THERAPEUTIC POTENTIAL OF PICORRHIZA KURROA IN PREVENTION AND TREATMENT OF HEPATIC DISORDERS: AN OVERVIEW

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ABSTRACT

The liver being vulnerable to wide variety of metabolic, toxic, microbial, circulatory and neoplastic insults is subjected to potential damage resulting in acute or chronic hepatic disorders. Viral hepatitis has always been a disease of major concern. The existence of atleast five distinct viral hepatitis agents has been documented namely HAV, HBV, HCV, HDV and HEV. Distinctive differences in symptoms of disease like onset, severity, prevalence, season, serological markers, clinical course etc lead to distinguish the causative agent. Liver disorders may be as acute or chronic hepatitis (inflammatory liver disease), hepatosis (non-inflamatory disorders) and liver cirrhosis (degenerative disorder resulting in fibrosis of the liver). An actual curative therapeutic agent has not yet been found. In fact most of the available remedies rather support or promote the process of healing or regeneration of the liver. The drugs available in the modern system of medicine are the corticosteroids and immunosuppressive agents which bring about only symptomatic relief and in most cases have no influence on the disease process. Their use is also associated with the risk of relapses and danger of side effects. In addition, two types of hepatitis B vaccines (plasma derived and recombinant) have also been developed and are available. These vaccines are too expensive and cannot be afforded by common patients. These vaccines also produce few side effects. Considering the non availability of effective, safe and cheap drugs for the cure of hepatic disorders, usefulness of alternate herbal therapy is currently being evaluated by scientists and clinicians. Picorrhiza kurroa is one of the most important herbs of ayurveda which forms an ingredient of many Indian herbal preparations used for the treatment of liver disorders. The alcoholic extract of Picrorrhiza kurroa has been shown to demonstrate significant hepato protective effect which appeared to be due to a mixture of two iridoid glycosides (picroside 1 and kutkoside) known as picroliv (kutkin). It has been found more active than a known hepatoprotective drug silymarin. Considering beneficial action of Picrorrhiza kurroa in protection of hepatic damage, an organic herbal formulation, Liver-Kidney-Care consisting of three medicinal herbs namely Picorrhiza kurroa, Boerhavia diffusa and Phyllanthus niruri has been developed by International Institute of Herbal Medicine (IIHM), Lucknow, India. This formulation is free of pesticides, insecticides, weedcides, toxins and harmful chemicals. Liver -Kidney - Care has been found to provide beneficial effect to patients of hepatic disorders attending the clinic of IIHM and several patients have been cured with the treatment of this herbal drug. Therefore, this herbal formulation alone can be used as alternative medicine in the treatment of hepatic disorders or it can also be used as adjunct / complimentary medicine.

Keywords: Picorrhiza kurroa, Picroliv, iridoid glycosides, viral hepatitis, hepatoprotective activity, Liver- kidney- Care.
INTRODUCTION
The liver being vulnerable to wide variety of metabolic, toxic, microbial, circulatory and neoplastic insults is subjected to potential damage resulting in acute or chronic hepatic disorders. Viral hepatitis has always been a disease of major concern. The existence of at least five distinct viral hepatitis agents has been documented namely HAV, HBV, HCV, HDV and HEV. Distinctive differences in symptoms of disease like onset, severity, prevalence, season, serological markers, clinical course etc lead to distinguish the causative agent. Hepatitis A is most often contracted through the fecal-oral route and it is self limiting school children are at particular risk. Hepatitis B is usually transmitted by parental inoculation of virus contacting material and so the others too have serious complications. The hepatitis B virus (HBV) is transmitted by horizontal and vertical routes and causes both acute and chronic liver diseases which are often associated with chronic sequelae including the development of hepatocellular carcinoma (HCC). An actual curative therapeutic agent has not yet been found. In fact, most of the available remedies rather support or promote the process of healing or regeneration of the liver. The drugs available in the modern system of medicine are the corticosteroids and immune suppressive agents which bring about only symptomatic relief and in most cases have no influence on the disease process. Further, their use is associated with the risk relapses and danger of side effects. Although, efforts are being made to develop drugs and vaccines for effective control of hepatitis, there is need to explore medicinal plants which are abundantly available in our country in order to develop safe, cheap and long acting hepatoprotective drugs. Extensive work has been carried out on few medicinal plants namely, Acacia catechu, Andrographis paniculata, Boerhaavia diffusa, Citrullus colocynthis, Eclipta alba, phyllanthus niruri, Picrorrhiza kurroa, Piper longum, Solanum nigrum, Terminalia arjuna, Tinospora cordifolia, Withania somnifera, Withania coagulans, Silymarin, Phyllanthus amarus using experimental animals. These plants exhibited significant hepatoprotective activity. The plant extracts showing promising results in animal model have been subjected for further screening against HBV infected human sera using Enzyme linked Immunosorbant Assay (ELISA). Amongst above plants, Picrorrhiza kurroa forms an ingredient of many Indian herbal preparations used for the treatment of liver ailments \[1-3\]. This review highlights the major findings of previous studies on Picrorrhiza kurroa.

Active Constituents
The alcoholic extract of Picrorrhiza kurroa contains two iridoid glycosides. Picroliv (Kutkin) and its two major irridoid glycosides viz. picroside I and kutkoside (Figure 2) have been isolated and described. Both picroside I and kutkoside were the cinnamoyl and vanilloyl esters of catalpol. The latter was prepared by alkaline hydrolysis of the mixture of picroside I and kutkoside followed by purification of the resulting product by chromatography. \[4\]

Picroliv is a standardized iridoid glycoside fraction obtained from root and rhizome of the plant picrorrhiza kurroa.

Many other active constituents have been identified including nine cucurbitacin glycosides, apocynin and dorsin. \[5\]
Botanical classification of *Picrorhiza kurroa* :

Kingdom : Plantae
Order : Angiosperm
Family: Scrophulariaceae
Genus: Picrorhiza
Species: *kurroa*

**FIGURE 1:-**
PICRRRHIZA KURROA: PLANTS AND RHIZOME

**FIGURE 2: STRUCTURE OF PICROLIV (KUTKIN)**
Hepatoprotective activity

Several research studies have shown that extracts of Picrorrhiza (P. kurroa) popularly known in India as “Kutkin” possess marked protective action on liver. Studies were conducted to evaluate hepatoprotective activity of alcoholic extract of P. kurroa and kutkin in some models of hepatic damage in rodents and the results showed that the alcoholic extract of the root and rhizome of P. kurroa exhibited hepatoprotective activity in rat and mastomys. The active principle was identified as kutkin and the kutkin free fraction of the extract were found to be devoid of any activity. Kutkin showed significant hepatoprotective activity in hepatic damage induced by galactosamine (in rats) and plasmodium berghei (in mastomys) as assessed by changes in several serum and liver biochemical parameters [2, 4]. Further, studies have been conducted to see the effect of picroliv on Plasmodium berghei induced hepatic damage in mastomys natalensis and the results showed that administration of picroliv, a standardized fraction of alcoholic extract of Picrorhiza kurroa (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 (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. In the liver, picroliv decreased the level of lipid peroxides and hydroperoxides and facilitated the recovery of superoxide dismutase and glycogen. Picroliv had no effect on the degree of parasitaemia [6].

In another experimental study, the investigations were carried out on the effect of oral administration of picroliv, obtained from total alcohol extractable rhizome of P. kurroa concurrently with toxication of rats for two weeks with carbon tetra chloride (CCl₄) and the results showed that administration of carbon tetra chloride to normal rats increased activities of hepatic 5'-nucleotidase, acid phosphatase, acid ribonuclease while the activities of succinate dehydrogenase, glucose 6-phosphatase, superoxide dismutase and cytochrome p450 were decreased. Levels of lipid peroxides, total lipids and cholesterol of liver were also increased. The activities of serum glutamate oxaloacetate transaminase, glutamate pyruvate transaminase and alkaline phosphatase were increased. Other serum parameters showing changes after CCL₄ were bilirubin, proteins, cholesterol, triglycerides and lipoprotein –X. Picroliv in doses of 6 and 12 mg / Kg provided a significant protection against most of the biochemical alterations produced by the CCL₄. The degree of protection afforded by picroliv, when administered simultaneously or as a pretreatment was almost equal [7]. Studies were conducted to see the protective action of picroliv on isolated rat hepatocytes against thioacetamide induced injury and the results showed that picroliv showed dose – dependent protective activity on isolated hepatocytes (ex-vivo) against thioacetamide - induced hepatic damage in the rat. It enhances the percentage of viable hepatic cells. Picroliv also antagonized the changes in the enzymes GOT, GPT and alkaline phophatase produced by thio-acetamide both in isolated hepatocyte suspension as well as in serum.
It was found to be more potent than silymarin, a known hepatoprotective agent\textsuperscript{[8]}. Picroliv, the active principle of P. kurroa and its main components which are a mixture of the iridoid glycosides, picroside 1 and kutkoside were studied \textit{in vitro} as potential scavengers of oxygen free radicals. The superoxide (O$_2^-$) anions generated in a xanthine-xanthine oxidase system, as measured in terms of uric acid formed and the reduction of nitroblue tetrazolium were shown to be suppressed by picroliv, picroside 1 and kutkoside. Picroliv as well as both glycosides inhibited the non-enzymatic generation of O$_2^-$ anions in aphenazine methosulphate NADH system. Malonaldehyde (MDA) generation in rat liver microsomes as stimulated by ascorbate Fe$^{2+}$ and NADPH-ADP-Fe$^{2+}$ systems was shown to be inhibited by the picroliv glycosides. Known antioxidants tocopherol (Vitamin E) and butylated hydroxy anisole (BHA) were also compared with regard to their antioxidant actions in the above system. It was found that BHA afforded protection against ascorbate Fe$^{2+}$ induced MDA formation in microsomes but did not interfere with enzymatic or non-enzymatic O$_2^-$ anion generation and tocoferal inhibited lipid peroxidation in microsomes by both peroxidant systems and the generation of O$_2^-$ anions in the non enzymatic system but did not find interfere with xanthine oxidase activity. This study shows that picroliv, picroside-1 and kutkoside possess the properties of antioxidants which appear to be mediated through activity like that of superoxide dismutase, metal ion-chelators and xanthine oxidase inhibitors. These results suggested that the hepatoprotective action of picroliv glycosides may be due to the prevention of lipid peroxidation and free radical generation during liver damage\textsuperscript{[9]}.

Effect of Picroliv, the active principle from Picrorrhiza kurroa, on glutathione metabolism in liver and brain of Mastomys natalensis infected with plasmodium berghei was studied and it was found that administration of Picroliv at a dose of 6mg/kg, po for two weeks showed significant protection against changes in liver and brain glutathione metabolism of plasmodium berghei infected Mastomys natalensis. The depletion of reduced glutathione level and inhibition of glutathione-s-transferase, glutathione reductase and glutathione peroxidase activities due to P. berghei infection were markedly reduced by picroliv. The increased levels of lipid peroxidation products in damaged tissue were also reduced along with recovery of glutathione metabolism\textsuperscript{[10]}.

Studies were also conducted to see the effect of picroliv on $\gamma$-glutamyl cycle in liver and brain of Mastomys natalensis infected with Plasmodium berghei and it was observed that the activation of $\gamma$ -glutamyl transpeptidase enzyme and decreased levels of cystine, sulphydryl groups as well as glutathione synthesis in both tissues due to P. berghei infection were reversed by picroliv. Enzymatic and non – enzymatic lipid peroxidation in microsomes \textit{in vitro} was significantly reduced by Picroliv along with recovery of reduced glutathione\textsuperscript{[11]}. The effect of Picroliv was investigated on oxidative modifications of serum lipoproteins in Plasmodium berghei infected Mastomys coucha and the results of the study showed that picroliv at the dose of 6mg/kg po for two weeks provided significant protection against the generation of lipid peroxidation products in serum $\beta$- lipoproteins of Plasmodium berghei infected M. coucha. Incubation of normal rat hepatocytes with very low density lipoproteins
or low density lipoprotein isolated from infected animals caused significant generation of lipid peroxides followed by a decrease in the viability of these cells, however, these effects were partially reversed with lipoproteins from infected and picroliv treated groups. High density lipoprotein from infected animals was not toxic to hepatocytes in vitro [12]. Picroliv (active principle from P. kurroa), its major components picroside 1, catapol, kutkoside 1, kutkoside were tested for the presence of anti hepatitis B virus surface antigen (anti HBs) like activity, HBs Ag. Positive serum samples obtained from hepatitis B virus (HBV) associated acute and chronic liver diseases and healthy HBs ag carriers were used to evaluate the anti HBs like activity of compounds / extract. The latter were mixed with serum sample and incubated at 37°C overnight followed by HBs Ag screening in the ELISA system. A promising anti- HBs Ag like activity was noted in Picroliv (and its major components) catalpol which differed from the classical neutralization. Picroliv also inhibited purified HBV antigens prepared from healthy HBsAg carriers [2,13]. Picroliv has been shown to possess dose dependent (0.75-12 mg/kg x 7 days) protective activity on isolated hepatocytes (ex-vivo) against paracetamol-induced hepatic damage in rats. It increased the percentage viability of the hepatocytes. Picroliv also restored the normal values of enzyme (glutamic oxaloacetic transminase [GOT], glutamic pyruvic transminase [GPT] and alkaline phophatase) both in isolated hepatocyte suspension as well as in the serum. Picroliv was found to be more potent than silymarin, a known hepatoprotective agent [14, 15].

In another study, picroliv has been shown to exhibit a significant dose dependent (3-12mg/kg po x 7 days ) protective activity against galactosamine induced hepatic damage in rats as evaluated on the isolated hepatocytes (ex. vivo) preparation. It markedly increased the percentage of viability of hepatocytes. It was also found to restore the galactosamine- induced changes in the levels of enzymes (GOT; GPT and alkaline phosphatase) both in isolated hepatic cells as well as in serum. Picroliv was also found to possess a marked anticholestatic effect. Picroliv was found to be more potent than silymarin, a standard hepatoprotective agent [16].

Picroliv has also been found to possess a dose (3-12 mg/kg, po for 7 days) dependent choleretic activity as evidenced by increase in bile flow and its contents (bile salts and bile acids). Significant anticholestatic activity was also observed against carbon tetrachloride induced cholestasis in conscious rat, anaesthetized guinea pig and cat. Picroliv was found to be more active than the known hepatoprotective drug silymarin [17]. An experimental study was conducted to evaluate hepatoprotective effect of Picroliv against Rifamicine-induced toxicity in animals. The results of the study showed that Picroliv exhibited significant hepatoprotective as well as an anticholestatic activity against rifamicine-induced hepatic damage. Rifamicine (50 mg/kg ipx6 days) resulted in the reduction of bile flow as well as its contents (bile salt and bile acids) in the conscious rat and anesthetized guinea pig. Further, it also caused a decrease in the viability and rate of oxygen consumption in
isolated rat hepatocytes. Picroliv treatment significantly reversed the altered parameter of bile and hepatocytes. Picroliv was found to be more active than known hepatoprotective drug silymarin. The modulation of rifamicin toxicity by picroliv indicated that this agent could be given simultaneously to tuberculosis patients to protect the liver from rifamicine induced toxicity\textsuperscript{[18-19]}. Considering the beneficial action of Picrorrhiza kurroa in protection of hepatic damage, International Institute of Herbal Medicine (IIHM), Lucknow, India, has developed an organic herbal formulation, “Liver – Kidney - Care” consisting of Bhumiamalaki - Phyllanthus niruri, 125 mg, Punarnava - Boerhavia diffusa, 100 mg and Katuki- Picrorrhiza kurroa, 100 mg. The above herbal combination at dose of one capsule twice daily within meals given to patients of hepatic disease attending the clinic of IIHM produced beneficial effect to patients. This above herbal combination are well known for its hepatoprotective effects singly or in combination with the best ever known hepatoprotective effects proved scientifically\textsuperscript{[20-21]}. Liver-Kidney-Care herbal formulation is free from pesticides, insecticides, weedicide and herbicides. This herbal formulation alone can be used as alternative medicine in the treatment of hepatic disorders or it can also be used as adjunct/complimentary medicine.

**DISCUSSION**

In the present days of environmental degradation, uncontrolled environmental stress, changing life style and expanding therapy with the potent drugs, the liver main organ of the human is continuously exposed to varieties of xenobiotics and therapeutic agents which interfere with the various functions of liver such as metabolic function, detoxicating function, secretory function and excretory function leading to liver disorders of varied nature including acute or chronic hepatitis (inflammatory liver disease), hepatosis (non-inflammatory disorders) and liver cirrhosis (degenerative disorder resulting in fibrosis of liver). The types of hepatitis may be virus induced hepatitis, drug/toxin induced hepatitis, and alcohol induced hepatitis and autoimmune hepatitis. Viral hepatitis, which is caused by at least five different and completely unrelated human pathogens known as hepatitis A,B, C, D, and E viruses (HAV, HBV, HCV, HDV and HEV), is of major concern since the essential lesion is an acute inflammation of entire liver and hepatic cell necrosis is associated with leucocytic reaction and infiltration. Thus, Hepatitis B virus infection can lead to cirrhosis, acute liver failure and liver cancer. There are about 45 million people in India carrying the Hepatitis B virus.

In spite of extensive studies carried out to develop therapeutic agents using diagnostic tests / enzyme assays and biomarkers, an actual curative therapeutic agent for hepatic disorders has not been found.

In fact, most of the available remedies rather support or promote the process of healing or regeneration of liver. The drugs available in
modern system of medicine such as immunoglobulin, ribavirin, lamivudine, famciclovir, fialuridine, vidarabine, interferon-alpha are the corticosteroid and immunosuppressive agents which may bring only symptomatic relief and in most cases have no influence on the disease process. Further, the use of above drugs is associated with the risk by relapses and danger of unwanted side effects/ adverse drug reactions. In addition, two types of hepatitis B vaccines (plasma derived and recombinant) have also been developed and are available. These vaccines are very expensive and have few side effects too.

Considering the non availability of effective, safe and cheap drugs for the cure of hepatic disorders, usefulness of alternate herbal therapy is currently being evaluated by scientists and clinicians throughout the world.

Extensive work has been carried out on few medicinal plants namely, Acacia catechu, Andrographis paniculata, Boerhaavia diffusa, Citrullus colocynthis, Eclipta alba, phylenthus nirruri, Picrorrhiza kurroa, Piper longum, Solanum nigrum, Terminalia arjuna, Tinospora cordifolia, Withania somnifera, Withania coaquulans, Silymarin, Phyllanthus amarus using experimental animals. These plants have exhibited significant hepatoprotective activity. The plant extracts showing promising results in animal model have been subjected for further screening against HBV infected human sera using Enzyme linked Immunosorbant Assay (ELISA). Picrorhiza kurrooa is one of the most important herbs of Ayurveda (the traditional system of medicine in India) which forms an ingredient of many Indian herbal preparations used for the treatment of liver ailments [1].

The results of the studies described above demonstrate that Picrorrhiza kurroa is effective in prevention and treatment of hepatic disorders. The presence of two major iridoid glycosides picroside I and Kutkoside in alcoholic extract of roots named as kutkin (picroliv), the active constituent of the plant Picrorrhiza kurroa has been found to be responsible in exhibiting hepato protective actively. Picroliv has been found to be more active than the known hepato-protective drug silymarin. It has been hypothesized that the hepato protective activity of this drug may be based on (1) Kutkins alter the structure of the outer membrane of the hepatocytes in such a way as to prevent penetration of the liver toxin into the interior of the cell, (2) Kutkins stimulate the action of nucleolar polymerase A, resulting in ribosomal protein synthesis and, thus stimulates the regenerative ability of the liver and formation of new hepatocytes, (3) Apocynin, is one of its constituents, has been found to exhibit powerful anti-inflammatory effects on a variety of inflammatory models [22]. Further, few studies conducted on experimental models have shown that the therapeutic activity of the plant towards hepatic damage/injury might be due to its antioxidant and choleric activity. Like silymarin, Picrorrhiza does possess significant antioxidant activity in vitro which may contribute to the hepatoprotective effect by reducing lipid peroxidation and free radical damage [9].

Chander et al found that Picrorrhiza and its main constituents, picroside-I and kutkoxide, inhibited the nonenzymatic generation of
O₂⁻ anions in a phenazine methosulphate NADH system, inhibited oxidative malonaldehyde generation by both the ascorbate-Fe2⁺ and NADPH-ADP-Fe2⁺ systems, and scavenged superoxide (O₂⁻) anions generated in a xanthine-xanthine oxidase system. In other words, Picrorhiza demonstrated antioxidant activity similar to that of superoxide dismutase, metal-ion chelators, and xanthine oxidase inhibitors [9]. Glutathione is vital to maintaining a variety of intracellular functions, including detoxification, antioxidation, tertiary protein configuration, and redox balance [23]. Picrorhiza was found to restore depleted glutathione levels in African desert rats infected with Plasmodium berghei (malaria). Several enzymes associated with glutathione function were also restored, including glutathione-S-transferase, glutathione reductase, and glutathione peroxidase [10].

Generation of lipid peroxides in African desert rats infected with Plasmodium berghei was significantly reduced by Picrorhiza at the oral dose of 6 mg/kg for two weeks, revealing Picrorhiza also possesses anti-lipid peroxidative effects [11]. The hepatoprotective action of Picrorhiza kurroa may be due to its ability to stimulate liver regeneration. Like silymarin, Picrorhiza may have an effect on liver regeneration. A 1992 study demonstrated stimulation of nucleic acid and protein synthesis in rat liver with oral administration of Picrorhiza. The authors stated the results were comparable to silymarin [24].

Another factor in the hepatoprotection of Picrorhiza may be its anti-inflammatory effects. Picrorhiza extracts were found to have an inhibitory effect on such pro-inflammatory cells as neutrophils, macrophages, and mast cells. [25] The authors suggested Picrorhiza extract inhibited membrane mediated activation of these cells (inhibited 8-adrenergic receptors). [26-27] The researchers found no effect of the Picrorhiza extract on prostaglandin production. [25]

Picrorhiza contains apocynin, a catechol, as one of its minor constituents. Apocynin has been found to exhibit powerful anti-inflammatory effects on a variety of inflammatory models. Apocynin was found to inhibit neutrophil oxidative burst in vitro without affecting beneficial activities such as chemotaxis, phagocytosis, and intracellular killing of bacteria [28-29]. In vivo animal models, apocynin inhibited lipopolysaccharide-induced emphysema in hamsters. [30]

Apocynin prevented the formation of ulcerative lesions in rats injected intracutaneously with Freund’s complete adjuvant. [31]
and reduced swelling in collagen-immunized rats. No effects on humoral and cellular immunity were observed after treatment with apocynin. \[^{32-33}\] Interestingly, the effective daily dose of apocynin was only 0.024 mg/kg. Such a dose is readily achieved from normal use of Picrorrhiza root instead of the concentrated apocynin extract \[^{32-33}\]. Several hepatotoxins, including paracetamol and ethynylestradiol, have a cholestatic effect on the production of bile. Picrorrhiza has been shown to reverse acetaminophen and ethynylestradiol-induced cholestasis, maintaining both bile volume and flow. Silymarin was tested simultaneously for comparison. Picrorrhiza was found to be a more potent choleretic and anticholestatic agent than silymarin.\[^{34}\] As for dosage/toxicity is concerned, picrorrhiza is poorly soluble in water and so is usually not taken as a tea. It is soluble in ethanol and so can be taken in tincture form (very bitter), but is usually administered as an encapsulated standardized extract (4% kutkin) \[^{35}\]. The usual adult dosage is 400 to 1500 mg/day, although daily doses as high as 3.5 g/day have been recommended for fevers \[^{36}\]. Picrorrhiza use is widespread in India and no major adverse reactions have been reported. The oral LD50 of kutkin is greater than 2600 mg/kg in rats \[^{37}\]. The LD50 of picrocide and kutkoside is greater than 1000 mg/kg in rats \[^{37}\]. By comparison, the maximum dose achievable with oral ingestion of picrorrhiza root is about 3-6 mg/kg. Considering beneficial action of Picrorrhiza kurroa in protection of hepatic damage/injury, an organic herbal formulation, Liver-Kidney-Care consisting of three medicinal herbs namely Picrorrhiza kurroa, Boerhavia diffusa and Phylanthus nirruri has been developed by International Institute of Herbal Medicine (IIHM), Lucknow, U.P., India. This formulation is free from pesticides, insecticides, weedcides toxins and harmful chemicals. Liver –Kidney –Care has been found to provide beneficial effect to patients of hepatic disorders attending the clinic IIHM and several patients have been cured with the treatment of this herbal formulation. As evidenced from encouraging results of this herbal formulation in treatment of patients with hepatic disorders, it can be recommended for the cases of fatty or sluggish liver, viral hepatitis, cirrhosis, hepatic enlargement, kidney stones, pyelonephritis, renal failure and urinary tract infection. It has capability to regulate fat metabolism in obesity and to improve appetite during convalescences. This herbal formulation has potential to eliminate hepatotoxic agents such as alcohol, chemical pollutant and drugs from the complex human system. Therefore, this herbal formulation alone can be used as alternative medicine in the treatment of hepatic disorders or it can also be used as adjunct / complimentary medicine. As a preventive treatment 1-2 capsules of Liver-Kidney-Care daily can be taken for any length of time without side effects.
Although beneficial results have been obtained with the treatment of Liver-Kidney-Care at dosage of 1-2 capsule twice a day within meal for at least one month to the patients, multidisciplinary clinical studies in human subjects using modern biotechnological tools and biomarkers may prove to be useful in understanding the biochemical mechanism of action of organic herbal formulation “Liver-Kidney-Care” containing hepatoprotective herb Picrorrhiza kurroa in prevention and treatment of hepatic disorders.

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