



A BIOACTIVE COMPONENT MARMESIN FROM *FERONIA LIMONIA* FRUIT PERICARP: A REVIEW

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Abstract: Plants serve as a vast source for many phytoconstituents that exhibit pharmacological properties. Identification of such types of potential plants is of great significance in medicine. It's a necessity to study the pharmacognostic characteristics of any plant before using it in the field of research and pharmaceutical formulation. *Feronia limonia* plant is well known for its medicinal properties. Wood apple has antioxidant, anticancer, antidiabetic, antimicrobial and hepatoprotective activity. In India, the fruit pericarp is used as a stomachic, diuretic, antidiabetic, antimicrobial, anticancer, cardiogenic and tonic to liver and lungs. Fruit pericarp of *Feronia limonia* contains marmesin and other components. Shell shows anti-fungal activity against gram positive and gram negative bacteria because of Psoralen. The fruit shells also contain anti-fungal compounds xanthotoxin, 2, 6-dimethoxybenzoquinone and osthonol. The structure elucidation was performed with the help of UV, IR, ¹H NMR, ¹³C NMR and mass spectra that confirmed the identity of Marmesin. It is a bioactive component furanocoumarin, which has a variety of pharmacological functions such as anti-inflammatory, antihepatotoxic, antiangiogenic, anticancer and antitumor activities. This article explains all about these things.

Keywords: Dihydrofuranocoumarin, Fruit pericarp, Pharmacological activities, Phytochemicals.

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INTRODUCTION

Feronia limonia Swingle (syn. *F. Elephantum correa*) is a common Indian tree belongs to the tribe Citrea and sub tribe Balsamocitrinae (Dreyer *et al.*, 1972). It is commonly known as 'Kaitha' in Hindi (Chopra *et al.*, 1956), wood apple or elephant apple in English and as 'Kapitha' in Sanskrit, belongs to the family Rutaceae. It is globally reported from India, Sri Lanka, Pakistan, Java and Malaysia. The plant is native of India

and Ceylon and is found throughout the plains of India (Kirtikar and Basu, 1935; The Wealth of India, 1956), particularly in dry situations. It occurs as wild or cultivated, up to an elevation of 1,500ft in Western Himalayas.

Feronia is a single species genus. The plant is small deciduous tree. It is moderate sized tree armed with straight sharp strong spine, 1.2-1.3 cm long. Two types of the plant are recognized



namely one with small acidic fruits and the other with large sweet ones. The pulp of ripe fruit is edible. The fruit is 5.0-6.3 cm in diameter, globosely hard, pericarp woody, rough grey colored, seeds numerous, small, compressed embedded in a sweetish aromatic edible pulp. Hammer is used to crack the hard rind of wood-apple fruit.

The plant is well known for its medicinal properties. The fruit is aromatic, sour-sweet, refrigerant cardio tonic, astringent, diuretic tonic to liver and lungs, good for throat, binding, antiscorbutic, alexipharmic. It is also used in treatment of diarrhea, dysentery, leucorrhoea, consumption, vomiting, blood impurities, fatigue, thirst, hiccough, cures cough, asthma, tumors, ophthalmic, gums strengthening, stomatitis, earache, sore throat useful in biliousness, topically it relieves the pain due to stings of wasps and other insects.

The fruit is much used in India as a liver and cardiac tonic and unripe fruit is alexipharmic, astringent to the bowels, removes itching of the body and increases 'vata', 'pitta', and 'kapha' and used in combination with bela and other medicines in diarrhea and dysentery. The presence of stigmasterol has been reported from the unripe fruit of this plant (Chopra *et al.*, 1969). The fruit pulp is used for affections of gum and throat. The pulp applied externally is a remedy for the bites of venomous insects, if not obtainable, the powdered rind may be used. Fruit pulp has anti-inflammatory, antipyretic, analgesic activity. In addition to this, wood apple also has antioxidant, anticancer, antidiabetic, antimicrobial and hepato-protective activity (Vidhya and Narain, 2011).

The seeds cure heart diseases, headache, an antidote to poisons, the oil is acrid, astringent, alexiteric, stops hiccough and vomiting, cure rat bites and all poisoning destroys biliousness. Three components described as having characteristic wood apple aroma are methyl hexanoate, ethyl-3-hydroxyhexanoate and butanoic acid (Macleod and Pieris, 1981).

Alkaloids, coumarins, fatty acids and sterols were found in fruit pericarp extraction of *Feronia limonia*. The presence of umbelliferone, dictamnine, xanthotoxol, scoparone, xanthotoxin, isopimpinellin, isoimperatorin and marmin has been reported (Reisch *et al.*, 1985).

The defatted seeds contain ample proteins, carbohydrates, fatty acids and lipids (Banerjee and Nigam, 1978; Gupta *et al.*, 1979).

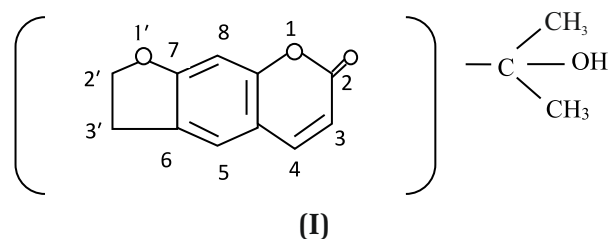
The main objective of this review article is to present the chemical constituents of this plant, responsible for its pharmacological activity.

COMPOUND DESCRIPTION

Compound FL-1, $C_{14}H_{14}O_4$, m.p. $189^{\circ}C$ ($M^{+}246$), white shining compound gave blue-violet fluorescence under UV light (Chatterjee and Mitra, 1949). The UV absorption maxima at 225, 250, 260, 300 and 337 nm were specific for dihydrofuranocoumarin (Chatterjee *et al.*, 1972). Appearance of peaks at $3440cm^{-1}$ and $1700cm^{-1}$ suggested the presence of tertiary hydroxyl group and α,β -unsaturated δ -lactone respectively. All experimental, UV and IR spectral data of compound FL-1 are given in table 1. The hydroxyl group was found to be alcoholic since it gave a negative test with ferric chloride. The compound gave no product with acetic anhydride and sodium acetate at room temperature but on heating the reaction mixture in an oil-bath at $130-140^{\circ}C$, monoacetate of the compound as formed which confirmed the presence of tertiary hydroxyl group in the molecule.

Spectral studies of the compound suggested the presence of a hydroxyisopropyl side chain. The 1H NMR signals at δ 1.22 (s, 3H, $-CH_3$), 1.36 (s, 3H, $-CH_3$) and 2.20 (bs, 1H , $-OH$) ppm confirmed the presence of hydroxyisopropyl side chain (Garg *et al.*, 1981). The fragment at m/z 59 also confirmed the presence of hydroxyisopropyl side chain (Silverstein *et al.*, 1981).

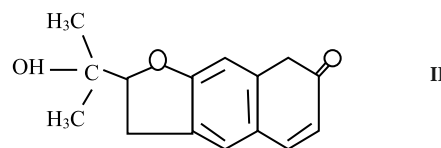
Thus, 1H NMR spectrum of the compound was consistent with dihydrofuranocoumarin containing a hydroxyisopropyl substituent and could be represented as I:



Signals at δ 6.20 (d, 1H, $J=9Hz$) and δ 7.60 (d, 1H, $J=9Hz$) ppm were assignable to the proton at C-3 and C-4 (Silverstein *et al.*, 1981). The 1H NMR spectrum also revealed the presence of two singlets, one at δ 7.22 (1H) and the other at δ 6.74

(1H) ppm assignable to C-5 and C-8 protons respectively (Murray *et al.*, 1982).

The only thing in the structure of compound FL-1 was the position of the side chain, present either at C-2' or C-3'. This was confirmed on the basis of ¹H NMR spectrum. The methylene and methyne protons on the dihydrofuran ring constitute an A₂X system which appears as a well-defined two protons doublet at δ3.20 (*J*=9Hz) and a one proton triplet at δ4.74 (*J*=9 and 9Hz) ppm (Garg *et al.*, 1980). It showed that the hydroxyisopropyl side chain was present at C-2' position. If the chain was present at C-3' position then a doublet corresponding to two protons should be present at δ3.75 ppm or at higher value due to the deshielding effect of the neighboring oxygen atom. On the basis of above evidences, the compound FL-1 is 2'-hydroxyisopropyl dihydrofuranocoumarin. It is represented as II: The ¹H NMR spectrum data of this compound is given in table 2.



Finally the structure of II as 2'-hydroxyisopropyl dihydrofuranocoumarin was confirmed by mass spectral data. The mass spectrum of the compound showed the molecular ion peak at *m/z* 246. The principal fragmentation pattern of 2'-hydroxyisopropyl dihydrofuranocoumarin, involves the loss of acetone from the molecular ion by elimination of the hydroxylated side chain with rearrangement of a hydrogen atom to give the ion, *m/z* 188 (Murray *et al.*, 1982). This then loses a hydrogen atom to give a highly stabilized ion of *m/z* 187 as a base peak. Fission of the hydroxyisopropyl side chain with retention of the charge on the smaller fragment to give an abundant ion at *m/z* 59, due to the protonated form of acetone, was also a characteristic feature of such coumarin (Silverstein *et al.*, 1981). All mass spectral data is given in table 1.

Table 1: Mass spectral data of compound FL-1.

Solubility	Chloroform, benzene, acetone and methanol
M.P.	189°C
R _f	0.65 (ethyl acetate)
Elemental Analysis: Calculated for C ₁₄ H ₁₄ O ₄	Found C : 68.54% C : 68.30% H : 5.70% H : 5.69%
UVλ _{max} ^{MeOH}	225, 250, 260, 300 (sh), 337nm
IRν _{max} ^{KBr}	3440, 3000, 1700, 1628, 1565, 1485, 1445, 1362, 1128, 960, 840cm ⁻¹
Mass spectra <i>m/z</i>	M+ 246, 228, 213, 188, 187, 166

Table 2: ¹H NMR spectrum data of compound FL-1.

Assignments	Chemical shifts (δ-ppm)	<i>J</i> values (Hz)
-CH ₃	1.22 (s, 3H)	
-CH ₃	1.36 (s, 3H)	
Ar-CH ₂ -CH<	3.20 (d, 2H)	9
Ar-CH ₂ -CH<	4.74 (t, 1H)	9, 9
H-3	6.20 (d, 1H)	9
H-8	6.74 (s, 1H)	
H-5	7.22 (s, 1H)	
H-4	7.60 (d, 1H)	9
-OH	2.20 (bs, 1H)	

The compound FL-1 as marmesin was confirmed by its m.p. and co-chromatography with an authentic sample of marmesin (Garg *et al.*, 1978).

PHYTOCHEMICAL ANALYSIS

Fruit pericarp of *Feronia limonia* contains 2,6-dimethoxybenzoquinone [$C_8H_8O_4$], psoralen (Bagul *et al.*, 2019), xanthotoxin [$C_{12}H_8O_4$] (Reisch *et al.*, 1985), ostheno (antifungal) (Patil *et al.*, 2012), amino acid, total amino acid (Thomas and Ponnammal, 2005) and three volatile flavour components like methyl hexanoate, ethyl-3-hydroxyhexanoate and butanoic acid. It also contains free fatty acids like palmitic, oleic, linoleic, linolenic acid, palmitoleic acid, stearic acids, β -sitosterol, β -amyrin and unsaponifiable matter lupeol, stigmasterol. In India, the fruit pericarp is used as a stomachic, diuretic, antidiabetic, antimicrobial, cardiogenic and tonic to liver and lungs. Small granules of fruit pericarp can be used for exfoliation purpose in skin care cosmetics, which help to remove the dead cells from the surface of the skin. Some recent reports identified its use in gastrointestinal disorders (Putta and Kilari, 2015). Shell shows anti-fungal activity against gram positive and gram negative bacteria because of psoralen.

Putta and Kilari (2014) also found significant antihyperglycemic, antihyperlipidemia activity of methanolic pericarp extracts of wood apple and significant protection against damage to kidney in streptozotocin induced diabetic rats. They suggested that antibacterial activity could be due to its antioxidant potential.

Hepatoprotective activity

In-vitro co-supplementation of methanolic extract or marmesin significantly minimized alteration in levels of AST and ALT and improved cell viability. Oral administration of methanolic extract or marmesin significantly prevented CCl_4 -induced elevation in the plasma markers of hepatic damage and hepatic lipid peroxidation and a decrease in hepatic antioxidants. *In-vivo* hepatoprotective potential of methanolic extract and marmesin was evident from the minimal alterations in the histo-architecture of liver (Jain *et al.*, 2012).

Anticancer activity

Marmesin exhibits significant anticancer activity against leukemia cells by induction of apoptosis and inhibits cell migration which is considered

critical for anti-leukemic agents. Furthermore, marmesin also inhibits tumor growth *in vivo* (Lin Dong *et al.*, 2017).

Adsorbent

The waste fruit shell of *Limonia acidissima* is used as an adsorbent. In this process, methylene blue dye was removed from any solution by using *Limonia acidissima* shell as an activated carbon. The effect of agitation time and concentration of dye on adsorption, effect of adsorbent dose, effect of temperature plays important role in the adsorptive removal of methylene blue dye (Bhadusha and Ananthabaskaran, 2011).

The *Limonia acidissima* hull (shell) powder is capable of removing chromium ions from aqueous solution up to 67.03% for an initial concentration of chromium 10 ppm and at a temperature of 30°C. The chromium adsorption ion performed by this plant hull powder is strongly affected by parameters such as contact time, initial chromium concentration, pH, adsorbent dosage, adsorbent particle size and temperature (Krishna and Sree, 2012).

The daily chromium requirement for adults is estimated to be 0.5-2µg of absorbable chromium. Excess amount of chromium ions in body can cause mutagenicity and carcinogenicity activity. Therefore controlled amount of chromium ion in drinking water as well as in human body is important (Chromium in Drinking-water, 1996).

Anti-bacterial activity

The rind of *Limonia acidissima* revealed antibacterial activity against *Staphylococcus aureus* and *Staphylococcus epidermidis* (Pandey *et al.*, 2014).

Anti-fungal activity

The fruit shell of *Limonia acidissima* has anti-fungal activity, due to the presence of psoralen, xanthotoxin, 2, 6-dimethoxybenzoquinone, sterol. A benzoquinone derivative 2, 6-dimethoxy-benzoquinone has been isolated from the chloroform extract of fruit shell which possesses antifungal activity (Bandara *et al.*, 1988).

CONCLUSIONS

Furanocoumarin has a furan ring fused coumarin nucleus, known as psoralen that shows photosensitizing effects towards skin. It exerts some interesting photobiological effects like

killing of bacteria, formation of mutants, inactivation of tumour cells, formation of giant cells, inactivation of viruses etc. Marmesin is one of the most prevalent linear dihydro-furancoumarin. It has benefits in the treatment of leucoderma, antifungal activity, phytoalexin, feeding deterrence effects and radical scavenging activity. The periodic determination of phytoconstituents is essential for standardization of raw material of the plant and its formulation in herbal drugs.

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