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REVIEW ON PHYTOCHEMICALS AND PHARMACOLOGICAL ACTIONS OF RUTA GRAVEOLENS L.

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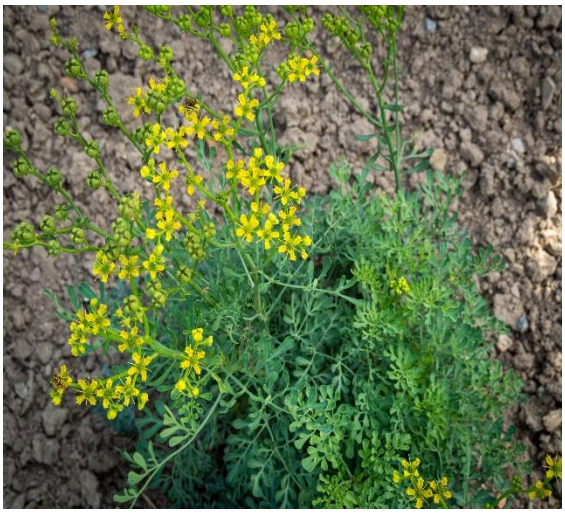
ABSTRACT:

The versatile plant rue, or Ruta graveolens L., is a member of the Rutaceae family. It is primarily rich in volatile oils, flavonoids, phenolic acids, alkaloids, and coumarins, which are secondary metabolites. Its many medical benefits have led to its widespread usage around the world. Numerous pharmacological effects, such as contraceptive, anti-inflammatory, antibacterial, antipyretic, antioxidant, analgesic, antihyperglycemic, free radical scavenging, hypotensive, antiviral, and antiplasmodial effects have been demonstrated for the extract and essential oil derived from this plant species. Furanoacridones and acridone alkaloids extracted from R. graveolens have been shown to have anticancer potential in vitro studies carried out using human cell lines. R. graveolens has been rapidly cloned by the use of in vitro methods. It has been successfully found that using hairy root culture is advantageous for increased synthesis of bioactive chemicals from this plant species. According to a survey of the literature, this plant species is intriguing to the pharmaceutical sector since it has the ability to have a variety of pharmacological effects.

INTRODUCTION :

The family of Rutaceae contains extremely wide variety of aromatic plants, mainly in tropical regions. Among them the rich are the genus Ruta[20]. It is now cultivated in many parts of the world. This plant is considered indigenous in South Europe and North Africa and it grows on waste stony ground [21-23]. The Rutaceae is one of the largest plant families with approximately 150 genera and 1,500 species distributed largely in tropical and subtropical parts of the world [24] . This family is known throughout the world for its citrus fruits such as oranges, lemons and grape fruit and also called as citrus family[25]. A variety of plants of the family Rutaceae are used in traditional system of medicine world-wide. Ruta graveolens L. is the most widely used medicinal plant in this family; it is also referred to as "Rue," "Sudab," or "Sadab" in Hindi. Despite being native to Europe, it may be found all over the world. It is an ornamental evergreen shrub of up to one-meter-tall and has considerable medicinal importance. More than 120 natural compounds mainly including acridone alkaloids, coumarines, essential oils, flavonoids, and furoquinolines have been found in the roots and aerial parts of this plant [26]. and is the main source of furanocoumarins such as psoralen, xanthotoxin (8-meth- 8710 oxypsoralen; 8-MOP) and bergapten (5-methoxypsoralen; 5-MOP).27This plant is commonly cultivated in India and is commonly called as sudab or sadab [21,23,3] .Two species of Ruta (genus) are reported to grow in India, of which Ruta graveolens (garden rue) is well known for its aromatic and medicinal uses[23] .In traditional system of medicine it is used as stimulant, emmenagogue, diuretic, and abortefacient, resolvent [2-4,28-32] .It is a perennial herbaceous or half-shrubby plant, reaching 2 to 2 1/2 feet in height, with a strong, heavy and unpleasant smell. Fruits are rough, grayish-brown, firm, spherical, and have four or five lobed tops. Seeds are ovoid, rounded on the back, flattish in front, angular, testa blackish, rough; embryo slightly curved from the base to the apex and is surrounded by scanty fleshy endosperm [28,31].



CHEMICAL CONSTITUENTS:

The chemical constituents present include rutin (2%), imperatorin, isoimperatorin, xanthotoxin, bergapten, psoralen. The alkaloids graveoline, gravelinine, rutamine, rutamarine, are also present in the herb[1,2]. Analysis of seeds gave following values; nitrogenous substances 21.6%, fixed oil 36.8%, and ash 13.8%. The oil from seeds is of drying type (iodine value; 189) and its fatty acid composition is as; palmitic acid 21.8%, stearic acid 9.1%, oleic acid 22.0% and linoleic acid 44.5%. The unsaponified matter contains ceryle alcohol, sitosterol and new coumarins[3] Methyl nonyleketone makes about 90% of the pure rue oil. Additionally, this plant has glucoside rutin[1]. The main chemical constituents of Ruta graveolens Linn are flavonoids. The flavonoid glycoside rutin (quercetin-3-β-rutinoside) is the most significant flavonoid that has been analysed.

All organs contained acridone alkaloids, although endodermal and circulatory tissues contained the highest concentrations. Quercetin is other major flavonoids found in Ruta graveolens and can also be obtained by rutin hydrolysis[4]. Ruta graveolens plants accumulate linear furanocoumarins (psoralens) and acridone or furoquinolone alkaloids. Hepatic aldehyde oxidase activity may be inhibited by whole extract, Quercetin, and Rutin, the two main flavonoids of Ruta graveolens, in a dose-dependent way[5,6].

PHARMACOLOGICAL ACTIONS:

1. Anti-oxidant Activity:

Inhibitory effects of 70% methanolic extract of leaves of Ruta graveolens on Guinea pig liver aldehyde oxidase enzyme shows 89-96% inhibition. Hepatic aldehyde oxidase activity may be inhibited by whole extract, Quercetin, and Rutin, the two main flavonoids of Ruta graveolens, in a dose-dependent way. The inhibitory effect of Quercetin on the enzyme was found to be more potent than menadione, the known specific inhibitor of aldehyde oxidase[7].

2. Anti-inflammatory Activity: Methanolic extract of Ruta graveolens with a concentration of 20 mg/kg and ethanolic extract with a concentration of 50 mg/kg showed maximum (90.9%) inhibition on carrageenan induced paw edema in wistar male rats. The effect was significantly higher than that of the standard drug Diclofenac sodium (72.72%)[8,9].

3. Anti-inflammatory and Antioxidant Activity: Rats with adjuvant-induced arthritis were given a methanolic extract of Ruta graveolens L. to study its anti-inflammatory and anti-oxidant properties. On the twenty-first day of adjuvant arthritis, Ruta graveolens methanolic extract showed the highest percentage of edema inhibition at a dosage of 20 mg/kg. The impact was greater than that of the common medication indomethacin. The activities of cycloxygenase-2 and myeloperoxidase and concentration of thiobarbituric acid reactive substance (TBARS) were decreased and the activities of antioxidant enzymes, vitamins C & E and reduced glutathione level were increased on treatment with methanolic extract of Ruta graveolens[8-10].

4. Cytotoxic Activity on Human Cancer Cell: Investigation of cytotoxic activity on human cancer cell lines of arborinine and furanoacridones isolated from Ruta graveolens Three kinds of human cancer cells were treated with the chemicals in vitro: A431 (skin epidermoid carcinoma), HeLa (cervix adenocarcinoma), and MCF-7 (breast adenocarcinoma). As positive controls, cisplatin and doxorubicin were employed. Arborine displayed the highest antiproliferative effects. Compounds 3, 4, 5 and 7 also displayed significant antiproliferative effects. Compounds 3, 4, and 7 were investigated in further detail. The administration of the chemicals to HeLa cells caused characteristic morphological signs of apoptosis, such as enhanced cell membrane permeability and cellular shrinkage, as shown by staining of the cell cultures. and granulation in the nucleus. When cell cultures were examined for the proportion of apoptotic cells, they were found to increase in a dose dependant manner. Most notably, compounds 3 and 7 enhanced apoptosis. The mRNA ratio of Bax/Bcl-2 (markers of apoptosis) was also dose dependently increased[11].

5 Anti-tumour Activity: Ehrlich ascites carcinoma (EAC), Dalton's lymphoma ascites (DLA), and L929 cells in culture were found to be susceptible to the anti-tumour activity of Ruta graveolens extract (IC100=16 mg/ml). It was also found to extend the life of animals bearing tumours. Additionally, extract of Ruta graveolens in isolated rat hearts exhibits a potential antiarrhythmic effect. Ruta graveolens extracts exhibit a considerable and rate-dependent prolongation of both the effective and functional refractory periods as well as the nodal conduction time When administered in conjunction with an extension of the life duration of animals harbouring tumours, the extract reduced the amount of solid tumours originating from DLA and EAC cells. The extract was found to scavenge hydroxyl radicals and inhibit lipid per oxidation at lower concentrations but the effect was minimal on higher concentration[12].

6. Anti-arrhythmic Activity: Alkaloidal in isolated rat hearts, Ruta graveolens extract exhibits possible antiarrhythmic properties. Ruta graveolens extracts greatly extend nodal conduction times and effective and functional refractory periods in a rate-dependent manner. The extract's effects are seen on both the slow and fast pathways of the node[13].

7. Antioxidative Activity: A variety of Ruta graveolens and Citrus sinensis extracts were tested for their ability to block the oxidation of L-DOPA, which is catalysed by mushroom tyrosinase. content of phenolic compounds and its cytotoxicity [14].

8. The results showed a correlation between the antimicrobial and cytotoxic activities of the extracts. Ruta graveolens extracts in methanol, petroleum ether, ethyl acetate, and water–methanol were found to have cytotoxic and antibacterial properties[15].

9. Micrococcus pyogenes var. is susceptible to the antibacterial properties of an alcoholic plant extract aureus and Esherichia coli· Psoralen present in this herb produce marked spasmolytic effect on isolated rabbit ileum [3].

11. The study examined the combined effects of two aqueous extracts one from Ruta graveolens and the other from Viola odorata with varying concentrations on the proliferation of Trichomonas vaginalis. The results showed that there is a variation of inhibition in different concentrations of two extracts and complete inhibition was seen with a concentration 10 mg/cm3 for 48 hrs[16].

12. Anti-androgenic action: Ruta graveolens was found to have anti-androgenic action in male albino rats, with a focus on sexual and aggressive behaviour. This activity was associated with a decrease in sperm motility and density

in cauda epididymis and testicular ducts. Decreased spermatogenic activity was observed in somniferous tubules, testosterone and FSH levels were found decreased and aggressive behaviour was also diminished[17.]

13 Anti-conceptive and Anti-Fertility Activity: Adult female Sprague-Dawley rats were used to investigate the anti-conceptive and anti-fertility properties of several Ruta graveolens extracts. The amount of resorbed embryos was greatly enhanced by the administration of various extracts. There was no significant effect on maternal weight gain, but some extracts showed a significant reduction in fatal weight. Administration of Hexane extract on post-coitum significantly decreased the number of females with born foetuses and increased the mortality rate among the born foetuses [18].

14 In adult Wistar male rats, ethanolic extracts of Cannabis sativa and Ruta graveolens demonstrated a markedly decreased spermatogenesis. Ruta graveolens had a greater impact than Cannabis sativa.Both the drugs showed significant reduction in the epididymal sperm counts [7].

15Aqueous extract of Ruta graveolens was tested at various concentrations to see if it might immobilise human sperm. The sperm immobilization effects of the extract appeared immediately in a dose-dependent manner and 100% of the sperms became immotile at a concentration of 100 mg/ml[19].

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