



HEPATOPROTECTION BY NATURAL PRODUCTS: A RECENT UPDATE

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Abstract

Liver is the largest gland in human body. It plays vital role in clearing the various toxic and chemical agents. It is also susceptible to diseases from these toxic and chemical agents. There are numerous commercially accessible medicine, ingestion of these medicine leads to consequences in medicine induced liver injury. Hepatotoxicity by drug is one of most leading cause of mortality and its prevalence increase exponentially day by day. Irrespective of enormous improvements in targeted drug, there are no entirely active drugs supportive liver function and provide safety of the organ without producing toxic effect. As a consequence, it is necessary to identify low toxic substitutes for the management of hepatotoxicity. There are many natural medicine such as plants source and nutraceuticals play essential characters in human health care: various scientific studies have showed that positive properties on liver protection can be recognized to the existence of phytochemicals. This review focuses on management of hepatotoxicity by the natural product.

Keywords: Hepatoprotection, hepatotoxicity, phytochemicals.

Introduction

Liver is the major organ in the human body. It perform numerous function including carbohydrate, lipid and protein metabolism and also help in clearing of many medicine, xenobiotic and synthetic compounds present in the body. Throughout this cleansing action, the toxic metabolite form that cause the hepatotoxicity rigorously (Dey *et al.*, 2013). These detoxification of the harmful chemicals, which results in various liver disease such as hepatotoxicity (Thompson *et al.*, 2017).

There are various reason for hepatotoxicity such as chemicals (pollution, carbon tetrachloride), (Dua *et al.*, 2019) drugs (anti-tubercular drug, anti-viral drug, opioids) and metals (Bawa *et al.*, 2019). During the hepatotoxicity cytokines are activated by the macrophages which is signal for hepatocytes inflammation (Mehta *et al.*, 2019). The usage of herbal product and ingesting of various nutraceutical play an important role in the well-being and many research has been specified in the, herbal product and nutraceutical have advantageous properties can be attributed to the existence of natural product which are known as phytoconstituents (Madrigal-santillán *et al.*, 2014).

There are many floras show a significant character in the social well-being protection. About more than 80% of the global community depend in the usage of conventional medication that is primarily basis on herbal resources (Areefa Shaik, A Elumalai, 2012). The approximately 7,500 floras have utilize in native well-being societies in the, ethnic communities of India. In short, the approximately 4,000 plants still unknown to population (Roy *et al.*, 2014). From the previous year nutraceutical also gain the popularity for the treatment of hepatotoxicity. "Nutraceutical" is defined as the diet or amount of diet that offers therapeutic or well-being benefits and also help in management of various disorder. There are various nutraceutical sources such as green vegetables, diary product (Nagpal *et al.*, 2012), fruits, nuts, grains, phytoconstituents and many more. Fisetin is one of the major constituents found in approximately all nutraceuticals (Kumar *et al.*, 2019a). From these nutraceuticals sources various constituents are extract such as

fisetin, vanillin (Abhinav Anand *et al.*, 2019), betaine (Kaur *et al.*, 2019), quercetin (Chellappan *et al.*, 2019; Prashar *et al.*, 2019; Khurshed *et al.*, 2020), crocin (from stigmas of *Crocus sativus*) (Dar *et al.*, 2017), curcumin (Som *et al.*, 2020; Garg *et al.*, 2019; Kaur *et al.*, 2018) for making herbal medicine. Screening of various phytoconstituents is importance to for treatment of hepatotoxicity and other disease also (Anand *et al.*, 2017). These phytoconstituents contain various activity such as antioxidants (Willd *et al.*, 2018; Kumar *et al.*, 2018a; (Farooq and Sehgal, 2018), antimicrobials (Sarma *et al.*, 2018), anti-inflammatory activity (Kumar *et al.*, 2018b; Prasad *et al.*, 2013; Kumar *et al.*, 2019b). All these activity are determine by in vivo method. Apart from this now days various software are available which detect these activity (Rao *et al.*, 2020) Currently 470 herbal medicine with well standard form are available in the markets (Gupta *et al.*, 2019). These herbal medicine help in treatment of liver disease and also improve nutrition level in body (Rajasekaran *et al.*, 2008). These nutraceutical also help to treat various kind of cancer patients (Muthuraman *et al.*, 2011; Kumar *et al.*, 2010; Patel, 2014).

Nutraceutical such as various citrus fruits like orange, grapes, lemons, lime, kiwi, tangerine these all are increase vitamins, minerals, antioxidants level in body (Motawe *et al.*, 2015). Moreover, the experimental evidence of the natural medications for treating the liver disease has a long history, and the use of traditional medicinal plants and nutraceuticals by a many individuals and the diverse constituents extract from these plant and nutraceuticals. Generally, hepatoprotective nutraceutical and plants contain a variety of chemical constituent like alkaloids, glycoside phenols, coumarins, essential oils, monoterpenes, vitamins, minerals, carotenoids, flavonoids and xanthenes (Madrigal-Santillán E, Madrigal-Bujaidar E and S, Valadez-Vega MC, 2013). There are numerous herbal product existing in the medicine system. Generally, this plant product and nutraceutical have utilize with combination with medicine for the treatment of hepatotoxicity (Saha *et al.*, 2019). So the present review is to explore the hepatoprotective effect by the natural product including plant and nutraceutical.

Table 1: Hepatoprotective plants evaluated using various *in vivo* animal models (continued)

S. No.	Botanical name	Family	Parts used	Screening method	Reference
1	<i>Aerva lanata</i>	Amaranthaceae	Root and flower	Carbon tetrachloride induced	(Ramachandra et al., 2011)
2	<i>Amaranthus caudatus</i> Linn	Amaranthaceae	Whole plant	Paracetamol induced	(Kumar et al., 2011)
3	<i>Anisochilus carnosus</i> Linn	Lamiaceae	Stem	Alcohol induced	(Nissar Ahmad Reshil, 2018)
4	<i>Asparagus racemosus</i>	Liliaceae	Root	Paracetamol induced	(Rahiman et al., 2014)
5	<i>Azima tetracantha</i>	Salvadoraceae	Leaves	Carbon tetrachloride induced	(T.Nargis Begum, 2016)
6	<i>Aegle Marmelos</i>	Rutaceae	Leaf	Alcohol induced	(Malairajan et al., 2007)
7	<i>Azadirachta indica</i>	Meliaceae	Aerial parts	Paracetamol induced	(Chattopadhyay, 2005)
8	<i>Berberis aquifolium,</i>	Berberidaceae	Rhizome	Carbon tetrachloride induced	(Feng et al., 2010)
9	<i>Commiphora wightii</i>	Burseraceae	Stem	Carbon tetrachloride induced	(Harjeet Singh et al., 2019)
10	<i>Carissa carindas</i>	Apocyanaceae	Root	Carbon tetrachloride induced + Paracetamol induced	(Hegde and Joshi, 2008)
11	<i>Cucumis trigonus Roxb.</i>	Cucurbitaceae	Fruit	Carbon tetrachloride induced	(Patil and Shaikh, 2015)
12	<i>Cassia fistula</i>	Fabaceae	Leaves	Carbon tetrachloride induced	(Kaur et al., 2020)
13	<i>Cajanus cajan</i> Linn	Leguminosae	leaves	Carbon tetrachloride induced + N-Nitrosodiethylamine induced	(Singh et al., 2011) Eze et al., 2019)
14	<i>Cajanus scarabaeoides</i> Linn	Fabaceae	Whole plant	Paracetamol induced	(Pattanayak et al., 2011)
15	<i>Clitoria ternatea</i> Linn	Fabaceae	Leaves	Paracetamol induced	(Nithianantham et al., 2011)
16	<i>Calotropis procera</i>	Asclepiaceae	Root bark	Paracetamol induced	(Setty et al., 2019)
17	<i>Curcuma xanthorrhiza</i> Roxb.	Zingiberaceae	Rhizome	Carbon tetrachloride induced + Paracetamol induced	(Devaraj et al., 2014) Pramono et al., 2018)
18	<i>Guazuma tomentosa</i>	Sterculiaceae	Leaves	Carbon tetrachloride induced	(Sharma et al., 2014)
19	<i>Ficus carica</i>	Moriaceae	Leaf	Rifampicin induced	(Gond and Khadabadi, 2008)
20	<i>Ficus religiosa</i> Linn.	Moriaceae	Stem bark	Paracetamol induced	(Pawar and Jhade, 2016)
21	<i>Fumaria officinalis</i>	Fumariaceae	Aerial parts	Carbon tetrachloride induced	(Udya Raj et al., 2012)
22	<i>Garcinia morella</i>	Clusiaceae	Fruit	Carbon tetrachloride induced	(Desr et al., 2017)
23	<i>Gmelina asiatica</i> Linn	Verbenaceae	Aerial parts	Carbon tetrachloride induced	(Ar and Gs, 2016)
24	<i>Euphorbia hirta</i>	Euphorbiaceae	Aerial parts	Carbon tetrachloride induced	(Dubey and Mehta, 2014)
25	<i>Hibiscus cannabinus</i>	Malvaceae	Leaves	Carbon tetrachloride induced + paracetamol induced	(Agbor and Oben, 2005)
26	<i>Hyptis suaveolens</i> Linn	Lamiaceae	Leaves	Acetaminophen induced	(Babalola et al., 2011)
27	<i>Ipomoea staphylina</i> Linn.	Convolvulaceae	Aerial Parts	Carbon tetrachloride induced	(Jeyadevi et al., 2019)
28	<i>Melia azedarach</i> Linn	Piperaceae	Leaves	Simvastatin induced	(Rao et al., 2012)
29	<i>Moringa oleifera</i>	Moringaceae	leaves	Cadmium induced	(Toppo et al., 2015) (Biswas et al., 2019) Farooq and Koul, 2019)
30	<i>Morinda citrifolia</i>	Moraceae	Fruit	Carbon tetrachloride induced	(Nayak et al., 2011)
31	<i>Myrtus communis</i>	Myrtaceae	Leaves	Paracetamol induced	(Rupesh et al.,)
32	<i>Myoporum lactum</i> Linn	Myoporaceae	Leaves	Carbon tetrachloride induced	(Venkat, 2017)

33	<i>Nelumbo nucifera</i>	Nelumbonaceae	Seed	Alcohol induced	(Pa and Meenakshi, 2017)
34	<i>Otostegia persica</i>	Lamiaceae	Aerial parts	Carbon tetrachloride induced	(Toori <i>et al.</i> , 2015)
35	<i>Picrorrhiza kurroa</i>	Scrophulariaceae	Rhizome	Galactosamine induced	(Negi <i>et al.</i> , 2007)
36	<i>Rubia tinctorum</i>	Rubiaceae	Root	Carbon tetrachloride induced	(Marhoume <i>et al.</i> , 2017)
37	<i>Leucas cilita</i> Linn	Lamiaceae	Whole plant	Carbon tetrachloride induced	(Qureshi <i>et al.</i> , 2010)
38	<i>Luffa echinata</i>	Cucurbitaceae	Fruit	Carbon tetrachloride induced	(Kumar <i>et al.</i> , 2012)
39	<i>Piper longum</i>	Piperaceae	Fruit	Isoniazid+ Rifampicin + Pyrazinamide induced	(Joseph, 2014)
40	<i>Silybium marianum</i>	Asteraceae	Seeds	Thioacetamide induced	(Asgary, 2014)
41	<i>Sida cordifolia</i>	Malvaceae	Roots	Alcohol induced	(Rejitha <i>et al.</i> , 2012; Khurana <i>et al.</i> , 2016)
42	<i>Solanum nigrum</i>	Solanaceae	Fruit	Carbon tetrachloride induced	(K.R Subash, K.S Ramesh, 2017)
43	<i>Sphaeranthus indicus</i>	Asteraceae	leaves	Carbon tetrachloride induced	(Mansoori <i>et al.</i> , 2018)
44	<i>Tinospora cordifolia</i>	Menispermaceae	Aerial parts	Carbon tetrachloride induced	(B. T. Kavitha1, S. D. Shruthi, 2011 ;Harjeet Singh <i>et al.</i> , 2019)
45	<i>Thunbergia laurifolia</i>	Acanthaceae	Leaves	Alcohol induced	(Palipoch <i>et al.</i> , 2019)
46	<i>Ocimum tenuiflorum</i>	Lamiaceae	Seed, Leaves	Paracetamol induced	(Chattopadhyay <i>et al.</i> , 1992) Sharma <i>et al.</i> , 2017)

Table 2: List of commonly consumed hepatoprotective nutraceutical evaluated using various *in vivo* models (continued)

S. No.	Biological Source	Family	Parts Consumed	Screening method	Reference
1	Carrot (<i>Daucus carota</i>)	Umbelliferae	Root	Paracetamol induced	(Jain <i>et al.</i> , 2017)
2	Cabbage (<i>Brassica oleracea</i>)	Brassicaceae	Leaves	Simvastatin induced	(Mohammed <i>et al.</i> , 2013)
3	Sugar leaf (<i>Stevia rebaudiana</i>)	Simvastatin	Leaves	Thioacetamide induced	(Das and Kathiriya, 2012)
4	Coconut oil (<i>Cocos nucifera</i>)	Arecaceae	Kernel	Paracetamol induced	(Zakaria <i>et al.</i> , 2011)
5	Tomato (<i>Solanum lycopersicum</i>)	Solanaceae	Pulp	Carbon tetrachloride induced	(Weremfo and Asamoah, 2011)
6	Cactus Pear (<i>Opuntia ficus-indica</i>)	Cactaceae	Fruit	Carbon tetrachloride induced	(Albano <i>et al.</i> , 2015)
7	Corn silk (<i>Zea Mays</i> Linn.)	Gramineae	stigmata	Isolated Rat Liver Perfusion	(Karami <i>et al.</i> , 2013)
8	Blueberry (<i>Vaccinium corymbosum</i>)	Ericaceae	Fruit	Carbon tetrachloride induced	(Liu <i>et al.</i> , 2019)
9	Lemon (<i>Citrus limon</i>)	Rutaceae	Fruit	Carbon tetrachloride induced	(Bhavsar <i>et al.</i> , 2008)
10	Chilly (<i>Capsicum annum</i>)	Solanaceae	Fruit	Lipopolysaccharide Induced	(Vasanthkumar <i>et al.</i> , 2017)
11	Red rice (<i>Oryza sativa</i>)	Poaceae	Seed	Paracetamol induced	(Sinthorn <i>et al.</i> , 2016)
12	Mango(<i>Mangifera indica</i>)	Anacardiaceae	Fruit	Carbon tetrachloride induced	(Motawe <i>et al.</i> , 2015)
13	Wheat (<i>Triticum aestivum</i>)	Poaceae	Grain	Carbon tetrachloride induced	(Motawe <i>et al.</i> , 2015)
14	Fennel (<i>Foeniculum vulgare</i>) Linn.	Umbelliferae	Bulbs	Carbon tetrachloride induced	(Yuan <i>et al.</i> , 2011)
15	Turmeric (<i>Curcuma longa</i>)	Zingiberaceae	Rhizome	Thioacetamide induced	(Salama <i>et al.</i> , 2013)
16	Garlic (<i>Allium sativum</i>)	Liliaceae	Bulb	Lead Induced	(Wu <i>et al.</i> , 2011)
17	Onion (<i>Allium cepa</i>)	Liliaceae	Bulb	Paracetamol induced	(Ozougwu and Eyo, 2014)
18	Red grapes (<i>Vitis vinifera</i>)	Vitaceae	Seed	Ethanol-Induced	(Hassan <i>et al.</i> , 2018)

19	<i>yam (Amorphophallus campanulatus)</i>	Araceae	Tubers	Carbon tetrachloride induced	(Sanjay jain, vinod k. dixit, 2009)
20	<i>Winter melon (Benincasa Hispida)</i>	Cucurbitaceae	fruits	Diclofenac sodium	(Rose <i>et al.</i> , 2015)
21	Beetroot (<i>Beta vulgaris</i>)	Amaranthaceae	Root	Carbon tetrachloride induced	(Rose and Sudha, 2014)
22	<i>Mustard seeds (Brassica juncea)</i>	Brassicaceae	Seed	Carbon tetrachloride induced	(Walia <i>et al.</i> , 2011)
23	Papaya (<i>Carica papaya</i>)	Caricaceae	Fruits	Carbon tetrachloride induced	(Mohammed <i>et al.</i> , 2017)
24	<i>Colocasia (Colocasia Antiquorum)</i>	Araceae	leaves, Corm	Carbon tetrachloride induced+ Paracetamol induced	(T. A. Tuse, 2009)
25	Taro (<i>Colocasia Esculenta</i>)	Araceae	Tender leaves, Corm	Thioacetamide induced	(Chinonyelum <i>et al.</i> , 2015)
26	<i>Coriander (Coriandrum sativum)</i>	Umbelliferaeae	Seed	Carbon tetrachloride induced	(A. Pandey, P. Bigoniya, V. Raj, 2014)
27	Cucumber (<i>Cucumis sativus</i>)	Cucurbitaceae	Fruits & Seeds	Paracetamol induced	(Palanisamy <i>et al.</i> , 2015)
28	Cumin (<i>Cuminum cymin</i>)	Apiaceae	Seed	Cisplatin induced	(Abbas and Naz, 2017)
29	Liquorice (<i>Glycyrrhiza glabra</i>)	Leguminosae	Root	Carbon tetrachloride induced	(Maksoud <i>et al.</i> , 2019)
30	Gooseberry(<i>Phyllanthus emblica</i>)	Phyllanthaceae	Fruit	Cisplatin induced	(Abbas and Naz, 2017)
31	Mint(<i>Mentha arvensis</i>)	Lamiaceae	leaves	Carbon tetrachloride induced	(Patil and Mall, 2012)
32	Curry leaf (<i>Murraya koenigii</i>)	Rutaceae	leaves	Carbon tetrachloride induced	(M. S. Pande, S. P. B.N Gupta, 2015)
33	Cardamom (<i>Elettaria cardamomum</i>)	Zingiberaceae	Seed	Gentamicin induced	(Aboubakr and Abdelazem, 2015)
34	Sesame (<i>Sesamum Indicum</i>) Linn.	Pedaliaceae	Seed	Carbon tetrachloride induced	(Cengiz and Kavak, 2012)
35	Clove(<i>Syzygium aromaticum</i>)	Myrtaceae	Bud	Paracetamol induced	(Sadia Kazi, 2016)
36	Bitter gourd (<i>Momordica charantia</i>)	Cucurbitaceae	Fruit	Acetaminophen Induced	(Zahra <i>et al.</i> , 2012)
37	Broccoli (<i>Brassica oleracea</i>)	<i>Brassicaceae</i>	Fruit	Carbon tetrachloride induced	(El-baz, 2012)
38	Pumpkin (<i>Cucurbita maxima</i>)	<i>Cucurbitaceae</i>	Fruit	Carbon tetrachloride induced	(Haldar <i>et al.</i> , 2011)
39	Pineapple (<i>Ananas comosus</i>)	Bromeliaceae	Fruit	Isoniazid induced	(Yantih and Harahap, 2017)
40	custard apple (<i>Annona squamosal</i>)	Annonaceae	Fruit	Isoniazid+ rifampicin induced	(Ts <i>et al.</i> , 2008)
41	Spinach (<i>Spinacia oleracea</i>)	Chinopodiaceae	leaves	Carbon tetrachloride induced	(Hr <i>et al.</i> , 2015)
42	Eggplant (<i>Solanum melongena</i>)	Solanaceae	Fruit	Carbon tetrachloride induced	(Raj <i>et al.</i> , 2016)
43	Avocado (<i>Persea Americana</i>)	Lauraceae	Fruit	Carbon tetrachloride induced	(Raj <i>et al.</i> , 2016)
44	Cucumber (<i>Cucumis sativus</i>)	Cucurbitaceae	Fruit	Alcohol induced	(Kumar <i>et al.</i> , 2019)

Conclusion

The rising attention in the scientific estimation of several herbal and nutraceuticals utilize in Ayurvedic structure of medication. Plants and nutraceuticals now days

gain the devotion as the strength advantageous nutrition and also a basis for the drug design procedure. Various natural drug obtain from nutraceutical abstract that are actually used to management of an extensive diversity of liver disorder.

During the previous senescence, the usage of natural product supplementation remained improved from 2.6% to 13%.

With the advancement of the herbal product and data-based studies prove that plant made medicine comprise various constituents that prevent from various kinds of hepatotoxicity. The usage of these herbal product also improve the quality of life. However, the rich antioxidant potential of the plant and nutraceutical essential to be explored in detail so that more hepatoprotective drugs can be formulated in an effective manner.

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