Antinociceptive and anti-inflammatory activity *in vivo* of variabilin isomer mixture isolated from marine sponge *Ircinia felix*

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Resumen

Actividad antinociceptiva y anti-inflamatoria in vivo de la mezcla de isómeros de variabilina aislada de la esponja marina *Ircinia felix*

Mediante el método de edema plantar inducida por carragenina en la pata de la rata, la mezcla de los isómeros de variabilina mostró actividad anti-inflamatoria, mientras que su actividad antinociceptiva fue confirmada por el método de contorsiones inducidas por ácido acético en ratones. Los resultados mostraron una actividad antinociceptiva alta y una actividad anti-inflamatoria moderada en las dosis de 150 y 200 mg/kg administradas por vía oral, en comparación con la actividad observada para los patrones empleados en las dosis evaluadas.
Palabras clave: Isómeros de variabilina – Actividad anti-inflamatoria - Actividad antinociceptiva.

Summary

Using the carrageenan-induced rat's paw edema method, variabilin isomer mixture previously isolated from the marine sponge *Ircinia felix*, showed anti-inflammatory activity. Mean while the antinociceptive activity was confirmed by the writhings test induced by intraperitoneal injection of acetic acid in mice. The results showed a high antinociceptive activity and a moderate anti-inflammatory activity in doses of 150 and 200 mg/kg by oral administration, in comparison with the observed activity of the standard substances in the evaluated doses.
Keywords: Variabilin isomer mixture - Anti-inflammatory activity - Antinociceptive activity.

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Introduction

Five furanosesterterpene tetronic acids were isolated as acetate and identified by spectroscopic methods as (+)-(7E,12E,20Z)-variabilin (Fig.1), (+)-(7E,13Z,20Z)-felixinin, (+)- (7Z,13Z,20Z)- felixinin, (+)-(8Z,13Z, 20Z)-strobilinin and (+)-(8E,13Z,20Z)-strobilinin, (1-3).

Recently, we have reported the antimicrobial activity against Gram (+) micro-organisms: *Micrococcus Lacteus*, *Staphylococcus aureus*, *Bacillus subtilis* and the Gram (-) micro-organisms: *Pseudomonas sp.*, *Enterobacter aerogenes* and *Escherichia coli*, antitumor activity and LC50 at 272 μg/mL in *Artemia salina* for these furanosesterterpene tetronic acid isomers. (4).

The present research aims to evaluate the antinociceptive and anti-inflammatory activity of the same furanosesterterpene isomer mixture.

Experimental

Materials and methods

Marine sponge

The marine sponge *Ircinia felix* was collected in the Bay of Santa Marta, Colombia, South America at the depth of 15-20 m. Voucher specimens described by Zea (5) have been deposited in the reference collection of the Institute de Investigaciones marinas de Punta Betín, Colombia "INVEMAR".

Extraction and isolation

Sample of variabilin isomer mixture employed in this study was isolated and identified from marine sponge *Ircinia felix* following the previous method described by Martínez *et al.*, (1-3).

Antinociceptive activity

Following the method described by Rahola 1991(6), the antiwrithing activity was evaluated employing OF1 twelve hours fasted female mice weighing 20 to 25 g.

Variabilin isomers were evaluated by oral administration in doses of 50, 100, 150 and 200 mg/kg. 3 groups each of 6 mice were employed for each dose, the vehicle [Tween 80: ethanol: water (1:1:22)] as a control, water as blank and the standard acetylsalicylic acid in a dose of 200 mg/kg.

One hour after the oral administration of the substances, the mice were injected intraperitoneal with 0.2 ml of 1% acetic acid. The mice were observed for the next 20 minutes and the number of writhings shown in each mouse was recorded. The data on antinociceptive activity

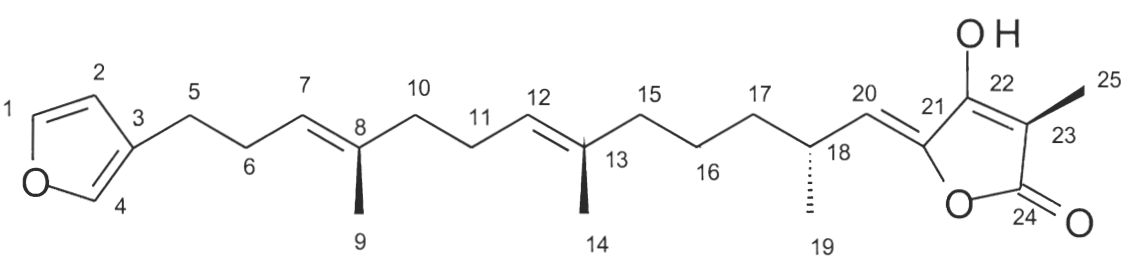

Figure 1. Chemical structure of variabilin.

Table 2. Mean of volume displaced and percentage of the anti-inflammatory effect.

Substance	Mean of volume displaced (mL)	Percentage of anti-inflammatory effect
Variabilin isomers 100 mg/kg	0.54 ± 0.04	29.6 ± 3.8
Variabilin isomers 150 mg/kg	0.27 ± 0.09	40.4 ± 3.9
Variabilin isomers 200 mg/kg	0.55 ± 0.04	42.6 ± 4.8
Indomethacine 6 mg/kg	0.27 ± 0.03	55.9 ± 1.5
Control	0.98 ± 0.06	0.0

percentage more or less similar to the inhibition percentage of the standard acetylsalicylic acid at the dose of 200 mg/kg, which means a potent antinociceptive effect of the isomers of the variabilin.

The behavior of the mice was normal without any significant changes equal to the behavior of the mice of the blank and the control.

Anti-inflammatory activity

The statistic analysis of the results for all the doses evaluated was realized with the data obtained at the third hour due to the high inflammation at this time and its lack at one hour of the carrageenan administration (8). The statistic analysis showed that there is a significant deference between the treatments but not between the blocks which means the anti-inflammatory activity of the compounds. Table 2 shows the mean of the volume displaced by the edema at the third hour and the percentage of the anti-inflammatory effect.

All the evaluated doses of variabilin isomers showed anti-inflammatory properties on the carrageenan-induced edema.

The percentage of the anti-inflammatory effect was 29.6%, 40.4% and 42.6% at the doses of 100, 150 and 200 mg/kg respectively, compared with 55.9% for the indomethacine in the dose of 6 mg/kg by oral administration. The result showed a significant anti-inflammatory effect of variabilin isomers at the doses of 150 and 200 mg/kg compared with the effect of the indomethacine at the dose of 6 mg/kg. From literature point of view variabilin showed anti-inflammatory activity when applied locally suppressing the mouse ear edema induced by 12-O-tetradecanoylphorbol 13-acetate and inhibited mouse paw edema induced by carrageenan (9).

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