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Short Communication

Tecomella undulata: A Potential Source of Anti-AIDS Agents

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Plant secondary metabolites are extensively used as drugs, fragrance, food, flavor, color, etc. Nearly 33% of the total drugs manufactured are either extracted directly from the plants or are elaborated from precursors derived from plant products. Preference for these plant-origin drugs is increasing enormously all over the world. With the resurgence of interest in ethno-botany, the recent biotechnological advances and GATT, many countries as well as WHO are taking keen interest in plants as sources of useful drugs, and are providing required encouragement for better utilization of the plant resources.

Tecomella undulata Smith (Bignoniaceae), locally known as Rohida, is a codominant species in the desert of western Rajasthan. Its wood is resistant to fungus and termite (Gupta *et al.*, 1969). The bark of its young branches is used for the treatment of syphilis and eczema. It possesses mild relaxant, cordiotonic and choleretic activities (Anonymous, 1976). In view of the wide ranging properties of *T. undulata*, a systematic chemical investigation of the plant was undertaken.

Previous investigations of *T. undulata* (Gujral *et al.*, 1979; Gupta *et al.*, 1969; Joshi *et al.*, 1986; Verma *et al.*, 1986) revealed the presence of lapachol, dihydrotectol, n-hentiacontanol, n-heptacosane, tecomin, veratric acid, quinones, chromone glucoside, undulatin, tecoside, etc. Present work reports the isolation of known betulinic, oleanolic and ursolic acids from the leaves of *T. undulata*.

The leaves of *T. undulata* were collected from Central Research Farm, CAZRI, Jodhpur, and dried under shade. The air dried leaves (4.4 kg) were powdered and soxhlet extracted first with petroleum ether (60 to 80°C) and subsequently with acetone. Petroleum ether was distilled off and the residue was chromatographed over a column of silica gel. It was eluted with petroleum ether and petroleum ether-ethyl acetate mixture of increasing polarity. Fractions of petroleum ether-ethyl acetate (19:1) mixture, showing similar spots on TLC, were combined, concentrated and kept overnight. The compound so obtained was filtered and recrystallized from ethyl acetate to afford betulinic acid (660 mg). Fractions of petroleum ether-ethyl acetate (9:1) mixture afforded oleanolic acid (2.37 g). The residue left after the removal of the solvent from acetone extract, was washed with petroleum ether and subsequently refluxed with chloroform (3 x 500 ml). The combined chloroform washings were concentrated and kept overnight, to afford ursolic acid (4.18 g). The isolated compounds

were characterized by interpreting IR, MS, ^{1}HNMR, ^{13}CNMR and DEPT spectral data. Their comparison with authentic samples (TLC, m.p., m.m.p.) confirmed the identity of compounds. The identification of other isolated triterpenes are under process.

A review of literature showed that ursolic acid (Xu *et al.*, 1996), oleanolic acid (Kashiwada *et al.*, 1998) and betulinic acid (Fujioka *et al.*, 1994) are potential inhibitors of human immunodeficiency virus (HIV) replication. This is because the EC_{50} (anti-HIV) values for ursolic, oleanolic and betulinic acids are 2.0, 1.7, 1.4 μg ml^{-1}, respectively, and the IC_{50} (toxicity) values for the above acids are 6.5, 21.8, 13 μg ml^{-1}, respectively.

These triterpenic acids have been reported (Kashiwada *et al.*, 1998) in the species *Syzygium claviflorum* (betulinic acid, 0.054%; oleanolic acid, 0.0037%; ursolic acid, 0.0055%), *Rosa woodii* (betulinic acid, 0.0035%; oleanolic acid, 0.0067%), *Prosopis glandulosa* (oleanolic acid, 0.0015%; ursolic acid, 0.0115%), *Turnstromia gymnandthera* (betulinic acid, 0.029%; oleanolic acid, 0.03%) and *Phoradendron juniperinum* (oleanolic acid, 0.29%). The concentration of betulinic, oleanolic and ursolic acids found in *T. undulata* in the present study are 0.015%, 0.054%, 0.0095%, respectively. These concentrations are higher in comparison to the concentrations reported in other species.

Derivatization of these acids afforded extremely potent anti-HIV compounds. The therapeutic index (T.I.) value, which is defined as IC_{50} divided by EC_{50}, of betulinic acid-3-O-3′,3′-dimethylsuccinate that has been derived from betulinic acid, is >20,000 (Kashiwada *et al.*, 1996). Oleanolic acid-3-O-3′,3′-dimethylsuccinate (ODS) showed extremely significant anti-HIV activity with EC_{50} value of 0.0005 μg ml^{-1} and T.I. value of 22400 (Kashiwada *et al.*, 1998). Interestingly, ODS is 24 times more effective than AZT, a drug which is presently used for checking the spread of AIDS. However, due to higher toxicity of ODS, it has lower T.I. value than AZT (22400 for ODS and 41667 for AZT).

Efforts are being made to further modify the oleanolic acid/betulinic acid and other related anti-HIV principles to reduce the toxicity and increase the T.I. In case this is successful, the ursolic, oleanolic and betulinic acids in *T. undulata* will make this plant "Green Gold" of Thar desert.

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