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THERAPEUTIC POTENTIAL OF OROXYLUM INDICUM: A REVIEW

Ahad A[1], Ganai AA[2], Sareer O[3], Najm MZ[1], Kausar MA[1], Mohd M[4], Siddiqui WA*[1].

[1]Department of Biochemistry, Faculty of Science, Jamia Hamdard, New Delhi-110062, India
[2]Department of Biotechnology, Faculty of Science, Jamia Hamdard, New Delhi-110062, India
[3]Department of Botany, Faculty of Science, Jamia Hamdard, New Delhi-110062, India
[4]Department of Pharmacognosy and Phytochemistry, Faculty of Pharmacy, Jamia Hamdard, New Delhi-110062, India

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Corresponding Author:
Dr. Waseem Ahmad Siddiqui, Department of Biochemistry, Faculty of Science, Jamia Hamdard, New Delhi-110062, India
was.sid12@gmail.com
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ABSTRACT

Medicinal properties of *Oroxylum indicum* L. Kurz are known for hundreds o years to various civilizations of the world. Scientific explorations of traditional belief o medicinal properties of *Oroxylum indicum* have got momentum mostly after the middl of the 20th century. In the present review, efforts have been made to sum up differen aspects of scientific studies on this medicinal plant. Scientific evidences are available o various medicinal aspects i.e. antimicrobial, antidiabetic, hepato-protective, anti inflammatory, anti-carcinogenic, immunomodulatory, nephro-protective, cardio protective, *etc*. to name a few. Most of these evidences are based on *in-vitro an* experimental studies.

NON-STANDARD ABBREVIATIONS

MS	Murashige and Skoog medium
mg	Milligram
g	Gram
kg	Kilogram
µg	Microgram
ml	Millilitre
L	Litre
BAP	6-benzylaminopurine
$AgNO_3$	Silver Nitrate
IBA	Indole-3-butyric acid
RAPD	random amplification of polymorphic DNA
BST	brine shrimp nauplii
WRG	wheat rootlet growth
LSG	lettuce seed germination
DNBS	dinitrobenzene sulfonic acid
BW	body weight
CCl_4	carbon tetrachloride
IC50	half maximal inhibitory concentration (IC50)
DPPH	2,2- diphenyl-1-picrylhydrazyl radical
FRAP	Ferric reducing antioxidant
OH^-	hydroxyl free radical
XTT	(2,3-bis-(2-methoxy-4- nitro-5-sulfophenyl)-2H-tetrazolium-5-carboxanilide) reagent
UV	ultraviolet
H_2O_2	hydrogen peroxide
DNA	Deoxyribonucleic acid
p.o.	per os (by mouth)
i.p.	intraperitoneally
v/v	volume/volume
AST or SGOT	aspartate aminotransferase or serum glutamic oxaloacetic transaminase
ALT or SGPT	alanine aminotransferase or serum glutamic pyruvic transaminase
ALP	Alkaline phosphatase
BUN	blood urea Nitrogen
LPO	Lipid peroxidation
HDL-C	high density lipoprotein-cholesterol
LDL-C	low density lipoprotein-cholesterol
VLDL-C	very low density lipoprotein-cholesterol
SRBC	Sheep red blood cell
[HA]	hemaglutinating antibody
DTH	delayed-type hypersensitivity
RD	Ranikhet disease
IBD	infectious bursal disease
HI	Hemagglutination inhibition
ND	Newcastle disease virus
DFNB	2, 4-dinitrofluorobenzene
MHI	mixed haemadsorption index antibody
MST	mean skin thickness
WIRS	water immersion plus restraint stress
HL-60 cell line	(Human promyelocytic leukemia cells) cell line
CEM	tumor cell lines
HCT-8, B-16	tumor cell lines
MDA-MB-435 S	melanoma cell lines
Hep 3D	hepatoma cell lines

INTRODUCTION

Since times immemorial, medicinal plants have been used virtually in all cultures as a source of medicine[1-2]. Fossil records have shown the use of plants as drugs since Middle Palaeolithic age i.e., approximately 60,000 years back[3]. The use of plants as medicines is not restricted to one system of medicine. The plants as medicines are capitalized in Ayurvedic, Greek, Islamic, Chinese, and Allopathic (Western) systems of medicines[4]. This indicates the

consensus among the nations upon the use of plants as medicines. Screening of medicinal plants on the basis of their presence at various geographical locations and their presumptive folklore use indicate a huge number of plant species that can be worked upon to yield a huge number of plant derived metabolites of important therapeutic significance. During the past decade, the traditional systems have gained importance in the field of medicine. In many developing countries, a large proportion of the population relies heavily on traditional practitioners, who are dependent on medicinal plants to meet the primary health care needs. Although, modern medicines are available, herbal medicines have often retained popularity for historical and cultural reasons. Growing interest has also prompted researcher to screen scientifically various claims regarding properties and uses of medicinal plant materials. Presently, both common consumers and healthcare professionals seek updated, authoritative information towards safety and efficacy of any recommended medicinal plant as drug prior to its use. The present attempt is to review and compile updated information on various aspects of *Oroxylum indicum*, a plant used in Indian system of medicine for variety of purposes. *Oroxylum indicum* belongs to the Family Bignoniaceae characterized by brown bark and large pinnate leaves. *Oroxylum* is a genus of medium sized, deciduous trees, distributed in India, Sri Lanka, Malaysia, China, Thailand, Philippines and Indonesia[5]. In India, the tree is indigenous to Eastern and Western Ghats and is also found in North-East regions[6]. *Oroxylum indicum* is commonly known as "Indian Trumpet tree" due to its resemblance to trumpet. The plant is known for its high commercial and economic importance. Several medicinal properties have been attributed to the plant not only in Ayurveda but also in Unani system of medicines[7]. Pharmacologically, it has been found to have astringent, anti-inflammatory, antihelminthic, antibronchitic, antileucodermatic, antirheumatic, anti-anorexic and many other medicinal properties[8].

Taxonomical Classification

Kingdom: Plantae
Division: Magnoliophyta
Class: Magnoliopsida
Order: Lamiales
Family: Bignoniaceae
Genus: *Oroxylum*
Species: *indicum*

Synonyms

Bignonia indica L.
Calosanthes indica Blume.

Vernacular Names

English: Broken bones plant, Indian calosanthes, Indian trumpet flower, Midnight horror, Tree of Damocles
Chinese: Handy pinyin, Mud huddle
Bengali: Sona, Khonha, Paharijora, Kani-Dingi, Hanghoal, Aklong-Singh, Thona Gach, Naori Chilana (Chaknma Tribe), Krong-Sa-Bang (Marma Tribe), Tou-Kharung Tripura Tribe), Kaak-Rakung (Tribe Halam), Kanai Dingi (Garo Tribe)
Hindi: Bhut-Vriksha, Dirghavrinta, Kutannat, Manduk (The Flower), Patrorna, Putivriksha, Shallaka, Shuran, Or Son, Vatuk
Kannada: Tattuna
Konkani: Davamadak
Nepalese: Tatelo
Malayalam: Palaqapayyani, Vashrppathiri, Vellappathiri
Marathi: Tayitu, Tetu
Sanskrit: Aralu, Shyonaka
Sri Lanka: Totila, Thotila
Tamil: Cori-Konnai, Palai-Y-Utaicci, Puta-Puspam (The Flower)
Telugu: Manduka-Parnamu, Pampena, Suka-Nasamu

Distribution

Oroxylum indicum is native to the Indian subcontinent, in the Himalayan foothills with a part extending to Bhutan and southern China, in Indo-China and the Malaysia ecozone. It is visible in the forest biome of Manas National Park in Assam, India. It is also found in Phillipines, Indonesia and Srilanka.

Ecology

Oroxylum indicum lives in relationship with the actinomycete *Pseudonocardia oroxyli* present in the soil surrounding the roots.

Botanical Description

Oroxylum indicum is a small to medium sized deciduous tree measuring upto 12 metres in height with light greyish brown, soft, spongy bark having corky lenticels, large pinnate, bipinnate or tripinnate ovate or elliptic leaves; lurid purple, fleshy, foetid flowers and large, flat, sword shaped capsules full of many flat and papery thin seeds with broad silvery wings. Leaves are large up to 1 – 5 m long, pinnate, bipinnate or tripinnate, leaflets are ovate or elliptic. They form enormous seed pods that hang down from bare branches. Those long fruits curve downward and resemble the wings of a large bird or dangling sickles or swords in the night. The fresh root bark is soft and juicy and creamish yellow to greyish in colour. The taste is sweet initially later becoming bitter. On drying, the bark shrinks, adheres closely to the wood and becomes faintly fissured[9]. Flowers are many large, purple and fleshy with perfect five stamens. Fruits are Capsule, large, flat, sword shaped, up to 90 cm x 9 cm valves woody. Seeds are many, flat, thin with broad silvery wing. The seeds are round with papery wings. Flowering starts in the cold season, from January to March and fruits are developed in April to July. The plant is also called as broken bones tree as when the long leaf and flower bearing stalks dry and fall from the tree, their accumulation beneath the tree resembles a pile of broken bones. The tree is a night bloomer and flowers are adapted to natural pollination by bats[10].

Microscopic Features

Microscopic studies of the roots of *Oroxylum indicum* revealed that the root cork consists of polyhedral cells with the fragments of pitted stone cells lying underneath the cork cell. The outer layer of cork is lignified while as the inner cork layer is non-lignified. Cortex is wide and made up of thin walled parenchymatous cells. Abundant crystal of calcium oxalate are scattered as such in parenchymatous cell of cortex. Phloem consists of thin walled radially arranged phloem parenchyma cells showing narrow tangential segments of sclerenchyma[11]. The microscopic carried out on the root bark of *Oroxylum indicum* revealed that the transverse section of the plant consist of cork, cortex, phloem and medullary rays. Cork consist of about 30 to 35 layers of tangentially running, polyhedral cells with the fragments of groups of tangentially running rectangular to oval, thick wall pitted stone cells lying underneath the cork cells. The outermost cork layer was consisting of about 15 to 20 rows of lignified

cells and rest of them inner cork layer was non-lignified. Cortex was wide. It was made up of thin walled parenchymatous cells. In the cortex stone cells and abundant lignified sclerides isolated or fairly in large groups showing a considerable variation in size and shape, walls of most of them were moderately thickened, striated and pitted. The abundant acicular crystals of calcium oxalate scattered as such in parenchymatous cells of cortex. Phloem forms the major part of the bark and was composed of broad radial strips separated by medullary rays. Phloem consists of about 25 to 30 layered, thin walled radially arranged phloem parenchyma cells showing narrow tangential segments of sclerenchyma. The phloem region is traversed by medullary rays, which are bi- seriate to tetra seriate and made up of thin walled cells.

Cultivation and Micro Propagation

The production, consumption and international trade in medicinal plants and phytomedicine have grown and are expected to grow further in the future. To satisfy growing market demands, surveys are being conducted to unearthen new plant sources of herbal remedies and medicines and at the same time develop new strategies for better yield and quality. This can be achieved through different methods including micro propagation[12]. It may help in conserving many valuable tree species in the process and may open new vistas in the forest biotechnology.

Oroxylum indicum is propagated naturally by seeds, which germinate in the beginning of the rainy season. Seedlings require moderate shade in the early stages. However, the seed set is poor and seed viability is low. Problems related with its natural propagation and indiscriminate exploitation for medicinal purpose has pushed *Oroxylum indicum* to the list of endangered plant species of India. According to the report of task force on conservation and sustainable use of medicinal plants, Planning commission, Government of India (2000), the estimated demand of *Oroxylum indicum* in Southern India is 500 kg per annum[13]. Various problems related with conventional propagation and high demand of planting material of medicinal and aromatic plants can be addressed by efficient and economical in-vitro propagation in a short span.

In an endeavour to develop micro propagation protocol, Sharad Tiwari, et al designed an efficient method to regenerate plant seedlings from callus cultures of nodal segments. During their experiments, they took seedling stem sections of *Oroxylum indicum* and cultured them on murashige and skoog (MS) medium with and without growth regulators. Callus proliferation started after 2 weeks of initial culture. They found the half-strength MS medium with 0.5 mgL^{-1} indole-3-butyric acid as the best rooting medium. When rooted plants were transferred to soil, they exhibited a normal development and grew successfully[14].

M. Gokhale and Y.K. Bansal developed a protocol for micro propagation of *Oroxylum indicum*. They took the seeds and germinated them under in-vitro conditions. After the formation of seedlings, they dissected the apical and axillary buds and inoculated them under aseptic conditions onto the sterile culture medium in test tubes on MS containing 3% sucrose, and plant growth regulators particularly cytokinins viz. BAP (1 mgl^{-1}), with additive $AgNO_3$ in different concentrations. Rooting of the regenerated shoots was achieved on medium (half-strength) containing IBA (1 mgl^{-1}) and $AgNO_3$ (1 mgl^{-1})[15].

Since the demand of *Oroxylum indicum* by pharmaceutical industry is exclusively escalating, the existence of *Oroxylum indicum* in natural population is high threatened. As an effort towards the conservation and collection strategies for this species, Jayaram K. and Prasad MNV assessed the genetic diversity in different accessions of *Oroxylum indicum* by RAPD. They found that the genetic diversity of this species is very low and depicted the possibility as difficulty in adapting to different environmental conditions. They stored the different accessions in the gene bank in their university and developed a nursery of the various varieties of the plant[16].

PHYTOCHEMISTRY

Oroxylum indicum has specific aromatic odour because of the presence of essential oils. The aromatic essential oil mainly contains phenols, fatty acids and aldehydes. Besides oil, the plant also contains polyphenolics, flavonoids and alkaloids.

- The leaves of this plant are reported to contain flavonoids namely chrysin, oroxylin-A, scutellarin, baicalein[17]. Leaves are also found to contain quercetin-3-o-α-L-arabinopyranoside, 1-(2-hydroxyethyl) cyclohexane-1, 4-diol, apigenin[18].
- Seeds of this plant are reported to contain ellagic acid[19].
- Root bark is reported to contain chrysin, baicalein, biochanin-A and ellagic acid[20]. The root bark has also been reported to contain two flavonoids 2, 5-dihydroxy-6, 7-dimethoxy flavone and 3, 7, 3', 5'-tetramethoxy-4'-hydroxyflavone[21].
- Stem bark is found to contain ellagic acid[22], chrysin, oroxylin-A, scutellarin, baicalein[23,24], 5-hydroxy 8-methoxy 7-o-β-D-glucopyranuronosyl flavone[25], stigmast-5-en-3-ol[26], pratensol[27], 3-(4-hydroxy phenyl) 2-propenoic acid[28] and flavonoid 3,4',5,7-tetrahydroxy-flavonol[29], 5-hydroxy 4',7-dimethoxy flavone[30], 7-o-methyl chrysin[31], dihydrooroxylin-A, methyl-3,4,5-trihydroxy-6-(5-hydroxy-6-methoxy-4-oxo-2-phenylchroman-7-yloxy)-tetrahydro-2H-pyran-2-carboxylate,5-hydroxyl-7-methoxy-2-(2-methoxy-6-(3,4,5-trihydroxy-6-(hydroxymethyl) tetrahydro-2H-pyran-2-yoloxy)phenyl)-4H-chromen-4-one[32]. Other chemical constituents contain prunetin and sitosterol from wood.
- Fruits are reported to contain oroxylin A, chrysin and ursolic acid[33], aloe-emodin[34].
- The seed oil contains caprylic, lauric, myristic, palmitic, palmitoleic, stearic, oleic, and linoleic acids[21].

Uses

The tree is often grown as an ornamental for its strange appearance. Materials used include the wood, tannins and dyestuffs. It is also a plant with edible leaves and stems. Young shoots and unripe fruits are eaten as vegetables. The tree is also frequently lopped for fodder[35]. Wood of the tree is used to make match boxes. Stem bark and fruits of the tree are used as mordant and yield colour dye[36].

ETHNO PHARMACOLOGY

Oroxylum indicum is an important herbal medicine in many Asian countries and is used in folk medicine as a cure of various diseases[37]. Each part of this plant possesses medicinal value. The root bark is well known tonic and

astringent useful in fever, diarrhoea, dysentry, bronchitis, intestinal worms, leucoderma, asthma, inflammation, anal troubles etc. It is diaphoretic and used in rheumatism. Tender fruits and seeds are refreshing and stomachic and used as expectorant, purgative and bitter tonic[38]. Leaves are emollient and contain anthraquinone and aloe-emodin[39]. The fruits are used in treating bronchitis, leucoderma, helminthosis, etc[40]. The seed extracts exhibit antimicrobial, analgesic, antitussive and anti-inflammatory properties[41]. In general, roots are used as astringent and for the treatment of tuberculosis[42]. Decoction of root bark is effective to cure nasopharyngeal cancer[43].

In Hindu medicine, the root, bark, stem, and leaf are prescribed for snake bite in diarrhoea and dysentry[44]. In some parts of India stem bark, fruits and leaves are used against jaundice. Bark is boiled in water and concentrated till colour changes to that of tea liquor. Cooled extract is taken with 2 tablespoons sugar in a glass of extract many times a day[45].

In Burma, Vietnam and the Philippines, the bark is used to treat dysentry and rheumatism[46].

In India, roots are used in Ayurvedic preparation called "Dasamoola" considered to be an astringent, anti-inflammatory, antihelminthic, antibronchitic, antileucodermatic, antirheumatic, antianorexic and for treatment of leprosy etc.[47]. It is also used in other Ayurvedic formulations such as amartarista, dantyadyarista, narayana taila, dhanawantara ghrita, brahma rasayana, chyavanaprasa awalwha, etc.[48]. The plant is reported to possess antiinflamatory, diuretic, antiarthritic, antifungal and antibacterial activity[49]. Stem bark of the plant is applied for the cure of scabies[50] and to treat arthritis[51]. Leaf decoction is given in treating stomachache, rheumatism, enlarged spleen[52]. Mature fruits of the tree are useful in treating cough, bronchitis, jaundice, piles, smallpox, dyspepsia, colic, leucoderma, pharyngodymia, cardiac disorder, helminthiasis, gastropathy, haemorrhoids and cholera. Root bark of this plant is an astringent used in diarrhoea, dysentry, rheumatism and ottorrhoea as it contains ellagic acid.

In Bangladesh, stem leaf, root, fruits and stem bark are used against tonsillitis, snake bite, rheumatoid arthritis, oedema, gynaecological disorders, colic, dysentry, skin disorder, epilepsy, antiseptic, diarrhoea cold, sudden unconsciousness, sex stimulant, fever, cholera, sore throat, astringent, jaundice, scabies, eczema, leucorrhoea, urinary problems, toothache, pus with urine, burning sensations in urinary tract, us with semen[53].

TOXICOLOGICAL STUDIES

A research work conducted to investigate the toxicological activities of the medicinal plant *Oroxylum indicum* has shown that the root and stem extracts of the plant are toxic for the brine shrimp nauplii[54].

Bioactivity studies of the *Oroxylum indicum* revealed that *Oroxylum indicum* exhibited moderate toxicity to the growth of brine shrimp (BST) nauplii and wheat rootlet growth (WRG), but was not toxic to the lettuce seed germination (LSG)[55].

Shrikant V. Joshi, et al, 2011, while evaluating the protective effect of aqueous extract of *Oroxylum indicum* root bark against DNBS-induced colitis in rats, performed the acute oral toxicity study on Wistar rats by feeding the overnight fasting rats with doses ranging from 175 mg/kg bw to 5000 mg/kg BW and found that the aqueous extract did not cause any mortality in the rats[56].

Similarly, Ashpak M. Tamboli, et al., determined the hypoglycemic activity of extracts of *Oroxylum indicum* Vent roots in animal models. They, while performing the acute toxicity tests, found that both the ethanolic and aqueous extracts were safe upto a dose of 5 g/kg BW a day[57].

Bichitra Nandy Tripathi, et al., 2011 studied the toxicity to find out the lethal dose of ethanolic extract of *Oroxylum indicum* in adult mice. *Oroxylum indicum* stem aqueous and ethanolic extract were administered orally in mice with graded doses (5 mg-3000 mg/kg BW) and mortality was observed for a period of 72 hours. The administration of aqueous extract did not produce any acute toxic symptoms (100% survival) at doses upto 2000 mg/kg BW[58].

Oroxylum indicum is being used as medicinal herb for thousands of years without any known adverse effects. There have been number of scientific studies conducted to evaluate the toxic effects of the plant. Almost all the studies conducted on *Oroxylum indicum* have shown that *Oroxylum indicum* is not toxic to humans and experimental animals even upto high doses.

PHARMACOLOGY

Antibacterial Activity

Oroxylum indicum is reported to possess antibacterial activity. The methanolic, ethyl acetate, and ethanolic extracts of stem bark of *Oroxylum indicum* were tested on three different species of gram positive and gram negative bacteria viz. Bacillus subtilis, E. coli, and Pseudomonas aeruginosa. All of the extracts were found to possess remarkable antibacterial properties[59].

The crude petroleum ether, methanolic and ethyl acetate extracts of root bark of *Oroxylum indicum* and the two compounds isolated from them, 2,5-dihydroxy 6,1-dimethoxyflavone (compound 1) and 3,7,3',5'-tetramethoxy 4'-hydroxyflavone (compound 2) have been found to have moderate to good antimicrobial and antifungal activity. The results of the study justified the use of this plant in the management of microbial infection[60].

The three fractions, hexane, CCL4 and chloroform obtained from methanolic stem bark extract of *Oroxylum indicum* were tested for antibacterial and antifungal activity by standard disc diffusion method against various gram-positive and gram-negative bacteria and some fungi such as *Bacillus cereus, Bacillus megaterium, Bacillus subtilis, Staphylococcus aureus, and Sarcina lutea. E. coli, Pseudomonas aeruginosa, Salmonella parathyphii, Salmonella typhi, Shigella boydii, Shigella dysenteriae, Vibrio mimicus, Saccaromyces cerevaceae, Candida albicans and Aspergillus niger*. All the extracts have been effective against both gram positive and gram negative bacteria as well as fungi and the properties were comparable with the effectiveness of standard antibiotic ampicillin[61].

The antifungal activity of dichloromethane extract of *Oroxylum indicum* has been studied against dermatophytes and wood rot fungi. The dichloromethane extract was found to have significant antifungal activity[62].

The antimicrobial activity of *Oroxylum indicum* has been studied against different strains of gram positive and gram negative bacteria[63].

The antibacterial activity of *Oroxylum indicum* has also been studied against staphylococcus aureus and E. coli. In acute toxicity test, antibacterial activity of acetone, water and ethanolic extracts was compared. Ethanolic extract possessed maximum activity against both strains of bacteria[64].

Antioxidant Activity

The production of different oxidative species and free radicals due to stress leads to adverse effects on various vital organs and tissues of body. Antioxidants are now standing on the mainstay of the treatment and prevention of several diseases[65]. Current research is directed towards finding naturally occurring antioxidants particularly of plant origin.

The antioxidant activity of *Oroxylum indicum* has been evaluated by in-vitro experiments. Antioxidant potential of methanolic extracts of different parts of *Oroxylum indicum* viz. root, root bark, stem, and stem bark, leaves and fruits was determined by performing DPPH, nitric oxide, superoxide anion and hydroxyl radical scavenging potential and reductive ability assay. Leaves and bark extracts showed maximum reductive ability and highest free radical scavenging activity than bark, stem and fruit extract[66].

The free radical scavenging potential of the different extracts of leaves of *Oroxylum indicum* has also been under in-vitro conditions by using DPPH assay. Crude ethyl acetate, methanolic and water extracts of leaves of *Oroxylum indicum* showed significant antioxidant activity with IC50 values of 49.0, 55.0 respectively at 100 µg/ml concentration[67].

The methanolic extract of stem bark of *Oroxylum indicum* has ability to scavenge DPPH, Superoxide and hydroxyl free radicals and inhibit lipid peroxidation in rat liver homolysates[68-69].

The free radical scavenging activity of the of stem bark of *Oroxylum indicum* has also been confirmed by different assays viz., total antioxidant assay and β-carotene bleaching assay. All the extracts viz. petroleum ether, benzene, chloroform, ethanol, and water showed antioxidant activity. However, ethanolic and chloroform extracts exhibited maximum antioxidant potential than other extracts[70].

Methanolic and aqueous extracts of stem bark of *Oroxylum indicum* have also been found to have diverse therapeutic potentials. Various properties including antioxidant property, cytotoxicity, and protection against oxidative DNA damage, Ferric reducing antioxidant (FRAP), free radical (DPPH and OH^-) scavenging activities as well as inhibitory effect on lipid peroxidation have also been confirmed. In the cytotoxicity test, cytotoxicity of the extracts has been characterized by XTT assay in MDA-MB-435 S and Hep 3D cell lines. Protection of DNA by the extracts against oxidative damage by UV-photolysis of H2O2 was studied. Both the extracts inhibited lipid peroxidation in a dosage dependent manner. Both extracts exhibited considerable free radical scavenging and ferric reducing abilities. The extracts demonstrated extensive cytotoxicity in both tested cell lines. Both extracts exhibited moderate levels of DNA protection against oxidative stress[71].

Antiinflammatory Activity

The root bark of *Oroxylum indicum* has been shown to inhibit chronic inflammation in rats. In the acute test conducted on experimental Wistar rats, carrageenan was used to induce rat paw edema in one group of animals and cotton pellet was used to induce chronic inflammation in second group. Pre-treatment with n-butanol fraction showed significant ($p<0.05$) anti-inflammatory activity at 3 hour when compared with control group. Further, it also significantly ($p<0.05$) reduced the increase in the weight of cotton pellet when compared with the control group and the results were comparable with that of standard diclofenac treated group of animals[72].

The antiinflamatory activity of stem bark of *Oroxylum indicum* has also been studied against the ear swelling in mice. Water extract was found to have obvious anti-inflammatory effects of lowering ear swell in mice.

Aqueous extract of leaves of *Oroxylum indicum* has been found to provide the relief to rats against carrageenan induced rat paw edema. To confirm the protective activity, an experiment was perform in which the inflammation was induced in the paws of rat by carrageenan injection. These experimental rats were administered with water extract of leaves of *Oroxylum indicum* at two dose levels of 150 mg/kg BW and 300 mg.kg BW/day. Both the doses exhibited significant antiinflammatory activity, with the dose level of 300 mg.kg bw/day exhibiting maximum anti-inflammatory activity. The significant anti-inflammatory activity has been attributed to the presence of different polyphenolic and flavonoid constituents present[73].

The aqueous and alcoholic extracts of *Oroxylum indicum* were also found to have significant antiinflammatory activity[74].

Analgesic Activity

Oroxylum indicum has been used since ages as analgesic agent. Pharmacologically, the activity was reported in the butanol extract of root bark of *Oroxylum indicum*. Two assay models, viz. tail flick and acetic acid induced writhing response, were employed to detect analgesic activity. For tail flick method, Wistar albino rats of either sex 200-250 g were selected. One group of animals was administered 100 mg/kg BW, p.o., and another group was administered standard drug morphine (10 mg/kg BW, i.p.). One hour after the administration, tail of the rat was placed on nichrome wire of an analgesiometer and the time taken by the animal to flick its tail was taken as reaction time. Analgesic activity was measured at 0 and 30 min. for acetic acid induced writhing; Swiss albino mice 20-25 g were selected. The n-butanol fraction was administered 100 mg/kg BW p.o. in one group. Another group received standard aspirin (25 mg/kg BW, i.p.). One hour after the administration, the injection of acetic acid 0.6 %v/v (10 ml v/v/kg BW, i.p.) was given and thereafter, the number of writhes was observed for upto 30 minutes. Reduction in number of writhing by any treatment as compared to vehicle treated animal was considered as a positive analgesic response, oral administration of n-butanol fraction significantly prolonged the reaction time in rats. Oral administration of n-butanol fraction also significantly reduced the number of writhing by 75.93 % as compared to aspirin 87.05 %. The analgesic activity has been attributed to the presence of flavonoids such as baicalein, ellagic acid, biochanin-A present in the roots of *Oroxylum indicum*[72].

Hepatoprotective activity

Oroxylum indicum has been found to offer liver protection against various experimentally induced damages. Different extracts of leaves of *Oroxylum indicum* showed significant hepatoprotective activity against CCL_4 induced hepatotoxicity in Wistar albino rats. Carbon tetrachloride injection lead to the significant increase in the level of SGPT, ALP, SGOT AND total bilirubin. Pet ether, ethanol, water and chloroform extracts administered orally at a dose of 300 mg/kg bw/day significantly altered the level of SGPT, ALP, SGOT AND total bilirubin towards the

normal. Ethanolic extract was found to be more effective than all other extracts[75].

The aqueous extract of *Oroxylum indicum* root bark has been found to have protective effect against paracetamol induced liver damage in experimental rats. This has been evident by significantly altered levels of serum enzymes (SGPT, ALP, SGOT AND total bilirubin) towards normal in experimental rats[76].

The hepatoprotective activity of stem bark of *Oroxylum indicum* against CCl_4 induced liver damage in mice has also been confirmed. Pet ether, chloroform, methanolic and aqueous extracts of stem bark of Oroxylum indicum were examined against carbon tetrachloride induced liver damage in mice using silymarin as control. Enzyme activities of SGPT, ALP and SGOT were analyzed. All the extracts were shown to have significant hepatoprotective activity, with the methanolic extract being more efficient[77].

The hepatoprotective effect of root bark of *Oroxylum indicum* has also been evaluated against carbon tetrachloride induced hepatotoxicity in experimental animals. Pre-treatment with the ethyl acetate and chloroform extracts prior to carbon tetrachloride induced liver damage, exhibited the liver protective action. Carbon tetrachloride treatment produced alteration in the activities of serum enzymes and the antioxidant status of the tissues, which was also manifested by abnormal histopathology. Pre-treatment with *Oroxylum indicum* restored all these changes upto normal[78]. All these studies confirmed the traditional uses of this plant as a potential hepatoprotective agent.

Nephroprotective Activity

Root decoction and leaves of *Oroxylum indicum* are widely used as prophylaxis for kidney disorders and to remove kidney stones in Indian system of medicine[79]. The ethanolic extract of roots of *Oroxylum indicum* has shown protective effect against cisplatin-induced renal injury in Wistar male albino rats. nephrotoxicity was induced by cisplatin (6 mg/kg bw i.p.) as evidenced by significant increase in BUN, serum creatinine, urinary total proteins, LPO levels and decreased creatinine clearance level. On administration of ethanolic extract at two dose levels 200 and 400 mg/kg BW for 3 days starting one hour prior to cisplatin administration significantly restored all the parameters towards normal. Histological studies also substantiated the results[80].

The nephroprotective activity of *Oroxylum indicum* has also been evaluated in experimental rats. It has been considered as a great discovery that several flavonoids have been found to possess nephroprotective activity. In an experiment, chrysin isolated from roots of *Oroxylum indicum* was evaluated for protective activity against cisplatin-induced nephrotoxicity.. Chrysin at a dose level of 40 mg/kg BW protected the kidney damage from nephrotoxic cisplatin in experimental rats. Animals which received chrysin reversed all the effects induced by cisplatin[81].

Antihyperlipidemic Activity

The antihyperlipidemic activity of *Oroxylum indicum* total root bark extract has been examined in cholesterol induced hyperlipidemic albino Wistar rat model. The root extract exhibited significant reduction in total cholesterol, total triglycerides, LDL-C, VLDL-C levels and remarkable increase in the levels of HDL-C when compared to standard Lovastatin drug. The atherogenic index and LDL-C: HDL-C risk ratio was also reduced to significant extent in the group treated with extract. The levels of SGOT and SGPT were also estimated and found to be significantly less than that of hyperlipidemic control group. The study scientifically proved the folklore use of *Oroxylum indicum* in cardiovascular disorders and as ingredient in various Ayurvedic formulations used in cardiovascular diseases[68].

Antidiabetic Activity

Antidiabetic properties of *Oroxylum indicum* have been evaluated in experimental animal models. The hypoglycemic activity of extracts of *Oroxylum indicum* (L) Vent roots has been studied in Wistar albino rats. In one study, the diabetes was induced in Wistar albino rats by a single intraperitoneal injection of Alloxan (120 mg/kg BW). In another study, the diabetes was induced as a result of insulin resistance by the single subcutaneous injection of dexamethasone (10 mg/kg BW). oral administration of ethanolic and water extracts of roots of *Oroxylum indicum* at the dose levels of 300 and 500 mg/kg bw for 21 days and 11 days respectively in two different studies showed a significant reduction in the serum glucose, triglyceride, total cholesterol levels and a significant increase in the liver and muscle glycogen levels, when compared with diabetic control groups. Sufficient reduction in serum glucose concentration was shown by aqueous and alcoholic extracts at 500 mg/kg BW after 21 days and 11 days by 50.92 % and 49.59 % respectively[82].

The methanolic and aqueous extracts of leaves of *Oroxylum indicum* have also been found to have antidiabetic activity against alloxan-induced diabetes in rats. Administration of methanolic and aqueous extracts at a dose level of 300 mg/kg bw for 21 days to Alloxan (120 mg/kg bw) induced diabetic rats significantly restored the serum biochemical parameters, viz., fasting blood glucose level, lipid profile, biomarker enzymes, serum total proteins, serum creatinine, serum urea, serum SGOT, SGPT and ALP, to normal. Methanolic extract induced more significant antidiabetic effect than aqueous extract[83].

Antihelminthic Activity

Antihelminthic activity of *Oroxylum indicum* has been studied under in-vitro conditions. In in-vitro experiment, *Oroxylum indicum* was evaluated for antihelminthic activity against equine strongyle eggs and compared to that of ivermectin, one of the most effective deworming agents. *Oroxylum indicum* was found to have significant antihelminthic activity by 0 % hatching of eggs at a dose of 2×10^{-1} g/L *Oroxylum indicum*. The results were quite comparable to the standard drug[84].

Immunomodulatory Activity

The fresh root of *Oroxylum indicum* is consumed with the traditional belief that it enhances immunity. This claim has been investigated in experimental animals. rats treated with n-butanol fraction (100 mg/kg bw) of *Oroxylum indicum* root bark for 22 consecutive days when challenged with sheep red blood cells (SRBC hemaglutinating antibody [HA] titter) and delayed-type hypersensitivity (DTH) reactions, showed a significant rise in antibody titre during secondary antibody responses, indicating a potentiating of certain aspects of the humeral response. The treatment also resulted in a significant rise in paw edema formation indicating increased host DTH response. Furthermore, histopathological analysis of lymphoid tissues showed an increase in cellularity such as

T-lymphocytes and sinusoids, in the treatment group. The plant was also found to have significant antioxidant activity. The reported immunomodulatory activity might be attributed to its ability to enhance specific immune responses (both humeral and cell-mediated) as well as its antioxidant potential[85].

The immunomodulatory properties of *Oroxylum indicum* have also been evaluated through estimation of hum oral and cell mediated immune response in broiler chicks. Day old broiler chicks were grown upto 7 days and divided into different groups. All the groups were vaccinated against Ranikhet disease (RD) virus on day 7 and day 28 except one group which served as unvaccinated control. All the groups of chicks were vaccinated against infectious bursal disease (IBD) on day 14. Two groups of chicks were fed *Oroxylum indicum* stem bark and root bark powder respectively each at 250 mg/kg BW. One group was fed levamisole at 10 mg/kg BW, which acts as standard drug. Humoral immune response was measured by hemagglutination (HA) test and Hemagglutination inhibition (HI) test against ND virus. Cell mediated immune response was studied on the basis of delayed hypersensitivity reaction or measured by contact sensitivity test with 2, 4-dinitrofluorobenzene (DFNB). Highest MHI antibody titter was found in levamisole treated group, followed by groups treated with root powder and stem powder of *Oroxylum indicum* respectively. Similarly six hours post DNFB challenge, a significant rise in mean skin thickness (MST) was observed in all the treated groups. The highest was observed in levamisole treated group, followed by groups treated with root powder and stem powder of *Oroxylum indicum* respectively. The findings suggested that the root bark of *Oroxylum indicum* possessed the significant immunomodulatory activity that its stem bark counterpart. Thus, Oroxylum indicum root bark powder may be recommended as safe and commercially beneficial immumomodulator[86].

Gastro Protective Activity

Oroxylum indicum has been used for ages for the treatment of various gastric disorders. The protective effect of alcoholic extract of root bark of *Oroxylum indicum* and its different fractions viz. pet ether, chloroform, ethyl acetate and n-butanol fractions has been studied against gastric ulcer in Wistar albino rats. The gastric mucosal damage was induced in rats by administration of ethanol. n-butanol fraction was also studied in water immersion plus restraint stress (WIRS) model. Alcoholic extract (300 mg/kg BW) and its different fractions (100-300 mg/kg BW) showed significant reduction in gastric ulceration against ethanol induced-gastric damage, with the n-butanol fraction being more effective. In WIRS model, pre-treatment with n-butanol fraction showed significant antiulcer and antioxidant activity in gastric mucosal homogenates. The study also showed the presence of certain flavonoids such as baicalein. The mechanism of gastro protective activity might be attributed to a decrease in gastric acid secretary and antioxidant activities leading to gastric cytoprotection, because of the presence of flavonoids[87].

Certain flavonoids isolated from the stem bark of *Oroxylum indicum* have also been confirmed to have gastroprotective activity[22].

Anticancer and antimutagenic Activity

The anticancer property of *Oroxylum indicum* has been evaluated in the experimental animals induced by different types of carcinogens, and in human cell lines by a number of experiments. Ethanolic extract of *Oroxylum indicum* was found to have antiproliferative effect on Hep 2 cell lines. Ethanolic extract exhibited cytotoxic activity against the Hep 2 cell lines at a concentration of 0.05 % [88].

Baicalein, the most abundant flavonoid present in the leaves of *Oroxylum indicum* has been isolated and tested on the viability and induction of apoptosis in the HL-60 cell line. pretreatment with baicalein for 24 hours caused a 50 % inhibition of HL-60 cells at concentrations of 25-30 μM. exposure of HL-60 cells to 10-20 μM baicalein for 36-48 hours caused the cells to accumulate at S or G2M phases. The result of the study indicated the baicalein has anti-tumor effect on human cancer cells[89].

The antimutagenic activity of methanolic extract of *Oroxylum indicum* has been evaluated in Trp-p-1 by Ames test. Baicalein was found to be the major antimutagenic component with an IC50 value of 2.78 ± 0.15 μM. the antimutagenicity mechanism was attributed to the presence of baicalein which acted as desmutagen and inhibited N-hydroxylation of Trp-p-2[90].

The toxicity study on tumor cells has revealed that *Oroxylum indicum* is having significant activity in the destruction and apoptosis of tumor cells. *Oroxylum indicum* has been found to have an IC50 value of 19.6μg/ml for CEM, 14.2 μg/ml for HL-60, 17.2 μMg/ml for B-16 and 32.5 μg/ml for HCT-8. On the sea urchin eggs, it also inhibit the progression of cell cycle since the first cleavage (IC50= 13.5 μg/ml)[91].

FUTURE DIRECTION OF RESEARCH

On the basis of previous studies already done on the plant, future studies can be focussed. *Oroxylum indicum* showed very promising results against various diseases in experimental animals, antioxidant properties in in-vitro and in-vivo studies against various free radicals and reactive oxygen species, antimicrobial properties in in-vitro studies against various microbes and immunomodulatory effects. The oxidative damage is one of the major causes of various diseases including cancer, diabetes and cardiovascular diseases. *Oroxylum indicum* is present in almost every part of Asia and its various properties like anticancer, antiinflammatory, antidiabetic and immunomodulatory effects may be further explored to provide additional protection and comfort to mankind at a very low cost due to its easy availability. *Oroxylum indicum* has been listed as a threatened plant because of the extensive cut-down of this plant for commercial purposes. Conservation should be done on a large scale through both in-situ and ex-situ methods in order to save this precious plant for the benefit of mankind.

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