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## Mini Review

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## Pharmacology of Xanthium species. A review

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### ABSTRACT

The genus *Xanthium* (Family Asteraceae) is represented by 25 species that are widely distributed in the world. Only a few species such as *Xanthium strumarium* and *Xanthium spinosum*, are studied for different pharmacological and phytochemical activities. These species has shown analgesic, anti-inflammatory, antiarthritic, cytotoxic, anti-angiogenesis and antiviral etc. in various established *in-vivo* and *in-vitro* experiments. Further studies are required to explore the therapeutic potential of already reported activities in term of clinical utility as well as the phytochemical and pharmacological studies on remaining species in the light of traditional uses.

**Keywords:** *Xanthium*, Asteraceae, *Xanthium strumarium*, *Xanthium spinosum*.

### INTRODUCTION

The genus *Xanthium* (Family Asteraceae) is represented by 25 species in the world. The *Xanthium* (cocklebur) is a genus of flowering plants in the sunflower tribe within the daisy family, native to the Americas and eastern Asia. However, widely distributed throughout the world [1]. The leaves are spirally arranged, with deeply toothed margins. Some species, notably *Xanthium spinosum*, are also very thorny with long, slender spines at the leaf bases.

The chemistry of this genus is quite homogeneous, sesquiterpene lactones being detected in all cases. The occurrence of some toxic kaurene glycosides has been reported. These compounds inhibit mitochondrial ADP/ATP translocation and produce nephrotoxic effects [2].

To the best of our knowledge, *Xanthium strumarium* and to some extent, *Xanthium spinosum* and *Xanthium spinosum*, are the only species of the genus that has been explored for phytochemically and pharmacologically, while the rest of the species are untouched.

### Pharmacological Activities

#### 1. Analgesic and antiinflammatory effects

*Xanthium strumarium*L., commonly known as cocklebur, is a species of annual plant belonging to the Compositae family, recorded in FDA Poisonous Plant Database. The fruit of *Xanthium strumarium* (XSF), Chinese name "Cang-Er-Zi", recorded in the current Chinese Pharmacopoeia, has been used in Traditional Chinese Medicine to treat nasal sinusitis, headache, urticaria and arthritis (Committee, 2010).

Hen *et al* (2007) demonstrated that the polar fraction of XSF has got most significant anti-inflammatory and analgesic properties in mice in a dose-dependent manner [3]. Bioassay-guided fractionation of ethanolic extract led to the isolation and identification of ten caffeoylquinic acids and three heterocyclics by HPLC-DAD-MSn from the active *n*-butanol fraction, implying that the active compounds are polar in nature. The isolated caffeoylquinic acids could partially explain the antinociceptive effect of *X. strumarium* polar extract.

Bader *et al* (2013) showed that the crude extract of *X. spinosum* roots from Jordanian origin dose-dependently inhibited the 5-LOX (IC<sub>50</sub>≅10µg/mL), COX-1(IC<sub>50</sub>≅50µg/mL), and 12-LOX (IC<sub>50</sub>≅170µg/mL) enzymatic pathways in intact pro-inflammatory cells. A direct activity at the level of PLA2 was not probable, but the extract induced the synthesis of the anti-inflammatory eicosanoid 15(S)-HETE, which may, in turn, inhibit this enzyme [4].

5-LOX bioguided fractionation of the crude extract led to the isolation of ziniolide, a known 12,8-guaianolide sesquiterpene lactone, from the hydroalcoholic fraction of then hexane extract (IC<sub>50</sub>=69µM). Both the plant extract and ziniolide are *in vitro* inhibitors of the phorbol-induced NFκB activation, a key regulator of the arachidonic pathway.

### Anti-arthritic activity

*Xanthium strumarium* L. fruit (Xanthiu fruit) has been traditionally used as a medicinal herb in China for the treatment of many ailments including rheumatoid arthritis. When it was experimentally studied by Lin et al (2014), it significantly suppressed paw swelling and arthritic score increased body weight loss and decreased the thymus index. The overproduction of TNF- $\alpha$  and IL-1 $\beta$  was remarkably suppressed in the serum of all EXS-treated rats, and in contrast, IL-10 was markedly increased. The level of COX-2 and 5-LOX was also decreased with EXS treatment.

Ten phenolic acid derivatives were identified from 14 detected peaks by HPLC-DAD with the reference substances and verified by LC-MS. These results suggest the potential effect of EXS as an anti-arthritis agent towards CFA-induced arthritis in rats. *Xanthium strumarium* has the potential to be regarded as a candidate for use in general therapeutics and as an immune-modulatory medicine in rheumatoid arthritis<sup>[1]</sup>.

### Antitrypanosomal activity

Talakai and co-worker (1995) showed the antitrypanosomal activity of crude 50% ethanolic extract of *Xanthium strumarium* leaves in vitro and in vivo<sup>[5]</sup>. The extract exhibited trypanocidal activity at all the four concentrations tested i.e. 5, 50, 500 and 1000 #g/ml, in vitro. In vivo trial revealed that the extract exerted an antitrypanosomal effect at dosage of 100, 300 and 1000 mg/kg, intraperitoneally. At 100 and 300 mg/kg doses, the survival period of the *Trypanosoma evansi* infected mice was significantly prolonged. However, the extract was found to be toxic to the animals at 1000 mg/kg dose.

### Anticancer Antiviral and Anti-angiogenesis effects

Xanthatin isolated from *X. spinosum* showed cytotoxicity against L1210 and Hep-G2 cell lines. Excellent inhibition of angiogenesis was observed; comparable to that of paclitaxel. Also, xanthatin provoked inhibitory activity against several viruses, a wide variety of virus including Herpes simplex, vaccinia and vesicular stomatitis in HEL cell cultures, feline corona, feline herpes in CRFK cell cultures, vesicular stomatitis virus, coxsackie virus B4 and respiratory syncytial virus in HeLa cell cultures. but with a therapeutic index <5<sup>[6]</sup>.

### Toxicity and unwanted effects

Despite its potential clinical use, *Xanthium strumarium* caused many side effects, such as depression, vomiting, abdominal pain, weakness, recumbency, paddling convulsions terminating in death between 6 and 96 h after ingestion have been reported in farm animals<sup>[7-10]</sup>. Microscopically, acute hepatic congestion and haemorrhage, centrilobular hepatocyte necrosis, with occasional binucleation together with discoid lysis of skeletal and cardiac muscle fibres are the changes which have been observed<sup>[11]</sup>. Hepatotoxicity induced by XSF has also been reported in humans and the clinic signs are similar to those observed in animals<sup>[7-8]</sup>.

Wang et al (2011) concluded that atractyloside and carboxyatractyloside induce hepatotoxicity in mice by induction of oxidative stress leading to lipid peroxidation in the liver<sup>[12]</sup>. Although some studies have focused on the side effects of XSF, its toxicity has not been well documented, and no conclusions about its hepatotoxic mechanisms have been proposed. These studies have raised considerable concerns about the adverse effects associated with the long-term use of XSF. To our knowledge, research on XSF-induced toxicity is scarce, presumably due to the multiple targeting sites involved in its in vivo toxic effect as well as the complexity of its multiple chemical ingredients, which can vary with geographical locations and the methods of processing of medicinal herbs<sup>[12]</sup>.

### CONCLUSIONS

It is concluded that only three species of the genus are explored for pharmacological and phytochemical studies, out of 25. It may be due to the toxicity of these studied species prevented the researcher from further exploration its therapeutic potential. However, this review clearly pointed out the species of genus *Xanthium* possessed marked hepatotoxic agents, therefore, should be carefully used for any therapeutic.

### Competing Interests

The authors declare that they have no competing interests.

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