Xanthanolides of *Xanthium italicum* Moretti and Their Biological Activity

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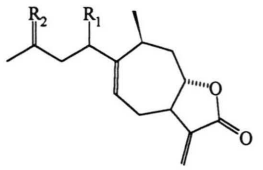
Seven xanthanolides were identified in the extract of *X. italicum* leaves. Antibacterial and cytotoxic activities were found for the total extract and its major constituents xanthinin and xanthatin.

The genus *Xanthium* (Asteraceae) includes a number of species, distributed from America over the whole world. The chemistry of this genus is quite uniform, xanthanolides being recorded in all cases [1]. We have now studied a species common in Bulgaria as a weed, *X. italicum* Moretti D. Löve. To the best of our knowledge, *X. italicum* has been object of a single early study and xanthinin (**1**) is the only compound found [2]. The present paper is the first report on isolation of the xanthanolides **2, 3, 4, 5** and **6** from the leaves of *X. italicum* (Fig. 1). These compounds were identified as xanthatin, xanthinosin, isoxanthanol, xanthanol and 2-hydroxyxanthinosin, respectively, by NMR and MS spectra in comparison with literature data [3–6]. It should be mentioned that the only detectable sesquiterpene lactones are with trans-fused lactone ring and according to McMillan [3] they are typical for the taxa placed in the "strumarium" morphological complex (*Xanthium strumarium* L.).

Further, the antibacterial and antiviral properties of the total leaves extract (LE) and the main xanthanolides **1** and **2** were studied. The results presented in Table I reveal that all the three samples have significant activity against gram-positive bacteria and show high cytotoxicity. Hence, a correlation between the cytotoxicity for animal cells and the antibacterial effect of the samples studied is evident. However, any relationship between the antiviral and antibacterial activity could be detected, as the total leaves extract (LE) was the only active sample towards pseudorabies virus (PsRV).



No.	R_1	R_2
1	OAc	O
2	H	O 2,3-dehydro-
3	H	O
4	OH	OAc, H
5	OAc	OH, H
6	OH	O

Fig. 1. Xanthanolides of *X. italicum*.

Experimental

Plant material

The leaves of *X. italicum* were collected in the vicinity of Sofia in July 1992. Voucher specimen (SOM-PR-150913) is deposited in the Herbarium of the Institute of Botany, Bulgarian Academy of Sciences.

Extraction and isolation

The air-dried plant material (80 g) was extracted with $CHCl_3$ and after evaporation of the solvent under reduced pressure the total leaves extract (LE) was obtained as a syrup (4.3 g). The extract was worked-up as described in ref. [7] and the obtained crude lactone fraction (1.3 g) was separated by column chromatography (SiO_2, 100 g) with toluene–acetone (8:1, v/v) to give the following lactones in order of their elution: **1** (450 mg), **2** (120 mg), **3** (17 mg), **4** (37 mg), **5** (40 mg) and **6** (46 mg). They were identified by their spectroscopic data.

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Table I. Antibacterial and antiviral[a] activity of *X. italicum* extract (LE), xanthinin (**1**) and xanthatin (**2**).

Sample	*S. aureus*		FPV			NDV			PsRV		
	$\varnothing_i$[b]	MIC [μg/ml]	$\varnothing_i$	$\varnothing_t$[c]	E[d]	$\varnothing_i$	$\varnothing_t$	E	$\varnothing_i$	$\varnothing_t$	E
LE	26	250	0	29	–	0	23	–	44	21	++
1	22	125	0	22	–	0	26	–	0	27	–
2	20	125	0	28	–	0	29	–	0	31	–

[a] 0.5% solutions of the samples in DMSO are used for antiviral screening.
[b] Diameter of inhibition zone (mm).
[c] Diameter of cytotoxicity zone (mm).
[d] Antiviral effect ($\Delta\varnothing = \varnothing_i - \varnothing_t$), E –, $\Delta\varnothing \leq 5$ mm, E++, $\Delta\varnothing = 21 - 40$ mm.

Spectral data

^{1}H NMR (250 MHz) and ^{13}C NMR (62.9 MHz) were run in $CDCl_3$ with TMS as int. standard on Bruker WM-250.

Mass spectra (EI-MS direct inlet 70 eV) were recorded on Jeol JMS D-300.

Biological activities

The antibacterial activity against *Staphylococcus aureus* and *Escherichia coli* was tested by a modification of the bioautography method [8]. The minimum inhibitory concentration (MIC) was determined by the method of serial dilution in broth towards *S. aureus* only, as no inhibition of gram-negative bacteria was detected. The antiviral screening was carried out by the agar-diffusion plaque-inhibition method [9, 10] against influenza virus A/chicken/Germany/27/Weybridge/H7N7 (FPV) [11]. Newcastle disease virus Russev strain (NDV) and pseudorabies virus A-2 strain (PsRV) grown in chick embryo fibroblast cultures [12].

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