



## PHYTOCHEMICAL COMPOSITIONS AND PHARMACEUTICAL IMPORTANCE OF XANTHIUM STRUMARIUM L

Manish Sharma\* Akash Gupta\*

\*Department of Botany, University of Rajasthan, JLN Marg, Jaipur, Rajasthan, India.

### Abstract

*Xanthium strumarium* L., belongs to family Asteraceae, is rich source of phytoconstituents which are being used for treatment of various life-threatening diseases. About 25 species of the plant have been recognized based on their morphology. Only two species of *Xanthium* including *Xanthium strumarium* and *Xanthium indicum* are reported in India that has been explored for phytochemically, and pharmacologically. *Xanthium strumarium* L. is the unique source of many biologically and pharmacologically important phytochemicals. Major Phytochemicals of *Xanthium* are steroids, alkaloids, terpenoids, saponins, tannins, flavonoids, proteins. Despite many medicinal uses, *Xanthium strumarium* causes many side effects like vomiting, abdominal pain, depression, paddling convulsions and even death in animals also. Induction of hepatotoxicity in human has also been reported. Pharmacological studies have generally confirmed the traditional use of extract of whole plant, root, leaves and fruits as an ailment for leukoderma, poisonous bites of insects, epilepsy, salivation, long standing cases of “malaria, rheumatism, tuberculosis, allergic rhinitis, Sinusitis, urticarial, rheumatoid arthritis, constipation, diarrhea, leprosy, lumbago, pruritus, and infections due to bacteria and fungus”.

**Keywords:** Asteraceae, Pharmacology, Phytochemicals, *Xanthium strumarium*.

### 1. Introduction

*Xanthium strumarium* L., belongs to family Asteraceae, is a cocklebur or burweed which can be commonly found throughout the tropical parts of India during the month of September to November. Its common name is ‘Chhota gokhru’ because the shape of its fruit looks like cow’s toe. It is also known as ‘Aadhasisi’ as this weed is used for the treatment of hemicranias. The plant is a significant source of phytochemicals, which are utilised to cure a variety of fatal diseases. Based on their morphology, about 25 species of the plant have been identified. In Europe, North America, and Brazil, *Xanthium strumarium* L. and *Xanthium spinosum* L. are used medicinally. In North America and Brazil, *Xanthium canadens* is utilised, while *Xanthium strumarium* is used in India, China, and Malaysia. Only two species of *Xanthium*, *Xanthium strumarium* and *Xanthium indicum*, have been studied from a phytochemical and pharmacological outlooks.

### 2. Taxonomical classification

Kingdom- Plantae

Phylum- Magnoliophyta

Class- Magnoliopsida

Order- Asterales

Family- Asteraceae

Genus- *Xanthium*

Species- *strumarium*

**Scientific name-***Xanthium strumarium* L.



**Vernacular names**-Chota dhatura, Chota gokhuru, Ghaghra (Hindi), Shankeshwar (Marathi), Marul-Umattai (Telugu), Godrian (Gujrati), Arishta, Medhya (Sanskrit), Bhede kurro, Ghangharaa, Kaastolo, Kuch Kuche (Nepali).

### 3. Distribution

Worldwide: *X. strumarium* is distributed mainly in temperate zones. In countries like Australia, India, South Africa, and the America, it grow widely as weed (Love and Dansereau, 1959). India: Assam, Bihar, Odisha, Madhya Pradesh, Maharastra, Uttar Pradesh Rajasthan: Jodhpur, Bikaner, Jaisalmer, Barmer, Sikar, Naguar, Jhunjhunu, Churu, and Ganganagar (Negi *et al.*, 2011).

### 4. Morphological features:

It is annual herb which grows upto 20-90 cm height. Stem is erect, branched, and hairy. Green, alternate, opposite, cauline leaves having 5-20 cm long and 4-16 cm wide petioles are present. Fruits are oval shaped having 2 chambered bur. These are 0.5 to 1.5 inch long and are covered with prickles. Flowers are small, unisexual, and green in color. Fruits are hard and woody, ovoid-globose and covered with spines and it ends with two stouts.

### 5. Phytochemical compositions.

*Xanthium strumarium* is the unique source of many biologically and pharmacologically important phytochemicals. Major Phytochemicals of *Xanthium* are steroids, alkaloids, terpenoids, saponins, tannins, flavonoids, proteins. Major phytochemicals which have been reported in *Xanthium strumarium* are- caffeic acids, xanthiazone, xanthiazone- (2-ocaffoyl)-b-D-glucopyranoside), xanthanol, isoxanthanol, tocophenol, chlorogenic caid, ferulic acid, 8-epixanthatin, 4-oxo-bedfordia, atractyloside etc. besides these, presence of many free amino acids viz. glutamic acid, alanyl-glycine, threonine, alanine, argino-mono hydrochloride, proline, valine, isoleucine, methionine have also been reported in the plant. Some important phytochemicals found in different parts (fruits, leaves, aerial parts, roots and whole plant) of *Xanthium strumarium* are summarized in table 1.

**Tab.1: Important phytochemicals found in different parts of *Xanthium strumarium* L.**

Name of plant parts	Bioactive compounds	Class of biological compounds	References
Fruits	Sibirolide A, sibirolide B, norxanthatolide A, norxanthantolide B, norxanthantolide C, norxanthantolide D	Sesquiterpenoids	Shi <i>et al.</i> , 2015
	1,5-di-O-caffeolyquinic acid, 3,4-caffeoylquinic acid methyl ester, 3,5-di-caffeoylquinic acid methyl ester, 4-O-caffeoyl quinic acid methyl ester, xanthiumnolic A, xanthiumnolic C, icariside D1, methylchlorogenate, caffeic acid ethyl ester	Phenylpropanoids	Hwang <i>et al.</i> , 2016, Han <i>et al.</i> , 2006, Tian <i>et al.</i> , 2013, Yuan, 2014, Cheng <i>et al.</i> , 2011,



			Kan <i>et al.</i> , 2011, Jiang <i>et al.</i> , 2017, Jiang <i>et al.</i> , 2013, Jiang, 2017, pandey and Rather, 2012, Qiu <i>et al.</i> , 2010, Shi <i>et al.</i> , 2015
	Laptolepisol D, dihydrodehydroliconiferyl alcohol, chushizisin E, similanol, diospyrosin, balanophoni A, fructusol A, syringaresinol	Lignanoids	Kan <i>et al.</i> , 2011, Yin <i>et al.</i> , 2016, Jiang <i>et al.</i> , 2018
	Daucosterol, beta-sitosterol	Steroids	Kan <i>et al.</i> , 2011
	Ononin, quercetin, allopatuletin, patuletin-3-glucuronide	flavonoids	Huang <i>et al.</i> , 2016, Yuan, 2014
<b>Leaves</b>	Xanthinin, xanthumin, xanthinol, isixanthanol, xanthatin, tomentosin, desacetyl-xanthanol	sesquiterpenoids	Winters <i>et al.</i> , 1969, McMillan <i>et al.</i> , 1975, Karmakar <i>et al.</i> , 2015
	Alpha-amyrin,	Triterpenoids	Kaur <i>et al.</i> , 2015
	Beta-sitoserol, 14-methyl-12,13-dehydro-sitosterol-heptadeconate	steroids	Kaur <i>et al.</i> , 2015, Kan <i>et al.</i> , 2011
<b>Aerial part</b>	1beta-hydroxy-5 alpha-chloro-8-epi-xanthatin, 11 alpha,13-dihydro-8 epi-xanthatin, 4-epi-xanthanol, inusoniolide, pungiolide A	Sesquiterpenoids	Han <i>et al.</i> , 2008, Mahmoud, 1998, Chen <i>et al.</i> , 2013, Wang <i>et al.</i> , 2013
	Lup-20(29)-en-3 beta-ol, lupenyl acetate, lupeol acetate, beta-amyrin, oleanolic acid	Triterpenoids	Cui, 2013, Wahab <i>et</i>



			<i>al.</i> , 2012, Li and Zhang, 2016, Sultana, 2014
	Stigmasterol, beta-sitosterol-3-O-beta-D-glucopyranoside	Steroids	Ingawale <i>et al.</i> , 2012, Sultana, 2014
<b>Roots</b>	Betulinic acid, botulin, erythrodiol	Triterpenoids	Ingawale <i>et al.</i> , 2018
	N-trans-feruloyl tyramine, 9,9'-o-di-(E)-feruloyl-(-)-secoisolariciresinol	Phenylpropanoids	Kan <i>et al.</i> , 2011
	Syringaresinol, 4-oxopinoresinol	Lignanoids	Ingawale <i>et al.</i> , 2018, Kan <i>et al.</i> , 2011
	Jatrocin B, cleomiscosin A, cleomiscosin C, Scopoletin	Coumarins	Kan <i>et al.</i> , 2011
	Stigma-4-en-beta-ol-3-one, beta-sitostenone, beta-daucosterol, beta-stigmasterol, 7-ketositosterol	Steroids	Kan <i>et al.</i> , 2011, Ingawale <i>et al.</i> , 2018
	5-hydroxy-3,6-dimethoxy-7-methyl-1,4-naphthalenedione, 5-methyluracil, uracil	Anthraquinones and naphthoquinones	Kan <i>et al.</i> , 2011, Ingawale <i>et al.</i> , 2018
<b>Whole plant</b>	Lupeol acetate	Triterpenoids	Li and Zhang, 2016
	Isovanillic acid, xanthiazone-(2-O-caffeoyl)-beta-D-glucopyranoside	Phenylpropanoids	Li and Zhang, 2016, pandey and Rather, 2012
	Ergosterol, taraxasteryl acetate	Steroids	Li and Zhang, 2016

## 6. Medicinal properties of the plant

Due to presence of various important phytochemicals, parts of *Xanthium strumarium* are being used for various medicinal purposes. Many researchers have shown that various plant parts have important pharmacological activities which are summarized in Table 2.

### 6.1. Larvicidal activity



It has been reported that seed extracts in methanol of *Xanthium strumarium* show larvicidal activity against *Aedes caspius* and *Culex pipiens* with LD<sub>50</sub> value of 531.07 µg/ml against 4<sup>th</sup> instart larvae of *Aedes caspius* and 502.32µg/ml for 4<sup>th</sup> instarlarvae of *Culex pipiens* (Fahd A. *et.al.*, 2017).

### 6.2. Anti-microbial activity

Xanthine was present in lower concentration in *Xanthium strumarium* essential oil. This phytochemical was isolated from extract of *Xanthium spinosum* L. and was found to be active against *Colltotrichum*, *T. reseau*, *B. cereus* and *S. aureus* (Ginestaa-Peris *et al.*, 1994). A study showed the effectiveness of cinnamic acid against *E. coli*, *P.aeruginosa*, *S.aureus* and *Salmonella* sp. and MIC values were found to be 1.0 mg /ml for all the bacterial strains (Chang *et al.*, 2001). Cinnamic acid was present in *Xanthium strumarium* extracts at the range of 22- 80 mg/g dry extract (Scherer *et. al.*, 2008). So, the compounds xanthin and cinnamic acid are responsible for the antimicrobial properties of *Xanthium strumarium*.

### 6.3. Anti-oxidant activity

In a study extracts of *Xanthium strumarium* plants were evaluated for their antioxidant and antiradical activities. IC<sub>50</sub> values were found to be 0.02 mg/ml and 0.09 mg/ml for antioxidant and antiradical activities respectively. These both activities were found to be better than ascorbic acid and α-tocopherol. (Javad Sharifi Rad *et al.*, 2013).

### 6.4. Anti-diabetic activity

The dried leaves and stems of *Xanthium strumarium* L. were tested for anti-diabetic efficacy using alcoholic and water extracts. Using a 21-day streptozotocin-induced diabetes model (STZ), the anti-diabetic potency was examined. The rats with diabetes were overweight and had high levels of triglycerides, cholesterol, and blood sugar. The blood glucose level, cholesterol level, and triglyceride level could all be reduced by continuously giving animals alcoholic and water extracts orally for 21 days at doses of 250 and 500 mg/kg, respectively. After 21 days of treatment, there was some improvement in the histological appearance of pancreatic cells in the STZ-induced groups. The findings show that *Xanthium strumarium* alcohol extracts have strong anti-diabetic efficacy (Joghee Suresh *et. al.*, 2014).

### 6.5. Anti-arthritis activity

In a study, it was found that extracts of *Xanthium strumarium* significantly suppress swelling and arthritic score. *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. (Bing Lin *et. al.*, 2014).

**Tab.2: Pharmacological activities shown by different parts of *Xanthium strumarium* L.**

Name of plant part	Extract	Activity	References
Fruit	Water	Anti-cancer	Hong <i>et al.</i> , 2004, Hong <i>et al.</i> , 2003, Zhao <i>et al.</i> , 2008, Yan <i>et al.</i> , 2010, Vaishnav and George, 2015, Pan <i>et al.</i> , 2013
	Water	Anti-inflammatory	An <i>et al.</i> , 2004, Yeom <i>et al.</i> , 2015, Huang <i>et al.</i> , 2011
	Methanolic		Kim <i>et al.</i> , 2005, Hossen <i>et al.</i> , 2016
	Ethanolic		Park <i>et al.</i> , 2015, Hasan <i>et al.</i> , 2011



	Methanolic	Analgesic effect	Kim <i>et al.</i> , 2005
	Ethanolic		Huang <i>et al.</i> , 2011, Kepenekci and Saglam, 2015
	Methanolic	Insecticidal	Talakal <i>et al.</i> , 1995, Gokce <i>et al.</i> , 2011, AI-Mekhlafi <i>et al.</i> 2017
	Ethanolic	Antioxidant	Ghahari <i>et al.</i> , 2017
	Methanolic		Ingawale <i>et al.</i> , 2018
	Water		Huang <i>et al.</i> , 2011
	Water	antimicrobial	Wang <i>et al.</i> , 2016
	Ethanolic		Gahari <i>et al.</i> , 2017
	Methanolic		Kim <i>et al.</i> , 2002
	Water	Anti-diabetic	Kupiecki <i>et al.</i> , 1974
	Methanolic		Ingawale <i>et al.</i> , 2018
	Water	antilipidemic	Li <i>et al.</i> , 2016, Li <i>et al.</i> , 2017
Water	antiviral	Liu <i>et al.</i> , 2009	
Leaves	Methanolic	Anti-inflammatory	Kim <i>et al.</i> , 2005, Khuda <i>et al.</i> , 2014
	Ethanolic	insecticidal	Talakal <i>et al.</i> , 1995, Chandel <i>et al.</i> , 2012
	Water		Chandel <i>et al.</i> , 2012
	Ethanolic	Anti-oxidant	Kamboj <i>et al.</i> , 2014
	Methanolic	Anti-microbial	Srinivas and Rajashekar, 2011, Devkota and Das, 2015, Yanar <i>et al.</i> , 2011
	Water		Devkota and Das, 2015, Wang <i>et al.</i> , 2016
Ethanolic	Sharifi <i>et al.</i> , 2016, Sharifi <i>et al.</i> , 2015,		
Aerial part	Ethanolic	Anti-cancer	Ferrer <i>et al.</i> , 2016, Vaishnav and George, 2015
	Methanolic		Hossen <i>et al.</i> , 2016

## 7. Toxicity

Despite many medicinal uses, *Xanthium strumarium* causes many side effects like vomiting, abdominal pain, depression, paddling convulsions and even death in animals also. Induction of hepatotoxicity in human has also been reported. It has been discovered that the plant's seeds and seedlings contain the glycoside carboxy-atractyloside, which is harmful to several animals, including horses, pigs, and cattle. If consumed in significant amounts, it can result in animal mortality and the dysfunction of several organs.

## 8. Conclusion

Many studies have been suggested that due to presence of active phytochemicals, different parts of *Xanthium strumarium* can be used to treat various life threatening agents. The plant can be utilized as rich sources of these important phyto-constituents by pharmaceutical industries to design and synthesize new medicines of various purposes.

## References



1. Afsar Shaik, Rajesh Kumar Kotha, P. Raveesha, Krishna Sree. Evaluation of anti-pyretic activity of methanolic whole plant extract of *Xanthium strumarium* against yeast induced pyrexia model in wistar rats. *Journal of pharmacy research*. 5 (12):5277-5279. 2012.
2. An H.J., Jeong H.J., Lee E.H., Kim Y.K., Hwang W.J., Yoo S.J. Xanthii Fructus Inhibits Inflammatory Responses in LPS-Stimulated Mouse Peritoneal Macrophages. *Inflammation*. 2004;28:263–270. doi: 10.1007/s10753-004-6049-9.
3. Bing Lin, Yong Zhao, Ping Han, Wei Yue, Xue-Qin Ma, Khalid Rahman, Cheng-Jian Zheng, Lu-Ping Qin, Ting Han. Anti-arthritic activity of *Xanthium strumarium* L. extract on complete freund's adjuvant induced arthritis in rats. *Journal of ethnopharmacology*. Vol. 55, issue 1, 2014. 248-255.
4. Chang, s.t., chen, p.f., chang, s.c. antibacterial activity of leaf essential oils and their constituents from *Cinnamomum osmophloeum*. *Journal of ethnopharmacology*. V. 77, page 123-127. 2001.
5. Chen J., Wang R., Shi Y.P. Chemical constituents from Xanthii Fructus. *Chin. Tradit. Herbal Drugs*. 2013;44:1717–1720. (In Chinese)
6. Cheng Z., Wang L., Chen B., Li F., Wang M.K. Chemical Constituents from *Fructus Xanthii*. *Chin. J. Appl. Environ. Biol.* 2011;17:350–352. doi: 10.3724/SP.J.1145.2011.00350. (In Chinese)
7. Fahd A. Al-Mekhlafi, Nael Abutaha, Ashraf M.A. Mashaly, Fahd A. Nasr, Khalid E. Ibrahim, Mohamed A. Wadaan. Biological activity of *Xanthium strumarium* seed extracts on different cancer cell lines and *Aedes caspius*, *Curex pipiens* (Diptera: Culicidae). *Saudi Journal of Biological sciences*. Volume 24, issue 4/ May 2017. 817-821.
8. Ginesta-peris, E. Garcia-breijo, f.j., primo- yufera, e. antimicrobial activity of xanthatin from *Xanthium spinosum* . letters in applied microbiology, v. 18, p. 206-208, 1994.
9. Han T., Li H.L., Hu Y., Zhang Q.Y., Huang B.K., Zheng H.C., Rahman K., Qin L.P. Phenolic acids in *Fructus Xanthii* and determination of contents of total phenolic acids in different species and populations of *Xanthium* in China. *J. Chin. Intergr. Med.* 2006;4:194–198. doi: 10.3736/jcim20060217. (In Chinese).
10. Han T., Zhang H., Li H.L., Zhang Q.H., Zheng H.C., Qin L.P. Composition of supercritical fluid extracts of some *Xanthium* species from China. *Chem. Nat. Compd.* 2008;6:814–816. doi: 10.1007/s10600-009-9208-2.
11. Hong S.H., Jeong H.J., Kim H.M. Inhibitory effects of Xanthii Fructus extract on mast cell-mediated allergic reaction in murine model. *J. Ethnopharmacol.* 2003;88:229–234. doi: 10.1016/S0378-8741(03)00232-0.
12. Hong S.H., Oh M.J., Lee E.J., Park J.H., Kim N.H., Rhee H.K., Kim H.M., Jung S.K. Processed Xanthii Fructus increases cell viability of mast cell line, RBL-2H3. *Orient. Pharm. Exp. Med.* 2004;4:60–64.
13. Hossen M.J., Kim M.Y., Cho J.Y. MAPK/AP-1-Targeted Anti-Inflammatory Activities of *Xanthium strumarium*. *Am. J. Chin. Med.* 2016;44:1111–1125. doi: 10.1142/S0192415X16500622.
14. Huang M.H., Wang B.S., Chiu C.S., Amagaya S., Hsieh W.T., Huang S.S., Shie P.H., Huang G.J. Antioxidant, antinociceptive, and anti-inflammatory activities of Xanthii Fructus extract. *J. Ethnopharmacol.* 2011;135:545–552. doi: 10.1016/j.jep.2011.03.057.



15. Hwang S.H., Wang Z.Q., Yoon H.N., Lim S.S. *Xanthium strumarium* as an Inhibitor of  $\alpha$ -Glucosidase, Protein Tyrosine Phosphatase 1 $\beta$ , Protein Glycation and ABTS<sup>+</sup> for Diabetic and Its Complication. *Molecules*. 2016;21:1241. doi: 10.3390/molecules21091241.
16. Ingawale A.S., Sadiq M.B., Nguyen L.T., Ngan T.B. Optimization of extraction conditions and assessment of antioxidant,  $\alpha$ -glucosidase inhibitory and antimicrobial activities of *Xanthium strumarium* L. fruits. *Biocatal. Agric. Biotechnol.* 2018;14:40–47. doi: 10.1016/j.bcab.2018.02.004.
17. Ishwarya S., Singh M.K. Evaluation of antioxidant and invitro cytotoxicity of crude fractions from the roots of *Xanthium strumarium*. *Int. J. Pharmtech Res.* 2010;2:2219–2223.
18. Javad Sharifi Rad, Seyedeh Mahsan Hoseini Alfatemi, Majid Sharifi Rad and Marcello Iriti. *In vitro* antioxidant and antibacterial activities of *Xanthium strumarium* L. extracts on methicillin-susceptible and methicillin-resistant *Staphylococcus aureus*. *Ancient science of life*. 2013. 33 (2):109-113.
19. Jiang H., Yang L., Liu C., Hou H., Wang Q., Wang Z., Yang B., Kuang H. Four new glycosides from the fruit of *Xanthium sibiricum* Patr. *Molecules*. 2013;18:12464–12473. doi: 10.3390/molecules181012464.
20. Jiang H., Yang L., Ma G.X., Xing X.D., Yan M.L., Zhang Y.Y., Wang Q.H., Yang B.Y., Kuang H.X., Xu X.D. New phenylpropanoid derivatives from the fruits of *Xanthium sibiricum* and their anti-inflammatory activity. *Fitoterapia*. 2017;117:11–15. doi: 10.1016/j.fitote.2016.12.007.
21. Jiang H., Yang L., Xing X.D., Zhang Y.Y., Yan M.L., Yang B.Y., Wang Q.H., Kuang H.X. Chemical constituents from fruits of *Xanthium sibiricum*. *Chin. Tradit. Herbal Drugs*. 2017;48:47–51. (In Chinese)
22. Joghee Suresh, Shanya Rajan, Nagamani. Anti-diabetic activity of aerial parts of *Xanthium strumarium*. *World journal of pharmacy and pharmaceutical sciences*. Vol 3, issue 3, 2185-2200. 2014.
23. Kan S.Q., Chen G.Y., Han C.R., Chen Z., Song X.M., Ren M., Jiang H. Chemical constituents from the roots of *Xanthium sibiricum*. *Nat. Prod. Res.* 2011;25:1243–1249. doi: 10.1080/14786419.2010.539182.
24. Karmakar U.K., Ishikawa N., Toume K., Arai M.A., Sadhu S.K., Ahmed F., Ishibashi M. Sesquiterpenes with TRAIL-resistance overcoming activity from *Xanthium strumarium*. *Bioorg. Med. Chem.* 2015;23:4746–4754. doi: 10.1016/j.bmc.2015.05.044.
25. Kaur M., Kamboj A., Rathour A., Saluja A.K. Isolation and Characterization of Constituents from the Leaves of *Xanthium strumarium* and their Evaluation for Antioxidant and Antimicrobial Potential. *Nat. Prod. Chem. Res.* 2015;3:168–173. doi: 10.4172/2329-6836.1000168.
26. Khuda F., Iqbal Z., Khan A., Shah Z.Y., Ahmad L., Nasir F., Hassan M., Shah I., Shah W.A. Evaluation of anti-inflammatory activity of selected medicinal plants of Khyber Pakhtunkhwa, Pakistan. *Pak. J. Pharm. Sci.* 2014;27:365–368.
27. Kim I.T., Park Y.M., Won J.H., Jung H.J., Park H.J., Choi J.W., Lee K.T. Methanol extract of *Xanthium strumarium* L. possesses anti-inflammatory and anti-nociceptive activities. *Biol. Pharm. Bull.* 2005;28:94–100. doi: 10.1248/bpb.28.94.
28. Li N., Zhang W.Z. Studies on Chemical Constituents of *Xanthium sibiricum* Patr. ex Widder. *J. Qiqihar Univ.* 2016;32:51–53. (In Chinese).





29. Love, D. and P. Dansereau. 1959. Biosystematic studies on *Xanthium*: taxonomic appraisal and ecological status. *Candian J. Botany* 37:173-208.
30. Mahmoud A.A. Xanthanolides and xanthane epoxide derivatives from *Xanthium strumarium*. *Planta Med.* 1998;64:724–727. doi: 10.1055/s-2006-957566.
31. McMillan C., Chavez P.I., Mabry T.J. Sesquiterpene lactones of *Xanthium strumarium* in a texas population and in experimental hybrids. *Biochem. Syst. Ecol.* 1975;3:137–141. doi: 10.1016/0305-1978(75)90017-4.
32. Negi JS, Negi PS, Rawat B, 2011. Chemical constituents and biological importance of *Swertia*: A review. *Current research in chemistry.* 3(1): 1-15.
33. Pan J.H., Wang Y.L., Xie M.R., Yu F.R. Inhibitory effect of xanthium extract on S180 cells growth and the impact on immune functions in tumor-bearing mice. *Chin. J. Clin. Res.* 2013;26:317–319. (In Chinese)
34. Pandey D.P., Rather M.A. Isolation and Identification of Phytochemicals from *Xanthium strumarium*. *Int. J. ChemTech Res.* 2012;4:266–271.
35. Park J.H., Kim M.S., Jeong G.S., Yoon J. Xanthii Fructus extract inhibits TNF- $\alpha$ /IFN- $\gamma$ -induced Th2-chemokines production via blockade of NF- $\kappa$ B, STAT1 and p38-MAPK activation in human epidermal keratinocytes. *J. Ethnopharmacol.* 2015;171:85–93. doi: 10.1016/j.jep.2015.05.039.
36. Qiu Y.L., Dai Y.H., Wang D., Cui Z. Chemical constituents in the fruits of *Xanthium sibiricum*. *Chin. J. Med. Chem.* 2010;20:214–216. (In Chinese)
37. Scherer R., Sismotto, M., Godoy, H.T. Antioxidant activity and related compounds of *Xanthium strumarium* extracts. *Phytochemistry*, 2009.
38. Shi Y.S., Li L., Liu Y.B., Ma S.G., Li Y., Qu J., Liu Q., Shen Z.F., Chen X.G., Yu S.S. A new thiophene and two new monoterpenoids from *Xanthium sibiricum*. *J. Asian Nat. Prod. Res.* 2015;17:1039–1047. doi: 10.1080/10286020.2015.1070146.
39. Shi Y.S., Liu Y.B., Ma S.G., Li Y., Qu J., Li L., Yuan S.P., Hou Q., Li Y.H., Jiang J.D., *et al.* Bioactive Sesquiterpenes and Lignans from the Fruits of *Xanthium sibiricum*. *J. Nat. Prod.* 2015;78:1526–1535. doi: 10.1021/np500951s.
40. Sultana A. *Ph.D. Thesis*. Federal Urdu University of Arts, Science and Technology; Karachi, Pakistan: 2014. Phytochemical Studies on the Chemical Constituents of *Xanthium strumarium* Linn., Synthesis in addition Bioactivities of 2, 3-Diaminonaphthalenimidazole Derivatives and Amides of Piperic Acid.
41. Tian J., Xia Y.F., Fang K.H. Simultaneous determination of eight phenolic acids in *Xanthium sibiricum* by HPLC. *Chin. Tradit. Pat. Med.* 2013;36:1623–1626. (In Chinese).
42. Vaishnav K., George L.B., Highland H.N. Induction of cell death through alteration of antioxidant activity in HeLa cervical cancer cells by *Xanthium strumarium* L. extract. *IOSR J. Pharm. Biol. Sci.* 2015;10:33–42.
43. Wahab A., Sultana A., Khan K.M., Irshad A., Ambreen N., Ali M., Bilal M. Chemical investigation of *Xanthium strumarium* Linn and biological activity of its different fractions. *J. Pharm. Res.* 2012;5:1984–1987.
44. Wang L., Wang J., Li F., Liu X., Chen B., Tang Y.X., Wang M.K. Cytotoxic sesquiterpene lactones from aerial parts of *Xanthium sibiricum*. *Planta Med.* 2013;79:661–665. doi: 10.1055/s-0032-1328482.



45. Winters T.E., Theodore A., Geissman D.S. Sesquiterpene lactones of *Xanthium* species. Xanthanol and isoxanthanol, and correlation of xanthinin with ivalbin. *J. Org. Chem.* 1969;34:153–155. doi: 10.1021/jo00838a033.
46. Yan G.H., Jin G.Y., Li G.Z., Cui C.A., Quan G.H., Jin D.S., Jin D.Z. The possible mechanism of inhibitory effect of *xanthium strumarium* on mast cells activated by compound 48/80. *Prog. Anat. Sci.* 2010;16:164–166. (In Chinese).
47. Yeom M., Kim J.H., Min J.H., Hwang M.K., Jung H.S., Sohn Y. *Xanthii Fructus* inhibits inflammatory responses in LPS-stimulated RAW 264.7 macrophages through suppressing NF- $\kappa$ B and JNK/p38 MAPK. *J. Ethnopharmacol.* 2015;176:394–401. doi: 10.1016/j.jep.2015.11.020.
48. Yuan H.E. *Master's Thesis*. Jinan University; Guangzhou, China: 2014. Study on the Chemical Constituents of *Herba Commelinae* and *Fructus Xanthii*. (In Chinese).
49. Zhao Y., Yang H., Zheng Y.B., Wong Y.O., Leung P.C. The Effects of *Fructus Xanthii* Extract on Cytokine Release from Human Mast Cell Line (HMC-1) and Peripheral Blood Mononuclear Cells. *Immunopharmacol.Immunotoxicol.* 2008;30:543–552.doi: 10.1080/08923970802135385.