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Phytochemicals & Pharmacological activity of *Xanthium strumarium*: An Updated Review

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Abstract

Therapeutic plants are of extraordinary worth in the field of treatment and fix of infections. Throughout the long term, logical examination has extended our insight into the compound constituents of the therapeutic plants, which decide the restorative properties. The purpose of this paper is to summarize the progress of modern research, and provide a systematic review on the traditional usages, phytochemistry, pharmacology of the X. strumarium. Plant parts like leaves, organic product, bark and seed have been accounted for having antidiabetic, antiulcer, calming, invulnerable modulator and pain- relieving movement. This survey tends to the tentatively validated realities and furthermore proposes the requirement for research on substance and pharmacological properties of Xanthium strumarium.

Keywords: *Xanthium strumarium L.; traditional usages; phytochemistry; pharmacology*

1. Introduction

Xanthium strumarium L. common medicinal plant belongs to family asteraceae. The plant occurs all over Pakistan, India, China, Eurasia and also in America. Local name of *Xanthium strumarium L.* is Common Cocklebur and Chota dhatura. The 20,000 species of its 950 genera are found worldwide as herbs, shrubs, trees and climbers [1]. It is a commonly found as a weed in roadsides, rice fields, hedges throughout the tropical parts of India. Xanthium strumarium is an annual herb, up to 1 m in height. *Xanthium strumarium L.* has stout stems, green, brownish or reddish-brown in color, often red-spotted that are rough and hairy. Fruits are cylindric to ovoid, two-chambered bur, 1 to 4 cm long, glandular, covered with hooked prickles, with two larger, longer incurved prickles projecting from the apex of the bur. A decoction of the root has been used in the treatment of high fevers. These medicinal properties are due to presence of chemical constituents such as steroids, alkaloids, flavonoids, triterpenoids, terpenoids, tannins, saponins, quinone, coumarin, protein, sugar and gum. It has many medicinal properties like antibacterial, antitumor, antitussive, antifungal, anti-inflammatory, antinociceptive, hypoglycaemic, antimitotic, antioxidant, antitrypanosomal, CNS depressant activity, diuretic effects, contact dermatitis, insecticidal and herbicidal activities [1].

Xanthium strumarium:

Botanical name	:	*Xanthium strumarium*
Family name	**:**	Asteraceae
Common name	**:**	Common Cocklebur, Cockleburr, Rough Cocklebur
Part used	**:**	The whole plant, especially root and fruit
Habitat	**:**	Australia, India, South Africa, and the Americas.

Fig 1. THE FRUIT OF *Xanthium strumarium strumarium*

Fig 2. WHOLE PLANT OF *Xanthium strumarium*

Phytochemical Screening

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 [2]. The phytochemical investigation of aerial parts of Xanthium strumarium Linn. has shown presence of sesquiterpene lactones, xanthanol, tomentosin and 8-epixanthatin over silica gel [3]. 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% [4]. A pentacyclictriterpene, 3β-acetoxy lup-20(29)-ene, stigmasterol and a fatty acid, palmitic acid has been isolated from aerial parts [5]. Kaemferol and quercetin flavonoids have been isolated from ethanol extract of flower [6]. Sephadex chromatography of n-butanol fraction of fruit found chlorogenic acid, ferulic acid, onion, for mononetin, xanthiazone and thiazinedione[7]. Phytosterols were isolated from fruit extract [8]. Moreover, xanthanolides and xanthatin were isolated from leaves [9]. Leaves were also found rich in ascorbic acid (113-115 mg %) [10]. 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-Dglucoside were reported from alcohol extract of leaves [11,12]. Hexane fraction of seeds estimated neutral lipids, fatty acids, fatty acid- esters, sterols and triterpenes in range of 0.1-1.6 mass% [13].

Pharmacological Activity

Anti-AR Effect

X. strumarium is a traditional medicine widely used in the treatment of nasal diseases, especially allergic rhinitis (AR). In modern pharmacological study, the mechanism of *X. strumarium* in treating AR has been studied extensively. In 2003, it was reported that WEX inhibited compound 48/80 (C 48/80)-induced systemic anaphylaxis in mice (0.01 to 1 g/kg, p.o.), and the mechanism may be related to the inhibition of histamine and TNF-α released from rat peritoneal mast cells (RPMC) [14,15]. In 2008, Zhao et al. found that WEX (0.25–1 mg/mL) can modulate the human mast cell-mediated and peripheral blood mononuclear cell (PBMNC)-mediated inflammatory and immunological reactions which induced by pro-inflammatory cytokines including interleukin (IL)-4, IL-6, IL-8, GM-CSF and TNF-α [16]. Furthermore, the MEX is found to possess the inhibitory effect on the activation of C 48/80 stimulated mast cells, and the mechanism was correlated to inhibit Ca^{2+} uptake and histamine release, and increase cAMP in RPMC [17]. In addition, in 2014, Peng et al. demonstrated that the caffeoylxanthiazonoside (CXT) (5, 10, 20 mg/kg, p.o.) isolated from the fruits of *X. strumarium* was helpful to alleviate the nasal symptoms of ovalbumin (OVA) induced AR rats via anti-allergic, down-regulating IgE, anti-inflammatory and analgesic properties [18].

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.

Tao et al. studied the inhibitory effect of xanthatin (1–40 μM), an active agent in *X. strumarium*, against lung cancer cells (Cell lines of A549, H1975, H1299, H1650 and HCC827) and its potential mechanisms [19,20,21]. It found that xanthatin could downregulate the STAT3, GSK3β and β-catenin, moreover, xanthatin could also trigger Chk1-mediated DNA damage and destabilize Cdc25C via lysosomal degradation [22,23]. In 1995, 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 IC_{50} (half maximal inhibitory concentration) values of 1.3 and 1.1 μg/mL, respectively [24]. Later, in 2002, it was reported that 1,8-epi-xanthatin epoxide has notable anti-tumor effect against A549 cells with IC_{50} value of 3.0 μM [25]. Furthermore, Wang et al. and Ferrer et al. reported that 8-epi-xanthatin-1α,5α-epoxide, 1β-hydroxyl-5α-chloro-8-epi-xanthatin and EEXA can inhibit the proliferation of A549 cells (IC_{50} = 9.5 μM, 20.7 μM and 52.2 μg/mL, respectively) [26,27].

Moreover, Zhang et al. reported that xanthatin (3.9–18.6 μM) inhibited the proliferation of MKN-45 cells by inducing G2/M cell cycle arrest and apoptosis [28]. Later, in 2015, Karmakar et al. found that xanthinosin (8 μM) and lasidiol p-methoxybenzoate (16 μM) potentiate both extrinsic and intrinsic TRAIL-mediated apoptosis pathways and also decreased the level of cell survival protein Bcl-2 in AGS cells [29]. Simultaneously, fructusnoid C (IC_{50} = 7.6 μM) also reported to exhibit cytotoxic effects on AGS cells [30]. EEXA and CFEEXA have been identified as the active ingredients against the growth of CT26 cells with IC_{50} values of 58.9 and 25.3 μg/mL, respectively [31].

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 1β-hydroxyl-5α-chloro-8-epi-xanthatin possessed significant in vitro cytotoxicity with an IC_{50} value of 5.1 μM against SNU387 cells [25]. Later, in 2017, the cytotoxic effects of MEX and EAFMEX on HepG2 cells were verified as LC_{50} (Lethal Concentration 50) values of 112.9 and 68.739 μg/mL. Furthermore, Liu et al. demonstrated that xanthatin (5–40 μM) can induce HepG2 cells apoptosis by inhibiting thioredoxin reductase and eliciting oxidative stress [32].

Additionally, an investigation in 1995 indicated that Xanthatin and 8-epi-xanthatin both have cytotoxic effects on SK-MEL-2 cells with ED_{50} values 0.5 and 0.2 μg/mL, respectively [33]. In 2012, the EEXS showed notable inhibitory activity on Mel-Ab cells through downregulation of tyrosinase via GSK3β phosphorylation at concentrations of 1–50 μg/mL [34]. Later, in 2013, Li et al. reported the anti-tumor effects of xanthatin both in vitro and in vivo. Previous results showed that xanthatin (2.5–40 μM) possess a remarkable anti-proliferative effect against B16-F10 cells, and the related mechanism probably associated with activation of Wnt/β-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 [35]. In 1994, DFEEXA was reported to be toxic to leukemia P-388 cells with an IC_{50} value of 1.64 μg/mL [29]. In addition, results of Nibret et al. showed that xanthatin has significant cytotoxic on HL-60 cells in 2011 [30]. Another report in 2017 reported that both MEX and EAFMEX have inhibitory effects on Jurkat cells, and EAFMEX showed higher toxicity to Jurkat cells when compared to MEX [29].

Anti-Inflammatory and Analgesic Effects

In 2004, it was reported that WEX (10, 100 and 1000 μg/mL) inhibited inflammatory responses in Lipopolysaccharide (LPS)-stimulated mouse peritoneal macrophages via decreasing IFN-γ, LPS-induced NO production and TNF-α production in a dose dependent manner [36]. 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-α, and MEX treatment (100 and 200 mg/kg/day, p.o.) clearly reduced carrageenan induced hind paw edema in rats [37]. In addition, MEX (100 and 200 mg/kg/day, p.o.) significantly reduced the amount of writhing induced by acetic acid, and increased jumping response latency in a hot plate test. 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 IC_{50} values of 0.47 and 11.2 μM, respectively [38]. By using LPS inhibition assay and animal model of inflammation (carrageenan induced hind paw edema), the MEXL (100, 200 and 400 mg/kg) showed obvious anti-inflammatory activity both in vitro (IC_{50} = 87 μg/mL) and in vivo [39]. A report in 2015 showed that MEXR (50–400μg/mL) can suppress inflammatory responses via the inhibition of nuclear factor-κB

(NF-κB) and signal transducer and activator of transcription 3 (STAT3) in LPS-induced murine macrophages [40]. Moreover, the WEX was found to restrain LPS-induced inflammatory responses through suppressing NF-κB activation, inhibiting JNK/p38 MAPK phosphorylation, and enhancing HO-1 expression in macrophages [41]. 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 [42]. In another study, Hossen et al. found the potential anti-inflammatory activity of MEXA on LPS-treated macrophages and an HCl/EtOH-induced mouse model of gastritis by inhibiting PDK1 kinase activity and blocking signaling to its downstream transcription factor, NF-κB [43]. 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 IC_{50} value of 8.73 μM [44].

Additionally, *X. strumarium* was confirmed to inhibit some other kinds of inflammatory and painful diseases. In 2011, Huang et al. suggested that WEX inhibited the development of paw edema induced by carrageenan, and exhibited inhibitory activity on acetic acid effect and reduced the formalin effect at the late-phase (0.1, 0.5 and 1.0 g/kg, p.o.) [45]. In addition, the NFEEX at doses of 0.5, 0.75 and 1.0 mg/ear showed strong anti-inflammatory activity in the croton-oil-induced ear edema test, and reduced the amount of writhing induced by acetic acid in mice in a dose-dependent manner (100, 200 and 400 mg/kg) [46]. A report in 2011 demonstrated the anti-inflammatory activity of xanthatin by inhibiting both PGE 2 synthesis and 5-lipoxygenase activity at doses of 100 and 97 mg/mL, respectively [39]. Furthermore, Park et al. first explained the anti-inflammatory mechanism of EEX, which inhibited TNF-α/IFN-γ-induced expression of Th2 chemokines (TARC and MDC) by blocking the activation of the NF-κB, STAT1 and ERK-MAPK pathways in HaCaT keratinocytes [47]. The hot plate test, acetic acid induced writhing test and formalin test were applied to evaluate the analgesic activity of EEX, and it showed significant analgesic activity at concentrations of 250 and 500 mg/kg body weight [48].

Insecticide and Antiparasitic Effects

In 1995, Talakal et al. reported that EEXL possess anti-plasmodial activity against *Trypanosoma evansi* both in vitro and in vivo. The EEXL exhibited trypanocidal activity at all the four tested doses at 5, 50, 500 and 1000 μg/mL in vitro, and it can significantly prolong the survival period of the *T. evansi* infected mice at concentrations of 100, 300 and 1000 mg/kg [49]. In 2011, xanthatin was demonstrated to be the dominating insecticidal active compound against *Trypanosoma brucei brucei* with an IC_{50} value of 2.63mg/mL and a selectivity index of 20 [35]. In addition, Go¨kce et al. showed that MEX exhibited both ingestion toxicity and ovicidal activity to *Paralobesia viteana* with an LC_{50} of 11.02% (*w*/*w*) [50]. In 2012, by using schizont inhibition assay, the anti-plasmodial activity of EEXL against *Plasmodium berghei* was assessed, and it showed significant activity (IC_{50} = 4 μg/mL) and high selectivity index in vitro [51]. Later, in 2014, Roy et al. found that WEXL had distinct insecticidal properties against *Callosobruchus chinensis* with strong toxicity, repellent properties, inhibited fecundity and adult emergence of the insects at 1%, 2% and 4% concentrations [52]. Moreover, it is reported that EEX revealed anti-nematode activity against *Meloidogyne javanica* in inhibiting egg hatching and inducing mortality among second stage juveniles (J2s) [53]. Furthermore, the effect of MEX on the mortality rates of *Aedes caspius* and *Culex pipiens* were investigated, and the results revealed that the LC_{50} values of MEX were found to be 531.07 and 502.32 μg/mL against *A. caspius* and *C. pipiens*, respectively [29].

Antioxidant 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 LC_{50} values of 10.28 and 40.40 μg/mL, respectively [54]. 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 [55]. 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 [45]. In the treatment with the MEXS (100 and 200 mg/kg, p.o. for 10 days), the contents of SOD, CAT, GSH and GPx were obviously increased in the diabetic rats' tissues [56]. Moreover, in 2011, Sridharamurthy et al. evaluated the antioxidant effect of EEXR and CEXR by the scavenging activity of free radicals such as DPPH, super oxide, nitric oxide, and hydrogen peroxide [57]. Results showed that the IC_{50} values of EEXR were 29.81, 495.30, 395.20 and 10.18 μg/mL, respectively, and the IC_{50} values of CEXR were 24.85, 418.30, 415.18 and 9.23

µg/mL, respectively. In addition, Kamboj et al. demonstrated that EEXL possessed strong scavenging capacity against DPPH, nitric oxide and hydrogen peroxide with IC_{50} values of 85, 72 and 62 µg/mL. In addition, the antioxidant activity was possibly due to the presence of compounds in the extracts like flavonoid and phenolic [58]. In 2015, hexadecanoic acid, α-amyrin and 14-methyl-12,13-dehydro-sitosterol-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 IC_{50} values of 106.4, 64.16, 76.18 µg/mL and 127.4, 83.96 and 84.4 µg/mL, respectively [59]. A study in 2017 revealed that the EOX displayed notable activity for DPPH radicals with an IC_{50} value of 138.87 µg/mL [60]. 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 [68].

Antibacterial and Antifungal Effects

In 1983, Mehta et al. reported that the WEXFT possessed antimicrobial properties against *Vibrio cholera* [61]. Later, a study in 1997 revealed 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 µg/mL, respectively [62]. 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* [63]. In 2015, Chen et al. also reported that β-sitosterol and β-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 [64]. 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 [65]. Moreover, Sharifi-Rad et al. 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 µg/mL, respectively; additionally, EOXL (30, 60 and 120 mg/mL) also exhibited obvious antibacterial activity against Shiga toxin-producing *Escherichia coli* [66,67]. Furthermore, Wang et al. revealed that WEX possessed antibacterial potentials against *S. aureus* and *E. coli* with MIC values of 31.25 and 7.81 mg/mL, respectively [68]. 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 µg/mL, respectively [60].

Similar to the antibacterial potentials, the antifungal activities of *X. strumarium* were also deeply investigated. In the year of 2002, Kim et al. found an antifungal constituent from *X. strumarium*, which was named deacetylxanthumin. It can inhibit mycelial growth and zoospore germination of *Phytophthora drechsleri* with a MIC value of 12.5 µg/mL [68]. In 2011, Yanar et al. used radial growth technique to test the antifungal activities of MEX against *Phytophthora infestans*, and the MEX showed the lowest MIC value of 2.0% *w/v* which was lower than the standard fungicide (Metalaxyl 4% + Mancuzeb 64%, MIC value was 2.5%, w/v) [69]. Later, in 2015, Sharifi-Rad et al. investigated the antifungal ability of EOXL on *Candida albicans* and *Aspergillus niger*, and the MIC values were 55.2 and 34.3 µg/mL, respectively [70]. In vitro, using the disk diffusion method, the EOXL exhibited strong inhibition against *Pyricularia oryzae* and *Fusarium oxysporum* with MIC values of 12.5 and 50 µg/mL, respectively [60]. Furthermore, the EOXL showed remarkable growth inhibition of a wide spectrum of fungal strains, such as *A. niger*, *Aspergillus flavus*, *F. oxysporum*, *Fusarium solani*, *Alternaria alternata* and *Penicillium digitatum* with both MIC and MBC (minimum bactericidal concentration) values of 8 µg/mL [71].

Antidiabetic 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 [72]. 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 [73]. 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 [74]. 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 [75]. In addition, it is reported that the CFMEXL exhibited notable inhibitory activity on α-glucosidase enzyme with the IC_{50} value of 72 µg/mL [76]. Similarly, another study found that MEX also had a strong α-glucosidase inhibitory effect with IC_{50} value of 15.25 µg/mL [61].

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 [57]. 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 [77]. 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 [78].

Antiviral Activity

In 2009, it was reported that the WEX (0.01, 0.1 and 1.0 g/kg, i.g., for 10 days) possessed antiviral activity against duck hepatitis B virus, and it can delay pathological changes [79]. In addition, five compounds were isolated from the fruits of *X. strumarium*, and their antiviral abilities were also evaluated. The results indicated that norxanthantolide F, 2-desoxy-6-epi-parthemollin, xanthatin, threo-guaiacylglycerol-8′-vanillic acid ether and caffeic acid ethyl ester exhibited notable activity against influenza A virus with IC_{50} values of 6.4, 8.6, 8.4, 8.4 and 3.7 µM, respectively by a cytopathic effect (CPE) inhibition method [80,81,82].

4. Conclusion

Future Perspectives

In summary, *X. strumarium*, which possesses anti- allergic rhinitis effects, anti-inflammatory and analgesic effects and anti-tumor effects, has been widely applied to clinical practice in many countries. In the meantime, many modern studies on *X. strumarium* were also carried out, and its pharmacological activities and chemical compositions have been preliminarily investigated. Nevertheless, how to find out the mechanism of pharmacological activities and its related compounds, develop clinical efficacy of *X. strumarium* and ensure medication safety are still extremely crucial now.

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