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Isolation and *in vitro* Biological Activities of a Rare Triterpenoid from the roots of *Trewia polycarpa*

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The *n*-hexane soluble fraction of the ethanolic extract of the roots of the plant *Trewia polycarpa* yielded a rare triterpenoid of taraxarane series, 3ß-acetoxytaraxaren-14-en-28-oic acid (I) whose identity has been confirmed by spectroscopic studies. This is the second report on the isolation of I from nature and first from the genus *Trewia*. Compound I exhibited prolongation of prothrombin time and also showed mild antibacterial and antifungal activities.

Trewia polycarpa Benth. (Euphorbiaceae) is used in the traditional Ayurvedic medicine under the name *Gambhari Prathinidhi*[1]. As no chemical or biological screening has been carried out on this plant, the roots which find use in medicine were taken up for the study. The roots of *T. polycarpa* were collected from Thiruthuraipoondi (Nagapattinam District, Tamil Nadu) and identified in the Survey of Medicinal Plants Unit (CCRAS, Govt. of India), Tirunelveli, Tamil Nadu. A voucher specimen has been retained in the herbarium of Sri Ramachandra Medical College and Research Institute, Chennai (Pharma No.02/98). Shade dried and coarsely powdered roots (2.5 kg) were extracted exhaustively with 90% ethanol (3x6 l) at room temperature. After 72 h the solvent was decanted, distilled over boiling water-bath and concentrated *in vacuo* to obtain the crude extract (yield: 44 g /1.75% w/w).

The ethanolic crude extract was successively shaken with *n*-hexane and chloroform. The *n*-hexane fraction on standing overnight afforded an amorphous powder which on column chromatography over silica gel (100-200 mesh) yielded a crystalline compound (I). [m.p. 289-291°; R_f 0.64

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(benzene:ethyl acetate, 19:1) and M.F. $C_{32}H_{50}O_4$]. Compound I answered positive Salkowski test for triterpenoids and has been identified as 3β-acetoxytaraxaren-14-en-28-oic acid based on the following spectral data.

IR: υ_{max}^{KBr} (cm^{-1}): 2936, 2859, 1734, 1687, 1474, 1451, 1388, 1377, 1365, 1297, 1241, 1215, 1143, 1026, 999, 930, 900, 832. ^1H NMR: (300 MHz, $CDCl_3$) δ_{ppm}: 0.84-0.95 (7x-Me), 2.03(1x-COMe), 2.30 (1H, dd, J=11.0 and 2.0 Hz, H-18), 2.38(2H, bd, J=8.0 Hz, H_2– 16), 4.45(1H, t, J=8.5 Hz, H-3α), 5.51 (1H, dd, J=7.55 and 3.03 Hz, H-15). ^{13}C NMR: (75 MHz, $CDCl_3$) δ_{ppm}: 37.6(C-1), 23.6 (C-2), 81.0 (C-3), 37.5 (C-4), 55.8 (C-5), 18.8 (C-6), 41.0 (C-7), 39.1 (C-8), 49.2 (C-9), 38.1 (C-10), 17.4 (C-11), 33.8 (C-12), 37.8 (C-13), 160.7 (C-14), 116.9 (C-15), 31.5 (C-16), 51.5 (C-17), 41.7 (C-18), 35.5 (C-19), 29.3 (C-20), 33.4 (C-21), 30.9 (C-22), 28.0 (C-23), 16.6 (C-24), 15.8 (C-25), 26.2 (C-26), 22.5 (C-27), 184.0 (C-28), 32.0 (C-29), 29.3 (C-30), 170.8 (CH_3COO), 21.2 (CH_3COO). The structure of I was further confirmed by 2D- COSY (^1H-^{13}C) studies.

A perusal of literature revealed that compound I has earlier been isolated from the roots of an African plant *Maprounea africana* Muell. -Arg. (Euphorbiaceae) and reported to possess inhibitory activity against HIV-1 reverse transcriptase[2]. However, this is the first report on the isolation of compound I from an Indian plant as well as the genus *Trewia* and second from a natural source.

Different concentrations of compound I were tested for

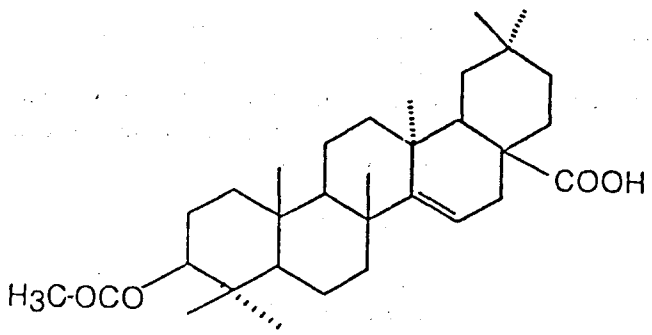
TABLE 1: EFFECT OF COMPOUND I ON PROTHROMBIN TIME.

Dose (μg)	Prothrombin Time (Sec)	INR Ratio
Control	13.3	
Aspirin 100	14.2	1.05
Compound I		
12.5	13.5	1.07
25.0	13.6	1.05
50.0	14.7	0.97
100.0	15.3	0.86

TABLE 2: ANTIMICROBIAL ACTIVITY OF COMPOUND I[a].

Microorganism	Compound I (μg)					Standard[b]
	62.5	125.0	250.0	500.0	MIC	
Bacteria						
Staphylococcus aureus	-	-	-	-	-	27.0
Streptococcus pyogenes	-	-	-	-	-	23.0
Escherichia coli	-	-	-	-	-	33.0
Pseudomonas aerugenosa	-	-	-	-	-	33.0
Salmonella typhi	-	-	-	-	-	25.0
Klebsiella pneumoniae	9.0	10.0	11.5	12.6	62.5	32.7
Fungi						
Candida albicans	-	7.0	7.0	9.0	125	39.0
Aspergillus niger	-	8.0	9.0	9.5	125	38.5
Cryptococcus neoformans	-	-	-	-	-	38.0
Penicillium sp.	-	-	-	-	-	43.0

[a]Values are mean of two sets of experiment (diameter of zone of inhibition in mm); [b]Standard for antibacterial studies - ciprofloxacin (5 μg); antifungal studies-clotrimazole (100 μg); MIC-μg/ml; - no inhibition; Diameter of disc or well - 6 mm; Solvent used for dissolving compound I and standards – DMSO.



(I)

the effect on prothrombin time[3] and on six bacteria and four fungi. The antibacterial activity was carried out by disc diffusion method[4] and antifungal activity by cup-plate method[5]. In the former study, the compound showed a concentration-dependent increase in prothrombin time compared to aspirin (Table 1). In the antimicrobial study, it exhibited mild antibacterial activity against *Klebsiella pneumoniae* and mild antifungal activity against *Candida albicans* and *Aspergillus niger* while no inhibition against other microbes was observed in the concentrations studied (Table 2). Minimum inhibitory concentration was studied by double dilution method.[5]

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Enhanced Transdermal Permeation of Bupropion Hydrochloride by Chemical Modification

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Bupropion, a monocyclic aminoketone is used primarily for the treatment of major depression. On oral administration, the drug undergoes extensive first pass metabolism. Delivery of bupropion via transdermal route would minimize some of the deficiencies associated with the oral delivery. In the present study, effect of various vehicles and penetration enhancers on diffusion kinetics of the salt and free drug through the human cadaver skin was studied using a modified diffusion

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