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Therapeutic Principles of Liver Diseases (Amraz-e-Jigar) & Hepatoprotective Medicine used in Unani System of Medicine-A Review Article

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Abstract.

Liver disease is one of the major causes of morbidity and mortality across the world. According to WHO estimates, about 500 million people are living with chronic hepatitis infections resulting in the death of over one million people annually. Medicinal plants serve as a vital source of potentially useful new compounds for the development of effective therapy to combat liver problems. Moreover herbal products have the advantage of better affordability and acceptability, better compatibility with the human body, and minimal side effects and are easier to store. Comprehensive scientific studies on safety and efficacy of these plants can revitalise the treatment of liver diseases. Unani System of Medicine has been treating liver diseases since centuries under the aegis of principles, which advise usage of specific drugs or therapy for a particular disease including liver diseases. To review the therapeutic principles along with Unani drugs documented in the treatment of liver diseases.

Keywords: Abnormal temperament Liver, Complementary medicine, Hepatoprotective drugs, Sue Mizaj, Unani Hepato protective, Unani medicine.

1. Introduction History and Background of liver Diseases:

Liver is the largest and unique organ, considered as source of hararat-e-ghariziya (innate heat) for body. So it was discussed much widely in Unani literature. Galen, (129-217 AD) even stated liver counterpart with sun, a source of energy for others planets. The basic functions are conveniently grouped under

(1) vascular functions

(2) excretory and secretory functions

(3) metabolic functions and

(4) Detoxifications functions.

In Unani Medicine (Greco-Arab Medicine), liver is an organ for production of akhlat (humours) and its four vital powers (quwaa) namely quwat-e- jaziba (power of absorption), quwat-e- ghaziya (power of digestion), quwat-e-masikah (power of retention) and quwat-e- dafiya (Power of excretion) perform all the functions related to liver. The derangement of function of any of these four powers produces derangement in temperament of humours. Moreover, deranged temperament of the humours leads to accumulation of mawad-e-fasida (morbid material) and ultimately pathological changes in the liver. The derangement of temperament of humours may be simple (saada) which need simple therapeutic measures or it may be compound (maddi) in which organic disturbance and quantitative changes take place in the liver cells. A number of liver diseases are mentioned in Unani Medicine, such as

A. Su-e- Mizaj (Abnormal/ Pathological temperament of the Liver),
B. Zauf-e Jigar (Dullness of Liver, Hepatosis or Hypocholeretic),
C. Sudda-e-Jigar (Hepatic obstruction),
D. Dard-e-Jigar (Hepatalgia),
E. Warm-e-Jigar (Hepatitis),
F. Zarba-e-Jigar (Trauma),
G. Dabila-e-Jigar (Hepatic Abscess),
H. Segar-e-jigar (Cirrhosis of Liver),
I. Su-ul-Qinaya (Anemia) and
J. Istiska (Ascites).

The liver is an organ about the size of a football. It sits just under your rib cage on the right side of your abdomen. The liver is essential for digesting food and ridding your body of toxic substances. Liver disease can be inherited. Liver problems can also be caused by a variety of factors that damage the liver, such as viruses, alcohol use and obesity. Over time, conditions that damage the liver can lead to scarring (cirrhosis), which can lead to liver failure, a life-threatening condition. But early treatment may give the liver time to heal.

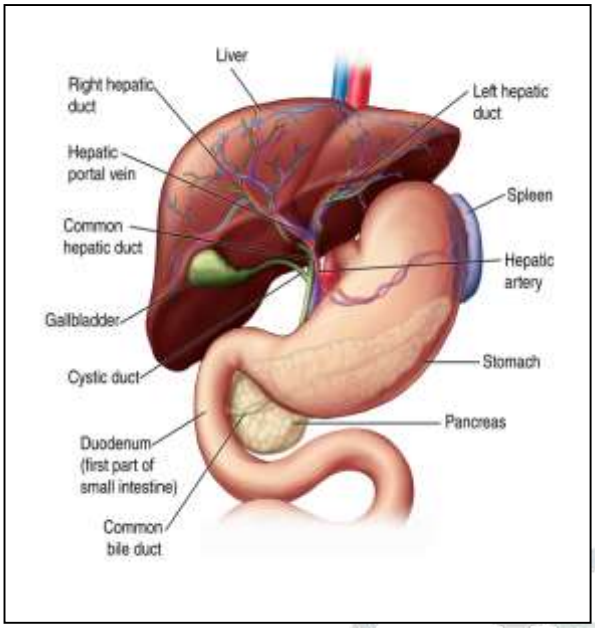

Fig. 1 Anatomy of healthy liver

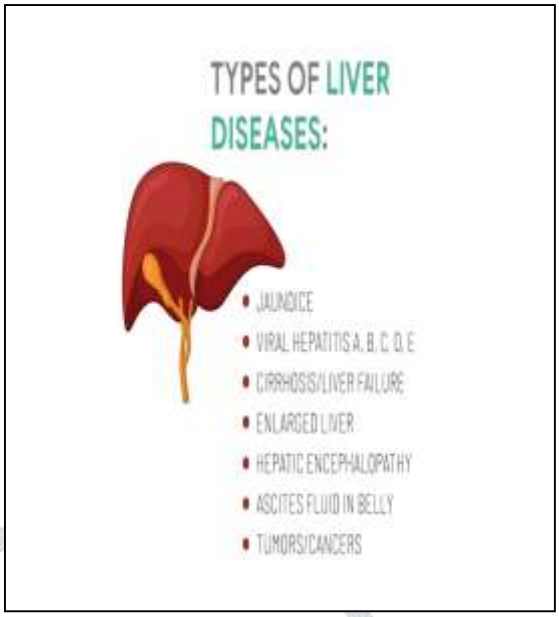

Fig. 2 list of liver diseases

The liver is the most important organ that plays an important role in maintaining various physiological processes in the body. It is involved in several vital functions, such as metabolism, secretion, and storage. It plays a central role in the detoxification and excretion of many exogenous and endogenous compounds. Hence, any injury to it or impairment of its function has grave implications for the health of the affected person. Every year, about 18,000 people are reported to die due to liver cirrhosis caused by hepatitis, although viral infection is one of the main causes for hepatic injury. It acts as a storage depot for proteins, glycogen, various vitamins, and metals. It also has a role in the regulation of blood volume by transferring the blood from the portal to the systemic circulation and its reticulo-endothelial system and participates in the immune mechanism. The human body identifies almost all drugs as foreign substances (i.e., xenobiotics) and subjects them to various chemical processes (such as metabolism) to make them suitable for elimination. This involves chemical transformations to (a) reduce fat solubility and (b) change biological activity. Although almost all tissues in the body have some ability to metabolize chemicals, smooth endoplasmic reticulum in liver is the principal “metabolic clearing house” for both endogenous chemicals (e.g., cholesterol, steroid hormones, fatty acids, and proteins), and exogenous substances (e.g., drugs). The central role played by the liver in the clearance and transformation of chemicals also makes it susceptible to drug-induced injury.

Hepatitis is an inflammation of the liver and is characterized by the presence of inflammatory cells in the tissue of the organ. There are five main viruses, referred to as types A, B, C, D, and E. These five types are of the greatest concern because of the burden of illness and death. The condition can be self-limiting or can progress to fibrosis (scarring) and cirrhosis. Hepatitis may occur with limited or no symptoms, but often leads to jaundice, anorexia, and malaise. Hepatitis is acute when it lasts less than 6 months and chronic when it persists for longer. Hepatic trouble, which includes parasites and viral infections; autoimmune diseases; and intoxication with various xenobiotics such as alcohol, herbal medicine, drugs, chlorinated solvents, peroxidized fatty acids, fungal toxins, industrial pollutants, and radioactive isotopes. In particular, types A and

C lead to chronic disease in hundreds of millions of people and, together, are the most common cause of liver cirrhosis and cancer.

About 1 million deaths per year are attributed to viral hepatitis infection, that is, hepatitis B virus (HBV) and hepatitis C virus (HCV) taken together, which is the leading cause of liver cirrhosis and cancer, accounting for 78% of cases. Nearly 1 out of every 3 people in the world (approximately 2 million people) has been infected by HBV and HCV. On World Hepatitis Day, July 28, 2013, the World Health Organization (WHO) and its partners focused on the fact that although the burden of disease caused by viral hepatitis is growing, it remains largely ignored or unknown to many policymakers, health workers, and the public.

2. Symptoms of Liver diseases:

Liver disease doesn't always cause noticeable signs and symptoms. If signs and symptoms of liver disease do occur, the may include:

A. Skin and eyes that appear yellowish (jaundice)
B. Abdominal pain and swelling
C. Swelling in the legs and ankles
D. Itchy skin
E. Dark urine color
F. Pale stool color
G. Chronic fatigue
H. Nausea or vomiting
I. Loss of appetite
J. Tendency to bruise easily

Make an appointment with your doctor if you have any persistent signs or symptoms that worry you. Seek immediate medical attention if you have abdominal pain that is so severe that you can't stay still.

3. Causes of liver Diseases:

Liver disease has many causes.

I. Infection of Liver diseases:

Parasites and viruses can infect the liver, causing inflammation that reduces liver function. The viruses that cause liver damage can be spread through blood or semen, contaminated food or water, or close contact with a person who is infected. The most common types of liver infection are hepatitis viruses, including:

A. Hepatitis A
B. Hepatitis B
C. Hepatitis C

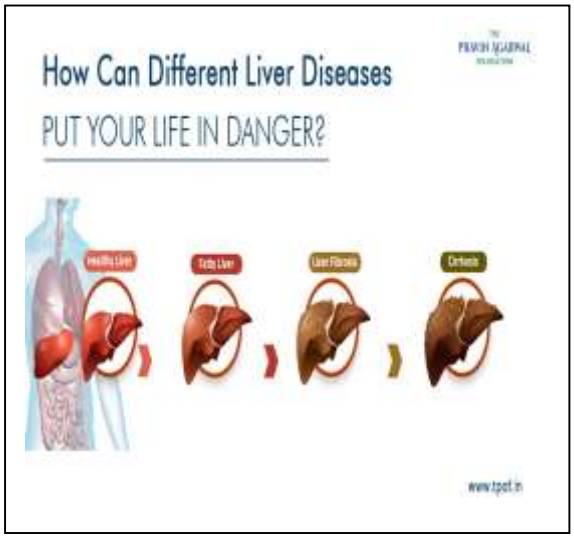

Fig.3 Healthy liver and infected liver

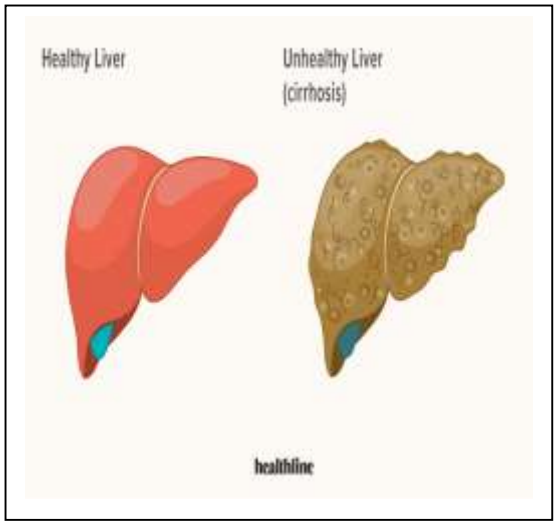

Fig.4 Healthy liver and infected liver

II. Immune system abnormality

Diseases in which your immune system attacks certain parts of your body (autoimmune) can affect your liver. Examples of autoimmune liver diseases include:

A. Autoimmune hepatitis

B. Primary biliary cholangitis

C. Primary sclerosing cholangitis

III. Genetics

An abnormal gene inherited from one or both of your parents can cause various substances to build up in your liver, resulting in liver damage. Genetic liver diseases include:

A. Hemochromatosis

B. Wilson's disease

C. Alpha-1 antitrypsin deficiency

IV. Cancer and other growths

Examples include:

A. Liver cancer

B. Bile duct cancer

C. Liver adenoma

V. Other

Additional, common causes of liver disease include:

A. Chronic alcohol abuse

B. Fat accumulation in the liver (nonalcoholic fatty liver disease)

C. Certain prescription or over-the-counter medications

D. Certain herbal compounds

4. Risk factors of Liver diseases:

Factors that may increase your risk of liver disease include:

A. Heavy alcohol use

B. Obesity

C. Type 2 diabetes

D. Tattoos or body piercings

E. Injecting drugs using shared needles

F. Blood transfusion before 1992

G. Exposure to other people's blood and body fluids

H. Unprotected sex

I. Exposure to certain chemicals or toxins

J. Family history of liver disease

Complications of liver disease vary, depending on the cause of your liver problems. Untreated liver disease may progress to liver failure, a life-threatening condition.

5. Prevention of Liver diseases:

To prevent liver disease:

A. Drink alcohol in moderation. For healthy adults, that means up to one drink a day for women and up to two drinks a day for men. Heavy or high-risk drinking is defined as more than eight drinks a week for women and more than 15 drinks a week for men.

B. Avoid risky behavior. Use a condom during sex. If you choose to have tattoos or body piercings, be picky about cleanliness and safety when selecting a shop. Seek help if you use illicit intravenous drugs, and don't share needles to inject drugs.

C. Get vaccinated. If you're at increased risk of contracting hepatitis or if you've already been infected with any form of the hepatitis virus, talk to your doctor about getting the hepatitis A and hepatitis B vaccines.

D. Use medications wisely. Take prescription and nonprescription drugs only when needed and only in recommended doses. Don't mix medications and alcohol. Talk to your doctor before mixing herbal supplements or prescription or nonprescription drugs.

E. Avoid contact with other people's blood and body fluids. Hepatitis viruses can be spread by accidental needle sticks or improper cleanup of blood or body fluids.

F. Keep your food safe. Wash your hands thoroughly before eating or preparing foods. If traveling in a developing country, use bottled water to drink, wash your hands and brush your teeth.

G. Take care with aerosol sprays. Make sure to use these products in a well-ventilated area, and wear a mask when spraying insecticides, fungicides, paint and other toxic chemicals. Always follow the manufacturer's instructions.

H. Protect your skin. When using insecticides and other toxic chemicals, wear gloves, long sleeves, a hat and a mask so that chemicals aren't absorbed through your skin.

I. Maintain a healthy weight. Obesity can cause nonalcoholic fatty liver disease.

6. General Principles of Treatment of Liver diseases in Unani system of medicine:

According to the Avicenna (1037 AD), while treating liver diseases, the tabeeb (physician) must know what is the normal temperament of the liver in that patient. Afterward, physician should assess the pathological temperament based on sign and symptoms, mentioned for respective type of su-e- mizaj and then accordingly use his skill to counteract the effect of pathological temperament (tadeel-e-mizaj) existing at the time of the disease but this counteraction must not be pushed extensively. In case of sudda-e-jigar (hepatic obstruction), try to relive the obstruction with the help of deobstruents (muftta-eh-sudad) such as Gentiana olivierii (Ghafis), Sphaeranthus indicus (Izkhar), Coriandrum sativum (Razyana/ Dhanaya), Cuscuta reflexa (Kasoos), Lupinus albus (Turmus) and Sphaeranthus indicus (Mundi). If dullness occurs in any of four quwaa (vital forces) or to empower the liver (islah), treatment should be provided with the drugs which essence like perfumes along with property of diuresis, astringent and deobstruent such as Cinnamomum zeylanicum (Darchini). Avicenna (1037 AD), particularly mentioned medicines with bitter taste, were mentioned favorable for liver e.g. Commiphora myrrha (Mur makki).

Tila and Zimad (Liniments and Ointments) were described briskly effective but were advised to use with cautions and should not be manipulated before tankiya (evacuation). Cichorium intybus (Kasni) and its other varieties, especially the bitter one, taken simply or as decoction (joshanda) or in the form of crushed juice (khisandah) was stated effective in all type of liver diseases. However in the case of extreme coldness in temperament of liver (pathological temperament), cichorium was advised to be consume mixed with honey.

According to Hippocrates (460-372 BC) and Galen (129-217 AD), muqawwi-e-Jigar (hepatoprotective/ liver tonics) drugs should be used along with other medicines.[4] Some muqawwi Jigar (hepatoprotective/ liver tonics) drugs, mentioned in Al-Qanoon which have been proven for their hepatoprotective effect Except Luk (Coccus lacca).

Avicenna [1037 AD] and other scholars also mentioned that worthiest time to take medicine in liver disease is, when the food has past the stomach and reaching toward the liver for further digestion or metabolism. Avicenna [1037 AD] also stated that during correction of temperament, providing extensive coldness endanger the possibility of anasarca or ascites and too much warmth/ hotness put vulnerability of zabol (atrophy of liver).

Razes [930 AD] in Alhawi, Avicenna [1037 AD] in Al-Qanoon and Azam khan in Akseer-e- Aazam, have documented principles about evacuation of the morbid material (istafraag) that it relies on morbid material (madda) position with respect to liver curvature. If morbid material (madda), present in concave portion of Liver, it iswise to expel through gut by purgatives. He also stated that it would be risky to expel the same through gut, if present in the convexity of liver as it should be evacuated through urine with the help of diuretics. Moreover, the drugs intended for diuresis should be grind in very fine particles than for purgation.

Stuffs / things injurious for Liver- eating another meal before complete digestion of first meal & improper dietary habits such as drinking cold water shortly after a sexual act, bath (hammam) or exercise harms liver and may cause istiska (ascites). In unavoidable circumstances, sips of water or small quantity of wine added with not too much cold water could be taken. Mucilaginous drugs and alcohol are

contraindicated and documented harmful, owning to their ability to produce obstruction in liver (sudda).

Therapeutic principles in abnormal/ pathological Temperament of liver (Su-e-Mizaj)

A. Su-e-Mizaj Haar Jigar (Abnormal / Pathological Hot Temperament of Liver)

Excess of coldness is injurious to liver, potentiate obstruction (sudda). Mild to moderate frigorific drugs (mubarrid adviyah) with additional deobstruent (mufattah), detergent (jali) and mild astringent properties were advised e.g. Cichorium intybus (Kasni) Berberis vulgaris (Zarishk) Tamarindus indicus (Tamarhindi)

Apium graveolens (Karafs) should be added additionally in compound formulations, in the presence of obstruction (sudda). Avicenna [1037 AD] proclaimed Apium a general deobstruent. Solanum nigrum (Mako)

The extract of Cichorium intybus (usarah- e-kasni), Physalis alkakengji (usarah-e- kakanaj), Solanum nigrum (usarah inab-us-salab/ Mako) each two parts, fresh Coriander sativum (usarah-e- kishneez tar) and Foeniculum vulgare (usarah-e- razyanaj) each one and half parts and with addition of half part of Crocus sativus (Zafran) should be ingested. Oil of Rose and oil of Pyrus malus (Tufah) are frigorific locally, should be applied on liver area before ingestion of the above extract (usarah). Allamah Karshi in Jamiul- Hikmat, has additionally recommended, venesection (fasd of bansleq/ abti) or application of leech on skin over liver area or around the anus, in presence of congestion in the liver.

Fig. 5 Jigreen Tonic for liver diseases

Compound formulations of Unani Medicine (murrakab adviyah) such as qurs- e-tabasheer,qurs- e-zarishk and qurs- e-kafoor were also described as beneficial.

Diet barley water (ma-ul-shaeer) as a diet was documented highly advantageous and vegetable soup combined with Cichorium intybus(Kasni), Solanum nigrum (Inbul Sa-al-lab/ Makoh), Green Coriander and Andropogon muricatus (Khas) were also stated as beneficial. Beet root, sour curdled milk (dahi), whey water, fresh apple juice, Punica granatum (pomegranate), Vitis vanifera (grapes), mulberry, vinegar (sirkah), and not too sweet melons were indicated as a diet in liver diseases. Unless a patient with good digestive system, fatty oily foods, meat and boiled eggs were stated harmful in patients of liver diseases.

B. Su-e-Mizaj Barid Jigar (Abnormal/ Pathological Cold Temperament of Liver)

Su-e-Mizaj Barid Jigar was mentioned, which produces zauf-e jigar (dullness of liver), dard-e-jigar (hepatalgia), su-ul-qinaya (anaemia) and istiska (ascitis). Compound formulations of Unani Medicine

(murakab adviyah) such as dawa- ul-kurkum, dawa-ul-luk, qurs-e-afsanteen, majoon falaasfa, itrifal-e-kabeer, tiryaqe kabeer and asanasaya were stated hot in temperament. So these drugs were used to counteract the coldness of liver which resulted in alteration (tadeel) of the disease condition and recovery. The wine of Artemisia absinthium (Afsanteen) containing Sikanjabeen has been stated worthwhile by Avicenna [1037 AD]. Moreover, tablet of Artemisia at bedtime has been proclaimed to accentuate its effects. In severe cases of this disease joshanda-e- sikanjabeen along with Qurs e luk should be administered. Decoction of Artemisia and Saussuria lappa (Qust) along with oil of almond and pistachio were mentioned also beneficial. Ointment (Zimad) prepared from Nardostachys jatamansi (Sumbulut-tibb), Metrocaria chamomile (Babunah), Andropogon schoenanthus (Izkhar) along with rose flower should be applied locally on the skin over liver area. Diet easily digestible meat, especially roasted has been allowed. Dry fruits in small quantity were advised effective.

C. Su-e-Mizaj Yabis Jigar (Abnormal/ Pathological Dry Temperament of Liver).

Vegetables and Drugs which are humectant (murattib) along with local application of humectant ointments and liniments (murattib zimad& oils) should be advised. Papaver somniferum (Khashkhash) has been mentioned for the treatment by Ahmad bin Rabban Tabri.

D. Su-e-Mizaj Ratab Jigar (Abnormal/ Pathological Wet Temperament of Liver).

Exercise, reduction in food and beverages and avoidance of liquid and liquid containing things have been constituted, the principles for treatment but also advised to avoid producing too much desiccation (tajfeef).

E. Su-e-Mizaj Haar Ybis Jigar (Abnormal/ Pathological Hot & Dry Temperament of Liver).

These patients should be treated with cold and moisture producing vegetables especially Endive (Kasni). Rice, spices and excessive pistachio should be avoided and respective liniments and ointments should be used locally.

F. Su-e-Mizaj Haar Ratab Jigar (Abnormal/ Pathological Hot & wet Temperament of Liver)

Humectants which possessed astringent property such as ma-ul jibn have been advised. Su-e-Mizaj Barid Ratab Jigar (Abnormal/ Pathological Cold & wet Temperament of Liver).Astringent (kabiz), demulscent (mulattif) and heat producing diets & drugs have been advised and if there were cold & moist morbid material, it has been advised that it should be evacuated (istafraag) gently either through ma-ul usool quwi or ayyaraj.

G. Su-e-Mizaj Barid yabis Jigar (Abnormal/ Pathological Cold and Dry Temperament of Liver).

Dawa-ul-luk,dawa-ul-kurkumand amrosiyah should be administered with ma-ul-usool and moist oils. Moreover, heat producing ointments should also be applied. Galen [129-217 AD] proclaimed treatment of su-e-mizaj barid yabis jigar and recovery toward health, a difficult one and also advised meat of one year goat's kid cooked in different ways should be used as it produces heat and moist in body.

7. Herbal Drugs used in liver diseases.

A. Foeniculum vulgare

Fennel (Foeniculum vulgare Mill. Family Umbelliferae) is an annual, biennial or perennial aromatic herb, depending on the variety, the leaves, stalks and seeds (fruits) of the plant are edible. Foeniculum vulgare is an aromatic herb whose fruits are oblong, ellipsoid or cylindrical, straight or slightly curved and greenish or

yellowish brown in colour. Volatile components of fennel seed extracts by chromatographic analysis include trans-anethole, fenchone, methylchavicol, limonene, α-pinene, camphene, β-pinene, β-myrcene, α-phellandrene, 3-carene, camphor, and cis anethole. Hepatoprotective activity of Foeniculum vulgare essential oil was studied using a carbon tetrachloride-induced liver fibrosis model in rats. The hepatotoxicity produced by chronic carbon tetrachloride administration was found to be inhibited by Foeniculum vulgare essential oil with evidence of decreased levels of serum aspartate aminotransferase, alanine aminotransferase, alkaline phosphatase and bilirubin.

B. Trigonella foenum graecum

Fenugreek (Trigonella foenum graecum) is an annual herb that belongs to the family Leguminosae. The seeds of fenugreek are commonly used as a spice in food preparations due to the strong flavour and aroma. The seeds are reported to have restorative and nutritive properties. Fenugreek seeds have antioxidant activity and have been shown to produce beneficial effects such as neutralization of free radicals and enhancement of antioxidant apparatus. The protective effect of a polyphenolic extract of fenugreek seeds against ethanol-induced toxicity was investigated in human Chang liver cells. Ethanolic treatment suppressed the growth of Change liver cells and induced cytotoxicity, oxygen radical formation and mitochondrial dysfunction. Incubation of FPEt along with EtOH significantly increased cell viability in a dose-dependent manner, caused a reduction in lactate dehydrogenase leakage and normalized GSH/GSSG ratio. The findings suggest that the polyphenolic compounds of fenugreek seeds on the other gastric and lung cancer cell lines included in the screen. The investigators suggested that garcinone E may be potentially useful for the treatment of certain types of cancer.

Fig. 6 Herbal drugs for liver diseases

Fig. 7 Herbal drugs for liver diseases

C. Garcinia mangostana Linn

Garcinia mangostana Linn. commonly known as " mangos teen", is a tropical evergreen tree and is an emerging category of novel functional foods sometimes called "super fruits" presumed to have a combination of appealing subjective characteristics, such as taste, fragrance and visual qualities, nutrient richness, antioxidant strength and potential impact for lowering risk of human diseases . The pericarps of G.

mangostana have been widely used as a traditional medicine for the treatment of diarrhea, skin infection and chronic wounds in South East Asia for many years. These are the nature's most abundant sources of xanthones, which are the natural chemical substances possessing numerous bioactive properties that help to maintain intestinal health, neutralize free radicals, help and support joints and cartilage functions and promotes immune systems. These are extracted from the rind of mangos teen containing 95% xanthones also isoflavones, tannin and flavonoids. Treatment of hepatocellular carcinomas with chemotherapy has generally been disappointing and it is most desirable to have more effective new drugs.

D. Jatropha curcas

Jatropha curcas Linn (Family: Euphorbiaceae), is an evergreen shrub, indigenous to America, but cultivated in most parts of India. This evergreen plant is common in waste places throughout India, especially on the Coromandel Coast and in Travancore; in the southern parts it is cultivated chiefly for hedges in the Konkan, and also in Malay Peninsula. Leaves are regarded as antiphrastic, applied to scabies; rubefacient for paralysis, rheumatism; also applied to hard tumours. Leaves also show antileukemic activity. Compounds that have been isolated from Jatropha curcas leaves include the flavonoids apigenin and its glycosides vitexin and isovitexin, the sterols stigmasterol, α -D-sitosterol and its α – Dglucosi e. Methanolic fraction of leaves of Jatropha curcas (MFJC) was evaluated against hepatocellular carcinoma induced by Aflatoxin B1.

Fig. 8 Herbal drugs for liver diseases

E. Silybum marianum

The protective effects of polyphenolic extract of Sily-bum marianum and Cichorium intybus on thioacetamide- induced hepatotoxicity in rat was investigated. The extracts were injected to the rats, at a dose of 25 mg kg-1 body weight together with thioacetamide at a dose of 50 mg kg body weight. Significant decrease in the activity of aminotransferase, alkaline phosphatase and bilirubin was observed in the groups treated with extracts and thioacetamide compared with the group that was treated only with thioacetamide. The level of Na+, K+ and liver weight between different groups was not significantly altered. This finding

suggested the hepatoprotective effect of Silybum marianum and Cichorium intybus extracts on liver cells due to the presence of flavonoids and their antioxidant effects.

F. Chamomile capitula

The effect of ethanolic extract of Chamomile recutita capitula (400 mg kg-1, P.O.) on blood and liver glutathione, Na+ K+- ATPase activity, serum marker enzymes, serum bilirubin, glycogen and thiobarbutiric acid reactive substances against paracetamol-induced liver damage in rats have been studied to find out the possible mechanism of Hepato protection. It was observed that extract of Chamomile recutita has reversal effects on the levels of abovementioned parameters in paracetamol hepatotoxicity suggesting its Hepato protective and / or Hepato stimulant activity.

Fig. 9 House hold remedies for liver diseases

G. Coccinia grandis

Alcoholic extract of the fruits of Coccinia grandis Linn (Curcubitaceae) was evaluated in CCl4-induced hepato-toxicity in rats and levels of AST, ALT, ALP, total proteins, total and direct bilirubin were evaluated. At a dose level of 250 mg/kg, the alcoholic extract significantly ($p<0.05$) decreased the activities of serum enzymes (AST, ALT and ALP) and bilirubin which were comparable to that of silymarin revealing its hepato-protective effect.

H. Wedelia calendulacea

The hepatoprotective activity of ethanolic extract of Wedelia calendulacea L. (Family: Asteraceae) was studied against CCl4-induced acute hepatotoxicity in rats. The treatment with ethanolic extract of Wedelia calendulacea showed a dose-dependent reduction in CCl4-- induced elevated serum enzyme activities with parallel increase in total proteins and bilirubin, indicating the extract could enhance the return of normal functional status of the liver comparable to normal rats. The weight of the organs such as liver, heart, lung, spleen and kidney in CCl4-induced hepatic damaged animals that received ethanolic extract of Wedelia calendulacea showed an increase over CCl4-treated control group.

I. Annona squamosa

The extracts of Annona squamosa (300 & 350 mg/kg bw) were used to study the hepatoprotective effect in isoniazid + rifampicin induced hepatotoxic model in albino Wistar rats. There was a significant decrease in total bilirubin accompanied by significant increase in the level of total protein and also significant decrease in ALP, AST, and ALT in treatment group as compared to the hepatotoxic group. In the histo pathological study, the hepatotoxic group showed hepatocytic necrosis and inflammation in the centrilobular region with portal triaditis. The treatment group showed minimal inflammation with moderate portal triaditis and their lobular architecture was normal

J. Flacourtia indica

The extracts of the aerial parts of Flacourtia indica (Burm. f.) Merr., were evaluated for hepato-protective properties. In paracetamol induced hepatic necrosis in rat models, all extracts were found to reduce serum aspartate transaminase (AST), serum alanine transaminase (ALT) and serum alkaline phosphatase (ALP). The most significant reduction of the serum level of AST and ALT were exhibited by petroleum ether and ethyl acetate extracts at a single oral of dose of 1.5g/kg of body weight with a reduction of 29.0% AST & 24.0% ALT level by petroleum ether extract, and 10.57% AST & 6.7% ALT level by ethyl acetate extract compared to paracetamol (3 g/kg of body weight) treated animals. Histopathological examination also showed good re-covey of paracetamol-induced necrosis by petroleum ether and ethyl acetate extracts. On the other hand, the methanol extract did not show any remarkable effect on paracetamol induced hepatic necrosis. The Hepatoprotective effects exhibited by petroleum ether and ethyl acetate extract might be mediated through the inhibition of microsomal drug metabolizing enzymes.

K. Swertia Chirata

Due to effect of Hepato toxicant (like ethanol, drugs, chemicals and others) serum aspartate aminotransferase , alanine aminotransferase , and alkaline phosphatase (ALP) activities and bilirubin level are increased, but liver glycogen and serum cholesterol levels are decreased. Histologically it produced Hepato cytic necrosis especially in the centrilobular region. Simultaneous treatments with Swertia chirata caused improvement at both biochemical and histo pathological parameters. Drug also possesses digestive, hepatic (conditions pertaining to the liver), tonic, astringent and appetizer properties and used in cough, dropsy and skin diseases. Swertia Chirata Simultaneous treatments with S. Chirata. (in different doses, viz. 20, 50, and 100 mg/kg body wt daily) and (CCl4) caused improvement at both biochemical and histo pathological parameters compared to that of (CCl4) treatment alone but it was most effective when S. chirata was administered in a moderate dose.

L. Cassia fistula (Amaltas)

Hepatoprotective activity of the n-heptanes extract of Cassia fistula (Fabaceae) leaves was investigated by inducing hepatotoxicity with paracetamol in rats. The extract at a dose of 400 mg/kg body wt. exhibited orally, significant protective effect by lowering the serum levels of transaminase (SGOT and SGPT), bilirubin and alkaline phosphatase. The effects produced were comparable to that of a standard Hepato protective agent.

M. Azadirachta indica (Neem)

Effect of A. indica leaf (Meliaceae) extract on serum enzyme levels (glutamate oxaloacetate transaminase, glutamate pyruvate transaminase, acid phosphatase and alkaline phosphatase) elevated by paracetamol in rats was studied with a view to observe any possible Hepato protective effect of this plant. It is stipulated that the extract treated group was protected from hepatic cell damage caused by paracetamol induction. The findings were further confirmed by histo pathological study of liver. The anti-hepatotoxic action of picroliv seems likely due to an alteration in the biotransformation of the toxic substances resulting in decreased formation of reactive metabolites.

N. Picrorhiza kurroa (Kutki)

Administration of picroliv, a standardized fraction of alcoholic extent of Picrorhiza kurroa (Scrophulariaceae) (3-12 mg/kg/day for two weeks) simultaneously with P. berghei infection showed significant protection against hepatic damage in Mastomys natalensis. The increased levels of serum glutamate oxaloacetate transaminase, glutamate pyruvate transaminase, alkaline phosphatase, lipoprotein-X (LP-X) and bilirubin in the infected animals were marked reduced by different doses of picroliv. In the liver, picroliv decreased the levels of lipid peroxides and hydroperoxides and facilitated the recovery of superoxide dismutase and glycogen.

O. Curcuma longa

Curcuma longa or turmeric is a member of Zingiberaceae family which is a perennial herb with short and thick rhizomes. Turmeric has been used extensively in traditional Chinese medicine and Unani medical system. Curcuma longa contains approximately 2% volatile oil, composed mainly of a- and bturmerone, monoterpenes, 5% curcuminoids, mainly curcumin, minerals, carotene and vitamin C. The active constituent of Curcuma longa is Curcumin, which is the yellow pigment of turmeric. The Hepato protective activity of the ethanol extract of Curcuma longa was investigated against paracetamol-induced liver damage in rats. At the dose of 600 mg/kg, paracetamol induced liver damage in rats as manifested by statistically significant increase in serum alanine aminotransferase and Aspartate aminotransferase and alkaline phosphatase. Pretreatment of rats with the ethanolic extract of Curcuma longa (100 mg/kg) prior to paracetamol dosing at 600 mg/kg statistically lowered the three serum liver enzyme activities. Moreover, treatment of rats with only the ethanolic extract of Curcuma longa (100 mg/kg) had no effects on the liver enzymes. This current result suggests that ethanolic extract of Curcuma longa has potent Hepato protective effect against paracetamolinduced liver damage in rats.

CONCLUSION

The Unique features of liver and capacity for regeneration lead to its frequent discussion in Unani Medicine. According to the concepts of Unani medicine, the four vital forces (quwaa) of liver are responsible for metabolism. The derangement in these forces produces pathological changes via derangement in temperament of humours. So the treatment includes measures for correction of the deranged temperament, evacuation of the morbid Humours and empowerment of liver.Diet, drugs and regimenal therapy have been advised to achieve these aims. Kasni (Cichorium intybus) has been stated effective in all kind of liver diseases. Moreover, drugs which possesses property of astringent, diuresis and deobstruation (mufftah-e-

sudad) such as Apium graveolens (Karafs), Gentiana olivierii (Ghafis), Sphaeranthus indicus (Izkhar), Coriandrum sativum (Razyana/ Dhanaya), Cuscuta reflexa (Kasoos), Lupinus albus (Turmus) and Sphaeranthus indicus (Mundi), have been advised strongly effective in liver diseases. Hepatoprotective drugs such as Rosa damascene (Ward), Crocus sativus (Zafran), Cinnamomum zeylenicum (Darchini), Berberis vulgaris (Zarishk), Myristica fra-grans (Joz Bua), Syzygium aromaticum (Qaranfal) have been proven for their potential hepato protective effects in various animal models except Coccus lacca (Luk), which still lacking consideration and should be tested for its Hepato protective activity. So management with Unani single drugs, compound products and supportive therapy must follow the therapeutic paradigms. These principle's will check complications due to mismanagement, encourage administration of specific drugs (drug of choice) for a particular pathological condition, and promote research on Unani drugs mentioned in the literature for the treatment of the pathological state of liver.

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