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Hepatoprotective Plants of Kashmir Himalaya

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Abstract
Liver is the site of various metabolic processes and is also responsible for the elimination of various xenobiotics from the body. Liver injury or liver dysfunction is a major health problem posing serious challenges to health care sector. According to WHO estimates, about 500 million people are affected by liver disorders. Plants are a source of various phytochemicals which could be used for the development of effective therapy to combat liver problems. In this review, attempt has been made to summarize the scientific data published on pharmacological activity of hepatoprotective plants used in traditional medicine by natives of Kashmir Himalayas.

Keywords: hepatoprotective plants, pharmacology, Kashmir Himalaya

1. Introduction
Liver being vital organ in body, is main site for various metabolic processes. Liver plays vital role in maintaining homeostasis of the body through these metabolic processes. Due to its centralized position in various life processes it is exposed to various xenobiotics as well. Liver toxicity induced by drugs is one of the major healthcare problems faced by the pharmaceutical industry and also drug regulatory agencies.
Elimination of harmful toxins is also one of the main fuctions of liver. As such alteration in its functions due to injury or exposure to harmful chemicals poses big challenge to the health of person. Though modern medicines have proven to be effective aginst various liver ailments, however they have little to offer in preventive therapies or cure of chronic liver ailments. As such under the phenomenon of "herbal renaissance" focus has now shifted towards plant-based medicines as they are offer better affordability, acceptability, and compatibility with minimal side effects.
Natural products are playing a vital role in health care for decades. Besides being source of vaious natural products, plants also produce phytochemicals, which serves as drugs or are key ingredients in formulation containing synthetic drugs. The selection of the plant species is a crucial factor for the ultimate success of investigation. Though random selection gives some hint, targeted collection based on chemotaxonomic relationships and ethnomedical information derived from Traditional Medicine are more likely to yield pharmacologically active compounds.

2. Area of study
Area of study of the current study is Kashmir Himalaya. Kashmir commonly called as the Kashmir Valley, is an integral but geologically younger part of the main Himalayan range. Politically it is an important province of the Jammu and Kashmir State accommodating much of its population and economic activity.
Kashmir lies between 33°20' and 34°54'N latitudes and 73°55' and 75°35'E longitudes, covering an area of 15,948 sq. km. Topographically, it is a deep elliptical bowl-shaped Valley bounded by lofty mountains of the Pir Panjal Range in the south and southwest and the Great Himalayan Range in the north and east, with 64% of the total area being mountainous. The Valley is an asymmetrical fertile basin stretching from southeast to northwesterly direction. Its diagonal length (from southeast to northwest corner) is 187 km, while the breadth varies considerably, being115.6 km along the latitude of Srinagar. The altitude of the floor of the Valley at Srinagar is 1600m (above the sea level) and the highest peak among its surrounding mountains is that of the Kolahoi or 'Gwashibror' (altitude 5,420m).Traversing the Valley is the river Jhelum and its tributaries, which feed many lakes for which Kashmir is famous.
In this study is summarized the scientific data published on Forty-eight (48) hepatoprotective plants used by inhabitants of Kashmir Himalayas under various local or Kashmiri names.

3. Methodology
A thorough survey of literature on the pharmacological profile of these plants was undertaken to collect the updated published data by using "Pubmed" and "Google Scholar" search engines. It was ensured that to test hepatoprotective activity well-established experimental models including carbon tetrachloride (CCl_4), thioacetamide, paracetamol, ethanol, and morphine induced liver damage were used. Furthermore, it was also ensured that the liver enzymes including aspartate transaminase (AST), alanine transaminase (ALT), alkaline phosphatase (APT), total protein (TP), and albumin (Alb) were used as a marker of liver injury. Literature search also included reversal of histopathological changes induced by toxin. Available data about the chemical constituent of the hepatoprotective plants and their toxicity has also been presented wherever it was available.
This study summarises in tabulated form (Table 1), the information about 48 hepatoprotective herbal drugs used in Kashmir Himalaya for the treatment of liver diseases including their botanical name, family, common name, local name/Kashmiri name, part of the plant used alongwith respective bibliographic references.

Table 1: Plants of Kashmir Himalayas with Hepatoprotective Activity.

S. No	Botanical Name	Family	Common name	Kashmiri name	Part used	References	Ref No.
1.	*Abelmoschus esculentus* (L.)	Malvaceae	*Okra, Lady's finger*	*Bhindi*	Whole plant	Saravanan S *et al.* 2013	[1]
2.	*Achillea millefolium* Linn.	Asteraceae	*Arrow-root, Bloodwort, Milfoil, Yarrow*	*Pahel gassa, Pahel kutch*	Whole plant	Gadgoli *et al*. 1995, Chauhan *et al.* 1994, Benedek 2007, Benedek 2006	[2, 3, 4, 5]
3.	*Achyranthes aspera* Linn	Amaranthaceae	*Chaff flower*	*Puthkunda*	Seeds, leaves	Khan N *et al.* 2015, Anantha KC *et al.* 2012, Kartik R *et al.* 2010, Krishnakumari S, *et al.*. 2006	[6, 7, 8, 9]
4	*Aconitum heterophyllum* Wall. ex. Royle,	Ranunculaceae	*Aconite*	*Patris*	Root	Subash AK *et al.* 2012	[1]0
5.	*Acorus calamus* Linn.	Araceae	*Sweet flag*	*Vai*	Whole plant	Ilaiyaraja N *et al.* 2011	[11]
6.	*Ailanthus altissima* (Mill) Swingle,	Simaroubaceae	*China-sumac, Stinktree, Tree of Heaven*	*Handoon*	Whole plant	Zhuo Z *et al.* 2015	[12]
7.	*Ajuga bracteosa* Wall. ex. Benth	Lamiaceae	*Bungle/ Nilkanthi.*	*Jan-i-adam*	Whole plant	Hsieh WT *et al.* 2011	[13]
8.	*Allium cepa* Linn.	Alliaceae	*Onion, Shallot*	*Gandh*	Bulb	Mete R *et al.* 2016	[14]
9.	*Allium sativum* Linn	Alliaceae	*Garlic*	*Rohan*	Bulb	Takemura S *et al.* 2017, Naji KM *et al.* 2017, Annamalai S *et al.* 2017, Oosthuizen C *et al.* 2017	[15, 16, 17, 18]
10.	*Amaranthus caudatus* Linn	Amaranthaceae	*Amaranth*	*Lissah, Haaskar*	Whole plant	Ashok Kumar BS *et al.* 2011	[1]9
11.	*Amaranthus spinosus* Linn.	Amaranthaceae	*Pigweed*	*Lissah,*	Whole plant	Rjeibi I *et al.* 2016, Mondal A *et al.* 2016, Zeashan H *et al.*2010, Zeashan H *et al.* 2009, Zeashan H *et al.* 2008	[20, 21, 22, 23, 24]
12.	*Angelica archangelica* Linn.	Apiaceae	*Angelica*	*Chohur*	Whole plant	Yeh ML *et al.* 2003, Hensel A *et al.* 2007, Raafat BM *et al.* 2013	[25, 26, 27]
13.	*Arctium lappa* Linn	Asteraceae	*Burdock*	*Phagorra*	Whole plant seeds	El-Kott AF *et al.* 2015, Kato *et al.* 1998, Fabrícia Souza Predes *et al.*2009	[28, 29, 30]
14.	*Arenaria serpyllifolia* Linn.	Caryophyllaceae	*Sandwort*	-	Aerial parts	Stocker P *et al.* 2004	[31]
15.	*Artemisia absinthium* Linn.	Asteraceae	*Absinth, Maderwort, Wormwood*	*Tethwan, Damer*	Whole plant	Saxena M *et al.* 2012, Amat N *et al.* 2010, Gilani AH *et al.* 1995	[32, 33, 34]
16	*Artemisia capillaris* Thunb	Asteraceae	*Absinth*	*Tethwan*	Whole plant	Janbaz KH *et al.* 2002, Gilani AH *et al.* 1993, Gilani AH *et al.* 1994, Wang ZQ *et al.* 2013	[35, 36, 37, 38]
17.	*Asparagus filicinus* Buch.-Ham. ex D.Don	Liliaceae	*Asparagus*	*Huleoon (Allipalli)*	Whole plant	Liu W *et al.* 2016	[39]
18.	*Asparagus officinalis* Linn	Liliaceae	*Garden aspargus*	*Aspargus*	Whole plant	Zhong C *et al.* 2015, Xiang J *et al.* 2014, Zhu X *et al.* 2010	[40, 41, 42]
19.	*Berberis lycium* Royle	Berberidaceae.	*Barberry.*	*Kawdach.*	Whole plant	Chand N *et al.* 2011	[4]3
20.	*Bupleurum longicaule var. himalayanse* (Kl.) Clarke	Apiaceae.	*Long-Stem Thorowax*	-	Root	Chou CC *et al.* 2003	[44]
21.	*Calendula officinalis* Linn.	Asteraceae	*Marigold.*	*Hamesh bahar.*	FlowerWhole plant	Preethi KC *et al.* 2009, Hamzawy MA *et al.* 2013, Rusu MA *et al.* 2005, Abdel-Aziem *et al.* 2014	[45, 46, 47, 48]
22.	*Capsella bursa-pastoris* (L.)	Brassicaceae.	*Shepherds purse*	*Kralmund.*	Whole plant	Kuroda *et al.* 1976	[49]
23.	*Carum carvi* Linn.,	Apiaceae.	*Caraway*	*Zeur*	Seeds	Samojlik I *et al.* 2010, Dadkhah A *et al.* 2011	[50, 51]
24.	*Celosia argentea* Linn.,	Amaranthaceae	*Cocks Comb*	*Mowal*	Whole plant	Hase K *et al.*. 1997, Hase K *et al.*. 1996	[52, 53]
25.	*Cichorium intybus* Linn.	Asteraceae	*Chicory*	*Wan-haandh*	Whole plant	Aktay G *et al.*. 2000, Ahmed B *et al.*. 2003, Zafar R *et al*.1998, Sultana S *et al.*1995	[54, 55, 56, 57]
26.	*Cuscuta chinensis* Lam.,	Cuscutaceae.	*Dodder*	*Kuklipoth*	Whole plant	Yen FL *et al.* 2007, Yen FL *et al.* 2008, Kim JS *et al.* 2017	[58, 59, 60]
27.	*Cydonia oblonga* Mill.,	Rosaceae	*Quince*	*Bumbchont*	Fruit	Mirmohammadlu M *et al.* 2015, Abliz A*et al.* 2014,	[61, 62]
28.	*Cynanchum auriculatum* Royle	Asclepiadaceae.	*Heart-Leaf Swallow-Wort*	-	Whole plant	Peng Y *et al.* 2015, Lv W *et al.* 2009, Peng YR *et al.* 2011	[63, 64, 65]
29.	*Cyperus rotundus* Linn.,	Cyperaceae	*Nut grass*	*Gaur gassa*	Rhizome	Chang *et al.*. 1984	[66]
31.	*Digitalis lanata* Ehrh.	Scrophulariaceae	*Grecian foxglove*	*Digitalis*	Whole plant	Durmaz I *et al.* 2016	[67]
32.	*Digitalis purpurea* Linn.,	Scrophuariaceae	*Common foxglove*	*Digitalis*	Whole plant	Fujino T *et al.* 2015	[68]

30.	*Eriobotrya japonica* Lindl.,	Rosaceae	*Loquat*	*Loquat*	Seeds, Leaves	Jiang WP *et al.* 2017, Jian T *et al.* 2017, Yoshioka S *et al.* 2010, Nishioka Y *et al.* 2002	[69, 70, 71, 72]
31.	*Ficus carica* Linn.,	Moraceae	*Fig*	*Anjoor*	Leaves Fruit	Stephen Irudayaraj S *et al.* 2017, Turan A *et al.*. 2016, Aghel N *et al.* 2011	[73, 74, 75]
32.	*Fumaria indica* (Hausskn.) Pugsley	Fumariaceae	*American fumitory*	*Shahtar*	Whole plant	Rao KS, Mishra SH. 1998	[76]
33.	*Glycyrrhiza glabra* Linn.	Papilionaceae.	*Licorice*	*Shanger*	Whole plant	Nose M., *et al.* 1994, Numuzaki, *et al.* 1994, Kuang Y *et al.* 2017, Hejazi II *et al.* 2017	[77, 78, 79, 80]
34.	*Linum usitatissimum* Linn.	Linaceae	*Flaxseed, flax, linseed.*	*Alish.*	Seeds	Endoh D *et al.* 2002, Hemmings SJ *et al.* 2004,	[81, 82]
35.	*Hemerocallis fulva* Linn.,	Liliaceae	*Daylilies*	-	Flower	Que F *et al.* 2007	[83]
36.	*Hypericum perforatum* Linn.,	Hypericaceae. (Clusiaceae)	*Common St. Johnswort*	*Basant*	Whole plant	Hohmann MS *et al.* 2015	[84]
37.	*Juglans regia* Linn.,	Juglandaceae.	*Walnut*	*Doon*	Leaf, Fruit	Eidi A *et al.* 2013, Shimoda H *et al.* 2009	[85, 86]
38.	*Marrubium vulgare* Linn.,	Lamiaceae	*White horehound*	*Troper*	Whole plant	Ettaya A *et al.* 2016, Elberry AA *et al.* 2010, Ahmed B *et al.* 2010	[87, 88, 89]
39.	*Medicago sativa* Linn.,	Papilionaceae.	*Alfalfa*	-	Whole plant	Al-Dosari MS 2012	[90]
40.	*Peganum harmala* Linn.,	Zygophyllaceae	*Rue*	*Isband*	Whole plant	Bourogaa E *et al.* 2015, Soliman AM *et al.* 2013	[91, 92]
41.	*Picrorhiza kurrooa* Royle. ex Benth,	Scrophulariaceae	*Kutki*	*Chobikhor*	Whole plant	Rastogi R *et al.* 2001, Saraswat B *et al.* 1999, Vaidya AB *et al.* 1996, Chaturvedi GN *et al.*.1996, Verma PC *et al.* 2009	[93, 94, 95, 96, 97]
42.	*Plantago lanceolata* Linn.	Plantaginaceae	*Plantain*	*Gulla*	Whole plant	Karpilovskaia *et al*... 1989	[98]
43.	*Podophyllum hexandrum* Royle,	Podophyllaceae	*May-apple*	*Ban Wangun*	Whole plant	Ganie SA *et al.* 2013, Ganie SA *et al.* 2011, Ganie SA *et al.* 2012	[99, 100, 101]
44.	*Portulaca oleracea* Linn.	Portulacaceae	*Purslane*	*Nunar*	Whole plant	Guoyin Z *et al.* 2017, Liu XF *et al.* 2015, Shi H *et al.* 2014	[102, 103, 104]
45.	*Rheum australe* D. Don	Polygonaceae	*Rhubarb*	*Pumbachalan*	Whole plant	Rokaya MB *et al.* 2012	[105]
46.	*Rosmarinus officinalis* Linn.,	Lamiaceae.	*Rosemary*	*Rosemary*	Whole plant	Amin A *et al.* 2005	[106]
47.	*Saussurea costus* (Falc.) Lipschitz	Asteraceae	*Costus*	*Kuth*	Whole plant	Chen HC, *et al.* Suhaib MJ *et al.* 1998	[107, 108]
48.	*Viscum album* Linn.,	Loranthaceae	*Mistletoe*	*Aal*	Whole plant	Kim WH *et al.* 2004	[109]

4. Conclusions

Medicinal plants are potential renewable natural resources and are generally considered to play a beneficial role in human health care. In view of adverse effects associated with the synthetic drugs, plants are safer, cheaper and much effective alternatives. The medicinal value of these plants lies in phytochemicals that produce a definite physiological action on the human body. Hepatoprotective activity of the plants in the current review need further investigation to translate it into the formulation of modern drugs after proper scientific evaluation of biomolecules, their mechanism of action, toxicity and appropriate standardization.

5. References

1. Saravanan S, Pandikumar P, Pazhanivel N, Paulraj MG, *et al*. Hepatoprotective role of *Abelmoschus esculentus* (Linn.) Moench, on carbon tetrachloride-induced liver injury. Toxicol Mech Methods. 2013; 23(7):528-36.
2. Gadgoli C, Mishra SH. Preliminary screening of *Achillea millefolium*, *Cichorium intybus* and *Capparis spinosa* for antihepatotoxic activity. Fitoterapia. 1995; 66(4):319-323.
3. Chauhan BL, Mohan AR. *et al*. Bioassay for evaluation of the hepatoprotective effect of LIV.52, a polyherbal formulation, on ethanol metabolism in chronic alcohol-exposed rats. Indian Journal of Pharmacology. 1994; 26(2):117-120.
4. Benedek B, Kopp B. *Achillea millefolium* L. s.l. revisited: recent findings confirm the traditional use. Wien Med Wochenschr. 2007;157(13-14):312-4.
5. Benedek B, Geisz N, Jäger W, Thalhammer T, Kopp B. Choleretic effects of yarrow (*Achillea millefolium* s.l.) in the isolated perfused rat liver. Phytomedicine. 2006; 13(9-10):702-6.
6. Khan N, Akhtar MS, Khan BA, Braga Vde A, *et al*. Antiobesity, hypolipidemic, antioxidant and hepatoprotective effects of Achyranthes aspera seed saponins in high cholesterol fed albino rats. *Arch Med Sci*. 2015; 11(6):1261-71.
7. Anantha KC, Siva RC, Manohar RA. Hepatoprotective effect of biherbal ethanolic extract against paracetamol-induced hepatic damage in albino rats. J Ayurveda Integr Med. 2012; 3(4):198-203.
8. Kartik R, Rao ChV, Trivedi SP, Pushpangadan P, Reddy GD. Amelioration effects against N-nitrosodiethylamine and CCl (4)-induced

hepatocarcinogenesis in Swiss albino rats by whole plant extract of *Achyranthes aspera*. Indian J Pharmacol. 2010; 42(6):370-5.
9. Krishnakumari S, Priya K. Hypolipidemic Efficacy of Achyranthes aspera on Lipid Profile in Sesame oil fed Rats. Anc Sci Life. 2006 Jan; 25(3-4):49-56.
10. Subash AK, Augustine A. Hypolipidemic effect of methanol fraction of *Aconitum heterophyllu*m wall ex Royle and the mechanism of action in diet-induced obese rats. J Adv Pharm Technol Res. 2012; 3(4):224-8.
11. Ilaiyaraja N, Khanum F. Amelioration of alcohol-induced hepatotoxicity and oxidative stress in rats by Acorus calamus. J Diet Suppl. 2011; 8(4):331-45.
12. Zhuo Z, Hu J, Yang X, Chen M, *et al*. Ailanthone Inhibits Huh7 Cancer Cell Growth via Cell Cycle Arrest and Apoptosis In Vitro and In Vivo. *Sci Rep*. 2015; 5:16185.
13. Hsieh WT, Liu YT, Lin WC. Anti-inflammatory properties of *Ajuga bracteosa* in vivo and in vitro study and their effects on mouse model of liver fibrosis. *J* Ethnopharmacol. 2011; 135(1):116-25.
14. Mete R, Oran M, Topcu B, Oznur M, *et al*. Protective effects of onion (Allium cepa) extract against doxorubicin-induced hepatotoxicity in rats. Toxicol Ind Health. 2016; 32(3):551-7.
15. Takemura S, Azuma H, Osada-Oka M, Kubo S, *et al*. S-allyl-glutathione improves experimental liver fibrosis by regulating Kupffer cell activation in rats. Am J Physiol Gastrointest Liver Physiol. 2018; 314(2):150-163.
16. Naji KM, Al-Shaibani ES, Alhadi FA, Al-Soudi SA, *et al*. Hepatoprotective and antioxidant effects of single clove garlic against CCl_4-induced hepatic damage in rabbits. BMC Complement Altern Med. 2017; 17(1):411.
17. Annamalai S, Mohanam L, Raja V, Dev A, *et al*. Antiobesity, antioxidant and hepatoprotective effects of Diallyl trisulphide (DATS) alone or in combination with Orlistat on HFD induced obese rats. Biomed Pharmacother. 2017; 93:81-87.
18. Oosthuizen C, Arbach M, Meyer D, Hamilton C, Lall N. Diallyl Polysulfides from *Allium sativum* as Immunomodulators, Hepatoprotectors, and Antimycobacterial Agents. J Med Food. 2017; 20(7):685-690.
19. Ashok Kumar BS, Lakshman K, Arun Kumar PA, Viswantha GL, *et al*. Hepatoprotective activity of methanol extracts of *Amaranthus caudatus* Linn. against paracetamol-induced hepatic injury in rats. Zhong Xi Yi Jie He Xue Bao. 2011; 9(2):194-200.
20. Rjeibi I, Ben Saad A, Hfaiedh N. Oxidative damage and hepatotoxicity associated with deltamethrin in rats: The protective effects of *Amaranthus spinosus* seed extract. Biomed Pharmacother.2016; 84:853-860.
21. Mondal A, Guria T, Maity TK, Bishayee A. A Novel Tetraenoic Fatty Acid Isolated from *Amaranthus spinosus* Inhibits Proliferation and Induces Apoptosis of Human Liver Cancer Cells. Int J Mol Sci. 2016; 17(10):1604
22. Zeashan H, Amresh G, Singh S, Rao CV. Protective effect of *Amaranthus spinosus* against D-galactosamine/lipopolysaccharide-induced hepatic failure. Pharm Biol. 2010; 48(10):1157-63.
23. Zeashan H, Amresh G, Singh S, Rao CV. Hepatoprotective and antioxidant activity of *Amaranthus spinosus* against CCl_4 induced toxicity. J Ethnopharmacol. 2009; 125(2):364-6.
24. Zeashan H, Amresh G, Singh S, Rao CV. Hepatoprotective activity of *Amaranthus spinosus* in experimental animals. Food Chem Toxicol. 2008; 46(11):3417-21.
25. Yeh ML, Liu CF, Huang CL, Huang TC. Hepatoprotective effect of *Angelica archangelica* in chronically ethanol-treated mice. Pharmacology. 2003; 68(2):70-3.
26. Hensel A, Deters AM, Müller G, Stark T, *et al*. Occurrence of N-phenylpropenoyl-L-amino acid amides in different herbal drugs and their influence on human keratinocytes, on human liver cells and on adhesion of Helicobacter pylori to the human stomach. Planta Med. 2007; 73(2):142-50.
27. Raafat BM, Saleh A, Shafaa MW, Khedr M, *et al*. Ginkgo biloba and Angelica archangelica bring back an impartial hepatic apoptotic to anti-apoptotic protein ratio after exposure to technetium 99mTc. Toxicol Ind Health. 2013; 29(1):14-22.
28. El-Kott AF, Bin-Meferij MM. Use of *Arctium lappa* Extract Against Acetaminophen-Induced Hepatotoxicity in Rats. Biochem Biophys Res Commun. 2015; 468(4):837-42.
29. Kato T, Hirose M, Takahashi S, Hasegawa R, *et al*. Effects of the lignan, arctiin, on 17-beta ethinyl estradiol promotion of preneoplastic liver cell foci development on rats. Anticancer Res. 1998; 18(2A):1053-1057.
30. Fabrícia Souza Predes; Sérgio Luis Pinto da Matta; Juliana Castro Monteiro, Tânia Toledo de Oliveira. Investigation of liver tissue and biochemical parameters of adult wistar rats treated with *Arctium lappa* L. Brazilian Archives of Biology and Technology, 2009, 52(2).
31. Stocker P, Yousfi M, Djerridane O, Perrier J, *et al*. Effect of flavonoids from various Mediterranean plants on enzymatic activity of intestinal carboxylesterase. Biochimie. 2004 Dec; 86(12):919-25.
32. Saxena M, Shukla S. Reversal of carbon tetrachloride-induced hepatic injury by aqueous extract of *Artemisia absinthium* in Sprague-Dawley rats. J Environ Pathol Toxicol Oncol. 2012; 31(4):325-34.
33. Amat N, Upur H, Blazeković B. In vivo hepatoprotective activity of the aqueous extract of *Artemisia absinthium* L. against chemically and immunologically induced liver injuries in mice. J Ethnopharmacol. 2010; 131(2):478-84.
34. Gilani AH, Janbaz KH. Preventive and curative effects of *Artemisia absinthium* on acetaminophen and CCl4-induced hepatotoxicity. Gen Pharmacol. 1995; 26(2):309-15.
35. Janbaz KH, Saeed SA, Gilani AH. Protective effect of rutin on paracetamol and CCl_4-induced hepatotoxicity in rodents. Fitoterapia. 2002; 73(7-8):557-63.
36. Gilani AH, Janbaz KH. Protective effect of *Artemisia scoparia* extract against acetaminophen-induced hepatotoxicity. Gen Pharmacol. 1993: 24(6):1455-8.
37. Gilani AH, Janbaz KH. Hepatoprotective effects of *Artemisia scoparia* against carbon tetrachloride: an

environmental contaminant. J Pak Med Assoc. 1994 Mar; 44(3):65-8.
38. Wang ZQ, Zhang XH, Yu Y, Tipton RC, *et al*. Artemisia scoparia extract attenuates non-alcoholic fatty liver disease in diet-induced obesity mice by enhancing hepatic insulin and AMPK signaling independently of FGF21 pathway. Metabolism. 2013 Sep; 62(9):1239-49.
39. Liu W, Ning R, Chen RN, Huang XF, *et al*. Aspafilioside B induces G2/M cell cycle arrest and apoptosis by up-regulating H-Ras and N-Ras via ERK and p38 MAPK signaling pathways in human hepatoma HepG2 cells. Mol Carcinog. 2016 May; 55(5):440-57.
40. Zhong C, Jiang C, Xia X, Mu T, *et al*. Antihepatic Fibrosis Effect of Active Components Isolated from Green Asparagus (*Asparagus officinalis* L.) Involves the Inactivation of Hepatic Stellate Cells. J Agric Food Chem.2015 Jul 8;63(26):6027-34.
41. Xiang J, Xiang Y, Lin S, Xin D, *et al*. Anticancer effects of deproteinized asparagus polysaccharide on hepatocellular carcinoma in vitro and in vivo. Tumour Biol. 2014 Apr; 35(4):3517-24.
42. Zhu X, Zhang W, Zhao J, Wang J, *et al*. Hypolipidaemic and hepatoprotective effects of ethanolic and aqueous extracts from *Asparagus officinalis* L. by-products in mice fed a high-fat diet. J Sci Food Agric. 2010; 90(7):1129-35.
43. Chand N, Durrani FR, Ahmad S, Khan A. Immunomodulatory and hepatoprotective role of feed-added *Berberis lycium* in broiler chicks. J Sci Food Agric. 2011; 91(10):1737-45.
44. Chou CC, Pan SL, Teng CM, Guh JH. Pharmacological evaluation of several major ingredients of Chinese herbal medicines in human hepatoma Hep3B cells. Eur J Pharm Sci. 2003; 19(5):403-12.
45. Preethi KC, Kuttan R. Hepato and renoprotective action of *Calendula officinalis* L. flower extract. Indian J Exp Biol. 2009; 47(3):163-8.
46. Hamzawy MA, El-Denshary ES, Hassan NS, Mannaa FA, Abdel-Wahhab MA. Dietary Supplementation of *Calendula officinalis* counteracts the Oxidative Stress and LiverDamage Resulted from Aflatoxin. ISRN Nutr. 2013 Feb 12; 2013; 538427. doi:10.5402/2013/538427
47. Rusu MA, Tamas M, Puica C, Roman I, *et al*. The hepatoprotective action of ten herbal extracts in CCl4 intoxicated liver. Phytother Res. 2005; 19(9):744-9.
48. Abdel-Aziem SH, Hassan AM, El-Denshary ES, Hamzawy MA, *et al*. Ameliorative effects of thyme and calendula extracts alone or in combination against aflatoxins-induced oxidative stress and genotoxicity in rat liver. Cytotechnology. 2014; 66(3):457-70.
49. Kuroda K, Akao M, Kanisawa M, Miyaki K. Inhibitory effect of *Capsella bursa –pastoris* on hepatocarcino-genesis induced by 3-methyl-4-(dimethylamino) azobenzene in rats. Cancer Res. 1976; 36(6):1900-1903.
50. Samojlik I, Lakić N, Mimica-Dukić N, Daković-Svajcer K, *et al*. Antioxidant and hepatoprotective potential of essential oils of coriander (Coriandrum sativum L.) and caraway (Carum carvi L.) (Apiaceae). J Agric Food Chem. 2010; 58(15):8848-53.
51. Dadkhah A, Allameh A, Khalafi H, Ashrafihelan J. Inhibitory effects of dietary caraway essential oils on 1, 2-dimethylhydrazine-induced colon carcinogenesis is mediated by liver xenobiotic metabolizing enzymes. Nutr Cancer. 2011; 63(1):46-54.
52. Hase K, Basnet P, Kadota S, Namba T. Immunostimulating activity of Celosian, an antihepatotoxic polysaccharide isolated from *Celosia argentea.* Planta Med. 1997; 63(3):216-9.
53. Hase K, Kadota S, Basnet P, Takahashi T, Namba T. Protective effect of celosian, an acidic polysaccharide, on chemically and immunologically induced liver injuries. Biol Pharm Bull. 1996; 19(4):567-72.
54. Aktay G, Deliorman D, Ergun E, Ergun F, Yesilada E, Cevik C. Hepatoprotective effects of Turkish folk remedies on experimental liver injury. J Ethnopharmacol. 2000; 73(1-2):121-9.
55. Ahmed B, Al-Howiriny TA, Siddiqui AB.Antihepatotoxic activity of seeds of *Cichorium intybus.* J Ethnopharmacol. 2003; 87(2-3):237-40.
56. Zafar R, Mujahid Ali S. Anti-hepatotoxic effects of root and root callus extracts of *Cichorium intybus* L. J Ethnopharmacol.1998; 63(3):227-31.
57. Sultana S, Perwaiz S, Iqbal M, Athar M.Crude extracts of hepatoprotective plants, *Solanum nigrum* and *Cichorium intybus* inhibit free radical-mediated DNA damage. *J* Ethnopharmacol. 1995; 45(3):189-92.
58. Yen FL, Wu TH, Lin LT, Lin CC. Hepatoprotective and antioxidant effects of *Cuscuta chinensis* against acetaminophen-induced hepatotoxicity in rats. J Ethnopharmacol. 2007; 111(1):123-8.
59. Yen FL, Wu TH, Lin LT, Cham TM, *et al*. Nanoparticles formulation of *Cuscuta chinensis* prevents acetaminophen-induced hepatotoxicity in rats. Food Chem Toxicol. 2008; 46(5):1771-7.
60. Kim JS, Koppula S, Yum MJ, Shin GM, *et al*. Anti-fibrotic effects of Cuscuta chinensis with in vitro hepatic stellate cells and a thioacetamide-induced experimental rat model. Pharm Biol. 2017; 55(1):1909-1919.
61. Mirmohammadlu M, Hosseini SH, Kamalinejad M, Esmaeili Gavgani M, *et al*. Hypolipidemic, Hepatoprotective and Renoprotective Effects of *Cydonia Oblonga* Mill. Fruit in Streptozotocin-Induced Diabetic Rats. Iran J Pharm Res. 2015; 14(4):1207-14.
62. Abliz A, Aji Q, Abdusalam E, Sun X, *et al*. Effect of *Cydonia oblonga* Mill. leaf extract on serum lipids and liver function in a rat model of hyperlipidaemia. J Ethnopharmacol. 2014; 151(2):970-4.
63. Peng Y, Ding Y. Pharmacokinetics and tissue distribution study of caudatin in normal and diethylnitrosamine-induced hepatocellular carcinoma model rats. Molecules. 2015; 20(3):4225-37.
64. Lv W, Zhang A, Xu S, Zhang H. Effects of general glycosides in *Cynanchum auriculatum* of Jiangsu province on liver fibrosis of rats. Zhongguo Zhong Yao Za Zhi. 2009; 34(19):2508-11
65. Peng YR, Ding YF, Wei YJ, Shu B, *et al*. Caudatin-2,6-dideoxy-3-O-methy-β-D-cymaropyranoside 1 induced apoptosis through caspase 3-dependent pathway in human hepatoma cell line SMMC7721. Phytother Res. 2011; 25(5):631-7.
66. Chang IM, Yun HS. Plants with liver-protective activities, pharmacology and toxicology of aucubin.

Advances in Chinese Medicinal Materials Research. World Scientific Press, Philadelphia, PA. 1984: 269-285.
67. Durmaz I, Guven EB, Ersahin T, Ozturk M, *et al*. Liver cancer cells are sensitive to Lanatoside C induced cell death independent of their PTEN status. Phytomedicine. 2016; 23(1):42-51.
68. Fujino T, Kuroda M, Matsuo Y, Kubo S, *et al* Cardenolide glycosides from the seeds of *Digitalis purpurea* exhibit carcinoma-specific cytotoxicity toward renal adenocarcinoma and hepatocellular carcinoma cells. Biosci Biotechnol Biochem. 2015; 79(2):177-84.
69. Jiang WP, Huang SS, Matsuda Y, Saito H, *et al*. Protective Effects of Tormentic Acid, a Major Component of Suspension Cultures of *Eriobotrya japonica* Cells, on Acetaminophen-Induced Hepatotoxicity in Mice. Molecules. 2017; 22(5):pii: E830.
70. Jian T, Ao X, Wu Y, Lv H, *et al*. Total sesquiterpene glycosides from Loquat (*Eriobotrya japonica*) leaf alleviate high-fat diet induced non-alcoholic fatty liver disease through cytochrome P450 2E1 inhibition. Biomed Pharmacother. 2017; 91:229-237.
71. Yoshioka S, Hamada A, Jobu K, Yokota J, *et al*. Effects of Eriobotrya japonica seed extract on oxidative stress in rats with non-alcoholic steatohepatitis. J Pharm Pharmacol. 2010; 62(2):241-6.
72. Nishioka Y, Yoshioka S, Kusunose M, Cui T, Hamada A, Ono M, Miyamura M, Kyotani S. Effects of extract derived from *Eriobotrya japonica* on liver function improvement in rats. Biol Pharm Bull. 2002; 25(8):1053-7.
73. Stephen Irudayaraj S, Christudas S, Antony S, Duraipandiyan V, Naif Abdullah AD, Ignacimuthu S. Protective effects of Ficus carica leaves on glucose and lipids levels, carbohydrate metabolism enzymes and β-cells in type 2 diabetic rats. Pharm Biol. 2017: 55(1):1074-1081.
74. Turan A, Celik I. Antioxidant and hepatoprotective properties of dried fig against oxidative stress and hepatotoxicity in rats. Int J Biol Macromol. 2016; 91:554-9.
75. Aghel N, Kalantari H, Rezazadeh S. Hepatoprotective Effect of Ficus carica Leaf Extract on Mice Intoxicated with Carbon Tetrachloride. Iran J Pharm Res. 2011; 10(1):63-8.
76. Rao KS, Mishra SH. Antihepatotoxic activity of monomethyl fumarate isolated from *Fumaria indica*. J Ethnopharmacol. 1998; 60(3):207-13.
77. Nose M, Ito M, Kamimura K, Shimizu M, Ogihara Y. A comparison of the antihepatotoxic activity between glycyrrhizin and glycyrrhetinic acid. Planta Med. 1994; 60(2):136-9.
78. Numuzaki K, Umetsu M, Chiba S. Effects of glycyrrhizin in children with liver dysfunction associated with cytomegalovirus infections. Tohoku J. Exp. Med. 1994; 172:147-153.
79. Kuang Y, Lin Y, Li K, Song W, *et al*. Screening of hepatoprotective compounds from licorice against carbon tetrachloride and acetaminophen induced HepG2 cells injury. Phytomedicine, 2017; 34:59-66.
80. Hejazi II, Khanam R, Mehdi SH, Bhat AR, *et al*. New insights into the antioxidant and apoptotic potential of *Glycyrrhiza glabra* L. during hydrogen peroxide mediated oxidative stress: An in vitro and in silico evaluation. Biomed Pharmacother. 2017; 94:265-279.
81. Endoh D, Okui T, Ozawa S, Yamato O, *et al*. Protective effect of a lignan-containing flaxseed extract against CCl_4-inducedhepatic injury. Vet Med Sci. 2002; 64(9):761-5.
82. Hemmings SJ, Westcott N, Muir A, Czechowicz D. The effects of dietary flaxseed on the Fischer 344 rat: II. Liver gamma-glutamyltranspeptidase activity.Cell Biochem Funct. 2004; 22(4):225-31.
83. Que F, Mao L, Zheng X. In vitro and vivo antioxidant activities of daylily flowers and the involvement of phenolic compounds. Asia Pac J Clin Nutr. 2007; 16(Suppl 1):196-203.
84. Hohmann MS, Cardoso RD, Fattori V, Arakawa NS, *et al Hypericum perforatum* Reduces Paracetamol-Induced Hepatotoxicity and Lethality in Mice by Modulating Inflammation and Oxidative Stress. Phytother Res. 2015; 29(7):1097-101.
85. Eidi A, Moghadam JZ, Mortazavi P, Rezazadeh S, Olamafar S. Hepatoprotective effects of Juglans regia extract against CCl4-induced oxidative damage in rats. Pharm Biol. 2013; 51(5):558-65.
86. Shimoda H, Tanaka J, Kikuchi M, Fukuda T, *et al*. Effect of polyphenol-rich extract from walnut on diet-induced hypertriglyceridemia in mice via enhancement of fatty acid oxidation in the liver. J Agric Food Chem. 2009; 57(5):1786-92.
87. Ettaya A, Dhibi S, Samout N, Elfeki A, Hfaiedh N. Hepatoprotective activity of white horehound (*Marrubium vulgare*) extract against cyclophosphamide toxicity in male rats. Can J Physiol Pharmacol. 2016; 94(4):441-7.
88. Elberry AA, Harraz FM, Ghareib SA, Nagy AA, *et al*. Antihepatotoxic effect of *Marrubium vulgare* and *Withania somnifera* extracts on carbon tetrachloride-induced hepatotoxicity in rats. J Basic Clin Pharm. 2010; 1(4):247-54.
89. Ahmed B, Masoodi MH, Siddique AH, Khan S. A new monoterpene acid from *Marrubium vulgare* with potential antihepatotoxic activity. Nat Prod Res. 2010; 24(18):1671-80.
90. Al-Dosari MS. In vitro and in vivo antioxidant activity of alfalfa (*Medicago sativa* L.) on carbon tetrachloride intoxicated rats. Am J Chin Med. 2012; 40(4):779-93.
91. Bourogaa E, Jarraya RM, Damak M, Elfeki A. Hepatoprotective activity of *Peganum harmala* against ethanol-induced liver damages in rats. Arch Physiol Biochem. 2015; 121(2):62-7.
92. Soliman AM, Abu-El-Zahab HS, Alswiai GA. Efficacy evaluation of the protein isolated from *Peganum harmala* seeds as an antioxidant in liver of rats. Asian Pac J Trop Med. 2013; 6(4):285-95.
93. Rastogi R, Srivastava A K, Rastogi AK. Long term effect of aflatoxin B (1) on lipid peroxidation in Rat liver and Kidney: effect of picroliv and silymarin. Phytother. Res. 2001; 15(4):307-10.
94. Saraswat B, Visen PK, Patnaik GK, Dhawan BN. Ex vivo and in vivo investigation of picroliv from *Picrorhiza kurroa* in an alcohol intoxication model in rats. Ethnopharmacol. 1999; 66(3):263-9.
95. Vaidya AB, Antarkar DS, Doshi JC, Bhatt AD, *et al*. *Picrorhiza kurroa* (kutki) Royle ex. Benth. as a

hepatoprotective agent- experimental and clinical studies. J Post Grad. Med. 1996; 42(4):105-8.
96. Chaturvedi GN, Singh RH. Jaundice of infectious hepatitis and its treatment with an indigenous drug Picrorhiza kurrooa. J Res. Indian Med, 1996; 1:1-14
97. Verma PC, Basu V, Gupta V, Saxena G, *et al*. Pharmacology and chemistry of a potent hepatoprotective compound Picroliv isolated from the roots and rhizomes of *Picrorhiza kurroa* royle ex benth. (kutki). Curr Pharm Biotechnol. 2009; 10(6):641-9.
98. Karpilovskaia ED, Gorban GP, Pliss MB, Zakharenko LN, *et al*. Inhibiting effect of the polyphenolic complex from *Plantago major* (Plantastine) on the carcinogenic effect of endogenously synthesized nitroso dimethylamine. Farmakol. Toksikol. 1989; 52(4):64-67.
99. Ganie SA, Zargar BA, Masood A, Zargar MA. Hepatoprotective and antioxidant activity of rhizome of *Podophyllum hexandrum* against carbon tetra chloride induced hepatotoxicity in rats. Biomed Environ Sci. 2013; 26(3):209-21
100. Ganie SA, Haq E, Masood A, Hamid A, *et al* Antioxidant and protective effect of ethyl acetate extract of *Podophyllum hexandrum* rhizome on carbon tetrachloride induced rat liver injury. Evid Based Complement Alternat Med, 2011, 238020. doi: 10:1155/2011/238020
101. Ganie SA, Amin S, Hamid R, Hamid A, *et al*. *Podophyllum hexandrum* aqueous extract as a potential free radical scavenger. Redox Rep. 2012; 17(2):54-62.
102. Guoyin Z, Hao P, Min L, Wei G, Zhe C, Changquan L. Antihepatocarcinoma Effect of *Portulaca oleracea* L. in Mice by PI3K/Akt/mTOR and Nrf2/HO-1/NF-κB Pathway. Evid Based Complement Alternat Med. 2017; 2017:8231358.
103. Liu XF, Zheng CG, Shi HG, Tang GS, *et al*. Ethanol extract from *Portulaca oleracea* L. attenuated acetaminophen-induced mice liver injury. Am J Transl Res. 2015; 7(2):309-18.
104. Shi H, Liu X, Tang G, Liu H, *et al*. Ethanol extract of *Portulaca Oleracea* L. reduced the carbon tetrachloride induced liver injury in mice involving enhancement of NF-κB activity. Am J Transl Res. 2014; 6(6):746-55.
105. Rokaya MB, Münzbergová Z, Timsina B, Bhattarai KR. Rheum australe D. Don: a review of its botany, ethnobotany, phytochemistry and pharmacology. J Ethnopharmacol. 2012; 141(3):761-74.
106. Amin A, Hamza AA. Hepatoprotective effects of *Hibiscus*, *Rosmarinus* and *Salvia* on azathioprine-induced toxicity in rats. Life Sci. 2005; 77(3):266-78.
107. Chen HC, Chou CK, Lee SD, Wang JC, *et al*. Active compounds from *Saussurea lappa* Clarks that suppress hepatitis B virus surface antigen gene expression in human hepatoma cells. Antiviral Res. 1995; 27(1-2):99-109.
108. Suhaib Ahmad MJ, Qadri SYH. Scientific evaluation of "Qusth" (*Saussurea lappa* Clarke.) with special reference to pharmacological studies. Post Graduate Department Ilmul Advia (Pharmacology), Government Nizamia Tibbia College, Hyderabad, Andhra Pradesh, 1998.
109. Kim WH, Park WB, Gao B, Jung MH. Critical role of reactive oxygen species and mitochondrial membrane potential in Korean mistletoe lectin-induced apoptosis in human hepatocarcinoma cells. Mol Pharmacol. 2004; 66(6):1383-96.