An Integrated Methodology for Chemical Product Design: Application to Cosmetic Emulsions

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An Integrated Methodology for Chemical Product Design: Application to Cosmetic Emulsions

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by

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Resúme étendu

Le passage des produits de base aux produits chimiques à haute valeur ajoutée, tels que les spécialités, les produits formulés et les dispositifs, a été une tendance dans l'industrie des procédés chimiques ces dernières années. En particulier, pour les industries chimiques traitant des produits de consommation, la vitesse de développement et de fabrication de ces produits est le facteur déterminant du succès de leur lancement, même au-dessus du coût de production (Charpentier, 2009). Si l'on tient compte du fait qu'il existe une pression permanente pour innover, il est facile de comprendre pourquoi il peut être si complexe de lancer de nouveaux produits qui répondent aux besoins des consommateurs (Cooper, 2013).

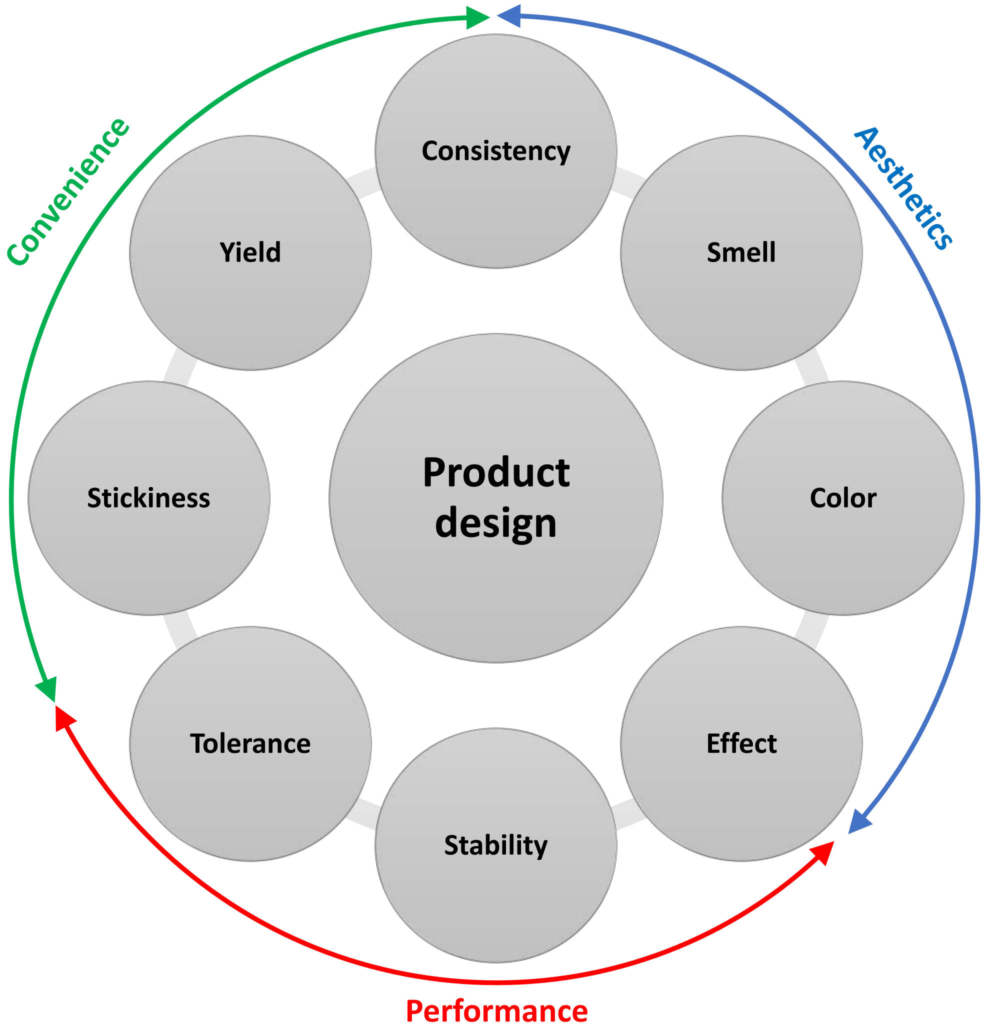
Dans la plupart des cas, un produit de consommation à base de produits chimiques pourrait être considéré comme un mélange d'un ou de plusieurs ingrédients clés qui sont responsables de la fonctionnalité du produit (ingrédients actifs) et d’autres ingrédients de soutien pour améliorer sa performance (Wibowo and Ng, 2002). L'ensemble des connaissances en génie chimique a identifié un besoin actuel de développement de produits efficaces et efficients pour les produits de consommation, qui sont considérés comme un groupe très diversifié par rapport aux produits chimiques de base (Costa et al., 2006). En ce sens, l'ingénierie des produits chimiques, la discipline couvrant l'ensemble du processus de conversion des besoins des clients et des nouvelles technologies en produits commercialisables, a été proposée il y a moins d'une décennie comme le troisième paradigme du génie chimique (Hill, 2009). Sur le plan conceptuel, l'ingénierie des produits chimiques pourrait être considérée comme l'inverse de l'ingénierie des procédés traditionnels. Il s'agit là d'une nouvelle façon de penser en génie chimique, car le processus de fabrication du produit a été l'objet d'étude classique (Bernardo and Saraiva, 2015). Dans ce contexte, la conception de produits chimiques (CPC) peut être considérée comme une facette de l'ingénierie des produits chimiques et être définie comme le cadre systématique de méthodologies et d'outils permettant de développer plus efficacement et plus rapidement des produits chimiques capables de répondre aux demandes du marché (Costa et al., 2006). Cependant, cette nouvelle vision ne s'est pas encore pleinement développée pour devenir le troisième paradigme prévu en génie chimique (Hill, 2009), peut-être à cause des relations complexes entre les technologies de manufacture et les diverses propriétés des ingrédients (Picchioni and Broekhuis, 2012).

Moggridge et Cussler (Moggridge and Cussler, 2000) été les premiers à proposer un ensemble cohérent de principes qui pourraient soutenir les activités de CPC. Par la suite, différentes méthodologies et outils ont été développés pour la conception de produits, la plupart suivant des procédures similaires (Bernardo et al., 2007; Costa et al., 2006; Hill, 2009; Ng et al., 2007; Wesselingh et al., 2007; Wibowo and Ng, 2002, 2001). Une étude de ces méthodologies indique que le point de départ commun à la plupart d'entre elles est l'identification des besoins des consommateurs et des propriétés d'utilisation finale correspondantes Cet objectif nécessite une interaction importante entre les différentes disciplines (marketing, psychologie, statistique, chimie, physico-chimie et thermodynamique, entre autres) afin de prendre en compte un large éventail d'aspects qui influencent la performance du produit et en même temps de rendre quantifiables les propriétés d'utilisation finale. L'un des défis restants consiste à convertir les évaluations des consommateurs, y compris les propriétés sensorielles, en termes mesurables qui pourraient guider la conception du produit (Cussler and Moggridge, 2011a).

Un autre défi concerne la génération et la sélection de produits qui répondent aux besoins des consommateurs mentionnés ci-dessus. Une alternative pour pallier le manque de modèles mathématiques fiables est d'utiliser les connaissances heuristiques disponibles. Comme dans la synthèse traditionnelle des processus chimiques, l'heuristique peut aussi être incorporée dans des algorithmes et diverses techniques d'optimisation (Costa et al., 2006; Hill, 2009; Moggridge and Cussler, 2000) pour formuler des produits chimiques et sélectionner les meilleurs candidats parmi différentes alternatives utilisant divers outils décisionnels (Constantinou et al., 1996; Eljack et al., 2005; Yunus et al., 2014, 2011). L'espace de recherche de candidats réalisables peut alors être réduit et l'investissement en temps et en ressources minimisé. Enfin, dans la dernière étape de la conception des produits, il est nécessaire d'intégrer des approches intégrées multi-échelles pour répondre à l'attention croissante portée aux exigences environnementales, sécuritaires et sociales, dans la transition vers une " ingénierie verte ". La prise en compte de tous les éléments rapprochera la conception du produit de la pratique dans l'industrie (Charpentier et McKenna, 2004 ; Edwards, 2006).

L'industrie cosmétique est l'un des secteurs où l'intégration des besoins des clients dans une procédure de conception systématique est essentielle. Les formulateurs de cosmétiques s'occupent de la préparation d'un produit économiquement et techniquement réalisable qui respecte les spécifications en termes de performance, de commodité et d'esthétique, comme le montre la Figure 1.

Figure 1 : Éléments de conception des produits cosmétiques. (Rähse, 2013)

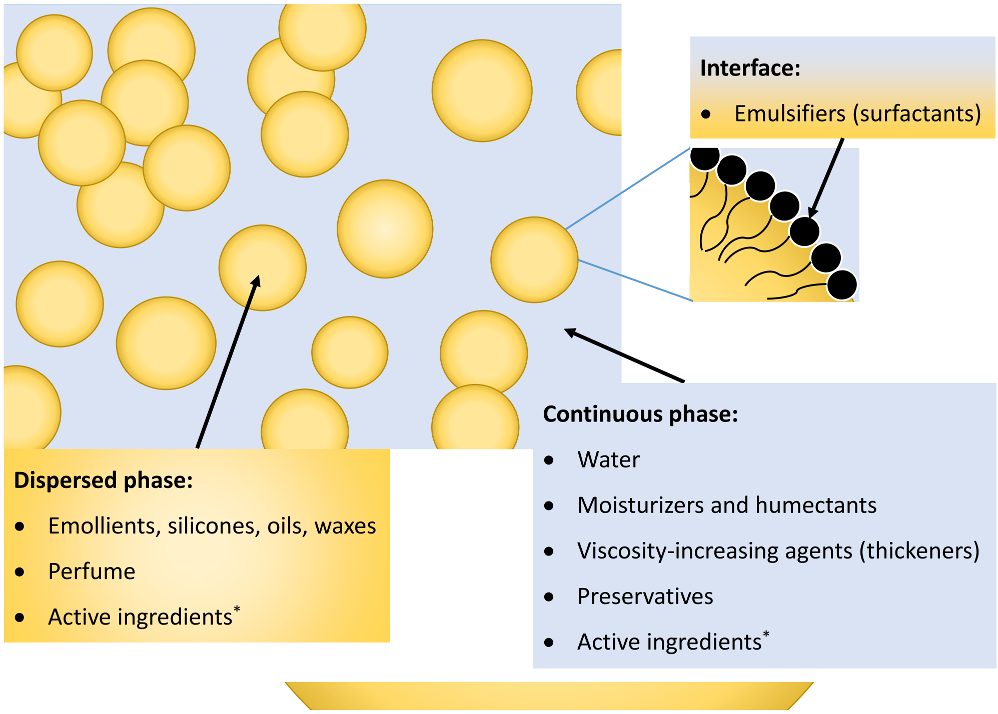


Bien que la principale préoccupation soit toujours la fonctionnalité, lorsque les consommateurs interagissent avec un produit cosmétique, ils perçoivent d'abord certaines de ses caractéristiques, comme la couleur, le parfum et la texture, à travers leur système sensoriel. Par exemple, lorsqu'une crème hydratante est appliquée sur la peau, les caractéristiques perçues comme la consistance, l'absorption, l'adhésivité et le gras sont simultanément évaluées par le consommateur et constituent une partie très importante de la valeur perçue du produit, en plus de protéger la peau de la sécheresse (Barel et al., 2001; Wibowo and Ng, 2001).

L'évaluation sensorielle de ces produits est donc une condition préalable à leur acceptation ou à leur rejet (Pensé-Lhéritier, 2015). Néanmoins, l'identification des attributs sensoriels des émulsions cosmétiques et la traduction de ces besoins en un ensemble de propriétés cibles souhaitées (mesures de performance) reste un sujet relativement peu exploré (Cussler et al., 2010).

L'industrie cosmétique mondiale peut être divisée en cinq grandes catégories : Les soins de la peau sont les plus importants, représentant plus d'un tiers du marché mondial, suivis par les soins capillaires avec près d'un quart (Statista, 2016). Parmi les produits de soins de la peau et des cheveux, une grande partie d'entre eux sont sous forme d'émulsions. Une émulsion peut être définie comme un mélange thermodynamiquement instable d'au moins deux liquides non miscibles ou partiellement non miscibles. Elle est stabilisée cinétique par des agents émulsifiants (tensioactifs ou émulsifiants) qui se trouvent à l'interface entre les deux phases liquides : l'une, la phase dispersée, sous forme de très fines gouttelettes dans l'autre, la phase continue (Knowlton and Pearce, 1993). Il existe de nombreux types d'émulsions cosmétiques (eau-dans-l'huile (E/H), huile-dans-l'eau (H/E), silicone dans l'eau, multiples, etc., mais les types H/E sont les plus courants pour les produits de soin de la peau et des cheveux. Jusqu'à 90 % des émulsions cosmétiques sont H/E (Lin, 2010), car elles ont tendance à être moins grasses et ont un coût inférieur à celui des autres formes, en raison de leur teneur plus élevée en eau. Les émulsions H/E cosmétiques ont un faible rapport de phase interne (Kostansek, 2012) - contenant généralement 10 à 35 % de phase dispersée - de sorte que l'ajout d'un agent émulsifiant approprié (par exemple des surfactants non ioniques avec des HLBs allant de 7 à 16) et l'agitation mécanique sont nécessaires pour créer une émulsion stable (Barel et al., 2001). Les principaux ingrédients d'une émulsion H/E cosmétique sont illustrés à la Figure 2.

Figure 2 : Composition d'émulsion cosmétique huile-dans-l'eau



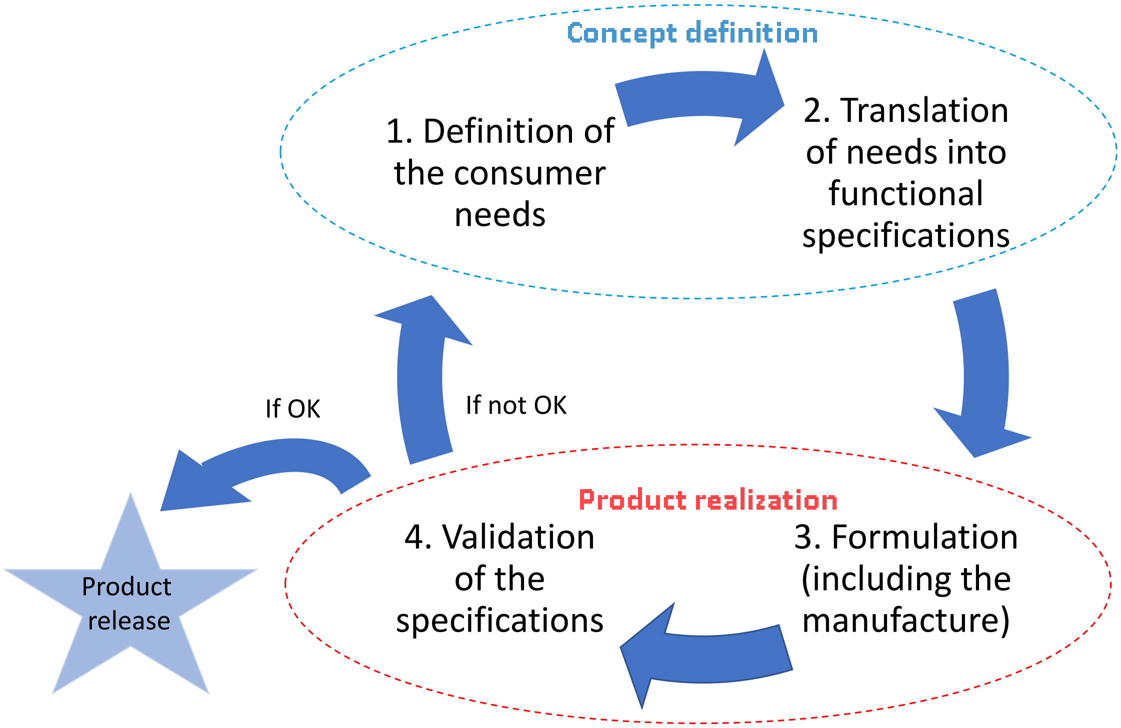
*Selon leur nature, les substances actives peuvent se retrouver dans une ou les deux phases (Barel et al., 2001).

En plus de l'importance du marché et de la relevance des produits à base d'émulsion (soins de la peau, soins capillaires, maquillage) où de telles méthodologies peuvent être utiles, une vaste collection de connaissances heuristiques sur la formulation et la fabrication est également disponible (Wibowo and Ng, 2001). Étonnamment, ces connaissances n'ont pas encore été intégrées dans une méthodologie et des modèles de propriétés qui pourraient servir à générer et sélectionner des prototypes réalisables, notamment dans le domaine des émulsions cosmétiques (Rähse, 2013, 2011; Rähse and Dicoi, 2009; Wibowo and Ng, 2001), pour accélérer la conception des produits cosmétiques. En ce sens, les émulsions cosmétiques sont de bons candidats pour développer des méthodologies de conception systématique, car de nombreux auteurs ont développé une base de connaissances pour les besoins des consommateurs, leur traduction en catégories nécessaires d'ingrédients et les propriétés d'utilisation finale avec des valeurs cibles et/ou des limites d'acceptation (Bagajewicz et al., 2011; Cheng et al., 2009; Lee et al., 2014; Mattei et al., 2012). L'objectif principal de cette étude est de fournir une méthodologie systématique qui contribue à la conception des produits formulés, sur la base de l'expérience cumulée de la communauté des chercheurs.

Proposition méthodologique pour la conception intégrée des produits formulés

Le processus traditionnel de conception cosmétique correspond à une succession cyclique de 4 étapes (Pensé-Lhéritier, 2016), comme le montre la Figure 3.

Figure 3: Cycle de conception des produits cosmétiques. Adapté de (Pensé-Lhéritier, 2016)

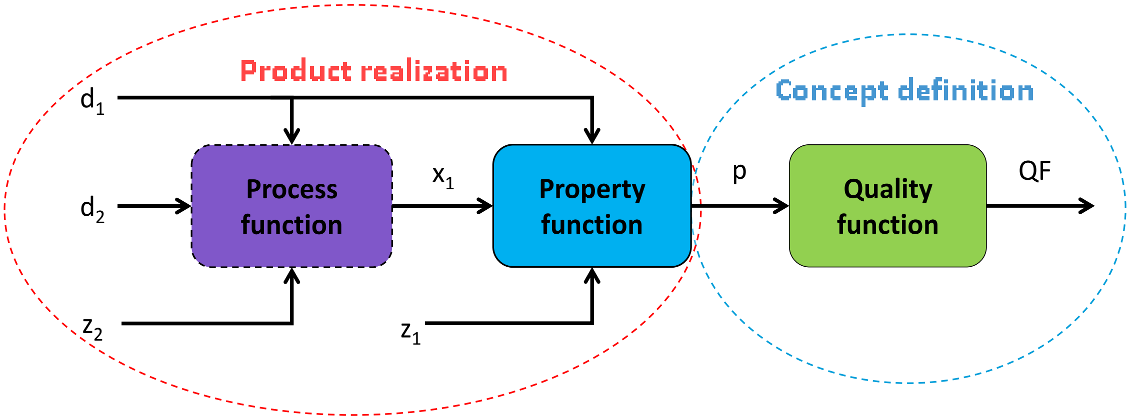


Les définitions susmentionnées peuvent être adaptées au contexte de la conception du produit formulé. Pour ce faire, on peut utiliser un modèle conceptuel assez bien établi comme le proposent Bernardo et Saraiva (2015), qui correspond à une représentation d'un problème de conception intégrée produit/processus à la Figure 4.

Définition du concept

Une caractéristique importante des produits de consommation est que les clients n'évaluent généralement pas leur valeur en fonction de spécifications techniques, mais plutôt en fonction de leur fonctionnalité et de leurs performances, souvent appelées facteurs de qualité(Costa et al., 2006). Comme les facteurs de qualité sont parfois qualitatifs et/ou subjectifs, il faut établir des paramètres de rendement.

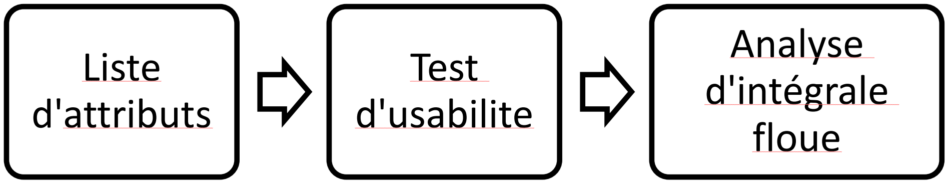
Figure 4: Conception conceptuelle des produits chimiques. Adapté de (Bernardo and Saraiva, 2015)



d_1 – Product design variables (process-independent)
d_2 – Process design variables
x_1 – Product state variables (process-dependent)
z_1 – Product operating variables (use conditions)
z_2 – Process operating variables
p – Product performance metrics
QF – Quality factors

Les facteurs de qualité (QF) sont liés aux mesures de performance des produits (p) par ce qu'on appelle une fonction qualité (Bernardo and Saraiva, 2004). Dans le cadre de ce modèle, la conception d'un produit formulé commence par l'inversion de la fonction qualité. Conceptuellement, cette inversion nécessite l'extraction d'informations (identification et estimation des paramètres p) sur un système à partir de données mesurées (attributs consommateurs QF), en association avec un modèle décrivant le comportement du système (Petit and Maillet, 2008). Comme pour la plupart des produits de consommation formulés, la définition des besoins des clients en matière de cosmétiques constitue le principal intrant requis par la méthodologie de conception et est généralement obtenue à partir de sources multiples, telles que les études de marché et de clientèle, les brevets, la littérature, entre autres (Mattei, 2014). L'évaluation de la performance cosmétique implique les cinq sens, d'où l'importance d'interpréter la réponse aux produits en fonction de leur perception (Nozawa and Uchida, 2009; Regué, 2011). De plus, la satisfaction est le résultat d'une combinaison de réponses sensorielles, émotionnelles et rationnelles à l'expérience d'utilisation du produit (SRL, 2018). L'ingénierie affective et Kansei étudient comment le plaisir et l'efficacité sont liés lors de l'utilisation d'un produit (Luo et al., 2011; Nagamachi, 1995). Étant donné que les produits cosmétiques sont conceptuellement conçus pour répondre aux attentes des consommateurs, l'utilisation de cette approche pourrait susciter un lien émotionnel avec le produit et améliorer l'expérience d'utilisation (Lokman and Kamaruddin, 2010). Dans ce contexte, il est important de définir un ensemble de mots ou d'attributs sémantiques (AS) qui décrivent mieux la perception du produit par l'utilisateur, comme le proposent Schütte et Eklund (Schütte and Eklund, 2005). En utilisant des techniques basées sur l'informatique douce (i.e. la logique floue), la spécificité du problème d'intérêt peut être prise en compte et les résultats obtenus peuvent être facilement interprétés (Zeng et al., 2008). Comme l'indiquent Camargo et al (2014), si l'on dispose de connaissances spécialisées sur l'application, l'initialisation de la mesure floue peut se faire par une identification basée sur la sémantique. Une telle méthode nécessite une évaluation manuelle de l'importance de chaque critère et de son interaction avec les autres critères au sein de l'agrégation pour évaluer la mesure floue sur chaque sous-ensemble (Camargo et al., 2011). Comme ces connaissances étendues sont rarement disponibles, la plupart du temps, la mesure floue doit être apprise à partir d'un ensemble de formation. Grabisch (1995b) a proposé un algorithme de rétro-propagation efficace pour approcher cette mesure floue de façon précise, en utilisant l'intégrale de Choquet (Choquet, 1954). Plus tard, Camargo et ses collaborateurs (2014) ont proposé une méthodologie intégrale floue pour intégrer les données des tests d'utilisabilité afin d'appuyer le processus de conception, et l'ont appliquée à la conception des semelles de masse. Cette méthode a été utilisée pour identifier et qualifier, en termes d'importance et d'interaction entre eux, l'ensemble d'attributs qui décrit le mieux les sentiments d'un groupe d'utilisateurs, comme le montre la Figure 5.

Figure 5 : Méthodologie générale de définition du concept



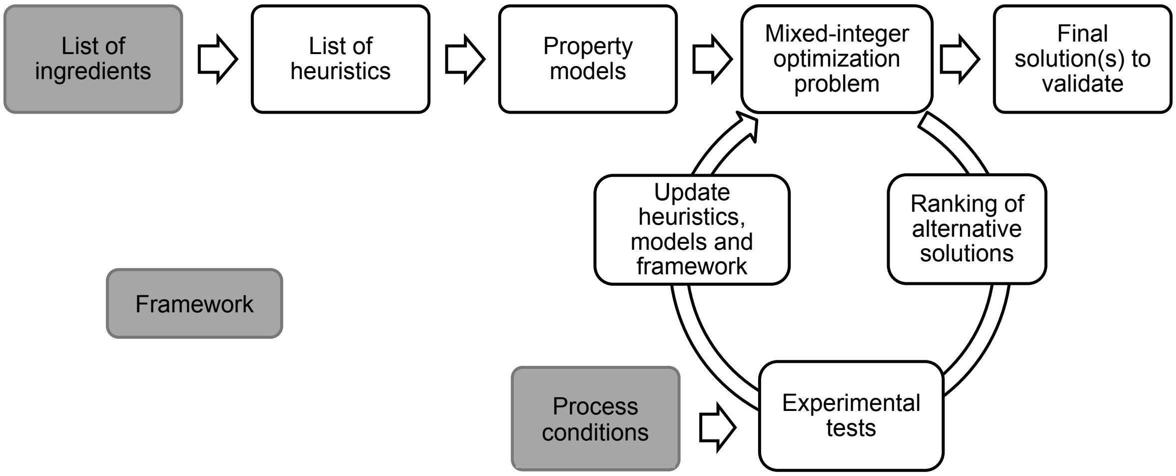
Les attributs sont collectés auprès de différentes sources disponibles, telles que les experts, la littérature et Internet par exemple - à partir de mots utilisés pour décrire le domaine de l'évaluation des émulsions cosmétiques. Ensuite, une sélection des attributs les plus pertinents est faite par l'exclusion des mots non pertinents ou répétés. Plusieurs techniques pourraient être utilisées, comme les diagrammes d'affinité, l'analyse factorielle ou l'analyse en composantes principales (ACP) (Camargo et al., 2014; Wortel and Wiechers, 2000). Un questionnaire est préparé pour évaluer l'ensemble de l'AS précédemment trouvée. Ensuite, les participants au test sont invités à noter un prototype sélectionné sur une échelle ordinale à 5 niveaux. Pour ce faire, on utilise actuellement la méthode différentielle sémantique (Camargo et al., 2014). L'un des prototypes peut être le produit le plus vendu pour la catégorie choisie ou tout autre produit à utiliser comme référence. Il est important de souligner que le but du test d'utilisabilité est de trouver la mesure floue qui minimise l'erreur quadratique d'un critère, de sorte qu'un résultat d'apprentissage, représenté par exemple par une acceptabilité globale ou une intention d'achat, devrait être inclus dans l'évaluation qui sert de score final global d'utilité (Camargo et al., 2014). Une fois les mesures floues calculées, les indices d'importance et d'interaction ont pu être estimés (indices Shapley et Murofushi et Soneda, respectivement (Grabisch, 1996). A partir de ces deux indices, un troisième, appelé indice composé, peut être calculé pour guider la phase de réalisation du produit.

Réalisation du produit

Compte tenu d'un cadre particulier, c'est-à-dire d'une liste d'ingrédients, et du nombre d'ingrédients différents dans une émulsion cosmétique, sa formulation doit être effectuée selon une procédure appropriée, qui tient en compte de leur interaction mutuelle dans la faisabilité de la préparation, de la stabilité et de l'efficacité de la ou des substances actives dans le véhicule (Barel et al., 2001).

La méthodologie proposée pour cette phase (Figure 6) est le fruit d'une collaboration internationale avec le PSE - CIEPQPF de l'Université de Coimbra au Portugal. L'équipe dirigée par le professeur Bernardo, qui a développé le modèle conceptuel illustré à la Figure 4, a beaucoup travaillé sur la génération et la sélection systématiques d'alternatives réalisables ainsi que sur des outils d'optimisation pour rechercher efficacement de grands domaines afin d'identifier le ou les produits menant aux spécifications requises.

Figure 6: Méthodologie générale de réalisation des produits

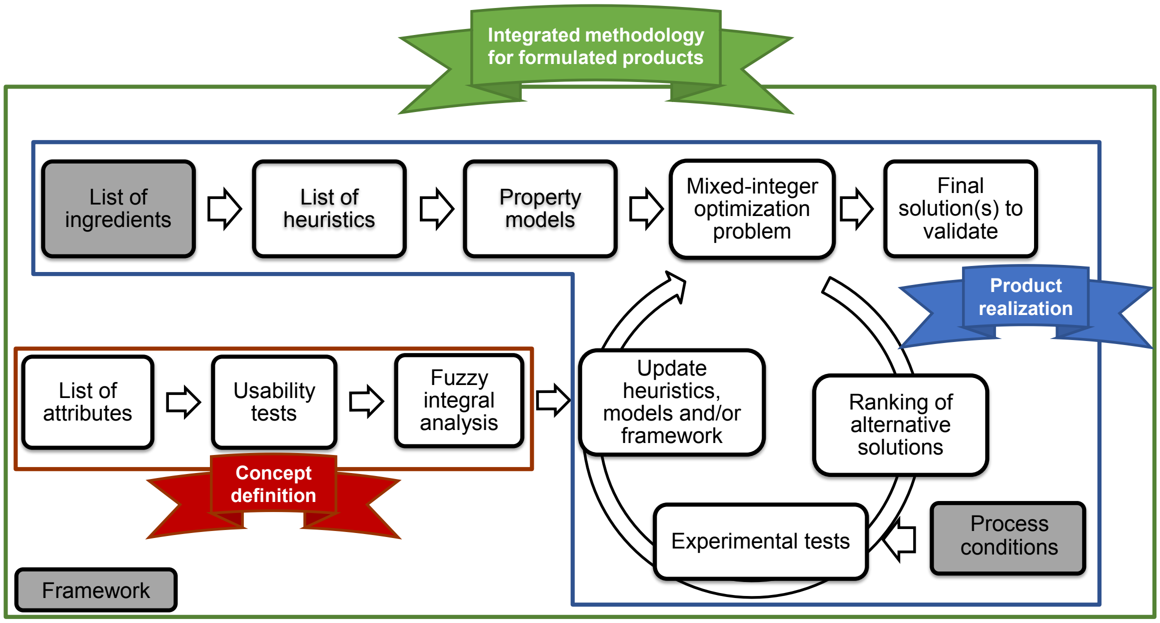


La première étape du processus de formulation est le choix des ingrédients (Rousseau, 2011). Comme les produits formulés contiennent souvent de 5 à 20 composants différents, tous les ingrédients candidats doivent être classés en fonction de leur(s) fonction(s) dans la formulation. Dans ce travail, l'information sur les ingrédients a été principalement tirée des spécifications des fournisseurs pour les ingrédients disponibles. Des bases de données ont été développées pour sélectionner les produits les plus appropriés à inclure dans la formulation, sur la base des spécifications du produit. Trois principaux types d'ingrédients ont été considérés pour la modélisation des émulsions H/E dans cette recherche: Emollients en phase dispersée, épaississants en phase continue et émulsifiants à l'interface. La sélection de ces ingrédients est basée sur plusieurs études réalisées par différents auteurs qui ont évalué l'impact de ces ingrédients sur les propriétés sensorielles, rhéologiques et texturales des émulsions cosmétiques (Barel et al., 2001; Korhonen et al., 2000; Lukic et al., 2012; Moravkova and Filip, 2014, 2013; Savary et al., 2013). La conception assistée par ordinateur des mélanges a été utilisée pour générer les alternatives, les tester et les évaluer afin d'identifier le produit conduisant aux caractéristiques définies *a priori.* Dans ce cas, l'optimisation des entiers mixtes a été utilisée comme un outil fondamental pour traiter les grands domaines discrets (Bernardo et Saraiva, 2015). En ce qui concerne les techniques, différentes méthodes d'optimisation (discrètes et/ou combinatoires) et différents algorithmes pour la génération et la sélection d'alternatives réalisables ont été mis en œuvre dans chaque cas. Au terme de ce processus assisté par ordinateur, les solutions finales identifiées au problème de conception du produit sont testées: Les mesures rhéologiques et certaines analyses de texture (fermeté, consistance, cohésion, indice de viscosité) sont les plus pertinentes à ce stade (Gilbert et al., 2013b; Savary et al., 2013).

Approche méthodologique intégrée pour la conception des produits formulés

Ensuite, une approche méthodologique générale est présentée pour la conception des produits formulés, dans laquelle une analyse de mesure floue à partir de la définition du concept, ainsi que des modèles heuristiques et de propriétés de la phase de réalisation du produit sont utilisés pour résoudre le problème de conception initial, comme le montre la Figure 7.

Figure 7: Approche méthodologique intégrée pour la conception des produits formulés



Example d'intégration des préférences des consommateurs et des connaissances heuristiques dans la conception des produits formulés

Un hydratant pour la peau peut être décrit comme un produit appliqué sur une peau humide ou sèche, qui est facile à étaler et agréable à utiliser (Kostansek, 2012). Les hydratants pour la peau sont utilisés pour maintenir la peau en bon état en maintenant son équilibre en huile et en eau (Eccleston, 1997). Bien que les besoins en matière de conditionnement dépendent fortement du type de peau (c.-à-d. peau normale, sèche, très sèche, sensible, etc.), les consommateurs recherchent toujours des produits qui peuvent soulager l'inconfort d'une peau sèche (Abrutyn, 2010). Les hydratants pour la peau procurent une sensation de peau saine grâce à l'utilisation d'hydratants (humectants et émollients), qui se présentent généralement sous la forme d'une émulsion H/E, stabilisée par une combinaison d'émulsifiants (surtout des surfactants non ioniques) et d'épaississants (alcools gras et polymères) (Barel et al., 2001).

Définition du concept

Dans cette étape, huit attributs signalés dans la documentation (Bagajewicz et al., 2011; Parente et al., 2010) ont été choisis pour être évalués pendant les tests d’usabilité représentés par deux mots dans la langue d'évaluation (c.-à-d. le français), comme le montre le Tableau 1. Chaque ensemble de mots a été sélectionné après avoir demandé à quatre experts de réfléchir à des mots-clés qui pourraient être utilisés pour décrire les hydratants pour la peau, puis de les classer manuellement dans chaque catégorie. Les deux termes les plus répétés ont été choisis pour représenter chaque attribut.

Tableau 1: Liste des principaux attributs des émulsions cosmétiques

Attribut	Symbol	Mot 1	Mot 2
Épaisseur	V	Épais	Mince* Mince
Possibilité d'étalement	S	Facile à étaler	Glisse facilement
Adhésivité	P	Collant	Lumière**
Facilité d'absorption	A	Facilement absorbé	Pénètre rapidement
Fraîcheur	F	Sensation de fraîcheur	Sensation de froid
Résidus	R	Blanchiment sur frottement	Résidus de feuilles
Graisse et huile	G	Graisseux	Sensation huileuse
Hydratation	H	Peau plus hydratée	Peau plus douce

*Indique que ces mots se trouvent à l'extrémité opposée de l'échelle des attributs.

Un questionnaire a été préparé et les participants ont été invités à appliquer un produit (Échantillon 1 - Crème ultra-nourrissante Bioderma® Atoderm) sur leurs bras et à répondre à l'ensemble des questions correspondant à chacun des mots du tableau 1, en utilisant une échelle ordinale à 5 niveaux allant de pas du tout à très beaucoup (Osgood, 1959). Deux dernières questions sur l'acceptabilité du produit permettraient à l'algorithme de l'analyse intégrale floue d'"apprendre" l'importance des attributs dans la performance globale.

Les trois valeurs les plus élevées sont indiquées en caractères gras. Ces résultats permettent de constater que la fraîcheur est l'attribut le plus important, suivie de la facilité d'absorption, des "résidus" et de l'adhésivité. Quant aux indices Murofushi et Soneda (interactions totales), on peut observer que l'attribut "résidus" interagit constamment avec d'autres attributs et figure parmi les attributs les plus hauts classés pour les interactions totales dans les deux cas. Il est à noter que les "résidus" ont aussi les valeurs les plus élevées d'interactions mutuelles, notamment avec facilité d'absorption et la fraîcheur.

Tableau 2: Valeurs normalisées des indices Shapley (poids relatifs), Murofushi et Soneda (interactions) et indice composé.

	V	S	P	A	F	R	G	H
Poids relatifs normalisés	0.13	0.04	**0.15**	**0.20**	**0.21**	**0.15**	0.05	0.07
Normalized Interactions normalisées	0.08	0.07	0.11	**0.22**	**0.18**	**0.20**	0.06	0.08
Indice composé	0.07	0.02	0.11	**0.29**	**0.25**	**0.20**	0.02	0.04

Dans la section suivante, on montre comment cette information des indices peut être utilisée pour guider le choix des solutions de rechange, en fonction du profil particulier de chaque produit échantillonné.

Réalisation du produit

Les humectants - comme la glycérine - et d'autres excipients - émollients, émulsifiants et épaississants - doivent être combinés d'une manière économiquement et techniquement réalisable pour répondre aux attentes des consommateurs. Les émollients, les surfactants non ioniques et les épaississants (polymères ou alcools gras) seront sélectionnés à partir d'une liste initiale de 36 ingrédients au total. Vecteurs des variables de décision - y (binaire) et x (continu) - les deux ont la dimension 36. Les variables de conception du produit, les paramètres de rendement et les spécifications souhaitées correspondantes pour la présente étude de cas sont présentés au Tableau 3. A partir d'une formulation de crème de base générique (Formulation K0-N0-N0-M1), qui résout le problème spécifié dans le Tableau 3 à un coût minimum, des modifications spécifiques ont été apportées afin de respecter des attributs différents pour l'échantillon évalué.

Tableau 3: Variables et spécifications de conception du produit

Variables de conception: choix des ingrédients y et quantité (masse) x
Nonionic surfactants: y_r, x_r Thickening polymers: y_n, x_n Fatty alcohols: y_m, x_m High spreading emollients: y_i, x_i Medium spreading emollients: y_j, x_j Low spreading emollients: y_k, x_k
Trouver les vecteurs $\boldsymbol{y}$ et $\boldsymbol{x}$ qui minimisent le coût, sous ▪ $\boldsymbol{2.0 \leq \gamma \leq 2.4}$ ▪ $\boldsymbol{3(x_{r1} + x_{r2}) \leq x_{r3} \leq 6(x_{r1} + x_{r2})}$ ▪ $\boldsymbol{2(x_{r1} + x_{r2}) \leq x_{r4} + x_{r5} + x_{r6} \leq 6(x_{r1} + x_{r2})}$,. ▪ $\boldsymbol{y_n, x_n}$ pour que log $\boldsymbol{\eta_1}$ et log $\boldsymbol{\eta_2}$ soient dans une intervalle idéale.

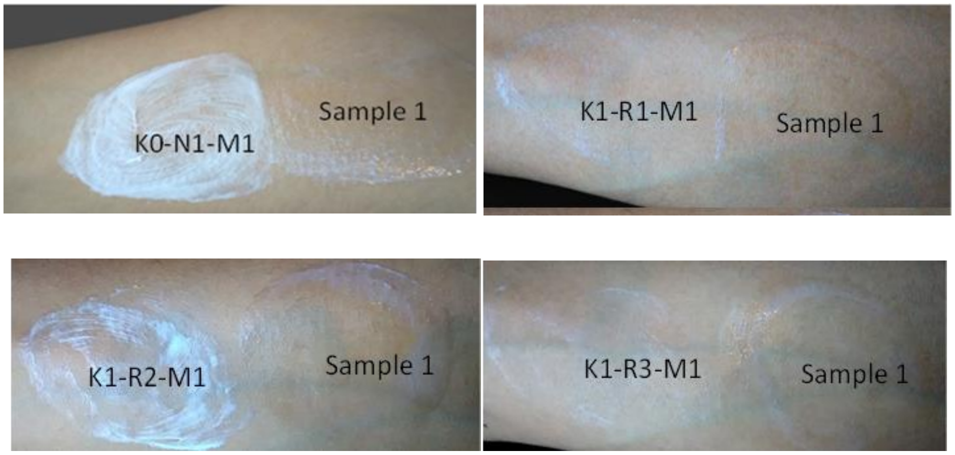
L'optimalité globale étant garantie, un classement correct des solutions à coût croissant est généré, toutes correspondant à des produits aux performances similaires (selon les modèles et heuristiques adoptés). La fonction d'objectif choisie est le coût total de la formulation en USD/kg, en considérant uniquement le coût unitaire de chaque ingrédient et en excluant les ingrédients fixes ou les coûts de fabrication. Le problème MINLP qui en résulte est ainsi résolu plusieurs fois en moins d'une seconde à l'aide de GAMS/BARON, en ajoutant successivement des coupes binaires interdisant les solutions précédentes y.

D'après les résultats obtenus dans le test d'utilisabilité de l'échantillon 1, la facilité d'absorption, la fraîcheur et les résidus étaient les attributs les plus importants de l'indice composé. En raison de l'interaction élevée entre ces attributs (voir le Tableau 2) et du fait que la formulation de base laisse plus de résidus blancs que l'échantillon 1 (voir Figure 8), le premier changement apporté à l'algorithme a consisté à mettre en œuvre une mesure de réduction des résidus blancs en ajoutant jusqu'à 2% d'émulsifiant faible HLB (Institute of Personal Care Science, 2016). Comme cette action permettrait non seulement d'abaisser le rapport huile/tensioactif et de permettre HLB<RHLB mais aussi d'augmenter la viscosité de la formulation finale, une série d'expériences a été réalisée pour comprendre comment chaque changement affecte les propriétés de l'émulsion, en particulier la viscosité et le résidu blanc. Les formulations ainsi obtenues sont présentées au Tableau 4.

Tableau 4: Alternatives de formulation fabriquées

Ingredient	**Cost (USD/kg)**	Formulations			
		K0-N1-M1	**K1-R1-M1**	**K1-R2-M1**	**K1-R3-M1**
Water		60.0%	60.0%	60.0%	60.0%
Xanthan gum (n1)	35	1.1%	1.1%	1.1%	1.1%
Cetyl Alcohol (m2)	7.4	4.0%	4.0%	4.0%	4.0%
Polysorbate 60 (r1)	15.5	0.5%	0.5%	0.5%	0.5%
PEG-100 Stearate (r3)	9.8	1.5%	1.5%	1.5%	1.5%
Glyceryl Stearate SE (r5)	**8.9**		**1.0%**	**1.0%**	**1.0%**
Sorbitan Stearate (r6)	12.5	1.3%	1.3%	0.5%	0.7%
Isopropyl Myristate (i4)	16.7	5.6%	5.6%	5.9%	6.8%
Paraffinum Liquidum (j7)	12.2	2.7%	2.7%	2.9%	3.2%
***Persea Grattisima* Oil (k2)**	16.7	1.0%	1.0%	1.2%	1.0%
Water		18.6%	17.6%	17.7%	16.5%
Glycerol		3.0%	3.0%	3.0%	3.0%
Preservative (Cosgard)		0.7%	0.7%	0.7%	0.7%
	Total	100%	100%	100%	100%
Cost (USD/kg)		**2.50**	**2.58**	**2.60**	**2.77**

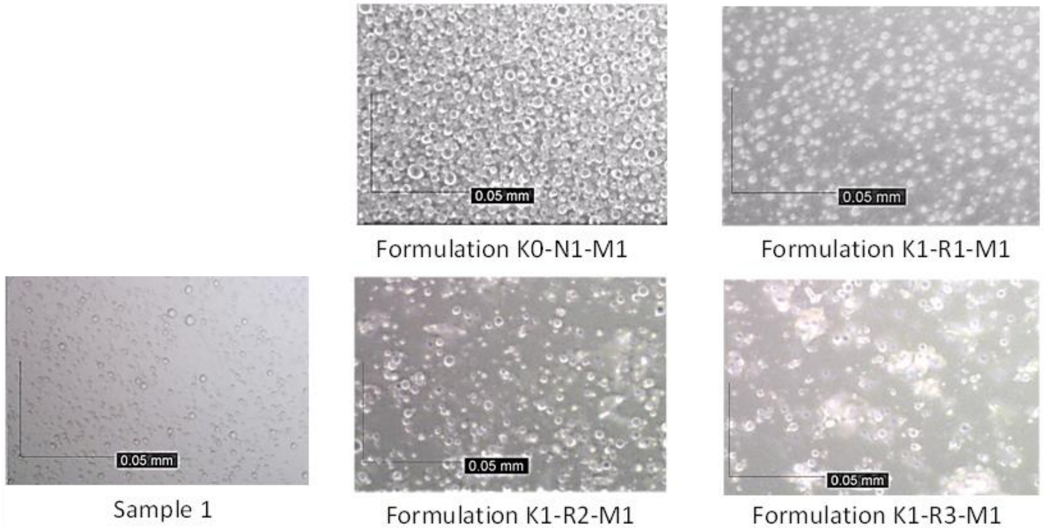
Figure 8: Résidus blancs des formulations dans l'échantillon 1



Comme on peut l'observer, les résidus blancs de K0-N1-N1-M1 sont beaucoup plus élevés que ceux de la formulation de l'échantillon 1, alors que pour la formulation K1-R1-M1 est très similaire aux résidus de l'échantillon 1, ce qui prouve que l'heuristique d'ajouter une petite quantité d'un surfactant HLB faible réduirait la formation de micro-mousse. C'était également le cas pour l'échantillon K1-R3-M1 mais pas pour K1-R2-M1, qui ne permettait pas HLB<RHLB.

Des microphotographies optiques représentatives (900X) des 4 émulsions et de l'échantillon 1 sont présentées à la Figure 9. On a observé que le cas de base (K0-N1-M1) avait une microstructure très différente de celle de l'échantillon 1. Avec des tailles de gouttelettes d'environ 5 µm. Il est à noter que la microstructure la plus similaire à celle de l'échantillon 1 est celle de la formulation K1-R3-M1.

Figure 9: Microphotographies (900X) d'échantillons dans le cas de l'échantillon 1


Formulation K0-N1-M1
Formulation K1-R1-M1
Sample 1
Formulation K1-R2-M1
Formulation K1-R3-M1

Le profil rhéologique des échantillons est présenté à la figure 10. En utilisant l'approximation de puissance, la viscosité finale η_2 a été calculé pour 5000 s-1, se situant entre 0,023 et 0,5 Pa.s pour tous les échantillons. Toutes ces formulations contiennent de la gomme xanthane comme polymère épaississant, ce qui confirme que le modèle de prédiction de la viscosité de l'émulsion est en fait correct. Les paramètres obtenus à partir de l'analyse de texture de toutes les émulsions d'échantillons préparés sont présentés au Tableau 6. L'alternative qui se rapproche le plus des paramètres rhéologiques et texturaux de l'échantillon 1 est également K1-R3-M1. Bien qu'aucun test sensoriel n'ait été effectué sur ces formulations, il a été rapporté que les paramètres de texture évalués ici correspondent bien aux caractéristiques sensorielles du produit final. En particulier, la fermeté est liée à l'adhésivité perçue par l'utilisateur, et la consistance, la cohésion et l'indice de viscosité sont tous en corrélation directe avec la glissance (Lukic et al., 2012).

Figure 10: Profil rhéologique des alternatives de solution pour l'échantillon 1

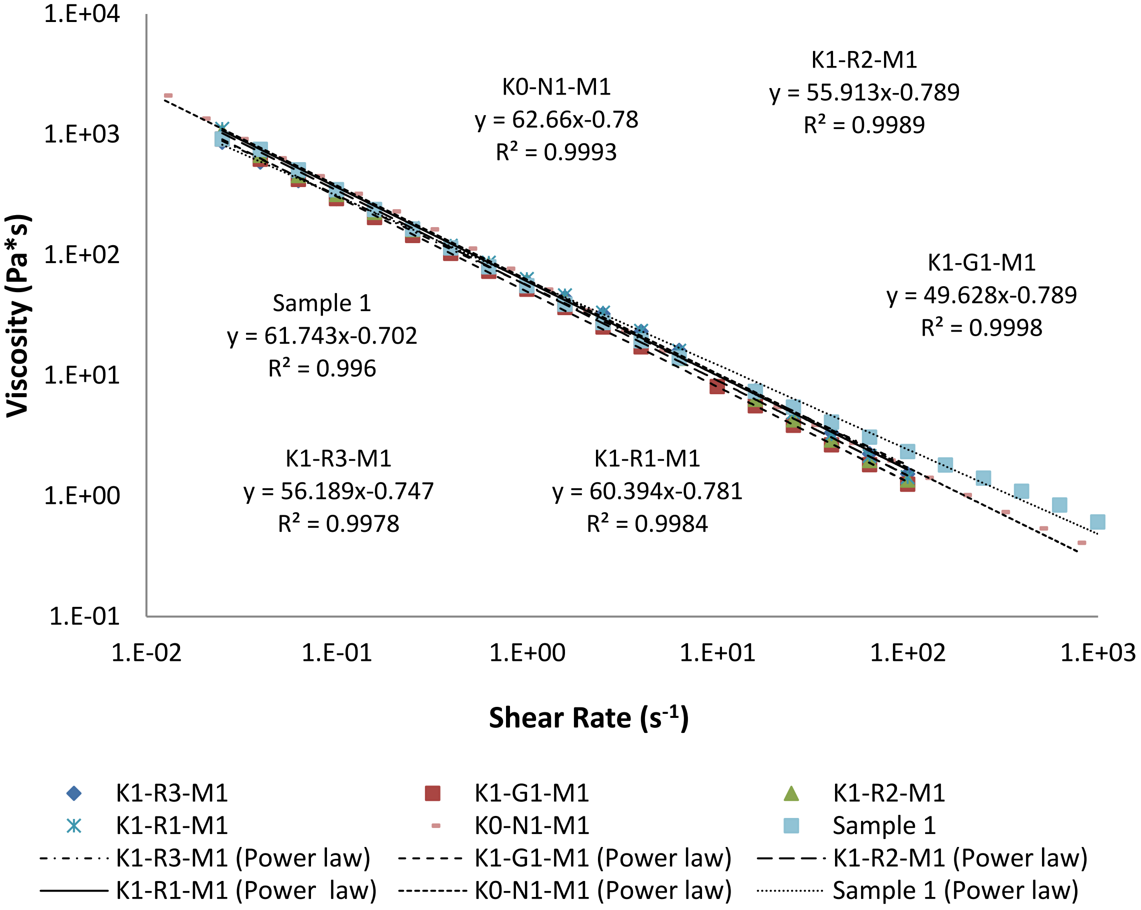


Tableau 6 : Paramètres de texture des alternatives dans l'échantillon 1

	Consistency (g.s)	Viscosity Index (g.s)	Firmness (g)	Cohesiveness (g)
K0-N1-M1	3979.7	445.4	154.6	199.1
K1-R1-M1	6711.4	694.1	285.7	403
K1-R2-M1	5078.6	536.7	199.2	245.2
K1-R3-M1	2131.4	246.5	81.3	105.8
Sample 1	2372.7	281.2	90.5	123.5

Dans cette recherche on a proposé une méthodologie basée sur l'optimisation pour la conception des produits formulés, qui intègre l'évaluation du consommateur ainsi que les règles heuristiques disponibles pour générer des alternatives de formulations. La méthodologie a été appliquée à deux échantillons commerciaux de crèmes hydratantes pour la peau, générant une série de solutions alternatives qui correspondent aux attentes des consommateurs avec un coût d'ingrédients minimum dans chaque cas. Ces solutions générées par ordinateur ont ensuite été fabriquées et évaluées. Les propriétés rhéologiques, texturales et microstructurales, ainsi que la quantité de résidus blancs des formulations alternatives qui ont intégré les informations fournies par les tests d'utilisabilité, sont plus similaires aux échantillons respectifs, d'où les informations sont venues en premier.

Comme cette méthodologie implique la participation de consommateurs non formés, il est possible de réduire le temps et les ressources consacrés à la conception des émulsions cosmétiques par rapport aux panels sensoriels, puisqu'il n'y a pas de formation des panels. Comparée à d'autres techniques quantitatives utilisées pour identifier les contributions statistiques des attributs (degré d'importance) ou la corrélation entre eux, comme l'ACP, cette méthodologie permet de calculer l'importance et l'interaction des attributs évalués, ce qui la rend précieuse pour le concepteur. Cela suggère qu'il s'agit d'une méthodologie utile non seulement pour recueillir des informations sur la perception qu'ont les consommateurs des caractéristiques sensorielles des produits cosmétiques, mais aussi pour guider la génération d'alternatives pour d'autres produits formulés.

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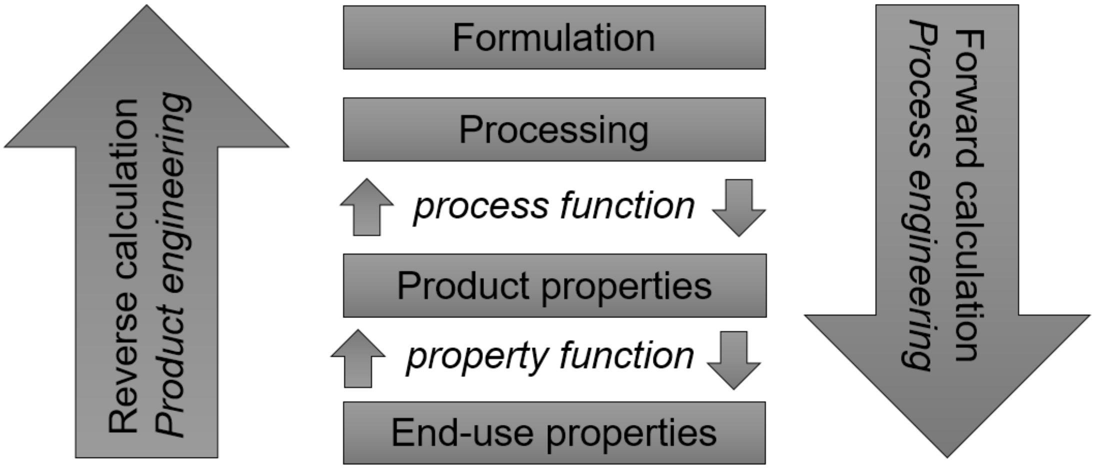
Introduction

The shift from commodities to high added-value chemical products, such as specialties, formulated products, and devices, has been a trend among chemical process industries in recent years. Due to growing competitiveness in the market, today companies must be able to launch new products faster while maintaining superior quality and performance, as a key to their success (Charpentier, 2010). In particular, for the chemical industries dealing with consumer products, the rate at which these products are developed and manufactured is the deciding factor in their successful launch, even more so than the cost of production (Charpentier, 2009). If one takes into account that there is a constant pressure to innovate in different markets, it is easy to understand why it could be so complex to launch new products that meet the consumers’ needs (Cooper, 2013).

A chemical-based consumer product could be seen in most cases as a mixture of one or more key ingredients that are responsible for the product’s functionality (active ingredients) and some supporting ingredients to enhance its performance (Wibowo and Ng, 2002). The body of knowledge in chemical engineering has identified a current need for an efficient and effective product development for consumer products, which are regarded as a very diverse group compared to commodity chemicals (Costa et al., 2006). In this sense, chemical product engineering, the discipline covering the whole conversion process of customer needs and new technologies into marketable products, was proposed less than a decade ago as the third paradigm of chemical engineering (Hill, 2009). Conceptually, chemical product engineering could be seen as the reverse of traditional process engineering. Figure 0-1 shows a conceptual notion of product engineering, which allows choosing the processing method and the formula based upon the desired properties of the product, and not to consider “use” properties as the result of the design process. This is a new way of thinking in chemical engineering, as the product manufacturing process has been the classical object of study (Bernardo and Saraiva, 2015). In this context, chemical product design (CPD) can be seen as one facet of chemical product engineering and be defined as the systematic framework of methodologies and tools to provide a more efficient and faster development of chemical products able to meet market demands (Costa et al., 2006). However, this new vision has not yet developed fully into the foreseen third paradigm in chemical engineering (Hill, 2009), perhaps because of the complex relationships between process technologies and the diverse ingredient properties (Picchioni and Broekhuis, 2012).

Figure 0-1: Chemical product engineering concept (Hounslow and Reynolds, 2006)



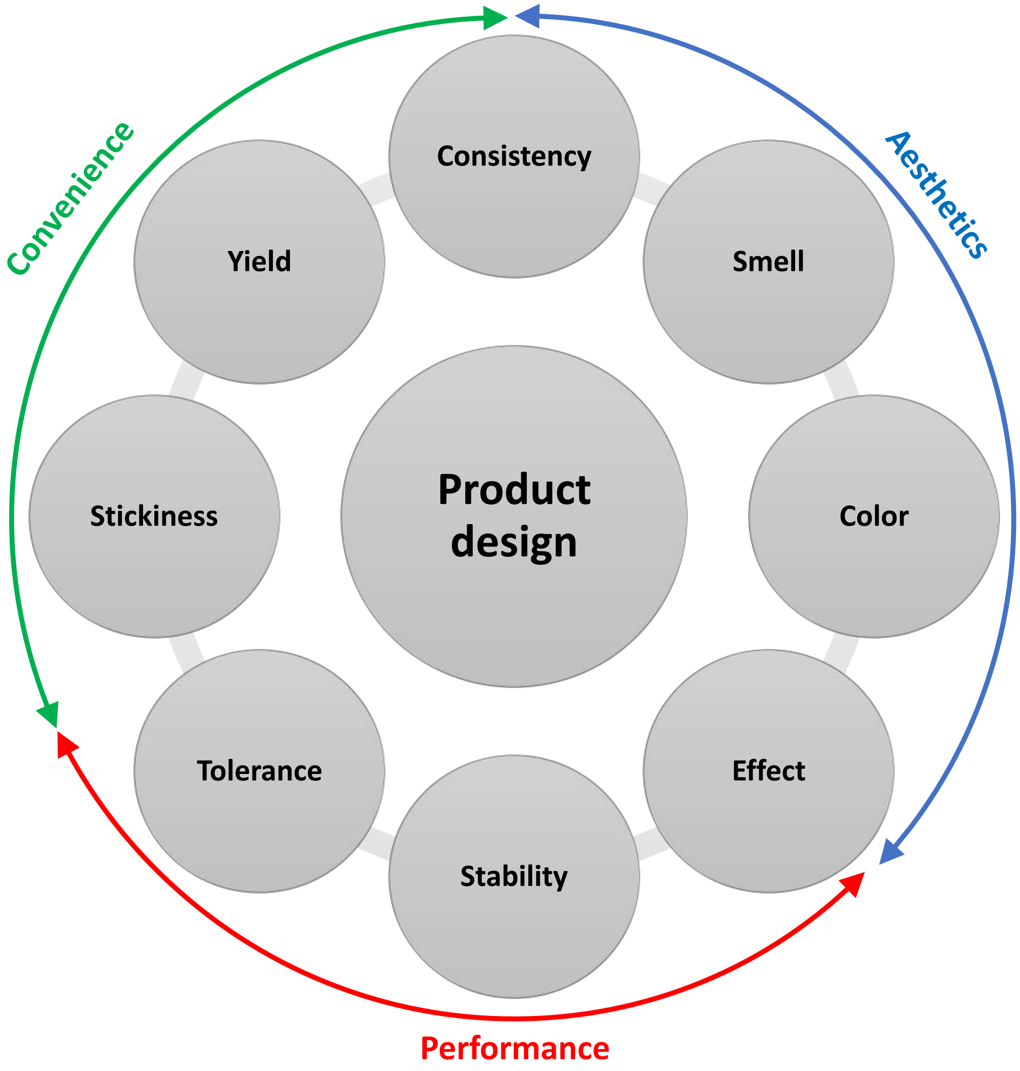
Moggridge and Cussler (Moggridge and Cussler, 2000) were the first to propose a consistent set of principles that could support CPD activities. After that, different methodologies and tools have been developed for product design, most of them following similar procedures (Bernardo et al., 2007; Costa et al., 2006; Hill, 2009; Ng et al., 2007; Wesselingh et al., 2007; Wibowo and Ng, 2002, 2001). A survey of these methodologies indicates that the common starting point of most of them is the identification of consumers' needs and the corresponding end-use properties. This objective requires significant interaction between different disciplines (marketing, psychology, statistics, chemistry, physical chemistry and thermodynamics, among others) to take into account a wide range of aspects that influence product performance and to make end-use properties quantifiable. One of the remaining challenges is converting consumer assessments, including sensory properties, into measurable terms that could lead the product design (Cussler and Moggridge, 2011a).

Another challenge concerns the generation and selection of products that fulfill the above-mentioned consumer needs. An alternative to overcome the lack of reliable mathematical models is to use available heuristic knowledge. As in the traditional chemical process synthesis, heuristics can also be incorporated into algorithms and diverse optimization techniques (Costa et al., 2006; Hill, 2009; Moggridge and Cussler, 2000) to formulate chemical products and to select the best candidates among different alternatives using diverse decision-making tools (Constantinou et al., 1996; Eljack et al., 2005; Yunus et al., 2014, 2011). The search space for feasible candidates can be then reduced, and time and resources investment minimized. Finally, in the last stage of product design, it is necessary to incorporate multiscale integrated approaches to address the increasing attention to environmental, safety, and social requirements, in the transition towards a “green engineering”. The consideration of all the elements brings the product design closer to the practice in the industry (Charpentier and McKenna, 2004; Edwards, 2006).

The cosmetic industry is one of the sectors in which integrating customer needs into a systematic design procedure is essential. As cosmetics are a category of ubiquitous consumer products that have been used for various purposes - namely to enhance personal appeal through decoration of the body, to camouflage flaws in the integument (skin, hair, nails, etc.), and to alter or improve upon nature (Barel et al., 2001) - by people of different cultures, the concept of needs can greatly vary. The focal market, therefore, constitutes a critical element for the success of the product, essentially placing the consumer at the heart of innovation (Pensé-Lhéritier, 2016). Moreover, there are many delivery systems in the cosmetics industry, greatly increasing the diversity of product options; some of them include aerosols (hair sprays); liquid foams (shaving foams); solutions (perfumes); suspensions (skin foundations); emulsions (hair conditioners, skin moisturizers); solid composites (soap bars), and powders (facial or baby powder). Novel product forms and increased performances, developed in cooperation with the customer, characterize the modern cosmetic product design (Rähse, 2013).

Cosmetic formulators deal with the preparation of an economically and technically feasible product that complies with the specifications in terms of performance, convenience, and aesthetics, as shown in Figure 0-2. While the primary concern is always functionality, when consumers interact with a cosmetic product, they first perceive some of its characteristics, like color, perfume, and texture, through their sensory system. For example, when a moisturizing cream is applied to the skin, perceived characteristics such as consistency, absorption, stickiness, and greasiness, are simultaneously assessed by the consumer and constitute a very important part of the perceived value of the product, apart from protecting the skin from dryness (Barel et al., 2001; Wibowo and Ng, 2001).

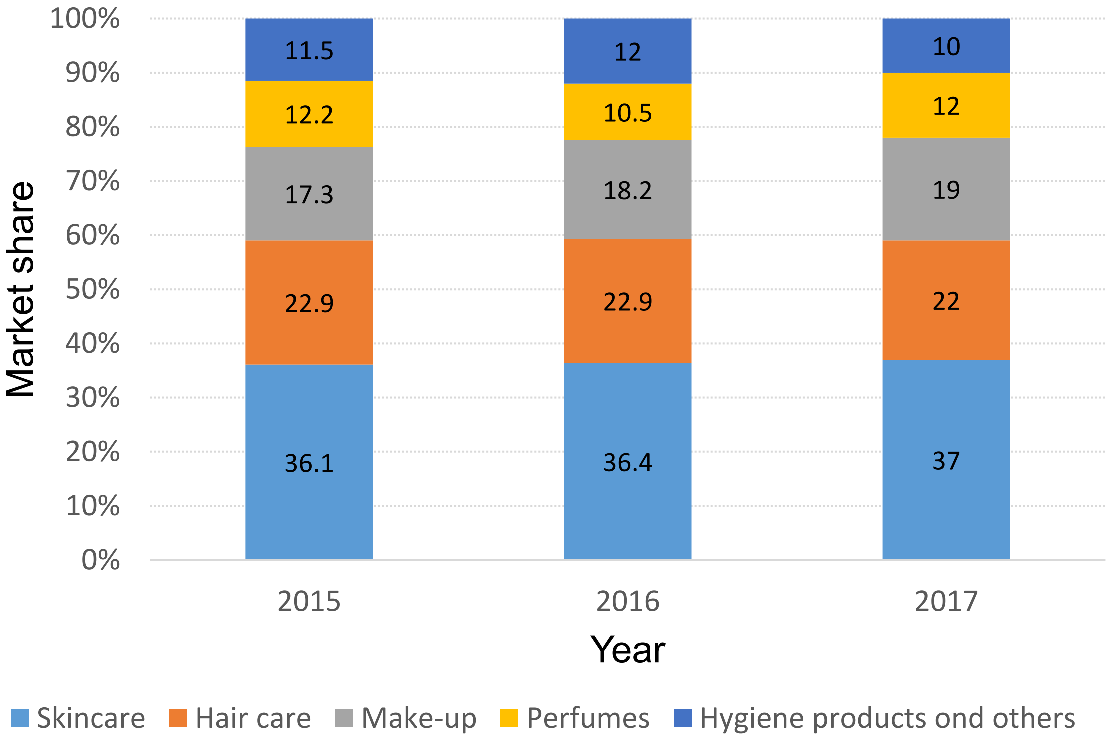
Figure 0-2: Elements of product design for cosmetics. (Rähse, 2013)



Therefore, a sensory assessment of these products is a prerequisite to accepting or rejecting them (Pensé-Lhéritier, 2015). Nevertheless, the identification of sensorial attributes for cosmetic emulsions and the translation of these needs into a set of desired target properties (performance metrics) remains a relatively unexplored subject (Cussler et al., 2010).

By 2014, the global cosmetic market was around 460 billion USD, and it is expected to reach 675 billion USD by 2020 (Research and Markets, 2015). The global cosmetic industry can be broken down into five main categories, as shown in Figure 0-3. Skin care is the largest one, accounting for more than a third of the worldwide market, followed by hair care with almost a quarter (Statista, 2016). Among skin care and hair care products, a great deal of them are in the form of emulsions (mostly oil in water) such as hydrating creams, lotions or hair conditioners and combing creams (Lin, 2010; Morávková and Stern, 2011).

Figure 0-3: Worldwide cosmetic market by product category (Statista, 2016)



In addition to the market relevance, and the important share of the emulsion-based products (skin care, hair care, make-up) where such methodologies can be valuable, a large collection of heuristic knowledge regarding formulation and manufacture is also available (Wibowo and Ng, 2001). Surprisingly, this knowledge has not been yet incorporated into a methodology along with property models, which could serve to generate and select feasible prototypes, particularly in the field of cosmetic emulsions (Rähse, 2013, 2011; Rähse and Dicoi, 2009; Wibowo and Ng, 2001), to accelerate the cosmetic product design process.

Considering the current state of the art of chemical product design (CPD), in particular the opportunities regarding integrated methodologies for formulated products, the research efforts should be concentrated on incorporating multidisciplinary aspects with hybrid experience/modelling tools to guide the product/process design of consumer-oriented products. In this sense, cosmetic emulsions are good candidates to develop systematic design methodologies, as many authors have developed a knowledge basis for consumer needs, their translation into necessary categories of ingredients, and the end-use properties with target values and/or boundaries of acceptance (Bagajewicz et al., 2011; Cheng et al., 2009; Lee et al., 2014; Mattei et al., 2012).

What is mainly envisaged with this study is to provide a systematic methodology that contributes to the design of formulated products, based on the cumulated experience of the research community.

Goals of the research

Given the detected opportunities regarding integrated methodologies for formulated product design and the importance of emulsions of the cosmetic industry, the aim of this research is to develop an integrated methodology for cosmetic emulsions design capable of coping with the consumer needs identification and translation into quantitative variables, which could serve as an input to solve a product/process design problem for cosmetic emulsions.

The specific objectives of the project are:

- To define a methodology for identifying consumers' needs regarding cosmetic emulsions.
- To select appropriate quantitative performance parameters to incorporate the consumer needs in a methodology for cosmetic emulsions design.
- To develop a suitable optimization and decision-making tool for an integrated modelling of cosmetic emulsions.
- To validate the applicability of the methodology by using a case study of cosmetic emulsion.

Structure of the document

This thesis is organized as depicted in Figure 0-4: Firstly, an overview of the chemical product design and the current methodologies are presented in chapter 1, along with a comprehensive classification of the existing contributions on integrated methodologies for chemical product design. This chapter focuses on selected articles and studies to identify key challenges and opportunities for formulated products. In chapter 2, the fundamental concepts and properties of emulsions in the context of cosmetic product design are introduced. Here, the main aspects related to the incorporation of the consumer assessment and the modelling of emulsified products in an integrative approach for formulated product design, are presented. Finally, the general methodology proposed as a contribution of this research is described. Next, in chapter 3, the author proposes the modeling of emulsified products, required to find the product formulation that renders a desired performance, using a specific case of cosmetic emulsion (hair conditioners). In chapter 4, the methodology for the identification of consumer needs and their integration with the modelling framework is illustrated using a skin-care product (skin moisturizer) as a case study. As a conclusion, in chapter 5, the main achievements, limitations, and perspectives for future work based on this contribution are highlighted.

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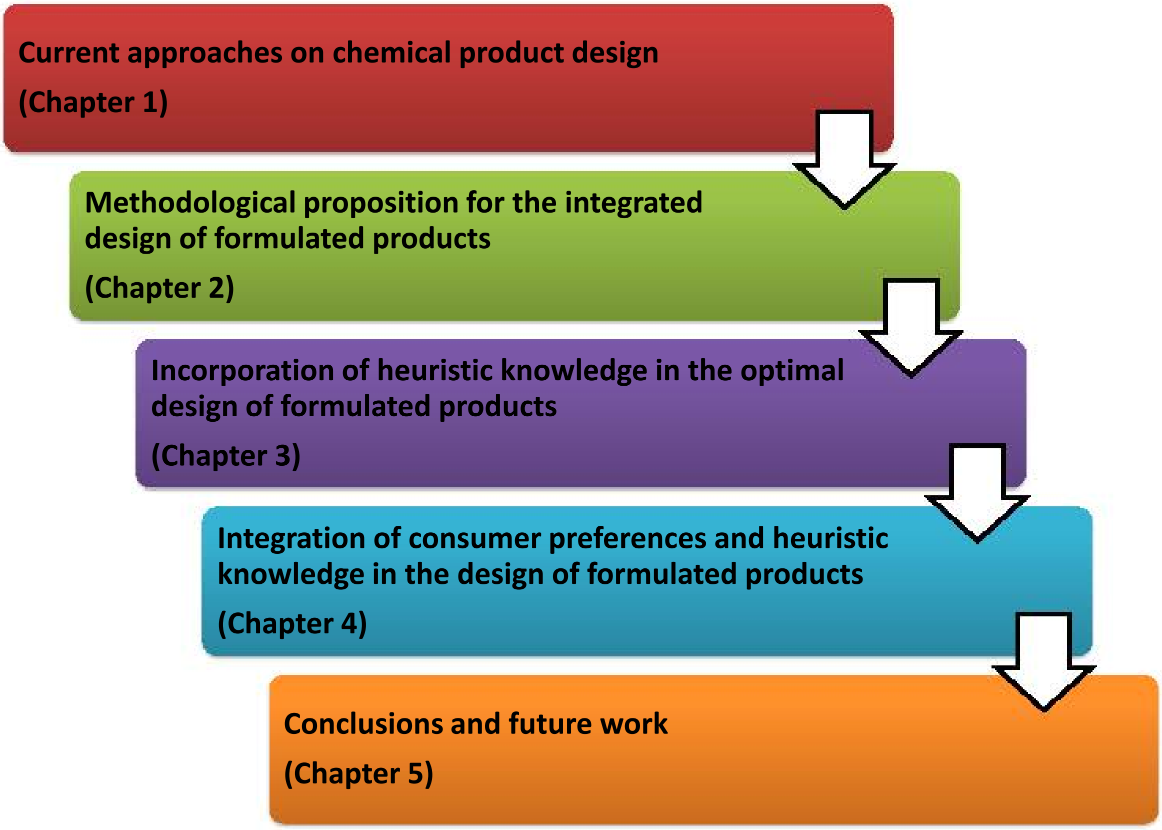
A peer-reviewed short communication resulting from the ESCAPE27 conference in 2017 was published in the book series *Computer Aided Chemical Engineering*, and also a full article appeared in the *Computers and Chemical Engineering Journal* this year. An abstract has been provisionally accepted for presentation at the ESCAPE29 conference in June 2019 too. In addition, two oral presentations at the AIChE Annual Meetings 2017 and 2018 and several poster presentations at different scientific events were delivered during this research.

Figure 0-4: Structure of the document



1. Current approaches on chemical product design: A study of opportunities identification for integrated methodologies

The shift from commodities to high added-value specialties and functional chemicals has been an increasing trend among the chemical manufacturers in recent years (Costa et al., 2006). Due to the growing worldwide competitiveness across all sectors, today companies must be able to do a quick development of new and differentiated products without compromising quality or performance, as a key element for their success (Charpentier, 2010). Frequently, the decision of a product launch is taken far from the processing plant or from the technical team, but in the marketing departments as a response to consumption trends. Then, in some particular sectors (e.g. personal care industry), the speed at which products are designed, developed and manufactured is the decisive factor, even above the cost of production (Charpentier, 2009). Consequently, the need for a rapid development of innovative chemical products becomes a major challenge for technical R&D departments (Cooper, 2013).

Traditionally, chemical product design has been made following an experiment-based trial-and-error approach at different scales in order to get a set of candidate products that meet the targeted performance (Eden, 2003; Mattei, 2014; Omidbakhsh et al., 2012; Zhang et al., 2017). Then, based upon different criteria (e.g. economics, process constrains, consumer feedback, etc.), a specific product is selected to be manufactured and commercialized. Such series of stages result in a very resource-consuming activity in product design and development. This approach becomes particularly difficult when dealing with multiple-species products in which their components, processing variables, and even use conditions, among other factors, could play a major role in the product performance. Consequently, different systematic methodologies for these types of products have been proposed as an alternative to reduce the time spent in the early stages of development (Zhang et al., 2016).

With the aforementioned considerations, the aim of the present chapter is to classify the most current contributions in the field of chemical product design. Particularly, it is intended to identify the key research opportunities for integrative methodologies, which involve mathematical modelling and experiment based components, product-process interactions, multi-scale and multidisciplinary approaches (consumer perception, business variables and sustainability) at different levels. The classification of the different research approaches was done by reviewing scientific literature before 2018, from the classic works to the most recent publications on the field. Based upon the reviewed material, a comprehensive description regarding integrated methodologies for chemical product design, focusing on their main contributions and their levels of integration for the case of formulated products is presented. This last feature distinguishes this study from previous reviews in the field or methodologies of chemical product design.

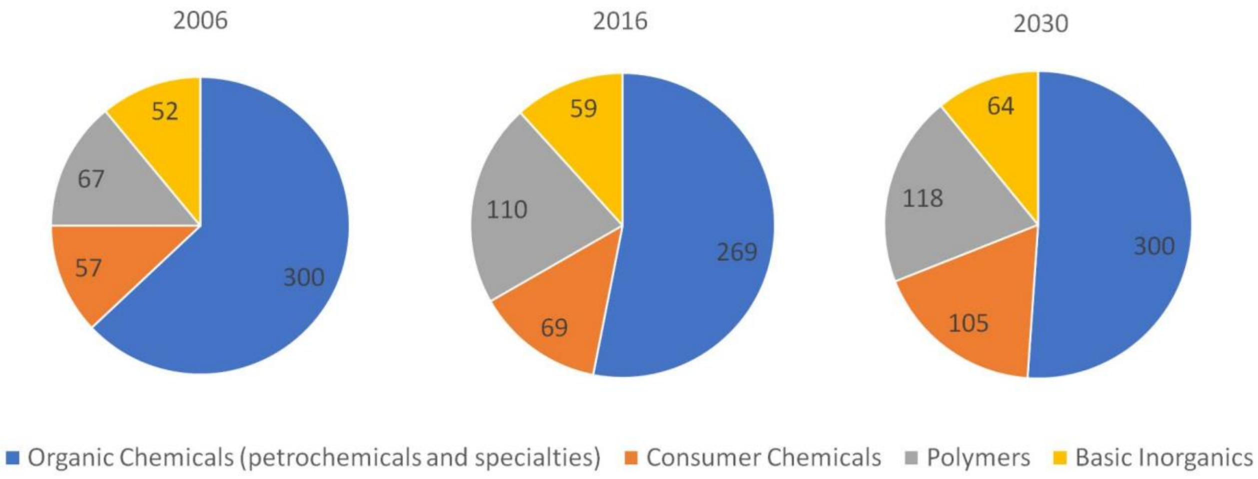
As a starting point, in the next section (§1.1) an overview of chemical product design research and the methodologies used in the current practice of chemical engineering along with a classification based on their type of integration are presented. Next, the applied searching methods for the various documents that supported the study are described (§1.2). Then, the main results are presented and discussed (§1.3). To conclude (§1.4), a set of opportunities in the field of integrative methodologies for multiple-species product design is identified for further research and development.

1.1 An overview on chemical product design

A chemical product can be defined as a system formed by different chemical substances, which is manufactured for one or more purposes (Cisternas, 2007). As there is a complex interaction of phenomena among the ingredients and during the manufacture of such systems (Schubert and Engel, 2004), the design procedure is in some cases, even a matter of art, relying mostly on the expertise of product developers. In this regard, the most recent paradigm of chemical engineering has focused on developing various methodologies to deal with product formulation and manufacture (Hill, 2009). This idea, named chemical product engineering, involves a backwards design methodology, from the identification of quality factors all the way to the manufacture of marketable products (Costa et al., 2006). Chemical product design (CPD) is considered a facet of chemical product engineering and it is defined as the systematic framework of methodologies and tools to provide a faster and more efficient development of chemical products able to meet market demands (Costa et al., 2006). Based upon open literature reports, 1988 was the first time CPD was mentioned in an academic publication (National Research Council, 1988). Since then, CPD has become a well-established research subject for almost two decades, consolidating with the milestone publication of the book "Chemical Product Design" by Moggridge and Cussler in 2001, and continuously evolving in different fields as described in most recent publications such as “Tools for Chemical Product Design: From Consumer Products to Biomedicine” edited by Achenie et al. (2017). Despite the large amount of research in the field during the last decades, CPD has not yet developed into the foreseen third paradigm in chemical engineering. A major reason for that is the lack of understanding over the complex relationships between product manufacturing technologies and material properties, at the different levels of the chemical supply chain, and among the different types of chemicals (Charpentier, 2002; Picchioni and Broekhuis, 2012).

As the development of chemical products has been led by the industry (Cisternas, 2007), they are generally classified by industrial sectors into 5 categories: Petrochemicals, specialties (e.g. paints, dyes, pigments, etc.), polymers, basic inorganic chemicals, and consumer chemicals (CEFIC, 2017). Though the latter group represented only 13.4% of total sales in 2016, it is expected to be the fastest growing category in the years to come in the EU: A 2.6% compound annual growth rate compared to 0.9% of the sector in general by 2030 (AT Kearney, 2012), as it is shown in Figure 1-1.

Figure 0-5: Chemical products sales in the EU (€MM) (AT Kearney, 2012; CEFIC, 2017, 2008).



Chemical products can also be classified depending if their design is process-centered or product-centered (Gani and Ng, 2015). In the first group, most commodities and single species products (small and large molecules) are found, whereas in the second group there are mostly multiple-species products (formulated and functional products) and devices sold directly to the consumer. In particular, this research takes into account the last group of products, focusing in formulated products, which are considered here as a mixture of one or more key ingredients responsible for the functionality of the product (active ingredients), and some supporting ingredients to enhance its performance (Wibowo and Ng, 2002), even if this definition could cover functional products as well.

Although the design process is different for each group of products, it generally consists on creating a product solution with certain functionality at acceptable cost, within a reasonable time, and in a sustainable way. The final result of the design process must be a competitive product in terms of appearance, performance, durability and price (Cussler and Moggridge, 2011a). Usually costly and time-consuming trial-and-error experimental procedures for the formulation and manufacture of chemical products are performed in the chemical industry (Charpentier, 2010). This traditional approach is lengthy, laborious and often constitutes the most resource-consuming part of the product development process (Liao et al., 2008). In this sense, the development of systematic strategies for product design has been gradually incorporated in the chemical industry and academia. Cussler and Moggridge (2001) were the first to propose a consistent set of principles that could support chemical product design activities through four general steps:

I. Needs definition
II. Generation of ideas
III. Selection of ideas
IV. Manufacture of the product

Over the last decade, and following similar principles with more or less steps, different methodologies and tools have been proposed to guide the formulated product design process (Bernardo et al., 2007; Costa et al., 2006; Hill, 2009; Ng et al., 2007; Seider et al., 2009; Wesselingh et al., 2007). Most of these methodologies share a common starting point involving a market research in order to identify consumers' needs and the corresponding end-use properties. Despite the variety of methods, one of the challenges to overcome at this stage is the transformation of consumer assessments, including sensory properties, into precise and measurable terms that could lead to the product design (Cussler and Moggridge, 2011a). The construction of these quantifiable terms requires significant interaction between different disciplines (chemistry, physical chemistry, thermodynamics, engineering, psychology, statistics, marketing research, etc.) to consider all aspects, involving measurable properties. When established, these quantifiable terms become major inputs in the development of new products (Favre and Bousquet, 2004). Although some progress has been made in this area, one of the main current challenges at this stage of the design process is related to the incorporation of sensorial attributes, due to the subjectivity of the appreciations (Pensé-Lhéritier, 2015).

Then, under these emerging methodologies, once the terms that describe consumer needs are defined, they are used to generate ideas of products using predictive and regressed models based upon the interaction of ingredients and processing variables. Here, the generation of feasible candidates, obtained with a variety of ingredients under different processing conditions, is accomplished by solving the models, and optimizing an objective function related with the product performance and some additional criteria (e.g. cost, safety, sustainability). This is normally done by using different algorithms and diverse optimization techniques (Costa et al., 2006; Cussler and Moggridge, 2011a; Hill, 2009). After the optimization, the product alternatives that best fulfill the aforementioned requirements are selected using heuristics (Hill, 2004; Wibowo and Ng, 2002, 2001) and/or various decision-making tools (Constantinou et al., 1996; Eljack et al., 2005; Yunus et al., 2014, 2011). Special emphasis has been placed on computer aided design methodologies, because the search space for feasible product alternatives is reduced compared with traditional trial-error approaches, so time and resources can be spared (Zhang et al., 2016). Beside the many components in multiple-species products, the processing conditions and the resulting microstructure also have an important impact on the product properties. The lack of quantitative structure-property relationships is considered to be an issue regarding this stage of the CPD.

Finally, at the last stage of product design, and after selecting the desired candidate product, it is necessary to make some adaptations in order to ensure a suitable production at industrial and commercial scale. Here, the classical tools of process design in the field of chemical engineering might be used at some levels. However, the complexity of the phenomena taking place from the molecular level up to the industrial production, and the economical and ecological factors involved in the scale of the production plants and the distribution network, compels for multiscale and multidisciplinary approaches to effectively cope with the CPD problem (Charpentier, 2009).

1.1.1 The need for integrated methodologies

There are several approaches to solve a CPD problem depending on the type of product, but they all require the integration of several domains and disciplines, especially for consumer formulated products. In that respect, Cheng et al. (2009) developed a holistic approach for the case of a skin-care cream, involving five groups of job functions: Management, Sales & Marketing, Research & Design, Manufacturing and Finance & Economics. Smith and Ierapepritou (2010) were the first to discuss the different integration strategies in their review, supported by data involving chemical product manufacturers. They established a general framework for integrative product design with three main strategies to incorporate: Consumer influence, product/process, and business requirements. At the same time, three solution approaches for the design problem were proposed: Model-based, experience-based, and hybrid model/experience based. Recently, Zhang et al. (2016) stated that hybrid systems (experience/model) should be employed to design product/process integrated solutions within a multiscale/multidisciplinary approach, when designing a formulated product.

Taking into account the aforementioned, this study considers three main levels of integration, as they represent the identified strategies to effectively deal with the difficult task of formulated product design: experience/modeling, product/process and multiscale/multidisciplinary approaches. The last level could be additionally sorted in four sublevels: multiscale; consumer insight (marketing, psychology, etc.), business decision variables (economics, finances and management, etc.), and the sustainability dimension, as it is shown in Figure 1-2. In the next sections, each one of these integrative approaches will be further explained.

1.1.2 Experience[1]/Modeling integration (EM)

Experimentation in CPD is normally useful when the underlying physico-chemical phenomena for the estimation of the target properties is not fully understood (or simply because the suitable mathematical models are not developed).

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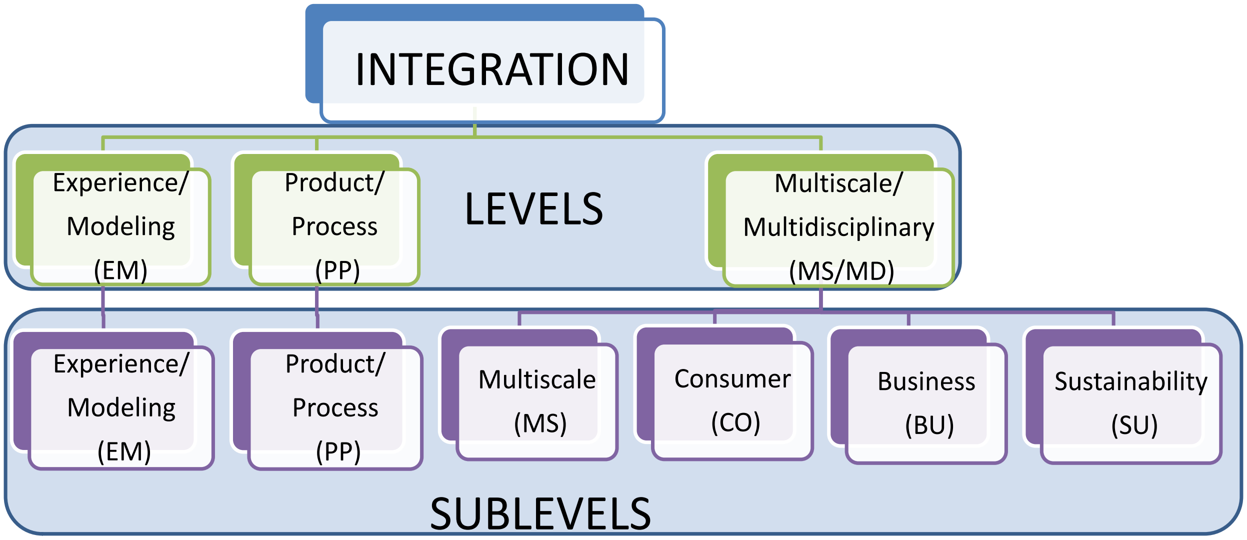
[1] Experience is here understood as a combination of the empirical knowledge derived from direct observation of and participation in experiments

Figure 0-6: Levels and sublevels of integration in CPD methodologies



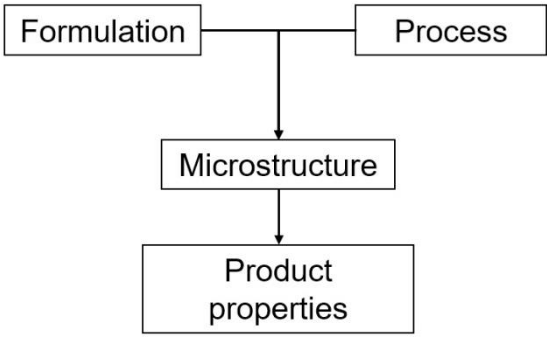
Therefore, in this case empirical knowledge and experience are needed to obtain the optimal formulations (Moulai Mostefa et al., 2006; Ng et al., 2007). On the other hand, when validated mathematical models for the estimation of all the target properties are available, a list of feasible candidates can be generated and tested by a model-based approach.

Nevertheless, in most cases such mathematical models are available for just a fraction of the target end-use properties or only for some type of specific products, that is why a hybrid experience/modeling integrated approach is more suitable, as it has been recently proposed (Mattei, 2014; Zhang et al., 2016). By combining the two above-mentioned approaches, the weaknesses of the one are covered with the strengths of the other (Gani and Ng, 2015): the uncertainties of the mathematical-based approach are compensated by rule-based techniques or heuristics, while the number of experiments is reduced through the model predictions and only carried out for the most promising candidates, saving up resources and time (Conte, 2010; Conte et al., 2011b, 2009a, 2009b; Contreras-Calderón et al., 2011).

1.1.3 Product/Process integration (PP)

As it was mentioned before, most formulated products are usually complex systems with different ingredients that interact to provide several functions required by the customers (Abildskov and Kontogeorgis, 2004). These systems are very often characterized not only by the quantity of each ingredient, but also by their microstructure; i.e. the relative spatial arrangement of each ingredient in the product (Bongers and Almeida-Rivera, 2012, 2009). In this sense, the microstructure is influenced by both the formulation and the process conditions (Figure 1-3).

Figure 0-7: Influence of microstructure on product properties. (Reproduced from Edwards 2006 with permission from ElSevier).



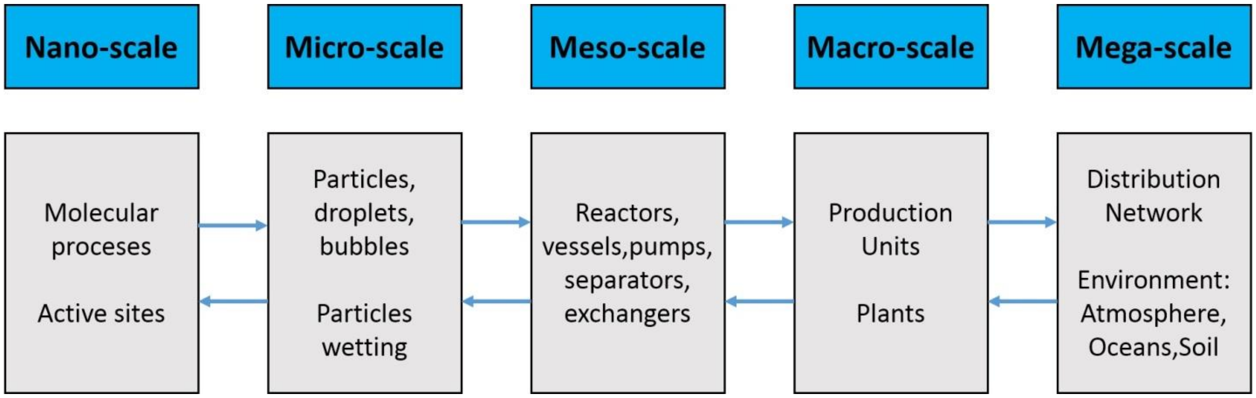
In some particular cases, the process could even determine both the product structure and its composition, for instance in the case of a crystalline solid (Bernardo, 2017). Bernardo and Saraiva (2005) illustrated how decisions regarding product formulation and microstructure interact with process design and operation, as well as how a decoupled sequential solution of product and process design problems may lead to suboptimal solutions.

1.1.4 Multiscale/Multidisciplinary integration (MS/MD)

Since the introduction of the triplet “molecular processes-product-process” engineering concept by Charpentier (2002), the term multiscale seems to be more than appropriate in CPD, as the design and manufacture of chemical products spans to a wide length and time scales (Charpentier and McKenna, 2004). This makes necessary to consider different interactions and complexity levels in order to describe phenomena at the nano-, micro-, meso-, macro-, and mega-scale, as shown in Figure 1-4. This task is required to identify and model the relationships between the different levels and scales.

As the development of modern products requires different disciplines over a wide scale range, multidisciplinary approaches have been proposed in the last few years, especially when a specific desired attribute needs to be attained (Gani and Ng, 2015). In this sense, the product design framework should take consider not only the product structure and composition, but also the manufacturing investments and costs, the associated supply chain, the marketing issues, such as the consumer behavior with respect to the product price, among other relevant factors that influence the product design (Bagajewicz, 2007).

Figure 0-8: Multiscale levels in product design. (Figure reproduced from Charpentier, 2002 with permission from ElSevier)



Integrative approaches, involving marketing, financial, economical and management issues on the business side, and product design and prototyping on the technical side, are necessary for the development of chemical-based products (Cheng et al., 2009; Ng, 2015). Multiscale and multidisciplinary integrated approaches are also being developed to address the increasing attention to environmental, safety and social requirements, to the transition towards sustainability, bringing the product design closer to the practice in the industry (Charpentier and McKenna, 2004; Edwards, 2006). Indeed, the modern industry is progressively adopting the principles of the "green chemistry" and "green engineering" (i.e. sustainability) in their designs to satisfy both the market requirements for specific end-use properties (nano- and micro-scales), and the social and environmental constraints of production processes and distribution networks (meso- and macro-scale) (Charpentier, 2016).

Hence, the main trends regarding the incorporation of multiscale/multidisciplinary approaches in formulated product design can be roughly divided into four sublevels: Those considering the multiscale (MS) nature of the design procedure itself; the ones dealing with the consumer (CO) understanding using disciplines like marketing, psychology, etc; those focused into business (BU) decision variables (economics, finances and management, etc.) and finally the ones considering the sustainability (SU) dimension.

1.2 Methods

In order to establish the scope and extent of literature to be covered and reviewed, a systematic procedure was adopted:

- The sources of information were defined with the following: online accessibility, English, French, German, Portuguese and Spanish as the languages, and a time span of nearly 30 years.
- The type of documents that were considered in the search included research and/or project reports, journal articles, book chapters, and dissertations in the chemical engineering field.
- The literature search was done by using Web of Science and Scopus engines, which include most scientific publications from major editors.

Initially, the research terms were combined by using the Boolean operators OR and AND, and wild cards like * to avoid issues with plurals or derived words. The search algorithm restricted to the title shown in (1.1) was used:

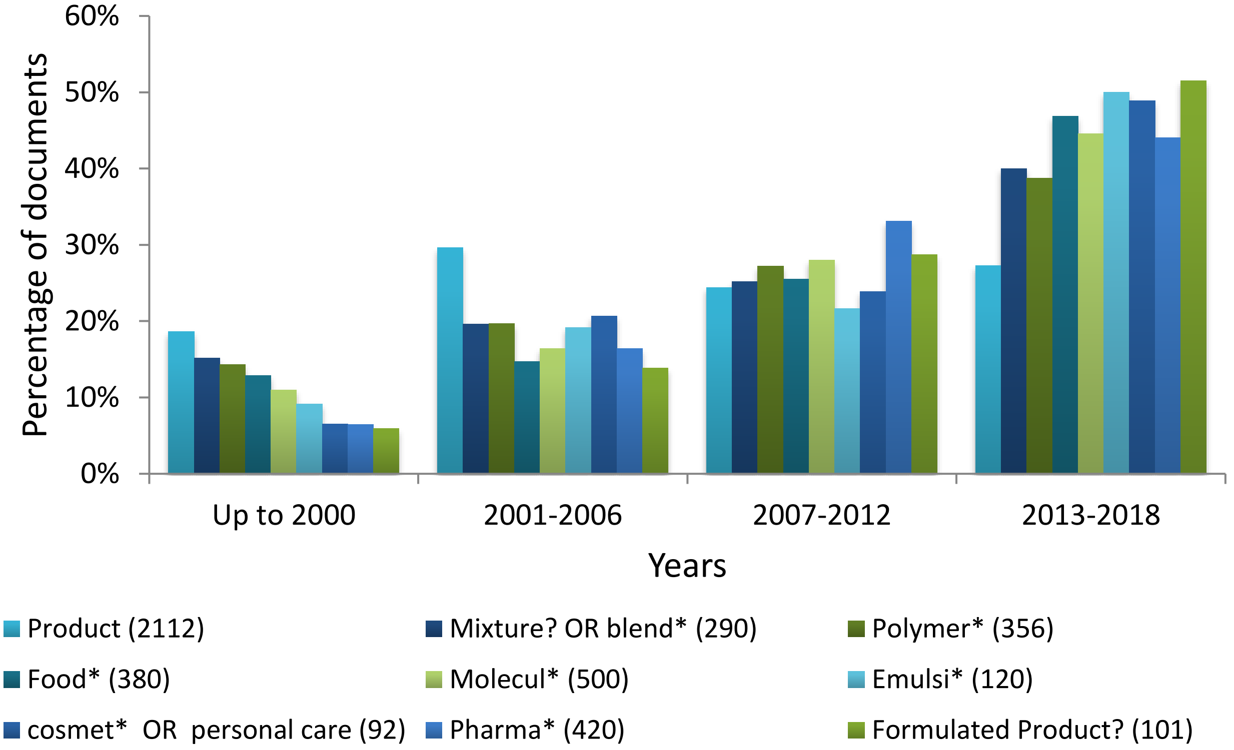
$$\text{(product) and (design} * \text{ OR develop} * \text{ OR formul} * \text{ OR engineer)} \qquad (0.1)$$

Then, as the main interest of this chapter was to select those documents, which could help to identify the major trends and main opportunities in the field of chemical product design, the list of documents was further restricted by using words in each of the levels and sublevels of integration mentioned in Figure 2. Finally, only those sources, which introduced a methodological approach that could be used as a framework to design chemical products, were selected to be further analyzed. For this, variations of the word “integration” and synonyms were emphasized, particularly looking after detailed information about the main steps for the systematic design of formulated products. If there was a lack of information based on these criteria, the document was only considered for statistical purposes and was not further analyzed in the study. The research was extended to other sources cited in the selected articles if they were likely to provide additional details on a particular methodology. However, it is worth saying that the inclusion of a particular document depended on its contained amount of information.

1.3 Results and discussion

More than two thousand documents were found with the aforementioned search algorithm (2085 in Scopus and 456 in Web of Science, with 429 common coincidences). Then, the commonest author and index keywords in these documents regarding product types were selected and placed instead of "product" in the search algorithm, in order to establish the different formulated product categories. The main product categories were: molecules, mixtures or blends, pharmaceuticals, emulsions, polymers, cosmetics and personal care, food, and formulated products. In order to determine the research trends on these product categories over the last years, three 6 year-intervals of time were selected starting in 2001, as it is shown in Figure 1-5.

Figure 0-9: Evolution of main product type publications (the number of documents is indicated in the brackets)

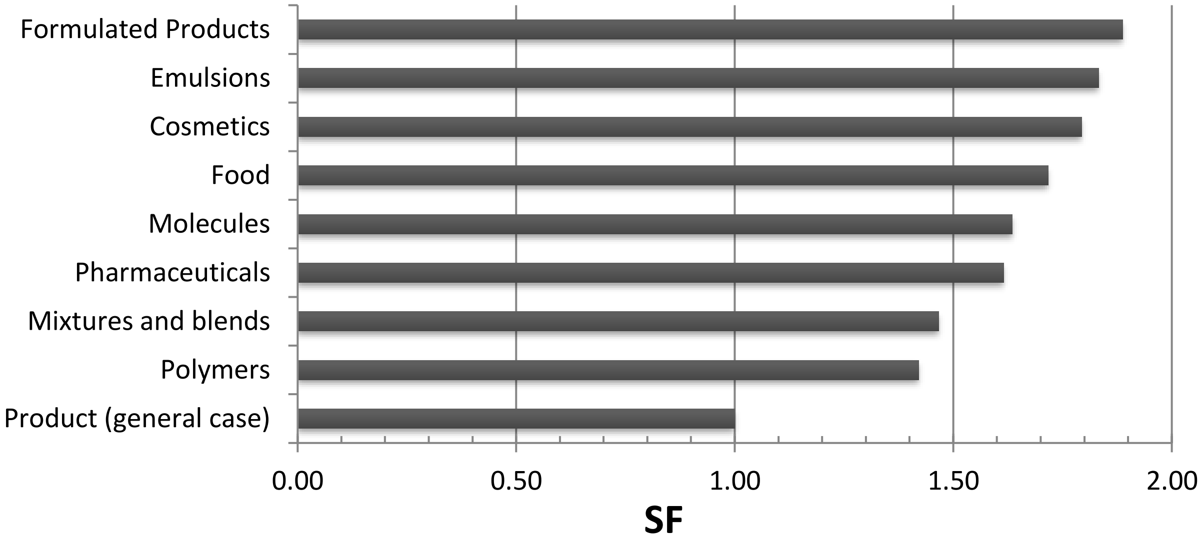


It can be observed that less than a fifth of the total publications in this field were done before 2001 and for all the specific product categories this fraction is even lower (max. 15%). Then, during the next period of time "product" design featured its highest peak, reaching 30% of the total number of documents on this subject, while the other product categories remained around 20%. Then the general ”product” term further made room for more specific types, in what could be considered a consolidation phase (2007-2012), where approximately a fourth of the documents in all categories was published. Finally, in the last 6 years (2013-2018), a specialization took place, accounting for around 40% of the total number of documents in every category, being the only exception the general case of “product” publications (27%).

In the case of “formulated products” for example, over half of the documents were produced in this period. This specialization is expected to continue, as the number of consumer formulated products in the market grows every year. To try to illustrate this, the percentage of documents published for each category in the last six years is compared with that of “product” publications (27%). Taking this number as a basis, a “specialization factor” (SF) for each product type was calculated according to (1.2) and shown in Figure 1-6. Here, it can be seen that formulated products, emulsions and cosmetics are on the top of the most specialized type of products.

$$\text{SF of X product type} = \frac{\text{\% of "X product type" publications in the last 6 years}}{\text{\% of “product” publications in the last 6 years}} \qquad (0.2)$$

Figure 0-10: Specialization factor by product type



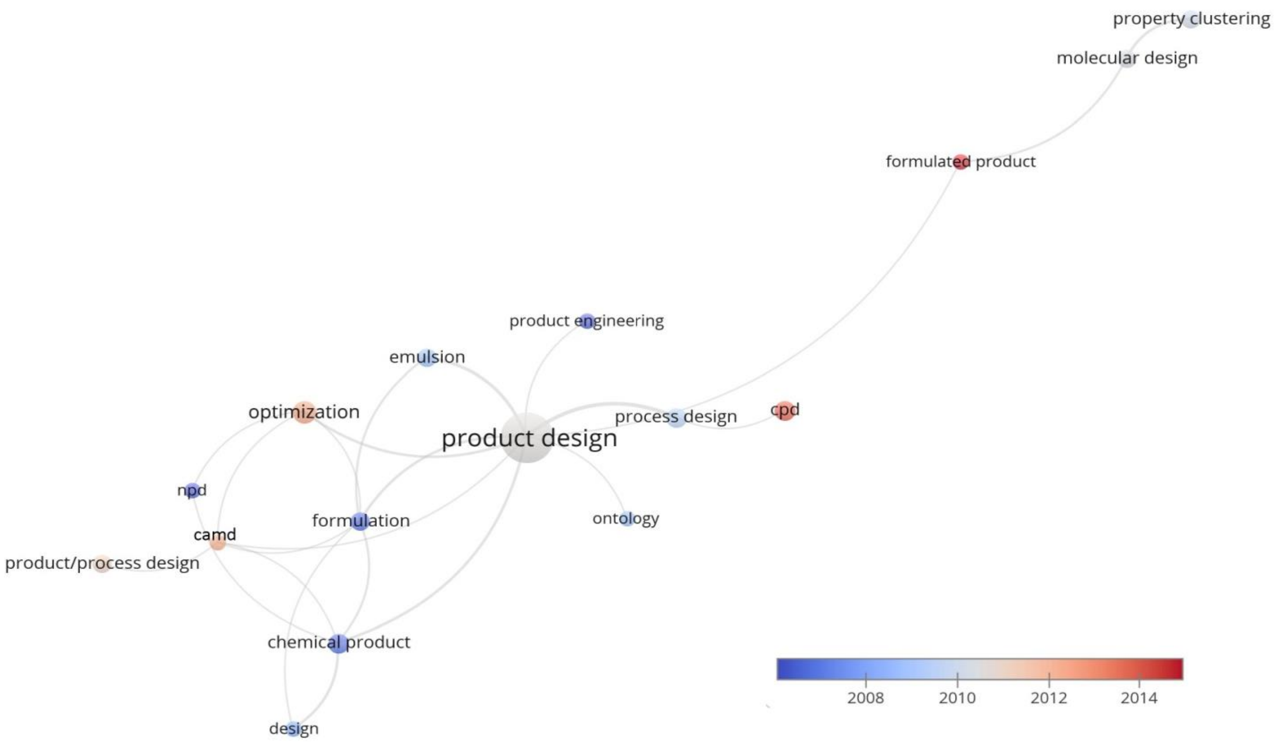
Then, by applying further restrictions regarding the content of the documents (see Section 1.2 - Methods), the list was reduced to 200 relevant sources containing information about the aforementioned levels of integration, related to any of these product categories, as it can be observed in Table 1-1.

Table 0-1: Type of selected contributions and their average publication year

Type of contribution	Perspective	Methodology	Review
Publications	35	157	8
Average publication year	2005.4	2009.7	2014.1

After making minor changes to the original author keywords among these 200 sources, like unifying singular and plural terms or British and American spelling, and using abbreviations instead of full sentences, such as NPD for new product development, those sources having at least 5 repetitions each (16 out of 386 in total) were selected, as shown in Figure 1-7.

Figure 0-11: Author keywords in selected sources on CPD



In this visualization made with VOSviewer®[2], the number of citations is proportional to the size of the circle under the tag, and its average publication year is indicated on a color scale.

When looking at the type of products used as examples or study cases among in these sources, “emulsions” are this time in the top position with examples in different categories such as cosmetics (Rähse, 2011), detergents (Mattei et al., 2014a, 2013a), food products (Norton et al., 2006), solvents (Coutinho et al., 2005) and pharmaceuticals (Schubert and Engel, 2004). Here, it is also important to notice the preference for the newest term “formulated product” (average publication year 2015) instead of that of “formulation” (average publication year 2006.8), which seems to reflect the industrial trend of using formulated products when speaking about “formulations that are reliably and repeatedly delivered to the target market and addressed to a specific consumer need” (AceForm 4.0, 2017).

The evolution of the keywords chosen by the authors of these documents was analyzed and it can be observed how they have gradually changed over time: In the first place, the most common term “product design” (average publication year 2010.6; 48 occurrences), but a few years earlier there were also used other, rather unassociated terms, such as “product engineering” (average publication year 2005; 5 occurrences), “NPD” (average publication year 2006.2; 5 occurrences), “chemical product” (average publication year 2006.9; 7 occurrences), “design” (average publication year 2008.2; 5 occurrences) and “molecular design” (average publication year 2010.3; 6 occurrences). More recently, “CPD” (average publication year 2013.7; 7 occurrences) appears on the scene, confirming what it was said above about the momentum this subject has gained in the current chemical engineering research. As expected, different authors highlight the importance of the process in the product design, with associated terms like “process design” (average publication year 2009.6; 7 occurrences) or “product/process design” (average publication year 2011; 6 occurrences). This integrative approach is illustrated for various product types, such as cosmetics (Bernardo, 2017; Bernardo and Saraiva, 2005), solvents (Cignitti et al., 2017), enzymes (Heitzig et al., 2010), detergents (Martín and Martínez, 2013a), pesticides (Morales-Rodríguez and Gani, 2009), pharmaceuticals (Reklaitis, 2007), biofuels (Voll et al., 2010) and food products (Norton et al., 2006).

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[2] http://www.vosviewer.com/

Finally, concerning the CPD problem solution, “optimization” (average publication year 2012.4) appears as the most common strategy, being mentioned as a keyword 10 times in these sources. Optimization is close related to “CAMD” (average publication year 2012.2; 5 occurrences), which stands for “computer-aided molecular/mixture design”, and is also a very popular tool, as it can accelerate the CPD design process. This technique has been successfully implemented by many authors for formulated products (Conte et al., 2012, 2011b, Mattei et al., 2014a, 2012; Omidbakhsh et al., 2012; Yunus et al., 2013), as it was reviewed by Zhang et al. (2016).

1.3.1 Integrative CPD methodologies

After analyzing the 157 documents focused in methodologies under the scope of the aforementioned levels and sublevels of integration (Figure 1-2), it was found that the three levels are rather equally represented, as shown in Table 1-2.

Table 0-2: Documents by type of integration levels

Integration level	EM	PP	MS/MD	Total
Number of publications	111	117	98	157
Average publication year	2009.9	2009.4	2010.7	2009.7
First publication year	1996	1996	1996	1996

*EM = Experience/modelling; PP = Product/Process; MS/MD = Multi-scale/Multidisciplinary

There are also no remarkable differences in the average year of publication for these groups of methodologies and they all share the same year for their first publication (1996), showing the awareness of the chemical engineering community about the importance of these levels when designing formulated products.

However, by considering the sublevels, some clearer trends can be distinguished (Table 1-3). On the one hand, business and consumer related methodologies are the most common in this category, having 72 and 63 documents, respectively (73% and 64% of the MS/MD cases). On the other hand, the least represented sublevels in the MS/MD category of integrated methodologies in the CPD scene are sustainability (SU – 18 documents) and multiscale (MS – 14 publications), accounting for only 18% and 14% of the documents, respectively. It is important to notice that these two sublevels are the latest to be first included in a methodology for chemical product design: 2006 for MS and 2008 for SU. As a matter of fact, multiscale integration is still regarded as one of the major challenges to be faced by the chemical process and product engineering (Charpentier, 2010; Garnier, 2014; Pohorecki et al., 2010; Zhang et al., 2018). Sustainability has only very late started to be taken into account in the field of CPD methodologies (2014.5 in average), despite the great importance it has for the chemical process industry (Grossmann, 2004).

Table 0-3: Documents by type of integration sublevels

Integration sublevel	EM	PP	MS	CO	BU	SU	Total
Number of publications	96	118	14	63	72	18	157
Average publication year	2009.9	2009.5	2011.6	2011.2	2010.5	2014.5	2009.7
First publication year	1998	1996	2006	2000	1996	2008	1996

*EM = Experience/modelling; PP = Product/Process; MS/MD = Multi-scale/Multidisciplinary; CO=Consumer; BU= Business; SU=Sustainability

As the main interest of this study is to classify the integrative methodologies in order to identify the key research opportunities for formulated products, the next step in the analysis was to investigate the comprehensiveness of the proposed methodologies. To do this, the number of different levels and sublevels of integration considered in each one of these 157 documents was counted. Tables 1-4 and 1-5 contain the publications grouped by the number of integrated levels and sublevels, respectively. Arabic digits were chosen for the number of levels, while Roman numerals were used for the number of sublevels.

Table 0-4: Methodologies by the number of combinations of integration levels

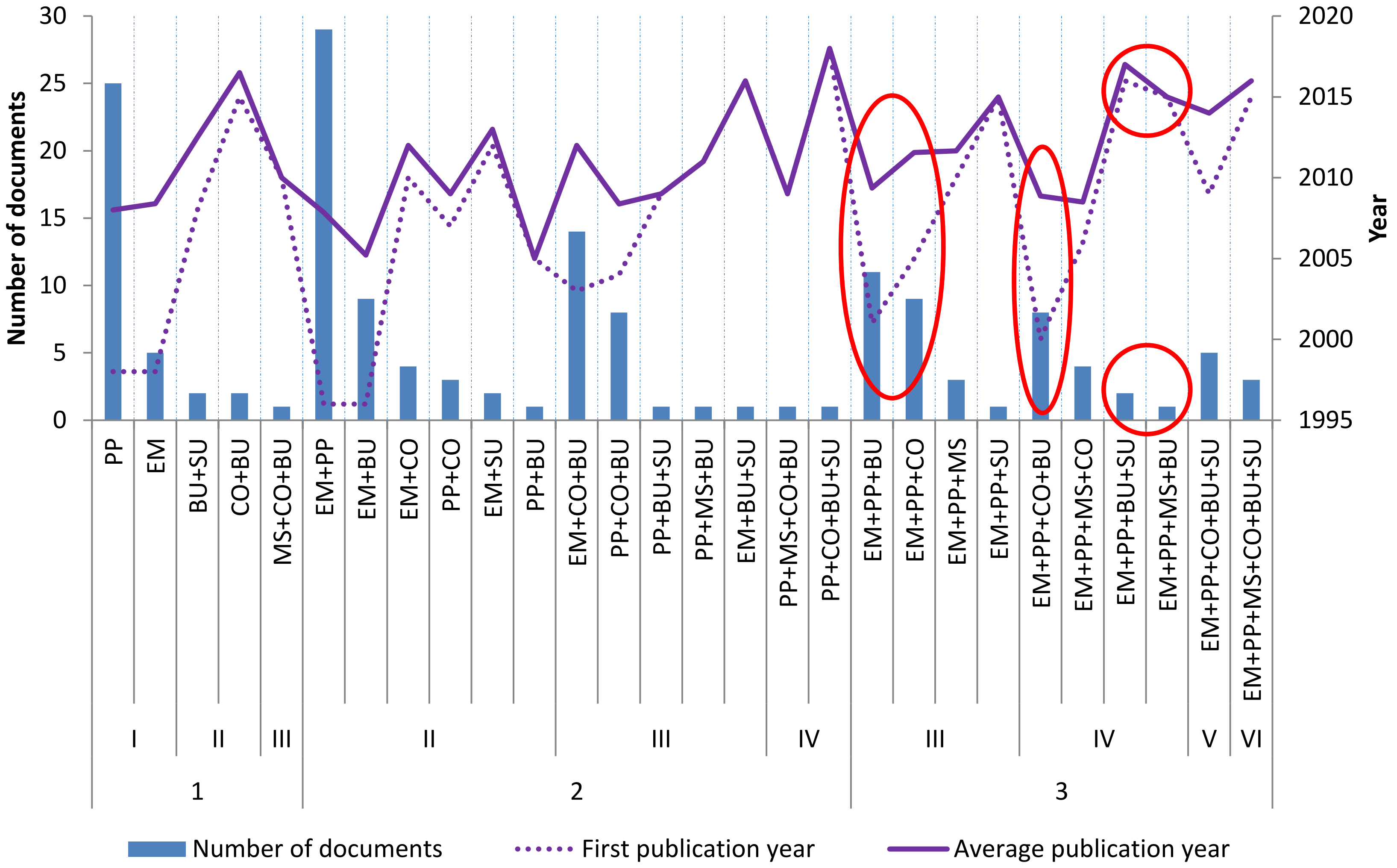
Number of levels	1	2	3	Total
Number of publications	35	75	47	157
Average publication year	2008.9	2009.1	2011.3	2009.7
First publication year	1998	1996	2000	1996

Table 0-5: Methodologies by the number of combinations of integration sublevels

Number of sublevels	I	II	III	IV	V	VI	Total
Number of publications	30	52	50	17	5	3	157
Average publication year	2008.1	2008.4	2010.8	2010.6	2014	2016	2009.7
First publication year	1998	1996	2001	2000	2009	2015	1996

As it can be seen, 78% of the identified sources (122) incorporate at least two of the three levels proposed in this study, and almost a third of all (47) sources incorporate the three main levels of integration. Among those, when considering the sublevels, around half of the methodologies consider at least four sublevels (25), but only 5% of total sources (7) come up to five or more sublevels, including three very recently published articles, which deliver a methodology with all the six sublevels (Fung et al., 2016; Ng, 2015; Zhang et al., 2017). The latest work is an integrated framework to conceive formulated products based on a multidisciplinary grand model proposed in the other two studies, which cover the product/process design coupled with an economic analysis to achieve an optimal solution of the CPD problem. Figure 1-8 presents detailed information about the 28 specific combinations found on each level and sublevel, to be able to explore the opportunities in the CPD domain.

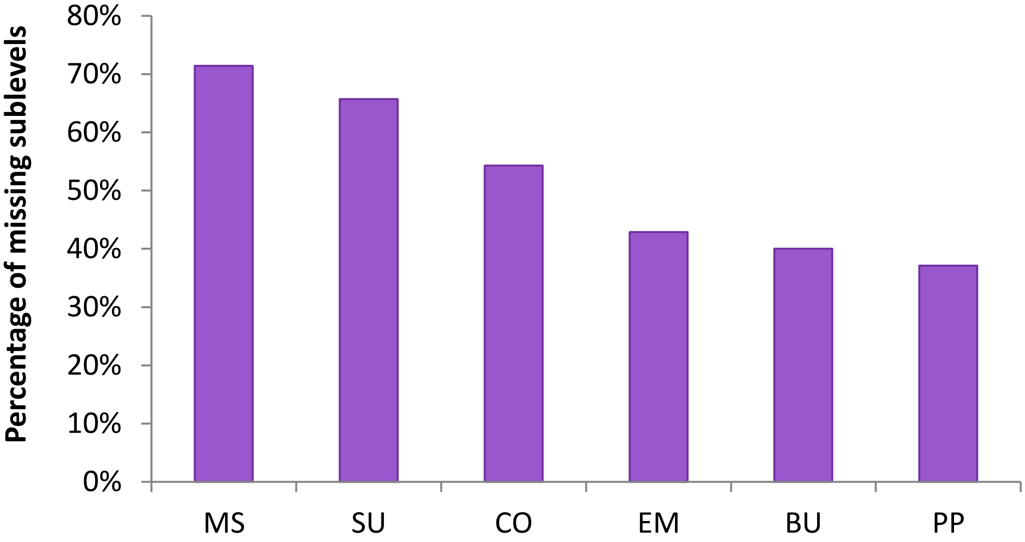
Figure 0-12: Detailed combinations of integration levels and sublevels



*EM = Experience/modelling; PP = Product/Process; MS/MD = Multi-scale/Multidisciplinary; CO=Consumer; BU= Business; SU=Sustainability

Noteworthy is, for example in the case of fully integrated methodologies (3 levels), the complexity of incorporating the multiscale and/or sustainability dimensions, which is reflected on both the number of documents, and the difference between the first and the average publication year for combinations without any of these sublevels (red ovals) and those considering them (red circles). This fact becomes more evident if we take the total number of missing combinations (35) and observe how many of them have not incorporated MS or SU sublevels: 71% and 66%, respectively. Figure 1-9 presents this feature for all the sublevels.

Figure 0-13: Sublevels in integrated methodologies for formulated product design



*EM = Experience/modelling; PP = Product/Process; MS/MD = Multi-scale/Multidisciplinary; CO=Consumer; BU= Business; SU=Sustainability

Appendix A summarizes 44 selected studies, many of them combining either three levels or four sublevels of integration. The focus is on their key contributions and opportunities for further integration and research in the field.

The main highlights of this analysis can be summarized as follows:

- Considering the importance of emulsions in the field of CPD (see Figures 1-6 and 1-7), many authors have developed a knowledge basis for the collection of the consumer needs, their translation into necessary categories of ingredients, and the end-use properties with target values and/or boundaries of acceptance, particularly in the case of cosmetics and personal care products (Bagajewicz et al., 2011; Bernardo, 2017; Bernardo and Saraiva, 2005; Cheng et al., 2009; Lee et al., 2014; Mattei et al., 2012).

- A large collection of heuristic knowledge regarding formulation and manufacture is available (Rähse, 2013, 2011; Rähse and Dicoi, 2009; Wibowo and Ng, 2001), and has not yet been incorporated in a systematic methodology along with property models, which could serve to both generate and select feasible prototypes, particularly in the field of cosmetic emulsions.

1.4 Conclusions

From this chapter it can be seen that systematic integrated approaches for formulated products are on the top of the current challenges in CPD. Nevertheless, only few methodologies have proposed an integration covering the different levels (experience/modelling, product/process and multiscale/ multidisciplinary approaches) and sublevels presented in this study. The classification made here could facilitate the task of creating new methodologies for formulated products.

Considering the current state of the art of CPD, in particular on the opportunities regarding integrated methodologies for formulated product design, the research efforts should be concentrated, on the one hand, in incorporating the consumer insight and business decision variables along with hybrid experience/modelling tools to guide the product/process design of a well-known structured product. To this respect, cosmetic emulsions seem to be a good candidate for formulated structured products, as it exists a large collection of available heuristic knowledge and property models in this field, which has not been incorporated in a systematic methodology for formulated product design. Finally, the inclusion of sustainability and/or multiscale dimensions in new fully integrated methodologies is one of the main challenges for chemical product design

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2. Methodological proposition for the integrated design of formulated products: Application to cosmetic emulsions

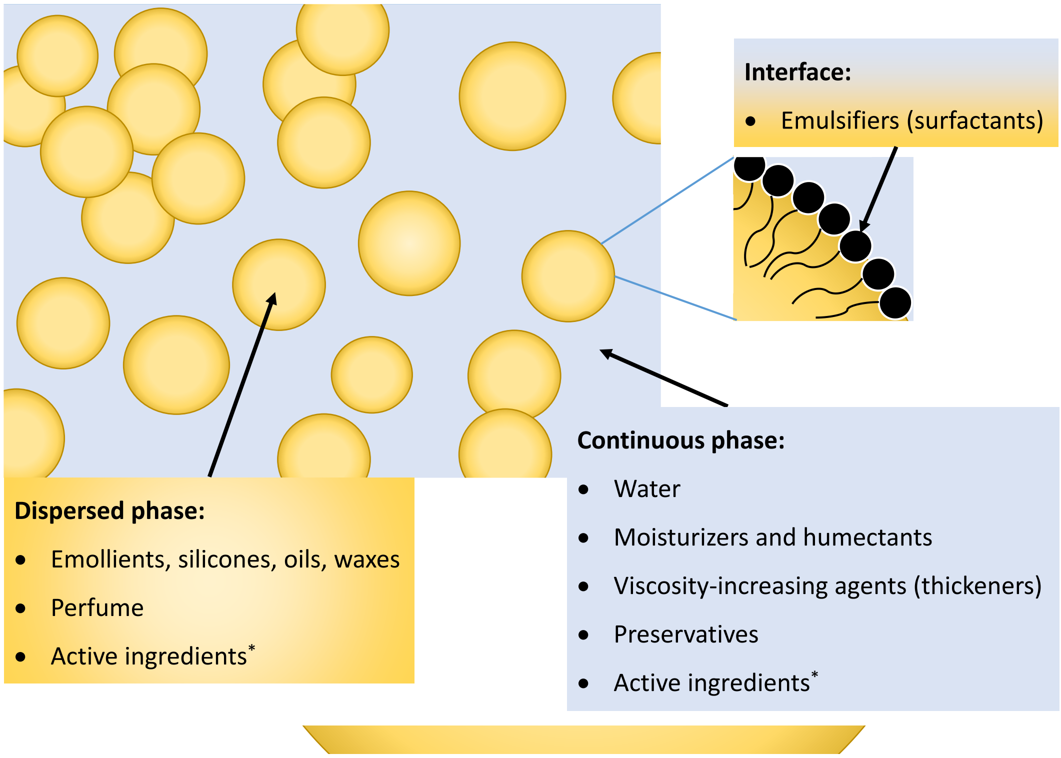
This chapter introduces the fundamental concepts and properties of emulsions (§2.1) in the context of cosmetic product design (§2.2). Then, the main aspects related to the incorporation of the consumer assessment (concept definition) (§2.3) and the modeling of emulsified products (product realization) (§2.4) in an integrative approach for formulated product design are presented. In the next section, the general methodology proposed as a contribution of this research is described (§2.5). Finally, some concluding remarks will be highlighted (§2.6).

2.1 Cosmetic emulsions

In general terms, a cosmetic formulation is composed of a variety of active and inactive (excipients and additives) ingredients (Rähse, 2013); the active ingredients are embedded into a matrix called the vehicle. With the aid of the vehicle, the active principle is delivered to the application site or to the target organ where the desired effect is achieved (Barel et al., 2001). Among the different type of cosmetic preparations, emulsions are of major interest because they are suitable vehicles for active ingredients of different nature (i.e. polar and non-polar). Emulsions are preferred because they are capable of delivering a variety of cosmetic benefits to the consumer, and their consumption steadily grows due to their many advantages: Their delivery form allows the formulation to combine otherwise incompatible ingredients into an effective, commercially desirable cosmetic product (Barel et al., 2001). In terms of active ingredients, water and oil soluble compounds can be incorporated in the same product, even if they would interact adversely with each other under normal circumstances (Pensé-Lhéritier, 2011). Emulsions also offer a great degree of formulation flexibility, permitting an easy modification of characteristics such as viscosity, feel and appearance (Knowlton and Pearce, 1993).

An emulsion can be defined as a thermodynamically unstable mixture of at least two immiscible or partially immiscible liquids. It is kinetically stabilized by emulsifying agents (surfactants or emulsifiers) that lie at the interface between the two liquid phases: one, the dispersed phase, in the form of very fine droplets inside the other, the continuous phase (Knowlton and Pearce, 1993). There are many types of cosmetic emulsions (water-in-oil (W/O), oil-in-water (O/W), silicone in water, multiple, etc., but the O/W type are the most commonly found for skin- and hair care products. Up to 90% of cosmetic emulsions are O/W (Lin, 2010), as these tend to feel less greasy and have a lower cost than other forms because of the higher water content. Cosmetic O/W emulsions are low internal phase ratio (Kostansek, 2012) - typically containing 10 to 35% dispersed phase - so the addition of a suitable emulsifier agent (for example nonionic surfactants with HLBs ranging from 7 to 16) along with the application of mechanical agitation are necessary to create a stable emulsion (Barel et al., 2001). The main ingredients of a cosmetic O/W emulsion are illustrated in Figure 2-1.

Figure 0-14: Cosmetic oil-in-water emulsion composition

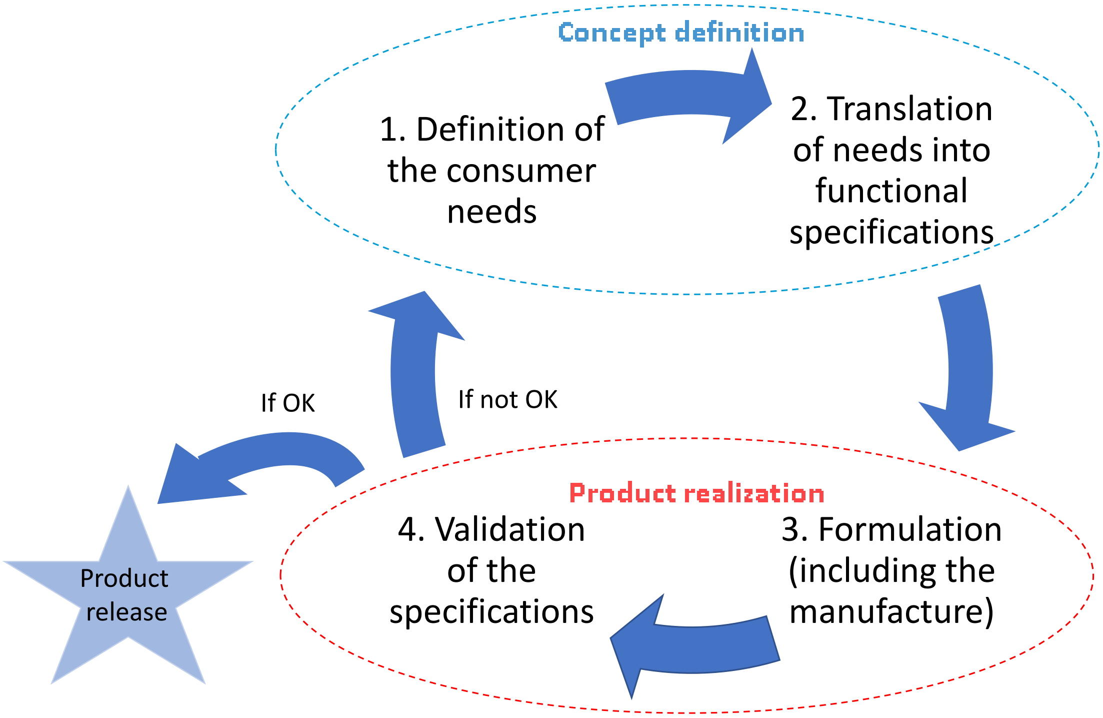


*Depending on their nature active substances can be found in one or both phases (Barel et al., 2001)

2.2 Cosmetics and formulated product design

The traditional cosmetic design process corresponds to a cyclic succession of 4 steps (Pensé-Lhéritier, 2016), as shown in Figure 2-2.

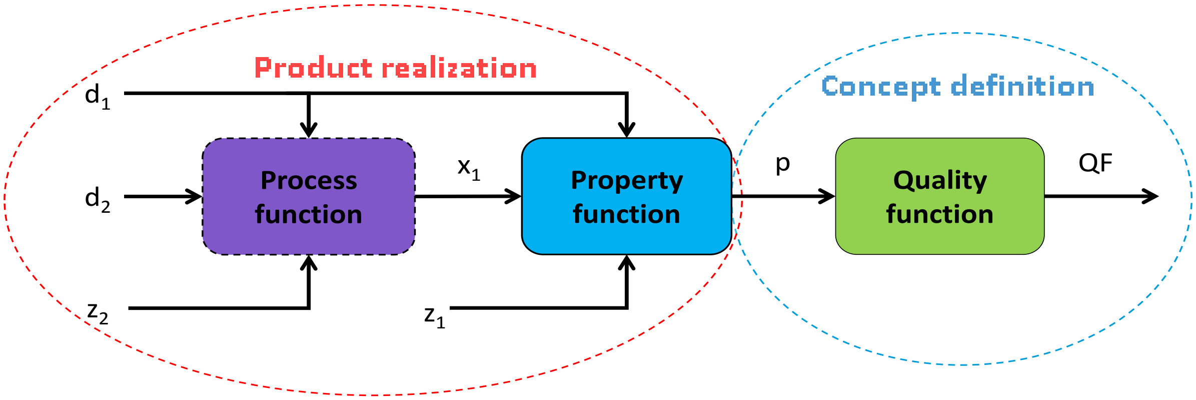
Figure 0-15: Cosmetic product design cycle. Adapted from (Pensé-Lhéritier, 2016)



The marketing team is normally responsible for steps 1 and 2, which constitute the concept definition. In this phase, the information on the consumer needs is translated to constitute the main functional specifications of the cosmetic product. Other secondary (galenics) or even tertiary (aesthetics) functions, regulations and standards need to be also specified before starting the formulation of the product in the laboratory (Pensé-Lhéritier, 2016; Rousseau, 2011). Steps 3 and 4, on the other hand, are under the direction of more technical teams, as they accord the physical product realization. After this phase, if the prototype meets the given specifications, the product is ready to be launched into the market; otherwise the process should start again.

The aforementioned definitions can be adapted into the context of formulated product design. This can be done using a fairly established conceptual model as proposed by Bernardo and Saraiva (2015), which corresponds to a representation of an integrated product/process design problem in Figure 2-3 .

Figure 0-16: Conceptual chemical product design. Adapted from (Bernardo and Saraiva, 2015)



d_1 – Product design variables (process-independent)
d_2 – Process design variables
x_1 – Product state variables (process-dependent)
z_1 – Product operating variables (use conditions)
z_2 – Process operating variables
p – Product performance metrics
QF – Quality factors

These authors also provided an example of this model using a cosmetic emulsion (Bernardo and Saraiva, 2005, 2004), which illustrate the functions, variables and parameters relevant to the design of a chemical product, as shown in Table 2-1.

Table 0-6: Conceptual design of a cosmetic lotion. Adapted from (Bernardo and Saraiva, 2005)

	Description	**Cosmetic lotion example**
QF	Product quality factors valued by customers	Skin feeling when poured and applied
p	Product physicochemical properties during usage	Emulsion viscosity
d_1	Product design variables (process independent): Ingredients used and their proportion	O/W emulsion components (water, emulsifier, thickener, oil, etc.)
x_1	Product state variables (process dependent): Product structure	Droplet size distribution of the oil phase
z_1	Product operating variables: external conditions during product usage	Shear rate of product application on skin
d_2	Process design variables: flowsheet configuration and equipment dimensions	Mixing equipment dimension
z_2	Process operating variables: operating procedure (recipe) and equipment operating conditions	Impeller speed, order of ingredients addition

In the next sections, the most important aspects for the concept definition and product realization of cosmetic emulsions from the perspective of consumer-oriented formulated products will be presented.

2.3 Concept definition

An important feature of consumer-products is that customers generally do not assess their value based on technical specifications, but rather according to functionality and performance attributes, which are often referred to as the quality factors (Costa et al., 2006). Table 2-2 lists some examples of typical quality factors for cosmetic emulsions like lotions, creams and pastes (Wibowo and Ng, 2001).

Table 0-7: Quality factors for lotions, creams and pastes. Taken from (Wibowo and Ng, 2001)

Functional	▪ Protects parts of the body ▪ Cleans parts of the body ▪ Provides a protective or decorative coating ▪ Causes adhesion to a surface ▪ Delivers an active pharmaceutical ingredient (API)
Rheological	▪ Can be poured easily ▪ Spreads easily when rubbed on the skin ▪ Does not flow readily under gravity but easy to stir ▪ Should give a uniform coating when applied to a surface ▪ Should not flow by itself, but can be squeezed out of the container
Physical	▪ Must be stable for a certain period of time ▪ Melts at a certain temperature ▪ Must release an ingredient at a controlled rate
Sensorial	▪ Feels smooth ▪ Does not feel oily ▪ Appears transparent, opaque, or pearlescent ▪ Does not cause irritation

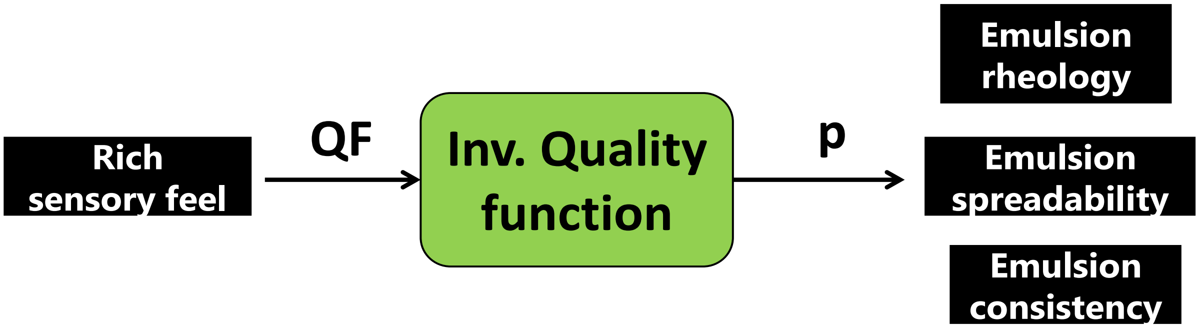
The consumer's needs interpretation uses product evaluation techniques to assess the characteristics or attributes of a product. These techniques are classified into objective and subjective assessments (International Federation of Societies of Cosmetic Science, 2008):

a) Objective, which relates to procedures carried out by trained personnel using either instrumental or sensory methods which produce directly reproducible and quantifiable results.

b) Subjective, which relates to procedures involving sensory test methods invariably carried out by untrained people under the supervision of trained organizers. Results obtained from panelists to panelists are usually not identical having been influenced by personal preference.

Because quality factors are sometimes qualitative and/or subjective, performance metrics need to be established. Quality factors (QF) are related to product performance metrics (p) through what is called a quality function (Bernardo and Saraiva, 2004). Under the scope of this model, designing a formulated product starts by the inversion of the quality function. Using a cosmetic emulsion as an example, a rich sensory feel as assessed by the consumer (QF) is associated with several parameters (p) like the emulsion rheology (Brummer and Godersky, 1999), the emulsion spreadability (Mentel et al., 2014), and also the emulsion consistency, as shown in Figure 2-4.

Figure 0-17: Quality function inversion



Conceptually, this inversion requires the extraction of information (identification and estimation of parameters p) about a system from measured data (consumer attributes QF), in association with a model describing the system's behavior (Petit and Maillet, 2008). Nevertheless, as the understanding of human perception, especially for touch, taste or smell, seem for the moment insufficient to build reliable models for this inversion, empirical correlations between quantitative parameters and consumer attributes are being used instead (Cussler et al., 2010). There is a wide array on the literature about the characterization of sensory cosmetic product attributes, mainly translated to textural and rheological properties (Gilbert et al., 2013b, 2013a; Lukic et al., 2012; Morávková and Stern, 2011; Nakano et al., 2013; Parente et al., 2010; Savary et al., 2013; Tang et al., 2015; Wittem et al., 2001; Wortel and Wiechers, 2000). For example, it is possible to describe properties of cosmetic emulsions, namely the integrity of shape and the penetration force, through oscillatory and creep recovery evaluation (Gilbert et al., 2013a). Some methods have also established a measurable relationship between consumer's and expert's sensory evaluation (Koehl et al., 2008).

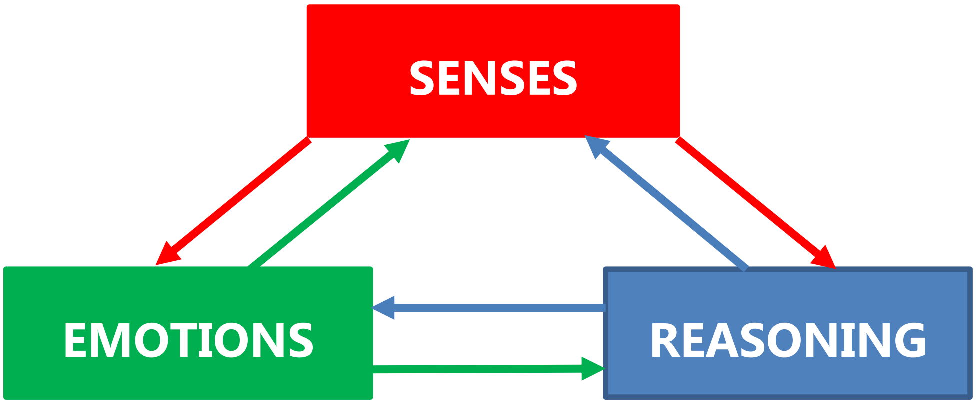
In the context of emulsions, Mattei (2014) proposed a robust knowledge basis for the collection of the consumer needs, and their translation into necessary categories of ingredients and end-use properties with target values and boundaries of acceptance. However, one of the main challenges identified in this research is related to the collection of the consumer needs and their translation into physical properties, specifically for some sensorial quality factors, due to the subjectivity of the appreciations (Pensé-Lhéritier, 2015). Table 2-3 summarizes some important consumer quality factors studied for cosmetic emulsions and the proposed translation into quantitative performance metrics.

Table 0-8: Consumer attributes translation for cosmetic emulsions

Consumer attribute (Quality factor)	Quantitative performance metrics (p)
Effectiveness	▪ Concentration of humectants (Bagajewicz et al., 2011) ▪ Concentration of cationic surfactants for hair conditioners (Iwata and Shimada, 2013) ▪ Appearance (gloss) (Gilbert et al., 2013b)
Thickness	▪ Viscosity (Bagajewicz et al., 2011) ▪ Penetration and compression force (Gilbert et al., 2013b)
Greasiness/Oiliness	▪ Concentration of insoluble substances (oil phase) (Bagajewicz et al., 2011) ▪ Friction coefficient (Nacht et al., 1981)
Smoothness	▪ Change in friction coefficient (Bagajewicz et al., 2011)
Creaminess	▪ $(\text{Thickness})^a \times (\text{Smoothness})^b$ (Bagajewicz et al., 2011)
Ease of spreading	▪ Contact angle (Bagajewicz et al., 2011) ▪ Texture analyzer (difficulty of spreading) (Gilbert et al., 2013b)
Absorption rate	▪ Diffusion and evaporation time to "steady state" (Bagajewicz et al., 2011)

As for most formulated consumer products, the definition of customer needs for cosmetics constitutes the main input required by the design methodology and is usually obtained from multiple sources, such as market and customer surveys, patent, literature, among others (Mattei, 2014). Cosmetic performance evaluation involves the five senses, hence the importance of interpreting the answer to the products according to how they are perceived (Nozawa and Uchida, 2009; Regué, 2011). Moreover, satisfaction is the result from a combination of sensory, emotional and rational responses to the experience of using the product (SRL, 2018), as illustrated in Figure 2-5. Several studies have shown that cooperation among senses reinforces the perception of an attribute and improve the individual's capacity to respond to a stimulus (Bosch, 2007; Guzman Alonso and Jiménez, 2018; Làdavas, 2008; van Ee et al., 2009).

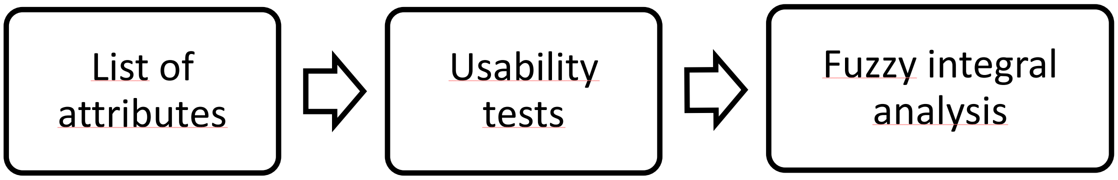
Figure 0-18: Consumer decision model. Adapted from (SRL, 2018)



Affective and Kansei engineering study how pleasure and efficiency are linked together during the experience of using a product (Luo et al., 2011; Nagamachi, 1995). These approaches were created to deal with this subjectivity and provide means to access the implicit emotion people have when interacting with the products and to translate those terms into product specifications, thus enabling the integration of users' emotions into the product design (Nagamachi and Lokman, 2011). Since cosmetics are conceptually designed to match the consumer expectations, using this approach could appeal for emotional connection with the product and improve the experience of use (Lokman and Kamaruddin, 2010). Under this scope, it is important to define a set of words or semantic attributes (SA) that better describe the user perception of the product, as proposed by Schütte and Eklund (Schütte and Eklund, 2005). An important limit of most approaches trying to elicit the importance level of each SA, is that most of them consider the set of SA as being mutually independent, underestimating the sensory interaction among them, which has a non-negligible impact on the final product design and its further acceptability to users (Augustine et al., 2010; Zeng et al., 2010; Zhu et al., 2010). Using soft computing based techniques (i. e. fuzzy logics), the specificity of the problem of interest can be taken into account and the obtained results may be easily interpreted (Zeng et al., 2008). Indeed when the mutual independence of attributes could be assumed, the traditional set of multicriteria techniques, such as the MAUT (Multiple-Utility Attribute Theory), could be used, and the global utility function could be treated as a weighted sum (Keeney and Raiffa, 1993). However, dealing simultaneously with the set of multidimensional semantic attributes and their interaction is not a trivial task. In order to be able to take interaction phenomena among attributes into account, a monotone set function, called *capacity* or *fuzzy* *measure* has been proposed to substitute the weight vector involved in the MAUT weighted sums calculation (Grabisch, 1995b). Such an approach can be regarded as taking into account not only the importance of each criterion but also the importance of each subset of criteria. From the above reasoning, we can see the behavior of the Choquet integral as a weighted average (i.e. an aggregation operator), where the utility values are represented by the fuzzy measures (Grabisch, 1996). The details of the definitions and computations of Choquet integral and fuzzy measures are in Appendix B.

As stated in Camargo et al (2014), if expert knowledge about the application is available, the initialization of the fuzzy measure can be done by an identification based on semantics. Such a method requires a manual assessment of the importance of each criterion and its interaction with the others within the aggregation to evaluate the fuzzy measure on each subset (Camargo et al., 2011). As such extensive knowledge is rarely available, so most of the time the fuzzy measure has to be learned from a training set. Grabisch (1995b) proposed an efficient retro-propagation algorithm to approximate this fuzzy measure in an accurate way, using the Choquet integral (Choquet, 1954). This means that, in the case of few little data, coefficients of the fuzzy measure which are not concerned with the data are kept as near as possible to the equilibrium point. Thus, this algorithm is still efficient when training data are limited. It also has a low computing time and a low memory cost (Schmitt et al., 2008). As the input range is not strictly defined in this study, learning is combined here to with a linear output based on linear error regression to ensure an accurate decision and a better convergence. Later, a fuzzy integral methodology to integrate data from usability tests in order to support design process was proposed by Camargo et al. (2014), and applied to the design of massing soles. This method was used to identify and qualify, in terms of importance and interaction among them, the set of attributes that best describes the feelings of a group of users, as shown in Figure 2-6.

Figure 0-19: General concept definition methodology



2.3.1 List of attributes

The attributes are collected from different available sources, such as experts, literature, and the Internet for example – from words used to describe the domain of cosmetic emulsions evaluation. Once the set of words defining the product attributes is established, the next step is the reduction in the quantity of words. Then, a selection of the most relevant attributes is made by the exclusion of the irrelevant or repeated words. Several techniques could be used, such as affinity diagrams, factor analysis or Principal Component Analysis (PCA) (Camargo et al., 2014; Wortel and Wiechers, 2000).

2.3.2 Usability tests

A questionnaire is then prepared to evaluate the entire SA previously found. Then, the participants of the test are asked to rate a selected prototype on a 5-level ordinal scale. For this purpose, the Semantic Differential Method SDM is currently used (Camargo et al., 2014). One of the prototypes can be the most sold product for the chosen category or any other product to be used as a reference. At this point it is important to underline that the aim of the usability test is to find the fuzzy measure that minimizes the square error of a criterion, so a learning output, represented for example by a global acceptability or a purchase intention, should be included in the evaluation which acts as an overall final utility score (Camargo et al., 2014).

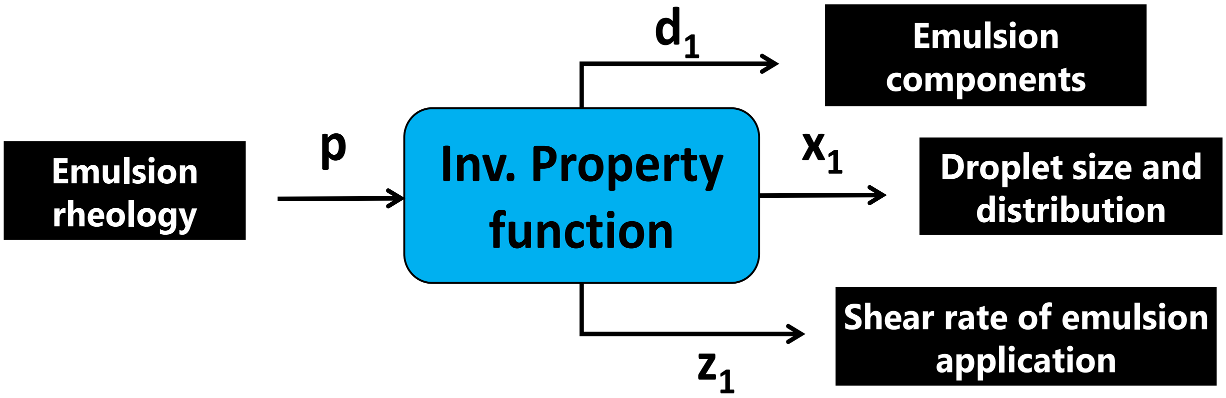
2.3.3 Fuzzy integral analysis

Once the fuzzy measures are calculated, the importance and interaction indices could be estimated (Shapley and Murofushi and Soneda indices, respectively). Once normalized, the Shapley index can be interpreted as a weighted average value of the marginal contribution of each criteria in all combinations, so the sum of the index of all SA is equal to 1 (Grabisch, 1996). On the other hand, the Murofushi and Soneda index represents the degree of interaction between two SA (Murofushi and Sugeno, 1991). These indices and their interaction (positive or negative) could be used to validate the relevance of the selected SA. This information is important, as an iterative process could be carried out in order to include a new SA or exclude an existing one (Camargo et al., 2014). From these two indices a third one called Composite index can be calculated. Latter could be used to guide the product realization phase, as it will be presented in chapter 4, using a skin moisturizer as an example.

2.4 Product realization

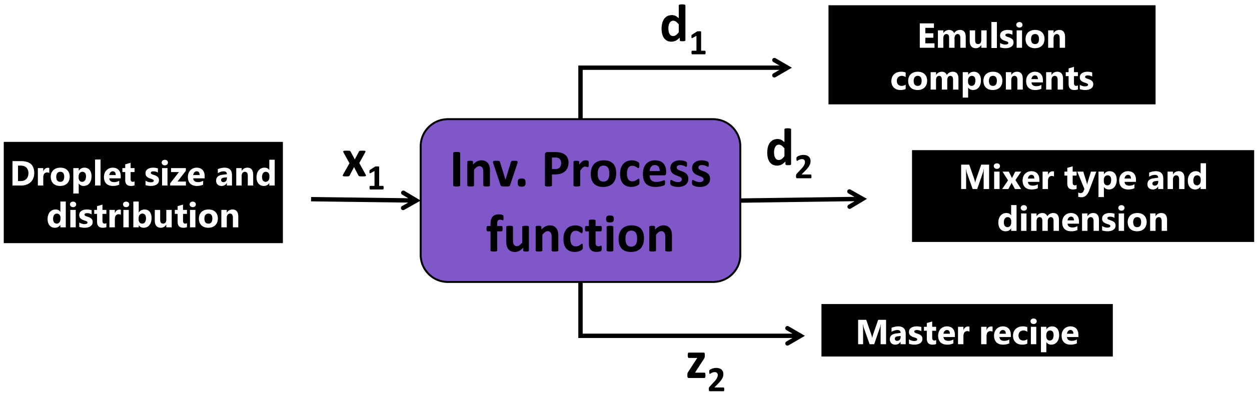
Given a particular framework, i.e. list of ingredients, and considering the number of different ingredients in a cosmetic emulsion (Table 2-1), its formulation should be conducted according to a suitable procedure, which takes into account the mutual interaction of them in the feasibility of preparation, stability and efficacy of the active substance(s) in the vehicle (Barel et al., 2001). The interrelationship between product design variables (d_1), use conditions (z_1) and microstructure (x_1) is called the property function. An example of the property function inversion in the case of a cosmetic lotion is illustrated in Figure 2-7. Here the models for the inversion of the function are more developed than in the case of the quality function (Cussler et al., 2010). For example, there are several models that predict the emulsion rheology (p) based on ingredients properties and droplet size and distribution (pair $\{d_1, x_1\}$) (Wibowo and Ng, 2001), and also on the shear rate during the application of the product (z_1), such as the Ostwald, Carreau or Cross models.

Figure 0-20: Property function inversion



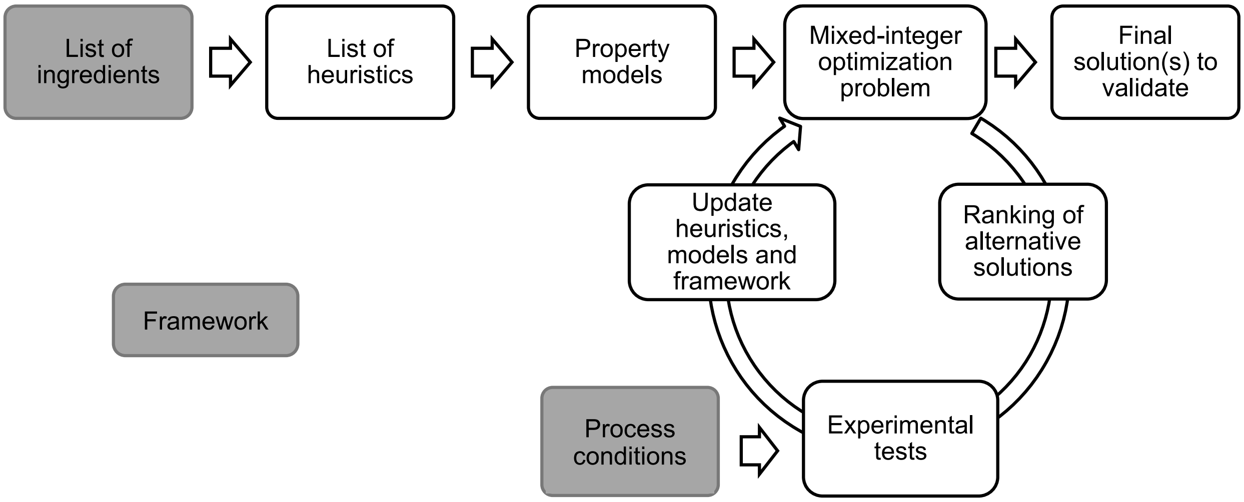
In addition, as emulsions are structured products, not only the composition but also the process conditions ought to be in the scope of the design work. The desired microstructure (x_1) may be attained by establishing suitable process design variables (d_2) and operating conditions (z_2) on a given formulation (d_1); the link between them is described as the process function. For example, in Figure 2-8, the droplet size and distribution of a cosmetic O/W emulsion (x_1) are mainly determined by its components (d_1) and by the processing variables and operating conditions, namely the mixer type and dimension (d_2) and the stirring speed (z_2), respectively (Lin, 2010).

Figure 0-21 : Process function inversion



The proposed methodology for this phase (Figure 2-9) resulted from an international collaboration with the Process Systems Engineering Group (PSE - CIEPQPF) at the University of Coimbra in Portugal. The team headed by Prof. Bernardo, who developed the conceptual model shown in Figure 2-3, has extensively worked on the systematic generation and selection of feasible alternatives along with optimization tools to efficiently search large domains in order to identify product(s) leading to the required specifications.

Figure 0-22: General product realization methodology



This work focuses on the design of a specific type of products (o/w cosmetic emulsions), so in the next subsections, the main general steps of the methodology applied to this case study will be explained. More details applied to the hair- and skin-care products are presented in chapters 3 and 4, respectively.

2.4.1 List of ingredients

The first step in the formulation process is the choice of the ingredients (Rousseau, 2011). As formulated products often include 5 to 20 different components, all the candidate ingredients must be classified depending on their function(s) in the formulation. In this work, ingredients information has been mainly taken from providers' specifications for the available ingredients. Databases were developed for selecting the most appropriate to be included in the formulation, on the basis of the product specifications.

Three main types of ingredients were considered for the modeling of O/W emulsions in this research: Emollients in the dispersed phase, thickeners in the continuous phase and the emulsifiers in the interface. The selection of these ingredients is based on several studies done by different authors who evaluated the impact of these ingredients in the sensorial, rheological and textural properties of the cosmetic emulsions (Barel et al., 2001; Korhonen et al., 2000; Lukic et al., 2012; Moravkova and Filip, 2014, 2013; Savary et al., 2013).

2.4.1.1 Emollients

When formulating emulsions, the dispersed phase should be first selected (Pensé-Lhéritier, 2011), and emollients constitute the main component of the dispersed phase, particularly in O/W emulsions. Emollients are required in the dispersed phase because they help to prevent soaping of formulations, they improve spread on skin, and the consumer-perceived benefits of a skin product are often a result of these ingredients remaining on the skin after evaporation of water and other volatile materials (Barel et al., 2001; Lukic et al., 2012; Savary et al., 2013). Some emollients, like mineral oil or petrolatum, have a heavy, oily skin feel that could affect consumer acceptance (Barel et al., 2001). Waxes are often used to increase the specific gravity of the dispersed phase, but also have a significant effect on the appearance, texture, and feel on application to skin of the product (Knowlton and Pearce, 1993). Greasiness is the main sensorial property of emollients, and among the most important physicochemical properties are the density, viscosity, melting point, relative polarity index (logP), and the required HLB (Muñoz and Alfaro, 2007; Wiechers et al., 2004). Regarding the rheological properties it is important to consider the viscosity and the yield stress value (Savary et al., 2013).

2.4.1.2 Emulsifiers

Emulsifiers are essential to stabilize the emulsions. This can be achieved by lowering the interfacial tension between the continuous medium and the dispersed droplets, and by providing colloidal stability to the latter (Kostansek, 2012). Due to the ability to adsorb at interfaces, surfactants are the preferred substances to accomplish this task in cosmetic emulsions (Rieger and Rhein, 1997). These amphiphilic molecules consist of a nonpolar lipophilic portion attached to a polar hydrophilic portion (Tadros, 2012). Surfactants can be divided up into three classes (Ansmann et al., 2005), depending on the nature of their hydrophilic portion:

- Ionic surfactants, which exhibit either an anionic or a cationic hydrophilic portion;
- Amphoterics, which have both negative and positive charged groups in the same molecule.
- Nonionic surfactants, which have no charge on the molecule but a polar group (often due to oxygen atoms) and a long fatty hydrocarbon chain.

The last class of surfactants is generally the first choice used for emulsions (Pensé-Lhéritier, 2011), because of their flexibility and well-understood physicochemical behavior (Ansmann et al., 2005). In fact, through different degrees of ethoxylation on fatty alcohols, a defined hydrophilic–lipophilic ratio can be attained, depending on the carbon number of the lipophilic alkyl chain and the number of hydrophilic ethoxy groups.

The type of surfactant and its physicochemical properties will influence the performance of the final product, namely with regard to droplet size and stability. Besides the strong correlation with performance and emulsion stability (Korhonen et al., 2000), emulsifiers have also been found to impact the desired sensory properties of the product such as color, odor, and consistency (Barel et al., 2001; Moravkova and Filip, 2013). Whereas from the theoretical point of view of the sensorial perspective, the choice of the emollients seems clear, the selection criteria for the emulsifiers still needs further research to unveil the exact influence of the emulsifier on skin feeling (Wiechers et al., 2004). Nevertheless, hydrophilic-lipophilic balance (HLB value) is probably the most popular tool to predict the effectiveness of the surfactants as emulsifiers (Mattei, 2014). This parameter is still relevant, along with some other physicochemical properties of the surfactants (surface tension, critical micelle concentration, solubility parameters, pH, molar weight, viscosity, cloud point, Krafft temperature, toxicity parameter, flash point, etc.) to correlate with some sensorial properties of the emulsions.

2.4.1.3 Thickeners

Thickeners are used to increase the viscosity of the continuous phase and mitigate the upward migration of the dispersed particles (stabilizers) (Barel et al., 2001; Moravkova and Filip, 2014; Muñoz and Alfaro, 2007). It has also been shown that thickeners could have relevant impact on skin feeling, namely when removing cream from the container and when spreading on the skin or on the hair, which can be checked in a flow curve (Moravkova and Filip, 2014). Table 2-4 summarizes the excipients to be considered in this model (emollients, thickeners, emulsifiers).

Table 0-9: Excipients in the modelling of emulsions

Ingredients	Parameters included in the modelling
Emollients	Density, viscosity, required HLB, greasiness, spreadability.
Emulsifiers	HLB value, molar volume, viscosity, cloud point, Krafft temperature, toxicity parameters, flash point.
Thickeners	Density, rheological behavior (viscosity, yield stress value, elastic and viscous modulus)

For the remaining components of the emulsion, they were included either as a fixed amount or neglected form all the formulations. In the case of active ingredients, such as moisturizers and humectants, which are used to guarantee the hydration of the *stratum corneum* of the skin or the hair cuticle, but also to control the impact on the body and the feel of the product (Knowlton and Pearce, 1993), they were added in a standard quantity. The same restriction was used for perfumes or preservatives. On the other hand, no coloring agents were considered in the manufacture of the emulsions.

2.4.2 Optimization problem

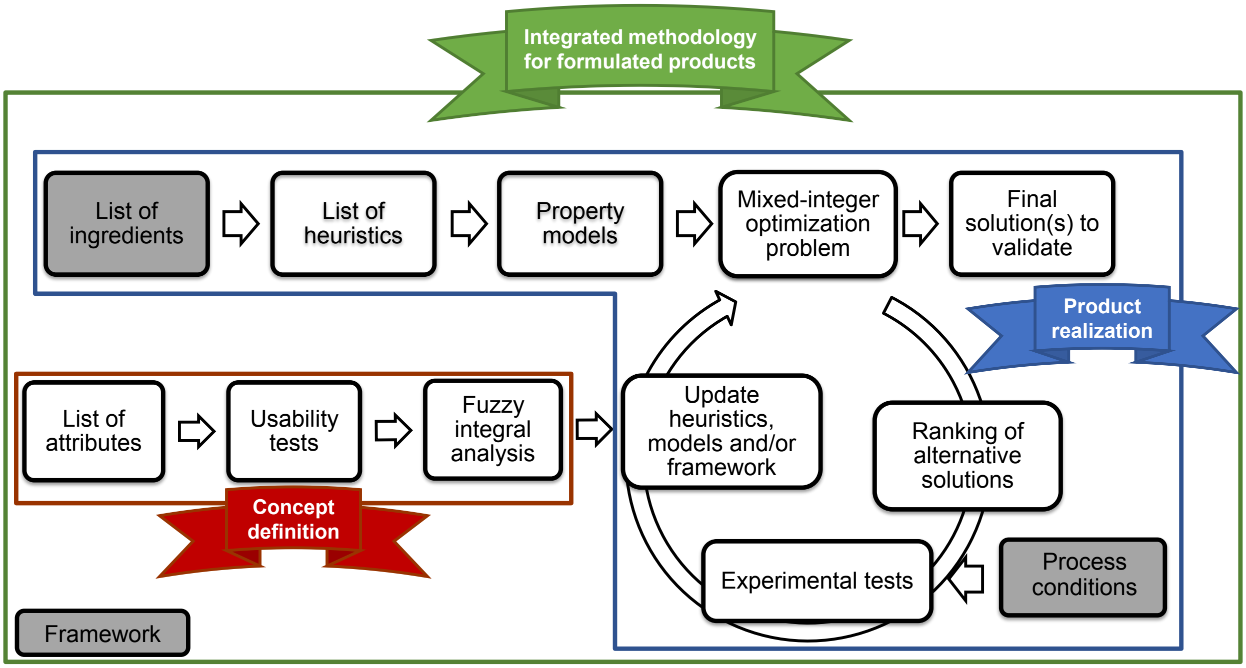
Computer-aided mixture design was used to generate the alternatives, and to test and evaluate them in order to identify the product leading to the *a priori* defined characteristics. In this case, Mixed-integer optimization was used as a fundamental tool to handle with large discrete domains (Bernardo and Saraiva, 2015). Regarding the techniques, different optimization methods (discrete and/or combinatorial) and algorithms for the generation and selection of feasible alternatives were implemented in each case.

At the end of this computer-assisted process, the final identified solutions to the product design problem are tested: Rheological measurements and some textural analyses (firmness, consistency, cohesiveness, index of viscosity) are the most pertinent ones at this stage (Gilbert et al., 2013b; Savary et al., 2013).

2.5 Integrated methodological approach for the design of formulated products

In this research, a general methodological approach is presented for the design of formulated products, in which a fuzzy measure analysis from the concept definition, along with heuristics and property models from the product realization phase are used to solve the initial design problem, as shown in Figure 2-10.

Figure 0-23: Integrated methodological approach for the design of formulated products



In the end, a list of feasible alternative formulations that relate to a given set of specifications of the final product is generated. The models, experiments, tools and databases used in the research are presented in Table 2-5.

Table 0-10: Summary of models, experience, tools and databases used in the research

	Models	Experience	Tools and databases
Process function		▪ Laboratory experiments	
Property function	▪ Viscosity ▪ HLB/RHLB ▪ Mixing rules	▪ Measurements of properties (rheology, microscopy, texture, stability) ▪ Empirical relationships	▪ Chemical databases (UL prospector, Cosing) ▪ Technical data from providers
Quality function	▪ Fuzzy integral analysis	▪ Usability tests ▪ Empirical relationships for correlating consumer attributes and performance parameters	

This work will focus on the design of a specific type of products (o/w cosmetic emulsions) and will be divided in two main phases: Starting with the product realization, a modelling approach of emulsified products will be proposed in order to find a product formulation (d1), along with the process conditions (d2, z2) that will render the desired specifications of the cosmetic emulsion (p). A first example of the modelling of emulsified products will be presented in chapter 3, using hair conditioners as a study case. Then, the product concept will be defined using a methodology for the selection of consumer attributes (QF) from usability tests that integrates the consumer's perception into the previous model, given the importance and interaction of selected attributes. These attributes are correlated to physico-chemical properties (p) that can be evaluated to assess the feasibility of the proposed alternatives. An example of the complete methodology (integration of concept definition and product realization) in the case of a skin moisturizer will be presented in chapter 4.

2.6 Conclusion

In the present chapter an integrated methodological approach enabling the design of emulsified cosmetic products has been proposed. The main aspects related to the concept definition and product realization were transformed in two phases: modelling of emulsified products and consumer assessment, respectively. Starting with a list of available ingredients, a modelling of emulsified products was proposed to find a product formulation, along with the process conditions, that will realize the desired specifications of the cosmetic emulsion. The relationship between product performance and ingredients selection along with process conditions need to be integrated using a set of property prediction models and heuristics to find a solution of such a complex problem, i.e. the product realization by simultaneously inverting the product and process functions. Then, to define the product concept, a methodology based on usability tests and fuzzy integral analysis is proposed to identify the most important consumer attributes and their interactions, and integrate them with the previous model. The output of the concept definition phase is transformed into additional heuristics that could guide the selection of the alternatives. In the next chapters, this general methodology will be used in the case of hair and skin-care products. Although the proposed methodology applies for all kinds of chemical products, it is particularly appropriate when dealing with multi-species consumer-oriented products.

3. Incorporation of Heuristic Knowledge in the Optimal Design of Formulated Products: Application to a Cosmetic Emulsion

Because of the growing competitiveness in the cosmetic sector, like in many other industrial domains dealing with chemical products, companies seek to reduce the time to market (Cooper, 2013). This is often the decisive point for successful product launch, even above the cost of production (Charpentier, 2010). Hence, chemical product design (CPD) has been proposed as a new way of thinking the chemical engineering discipline, where the product manufacture process has been the classical object of study (Cussler and Moggridge, 2011; Bernardo and Saraiva, 2015). CPD has been constructed as a systematic framework of methodologies and tools, whose aim is to provide a more efficient and faster development of products able to meet market demands (Costa et al., 2006). However, CPD has not yet developed into the foreseen third paradigm of chemical engineering (Hill, 2009), maybe because of the incomplete understanding of sensorial product attributes (Cussler et al., 2010), and also of complex interactions between materials and their impact in product performance (Picchioni and Broekhuis, 2012).

In the product engineering field, chemical products are generally classified into three categories: molecules, formulated products, and functional products and devices (Gani and Ng, 2015). Under this classification, most cosmetics would fall in any of the last two categories, as they could be seen as a mixture of one or more key ingredients responsible for the product's functionality (active ingredients) with other supporting ingredients to enhance the mixture performance (Wibowo and Ng, 2002). Cosmetics can also be classified according to their physical form or delivery system, and emulsions are probably the most commonly used due to their numerous advantages (Knowlton and Pearce, 1993). Only among the skincare and hair-care segments, a considerable number of products, such as hydrating creams, body lotions, conditioners and combing creams, are formulated as emulsions (Morávková and Stern, 2011). Traditionally, emulsified cosmetic product design has been made following an experiment-based trial-and-error approach, seeking formulations that meet targeted performance (Barel et al., 2001), including product sensorial attributes that are critical for consumer acceptance

(Pensé-Lhéritier, 2015). Such trial-and-error procedures are very resource-consuming, especially during early stages of product design or reformulation (Conte et al., 2011b).

A more systematic search for the optimal product may be supported by computer-aided methods, known in literature as computer-aided molecular/mixture design (CAMD) methods (Achenie et al., 2002). These are based on a set of fundamental units that may compose the desired product and models to estimate product properties from the type and number of those units. A systematic search for the right combination of units may then be made, often using mixed-integer optimization. These methods may be very effective in the case of relatively small molecules described as a combination of molecular groups and with properties predicted using reliable group contribution methods (Gani, 2004). They have also been applied with success to relatively simple liquid formulations, once mixture properties may be reasonably estimated (Achenie et al., 2002; Conte et al., 2012, 2011b; Yunus et al., 2013). For more complex formulated products, often having specific microstructural features, the lack of adequate property models hinders such systematic searches (Bernardo and Saraiva, 2015; Gani and Ng, 2015). In these more complex domains, product design then relies on less structured knowledge, such as databases of often used ingredients and heuristic rules regarding ingredients functionality and its recommended/allowed concentrations. Several product design procedures incorporating such heuristic knowledge have been proposed, most of them for specific product families, e.g., creams and pastes (Wibowo and Ng, 2002, 2001), pharmaceutical tablets and capsules (Fung and Ng, 2003), emulsions (Mattei et al., 2012; Schubert and Engel, 2004), and detergents (Martín and Martínez, 2013a). It is also worth mentioning the method proposed by Lee et al. (2014) in the scope of personal care products, which is based on case-based reasoning, i.e., reuse and revision of knowledge acquired in previous developed product formulations.

Recently, Fung et al. (2016) presented a general framework for chemical product design using rules and model-based methods, as well as tools, databases, and experiments, supported by a hand lotion case study. Also, Zhang et al. (2017) proposed a comprehensive framework applicable to several classes of formulated products, handling several sources of information and knowledge, including heuristic-based and model-based methods. For instance, when a solvent is being developed using this methodology, the product may be designed using CAMD tools incorporating the necessary property models for the main components of the liquid mixture; meanwhile the other more complex ingredients of the mixture (e.g. emulsifiers) are decided based upon heuristics. In this case, heuristics are often stated as logical conditions and thus logic-based mixed-integer programming is used (Raman and Grossmann, 1991). In the above-mentioned methodologies, heuristic rules and property models are used as complementary sources of knowledge, but no physical prototypes are prepared to validate the design approach. In this direction, this work focused on cosmetic emulsions design, converting heuristic rules into mathematical forms that were explicitly included in the optimal design problem, side by side with property models. Then, a lab scale validation of the designed products, as obtained from the solution of the optimization algorithm, was carried out. As far as we know, this is the first attempt to fully integrate heuristic knowledge into an optimization-based CAMD tool using a specific product case, whose resulting alternatives were manufactured and evaluated using different performance indicators, proving evidence of the applicability of the methodology.

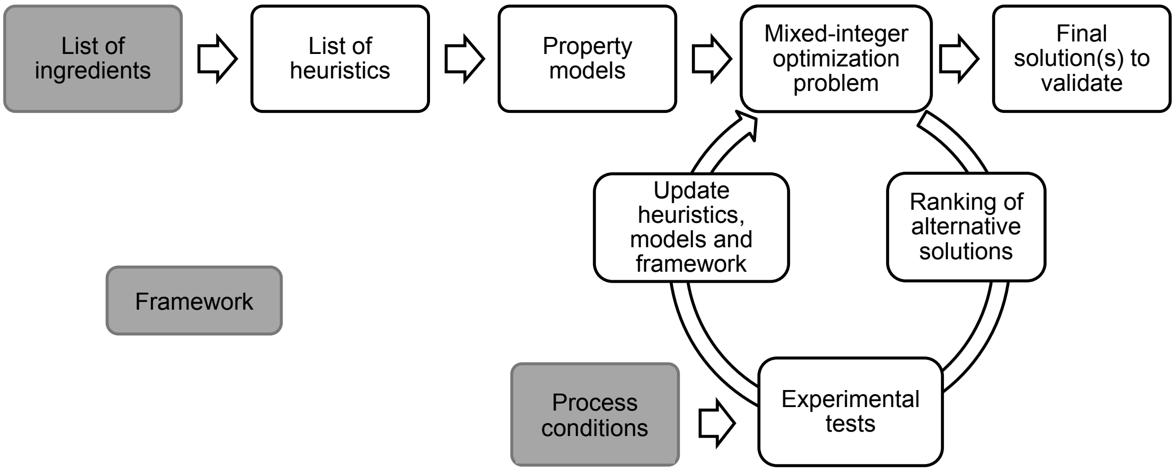
In this contribution, the design problem is formulated from an initial (long) list of available ingredients, a subset of which is to be selected. New molecular entities are thus not being equated. As a study case, we have considered the field of cosmetic emulsions, particularly an example of a rinse-off hair conditioner. The domain of cosmetic formulations has an extensive history, handles hundreds of different ingredients, and it is rich in heuristic knowledge, namely regarding qualitative function of ingredients, their incompatibilities and positive synergies, as well as their impact on sensorial attributes (Barel et al., 2001; Gilbert et al., 2013b; Laba, 1993; Sakamoto et al., 2017). It was therefore selected as a prime area of application in which the incorporation of heuristic knowledge in an optimization-based method may likely be fruitful and easy to validate at a lab scale (Arrieta-Escobar et al., 2017).

3.1 Overall Methodology

Although initially developed in the scope of cosmetic emulsions, the basic ideas and tools of the methodology here proposed (Figure 2-9, here 3-1) are applicable to any formulated product, whose specific functionalities result from the proper blend of ingredients and specific interactions between them.

The methodology starts with a list of available ingredients organized by their main function (e.g., emollients, emulsifiers, thickeners). A binary variable is associated to each ingredient, indicating whether that ingredient is selected to be part of the formulation or not. Then, available heuristics regarding choice of ingredients and their amounts are listed and modelled as algebraic restrictions. Some heuristics are first stated as logical conditions and then translated into algebraic constraints involving binary variables, as it will be explained in section 3.2 (Raman and Grossmann, 1991; Williams, 2013). Heuristic-related restrictions, together with other known limits (technical and/or legal), define a reduced design space, compared to the initial design space covering all possible combinations of ingredients in all possible proportions. The search in this reduced space is then guided by available property models relating product composition to key physicochemical properties or sensorial attributes.

Figure 0-24: General product realization methodology for the design of formulated products



Let y be the vector of binary variables associated with the choice of ingredients and x the vector of corresponding mass fractions. Let p be the vector of product performance metrics, including well-defined physico-chemical properties (e.g., rheological profile of a cream-like product) and also metrics related to more subjective sensorial attributes (e.g., greasiness of a cream-like product measured in a scale derived by sensorial tests). Product quality is often evaluated in terms of the deviation of p from target values p^* (product performance specifications). Property models, also known as the property function, are any relationship between metrics p and product composition, here represented by the set of equations $h(x, y, p) = 0$ (Bernardo and Saraiva, 2015). Heuristic rules represent additional knowledge that is incorporated in the problem formulation as the set of constraints $g_1(x, y, p) \leq 0$. Finally, let f be a global objective function to be minimized, accounting for both product quality and cost. The problem of optimal product formulation may then be stated as the following optimization problem:

$$\begin{aligned} &\min_{x,y} f(x, y, p, p^*) \text{ [product performance]} \\ &s.t. \quad h(x, y, p) = 0 \text{ [property function]} \qquad (0.3) \\ &\qquad\;\; g_1(x, y, p) \leq 0 \text{ [heuristic-related restrictions]} \\ &\qquad\;\; g_2(x, y, p) \leq 0 \text{ [other restrictions]} \end{aligned}$$

Problem (3.1) does not incorporate the role of the product manufacturing process. Let u and v be continuous and binary design variables regarding the manufacturing process (including its scale-up). Then, the final product state s (e.g., microstructural attributes, homogeneity of active ingredients) is a function of x, y, u and v. This is known as the process function, which often includes mass, energy and momentum balances, and other models describing materials transformation during processing, and is here represented by the set of equations $h_2(u, v, x, y, s) = 0$. In this extended design domain, the property function should now include product state variables s, which clearly have a role in defining product properties. The property function is then written as: $h_1(x, y, p, s) = 0$. Heuristics relating the choice of ingredients (x, y) with the design of the manufacturing process (u, v) should also be considered. Problem (3.1) may then be extended to the following optimization formulation integrating both product and process design decisions:

$$
\begin{aligned}
&\min_{x,y,u,v} f(u, v, x, y, p, p^*) \text{ [product/process performance]} \\
&s.t. \quad h_1(x, y, p, s) = 0 \text{ [property function]} \\
&\qquad h_2(u, v, x, y, s) = 0 \text{ [process function]} \\
&\qquad g_1(x, y, u, v) \leq 0 \text{ [heuristic-related restrictions]} \\
&\qquad g_2(x, y, u, v) \leq 0 \text{ [other restrictions]}
\end{aligned}
\tag{0.4}
$$

More than a single optimal solution, which due to model uncertainties may only be called optimal in a strictly mathematical sense, one is interested in a small set of promising solutions to be subjected to experimental tests. A set of solutions with different combinations of ingredients may be generated through successive solutions of problems (3.1) or (3.2), adding integer cuts that prohibit previous integer solutions (Tsai et al., 2008). More precisely, in order to generate S solutions, one first solves the original problem obtaining $y^{(1)}$. Then, one solves the problem again but with the binary cut $y \neq y^{(1)}$, thus obtaining a new formulation $y^{(2)}$. Next, we solve the problem one more time, now with two cuts: $y \neq y^{(1)}$ and $y \neq y^{(2)}$. And so on, until obtaining $y^{(S)}$. The binary cut $y \neq y^{(k)}$ is imposed through the constraint

$$\sum_i \left| y_i - y_i^{(k)} \right| \geq 1 \ ,$$

which may be simplified to the differentiable form:

$$\sum_{i:y_i^{(k)}=0} y_i - \sum_{i:y_i^{(k)}=1} (1 - y_i) \geq 1 \, .$$

When generating the s-th solution, one must prohibit all $(s - 1)$ previous solutions and thus the restriction above is written for $k = 1, \dots s - 1$. It should be noted that if all solutions are obtained to global optimality, then they are a well ranked list of alternatives according to the objective function f.

The list of solutions thus obtained constitutes a plausible set of alternative product formulations to be produced, tested in the laboratory and assessed by customers. In principle, all performance metrics p should be evaluated. The methods used are naturally case-dependent and thus are not here discussed. In the example of section 3.4, testing of the alternative formulations, for a hair conditioner, include rheological and textural measurements.

Finally, as sketched in Figure 3-1 above, computer-generated alternatives and their realization should evolve in successive cycles where results from experimental tests are fed back to problem formulation (3.1) and (3.2), in the form of updated models and heuristics. Successive cycles should desirably result in a decreasing number of alternatives under study until all product specifications are met.

Remarks

In the practical case of section 3.3, the process function is not studied and thus only a problem of type (3.1) is formulated and solved. The incorporation of processing aspects, including scale-up and useful associated heuristics (e.g., mixing intensity, processing temperatures and heating/cooling rates depending on selected ingredients) could the subject of coming research.

Product design problems are certainly multi-objective, with the typical conflicting pair being product performance *vs.* production cost. In formulations (3.1) and (3.2) above, a global objective f is considered, which may be an effective approach if for instance deviations from a target quality are modelled using quality loss functions in a monetary basis (Bernardo and Saraiva, 2015, 2005). If, however, disaggregated results are required, for instance in the form of a Pareto curve, then multi-objective optimization tools should be used, such as the ε-constraint method (this will be illustrated in section 3.4 with a Pareto graph of a product sensorial index *vs.* cost of raw-materials).

Most heuristic rules have a linear formulation, as will be explained in the next section. In general, however, property and process functions are likely to be non-linear and thus problems (3.1) and (3.2) will be MINLP problems. Global optimization methods are thus needed, moreover to guarantee a correct rank of product alternatives. Nevertheless, in the case study of section 3.3, problem (3.1) is formulated as a MILP problem and then, global optimality is guaranteed using standard optimization solvers.

3.2 Modelling of Heuristic Rules

In order to incorporate available heuristic knowledge into an overall optimal product design formulation, heuristics should be first modelled using binary variables and propositional logic. The modelling techniques described below have roots on classical operations research problems (Williams, 2013) and have been widely used in process synthesis (e.g., Raman and Grossman, 1991; Grossmann et al., 1999). A related topic is disjunctive programming (Balas, 1985; Raman and Grossmann, 1994) which has been recently applied to optimal product formulation (Jonuzaj et al., 2016), but its application to our modelling task will not be here discussed.

The simplest rules are often recommended (or regulatory) limits for the quantity of some ingredients. Let y be the vector of binary variables associated with the choice of ingredients and x the vector of corresponding mass fractions. Then, recommended limits for ingredient i are easily modelled through the linear constraints $Ly_i \leq x_i \leq Uy_i$. If ingredient i is chosen ($y_i = 1$), then the desired limits L and U are imposed. If, otherwise, ingredient i is not chosen ($y_i = 0$), the above restrictions result in $x_i = 0$. If no heuristic limits are known, one simply writes $0 \leq x_i \leq y_i$. Other types of simple rules are the limits on the total number of ingredients or on the number of ingredients belonging to a certain class. These are easily modelled adding up corresponding binary variables. For instance, if the formulation should have between M and N ingredients of the subset $\{k\}$, one writes $M \leq \sum_k y_k \leq N$.

More sophisticated heuristics are often initially stated as logical expressions, which in the language of propositional logic are denominated as sentences. These are composed of unit propositions (here designated by capital letters $P, Q, R, \ldots$) linked by logical operators: “or”, “and”, “not”, “implies”, “if and only if”, “exclusive or” (with respective symbols $\vee$, $\wedge, \sim, \Rightarrow, \Leftrightarrow$, $\dot{\vee}$). Sentences may be simple (e.g., $P \Rightarrow Q$) or compound [e.g. $(P \wedge \sim Q) \Leftrightarrow R$].

In general, each unit proposition P may be associated with the satisfaction of a general constraint $g(x, y) \leq 0$, involving both continuous and binary variables, x and y, respectively. One then writes: $P \leftrightarrow g(x, y) \leq 0$. Here, we will describe two particular cases of this general relationship and illustrate its usefulness.

3.2.1 Case 1

Each unit proposition P_i is associated with a single binary variable y_i: $P \leftrightarrow y_i$.

Simple sentences composed of unit propositions $\{P_i\}$ are easily translated into linear constraints in the binary variables $\{y_i\}$. For instance, regarding the choice of ingredients 1 and 2, $P_1 \vee P_2$ is represented by $y_1 + y_2 \geq 1$, $P_1 \wedge P_2$ by the two restrictions $y_1 \geq 1$ and $y_2 \geq 1$, and $P_1 \Rightarrow P_2$ is logically equivalent to $\sim P_1 \vee P_2$, which is in turn represented by $1 - y_1 + y_2 \geq 1$(see Raman and Grossmann, 1991, for a complete list of equivalences). In the case of compound sentences, there is also a systematic approach. First, one converts the sentence into the conjunctive normal form using basic properties of logical operations (e.g., distributive property, De Morgan’s laws). The conjunctive normal form is a conjunction of sentences, each one being a disjunction of unit propositions P_i or $\sim P_i$. This normal form is then easily translated to a set of linear constraints in the binary variables $\{y_i\}$. This procedure is better understood with an example.

Example 1. The rule to be modeled is: “if ingredients 1 or 2 are chosen then ingredients 3 and 4 must be chosen”. In proposition logic, one has the sentence:

$$(P_1 \vee P_2) \Rightarrow (P_3 \wedge P_4).$$

Using the definition of implication, this is equivalent to:

$$\sim (P_1 \vee P_2) \vee (P_3 \wedge P_4).$$

Then moving the negation inwards, one obtains:

$$(\sim P_1 \wedge \sim P_2) \ \vee (P_3 \wedge P_4).$$

Recursively distributing “∨” over “∧” results in:

$$[\sim P_1 \vee (P_3 \wedge P_4)] \wedge [\sim P_2 \vee (P_3 \wedge P_4)]$$
$$\Leftrightarrow (\sim P_1 \vee P_3) \wedge (\sim P_1 \vee P_4) \wedge (\sim P_2 \vee P_3) \wedge (\sim P_2 \vee P_4)],$$

Finally, the translation to linear constraints is:

$$1 - y_1 + y_3 \geq 1;\ 1 - y_1 + y_4 \geq 1;\ 1 - y_2 + y_3 \geq 1;\ 1 - y_2 + y_4 \geq 1.$$

3.2.2 Case 2

The proposition P is associated with the satisfaction of the constraint $g(x) \leq 0$: $P \leftrightarrow g(x) \leq 0$. In this case, an extra binary variable z is associated with the satisfaction of the constraint: $P \leftrightarrow z \leftrightarrow g(x) \leq 0$.

Different $g - z$ logical associations may then be useful, such as $z = 1 \Rightarrow \ g(x) \leq 0,\ g(x) \leq 0 \Rightarrow \ z = 1$, or both the implications. These implication sentences may be modelled using the so-called big-M technique (Raman and Grossmann, 1991).

Case 2.1. The implication $z = 1 \Rightarrow g(x) \leq 0$ is modelled by the constraint $g(x) \leq U_g(1 - z)$, where U_g is an upper bound for $g(x)$ such that $g(x) \leq U_g$ is certainly non-active. If $z = 1$, then the constraint $g(x) \leq 0$ is "activated". If otherwise $z = 0$, then $g(x) \leq U_g(1 - z)$ results in the non-active constraint $g(x) \leq U_g$.

Case 2.2. The reciprocal implication $g(x) \leq 0 \Rightarrow z = 1$, translated by the constraint $g(x) \geq L_g z + \varepsilon$, where L_g is a lower bound for $g(x)$ and ε a small positive tolerance to guarantee that, when $z = 1$, $g(x)$ is strictly positive.

Case 2.3 The equivalence $z = 1 \Leftrightarrow g(x) \leq 0$ may be written as the two implications in cases 2.1 and 2.2 and thus it is represented by the two constraints $L_g z + \varepsilon \leq g(x) \leq U_g(1 - z)$.

Example 2. Here heuristic 3 of Table 3-5 is considered to be used in the case study of section 3-3. The heuristic is first stated as follows: "When no thickening polymer is used, the concentration of fatty alcohols is at least twice the cationic surfactants' in a molar base". The rule involves three different subsets of ingredients: thickening polymers – set $\{n\}$, fatty alcohols – set $\{m\}$, and cationic surfactants – set $\{r\}$. The heuristic is thus written as the implication:

$$y_n = 0, \forall n \Rightarrow g(x) \leq 0, \text{ with } g(x) = 2\sum_r \frac{x_r}{M_r} - \sum_m \frac{x_m}{M_m}, \tag{0.5}$$

where M designates molar mass (g/mol). Next, this implication is decomposed into two simpler logical sentences, using an auxiliary binary variable z:

$$y_n = 0, \forall n \Leftrightarrow z = 1 \tag{0.6}$$

$$z = 1 \Rightarrow g(x) \leq 0 \tag{0.7}$$

Sentence (3.4) may be modelled using the approach of case 1 above. There are three possible polymer thickeners belonging to set $\{n\}$. On then writes: $(\sim P_1 \wedge \sim P_2 \wedge \sim P_3) \Leftrightarrow Z$, with P_n being the unit proposition "thickener n is chosen" and Z the proposition "$z = 1$". Unfolding the equivalente into two implications, one has:

$$[(\sim P_1 \wedge \sim P_2 \wedge \sim P_3) \Longrightarrow Z] \wedge [Z \Longrightarrow (\sim P_1 \wedge \sim P_2 \wedge \sim P_3)].$$

Converting this sentence to the conjunctive normal, one obtains:

$$(P_1 \vee P_2 \vee P_3 \vee Z) \wedge (\sim P \vee \sim Z) \wedge (\sim P_2 \vee \sim Z) \wedge (\sim P_3 \vee \sim Z).$$

This is easily translated into the following set of linear restrictions:

$$z \geq 1 - (y_1 + y_2 + y_3),$$
$$z \leq 1 - y_1, z \leq 1 - y_2, z \leq 1 - y_3.$$

Sentence (3.5) corresponds to case 2.1 above and thus is represented by $g(x) \leq U_g(1-z)$, with $g(x)$ given by the expression in (S1) with the upper bound $U_g = 2$.

3.3 Hair Conditioner Case Studies

A rinse-off conditioner is a cream-like product applied to wet, freshly washed hair, and rinsed out after a couple of minutes. It improves hair combing and several hair sensorial attributes, mainly through adsorption of cationic surfactants to the hair surface (Idson, 1967). Typically, it is an O/W emulsion containing 10 to 25 % oil phase, stabilized with a combination of emulsifiers (cationic surfactants) and thickeners (Barel et al., 2001). The oil phase is rich in emollients that improve the spread of the product.

3.3.1 List of Ingredients

These three main groups of ingredients – emulsifiers, thickeners and emollients – will be considered in this case study and a suitable combination to be used within each group selected. All parameters used for the modelling of these products are presented in Appendix C.

3.3.1.1 Emulsifiers

Hair conditioning emulsifiers are usually cationic surfactants that define to a great extent sensorial properties, such as consistency and feel of use (Barel et al., 2001). Table 3-1 shows the list of cationic surfactants considered as possible components of the product formulation, together with some heuristic rules to define the effect of surfactants on the desired “feel of use” attribute of the final product. Most consumers classify products in three alternative categories (moist and lubricating, moist and soft, or soft and moist), and some proportions of surfactants are known to provide a certain classification. For instance, a product perceived as “moist and soft” typically has a molar fraction ratio $x_{r3}\colon x_{r2}$ going from 1:2 to 1:4 and does not have surfactant $r1$ (Iwata and Shimada, 2013).

Table 0-11: List of available cationic surfactants and heuristics for feel of use attribute

	Cationic surfactant (*r*)	Moist and lubricating	Moist and soft	Soft and moist
1	Steartrimonium Chloride (STAC)	1 to 4 parts	-	2 to 4 parts
2	Cetrimonium Chloride (CTAC)	1 to 4 parts	2 to 4 parts	-
3	Behentrimonium Chloride (BTAC)	-	1 part	1 part
4	Stearamidopropyl Dimethylamine	-	-	-
5	Behenamidopropyl Dimethylamine	-	-	-

3.3.1.2 Thickeners

Thickeners used in hair conditioners are often water-soluble polymers and/or fatty alcohols (Table 3-2). They increase the viscosity of the product and thus influence how it is felt to the touch. Skin creams and conditioners have a similar consistency and thus data regarding skin creams will be here used.

Table 0-12: List of thickeners used in the case study

	Thickening polymer (*n*)	Fatty alcohol (*m*)
1	Hydroxypropyl Starch Phosphate	Stearyl alcohol
2	Hydroxyethyl Cellulose	Cetyl alcohol
3	Hydroxypropyl Guar	Cetearyl alcohol

For skin creams, the consumer evaluation of skin feeling has a strong correlation with the product rheological profile (Brummer and Godersky, 1999). More precisely, the primary feeling is correlated to the high viscosity η_1, perceived on the onset of flow of the product, under low applied stress, while the secondary feeling corresponds to a much lower final viscosity η_2, when the product is being applied under higher stress (the cream has a strong shear-thinning behavior). Sensorial tests indicate that the ideal cream should have an "initial" viscosity η_1 between 1350 and 3500 Pa.s and a "final" viscosity η_2 between 0.023 and 0.500 Pa.s. Also, the "final" viscosity is perceived at a typical shear rate of ~500 s^{-1}, corresponding to the cream application over small areas (Brummer and Godersky, 1999). Composition-viscosity data for polymer thickened aqueous solutions are available for several polymers (Prospector®, 2017). These data, together with a reliable theoretical model to predict the effect of the dispersed phase (Pal, 2001), were used to construct equations of the type $log(\eta) = a + bx_n + c\phi$ (average relative errors 22%), for each polymer n in Table 2 and for both η_1 and η_2 (ϕ is the mass fraction of the oil phase). Since usually only one polymer is used, mixing rules are not needed. Also, often no polymers are used at all and only fatty alcohols are enough to attain a good product's consistency. In that case, fatty alcohols should be present in a concentration at least twice of cationic surfactants', in a molar base (Nakarapanich et al., 2001). This and other heuristic rules will be modelled as algebraic restrictions and included in the design problem formulation, as explained further below.

3.3.1.3 Emollients

Emollients are required in the oil phase to improve the spreadability of the product. A proper combination of three or more emollients of high, medium and low spreading types provides the complete profile for a well-performing product (Ansmann et al., 2005). Table 3-3 presents the list of emollients of three different types initially considered as possible ingredients of the formulation.

Table 0-13: List of emollients used in the product modeling

	High spreading (*i*)	**Medium spreading (*j*)**	**Low spreading (*k*)**
1	Cyclopentasiloxane (C5)	C12-C15 Alkyl benzoate	Oleyl erucate
2	Isoamyl cocoate	Glyceryl stearate	*Persea gratissima* oil
3	Diethylhexyl carbonate	Cetyl ethylhexanoate	PPG-15 stearyl ether
4	Isopropyl Myristate	Cetearyl Isononanoate	Cetyl Dimethicone NP**
5	Isopropyl palmitate	Cetyl Dimethicone MP*	PPG-14 butyl ether
6	Decyl cocoate	PPG-3 Myristyl ether	Triisostearin
7	Ethylhexyl palmitate	*Paraffinum Liquidum*	Dimethicone
8	Phenoxyethyl caprylate	Octyldodecanol	
9	Caprylic/Capric triglyceride		

*MP = Medium polarity; **NP=Non-polar

Emollients are also responsible for the remaining sensorial characteristics (greasiness) after other materials have evaporated (Barel et al., 2001). The greasiness value (γ) of a mixture of emollients can be estimated as a weighted average from individual values available for a wide range of ingredients (Mentel et al., 2014). A typical product specification is a greasiness value γ in the middle of the scale: between 2.0 and 2.4 (Bagajewicz et al., 2011).

3.3.2 Formulation of the optimal design problem

Product design variables, performance metrics and corresponding desired specifications for the present case study are shown in Table 3-4. Main decision variables together with product attributes and performance metrics are also presented in Table 3-4.

Table 0-14: Product design variables and specifications

Design variables: choice of ingredients y and mass percentages x
cationic surfactants: y_r, x_r thickening polymers: y_n, x_n fatty alcohols: y_m, x_m high spreading emollients: y_i, x_i medium spreading emollients: y_j, x_j low spreading emollients: y_k, x_k
Product attributes/properties
1. Feel of use $= f(x_r)$ (see Table 3-1) 2. Consistency/feel to the touch: related to viscosities η_1 and η_2 (both function of x_n, x_m and ϕ) or to fatty alcohols content 3. Greasiness $\gamma = f(x_i, x_j, x_k)$
Specifications
1. "Soft and moist" 2. $\eta_1 \in [1350,3500]$ (Pa.s) and $\eta_2 \in [0.023,0.500]$ (Pa.s), or satisfy heuristic 3 (see Table 3-5) 3. $\gamma \in [2.0,2.4]$

A sample of the heuristic rules incorporated in the problem formulation is presented in Table 3-5, together with respective linear restrictions.

Table 0-15: Sample of heuristics used in the problem formulation

Heuristic	**Mathematical formulation**
1. There should be at least two but no more than three cationic surfactants.	$2 \leq \sum_r y_r \leq 3$
2. Cationic surfactants at about 20% of the oil phase should stabilize the emulsion.	$0.16\phi \leq \sum_r x_r \leq 0.24\phi$
3. When no thickening polymer is used, the concentration of fatty alcohol is at least twice the cationic polymers' in a molar base.	Let $z \in \{0,1\}$: $z = 1 \Leftrightarrow \sum_n y_n = 0$ $z = 1 \Rightarrow \sum_m \frac{x_m}{M_m} \geq 2\sum_r \frac{x_r}{M_r}$
4. If heuristic 3 holds, then product viscosity profile is expected to be satisfactory.	$z = 1 \Rightarrow \eta_1$ and η_2 are within specifications
5. At least one emollient of each type should be used: high, medium and low spreading.	$\sum_i y_i \geq 1;\ \sum_j y_j \geq 1; \sum_k y_k \geq 1$

Heuristics stated as logical conditions, like heuristic 3, need to be first converted to algebraic restrictions. Other restrictions such as regulatory and/or recommended composition limits were also considered, but are not listed. As it will be presented in the next sections, two different case studies were considered to illustrate the product realization phase of the methodology.

3.3.3 Case Study 1

This case study corresponds to the first short communication that was presented for the ESCAPE27 and later published in *Computer Aided Chemical Engineering*

The chosen objective function is the total cost, which is set up to be minimized. The desired product performance is specified as follows:

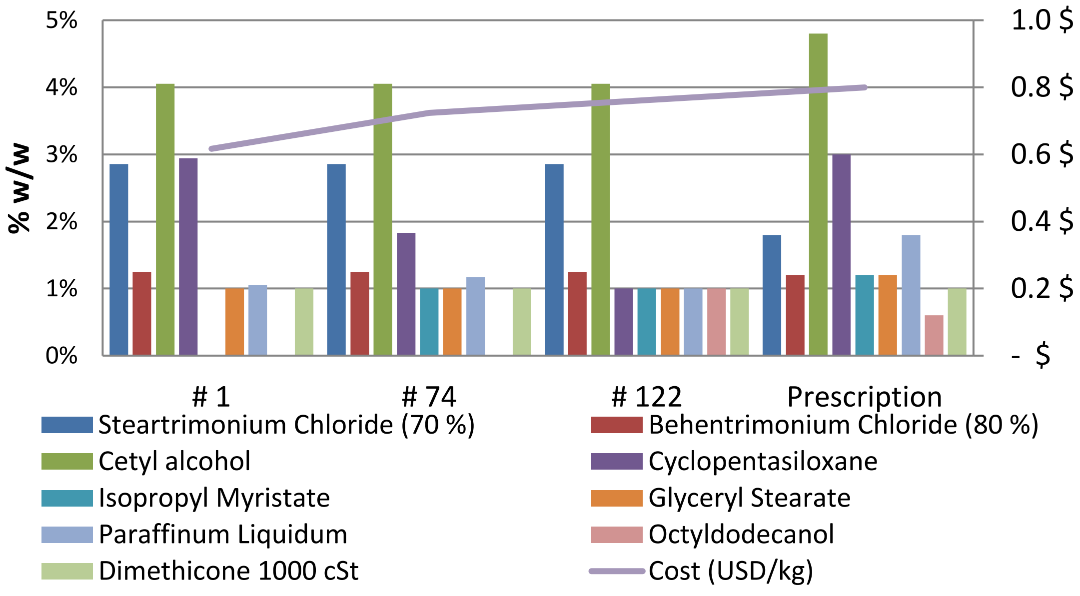
- “feel of use” attribute is set to “Soft and Moist”;
- greasiness is set between 2 and 2.4 (and thus softness is also bounded);
- viscosity η_1 between 120 and 500 Pa.s, and viscosity η_2 between 0.023 and 0.500 Pa.s.

The resulting model is a small MILP problem with 87 variables (33 of which binary) and 112 restrictions, prior to addition of integer cuts. The problem is solved in less than 1 s using GAMS/CPLEX.

3.3.3.1 Results

Through successive problem solution adding integer cuts, a list of 329 formulations under 0.8 USD/kg was obtained. In Figure 3-2, three selected alternatives (# 1, # 74 and # 122) are presented, each one representing the highest ranked combination of different ingredients, put alongside a sample formulation for rinse-off conditioner (Prescription 5.19 - Iwata and Shimada, 2013).

Figure 0-25: Alternative formulations for a “Soft and Moist” rinse-off conditioner



All these alternative formulations have a lower cost but similar performance parameters compared to the prescription (γ = 2.33 *vs.* 2.40; μ = 0.52 *vs.* 0.53; viscosity within specifications) and could serve as initial candidates in a reformulation or even in a new product development.

3.3.4 Case Study 2

This case study can be considered as an extension of the previous one, as it incorporates the product performance evaluation together with the economic goal. This study was already published (Arrieta-Escobar et al., 2018) in the journal *Computers and Chemical Engineering.*

Product design variables, performance metrics and corresponding desired specifications for the present case study were listed in Table 3-4. Cationic surfactants, thickeners (polymers or fatty alcohols) and emollients were selected from an initial list with a total of 35 ingredients, organized as in the above Tables 1 to 3. The formulation also includes Water, Glycerol and three additional minor ingredients (Disodium EDTA, Propylparaben and Perfume). These five ingredients are mandatory and thus their selection will not be equated. The mass percentage of the last four is also fixed (details are given in section 3.3.4.1.2, where the manufacturing procedure is described).

The desired product performance is specified as follows:

- "Feel of use" attribute is set to "moist and soft", according to heuristics in Table 3-1, implies that cationic surfactants $r2$ and $r3$ must be chosen and in amounts such that x_{r2} is 2 to 4 times x_{r3}, and that cationic surfactant $r1$ is not chosen.
- A cream-like consistency and corresponding feel to the touch is aimed (viscosities η_1 and η_2 within the known ideal ranges for a cream). Regarding specification (ii), one has the above-mentioned property models of the type $log(\eta) = a + bx_n + c\phi$, for both $\eta_1$and η_2.
- Greasiness value γ between 2.0 and 2.4. If no thickeners n are chosen, then heuristic 3 (below described) is activated. Specification (iii) is easily imposed through a linear mixing rule to estimate γ from known individual values for each emollient. The feasible design space is further reduced through other heuristic rules, a sample of which is given in Table 3-5, together with the corresponding mathematical formulation. The modelling of heuristic 3 is described in detail in example 2 of section 3.

The chosen objective function is the total cost of the formulation in USD/kg, only considering the unit cost of each ingredient and excluding fixed ingredients. The problem of finding the best formulation may then be stated as: "find vectors y and x that minimize cost, subject to property models (for $log(\eta_1)$, $log(\eta_2)$ and γ), product specifications ($2x_{r3} \leq x_{r2} \leq 4x_{r3}$, desired intervals for $log(\eta_1)$, $log(\eta_2)$ and γ) and a list of heuristic-related restrictions. This is a MILP problem with 87 variables (36 of which binary) and 112 restrictions, which is solved in less than 1 s using GAMS/CPLEX. The problem is solved several times, successively adding binary cuts prohibiting previous solutions y. Since global optimality is guaranteed, a correct rank of solutions with increasing cost is generated, all corresponding to products with similar performance (according to the models and heuristics adopted).

3.3.4.1 Experimental tests

3.3.4.1.1 Materials

The emulsifiers used for the preparation of samples were Behentrimonium Chloride (BTAC) 85% (Incroquat® Behenyl TMC-85, Croda, USA) and Cetrimonium Chloride (CTAC) 30% (Quartamin® 60, Kao, Mexico). Samples differed in seven components of the oil phase: *Paraffinum Liquidum* (Mineral Oil USP, DISAN, Colombia), Glyceryl Stearate (Cithrol® GMS 40-PA, Croda, Brazil), Octyldodecanol (Eutanol® G, BASF, Mexico), Cyclopentasiloxane (Xiameter® PMX-245, Dow Corning, China), Dimethicone (Xiameter® PMX-200 Fluid, Dow Corning, China) Stearyl Alcohol (ThaiOl 1898, TFA, Thailand) and Cetyl Alcohol (EcoRol 16/98P, PT Ecogreen Oleochemicals, Indonesia). Ingredients that were common to all samples (Glycerol, Disodium EDTA, Propylparaben and Perfume) were provided by local producers.

3.3.4.1.2 Emulsion processing

All sample emulsions were prepared for a total weight of 500 g. Initially, 1 g Disodium EDTA was added to 150 g distilled water (Phase A) and heated to 80ºC. In the meantime, the corresponding oily ingredients of each sample were mixed (Phase B) and then heated to 80ºC under manual stirring. When both phases reached the desired temperature, Phase B was added to Phase A under continuous agitation using a high-performance dispersing mixer Ultraturrax, (IKA, Germany) at minimum speed (around 2300 rpm) for 10 min. If the sample contained Dimethicone, it was added after the second minute of this step. After completing the homogenization, the emulsion was cooled down by adding the remaining water with 15 g Glycerol (Phase C), and by locating the mixing vessel within an ice-cold water bath. At this point, the emulsion was stirred with a propeller (Heidolph, Kelheim, Germany) at 1000 rpm for 10 minutes. Finally, Cyclopentasiloxane (if selected), Propylparaben and Perfume (Phase D) were added to the mixture when the temperature of the emulsion was below 40ºC and then kept under stirring for an additional period of 15 min (at 200 rpm). When needed, the pH value was adjusted to 3.7 ± 0.5 using a Lactic Acid Solution (85%), as the isoelectric point of hair shaft is 3.67 (Gavazzoni Dias et al., 2014). All the samples were stored in polyethylene containers under dry and dark conditions.

3.3.4.1.3 Microscopy

Homogeneity and stability of each sample emulsion were verified by optical microscopy (Motic B3-223 Professional Series, Hong Kong, China), using a 400X magnification. The droplet size was measured using Motic Images plus 2.0 software. A small amount of each sample was put on a glass slide, covered with a coverslip and pressed to make it as thin as possible. All samples were examined 1 month after preparation to assure long term stability.

3.3.4.1.4 Rheological measurements

Steady-flow properties were measured on a rotational rheometer Bohlin CVOR 200 (Malvern Instruments, Southborough, USA) with a cone-and-plate geometry. The cone diameter was 40 mm and the gap angle between the cone and plate was 4º. The shear rates were measured from 0.001 to around 2000 s^{-1}, with a logarithmically increasing scale (30 points). All samples were tested 1 week after preparation to assure that the emulsions were stable. The cone-and-plate gap was carefully filled with a defined amount of product, and any extra sample was wiped with a metal spatula. All measurements were conducted at least in duplicate. The measuring temperature was 20 ± 0.1ºC.

3.3.4.1.5 Texture analysis

The characterization of textural properties was performed to assure that the obtained products were suitable as hair conditioning emulsions, considering the reported properties of such products. The textural properties were measured with Texture Analyzer TA.XT Plus (Stable Micro Systems Ltd., Godalming, U.K.) using a suitable method specified by the equipment manufacturer. An A/BE Back Extrusion Rig was used, which included: Locating Base Plate, Sample Containers (50mm internal diameter) and Compression Discs (35mm diameter). To accurately determine the textural properties of the hair conditioner, samples were put in the Sample Containers (75% full) and kept at a specific temperature of 20 ± 0.2ºC. The disc penetrated 25 mm deep inside the sample at a rate of 2.0 mm/s, and the force exerted (up and down) was automatically measured. The following parameters were calculated: firmness, consistency (related to hardness), cohesiveness and index of viscosity (related to adhesiveness). Each sample was analyzed in duplicate and average values were calculated for all parameters (expressed as positive values).

3.3.4.2 Results

3.3.4.2.1 Optimal formulations

Table 3-6 shows a rank of nine formulations with increasing cost generated using binary cuts and then all have a different combination of ingredients. As observed, all alternatives contain the same quantity of CTAC and BTAC as emulsifiers, but different contents of emollients and thickeners in phases B and D, and water in Phase C. It is to underline that none of these formulations contain thickening polymers, as the option of using fatty alcohols in a sufficient amount (heuristic 3) turned out to be cheaper. All nine alternatives were prepared and tested as described in section 3.3.4.1.2 above.

3.3.4.2.2 Visual inspection and stability

Most of the sample products exhibited the expected creamy consistency, characteristic of this type of personal care products. The exceptions were Formulations 5 and 9, which both had a rather runny appearance. All samples were stable (no phase separation) after being centrifuged at 10000 rpm for 10 min.

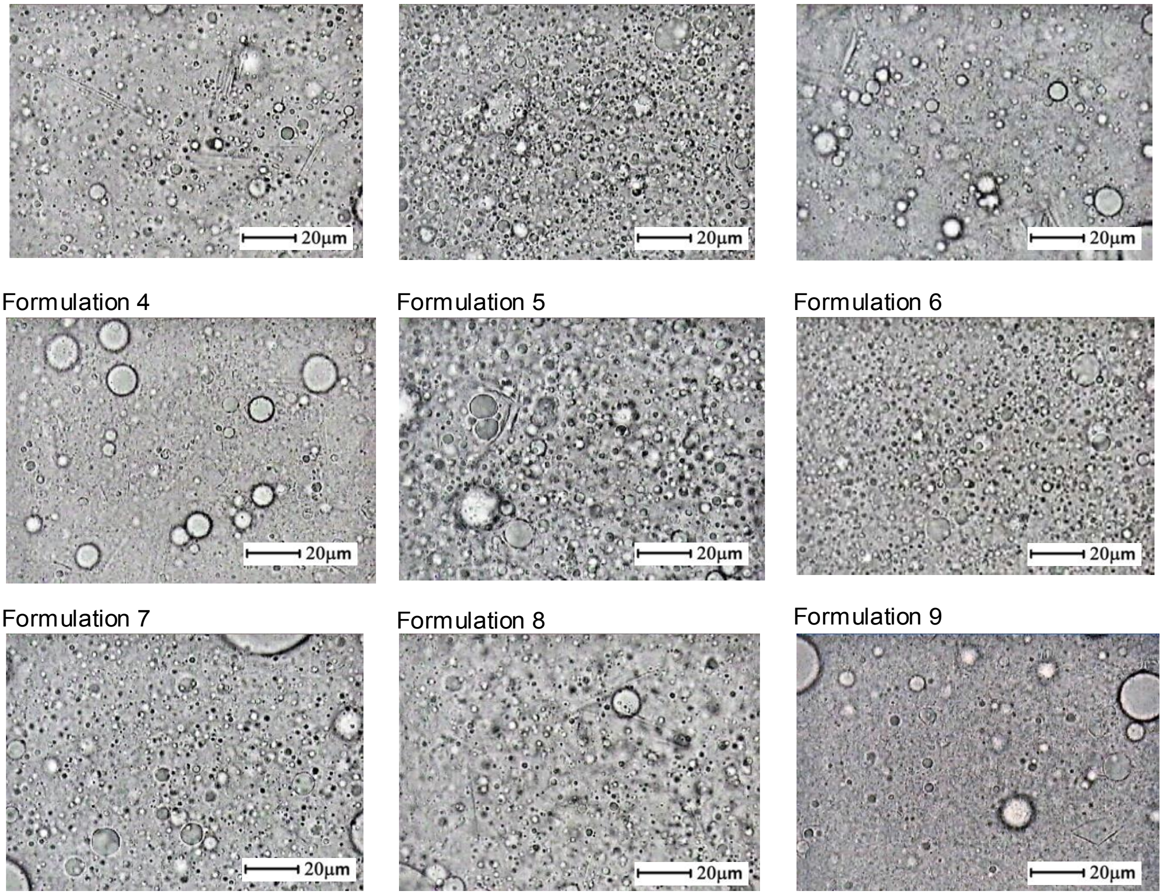
Table 0-16: Nine alternative formulations with increasing cost

Phase	Ingredient	Cost $/kg	Formulation								
			#1	**#2**	**#3**	**#4**	**#5**	**#6**	**#7**	**#8**	**#9**
A	Water		60.0%	60.0%	60.0%	60.0%	60.0%	60.0%	60.0%	60.0%	60.0%
	Disodium EDTA		0.2%	0.2%	0.2%	0.2%	0.2%	0.2%	0.2%	0.2%	0.2%
B	Cetyl Alcohol ($m2$)	2.4	4.1%	4.1%	-	4.1%	-	4.1%	4.1%	4.1%	-
	Stearyl Alcohol ($m1$)	2.4	-	-	4.5%	-	4.5%	-	-	-	4.5%
	CTAC (30%) ($r2$)	2.6	6.7%	6.7%	6.7%	6.7%	6.7%	6.7%	6.7%	6.7%	6.7%
	BTAC (85%) ($r3$)	10.0	1.2%	1.2%	1.2%	1.2%	1.2%	1.2%	1.2%	1.2%	1.2%
	Glyceryl stearate ($j2$)	6.0	1.0%	-	1.0%	1.0%	-	1.0%	-	-	1.0%
	Paraffinum Liquidum ($j7$)	1.3	1.1%	1.1%	1.1%	-	1.1%	1.4%	-	1.0%	-
	Octyldodecanol ($j8$)	7.0	-	1.0%	-	-	1.0%	1.0%	1.0%	-	-
	Dimethicone ($k7$)	3.1	1.0%	1.0%	1.0%	2.6%	1.0%	1.0%	2.6%	1.0%	2.6%
C	Water		18.1%	18.1%	17.7%	18.1%	17.7%	18.1%	18.1%	16.6%	17.7%
	Glycerol		3.0%	3.0%	3.0%	3.0%	3.0%	3.0%	3.0%	3.0%	3.0%
D	Cyclopentasiloxane ($i1$)	3.5	2.9%	2.9%	2.9%	2.4%	2.9%	1.6%	2.4%	5.5%	2.4%
	Propylparaben		0.2%	0.2%	0.2%	0.2%	0.2%	0.2%	0.2%	0.2%	0.2%
	Perfume		0.5%	0.5%	0.5%	0.5%	0.5%	0.5%	0.5%	0.5%	0.5%
		Total	**100%**	**100%**	**100%**	**100%**	**100%**	**100%**	**100%**	**100%**	**100%**
	Cost (USD/kg)		0.60	0.61	0.61	0.62	0.62	0.63	0.63	0.63	0.63

3.3.4.2.3 Microscopy

Representative optical microphotographs (400X) of the nine sample emulsions are presented in Figure 3-3, evidencing that all hair conditioners exhibited a similar microstructure, with droplet sizes ranging from 0.5 to 5 μm. It should be noted that all samples were prepared following the exact same procedure. This could explain the similarities in droplet size, which is known to be a strong function of processing conditions. The understanding of the impacts of the processing conditions in the product structure and in its performance is out the scope of this work and will be explored in a further study.

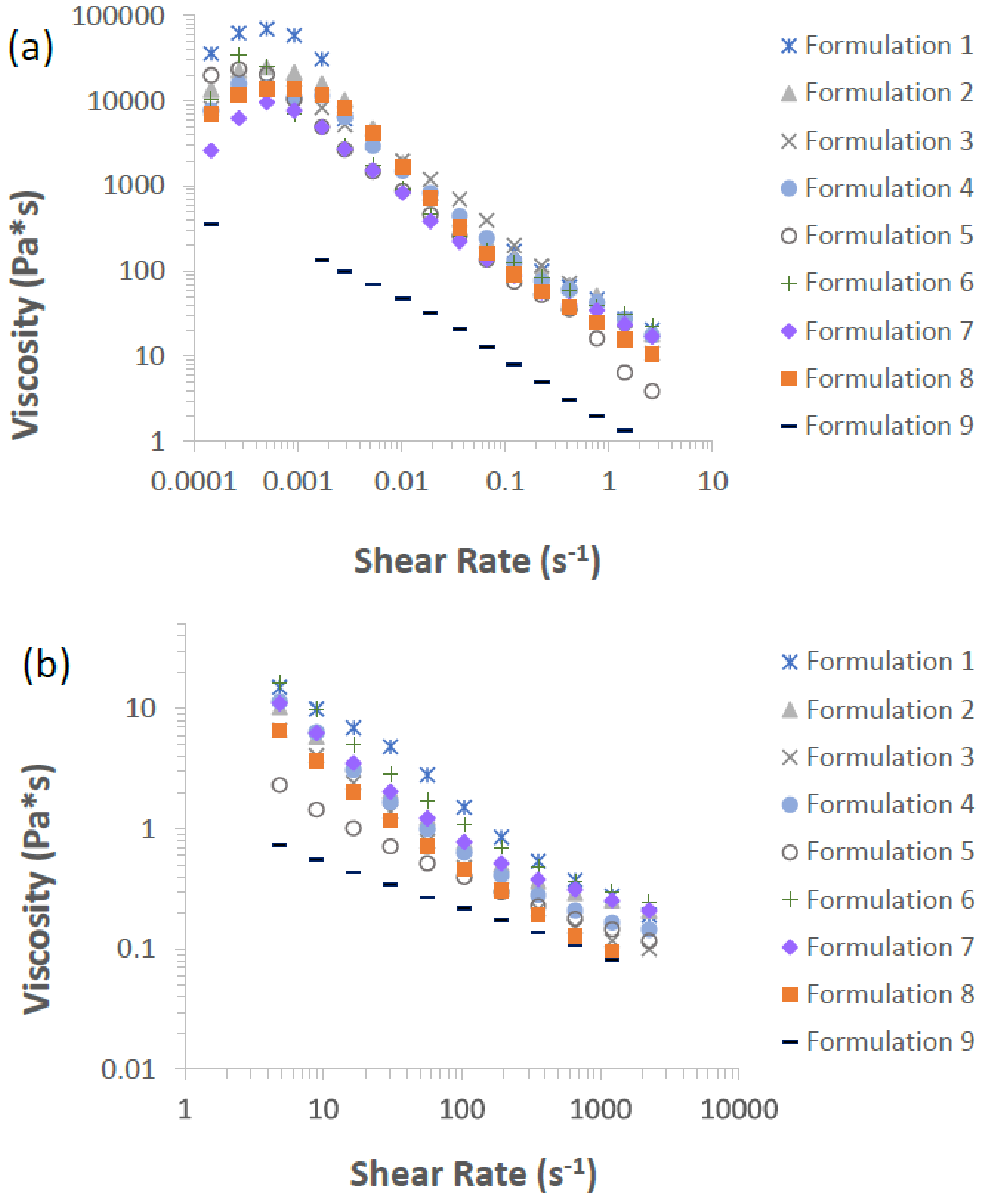
Figure 0-26: Photomicrographs of investigated samples (400X)


Formulation 1
Formulation 2
Formulation 3
Formulation 4
Formulation 5
Formulation 6
Formulation 7
Formulation 8
Formulation 9

3.3.4.2.4 Rheological measurements

The viscosity of the nine samples at different exerted shear rates is presented in Figure 3-4. The plot is divided in two sections to facilitate the analysis: Figure 3-4(a) for the low shear rate section (below 10 s^{-1}) and Figure 3-4(b) for the high shear rate section (above 10 s^{-1}).

Figure 0-27: Rheological profiles of tested formulations at low (a) and high (b) shear rates.



All samples 1 to 8 all have a viscosity profile within specifications: an initial viscosity η_1 between 1350 and 3500 Pa.s (Figure 3-4(a), point just before the strong shear-thinning region, ~0.003 s^{-1}) and a final viscosity η_2 between 0.023 and 0.5 Pa.s (see Figure 3-4(b), η_2 at about 500 s^{-1}). All these formulations do not contain thickening polymers but instead a significant amount of fatty alcohols, according to heuristic 3 (Table 3-5).

These results then show that the assumed heuristic 3 is in fact correct. Only Formulation 9 exhibited a different behavior from the rest of the formulations, consistently showing a lower viscosity, moreover at low shear rates. Though the microscopic image of this sample is very similar with the others, it is common to observe differences in the viscosity of some emulsions using fatty alcohols, due to the formation of aggregates (Sakamoto et al., 2017) and the different content of Dimethicone, which seem to have an antagonism together.

3.3.4.2.5 Texture analysis

The parameters obtained from the textural analysis in all prepared sample emulsions are presented in Figure 3-5 as box plots[3], where whiskers extend to 5th and 95th percentile. Except for Formulation 7, all samples are within this range and for all parameters. Although no sensorial tests were performed on these formulations, it has been reported that the textural parameters here evaluated do correlate well with the sensorial attributes of the product. In particular, firmness is related to the texture as perceived by the user, and consistency, cohesiveness and index of viscosity all directly correlate with slipperiness (Lukic et al., 2012). As these textural parameters for all obtained formulations were found to be similar, this indicates that main sensorial attributes are similar as well. However, there remains a need for conducting a sensory evaluation, namely regarding “feel of use” and greasiness, the key sensorial attributes initially specified (Table 3-4).

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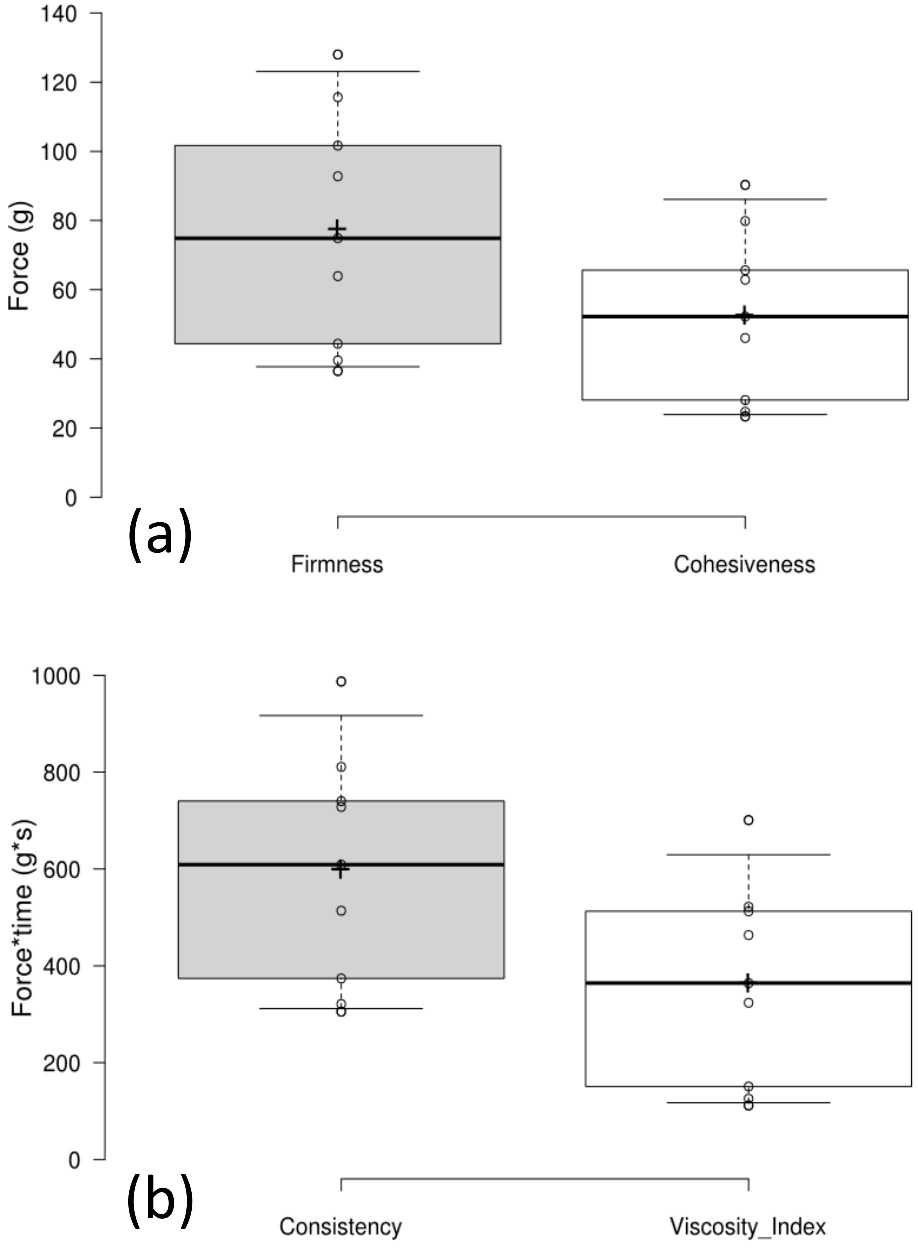
[3] http://shiny.chemgrid.org/boxplotr/

Figure 0-28: Results of texture analysis: (a) firmness and cohesiveness; (b) consistency and viscosity index



3.4 **Discussion**

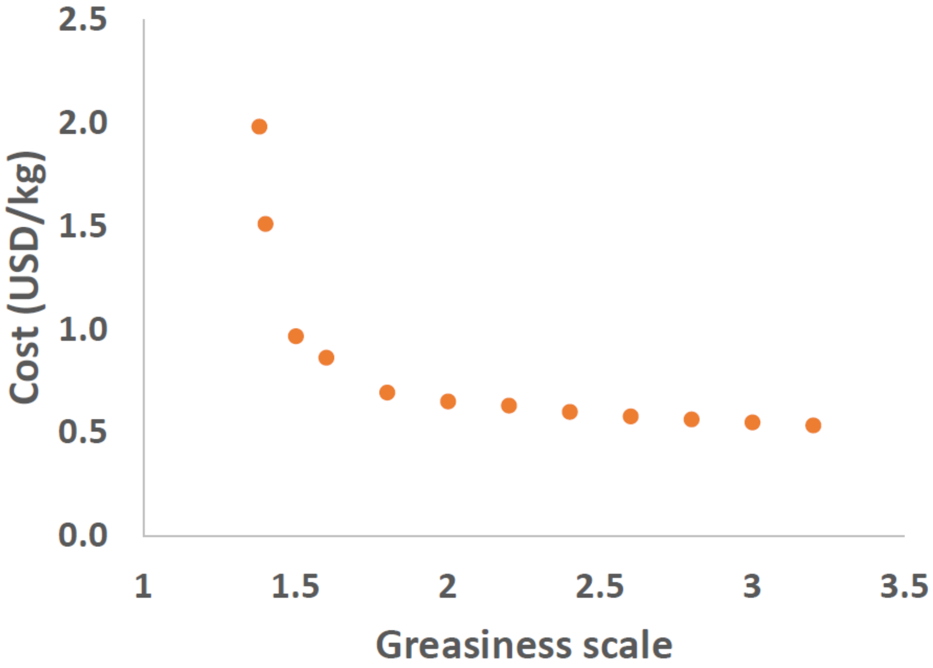
For illustrative purposes, Table 3-7 shows how sensible the optimal solution is (first solution without any binary cuts) to variations in the cost of two ingredients, Cyclopentasiloxane and Dimethicone, with a total of 9 scenarios. In the scenarios of the first two rows of Table 3-7, the optimal product formulation remains the same (the one in column #1 of Table 3-6) and the minimum cost varies in the expected proportion. Conversely, in the scenarios of the third row (40% increase in the cost of Cyclopentasiloxane), the same combination of ingredients is selected but the level of Cyclopentasiloxane decreases to its lower bound of 1% and the quantity of other emollients increases in order to comply with a total of 6% in the set of emollients.

Table 0-17: Optimal product cost increase with variations in the costs of Dimethicone and Cyclopentasiloxane.

		Dimethicone cost increase		
		0%	**20%**	**40%**
Cyclopentasiloxane cost increase	**0%**	0.0%	1.0%	2.1%
	20%	3.4%	4.4%	5.4%
	40%	6.1%	7.2%	8.2%

To illustrate how multiple objectives may be handled, we now consider product greasiness *vs.* cost. The original problem was formulated with the specification of greasiness value γ between 2.0 and 2.4 and all optimal solutions of Table 3-7 converged to the upper limit of 2.4 (heavier emollients perceived as more greasiness are cheaper). A Pareto curve showing the greasiness/cost trade-off may thus be constructed solving the problem with the constraint $\varepsilon - 0.4 \leq \gamma \leq \varepsilon$ for decreasing values of ε. Such a curve is shown in Figure 3-6 with values of ε between 1.38 and 3.2. All points in the figure correspond to optimal solutions that have converged to $\gamma = \varepsilon$. These results may be read as the additional cost one has to pay for a product with a lower greasiness value, more adequate for greasy hair. For example, taking a greasiness value of 2.4 as a base, if we set this value to 1.4, the minimal cost for a formulation would increase from 0.60 to 1.51 USD/kg. Indeed, a formulation with lower values of greasiness requires less greasy emollients, which are in general more expensive than more greasy emollients.

Figure 0-29: Pareto curve of product greasiness *vs.* cost



In a scenario with an increasing number of ingredients, it will be expected a much greater number of equally performing feasible alternatives, along with a higher level of uncertainty due to the synergies and antagonisms of the new ingredients. The first issue could be partially addressed by better understanding the critical performance parameters and incorporating them in a multi-objective optimization function with a multicriteria decision-making tool that allow the designer to choose the solution that better suits the required performance goals. This approach will be further explored in a future contribution. Besides, to cope with a higher level of uncertainty, in the practice, designers use a chassis formulation as a base, on which they perform small changes using experimental design (Claeys-Bruno et al., 2009; Ochoa et al., 2017), in order to adjust the optimal level of a new ingredient.

3.5 **Conclusions**

We have proposed an optimization-based methodology for the design of formulated products, which explicitly incorporates available heuristic rules. These may be initially stated as logical constraints that are easily translated into algebraic restrictions using binary variables and propositional logic. The methodology was applied to a cosmetic emulsion example, being generated a rank of alternative solutions that fulfill expected properties with minimum ingredient costs. In the first case, a list of feasible alternatives, which have a lower cost but similar performance parameters compared to a prescription was obtained. This list could serve as initial candidates in a reformulation scenario. In the second case, the computer-generated solutions were also manufactured and tested. The rheological, textural and microstructural properties of the alternative formulations show that most of them are similar, and so any of them could serve as a starting point in a new product development process. Consumer assessment, along with other heuristics related to manufacture could also be integrated to improve the methodology. It was thus suggested that is possible to reduce the time and resources spent in cosmetic emulsions design compared with the traditional trial-and-error methods.

4. Integration of Consumer Preferences and Heuristic Knowledge in the Design of Formulated Products: Application to a Cosmetic Emulsion

The design of optimal mixtures is an important challenge in many industrial sectors, namely for formulated products like cosmetics (Zhang et al., 2017). Due to the large number of different combinations of ingredients and their levels of use, a critical issue is how to define a reduced search space using available knowledge. For that purpose, besides key physicochemical properties of the final product, it is of paramount importance to account for the performance of the product as perceived by the final consumer.

In the previous chapter a method to find a set of plausible product formulations was proposed, based on mixed-integer programming and explicitly including available heuristic rules modeled as algebraic restrictions, and here the method is extended to include consumer assessment. Starting with a list of product attributes directly valued by consumers, the importance level of each of them and the interactions between them are determined from data of usability tests made on an on-market product, by using fuzzy measures, in particular the Choquet integral (Camargo et al., 2014). These consumer parameters can then be incorporated into the optimal design problem formulation as further restrictions, along with heuristic rules and property models.

A case study of skin moisturizers is presented, being considered an initial design space with 36 possible main components (6 non-ionic emulsifiers, 24 emollients and 6 thickeners). Consumer preference parameters are classified in 8 groups of attributes (thickness, ease of spreading, stickiness, easy of absorption, freshness, residues, greasiness/oiliness and moisturization) and are calculated for two commercially available skin moisturizers by means of usability tests on 32 women for each product. After computing the survey data, indices of importance and interactions showed that some of the most relevant attributes were residues, thickness, and greasiness. A small set of alternative formulations was then generated using a series of actions based on these attributes and then manufactured at a lab scale. As a result, each action led a basic formulation to become more similar in terms of rheological and textural properties, when compared to the commercial products used in the survey. This proposed method could be well adapted to accelerate reformulation processes, estimate the relevance of consumer attributes or to guide the selection of alternatives in reformulation of benchmarking processes.

4.1 Introduction

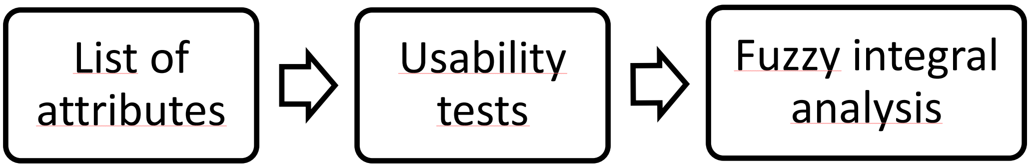
In the highly competitive market, consumer acceptance has become an important factor in the product design process. Therefore, the prediction of acceptability is essential in product development, especially in the domain of cosmetic products, whose performance assessment integrates not only functional but also sensorial characteristics (Wortel and Wiechers, 2000). Normally, an objective evaluation (sensorial profiling) is made by a panel of experts under determined conditions (Civille and Dus, 1991), which makes it very expensive to implement. When there are limited resources, acceptance tests are frequently used during early stages of cosmetic product development to help understand these attributes (Huber, 2017). For this, consumer surveys and household tests are generally made prior to new developments or important reformulation processes (Gagnaire and Freyssinet, 2016; Rähse and Hoffmann, 2003).

Among the different methodologies to elucidate consumer response to a certain product, "Affective Engineering" or "Kansei Engineering" approaches can be used (Luo et al., 2011; Yang, 2011). In a Kansei engineering approach, semantic attributes have been used to describe the affective responses of consumers to products (Shieh et al., 2017). These words describe the domain or the product to be evaluated as it is perceived during its use (Schütte and Eklund, 2005). Traditional techniques used in Kansei design, such as PCA (Principal Components Analysis) or multi-factorial analysis, are useful to reduce the semantic space and identify the contribution of the attributes (degree of importance) or the correlation among them, but they are not able to quantify the interactions ("synergistic" or antagonist effects") of groups of SA. This aspect is particularly relevant for cosmetics as there is an important influence of the sensory interaction on the users' perception and assessment of the product.

Fuzzy measures have been applied to the subjective evaluation of different attributes, such as color (Tanaka and Sugeno, 1991) or texture (Schmitt et al., 2008) and in particular the studies of Grabisch (Grabisch, 2007). Recently a methodology to integrate the user's perception and identify the importance and interaction of consumer attributes, based on fuzzy measures, was proposed by Camargo et al. (2014). This methodology combines a Hybrid

Kansei Engineering approach (Matsubara and Nagamachi, 1997), which uses a prototype or mock-up to elicit the product attributes, with a fuzzy integral analysis, namely the Choquet integral (Choquet, 1954). The main advantage of this approach is the possibility to consider the attributes relevance, based on the user's preferences, and the interactions among them. In this contribution, the methodology of Camargo et al. (2014) will be adapted (see Figure 4-2) for cosmetic emulsions in order to understand the importance level of each quality factor (Shapley index) along with the synergy or redundancy among them (Murofushi and Soneda indices). The main stages of this methodology are described in detail in the original paper, and here only some aspects will be mentioned in the context of a skin moisturizer.

Figure 0-30: Concept definition methodology. Adapted from (Camargo et al., 2014)

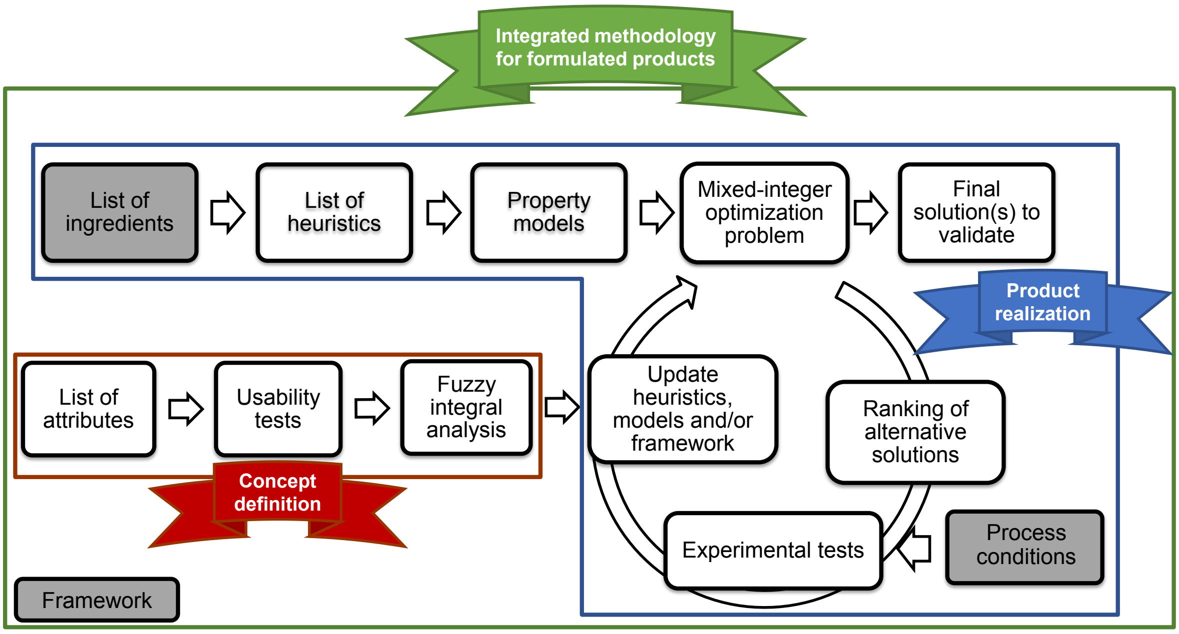


4.1.1 Integrated methodology for formulated product design

An integrated methodology for the design of formulated products consisting of two main phases: concept definition, in which the main attributes of the product are defined using the fuzzy integral methodology described above, and product realization, in which product modelling is carried out using heuristics and property models to propose a set of feasible alternatives. Although initially developed in the scope of cosmetic emulsions, the basic ideas and tools of the methodology here proposed (Figure 4-1) are applicable to any formulated product, whose specific functionalities result from the mixtures of functional ingredients and specific interactions between them.

This concept definition methodology will be integrated to the product realization phase, which has already been presented in the context of hair conditioners (Arrieta-Escobar et al., 2018), except for the inclusion of the concept definition phase. The output of the concept definition phase can be considered as a new set of heuristics that will guide the selection process of the alternatives, as shown in Figure 4-1. Because the main purpose of the current chapter is to present the integration of the concept definition phase with the product realization phase, a skin moisturizer study case will serve as an example to explain the integrated methodology in the next section.

Figure 0-31: Integrated methodological approach for the design of formulated products



4.2 Skin moisturizer case study

A skin moisturizer can be described as a product applied to wet or dry skin, which is easy to spread and pleasant to use (Kostansek, 2012). Skin moisturizers are used to keep in good condition the skin by maintaining its balance of oil and water (Eccleston, 1997). Although conditioning needs depend heavily on the type of skin (i.e. normal, dry, very dry, sensitive skin, etc.) consumers always search for products that can relief the discomfort of a dry skin (Abrutyn, 2010). Skin moisturizers provide a healthy skin feeling thanks to the use of moisturizers (humectants and emollients), which are typically delivered in the form of an O/W emulsion, stabilized with a combination of emulsifiers (mostly nonionic surfactants) and thickeners (fatty alcohols and polymers) (Barel et al., 2001).

4.2.1 Concept definition phase

4.2.1.1 List of attributes

In this stage, 8 attributes reported in the literature (Bagajewicz et al., 2011; Parente et al., 2010) were chosen to be evaluated during the usability tests, and a pair of words in the language of evaluation (i.e. French), as shown in Table 4-1. Each set of words was selected after asking four experts to brainstorm keywords that could be used to describe skin moisturizers, and then to manually classify them in each category. The two most repeated terms were selected to represent each attribute.

Table 0-18: List of main attributes for cosmetic emulsions

Attribute	Word 1	Word 2
Thickness	Thick	Thin*
Spreadability	Easy to spread	Glides easily
Stickiness	Sticky	Light*
Ease of absorption	Easily absorbed	Penetrates quickly
Freshness	Fresh sensation	Cold sensation
Residues	Whitening on rub-out	Leaves residues
Greasiness/oiliness	Greasy	Oily sensation
Moisturization	More hydrated skin	Softer skin
*Indicates that these words are at the opposite end of the attribute scale		

4.2.1.2 Usability tests

A questionnaire was prepared, having two main sections. According to ASTM E1490-(03) products should be tested with respect to skin type needs, so a first series of questions (hair and eyes color, skin phototype etc.) helped to determine whether the user could participate or not in the test (90% of the participants should have the same type of skin) and also minimized the risk of having adverse reactions using the product (i.e. users with sensitive skin). Then, other questions regarding the frequency of use and the main criteria when purchasing a skin moisturizer were also asked.

In the second part of the test, the participants were told to apply the product on their arms, and to answer the set of questions corresponding to each one of the words in Table 4-1, using a 5-level ordinal scale from not at all to very much (Osgood, 1959). Two final questions about product's acceptability would allow the algorithm in the fuzzy integral analysis to "learn" how important the attributes were to the overall performance. The complete survey form – in French (original) and English – and the complete results are presented in Appendix D.

4.2.1.3 Fuzzy integral analysis

After calculating the fuzzy measures, the different scores and indices of the attributes will be used to guide the selection of the alternative formulations in the next phase.

4.2.2 Product realization phase

Humectants - like glycerin – and other excipients – emollients, emulsifiers, and thickeners – should be combined in an economically and technically feasible fashion to fulfill the consumers' expectations. For this purpose, the product modelling was made for these groups of ingredients – emulsifiers, thickeners and emollients – considering a fixed amount of glycerin as humectant, using the methodology explained in section 2.2.

4.2.2.1 List of ingredients, heuristics and property models

- Emollients

Emollients are required in the oil phase to improve the spreadability of the product. A proper combination of three or more emollients of high, medium and low spreading types provides the complete profile for a well-performing product (Ansmann et al., 2005). Table 4-2 contains the list of emollients initially considered in the formulation, grouped by its spreading properties.

Table 0-19: List of emollients used in the skin moisturizer formulation

	High spreading (*i*)	**Medium spreading (*j*)**	**Low spreading (*k*)**
1	Cyclopentasiloxane (C5)	C12-C15 Alkyl benzoate	Oleyl erucate
2	Isoamyl cocoate	Ethylhexyl stearate	*Persea gratissima* oil
3	Diethylhexyl carbonate	Cetyl ethylhexanoate	PPG-15 stearyl ether
4	Isopropyl Myristate	Cetearyl Isononanoate	Cetyl Dimethicone NP**
5	Isopropyl palmitate	Cetyl Dimethicone MP*	PPG-14 butyl ether
6	Decyl cocoate	PPG-3 Myristyl ether	Triisostearin
7	Ethylhexyl palmitate	*Paraffinum Liquidum*	Dimethicone
8	Phenoxyethyl caprylate	Octyldodecanol	
9	Caprylic/Capric triglyceride		

*MP = Medium polarity; **NP=Non-polar

The residual film of the emollient helps to lubricate and reduce the friction exerted on the skin surface (Dederen et al., 2012). The greasiness value (γ) of a mixture of emollients was estimated here as a weighted average from individual values (Mentel et al., 2014). Typical greasiness values γ for skin moisturizers are in the range from 2.0 and 2.4 on a 5 point scale (Bagajewicz et al., 2011). The required HLB value of the emollients was obtained directly from the provider or from other available sources (Pensé-Lhéritier, 2016).

- Emulsifiers

Skin moisturizer emulsifiers are usually a suitable combination of at least two nonionic surfactants (Rieger and Rhein, 1997) used at a minimum level of 2% and up to 5% (Rähse, 2013). The final HLB value of the combination – a mixture of high, medium and low HLB -

should be between 8 and 15 to assure O/W emulsions and a surfactant/oil phase ratio 1:4 to 1:6 should be kept to stabilize the resulting emulsion (Iwata and Shimada, 2013). In Table 4-3 is presented the list of non-ionic surfactants considered as possible components of the product formulation, along with the proper amount required to stabilize the emulsions.

Table 0-20: List of nonionic surfactants and their combination rule

	Nonionic surfactant (*r*)	**HLB**	**Combination rule** (Iwata and Shimada, 2013)
1	Polysorbate 60	14.9	1 part Medium HLB (9-15) 3 to 6 parts High HLB (>16) 2 to 6 parts Low HLB (<8)
2	Polysorbate 80	15	
3	PEG-100 Stearate	18.8	
4	Sorbitan Oleate	4.3	
5	Glyceryl Stearate SE	5.8	
6	Sorbitan Stearate	4.7	

- Thickeners

Thickeners used in skin moisturizers are water-dispersable polymers and fatty alcohols (Table 4-4). Normally, they are used in combination in skin care emulsions, as these formulations are more prone to destabilization (Iwata and Shimada, 2013).

Table 0-21: List of thickeners used in the skin moisturizer case study

	Thickening polymer (*n*)	**Fatty alcohol (*m*)**
1	Xanthan Gum	Stearyl alcohol
2	Hydroxyethyl Cellulose	Cetyl alcohol
3	Hydroxypropyl Guar Gum	Cetearyl alcohol

Thickeners not only increase the viscosity of the product, but depending on its nature, they can even influence the product's perception (Wang et al., 1999). It has been shown that the consumer evaluation of skin feeling has a strong correlation with the product rheology (Brummer and Godersky, 1999). More precisely, the primary feeling is correlated to the viscosity perceived on the onset of flow of the product (low stress viscosity η_1), while the secondary feeling corresponds to a much lower final viscosity, perceived during the product's application (high stress viscosity η_2). Under such circumstances, an ideal cream η_1 value should be between 1350 and 3500 Pa.s (between 120 and 500 Pa.s a lotion) and η_2 between 0.023 and 0.500 Pa.s. This last viscosity interval corresponds to a shear rate of ~500 s^{-1}, if the application is over small areas like the face, or ~5000 s^{-1}, if the application is over large areas like the body (Brummer and Godersky, 1999).

Composition-viscosity data for polymer thickened aqueous solutions are available for several polymers (Prospector®, 2017). These data, together with a reliable theoretical model to predict the effect of the dispersed phase (Pal, 2001), were used to construct equations of the type $log(\eta) = a + bx_n + c\phi$ (average relative errors 22%), for each polymer n in Table 4-4 and for both η_1 and η_2 (ϕ is the mass fraction of oil phase). Since only one polymer is used, mixing rules are not needed. Fatty alcohols will be used at a 2-4% concentration.

4.2.2.2 Optimization problem

Product design variables, performance metrics and corresponding desired specifications for the present case study are shown in Table 4-5. Emollients, nonionic surfactants, and thickeners (polymers or fatty alcohols) will be selected from an initial list with a total of 36 ingredients, organized as in the above Tables 4-2 to 4-4. Vectors of decision variables - y (binary) and x (continuous) - both have dimension 36. The formulation also includes a fixed amount of mandatory ingredients, namely the humectant (3% Glycerol) and the preservative (0.7% Cosgard®).

Table 0-22: Product design variables and specifications

Design variables: choice of ingredients y and mass percentages x
Nonionic surfactants: y_r, x_r
Thickening polymers: y_n, x_n
Fatty alcohols: y_m, x_m
High spreading emollients: y_i, x_i
Medium spreading emollients: y_j, x_j
Low spreading emollients: y_k, x_k
Find vectors $\boldsymbol{y}$ and $\boldsymbol{x}$ that minimize cost, subject to
▪ $\mathbf{2.0 \leq \boldsymbol{\gamma} \leq 2.4}$
▪ $\mathbf{3}(\boldsymbol{x_{r1}} + \boldsymbol{x_{r2}}) \leq \boldsymbol{x_{r3}} \leq \mathbf{6}(\boldsymbol{x_{r1}} + \boldsymbol{x_{r2}})$
▪ $\mathbf{2}(\boldsymbol{x_{r1}} + \boldsymbol{x_{r2}}) \leq \boldsymbol{x_{r4}} + \boldsymbol{x_{r5}} + \boldsymbol{x_{r6}} \leq \mathbf{6}(\boldsymbol{x_{r1}} + \boldsymbol{x_{r2}})$,
▪ $\boldsymbol{y_n}, \boldsymbol{x_n}$ so log $\boldsymbol{\eta_1}$ and log $\boldsymbol{\eta_2}$ are within the ideal range

The chosen objective function is the total cost of the formulation in USD/kg, only considering the unit cost of each ingredient and excluding fixed ingredients or manufacture costs. The resulting MINLP problem is solved several times in less than 1 second using GAMS/BARON. successively adding binary cuts prohibiting previous solutions y. Since global optimality is guaranteed, a correct rank of solutions with increasing cost is generated, all corresponding to products with similar performance (according to the models and heuristics adopted).

4.2.2.3 Experimental tests

4.2.2.3.1 Materials

The ingredients used in the preparation of samples were Polysorbate 60 (Tween^{TM} 60-SS-(RB), Croda, UK), Polysorbate 80 (TEGO® SMO 80 V, Evonik, Germany), PEG-100 Stearate (SP Myrj^{TM} S100 MBAL-PA-(RB), Croda, UK), Glyceryl Stearate (Cithrol® GMS 40 SE MBAL-PA-(SG), Croda, Singapore), Sorbitan Stearate (SP Span^{TM} 60 MBAL-PA-(SG), Croda, Singapore), Sorbitan Oleate (SP Span^{TM} 80 MBAL-PA-(RB), Croda, UK), *Persea gratissima* oil (Avocado Oil, Provital group, Spain), Cetyl Alcohol (Lanette® 16, BASF, Germany), Isopropyl Myristate (Tegosoft® M, Evonik, Germany), Xanthan Gum (Rheocare® XGN, BASF, Germany), Dehydroacetic acid (and) Benzyl alcohol (Cosgard - *Geogard® 221*, Bioflore, Belgium). The humectant (Glycerol USP) and the *Paraffinum Liquidum* (Mineral Oil USP*)* were found in a local cosmetic store.

4.2.2.3.2 Emulsion processing

All sample emulsions were prepared for a total weight of 200 g. Initially, Xanthan gum was added to a beaker containing distilled water (Phase A). The gum was carefully added, aiming for the center of the vortex made by the propeller (Heidolph, Kelheim, Germany) at 800 rpm, while heating to 60ºC. In the meantime, the corresponding oily ingredients of each formulation were mixed (Phase B) and also heated to 60ºC under manual stirring. When both phases reached the desired temperature, Phase B was added to Phase A under continuous agitation using a high-performance dispersing mixer Ultraturrax (IKA, Germany) at minimum speed (around 2300 rpm) for 10 min. After the homogenization, the emulsion was cooled down following two different procedures:

- Manufacture procedure I: by adding the Phase C and simultaneously putting the beaker inside an ice-cold water bath.
- Manufacture procedure II: only by putting the beaker inside an ice-cold water bath (in this case the total amount of water was in Phase A).

During the cooling stage, the emulsion was stirred using the propeller at 800 rpm for 10 minutes. Finally, the preservative (Phase D) was added to the mixture when the temperature of the emulsion was below 40ºC and then kept under stirring for an additional period of 15 min (at 200 rpm). All the samples were stored in polyethylene containers under dry and dark conditions.

4.2.2.3.3 Rheology

Rheological analysis was performed on a rotational viscometer ARES (TA Instruments, New Castle, USA). The flow behavior was studied by continuous shear investigations, which were performed to evaluate the shear response (Pa*s) as a function of shear rate (s^{-1}) (from 0.01 to around 100 s^{-1}) with a logarithmically increasing scale (5 points), using parallel pates (25mm). All samples were tested 1 week after preparation to assure that the emulsions were stable. The gap between the disc and the plate (0.5 mm) was carefully filled with a sample of the product, and any left material was removed using a metal spatula. All measurements were conducted at least in duplicate. The measuring temperature was 20 ± 0.1ºC.

4.2.2.3.4 Textural analysis

The textural properties of the skin moisturizer samples were measured using a Texture Analyzer TA.XT Plus (Stable Micro Systems Ltd., Godalming, U.K.) featuring a load cell of 30 kg, with an A/BE back extrusion rig, which included a locating base plate, sample containers (50mm internal diameter), and compression discs (35mm diameter). After penetrating the sample (25 mm deep) at a rate of 2.0 mm/s, the probe returned to the initial position. Following this procedure, the firmness, consistency (related to hardness), cohesiveness, and index of viscosity (related to adhesiveness) of the samples were measured in duplicate and average values were calculated for all parameters (all expressed as positive values). All the measurements were taken at room temperature of 20 ± 0.2ºC

4.2.2.3.5 Microscopy

Emulsions were observed using a portable microscope Dino-Lite® Edge AM7515MT8A (Taipei, Taiwan), with a magnification of 900x, and images were captured with the in-built camera 5Mpixels (2592x1944). For this, a small amount of each sample was mounted on a glass slide along with a drop of distilled water under a cover slip. All samples were examined 2 months after preparation to assure long term stability.

4.2.2.3.6 White residues on rubbing-out

An adaptation to the descriptive skin feel analysis method described by ASTM E1490-(03) was implemented here to establish a qualitative comparison of the white residues left by two products during rubbing-out: 0.1g of each product was spread on the mid-section of the forearm, using for one product the index and for the other product the middle finger (both of the opposite hand). The white residue of both samples was compared after 15 circular rubs at a rate of 2 strokes per second (a watch was used in regulation of the timing).

4.2.2.4 Heuristics update

In this step the integration of the consumer assessment in the product realization phase takes place. Depending on the experimental tests and the ranking of attributes and their interactions, a series of heuristics could be transformed into additional restrictions in the algorithm, as shown in Table 4-6 below. These actions are taken to increase or reduce the value of a specific attribute, depending on the case.

Table 0-23: Heuristics to guide the selection of alternatives based on the attributes.

Attribute	Actions to increase	Actions to reduce
Thickness	▪ Adjust viscosity target value in the algorithm ▪ Increase fatty alcohol content (Iwata and Shimada, 2013)	▪ Replace part of surfactants to those that have lauryl or oleyl alkyl group ▪ Add branched-chain higher alcohol (i.e. Octyldodecanol) (Iwata and Shimada, 2013)
Residues		▪ Add up to 2% low HLB emulsifier and allow HLB<RHLB ▪ Add silicones to the formulation (Institute of Personal Care Science, 2016)[4]
Greasiness /oiliness	Adjust greasiness target value in the algorithm	

4.3 Results and discussion

4.3.1 Concept definition phase

The usability tests were conducted during two main popular events in the city of Nancy (France). The participants of the first group (sample 1) were recruited during *Cité Santé*[5] 2018

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[4] White residues after rubbing-in are mainly related to the generation of microfoam (emulsifiers catching air) so the use of silicones could also reduce this problem. Another possible solution is to add up to 2% low HLB emulsifier. This will not only remove the microfoam, but also increase the viscosity of the formulation.

[5] https://www.salon-citesante.com/

(March 23rd and 24th), and the second group during the International Fair of Nancy[6] 2018 (May 25th to 4th June). As mentioned before, in the first part of the usability test, users were asked to answer some questions to determine if they were able to participate in the test. In both groups, at least 93% of the participants (30 out 32) had normal to dry skin[7]. Besides, age ranges and frequency of use distribution was similar too, as it can be observed in Tables 4-7 and 4-8, respectively. The products were wrapped in aluminum foil to prevent the participants to be biased by the brand.

Table 0-24: Age distribution of the participants in the usability tests

Age range	**18-29**	**30-39**	**40-49**	**>50**
Sample 1	16	5	5	6
Sample 2	15	6	5	6

Table 0-25: Frequency of skin moisturizer use among the participants

Frequency of use	**Twice a day or more**	**Once a day**	**Sometimes a week**	**Sometimes a month**	**Sometimes during the winter**	**Total**
Sample 1	3	8	8	10	3	32
Sample 2	2	10	12	6	2	32

From a given list, users were asked to rank the 5 most important criteria they consider when purchasing a skin moisturizer. The most important attributes corresponded to rational or functional attributes (weighted average of 76%) of the product, while the rest were more emotional or sensorial aspects, as shown in Figure 4-3.

Figure 0-32: Criteria when selecting a skin moisturizer as assessed by the users

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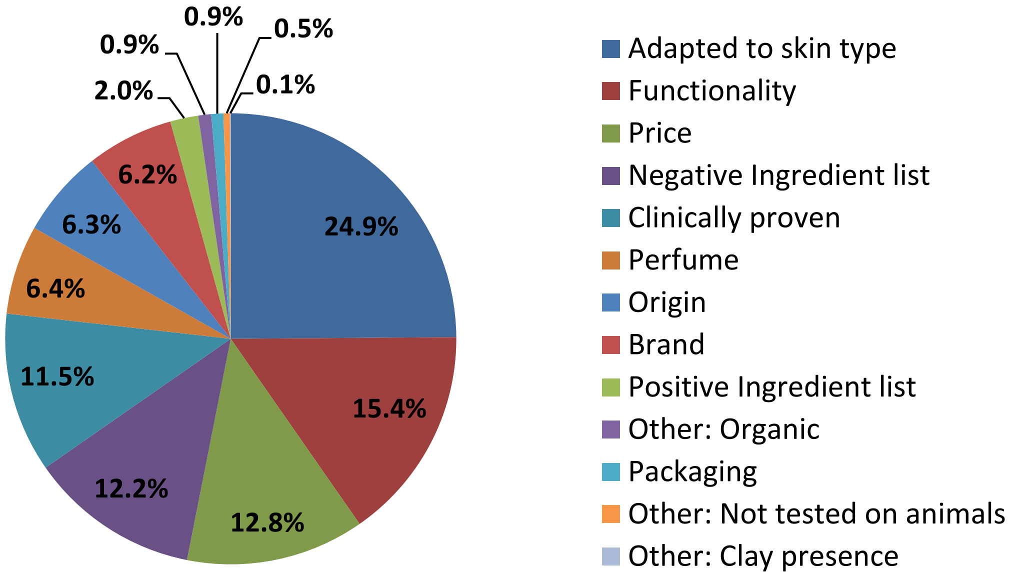
[6] http://www.foireinternationale-nancy.com/

[7] The data were used to complete a diagnosis test available online https://www.bioderma.fr/fr/club-bioderma/mes-diagnostics/diagnostic-corps?evolution=1

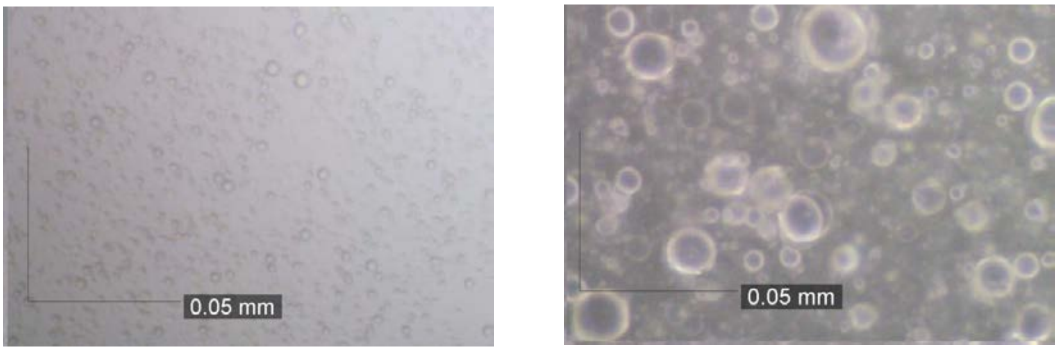


Regarding the second part of the test, the two skin moisturizers were commercially available products:

- Sample 1: Bioderma® *Atoderm* Ultra-nourishing Cream (France)
- Sample 2: NIVEA® Body cream Sun protection FPS 15 (Colombia)

These two products are suitable for body, face and hands use and intended for dry skin. From their ingredients list, it can be seen that they are both o/w emulsions stabilized using a combination of nonionic and anionic surfactants (Glyceryl Stearate and neutralized Stearic/Palmitic acids in both products), along with Cetyl Alcohol and polymeric thickeners. Nevertheless, they present different characteristics, both in their excipients and active ingredient composition and in their physicochemical properties. Sample 1 contains more than 15 different emollients (*Paraffinum Liquidum*, Cetearyl Isononanoate and Cyclopentasiloxane, etc.) and moisturizers (Xylitol, Mannitol, Rhamnose, etc.), while sample 2 has much fewer of these ingredients and includes some UV filters (Butyl Methoxydibenzoylmethane, Octocrylene, and Phenylbenzimidazole Sulfonic Acid). The complete list the ingredients contained in these two skin moisturizers is presented on Appendix E. From their appearance, Sample 1 could be classified as a cream and Sample 2 as a lotion (Iwata and Shimada, 2013). Under the microscope, both emulsions also look very different, the particle size for sample 1 being significantly smaller than for sample 2, as shown in Figure 4-4.

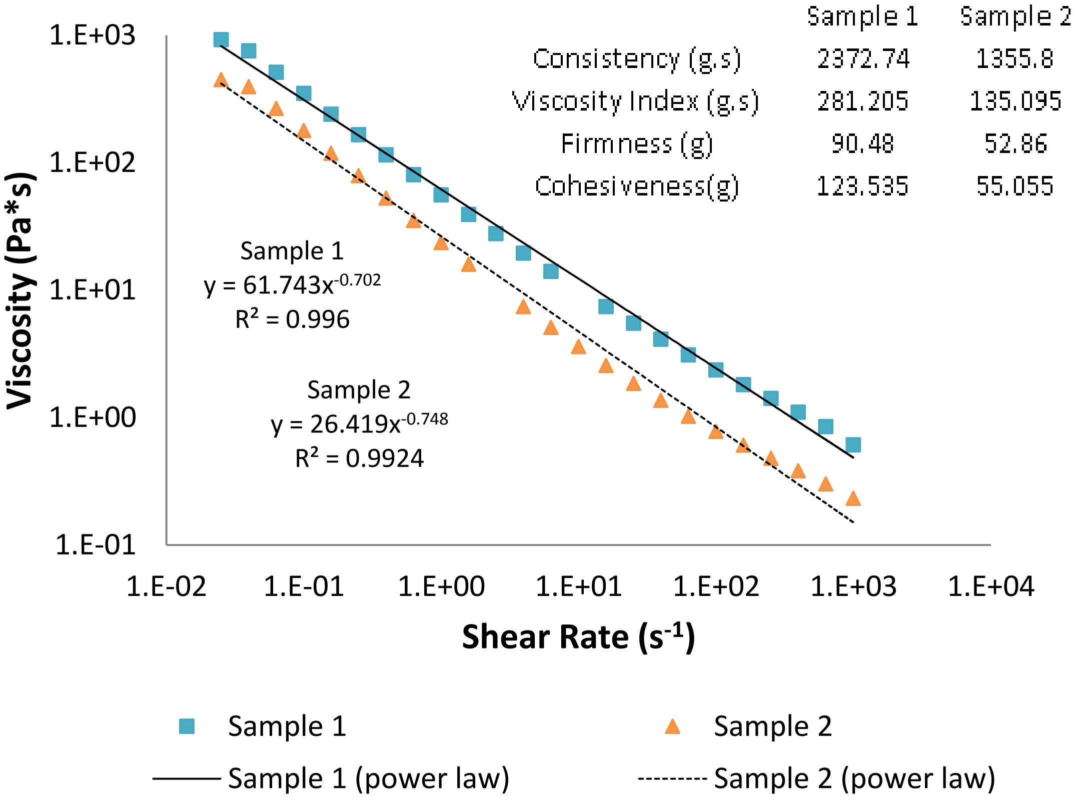
Figure 0-33: Photomicrographs of commercial samples (900X)



Sample 1 Sample 2

The rheological and textural profiles of the two samples are shown in Figure 4-5, confirming that sample 1 is much more viscous than the sample 2. These differences were also clear for the participants of the test, even if they were untrained consumers and had no common references of the attributes' scales. The ability of the regular consumers to find differences in cosmetic products has been reported before in other studies (Parente et al., 2011).

Figure 0-34: Rheological and textural profiles of the commercial samples in the usability tests



	Sample 1	Sample 2
Consistency (g.s)	2372.74	1355.8
Viscosity Index (g.s)	281.205	135.095
Firmness (g)	90.48	52.86
Cohesiveness(g)	123.535	55.055

Table 4-9 contains the resulting average values of each attribute. Collected data were verified in order to evaluate its consistency (correlation with the normal distribution above 0.92 for all attributes - see Appendix D).

Table 0-26: Average and variance parameters for the evaluated attributes

Attribute	**Symbol**	**Sample 1**		**Sample 2**	
		Mean	Variance	Mean	Variance
Thickness[a,b]	V	0.46	0.059	0.26	0.046
Spreadability[a,b]	S	0.75	0.028	0.84	0.032
Stickiness[a,b]	P	0.45	0.036	0.72	0.051
Ease of absorption[a,b]	A	0.35	0.055	0.61	0.105
Freshness[a,b]	F	0.31	0.040	0.45	0.052
Residues[b]	R	0.30	0.043	0.24	0.032
Greasiness/oiliness[a,b]	G	0.74	0.040	0.46	0.067
Moisturization[a,b]	H	0.61	0.039	0.73	0.042
Overall performance[a,b]	C	0.43	0.074	0.57	0.086
[a]Different mean, t test (p<0.05), [b]Same variance, F test (p>0.05)					

As it can be observed, the mean score for each attribute is different between the two samples, except for the “residues” score. Here it is important to mention that both samples had low values in the “residues” attribute score, which means that the emulsions left almost no residue or whitening.

In Table 4-10, the Shapley indices for each attribute computed from the fuzzy integral analysis are shown.

Table 0-27: Shapley index for the evaluated attributes

	V	**S**	**P**	**A**	**F**	**R**	**G**	**H**
Sample 1	1.05	0.35	1.19	**1.57**	**1.65**	**1.22**	0.38	0.59
Sample 2	**1.36**	0.34	0.85	0.94	**1.26**	**1.74**	0.82	0.68

The three highest values for each sample are marked in bold characters. From these results, it is possible to see that “freshness” is the most important attribute for Sample 1 (1.65), followed by “ease of absorption” (1.57) and “residues” (1.22). The first two attributes were poorly graded in the test (0.31 and 0.35 in Table 4-9, respectively), which suggests that the heavy emollience of the product could have an influence on the overall score. In fact, Sample 1 contains Mineral Oil, an occlusive ingredient that hinders water evaporation from the skin, which is usually related with a low freshness sensation (Parente et al., 2010). Regarding “residues”, the score (0.3) in Table 4-9 could indicate that having low quantity of residues after rubbing-out is one of the most important features for the consumers when rating the product. In the case of Sample 2, “residues” has the highest index (1.74) followed by “thickness” (1.36) and “freshness” (1.26). Among these attributes, “thickness” is also the lowest rated attribute (0.26 in Table 4-9), which could indicate that the sample 2 is perceived as not being thick enough, thus affecting the overall performance score of the product.

Table 4-11 contains the Murofushi and Soneda (total interactions) indices, for the two evaluated samples. The three highest values for each pair of attributes and also for the total interactions are marked in bold characters. It can be observed that the attribute “residues” is consistently interacting with other attributes and appears amongst the highest ranked attributes for total interactions in both cases (4.00 for Sample 1 and 4.02 for Sample 2). Noteworthy is that “residues” also has the highest values of mutual interactions; namely with “ease of absorption” (1.46) and “freshness” (1.15) in the case of sample 1, and with “thickness” (0.69), “stickiness” (0.97) and “moisturization” (-0.85) in the case of sample 2. The positive or negative sign means that the effect is synergistic or redundant, respectively (Grabisch, 1996).

Table 0-28: Interaction index among attributes (Murofushi and Soneda index)

		V	S	P	A	F	R	G	H	Total interactions
Sample 1	**V**	-	0.31	-0.30	0.10	0.13	0.51	0.10	0.15	1.60
	S		-	0.31	0.28	0.11	0.21	-0.14	-0.10	1.48
	P			-	0.41	-0.29	0.63	0.01	0.21	2.18
	A				-	**1.15**	**1.46**	0.81	-0.22	**4.44**
	F					-	**0.98**	0.06	0.85	**3.57**
	R						-	0.11	0.08	**4.00**
	G							-	0.03	1.27
	H								-	1.64
Sample 2		**V**	**S**	**P**	**A**	**F**	**R**	**G**	**H**	**Total interactions**
	V	-	0.39	0.00	-0.05	0.29	**0.69**	0.29	0.40	2.10
	S		-	0.04	0.05	0.20	0.37	0.02	-0.06	1.13
	P			-	-0.11	0.14	**0.97**	-0.58	0.55	2.39
	A				-	-0.15	0.52	0.47	0.27	1.62
	F					-	0.47	0.67	0.39	2.30
	R						-	-0.16	**-0.85**	**4.02**
	G							-	0.30	**2.49**
	H								-	**2.82**

Finally, the composite index, which integrates the normalized Shapley and Murofushi and Soneda indices, is presented in Table 4-12. In the case of sample 1, “ease of absorption” (0.29) and in the case of sample 2 “residues” (0.34), are the most important attributes under this metric. “Residues” and “freshness” had consistently one of the highest composites indices (0.20 and 0.25, for sample 1 and 0.34 and 0.14 for sample 2, respectively).

Table 0-29: Normalized values of Shapley (relative weights), Murofushi and Soneda (interactions) and composite indices.

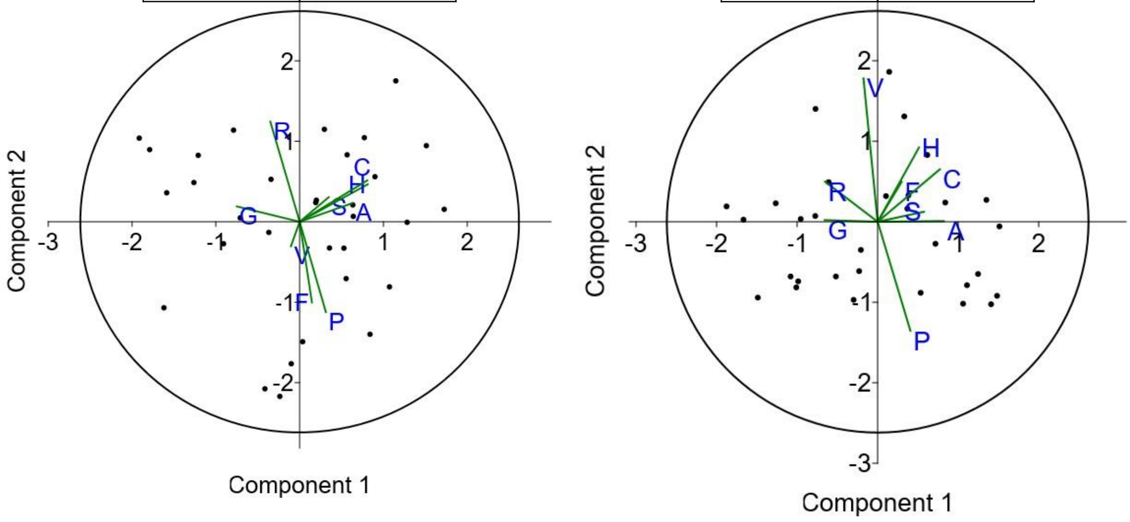
		V	S	P	A	F	R	G	H
Sample 1	Normalized relative weights	0.13	0.04	0.15	0.20	0.21	0.15	0.05	0.07
	Normalized interactions	0.08	0.07	0.11	0.22	0.18	0.20	0.06	0.08
	Composite index	0.07	0.02	0.11	**0.29**	**0.25**	**0.20**	0.02	0.04
Sample 2	Normalized relative weights	0.17	0.04	0.11	0.12	0.16	0.22	0.10	0.09
	Normalized interactions	0.11	0.06	0.13	0.09	0.12	0.21	0.13	0.15
	Composite index	**0.14**	0.02	**0.10**	0.07	**0.14**	**0.34**	**0.10**	0.09

The same data exploration was made using principal component analysis (PCA), as it is shown in Figure 4-6. Despite the percentage of variance explained by the principal components for both samples being slightly under 60% (Hair et al., 2009), some confirmatory trends can be observed, such as "residues" in Sample 1 or "thickness" in sample 2 being very close to the PC1, which accounts for 36% and 39% of the variance of data in each case, respectively. Nevertheless, this technique does not seem particularly helpful to elicit the most important attributes for the evaluated samples and does not shed any light about the interactions between them, when compared with the methodology here proposed.

Figure 0-35: PCA for the evaluated attributes

Sample 1	Variance
PC1	36%
PC2	18%

Sample 2	Variance
PC1	39%
PC2	17%



In the next section, it is shown how this information of the indices can be used to guide the selection of alternatives, based on the specific profile of each sample product.

4.3.2 Product realization phase

Starting from a generic basic cream formulation (Formulation K0-N0-M1), which solves the problem specified in Table 4-5 at a minimum cost, specific changes were made in order to comply with different attributes for the two evaluated samples (Cases 1 and 2). For this, additional heuristics from Table 4-6 were included in the algorithm as restrictions that allowed searching for feasible alternatives that increased or reduced the level of the aimed attribute. The resulting formulations are presented in Table 4-13. The name of the formulations was given according to the following parameters:

- The first letter indicates if the product is a cream (K) or a lotion (L), while the number corresponds either to the base case (0) or to the commercial samples (1 or 2)
- The second part also contains letters and numbers. The letter corresponds to the aimed attribute(s) - R for “Residues”, G for “Greasiness/oiliness” and V for “Thickness”, etc. - and the number is a counter for the sample at this stage.
- The last part indicates the manufacture procedure: M1 for Procedure I or M2 for Procedure II (see section 3.2.3.2)

In the end of this section a third case will be presented, in which a Pareto front is built to support the decision making for a tradeoff of three different goals (total cost, greasiness and hazard index).

Table 0-30: Alternative formulations manufactured

Phase	**Ingredient**	**Cost (USD/kg)**	**Skin moisturizers composition (w/w%)**								
			K0-N1-M1	**K1-R1-M1**	**K1-R2-M1**	**K1-R3-M1**	**K1-G1-M1**	**K1-R3-M2**	**K1-G1-M2**	**L2-R3V1-M1**	**K2-R3V1-M1**
A	**Water**		60.0%	60.0%	60.0%	60.0%	60.0%	76.5%	77.6%	60.0%	60.0%
	Xanthan gum (n1)	35	1.1%	1.1%	1.1%	1.1%	1.1%	1.1%	1.1%	0.6%	1.1%
B	**Cetyl Alcohol (m2)**	7.4	4.0%	4.0%	4.0%	4.0%	4.0%	4.0%	4.0%	4.0%	4.0%
	Polysorbate 60 (r1)	15.5	0.5%	0.5%	0.5%	0.5%	0.5%	0.5%	0.5%		
	Polysorbate 80 (r2)	15.0								0.5%	0.5%
	PEG-100 Stearate (r3)	9.8	1.5%	1.5%	1.5%	1.5%	1.5%	1.5%	1.5%	1.5%	1.5%
	Sorbitan Oleate (r4)	16.2								0.7%	0.7%
	Glyceryl Stearate SE (r5)	8.9		1.0%	1.0%	1.0%	1.5%	1.0%	1.5%	1.0%	1.0%
	Sorbitan Stearate (r6)	12.5	1.3%	1.3%	0.5%	0.7%		0.7%			
	Isopropyl Myristate (i4)	16.7	5.6%	5.6%	5.9%	6.8%	7.1%	6.8%	7.1%	6.7%	6.7%
	Paraffinum Liquidum (j7)	12.2	2.7%	2.7%	2.9%	3.2%	1.9%	3.2%	1.9%	3.1%	3.1%
	***Persea Grattisima* Oil (k2)**	16.7	1.0%	1.0%	1.2%	1.0%	1.0%	1.0%	1.0%	1.0%	1.0%
C	**Water**		18.6%	17.6%	17.7%	16.5%	17.6%			17.2%	16.7%
	Glycerol		3.0%	3.0%	3.0%	3.0%	3.0%	3.0%	3.0%	3.0%	3.0%
D	**Preservative (Cosgard)**		0.7%	0.7%	0.7%	0.7%	0.7%	0.7%	0.7%	0.7%	0.7%
		Total	100%	100%	100%	100%	100%	100%	100%	100%	100%
		Cost (USD/kg)	**2.50**	**2.58**	**2.60**	**2.77**	**2.63**	**2.77**	**2.63**	**2.61**	**2.77**
		Greasiness	**2.4**	**2.4**	**2.4**	**2.4**	**2.2**	**2.4**	**2.2**	**2.4**	**2.4**

4.3.2.1 Case 1 - Sample 1

All the manufactured products exhibited the expected creamy consistency of this type of cosmetic emulsions. All the samples were stable (no phase separation) after being centrifuged at 10000 rpm for 10 min. From the results obtained in the usability test of Sample 1, ease of absorption, freshness, and residues were the most important attributes by the composite index. Due to the high interaction between these attributes (see Table 4-11), and the fact that the base formulation left more white residues than the Sample 1 (Figure 4-7), the first change made to the algorithm was to implement one of the actions found to reduce the white residues by adding up to 2% low HLB emulsifier (see Table 4-6). As this action would not only lower the oil/surfactant ratio and allow HLB<RHLB but also increase the viscosity of the final formulation, a series of experiments were performed to understand how each change affected the emulsion properties, especially the viscosity and the white residue.

- Formulation K1-R1-M1 is essentially K0-N1-M1 + 1% Glyceryl Stearate. This could be considered a classical corrective action and is only chosen here to compare with a more systematic approach to solve the problem.
- Formulation K1-R2-M1 includes 1% Glyceryl Stearate but compensates with the addition of other emollients to keep the minimal oil/surfactant ratio (1:4) allow HLB=RLHB.
- Formulation K1-R3-M1 includes 1% of a low HLB surfactant and allows 0.5 ≤ RLHB-HLB ≤ 1.

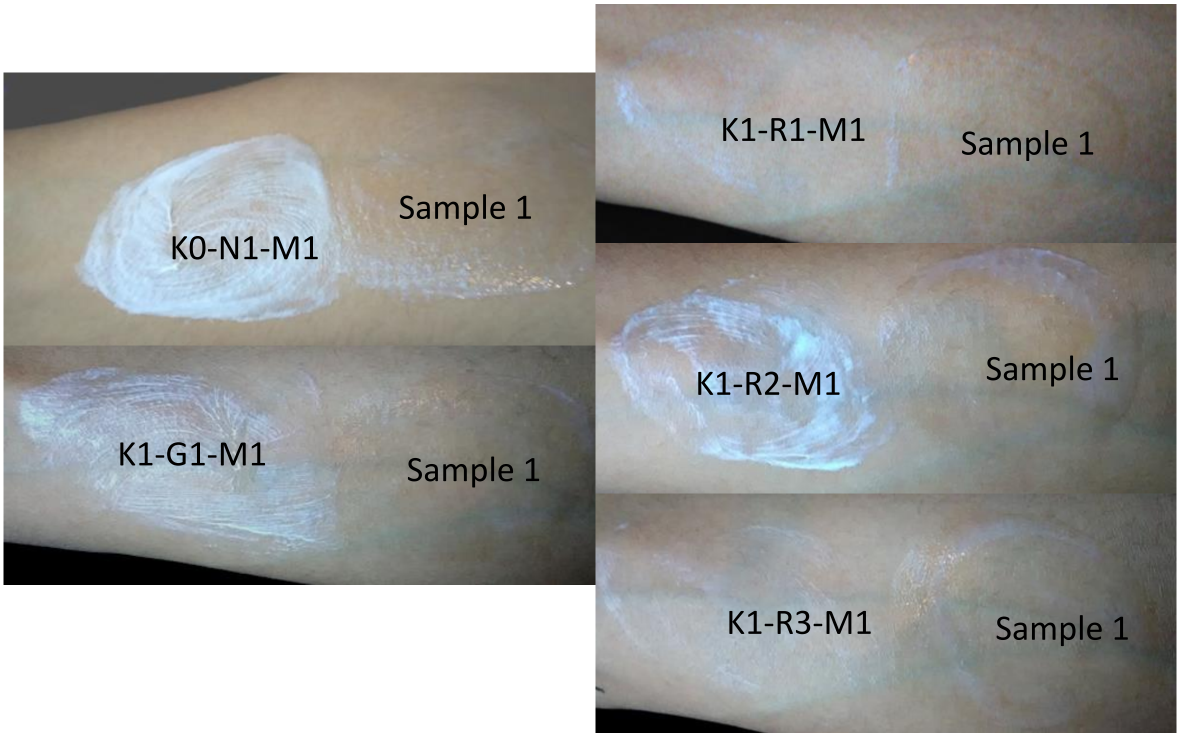
Then, another formulation K1-G1-M1 is made ignoring the attributes indices of the previous section and only taking into account the high value given to the attribute greasiness. This could be considered as an approach to generate alternative formulations, based on the consumer assessment but disregarding the importance and interactions of the attributes. In this example, the maximal value of γ in the algorithm was 2.2 instead of 2.4.

Two additional formulations following the manufacture procedure II were prepared, namely K1-R3-M2 and K1-G1-M2.

4.3.2.1.1 Residues

In Figure 4-7 are the white residues left by each one of the alternative formulations compared to Sample 1, according to the method described in section 4.3.2.3.

Figure 0-36: White residue of formulations in Case Sample M1

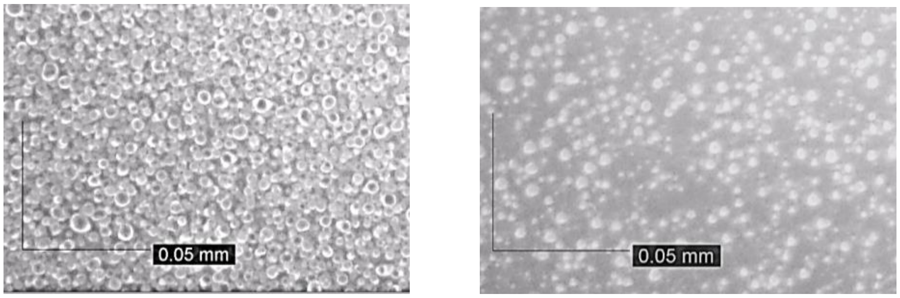


As it can be observed, the white residues of K0-N1-M1 are much higher than the Sample 1 formulation, while for the formulation K1-R1-M1 is very similar to the residues of sample 1, proving that the heuristic about adding a small amount of a low HLB surfactant would reduce the micro-foam generation. This was also the case for sample K1-R3-M1 but not for K1-R2-M1, which did not allow HLB<RHLB. Although K1-G1-M1 was trying to reduce the greasiness of the base formulation (K0-N1-M1), it also performed better in the white residues when compared to it. The use of different quantities of emollients also has an impact on the residues left by the product, as it has been said before.

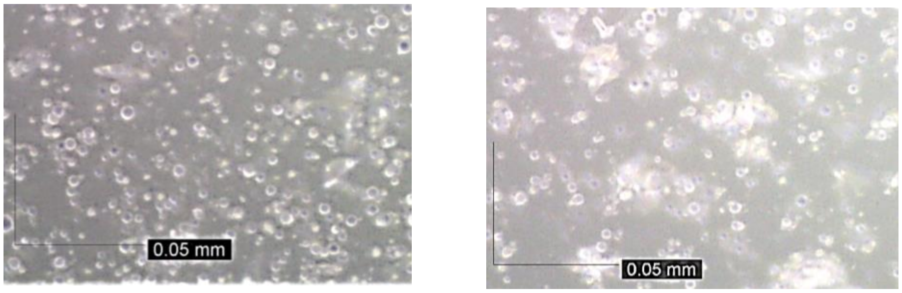
4.3.2.1.2 Microscopy

Representative optical microphotographs (900X) of the 5 sample emulsions following manufacture procedure M1 and the sample 1 are presented in Figure 4-8 and those with procedure M2 in Figure 4-9. It was observed that the base case (K0-N1-M1) had a very different microstructure, when compared to Sample 1. With droplet sizes around 5 µm. It should be noted that the most similar microstructure to sample 1 is the one of formulation K1-R3-M1. In the case of M2, it can be seen that the manufacture procedure M2 changes the microstructure of the emulsion, making the emulsions coarser. This phenomenon has been reported by other authors (Lin, 2010).

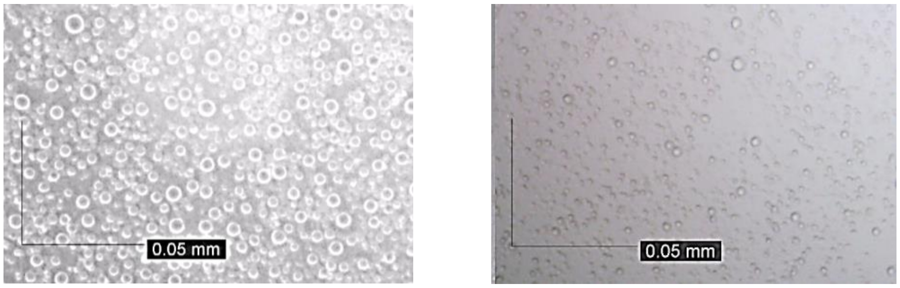
Figure 0-37: Microphotographs (900X) of samples in case Sample 1-M1



Formulation K0-N1-M1 Formulation K1-R1-M1

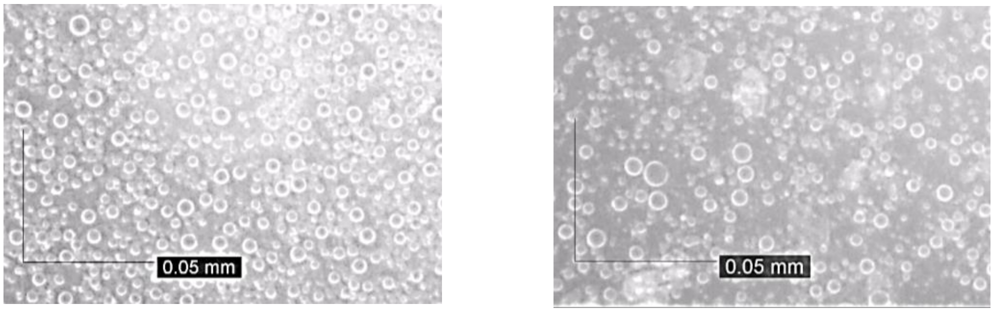


Formulation K1-R2-M1 Formulation K1-R3-M1

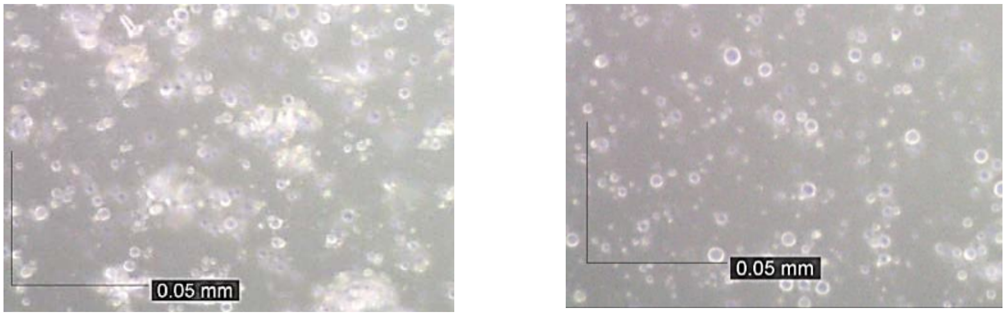


Formulation K1-G1-M1 Sample 1

Figure 0-38: Microphotographs (900X) of samples in case Sample 1-M2



Formulation K1-G1-M1 Formulation K1-G1-M2



Formulation K1-R3-M1 Formulation K1-R3-M2

4.3.2.1.3 Rheology and textural analysis

The rheological profile of these 6 samples is presented in Figure 4-10. Using the power approximation, the final viscosity η_2 was calculated for 5000 s^{-1}, lying between 0.023 and 0.5 Pa.s for all samples. All these formulations contain xanthan gum as thickening polymer, which confirms that the model for the prediction of the emulsion viscosity is in fact correct.

The parameters obtained from the textural analysis in all prepared sample emulsions are presented in Table 4-14. The alternative that comes closer to the rheological and textural parameters of Sample 1 is also K1-R3-M1. Although no sensorial tests were performed on these formulations, it has been reported that the textural parameters here evaluated do correlate well with the sensorial attributes of the final product. In particular, firmness is related to the tackiness as perceived by the user, and consistency, cohesiveness and index of viscosity all directly correlate with slipperiness (Lukic et al., 2012).

Figure 0-39: Rheological profile of the alternatives in Case Sample 1-M1

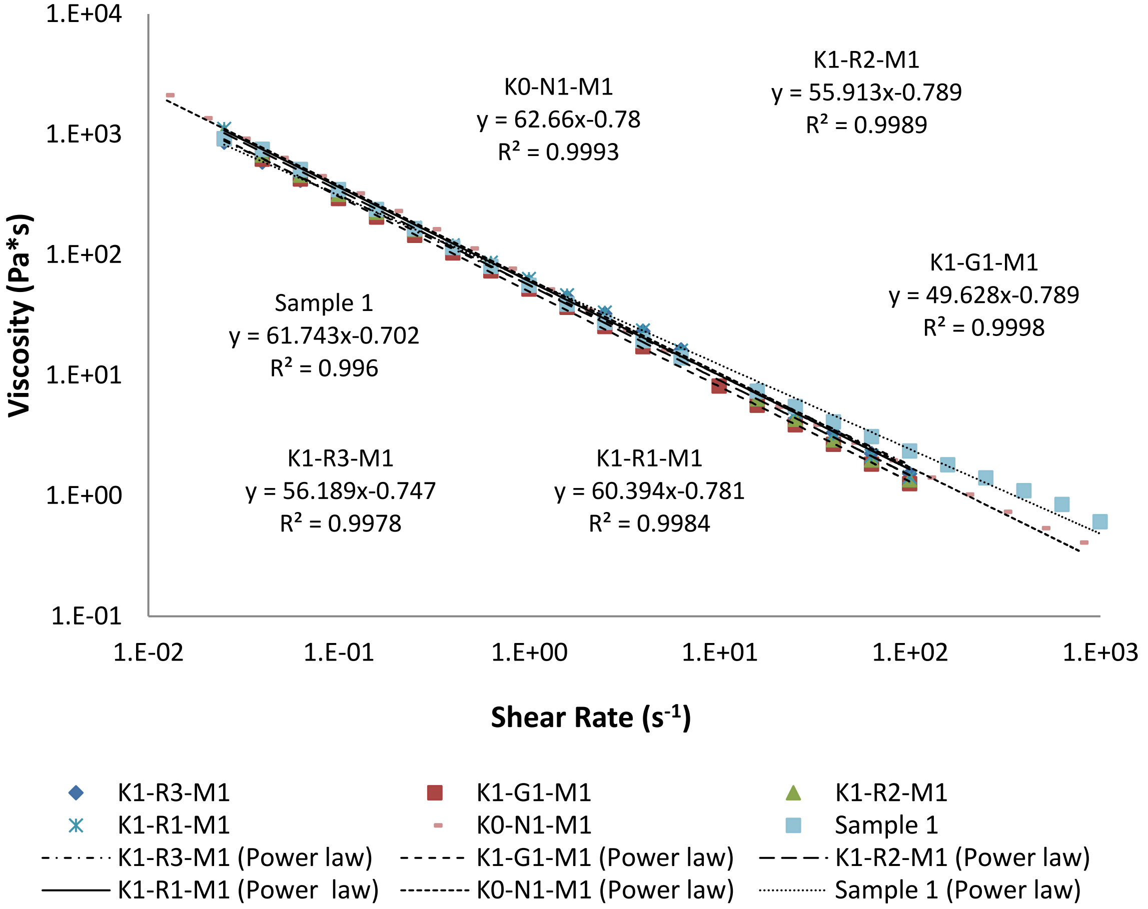


Table 0-31: Textural parameters of the alternatives in Case Sample 1 M1

	K0-N1-M1	K1-R1-M1	K1-R2-M1	K1-R3-M1	K1-G1-M1	Sample 1
Consistency (g.s)	3979.7	6711.4	5078.6	2131.4	6228.0	2372.7
Viscosity Index (g.s)	445.4	694.1	536.7	246.5	623.6	281.2
Firmness (g)	154.6	285.7	199.2	81.3	244.3	90.5
Cohesiveness(g)	199.1	403.0	245.2	105.8	289.0	123.5

Regarding the changes in the manufacture procedure, this also influences the rheological and textural properties of the emulsions, making the formulation K1-R3-M2 less similar to Sample 1, than the one produced following the Procedure I, as it can be seen in both Figure 4-11 and Table 4-15. Regarding the textural properties, it does not seem to be a clear trend on the impact of the manufacture procedure, as for K1-R3-M1 the values of the textural parameters increased but for K1-R3-M1 decreased.

Figure 0-40: Rheological profile of the alternatives in Case Sample 1-M2

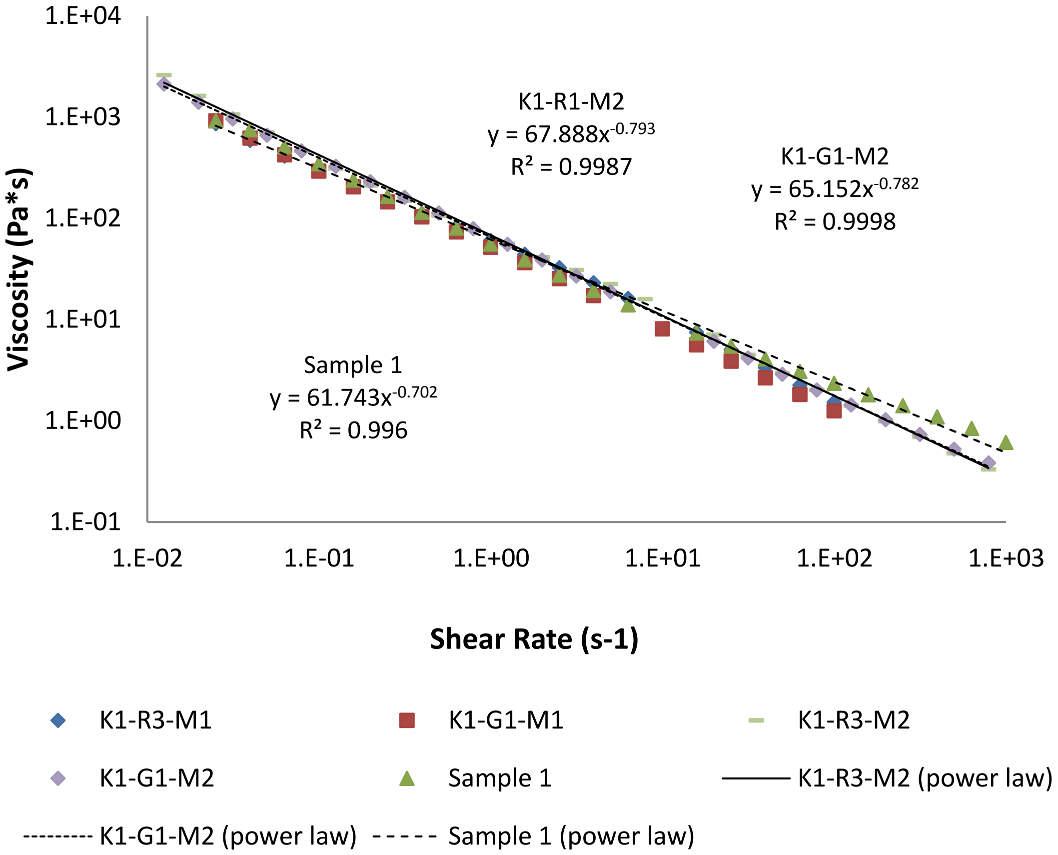


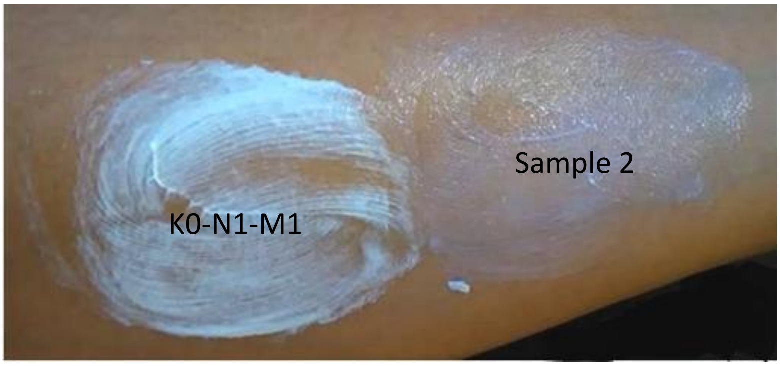
Table 0-32: Textural parameters of the alternatives in Case Sample 1 M2

	K1-R3-M1	K1-G1-M1	K1-R3-M2	K1-G1-M2	Sample 1
Consistency (g.s)	2131.4	6228.0	4845.5	4822.1	2372.7
Viscosity Index (g.s)	246.5	623.6	485.3	504.9	281.2
Firmness (g)	81.3	244.3	197.4	194.5	90.5
Cohesiveness(g)	105.8	289.0	228.7	221.6	123.5

4.3.2.2 Case 2 - Sample 2

For sample 2, the starting point is Formulation K1-R3-M1, as residues is the most important attribute too (0.34 in the composite index; see Table 4-12), and K0-N1-M1 left considerably more residues than Sample 2, as it can be observed in Figure 4-12.

Figure 0-41: White residue of formulation K0-N1-M1 vs. Sample 2



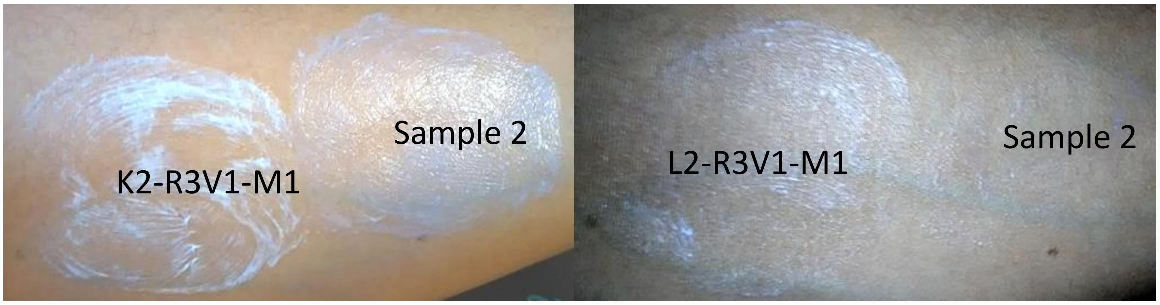
The next action was targeting the thickness, as there was no reliable action to correct and easily evaluate the change of the freshness attribute. Two different actions were taken, to understand if any of the actions led to a closer version of the commercial sample.

- Formulation K1-R3V1-M1, which comes from the action on the choice of the surfactants, preferring those having oleyl instead of stearyl groups (see Table 4-6).
- Formulation L2-R3V1-M1, which considers the same changes and also the viscosity parameters of a lotion (see section 3.2.1.3.)

4.3.2.2.1 Residues

The comparison of each alternative formulation with Sample 2 regarding residues is shown in Figure 4-13. Here, formulation L2-R3V1-M1, which had into account the residues and the two actions regarding the viscosity of the lotion (restrained values for final viscosity and emulsifiers with oleyl groups), had the best results when compared to the similar alternative K2-R3V1-M1, which only considered the change of the emulsifiers.

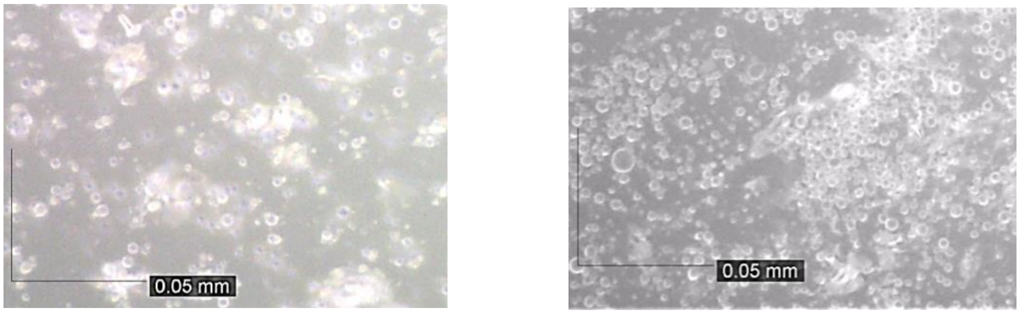
Figure 0-42: White residue of formulations in Case Sample 2



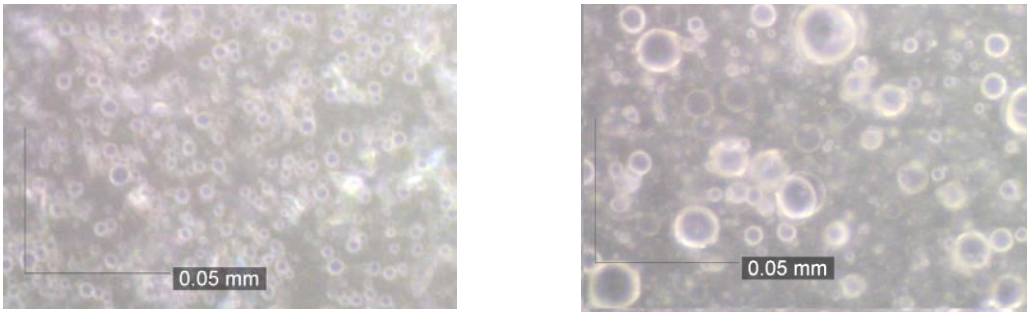
4.3.2.2.2 Microscopy

The microphotographs (900X) of the alternatives in the case of sample 2 are presented in Figure 4-14, showing that the base case (K1-R3-M1) had a very different microstructure, when compared to Sample 2, but the formulation L2-R3V1-M1 is much more similar.

Figure 0-43: Microphotographs (900X) of samples in case sample 2



Formulation K1-R3-M1 Formulation K2-R3V1-M1



Formulation L2-R3V1-PI Sample 2

4.3.2.2.3 Rheological and textural analysis

The viscosity of these four alternatives at different exerted shear rates is presented in Figure 4-15. Using the power approximation, the final viscosity η_2 was calculated for 5000 s^{-1}, lying between 0.023 and 0.5 Pa.s for all samples. In this case it is possible to observe the value of η_1 for the Formulation L2-R3V1-M1 and the sample 2, which lie between the ideal limits for lotions (120000 - 350000 Pa). Regarding the textural properties, both formulations (L2-R3V1-M1and K2-R3V1-M1) also have very similar values when compared to Sample 2, as shown in Table 4-16.

Figure 0-44: Rheological profile of the alternatives in Case sample 2

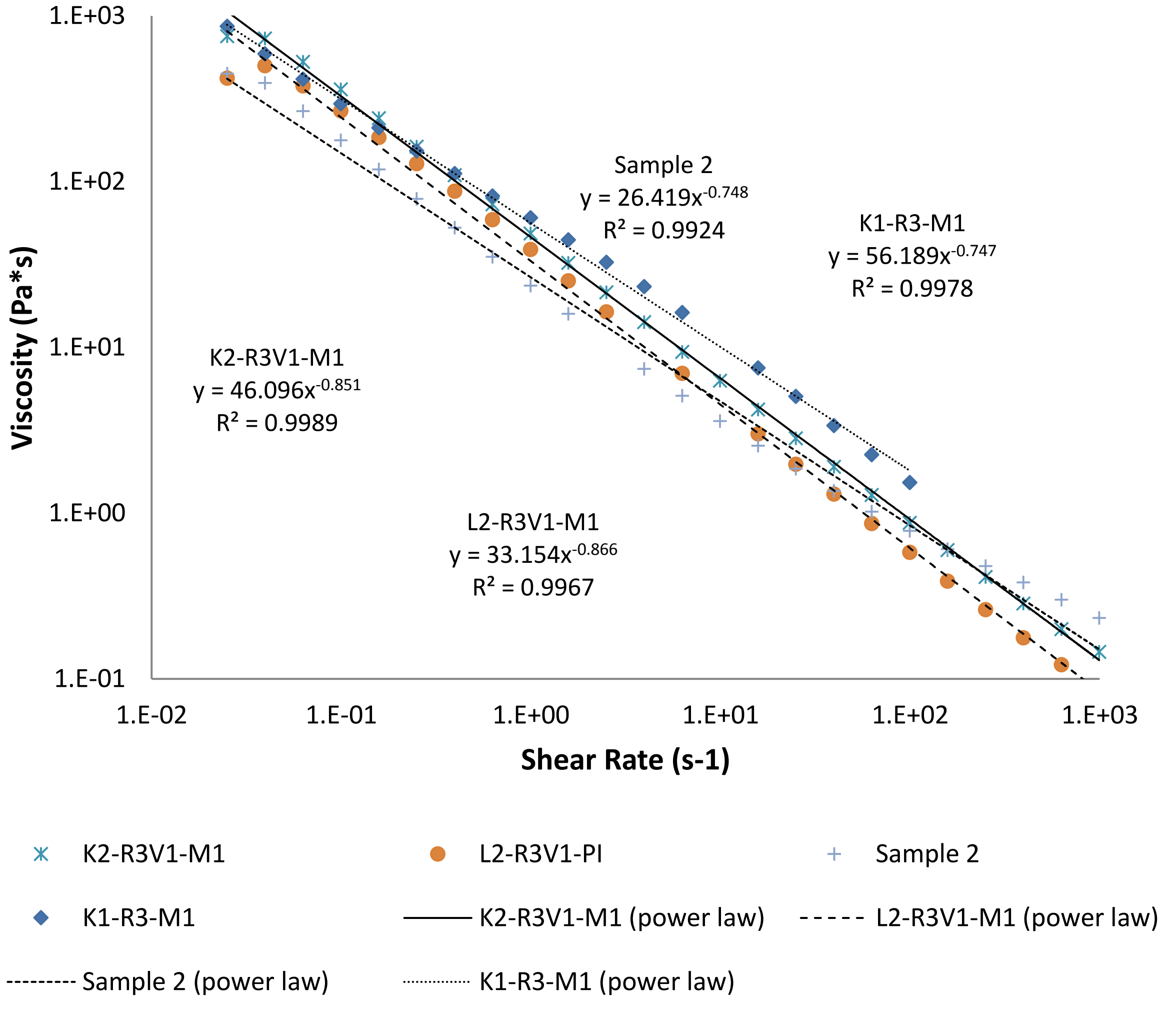


Table 0-33: Textural parameters of the alternatives in Case sample 2

	K1-R3-M1	L2-R3V1-PI	K2-R3V1-M1	Sample 2
Consistency (g.s)	2131.4	1929.3	2020.6	1355.8
Viscosity Index (g.s)	246.5	204.7	227.9	135.1
Firmness (g)	81.3	73.3	78.7	52.9
Cohesiveness(g)	105.8	89.6	98.6	55.1

4.3.2.3 Case 3 - Multi-objective approach

Besides product greasiness and cost, a third feature - hazard score - was brought here to illustrate how a multiobjective optimization could be implemented in this context. Hazard score[8] is an indicator, which rates cosmetic ingredients based on their data availability and the number of studies available in the open scientific literature. The ratings are given on a numerical scale from 1 to 10, 10 being the most "dangerous" (see Figure 4-16). The EWG's *Skin Deep Database* was created to be a helpful tool to empower the consumers and is among the most popular resources as a cosmetic safety reference in America. It is important to mention that the choice of this particular indicator is merely practical, as it is a numerical score fitting the purpose of the example.

Figure 0-45: Hazard score as proposed by EWG (2018)

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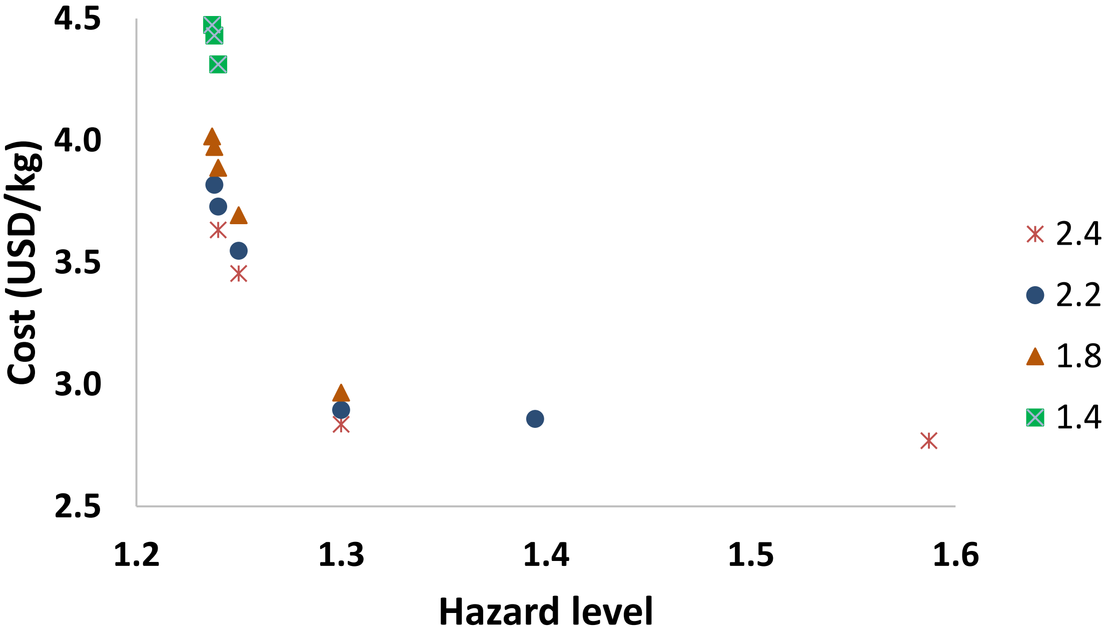
[8] . The ratings reflect potential health hazards but do not account for the level of exposure or individual susceptibility, factors which determine actual health risks, if any https://www.ewg.org/skindeep/

The original problem was formulated with the specification of a fixed greasiness value γ between 1.4 and 2.4 and a hazard score (*HS*) up to 1.6. All optimal solutions converged to the upper limit (more “dangerous” ingredients and “greasy” emollients are cheaper). A Pareto curve showing the hazard score/cost trade-off for different greasiness values may thus be constructed solving the problem with the constraint $0 \leq \mathrm{HS} - 1 \leq \varepsilon$ for decreasing values of ε. Such a curve is shown in Figure 4-17 with values of ε between 0.24 and 0.58. All points in the figure correspond to optimal solutions that have converged to $HS - 1 = \varepsilon$. These results may be read as the additional cost one would have to pay for a product with a lower hazard score, depending on the desired greasiness value. For example, taking a greasiness value of 2.4 as a base, the minimal HS is 1.58. If now the greasiness value is set to 1.4 and it is desired to reduce the HS to 1.24, the minimal cost for a formulation would increase 65%, from 2.77 to 4.48 USD/kg. Indeed, a formulation with “less greasy” and “safer” ingredients excludes the use of Mineral Oil ($\gamma = 3.8; HS = 3$), which is cheaper than emollients with lower values of greasiness.

Figure 0-46: Pareto curve of product greasiness *vs.* hazard score *vs.* cost



4.4 Conclusions

We have proposed an optimization-based methodology for the design of formulated products, which incorporates the consumer assessment along with available heuristic rules to generate alternatives of formulations. The methodology was applied to two commercial samples of skin moisturizers, being generated a series of alternative solutions that correspond to the consumers’ expectations with minimum ingredient costs in each case. These computer-generated solutions were then manufactured and evaluated. The rheological, textural and microstructural properties, along with the amount of white residues of the alternative formulations that integrated the information provided by the usability tests, are more similar to the respective samples, from which the information came in the first place.

As this methodology involves the participation of untrained consumers, it is possible to reduce the time and resources spent in cosmetic emulsions design compared with sensorial panels, as there is no panel training involved. Compared to other quantitative techniques used to identify statistical contributions of the attributes (degree of importance) or correlation among them, like PCA, this methodology allows to calculate the importance and the interaction of the evaluated attributes, which makes it valuable to the designer. This suggests that this is a useful methodology not only to gather information about consumers’ perception of the sensory characteristics of cosmetic products, but also to guide the generation of alternatives for other formulated products.

5. Conclusions and future work

The main purpose of this work was to propose a systematic methodology for the design of chemical-based products. For this, consumer-oriented formulated products have been considered, with focus on cosmetic emulsions. This research introduced a methodology to find a set of plausible formulations for emulsified cosmetic products, based on a fuzzy integral analysis of the consumer preferences, integrated to a mixed-integer optimization tool that incorporates available heuristic rules and property models.

In the first chapter, a classification of the current contributions in the field of chemical product design methodologies was presented. Particularly, the key research opportunities in integrative methodologies, which involve mathematical modelling and experiment based components, product-process interactions, multi-scale and multidisciplinary approaches (consumer perception, business variables and sustainability) at different combinations were highlighted. This classification could facilitate the task of creating new systematic integrated methodologies for formulated products, as only few methodologies have proposed an integration covering the different levels (experience/modelling, product/process and multiscale/ multidisciplinary approaches) and sublevels presented in this study. Considering the opportunities regarding integrated methodologies for formulated product design, this research concentrated in incorporating the consumer insight and business decision variables along with hybrid experience/modelling tools to guide the product/process design of cosmetic emulsions, as it exists a large collection of available heuristic knowledge and property models in this field, which had not been included in a systematic methodology for formulated product design.

In that sense, in the next chapters, the main features related to the consumer assessment and the modelling of emulsified cosmetic products, combining a classical approach of cosmetic product development (concept definition and product realization phases) with a conceptual framework for chemical product design (quality, property and process functions) were introduced. Using hair conditioners as an example, an optimization-based methodology for the design of formulated products, which explicitly incorporates available knowledge about product performance and ingredients selection was proposed. These heuristic rules were initially stated as logical constraints and then translated into algebraic restrictions using binary variables and propositional logic, and then combined with suitable property models to find a solution that fulfill the expected properties with minimum ingredient costs, i.e. realize a product by simultaneously inverting the product and process functions. A set of these computer-generated alternative formulations were manufactured and tested (rheological, textural and microstructural properties), showing that most of them could serve as a starting point for a reformulation or a new product development.

Then, in order to define the product concept, a methodology based on usability tests and fuzzy integral analysis was proposed to identify the most important attributes and their interactions, and include the quality function in the previous modelling. The output of the concept definition phase was transformed into additional heuristics that guided the selection of the alternatives in the product realization phase. To illustrate this, the methodology was applied to two commercial samples of skin moisturizers, generating a series of alternative solutions that corresponded to the consumers' expectations with minimum ingredient costs in each case. Their rheological, textural and microstructural properties, along with the quantity of white residues of the alternative formulations showed that by integrating the consumers' perception provided by the usability tests, it is possible to obtain similar prototypes, when compared to the commercial samples. This methodology could be then well adapted to accelerate reformulation or benchmarking processes.

As the proposed methodology involves the participation of untrained consumers and a computer-assisted alternative solutions generation, it was thus demonstrated that is possible to reduce the time and resources spent in traditional cosmetic emulsions design, which uses long cycles of trial-and-error methods and usually needs costly sensorial panels. This suggests that this is a useful methodology not only to gather information about consumers' perception of the sensory characteristics of the products, but also to incorporate this information to guide the generation of alternative formulations in an integrated methodology for cosmetic product design. Although this general methodology was illustrated using hair and skin-care emulsified products as examples, it could be used for more types of chemical products, being particularly appropriate when for multi-species consumer-oriented products.

5.1 Limitations and perspectives

As this is a first approach to an integrated methodology for formulated products, it is difficult to cover in detail all the aspects of the problem. Here, some limitations to this contribution will be highlighted in order to shed some light on the future work that could derivate from it.

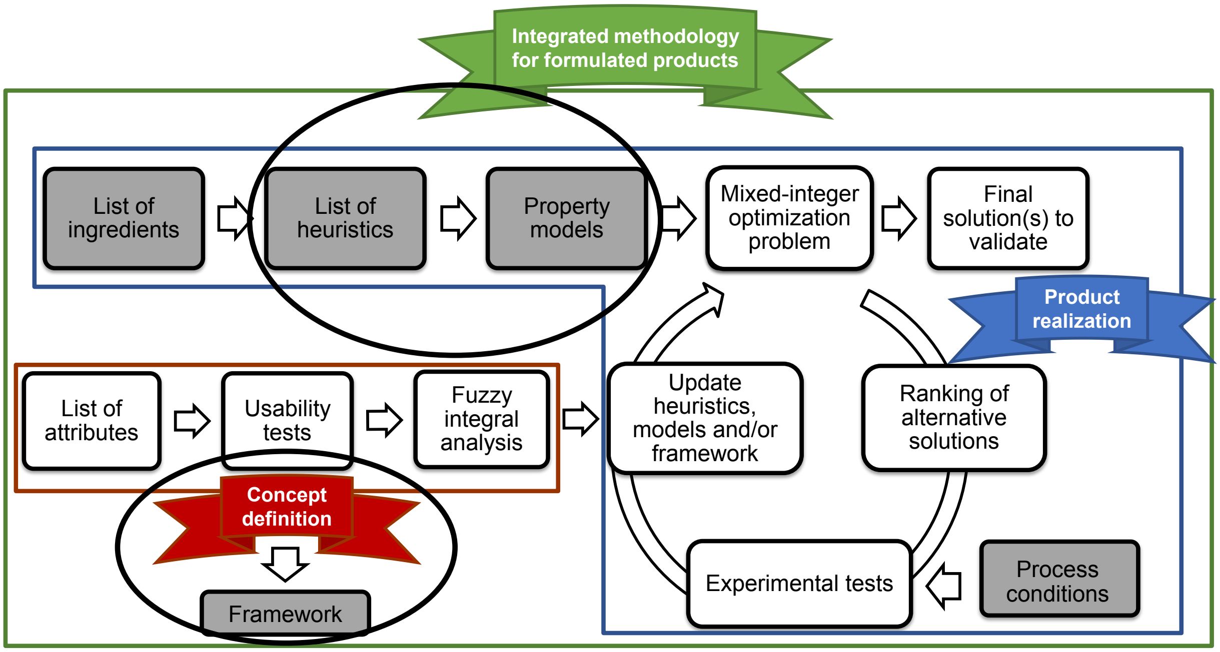
Regarding the integration of the different levels and sublevels, this methodology considered the consumer insight and business decision variables along with hybrid experience/modelling tools to solve the product design problem. Nevertheless, other variables, such as the selling price or the demand of the product to be launched, need to be considered in a competitive market too (Bagajewicz, 2017; Chan et al., 2018). Also, the inclusion of sustainability and/or multiscale dimensions in new fully integrated methodologies continues to be of the main challenges for chemical product design.

In the concept definition phase, the treatment of the semantic attributes resulting from the Kansei process could be refined by using clustering algorithms to make more robust the selection process of the initial terms. Another topic is the translation of the consumer needs into product properties with target values and boundaries of acceptance. Here we considered some correlations that have been reported between the consumer attributes and rheological and textural properties of the products, but additional efforts should be made to establish reliable quantitative relations between these factors.

When designing an emulsion, it is also recommended that the manufacturing process is designed simultaneously within the product realization phase. In this contribution we considered the interaction of the processing conditions when manufacturing the formulations in the experiment tests, but the impact of other variables (such as the processing temperature) should also be studied. If, for example, different processing temperatures are pondered, some properties of the emulsifiers at the interface change, increasing or lowering its HLB value (Förster et al., 1995). In this case, the HLB approach is insufficient and would require the adoption of other concepts, such as PIT (Förster et al., 1992) or CAPICO (Rieger and Rhein, 1997). Also, the consideration of "natural" cosmetic emulsions could be of particular interest, due to the greater demand of this type of products by the consumers. However, this might be challenging, as only a limited number of ingredients for natural products are available, and the impact they have on properties such as "residues" will require further research to be optimized (Huber, 2017).

In what concerns the general methodology itself, some improvements could also be made. For example, in this contribution the framework (ingredients and process conditions) was predefined to O/W emulsions, but it could be enlarged and be integrated with the product concept definition. For this, not only the list of ingredients and the process conditions but also the heuristics and the property models should be encompassed within the framework, depending on the results of the concept definition phase, as shown in Figure 5-1.

Figure 0-47: Integrated methodology for formulated products



Finally, from a global perspective, the recent advances achieved in other fields could be included in future studies:

- Synesthesia, understood as the perception of an experience obtained by stimuli that are not normally associated with this experience (Stein, 2012), presents a great opportunity for innovative concepts in the field of cosmetics, by the application of neuro-scientific techniques, such as electromyography, electrodermal activity, heart rate, blood pressure, biometrics, facial expression analysis, augmented and virtual reality, among others (Guzman Alonso and Jiménez, 2018; Jiménez et al., 2016).
- Industry 4.0 appears also as a promising area, in which various digitalization technologies will connect, model and automate design, manufacturing and supply chains systems (AceForm 4.0, 2017). Through IoT (Internet of things), for example, a greater access and sharing of data across the supply chain (from the raw material providers up to the consumer) could be attained ("Industry 4.0 Top Challenges for Chemical Manufacturing," 2017).

A. Integrated chemical product design methodologies

Number	Main contribution	Challenges and Opportunities	Integration level and sublevel*			Reference
			EM	PP	MS/MD	
1	Microeconomics influences product design: pricing, supply and demand. A model to predict consumer preference for skin moisturizing lotions. This model allows to distinguish the formulation that leads to the consumer most preferred skin lotion from the most profitably one in a quantitative fashion. In the latter case, the selling price is also determined simultaneously with the optimal formulation.	Process variables incorporation and inclusion of subjective consumer attributes.	EM		CO, BU	(Bagajewicz, 2007)
2						(Bagajewicz et al., 2011)
3	An optimization-based methodology that conceptualizes the problem of simultaneous product and process design; handles both parameter and model uncertainties; rationalizes optimal decisions in face of the actual level of uncertainty and identifies the problem levels whose uncertainty reduction is more valuable. The problem formulation integrates product quality, as assessed by customers, a model predicting lotion viscosity as a function of its composition and a process model linking process design and operation with lotion composition and microstructure.	Inclusion of consumer subjective attributes	EM	PP	CO	(Bernardo and Saraiva, 2004)
4						(Bernardo and Saraiva, 2005)
5	5 product design domains: Product Manufacturing Process, Product composition and structure, Product use conditions, Product performance (Performance metrics through constitutive and operational properties) and Product Quality. These domains are related to 3 basic design functions: Process function, Property function and quality function.					(Bernardo et al., 2007)
6						(Bernardo and Saraiva, 2015)
7	Methodology composed of 9 levels of increasing degree of complexity where decisions are made to proceed from one level to another, while stressing the relevance of modeling towards more time- and cost-effective process synthesis. The whole design methodology spans from how the new product can enlighten the consumer, financial and supply chain boundary conditions, through an optimal flowsheet able to produce the desired product cost effectively.	Experimental component is missing		PP	CO, BU	(Bongers and Almeida-Rivera, 2009)
8						(Bongers and Almeida-Rivera, 2012)

*EM = Experience/modelling; PP = Product/Process; MS/MD = Multi-scale/Multidisciplinary; CO=Consumer; BU= Business; SU=Sustainability

Number	Main contribution	Challenges and Opportunities	Integration level and sublevel*			Reference
			EM	PP	MS/MD	
9	An algorithm that includes the property contributions predicted by combined group contribution and connectivity indices methods (GC+ technique) into the cluster space, as a solution of property based molecular design problems. The developed algorithm has the ability to combine a variety of property models based on group contribution expressions and topological indices based QSAR/QSPR's. It utilizes molecular property operators formed from signatures to solve the reverse problem of obtaining the molecular structures that satisfy the property targets estimated during the process design step.	Limited to properties for which group contribution models are available. Different topological indices in the reverse problem.	EM	PP	BU	(Chemmangattuvalappil et al., 2010a)
10						(Chemmangattuvalappil et al., 2010b)
11	An integrative approach, involving marketing and management issues on the business side, and product design and prototyping on the technical side, is proposed for the development of chemical-based products. For the former, objective-time chart, RAT2IO modules and workflow diagrams are used for project management. For the latter, the integration of experiments, modeling and synthesis expedites product conceptualization and prototyping.	Process variables incorporation	EM	PP	CO, BU, SU	(Cheng et al., 2009)
12	The emphasis is put on the connection between customer preference, product quality, corresponding product attributes/technical specifications, as well the economic benefits such as product pricing, product sales profit, predicted market share, initial capital investment, and operating cost. This study proposes the major economic analyses and related activities to be carried out at the early stage of product development. The proposed economic analysis in this study would assist, or sometimes alter, the decision on both what to make and how to make.	Further investigate the sensitivity of the target price of the new product on economic returns.				(Cheng et al., 2016)

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Number	Main contributions	Challenges and Opportunities	Integration level and sublevel*			References
			EM	PP	MS/MD	
13-18	These works highlights new features of the virtual process-product design lab (VPPDL), which handles the design of mixtures and formulated products, by integrating modeling and experiments. The VPPDL software is based on this decomposition strategy and is crucial to trim down the number of experiments, reducing the resources invested and shortening the product development time. The problem of non-availability of data has been overcome with the generation of pseudo-data with a GC based model. The product design problem consists of 3 stages: computer-aided design (Stage 1), which generates a list of feasible candidates, experimental planning (Stage 2), which generates a list of experiments and checks the available experimental set-ups, and experimental testing (Stage 3), which measures the necessary data and verifies the desirable attributes of the final product.	Quantify (if possible) sensorial factors and cosmetic properties (appearance, turbidity, odor, skin feeling, stickiness, etc.)	EM	PP		(Conte et al., 2012, 2011a, 2011b, 2010, 2009a, 2009b)
19	Provide a review of the scope of chemical product engineering by discussing its emergence within chemical engineering. The idea of a chemical product pyramid is introduced in this article to systematize the relationships between the product recipe, materials' physicochemical properties, process variables, product structural attributes, usage variables and product quality factors.	Convert customer needs to technical specifications; modeling and optimization approaches for chemical product design; predictive capabilities for physical properties; systematic approaches supporting chemical product design.	EM	PP	CO, BU, SU	(Costa et al., 2006)

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Number	Main contributions	Challenges and Opportunities	Integration level and sublevel*			References
			EM	PP	MS/MD	
20	A computer-aided modeling framework capable of handling the modeling needs for product-process design and analysis. The systematic and efficient development of multi-scale models, their interconnections, analysis, parameter regression and solution through the modeling framework.	Adding a mass transfer model to improve the model performance.	EM	PP	MS	(Heitzig et al., 2010)
21	8 steps methodology for functional products design: (i) product definition with an analysis of customer needs; (ii) technical product requirements; (iii) product performance relationship and derivation of property prediction models; (iv) product candidate generation; (v) product candidate selection; (vi) process design; (vii) risk analysis; and finally (viii) business case analysis	Methodology for structured products, especially for design problems where complete data are unavailable.		PP		(Hill, 2009)
22	A knowledge-based collaborative platform for translating the product requirements and providing decision support to formulators in their attempt to select the most appropriate formulae. A knowledge-based artificial intelligence technique, namely case-based reasoning that utilizes the knowledge gained in solving similar past cases.	Integration of fuzzy logic to help formulators determine the quantitative values of the parameters, such as time and temperature, for developing chemical products.			CO	(Lee et al., 2014)

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Number	Main contributions	Challenges and Opportunities	Integration level and sublevel*			References
			EM	PP	MS/MD	
23	The problem becomes a multi-objective optimization that is solved using the e-constraint method with global optimization techniques to minimize of the environmental impact while minimizing the production cost for a couple of case studies The complexities in the models that describe the performance or process constraints may result in non-global optimal solutions and thus we have to evaluate the best model for the different constraints which has the accuracy needed but which does not add further complexities.	Process constraints such as slurry viscosity and density, ingredients mixing and agglomeration constraints or finishing requirements for better customer acceptance such as perfumes or aesthetics can be added which will help design the best product with the lowest cost.	EM	PP	CO,BU,SU	(Martín and Martínez, 2013a)
24						(Martín and Martínez, 2013b)
25	The methodology consists of a model-based framework involving 7 sequential hierarchical steps: starting with the identification of the needs to be satisfied by the product and then adding one-by-one the different classes of chemicals, until a formulation is obtained. Structured databases, appropriate pure component as well as mixture property models, rule-based selection criteria and CAMD techniques are employed together to obtain one or more candidate formulations, which satisfy the desired needs (target properties).	Virtual formulation design and verification of emulsified products.	EM	PP		(Mattei et al., 2012)
26			EM	PP	CO	(Mattei et al., 2013a)

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Number	Main contributions	Challenges and Opportunities	Integration level and sublevel*			References
			EM	PP	MS/MD	
27	A systematic analysis of the model performance against experimental data is carried out using data for a wide range of nonionic surfactants covering a wide range of molecular structures. The group parameter estimation has been performed using a data set of experimental measurements covering a large variety of nonionic surfactants including linear, branched, and phenyl alkyl ethoxylates; alkanediols; alkyl mono- and disaccharide ethers and esters; ethoxylated alkyl amines and amides; fluorinated linear ethoxylates and amides; polyglycerol esters; and carbohydrate derivate ethers, esters, and thiols.	The addition of a temperature-dependent term. Extension of the data set, possibly by considering measurements indirectly obtained through the observation of the same physical properties.	EM	PP	CO	(Mattei et al., 2013b)
28	The mathematical formulation of a standard product design problem is presented, together with the list of both the pure component properties (related to nonionic surfactants) and the mixture properties (relevant to the overall products as emulsions) needed for the solution of the design algorithm. Predictive models for properties such as the density, the viscosity, the surface and the interfacial tension, but also the type of emulsion expected (through the hydrophilic–lipophilic balance), and its stability (through the hydrophilic–lipophilic deviation), forming a robust chemical product design tool.	Development of group-contribution methods for the pure component properties of ionic surfactants (adequate new first order groups are needed). Development of predictive, reliable models able to efficiently describe both the binary and the ternary phase diagrams involving surfactants.	EM			(Mattei et al., 2014a)
29	List of consumer assessments and target properties. The model libraries, the structured databases and the generic workflow are integrated through product design ontology, developed to represent the associated knowledge.	Stability issues such as the verification of the solubility of the ingredients in the solvent mixture and the verification of the stability of the formulation as an emulsion are needed.	EM	PP	CO, BU	(Mattei et al., 2014b)

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Number	Main contributions	Challenges and Opportunities	Integration level and sublevel*			References
			EM	PP	MS/MD	
30	A framework, which allows the user to cover a wide range of problems at different scales (of length and time) and disciplines of chemical engineering and science in an easy and efficient manner; achieving in this way the development of a product-process with the desired end-use characteristics. It is a combination of different computational tools, such as, property prediction packages, modeling tools, simulation engines, solvent selection software, etc.	Reliable multiscale models must be available in a model-library and used through an appropriate model-based framework, that can also help to generate models, when they are not available.		PP	MS, CO BU	(Morales-Rodríguez and Gani, 2009)
31	Multiscale objective-oriented process synthesis and development (MOPSD) relates business decision-making to the design and development of products and processes. Business decisions are made in a hierarchical manner, from corporate goals, marketing decisions, product design, to plant design and development. To implement such a framework, the RATIO concept is introduced. The objective, information, tools, time needed, activities, and human and monetary resources for completing each step of the business project are identified.	The gap between business personnel, and chemists and chemical engineers within the company has to be narrowed to produce the right product, improve product quality, lower production cost and reduce time-to-market.		PP	MS, CO, BU	(Ng, 2004)
32	This paper introduces a novel methodology in chemical product design by incorporating fuzzy and bi-level optimization into the molecular design techniques. By incorporating fuzzy optimization into the methodology, property weighting factors in a multi-objective optimization problem are able to be addressed systematically without bias and the optimal product can be identified. Bi-level optimization is utilized to determine the property target ranges which are undefined.	Uncertainty of property models. Sensitivity analysis on the property target ranges.	EM	PP	CO, BU	(Ng et al., 2014a)

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Number	Main contributions	Challenges and Opportunities	Integration level and sublevel*			References
			EM	PP	MS/MD	
33	A novel methodology is developed for the design of optimum molecules used in chemical processes by considering and optimizing both property superiority and robustness. Fuzzy optimization approach is extended in this work to address and trade off property superiority and robustness simultaneously.	Extend to the design of mixtures or blends, such as formulated products.	EM	PP	CO, BU	(Ng et al., 2014b)
34	Summarizes Integrated Product/process CAMD methodologies. Current challenges and future opportunities in the field of chemical product design using computer-aided molecular design (CAMD) tools are highlighted.	The estimation of property related to structured products as well as non-organic compounds needs to be explored.	EM	PP	MS, CO, BU, SU	(Ng et al., 2015)
35	This methodology starts with defining needs for a new product and generating ideas. It then screens the candidate ingredients, using design of experiment techniques, and develops a model for each response. It then inverts the models using a nonlinear optimization technique, and obtains an optimal design for the product based on the desired properties.	This methodology should be applicable in other chemical product formulation developments.	EM	PP	CO	(Omidbakhsh et al., 2012)
36	Process engineering was launched about a decade ago, but so far has not yet developed into the foreseen third paradigm in chemical engineering. A plausible explanation for this slow progress can be found in the complex relationship between product manufacturing technologies and material properties. Process technology mainly affects molecular properties and therefore the specifications of chemicals further down the value chain where processing technology largely determines the shape and structure of the end-product.	Relationship between chemistry and composition at the molecular scale and the behavior of formulated products to process engineering during chemical substance manufacture, shaping and structuring.		PP	BU	(Picchioni and Broekhuis, 2012)

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Number	Main contributions	Challenges and Opportunities	Integration level and sublevel*			References
			EM	PP	MS/MD	
37	Find solutions for the complicated technical problems in chemical product development, as well as in the design and operation of the manufacture processes. The characteristics of product synthesis, process operation, and product quality control are investigated in coupled with computer aided monitoring, online modeling, simulation and operation optimization.	Application to other formulated products	EM	PP	MS, CO	(Qian et al., 2006)
38	New perspectives and strategies of chemical product design are provided. Innovation map to guide the technology-development process and the Stage-Gate product-development process (SGPDP). The innovation map relates the technological components of product developments to the technical advantages and the satisfaction of the customer-value proposition.	Satisfy more complex customer and technical requirements. There is less emphasis on the design of manufacturing processes – primarily because these process designs depend heavily on the technology platforms.		PP	CO, BU	(Seider et al., 2009)
39	4 steps procedure: Consumer preference identification; attribute-based methods; problem formulation; multiobjective optimization. The integrated framework specifically considers the unique set of challenges and design requirements associated with chemical-based consumer product by incorporating consumer influence, empirical property models, and subjective product evaluation. Appropriate multidisciplinary consideration, including an integrated product–process strategy.	The absence of credible modeling approaches has limited integrative application. Construct standard frameworks and mechanisms to facilitate integration.		PP	CO, BU	(Smith and Ierapepritou, 2009)

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Number	Main contributions	Challenges and Opportunities	Integration level and sublevel*			References
			EM	PP	MS/MD	
40	A centralized framework was developed that combines property clustering with chemometric techniques like principal component analysis (PCA) and partial linear regression onto latent surfaces (PLS) to solve the design problem in a property descriptor sub-domain. Visualize the reverse problem formulation using the combination of property clustering and chemometrics provides a framework to solve property driven processes without commitment to components and/or structures a priori.	Simultaneous molecular and microstructure design (including polymorphism) to occur, avoiding the heavy combinatorial expense typically associated with solving problems in the meso-scale.	EM	PP	MS, CO	(Solvason et al., 2010)
41	A systematic procedure is presented for the synthesis and development of manufacturing processes for creams and pastes: Step 1. Product conceptualization Step 2. Identification of product quality factors Step 3.Selection of ingredients and product microstructure Step 4. Generation of process alternatives Step 5. Product and process evaluation alternatives	The procedure can be extended to other types of product delivery systems. Integration of software into a coherent environment would further improve the development process.	EM	PP	CO, BU	(Wibowo and Ng, 2002, 2001)
42	A systematic methodology for design of tailor-made blended products is formulated as a Mixed Integer Nonlinear Programming (MINLP) model. It has 4 main tasks. 1) Problem definition: the product needs are identified, translated into target properties and the bounds for each target property are defined. 2) Target property models are retrieved from a property model library. 3) A mixture/blend design algorithm is applied to obtain the mixtures/blends that match the design targets. 4) The mixture target property values are verified (virtual).	Add an experimental component to verify the designed products	EM		CO	(Yunus et al., 2011)
43			EM	PP		(Yunus et al., 2013)
44						(Yunus et al., 2014)

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B. Fuzzy measures and the Choquet integral

These definitions are part of the original article written by Camargo et al. (2014)

Let us denote $X=\{C_1, \dots, C_n\}$ as the set of *n* criteria, and *P* as the power set of *X*, i.e. the set of all subsets of *X*.

Definition 1. *A* fuzzy measure *or* capacity, *μ*, defined on *X* is a set function *μ*:

$$P(X) \rightarrow [0,1]$$

verifying the following axioms:

1. $\mu(\varnothing)=0,\ \mu(X)=1,$ (D-1)

2. $A \subseteq B \Rightarrow \mu(A) \leq \mu(B)$ (D-2)

Fuzzy measures generalize additive measures, by replacing the additivity axiom

$(\mu(A \cup B) = \mu(A) + \mu(B),\ A \cap B = \varnothing)$ (D-3)

with a weaker one (monotonicity).

In this context, *μ*(*A*) represents the importance, or the degree of trust in the decision provided by the subset *A* of X. The next step in building a final decision, is to combine the partial confidence degree according to each criterion into a global confidence degree, taking those weights into account.

Definition 2. Let *μ* be a fuzzy measure on *X*. The discrete Choquet integral of $\varphi = [\varphi_1, \dots, \varphi_n]^t$ with respect to *μ*, noted $C\mu(\varphi)$, is defined by:

$$C_\mu(\varphi) = \sum_{j=1,n} \varphi(j)\left[\mu\left(A_{(j)}\right) - \mu\left(A_{(j-1)}\right)\right] \tag{D-4}$$

Where the notation $(\cdot)$ corresponds to a permutation on the source indexes, such that $(i) \leq (j) \Rightarrow \varphi_{(i)} \leq \varphi_{(j)}$. Also $A_{(j)}$={(j),…, (n)} represents the [j..n] associated criteria in increasing order and $A_{(n+1)} = \emptyset$.

From the above definitions, we can see that the behavior of the Choquet integral as an aggregation operator entirely relies on the fuzzy measure used. There are several methods to determine the most adequate fuzzy measure to be used for a given application. The calculation of the Choquet integral requires the assessment of any set of *P(X)*. Several ways to automatically set the 2^n-2 values exist (Grabisch, 1995a). When using optimization techniques, the aim is to find the fuzzy measure that best minimizes a criterion on the training set that has the square error.

Considering (x^k, y^k), $k = 1, \ldots, l$, l learning samples where $x^k = [x^k_1, \ldots, x^k_n]^t$ is a n-dimensional vector, and y_k the expected global evaluation of object k, the fuzzy measure can be determined by minimizing (Grabisch, 1995a):

$$E^2 = \sum_{k=1,l} (C_\mu(x^k_1, \ldots, x^k_n) - yk)^2. \tag{D-5}$$

Importance Index: The importance of each SA, also called the Shapley index, is based on the definition proposed by Shapley in game theory (Shapley, 1953). Let a fuzzy measure μ and a criterion i be considered. The main expression is given in (D-2) and so on for each SA

$$\sigma(\mu,i)=\frac{1}{n}\sum_{t=0}^{n-1}\frac{1}{\binom{n-1}{t}}\sum_{\substack{T\subseteq x\setminus i\\ |T|=i}}\left[\mu(T\cup i)-\mu(T)\right] \tag{D-6}$$

The Shapley value can be interpreted as a weighted average value of the marginal contribution $\mu(T \cup i) - \mu(T)$ of criteria i alone in all combinations. And the sum of the index of all SA is equal to 1, so $\sum_{i=1,n} \sigma(\mu, i) = 1$

Interaction Index: The interaction index, also called the Murofushi and Soneda index (Grabisch, 1996; Murofushi and Sugeno, 1991), represents the positive or negative degree of interaction between two SA. As the fuzzy measure is non-additive, then some sources interact. The marginal interaction between i and j, conditioned to the presence of the elements of combination $T \subseteq X \setminus ij$, is given by

$$(\Delta_{i,j}\mu)(T) = \mu(T \cup ij) + \mu(T) - \mu(T \cup i) - \mu(T \cup j) \tag{D-7}$$

$$I(\mu, ij) = \sum_{T \subseteq Xij} \frac{(n-t-2)!\,t!}{(n-1)!} (\Delta ij \mu)(T) \tag{D-8}$$

C. Ingredients database

Emollient	Thickener	Humectant
Fatty alcohol	Emulsifier	Other additives

Ingredient - INCI Name	Commercial name (Supplier)	CAS	Cost (USD/kg)	Greasiness	RHLB	HLB	Hazard Index
Cyclopentasiloxane	XIAMETER™ PMX-0245 (Dow Corning) BELSIL® CM 1000 (Wacker)	541-02-6	28.9	2	7.5		3
Isoamyl Cocoate	Tegosoft AC (Evonik)	-	23	1.8			1
Diethylhexyl Carbonate	Tegosoft DEC (Evonik)	14858-73-2	30	1.8			1
Isopropyl Myristate	Crodamol IPM (CRODA) Tegosoft M (Evonik) IPM (BASF)	110-27-0	16.7	1.8	12		1
Isopropyl Palmitate	Crodamol IPP (CRODA) Tegosoft P (Evonik) IPP (BASF)	142-91-6	16.7	3	12		1
Decyl Cocoate	Tegosoft DC (Evonik)	-	23.9	3			1
Ethylhexyl Palmitate	Crodamol OP (CRODA) Tegosoft OP (Evonik) Cegesoft C24 (BASF) ETHYLHEXYL PALMITATE (FACI)	29806-73-3	14.3	3	8		1
Phenoxyethyl Caprylate	Tegosoft XC (Evonik)	23511-73-1	24	1.8			1
Caprylic/Capric triglyceride	Crodamol AB (CRODA) Tegosoft TN (Evonik) Myritol 312 or 318 (BASF)	73398-61-5	15.8	3	5		1
C12-15 Alkyl benzoate	Crodamol OS (CRODA) Tegosoft OS (Evonik) Cetiol AB (BASF)	68411-27-8	20.1	1.3	13		1
Ethylhexyl stearate	Tegosoft OS (Evonik) Cithrol OS (CRODA)	22047-49-0	18.31	1.3	8		1
Cetyl ethylhexanoate	Tegosoft CO (Evonik) Schercemol™ CO Ester (Lubrizol)	59130-69-7	25	1.3			1
Cetearyl Isononanoate	Tegosoft CI (Evonik) Crodamol GTCC (CRODA) Cetiol SN (BASF)	111937-03-2	18.6	1.3	9.1		1
Cetyl Dimethicone (high viscosity, medium polarity)	Abil Wax 9801 (Evonik) DOWSIL™ 2502 (Dow Corning)	191044-49-2	19	3.8			1
PPG-3 Myristyl Ether	Tegosoft APM (Evonik) Arlamol™ PM3 (CRODA EEUU)	63793-60-2	25.4	1.3			1
Paraffinum liquidum	Mineral Oil PRIMOL™/MARCOL™ (ExxonMobil)	8012-95-1	1.3	3.8	11		3

Ingredient - INCI Name	**Commercial name - Supplier**	**CAS**	**Cost (USD/kg)**	**Greasiness**	**RHLB**	**HLB**	**Hazard Index**
Octyldodecanol	Tegosoft OER (Evonik) Eutanol G (BASF)	5333-42-6	22.7	1.3	10.9		1
Oleyl Erucate	Tegosoft G20 (Evonik) Cetiol J 600 (BASF)	17673-56-2	23.9	2			1
Persea Gratissima Oil	Avocado Oil (Provital Group) Lipovol® A (Vantage Specialty ingredients)	8024-32-6	16.7	2	7		1
PPG-15 Stearyl Ether	Tegosoft E (Evonik) Cetiol E (BASF) MARLOSOL ST 9150 P (Sasol) Arlamol E (CRODA)	25231-21-4	21.75	2	7		1
Cetyl Dimethicone (very high viscosity, nonpolar)	Abil wax 9840 (Evonik) MIRASIL CETYL DM (ELKEM) PECOSIL® AS-16 (Phoenix Chemical)	191044-49-2	35	3.2			1
PPG-14 Butyl Ether	Tegosoft PBE (Evonik) Arlamol™ PB14 (CRODA)	9003-13-8	23	3.2			1
Triisostearin	Tegosoft TIS (Evonik) PELEMOL® GTIS (Phoenix Chemicals) Crodamol GTIS (CRODA)	26942-95-0	30	3.2	8		1
Dimethicone 1000 CSt	Abil 350 (Evonik) XIAMETER™ PMX-200 (Dow Corning)	9006-65-9 63148-62-9	29.3	3.2	5		3
Stearyl Alcohol	Lanette 18 (BASF) Crodacol™ S95 (CRODA) KALCOL® 8098L (KAO)	112-92-5	7.4		15.5		1
Cetyl Alcohol	Lanette 16 (BASF) Crodacol™ C95 (CRODA) KALCOL® 6098L Cetyl alcohol (KAO)	36653-82-4	7.4		16		1
Cetearyl Alcohol	Lanette D (BASF) Crodacol™ 1618 (CRODA) KALCOL® 6850L Cetearyl Alcohol (KAO) Nafol 1618 (Sasol)	67762-27-0	10.3		15.5		1
Xanthan Gum	Rhodicare H (Solvay) Rheocare® XGN (BASF)	11138-66-2	35				1
Hydroxyethyl Cellulose	Natrosol 250 HHR (Ashland) CELLOSIZE™ PCG-10 (Dow)	9004-62-0	50.5				1
Hydroxypropyl Guar Gum	Jaguar HP 105 (Solvay) N-Hance™ HP-40 Hydroxylpropyl Guar (Ashland)	68442-94-4 39421-75-5	47.8				1
Hydroxypropyl Starch Phosphate	Structure XL (Akzo Nobel) AGENAJEL 20.383 (AGRANA Starch)		27.8				1

Ingredient - INCI Name	**Commercial name - Supplier**	**CAS**	**Cost (USD/kg)**	**Greasiness**	**RHLB**	**HLB**	**Hazard Index**
Glyceryl Stearate SE	Cithrol GMS 40 SE (CRODA)	11099-07-3	8.9	1.3		5.8	1
Sorbitan Monostearate	SP Span 60 MBAL (CRODA) TEGO SMS (Evonik) KAOPAN SP-S-10 (KAO) SABOSORB MS (SABO)	1338-41-6	12.5			4.7	1
Sorbitan Monooleate	Span 80 (CRODA) TEGO® SMO V (Evonik) KAOPAN® SP-O-10 (KAO) SABOSORB MO (SABO)	1338-43-8	16.2			4.3	1
PEG-100 Stearate	Myrj S100 (CRODA) Sympatens-BS/1000 G (KLK Oleo Europe)	9004-99-4	9.8			18.8	3
Polysorbate 60 Polyoxyethylene (20) sorbitan monostearate	Tween 60 (CRODA) TEGO SMS 60 (Evonik) SABOSORB MSE (SABO) KAOPAN® TW-S-120 (KAO)	9005-67-8	15.5			14.9	3
Polysorbate 80 Polyoxyethylene (20) sorbitan mono-oleate	Tween 80 (CRODA) TEGO® SMO 80 V (EVONIK) SABOSORB MOE (SABO) KAOPAN® TW-O-120 (KAO) Alkamuls® T80-C (Solvay)	9005-65-6	15			15	3
Glycerol		56-81-5					2
Propylen Glycol		57-55-6					1
Methylparaben		99-76-3					4
Propylparaben		94-13-3					7
Sorbic Acid/Potassium sorbate		110-44-1					2.5
Lecithin		8002-43-5					1
Tocopherol		1406-18-4			6		1
Citric Acid							2
Sodium Hydroxide							3.5

D. Survey for the usability tests (Questionnaire and Results)

English version (translated)

Questionnaire: Body cream test

For a study on the keywords used to describe the sensory properties of body creams, we thank you in advance for your response to our questionnaire.

Profile

Color:

Eyes [ ] Blue [ ] Green
[ ] Brown [ ] Black
[ ] Gray

Hair [ ] Blond [ ] Red [ ] Light brown
[ ] Brown [ ] Dark brown [ ] Black

Skin [ ] PhT 1 [ ] PhT 2
[ ] PhT 3 [ ] PhT >4

Gender : [ ] Woman [ ] Man

Age: [ ] < 20 years old [ ] 20-29 years [ ] 30-39 years old
[ ] 40-49 years old [ ] 50-59 years old [ ] > 60 years old

1. **You would say your skin is:**
   [ ]Dry [ ] Normal [ ] Greasy [ ] Sensitive [ ] Damaged

2. **Where are you most often?**
   [ ] Indoors [ ] Outdoors [ ] In a place with air conditioning

3. **Do you sunbathe (incl. UV)?**
   [ ] Yes [ ] No

4. **Do you use body cream?**
   [ ] Twice a day or more
   [ ] Once a day
   [ ] Sometimes a week
   [ ] Sometimes a month
   [ ] Sometimes during the winter
   [ ] Never

5. **You feel that your skin (of the body)**
   [ ] Is sometimes tight
   [ ] Is always tight
   [ ] It's rough and sometimes it has patches
   [ ] It has patches and sometimes it itches
   [ ] It itches intensely
   [ ] You don't have any of these problems

6. **Rank the five (5) most important criteria in choosing a cosmetic product for the body**
   [ ] Price
   [ ] Brand
   [ ] Packaging
   [ ] Functionality (nourishing, repairing, protective...)
   [ ] Adapted to your skin type (dry, greasy, normal...)
   [ ] Positive list of ingredients
   [ ] Negative list of ingredients
   [ ] Perfume
   [ ] Clinically proven
   [ ] Origin (Produced in some country, local ingredients...)
   [ ] Other? ____________________
   [ ] Other ? ____________________

B. Product test: You will be testing a body cream and will be asked to answer a few questions about the experience of use

No	**Question**	**fully agree**	**agree**	**balanced**	**disagree**	**fully disagree**	**does not wish to answer**
1	Is the cream thick?						
2	Do you think that this product is easy to apply?						
3	Is this cream sticky?						
4	Is the product easily absorbed through the skin?						
5	Did this cream feel cool to you?						
6	Does the cream leave white marks on your skin?						
7	Do you feel that this cream is greasy?						
8	Is your skin more hydrated with this product?						
9	Does the texture of the cream seem thin to you?						
10	Does this cream glide easily on the skin?						
11	Is the cream light?						
12	Does this product penetrate quickly?						
13	Does the cream produce a feeling of freshness during application?						
14	Do you feel any cream residues on your skin?						
15	Does the product leave an oily feeling on the skin?						
16	Does your skin feel softer after using this cream?						
17	Would you be convinced by the use of this product in your daily life?						
18	Would you buy this cream for you?						

French version (original)

Questionnaire : test crème pour le corps

Pour une étude sur les mots clé utilisés pour décrire des propriétés sensorielles des crèmes pour le corps, nous vous remercions d'avance de bien vouloir répondre à notre questionnaire.

Profil des répondants

Cheveux [ ] Blonds [ ] Roux [ ] Châtains clairs
[ ] Châtains [ ] Châtains foncés/Bruns [ ] Noirs

Couleur :

Yeux [ ] Bleus [ ] Verts
[ ] Marrons [ ] Noirs
[ ] Gris

Peau [ ] PhT 1 [ ] PhT 2
[ ] PhT 3 [ ] PhT >4

Sexe : [ ] Femme [ ] Homme

Âge : [ ] < 20 ans [ ] 20-29 ans [ ] 30-39 ans
[ ] 40-49 ans [ ] 50-59 ans [ ] > 60 ans

1. **Considérez-vous que votre peau (corps) est ?**
   [ ] Sèche [ ] Normale [ ] Grasse [ ] Sensible [ ] Irritée

2. **Dans quel lieu vous trouvez-vous le plus souvent?**
   [ ] A l'intérieur [ ] A l'extérieur [ ] Dans un endroit climatisée

3. **Prenez-vous des bains de soleil (UV compris)?**
   [ ] Oui [ ] Non

4. **Utilisez-vous de la crème pour le corps?**
   [ ] 2 fois par jour
   [ ] 1 fois par jour
   [ ] Quelques fois par semaine
   [ ] Quelques fois par mois
   [ ] Des fois pendant l'hiver
   [ ] Jamais

5. **Sentez-vous que votre peau (corps)?**
   [ ] Tiraille occasionnellement
   [ ] Tiraille sans cesse
   [ ] Est rugueuse et parfois a des plaques
   [ ] A des plaques et parfois vous démange
   [ ] Vous démange intensément
   [ ] N'a aucun de ces problèmes

6. **Classez les <u>cinq critères les plus importants</u> dans le choix d'un produit cosmétique pour le corps**
   [ ] Prix
   [ ] Marque
   [ ] Emballage
   [ ] Description fonctionnelle (nourrissante, réparatrice, protectrice…)
   [ ] Adaptée à votre type de peau (sèche, normale, mixte…)
   [ ] Présence de certains ingrédients
   [ ] Absence de certains ingrédients
   [ ] Odeur/Parfum
   [ ] Efficacité prouvée
   [ ] Origine (Produit en France, Ingrédients locaux…)
   [ ] Autre, lequel ? ____________________
   [ ] Autre, lequel ? ____________________
   [ ] Autre, lequel ? ____________________

B. Test du produit : Vous allez tester une crème pour le corps est on vous demandera de répondre a quelques questions par rapport a l'expérience d'usage

No	Question	tout à fait d'accord	d'accord	mitigé	pas d'accord	pas du tout d'accord	ne souhaite pas répondre
1	Est-ce que la crème est épaisse?						
2	Sentez-vous que ce produit est facile à appliquer?						
3	Cette crème est-elle collante?						
4	Est-ce que le produit est absorbé facilement par la peau?						
5	Cette crème vous a-t-elle parue froide?						
6	Est-ce que la crème laisse des traces blanches sur votre peau?						
7	Sentez-vous que cette crème est grasse?						
8	Votre peau est-elle plus hydratée avec ce produit?						
9	La texture de la crème vous paraît-elle fluide?						
10	Cette crème glisse-t-elle facilement sur la peau?						
11	La crème est-t-elle légère?						
12	Est-ce que ce produit pénètre rapidement?						
13	La crème produit-elle une sensation de fraîcheur pendant l'application?						
14	Sentez-vous des résidus de crème sur votre peau?						
15	Le produit laisse-t-il une sensation huileuse sur la peau?						
16	Est-ce que votre peau semble plus souple après utilisation de cette crème?						
17	Seriez-vous convaincu par l'utilisation de ce produit dans votre vie quotidienne?						
18	Est-ce que vous achèteriez cette crème pour vous?						

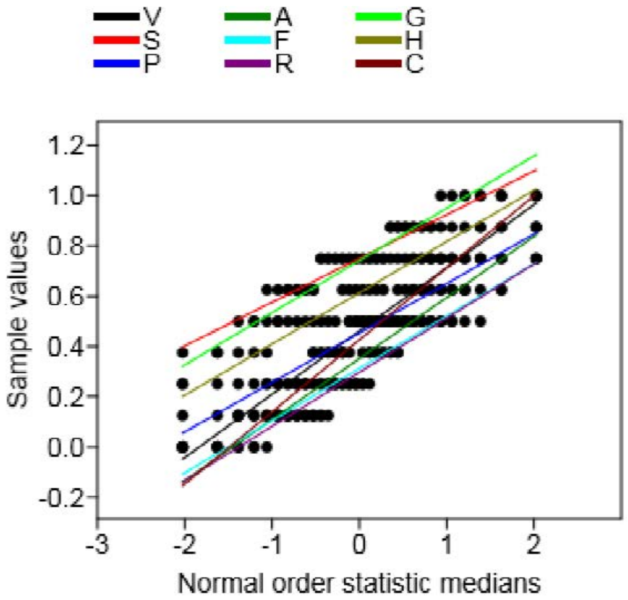
Results of the survey

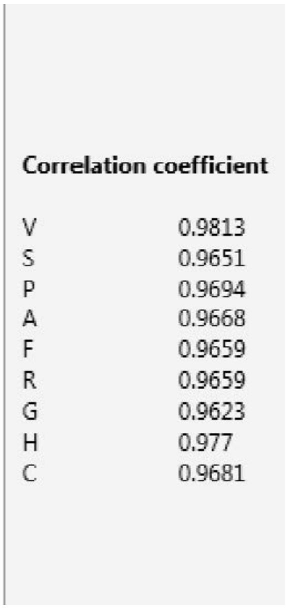
For each sample more than 32 volunteers participated in the survey, but some of them did not fit the test conditions, so their answers are not showed here.

Sample 1	**V1**	**S1**	**P1**	**A1**	**F1**	**R1**	**G1**	**H1**	**V2**	**S2**	**P2**	**A2**	**F2**	**R2**	**G2**	**H2**	**C1**	**C2**
#Question	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**	**13**	**14**	**15**	**16**	**17**	**18**
2	4	1	4	1	4	4	4	3	4	4	4	4	3	4	4	3	4	4
3	2	2	3	2	3	5	2	2	2	2	2	2	2	5	2	3	3	3
4	2	2	2	3	4	4	2	2	2	2	2	3	4	2	2	2	2	2
5	4	2	1	4	4	4	1	4	2	2	4	5	3	1	1	4	5	4
6	3	4	2	4	5	4	2	4	2	2	4	4	3	2	1	4	4	5
7	1	2	3	4	1	5	3	3	3	5	1	5	5	4	2	3	4	4
8	3	2	3	4	5	5	3	2	2	2	3	5	3	2	2	2	3	3
9	3	2	2	3	4	5	2	3	2	2	4	5	5	1	1	3	3	4
11	3	3	2	4	4	4	1	3	4	2	2	5	3	4	1	5	5	5
12	1	2	3	3	5	5	3	2	1	1	4	3	3	5	4	1	1	2
16	1	2	3	4	3	5	2	3	3	2	2	3	1	5	1	2	5	5
17	2	3	4	3	5	5	2	2	2	2	3	4	4	4	2	2	3	3
19	4	2	3	2	5	4	3	1	1	1	2	4	3	2	3	1	2	2
21	5	2	4	3	4	5	2	2	2	2	2	3	2	4	2	2	2	2
23	5	2	3	3	5	3	2	3	1	1	2	3	2	5	3	3	3	3
25	3	1	4	5	3	5	2	3	2	1	2	5	3	5	2	3	4	4
27	5	1	3	4	5	5	1	3	3	2	3	5	4	4	1	4	4	4
28	2	1	2	4	5	5	2	1	5	1	5	4	1	4	1	4	4	4
29	2	2	4	3	5	5	2	2	2	1	3	3	4	2	2	3	3	4
30	3	1	1	4	4	5	1	1	1	1	3	4	2	1	2	3	2	2
32	3	1	1	3	2	5	1	2	1	2	2	2	3	2	4	3	3	3
33	2	3	2	5	5	5	1	2	4	1	4	5	4	5	5	2	2	1
34	1	4	1	3	5	4	1	3	3	2	3	5	4	3	1	3	4	4
35	2	2	2	3	4	4	2	2	2	2	3	3	2	2	4	2	2	2
36	1	1	2	3	4	5	2	1	1	1	4	2	5	2	2	1	1	3
38	2	3	3	2	4	5	2	2	5	2	4	2	4	1	2	1	2	2
39	1	4	1	4	4	3	1	3	4	3	4	4	4	1	1	3	5	5
40	3	2	5	3	5	5	2	3	2	1	4	5	5	2	2	4	4	5
42	4	3	2	4	5	5	2	2	2	1	3	5	4	3	1	3	3	3
43	5	2	1	5	5	5	1	3	1	1	1	4	5	1	1	3	5	5
44	3	4	2	2	5	5	4	2	3	1	2	1	4	4	3	2	3	3
45	2	2	4	4	2	4	2	2	3	3	3	5	3	5	2	3	3	3

Sample 2	**V1**	**S1**	**P1**	**A1**	**F1**	**R1**	**G1**	**H1**	**V2**	**S2**	**P2**	**A2**	**F2**	**R2**	**G2**	**H2**	**C1**	**C2**
#Question	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**	**13**	**14**	**15**	**16**	**17**	**18**
1	4	1	4	1	2	4	4	1	1	1	1	1	1	4	4	1	1	2
3	3	2	5	2	5	5	4	2	1	1	3	2	2	5	5	2	2	3
5	2	1	5	3	3	5	3	1	5	1	2	3	2	2	3	2	2	2
6	4	2	4	3	5	5	3	1	1	1	2	3	1	2	4	1	1	2
7	5	1	5	2	3	5	5	2	1	1	1	1	1	5	5	1	3	2
8	3	2	4	3	4	5	2	2	2	2	3	3	3	2	3	2	3	3
9	5	2	5	2	4	4	2	3	4	2	2	2	2	5	2	5	2	2
10	2	2	1	2	3	5	5	1	5	1	4	1	1	2	4	1	1	1
11	1	3	2	1	5	5	3	1	1	1	1	1	3	3	1	1	1	1
13	4	1	2	2	3	5	2	2	1	1	2	1	2	5	4	2	2	1
14	4	2	3	2	4	4	3	2	2	2	2	2	2	4	3	2	2	2
15	5	1	5	1	5	5	3	1	2	1	1	2	3	5	5	3	2	2
16	5	1	3	2	5	5	3	3	2	1	2	3	5	3	3	5	2	2
17	3	2	2	1	5	5	2	1	2	2	2	1	2	5	5	1	2	3
18	3	1	4	4	5	5	2	1	1	1	1	3	2	4	1	2	3	4
19	5	2	3	3	5	5	3	3	2	2	2	3	3	2	2	3	4	4
20	4	1	5	1	4	5	3	2	1	1	1	1	3	3	3	2	3	3
21	5	4	5	4	2	2	2	2	1	1	1	5	2	2	2	2	5	5
24	4	1	5	1	5	5	5	2	2	2	1	1	2	5	5	2	2	2
25	3	2	2	5	5	5	2	2	2	2	3	5	5	2	2	3	5	5
26	1	1	3	5	4	5	3	1	1	1	4	4	2	2	2	3	3	3
27	5	1	4	4	5	5	2	2	1	1	3	4	4	3	2	2	3	3
28	3	4	1	4	3	5	3	3	2	2	1	4	3	2	4	3	4	4
29	4	4	4	3	4	5	4	3	2	2	2	3	3	3	2	3	4	5
31	4	3	2	4	5	4	2	2	2	2	3	4	2	2	4	4	5	5
32	5	1	5	1	5	5	4	2	1	2	1	1	2	5	5	1	2	1
33	5	1	5	1	3	3	4	2	1	1	1	1	1	5	4	2	2	2
34	4	1	3	1	5	5	5	1	1	1	1	2	1	5	5	2	1	1
35	4	4	4	4	4	4	4	4	2	3	2	4	2	4	3	2	4	4
37	3	2	5	2	3	5	2	1	1	1	2	2	2	2	5	2	2	3
38	4	1	4	3	5	5	1	2	2	1	3	4	5	2	2	1	3	4
39	4	3	4	5	2	4	1	2	3	2	2	4	2	4	3	4	3	3

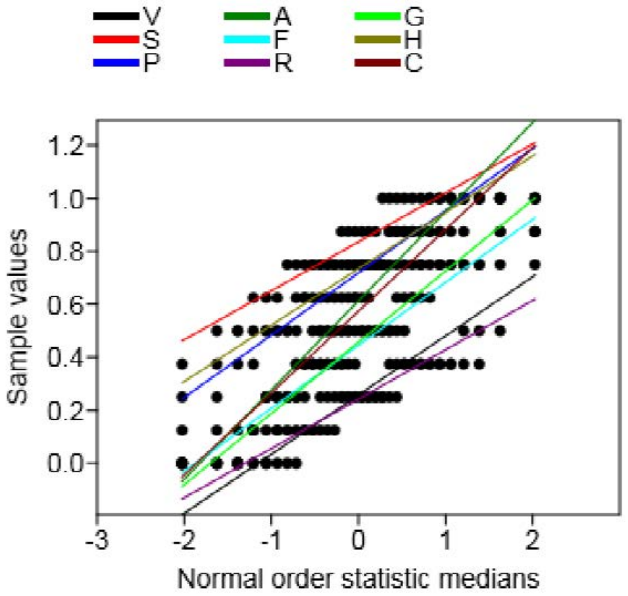
Sample 1. Normal correlations

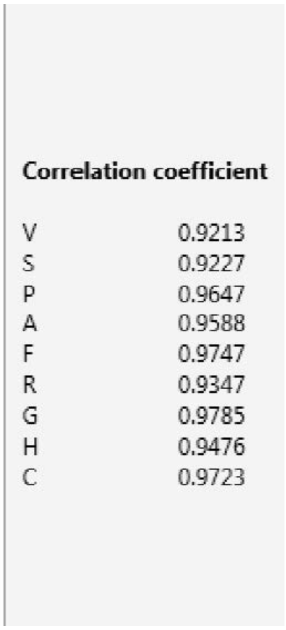




Correlation coefficient	
V	0.9813
S	0.9651
P	0.9694
A	0.9668
F	0.9659
R	0.9659
G	0.9623
H	0.977
C	0.9681

Sample 2. Normal correlations





Correlation coefficient	
V	0.9213
S	0.9227
P	0.9647
A	0.9588
F	0.9747
R	0.9347
G	0.9785
H	0.9476
C	0.9723

E. Ingredients of the commercial skin moisturizers for the usability tests

[9]

[10]

Ingredient	Sample 1	Sample 2
1	Water	Water
2	Paraffinum Liquidum	C12-15 Alkyl Benzoate
3	Glycerin	Glycerin
4	Cetearyl Isononanoate	Cetyl Alcohol
5	Glyceryl Stearate	Alcohol Denat
6	PEG-100 Stearate	Butyl Methoxydibenzoylmethane
7	Myreth-3 Myristate	Octocrylene
8	Steareth-21	Phenylbenzimidazole Sulfonic Acid
9	Cyclopentasiloxane	Dimethicone
10	Acrylates/ C-10-30 Alkyl Acrylate Crosspolymer	Palmitic Acid
11	Caprylyl Glycol	Cetyl Palmitate
12	Cetyl Alcohol	Stearic Acid
13	Disodium EDTA	Phenoxyethanol
14	Palmitic Acid	Glyceryl Stearate
15	Stearic Acid	Sodium Hydroxide
16	Xylitol	Tapioca Starch
17	Mannitol	Carbomer
18	Rhamnose	Methylparaben
19	Sodium Hydroxide	Trisodium EDTA
20	Sodium Dihydroacetate	Tocopheryl Acetate
21	Xylitylglucoside	Myristic Acid
22	Anhydroxylitol	Arachidic Acid
23	Niacinamide	Aloe Barbadensis Leaf Juice Powder
24	Glucose	Oleic Acid
25	Fructooligosaccharides	Benzoic Acid
26	Caprylic/Capric Triglyceride	Linalool
27	Laminaria Ochroleuca Extract	Limonene
28	BI475	Buthylphenyl Methylpropional
29		Benzyl Alcohol
30		Perfume

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[9] Taken from https://www.easyparapharmacie.com/. Visited on 12.10.2018
[10] Taken from https://www.nivea.com.mx/. Visited on 12.10.2018

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An integrated methodology for chemical product design: Application to cosmetic emulsions

The design of optimal mixtures is a major challenge in many industrial sectors, especially for formulated products such as cosmetics. Due to the large number of different combinations of ingredients and their quantities, a critical issue is how to define a narrow search space using available knowledge. For this purpose, besides considering some key physicochemical properties of the final product, it is of paramount importance to take into account the performance of the product as perceived by the final consumer. Here, we have proposed a methodology to find a set of plausible formulations for emulsified cosmetic products, based on a fuzzy integral analysis of the consumer preferences and integrated into a mixed-integer optimization tool that incorporates available heuristic rules and property models. Two case studies of cosmetic emulsions were given to illustrate the methodology. In a first example using hair conditioners, the rheological, textural, and microstructural properties of nine alternative formulations manufactured at a lab scale were measured to validate the modelling of emulsified products. Then, two commercial samples of skin moisturizers were tested to identify the most relevant consumer attributes using fuzzy measures. Based on this assessment, ten computer-generated solutions with minimum ingredient costs were also manufactured and evaluated, showing that the proposed methodology could be well adapted to accelerate reformulation or benchmarking processes. Using this approach, product designers could also estimate the relevance and interactions of subjective consumer attributes and guide the design of other formulated products.

Keywords: Product design, emulsions, cosmetics

Une méthodologie intégrée de conception de produits chimiques: Application sur des émulsions cosmétiques

La conception de mélanges optimaux est un défi important dans de nombreux secteurs industriels, notamment pour les produits formulés comme les cosmétiques. En raison du grand nombre de combinaisons différentes d'ingrédients et de leurs niveaux d'utilisation, une question cruciale est de savoir comment définir un espace de recherche réduit en utilisant les connaissances disponibles. Pour cela, outre la prise en compte de certaines propriétés physico-chimiques essentielles du produit final, il est d'une importance capitale de tenir compte de la performance du produit telle que perçue par le consommateur final. Ici on a proposé une méthodologie pour trouver un ensemble de formulations plausibles de produits cosmétiques émulsifiés, basée sur une analyse intégrale floue des préférences du consommateur, intégrée à un outil d'optimisation d'entiers mixtes qui intègre des règles heuristiques disponibles et des modèles de propriétés. Deux études de cas d'émulsions cosmétiques ont été présentées pour illustrer la méthodologie. Dans un premier exemple utilisant des après-shampooings, les propriétés rhéologiques, texturales et microstructurales de neuf formulations alternatives, fabriquées en laboratoire, ont été mesurées pour valider la modélisation des produits émulsifiés. Ensuite, deux produits commerciaux de crèmes hydratantes ont été testés pour identifier les attributs les plus pertinents pour les consommateurs, en utilisant des mesures floues. Sur la base de cette évaluation, dix solutions, générées par ordinateur avec des coûts minimaux d'ingrédients ont également été fabriquées et évaluées, ce qui montre que la méthodologie proposée pourrait être bien adaptée pour accélérer les processus de reformulation ou d'étalonnage. En utilisant cette approche, les concepteurs de produits pourraient également estimer la pertinence et les interactions des attributs du consommateur et guider la conception d'autres produits formulés.

Mots clés: Conception de produits, émulsions, cosmétiques