A Review of Pharmacology of Phytochemicals from Indian Medicinal Plants

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Abstract

In recent years, research on medicinal plants has attracted a lot of attention globally. Large body of evidence has accumulated to demonstrate promising potential of medicinal plants used in various traditional, complementary and alternative systems. Several Indian medicinal plants have been studied for pharmacological activity in recent years. To understand the mechanism of action, the researchers have worked at molecular levels and several significant phytochemicals have been isolated. The present review is aimed at compiling data on promising phytochemicals from Indian medicinal plants that have been tested in various disease models using modern scientific methodologies and tools.

INTRODUCTION

Medicinal herbs are significant source of synthetic and herbal drugs. In the commercial market, medicinal herbs are used as raw drugs, extracts or tinctures. Isolated active constituents are used for applied research. For the last few decades, phytochemistry (study of plants) has been making rapid progress and herbal products are becoming popular.

To facilitate the readers to look at their areas of interest, we have tried to discuss potential phytochemcials in this article. In the review pharmacological investigations on phytochemicals have been discussed according to human anatomy.

DIGESTIVE SYSTEM

GASTRO-PROTECTIVE PHYTOCHEMICALS

Bergenin and neobergenin belongs to isocoumarin group of phytochemicals. They have been isolated from leaves and roots of Fluggea micrcarpa Blume (Euphorbiaceae). The two isocoumarins demonstrated significant protection against aspirin-induced peptic ulcer and pylorus-ligation in animal models. The mechanism of gastro-protective action of bergenin and neobergenin was attributed to increased prostaglandin production [1].

Luvangetin, a pyranocoumarin isolated from seeds of Aegle marmelos Correa (Rutaceae) has gastro-protective action similar to bergenin and neobergenin however mode of action was thought to be different [2].

HEPATOPROTECTIVE PHYTOCHEMICALS

Eclipta alba L. is used as hepatoprotective in Ayurveda. In rats against carbon tetrachloride induced hepatotoxicity. In vivo studies with active fractions from ethanolic extract of Eclipta alba leaves were undertaken. One fraction was containing wedelolactone and other fraction was containing apigenin, 4-hydroxybenzoic acid and protocatcheuic acid. The second fraction was found to be more active hepatoprotective[3].

Kutkins isolated from Picrorhiza kurrooa ex Benth. (Scrophulariaceae) has shown significant curative activity in vitro in primary cultured rat hepatocytes against toxicity induced by thioacetamide, galactosamine, and carbon tetrachloride[4]. In another study, active constituent of Picrorhiza kurrooa showed a dose dependent hepatoprotective activity against oxytetracycline induced hepatic damage in rats[5].

Hepatoprotective activity of C-phycocyanin isolated from Spirulina platensis L. was investigated. Intraperitoneal administration of single dose of phycocyanin in a dose of 200mg/kg one to three hours prior to carbon tetrachloride and R-(+)-pulegone, demonstrated significant hepatoprotective activity[6].

Ursolic acid isolated from leaves of Eucalyptus terelicomisdemonstrated hepatoprotective effect against thiacetamide, galactosamine and carbon tetrachloride in rats. Pretreatment with ursolic acid increased the viability of liver

cells. In large doses, ursolic acid demonstrated choleretic effect. Further the authors concluded that hepatoprotective activity of ursolic acid was comparable to silymarin[7].

Bioassay guided activity of fruit extract of Terminalia belerica identified 3, 4, 5-trihydroxy benzoic acid (gallic acid), as hepatoprotective principle [8].

CHOLRETIC PHYTOCHEMICALS

Andrographis paniculata Nees. is well known medicinal plant for its usefulness in liver diseases. In Ayurveda it is known as Bhunimba or Kalmegha. It is used as bitter tonic and febrifuge. Because of bitter taste it is popularly known king of bitters. It contains diterpene lactones (andrographolide, neoandrographolide and kalmeghin).

Andrographolide produced dose dependent chloretic effect evidenced by increase in bile flow, bile salt and bile acids in animal models. The cholretic effect of Andrographis paniculata was found to be better than silymarin[9].

ANTISPASMODIC PHYTOCHEMICALS

Chebulin an anthraquinone glycoside found in flowers of Terminalia chebula Retz (Combretaceae) popularly known as haritaki in Ayurveda has antispasmodic activity similar to papaverine [10]. Chebulin is however considered to be purgative principle of Terminalia chebula.

ANTIDIARRHEAL PHYTOCHEMICALS

Anti diarrheal activity of piperine, the principle alkaloid of Piper longum and Piper nigrum L. (Piperaceae) was investigated against diarrhea induced by castor oil, magnesium sulphate and arachidonic acid in rats. Piperine significantly inhibited diarrhea produced by above laxatives and aperients at a dose of 8 and 32 mg/kg p.o. dose. It further inhibited castor oil induced enter pooling explaining prostaglandin inhibiting effect[11].

RESPIRATORY SYSTEM

BRONCHODILATOR PHYTOCHEMICALS

Experiments conducted with Tylpohorine a phenanthroindalizidine alkaloid present in Tylophora asthmatica (L. f.) Wight & Arn. (Asclepiadaceae) in various animal models have shown significant anti-inflammatory, anti-anaphylactic and anti-spasmodic activities. Bronchodilator activity of Tylophora asthmatica is attributed to tylophorine [12].

CARDIOVASCULAR SYSTEM

HYPOLIPIDEMICS

Guggulsterones found in Commiphora mukul have been reported to inhibit cholesterol synthesis in the liver via antagonism to the farsenoid X receptor and the bile-acid receptor[13]. Since then several clinical trials have been carried out with standardized extract of Commiphora mukul in treating hypercholesterolemia [14,15, 16].

ANTIARRHYTHMIC

Jatamansone a sesquiterpene ketone found in Nardostachys jatamansi DC (Valerianaceae) has been reported to have antiarrhythmic activity however details of the study are missing[17].

NERVOUS SYSTEM

NOOTROPICS

Bacosides belong to group of compounds known as triterpenoid saponins [18]. They are considered to be active constituents of Bacopa monnieria L. (Scrophulariaceae) popularly known as Brahami in Ayurveda[19]. Bacoside-A and bacoside-B have been identified. The bacoside- A content of Bacopa monnieria L. is about 2.5-3.0%.

Extensive pharmacological studies with standardized extracts of Bacopa monniera Linn has demonstrated that the medicinal plant improves the acquisition, retention and retrieval of learned tasks. A study found that bacosids A and B were active in facilitating effects of Bacopa monniera Linn. on learning schedules[20]. The bacosides further decreases the incidence of retrograde amnesia produced by immobilization induced stress, electro-conclusive shock and scopolamine. Bacoside A and B were found to facilitate the capacity for mental retention in rats and were active in both positive and negative reinforcement experiments [21].

ANTI-ANXIETY

Ginkgo biloba is well known for its pharmacological activities. The medicinal plant contains bioflavonoids, pronathocyanidins, diterpenes and a toxic compound ginkgolic acid. In an experimental study, aimed at anxiolytic activity of ginkgolic acid conjugates (including several salicylates) demonstrated significant anxiolytic activity. In contrast, toe commercial preparations EGb 761 and Ginkocer (devoid of ginkgolic acid conjugates failed to evoke significant anxiolytic activity [22]. The study was concluded that ginkgolic acid conjugates might be the active constituents of Ginkgo biloba responsible for the anxiolytic activity.

ANALGESICS

Gossypin is a bioflavonoid obtained from yellow petals of Hibiscus vitifolius L. (Malvaceae). It has anti-nociceptive activity similar to opium alkaloids and involving multi-neurotransmitter systems. It acts through cholinergic and GABAergic pathways. It seems to have potential analgesic activity with free from tolerance and dependence [23]. Cerpegin is an oxazolone alkaloid isolated from Ceropegia juncea Roxb [24]. It has shown analgesic effect against acetic acid induced writhing in mice [25].

ANTI-INFLAMMATORY

Gossypin was found to significantly reduce the rat paw, edema and the increased vascular permeability induced by various phlogistic agents. It produced significant inhibition of the accumulation of pouch fluid and granulation tissue formation in the carrageenin induced granuloma pouch in rats. Gossypin was also found effective against the adjuvant and formalin induced chronic arthritis in rats [26].

Betulinic acid, a triterpene isolated from Nelumbo nucifera L. demonstrated significant anti-inflammatory activity when tested in carrageenin and 5-hydroxytryptamine induced paw edema. The activity was comparable to betamethasone and phenylbutazone [27].

Premnazole, an isoxazole alkaloid isolated from Premna integrifolia L. and Gmelina arborea L. (Verbenaceae) demonstrated significant anti-inflammatory activity in reducing cotton pellet-induced granuloma formation in rats. The anti-inflammatory activity was comparable to that of phenylbutazone[28]. Gangetin-a pterocarpenoid isolated from Desmodium gangeticum has been reported to have anti-inflammatory and analgesic activities[29].

TRANQUILLIZER PHYTOCHEMICALS

Jatamansone a sesquiterpene ketone found in Nardostachys jatamansi DC (Valerianaceae) has been reported to have tranquillizer activity however details of the study are missing[30].

ANTICONVULSANT PHYTOCHEMICALS

Jatamansone sesquiterpene ketone found in Nardostachys jatamansi DC (Valerianaceae) and pongamol, a flavonoid found in Pongamia pinnata (L.) Merr. (Fabaceae) are reported to have significant anticonvulsant activity[31, 32].

CENTRAL NERVOUS SYSTEM DEPRESSANTS

PHYTOCHEMICALS

In a study CNS activity of swertiamarin, a secoiridoid glycoside obtained from Swertia chirata - (Wall.) C.B.Clarke. was evaluated. It was found that swertiamarin significantly reversed the mangiferin-induced CNS-stimulating effects in albino mice and rats [33].

NEPHROPROTECTIVE PHYTOCHEMICALS

Lupeol isolated from stem bark extract of Crataeva nurvala.Buch.-Ham. (Capparaceae) offered significant activity against free radical induced nephrotoxicity in rats[34].

ANTIOXIDANT PHYTOCHEMICALS:

Rubidianin, an anthraquinone isolated from alcoholic extract of Rubia cordifolia has demonstrated significant antioxidant activity. It prevented lipid peroxidation induced by ferrous sulphate and t-butylhydroperoxide. Rubidianin depicted activity in dose-dependent manner. The anti-oxidant activity of rubidianin was found to be better than mannitol, vitamin e and p-benzoquinone [35].

ANTICANCER PHYTOCHEMICALS

In vitro anti cancer studies have demonstrated that bioflavonoids like luteolin and quercetin have the power to inhibit the proliferation of cells in human carcinoma of larynx and sarcoma-180 cell lines [36]. Phenanthroindolizidine alkaloids pergularinine and tylophorinidine isolated from Pergularia pallida (Roxb.) Wight & Arn. (Asclepiadaceae) inhibited the growth of Lactobacillus leichmanni cells by binding to thymidylate synthetase[37].

Withanolides, the active constituents of Withania somnifera Dunal (Solanaceae) are group of pharmacologically active compounds present in roots and leaves. The chemistry of withanolides has been studied and they are basically steroidal lactones. Withanolides are similar to ginsenosides (the active constituents of Panax ginseng) in structure and activity. They are believed to be immunomodulator, which most probably accounts for anticancer activity. Withaferin-A is best studied withanolide[38].

Withaferin- A isolated from the roots of Withania somnifera, reduced survival of V79 cells in a dose-dependent manner. LD50 for survival was 16 microM. One-hour treatment with a non-toxic dose of 2.1 microM before irradiation significantly enhanced cell killing, giving a sensitizer enhancement ratio (SER) of 1.5 for 37% survival and 1.4 for 10% survival. SER increased with drug dose, but at higher doses the increased lethality appears to be due to two effects

i.e. drug toxicity and radio sensitization. The drug induced a G2/M block, with a maximum accumulation of cells in G2-M phase at 4 h after treatment with 10.5 microM withaferin A in 1 h[39].

Withaferin- A showed marked tumour-inhibitory activity when tested in vitro against cells derived from human carcinoma of nasopharynx (KB). It also acted as a mitotic poison arresting the division of cultured human larynx carcinoma cells at metaphase and in HeLa cultures similar to star -metaphase. It also produced significant retardation of the growth of Ehrlich ascites carcinoma, Sarcoma 180, Sarcoma Black (SBL), and E 0771 mammary adenocarcinoma in mice in doses of 10, 12, 15 mg./kg body-weight. Growth of Ehrlich ascites carcinoma was completely inhibited in more than half the mice, which survived for 100 days without the evidence of growth of the tumour. Withaferin-A arrested mitosis in embryonic chicken fibroblast cells[40].

Withaferin-A isolated from the alcoholic extra ct of Withania somnifera showed significant antitumor and radio sensitizing effects in experimental tumors in vivo, without any noticeable systemic toxicity. Withaferin A gave a sensitizer enhancement ratio of 1.5 for in vitro cell killing of V79 Chinese hamster cells at a non-toxic concentration of approximately 2 microM[41].

A free radical scavenging, anti-tumour and anti-carcinogenic activity of gossypin has been reported[42]. Antitumor activity of total alkaloid fraction of Solanum pseudocapsicum L. (Solanaceae) leaves has been reported[43].

In animal studies, plumbagin, napthoquinone from Plumbago rosea L. (Plumbaginaceae) has shown anti tumour activity. The antitumour and radimodifying properties of plumbagin were tested on mouse Ehrlich ascites carcinoma. Plumbagin produced inhibition of exponentially growing tumours. When radiation was combined with plumbagin, mouse survival was increased by 120 days. However mode of action of anti cancer activity of plumbagin remains unclear[44].

CHEMOTHERAPEUTICALLY USEFUL PHYTOCHEMICALS

ANTIMICROBIAL

Clausenol a carbazole alkaloid isolated from alcoholic extract of stem-bark of Clausena anisata (Willd) Hook (Rutaceae) has shown antibacterial activity [44,45]. The phytochemical was found to be active against bacteria and fungi. Preliminary investigations of xanthochymol, active principle of Garcinia xanthochymus Hook.f. (Guttiferae) demonstrated antimicrobial activity [46].

ANTI-FUNGAL

In 1970 a study reported antifungal activity of Withaferin A[47]. Fungistatic activity of Zaluzanin-D isolated from Vernonia arborea L. (Asteraceae) was reported[48]. Lignans (termilignan and thannilignan), 7-hydroxy-3', 4'-(methylenedioxy) flavone and anolignan B isolated from Terminalia belerica (Gaertn.) Roxb. (Combertaceae) have significant antimalarial and antifungal activities [49].

Glycyrrhizin, triterpenoid saponin found in Glychyrrhiza glabra L. (Fabaceae) inhibited the plaque formation in DNA and RNA viruses. It has been proposed that glycyrrhizin blocks the first steps on viral replication as well as the viron exit from the capside [50].

ANTI-LEISHMANIAL

Amarogentin, a secoiridoid glycoside isolated from Swertia chirayita (Roxb ex. Flem) Karst] (Gentianaceae) is inhibitor of topoisomerase I enzyme of Leismania donovani [51,52]

ANTHELMINTIC PHYTOCHEMICALS

Palasonin (terpene anhydride), active principle isolated from seeds of Butea monosperma L. (Fabaceae) inhibited glucose uptake and depleted the glycogen content in Ascaridia galli. In another study interaction of palasonin with glycolytic enzymes and succinic acid production in Ascaris lumbricoides was postulated as possible mechanism of action [53,54].

Gentistein, the active compound of Flemingia vestita Benth. (Fabaceae) was investigated for anthelmintic activity against Fasciolopsis buski, the large intestinal fluke of swine and human host. Genistein induced effect on the activity of nitric oxide synthase which may be the possible mode of action [55].

HYPOGLYCEMIC PHYTOCHEMICALS

Swerchirin, xanthone from Swertia chirayita (Roxb ex. Flem) Karst] (Gentianaceae) has hypoglycemic activity. Researchers compared the effects of mode of action of three different hypoglycemic agents; centipiperalon, tolbutamide and swerchirin in normal as well as diabetic rats. Except in rats with severe pancreatic damage, swerchirin showed better glucose lowering effect compared to tolbutamide [56].

Karanjin, a flavone showed significant hypoglycemic activity with a single dose of 0.5 mg/kg in normal rats.

However it was ineffective in alloxan- induced diabetic rats[57].

ANTIOXIDANT PHYTOCHEMICALS

Apocynin isolated from Picrorhiza kurroa Royle. ex Benth. (Scrophulariaceae) is a potent NADPH oxidase inhibitor and has anti-oxidant and anti-inflammatory activity[58].

REPRODUCTIVE SYSTEM

ANTIFERTILITY PHYTOCHEMICALS

Solasodine an alkaloid of Solanum xanthocarpum L. (Solanaceae) demonstrated antifertility activity in male and dogs. The alkaloid on oral administration resulted in inhibition of spermatogenesis and sperm motility. The mechanism of action of solasodine may be attributed to inhibition of testosterone release. Solasodine seems to be valuable antifertility agent of plant origin [59].

Embelin a plant benzoquinone and active constituent of Embelia ribes Burm (Myrsinaceae) is another valuable antifertility agent of plant origin. Several animal studies have proved efficacy of embelin as antifertility agent. Several theories have been postulated for its anti fertility activity but authentic one is still to come. Plumbagin, napthoquinone from Plumbago rosea L. (Plumbaginaceae) has anti fertility activity similar to embelin[60].

SPERMOPIOTIC PHYTOCHEMICALS

Mucuna prurita Baker (Fabaceae) is well known spermopiotic plant of Ayurveda. In a study the total alkaloidal content (mucuadine, mucuadinine, mucucuadinine, pruriendine, mucunine, mucunadine, nicotine) of Mucuna prurita demonstrated increased spermatogenesis in albino rats[61].

ANTI-IMPLANTATION PHYTOCHEMICALS

Embelin demonstrated 100 per cent anti-implantation activity in albino rats and rabbits when given in a dose of 10mg/kg.

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