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Short report

Antileishmanial and antifungal activities of xanthanolides isolated from *Xanthium macrocarpum*

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Abstract

Seven xanthanolides, xanthinosin, xanthatin, 4-hydroxyxanthinosin, xanthinin, 4-epiisoxanthanol, 4-epixanthanol, 2-hydroxyxanthinosin and 4-oxobedfordia acid, were isolated from the fruits of *Xanthium macrocarpum*. A valuation of the antifungal activity of these xanthanolides against *Candida albicans*, *Candida glabrata* and *Aspergillus fumigatus* and of their antileishmanial activity against *Leishmania infantum* and *Leishmania mexicana* is presented.

Keywords: *Xanthium macrocarpum*; Xanthanolides; Antifungal activity; Antileishmanial activity

1. Plant material

Xanthium macrocarpum DC (Asteraceae), fruits and leaves collected at Fresnes-sur-Loire, France, in September and October 2001, was identified by M. Lavault, Department

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of Pharmacognosy, University of Angers, France. A voucher specimen was deposited in the same department.

2. Uses in traditional medicine and other reported activities

X. macrocarpum has been traditionally used for the treatment of catarrhs, scrofula and leprosy [1]. *Xanthium* species are sources of sesquiterpene lactones, which are known to possess antiviral, antibacterial [2], antimalaric [3], antitrypanosomal [4] and fungicidal activities [5].

3. Previously isolated constituents

Xanthatin, xanthinin, xanthanol and isoxanthanol [6].

4. Tested material

From the fruits: xanthinosin (0.32%) [7], xanthatin (0.02%) [6,8], 4-hydroxyxanthinosin [9] (0.0002%) [9], xanthinin (0.0002%) [8,10], 4-epiisoxanthanol (0.009%) [8], 4-epixanthanol (0.009%) [8] and 2-hydroxyxanthinosin (0.0003%) [11]. 4-Oxobedfordia acid (0.0005%) [12] and flavone jaceidin (0.0004%) [13] were also isolated.

From the leaves: xanthathin (0.033%) [6,8], xanthinin (0.04%) [8,10], xanthinosin (0.008%) [7], 2-hydroxyxanthinosin (0.002%) [11], 4-epiisoxanthanol (0.025%) [8], 4-epixanthanol (0.03%) [8] and 4-oxobedfordia acid (0.01%) [12].

5. Studied activity

Antifungal screening activity by paper disk diffusion [14]. Fungistatic and fungicidal activities by broth microdilution method [15]. Antileishmanial activity by fluorimetric microdilution method [16].

6. Used microorganism

Listed in Table 1.

7. Results

Reported in Table 1. Xanthatin and xanthinin exhibited significant fungistatic activities with MIC 80 at 32 μg/ml. No significant fungicidal activities were revealed for these two

Table 1
Antifungal and antileishmanial activities of xanthanolides from *X. macrocarpum*

Microorganism	Xanthinosin	Xanthatin	4-Hydroxyxanthinosin	Xanthinin	4-Epiisoxanthanol	4-Epixanthanol	2-Hydroxyxanthinosin	Jaceidin	Amphotericin B[b]
Diameters of inhibitions zones/MIC$_{80}$ (μg/ml)									
C. albicans	30/125	27/32	21/250	20/32	–[a] />250	–[a]/>250	–[a]/>250	–[a]/>250	31/2
C. glabrata	–[a]/>250	27/32	–[a]/>250	–[a]/>250	–[a]/>250	–[a]/>250	–[a]/>250	–[a]/>250	32/2
A. fumigatus	–[a]/>250	–[a]/>250	–[a]/>250	–[a]/>250	–[a]/>250	–[a]/>250	–[a]/>250	–[a]/>250	31/2
IC$_{50}$ (μg/ml) ± S.D.									
L. infantum	35 ± 7	38 ± 5	>100	3.6 ± 0.8	24 ± 21	38 ± 14	>100	>100	0.02 ± 0.01
L. mexicana	44 ± 3	42 ± 7	>100	4.7 ± 0.2	40 ± 8	35 ± 14	>100	>100	0.05 ± 0.01

[a] No activity (diameter of the inhibition zone less than 12 mm).
[b] Reference positive.

compounds (data not shown). Five of the xanthanolides tested were found to be leishmanicidal, xanthinin being the most active compound.

8. Conclusion

Five xanthanolides exhibited an antileishmanial activity. Among them, xanthatin and xanthinin also exhibited an antifungal activity. α-Methylene-γ-butyrolactone group is requested for the antileishmanial activity, and this explains why jaceidin appears inactive. However, the active functional group has not been identified in the case of already reported antileishmanial sesquiterpenoids [17]. As for the antifungal activity, it seems to be related with the presence of the unsaturated carbonyl group in the cyclopentanone ring like in xanthatin, whereas the other isolated xanthanolides were inactive [18]. In the case of xanthinin, a possible metabolisation leading to an unsaturated carbonyl group by the elimination of an acetate ion could thus explain its activity. Lipophilicity is another factor to be considered to explain the lower activities of the other xanthanolides. In fact, a low polarity seems to be required for sesquiterpene lactones to pass through the fungal cell wall [19].

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