International Journal of Health Sciences and Research
DOI: https://doi.org/10.52403/ijhsr.20210426
Vol.11; Issue: 4; April 2021
Website: www.ijhsr.org
Review Article *ISSN: 2249-9571*

Scientific Validation on *Siddha Sashtric* Polyherbal Formulation "*Raasa Amirthathy Chooranam*" for Tuberculosis - A Review

Vimalan M[1], Antony Duraichi R[2]

[1]PG Scholar, Department of Gunapadam, [2]Lecturer, Department of Gunapadam,
Government Siddha Medical College, Palayamkottai, Tirunelveli, Tamil Nadu, India.

Corresponding Author: Vimalan M

ABSTRACT

Siddha medicines include 32 types of internal medicines and 32 types of external applications. Herbal drugs are given in the forms like *choornam* (powder), *ilagam*, *Mathirai* (tablets), *thylam* (oil) and mineral preparations in the form of *parpam* (white calcinated powder), *chendooram* (red in color) etc. The *siddha* formulation '*Raasa amirthathy chooranam*' is a polyherbal formulation consists of 21 herbal ingredients. According to siddha literature, the ingredients in this formulation have therapeutic effects on *Uzhzhurukki* can be correlated with tuberculosis in modern medical science. Present review focuses on the composition, traditional uses of the Siddha sashtric polyherbal formulation "*Raasa amirthathy chooranam*" along with the scientific analysis of its pharmacological action. The current review provides a background for the various pharmacological actions of the ingredients of the formulation. Analyzing various research articles, the ingredients of this formulation possesses Anti tuberculosis, Anti microbial, Hepato protective, Anti inflammatory, Antioxidant and Immuno modulatory activity which will improve the symptoms of illness as well as prevent the complications of disease. This review explains the phyto constituents and pharmacological actions of each ingredients of *Raasa amirthathy chooranam* that has been mentioned in *Vaiththiya Saarasangirakam*, 1968, Page No 433 classical siddha literature.

Key Words: *Raasa amirthathy chooranam*, tuberculosis, polyherbal formulation.

INTRODUCTION

Herbal medicines as the major remedy in Siddha system of medicine have been used in medical practices since antiquity. The practices continue today because of its biomedical benefits as well as place in cultural beliefs in many parts of the world and have made a great contribution towards maintaining human health. Approximately 60% of the population use traditional medicines to treat medical illnesses.

Tuberculosis is a contagious infection that usually attacks the lungs. It can also spread to other parts of the body. It is caused by bacteria (Mycobacterium tuberculosis). It is curable and preventable. It remains the leading cause of death from an infectious disease among adults worldwide with more than 10 million people becoming newly sick from tuberculosis each year. Herbal drugs are gaining worldwide popularity because of lesser side effects, cost effectiveness and easy availability to poor people particularly in developing countries.

In Siddha sashtric text *Vaiththiya Saarasangirakam, Raasa amirthathy chooranam*, a polyherbal formulation is mentioned for Tuberculosis. This review focuses the chemical constituents, therapeutic actions of 21 ingredients of

Raasa amirthathy chooranam to get better results in clinical application in managing Tuberculosis by Siddha aspect.

MATERIALS AND METHODS

Type of Study: Literature Review

The information on Siddha formulation "*Raasa amirthathy chooranam*" was acquired from Siddha text book of *Vaiththiya Saarasangirakam* and by literature searching in electronic databases such as Pub Med, Google-Scholar etc for publications.

RESULTS AND OBSERVATIONS

Table 1: Ingredients of *Raasa amirthathy chooranam*

S. NO	INGREDIENTS	FAMILY	CHEMICAL CONSTITUENTS	THERAPEUTIC ACTIONS
1	Elattaria cardamomum(F)[1]	Zingiberaceae	Cineole, limonene, terpinolene, myrcene, linalool, alpha terpinyl acetate	➢ Anti tuberculosis ➢ Chemo preventive ➢ Immunomodulatory ➢ Anticancer
2	Cinnamomum verum(B)[2]	Lauraceae	Eugenol, E- cinnamyl acetate, cinnamaldehyde, caryophyllene oxide	➢ Anti tuberculosis ➢ Anti microbial ➢ Antioxidant ➢ Anticancer ➢ Anti inflammatory ➢ Anti diabetic
3	Glycyrrhiza glabra(R)[3]	Fabaceae	Glycyrrhizin, glabrin, liqurtin, semilicoisoflavone, methoxyficifolinol	➢ Anti tuberculosis ➢ Anti inflammatory ➢ Anti ulcer ➢ Antioxidant ➢ Anti cancer ➢ Hepato protective
4	Cuminum cyminum(F)[4,5]	Apiaceae	Cuminaldehyde, cuminol, cymene, cuminoside, cimonene, eugenol	➢ Anti tuberculosis ➢ Digestive ➢ Antimicrobial ➢ Hepato protective ➢ Anti inflammatory ➢ Bio enhancer activity
5	Nigella sativa(S)[14]	Ranunculaceae	Thymol, thymoquinone, melanthin, campesterol, longitolene	➢ Anti tuberculosis ➢ Bronchodilator ➢ Antimicrobial ➢ Hepato protective ➢ Renal protective ➢ Immunomodulatory
6	Trigonella foenum graecum(S)[15]	Fabaceae	Trigonelline, diosgenin, prolomin, Scopoletin, coumarin, phytic acid	➢ Anti microbial ➢ Anti oxidant ➢ Anti diabetic ➢ Hepato protective
7	Hyoscyamus niger(S)[16]	solanaceae	Hyoscyamine, hyoscine, scopolamine, atropine	➢ Anti microbial ➢ Anti inflammatory ➢ Analgesic ➢ Sedative
8	Piper cubeba(F)[17]	Piperaceae	β – caryophyllene, epi – cubebol, cubebol, Y – cadinene	➢ Anti tuberculosis ➢ Anti bacterial ➢ Antioxidant ➢ Nephroprotective ➢ Anti inflammatory
9	Piper longum(F)[6]	Piperaceae	Piperine, piperlongumine, sylvatin, sesamin, pipermonaline, piperundecalidine	➢ Anti tuberculosis ➢ Carminative ➢ Immunomodulatory ➢ Antioxidant ➢ Anti inflammatory ➢ Hepatoprotective
10	Embelia ribes(F)[7]	Myrsinaceae	Embelin, embolic acid, embelinol, christembine, cinnamic acid, rapanon	➢ Antioxidant ➢ Cardio protective ➢ Antimicrobial
11	Crocus sativus(P)[18]	Iridaceae	Crocin, picrocrocin, crocetin, safranal	➢ Antitussive ➢ Anti inflammatory ➢ Antioxidant ➢ Antimicrobial
12	Nardostachys jatamansi(R)[8]	Valerianaceae	β – eudesmol, elemol, β –sitisterol, algelicin, jatamansin	➢ Anti cancer ➢ Antioxidant ➢ Hepatoprotective ➢ Anti bacterial

Table 1: Continued…				
13	Rubia cordifolia(R)[19]	Rubiaceae	Rubiadin, manjistin, alizarin, garancin, purpurin, xanthopurpurin	➢ Anti tuberculosis ➢ Hepato protective ➢ Anti microbial ➢ Anti inflammatory ➢ Anti cancer
14	Picrorhiza kurroa(R)[20]	Plantaginaceae	Picroside I&II, d – mannitol, kutkiol, kutki sterol, apocynin	➢ Hepato protective ➢ Anti inflammatory ➢ Antioxidant ➢ Immunomodulatory
15	Piper longum(R)[9]	Piperaceae	Piperine, piperlongumine, sylvatin, sesamin, pipermonaline, piperundecalidine	➢ Antibacterial ➢ Antidiabetic ➢ Anti hyperlipidemic
16	Myristica fragrans(Nut)[10]	Myristicaceae	Myristicin, myristic acid, elemicin, safrole, trimyrishtin, myrcene	➢ Anti inflammatory ➢ Immunomodulatory ➢ Antioxidant ➢ Carminative ➢ Hepatoprotective ➢ Anti microbial
17	Syzygium aromaticum (Bud)[11]	Myrtaceae	Myricetin, eugenol, eugenol acetate, limonin, ferulic aldehyde	➢ Anti tuberculosis ➢ Anti cancer ➢ Hepato protective ➢ Antioxidant ➢ Anti inflammatory ➢ Anti microbial
18	Myristica fragrans(Aril)[12]	Myristicaceae	Myristicin, myristic acid, elemicin, safrole, trimyrishtin, myrcene	➢ Anti inflammatory ➢ Immunomodulatory ➢ Antioxidant ➢ Anti microbial ➢ Radio protective
19	Alpinia galanga(Rh)[13]	Zingiberaceae	Alpinin, galangol, galangin, campheride, galanolactone	➢ Anti tuberculosis ➢ Immuno stimulating activity ➢ Antioxidant ➢ Anti inflammatory ➢ Anticancer ➢ Carminative
20	Plumbago zeylanica(R)[21]	Plumbaginaceae	Plumbagic acid, lupeol, uridine, daucosterol, tachioside, norcanelilline	➢ Anti tuberculosis ➢ Hepato protective ➢ Nephroprotective ➢ Antioxidant
21	Cassia angustifolia(L)[22]	Caesalpiniaceae	Rutin, scutellarein, quercimeritrin, sennoside A & B	➢ Antioxidant ➢ Anti inflammatory ➢ Anti microbial

F – Fruit, B – Bark, R – Root, Rh – Rhizome, S – Seed, L – Leaf, P – Pollen grains.

PHARMACOLOGICAL ACTIVITIES OF INGRDIENTS RELATED TO TUBERCULOSIS:

Elattaria cardamomum:

Antituberculosis activity[23]:

Mature seeds of E. cardamomum and mature rhizomes of Z. officianale and C. longa were air dried and extracted with 99% ethanol using a Soxhlet apparatus for 6-8 hours. The extracts were concentrated to dryness using a rotary evaporator and tested anti-mycobacterial activity by Luciferase reporter phage (LRP) assay against standard strain of M. tuberculosis H37RV at three different concentrations (25, 250 and 500 µg/ml). The results revealed that all the three plants have potential antituberculosis activity.

Cinnamomum verum:

Antituberculosis activity[24]:

Antituberculosis activity of extracts was tested by agar dilution & Microscopic Observation of Drug Susceptibility Assay (MODS).50% inhibition (IC50) was calculated by Resazurine Microtitre Assay (REMA).The combined effect of the extracts with INH was evaluated by checkerboard titrations. Minimum Inhibitory Concentration (MIC) of aqueous &methanolic extracts of both plants showed 10 mcg/ml by agar dilution method. Acquous (CAS) & methanolic (CMS) extracts of Cinnamomum showed MIC value of 0.5 & 2 mcg/ ml respectively.

Anti microbial activity[25]:

Extraction with an aqueous system from the dried stem barks of C. verum yielded 2.5% of the dried plant. Among 10 test strains of bacteria, C. verum showed inhibitory effect on the growth of Klebsiella pneumoniae ATCC 10031, Staphylococcus epidermidis ATCC 12228 and E. coli ATCC 25922 in an agar diffusion test. The Minimal Inhibitory Concentrations (MICs) and the Minimal Bactericidal Concentrations (MBCs) were in the range of 4-16 and 16-32 g L-1, respectively.

Glycyrrhiza glabra:

Anti tuberculosis activity[26]:

Bioactivity guided isolation of Glycyrrhiza glabra (Leguminosae / Fabaceae) roots resulted in the characterization of 18β-glycyrrhetinic acid as a major anti-tubercular agent. Further, GA-1 was semi-synthetically converted into its nine derivatives, which were in-vitro evaluated for their antitubercular potential against Mycobacterium tuberculosis H37Rv using BACTEC-460 radiometric susceptibility assay. All the derivatives were active, but the benzylamide (GA-8, MIC 12.5μg/ml) and ethyl oxylate (GA-3, MIC 25.0 μg/ml) derivatives were significantly active against the pathogen. This was further supported by the molecular docking studies, which showed adequate docking (LibDock) scores for GA-3 (120.3) and GA-8 (112.6) with respect to the standard anti-tubercular drug, rifampicin (92.94) on the DNA-directed RNA polymerase subunit beta (rpoB) target site. Finally, the in silico pharmacokinetic and drug-likeness studies showed that GA-3 and GA- 8 possesses drug-like properties

Hepato protective activity[27]:

Glycyrrhizaglabra extract was added to the carp primary hepatocytes before (pre-treatment), after (post-treatment) and both before and after (pre- and post-treatment) the incubation of the hepatocytes with CCl_4. CCl_4 at 8 mM in the culture medium produced significantly elevated levels of lactate dehydrogenase (LDH), glutamate oxalate transaminase (GOT), glutamate pyruvate transaminase (GPT) and malondialdehyde (MDA) and significantly reduced levels of superoxide dismutase (SOD) and glutathione peroxidase (GSH-Px). Pre-treatment (5 μg/ml) and pre- and post-treatment (5 and 10 μg/ml) of the hepatocytes with *Glycyrrhizaglabra* extract significantly reduced the elevated levels of LDH, GOT, GPT and MDA and increased the reduced levels of SOD and GSH-Px by CCl_4; post-treatment of the hepatocytes with *Glycyrrhizaglabra* extract at 5 μg/ml reduced the GPT and GOT levels and increased the GSH-Px level, but had no effect on the other parameters at all the studied concentrations.

Cuminum cyminum:

Anti tuberculosis activity[28]:

Essential oils were used with cumin, cloves, cinnamon, laurel and anis to determine Minimum Inhibitory Concentration (MIC) against Mycobacterium tuberculosis strains. The MICs were determined on M. tuberculosis H37Rv sensitive to all five first line antituberculosis drugs (streptomycin, isoniazid, rifampicin, ethambutol and pyrazinamide), two H37-Rv (CH-8 and CH-15) isoniazid-resistant, two H37Rv (CH-07 and CH-09) rifampicin-resistant, two H37Rv (CH-03 and CH-06) streptomycin-resistant, and two H37Rv (CH-09 and CH-10) ethambutol-resistant using the microplate alamar blue assay. The results obtained showed that the cumin and cinnamon essential oils showed a MIC of 12.5 μg/ml against reference strain H37Rv.

Hepato protective activity[29]:

Administration of cisplatin raised the level of LFT's enzymes and also reduced the level of antioxidant enzymes in the liver of the mice. Administration of Cuminum cyminum, Phyllanthusemblicus extract and silymarin remarkably showed the hepatoprotective effect in the albino mice. Administration of C. cyminum, P. emblica

and silymarin decreased the level of ALT, AST, and ALP along with increasing the level of Total protein content. It also increased the level of antioxidant enzymes in the liver of mice showing its hepatoprotective activity. We found C. cyminum has a better hepatoprotective effect than P. emblica.

Anti microbial activity[30]:

Three groups of microorganisms [aerobic bacterial mixture, anaerobic bacterial mixture and Enterococcus faecalis (E .faecalis)] were isolated from the teeth with persistent apical periodontitis. Zone of inhibition (ZOI), minimum inhibitory concentration (MIC), minimum bactericidal concentration (MBC), minimum biofilm inhibitory concentration (MBIC) and time-kill tests were performed to assess the antimicrobial efficacy of the medicaments. Further, a cytocompatibility analysis of the medicaments was performed on L929 fibroblasts. Co-trimoxazole showed the greatest ZOI followed by cumin and CHX. The smallest MIC and MBC belonged to co-trimoxazole followed by cumin and CHX for all groups of bacteria except for *E. faecalis* for which the MBC of cumin was smaller than co-trimoxazole. The results of time-kill assay revealed that all medicaments totally inhibited the bacterial growth in all groups after 24 h. CHX was the most cytotoxic solution while there were no significant differences between the cytocompatibility of different concentrations of cumin essential oil and co-trimoxazole.

Nigella sativa:

Anti tuberculosis activity[31]:

In Middlebrook broth, fluorescence test for tuberculosis was negative with thymoquinone 20, 40 and 80 µg/ml and streptomycin 1.25 µg/ml up to day 14th. With controls, thymoquinone 2.5, 5 and 10 µg/ml fluorescence was detectable from day 10 to 14. In Middlebrook agar, there was no visible growth of tubercle bacillus with thymoquinone 20, 40 and 80 µg/ml and streptomycin 1.25 µg/ml, however, with controls, thymoquinone 2.5 and 5 µg/ml abundant and with 10 µg/ml few colonies were observed.

Anti microbial activity[32]:

Filter paper discs impregnated with the diethyl ether extract of *Nigella sativa* seeds (25–400 µg extract/disc) caused concentration dependent inhibition of Gram-positive bacteria represented by *Staphylococcus aureus*. Gram-negative bacteria represented by *Pseudomonas aeruginosa* and *Escherichia coli* (but not *Salmonella typhimurium*) and a pathogenic yeast *Candida albicans*. The extract showed antibacterial synergism with streptomycin and gentamicin and showed additive antibacterial action with spectinomycin, erythromycin, tobramycin, doxycycline, chloramphenicol, nalidixic acid, ampicillin, lincomycin and sulphamethoxyzole-trimethoprim combination. The extract successfully eradicated a non-fatal subcutaneous staphylococcal infection in mice when injected at the site of infection.

Hepato protective activity[33]:

The in vitro and in vivo findings of this study demonstrated that the NSSE has protective effects against APAP-induced hepatotoxicity and metabolic disturbances by improving antioxidant activities and suppressing both lipid peroxidation and ROS generation.

Trigonella foenum graecum:

Anti microbial activity[34]:

The inhibitory effect of fenugreek oil was tested against four microorganisms: three bacteria: Escherichia Coli, Staphylococcus aureus, and Salmonella typhimurium and one Mould: Aspergillus niger. The results indicated that the oil has a Potent antimicrobial activity against all tested microorganisms. The Highest antimicrobial activity among the bacteria was detected Against E. coli, where the inhibition zone diameter was 20 mm.

However, the highest antimicrobial activity against all tested Organisms was found against Aspergillus niger where a complete Inhibition (100%) was recorded.

Hepato protective activity[35]:

Hepatic injury in rats was induced separately by administration of equal mixture of CCl4 and olive oil (50% v/v, 1.25 ml/kg, ip). Liver damaged was monitored by raised biochemical marker enzymes (SGOT, SGPT, and alkaline phosphatase). CCl4 was administered twice a week, on every first and fourth day of all 14 days. The extract at the dose of 250 mg/kg b. wt. was evaluated by inducing hepatotoxicity with CCl4 and using silymarin (100 mg/kg) as the reference standard. Biochemical parameters like, SGOT, SGPT and serum bilirubin level were analysed. A section of liver was subjected to histopathological studies. Based on the above studies, it is reported that the methanol extract of TFG possess significant hepato-protection against CCl4 induced hepatotoxicity in albino rats.

Piper cubeba:

Antibacterial activity[36]:

The evaluation of the antibacterial activity has been done by broth microdilution technique for determination of the minimum inhibitory concentration and the minimum bactericidal concentration against Porphyromonas gingivalis, Prevotella nigrescens, Actinomyces naeslundii, Bacteroides fragilis and Fusobacterium nucleatum. It was possible to make an analysis regarding the relationship between structure and antimicrobial activity of derivatives against microorganisms that cause endodontic infections. The most promising were minimum inhibitory concentration =50 µg/ml against P. gingivalis by (2) and (3), and minimum inhibitory concentration =100 µg/ml against B. fragilis by (6). Cytotoxicity assays demonstrated that (1) and its derivatives do not display toxicity.

Anti tuberculosis activity[37]:

A novel piperine dimer, named chabamide, was isolated from stems of Piper cubeba Hunter and its structure was elucidated on the basis of spectroscopic evidence. Chabamide showed antimalarial activity with an IC 50 value of 2.7 µg/ml and antituberculosis activity with the minimum inhibitory concentration (MIC) of 12.5 µg/ml.

Piper longum:

Hepato protective activity[38]:

On Administration of the aqueous extract of fruits of Piper longum along with the anti TB drugs, the levels of lipid peroxides in Liver homogenate as well as serum are significantly decreased ($p<0.001$) compared to the group treated with antitubercular drugs. Similarly on administration of piperine along with anti TB drugs, lipid peroxides in serum and in liver homogenate are signficantly reduced ($p<0.001$) compared to the group treated with antitubercular drugs. The levels of reduced Glutathione are also significantly reduced ($p<0.001$) in the Group treated with anti tubercular drugs compared to normal Control. Administration of extract of fruits of Piper longum and piperine along with the anti TB drugs significantly increased the levels of reduced glutathione ($p<0.001$) Histopathological studies indicate no significant change between the control and the group administered with Antitubercular drugs. On extending the study of Hepatoprotective effect to infected animals, it was again observed that there was a significant increase ($p<0.001$) in lipid peroxides in liver homogenate of animals on Administration of anti TB drugs. The levels were lowered significantly ($p<0.001$) on administration of extract of fruits of Piper longum with anti TB drugs compared to the group treated with antitubercular drugs. There was a significant decrease ($p<0.05$) in reduced glutathione levels in the group treated with anti TB drugs. On administration of extract of fruits of Piper longum with anti TB drugs a significant increase ($p<0.001$) in the levels of reduced

glutathione is observed compared to the group treated with antitubercular drugs.

Anti tuberculosis activity[39]:

A bioassay guided fractionation of Pippali (Piper longum L.) was performed in five different organic solvents and their activities were monitored against different pathogenic bacteria including MDR Mycobacterium. Different fractions were screened for the bioactivity against Mycobacterium, and the structure of bioactive compound was characterized with H 1 and C 13 NMR. An ethyl acetate fraction of Pippali extract was found active against M. smegmatis (3000µg ml -1) and M. tuberculosis (39 µg ml -1). It also shows very significant activity against other bacterial strains like E.coli (152 µg ml -1), Staphylococcus aureus (14 µg ml-1), Salmonella typhi (180 µg ml -1), Enterococcus faecalis (15 µg ml -1), and Pseudomonas aeruginosa (52 µg ml -1). This fraction of ethyl acetate was then purified and characterized as piperine [5-(1, 3-benzodioxol-5-yl)-1-piperidin-1-ylpenta-2,4-dien-1-one], a well known alkaloid from this plant. Bioactivity guided fractionation concludes that Piperine is the only active ingredients in various fractions of fruit extract evaluated for antibacterial activity.

Embelia ribes:

Antimicrobial activity[40]:

The antimicrobial activity against two micro-organisms were tested using disc diffusion method and cytotoxicity of GNPs and SNPs was determined against MCF-7 cell lines at different concentrations by MTT assay. Both the GNPs and SNPs prepared from E. ribes comparatively showed promising results thereby proving their clinical importance.

Crocus sativus:

Antimicrobial activity[41]:

The antimicrobial activity was determined by the evaluation of the minimum inhibitory concentration using the agar well plate procedure. The most effective extract was SPE with a minimum inhibitory concentration varying between 500 µg/mL, 250 µg/mL, 125 µg/mL, 62.5 µg/mL, 31.25 µg/mL, 15.63 µg/mL.

Nardostachys jatamansi:

Hepatoprotective activity[42]:

A 50% ethanolic extract of the rhizomes of N. jatamansi is shown to possess hepatoprotective activity. Pretreatment of rats with the extract (800 mg/kg body wt, orally) for three consecutive days significantly ameliorated the liver damage in rats exposed to the hepatotoxic compound thioacetamide. Elevated levels of serum transaminases (aminotransferases) and alkaline phosphatase, observed in thioacetamide alone treated group of animals, were significantly lowered in N. jatamansi pretreated rats. Pretreatment of the animals with the extract also resulted in an increase in survival in rats intoxicated with LD90 dose of the hepatotoxic drug.

Antibacterial activity[43]:

Antibacterial activity was evaluated by agar well diffusion assay and broth microdilution assay. The study revealed that N. jatamansi extract is sensitive to all tested bacterial strains. The zones of inhibition and MIC ranged from 8-22 at a concentration of 1-5 mg/mL and 0.3-0.6 mg/mL, respectively. Methanolic extract of N. jatamansi showed marked inhibition of carbonic anhydrase (IC 50 712.41±0.001 µg/mL) when compared with standard acetazolamide.

Rubia cordifolia:

Anti-mycobacterial activity[44]:

Anti-mycobacterial activity of Rubia cordifolia leaves were tested on DCM and ethanolic extracts against H37Rv strain of Mycobacterium tuberculosis using the green fluorescence protein microplate assay (GFPMA). The ethanolic crude extract (K2F-3) was less active than the DCM (K2F-1) crude extract, with MIC90 of 57.3 and 44.5 µg/ml respectively as shown in Table 1 and Table 2 respectively.

Fractionation of the crude extracts by preparative chromatography, eluting with 5% methanol-DCM afforded four sub-fractions from each crude. The sub-fractions from the ethanol crude demonstrated better activity compared to those obtained from the DCM crude.

Hepato protective activity[45]:

Rubiadin at a dose of 50, 100 and 200 mg/kg was administered orally once daily for 14 days. The substantially elevated serum enzymatic activities of serum glutamic oxaloacetic transaminase (SGOT), serum glutamate pyruvate transaminase (SGPT), serum alkaline phosphatase (SALP) and γ-glutmyltransferase (γ-GT) due to carbontetrachloride treatment were dose dependently restored towards normalization. Meanwhile, the decreased activities of glutathione S-transferase and glutathione ruductase were also restored towards normalization. In addition, rubiadin also significantly prevented the elevation of hepatic melondialdehyde formation and depletion of reduced glutathione content in the liver of CCl4 intoxicated rats in a dose dependent manner. Silymarin used as standard reference also exhibited significant hepatopretective activity on post treatment against carbon tetrachloride induced hepatotoxicity in rats. The biochemical observations were supplemented with histopathological examination of rat liver sections. The results of this study strongly indicate that rubiadin has a potent hepatoprotective action against carbon tetrachloride induced hepatic damage in rats.

Anti microbial activity[46]:

55 plant methanolic extracts were investigated for antimicrobial activity against, thirteen phytopathogens of Gossypium using agar ditch diffusion method. Results from the in vitro antimicrobial assays indicated that six plant extracts exhibited antimicrobial activity, in which highest activity was observed from the root extracts of R. cordifolia and G. glabra. Qualitative phytochemical tests, Column chromatography and of these two active root extracts demonstrated the presence of phyto compounds VIZ, anthraquinones and flavonoids as major active constituents respectively.

Picrorhiza kurroa:

Hepato protective activity[47]:

P. kurroa by itself had no cytotoxic effects on the liver slices at a wide range of concentrations (0.5-0.1%; data not shown). Percent release of LDH from slices treated with the highest concentration (20 mg/ml) of P. kurroa extract alone (8.5%± 0.14) was found to be similar to that in the case of control Untreated slices (10.2%±2.6) [Table 3]. In all the experiments, Three concentrations of P. kurroa, viz., 20 mg/ml, 10 mg/ml and 0.5 mg/ml were used, while the time course for the release of cytotoxicity marker enzyme was followed only for the highest concentration of P. kurroa (20 mg/ml). P. kurroa, when added along with ethanol, inhibited the release of all three marker enzymes in a concentration-dependent manner. Ascorbic acid (10 mM) was used as a standard antioxidant and protected the liver slices from the cytotoxic effect of ethanol.

Piper longum (root):

Anti bacterial activity[48]:

Antibacterial activity of piperlongumine was evaluated against 18 clinically isolated strains, including identified strains belongs to Klebsiella pneumoniae, Pseudomonas aeruginosa and Staphylococcus aureus, using the agar-well diffusion method. All the clinical strains showed concentration dependent susceptibility towards the constituent piperlongumine (25, 50, 100µg/100µL). It exhibited significant zone of inhibition against both the clinical and ATCC and MTCC strains. The antibacterial activity was more pronounced against Klebsiella pneumonia (24.00±0.12 mm) and Pseudomonas aeruginosa (20.00±0.12 mm)

while it was moderate on Staphylococcus aureus (16.47±0.18 mm).

Myristica fragrans:

Anti microbial activity[49]:

Acetone extract has shown the strongest antibacterial and antifungal activity with Staphylococcus aureus (13.8 ± 0.42 mm) and Aspergillus niger (14.4 ± 0.37 mm), respectively. GC–MS analysis of acetone extract has revealed the presence of 32 compounds of extract representing 99.49%. Sabinene (28.61%) has shown the highest occurrence in the extract. B-Pinene (10.26), α-pinene (9.72), myristicin (4.30%), isoeugenol (2.72%), p-cymene (1.81%), carvacrol (1.54%), eugenol (0.89%) and β-caryophellene (0.82%) were reported as possible contributor for antioxidant and antimicrobial activity of nutmeg.

Hepatoprotective activity[50]:

Myristicin, one of the major essential oils of nutmeg, was found to possess extraordinarily potent hepatoprotective activity. Myristicin markedly suppressed LPS/D-GalN-induced enhancement of serum TNF-α concentrations and hepatic DNA fragmentation in mice. These findings suggest that the hepatoprotective activity of myristicin might be, at least in part, due to the inhibition of TNF-α release from macrophages.

Syzygium aromaticum:

Anti tuberculosis activity[51]:

Methanolic and acetone extract of Syzygium aromaticum exhibited very good anti-TB activity having MIC of 0.8 µg/ml and 12.5 µg/ml respectively.

Hepato protective activity[52]:

30 Healthy Rabbits weighing 2kg on average were divided into 3 equal groups. Group A was taken as control group having no intervention while group B was given paracetamol 500mg BD for 10 days followed by SyzygiumAromaticum powder 100mg BD for next 10 days. Group C was given paracetamol 500mg BD and Syzygium Aromaticum powder 100mg BD for 20 days. Blood samples were taken from ear lobes through 24 gauge canula for liver enzymes at days 1, 10 and 20 and analyzed in ISRA Laboratory. Mean and standard deviation were calculated and p-value <0.05 was taken as significant. The data was entered and analyzed by using SPSS version 16. There was no rise in liver enzymes in group A at any stage of the study. Liver enzymes ALT, AST, GGT, ALP and LDH markedly increased in group B in initial 10 days but declined in next 10 days. There was no significant rise in liver enzymes in group C at any level of the study.

Anti microbial activity[53]:

The zone of inhibition in clove ethanolic extract against all the food associated bacteria was in the range of 25mm to 32mm and in molds the percent mycelial growth inhibition ranged from 70% to 100%.The clove ethanolic extract exhibited the maximum zone of inhibition against E. coli. The MIC values of clove ethanolic extract for different bacterial isolates ranged from 5.0 mg/ml to 20mg/ml and 10 mg/ml to 20mg/ml against molds.

Myristica fragrans (aril part):

Anti microbial activity[54]:

In poison food medium method, the essential oil showed complete zones of inhibition against Fusarium graminearum at the all tested doses. For other tested fungi and bacteria, they gave good to moderate zone inhibition.

Alpinia galanga:

Anti tuberculosis activity[55]:

1´ acetoxychavicol acetate, the reference standard used, was present in all the three extracts. The acetone and ethanolic extracts were active in axenic (aerobic and anaerobic) and intracellular assays. The aqueous extract did not demonstrate activity under the defined assay parameters.

Plumbago zeylanica:

Anti tuberculosis activity[56]:

Plumbagin analogs, obtained from Plumbago zeylanica (Family-Plumbaginaceae), have been synthesized. Out of the various synthesized analogs, the antitubercular activity of compound a and b was evaluated using standard H 37 Rv and S, H, R, and E sensitive M tuberculosis strains using LRF assay method. Compound a showed strong activity against both standard H 37 Rv and S, H, R and E sensitive M. tuberculosis strains as compared to standard Rifampicin. The other compounds are proved to be more active against standard H 37 Rv and S, H, R and E sensitive M. tuberculosis strain as compared to Rifampicin.

Hepato protective activity[57]:

Hepatotoxicity was induced in male Wistar rats by intra peritoneal injection of CCl4 (0.1 ml/kg/day for 10 days). Extracts of P. zeylanica rhizome were administered to the experimental rats (25 mg/kg/day, po for 14 days). The hepatoprotective effect of these extracts was evaluated by the assay of liver function biochemical parameters (Protein, Cholesterol, Bilirubin, Alanine amino transaminase, and Aspartate amino transaminase activities). In rhizome extract-treated animals, the toxic effect of CCl4 was controlled significantly by restoration of the levels of Protein, Cholesterol, Bilirubin Alanine amino transaminase and Aspartate amino transaminase as compared to the control cohort, which evidenced the hepatoprotective activity. Rhizome extract of P. zeylanica possesses significant hepatoprotective activity.

Cassia angustifolia:

Anti microbial activity[58]:

Methanolic extraction of plant showed notable antifungal activities against Aspergillusniger, Aspergillus terreus, Aspergillus flavus, and Aspergillus fumigatus C.Angustifolia was very highly active against A. terreus(6.01±0.27). Aspergillus was found to be sensitive to all test medicinal plants and mostly comparable to the standard reference antifungal drug amphotericin B and Fluconazole to some extent.

CONCLUSION

This review especially exposes the ingredients of *Raasa Amirthathy Chooranam* have Anti tuberculosis, Anti microbial, Hepato protective, Anti inflammatory, Antioxidant and Immuno-modulatory activity. These pharmacological activities and Chemical constituents contribute major role in treatment of tuberculosis. Furthermore this formulation should be subjected to preclinical evaluations to understand the safety and better effectiveness of herbal medicine before prescribing to the patients.

Acknowledgement: None

Conflict of Interest: None

Source of Funding: None

REFERENCES

1. Samir qiblawi, Awdah Al – Hazimi et al,. Chemopreventive effects of Cardamom on chemically induced skin carcinogenesis in swiss albino mice. Journal of medicinal food 2012; 15(6): 576-580.
2. Neetu singh, Amerender Singh rao et al,. Phytochemical and pharmacological review of Cinnamomum verum J. Presl – a versatile spice used in food and nutrition. Food chemistry 2020; 338, 127773.
3. Rajandeep kaur, Harpreet Kaur et al,. Glycyrrhiza glabra: a phytopharmacological review. International journal of pharmaceutical sciences and research 2013; 4(7): 2470.
4. Krishnapura srinivasan. Cumin and black cumin seeds: traditional uses, chemical constituents, and nutraceutical effects. Food quality and safty 2008; 2(1):1-16.
5. Johri R K. Cuminum cyminum and carum carvi: an update. Pharmacognacy reviews 2011; 5(9): 63-72.
6. Vaishali yadav, anuja Krishnan et al,. A systematic review on piper longum L.: bridging traditional knowledge and

pharmacological evidence for future translational research. Journal of ethnopharmacology 2020; 247,112255.
7. Uma bhandari, Nazam Ansari M et al,. Cardioprotective effect of aqueous extract of Embelia ribes Burm fruits against isoproterenol – induced myocardial infarction in albino rats. Csir 2008.
8. Shilpee chaudhary, Kodangala Subraya et al,. Evaluation of antioxidant and anticancer activity of extract and fractions of Nardostachys jatamansi DC in breast carcinoma. BMC complementary and alternative medicine 2015; 15(1): 1-13.
9. Shaik abdul nabi, ramesh babu kasetti et al,. Antidiabetic and antihuperlipidemic activity of piper longum root aqueous extract in STZ induced diabetic rats. BMC complementary and alternative medicine 2013; 13(1): 37.
10. Rahul checker, Suchandra chatterjee et al,. Immunomodulatory and radioprotective effect of lignans derived from fresh nutmeg mace in mammalian splenocytes. International immunopharmacology 2008; 8(5): 661-669.
11. Arunava Das , Harshadha K et al,. Evaluation of therapeutic potential of eugenol – a natural derivative of syzygium aromaticum on cervical cancer. Asian pacific journal of cancer prevention 2018; 19(7): 1977.
12. Yukihiro ozaki, Soekeni Soedigdo et al,. Anti-inflammatory effect of mace, aril of myristica fragrans Houtt., and its active principles. The Japanese journal of pharmacology 1989; 49(2): 155-163.
13. Chudiwal AK, jain DP et al,. Alpinia galanga Willd. – an overview on phyto – pharmacological properties. CSIR 2010.
14. Aftab ahmad, Asif Husain et al,. A review on therapeutic potential of Nigella sativa: A miracle herb. Asian pacific journal of tropical biomedicine 2013; 3(5): 337-352.
15. Shailima rampogu, Saravanan parameswaran et al,. Exploring the therapeutic ability of fenugreek against type II diabetes and breast cancer employing molecular docking and molecular dynamics simulations. Evidence based complementary and alternative medicine 2018; 1943203:12.
16. Aaparna K, Abhishek J Joshi et al,. Phyto-chemical and phyto pharmacological profiles of Hyocyamus niger Linn – A review. Pharma science monitor 2015; 6(1): 153-159.
17. Wasim ahmad, Azhar hasan et al,. An appraisal of medicinal properties of piper cubeba. UNIMED Kulliyat 2012; 13(18): 5-7
18. Srivastava R, Ahmed H et al,. Crocus sativus L.: a comprehensive review. Pharmacological reviews 2010; 4(8): 200.
19. Nilambari deshkar, Shrikant tilloo et al,. A comprehensive review of Rubia cordifolia Linn. Pharmacognosy reviews 2008; 2(3): 124-134.
20. Deepica soni, Abhinav grover. Picrosides from Picrorhiza kurroa as potential anti-carcinogenic agents. Biomedicine and pharmacotherapy 2019; 109: 1680-1687.
21. Jai C tilak, Soumyakanti adhikari et al,. Antioxidant property of Plumbago zeylanica, an Indian medicinal plant and its active ingredient, plumbagin. Redox report 2004; 9(4): 219-227.
22. Khaled bellassoued, Houda hamed et al,. Antioxidant and hepatoprotective effects of cassia angustifolia extract against carbon tetrachloride – induced hepatotoxicity in rats. The journal of metabolic diseases 2019;
23. Jyothi PV arun 2014, 'Identification of lead compounds with anti-tuberculosis activity in indigenous spices of Kerala', M.Sc thesis, Kerala university, Thrissur.
24. Shashikant vaidya, jaishankar Sharma et al,. Assessment of anti-tuberculosis activity of extracts of Cinnamomum verum and Solanum surattense along with isoniazid. European respiratory journal 2016; 48(60).
25. Puangpronpitag D, sittiwet C. Antimicrobial properties of Cinnamomum verum aqueous extract. Asian journal of biological sciences 2009; 2(2): 49-53.
26. Kalani, Komal et al,. Anti-tubercular agents from Glycyrrhiza glabra. Current topics in medicinal chemistry 2015; 15(11): 1043-1049.
27. Guojun yin, Liping Cao et al,. Hepatoprotective and antioxidant effects of Glycyrrhiza glabra extract against carbon tetrachloride – induced hepatocyte damage in common carp. Fish physiology and biochemistry 2011; 37(1): 209-216.
28. Andrade-ochoa Sergio et al,. Evaluation of antimycobacterium activity of the essential oils of cumin, clove, cinnamon, laurel and anis. Advances in biological chemistry 2013; 3(5):480-484.

29. Nahid abbas, Mamuna naz et al. Comparative study of hepatoprotective effect produced by Cuminum cyminum, fruits of Phyllanthus emblicus and Silymarin against cisplastin – induced hepatotoxicity. International journal of pharmaceutical sciences and research 2017; 8(5): 2026-32.
30. Abbas abbaszadegan, Ahmad gholami et al,. Antimicrobial and cytotoxic activity of Cuminum cyminum as an intracanal medicament compared to chlorhexidine gel. Iranian endodontic journal 2015; 11(1): 44-50.
31. Muhammad akram randhawa. In vitro antituberculosis activity of thymoquinone, an active principle of Nigella sativa. Journal of ayub medical college abbottabad 2011; 23(2): 78-81.
32. Hanafy MSM, Hatem ME. Studies on antimicrobial ctivity of Nigella sativa seed. Journal of athnopharmacology 1991; 34(2-3): 275-278.
33. Gareeballa osman adam, Mahbubur rahman et al,. Hepatoprotective effects of Nigella sativa seed extract against acetaminophen – induced oxidative stress. Asian pacific journal of tropical medicine 2016; 9(3): 221-227.
34. Abdel moneim E sulieman et al,. The chemical composition of fenugreek and the antimicrobial properties of its seed oil. Gezira j of eng. & applied sci. 2008; 3(2): 52-71.
35. Shaileyee das. Hepatoprotective activity of methanol extract of fenugreek seeds on rat. International journal of pharmaceutical sciences and research 2014; 5(4): 1506.
36. Karen rezende, Rodrigo lucarini et al,. Antibacterial activity of cubebin isolated from Piper cubeba and its derivatives against microorganisms that cause endodontic infections. Revista brasileira de farmacognosia 2016; 26(3): 296-303.
37. Thitima rukachaisirikul, Samran prabpal et al,. Chabamide, a novel piperine dimer from stems of piper cubeba. Planta medica 2002; 68(9): 853-855.
38. Prema gurumurthy, vijayalatha et al,. Hepato protective effect of aqueous extract of Piper longum and piperine when administered with antitubercular drugs. The bioscan 2012; 7(4): 661-663.
39. Singh C, Santosh kumar singh et al,. Antimicobacterial activity of Piper longum L. Fruit extracts against multi drug resistant Mycobacterium spp. International journal of phytomedicine 2011; 3(3): 353-361.
40. Manikandan dhayalan et al,. In vitro antioxidant, antimicrobial, cytotoxic potential of gold and silver nanoparticles prepared using Embelia ribes. Natural product research 2016; 31(4): 465-468.
41. Adil farooq wali et al,. Antioxidant, antimicrobial, antidiabetic and cytotoxic activity of Crocus sativus L. Petals. Applied sciences 2020; 10(4): 1519.
42. Shakir ali et al,. Nardostachys jatamansi protects against liver damage induced by thioacetamide in rats. Journal of ethnopharmacology 2000; 71(3): 359-363.
43. Tayyeba rehman, saeed ahmad et al,. Evaluation of antibacterial and carbonic anhydrase inhibitory potential of methanolic extract Nardostachys jatamansi dc rhizome. Acta poloniae pharmaceutica 2017; 74: 1471-1476.
44. Makgatho ME, Nxumalo et al,. Evaluation of the anti-mycobacterial, anti-oxidative and anti-proliferative activities of Rubia cordifolia ethanolic leaf extract sub-fractions in human lymphocytes and neutrophils. Afr j tradit complement altern med. 2017; 14(5): 181-187.
45. Guntupalli M mohana rao et al,. Hepatoprotective effects of rubiadin, a major constituent of Rubia cordifolia Linn. Journal of ethnopharmacology 2006; 103(3): 484-490.
46. Naidu KC, Ramya lalam et al,. Antimicrobial agents from Rubia cordifolia and Glycyrrhiza glabra against phytopathogens of Gossypium. International journal of pharm tech research 2009; 1(4): 1512-1518.
47. Sangeeta sinha, jyoti bhat et al,. Hepatoprotective activity of Picrorhiza kurroa extract against alcohol cytotoxicity in mouse liver slice culture. International journal of green pharmacy 2011; 5(3).
48. Raja naika, prasanna KP et al,. Antibacterial activity of piperlongumine an alkaloid isolated from methanolic root extract of Piper longum L. Pharmacophore 2010; 1(2): 141-148.
49. Ashish deep gupta et al,. Chemistry, antioxidant and antimicrobial potential of nutmeg. Journal of genetic engineering and biotechnology 2013; 11(1): 25-31.

50. Tatsuya morita, keiko jinno et al,. Hepatoprotective effect of myristicin from nutmeg on lipopolysaccharide/D-galactosamine-induced liver injury. Journal of agricultrre and food chemistry 2003; 51(6): 1560-1565.
51. Rajandeep kaur, harpreet kaur. Antitubercular activity and phytochemical screening of selected medicinal plants. Oriental journal of chemistry 2015; 31(1): 597-600.
52. Sadia kazi, palwasha abbasi et al,. Syzygium aromaticum: a potential hepatoprotective agent. JSZMC 2016; 7(2): 956-959.
53. Ram kumar pundir et al,. Antimicrobial activity of ethanolic extracts of Syzygium aromaticum and Allium sativum against food associated bacteria and fungi. Ethnobotanical leaflets 2010; 3:11.
54. Guridip singh, marimuthu P et al,. Antimicrobial and antioxidant potentials of essential oil and acetone extract of Myristica fragrans aril. Journal of food science 2005; 70(2): 141-148.
55. Pooja gupta, purva bhatter et al,. Evaluating the anti Mycobacterium tuberculosis activity of Alpinia galangal L. Axenically under educing oxygen conditions and in intracellular assays. BMC complementary and alternative medicine 2014; 14(1): 84.
56. Nishi nayak, meenakshi bajpai et al,. Plumbagin analogs-synthesis, characterization and antitubercular activity. Journal of advanced pharmaceutical technology & research 2014; 5(1) 28.
57. Iftikhar aslam tayubi et al,. Hepatoprotective activity of Plumbago zeylanica L. Against carbon tetrachloride induced hepatotoxicity in rats. International journal of scientific innovations 2018; 1.
58. Ali Hussein al-marzoqi et al,. Determination of metabolites products by Cassia angustifolia and evaluate antimicrobial activity. Journal of pharmacognosy and phytotherapy 2016; 8(2): 25-48.

How to cite this article: Vimalan M, Antony Duraichi R. Scientific validation on siddha sashtric polyherbal formulation *"raasa amirthathy chooranam"* for tuberculosis – a review. *Int J Health Sci Res.* 2021; 11(4): 197-209. DOI: *https://doi.org/10.52403/ijhsr.20210426*

******