

## A BRIEF REVIEW ON PHYTOCHEMISTRY AND PHARMACOLOGICAL ACTIVITY OF *XANTHIUM STRUMARIUM L.*

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### خلاصہ

*Xanthium strumarium L.* طبی اہمیت کی حامل ایک جڑی بوٹی ہے۔ اس کا تعلق خاندان Compositeae کے جنس *Xanthium* سے ہے۔ یہ پاکستان، انڈیا، چین، یوریشیا اور امریکا میں بھی پایا جاتا ہے۔ عموماً چھوٹا گھرو جبکہ تجارتی تاکا لبر کے نام سے جانا جاتا ہے۔ فائیکو کیمیائی تجزیہ کے مطابق یہ کئی نامیاتی درجات کا مجموعہ ہے جیسے ٹریپیز، سیکویو ٹریپیز، لیکٹونز، فلیوینونز، الکیلاڈز، کیونونز، فینولز، فایٹو اسٹرولز، نامیاتی ترشہ، سکوربک ایسڈ، اما نیو ایسڈ اور پروٹینز۔ روایتی حکمت میں اس کی نامیاتی کشید بہت سے امراض مثلاً انفیکشن، الرجی، بخار، لمبریا، قبض، کھانسی، سردی، ڈائیریا، ٹی بی اور کیڑے کے ڈنک کے علاج کے لیے استعمال ہوتے ہیں۔ یہ خواص اس پودے میں موجود طبی افادیت کے حامل اجزاء کی بدولت ہیں جیسے *carboxyatractyloside* (ہائپو گلیسمک)، *caffeoylquinic acid* (اینٹی ہائپر گلیسمک)، *xanthumin* (اینٹی مائیکرو بیل)، *xanthinin* (اینٹی پلاسموڈیل)، *caffeoylquinic acid* (اینٹی انفلامٹری)، *xanthatin*, *sesquiterpene xanthanolides* (اینٹی ٹیومر) اور *terpenes* (اینٹی آکسڈنٹ) ہیں۔ علاوہ ازیں *X. strumarium* زمین سے دھاتوں کو بھی جذب کر سکتا ہے۔ اس نظر ثانی تبصرہ کا مقصد *X. strumarium* کے *phytochemical* اور *pharmacological* خواص کو اجاگر کرنا ہے تاکہ محقق اس کے مزید طبی عامل دریافت کرنے میں حوصلہ مند بھی ہوں جو انسانی صحت کے لیے فائدہ مند بھی ہوں۔ مزید یہ کہ صنعتی علاقوں میں اس کی کاشت سے زمین کو جیومیٹیل سے پاک کیا جاسکتا ہے۔

### Abstract

*Xanthium strumarium* Linn. is one of the medicinally valuable herb belongs to genus *Xanthium* of family Compositeae. The plant occurs all over Pakistan, India, China, Eurasia and also in America. The trade name is Cocklebur and Chotadhatra while generally known as Chotagokhru. Phytochemical analysis have highlighted existence of various classes of organic compounds mainly terpenes, sesquiterpenes, lactones, flavonoids, alkaloids, quinines, phenols, phytosterols, organic acids, ascorbic acid, amino acids and proteins. Plant extracts in organic solvents have been experienced in traditional medicine for the treatment of bacterial and fungal infections, allergy, fever, malaria, diarrhea, constipation, cough, headache, tuberculosis and insect bite. These medicinal properties are due to presence of pharmacological constituents such as *carboxyatractyloside* (hypoglycemic), *caffeoylquinic acid* and *caffeic acid* (anti-hyperglycemic), *xanthumin* (anti-microbial), *xanthinin* (anti-plasmodial), *caffeoylquinic acid* (anti-inflammatory), *xanthatin*, *sesquiterpene xanthanolides* (anti-tumor) and *terpenes* (anti-oxidants). Besides these *X. strumarium* has potential to accumulate heavy metals from soil. Therefore it may consider to cultivate near industrial areas for phytoremediation. This review is done to explore phytochemicals and pharmacological properties in order to collect its variable properties as a medicinal agent that encourage researchers for further isolation and quantification of phytochemicals beneficial for human health.

**Key words:** Phytochemicals, Pharmacology, Anti-microbial, Anti-hyperglycemic

### Introduction

The plant *Xanthium strumarium* is a member of the the largest family i.e. Compositeae, of flowering plant (Angiosperm). The flowers are gathered on inflorescence recemose which appears as stars therefore, also known as Asteraceae. The 20,000 species of its 950 genera are found worldwide as herbs, shrubs, trees and climbers (Chopra, 1994). The whole family is valuable in different aspects, lettuce and artichoke are edible, sunflower and niger seeds are natural source of edible oil. Marigold, daisy and zinnia are ornamental plants. Parthenium is famous for rubber and oaks for building material (Pandey, 2001). In addition besides having economic importance the family exhibits pharmacological properties like *Artemisia* is antimalarial and *calendula* is used for healing wounds whereas *pulicaria* is an insecticidal plant (Muley et al., 2009).

*Xanthium* is a medicinally important genus of compositeae family. It comprises of nearly 25 species distributed throughout the world, four of them *X. macrocarpum*, *X. sibiricum*, *X. spinosum* and *X. strumarium* are also

occurred in Eurasia (Pandey *et al.*, 2012). *X. strumarium* Linn. is a medicinal plant. It is distributed to almost all over of Pakistan (Syed, 1989). Cocklebur and chotadhatura are the trade names of the weed though commonly known as *Chotagokhru*. This is because of its fruit that turns from green to yellow upon ripen, this ability derived from Greek word 'xanthose' which means 'yellow' in addition 'strumarium' that define 'swelling alike beanbag' (Anooj, 2010, Zabta, 2006).

*X. strumarium* Linn. Is an annual erect herb. Its fruit is oblong, hard and covered with hooked bristles. White or green flowers located on monoecious, axillary raceme capitulum. Male head embraces with many flowers, is 5-toothed with tubular corolla, situated at the top of branch whereas axillary located female head has no corolla (Jafri, 1966, Ravindra, 2003). The weed is propagated through seeds and blooms from August to February (Pullaiah, 2006).

### Phytochemical profile

The phytochemical screening of various solvent extracts of this herb has determined the presence of various classes of organic compounds mainly flavonoids, alkaloids, tannins, anthraquinones, terpenoids, glycosides, ascorbic acid, organic acids and others (Farooq *et al.*, 2014). The phytochemical investigation of aerial parts of *Xanthium strumarium* Linn. has shown presence of sesquiterpene lactones, xanthanol, tomentosin and 8-epi-xanthatin over silica gel (Mangel *et al.*, 1993). Further study of aerial parts has found nitrogen 7.5% and protein 46.87% and amino acids were estimated in range of 2-14mg/100g whereas vitamin B 1.4% by (Kumar and Rawat, 2008). A pentacyclitriterpene, 3 $\beta$ -acetoxy lup-20(29)-ene, stigmasterol and a fatty acid, palmitic acid has been isolated from aerial parts (Aneela *et al.*, 2012). Kaemferol and quercetin flavonoids have been isolated from ethanol extract of flower (Kapoor and Ranga, 2003). Sephadex chromatography of n-butanol fraction of fruit found chlorogenic acid, ferulic acid, onion, for mononetin, xanthiazone and thiazinedione (Ting Han *et al.*, 2006). Phytosterols were isolated from fruit extract (Itsuo *et al.*, 1965). Moreover xanthanolides and xanthatin were isolated from leaves (Saxena and Mondal, 1994). Leaves were also found rich in ascorbic acid (113-115 mg,%) (Isamu, 1947). Ethyl acetate extract of stem and ether extract of leaves, both contained phytosterols, xanthinine, triterpenes, strumasterol and oleic acid while 3,4-dihydroxy cinnamic acid and B-sitosterol-D-glucoside were reported from alcohol extract of leaves (Bisht and Rambir, 1978, Khafagy *et al.*, 1974). Hexane fraction of seeds estimated neutral lipids, fatty acids, fatty acid- esters, sterols and triterpenes in range of 0.1-1.6 mass% (Uchenko and Glushenkova, 2000).

Many researchers have analyzed inorganic profile after charring following ashing. (Iqbal *et al.*, 2011) reported Na = 11, K = 16.6, Ca = 12.5 and Cl = 60.6 mg / Kg, in Mardan species. The said plant growing in industrial area of Rawalpindi (Pakistan), was studied for heavy metal accumulation ability in shoots and roots by (Ashfaq *et al.*, 2011). They found Pd 9, Cu 126 and Zn 66.2 mg/Kg in roots while 27, 15.3 and 28 mg/Kg of Pd, Cu and Zn respectively in shoots. Moreover the content of Zn, Cd, Pd, Fe and Cu in 3.64, 0.13, 1.57, 2.20 and 2.12 mg/Kg respectively has been determined from *X. strumarium* growing in Kohat (Iqbal *et al.*, 2010).

### Medicinal Importance

The herb *Xanthium strumarium* Linn. is being credited for medicinal value for a long time in China, Malaysia, Indo-Pak and America. The whole plant possesses anti-oxidant, analgesic, sedative and diuretic properties. Besides these sialogogue, emollient, sudorific, and emollient pharmacological activities were also observed in the herb (Zabta, 2006). In Ayurveda the decoction of plant is given to treat malaria and urinary diseases. The leaves are astringent and are given in herpes and scrofula (Pullaiah, 2006). In addition the oil obtained through steam distillation of leaves shows potential against pathogen. A tonic of leaves with honey is used for cough and fever. Moreover a mixture of leaves, sugar and black pepper is given in blood dysentery (Umberto, 2012). In China its fruit has been used to cure headache, nasal sinusitis and arthritis (Ting *et al.*, 2006). As the fruit of the plant possesses anti-inflammatory property, it is useful for small pox, to cure urinogenital infections and hormonal activity (Krishnan, 2000). A decoction of roots is applied locally over boils and in cancer therapy (Narayan and Purohit, 2003). The plant demonstrates anthelmintic and cooling properties. It is useful to improve voice, appetite and memory. The powdered aerial parts of the plant applied on poisonous insects and snake bite (Sastri, 1976).

### Pharmacological profile

**Anti-oxidant activity:** The fruit of *X. strumarium* possesses radical scavenging property. The potential was found 138.87  $\mu$ g/ml in DPPH assay in contrast of Ascorbic acid in addition, 32.76  $\mu$ mole activity/mg protein was observed in catalase by measuring the initial rate of H<sub>2</sub>O<sub>2</sub> disappearance (Ghahari *et al.*, 2017). Antioxidant potential was also determined in ethyl acetate fraction of aerial parts by DPPH method. The fraction found excellent with 71% inhibition and EC<sub>50</sub>= 938 $\mu$ g/ml in contrast of Ascorbic acid (Aneela *et al.*, 2017).

**Antihyperglycemic activity:** A water insoluble glycoside (potassium carboxyatrectyloside) has been isolated from aqueous extract of aerial part of *X.strumarium* by flash evaporation of 7:3 tetra hydrofurane: water. The glycoside exerted adenine nucleotide translocation inhibition through mitochondrial membrane (John *et al.*, 1976). In addition a phenolic compound, Caffeic acid was also obtained from aqueous- methanol fraction of fruit of this plant possessing anti hyperglycemic property. It was experienced onto insulin resistant diabetic rats in a dose dependent way, a decrease of plasma glucose was observed that was not found in normal rats (Feng-Lin *et al.*, 2000). More over Methyl-3,5-di-O-Caffeoylquinic acid isolated through column chromatography of ethyl acetate fraction of fruit, was found as a preventive agent for diabetic complications. It exhibited inhibition of galacticol formation in the rat lens and in erythrocytes incubated with glucose concentration (Ha Na *et al.*, 2013).

**Antimicrobial activity:** The ethyl acetate fraction of aerial parts of this plant was screened for antimicrobial activity. The fraction exhibited significant antibacterial activity against *B.cereus*, *B. subtilis* and *B. thuringiensis* gram positive bacteria whereas found good against *K. pneumoniae* gram negative bacteria exhibited zone of inhibition 26, 34, 30 and 22 mm respectively. The MIC values observed were 88, 120, 102 and 56mg/ml respectively, taking Gentamicin as standard. The methanol fraction showed moderate activity against *S. faecalis* 13mm. The same fraction was also found excellent against fungal strains *A. flavus*, *A. niger*, *Penicillium* species and *Rhizopus* with 19,15,12 and 16 mm zone of inhibition along with MIC values of 320, 100, 149 and 300 mg/ml using Gresiofulvinas standard drug (Aneela *et al.*, 2012, Aneela *et al.*, 2017).

A sesquiterpene xanthanol was isolated from ethylacetate fraction of aerial parts of this plant. The compound was found significantly active against *S.aureus* and *B.subtilis* at 25 and 23 mg/ml in contrast of 0.5mg/ml streptomycin sulphate as reference. (Jawad *et al.*, 1988). Moreover soxhleted ether extract of leaves of *X.strumarium* exhibited good antibacterial activity. The activity might be due to an active crystalline compound *Xanthumin* that has molecular formula  $C_{17}H_{22}O_5$  (Gupta and Gupta, 1975).

**Anti-plasmodial Activity:** The dose based examination of ethanolic extract of leaves on mice upon application of 150 mg/kg/day over *Plasmodium berghei* infected mice, showed sustain ability for 29 days. It was similar to standard drug Chloroquin (5mg/kg/day). It reflected presence of compound possessing anti-plasmodial activity and leaves extract is active for treatment of malaria (Sanjeev *et al.*, 2012). Moreover the aqueous extract of aerial parts of the plant inhibited the growth of *Plasmodium falciparum* at  $EC_{50}$  10  $\mu$ g/ml. The activity was due to Xanthinin in the extract as an active component (Tran *et al.*, 2003).

**Anti-trypanosomal Activity:** The crude ethanolic extract of aerial parts of *X. strumarium* was analyzed for anti-trypanosomal behavior in mice through vivo trial. The extract was effective at 100 and 300 mg/kg. on specimen infected by *trypanosome evansi*. However, it was found toxic at 1000 mg/kg (Talakai *et al.*, 1995).

**Insecticidal activity:** The crude methanol extract of whole plant exhibited 100% mortality for *Callosbruchus analis* in comparison of standard drug Permethrin (100% activity at 235.7 $\mu$ g/cm). It proved *X.strumarium* as a natural insecticide (Fazli, 2012).

**Anti-inflammatory Activity:** The potential to treat inflammation was determined by croton-oil-induced edema test of n-butanol fraction of whole plant. The results showed highest activity 0.5, 0.75 and 1.0 mg/ear with reference Indomethacin (0.3 mg/ear). Furthermore the fraction led to the isolation of Caffeoylquinic acid that implied polar nature of active compounds in it (Han *et al.*, 2007).

**Anti-arthritic activity:** The immune-modulatory potential to prevent rheumatoid arthritis was observed in extract of fruit *X.strumarium*. A significant suppress in paw swelling and arthritis level was observed upon administration of 300-75 mg/kg once a day of extract using methotrexate 3mg/kg/twice a week on Freund Adjuvant induced rats (Lin *et al.*, 2014).

**Diuretic activity:** The 65% hydroalcoholic solution of aerial parts of *X. strumarium* was evaluated for diuretic potential in wistar rats. Similar effects to that of reference Furosemide (5mg/kg) was found at the dose of 100, 200 and 400mg/kg extract. The plant was found safe with no toxicity and death at 2000mg/kg, limited dose of standard (Dra *et al.*, 1999).

**Cytotoxic activity:** A compound 3,4-dihydroxy benzaldehyde isolated from fruit was appeared as a competitive inhibitor of phosphotransferase CKII activity with  $IC_{50}$  of 783 $\mu$ M with respect to ATP (Bang *et al.*, 2008). The methanol and ethyl acetate fractions of seeds exhibited higher cytotoxicity to Hep- G2, A-549 and Human-T cell line. The same methanol fraction showed 100% mortality after 24 hr for *Aedes caspius* with  $LC_{50} = 531 \mu$ g/mL (Fahd *et al.*, 2017). Furthermore in vitro cytotoxic activity was determined in methanol extract of leaves against

human tumor cell line of HCT-15, A-549, SK-OV-3, SK-MEL-2 and XF-498 with reference Doxorubicin. The cytotoxic compounds xanthatin, 8-epi-xanthatin and 8-epi-tomentosin were isolated from this bioactive fraction (Jong *et al.*, 1995). In addition, cytotoxic xanthanolides were also isolated through Si-gel CC technique of Et<sub>2</sub>O-Petrol (1:2) fraction of aerial parts (Saxena and Manju, 1995).

**Toxicity and growth inhibition activity:** *Xanthium strumarium* also exhibited medium to moderate toxic effects on mammals when ingested in sufficient amount. The effective principle component is Carboxyatractyloside that is present in germinating seeds but not in mature plant (Witte *et al.*, 1990). The toxicosis signs, vomiting and abdominal pain appeared after 6 to 9 hrs of ingestion of seed. It then results into hypoglycemia and hepatic damage then finally to death (Masvingwe and Mavengwa, 1998). Moreover Potassium carboxyatractyloside occurring in aerial parts demonstrated growth regulating property of wheat coleoptiles at 10<sup>-3</sup>, 10<sup>-4</sup> and 10<sup>-5</sup> M whereas chlorosis was observed within leaf whorl at 10<sup>-3</sup> and 10<sup>-4</sup> M (Horace, 1983).

## Conclusion

The present review has confirmed *Xanthium strumarium* L. as a beneficial medicinal plant. Extracts of whole plant is experienced in traditional medicine to treat fever, allergy, cough, infections, tumours and insect bite. The bioactive potential is due to biologically active xanthatin, Xanthumin, sesquiterpene xanthanol, terpenes, caffeic acids, carboxyatractyloside, xanthinin, caffeoylquinic acid, xanthanolides, 8-epi-tomentosin, 3,4-dihydroxy benzaldehyde, ascorbic acid and phytosterols. As the *X. strumarium* can accumulate heavy metals from soil, may be used as a natural phytoremediator of heavy metals near industrial sites. The pharmacologic characters of plant need to cultivate it on large scale to provide safe, efficient and less expensive medication.

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