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# Traditional Indian Medicine: A Systematic Review and Meta-analysis of Clinical Outcome in Non-Alcoholic Fatty Liver Diseases

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**Abstract**

Background: A fast developing liver condition called non-alcoholic fatty liver disease (NAFLD) is closely related to the metabolic syndrome. Since there are currently no particular pharmaceutical treatments for NAFLD, lifestyle and dietary changes are the main focus of current treatment. Over centuries of use, a number of substances mentioned in Ayurvedic writings have demonstrated positive effects in patients. However, there is disagreement among the results of several randomized clinical trials (RCTs) about the effectiveness of herbs in treating non-alcoholic fatty liver disease (NAFLD).The purpose of this study is to conduct a systematic review and meta-analysis of the data to assess the efficacy and security of medications with Ayurvedic references. Methodology: To find pertinent studies, the electronic databases PubMed, Web of Science, Embase, Cochrane library, and ARP were searched up to May 2022. Utilizing a modified Jadad Scale, the studies' quality was assessed. Using the Cochrane Risk of Bias Tool, the risk of bias was evaluated. The search turned up 1352 studies, but only 18 of them were ultimately assessed. A statistical analysis revealed a substantial decrease in the levels of AST (SMD: -0.91, 95% CI: -1.04, 0.08), ALT (SMD = 0.91; 95% CI: 1.53, 0.28; P 0.00001), and fatty liver (RR: 2.42, 95% CI: 1.52, 3.86).Conclusion: Based on the scant information that is currently available, Ayurvedic medicines have shown effective in treating NAFLD. To produce better evidence, more high-quality RCTs with sizable sample numbers and standardized Ayurvedic medications that take histological outcomes into account must be done.

**Keywords:** Ayurveda, Herbal Medicine, Non- Alcoholic Fatty Liver Disease, Meta-analysis, Systematic Review, Yakrit Roga

## Introduction

Non-alcoholic fatty liver disease (NAFLD), which affects over one-fourth of the world's population, is the most prevalent liver ailment to develop globally recently.(1,2) NAFLD, a disorder closely related to metabolic syndrome, develops when too much fat builds up in the liver cells without drinking alcohol. The prevalence of NAFLD is between 6 and 35 percent worldwide. NAFLD ranges from simple steatosis without cirrhosis to nonalcoholic steatohepatitis (NASH), which may accompany or without cirrhosis, in the absence of a significant history of alcohol usage. NASH is a progressive condition that affects 30–40% of people with elevated liver enzymes and around 5-7% of the general population. Hepatocellular carcinoma (HCC) has a prominent non-viral etiology that is quickly being known as NAFLD (3). According to estimates, one-third of adult Americans in the United States have NAFLD, compared to 20% to 30% in Europe and the Middle East.(4) Recent research conducted in several regions of India has shown that the prevalence of NAFLD ranges from 9 to 35%.(1) The increased frequency of NAFLD can also be attributed to the fact that the metabolic syndrome's hepatic manifestation is frequently associated with obesity.(5) Indians are more prone to insulin resistance or metabolic syndrome and its symptoms, such as NAFLD, as a result of urbanization and associated changes, such as a high-fat and carbohydrate-rich diet, sedentary lifestyle, and a higher hereditary propensity for diabetes mellitus.(6)

In the Indian subcontinent, ayurvedic medicine (AyM) has a long history of safely and successfully treating liver disorders. The plant-based medicines used alone or in combination with specific metals and minerals that have undergone rigorous pharmaceutical processes to become therapeutically active nanoparticles are included in the material-medica of AyM.(7) According to the ancient system of Ayurveda, NAFLD can be viewed as a combination of the diseases Yakt Roga (liver illness) and Medoroga (obesity). Yakt Roga (liver disease) encompasses a wide range of illnesses, from straightforward hepatic steatosis through hepatomegaly to liver cirrhosis. The main etiological causes of NAFLD are vidh (spicy food) and abhiyand hra (food that blocks channels or a fatty diet). Rakta kapha dui is caused by these two factors.(8) Various therapies based on herbal, metal/mineral, or multi-ingredient composition as described in old Ayurvedic scriptures have been used in several clinical trials. Similar to it, several patented or proprietary products are also in use.(9) Numerous studies have been released that raise questions about the safety and toxicity of Ayurvedic medicines, particularly those with herbomineral and mineral origins.(10)

## Need of Study

At this time, there is no one preferred pharmaceutical treatment for NAFLD. Changes in lifestyle and food are suggested, and therapy is geared toward addressing the risk factors for NASH (insulin resistance and reduced fatty acid transport to the liver). Plant-based substances with possible hepatoprotective effects have also been utilized, with varying degrees of success.(11,12) Considering the disease's national and global prevalence, clinical picture, prognosis, and the search for hepato-protective interventions, ayurvedic medicine can be a successful treatment choice for NAFLD, both as a stand-alone and adjuvant therapy. A systematic review of the quantity and caliber of data supporting the security and efficacy of Ayurvedic medicine therapies in NAFLD has been made. The evaluation of the data supporting the effectiveness and safety of Ayurvedic medicine (AyM) may result in significantly more effective NAFLD treatment alternatives. The study is laid out in accordance with the PRISMA report checklist.(13)

## Materials & Method

### Search Strategy

Up until May 2022, the electronic databases were thoroughly searched using PubMed, Web of Science, Embase, Cochrane library, and ARP (AYUSH Research Portal, Government of India). The information was limited to relevant RCTs that looked into how herbal or Ayurvedic treatments affected patients with NAFLD. Table 1 explains the methodology used for literature retrieval.

**Table 1: Strategy employed for literature retrieval**

| | |
|---|---|
| NAFLD | "Nonalcoholic fatty", "Non-alcoholic fatty", "Non-alcoholic fatty liver disease" [mesh], "Nonalcoholic" AND "fatty liver" [mesh], "Non-alcoholic" AND "fatty liver" [mesh], NAFLD, "Nonalcoholic steatohepatitis" |
| Ayurveda | "Phytotherapy", "Herbal medicine", "Plant preparation", "Ayurveda medicine", "Complementary medicine", "Drugs, Ayurveda herbal" [Mesh], "Medicine, traditional" [Mesh], "Plant preparations" [Mesh], "Medicinal plant", "Plant medicinal product", "Herb". |

### Eligibility criteria and screening

Each study's title, abstract, and complete text were examined to see if they met the inclusion criteria. Two levels of evaluation were included in the screening procedure for inclusion. The title and abstract were checked at the preliminary stage, and the following papers were not included in the initial round of screening: (1) Non-randomized trial; (2) protocol, review, and meta-analysis; (3) dietary, nutraceutical, fortified food, and probiotic studies; and (4) investigations of other diseases in NAFLD patients. The second stage involved conducting a full-text review to weed out any RCTs not connected to AYM, studies employing metabolites obtained from herbal sources, or substances not mentioned in Ayurvedic literature. Studies evaluating the impact of AyM on at least one of the following anthropometric variables (WC, body weight, BMI), blood lipid profiles (TG, TC, HDL, LDL), glycemic indices (FBS, HOMA-IR, serum insulin, and HbA1c) in subjects with diagnosed NAFLD were also included in the review.

### Data extraction & analysis

In accordance with the inclusion criteria previously specified, the titles and abstracts were separately evaluated by two reviewers (PC & NL). Additionally, studies with potential relevance were gathered and thoroughly evaluated. The following details were added to a standard data extraction table: (i) the authors' names; (ii) the publication year; (iii) the intervention; (iv) the sample size; (v) the patients' average ages; (vi) the length of the intervention; and (vii) the outcome indicators. Microsoft Excel 2016 was used to extract and record data, and Zotero 6.0 was used to manage and categorize references. The RoB 2 tool was used to evaluate the Risk of Bias.(14) The modified Jadad scale was used to evaluate the reporting quality of the studies that were a part of the review.(15,16) High-quality studies were defined as RCTs with a score of at least 4, whereas low-quality trials were defined as those with a score of less than 4.

### Outcome indicators

The effect of the intervention on the degree of fatty liver as determined by ultrasonography, fibroscan, or NAFLD Activity score (NAS), as well as changes in alanine transaminase (ALT), and aspartate transaminase (AST) levels, was the primary outcome. Gammaglutamyl transferease (GGT), total cholesterol (TC), triglycerides (TG), high-density lipoproteins (HDL), low-density lipoproteins (LDL), fasting blood glucose (FBS), HOMA-IR, and BMI alterations are among the secondary outcomes.

**Statistical analysis**

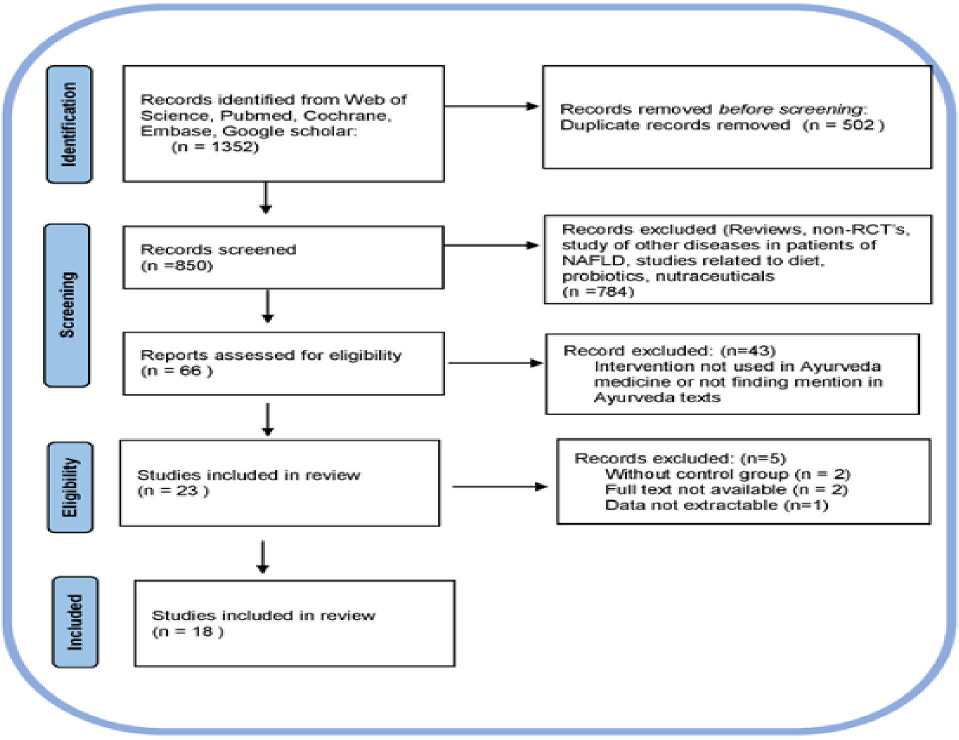
All of the secondary outcomes were reported using the Standard Mean Difference (SMD). The risk ratio (RR) and 95% CI were used to evaluate the dichotomous data. The overall aggregate effect of interventions was evaluated using the Cochrane review manager program RevMan 5.4.1. An effect size with a 95% confidence interval (CI) was employed in the combined analysis. The I2 test was used to evaluate heterogeneity. A fixed-effect model was used to synthesize the data if there was no heterogeneity (I2 50% and P > 0.1); otherwise, a random-effect model was employed if there was heterogeneity (50% I2 75%). Plots of forests were used to display the results.

## Results

### Study identification and selection

The initial screening procedure was carried out in accordance with the PRISMA recommendations as outlined in the flowchart in Fig. 1. Initial searches in the chosen electronic databases and allied sources turned up a total of 1352 studies. 850 possibly pertinent articles were chosen from this group and kept for additional screening. The titles and abstracts were then scrutinized. Additional 784 studies were disqualified for a variety of factors, including reviews, non-RCTs, research on comorbidities, food, and nutraceuticals. Then, 66 papers were chosen for additional evaluation. The assessment involved reading the complete texts, and as a result, 43 studies on herbal medications and therapies that weren't present in Ayurvedic writings were further disregarded. Finally, 23 studies were determined to be final selection-eligible. Five of these studies were eliminated due to single-arm design or inability to retrieve data. Finally, 18 English-language papers were discovered to meet the inclusion criteria and were added to the systematic review.(8,17-33).

**Fig 1 PRISMA flow diagram showing selection methodology of included studies. Out of 1352 studies identified, only 18 studies were finally included in the review**

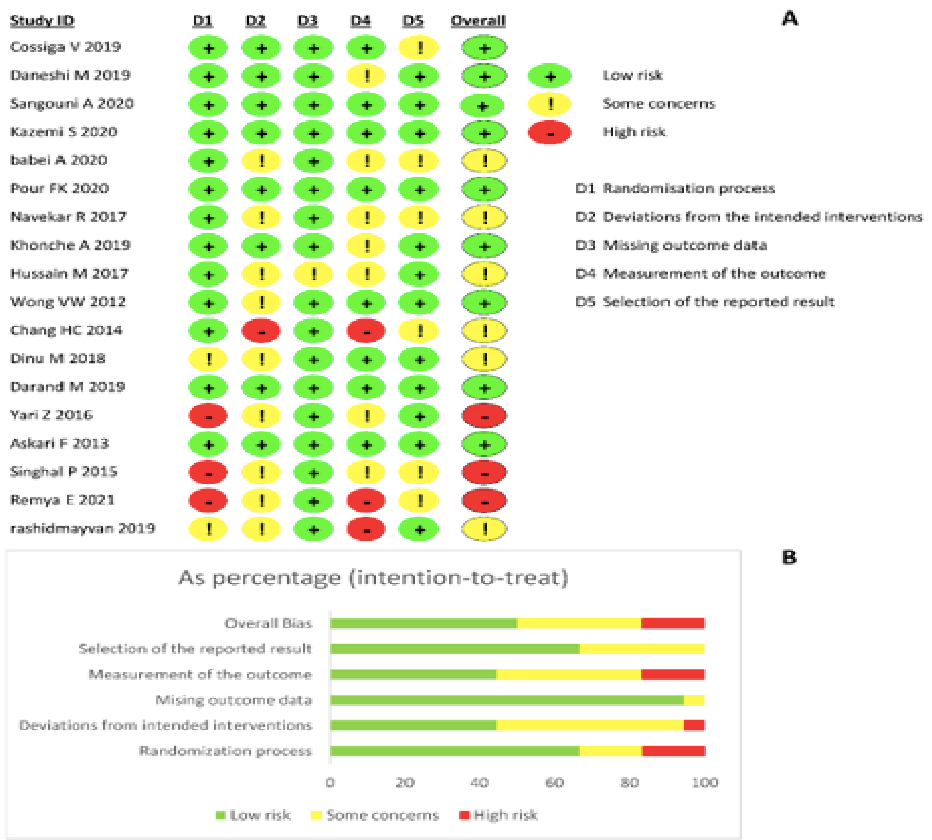


**Study characteristics & quality assessment**

For a systematic evaluation, 1097 participants from the 18 randomized clinical trial studies were considered, of whom 553 were assigned to the intervention group. Figure 2 depicts the assessment of the danger of bias.

Each study (PC & NL) was reviewed individually by two writers independ-ently. Every study had primary outcomes that were precisely defined. Five studies, however, did not disclose their previous sample size calculation technique. Thirteen had clearly specified protocols for allocation concealment and randomization. Thirteen studies included a total of 46 individuals who were deemed dropouts, whereas the number of dropouts in five RCTs was not reported. The participants' average age was 45.75. 14 trials lasted 12 weeks, while 2 investigations lasted 24 weeks and 8 weeks apiece. Using a modified Jadad score, the published studies' quality was evaluated. Three studies were deemed to be of low quality since they had a score of four or less. Only one study reported using liver biopsy to measure histological response as a primary endpoint for assessing the effectiveness of the intervention.

**Fig 2 (A) Risk of Bias of included studies; (B) Graph showing Risk of Bias**




**Intervention and control comparison**

The clinical studies evaluated fifteen different therapies in total. Three studies (8,28,30) compared dietary and lifestyle changes to 15 RCTs, while 15 RCTs were evaluated against a placebo. In five studies(20,21,29,31,32), participants were also counseled on dietary and lifestyle changes. Table 2 includes a list of the therapies evaluated in the included studies.

**Table 2: Characteristics of the studies included in the review**

| S.No. | Authors | Intervention | Control | Additional confounders | Total No. of Patients | No. of Patients in Intervention group | No. in Control group | Mean age of Participants | Duration | No of dropouts |
|---|---|---|---|---|---|---|---|---|---|---|
| 1 | Askari F 2013 | Cinnamomum zeylanicum Blume | Placebo | Dietary advice + Exercise | 50 | 23 | 22 | 42.2 | 12 weeks | 5 |
| 2 | Babaei A 2020 | Trigonella foenum-graecum L. (Hydro Alcoholic extract) | Placebo | Lifestyle changes | 30 | 13 | 11 | 39.3 | 3 months | 6 |
| 3 | Chang HC 2014 | Hibiscus sabdariffa | Placebo | None | 36 | 19 | 17 | 37.94 | 12 weeks | 4 |
| 4 | Cossiga V 2019 | Berberis aristata, Elaeis guineensis and Coffea canephora | Placebo | None | 49 | 26 | 23 | 54.2 | 24 weeks (6 months) | 0 |
| 5 | Daneshi M 2019 | Elettaria cardamomum L. | Placebo | None | 87 | 43 | 44 | 50 | 3 months | 6 |
| 6 | Darand M 2019 | Nigella sativa L | Placebo | Exercise and balanced diet | 50 | 22 | 21 | 47.4 | 12 weeks | 7 |
| 7 | Hussain M 2017 | Nigella sativa L | Placebo | None | 70 | 35 | 35 | 37 | 12 weeks | 0 |
| 8 | Kazemi S 2020 | Sumac (Unani Med) | Placebo | Calorie deficit diet | 84 | 40 | 40 | 41.6 | 12 weeks | 4 |
| 9 | Khonche A 2019 | Nigella sativa L | Placebo | None | 120 | 60 | 60 | 46.64 | 12 weeks | 0 |
| 10 | M Dinu 2018 | Triticum turgidum subsp. | Control Whea | None | 40 | 20 | 20 | 55.2 | 3 months | Not Shown |

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | turanicum (Khorasan | t | | | | | | | |
| 11 | Navekar R 2017 | Curcuma longa L. | Placebo | None | 46 | 21 | 21 | 41.23 | 12 weeks | 4 |
| 12 | Pour FK 2020 | Crocus sativus L. | Placebo | None | 76 | 38 | 38 | 42.7 | 12 weeks | 3 |
| 13 | Rashidmayvan 2019 | Nigella sativa L. oil | Placebo | None | 44 | 22 | 22 | 40.61 | 8 weeks | Not Shown |
| 14 | Remya E 2021 | Sharpunkhadi powder | Placebo | Dietary advice + Lifestyle changes | 83 | 43 | 40 | Not specified | 8 weeks | Not Shown |
| 15 | Sangouni A 2020 | Allium sativum, L. (Garlic) | Placebo | None | 90 | 42 | 40 | 45.75 | 12 weeks | 6 |
| 16 | Singhal P 2015 | Arogyavardhini vati & triphla guggul | Pathya & Diet Lifestyle | None | 32 | 21 | 11 | Not specified | 3 months | Not Shown |
| 17 | Wong VW 2012 | Phyllanthus urinaria | Placebo | None | 60 | 40 | 20 | 50 | 24 weeks | 1 |

**Outcome**

Changes in liver function (AST, ALT, GGT), lipid profile (TG, TC, HDL, LDL), hyperglycemia, (FBS, HOMAIR, QUICKI), inflammatory markers (hs-CRP, TNF-), and BMI are among the reported findings of the investigations. Table 3 summarizes these results.

Only the results at the conclusion of the trial period were published; no study attested to the follow-up information following the conclusion of the intervention period.

However, all of the RCTs that were published showed outcomes in the intervention group that were statistically superior to those in the control group. Additionally, no RCT revealed any unfavorable outcomes from the intervention.Figure 3-6 displays how interventions affect results.

| **S.No.** | **Authors** | **Intervention** | **Radiological/ Histological Assessment** | **Liver Function Profile** | **Body weight** | **weight Blood Sugar** | **Lipids** | **Others** | **Jadad Score** |
|---|---|---|---|---|---|---|---|---|---|

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| 1 | Askari F 2013 | Cinnamomum zeylanicum Blume | - | AST, ALT, GGT | BMI | FBS, HOMAIR, QUICKI | TC, TG, LDL, HDL | hsCRP, TNF-α | 4 |
| 2 | Babaei A 2020 | Trigonella foenum-graecum L. (Hydro Alcoholic extract) | Fibroscan | AST, ALT, GGT | BMI | FBS | TC, TG, LDL, HDL | - | 7 |
| 3 | Chang HC 2014 | Hibiscus sabdariffa | Fibroscan | AST, ALT, GGT | BMI | FBS | TC, TG, LDL, HDL | - | 5.5 |
| 4 | Cossiga V 2019 | Berberis aristata, Elaeis guineensis and Coffea canephora | Fibroscan | AST, ALT, GGT | BMI | FBS, HOMAIR | TC, TG, LDL, HDL | - | 7 |
| 5 | Daneshi M 2019 | Elettaria cardamomum L. | USG | - | - | FBS, QUICKI, HOMA-IR | TC, TG, LDL, HDL | - | 7 |
| 6 | Darand M 2019 | Nigella sativa L | Fibroscan | AST, ALT | BMI | FBS | TC, TG, LDL, HDL | hsCRP, TNF-α | 7 |
| 7 | Hussain M 2017 | Nigella sativa L | USG | AST, ALT | BMI | - | - | - | 5 |
| 8 | Kazemi S 2020 | Sumac (Unani Med) | Fibroscan | AST, ALT | BMI | HbA1C, Quicki, HOMA-IR | - | hsCRP, TNF-α | 7 |
| 9 | Khonche A 2019 | Nigella sativa L | USG | AST, ALT | - | - | TC, TG, LDL, HDL | - | 7 |
| 10 | M Dinu 2018 | Triticum turgidum subsp. turanicum | USG | AST, ALT, ALP | - | FBS | TC, TG, LDL, HDL | hsCRP, TNF-α | 4 |

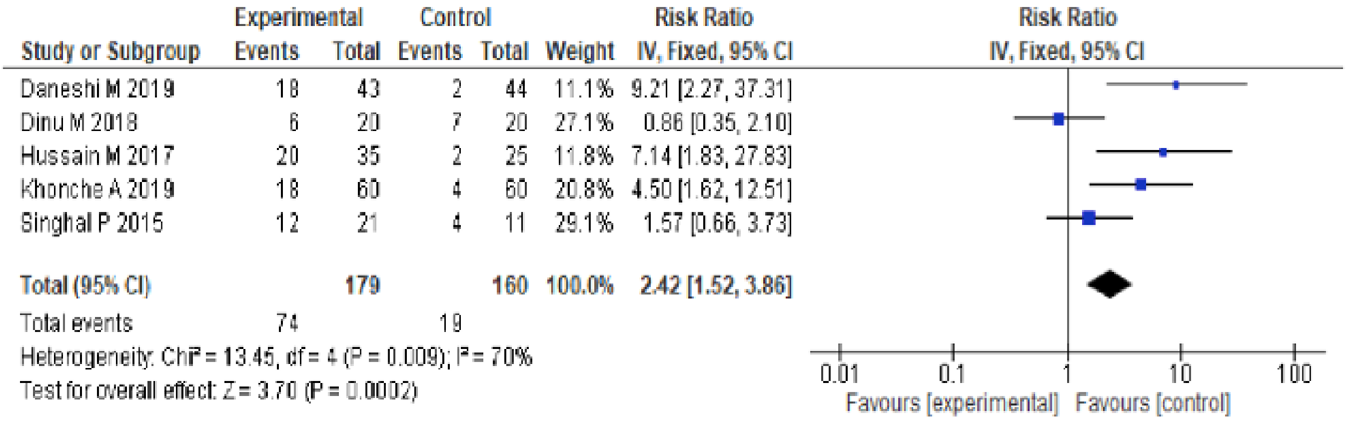
| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | (Khorasan | | | | | | | |
| 11 | Navekar R 2017 | Curcuma longa L. | - | AST, ALT | BMI | FBS, HOMAIR | - | - | 7 |
| 12 | Pour FK 2020 | Crocus sativus L. | - | AST, ALT | BMI | - | - | hsCRP, TNF-α | 7 |
| 13 | Rashidmayvan 2019 | Nigella sativa L. oil | - | AST, ALT, GGT | BMI | FBS | TC, TG, LDL, HDL | hsCRP, TNF-α | 5 |
| 14 | Remya E 2021 | Sharpunkhadi powder | - | - | - | FBS | TC, | - | 4 |
| 15 | Sangouni A 2020 | Allium sativum, L. (Garlic) | - | GGT | BMI | FBS, HOMAIR | TG, HDL | - | 7 |
| 16 | Singhal P 2015 | Arogyavardhini vati & triphla guggul | USG | AST, ALT | BMI | FBS | TC, TG, HDL | - | 3 |
| 17 | Wong VW 2012 | Phyllanthus urinaria | NAS | AST, ALT | BMI | FBS | TC, TG, LDL, HDL | - | 6 |

ALT - Alanine transaminase; AST- Aspartate transaminase; GGT- Gamma-glutamyl transferase; TC - Total cholesterol; TG – Triglycerides; HDL - High-density lipoproteins; LDL - Low-density lipoproteins; FBS - Fasting blood glucose; HOMA-IR - Homeostatic Model Assessment for Insulin Resistance; BMI – Body mass index; TNF- α – Tumor necrosis factor-alpha; hsCRP – high sensitivity C-reactive protein.

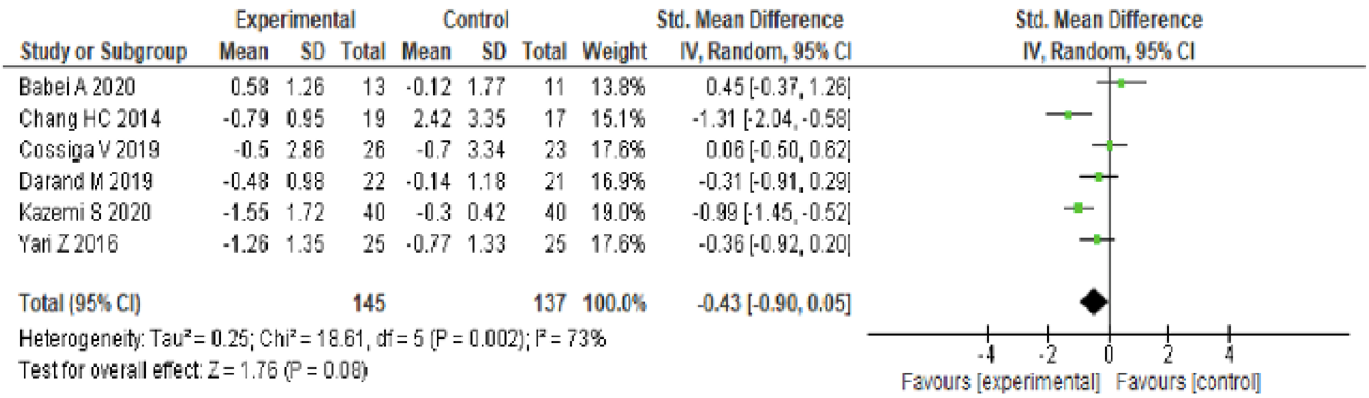
**Effect of intervention on grades of fatty liver and liver stiffness**

Five investigations described variations in the ultrasonographic grades of fatty liver. 339 patients were engaged in these research, with 179 assigned to the intervention group and 160 to the control group. Fixed effects analysis of the combined data from these studies showed a substantial decline in the grades of fatty liver (RR: 2.42, 95% CI: 1.52, 3.86; Figure 3A). Six studies including 282 patients—145 in the herbal intervention group and 137 in the control group—reported changes in liver stiffness with herbal intervention. Using random effects analysis, the combined data from these studies revealed a statistically insignificant decrease in liver stiffness (SMD: -0.43, 95% CI: -0.90, 0.05; Figure 3B).

**Fig 3: Forest Plot showing effect of intervention on (A) Grades of Fatty Liver; (B) Liver Stiffness**




A) Forest Plot of effect of herbal intervention on grades of Fatty Liver - USG




B) Forest Plot showing effect of herbal intervention on Liver Stiffness

**Effect of intervention on liver enzymes**

In 15 investigations, the impact on AST & ALT was evaluated. 811 participants were enrolled in these investigations, 425 of whom were in the intervention group and 386 were in the control group. Using random effects analysis, the pooled data from these trials showed a substantial decrease in the levels of AST (SMD: -0.91, 95% CI: -1.04, 0.08; Figure 4A) and ALT (SMD = 0.91; 95% CI: 1.53, 0.28; P 0.00001) (Figure 4B). There were only four studies that noted changes in GGT levels. 227 patients were engaged in these research, with 115 assigned to the intervention group and 112 to the control group. GGT levels significantly improved as a result of the aggregated effect of four investigations (SMD = -0.36, 95% CI: -0.69, -0.04; p0.05; Figure 4C).

**Effect of intervention on lipid profile**

In 12 research, the impact on total cholesterol (TC) was evaluated. 566 patients were engaged in these studies, with 301 assigned to the intervention group and 265 to the control group. Random effects analysis of the pooled data from these studies revealed a negligible decrease in TC levels (SMD: -0.38, 95% CI; -0.77, 0.01' Figure 5A). 13 studies encompassing 714 patients, 376 in the intervention group and 338 in the control group, evaluated the effect on HDL and TG. HDL concentrations significantly

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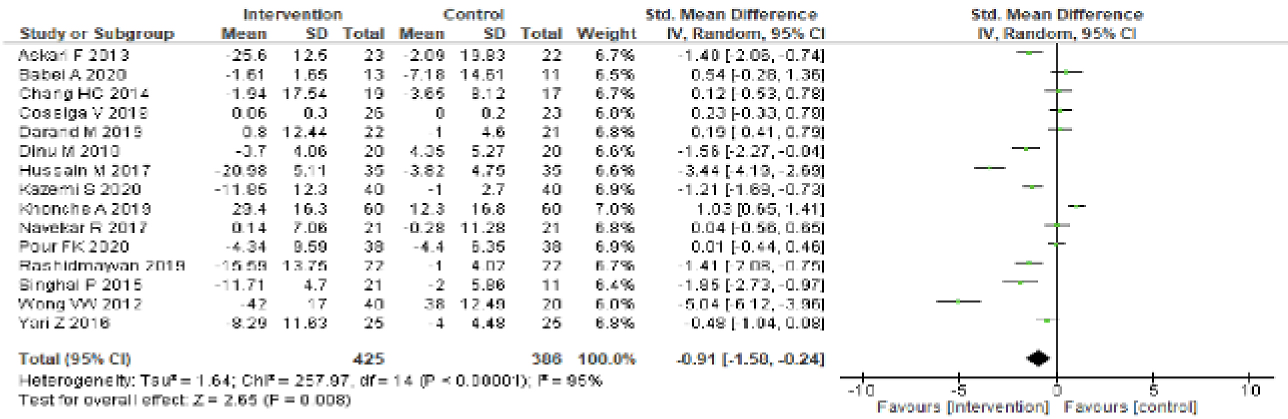
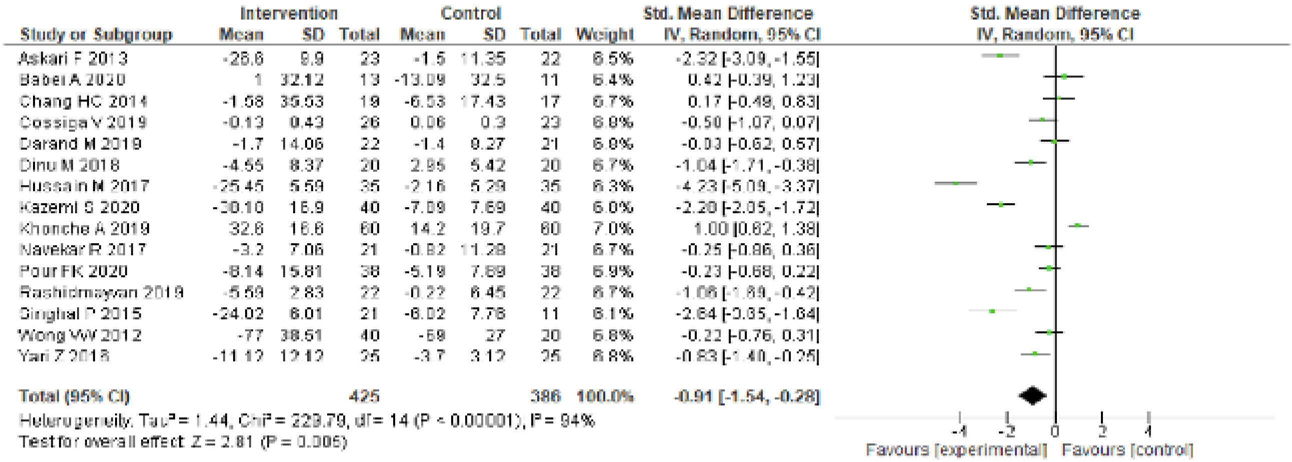
increased (SMD: 0.43, 95% CI: -0.11, 0.75; Figure 5B). These trials' combined data showed that TG levels have significantly improved (SMD: -0.46, 95% CI: -0.79, -0.13; Figure 5C). With 313 individuals in the intervention group and 285 in the control group, 598 participants were involved in eleven trials that evaluated the intervention's effects on LDL. LDL levels significantly decreased (SMD: -0.54, 95% CI: -0.95, -0.12; Figure 5D).

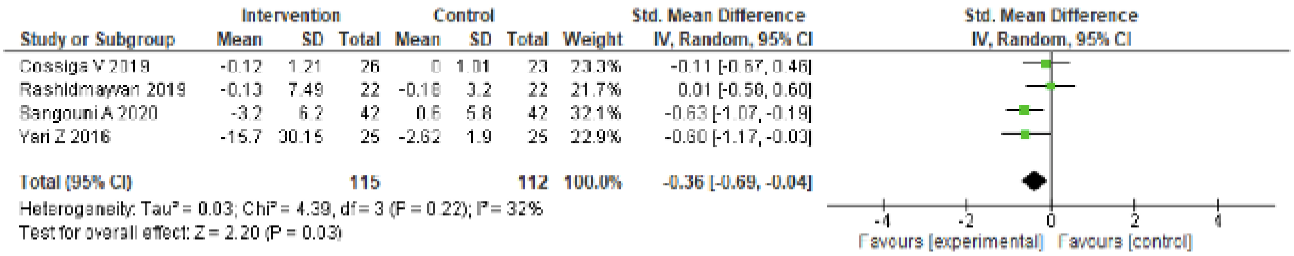
**Fig 4: Forest Plot Showing effect of intervention on changes in (A) AST (Aspartate Transaminase; (B) ALT (Alanine transaminase); (C) GGT (Gamma Glutamyl Transferase)**




A) Forest Plot showing effect of intervention on AST




B) Forest Plot showing effect of intervention on ALT




C) Forest Plot showing changes in GGT

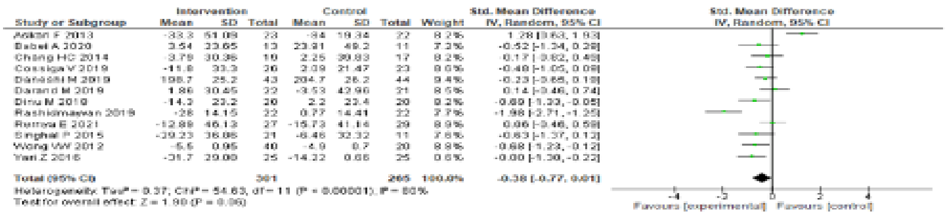
**Effect of intervention on glycemic profile**

13 research examined the impact on FBS. 641 participants were enrolled in these investigations, 339 of whom were in the intervention group and 302 were in the control group. Using random effects analysis, the combined data from these studies revealed a highly significant improvement in FBS levels (SMD: -0.34, 95% CI: -0.61, -0.07; Figure 6A). Seven studies including a total of 437 patients—220 in the intervention group and 217 in the control group—assessed the effectiveness of the HOMA-IR intervention. Again, levels of HOMA-IR significantly improved (SMD: -0.66, 95% CI: -1.57, 0.24; Figure 6B).

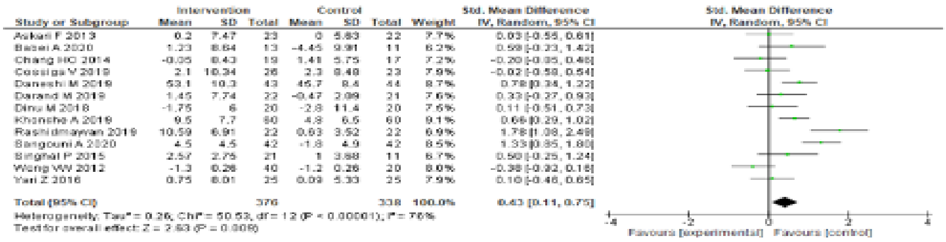
**Effect of intervention on BMI**

In 14 research, the influence on BMI was evaluated. 735 participants were enrolled in these investigations, 387 of whom were in the intervention group and 348 were in the control group. The combined results from these trials, when subjected to random effects analysis, show a significant reduction in BMI levels (SMD: -0.28, 95% CI: -0.51, -0.04; Figure 6C).

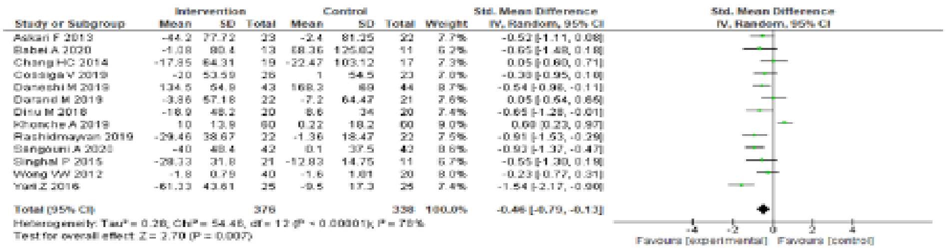
**Fig 5: Forest Plot Showing effect of intervention on changes in (A) Total Cholesterol; (B) HDL (High Density Lipoproteins); (C) Triglycerides; (D) LDL (Low Density Lipoproteins)**



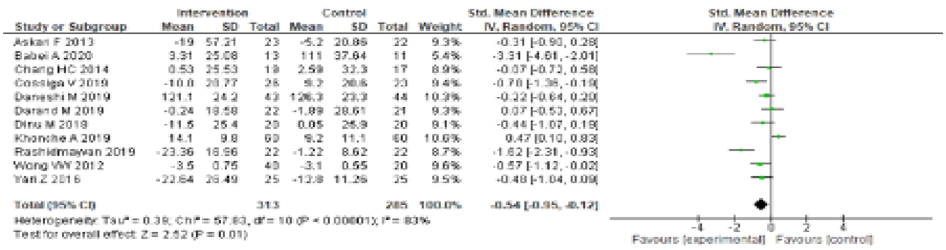

A) Forest Plot showing effect on Total Cholesterol




B) Forest Plot Showing changes in High Density Lipoproteins




C) Forest Plot showing changes in Triglycerides

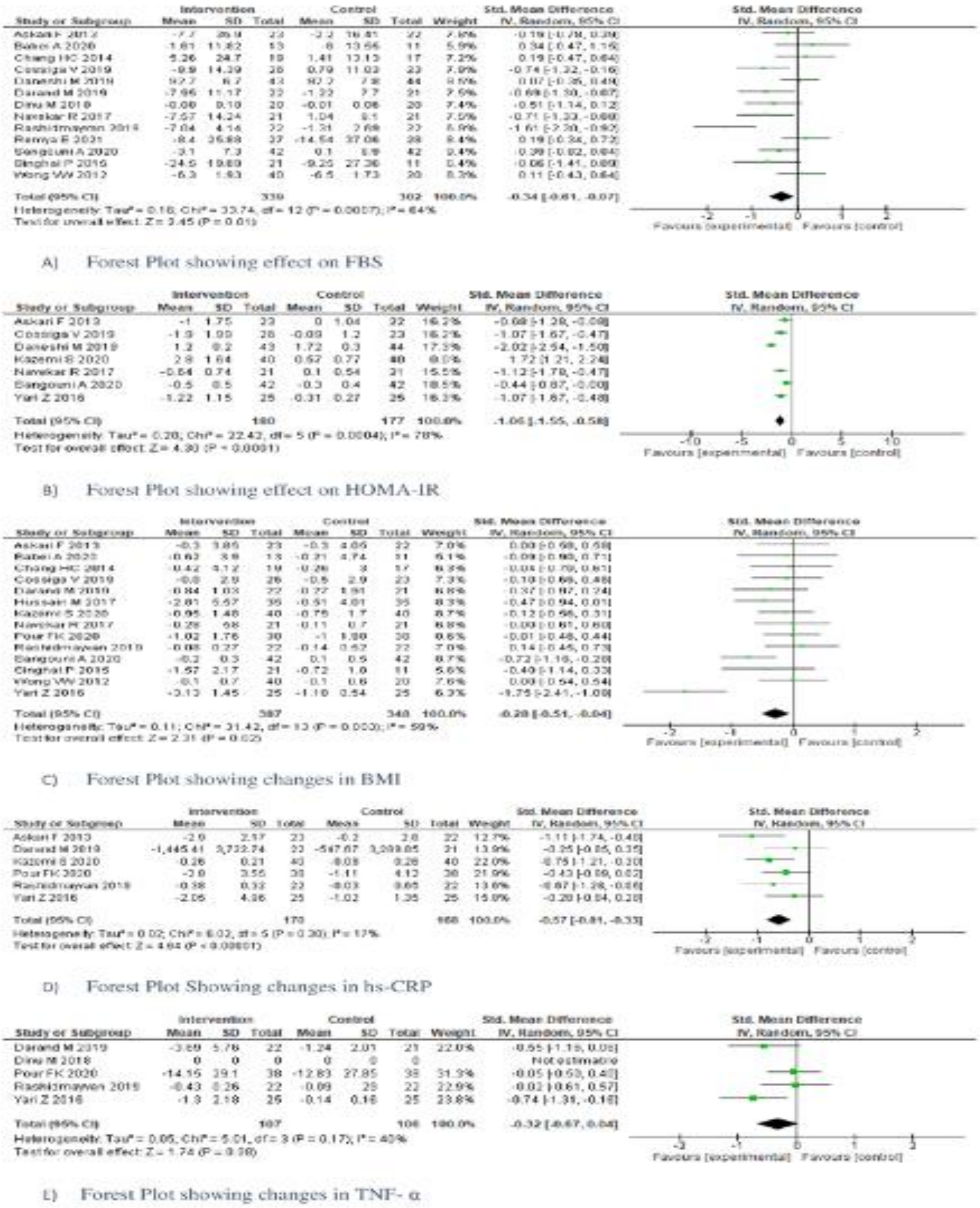



D) Forest Plot Showing changes in Low Density Lipoproteins

**Effect on inflammatory markers**

Six studies evaluated the impact on hs-CRP. 338 individuals were enrolled in these investigations, 170 of them were in the intervention group. Using random effects analysis, the combined data from these trials show a substantial decrease in hs-CRP levels (SMD: -0.57; 95% CI: -0.81, -0.33; Figure 6D). Five studies evaluated the impact on TNF-. 213 patients were involved in these research, 107 of whom were in the intervention group. TNF- levels have been significantly reduced in these studies' combined data utilizing random effects analysis (SMD: -0.32; 95% CI: -0.67, -0.04; Figure 6E).

**Fig 6: Forest Plot Showing effect of intervention on changes in (A) FBS (Fasting Blood Glucose); (B) HOMA-IR; (C) BMI; (D) hs-CRP; (E) TNF- α**



**Discussion**

For millennia, the Indian subcontinent has employed ayurvedic remedies. The foundational ideas for healthy living, a sound eating plan, and ideal seasonal behaviors are laid out in the Ayurvedic writings. Ancient Ayurvedic writings with a long history of safe and successful use contain the therapies that were examined in this systematic review. While some, like Phyllanthus and Arogyavardhini vati, are specifically employed as remedies, others, like Phyllanthus, are consumed as food. There is a dearth of studies focused on the efficacy of Ayurvedic multiingredient formulations and single herbs in treating NAFLD, despite the fact that many of these formulations and herbs are proven to benefit liver functioning. In this systematic review, RCTs involving therapies that are mentioned in Ayurvedic scriptures were identified and their effectiveness in treating NAFLD was assessed.

There were 18 such RCTs with 1097 participants. The studies were of good quality, and all but four of them adequately reported the RCT's methodological components. In contrast, the majority of trials explicitly described the blinding procedures, inclusion and exclusion criteria, and the percentage of dropouts. Only fourteen studies had the description of the randomization technique available. The other fourteen involved assessments over 12 weeks, while two investigations were carried out over 24 weeks and two over 8 weeks apiece. No negative medication responses were documented in any of the experiments. Although the research-based evidence is insufficient to prove AyM's involvement in the treatment of NAFLD, the outcomes have been encouraging. The results of this systematic review and meta-analysis showed that the interventions that are mentioned in Ayurvedic scriptures are helpful. In comparison to a placebo, these AyM were more effective with reducing AST and ALT levels and reversing the fatty liver alterations. The study's specific interventions, such as the cardamom, fenugreek, cinnamon, and garlic, are all staples of the Indian diet. However, there is a significant range in the epidemiology of NAFLD in the Indian subcontinent, ranging from 9 to 35% (1). This contradiction may be explained by the fact that, despite the fact that these interventions are considered dietary components, they are used in a non-standardized dose that is added to the deep-frying process, which likely cancels their beneficial effects on NAFLD.

The current analysis had a number of drawbacks. First, the studies' sample sizes were too tiny to reliably predict the results. Eight of the papers described sample size calculation. A sample size calculation entails figuring out the bare minimum of participants needed to make an estimation of a treatment effect that is clinically useful. A limited sample size may lower the standard of the study and cause statistical outliers when determining how effective an intervention is.

Not all studies conducted histological examinations to evaluate the effectiveness of treatments for NAFLD. The majority of research evaluated changes in the grading of the fatty liver based on ultrasonography and fibro scan, which is the primary outcome. Although AST and ALT levels dramatically decreased, alterations in liver enzymes cannot be used as the only indicator of treatment effectiveness in NAFLD (32). In clinical practice, there have been several situations where ultrasonography unintentionally revealed fatty liver alterations despite average AST and ALT readings.

The other three research included lifestyle changes and diet management; fifteen investigations were undertaken in comparison to placebo. For a more thorough analysis of the therapies' efficacy, the suggested medications of choice should be compared to them.

The role of AyM as an additional resource for controlling NAFLD should be examined by carrying out high-quality RCTs because there are few therapy alternatives for NAFLD. The results of such RCTs should concentrate on the hepato-protective effects of Ayurvedic medicines while also working to establish high-quality evidence of their efficacy and safety.

The pooled analysis of studies revealed significant heterogeneity (I2 = 66.30%). It can be explained by the fact that there were few research included in the analysis, though.(34) NAFLD is a hepatic indication of metabolic syndrome, and symptomatic patients should receive holistic care by include subjective assessment.

**Conclusion**

Since the beginning of time, traditional products have been used, and numerous of them have also been investigated for their efficacy in NAFLD. These have produced favorable results. According to the few information that is currently available, ayurvedic medicines have been effective in treating NAFLD. To be used as a therapeutic option for NAFLD, Ayurvedic medications need to be supported by more thorough research over an extended period of time. As a result, RCTs including traditional Ayurvedic medicines should be carried out strictly in accordance with CONSORT principles, with a bigger sample size and a focused methodology. The results of histological analysis should also be evaluated.

**Ethical Statement**

Since there are no human or animal studies involved in this investigation, the ethical statement is not applicable.

**Conflict of Interest**

Nil

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