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Review Article

A Review of Phytopharmacological Studies on Some Common Flowers

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ABSTRACT

Flowers of *Nelumbo nucifera* Gaertn, *Hibiscus rosa-sinensis* L., *Calendula officinalis* L., *Datura metel* L., *Jasminum sambac* L Aiton., *Mimusops elengi* L., *Nyctanthes arbor-tristis* L., *Saraca asoca* (Roxb.) Wilde., *Tabernaemontana divaricata* (L.) R. Br. ex Roemer and Schultes., and *Ixora coccinea* L. are very popular for their aesthetic and spiritual appeal. Indigenous treatment systems found these flowers very useful in curing various ailments. Their phytochemical profiles are very impressive and several promising bioactive compounds were isolated and characterized. Synergism in some flower extracts produces antioxidant and anti inflammatory activities both in vitro and in vivo. Flower metabolome is a valuable resource to search for novel bioactive compounds.

INTRODUCTION

Lord Buddha while on a long journey fell ill and Jain physicians cured his illness with a drop of nectar served on the lotus petal. Jains being strict adherents to the ahimsa begun exploring flowers as novel and pious way of curing diseases and thus originated 'Pushpa Ayurveda' or flower therapy. It describes various practices such as 'darsanam', 'sparsha vidhanam', 'alepanam', 'nasya vidhanam' etc detailing the essential protocols associated with this particular branch of of ayurveda. Ayurveda and siddha systems documents unique medicinal properties of some flowers as distinct from other parts of the plant[1].There mentioned about rasayana medicines made with 18000 kinds of flowers[2]. 'Kaiyadevanighantu' is an ayurvedic text mainly devoted to the therapeutic implication of flowers of many medicinal plants[3]. Such a vast and ancient wisdom of health care should put into effective use in tackling the contemporary challenges of medical science and this is the reason behind the extensive research going on the phytochemical and pharmacological properties of different flowers. Demand for novel drugs is ever increasing and researchers turn more and more to nature as a source of valuable molecules. Here the authors focus on 10 flowers which are popular remedies for a host of diseases and in which significant phytochemical and pharmacological studies are carried out or are going on. Also a humble effort is made to converge discussions from such studies to a balanced and futuristically valuable perspective, encompassing this particular research area.

Lotus flower (Nelumbo nucifera Gaertn of family Nelumbonaceae)

Lotus flower or 'Thamara' occupy a unique place in indian psyche because of its aesthetic, spiritual and therapeutic values. Ayurveda describes lotus flowers as sweet cooling, astringent and diuretic. There are special references to the medicinal uses of different parts of the flower with detailed descriptions on the methods of use[4]. In ayurveda and other indigenous practices flower formulations are used to treat diarrhoea, diseases of the liver, cough, menorrhagia and bleeding piles[3,4]. 'Aravindasavam' is a ayurvedic paediatric tonic with lotus flower as its main ingredient[5]. Flower contains flavonoids, arbutin, alkaloids, steroids, phenols and tannins[6,7]. Pharmacological and toxicological studies show that flower has antidiabetic, hypoglycemic and hypolipidemic properties[8- 11]. A possible mechanism involved in the hypoglycemic property is that it stimulates insulin secretion from beta cells of islets of Langerhans[12], but arriving at such a conclusion requires further studies. Several flavonoids and Isorhamnetin glycosides having antioxidant property were isolated from the stamens[13,14]. They augmented antioxidant defence systems in experimental animals by decreasing lipid hydroperoxides, increasing superoxide dismutase and glutathione levels.This might also help in understanding lotus flower's multifaceted roles as cardioprotective tonic[15], potential acetylcholinesterase inhibitor to treat alzheimer's disease (Hint:ayurvedic remedy for insomnia and restlessness)[16], and an antitumour agent[17]. This flower is also rich in secondary metabolites having antibacterial and other antimicrobial properties[18,19,20]. Moreover several studies confirmed its antiplatelet and haemostatic potential[21]. Shim et.al shown that kaemferol from stamens exert antiallergic effect by downregulating FcepsilonRI expression and degranulation[22]. Recent research shown that flower stalk extracts has antiulcer activities[5]. Most of the above studies also prove that white lotus flowers are medicinally more valuable than the pink ones.

Hibiscus flower (Hibiscus rosa-sinensis L. of family Malvaceae)

Hibiscus flower is extensively mentioned in Ayurveda and siddha systems and continue to be a prominent herbal

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remedy of indigenous practices across the world to treat hair fall, piles, hemorrhage, menorrhagia, leucorrhoea, dysuria, hypertension, cough, diseases of pittam, and as emmenagogue, abortifacient and contraceptive[1,3,23,24]. Many of these claims are substantiated by research. Local wisdom in northern parts of Karnataka advocates consuming 5 to 6 fresh petals to cure diabetes[25] and flower has proven hypoglycemic effect[26]. Upadhyay et.al.demonstrated hair retarding effect of flower extract against the traditional use of flower as hair promoting tonic[27]. Phytochemical analysis of the flower yielded indole alkaloids, reducing sugars,saponins,tannins and terpenoids and aqueous extracts shows the presence of cardiac glycosides, saponins[28], flavonoids such as quercetin and cyanidin[29]. Many of this secondary metabolites are responsibles for different properties such as haemoprotective[30] or antibacterial activities[31,32,33]. Siddiqui et.al isolated four new compounds from the hydroalcoholic extracts and compared the hypotensive activity of extract and individual compounds. He found that extract exhibited higher activity than the isolated compounds and suggested synergism among components[34]. One of the important property studied was flowers' unique antifertility property, acting through antiestrogenic activity and thereby preventing implantation[35]. There are also reports on its antispermatogenesis activity[36,37,38]. Flower has hypolipidemic effect as suggested by numerous studies[39,40,41]. In an interesting experiment monosodium glutamate (MSG) induced obesity in rats was effectively treated with powder of flower dissolved in normal saline[42] thereby proving its antiobesity and anti-atherogenic potential. Researchers also demonstrated the antianxiety activity[43] and immunostimulatory effect of flower extracts acting via cell mediated and humoral antibody activation of T and B cells[44].

Marigold flower (Calendula officinalis L. of Asteraceae)

To heal a wound, apply crushed calendula flowers and this property is popular among both the traditional practitioners and modern researchers[45]. Flower extract acts simultaneously on several fronts and effectively deal with different aspects of wound healing that include proliferation and migration of fibroblasts- anti inflammatory triterpenes playing an active role[46], angiogenesis as demonstrated by neovascularization of rats cutaneous wounds and chick chorioallantoic membrane[47,48] and speed up epithelization, with a significant increase in the hydroxyproline and hexosamine presence[49,50]. Moreover oral treatment also improved overall physiological parameters associated with wound healing in animal trials[51]. Inspired by these promising results there are numerous efforts to decipher the phytochemical profile of this flower and several compounds that include flavonol 3 o glycosides[52] flavoxanthin, auroxanthin[53], glycosides of oleanolic acid[54], triterpenoid monoesters[55], ionone glucosides, sesquiterpene oligoglycosides[56], triterpenoid oleanene,[57] triterpenoid alcohols[58], carotenoids[59] etc were isolated from the flower. Many anti Inflammatory substances such as faradiol 3- o- laurate, palmitate and myristate are also isolated[60,61]. They act by scavenging free radicals and inhibiting inflammation mediators cytokines and prostaglandins[62]. Faradiol-3-myristic acid ester and faradiol- 3-palmitic acid ester contribute to antiphlogistic activity of extracts[63]. Antioxidant activities by free radical scavenging, DNA protection, triggering of cellular antioxidants are mainly done by polyphenols present in the extract[64-67]. Existence of flavonols which are anti-genotoxic at nano concentrations and genotoxic at micromolar concentrations -a case of hormesis has been reported[68]. Laser radiation treatment could enhance flower extracts' antitumor performance manyfold. This activity probably involved cell cycle arrest at the G1/G0 stage, proliferation of peripheral blood lymphocytes[69] and inhibition of key enzymes involved in metastasis[70]. Immunostimulatory polysaccharides are present in the flower extract[71]. Traditional use to treat gastrointestinal ulcers, abdominal cramps and constipation are supported by research[72,73]. Flower is hepatoprotective[74] and neuroprotective[75,76] while essential oil is sun protective[77]. Baicalein like compound in the extract is capable of effectively inhibiting HIV-1 reverse transcriptase in a cell free system[78]. Clinical trials proved that toothpaste containing flower extract helped to reduce of gingivitis[79]. Antibacterial, antifungal[80,81] and molluscicidal activities[82] are also reported for various flower extracts.

Datura flower (Datura metel L. of family Solanaceae)

Ayurveda classify this flower of 'Tamasic' nature as it contains toxins that induce sleep or creates nausea[2]. In Ayurveda and siddha traditions there are many medicinal uses for datura flower. It is used to cure eye diseases, psychosis, epilepsy, fever, delirium, burning sensation, boils, dysuria, dog bite, scorpion sting poisoning, earache, asthma and skin diseases[1]. In chinese medicine it is a good remedy for skin inflammation and psoriasis. Brazilians and Vietnamers smoke dried flowers as antiasthmatic cigarettes[83]. Floral extract was given orally as an anaesthetic[84]. Compounds such as melatonin and serotonin playing a significant protective role to young plant reproductive tissues are neurologically active[85]. Mature flower contains steroids, alkaloids, phenolic compounds, flavonoids, and tannins, many these compounds may contribute to its antibacterial activity[86]. Many antimicrobial compounds were isolated and characterised[87]. Yangjinhualine A is a novel compound isolated from flower as white amorphous powder[88]. Flower has more phenolics compounds than other parts and has good antioxidant activity[89]. Withanolides, a group of C28 steroidal lactones with a characteristic α, β-unsaturated δ-lactone ring (moiety responsible for compounds' cytotoxic and antitumour properties) are isolated from flower[90,91]. Antipsoriasis fraction of flower contains withanolide compounds namely baimantuoluoline A, B, C, withafastuosin E and withametelin C[92].

Jasmine flower (Jasminum sambac L. Aiton of family Oleaceae)

Jasmine is a flower for constant use,it eradicates slesma (Phlegm), endows good vision and whim, and kills lice in hair- says pushpaayurveda[2]. One of the clinical studies suggest that jasminum flowers is an effective and

inexpensive method to suppress puerperal lactation[93]. Methanol extract shows the presence of alkaloids, flavonoids, terpenoids, carbohydrates, proteins, phenols, tannins, saponins and phytosterols and inhibit lipid peroxidase activity[94]. Ethanolic extract revealed the presence of coumarins, cardiac glycosides, essential oils,flavonoids, phenolics, saponins, and steroids .Animal studies cleared use of flower for jasmine tea, traditional medicines and food industries. Its flavonoid component have a vasorelaxation property, exerting its influence on endothelial cells through muscarinic receptors and or by stimulating nitric oxide release[95]. Flower essential oil is found to inhibit bacterial growth and mechanism proposed is bacterial cell membrane disturbances[96].

Elengi flower (Mimusops elengi L. of family Sapotaceae)

Mimusops elengi of sapotaceae family has a mesmerising fragrance and different parts of plant are mentioned in ayurveda and other traditional systems for many of their medicinal properties. Flowers are recommended for dental diseases, cardiac and eye diseases[1,7]. A snuff made from the dried and powdered flowers is given in a disease called 'Ahwah', prevalent in Bengal. The powdered flowers induce a copious defluxion from the nose and relieve the pain in the head. Water distilled from the flowers is used by the natives of Southern India, both as a stimulant medicine and as a perfume[97]. Even dry corolla retains its fragrance. Liquid CO2 extraction of fresh and dry flowers show that fresh flowers yield good volatiles composition than the dry flowers.It contains phenol, benzyl alcohol phenyl ethyl alcohol, anisyl alcohol ,carvacrol , E-cinnamyl alcohol. A total of 74 compounds that consists alkaloids, flavonoids, phenolics and tannins identified through different extraction protocols[7,98,99]. Methanolic extract found to inhibit growth of a number bacterial pathogens[100,101]. Antibacterial and anti inflammatory property of flower oil was demonstrated by microdilution antibacterial assay and cyclo oxygenase inhibitory screening assay respectively[102]. In a study evaluating Thai and Indian claim of flower as a good brain tonic, rats pretreated with flower extract shown only milder symptoms of brain damage against ischemia reperfusion. This neuroprotective effect is due to antioxidant and anti inflammatory properties of various bioactive polyphenols such as protocatechuic acid, chlorogenic acid,caffeic acid, rutin and luteolin- 7 -O glucoside present in flower[103]. Other promising reports include cognitive enhancing activity[104] hypoglycemic, hypolipidemic effects[105] and diuretic potential[106]. Pharmacognostical studies helped to identify potent wound healing principles such as β-sitosterol, lupeol, gallic acid and eugenol and also suggested safe dose for flower extracts' oral consumption[107].

Night jasmine flower (Nyctanthes arbor-tristis L. family Oleaceae)

The bright orange corolla tube of Nyctanthes flower contains a pigment nyctanthin and Buddhists monks were fond of using it to colour their robes[108]. Ayurveda characterise flower as astringent, stomachic and carminative and of provoking menstruation[109]. Many diverse properties of flower extracts were examined. Activity guided fractionation of ethanol extract of flowers yielded antimalarial cyclohexyl ethanoid namely rengyolone which is active against Plasmodium falciparum[110]. On the other hand a pure compound namely NCS-2 isolated from the chloroform extract is larvicidal against early instars of common filarial vector, culex quinquefasciatus[111]. Various flower extracts are antibacterial, cytotoxic and antifungal[112-114]. A benzofuranone,3,3a,7, 7a-tetrahydro-3a hydroxy-6(2H)-benzofuranone having significant antibacterial activity against both gram positive and gram negative bacteria was isolated from the flower[115]. Antidiabetic activity of flower extract in more effective than leaf extract[116]. Similarly immunostimulant properties of flower are also reported[117] and treatment with ethanol extract cleared entamoeba histolytica infections in rat caecum[118]. Phytochemical studies revealed the presence of alkaloids, tannins, triterpenoids, glycosides and flavonoids as well as the significant antioxidant properties of phenolic compounds of this flower[119,114]. On the other hand flower extracts hepatoprotective activity against CCl_4 induced liver damage in rats[120] and membrane protective role against H_2O_2 damage in chick lymphocytes[121] are worth mentioning.Interestingly orange coloured calyx has more antioxidant activity than other parts[122] and a carotenoid aglycone namely crocetin with good membrane stabilising property was isolated from this part[123].

Ashoka flower (Saraca asoca Roxb. Wilde of family Fabaceae)

Saraca asoca (Roxb.) Wilde, or saraca indica is another prestigious plant in Indian traditions but overexploitation and habitat loss forced its entry in to the IUCN redlist of vulnerable species. In ayurveda dried floweres of asoca are used in diabetes and haemorrhagic dysentery, in sidtha tradition it is given for bloody stools.Flower buds soaked in cold water for 1-2 hours is a health tonic[1]. Early investigation into the antidiabetic and anticancer properties of the flower extracts were conducted[124]. Flower essential oil analysis shows presence of 28 compounds such as *E*,*E*-*α*-farnesene and sesquiterpene hydrocarbon type constituents[125]. Compounds such as tannins, steroids glycosides, saponins, flavonoids and gallic acid are present in the flower[126]. When Gallic acid and quercetin were quantified among different plant parts, flower has maximum amount, corroborating its effective antioxidant properties[127]. Later It is also found that free radical scavenging activity is higher in fresh flower than the dried flower[128] and this effect might involve inhibition of xanthine oxidase, a key enzyme linked to inflammation[129]. Antihyperglycemic and antioxidant studies show that phytosterols and flavonoids may act in many fronts such as activating enzymatic antioxidants, free radical scavenging while hyperglycemic effect may be due to increased pancreatic secretion of insulin or by the release of insulin from its bound form[130]. Ethyl acetate fraction containing phenolic compounds gallic acid, β-sitosterol and anthocyanidin, pelargonidin-3,5-diglucoside, cyanidin-3, 5-diglucoside is promising because in vitro and in vivo trials shown that this fraction effectively decrease aldose reductase activity (a prominent reason behind many

diabetic related complications) and diabetic induced cataractogenesis[131]. Antibacterial property against clinical pathogens is also reported for flower[132,133].

Crepe jasmine flower (Tabernaemontana divaricata (L.) R. Br. ex Roemer and Schultes of family Apocynaceae)

Tabernaemontana divaricata is a popular medicinal plant among the traditional medicinal systems of the world. Flower juice mixed with little amount of breast milk gives good relief to infected eyes.There are many reports on the antibacterial efficacy of flower extracts against ocular pathogens[134], *Staphylococcus aureus* and *Escherichia coli*[135]. Two novel compounds from flowers namely ethyl-4-n-octyl benzoate and ethyl-4- n-decyl benzoate show significant antibacterial and antiradical activity[136]. Apart from the antimicrobial activities, various extracts of flowers are hypoglycemic,[137] anxiolytic,[138] anticonvulsant[139] and prevent implantation[140]. Ethnomedical use of flower extract in epileptic patients is corroborated by anticonvulsant studies in animal models[141]. A much researched area is its gastroprotective ability. Administration of methanol flower extract significantly reduced gastric juice volume, acidity and ulcer indices in experimental animals. It is suggested that antioxidant and antiinflammatory properties of various alkaloid and flavonoids contents in flower extracts might be acting in a synergistic way to give antiulcer property[142]. Nevertheless there are efforts to identify the most bioactive compounds and several indole alkaloids are reported as potential candidates[143].

Ixora flower (Ixora coccinea L. of family Rubiaceae)

Ixora coccinea is an important plant in ayurveda and flowers are used to treat various ailments such as leucorrhoea, dysentery, dysmenorrhoea, hemoptysis, hypertension etc[144]. Ayurvedic claim of flower as an effective remedy for diarrhea and dysentery is evaluated by administrating of aqueous extracts in experimental models. Alkaloids, flavonoids, tannins, glycosides present might act in a synergistic way on different mechanism to bring the desired effect[145,146]. Antibacterial and antifungal activities of flower extracts are reported[146,147]. In another study high phenolic and corresponding antioxidant activity is noted in flower than other parts[148]. Wormicidal,[149] antiinflammatory and analgesic property are also reported for the flower extract[150]. An ayurvedic oil preparation from flowers of ixora coccinea and cortus sativum when applied on tumour, is found to arrest its further growth[151]. Similarly topical application of ixora flower extract also inhibited growth and delayed the onset of papilloma formation[152]. On the other hand intraperitoneal administration of flower extract increased the lifespan of tumour bearing mice[153]. Significant antigenotoxic property of the hexane extract of the flower led to the isolation of the triterpenoid ursolic acid as the active ingredient[154]. Chemoprotective effect of active fraction alone[155] or in combination with cyclophosphamide helped to reduce malignancy[156]. Recently another novel terpenoid Ixoroid is isolated from the flower[157].

DISCUSSION

Notwithstanding the morphological, anatomical and functional uniqueness, flowers present a very comprehensive biochemical profile that include alkaloids, flavonoids, tannins, triterpenoids, glycosides, saponins, phytosterols phenols etc. These secondary metabolites are responsible for the diverse biological activities of flower including antioxidant, antimicrobial, hyperglycemic, hypolipidemic, and whole lot of other biological properties- from being a general health tonic to one that specifically inhibit reverse transcriptase enzyme activity. Secondary metabolite composition of a flower may be different from other parts of plant, or within the different parts of same flower or among different varieties of a species. In Ixora high phenolic content is noted in flower extracts than other parts. When gallic acid and quercetin were quantified among different plant parts of Saraca, flower topped the list. Similarly, white lotus flower extract is therapeutically more valuable than pink variety and orange coloured calyx of Nyctanthes has more antioxidant activity than other parts of flower. Biochemical composition of flower extracts depend on extraction protocols adopted. Fresh flowers of mimusops are richer in volatiles and that of Saraca are biologically more active than dry flowers. Activity guided fractionation helped to isolate and characterise several novel bioactive compounds from the flowers, such as antigenotoxic ursolic acid from ixora and antimalarial rengyolone from nyctanthes. Conversely in several studies successful activity is prominent in extracts, suggesting synergism between compounds. Hypotensive activity of hibiscus flower extracts is higher than its individual components.Moreover some odd methods found to enhance performance of flower extracts. In Calendula Laser radiation treatment could enhance flower extracts antitumor performance manyfold. Scope of such unique attempts at appropriating incredible ‘biochemical libraries’ of flowers into drug development and disease fighting is ever increasing. Undoubtedly ethno medical practices such as push ayurveda has been one of the main guiding principle in the search for valuable natural products. Many of the noble results of pushpay ruveda might be outcome of synergism among components of flower leading to the activation of body’s several defence strategies. Importance was on promoting good health rather than relying on any single compound to fight disease. This concept is gaining momentum in modern medicine too, where ‘get a super molecule to target a specific disease’ is the norm. Phytopharmacological research in flower metabolomes will help several traditional treatment systems to attain status of rational and evidence based medical practices. It will also complement modern techniques such as reverse pharmacology, combinatorial chemistry and computational biology in the development of smart drugs that assure health for all.

CONCLUSION

Flowers which are used as popular remedies are rich source of biologically active secondary metabolite. Activity guided fractionation could isolate and characterize many compounds. Extracts or isolated

compounds produced good antimicrobial, antioxidant, anti inflammatory activities both invitro and invivo.

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