

Contribution of Ethnopharmacology in Ameliorating Toxicity of Vital Organs

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SUMMARY

Ethnopharmacology is an integrated system of traditional medicines which are extracted from plants. These traditional medicines are employed as therapeutic agents owing to their abrogative potential against different diseases. These drugs are extensively studied to elucidate their mitigative properties against various sorts of diseases. Vital organs such as the lungs, kidney, liver, and heart are continuously exposed to several toxicities due to various sorts of toxicants which include environmental contamination, xenobiotics, and underlying conditions of particular diseases. Various sorts of Ethnopharmacological drugs are extensively used as ameliorative agents against liver, renal, lung, heart, and testicular toxicities in both humans and animals. Furthermore, various drug and food regulatory authorities such as WHO approved thousands of ethnopharmacological drugs as safe agents for oral intake. Overall, the findings highlight the potential of ethnopharmacological drugs as a source of new therapeutic approaches for the treatment of vital organ toxicity in humans and animals. In conclusion, ethnopharmacological drugs have shown promising results in mitigating the effects of vital organ toxicity. Further research is needed to fully understand the mechanisms of action and potential therapeutic benefits of these drugs. This chapter will encompass all the aspects of ethnopharmacological drugs and their role in the amelioration of vital organ toxicity.

INTRODUCTION

Ethnopharmacology is an integrated study associated with the analysis of traditional medicines and their biological role on the basis of their description, observation as well as experimental examination (Rivier & Bruhn 1979). The definition was later modified by Bruhn & Holmstedt (1981) as “ethnopharmacology is a multidisciplinary scientific investigation of bioactive substances that have been conventionally utilized or identified by man”. According to Fabricant & Farnsworth (2001), ethnopharmacology is an exceptionally diversified field that involves pharmacology, botany, chemistry, and biochemistry as well as various other subjects such as linguistics, history, archaeology, and anthropology. Ethnopharmacology was initially introduced in 1967 at an international conference held in San Francisco to

emphasize the multidisciplinary approach of conventional psychotropic drugs (Efron et al., 1967).

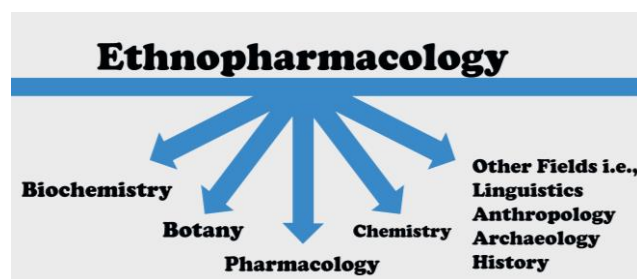


Fig 1. Diverse fields in ethnopharmacology

Traditional medicines vary in different regions as well as countries of the world and entail an extensive range of therapies and practices. These medicines are referred to as complementary or alternative medicines (Khamkar et al., 2015). About 70-80 percent people of in developed countries use

complementary medicine because they assume that these medicines are totally organic as well as risk-free and can be used as a treatment for chronic, painful, or fatal diseases (UNESCO, 2013). From 1981 to 2007, major sources of active components of medicine were natural products and more than half of the drugs approved since 1994 were extracted from natural products. Furthermore, 13 drugs obtained from natural resources were permitted during 2005-2007 (Harvey, 2008). During the time period of 1981-2002, almost 75 percent of anti-infectious medicines and 60 percent of anticancer remedies were obtained from natural sources, moreover, 61 percent of all new chemical compounds that were present globally in the same time periods were found to be derived from natural products (Newman et al., 2003).

PROTECTIVE ROLE OF VARIOUS ETHNOPHARMACOLOGICAL DRUGS AGAINST TOXICITY OF VITAL ORGAN

Hepatotoxicity and ethnopharmacological medicines

The liver is an important body organ that primarily regulates the metabolism of exogenous as well as endogenous agents (Senthilkumar et al., 2014). It has a key role in detoxification as well as the eradication of drugs and their metabolites. Hepatic damage can be induced due to infection, alcohol consumption, medications, xenobiotics, malnutrition, and anemia (Mroueh et al., 2004). These factors promote reactive oxygen species (ROS) production which is considered as prime cause of hepatotoxicity (Sanchez-Valle et al., 2012). Reactive oxygen species are reported to instigate lipid peroxidation by oxidizing molecules which are present in the cellular membranes as well as tissues. Furthermore, excessive generation of ROS can induce oxidative stress (OS) which leads to inflammatory as well as apoptotic responses. Synthetic medicines that are employed against hepatic disorders have deleterious side effects therefore the use of traditional medicinal plants (Tab 1) is now becoming a global trend (Li et al., 2015).

Rhodiola imbricata, also named arctic or golden root, is a traditional herbal medicine used in Mongolia, Soviet Republics, China, and Tibet (Kelly, 2001). It possesses the ability to increase the level of antioxidant markers in the liver and is therefore designated as a hepatoprotective medicine (Senthilkumar et al., 2014). *Fufang Zhenzhu Tiaozhi*, a capsule made from the combination of eight traditional Chinese medicinal herbs is documented to exhibit a hepatoprotective effect against toxicity induced by the fatty liver (non-alcoholic) as well as type 2 diabetes mellitus (Bei et al., 2019; Wang et al., 2021). *Hippophae rhamnoides* L. also named as sea buckthorn is a deciduous shrub which belongs to the Elaeagnaceae family and is reported to be involved in nitrogen fixation [Fig 2., (Hou

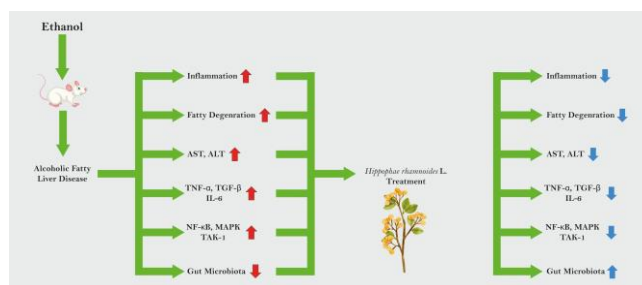


Fig 2. *Hippophae rhamnoides* mitigate ethanol induced fatty liver disorder.

et al., 2017)]. This plant has multiple medicinal as well as edible applications and it has been used in Europe and Asia for centuries (Kosman et al., 2009; Tian et al., 2020).

Zhao et al. (2022) used the extract of this plant as a stupendous hepatoprotective drug against liver injury induced by the accumulation of fats. It is documented that many natural remedies that improve liver function during various sorts of damage have the ability to modify intestinal flora while sea buckthorn alleviated the inflammation as well as fatty degeneration of liver cells induced by ethanol in mice. It also reconstructed the structure of gut microbiota which reverses the development of alcoholic fatty liver. Moreover, it attenuated Transforming growth factor-β-activated kinase 1-

Tab 1. Ethnopharmacological plants against hepatotoxicity

Plant	Common Name	Effect against Hepatotoxicity	Reference
<i>Citri Reticulatae Pericarpium</i>	Chenpi	It plays essential role in the treatment of multiple liver disorders and acts as an anti-inflammatory as well as antioxidative agent.	(Yu et al., 2018).
<i>Antrodia cinnamomea</i>	Antrodia cinnamomea	It is a medicinal fungus which is hosted by the trunks of <i>cinnamomum kanehirai</i> Hayata. It is reported to protect liver from fatty liver disorder (non-alcoholic) by reducing OS, inflammation as well as lipogenesis and promotes β-oxidation of fatty acid	(Lu et al., 2013; Cao et al., 2022)
<i>Dendrobium</i>	Orchid	It demonstrates hepatoprotective potential against CCl4-induced acute liver injury via regulating Nrf-2 signaling pathway as well as it enhances the metabolism of lipids and elevates the level of antioxidant enzymes.	(Li et al., 2019; Zhou et al., 2020; Huang et al., 2019; He et al., 2019)

Tab 2. Traditional Chinese medicinal formulas used in the treatment of renal disorders

Formula	Herbs	Effect on Kidney	References
Liu-Wei-Di-Huang Wan	Rhizoma Rehmanniae Preparata; Fructus Corni; Rhizoma Dioscoreae; Rhizoma Alismatis; Cortex Moutan Radicis; Poria	Protect kidney against diabetic nephropathy (type 2 diabetes mellitus)	Hsu et al., 2014
Wuling San	Polyporus (<i>Polyporus umbellatus</i> Fries); Poria (<i>Poriacocos</i> Wolf); Alismatis rhizome (<i>Alisma orientale</i> Juz.); Cinnamomi cortex (<i>Cinnamomum cassia</i> J. Presl); <i>Atractylodis macrocephalae</i> rhizome	Increases urinary volume and reduced average body weight in patients suffering from nephritic syndrome. Ameliorate diabetic nephropathy induced renal edema. Anti-hyperuricemic as well as anti-inflammatory effects against hyperuricemia with kidney dysfunction	Jin et al., 2012; Xiong et al., 2011; Yang et al., 2015
Mixture of <i>Astragalus membranaceus</i> and <i>Salvia miltiorrhiza</i>	<i>Astragalus membranaceus</i> ; <i>Salvia miltiorrhiza</i>	Relieve proteinuria, reduce mortality as well as improve renal function as a consequence of chronic kidney disease. Ameliorate kidney pathology as well as metabolism, restore structure of intestinal flora and barrier, increase the number of probiotics that produce butyric as well as lactic acid i.e., <i>Akkermansia</i> and <i>Lactobacillus</i> .	Hsieh et al., 2017; Huang et al., 2018; Han et al., 2021

induced (TAK1), Mitogen-activated protein kinases (MAPKs) as well as nuclear transcriptional factor NF-κB activation. These biochemical changes mediated by sea buckthorn ameliorated the ethanol-induced alcoholic fatty liver disease.

Khaya senegalensis commonly known as a dry zone mahogany is a medicinal plant used by Nupes of Nigeria as well as in other regions of Africa (Adebayo et al., 2003). *Khaya senegalensis* is proven to attenuate nephrotoxicity induced by malarial parasites (Adetutu et al., 2015). *Phyllanthus niruri* is a

Tab 3. Traditional medicinal plants to cure testicular toxicity.

Plant	Common Name	Effect	Reference
<i>Morinda officinalis</i>	Indian Mulberry	Improve sexual function of male mice. Protect human sperm DNA from oxidative stress	Wu et al., 2015
<i>Nigella sativa</i>	Black Cumin; Habbatus Sauda; Kalonji	Its oil can attenuate testicular toxicity and enhance sperm quality	Ping et al., 2014
<i>Moringa oleifera</i> Lam.	Drumstick tree	It can modulate the gene expressions related to Sertoli and spermatogonial cell. Enhances blood and intratesticular hormonal milieu.	Matic et al., 2018; Nayak et al., 2020
<i>Mucuna pruriens</i>	Magic velvet bean	Treat hypoactive sexual desire disorder and improve the sexual behaviors as well as improve functional proteins of testes.	Tangrisakda et al., 2022
<i>Pogostemon cablin</i> (Blanco) Benth	Patchouli	Various extracts from the leaves of this plant can attenuate testicular toxicity via reducing OS, increasing sperm count, motility as well as viability.	Ijaz et al., 2022
<i>Taraxacum officinale</i> L.	Dandelion	It can reduce OS and inflammation meanwhile increasing the level of luteinizing hormone and testosterone.	Abdel-Magied et al., 2019
<i>Tamarindus indica</i> Linn.	Tamarind	It can treat diabetes induced testicular toxicity via increasing the level of serum insulin, sperm viability, sperm count and seminal vesicular fructose which is used by spermatozoa. Moreover, it attenuated OS and recovered antioxidant enzymes.	Maiti, 2017

Renal toxicity and ethnopharmacological medicines

The kidney is an important organ with significant cellular complexity as well as functional diversity such as maintenance of composition, pressure, and volume of blood, as well as eradication of nitrogenous wastes (Little & McMahon 2012). Acute kidney injury (AKI) is a common problem linked with high levels of morbidity as well as death. According to previous literature, one out of every five adults and one out of every three children suffer from acute kidney injury (Susantiphong et al., 2013). Various renal toxicants and infections are considered the primary causes of acute kidney injury (Barnett et al., 2019).

widely used ethnopharmacological plant in South and Southeast Asia (Giribabu et al., 2017) and is commonly named a stone breaker or Chanca Piedra in Brazil which is used to cure renal as well as ureteric calculi (Calixto et al., 1998). Research demonstrates that *P. niruri* prevents stone formation in renal tissues by inhibiting the growth of urate crystals (Freitas et al., 2002) alternating the renal stone composition and making it more delicate as well as easily dissolvable (Barros et al., 2006). Furthermore, it induces relaxation of the urethra as well as diminishes the excretion of crystallization promoters such as calcium in the urine (Boim et al., 2010). This medicinal herb is an effective treatment for hemorrhagic cystitis as well as it relieves diabetes mellitus-induced kidney damage by inhibiting OS, apoptosis, inflammation, and kidney proliferation (Boeira et al., 2011; Giribabu et al., 2017). Some other plants that are

used against diabetic nephropathy include *Murraya koeingii* and *Brassica juncea* (Grover et al., 2003). Several traditional Chinese medicine formulas that consist of multiple types of herbs are widely used to treat kidney disorders (Tab 2).

Testicular toxicity and ethnopharmacological medicines

Testes are reproductive organs which are primarily responsible for reproduction and are present outside the human body (Seevagan et al., 2019). They perform endocrine as well as exocrine functions (Tiwana and Leslie, 2017). Toxicity of testicles is the primary cause of infertility and can be induced by multiple factors including nutritional, environmental, and hormonal imbalances (Dubey et al., 2018).

The heart is a vital organ made up of cardiac muscles, involved in the distribution of oxygenated blood throughout the body. It carries oxygenated blood to the body's organs while pumping deoxygenated blood toward the pulmonary system (Kenny et al., 2011). According to a report published by WHO, cardiovascular disorders are the major cause of death worldwide (WHO, 2019). Cardiac Muscle damage, electrophysiological disturbances, and vascular endothelial dysfunction are some of the factors that can contribute to cardiovascular toxicity (Singh., 2016). Cardiotoxicity is induced by various drugs including anticancers such as chemotherapeutics as well as different kinds of anti-depressants (McGowan et al., 2017). Furthermore, air pollution (Rao, 2018) and plastic exposure (Posnack, 2021) as well as excessive consumption of alcohol can lead to severe

Tab 4. Ethnopharmacological plants against cardiotoxicity.

Plant	Common Name	Effect against cardiotoxicity	Reference
<i>Cnidium monnieri</i> (L.) Cuss <i>Saussurea lappa</i>	Monnier's snowparsley Costus	It can reduce systolic blood pressure (Ogawa et al., 2007) and demonstrates strong vaso-relaxing effect. Moreover, it alleviates cardiac hypertrophy as result of renovascular hypertension via inhibiting OS, lipid metabolism and NF-kB in cardiac tissues. It attenuated Ehrlich Solid Tumour (a tumour that promotes breast cancer) prompted cardiotoxicity via improved the levels of sodium and high-density lipoproteins. Furthermore, it enhances lipid profiles and electrolytes in cardiac tissues and also increased apoptosis against cancerous cells.	Chiou et al., 2001; Chen et al., 2011 Elgharabawy et al., 2021
<i>Glycyrrhiza glabra</i>	Licorice	It mitigated Doxorubicin induced cardiotoxicity through regulating the metabolism and homeostasis of lipids, diminishing OS, sustaining the functions of mitochondria and prevented cardiac heteropathy.	Upadhyay et al., 2020
<i>Platycodon grandiflorum</i>	Baloon flower or Chinese bellflower	It is reported to cure anthracycline (a chemotherapeutic drug applied against breast cancer) induced cardiotoxicity. It protects cardiac tissues from systolic dysfunction as well as myocardial injury.	Hao et al., 2020

Cerely (*Apium graveolens* L.) is a widely used traditional folk medicine to treat multiple diseases like gastrointestinal disorders and rheumatism. (Maruyama et al., 2009). The seeds of this plant are used as a sedative, hypotensive, diuretic, and spasmolytic agent as well as to enhance fertility (Al-Asmari et al., 2017; Kooti et al., 2017). The oils of celery have the potential to reduce OS in testes and enhance the function of sperms. Moreover, it can increase the level of testosterone (Helal, 2014; Khiabani, 2014; Madkour, 2014; Shalaby and El-Zorba, 2010). Cistanche (*Cistanche Hoffmy*) is a traditional plant which is used as a therapeutic approach for testicular dysfunction and is reported to enhance the sexual function of males via increasing testosterone production (Tab 3). This plant is commonly found in the semi-arid regions of India, Mongolia, and China (Wang et al., 2016). Cistanche upregulates steroidogenic enzymes in order to attenuate testicular toxicity (Jiang et al., 2016). *Urtica dioica* is a folk medicine which is documented to increase sperm count and motility. It also helps in maintaining the normal diameter of seminiferous tubules and sperm cell morphology as well as increasing the testosterone level and quality of spermatozoa (Jalili et al., 2014).

cardiovascular disorders including cardiac arrhythmias and dilated cardiomyopathy (DCM) (Xi et al., 2017). These abnormalities can disrupt blood circulation as well as continuous flow. Moreover, inflammation as well as OS play a central pathogenic role inducing cardiovascular toxicity (Kovacic and Thurn, 2005; Juni et al., 2013).

Sweet marjoram (*Origanum majorana* L.) is a native plant to the Mediterranean region and planted in many other countries of Europe, North Africa, and Asia (Bina and Rahimi, 2017). It is effective against thrombocytosis, granulocytosis, and erythrocytosis as well as against increased heart weight, OS, and myocardial infarction (Ramadan et al., 2013). *Ginkgo biloba* L., a deciduous plant of the genus Ginkgo usually known as a living fossil (Hassan et al., 2020), which is extensively used for various purposes such as medicine, ornamental, food, material, and greening (Tab 4). Extract of *Ginkgo biloba* L. can be used against myocardial infarction as it can diminish the deposition of cholesterol in peripheral tissues, counter atherosclerosis production, and prevent damage to vascular endothelial cells (Chen et al., 2014).

Cardiovascular diseases and ethnopharmacological medicines

Ethnopharmacological drugs and their therapeutic action against lung toxicity

Lungs are considered important organs of the respiratory system which are responsible for the exchange of gases between blood and its environment (Lutfi, 2017). Lungs divide into many portions, which are further segmented into more than 300

ethnopharmacological plant which is usually found in Africa and Asia (Zahidin et al., 2017). It is applied against various disorders in animals such as anthrax in cattle as well as camel (Giday and Teklehaymanot 2013), bovine mastitis (Mubarack et

Tab 5. Ethnopharmacological plants against Pulmonotoxicity.

Plant	Common Name	Effect against Pulmonotoxicity	Reference
<i>Selaginella doederleinii</i>	Spikemoss or Club moss	It protects lungs from toxicity induced by lungs cancer via prompting mitochondrial pathways and promoting apoptosis of cancerous cells.	Sui et al., 2016
<i>Abutilon pannosum</i>	Ragged Mellow or Peeli Boti (Urdu)	It protected the lungs toxicity via reducing OS, inflammation, apoptosis and improved antioxidant enzymes of lungs.	Khalil et al., 2020
<i>Zataria multiflora</i>	Avishane-shirazi (Persian)	It mitigates cisplatin induced lung damage by increasing the activity of the antioxidant defense system, scavenging the ROS that induce lipid peroxidation as well as via quenching free radicals.	Habibi et al., 2020

million alveoli primary sites for gaseous exchange (Chaudhry & Bordoni 2022). Many harmful reactions take place inside the lungs which are responsible for cancer, asthma, and chronic obstructive pulmonary disease, because of exposure of the lungs to different toxicants such as cigarette smoke, nitrogen oxides, industrial contaminants, ozone, and many other substances (Kovacic & Somanathan 2009).

Ziziphora tenuior L. is a traditional medicinal plant which is enriched with various flavonoids, polyphenolic, and phenolic compounds usually found from Southwest Asia to Eastern Europe (Mehmood et al., 2010). In traditional medicine (Tab 5), it is broadly used as herbal tea to cure asthma and gastrointestinal disorders (Pirbalouti et al., 2010). The extract of *Z. tenuior* exhibits pulmonary protective function against chlorpyrifos-induced lung toxicity owing to its free radical scavenging action as well as anti-inflammatory properties (Kianpour et al., 2021). *Andrographis paniculata* (Burm.f.) Nees is a medicinal plant and is a member of the family Acanthaceae. It is well known for its curative potential against respiratory tract infections, sore throat, diarrhea, and liver disorders in Southeast Asian countries such as India and China (Hossain et al., 2014). It has the ability to attenuate cisplatin-induced lung damage by enhancing the activity of the antioxidant defense system, and scavenging free radicals that induce liver peroxidation and peroxidative damage (Habibi et al., 2018).

THERAPEUTIC ACTION OF ETHNOPHARMACOLOGICAL DRUGS AGAINST VITAL ORGAN TOXICITY IN ANIMALS

Multiple ethnopharmacological medicines are applied to cure various disorders in animals. *Herniaria hirsuta* L. (hairy rupturewort) is a plant of the genus *Herniaria* (Caryophyllaceae) which is commonly reported in North Africa, Asia as well as Europe. It possesses the ability to lower cholesterol levels in the bile of dogs. Furthermore, it has the ability to dissolve existing gallstones and prevent the formation of new gallstones (Dooren et al., 2015). *Acalypha indica* is an

al., 2012), constipation, and maggot wound (Pandit, 2010), as well as its paste is applied on the skin of goat, chicken and cow for wounds treatment (Selvaraju et al., 2011).

Licorice is a root of *Glycyrrhiza* plant, a member of the family Leguminosae, and used as a traditional medicine since bygone times (Shibata 2000). It is used as a feed additive, and its constituents can elevate the production efficiency of broilers, rabbits, sows, and pigeons and keep their intestine healthy (Ibrahim et al., 2020). Moreover, it improves immunity along with the meat quality of animals (Luo et al., 2019). Chamomile (*Matricaria recutita* L.) is a popular traditional medicine that is used against gastrointestinal disorders including diarrhea (Alanís et al., 2005).

CONCLUSION

In conclusion, ethnopharmacology has emerged as a promising field in mitigating vital organ toxicity in both humans and livestock. The use of natural products with medicinal properties has gained widespread attention in recent years due to their potential therapeutic benefits and minimal side effects. Ethnopharmacology has the potential to offer safe and effective alternatives for the prevention and treatment of vital organ toxicity, improving the health and well-being of humans and livestock alike. However, it is important to note that further studies are needed to fully understand the pharmacological mechanisms and potential risks associated with these natural remedies.

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