



A Review on the Most Important Medicinal Herbs Native to Iran with Anti-Acetaminophen Toxicity

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Abstract: Acetaminophen is an analgesic and anti- fever drug, which can be toxic in high doses and leads to hepatic and renal injury. Acetaminophen poisoning can cause many complications and injuries in the body including vomiting, diarrhea, malaise, shock, jaundice, and liver failure and in some cases will lead to myocardial and kidney damage. Against all toxic and destructive effects of drugs like acetaminophen, some compounds are found that can partially restrain poisoning of abuse such compounds. In this review article, medicinal plants native to Iran have been reported, which are used to protect acetaminophen toxicity. In this review study, searching the articles with key words such as acetaminophen, hepatotoxicity, herbs, extracts, and essential oils were used. Searching the articles was conducted through databases of income in Iran like Google Scholar, ISI January, MegaIran, and a number of other databases. Medicinal plants including green tea, turmeric, cress, dandelion, and capers are the most important medicinal plants against the toxicity of acetaminophen. It seems that pharmacological bioactive and antioxidants substances obtaining from plant and biological materials are anti- acetaminophen poisoning.

Keywords: *liver, Toxicity, Acetaminophen, Herbs, Iran.*

Introduction

Acetaminophen is the drug from analgesics category and derivatives of Para amino phenol which is an appropriate substitute for aspirin in the treatment of mild to moderate muscle aches, joint pain, headache, fever, post-operative pain, pain after childbirth, etc. [1].

Acetaminophen is an analgesic and antipyretic drug which is toxic in high levels and causes hepatic and renal damages [2]. Physicians haven't enough information about complications of this drug and its treatment details, its preparation and its metabolism is easy without a prescription; therefore, prescribing and consumption is high [3,4]. Poisoning with Acetaminophen can cause side effects to the

body, especially the liver damage and also die. Acetaminophen poisoning is usually associated with vomiting, diarrhea, malaise, shock, jaundice, liver failure, and in some cases will lead to myocardial and kidney damage [5]. Against all toxic and destructive effects of drugs like acetaminophen, that can partially prevent poisoning, there are some antidotes. Among these compounds, the active ingredients of plant extracts are promising [6-8]. Using herbs to treat diseases has long been common in human societies and were considered up to about half a century ago as one of the most important suppliers of drugs for the treatment of diseases [9-12]. Studies have shown that medicinal plants with flavonoids and phenolic compounds have

many biological effects including antioxidant properties [13-27]. In this review article, medicinal plants native to Iran has been reported, which are used to protect acetaminophen toxicity.

Methods

In this review article of literature searches were conducted using key words such as acetaminophen, hepatotoxicity, herbs, extracts, and essential oils. Searching the articles was implemented from databases inside and outside of Iran like Google Scholar

databases, ISI January, Mega Iran, and a number of other sites.

Results and Discussion

In Iran, five plants are used as liver protective against acetaminophen. Medicinal herbs including green tea, turmeric, cress, dandelion, and capers are the most important medicinal plants against acetaminophen toxicity. The mentioned medicinal herbs with additional information have been presented in Table 1.

Table1: Iranian native medicinal plants with liver protective against the acetaminophen with Persian name, scientific name, family name.

S.No	Scientific Name	Family Name	Persian name	Description
1	Camellia sinensis L.	Green tea		Administration of 7 mg green tea extract in mice for 30 days resulted in a significant reduction in ALT and AST levels in the experimental group than the acetaminophen group. Histopathological examinations also revealed reduction of hepatic necrosis, congestion and the accumulation of inflammatory cells and red blood cells [28].
2	Curcuma longa	Turmeric	Turmeric	Dose of 1000 mg kg of turmeric extract reduces the scope of liver necrosis, inflammation and reduces also congestion in the liver cells [29].
3	Lepidium sativum cruciferua L.	Shahi	Shahi	Shahi extract at a dose of 1000 mg kg in mice showed that ALP, GPT, GOT and MDA were significantly lower in rats [30].
4	Taraxacum syriacum	dandelion	dandelion	Dandelion extract at a dose of 200 mg of acetaminophen poisoning causes reduced toxic doses (700 mg kg ip) [31].
5	Capparis spinosa	Capparidaceae	Capers	capers aqueous extract at a dose of 200 milligrams per kilogram of feed, reduces enzymes including ALT, AST, ALP and total bilirubin increases by toxic dose of acetaminophen [32].

Herbal medicines are the most important part of traditional medicine that have a long history in human life [27]. Based on the obtained results, herbs, green tea, turmeric, cress, dandelion, capers, green tea are the most important herbals against Acetaminophen. Among the properties of green tea, the anti-inflammatory, anti-bacterial, anti-viral effects can be mentioned while this plant has the function of wound healing [33,34].

The main active ingredient of turmeric herb is curcumin which is effective in various diseases [35,36]. Green tea contains flavenoles, aglycones, theanine, and aromatic compounds [37]. Dandelion has been used for treating gastrointestinal disorders such as anorexia, indigestion and insomnia, eye

problems, treatment of rheumatism and skin diseases. It is also used as diuretic, laxative, treatment of anemia, inflammation, jaundice treatment, detoxifies, blood purifier, and fever such as eczema [38-40]. It seems that bioactive substances with natural antioxidant and pharmacological activities are effective anti-poisoning agents which can be used against diseases or toxic effects of agents such as acetaminophen [41,42].

The exact mechanisms of these plants are not clear. It is clear that acetaminophen causes oxidative stress, increases hepatocytes and decreases the level of glutathione (GSH), as well as the total antioxidant capacity. Antioxidants have been shown to combat oxidative stress and increase the body antioxidant capacity [43-50].

These plants with their antioxidant activity can help treating or preventing other diseases, too.

References

1. Tatti R, Abolghasemi SJ, Tatina M, Nasre Tajan M (2012) Influence of prebiotic immune wall on growth performance, body composition and immune physiological variables in juvenile great sturgeon, *Huso huso*. *Annals of Biological Research*, 3(9); 4435-4441.
2. Goldstein RS, Schnellman RG (1996) Toxic response of the kidney. 117-142, In: Klaassen, CD, Amdur, MO and Doll, J, (Eds). *Casarett and Doull Toxicology: the basic science of poisons*. McGraw- Hill Co., New York, 1100p.
3. Laura P, Philip R, Jack A (2003) Acetaminophen-induced hepatotoxicity. *Toxicology*, 31:1499-1506.
4. Rowden AK, Norvell J, Eldridge DL, Krik MA (2005). Update on acetaminophen toxicity. *Medical Clinics of North America*, 89(6): 1145-1159.
5. Kumar V, Abbas AK, Fausto N Robbins (2005) *Cotran Pathologic Basis of Diseases*. 7th ed. Elsevier Saunders: Philadelphia; p 25-26, 428.
6. Baradaran A, Nasri H, Nematbakhsh M, Rafieian-Kopaei M (2014) Antioxidant activity and preventive effect of aqueous leaf extract of Aloe Vera on gentamicin-induced nephrotoxicity in male Wistar rats. *Clinica Terapeutica*; 165(1):7-11.
7. Ghaed F, Rafieian Kopaei M, Nematbakhsh M, Baradaran A, Nasri H (2012). Ameliorative effects of metformin on renal histologic and biochemical alterations of gentamicin-induced renal toxicity in Wistar rats. *J Res Med Sci*; 17 (7):621-625.
8. Heidarian E, Movahed Mohammadi GH, Saffari J, Ghatreh-Samani K (2013) Protective Effect of Hydroethanolic Extract of Cress against Hepatotoxicity due to Acetaminophen in Rats. *J Mazand Univ Med Sci*; 23(102):73-84.
9. Baharvand-Ahmadi B, Bahmani M, Naghdi N, Saki K, Baharvand-Ahmadi S, Rafieian-Kopaei M (2015) Review on phytochemistry, therapeutic and pharmacological effects of myrtus (*Myrtus communis*). *Der Pharmacia Lettre*; 7(11):160-165
10. Ghasemi Pirbalouti A, Momeni M, Bahmani M (2013) Ethnobotanical study of medicinal plants used by Kurd tribe in Dehloran and Abadan Districts, Ilam Province, Iran. *African journal of traditional, complementary, and alternative medicines*; 10(2):368-385
11. Bahmani M Rafieian-Kopaei M (2014) Medicinal plants and secondary metabolites for leech control. *Asian Pacific Journal of Tropical Disease* ; 4(4): 315-316.
12. Bahmani M, Banihabib E Rafieian-Kopaei M, Gholami-Ahangaran M (2015) Comparison of disinfection activities of nicotine with copper sulphate in water containing *Limnatis nilotica*. *Kafkas Univ Vet Fak Derg*; 21 (1): 9-11
13. Bahmani M, Sarrafchi A, Shirzad H, Rafieian-Kopaei M (2016) Autism: Pathophysiology and promising herbal remedies. *Current Pharmaceutical Design*; 22(3):277-285.
14. Bahmani M, Shirzad H, Rafieian S, Rafieian-Kopaei M (2016) *Silybum marianum*: Beyond Hepatoprotection. *Journal of Evidence-Based Complementary and Alternative Medicine* 2015; 20(4):292-301.
15. Asadi-Samani M, Rafieian-Kopaei M, Azimi N Gundelia (2013). A systematic review of medicinal and molecular perspective. *Pak J Biol Sci*; 16: 1238-47.
16. Baharvand-Ahmadi B, Bahmani M, Naghdi N, Saki K, Baharvand-Ahmadi S, Rafieian-Kopaei, M (2015). Medicinal plants used to treat infectious and non-infectious diseases of skin and skin appendages in city of Urmia, northwest Iran. *Der Pharmacia Lettre* ; 7(1):189-196

Conclusion

The plants presented in table 1 have all antioxidant activities. Hence, they may induce, at least in part, their effects by their antioxidant properties.

17. Baharvand-Ahmadi, B, Bahmani, M, Tajeddini, P, Naghdi, N, Rafieian-Kopaei, M (2016). An ethno-medicinal study of medicinal plants used for the treatment of diabetes. *Journal of Nephropathology*; 5(1): 44-50.
18. Baharvand-Ahmadi, B, Bahmani, M, Zargaran, A, Eftekhari, Z, Saki, K, Baharvand-Ahmadi, S, Rafieian-Kopaei, M (2015) *Ruta graveolens* plant: A plant with a range of high therapeutic effect called cardiac plant. *Der Pharmacia Lettre*; 7(11): 172-173
19. Delfan B, Kazemeini, H, Bahmani, M (2015) Identifying Effective Medicinal Plants for Cold in Lorestan Province, West of Iran. *Journal of Evidence-Based Complementary and Alternative Medicine* 20 (3): 73-179.
20. Ebrahimie M, Bahmani M, Shirzad H, Rafieian-Kopaei M, Saki KA (2015). Review Study on the Effect of Iranian Herbal Medicines on Opioid Withdrawal Syndrome. *Journal of Evidence-Based Complementary and Alternative Medicine*; 20(4):302-309.
21. Mirhosseini M, Baradaran A, Rafieian-Kopaei M (2014) *Anethum graveolens* and hyperlipidemia: A randomized clinical trial. *J Res Med Sci* 19:758-61.
22. Nasri H, Rafieian-Kopaei M (2013) Tubular Kidney Protection by Antioxidants. *Iran J Public Health*; 42(10):1194-6.
23. Nasri H, Sahinfard N, Rafieian M, Rafieian S, Shirzad M, Rafieian-kopaei M (2014) Turmeric: A spice with multifunctional medicinal properties. *J Herbmed Plarmacol* 3(1): 5-8.
24. Nasri H, Behradmanesh S, Ahmadi A, Rafieian-Kopaei M (2013). Impact of oral vitamin D (cholecalciferol) replacement therapy on blood pressure in type 2 diabetes patients; a randomized, double-blind, placebo controlled clinical trial. *J Nephropathol.* 2014 Jan; 3(1):29-33. doi: 10.12860/jnp.2014.07. Epub Dec 25.
25. Rafieian-Kopaei M, Asgary S, Adelnia A, Setorki M, Khazaei M, Kazemi S, Shamsi F (2011) The effects of cornelian cherry on atherosclerosis and atherogenic factors in hypercholesterolemic rabbits. *J Med Plants Res.* 5(13):2670-2676.
26. Sarrafchi A, Bahmani M, Shirzad H, Rafieian-Kopaei M (2015). Oxidative stress and Parkinson's disease: New hopes in treatment with herbal antioxidants. *Current Pharmaceutical Design*; 22(2):238-246.
27. Sewell RDE, Rafieian-Kopaei M (2014) The history and ups and downs of herbal medicine usage. *J Herbmed Pharmacol.* 3(1):1-3.
28. Sadat Khorsandi LF, Javadnia M, Orazizadeh A, Abdolahi M (2010) Effect of green tea (*Camellia sinensis* L.) extract on acetaminophen induced acute hepatotoxicity in mice. *Iranian Journal of Medicinal and Aromatic Plants* 26(1): 22-29.
29. Khorsandi LS, Taheri-Mobarakeh M, Kalantari HA (2006). The Protective Effect of turmeric extract in acute liver toxicity induced by acetaminophen in mice. *Zanjan University of Medical Sciences*, 14 (55): 29-23.
30. Heidarian E, Rafieian-Kopaei M (2013) Protective effect of artichoke (*Cynara scolymus*) leaf extract against lead toxicity in rat. *Pharm Biol.*, 51(9):1104-9.
31. Nazari A, Ghasvand A, Hassanzadeh G, Rashidipour M, Ahmadi S (2013) The identification of chemical compounds of *Taraxacum Syriacum* Boiss (Gasedak) and assessing its extract effect on Acetaminophen induced nephro-toxicity in rat. *Yafteh.* 15(2):15-24
32. Eslami M, Farokhi F (2014) The effect of aqueous extract of fruits capers (*Capparis spinosa*) on the toxicity induced by acetaminophen in mice. *Journal of animal physiology and developmental*; 28 (8)1:55-62.
33. Asadi SY, Parsaei P, Karimi M, Ezzati S, Zamiri A, Mohammadizadeh F, Rafieian-Kopaei M (2013). Effect of green tea (*Camellia sinensis*) extract on healing process of surgical wounds in rat. *Int J Surg.* 11(4):332-7.
34. Parsaei P, Karimi M, Asadi SY, Rafieian-Kopaei M (2013) Bioactive components and preventive effect of green tea (*Camellia sinensis*) extract on postlaparotomy intra-abdominal adhesion in rats. *Int J Surg.* 2013; <http://dx.doi.org/10.1016/j.ijssu.08.014>.

35. Asgari S, Setorki M, Rafeian-Kopaei M, Heidarian E, Shahinfard N, Ansari R (2012) Postprandial hypolipidemic and hypoglycemic effects of *Allium hertifolium* and *Sesamum indicum* on hypercholesterolemic rabbits. *Afr J Pharm Pharmacol*; 6(15):1131-5.
36. Kohli K, Ali J, Ansari M, Raheman Z (2005) Curcumin: a natural antiinflammatory agent. *Indian J Pharmacol* 37 (3):141-7.
37. Hamilton JM (2001) Anticarcinogenic properties of tea (*Camellia sinensis*). *Journal of Medical Microbiology* 50: 299-302.
38. Chakurski I, Matev M, Koichev A (1981) Treatment of chronic colitis with anherbal combination of *Taraxacum officinale*, *Hipericum perforatum*, *Melissa officinalis* and *Foeniceum vulgare*. *Vutr Boles* 20: 51-4.
39. Fang J (2001) Effect of Fu-zhevg qu-xie on gastric disease infected with *Campylobacter pyloridis*. *Chin J Mod Devtrad Med*, 11:150-2.
40. Liux Han W, Sun D(2003). Treatment of intestinal metaplasia and atypical hyperplasia of gastric mucosa with xiao wei yan powder. *Chin Hotsa Chih* 12:602-3.
41. Shirzad H, Taji F, Rafeian-Kopaei M (2011) Correlation between antioxidant activity of garlic extracts and WEHI-164 fibrosarcoma tumor growth in BALB/c mice. *J Med Food*. Sep; 14(9):969-74.
42. Baradaran A, Nasri H, Rafeian-Kopaei M(2014). Oxidative stress and hypertension: Possibility of hypertension therapy with antioxidants. *J Res Med Sci*.19(4):358-67.
43. Akhlaghi M, Shanian Gh, Rafeian-Kopaei M, Parvin N, Saadat M, Akhlaghi M(2011) Citrus aurantium Blossom and Preoperative Anxiety. *Revista Brasileira de Anestesiologia* 61(6):702-712.
44. Hasanpour Z, Nasri H, Rafeian-Kopaei M, Ahmadi A, Baradaran A, Nasri P (2015) Paradoxical Effects of Atorvastatin on Renal Tubular Cells An Experimental Investigation. *Iran J Kidney Dis* ;9(3):215-20.
45. Karimi A, Moradi MT (2015) Total phenolic compounds and in vitro antioxidant potential of crude methanol extract and the correspond fractions of *Quercus brantii* L. acorn. *J Herbmed Pharmacol*; 4(1): 35-39.
46. Rafeian-Kopaei M, Nasri H, Nematbakhsh M, Baradaran A, Gheissari A, Rouhi H, Ahmadi Soleimani M, Baradaran-Ghahfarokhi M, Ghaed-Amini F, Ardalan M(2012). Erythropoietin ameliorates genotoxicity-induced renal toxicity: A biochemical and histopathological study. *J Nephropathology*; 1(2): 109-116.
47. Ilkhanizadeh B, Mehrshad A, Seddighnia A, Zarei L (2017) Comparison between effects of free and niosomal formulations of *Artemisia annua* L. (asteraceae) on chronic myelogenous leukemia (K562) cell line. *International Journal of Pharmacology*; 13(2):191-197.
48. Behroozi-Lak T, Zarei L, Molody-Tapeh M, Farhad N, Mohammadi R (2016) Protective effects of intraperitoneal administration of nimodipine on ischemia-reperfusion injury in ovaries: Histological and biochemical assessments in a rat model. *Journal of Pediatric Surgery* June 05.
49. Zarghani, SS, Soraya, H, Zarei, L, Alizadeh, M(2016) Comparison of three different diet-induced non alcoholic fatty liver disease protocols in rats: A pilot study. *Pharmaceutical Sciences*; 22(1):9-15.
50. Bakhtiary Z, Shahrooz R, Ahmadi A, Zarei L (2015) Protective effects of ethyl pyruvate on sperm quality in cyclophosphamide treated mice. *Iranian Journal of Reproductive Medicine* 291-296.