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REVIEW

A Brief Review on Chemical Constituents of Some Medicinally Important Species of the Genus *Plumeria*

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The present communication deals with a brief review of some species from *Plumeria* (family—Apocynaceae) which are used in the treatment of various ailments like bitter tonic, expectorant, purgative skin diseases, diuretic, antipsychotic, antitumor agents and as inhibitors of human immuno-deficency virus type-1 (HIV-1).

INTRODUCTION

Species of Genus *Plumeria* have been investigated for iridoids and triterpenoids and some of these have been found to exhibit algicidal, antibacterial, cytotoxic and plant growth inhibiting activity.[1-6]

A survey of the literature reveals that the following *Plumeria* species have attracted the attention of chemists to carry out phytochemical and biological investigations:

P. acuminata

Isolation of antigenotixins from this species was reported.[7] The plant was reported to be an animal killer.[8, 9] Pharmacological action of the leaves was reported by Muir *et al.*[10] Herrera *et al.* have studied some Philippine plants as possible sources of antifertility agents.[11]

P. acutifolia

From the leaf of the title plant plumeric acid (1, R = H) and methyl plumeriate (1, R = Me) were obtained. An injection formulation containing 10 mg of plumeric acid and 5 g powdered glucose, showed antitumor activity with 100% effective in inhibiting Yoshida sarcoma cells *in vitro*.[12]

Freshly picked, mature, green leaves of this plant were tested for antimutagenic activity by using its bioassay. Bioassay results indicated that the CCl_4 extract has antimutagenic activity. This extract was fractionated and subjected to sequential

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flash column chromatography. Three of the TLC-pure isolates exhibited antimutagenic activity. One of these is a triterpenoid derivative.[13]

Structure assignments of plumieride and its acetyl derivative isolated from stem bark of the plant were studied.[14]

Mahdihassan reported some anticancerous activity of this plant.[15] A study about some folk medicines including the title plant of Singhbbum (Bihar) has been done by Chandra *et al.*[16] Pharmacological studies of this plant have been also reported by Siddiqui *et al.*[17]

P. alba

The leaves, stems, flowers and latex of the title plant have been analyzed for their total soluble sugars, reducing sugars and free amino acids. Their latex was also analyzed qualitatively for sugars and amino acids. Sucrose, glucose, raffinose, proline, tryptophan and tyrosine were found. The highest percentage of total soluble proteins was found in the leaves and stem. The flowers showed a higher quantity of sugars than other parts of the plant.[18]

Flowers of this species was also reported to contain several flavonoids.[19] Subramanian *et al.*[20] studied the optical microscopic properties on the structure and secretion of resin glands in this plant.

Preliminary phytochemical screening has been carried out in 12 laticiferous members belonging to family Apocynaceae including *P. alba*. Based on the qualitative analysis of carbohydrates and amino acids, an artificial key has been suggested which may help in delineation of closely related taxa of the family.[21]

P. bicolor

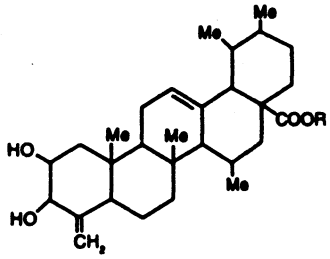
The chloroform extract of the stem bark of the title plant afforded three new compounds *i.e.* 3β-hydroxy-plumerian-12-ene (2), 3β-acetoxy-plumerian-12-ene (3) and tetratriacontanol ferulate (4) along with the known compounds *viz.* allamandin (5), 2,5-dimethoxy-*p*-benzoquinone (6), sioplumericin (7), plumericin (8), allamcin (9) and fulvoplumiericin (10). (This is the first report of the isolation and characterization of chemical constituents from this species).[22] Some of the known compounds were reported for their biological activities when evaluated with a panel of cell lines composed of murine lymphocytic leukemia (P-388) and a number of human cancer cell-types (breast, colon, fibrosarcoma, lung, melanoma and KB).[23]

P. elegans

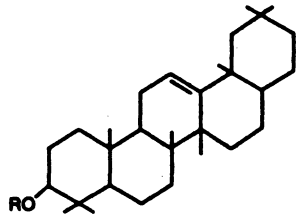
Lectins were isolated and characterized from this species. Hemagglutination of papain or neuraminidase treated human erythrocytes by extraction of the plant was inhibited by porcin stomach mucin. Lectin accounting for 23% of activity in this plant had a molecular weight 8100. Phycobiliproteins were not associated with lactin.[24] Lectins were also isolated from this plant by Fish *et al.*[25] The plant also contains a good amount of amino acids.[26]

P. obtusa

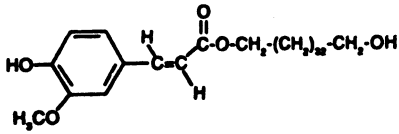
From the fresh leaves of the title plant, pentacyclic triterpenoids along with



(1)



(2) R = H
(3) R = Ac



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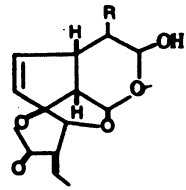
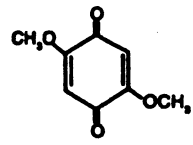


(5) R = COOMe
(9) R = H



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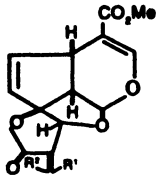
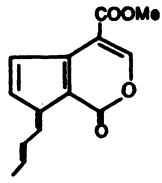
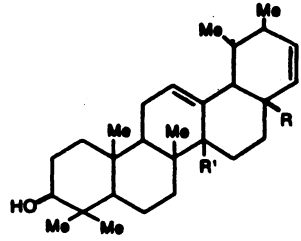


(7) R¹ = H, R² = Me
(8) R¹ = Me, R² = H



(10)



(11) R = CH_2OEt, R¹=Me
(12) R = CO_2H, R¹ = Me
(13) R = CH_2OEt, R¹=CO_2H

coumarin derivative have been isolated. Two new triterpenes "obtusin and obtusilic acid" were characterized as the 24-E and 27-Z *p*-coumaric esters of the novel 3β,24-dihydroxyurs-12-en-28-oic acid and 3β,27-dihydroxyurs-12-en-30-oic acid, respectively, through chemical and spectral studies. Some known compounds as kaneroside, oleandrin, α-amyrin, neriucoumaric acid, isoneriucoumaric acid, alphitolic acid, oleanonic acid, methyl-*p*-E-coumarate and scopoletin have also been reported.[27]

A new triterpenoid, obtusilinin (11) and 27-*p*-Z-coumaroyloxyursolic acid

were also reported. Their structures were established as 3β-hydroxy-27-p-Z-coumaroyloxyolea-12-en-28-oic acid and 3β-hydroxy-27-p-Z-coumaroyloxyurs-12-en-28-oic acid respectively.[28]

From the fresh leaves of this plant two new pentacyclic triterpenoids, obtusic acid (12) and obtusilinic acid (13), were isolated.[29]

Five pentacyclic triterpenoids of the Ursana series were isolated from the plant. These compounds have not been reported from the natural sources[30] The fresh spring leaves of the plant contains pentacyclic triterpenoids. A new triterpene, obtusalin (14), was characterized as 3β-27-dihyroxylup-12-ene through chemical and spectral methods, while the other three were betulinic, oleanolic and ursolic acids.[31] From the leaves also, coumarobtusanoic acid (15) and coumarobtusana (16) were isolated. A known triterpene, 27-p-E-coumaroyloxyursolic acid, was also identified.[32]

P. rubra

From a water-soluble extract of the stem bark of the title plant, a novel flavan-3-ol glycoside, plumerubroside (17), was isolated. Its structure and conformation established it as (2R, 3S)-3,4′-dihydroxy-7,3′,5′-trimethoxy- flavan-5-O-β-D-glucopyranoside.[33]

Heartwood of this plant gave six compounds. Plumericin and isoplumericin showed molluscicidal, cytotoxic and antibacterial activities, 4-hydroxy-acetophenone showed weakly cytotoxic activity, whereas the remaining glycosidic compounds plumieride, 13-O-coumaroylplumieride, protoplumericin-A, were also isolated and characterized.[34]

The stem bark of the plant yielded plumerine, a novel lupin alkaloid (18). The presence of these were the first example of the occurrence of bicyclic lupin alkaloids in subfamily Plumerioideae a of the Apocynaceae.[35]

The essential oil known as "Common yellow" growing in Hawaii was extracted and analysed with GC and GC-MS and a total of 74 compounds were identified. Compounds, linalol, phenylacetaldehyde, transfarnesol, β-phenylethyl alcohol, geraniol, d-terpeneol, neral and geranial were found in major quantity in the floral scent of flowers.[36] β-Phenylethyl alcohol, phenylacetaldehyde and methyl cinnamate were also found to make a major contribution to the floral spicy scent of this flower.[37] The leaves of the title plant showed antifertility action on adult male albino rats when treated at the daily dose of ½ leaf/rat for 10 or 20 days. The test substances effectively inhibited fertility of the male rat by involution of the genital structures evidenced by sterile matings with proestrous females.[38] From the bark of the plant collected in Indonesia, six cytotoxic constituents were characterized. There iridoids, *viz.* fulvoplumierin, allamcin, and allamandin, as well as 2,5-dimethoxy-*p*-benzoquinone were found to be active constituents of the petroleum-ether and $CHCl_3$-soluble extracts. Cytotoxic compounds were also isolated from the water-soluble extract of the bark as iridoid plumericin and the lignan liriodendrin (19). Each of these substances showed general cytotoxic activity when evaluated with a panel of cell lines composed of murine lymphocytic leukemia (P-388) and a number of human cancer cell-types (breast, colon, fibrosarcoma, lung, melanoma, KB). Five additional iridoids,

15-demethylplumieride (20), α-allamcidin (21), β-allamcidin (22), and 13-*o*-trans-*p*-coumaroylplumieride (23) were obtained as inactive constituents. 2,5-Dimethoxy-*p*-benzoquinone was a novel natural product, and its structure was detected by spectroscopic methods and by conversion to plumieride. The configuration of the C-4 stereocenter was unambiguously assigned for (21) and (22).[39]

Some plant latexes of the family *Apocynaceae* were investigated for the presence of acid phosphatase and ATPase. The richest sources of the enzymes ATPase were found in the latex of *P. rubra*.[40]

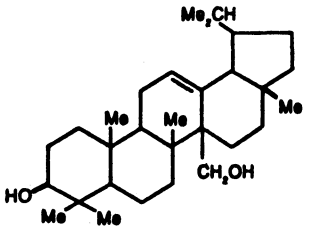
The stem of the title plant showed the presence of phenolic contents. The leaves contain high concentration of *o*-dihydroxyphenol.[41] From this plant two new oleanene triterpenes were also isolated and their structures were established as 6α-hydroxy-3-epi-oleanolic acid and 3α,27-dihydroxy-olean-12-ene by means of chemical and spectral methods.[42]

The decorticated stem of the plant afforded fulvoplumierin, amyrin, lupeol, β-steroid and plumieride.[43]

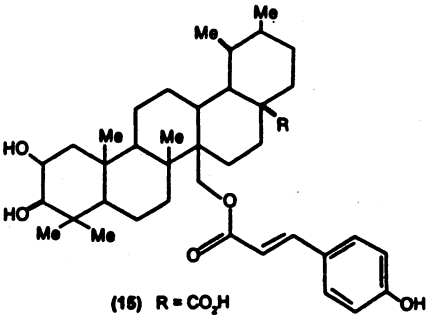
From the powdered roots of this species (grown in Egypt) plumericin was isolated in yields of 0.08 and 0.1%. Fulvoplumierin was also isolated from the stem bark of this plant in yields of 0.20 and 0.24%.[44]

Ethanolic (96%) extract of the stem bark, stem wood, roots and leaves of this plant (grown in Egypt) yielded plumieride (24). Evaporating the alcohol, taking up the residue with water, filtering, removing excess Pb with 5% Na_2HPO_4, decolorizing the filtrate with charcoal, extracting with EtOAc, washing with 2N-Na_2CO_3 and water, evaporating and crystallizing from 70% EtOH. Fulvoplumierin was quantitatively detected by treating with $FeCl_3$ in H_2SO_4 and assaying colorimetrically. The percentages of fulvoplumierin found in the young stem (0.2), stem wood (0.47), leaves (0.45), roots (0.52) and stem (0.96).[45]

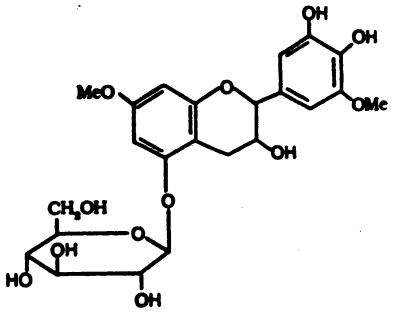
Inhibition of human immunodeficiency virus *Revers transcriptas* is currently considered a useful approach in the prophylaxis and intervention of acquired immunodeficiency system (AIDS), and natural products have not been extensively explored as inhibitors of this enzyme. The reverse transcriptase assay developed for the detection of the enzyme in virons involving polyadenylic acid, oligoleoxythymidylic acid (poly rA. oligo dT.) and radiolabeled thymidine 5′-triphosphate (TTP), can be applied as a simple method for screening the human immunodeficiency virus type-1 reverse transcriptase (HIV-1RT) inhibitory potential of natural products. One hundred fiftysix pure natural products were examined in this system. Benzophenanthridine alkaloids, such as fagaronine chloride and nitidine chloride, which are known inhibitors of *avian myelobblastosis virus* reverse transcriptase, demonstrated potent activity in the HIV-1RT system. Additional inhibitors found were columbamine iodide and other protoberberine alkaloids, the isoquinoline alkaloid *o*-methyl-psychotrine sulphate, and the iridoid fulvoplumierine. A number of alkaloids, as well as compounds of many other structural classes, were tested and found to be inactive. Out of 100 plant extracts evaluated, 15 extracts showed significant inhibitory activity. Polyphenolic compounds were found to be responsible for the activity demonstrated by the majority of plant extracts. The method also proved useful in directing an isolation



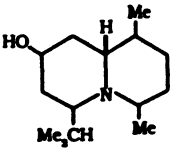
(14)



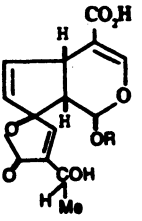
(15) R = CO_2H
(16) R = Me



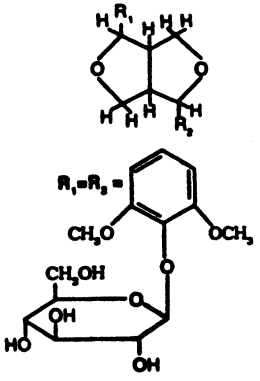
(17)



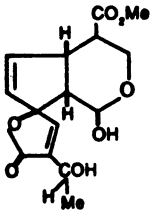
(18)



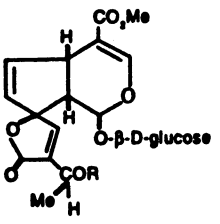
(20) R=β-D-glucopyranosyl



(17)



(21), α-OH
(22), β-OH



(23), R=trans-p-coumeroyl
(24), R=H

procedure with the title plant to yield fulvoplumierin as an active compound (IC_{50} 45 μg/mL).[46]

Phytochemical studies of this plant have resulted in the isolation of taraxasteryl acetate, lupeol, stigmasterol, oleanolic acid, cycloart-22-ene-3α,25-diol and rubrinol (m.p. 244°C), a new triterpene of the Ursane series. Its structure was found to be 3β, 30-dihydroxy-12-ursene. The antimalarial testing showed it to be

active against *Bacillus anthracis, Pseudomonas aeruginosa, Pseudomonas pseudomallei* and *Corynebacterium pseudodiphthericum.*[47]

Volatile compounds of an alcoholic extract from flowers of the title plant were isolated by continuous liquid-liquid extraction with isopentane. The extract was analysed by HR-GC and GC-MS techniques. A total of 27 compounds were identified out of which 16 were reported for the first time in the flower.[48]

Preliminary screening for antibacterial and antitumor activities of Papua New Guineen native medicinal plants was carried out by Sundarrao *et al.*[49]

P. sericifolia (C. Wright)

From the stem of the title plant alkaloid vincubine, which previously was isolated from *Catharathus roseus*, was also isolated in (3–3.5%) yield.[50]

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