Review

Ethnomedicinal, pharmacological and phytochemical evaluation of *Xanthium strumarium* L.

Yaseen Khan[1*], Sulaiman Shah[2], Shakir Ullah[3]

Abstract— *Xanthium strumarium* is a common medicinal plant belong to family Asteraceae. It is broadly dispersed in North America and south Asia. It is a dominant plant specie in southern region of China and in northern areas of Pakistan. Usually, it's appear in spring, the plant parts i.e. leaves, root, stem and seed are used in traditional medicine for the treatment of various health problem such as 'leucoderma, epilepsy, salivation, malaria, rheumatism, tuberculosis, allergic rhinitis, sinitis, urticaria, rheumatoid arthritis, constipation, diarrhoea, leprosy, lumbago, pruritis, bacterial and fungal infections'. The plant contains various bioactive compounds including proteins, carbohydrates, phenols, tannins, flavonoids, saponins, sesquiterpene, lactones, glycoside and polysterols. This comprehensive study provide the description, phytochemical constituents and pharmacological activities of the *X. strumarium*. Moreover, the antibacterial, antitumor, antitussive, antifungal, anti-inflammatory, ant nociceptive, hypoglycemic, antimitotic, antioxidant, antitrypanosomal, insecticidal and herbicidal activities has been reviewed. The current review aims at pharmacological and phytochemical properties of *X. strumarium*. This review will serve as a base for further inquiry and exploitation of *X. strumarium*.

Keywords— Ethnomedicinal study, Medicinal constituent, Phytochemical property, *Xanthium strumarium*

Introducation

Asteraceae is a massive plant family, it is also called Compositae. This family of the flowering-plant order Asterales, with more than 1,620 genera and 23,600 species having herbs, shrubs, and trees dispersed throughout the world. *Xanthium strumarium* is a medicinal plant, generally called 'cocklebur or bur weed' commonly found as a weed in roadsides, rice fields, gounds, hedgerows throughout the tropical parts in Pakistan [1, 2]. The word "xanthium" is derived from an ancient greek word "xanthos" meaning yellow and "strumarium" means "cushion like swelling," with reference to the seed pods, which turn from green to yellow as they ripen (later they become deep yellow to brown) [3]. Nearby, this plant is recognized by numerous names such as Geshkay in Pakistan, Cang er zi in China and Woolgarie bur in North America.

X. strumarium is an annual plant, having 1 to 1.2 m height. The stems is stout, rough, green or brownish in color, frequently red-spotted and hairy. The leaves are alternate, dull green on the upper surface and paler below, with short bristly hairs on both surfaces [Fig. 1]. The plant is broad, and 3-5 lobed, 30-180 mm long by 30-180 mm wide on long petioles (stalks). *X. strumarium* flowers are yellowish green, located in spherical apical capitula, inconspicuous, in the leaf axils. The corolla is true, tubular; stamens free. The involucre upon fruiting turns into dense ligneous prickly pericarp. The fruit is called a bur (geshkai), its oval in shaped and it is about 1.3-3.5 mm long, brown in color [Fig. 2].

Each bur has two stout, curved or straight horns and is covered with hooked spines. The seed have capability to spread easily dispersed through animals as the fruits have hooked bristles and two strong hooked beaks [4]. Flowering time in Pakistan is from August to September. The flowering session of *X. strumarium* is from July to October, and the seeds ripen from August to October. The flowers are monoecious, and pollinated by insects. The plant is self-fertile. The fruits are reaped when ripe and dehydrated for use [5]. Usually herbivores eat young plants, various plants found to be toxic, and can be poisoned if the animals consume them in sufficient quantity. In Western literature, xanthium is not labelled as a medicinal plant, but it is recognized as a toxic plant especially for grazing animals [3]. It has been documented to cause huge destruction in cattle, horses, goats, pigs and sheep [6], and reduced weight gain in poultry [7]. The plant produces allergic contact dermatitis in susceptible humans. *X. strumarium* has many medicinal properties like cooling, laxative, fattening, anthelmintic, tonic, digestive, antipyretic, improves appetite, voice, complexion anodyne, Ant rheumatic, appetizer, diaphoretic, diuretic, emollient and sedative [8]. The plant is considered to be useful in treating long-standing cases of malaria, rheumatism, diseased kidneys, and tuberculosis. It is also used as an adulterant for *Datura stramonium*. The fruits of *X. strumarium* has the properties like anodyne, antibacterial, antifungal, antimalarial, Antirheumatic, antispasmodic, antitussive, cytotoxic, hypoglycemic and stomachic [9]. They are used internally in the treatment of allergic rhinitis, sinusitis, catarrh, rheumatism, rheumatoid arthritis, constipation, diarrhea, lumbago, leprosy and pruritus [10]. A decoction of the root has been used in the treatment of high fevers and to help a woman expel the afterbirth and a decoction of the seeds has

• *Corresponding author: Yaseen Khan*
[1] *Key Laboratory of Plant Nutrition and Agri-environment in Northwest China, Ministry of Agriculture, College of Natural Resources and Environment, Northwest A&F University, Yangling, Shanxi, China*
Email: Yaseenkhan3444@gmail.com
[2] *Department of Botany, University of Malakand Chakdara, Khyber Pakhtoonkhwa, Pakistan*
[3] *Key Laboratory of Plant Ecology, Northeast Forestry University, Harbin, 150040, China*

been used in the treatment of bladder complaints by local peoples. The dried leaves of *X. strumarium* are a source of tannin, that's the reason is poisonous to grazing animals [11].

X. strumarium was cultivated as a leafy vegetable in China, young floral tops and the two leaves below are boiled in water and eaten as a pot-herb in Assam (India) [11]. The herb as such is suspected to be poisonous, but the toxic substances are removed by washing and cooking [7]. A highly toxic glycoside (Carboxyatractyloside) is present in the seeds and seedlings of *X. strumarium*. The amount of the chemical was measured to be 0.457 % in the seeds and 0.12% in the seedling at the two-leaf stage. The poison occurs only in the cotyledons or seed leaves of the seedlings. The toxin readily vanishes after germination [11].

This review article is prepared from scientific literature. The literature cited for this review includes publications and books being published in well reputed journals. This paper provides a review of the available knowledge about pharmacological and phytochemical properties of *X. strumarium.*

Ethno medicinal uses of X. strumarium

X. strumarium is used a believed medicine in North America, China, Malaysia and Pakistan. According to Ayurveda, the plant has cooling, laxative, fattening, anthelmintic, alexiteric, tonic, digestive, antipyretic activities and improves appetite, voice, complexion and memory. It cures leucoderma, biliousness and poisonous bites of insects, epilepsy, salivation and fever [12]. It is reported that it is used by various Native American tribes to relieve constipation, diarrhea and vomiting, in China usually it is used for headache, ulcers and sinus problems [13]. It is also reported that the plant is useful in treating long-standing cases of malaria and is used as an adulterant for *D. stramonium* [13]. The leaves and roots are used for their anodyne, ant rheumatic, ant syphilitic, appetizer, diaphoretic, diuretic, emollient, laxative and sedative activities. An infusion of the plant has been used in the treatment of rheumatism, diseased kidneys and tuberculosis [14]. It has also been used as a liniment on the armpits to reduce perspiration. The fruits contain a number of homeopathically active compounds including glycosides and phytosterols. They are anodyne, antibacterial, antifungal, antimalarial, antirheumatic, antispasmodic, antitussive, cytotoxic, hypoglycemic and stomachic. They are used internally in the treatment of allergic rhinitis, sinusitis, urticarial, catarrh, rheumatism, rheumatoid arthritis, constipation, diarrhea, lumbago, leprosy and pruritus [15]. They are also used externally to treat pruritus and small pox. The root is a bitter tonic and febrifuge [13]. It has historically been used in the treatment of scrofulous tumors and used locally on ulcers, boils and abscesses [16]. The paste of green spiny fruits is used against migraine and the juice of leaves and fruits is believed to be useful for smallpox and the roots are used for cancer [13, 16]. The burs are used in China as a tonic, diuretic and sedative [7]. A decoction of the root has been used in the treatment of high fevers, leucorrhoea and to help a woman expel the afterbirth. Seeds contain 25–30% oil, which has resembles with sunflower oil and is used for treating bladder infections, herpes and erysipelas. The dried leaves are a source of secondary metabolites specially tannin. A yellow dye is obtained from the leaves [7]. The seed powder has been used as blue body paint [15]. The dried plant repels weevils from stored wheat grain [17].

X. strumarium is suspected to be poisonous but the toxic substances are removed by washing and cooking [10]. *X. strumarium* consider also a toxic herb in traditional Chinese medicine. It has various toxic effect on human body. The toxic symptoms in humans include dizziness, drowsiness, coma and generalized tonic seizure, appearance of jaundice, hepatomegaly, impairment of liver function, proteinuria, cylindrica, and hematuria [18]. The toxic substance soluble in water is extensively used for the treatment of sinus congestion. It has not been blamed for any harmful effects among Western consumers, and has not been banned by any health department in any country [7]. Yet, it is a herb that should be investigated, as will be done here. Because of its multi activity, in particular, antitumor, anticancer activity, so much attention is paid towards the herb [18]. The herb is suspected of causing allergy only in autumn when it is in the pre-fruiting stage [19]. *X. strumarium* is classified in modern Materia Medicas as either a herb for dispelling wind chill or a herb for dispelling wind damp. Its modern uses are mainly for allergy-type disorders, specifically allergic rhinitis, atopic dermatitis, chronic par nasal sinusitis and chronic eczema [3].

Chemical constituents of *X. strumarium*

The above ground parts of the plant comprise a mixture of anonymous secondary metabolites specially, alkaloids, which are supposed to be toxic. Moreover, the upper parts of the plant contain sesquiterpene lactones, xanthumin, xanthatin, xanthostrumarin, atractyloside, phytosterols, xanthanol [Fig. 4], isoxanthanol, xanthinosin [Fig. 3], 4-oxo-bedfordia acid [22-26], γ-tocopherol [20], thiazinedione [21] and linoleic acid. The main toxic compound isolated from the plant has been identified as carboxyatractyloside, a kaurene glycoside previously called xanthostrumarium [22]. In addition to carboxyatractyloside CAT, potentially toxic ingredients include several sesquiterpene lactones (e.g. guaianolides, germacranolides, and elemanolides) [23].

Above ground parts also comprises three xanthanolide and xanthanetype sesquiterpenoids, 11α,13-dihydroxanthatin, 4β,5β- epoxyxanthatin-1α,4α-endoperoxide, 1β,4β,4α,5α–diepoxy xanth 11(13)-en-12-oic acid [24], a dimeric xanthanolide, sesquiterpene lactones [25], 8-epixanthatin, 2-epixanthumin and 8-epi-xanthatin-5β-epoxide. The phenols isolated are caffeic acid, potassium3-O-caffeoylquinate, 1-O-caffeoyl quinic acid, chlorogenic acid, 4-O-caffeoylquinic acid, 1,4-di-O-caffeoylquinic acid, 1,5-di-O-caffeoylquinic acid, 3,5-di-O-caffeoylquinicacid, 4,5-di-O-caffeoylquinic acid, 1,3,5-tri-O-caffeoylquinic acid, 3,4,5-tri-O-caffeoylquinic acid, and cynarin [26, 27].

The poisonous principles of the seeds are hydroquinone, choline and a third more toxic unidentified compound. Besides these, the seeds also contain considerable amount of iodine [8, 14].

The fruits are rich in vitamin C. Thiazinediones isolated from the fruits are 7-hydroxy methyl-8,8-dimethyl- 4,8 dihydrobenzol [1,4], thiazine-3,5-dione-11-O-β-dglucopyranoside [28], 2-hydroxy-7 hydroxymethyl-8,8-dimethyl-4,8 dihydrobenzol [1,4], thiazine-3,5-dione-11-O- β-d glucopyranoside, 7-

hydroxymethyl-8,8-dimethyl-4,8- dihydrobenzo [1, 3], thiazine-3,5-dione, 7-hydroxymethyl-8,8- dimethyl-4,8-dihydrobenzol [1, 4], thiazine-3,5-dione-(2-Ocaffeoyl)-β d-glucopyranoside, ferulic acid, formononetin and ononin [28].

Figure 1 ***Xanthium strumarium***

Figure 2 Seed of ***Xanthium strumarium***

The powdered shell of fruit can be used for making activated carbon. The shells contain 15.9% pentosans and can be used as a raw material for the synthesis of furfural [28]. The young fruit contains glucose, fructose, sucrose, organic acids, phosphatides, potassium nitrate, β-sitosterol, γ-sitosterol, β-d-glucoside of β-sitosterol called strumaroside [30-32]. The total free amino acid content is 1.65%. It includes amino-n-butyric acid, arginine, aspartic acid, cystine, glutamic acid, methionine, proline, tryptophan in micromoles per milligram dry weight [33, 34]. The stem oil is characterized by large amounts of monoterpenes with 49.4% and sesquiterpenes with 29.1%. The leaf oil is also characterized by higher amounts of monoterpenes by 55.8% than sesquiterpenes with 26.4%. The oil is light yellow, odorless and has the same taste as other vegetable oils. Oil contains d-limonene, d-carveol, α-ionone terpinolene, β-caryophyllene and p-cymene with 35.0%, 25.0%, 10.5%, 7.0%, 6.0% and 5.0% respectively [35, 36].

Pharmacological activity of *X. strumarium*

Antiviral effect

X. strumarium is reported as an antiviral activity against duck hepatitis B virus in 2009, and it can delay pathological changes [37]. Furthermore, five compounds were sequestered from the fruits of *X. strumarium*, and their antiviral abilities were also assessed. The results showed that norxanthantolide F, 2-desoxy-6-epi-parthemollin, xanthatin, threo-guaiacylglycerol-80-vanillic acid ether and caffeic acid ethyl ester exhibited notable activity against influenza A virus with IC50 values of 6.4, 8.6, 8.4, 8.4 and 3.7 μM, respectively by a cytopathic effect (CPE) inhibition method [7, 13].

Antibacterial and Antifungal Effects

X. strumarium is reported the WEXFT possessed antimicrobial properties against Vibrio cholera in 1983 [38]. Later, a study in 1997 exposed that the xanthatin isolated from the leaves of *X. strumarium* had notable potent activities against Staphylococus epidermidis, Bacillus cereus, Klebsiella pneumoniae, Pseudomonas aeruginosa and Salmonella fyphi with minimum inhibitory concentration (MIC) values of 31.3, 62.5, 31.3, 125 and 125 g/mL, respectively [39]. In addition, it is reported that MEXL (500 and 100 mg/mL) exhibited strong activity against K. pneumoniae, Proteus vulgaris, P. aeruginosa, Pseudomonas putida, Salmonella typhimurium, B. cereus, Bacillus subtilis and S. epidermidis [40]. In 2015, sitosterol and -daucosterol isolated from the *X. strumarium* have significant inhibitory effects against Escherichia coli, with MIC values of 0.17 and 0.35 mg/mL, respectively [41]. By using the disc diffusion method, Devkota et al. determined the antibacterial activity of MEXL and WEXL, and results showed that the two extracts inhibited growth towards K. pneumoniae, Proteus mirabilis, E. coli, B. subtilis, Enterococcus faecalis and Staphylococcus aureus at concentrations of 50, 100, 150, 200 and 250 mg/mL [42]. Moreover, it is revealed that EOXL can significantly suppress the growth of S. aureus, B. subtilis, K. pneumoniae and P. aeruginosa with MIC values of 0.5, 1.3, 4.8 and 20.5 g/mL, respectively; additionally, EOXL (30, 60 and 120 mg/mL) also exhibited obvious antibacterial activity against Shiga toxin-producing Escherichia coli [43, 44]. Later it is discovered that WEX possessed antibacterial potentials against S. aureus and E. coli with MIC values of 31.25 and 7.81 mg/mL, respectively [45]. Using the disk diffusion, the antibacterial activity of EOXF on Rathayibacter toxicus and Pyricularia oryzae was evaluated, and the MIC values were 25 and 12.5 g/mL, respectively [46].

Antilipidemic Effect

Recently, investigations into the Antilipidemic effects of X. strumarium have been conducted. In 2011, the CEXR and EEXR were evaluated for anti-lipidemic activity in Triton WR-1339 induced hyperlipidemia in Swiss albino rats. The results showed that CEXR and EEXR (200 and 400 mg/kg p.o.) can significantly decrease the contents of plasma cholesterol, TG, LDL, and VLDL and increase plasma HDL levels, which was possiblely related to their significant antioxidant activity [7, 28]. Later, in 2016, Li et al. found that WEX (570 and 1140

mg/kg, p.o., for 6 weeks) could improve the synthesis of fatty acid and TG, thus decreased the circulating free fatty acid (FFA) levels, indicating that WEX is involved in solving the abnormality of FFA in the circulation, which is executed by promoting the storage of the excess fat, rather than the elimination of added fat [47]. Furthermore, after treatment with WEX (3.7 and 11.11 g/kg, p.o., for 4 weeks), the blood glucose, TC, TG, LDLC levels decreased and HDLC levels increased in diabetic mice [48].

Anti-diabetic Effect

In 1974, Kupiecki et al. found that the WEX (15 and 30 mg/kg, i.p.) exhibited potent hypoglycemic activity in normal rats in a dose-dependent manner [49]. In 2000, the antidiabetic effect of caffeic acid isolated from *X. strumarium* was investigated on both streptozotocin-induced and insulin-resistant rat models. The results showed that caffeic acid (0.5–3.0 mg/kg, i.v.) can decrease the plasma glucose level via increasing the glucose utilization [50]. In 2011, Narendiran et al. found that MEXS at the doses of 100 and 200 mg/kg (p.o., for 30 days) had remarkable diabetic activity in normal-glycemic and streptazocin induced hyperglycemic rats [51]. A report in 2013 demonstrated that the methyl-3,5-di-O-caffeoylquinate showed strong ability to counteract diabetic complications via competitive inhibition of aldose reductase (AR) and galactitol formation in rat lenses [52]. In addition, it is reported that the CFMEXL exhibited notable inhibitory activity on glucosidase enzyme with the IC50 value of 72 g/mL [122]. Similarly, another study found that MEX also had a strong glucosidase inhibitory effect with IC50 value of 15.25 g/mL [53].

Anti-oxidant Effect

In 2010, it was reported that CEXR and MEXR showed significant free radical scavenging activity by 1, 1-diphenyl-2-picrylhydrazyl (DPPH) method with LC50 values of 10.28 and 40.40 g/mL, respectively [53]. After administration of PEEXW (250 and 500 mg/kg, p.o., for 20 days), the contents of superoxide dismutase, glutathione peroxidase, glutathione reductase and catalase significantly increased in rats' brain [54]. Later, in 2011, Huang et al. found that WEX exhibited 70.6% to 76.4% and 35.2% to 79.1% scavenging activity on 2,2′-Azinobis-(3-ethylbenzthiazoline-6-sulphonate) (ABTS) radicals and DPPH radical scavenging in the concentration of 0.05–0.2 mg/mL; simultaneously, the reducing activity of WEX increased and liposome protection effect enhanced in a concentration-dependent manner with the same doses [55]. In 2015, hexadecanoic acid, amyrin and 14-methyl-12, 13-dehydrositosterol-heptadeconate were isolated from the leaves of X. strumarium, and their antioxidant potential was also evaluated. These three chemical components showed significant antioxidant activity in a dose dependent manner by DPPH and hydroxyl radical assay methods with the IC50 values of 106.4, 64.16, 76.18 g/mL and 127.4, 83.96 and 84.4 g/mL, respectively [54]. A study in 2017 revealed that the EOX displayed notable activity for DPPH radicals with an IC50 value of 138.87 g/mL [54]. Furthermore, the antioxidant effects of the MEX obtained by the response surface methodology were measured by the scavenging activity towards the DPPH radical and Ferric ion reducing antioxidant power (FRAP). These results showed that methanol concentration and solid to solvent ratio were demonstrated to possess obvious effects on DPPH and FRAP values [7].

Anti-Inflammatory and Analgesic Effects

In 2004, it was reported that WEX (10, 100 and 1000 g/mL) inhibited inflammatory responses in Lipopolysaccharide (LPS)-stimulated mouse peritoneal macrophages via decreasing IFN-, LPS-induced NO production and TNF-_ production in a dose dependent manner [56]. Furthermore, in 2005, Kim et al. evaluated the anti-inflammatory and anti-nociceptive activities of MEX both in vitro and in vivo, it showed that the MEX (30, 60 and 90 mg/mL) can down-regulate the production of NO, PGE 2 and TNF-_, and MEX treatment (100 and 200 mg/kg/day, p.o.) clearly reduced carrageenan induced hind paw edema in rats [57]. Later, in 2008, xanthatin and xanthinosin were reported to inhibit LPS-induced inducible nitric oxide synthase and cyclooxygenase-2 (COX-2) expression in microglial BV-2 cells with IC50 values of 0.47 and 11.2 _M, respectively [58]. A report in 2015 showed that MEXR (50–400-g/mL) can suppress inflammatory responses via the inhibition of nuclear factor-_B (NF-_B) and signal transducer and activator of transcription 3 (STAT3) in LPS-induced murine macrophages [59]. In 2016, Hossen et al. demonstrated that the inhibitory effect of MEX on the inflammatory disease possibly related to signaling inhibition of MAPK and AP-1 [60]. Later, in 2017, Jiang et al. found a new phenylpropanoid derivative named Xanthiumnolic E isolated from *X. strumarium*, which has notable inhibitory effect on LPS-induced nitric oxide (NO) production with IC50 value of 8.73 -M [61]. Additionally, X. strumarium was confirmed to inhibit some other kinds of inflammatory and painful diseases.

Anti-Tumor Effect

Anti-tumor effects are also regarded as primary pharmacological properties of *X. strumarium*, and have been extensively investigated in lung cancer, breast cancer, cervical cancer, colon cancer, liver cancer, meningioma, and leukemia. Ahn et al. isolated three cytotoxic compounds from the leaves of *X. strumarium*, among them, xanthatin and 8-epi-xanthatin possessed obvious anti-tumor activity on A549 cells with IC50 (half maximal inhibitory concentration) values of 1.3 and 1.1 g/mL, respectively [61]. Later, in 2002, it was reported that 1, 8-epi-xanthatin epoxide has notable anti-tumor effect against A549 cells with IC50 value of 3.0 M [69]. Furthermore, Wang et al. and Ferrer et al. reported that 8-epi-xanthatin-1, 5 -epoxide, 1-hydroxyl-5 -chloro-8-epi-xanthatin and EEXA can inhibit the proliferation of A549 cells (IC50 = 9.5 M, 20.7 M and 52.2 g/mL, respectively) [62, 63].

In 2007, by using Cell Titer 96 assay in vitro, Ramı'rez-Erosa et al. found that xanthatin and xanthinosin, two sesquiterpene lactones isolated from the burs of *X. strumarium*, obviously restrain the proliferation of breast cancer MDA-MB-231 cells with the IC50 values of 13.9 and 4.8 g/mL, respectively [59].

Furthermore, Takeda et al. studied the mechanism of xanthatin against breast cancer MDA-MB-231 cells in 2011, and the results indicated that xanthatin (5–25 M) inhibits cell growth via inducing caspase independent cell death which were irrelevant with FTase inhibition [58]. In addition, xanthatin (2.5–10 M) can also up-regulate GADD45 tumor sup-

pressor gene, and induce the prolonged expression of c-Fos via N-acetyl-L-cysteine-sensitive mechanism [62, 63]. In 2015, Vaishnav et al. demonstrated that WEX with a concentration of 12.5–50 g/mL were able to induce death in HeLa cervical cancer cells by altering the antioxidant levels [63]. Furthermore, the anti-tumor effects of *X. strumarium* on liver cancers have also been reported in recent years. In 2013, Wang et al. found that the 1-hydroxyl-5 -chloro-8-epi-xanthatin possessed significant in vitro cytotoxicity with an IC50 value of 5.1 M against SNU387 cells [19]. Later, in 2017, the cytotoxic effects of MEX and EAFMEX on HepG2 cells were verified as LC50 (Lethal Concentration 50) values of 112.9 and 68.739 g/mL [64]. Some previous results showed that xanthatin (2.5–40 M) possess a remarkable anti-proliferative effect against B16-F10 cells, and the related mechanism probably associated with activation of Wnt/ -catenin pathway as well as inhibition of angiogenesis. Meanwhile, the in vivo evidence in mice (xanthatin, 0.1–0.4 mg/10 g, i.p.) also verified the results mentioned above [65].

TABLE 1. Chemical constituents isolated from *X. strumarium*

Classification	Chemical compound	Part of plant	References
Sesquiterpenoids	Sibirolides	Fruit	[13]
	Norxanthantolides	Fruit	[13]
	xanthinin	Leaves	[15]
	xanthumin	Leaves	[15]
	xanthanol	Leaves	[15]
	xanthanol Acetate	Leaves	[15]
	Isoxanthanol	Leaves	[15]
	xanthumanol	Leaves	[16]
	deacetoxylxanthumin	Leaves	[16]
	xanthatin	Leaves	[16]
	xanthinosin	Leaves	[16]
	tomentosin	Leaves	[16]
	xanthnon	Aerial parts	[21]
	pungiolide D	Aerial parts	[25]
	5-azuleneacetic acid	Aerial parts	[21]
Triterpenoids	betulin	Root	[28]
	erythrodiol	Root	[28]
	betulinic acid	Root	[28]
	lup-20(29)-en-3-ol	Aerial parts	[27]
Triterpenoids	lupenyl acetate	Aerial parts	[29]
	lupeol acetate	Whole plants	[30]
	a-myrin	Leaves	[32]
	Oleanolic acid	Arial parts	[31]
Phenylpropenoids	Xanthiumnolic A	Fruits	[40]
	Xanthiumnolic C	Fruits	[40]
	Chlorogenic acid	Fruits	[34]
	N-trans-feruloyl tyramine	Roots	[39]
	1,3-di-O-caffeoylquinic acid	Fruits	[34]
	ferulic acid	Fruits	[43]
	caffeic acid	Fruits	[36]
	isovanillic acid	Whole plants	[30]
	7-(4-hydroxy-3-methoxyphenyl)-1-phenylhept-4-en-3-one	Roots	[28]
Phenylpropenoids	coniferine	Fruits	[45]
	arbutin	Fruits	[45]
	icariside F2	Fruits	[45]
	icariside D1	Fruits	[45]
	caffeic acid choline ester	Fruits	[38]
Lignanoids	xanthiumnolic B	Fruits	[40]

	leptolepisol D	Fruits	[48]
	chushizisin E	Fruits	[48]
	diospyrosin	Fruits	[48]
	balanophonin A	Fruits	[48]
	dehydrodiconiferyl alcohol	Fruits	[48]

Precautions

X. strumarium is poisonous to mammals. It is reported to have medium to strong allergenic effects. The toxic principle is a sulphated glycoside, carboxyatractyloside, found in the seeds and during the two-leaf seedling stage [66]. The mature plant is reported as non-toxic, although toxicosis has been reported in cattle which had ingested mature plants with burs despite the general belief that ingestion of burs should be limited by mechanical injury during mastication.

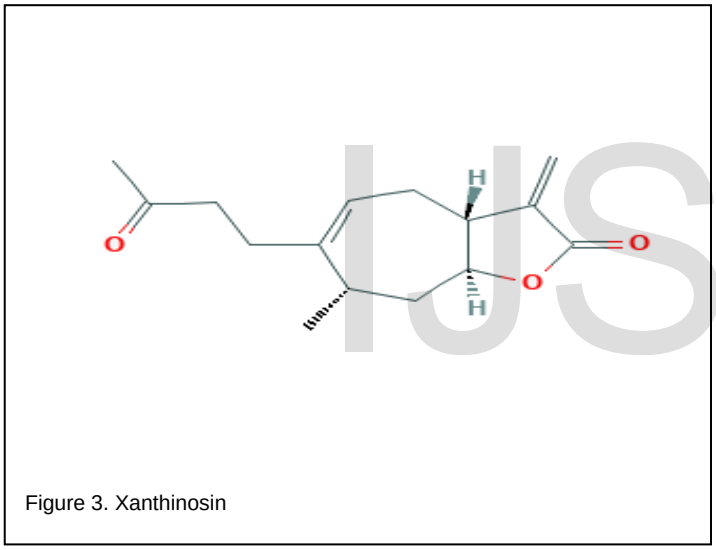

Figure 3. Xanthinosin

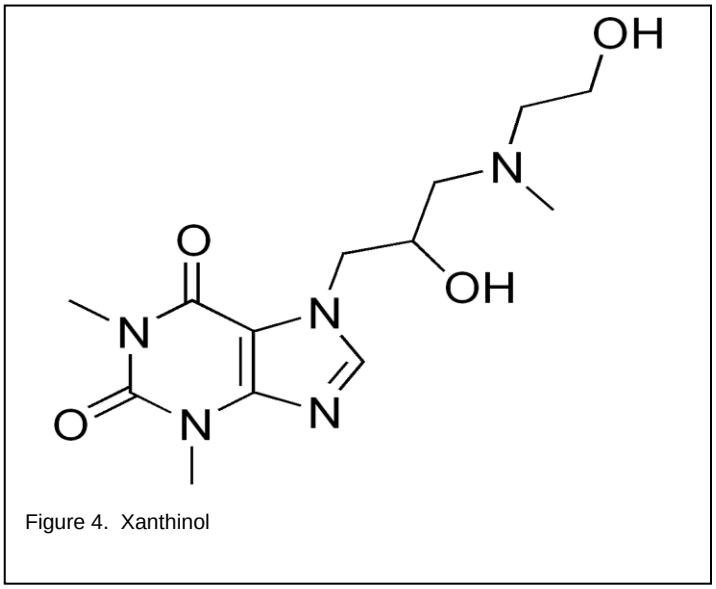

Figure 4. Xanthinol

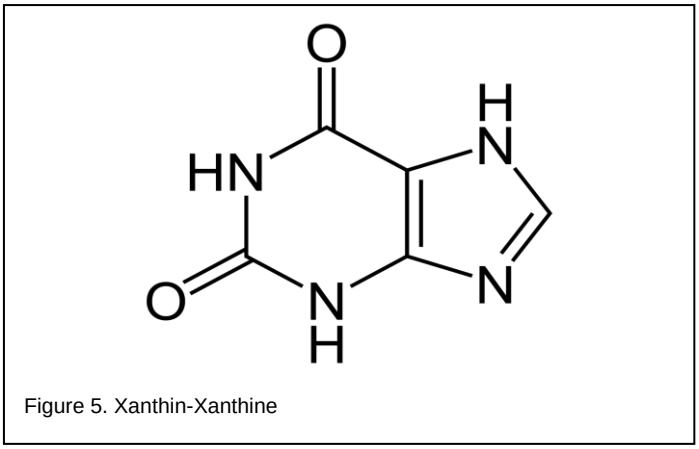

Figure 5. Xanthin-Xanthine

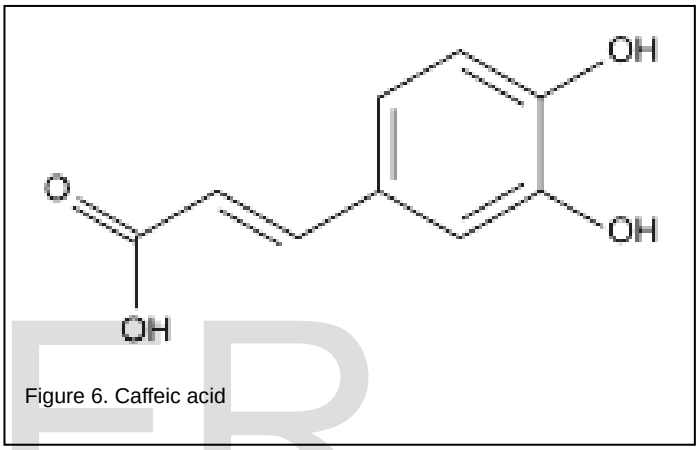

Figure 6. Caffeic acid

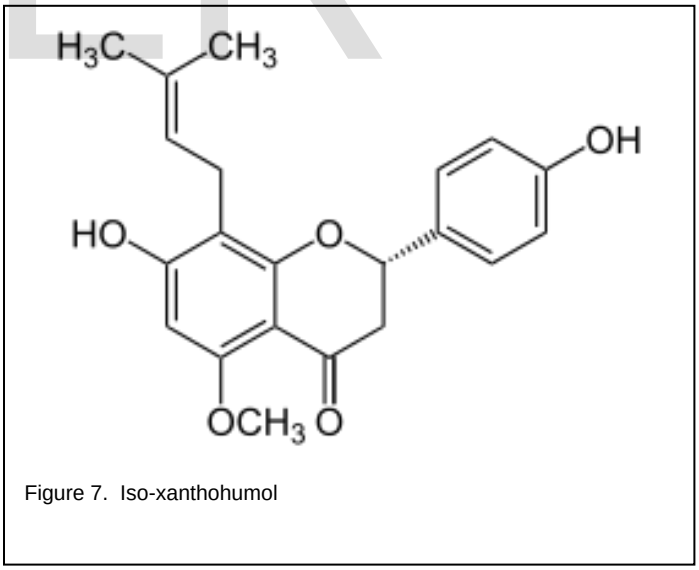

Figure 7. Iso-xanthohumol

Contact dermatitis

The plant is suspected to cause air-borne contact dermatitis. In a study, patch tests with a 15% aqueous extract of airdried leaves showed a severe positive reaction. The titre of contact hypersensitivity with the plant extract was more than 1:100,000 and for *Parthenium hysterphorus* it was 1:10, indicating a high degree of hypersensitivity to *X. strumarium*. Further tests in 14 other patients revealed a high prevalence of cross sensitivity between the two plants [67]. The antigens in the

two plants seem to be very similar [68].

CONCLUSION

This review reveals that the plant has potent in Ethno & pharmacological activities. The plant is traditionally used to be useful inepilepsy, salivation, long-standing cases of malaria, rheumatism, tuberculosis, allergic rhinitis, sinitis, urticaria, rheumatoid arthritis, constipation, diarrhoea, leprosy, lumbago, pruritis, and inflections due to bacteria and fungus. Most of the biological effects can be clarified by the high amount of xanthatin, xanthanolide sesquiterpene lactones, desacetyl xanthumin, xanthanol, xanthumin, thiazinedione, desacetyl xanthumin, carboxyatractyloside, caffeic acid derivative and its quinic acid derivatives present in all plant parts. Today the plants are the almost exclusive source of drugs for a majority of the world's population. Therefore, it remains a challenge for scientists to provide efficient, safe and cheap medications, especially for rural areas for that we need more research work. Their quantification of individual phytoconstituents as well as pharmacological studies should be further investigated.

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