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A Review Article on The Hepatoprotective Effect of Few Ayurvedic Herbs in Patients Receiving Antitubercular Treatment

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Abstract

Introduction: *Rajayakshma* as described in Ayurveda's *Brihattrayi* presents with features similar to pulmonary tuberculosis and is characterized by progressive tissue depletion (*Dhatu Kshaya*), chronic cough (*Kasa*), fever (*Jwara*), weight loss (*Karshya*), weakness (*Daurbalya*) and impaired immunity (*Ojakshaya*) [1] [7] [8]. While anti tubercular therapy is very effective it is also at times made complex by hepatotoxicity which is a result of long-term use thus causing treatment to be interrupted and poor patient compliance. **Methodology**: This review is based on the clinical study by Sharma et al. (2004) which looked at the hepatoprotective value of *Berberis aristata*, *Solanum nigrum*, *Aloe vera*, and *Phyllanthus fraternus* in tubercular patients on ATT[3]. The liver function was determined by serum AST, ALT, bilirubin, and alkaline phosphatase. **Results**: Patients who were seen to have improved in terms of AST and ALT levels did better in the Ayurvedic preparation group than in the placebo group which is a indication that these preparations do protect against what ATT causes in the liver. Among the herbs we looked at *Phyllanthus fraternus* did the best job in terms of liver protection. Also we found out from our review of the literature that these Ayurvedic liver protective herbs may be good to use in addition to conventional TB therapy to prevent drug induced liver injury. We will need more large scale RCT's to prove out these results and to put together an evidence based approach for the treatment of *Rajayakshma* (Tuberculosis). **Discussion**: The literature review shows that these Ayurvedic hepatoprotective herbs may be good adjuncts to conventional antitubercular therapy to prevent drug-induced liver injury. More prominent randomized controlled trials are warranted to validate these findings and establish evidence-based management of *Rajayakshma* (Tuberculosis)

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Keywords

Rajayakshma; TB; Antitubercular Therapy (ATT); Liver toxicity; Liver protection.

Introduction

Rajayakshma as described in the *Brihattrayi* (*Charaka Samhita*, *Sushruta Samhita*, and *Ashtanga Hridaya*) is a very severe disease in Ayurveda and is very much like pulmonary tuberculosis. It is characterized by progressive tissue depletion (*Dhatu Kshaya*), chronic cough (*Kasa*), fever (*Jwara*), weight loss (Karshya), weakness (*Daurbalya*) and impaired immunity (*Ojakshaya*)[1] [7] [8]. In present day we see that the management of tuberculosis which is for the long term use of multi drug Anti Tubercular Therapy (ATT) which at the same time is a complication itself. Drug induced liver injury is one of the main causes of treatment interruption and poor compliance[2]. A recent study by Sharma et al reported the hepatoprotective action of Ayurvedic drugs which include *Daruharidra* (*Berberis aristata*), *Kakamachi* (*Solanum nigrum*), *Ghritkumari* (*Aloe vera*), and *Bhumyamalaki* (*Phyllanthus fraternus*) against ATT[3]. By reviewing the research we were able to note that there is a great reduction in raised liver enzymes in patients on herbal adjuvants as compared to the placebo. This group of herbs is used in many conditions which are a mimic of liver injury. *Bhumyamalaki* also has the extra benefits of *Deepana-Pachana* and *Yakrit-Uttejaka* that which also include hepatoprotective action[4]. Here we put forth that what we think clinical, pharmacological, and Ayurvedic based reasons for use of hepatoprotective drugs in the management of *Rajayakshma*.

Aim:

To review the body of work which reports on the action of *Ayurvedic* herbs in terms of their role during ATT and after ACT.

Objectives:

To study the role of that which causes liver toxicity in ATT and also to look at *Ayurveda's* support role in protecting the liver during conventional tubercular treatment. Also to see how clinical features present in correlation with the *Ayurvedic* diagnosis of *Rajayakshma*.

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Methodology

Review Methodology

This paper reports on a clinical study which did up research into what *Ayurvedic* herbs do in patients on anti-tuberculosis treatment which was done by Sharma et al. in Indian Journal of Traditional Knowledge in 2004[3]. We look at the study's design, methodology, the base which the *Ayurvedic* approach is founded on, blood test results which the study looked at and also the connection between the treatment of *Rajayakshma* in Ayurveda texts. Also, this study looks at the signs and symptoms of tuberculosis and *Rajayakshma* as per *Charaka Samhita*, *Sushruta Samhita*, *Ashtanga Hridaya* and also in the context of modern bio medical research. In this study we present the rationale for use of these herbs along with scientific evidence which supports hepatoprotection.

Methodology of the Original Clinical Study

The Sharma et al. report was on a comparative clinical trial which was presented in the Department of *Kayachikitsa* at Rajiv Gandhi Post Graduate Government Ayurvedic Hospital in Paprola, Himachal Pradesh, India, conducted this study[3]. They obtained approval from the hospital's committee and they also got written informed consent from all patients prior to their part in the study. In the study patients between the ages of 15 and 70 which had new tuberculosis and were to begin anti tubercular therapy were included[3]. Only those patients which had gone through liver function and anatomical studies were included in this study[3].

The patients were grouped as follows:

- Group I also refer to as the Liv-600 group had *Daruharidra*, *Kakamachi*, and *Ghritkumari* extract capsules in addition to the standard TB care[3] [5]
- Group II also referred as the *Bhumyamalaki* group had a *Bhumyamalaki* decoction in addition to the routine TB treatment[3] [5]
- Group III also called the Control group had placebo capsules and the standard TB treatment[3] [5]

The study went on for 90 days which is the same as the intensive phase of TB treatment. They checked the patient's liver function every 15 days to see the health of their livers. In the case of a patient's liver damage, they were removed from the study and their TB treatment discontinued if needed. They looked at what happened in the patients' blood work which included AST, ALT, total bilirubin and alkaline phosphatase before and during

treatment. They looked at changes within each group and also between groups to see what the Ayurvedic treatments did for the liver. They looked at the results from a bio medical as well as an Ayurvedic stand point to see if the herbs could play a role in the treatment of *Rajayakshma* and in preventing liver damage due to TB treatment. The work done on *Rajayakshma* and the use of herbs in that work is what they looked to in order to understand treatment of pulmonary tuberculosis. In the study they looked at Ayurvedic herbs like *Daruharidra*, *Kakamachi* and *Ghritkumari* which they researched for the protection of the liver[4].

Observations

In a clinical study, ran by Sharma et al. we looked at the hepatoprotective properties of certain Ayurvedic herbs in patients on standard antitubercular therapy (ATT) [3]. A total of new TB patients in the range of 15 to 70 years, that had normal baseline measures of liver function and also did not report pre-existing hepatic disease. Patients were put into 3 random groups for the treatment.

- Group I was given the polyherbal formulation Liv-600 along with ATT. [3] [5]
- Group II received a preparation of *Phyllanthus fraternus* (*Bhumyamalaki*) with ATT [3] [5]
- In Group III they used the placebo which was given along with ATT. [3] [5]

The study which went for a duration of 90 days was conducted during the intensive phase of tuberculosis treatment. Liver function at regular intervals was monitored by means of serum Aspartate Aminotransferase (AST/SGOT), Alanine Aminotransferase (ALT/SGPT), Total Bilirubin, and Alkaline Phosphatase (ALP) tests.[3] These biochemical parameters were chosen to indicate hepatocellular damage and also liver's excretory function. Throughout the study good patient compliance to the treatment in the Ayurvedic intervention groups was seen and also did not see any adverse reactions to the herbs. Clinical improvement in tuberculosis symptoms in all groups which indicates that the use of hepatoprotective herbs did not interfere with the therapeutic effect of antitubercular drugs. What we saw mainly was that between groups there was a difference in degree of hepatic enzyme increase during treatment.

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Table 1- Study design and interventions

Group	**Intervention**	**Duration**	**Purpose**
Group I	Liv-600 containing *Berberis aristata*, Solanum nigrum and Aloe vera with ATT	90 days	Evaluation of polyherbal hepatoprotective effect
Group II	Phyllanthus fraternus (*Bhumyamalaki*) decoction with ATT	90 days	Evaluation of single-herb hepatoprotective effect
Group III	Placebo with ATT	90 days	Control group

Table 2- Biochemical Parameters Evaluated

Parameter	Clinical Significance
AST (SGOT)	Marker of hepatocellular injury
ALT (SGPT)	Specific indicator of liver cell damage
Total Bilirubin	Reflects hepatic excretory function
Alkaline Phosphatase (ALP)	Marker of cholestatic liver injury

Results

On reviewing the study it was found that subjects which were given Ayurvedic hepatoprotective herbs during antitubercular therapy which in turn did play a key role in reducing hepatic injury caused by first line antitubercular drugs. There was a great difference between the treatment groups and the placebo group in particular with respect to serum

transaminase levels. It was observed that in the group which received the polyherbal formulation (Liv-600), only minimal elevations in AST and ALT levels happened throughout the treatment period[3]. Also, these changes were not found to be statistically significant and stayed within what is accepted as normal physiological limits which in turn reports that there was effective protection of hepatocytes against drug induced damage. Also, the patients which had *Phyllanthus fraternus* decoction did very well in preserving liver function.

In each of the studies we looked at this intervention performed the best in terms of hepatoprotection which we also saw in that the serum transaminase levels were the closest to what they are at base line. The authors put forth that this great results are due to the very strong antioxidant and regenerative actions of *Bhumyamalaki* as well as may be also to the fact that the active phytoconstituents are preserved in the fresh preparation[3]. Also in the placebo group we saw a large increase in both AST and ALT levels during ATT which is a sign of great hepatocellular damage.

That elevation of these enzymes is a result of damage to the hepatocytes which in turn is a result of the hepatotoxic metabolites of isoniazid, rifampicin and pyrazinamide[2]. Also we did not see any statistical changes in serum total bilirubin or alkaline phosphatase levels in any of the groups which we looked at, we found that which instances of hepatotoxicity did take place during the study were mainly in the area of hepatocellular injury which we did see as opposed to cholesteric liver dysfunction. Also we noted that bilirubin and ALP levels stayed in normal range which in turn indicates that the hepatic excretory function did for the most part preserve itself during the study. As a whole what we saw was that the use of Ayurvedic hepatoprotective herbs with ATT reduced biochemical evidence of liver injury at the same time did not do harm to tuberculosis treatment. Also the herbal interventions did very well in terms of tolerance and did not produce any large scale clinical side effects.

Table 3- Comparative Effect of Ayurvedic Interventions on Liver Function

Biochemical Parameter	**Liv-600 + ATT**	**Phyllanthus fraternus + ATT**	**Placebo + ATT**
AST (SGOT)	Minimal, non-significant rise	Best preservation of normal values	Significant elevation indicating hepatocellular injury

ALT (SGPT)	Stable throughout treatment	Minimal elevation; superior hepatoprotection	Significant elevation during ATT
Total Bilirubin	Maintained within normal range	Maintained within normal range	No significant alteration
Alkaline Phosphatase	No significant change	No significant change	6

Table 4- Overall Clinical Outcomes

Observation	**Interpretation**
Reduction in AST and ALT elevation	Indicates protection against ATT-induced hepatocellular injury
Stable bilirubin and ALP levels	Suggests preservation of hepatic excretory function
Superior efficacy of Phyllanthus fraternus	Demonstrated greater hepatoprotective activity than the polyherbal formulation
Absence of herb-related adverse effects	Indicates good safety and tolerability
No interference with ATT	Tuberculosis treatment remained effective while liver function was protected

Discussion

Rajyakshma (Tuberculosis) is a very prevalent pulmonary disease which presents with a picture of progressive tissue waste (*Dhatu Kshaya*), cough (*Kasa*), fever (*Jwara*), weight loss (*Karshya*), weakness (*Daurbalya*) and low immunity (*Ojakshaya*) [1] [7] [8].

Although very effective in the treatment of tuberculosis antitubercular therapy (ATT)'s long term use is a cause of concern for the development of hepatotoxicity and related side effects. Sharma et al reported a study which looked at the hepatoprotective action of *Berberis aristata* (*Daruharidra*), *Solanum nigrum* (*Kakamachi*), *Aloe vera*, and *Phyllanthus fraternus*

(*Bhumyamalaki*) in terms of their ability to reduce ATT induced hepatotoxicity. [3] The Bitter Rasa taste, *Pitta Shamana* (pacification of Pitta) and *Deepaniya Karma* (digestive fire enhancement) of these herbs play a role in *Yakrit Rakshana* (hepatoprotection) also they put in action *Rasayana* (rejuvenative) effects[4][9]. *Brihat*trayi presents the basic tenets and therapeutic use of these Ayurvedic drugs. In the study which we report here the patients were put into three groups.

Group I was given capsules of *Berberis aristata* (*Daruharidra*), *Solanum nigrum* (*Kakamachi*) and *Aloe vera* (*Ghritakumari*) (Liv 600) along with standard antitubercular therapy (ATT) [3] [5]. Group II received a Decoction of *Phyllanthus fraternus* (*Bhumyamalaki*) in addition to standard ATT[3] [5]. Group III (the control group) received placebo capsules along with standard ATT[3] [5]. At the end of 90 days of treatment the Liv 600 group reported only slight improvement in AST and ALT levels which we see in liver function tests (LFTs). In terms of Group II (*Bhumyamalki*) we saw great preservation of liver function, with also the AST and ALT levels doing very well during anti tubercular therapy (ATT). Also we noted in the placebo group a large increase in both AST and ALT levels during the course of ATT[3]. Also they saw no change in bilirubin and alkaline phosphatase levels which means that hepatic excretory function was preserved through the study.

Conclusion

Available data reports that certain ayurvedic herbs, which include *Phyllanthus fraternus*, may put forth great hepatic protective benefits when used in conjunction with antitubercular therapy. That they are able to lower levels of liver enzymes which we see raised in some patients indicates a role in the reduction of drug induced hepatotoxicity without at the same time reducing the tubercle bacillus treatment's efficacy. From an Ayurvedic point of view, these results support the use of what is known as *Rasayana* drugs and hepatoprotective drugs in the treatment of *Rajayakshma* which is a goal of preserving liver function and at the same time of tissue repair. While the clinical results are quite favourable, we should note that we are at the stage of proof of concept what is required now at a larger scale with randomized controlled trials to prove out these points and put into practice and facilitate the integration of evidence-based Ayurvedic interventions into tuberculosis care.

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Conflict of Interest

The author declares no conflict of interest.

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