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SESQUITERPENE LACTONES FROM *VERNONIA*

JOÃO LUIS CALLEGARI LOPES

Departamento de Física e Química, Faculdade de Ciências Farmacêuticas de Ribeirão Preto, USP,
Via do Café s/n, 14090 Ribeirão Preto, SP, Brasil

Some informations about the sesquiterpene lactones isolated from Brazilian species of Vernonia *are described, as well the results of tests developed with such compounds with respect to their anti-feedant, molluscicide, antimicrobial and analgesic properties.*

Key words: sesquiterpene lactones – *Vernonia*

Compositae is one of the largest and most familiar families of Flowering Plants, and has attracted organic chemists, botanists and pharmacologists for long time, specially for the large diversity of chemical constituents, taxonomic complexity, economic importance and biological applications.

Among the recognized 13 tribes of this family is the Vernonieae, a pantropical tribe containing about 1500 species. This tribe is well represented by the large genus *Vernonia* with more than 1000 species, from which 200 species (20%) are estimated of occurring in Brazil. A recent compilation from Chemical Abstracts showed that only 150 species (15%) were subject of any chemical analysis although the literature already contains a considerable number of reports on constituents of the *Vernonia*. The considerable number of non-investigated species and the abundance in Brazil justify a more intense investigation of the genus by Brazilian phytochemists.

The Chemistry of the genus *Vernonia* has been investigated chemically by many authors (Fischer et al., 1979; Seaman, 1982). Several types of natural products are present, but undoubtedly the most common are the sesquiterpene lactones containing an endocyclic 7 (11) double bond and an acetate group at C-13, known as glaucolides and hirsutinolides. A relative large number of sesquiterpene lactones have been related as possessing different types of bioactivity (Picman, 1986), and this activity seems to be associated with the presence of an α-methylene-δ-lactone and/or cyclopentenone ring moieties in the structure of the compounds.

The present report contains informations about the sesquiterpene lactones isolated from Brazilian species of *Vernonia*: *V. pedunculalata* DC, *V. scorpioides* (Lam.) Pers., *V. eremophila* Mart., *V. fruticulosa* Mart., as well the results of biological tests developed with such compounds. While in these four species sesquiterpene lactones have been detected, in others three species, *V. westiniana* Less, *V. discolor* Less and *V. mucronulata* Less there was no evidence of the presence of these compounds, although Jakupovic et al. (1987) have mentioned the occurrence of two terpenoids of glaucolide type in *V. westiniana*. From *V. pedunculata* were isolated compounds **4**, **5**, **6** (Lopes, 1980); from *V. scorpioides* compound **9** (Lopes, 1980) from *V. eremophila* compounds **1**, **7**, **8** (Alarcon, 1989) and from *V. fruticulosa* compound **1** (Nagamiti, 1987). The sesquiterpene lactones **2** e **3** were prepared from **1** by hydrogenation at room temperature in presence of PtO_2.

The sesquiterpene lactones have been submited to some biological tests and the results are following described. The anti-feedant properties of 15-deoxygoyazenzolide, eremantholide C and scorpioidine have been tested with *Locusta migratoria* (L.) (Table I). The anti-feedant activity of the three substances was different. Thus scorpioidine (**9**) showed the higher inhibition of feeding by *Locusta* and the activity incresead with an increase on the concentration of the substance. Results of a large number of experiments with sesquiterpene lactones described on the literature (Picman, 1986) suggest that these compounds are related with plant defense against herbivorous insects.

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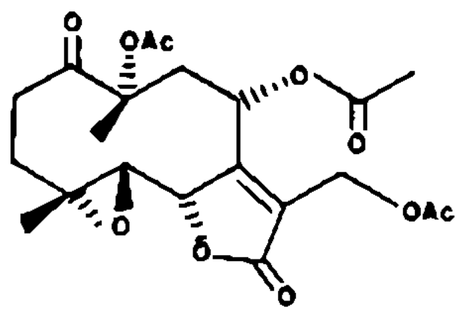
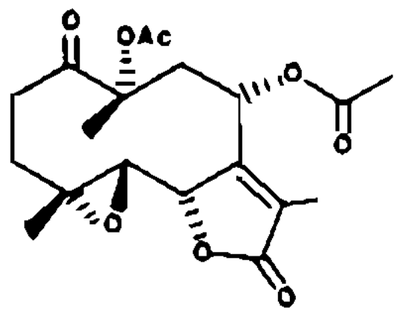
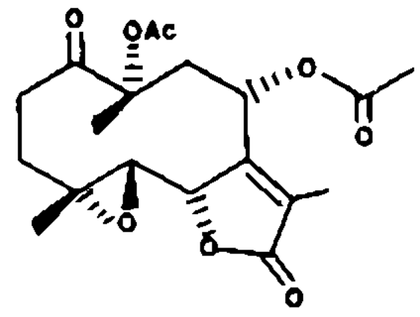
1 

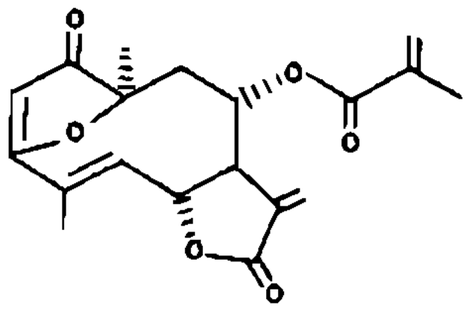
Glaucolide B

2 

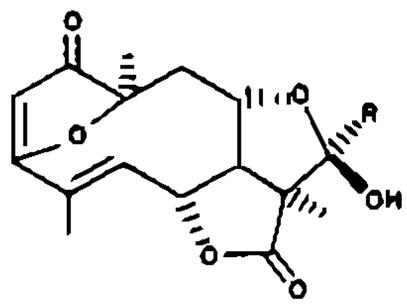
13-desacetoxy-glaucolide B

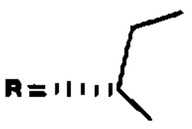
3 

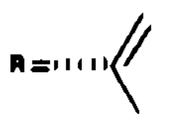
dihydrodesacetoxy-glaucolide B

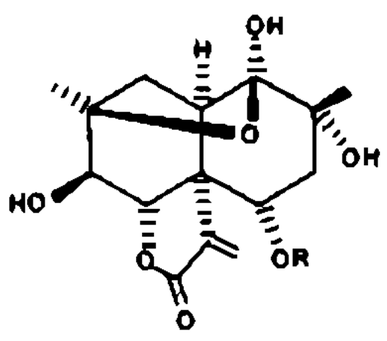
4 

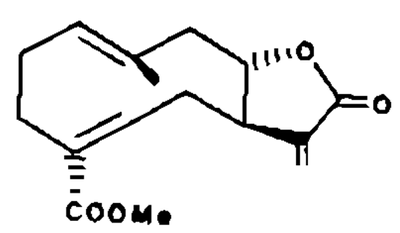
15-deoxygoyazenzolide



5 R=  eremantholide B

6 R=  eremantholide C



9 

scorpiodine

7 R = Ac 8-α-acetoxy-2-epi-vernomargolide-1,4-cyclohemiacetal

8 R = H 8-α-hydroxy-2-epi-vernomargolide-1,4-cyclohemiacetal

TABLE I

Feeding inhibition by sesquiterpene lactones

Compound	Concentration (% wt.)	Percentage of inhibition
Scorpiodine	1.0	98
	0.1	93
	0.01	43
eremantholide C	0.1	41
15-deoxygoyazenzolide	0.1	62

Some sesquiterpene lactones have been described as having quite potent molluscicide properties (Marchant et al., 1984). Compounds **1**, **2**, **3**, **4**, **6** and **7** have been assayed against snails and eggs of *Biomphalaria glabrata* (Table II). Glaucolide B (**1**) was the most toxic compound, it caused 90% mortality and 100 ppm and 40% mortality at 40 ppm to adult forms within 24 h and 73% mortality at 100 ppm to embryonic forms after 24 h. To investigate the effect of the α, β-unsaturated lactone function on activity, glaucolide B was converted by catalytic hydrogenation to derivatives **2** and **3**, and resulting compounds were without activity. Compound **7** with an α, β-unsaturated lactone function presented non significant activity while compound **4** with this moiety and a cyclopentenone ring were inactive.

TABLE II

Results of molluscicidal tests with *Biomphalaria glabrata* snails and eggs

Compounds	% Activity (Concentration in ppm)	
	Snails	Eggs
Glaucolide B	40 (10)	3 (10)
	90 (100)	73 (100)
13-desacetoxyglaucolide B	10 (100)	0 (100)
Dihydrodesacetoxyglaucolide B	0 (100)	0 (100)
15-deoxygoyazenzolide	0 (100)	0 (100)
Eremantholide C	0 (100)	0 (100)
8-α-acetoxy-2-epi-vernomargolide--1,4-cyclohemiacetal	20 (10)	0 (10)
	30 (100)	0 (100)

TABLE III

Antifungic and antibacterial activities of sesquiterpene lactones

Samples	Microorganisms								
	B.c.	S.a.	S.e.	E.c.	C.a.	C.t.	C.g.	C.n.	C.s.
Glaucolide B	10	12	NT	–	–	–	–	–	+
13-desacetoxyglaucolide B	–	–	–	–	–	NT	NT	NT	NT
13-dihydrodesacetoxyglaucolide B	–	–	–	–	–	NT	NT	NT	NT
15-deoxygoyazenzolide	–	–	–	–	–	–	–	–	–
Eremantholide B	12	12	NT	–	–	10	10	9	–
Eremantholide C	–	–	–	–	–	–	–	–	–
8-α-acetoxy-2-epi-vernomargolide--1, 4-cyclohemiacetal	–	–	–	–	–	–	–	–	–
Chloramphenicol	15	9	10	12	–	–	–	–	–
Nystatin	–	–	–	–	18	15	10	14	–
Solvent (DMSO/H_2 1:1)	–	–	–	–	–	–	–	–	NT

Microorganisms: B.c. *Bacillus cereus;* S.a. *Staphyllococcus aureus;* S.e. *Staphyllococcus epidermidis;* E.c. *Escherichia coli;* C.a. *Candida albicans;* C.t. *Candida tropicalis;* C.g. *Candida glabrata;* C.n. *Criptococcus neofarmans;* C.s. *Clasdosporium sphaesrospermum.*
Biossays carried out by the method of agar diffusion (1 mg/ml) except for *C. sphaesrospermum,* assayed by biochromatography. Results expressed by the maximum diameter (mm). Concentration antibiotics = 30 μg/ml. NT: non tested, – no inhibition of growth (inactive compound).

The sesquiterpene lactones **1**, **2**, **3**, **4**, **5**, **6** and **7** were assayed for their antimicrobial activity (Table III). Many compounds of this class possess antibacterial and anti-fungal activities (Picman & Towers, 1983; Picman, 1986; Davino, 1989). Results of the screening shown that glaucolide B (**1**) and eremantholide B (**5**) inhibited the growth of bacteria and only eremantholide B was weakly active against fungus.

Finally, glaucolide B exhibited weak analgesic activity in the mouse writhing test, eliciting a 58% response at a dosage of 160 mg/kg compared with indomethacin's 50-60% response at 5 mg/kg. No effect was observed with the hydrogenation products of glaucolide B (**2** and **3**). No effects were observed with glaucolide B on the rat paw edema induced by carrageenin and dextran.

ACKNOWLEDGMENTS

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