

HEPATOTOXICITY AND ITS MANAGEMENT IN UNANI SYSTEM OF MEDICINE: A REVIEW

***Hushan Jahan¹, ²Hifzul Kabir and Zeba Afrin¹**

¹PG Scholar, Deptt. of Ilmul Advia, School of Unani Medicine, Jamia Hamdard.

²Assistant Professor, Deptt of Ilmul Advia, School of Unani Medicine, Jamia Hamdard.

Article Received on
10 May 2017,

Revised on 30 May 2017,
Accepted on 20 June 2017

DOI: 10.20959/wjpr20177-8839

***Corresponding Author**

Hifzul Kabir

Assistant Professor, Deptt of
Ilmul Advia, School of
Unani Medicine, Jamia
Hamdard.

ABSTRACT

Liver diseases are a major worldwide health problem in developing countries that is a serious challenge to the world. In today's scenario excessive drug therapy, environmental pollutants, hepatic cancer and alcoholic intoxicants are the main causes of liver disorders. The Herbal products of traditional medicines (Unani, Ayurveda, etc.) play a major role in health care of developing countries. Unani drugs constitute an important part in the traditional system of medicine (TSM) in India and abroad. Due to the realization about safety of TSM products the demand is increasing day by day. In Unani system of medicine there are so many traditional formulations used since long for several chronic disorders. The compound formulations (like Jawarish Jalinoos,

Majoon dabidul ward, Muravvaqin, Jawarish Aamla etc) as well as single drugs of Unani system of medicine are playing a great role for the treatment of various liver disorders. In this review aspects of protective role of different types of Unani formulations in various liver disorders shall be discussed.

KEYWORDS: Unani medicine, Hepatotoxicity, Medicinal plants.

INTRODUCTION

The liver is known as Kabid in Unani system of medicine and it is considered the main site of metabolism for drugs and other exogenous compound.^[1] It involves in various important functions like maintenance, performance and regulating the homeostasis of the body. The major functions of liver are metabolism of carbohydrate, protein and fat, detoxification of unwanted substances, secretion of bile and storage of vitamin.^[6]

According to Tibbe Unani liver is known as Matbakh(Kitchen) of the body and have a most pivotal role to play in human health and diseased condition. As per the concept of Unani system of Medicine there are four Quwa (Energy) present in the liver(Kabid) viz Quwwat- e- Jaziba, Quwwat-e- maska, Quwwat- e- Hazima and Quwwat- e- Dafeaa.^[2]

Liver is organ that is exposed to various drugs which are carried from GIT via the portal vein and also to the metabolites produced.^[1] It is the important organ in the toxicity of drugs because it is the major site of metabolism and elimination of noxious substances. Liver is functionally involved between the site of absorption and systemic circulation.^[3]

➔ Hepatotoxicity is the effect of harmful or poisonous or toxic substances on the liver or it is also described as chemical driven liver damage. Main causes for liver disease are as follows:

- **Drugs or toxins:** Various drugs when taken in overdoses and sometimes in therapeutic range can lead to the injury. For example acetaminophen, isoniazid NSAIDs (aspirin, ibuprofen, diclofenac) and glucocorticoids.^[4]
- **Detoxification:** detoxification of the harmful chemicals occurs in the liver, which in turn results in various hepatic diseases.
- **Infections:** hepatitis^[1]
- **Chronic alcoholism**^[4]
- **Immunological response**^[5]
- **Ischaemia**^[4]
- **Cholesterol or triglycerides**^[6]
- **Obstruction of bile flow**(such as in cholestasis)^[1]
- **Natural products**(Amantia mushroom, aflatoxins).^[6]
- **Industrial toxins**(ccl4, arsenic and vinyl chloride)^[4]
- **Herbal and alternative remedies-** Ackee fruit(Blighia sapida), camphor, pyrrolizidine alkaloids.^[5]

Hepatotoxins are the chemicals that produced liver injury. 5% of all the hospital admissions are due to drug induced liver injury and 50% of all acute liver failure.^[6]

HEPATOTOXIC DRUGS^[6]

| | |
|---------------------------------------|--|
| Anti tubercular drugs | Rifampicin Isoniazid Pyrazinamide |
| Non Steroidal Anti inflammatory Drugs | Acetaminophen Nimesulide Diclofenac Ibuprofen Sulinac |
| Anti Retroviral Drugs | Protease inhibitor: Ritonavir Indinavir Nelfinavir Nucleoside analogues reverse transcriptase inhibitors: Lamivudine Tenofovir Stavudine Zidovudine Non- nucleoside analogues reverse transcriptase inhibitors: Nevirapine Efavirenz Emtricitabine |
| Anti hyperlipidemic Drugs | Statins Atrovastatin Lovastatin Simvastatin Niacin Fibrates |
| Anesthetic agents | Halothane Chloroform Enflurane Nitrous oxide |
| Antiepileptic Drugs | Carbamazepine Valporic acid Felbamate Phenytoin |
| Anti Depressants Drugs | Aminaprine Imipramine |
| Anti Hypertensive Drugs | Methyl dopa |
| Other Drugs | Antibiotics (Amoxicillin, Ciprofloxacin) Oral contraceptives Anti fungal(Fluconazole and Itraconazole) |

CLASSIFICATION OF LIVER DISEASE IN UNANI SYSTEM OF MEDICINE

Ittehabi (inflammatory): caused with the changes in Akhlaat found in the liver.

For example Warm-e- Kabid(Hepatitis), Cirrhosis of liver(Talayyif-ul-Kabid) and Ascitis(Istisqa).^[7]

Ghair Iltehabi(non inflammatory): caused due to the weakness of Quwa(faculties).^[7]

Amraz- e- Shirki: liver diseases may be caused with the involvement of other organ of the body.^[8]

CLASSIFICATION OF LIVER DISEASES ACCORDING TO THE MIZAJ (TEMPERAMENT)^{[7], [9]}

1. **Su- e- Mizaj Sada:** it may be of the following types:

- Su-e-Mizaj Har
- Su-e- Mizaj Barid
- Su-e- Mizaj Yabis
- Su-e- mizaj Ratab
- Su-e- Mizaj Har Barid
- Su-e- Mizaj Har Yabis
- Su-e- Mizaj Barid Ratab
- Su-e- Mizaj Barid Yabis

2. **Sue Mizaj Ma'ddi**

- Su-e- Mizaj safrawi
- Su-e- Mizaj Damvi
- Su-e- Mizaj Balghami
- Su-e- Mizaj Saudawi

CLASSIFICATION OF LIVER DISEASES ACCORDING TO AKHLAT(Humors)^[9]

Warm e Kabid is of four types

- Warm- e Safrawi
- Warm-e – Balghami
- Warm-e-Damvi
- Warm-e- Saudawi

CLINICAL FEATURES OF HEPATOTOXICITY AS PER THE CONCEPT OF TIBB-E- UNANI

According to the Unani System of Medicine the diagnosis of liver diseases is based upon the Pulse, urine and the stool.

There are some concepts mentioned in classical literature:

- The color of urine, stool and the sweat of a diseased patient varies from yellow to dark yellow.^[7]
- In warm e kabid Had(Acute hepatitis), the color of urine is reddish brown.^[9]
- According to the concept of zakarya Razi(A Famous scholar), liver becomes enlarged and tender in chronic hepatitis and patient of Jaundice passes clay colored stool.^{[9], [10]}
- Pain and tenderness in hepatic region, Dryness of the tongue, constipation, anorexia, general weakness, pruritus and hepatic enlargement are the signs of acute inflammation of liver.^[7]

MANAGEMENT OF HEPATOTOXICITY IN TIBB- E- UNANI^[9]

- To eradicate the cause of disease is the first line of treatment.
- Anti inflammatory drugs(Muhallil- e- Auram)
- Diuretics and purgative of Yellow bile(Mudir and Mushil-e- Safra)
- Use of deobstruents(Mufatteh),s and Detergent(Jaali) drugs are also reported.
- According to Razi, the diet of the patient should be light and easily digestible.

MEDICINAL HERBS USED IN LIVER DISEASES

Aegle marmelos

Aqueous and ethanolic extract of fruit pulp of *A. marmelos* was tested in mice against the CCl₄ induced liver injury. Biochemical parameters like SGOT (Serum Glutamate Oxaloacetate Transaminase), SGPT(Serum Glutamate Pyruvate Transaminase and ALP were analyzed. Results of the study shows the significant activity of *A. marmelos* and also confirms that *A. marmelos* is a potent hepatoprotective agent in the traditional system of medicine.^[11]

Andrographis paniculata

Methanolic extract and andrographolide free methanolic extract of the plant were tested against the CCl₄ induced liver damage in rats. SGOT, SGPT, serum alkaline phosphatase,

serum bilirubin and triglycerides were the parameters to be assessed. Study suggests the antihepatotoxic activity of *Andrographis paniculata*.^[12]

Azadirachta indica

The extract of the leaf of *A. indica* was studied in rats against the paracetamol induced hepatic damage. Biochemical parameters to be assessed were glutamate oxaloacetate transaminase, glutamate pyruvate transaminase, acid phosphatase and alkaline phosphatase. Study shows that the group treated with the extract shows the protection from liver cell damage. The histopathological study also confirmed the above findings.^[13]

Berberis tinctoria

The methanolic extract of *B. tinctoria* leaves was evaluated for hepatoprotective and antioxidant potential in experimental animal model. The acute toxicity was induced by Paracetamol at the dose of 750mg/kg in Wistar rats. The biochemical parameters to be assessed were serum glutamate oxalate transaminase and serum Glutamate Pyruvate Transaminase (SGOT and SGPT), alkaline phosphatase (ALP), bilirubin and total protein. Results of the study showed that methanol extract of *B. tinctoria* leaves at the dose of 150mg/kg and 300mg/kg produced significant effects by decreasing the levels of serum enzymes, bilirubin and lipid peroxidation while it significantly increased the levels of glutathione (GSH), catalase (CAT) and super oxide dismutase (SOD) in a dose dependent manner. These results suggest that the hepatoprotective effect is probably by antioxidant effect on hepatocytes.^[14]

Capparis spinosa

Ethanollic bark extract of *C. spinosa* was studied in animal model against the CCl₄ induced liver damage in rats. Biochemical parameters assessed were alanine transaminase, aspartate transaminase and duration of sleep. Results showed that the group that was treated with extract had a significant decrease in levels of serum enzymes activities in comparison with CCl₄ treated group. The study reveals that *C. spinosa* has a significant protective effect against CCl₄ hepatic damage.^[15]

Cassia fistula

The study was conducted on n- heptanes extract of *Cassia fistula* leaves in experimental animal model. Hepatotoxicity was induced with paracetamol in rats. The dose of extract was 400mg/kg orally. The parameters to be assessed were transaminases (SGOT and SGPT),

bilirubin and alkaline phosphatase (ALP). A significant protective effect was produced by lowering the levels of enzymes.^[16]

Curcuma longa

In this study the curcuma longa was evaluated at the dose of 600mg/kg orally in experimental rats. The hepatotoxic agent taken was paracetamol. Results of the study suggest that it has significant protective effect on liver cells damage caused by paracetamol. The effect may be due to its active constituent curcumin.^[17]

Eclipta Alba

Ethanol/water (1:1) extract of *Eclipta Alba* was studied at subcellular levels in rats against (CCl₄) -induced hepatotoxicity. Study showed the loss of hepatic lysosomal acid phosphatase and alkaline phosphatase by (CCl₄) was significantly restored by *Eclipta Alba*. The results of the study also suggest that hepatoprotective activity of *Eclipta Alba* is by regulating the levels of hepatic microsomal drug metabolising enzymes.^[18]

Ficus carica

In the study antihepatotoxic activity of petroleum ether (60-80°C) extract of leaves of *Ficus carica* against the rifampicin at the dose of 50mg/kg orally in rats was tested. The biochemical parameters assessed were serum levels of glutamic oxaloacetate transaminase, glutamic pyruvic transaminase, bilirubin and histological changes in liver. Liver weights and pentobarbitone sleeping time were also monitored. Results of the study indicated the promising hepatoprotective activity of *ficus carica* as there was significant reversal of biochemical, histological and functional changes induced by rifampicin treatment in rats by petroleum ether extract treatment.^[19]

Lepidium sativum

Hepato-protective activity of methanolic extract of *Lepidium sativum* at a dose of 200 and 400 mg/kg was evaluated against CCl₄-induced liver damage in rats. Results of the study suggested significant reduction in the level of all biochemical parameters that were elevated by CCl₄ administration.^[20]

Prostechea michuacana

In this study methanol, hexane and chloroform extracts of *Prostechea michuacana*(PM) were evaluated for hepatoprotective activity in experimental animal model. The liver toxicity was

produced by CCl₄ in albino rats. Pretreatment administration of methanolic extract reduced the biochemical parameters of liver injury. The extract of PM was administered at the dose of 200, 400 and 600mg/kg. The protective effect was measured by monitoring the serum enzymes. Results showed the significant hepatoprotective effect of methanolic extract of orchid as reflected by reduction in the increased activity of serum enzymes, and bilirubin. These results suggested that methanolic extract of PM could protect paracetamol-induced lipid peroxidation by eliminating the harmful effects of toxic metabolites of paracetamol. This protective effect was comparable with silymarin. Hexane and chloroform extracts did not show any apparent effect.^[21]

Terminalia arjuna

The hydroalcoholic extract of the *Terminalia arjuna* was evaluated for its hepatoprotective activity in Albino Wistar mice. The general behavior of the animals has been studied in comparison to control group with the *Terminalia arjuna* extract treated animals. A gross pathology and histology have also been studied. Study showed that SGOT, SGPT and sALP clearly direct the hepatoprotective effectiveness of hydroalcoholic extract of *Terminalia arjuna*.^[22]

Picrorhiza kurroa

In the study picroliv, that is a standardized fraction of alcoholic extract of *Picrorhiza kurroa* at the dose of (3-12 mg/kg/day for two weeks) simultaneously with *P. berghei* infection was administered. Results of study showed significant protection against hepatic damage in *Mastomys natalensis*. The increased levels of serum glutamate oxaloacetate transaminase (GOT), glutamate pyruvate transaminase (GPT), alkaline phosphatase, lipoprotein-X (LP-X) and bilirubin in the infected animals were markedly reduced by different doses of picroliv. Picroliv also decreased the levels of lipid peroxides and hydroperoxides and facilitated the recovery of superoxide dismutase and glycogen in the liver.^[23]

Solanum nigrum

In Unani system of medicine the drug is known as *Mako*. The extract of *Solanum nigrum* (SNE) was investigated on thioacetamide (TAA)-induced liver fibrosis in mice. Results showed that SNE decreased the hepatic hydroxy proline and α - smooth muscle acting protein levels in TAA treated mice. The extract inhibited TAA-induced collagen (α 1) (I), transforming growth factor- β 1 (TGF- β 1) and mRNA levels in the liver. Histological studies also confirmed that SNE reduced the degree of fibrosis caused by TAA treatment.^[24]

In other study, the protective effects of aqueous extract of *Solanum nigrum* was investigated in experimental rats. Toxicity was produced by CCl₄. The results showed that aqueous extract of Mako has the significant hepatoprotective potential.^[25]

Swertia Chirata

In this study *S. Chirata* (Gentianaceae). at different doses, viz, 20, 50, and 100 mg/kg body wt daily) was administered simultaneously. The toxicity was induced by CCl₄ in experimental rats and the hepatoprotective effect of chirayata was evaluated. Results obtained from the study showed the improvement in biochemical as well as histopathological parameters compared to CCl₄ treated group and the protective effect was more obvious when chirayata was administered in moderate dose(50mg/kg body wt).^[26]

Glycyrrhiza glabra

Glycyrrhizin is the active constituent of *Glycyrrhiza glabra*. Basically it is a triterpine saponin. Various studies shows hepatoprotective potential of Glycyrrhizin.(13) According to the study conducted by Japanese researcher glycyrrhizin promote the regeneration of liver cells and inhibits the fibrosis at the same time. The study was conducted on experimental rats and toxicity was induced by CCl₄. The results also indicate that restore the liver structure and function from the damage due to carbon tetrachloride.^[27]

Foeniculum vulgare

In this study essential oil of *Foeniculum vulgare* was evaluated for its hepatoprotective activity against CCl₄ induced liver toxicity in experimental rats. Results suggested that the hepatotoxicity produced by CCl₄ administration was found to be inhibited by the essential oil of *Foeniculum vulgare* and decreased level of serum aspartate aminotransferase, alanine aminotransferase, alkaline phosphatase and bilirubin.^[28]

COMPOUND FORMULATIONS USED IN UNANI SYSTEM OF MEDICINE

There are more than 300 preparations in the Indian systems of medicine for the treatment of jaundice and chronic liver diseases.^[29]

Jawarish-e-Amila sada

Jawarish-e- Amila Sada is a semisolid preparation used in Unani System of Medicine. A study was performed using the Jawarish Amla Sada(JAS) against CCl₄ induced hepatotoxicity in Wistar Rats. Parameters analyzed were (SGOT, SGPT, TB, CHO and TG).

Toxicity was induced by CCl₄. Study showed that CCl₄ induction caused significant elevation in level of liver enzymes. CCl₄ induction resulted in severe loss of hepatic architecture in the form of intense peripheral and central vein necrosis, fatty changes, etc., when compared to normal control group. The percentage of protection with silymarin was 47.24%, 72.34%, 94.67%, 91.52% and 87.80%, respectively.

Animals treated with aqueous slurry of JAS at two different doses 0.7 and 1.0 g/kg showed a significant reduction in the levels of biochemical parameters. The percentage protection offered by JAS at low dose was found to be 29.43%, 56.03%, 63.82%, 80.65% and 66.95% for SGOT, SGPT, TB, CHO and TG, respectively. At high dose of JAS showed the percentage protection of 42.51%, 79.13%, 90.43%, 97.74% and 85.13% for SGOT, SGPT, TB, CHO and TG, respectively.^[30]

Jigreen

Jigrine is an Unani formulation in the form of syrup containing 14 single drugs. In this study the effects of Jigreen was studied against the alcohol(40% alcohol 2ml/100 g, po for 21 days), CCl₄(1:1 in groundnut oil, 0.1ml/Kg SC. On 20th day) and paracetamol(750mg/kg, ip) induced hepatic damage in rats.

Oral pretreatment with Jigreen was done at the dose of 0.5 ml and 1.0ml/kg for 7 days. Biochemical parameters like SGOT, SGPT, serum bilirubin, plasma prothrombin time and tissue lipid peroxides were estimated to assess the liver function. The level of liver enzymes(serum transaminases, bilirubin, plasma prothrombin time and lipid peroxides) was found elevated due to alcohol - CCl₄ and paracetamol treatment. These effects were progressively reduced by pretreatment doses of Jigrine. The study confirms the hepatoprotective activity of Jigrine and attributes it to the antioxidant property of the formulation.^[31]

Majoon Dabeed ul ward(MD)

In this study Majoon-e-Dabeed-ul-ward (MD), an Unani formulation was evaluated for hepatoprotective activity against acetaminophen (APAP; 2 g/kg p.o.)-induced liver damage.

Study showed that levels of liver enzymes [aspartate transaminase (AST), alanine transaminase (ALT), serum alkaline transaminase (SALP), lactate dehydrogenase (LDH), bilirubin, albumin, urea and creatinine] increased in APAP treated group while treatment with

MD (250,500 and 1,000 mg/kg p.o.) reverse the altered levels of AST, ALT, SALP, LDH, bilirubin, albumin, urea and creatinine in a dose-dependent manner. Results of the study showed that there was a significant restoration in LPO, GSH content and metabolic enzymes (ATPase and G-6-pase) after the treatment with MD. Thus the herbal formulation, MD showed hepatoprotective efficacy against APAP-induced liver damage.^[32]

Qurs-e- Rewand

The present study was done to evaluate the effect of Qurs e Rewand, a Unani formulation on sleep duration in sodium pentobarbital (PB) induced sleeping in mice. It is commonly used compound hepatoprotective drug. Animals were divided in different groups. Extract of Qurse Rewand was administered orally at the dose of (50mg/kg b. w.) and (100 mg/kg b. w.) respectively as single and double dose for 7 days. Silymarin was given at the dose of 100mg/kg b.w. Toxicity was induced by CCl₄ that was given 2ml/kg through the intraperitoneal route on 8th day of the study. After two hours interval these groups were administered sodium pentobarbitone at the dose 30mg/kg b.w. intraperitoneally. The sleeping time was observed by CNS activity as pinna, sound and righting reflex in each animal at every five minutes.

The results obtained, indicated the significant reduction ($P \leq 0.05-0.001$) in the onset and duration of pentobarbitone-induced sleep in mice treated with the test drug.

The results suggest that Qurs e Rewand shortened the pentobarbital hypnosis without major toxic effect and also suggest that QR was more potent in double dose than single dose. The shortening of duration is almost equal to the standard drug. Thus it can be concluded that the drug is safe and can be used in high doses.^[33]

Qurs-e- Tabasheer

The present study was undertaken to investigate the antihyperglycemic, antihyperlipidemic and hepatoprotective activity of an unani formulation “Qurs Tabasheer” in streptozotocin (STZ) induced diabetic wistar rats. The study showed that STZ produced a marked increase in the serum glucose, Total Cholesterol, LDL cholesterol, VLDL Cholesterol, Triglycerides and reduced the HDL level. The hepatoprotective activity was evaluated through estimating levels of various liver enzymes viz. Hexokinase, Glucose-6-Phosphatase and Fructose-1-6-biphosphatase in STZ diabetic wistar rats.

The level of Hexokinase and Glucose-6-Phosphatase was decreased to a significant level while the level of fructose-1-6-biphosphatase was augmented in STZ-induced diabetic wistar rats. Treatment with Qurs Tabasheer extract for 28 days to STZ-induced diabetic rats significantly reduces the level of serum glucose, total cholesterol, triglycerides, glucose-6-phosphatase and fructose-1-6-biphosphatase, while magnitude of HDL cholesterol and hexokinase was more potent. Thus the study confirms the hepatoprotective activity, anti hyperglycemic activity and antihyperlipidemic activity of Qurs-e- tabasheer.^[34]

Qurs-e-Zarisk Sagheer

The present study was designed to investigate the hepatoprotective effect of Qurs e Zarishk Sagheer(QZS) against the CCl₄ induced liver damage in rats. Hydroalcoholic extract was used at the dose 700mg/kgbw and 230 mg/kg bw respectively. Silymarin was taken as a standard drug at the dose 100mg/kg orally once a day. Biochemical parameters viz Serum Glutamate Oxaloacetate Transaminase, Serum Glutamate Pyruvate Transaminase and TBARS were assessed. Histological studies of liver tissues of all the animals were also determined. The study showed gross elevation of liver enzymes as well as histological changes in the animals that were treated with CCl₄, while the test drug showed significant enzymes lowering activity in both lower and higher doses, which was comparable with that of Silymarin. Better results were found in extract treated animals. The study demonstrated that QZS possesses significant liver enzyme lowering effect in CCl₄ induced hepatic injury indicating hepatoprotective effect.^[35]

Kabideen

The present study was designed to evaluate the self prepared (SP) and market sample (MS) of Kabideen(Syrup) for hepatoprotective activity against paracetamol induced hepatotoxicity in albino rats of either sex. at a dose of 5.25 ml/kg body weight. Various biochemical parameters of liver function including serum total bilirubin, total protein, aspartate transaminase (AST), alanine transaminase (ALT), alkaline phosphatase (ALP), total cholesterol and lipid peroxidation were assessed. The histopathological study of liver tissue was also conducted. Results of the study suggested that the level of marker enzymes in the animals treated with paracetamol (750 mg/kg intraperitoneally) were markedly elevated. That indicate the severe damage of liver cells. While the animals treated with two samples of Kabideen showed significant reduction in serum markers. Thus the study indicates the

significant hepatoprotective effect possessed by the test drug. However, the effect of self prepared sample was more striking.^[36]

Sharbat-e- Deenar

Study was done to investigate the hepatoprotective and antioxidant effect of Shrbat-e-Deenar(SD) against the CCl₄ induced liver damage in rats. Hepatoprotective activity was estimated by giving SD at the doses 1, 2 and 4ml/kg orally after CCl₄ intoxication at the dose 1.5ml/kg intraperitoneally for 48 hours in experimental animals. The antioxidant activity was evaluated by DPPH assay, H(2)O(2) assay and total phenolic contents. Results of the study showed the elevation in the levels of biochemical parameters as well as histological deterioration due to the exposure of CCl₄. Therapy with SD showed a marked protection on these parameters(alanine transaminase, aspartate transaminase, albumin and Urea). Treatment with SD also showed a protective effect by restoring the level of lipid peroxidation, reduced glutathione and glucose-6- phosphatase. SD treated groups also showed the significant recovery in the level of hexobarbitone sleeping time and bromosulphthalein retention time. Histopathological study also showed recovery in the architecture of liver cells. Thus the study evaluated that Sharbat-e- Deenar exhibits the hapatoprotective effect which may be due to its antioxidant activity.^[37]

Murawwaqein

Murawwaqein is a frothless juice of Mako(*Solanum nigrum*) and Kasni(*Cichorium intybus*) leaves. It is used as hepatoprotective in Unani system of Medicine.

The present study was undertaken to assess the hepatoprotective activity of Murawwaq of Mako and Murawwaq of Kasni and Murawwaqein against Rifampicin induced hepatic damage in Wistar rats. Rifampicin was given in suspension form orally for 30days to induce the toxicity. Murawwaq of Mako, Murawwaq of Kasni and Murawwaqein along with Rifampicin were administered to the concurrent group. Treated group was given Murawwaq of Mako, Murawwaq of Kasni and Murawwaqein for next 20 days after withdrawl of Rifampicin. Results of the study showed that Murawwaq of Mako, Kasni and Murawwaqein significantly prevented the changes in the level of biochemical parameters like serum bilirubin, SGPT, SGOT and SALP. Results of histopathological analysis also suggest that there were significant reversed changes in degeneration and liver fibrosis in concurrent and treated groups. Thus study can be concluded that Murawwaq of Mako, Murawwaq of Kasni and Murawwaqein prevent and reversed the liver damage caused by Rifampicin.^[38]

Other than above described formulations the following preparations are also mentioned as liver tonic and hepatoprotective in classical Unani literature.

These are Jawarish Jalinoos, Jawarish-e-Amila luluvi, Jawarish-e-Tabashir, Qurs-e-gul, Sharbat-e-anarshreen, Sherbeth-e-deenar, Muffarah-e-Ahmedi, Majoon Dabidul ward, Dawa ul kurkum Kabir, Dawa ul kurkum Sagheer, Dawa ul misk Motadil, Habb e Kabid Naushadri.^{[7], [39]}

CONCLUSION

The classical literature of traditional system of medicine described the use of plants for the treatment of various diseases. In this review it is obvious that single drugs obtained from medicinal plants and compound polyherbal formulations play an important role in various liver diseases. Different medicinal plants and their extracts have potent hepatoprotective activity in various experimental animal models. The hepatoprotective activity is probably due to the presence of flavonoids, phenolic compounds, polyphenols etc. the results of several studies indicate that extracts of medicinal herbs have marked potential for use in liver disorders. The present review gives a brief knowledge about the hepatotoxicity, medicinal herbs and polyherbal compound formulations used in Unani system of Medicine for liver ailments.

REFERENCES

1. *DRUG HEPATOTOXICITY*. TIMBRELL, JOHN A. 1983, Br. J. clin. Pharmac., 15: 3- 14.
2. *Liver Tonics Used In Unani System of Medicine with Reference to Their Hepatoprotective Effect*. Shazia Khan, Hifzul Kabir. New Delhi : Jamia Hamdard, 2007. Research Advances and Traditional Medicine. pp. 121- 130.
3. *Current Concepts of Mechanisms in Drug-Induced Hepatotoxicity*. Stefan Russmann, Gerd A. Kullak-Ublick and Ignazio Grattagliano. 2009, Current Medicinal Chemistry, 16: 3041- 3053.
4. Harrison's. *Principles of Internal Medicine*. McGraw Hill : the Mc Graw Hill companies, 2008; 2: 1949- 1952.
5. *Drug-Induced Hepatotoxicity*. William M. Lee, M.D. 2003, The new england journal of Medicine, pp. 474- 485.
6. *Drug-Induced Hepatotoxicity: A Review*. Aashish Pandit, Tarun Sachdeva and Pallavi Bafna. 5, 2012, Journal of Applied and Pharmaceutical Science, 2: 233- 243.

7. Ibn-e-Sina. *Alqanoon fil tibb*(Urdu Translation by HKm Ghulam Hussain Kantoori). Delhi : Aijaz Publishing House, 2007.
8. Khan, Hkm Aazam. *Qarabadeen- e- Aazam*. Delhi : Sheikh Mohammad Basheer and Sons Urdu Bazar Lahore, YNM. p. 35.
9. Razi, Zakariya. *Kitab- ul- Havi*. New Delhi : CCRUM, 2000; 47- 62.
10. Tabri, Rabban. *Firdaus- ul- Hikmat*. Lahore : Idara Matnuaat-e- Slemani, Urdu Bazar Lahore, 2002; 588- 549.
11. Rajasekaran C., Kalaivani T., Ramya S. and Jayakumararaj R. 8, 2009, Journal of Pharmacy Research, 2: 1419- 1423.
12. *Hepatoprotective activity of Andrographolide from Andrographis paniculata against Carbontetrachloride*. SharmaA., Handa SS and. 1990, Indian J. med., Res.
13. *Hepatoprotective activity of Azadirachta indica leaves on paracetamol induced hepatic damage in rats*. Chattopadhyay R.R, Sarkar S.K, Ganguly S, Banerjee R.N, Basu T.K, Mukherjee A. 8, 1992, Indian J Exp Biol., 30: 738- 740.
14. *Hepato Protective and Antioxidant Role of Berberis tinctoria Lesch Leaves on Paracetamol Induced Hepatic Damage in Rats*. KANDA SAMY MURUGESH, VEERENDRA CHANNABASAPPA YELIGAR, BHIM CHARAN MAITI and TAPAN KUMAR MAITY. 2005, Iranian Journal of Pharmacology and Therapeutics, 4: 64-69.
15. *Hepatoprotective Activity of Capparis spinosa Root Bark Against CCl₄ Induced Hepatic Damage in Mice*. Nasrin Aghela, Iran Rashidib and Amir Mombeinia. 4, 2006, Iranian Journal of Pharmaceutical Research, 6: 285- 290.
16. *Hepatoprotective activity of Cassia fistula*. Bhakta T, Banerjee S, Subhash C. M, Tapan K.Maity, Saha B.P, Pal M. 3, 2001, Phytomedicine., 8: 220- 224.
17. *Hepatoprotective effects of Curcuma longa rhizomes in paracetamolinduced liver damage in rats*. MN, Somchit. 2002. Proceedings of the Regional Symposium on Environment and Natural Resources. pp. 698- 702.
18. *Hepatoprotective effect of the ethanol/water extract of Eclipta Alba*. Saxena A.K, Singh B, Anand K.K. 3, 1993, J Ethnopharmacol, 40: 155- 161.
19. *Hepatprotective Activity of ficus carica Leaf Extract on Rifampicini Induced Hepatic Damage in Rats*. Khadabadi, N.Y. Gond and S.S. 3, 2008, Indian Journal of Pharmaceutical Science, 70: 364- 366.
20. *Hepato-protective effect of Lepidium sativum against car-bontetrachloride-induced damage in rats*. Afaf I, Abuelgasim, Nuha HS, Mohammed AH. 2008, Res Journal of Animal Veterinary Science, 3: 20-23.

21. *Hepatoprotective and Inhibition of Oxidative Stress of Prostechea michuacana*. Rosa MP, Gutiérrez, Rosario VS. 1, 2009, Rec Nat Prod, 3: 46- 51.
22. *Hydroalcoholic Extract of Terminalia arjuna: A Potential Hepatoprotective Herb*. Subasini U., Rajamanickam G.V., Dubey G.P., Prabu P.C. 2, 2007, Journal of Biological Sciences, 7: 255- 262.
23. *Evaluation of Picrolive from Picrorhiza kurroa in Mastomys natalensis infected with Plasmodium berghei*. Chandar R, Dwivedi Y, Rastogi R, Sharma SK, Garg NK, Kapoor NK, Dhawan BN. 7, 1990, International Journal on Medicinal Research, 34: 1330-- 1334.
24. *Inhibitory effect of Solanum nigrum on thioacetamide-induced liver fibrosis in mice*. Chang-Chi H, Hsun-Lang F and Wen-Chuan L. 2008, J Ethnopharmacol, 119: 117- 121.
25. *A REVIEW ON HEPATOPROTECTIVE HERBAL DRUGS*. Kumar, Anil. 1, 2012, INTERNATIONAL JOURNAL OF RESEARCH IN PHARMACY AND CHEMISTRY, 2: 92- 102.
26. *Antihepatotoxic activity of Swertia chirata on paracetamol and galactosamine induced hepatotoxicity in rats*. Karan M, Vasisht K, Handa S.S. 2, 1999, Phytotherapy Research, 13: 95- 101.
27. *Herbal medicine in Treatment of Liver Diseases*. Stickel F, Schuppan, D. 2007, Digestive and Liver Disease, 39: 293- 304.
28. *Fenugreek (Trigonella foenum graecum) seed extract prevents ethanol-induced toxicity and apoptosis in chang liver cells*. Subramanian Kaviarasan, Nalini Ramamurty, Palani Gunasekaran Elango Varalakshmi and Carani Venkatraman Anuradha. 3, 2006, Alcohol & Alcoholism, 41: 267- 273.
29. *HEPATOPROTECTIVE HERBAL MEDICINE: A REVIEW*. Chandan Das, Ashutosh Mishra, Manas Ranjan Mishra, Dushmantha Kumar Pradhan, Malarkodi Velraj, Sujit Dash, Durgacharan Sahoo. 1, 2012, Int RJ Pharm Sci, 3: 0001- 00012.
30. *Efficacy of a traditional unani formulation Jawarish-e-Amla Sada against CCl₄ induced liver toxicity in Albino Wistar Rats*. Sunita Shailajan, Mayuresh Joshi, Dipti Singh, dipti Gurjar, Bhavesh Tiwari. 2015, International Journal of Green Pharmacy, pp. 100- 103.
31. *HEPATOPROTECTIVE ACTIVITY OF "JIGRINE" ON LIVER DAMAGE CAUSED BY ALCOHOL - CARBONTETRACHLORIDE AND PARACETAMOL IN RATS*. VIVEK KAPUR, K.K. PILLAI, S.Z. HUSSIAN, D.K. BALANI. 1994, Indian Journal of Pharmacology, 26: 35- 40.

32. *Evaluation of Hepatoprotective Efficacy of Majoon-e-Dabeed-ul-ward Against Acetaminophen-Induced Liver Damage: A Unani Herbal Formulation.* Shukla, Arvind Kumar Shakya and Sangeeta. 2011, DRUG DEVELOPMENT RESEARCH, 72: 346- 352.
33. *Effect of Qurs-e-Rewand (A Hepatoprotective Unani Formulation) on Pentobarbitone induced Sleeping in Mice.* Khan, Shamshad Alam & Naeem A. 3, 2015, Journal of Medical Science and Clinical Research, 3: 4885- 4890.
34. *Improved glycemic control, pancreas protective and hepatoprotective effect by traditional poly-herbal formulation "Qurs Tabasheer" in streptozotocin induced diabetic rats.* Danish Ahmed, Manju Sharma, Alok Mukerjee, Pramod W Ramteke and Vikas Kumar¹. 10, 2013, BMC Complementary and Alternative Medicine, 13: 1- 15.
35. *The Effect of Qurs-e-Zarishk Sagheer(A Compound Unani Formulation) on Liver Enzymes in CCl₄ Induced Hepatotoxicity in Rats.* Shamshad Alam, 1Naeem. A. Khan and Mohammad. Nasiruddin. 4, 2014, HIPPOCRATIC JOURNAL OF UNANI MEDICINE, 9: 1- 12.
36. *Hepatoprotective Activity of A Unani Polyherbal Formulation "Kabideen" in Paracetamol Induced Liver Toxicity in Rats.* Mahim Zameer, Abdur Rauf and Iqbal Ahmad Qasmi. 4, 2014, HIPPOCRATIC JOURNAL OF UNANI MEDICINE, 9: 41- 50.
37. *Hepatoprotective Efficacy of Sharbat-e- Deenar against carbon tetrachloride- induced liver damage.* Shakya AK, Saxena M, Sharma N, Shrivastava S, Shukla S. 2, 2012, J Environ Pathol Toxicol Oncol, 31: 131- 141.
38. *Effect of Murawwaq of Mako, Murawwaq of Kasni and Murawwaqein on Hepatotoxicity Induced by Rifampicin in Rats Just After the Rainy Season(August- Septmber).* N. Khatoon, H. Kabir, S. Javed, M.Asif, S. Fatima and M.N.Khan. 2, 2009, Hamdard Medicus, 52: 48- 53.
39. Kabir, Hifzul. *Morakkabat (Unani Formulations).* Aligarh : Shamsheer Publisher and Distributors, 2003.