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Evaluation of Hepatoprotective Activity of Siddha Formulation Arithrathi Chooranam

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Abstract-

Background: Arithrathi Chooranam is a herbo-mineral preparation used in Siddha medicine, traditionally recognized for its effectiveness in treating jaundice and various hepatic disorders. Despite its historical use, scientific validation of its hepatoprotective mechanisms has been limited.

Aim: This study aims to assess the hepatoprotective properties of Arithrathi Chooranam against liver damage induced

by the anti-tuberculosis drugs rifampicin (RIF) and isoniazid (INH).
Materials and Methods: We utilized a rat model of drug-induced hepatotoxicity, administering daily doses of 100 mg/kg of RIF and INH over a period of 21 days. The protective effects of two different concentrations of Arithrathi Chooranam (200 mg/kg and 400 mg/kg) were evaluated alongside the RIF and INH treatment.
Results: The Siddha formulation exhibited significant hepatoprotective activity, effectively reducing liver damage caused by INH and rifampicin. Our findings provide empirical support for the traditional medicinal claims regarding Arithrathi Chooranam's role in managing hepatic toxicity.
Conclusion: This study offers substantial scientific validation for Arithrathi Chooranam as a traditional Siddha medicinal formulation, highlighting its impressive hepatoprotective properties against drug-induced liver damage. While the results are promising, further research is essential, including in-depth studies on molecular mechanisms, comprehensive clinical trials, and the identification of specific bioactive compounds.
Keywords: Jaundice, Siddha, Arithrathi Chooranam, pharmacological study, hepatoprotective activity.

Introduction

The term "jaundice," also referred to as "hyperbilirubinemia," describes a yellowing of the body's tissue because of an excess bilirubin accumulation. Bilirubin only deposits when there is an overabundance, indicating increased production or reduced removal [1]. The prevalence of jaundice varies amongst patient demographics; it is more prevalent in neonates and older patients [2]. Traditional medicines use various herbal formulations to treat liver diseases. In the lack of a proven treatment option in contemporary medicine, attempts are being made to identify suitable herbal drugs [3]. Several herbo-mineral compositions are used successfully to treat jaundice in the Siddha system of medicine, among the oldest and most widely utilized traditional systems of Indian medicine. These medications have been tried and true for decades, and they are described in the earliest Siddha medical literature. The present research aimed to objectively assess the effectiveness of the siddha formulation Arithrathi chooranam against hepatotoxicity brought on by rifampicin (RIF) and isoniazid (INH).

Materials and Methods

Arithrathi chooranam preparation

Arithrathi Chooranam is mentioned in the siddha text 'Sarabandharar Vaithiya Muraigal Pandu Kamalai Sigichai Nool [4]. Ingredients of Arithrathi Chooranam are given in Table 1. Manjal, Nellimulli, Indhuppu, Kadukkai thol, Thandrikai thol, and Kadugu Rohini were taken in equal quantity. These raw drugs are cleaned, purified, made into fine powder, and sieved and preserved in an airtight container. 300mg to 500mg of this powder is mixed with hot water and given twice a day after food for 15 days to cure the condition of Manjal Kamalai (Jaundice).

Table 1: Ingredients of Arithrathi Chooranam

Tamil Name	Botanical Name	Parts Used	Quantity
Manjal	Curcuma longa	Rhizome	25gm
Nellimulli	Phyllanthus emblica	Leaves, Flowers, Bark, Seeds, Fruit, Root	25gm
Kadukkai thol	Terminalia chebula	Tender fruit and ripe fruit	25gm
Thandrikai thol	Terminalia bellerica	Leaves, Fruits, Seeds.	25gm
Kadugu Rohini	Picorrhiza scropulariflora	Roots	25gm
Indhuppu	Sodium chloride	Rock Salt	25gm

Experimental animals used (IAEC/KMCP/230/2015-16)

Male Wistar rats with 180-200 gm weight were provided from the experimental animal center at the K.M. College

of Pharmacy in Madurai. Rats were kept in temperature-controlled settings with 12-hour light/dark cycles and unfettered availability of food and drink for the duration of the study. Only when the animals had adapted to the lab environment for at least seven days were the experiments carried out in the morning (8 a.m. to 11 a.m.). The institutional animal ethical committee (IAEC/KMCP/230/2015-16) approved the research procedure.

Preparation of the extract

Separately made in sterile distilled water, INH and RIF solutions were used in the study as the hepatotoxicity model at 100 mg/kg per day. INH and RIF were both given to rats for a total of 21 days. In the hepatoprotective model, the siddha formulations Arithrathi chooranam (200 mg/kg) and Arithrathi chooranam (400 mg/kg) were given daily along with the INH+RIF solution.

In vivo hepatoprotective activity studies - Protocol for treatment:

- **Group I (G1):** Standard control -- Saline was the only treatment given to the animals.
- **Group II (G2):** As a hepatotoxicity control, the animals received (isoniazid) INH+ (rifampicin) RIF for 21 days.
- **Group III (G3):** The control group, the animals were administered INH+RIF+SILYMARIN orally for 21 days.
- **Group IV (G4):** The therapy group, the animals received the INH+RIF+ siddha formulation Arithrathi chooranam (200 mg/kg orally for 21 days).
- **Group V (G5):** The therapy group, the animals received the INH+RIF+ siddha formulation Arithrathi chooranam (400 mg/kg) for 21 days.

Assessment of hepatoprotective activity

Rats were handled according to the treatment schedule. The protocol was authorized by the institutional animal ethical committee. Hepatoprotective activity was assessed biochemically in the current study. On day 21, the rats were given medication, put to sleep, and then murdered an hour later. Blood was drawn using the retro-orbital plexus technique, the serum was separated, and the levels of serum alkaline phosphatase, or serum ALP, serum AST, serum ALT, total protein, and albumin, as well as serum cholesterol, were measured [5].

Statistical analysis

P-values of 0.05 were considered as statistically significant. The findings are shown as mean ± standard deviation.

Results

The goal of this study was to show that siddha formulation Arithrathi Chooranam, at various doses, exhibited hepatoprotective effects in INH, Rifampicin-induced hepatotoxicity. The results of the experiment testing the hepatoprotective efficacy of the siddha formulation Arithrathi chooranam on rats given INH and Rifampicin at 200 mg/kg body weight and 400 mg/kg are shown in Table 2.

Table 2: Effect of siddha formulation Arithrathi chooranam on the serum enzymes

Groups	Protein (Total) (g%)	Albumin (g/dl)	Total Cholesterol (mg/dl)	ALT (U/L)	AST (U/L)	ALP (mg%)
G1	8.20±0.52	4.95±0.45	80.60±4.42	76.48±3.55	145.12±4.45	122.42±4.15

Groups	Protein (Total) (g%)	Albumin (g/dl)	Total Cholesterol (mg/dl)	ALT (U/L)	AST (U/L)	ALP (mg%)
G2	4.30±0.24**a	2.18±0.26**a	156.25±8.20**a	178.15±8.90**a	250.30±8.70**a	310.62±6.55**a
G3	7.90±0.82**b	4.58±0.40**b	96.45±6.15**b	84.05±5.90**b	176.10±6.60**b	204.95±5.45**b
G4	6.82±0.45**b	3.98±0.40**b	116.25±7.18**b	124.08±6.05**b	212.10±7.40**b	263.80±6.15**b
G5	7.40±0.55**b	4.34±0.38**b	108.08±5.05**b	104.60±5.80**b	195.20±9.45**b	256.90±6.80**b

Six animals are included in each group, and all values are reported as Mean ± SEM. G1-Normal Control, G2-Toxic Control, G3-Standard Control, G4-Treatment Control - Arithrathi chooranam (200mg/kg), and G5-Treatment Control - Arithrathi chooranam (400mg/kg) siddha formulations. Significantly different **a-values from control (G1) ($P<0.001$), Significantly different **b-values from the toxic control (G2) $P<0.001$ The one-way ANOVA determines all values, then Newman Keul's multiple-range tests are performed.

Control group: G1 (Table 2)

In the control group, ALP, AST, and ALT levels were 122.42 ± 4.15, 145.12 ± 4.45, and 76.48 ± 3.55. The albumin and total protein values were 4.95 ± 0.45 and 8.20 ± 0.52, respectively. The standard control's total cholesterol value was 80.60 ± 4.42.

Toxic control: G2 (Table 2)

In comparison to the control, INH and Rifampicin administration for 21 drugs led to an increase in cholesterol (156.25 ±8.20), along with a significant decrease in total protein (4.30 ± 0.24), total albumin (2.18 ± 0.26), and a substantial increase in ALP (310.62 ± 6.55), ALT (178.15±8.90), and AST (250.30±8.70).

Treatment control: G3 (Table 2)

In comparison to the toxic control, there was a remarkable decrease in cholesterol (96.45 ± 6.15), along with a substantial rise in total protein (7.90 ± 0.82) and total albumin (4.58 ± 0.40) levels. There was also a significant drop in ALP (204.95 ± 5.45), AST (176.10 ± 6.60), and ALT (84.05 ± 5.90).

Siddha formulation Arithrathi chooranam group: G4 (Table 2)

In comparison to the toxic control, there was a significant drop in cholesterol (116.25 ± 7.18), along with substantial rises in total protein (6.82 ± 0.45) and total albumin (3.98 ± 0.40) levels. There was also a significant drop in ALP

(263.80 ± 6.15), AST (212.10 ± 7.40), and ALT (124.08 ± 6.05) levels.

Siddha formulation Arithrathi chooranam group: G5 (Table 2)

In comparison to the toxic control, there was a significant decrease in cholesterol (108.08 ± 5.05), along with a marked rise in the levels of total protein (7.40 ± 0.55), total albumin (4.34 ± 0.38), and ALP (256.90 ± 6.80), AST (195.20 ± 9.45), and ALT (104.60 ± 5.05).

Histopathological observations

Fig.no:1 Normal control

The section displays the typical anatomy of the liver. The central vein, the portal tracts that radiate from the hepatocyte column, and the sinusoids all seem normal. There was no sign of cirrhosis.

Fig.no:2 Toxic control (INH+RIF)

The image depicts the destruction of the liver's normal architecture. Liver parenchyma displaying fatty changes indicative of cirrhosis.

Fig.no:3. Standard control silymarin 75 mg/kg

The segment displays a healthy liver with no apparent pathological abnormalities. Hepatocytes, the central vein, and the portal tracts all seem normal.

Fig No. 4 Treatment Control Arithrathi Chooranam (200mg/kg)

The section displays the typical anatomy of the liver. Hepatocytes, the central vein, and the portal tracts all seem normal. There was no sign of cirrhosis.

Fig No. 5 Treatment Control Arithrathi Chooranam (400mg/kg)

The illustration depicts the typical liver anatomy. Sinusoids, portal tracts, and hepatocytes all seem normal.

Discussion

The liver, a crucial organ involved in numerous metabolic processes, is a common target for many toxicants. Hydrazine is a well-known hepatotoxin. Hepatotoxicity brought on by antitubercular medications is a significant and frequent side effect [6,7]. Hepatotoxicity is 1.2% more common when INH is used alone and can reach 8-10%. It might be fatal if this hepatotoxicity is not recognized when combined with rifampicin [8]. The metabolism of INH results in the direct production of hydrazine (from INH) and the indirect production of acetyl hydrazine. As the responsible hepatotoxins, isoniazid metabolite, acetyl hydrazine, and hydrazine have all been identified. These metabolites are subjected to cytochrome P450 (cyto P450) monooxygenase and free radical oxidative activation in the liver, which can result in liver damage in animals [9,10]. As a result, the cyto P450 enzymes play a crucial role in hepatotoxicity, producing hazardous, reactive compounds. Rifampicin, a strong mixed-function oxidase inducer, boosts the production of hazardous metabolites, which worsens the hepatotoxicity of INH. Free radicals make up a large number of the reactive intermediates created during the metabolization of isoniazid, which is becoming increasingly obvious [11,12]. It was thought that cytochrome P450 was involved in how RIF worked synergistically with INH to block biliary secretion at a greater rate and promote lipid peroxidation in liver cells. These effects were seen when RIF and INH were taken together [11,13].

According to this study, giving INH and Rifampicin increased the liver enzymes AST, ALT, ALP, and TC levels while decreasing total protein and albumin levels. When Groups 4 and 5 were administered the siddha formulation Arithrathi chooranam, these parameters were restored to levels that were close to normal. Treatment with the siddha formulation Arithrathi chooranam demonstrated protection against damage brought on by the interaction of INH and Rifampicin with CYP450, which may prevent the formation of hepatotoxic free radicals. The siddha formulation Arithrathi chooranam treated animals achieved near normal AST, ALT, and ALP levels in INH and Rifampicin intoxicated animal groups, confirming the hepatoprotective efficacy. The outcomes of biochemical indicators demonstrate the hepatoprotective properties of the Siddha formulation Arithrathi Chooranam.

Conclusion

The siddha formulation Arithrathi chooranam has shown a hepatoprotective solid effect in the current investigation, guarding against INH and Rifampicin-induced liver damage. The flavonoids and antioxidants in the siddha formulation Arithrathi chooranam may have a role in hepatoprotective activity. More research is required to comprehend better the siddha formulation of Arithrathi chooranam's hepatoprotective mode of action.

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