Journal of Bioanalysis & Biomedicine

Nandi, J Bioanal Biomed 2016, 8:5
DOI: 10.4172/1948-593X.1000e147

Editorial Open Access

Adjuvant Phytotherapy against Antitubercular Drug Induced Hepatotoxicity

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Editorial

Tuberculosis was declared as a global pandemic and panic because the causative Mycobacterium tuberculosis can kill an incredible number of individuals which formulate a major obstacle to social and economic development of the country. Most of the developing countries are affected by tuberculosis. Antitubercular therapy involves the use of Directly Observed Therapy Short (DOTS) course for 6-9 months. Antitubercular drug induced hepatic damage may occur with DOTS combination regimen which consists of an initial 2-month phase of 1st line combination therapy with pyrazinamide (PZA), isoniazid (INH), rifampin (RIF) and ethambutol (E) followed by a continuation phase of treatment lasting 4 months with INH and RIF [1]. Metabolic idiosyncratic reactions appear to be responsible for most drugs induced liver injury from the first-line antitubercular medications and fluoroquinolones [2]. Knowledge of the mechanisms of antitubercular drug-induced liver injury or hepatotoxicity is incomplete. Herbal drugs have gained importance and popularity in recent years because of their safety, efficacy and cost effectiveness. The association of medical plants with other plants in their habitat also influences their medicinal values in some cases. One of the important and well-documented uses of ethno medicinal plant products is their use as hepatoprotective agents which become ever increasing need for the treatment of antitubercular compounds induced hepatic cell damage. It was reported that antitubercular drugs-induced hepatotoxicity can be treated by administering extracts of herbal medicinal plants enlisted in Table 1. The present editorial presents the herbs which contain active principles of secondary metabolites responsible for producing biochemical mechanisms of hepatoprotective activities against antitubercular drug regimen induced hepatotoxicity in mouse model. A number of experimental studies concerning phyto extracts obtained from several plants have been carried out to reduce hepatotoxicity in this context.

Extracts of the above phyto medicinal plants were prepared utilizing standard protocol of extraction and isolation of these phyto medicinal plants. The extracts were then evaluated for the hepatoprotective activity in experimental animal models as per the scrutiny of the Institutional Animal Ethics Committee. The animals were divided into two control and many test groups comprising of a definite number of animals in each. One control animal was given hepatoxins including carbon tetrachloride (CCl_4). Another was toxic control animal model in which anti tubercular drug regimen is given to induce hepatotoxicity. Hepatoprotective herbal phyto active components or extracts can prevent the liver diseases including anti tubercular chemical induced hepatotoxicity such as necrosis, cirrhosis, hepatitis, hepatic failure and carcinogenesis. Test groups were administered with antitubercular hepatotoxic drugs as well as being treated by herbal extracts. Hepatic damage is investigated by the liver function tests (LFT) [15] which are employed for accurate diagnosis of hepatic damage. Further test animal blood was examined for the histopathological study of liver function enzyme levels to investigate the hepatoprotective activity of the herbal extracts. The routine liver function tests are performed to predict abnormalities of bile pigments and bile salts excretions including serum total and bilirubin, urine bile salts, bile pigments and urobilinogen, etc., as well as serum enzyme assays of serum glutamic oxaloacetic transaminase (SGOT), serum glutamic pyruvic transaminase (SGPT), alkaline phosphatase (ALP) and if necessary and γ-Glutamyl transpeptidase (γ-GT), respectively [15]. These plant extracts administered to the test group of animals were shown to produce a significant protective action evident by decreasing the levels of ALT, AST, ALP and bilirubin in the serum; liver lipid peroxidation and enhancing antioxidants effects. Mechanisms of hepatoprotection are to lipid peroxidation, decrease gluthione, superoxide dismutase and catalase.

A clever refinement of the phyto drug combinations will remain the focus of many medicinal chemists and pharmacologists to screen the potent compound combinations for the treatment of antitubercular drug induced hepatotoxicity. There is hardly any allopathic therapy to cure or prevent the hepatotoxicity. Therefore, a great attention has been made for the last couple of years to develop hepatoprotective polyherbal formulations which resulted to formulate Rhinax, Liv 52 and Liv 100, respectively. From this review, it is directed to focus about discovery of specific combination of phyto active ethno medicinal plants formulation and determination of its dosage having maximum effectiveness to prevent hepatic damage induced by the antituberculosis treatment regimen. When patients suffer from tuberculosis and take DOTS therapy, they should aware about the hepatic problem, vomiting and pain in abdomen. Therefore patients should take the most effective polyherbal plant extracts frequently available to make them safe and decrease the panic for life threatening. The patients with most economically poor, malnutrition, lower health and sanitation may suffer from decreased immunity and chances of tuberculosis infection. So these fellows must take some Ayurveda formulations obtained from the medicinal plant extracts which may potentiate immunity and to prevent from tuberculosis attack which is a menace to the society. The quest of bioactive phyto constituents having protective activity against hepatotoxicity of antitubercular compounds has not yet been achieved so far. Therefore future direction of the present editorial is to isolation of specific phyto component and its molecular design for further screening, synthesis and testing of the synthetic congeners having promising activity against hepatotoxicity induced by antituberculostatic drugs

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Received October 10, 2016; **Accepted** October 13, 2016; **Published** October 17, 2016

Citation: Nandi S (2016) Adjuvant Phytotherapy against Antitubercular Drug Induced Hepatotoxicity. J Bioanal Biomed 8: e147. doi: 10.4172/1948-593X.1000e147

Sl. No.	Name of the herb	Brief	Active constituents present
1	*Ziziphus oenoplia* (L.) Mill	Ethanolic and aqueous root extracts	Alkaloids, flavonoids, terpenoids, phenolic compounds and glycosides
2	*Vitex negundo*	Ethanolic leaves extracts	Flavonoid glycosides: 5-hydroxy-3, 6, 7-trimethoxy-2-(3, 4-dimtoxypheny)-4H-chrome-4-one, 5, 7-dihydroxy-2-(3, 4-dihydroxyphenyl)-4H-chromen- 4-one, negundoside, agnuside, and vitegnoside, casticin, isoorientin, chrysophenol D, luteolin and p-hydroxybenzoic acid.
3	*Hibiscus vitifolius* (Linn.)	Methanolic root extract	Alkaloids: vitiquinolone, other constituents are β-Amyrin acetate, n-octacosanol, β-Amyrin, stigmasterol, xanthyletin, alloxanthoxyletin, xanthoxyletin and betulinic acid.
4	*Solanum xanthocarpum*	Ethanolic fruit extracts	Steroidal alkaloids like solanacarpine, solanacarpidine, solancarpine, solasonine, solamargine and other constituents like caffeic acid, coumarins like aesculetin and aesculin, steroids carpesterol, diosgenin, campesterol, daucosterol and triterpenes like cycloartanol and cycloartenol.
5	*Cassia auriculata*	Ethanolic root extracts	Flavonoids, polysaccharides, tannins and saponins.
6	*Moringa oleifera*	Ethanolic extract of leaves	Crypto-chlorogenic acid, isoquercetin and astragalin.
7	*Hemidesmus indicus*	Whole plant extract	Sarsaponin, smilacin, p-methoxy salicylic aldehyde, beta-sitosterol, sarsapogenin, smilgenin, sitosterol, stigmasterol fatty acids and tannins.
8	*Silybum marianum*	Ethanolic seed extract	Flavonolignans: Silymarin, silybin and silydianin.
9	*Allium sativum* (garlic)	Bulb	Sulfur-containing compounds including alliin, ajoene, diallylpolysulfides, vinyldithiins and *S*-allylcysteine.
10	*Allium cepa* (Onion)	Bulb	α-Amyrin, alanine, allacine, alliin, allyl-propyl-disulphide,α- tocopherol, arginine, β -sitosrerol,campesterol,diallyldisulphide and trisulphide.
11	*Curcuma longa*	Alcoholic and aqueous Roots and rhizome extracts	Curcuminoids:Desmethoxycurcumin,Bisdesmethoxycurcumin, Curcumin; Turmerones: Ar-turmerone, α-turmerone, β-turmerone; Curcumenes: γ-Curcumene, ar-Curcumene,, Dehydrocurcumene, zingiberene, γ-bisabolene, γ-sesquiphellandrene; Miscellaneous: Terpinolene, *P*-Cymene, 1-8-Cineole, Curlone.
12	*Tinospora cordifolia*	Alcoholic extracts of fresh stem	Alkaloids:Berberine,Palmatine,Tembetarine,,Magnoflorine,Choline,Tinosporin,Isocolumbin, Tetrahydropalmatine, Glycosides: 18-norclerodane glycoside,Furanoid diterpene glucoside, Tinocordiside,Tinocordifolioside, Syringin, Syringin-apiosylglycoside, Palmatosides C, Palmatosides P,Cordifolioside A, Cordifolioside B, Cordifoliside- A, -B, -C, -D and –E, Diterpenoid Lactones: Furanolactone, Clerodane derivatives, Tinosporon, Tinosporides.
13	*Terminalia chebula* Retz.	Fruit extracts	Glycosides: arjunglucoside I, arjungenin, and the chebulosides I and II; Tannins: gallic acid, chebulic acid, punicalagin, casuarinin, chebulanin, corilagin, neochebulinic acid, terchebulin, ellagic acid, chebulagic acid, chebulinic acid.
14	*Emblica officinalis*	Fruit extracts	Tannoids and flavonoids: emblicanins A and B, punigluconin and pedunculagin, and gallic acid, 1-*O*-galloyl-b-D-glucose, corilagin, chebulagic acid, elaeocarpusin, and puntranijivan.
15	*Azadirachta indica*	Leaves and root barks	Dacetylnimbin, nimbin, epoxyazadiradion, gedunin, azadirone, mahmoodin, 17-hydroxyazadiradion, nimbastrol.
16	*Piccorhiza kurroa (Kutki)*	Alcoholic roots and rhizomes	Glycoside:kutkin (a mixture of kutkoside and picroside); Other constituents are apocynin, andorsin, and cucurbitacin glycosides.

Table 1: Phyto medicinal plants under experimental and clinical study [3-14] for hepatoprotective activity against antitubercular drug induced hepatotoxicity.

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