CYTOTOXIC DYSORONE E AND OTHER CONSTITUENTS OF THE LEAVES OF *DYSOXYLUM ROSEUM*(MELIACEAE) FROM NEW CALEDONIA

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Résumé *: cinq triterpènes nouveaux de type apotirucallane dénommés dysorone A-E ont été isolés des feuilles de* Dysoxylum roseum, *en même temps qu'un dérivé aromatique possédant une fonction époxyde, qui a reçu le nom de dysoroxide. Le triterpène majoritaire, la dysorone E, est modérément cytotoxique in vitro vis à vis des cellules du carcinome buccal humain du type KB (ED_{50} 3.5 µg/ml).*

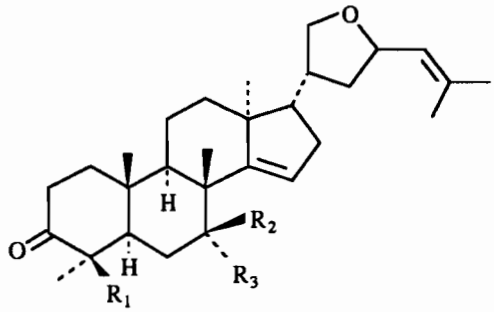
Abstract *: chemical investigation of the biologically active compounds in* Dysoxylum roseum *leaves has led to the isolation and characterisation of five new apotirucallane-derived triterpenes called dysorone A-E and an aromatic epoxide called dysoroxide. The major compound, dysorone E , exhibits moderate cytotoxic activity in vitro against the growth of KB human buccal carcinoma cells (ED_{50} 3.5 µg/ml).*

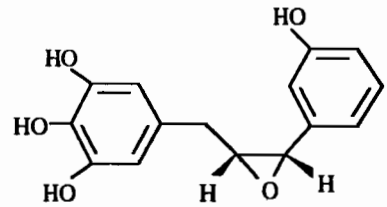
Dysoxylum roseum C.DC. belongs to a genus with varied ethno-medical uses in Polynesia, India, Malaysia, and other regions of the Pacific (1). Members have been shown to possess antibacterial (2), CNS depressant and antiinflammatory (3), immunomodulatory (4) and cardioactive (5) activities. *Dysoxylum roseum* grows as a tree and the leaves collected in the Rivière Bleue forest reserve, New Caledonia, were tested in systematic study of New Caledonia plants for bioactive agents.

Preliminary biological screening indicated cytotoxic and antibacterial activities for the methanolic extracts of the barks and the leaves, respectively against KB cells and *Staphylococcus aureus*. Only the extract from the bark showed immunomodulatory activities using tests based on interleukine production by activated macrophages.

The MeOH extract was fractionated by various chromatograhic procedures with fractions monitored for cytotoxicity. This led to the isolation of novel apotirucallane-derived (3,6) triterpenes, dysorone A-E and an epoxide, dysoroxide.

Dysorone A-E were characterised by their ^{1}H and ^{13}C nmr, $^{1}H/^{1}H$ COSY , $^{1}H/^{13}C$ HETCOR and long range HETCOR data. Their negative $[\alpha]_D$ indicates triterpenoids belonging to the tirucallane rather to the euphane series (7). Other data collected include hrms, ir, uv and mp. Similar data identified dysoroxide as 1-(3',4',5'-trihydroxyphenyl)-3-(3",5"-dihydroxy-phenyl)-propan-2,3-epoxide.





Dysorone A	$R_1 = CH_2OH$,	$R_2,R_3 = O$	Dysoroxide
Dysorone B	$R_1 = CH_2OH$,	$R_2 = H, R_3 = OH$	Mp, 213-215°
Dysorone C	$R_1 = CH_3$,	$R_2,R_3 = O$, D^1	Heirms, m/z 290, M^+
Dysorone D	$R_1 = CH_3$,	$R_2 = H, R_3 = OH$, D^1	UV λ max 280 nm
Dysorone E	$R_1 = CH_2OH$,	$R_2,R_3 = O$, D^1	

The cytotoxic activity of each isolated compound was evaluated by the ability to inhibit the *in vitro* growth of KB human buccal carcinoma cells. Only Dysorone E was active with ED_{50} of 3.5μg/ml.

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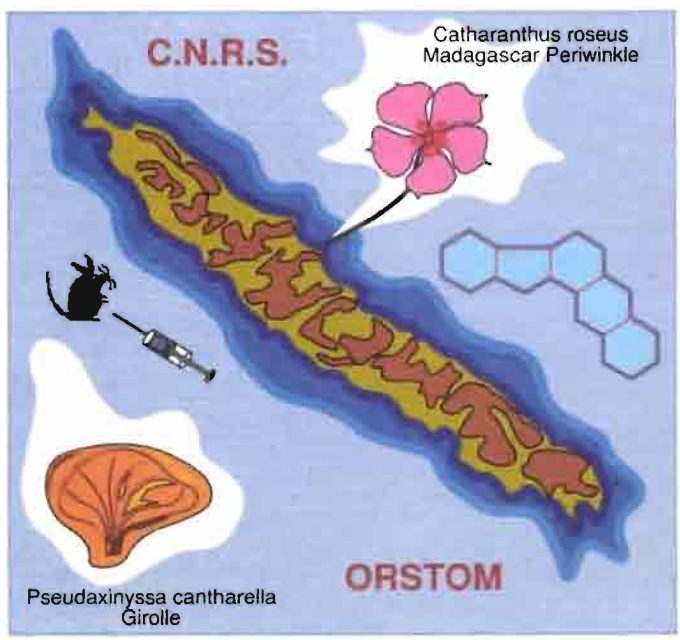

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