



CLINICAL TRAIL

Randomized Clinical trial on the efficacy of KB yoga in Non Alcoholic Fatty Liver Disease

Vivek Palengara¹, Manojkumar N²

¹Professor, Department of Dravyagunavijnanam, VPSV Ayurveda College, Kottakkal, Malappuram, Kerala

²Professor and Head of the Department, Department of Dravyagunavijnanam, VPSV Ayurveda College, Kottakkal, Malappuram, Kerala

*Email: drvivekp@gmail.com

ARTICLE HISTORY

Received: 05 October 2025
Accepted: 08 December 2025
Available online
Version 1.0 : 31 December 2025

Keywords

Non-alcoholic fatty liver disease, Kirātatikta, Bhringarāja, Leucas aspera, randomized controlled trial

Additional information

Peer review: Publisher thanks Sectional Editor and the other anonymous reviewers for their contribution to the peer review of this work.

Reprints & permissions information is available at <https://keralajournalofayurveda.org/index.php/kja/open-access-policy>

Publisher's Note: All Kerala Govt. Ayurveda College Teacher's Association remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Copyright: © The Author(s). This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution and reproduction in any medium, provided the original author and source are credited (<https://creativecommons.org/licenses/by/4.0/>)

CITE THIS ARTICLE

Vivek P, Manojkumar N. Randomized Clinical trial on the efficacy of KB yoga in Non Alcoholic Fatty Liver Disease. Kerala Journal of Ayurveda. 2025;4(4):60-68. <https://doi.org/10.55718/kja.491>



Abstract

Background: Non-alcoholic fatty liver disease (NAFLD) is the most prevalent chronic liver disorder worldwide, strongly associated with obesity, metabolic syndrome, and type 2 diabetes. Conventional management is limited, and effective Ayurvedic interventions may provide cost-effective alternatives. Kirātatikta (*Andrographis paniculata* (Burm.f.) Nees) and Bhringarāja (*Eclipta prostrata* (L.) L) are traditionally prescribed in liver disorders, but clinical evidence in NAFLD is scarce.

Objective: To evaluate the efficacy of KB Yoga (combination of Kirātatikta and Bhringarāja) in comparison with Droṇapuṣpī (*Leucas aspera* (Willd.) Link)) in patients with NAFLD.

Methods: A randomized controlled clinical trial was conducted at VPSV Ayurveda College Hospital, Kottakkal. Participants aged 30–60 years with NAFLD, confirmed by elevated ALT/AST and ultrasound, were randomized to receive either KB Yoga tablets (450 mg) or Droṇapuṣpī tablets (500 mg) for the study period. Primary outcomes were changes in ALT and AST levels; secondary outcomes included gastrointestinal and constitutional symptom relief assessed by the Gastrointestinal Symptom Rating Scale. Statistical analysis was performed using Mann-Whitney U test and Wilcoxon signed-rank test.

Observations: A total of 106 participants were randomized (53 in each group). In the KB group, mean ALT decreased from 114.7 to 55.08 IU/L and AST from 73.34 to 44.06 IU/L ($p < 0.05$). Both enzymes also decreased significantly in the control group, but between-group comparisons favored KB (ALT: 55.08 ± 15.70 vs. 64.53 ± 24.02 , $p = 0.017$; AST: 44.06 ± 12.51 vs. 50.25 ± 17.48 , $p = 0.043$). Subjective symptom assessment showed significant within-group improvements in both arms, with slightly greater resolution of gastrointestinal complaints in the KB group.

Discussion and Conclusion: KB Yoga demonstrated superior hepatoprotective efficacy compared with Droṇapuṣpī in NAFLD, with significant reductions in ALT and AST and parallel improvement in gastrointestinal and constitutional symptoms. Its dual metabolic and anti-inflammatory mechanisms, alongside classical Ayurvedic indications, support its use as a cost-effective and readily available intervention for NAFLD. Further trials with imaging and biomarker endpoints are warranted.

Introduction

Fatty liver disease can be defined as the deposition of fat exceeding 5% of liver weight or affecting more than 30% of hepatocytes. It can arise either from excess fat entry into the liver (e.g., obesity, diabetes, hyperlipidaemia) or impaired metabolism due to liver injury (e.g., alcohol, toxins, drugs, malnutrition, or systemic illness).^{1,2} Morphologically, it is classified as macrovesicular fatty liver, characterized by large fat droplets displacing the nucleus, or microvesicular fatty liver, with tiny droplets accumulating within hepatocyte organelles. While macrovesicular change is commonly linked to alcoholism, obesity, and diabetes, microvesicular fatty change is seen in acute fatty liver of pregnancy, Reye's syndrome, and certain drug toxicities. The pathogenesis involves disturbances of lipid metabolism, i.e. increased fatty acid entry or synthesis, reduced oxidation, enhanced triglyceride esterification, or impaired lipoprotein export.²

Non-alcoholic fatty liver disease (NAFLD) has considered as the commonest chronic liver disorder, affecting about 25-30% of adults globally, and is strongly associated with metabolic syndrome, obesity, and type 2 diabetes. NAFLD begins as fatty liver (NAFL), which is generally benign, and steatohepatitis (NASH), a progressive form with inflammation, hepatocyte injury, and fibrosis that can advance to cirrhosis and hepatocellular carcinoma. Cardiovascular disease remains the leading cause of mortality in NAFLD, followed by cancer and liver failure. NASH patients with cirrhosis are at the highest risk, with up to 20% developing cirrhosis and a yearly 1-2% risk of HCC. The global prevalence of NAFLD is around 32%, higher in men, and projected to rise significantly by 2030, especially in the Americas and Southeast Asia.³⁻⁵

In India, NAFLD is increasingly finding as a health problem in clinical practice, with prevalence estimates ranging from 9% to 53%. The pooled prevalence is 38.6% among adults and 35.4% among children, with even lean individuals showing susceptibility due to higher abdominal adiposity, insulin resistance, and atherogenic dyslipidaemia characteristic of Indians.^{6,7} Urbanization, sedentary lifestyles, and dietary patterns further contribute to risk. Kerala shows a particularly high burden, with nearly 50% prevalence in adults well above the global average.⁸

Currently, no established management strategies exist for non-alcoholic fatty liver disease (NAFLD). Among the numerous herbal drugs mentioned in Ayurveda, a combination of *Kiratatikta* [*Andrographis paniculata* (Burm.f.) Nees] and *Bhringaraja* [*Eclipta prostrata* (L.) L] are widely prescribed by traditional physicians for liver disorders. Both drugs are well-documented in classical texts, either as single agents or in

formulations such as Sudarśanāsava, Sudarśanam guṭika, and Bhringarājāsava, and have shown clinical benefits.⁹⁻¹⁵ Despite their frequent use, particularly in combination, there is very limited documented scientific data validating their efficacy in liver pathologies especially in NAFLD. In contrast, efficacy of *Dronapushpi* [*Leucas aspera* (Willd.) Link]) has been reported clinically in NAFLD, but its seasonal availability and higher cost pose limitations for wider application.¹⁶ Kiratatikta and Bhringaraja, being readily available throughout the year and cost-effective, offer a practical alternative. However, while pharmacognostical and phytochemical parameters of each drug individually are known, similar data for their combination is lacking. Therefore, this study was undertaken to evaluate the clinical efficacy of the combination of Kiratatikta Bhringaraja (hereafter the term KB yoga will be used) against Dronapushpi in NAFLD. The study was a randomized controlled clinical trial conducted at OPD of VPSV Ayurveda College Hospital, Kottakkal. Its primary objective was to compare the efficacy of KB Yoga tablet and Dronapushpi tablet on elevated liver enzymes (AST and ALT), and secondary objectives were assessing the effect of KB Yoga on subjective symptoms.

Methodology

Recruitment of participants - NAFLD Participants, diagnosed as per the diagnostic criteria, attending the OPDs of VPSV Ayurveda College Hospital were selected sequentially as per the inclusion criteria and allocation concealment was done using a computer-generated sequence. Sample size was 53 in both the groups. Ethics committee approval was obtained on 07/07/2020, Proceedings No: IRB/CI/O3/20; dated 30-09-2020, Ref IRB/Doc/03/20 dated 07-07-2020 and also registered in CTRI (CTRI/2021/07/034920).

Diagnostic Criteria - NAFLD was diagnosed based on elevated ALT and AST levels in liver function tests, as per the World Gastroenterology Organisation global guidelines, together with liver ultrasound confirmation NAFLD, which was done within six months prior to recruitment.

Inclusion Criteria and exclusion criteria - Participants were included if they were diagnosed with fatty liver disease, presented with mild to moderate elevation of ALT and AST levels (less than five times the upper limit), had ALT higher than AST levels, were between age 30 and 60 years irrespective of gender, and had provided informed consent. Those with uncontrolled hypertension or diabetes mellitus, diagnosed with viral hepatitis, Wilson's disease, drug-induced fatty liver, or had liver cirrhosis or were undergoing Ayurvedic treatment for other conditions with a history of ischemic heart disease, stroke, cancer treatment, insulin therapy, pregnancy, lactation, or prolonged bed rest were excluded.

Preparation of the drug - The test drug (KB Yoga) was prepared by mixing equal parts of *Kiratatikta* [*Andrographis paniculata* (Burm.f.) Nees] and *Bhringaraja* [*Eclipta prostrata* (L.) L], boiled with 16 times water, reduced to 1/8th, filtered to obtain the decoction, and then processed into 450 mg tablets by a GMP-certified company after quality testing.¹⁷ The control drug, Dronapushpi [*Leucas aspera* (Willd.) Link] was prepared by powdering and sieving the plant material, followed by repeated bhāvana with its fresh swarasa as per Sārṅgadhara Samhitā, dried, powdered, and converted into 500 mg tablets, also manufactured by a GMP-certified company.¹⁸ The dose of the trial drug was fixed by calculating the total soluble particles in the Kashaya of KB yoga (98 ml) and that of the control from the previous study.¹⁶ by The details of intervention is shown in the table number 1.

Table no. 1 - Details of intervention given

Particulars	Group A (Test Drug)	Group B (Control Drug)
Sample Size	53	53
Drug	KB Yoga tablet	<i>Dronapushpi</i> tablet
Dose	450 mg (2 tablets twice daily)	500 mg (1 tablet twice daily)
Route of Administration	Oral	Oral
Time of administration	Morning and night 1hour before breakfast and dinner	Morning and night 1hour before breakfast and dinner
Anupana	Luke warm water (boiled and cooled)	Luke warm water (boiled and cooled)
Duration	45 days	45 days

Table no. 2: Comparison of effect of Alanine transaminase and Aspartate transaminase values before and after in trial group

Variables	Mean	Median (IQR)	SD	Wilcoxon Signed Rank Value	P Value
ALT BT	114.7	100 (81.5-141)	39.64	-6.275	<0.001
ALT AT	55.08	51 (44-63)	15.69		
AST BT	73.34	64 (58-77.5)	26.02	-6.327	<0.001
AST AT	44.06	41 (35-47)	12.51		

Table no.3: Comparison of Alanine transaminase and aspartate transaminase values before and after comparison of treatment in control group

Variables	Mean	Median (IQR)	Sd	Wilcoxon Signed Rank Value	P Value
ALT BT	106.85	99(84-120.5)	34.98	-6.335	<0.001
ALT AT	64.53	59(48.5-78.5)	24.018		
AST BT	72.7	64(55.5-77.5)	29.882	-5.928	<0.001
AST AT	50.25	45(39-57)	17.482		

Table no. 4: ALT and AST - Mean comparison of after treatment values between the groups

Variable	Trial			Control			Mann Whitney U Test	P Value
	Mean	Median	SD	Mean	Median	SD		
ALT(AT)	55.08	15.698	51	64.53	24.018	59	1026.5	0.017
AST(AT)	44.06	12.509	41	50.25	17.482	45	1084.5	0.043

The trial adhered to an intention-to-treat analysis, with the first review results carried forward for dropouts. Biochemical parameters, ALT, and AST were evaluated before and after treatment. Subjective parameters i.e. fatigue, nausea, acid regurgitation, vomiting, abdominal pain, eructation, heartburn, abdominal heaviness, abdominal distension, increased flatus and altered bowel habits such as increased or decreased passage of stool, loose stools, urgent need for defecation, and anorexia were assessed by using Gastrointestinal Symptom Rating Scale¹⁹. Since both objective and subjective parameters were not following normality, Mann-Whitney U test was carried out for between group comparison and with in group by Wilcoxon Signed rank test. There were no follow-up assessments.

Observations

A marked and statistically significant reduction were observed in serum liver enzymes following treatment. ALT decreased from a baseline mean of 114.7 IU/L to 55.08 IU/L ($p < 0.05$), and AST from 73.34 IU/L to 44.06 IU/L ($p < 0.05$) in trial group as shown in the table number 2. In control group also, statistically significant reduction of ALT and AST can be visible (Table no.3).

Post-treatment analysis indicating that the trial group showed significantly greater improvement than control group in key liver function parameters. ALT and AST values were reduced in the trial group (ALT: 55.08 $\pm$ 15.70 vs. 64.53 $\pm$ 24.02, $p = 0.017$; AST: 44.06 $\pm$ 12.51 vs. 50.25 $\pm$ 17.48, $p = 0.043$), indicating better hepatic enzyme normalization (table no. 4)

Subjective symptom assessment showed significant improvement in all recorded gastrointestinal complaints (table no. 5).¹⁹ Fatigue, nausea, acid regurgitation, vomiting, abdominal pain, eructation, heartburn, abdominal heaviness, abdominal distension, increased flatus, altered bowel frequency, loose stools, urgency for defecation, and anorexia all showed significant reductions in median symptom scores ($p < 0.01$ for all variables). The largest median reductions were observed in abdominal heaviness, acid regurgitation, loose stools, and urgency of defecation, which often resolved completely post-treatment. Overall, the trial drug produced significant biochemical and clinical improvements within the group, with the most pronounced effects seen in hepatic enzyme normalization, lipid profile optimization, and symptom resolution.

In control group also, there were notable improvements in most recorded gastrointestinal and systemic complaints (table no.6). Fatigue, nausea, acid regurgitation, abdominal pain, eructation, heartburn, abdominal heaviness,

abdominal distension, increased flatus, altered bowel habits (both increased and decreased passage of stools), loose stools, urgency of defecation, and anorexia all revealed statistically meaningful reductions in symptom scores ($p < 0.05$ for all).

For subjective symptom scores, both groups reported marked improvement, with most gastrointestinal and constitutional complaints approaching minimal or zero scores (table no. 7). No statistically significant differences were shown between groups for fatigue, nausea, acid regurgitation, abdominal pain, eructation, heartburn, abdominal heaviness, abdominal distension, increased or decreased passage of stools, or urgency of defecation ($p > 0.05$ for all). Vomiting scores were zero in both groups post-treatment as there were no one presented with the complaint of this symptom. A significant difference was seen for loose stools, with the control group showing a slightly higher mean score (0.08 ± 0.27) compared to zero in the trial group ($p = 0.042$). Anorexia showed a trend of improvement in the trial group but statistically insignificant ($p = 0.08$).

Table no. 5: Subjective parameters - Before and after treatment comparison in trial group

Symptoms	SD	Median (IQR)	Wilcoxon Sign Rank Value	p Value
Fatigue (BT)	0.89	0.0(0.0-1.0)	-4.244	<0.001
Fatigue (AT)	0.32	0.0(0.0-0.0)		
Nausea (BT)	0.745	0.0(0.0-1.0)	-4.4	<0.001
Nausea (AT)	0.295	0.0(0.0-1.0)		
Acid regurgitation (BT)	0.958	1.0(0.0-2.0)	-5.427	<0.001
Acid regurgitation (AT)	0.503	0.0(0.0-1.0)		
Vomiting (BT)	0.495	0.0(0.0-1.0)	-3.638	<0.001
Vomiting (AT)	0.00	0.0(0.0-0.0)		
Abdominal pain (BT)	1.013	2.0(0.0-2.0)	-4.916	<0.001
Abdominal pain (AT)	0.434	0.0(0.0-0.5)		
Eructation (BT)	1.028	1.0(0.0-2.0)	-4.817	<0.001
Eructation (AT)	0.409	0.0(0.0-0.0)		
Heart burn (BT)	0.854	1.0(0.0-2.0)	-5.224	<0.001
Heart burn (AT)	0.342	0.0(0.0-0.0)		
Abdominal Heaviness (BT)	0.695	2.0(1.0-2.0)	-6.33	<0.001
Abdominal Heaviness (AT)	0.503	0.0(0.0-1.0)		
Abdominal Distension (BT)	0.875	0.0(0.0-2.0)	-4.523	<0.001
Abdominal Distension (AT)	0.295	0.0(0.0-0.0)		
Increased flatus (BT)	0.781	1.0(0.0-2.0)	-5.445	<0.001
Increased flatus (AT)	0.295	0.0(0.0-0.0)		
Increased passage of stools (BT)	0.723	0.0(0.0-1.0)	-4.001	<0.001
Increased passage of stools (AT)	0.267	0.0(0.0-0.0)		
Decreased passage of stools (BT)	0.495	0.0(0.0-0.0)	-2.714	0.007
Decreased passage of stools (AT)	0.192	0.0(0.0-0.0)		
Loose stool (BT)	0.696	1.0(0.0-1.0)	-5.069	<0.001
Loose stool (AT)	0.0	0.0(0.0-0.0)		
Urgent need of defaecation (BT)	0.607	0.0(0.0-1.0)	-4.413	<0.001
Urgent need of defaecation (AT)	0.137	0.0(0.0-0.0)		
Anorexia (BT)	0.657	0.0(0.0-1.0)	-3.542	<0.001
Anorexia (AT)	0.0	0.0(0.0-0.0)		

Table no.6: Subjective parameters - Comparison of before and after treatment in control group

Symptoms	SD	Median (IQR)	Wilcoxon Sign Rank Value	p Value
Fatigue(BT)	0.927	0.00(0.00-2)	-4.54	<0.001
Fatigue(AT)	0.361	0.0(0.0-0.0)		
Nausea(BT)	0.894	0.00(0.00-1.5)	-4.284	<0.001
Nausea(AT)	0.342	0.0(0.0-0.0)		
Acid regurgitation(BT)	0.807	2.0(1.0-2.0)	-5.929	<0.001
Acid regurgitation(AT)	0.51	0.0(0.0-1.0)		
Vomitting(BT)	0.354	0.0(0.0-0.0)	-1.89	0.06
Vomitting(AT)	0	0.0(0.0-0.0)		
Abdominal pain(BT)	0.993	2.0(0.0-2.0)	-4.875	<0.001
Abdominal pain(AT)	0.542	0.0(0.0-0.0)		
Eructation(BT)	0.778	1.0(1.0-2.0)	-5.719	<0.001
Eructation(AT)	0.466	0.0(0.0-0.0)		
Heart burn(BT)	0.818	1.0(0.0-2.0)	-5.058	<0.001
Heart burn(AT)	0.454	0.0(0.0-0.0)		
Abdominal Heaviness(BT)	0.77	2.0(1.0-2.0)	-5.937	<0.001
Abdominal Heaviness(AT)	0.541	0.0(0.0-1.0)		
Abdominal Distension(BT)	0.913	1.0(0.0-2.0)	-4.71	<0.001
Abdominal Distension(AT)	0.395	0.0(0.0-0.0)		
Increased flatus(BT)	0.772	1.0(0.0-2.0)	-5.436	<0.001
Increased flatus(AT)	0.354	0.0(0.0-0.0)		
Increased passage of stools(BT)	0.593	0.0(0.0-0.0)	-2.887	0.004
Increased passage of stools(AT)	0.267	0.0(0.0-0.0)		
Decreased passage of stools(BT)	0.521	0.0(0.0-0.0)	-2.53	0.011
Decreased passage of stools(AT)	0.192	0.0(0.0-0.0)		
Loose stool (BT)	0.74	0.0(0.0-1.0)	-4.564	<0.001
Loose stool (AT)	0.267	0.0(0.0-0.0)		
Urgent need of defaecation (BT)	0.602	0.0(0.0-1.0)	-4.066	<0.001
Urgent need of defaecation (AT)	0.192	0.0(0.0-0.0)		
Anorexia (BT)	0.723	0.0(0.0-1.0)	-4.134	<0.001
Anorexia (AT)	0.233	0.0(0.0-0.0)		

Table no.7: Subjective parameters - Mean comparison of after treatment values of between the groups

Variable	Trial			Control			Mann Whitney U Test	P Value
	Mean	Median	SD	Mean	Median	SD		
Fatigue(AT)	0.11	0.0(0.0-0.0)	0.32	0.15	0.0(0.0-0.0)	0.361	1351.5	0.568
Nausea(AT)	0.09	0.0(0.0-0.0)	0.295	0.13	0.0(0.0-0.0)	0.342	1351.5	0.542
Acid regurgitation (AT)	0.3	0.0(0.0-1.0)	0.503	0.32	0.0(0.0-1.0)	0.51	1378.5	0.835
Vomitting(AT)	0	0.0(0.0-0.0)	0	0	0.0(0.0-0.0)	0	1404.5	1
Abdominal pain(AT)	0.25	0.0(0.0-0.5)	0.434	0.23	0.0(0.0-0.0)	0.542	1318	0.438
Eructation(AT)	0.21	0.0(0.0-0.0)	0.409	0.23	0.0(0.0-0.0)	0.466	1399	0.961
Heart burn(AT)	0.13	0.0(0.0-0.0)	0.342	0.21	0.0(0.0-0.0)	0.454	1321.5	0.41
Abdominal Heaviness(AT)	0.45	0.0(0.0-1.0)	0.503	0.47	0.0(0.0-1.0)	0.541	1392.5	0.93
Abdominal Distension(AT)	0.09	0.0(0.0-0.0)	0.295	0.19	0.0(0.0-0.0)	0.395	1272	0.166
Increased flatus(AT)	0.09	0.0(0.0-0.0)	0.295	0.09	0.0(0.0-0.0)	0.354	1380.5	0.754
Increased passage of stools (AT)	0.08	0.0(0.0-0.0)	0.267	0.08	0.0(0.0-0.0)	0.267	1404.5	1
Decreased passage of stools (AT)	0.04	0.0(0.0-0.0)	0.192	0.04	0.0(0.0-0.0)	0.192	1404.5	1
Loose stool (AT)	0	0.0(0.0-0.0)	0	0.08	0.0(0.0-0.0)	0.267	1298.5	0.042
Urgent need of defaecation (AT)	0.02	0.0(0.0-0.0)	0.137	0.04	0.0(0.0-0.0)	0.192	1378	0.56
Anorexia (AT)	0	0.0(0.0-0.0)	0	0.06	0.0(0.0-0.0)	0.233	1325	0.08

Discussion

In this trial, the KB formulation produced a large and clinically meaningful fall in transaminases, with mean ALT decreasing from ~114.7 to 55.08 IU/L and AST from ~73.34 to 44.06 IU/L. These changes are substantial, representing a roughly 50% fall in mean ALT along with important reductions in AST, which is indicating an intervention that reduces hepatocellular inflammation and the systemic drivers of hepatic steatosis.

The reductions in ALT and AST observed in the present trial may be mechanistically explained by complementary actions of *Andrographis paniculata* and *Eclipta prostrata*. Reduced hepatic lipid influx and de novo lipogenesis may be the plausible contributors: andrographolide, the major constituent of *A. paniculata*, has been reported to suppress fatty-acid uptake (FATP2) and lipogenic transcription factors, thereby lowering intrahepatic fat accumulation and limiting lipotoxic stress on hepatocytes.²⁰ In parallel, bioactive coumestans from *E. prostrata*, particularly wedelolactone, have been reported to activate AMPK and up-regulate PPAR α /LPL/LDLR pathways, promoting fatty-acid oxidation and lipid clearance.²¹ Taken together, these metabolic effects may align with the combined improvements in transaminases and lipid parameters documented in this study.²²

Anti-inflammatory mechanisms may also be relevant. Andrographolide has been reported to attenuate NF- κ B signalling and NLRP3 inflammasome activity, reducing pro-inflammatory cytokines and thereby protecting hepatocytes from further injury.²³ Wedelolactone exerts similar inhibitory effects on NF- κ B and downstream mediators such as iNOS, COX-2, and TNF- α , which could synergistically reduce hepatic inflammation and necrosis.²⁴ These overlapping anti-inflammatory actions therefore offer a coherent mechanistic explanation for the observed biochemical improvements.

The antioxidant and cytoprotective properties of both plants in KB likely contribute to the observed biochemical improvements. Flavonoids, coumestans and triterpenes restore hepatic antioxidant enzymes (SOD, GPx, catalase), decrease lipid peroxidation and stabilise hepatocyte membranes. Preclinical studies also show antifibrotic activity of andrographolide and *Eclipta* extracts via modulation of stellate-cell activation and fibrogenic signalling, suggesting potential to slow progression from steatosis to fibrosis.^{25,26} These mechanisms align with symptom improvements noted in the trial, including reductions in fatigue, malaise, abdominal heaviness and post-prandial fullness, likely mediated by lower systemic inflammation, improved hepatic lipid/bile handling and reduced hepatic-driven dysbiosis.

The literature consistently demonstrates hepatoprotective, anti-inflammatory, antioxidant and metabolic-regulating effects for *A. paniculata* and *E. prostrata*, though confirmation of causal pathways will require biomarker-based studies incorporating lipidomic, cytokine, inflammasome and microbiome profiling.²⁷

Leucas aspera contains flavonoids, diterpenes, triterpenes and phenolics with reproducible antioxidant, anti-inflammatory, prostaglandin-modulatory and antimicrobial actions that explain hepatoprotective and gastrointestinal benefits. Preclinical models show enhanced antioxidant defenses, reduced lipid peroxidation and attenuation of necrosis, along with prostaglandin antagonism and mucosal protection that improve abdominal pain, nausea, reflux and bloating. These actions provide a coherent rationale for modest ALT/AST reductions and symptomatic relief, though direct NAFLD-specific metabolic effects remain unestablished.²⁸⁻³⁰

In contrast, KB offers a stronger mechanistic basis for the larger transaminase declines observed (ALT $\approx$ 114.7 $\rightarrow$ 55.1 IU/L; AST $\approx$ 73.3 $\rightarrow$ 44.1 IU/L). Andrographolide inhibits fatty-acid uptake and lipogenesis (FATP2, lipogenic transcription factors) and suppresses NF- κ B/NLRP3-mediated inflammation, while wedelolactone activates AMPK and PPAR α /LPL/LDLR pathways, enhancing fatty-acid oxidation and exerting potent anti-inflammatory and antifibrotic effects. Together, these multimodal actions reduce hepatic fat influx, increase fat disposal, diminish necroinflammatory injury and restore antioxidant capacity-mechanistically aligning with the magnitude of biochemical and symptomatic improvement seen in the trial. By contrast, the published pharmacology of *Leucas aspera* emphasises antioxidant, antimicrobial, prostaglandin-modulatory and gastroprotective effects that plausibly reduce hepatocyte oxidative injury and improve dyspeptic/visceral symptoms, but it lacks direct, modern NAFLD-specific evidence for interventions on hepatic lipid handling, AMPK activation, PPAR α upregulation, or inflammasome modulation at the level and breadth demonstrated for KB; the principal *L. aspera* data therefore better explain symptomatic and hepatoprotective effects via membrane stabilization, reduction of lipid peroxidation and mucosal protection rather than a coordinated metabolic programme that lowers hepatic steatosis.³¹⁻⁴¹ In short, KB's multimodal, complementary targeting of both the metabolic drivers (lipid uptake and lipogenesis) and the inflammatory/oxidative injury pathways central to NAFLD gives it a stronger mechanistic expectation of superior between-group biochemical efficacy (ALT/AST and lipid endpoints) and secondary symptomatic benefit compared with dronapushpi, whereas *L. aspera* provides a plausible but narrower hepatoprotective and symptom-modifying profile.

Kiratatikta, described with *Tikta rasa*, *Laghu-Ruksha guna*, *Sheeta veerya* and *Katu vipaka*, is classically indicated as *jvaraghna*, *kapha-pittahara*, *yakrituttejaka* and *raktashodhaka*.⁴² These attributes support *Deepana-pachana* and *ama-pachana* actions, correcting *jatharagni* and reducing meda-related metabolic residues that correspond to lowered hepatic lipid influx and improved fat metabolism. *Bhringaraja* (*Eclipta prostrata*), described with *Katu-Tikta rasa*, *Laghu-Ruksha guna*, *Uṣṇa veerya* and *Katu vipaka*, is classically indicated as a *yakrit-hara* and *rasayana* drug.⁴³⁻⁴⁵ Its *srotoshodhana* of *rasavaha* and *medovaha srotas* plausibly corresponds to lipid clearance, and its *kapha-hara* and *medo-lekhana* effects reduce meda-accumulation in the liver, aligning with modern evidence of wedelolactone-mediated AMPK/PPAR α activation and improved fatty-acid oxidation.⁴⁶

In addition, both drugs contribute *raktashodhaka*, *śoṭha-hara* and *rasayana* effects that help reduce inflammatory load, stabilise hepatocytes and support *dhatu-balya*. This Ayurvedic reasoning parallels experimental findings of NF- κ B and inflammasome inhibition by andrographolide-like bitter principles and wedelolactone, reduction in oxidative stress through restoration of SOD, catalase and glutathione peroxidase, and anti-fibrotic modulation of stellate-cell activity.⁴⁷ Thus, the *tikta-katu rasa*, *laghu-ruksha guna* and combined *sheeta-uṣṇa veerya* of KB yoga provide synergistic *kapha-pittahara*, *medo-lekhana* and *yakrit-hara* actions that offer a coherent Ayurvedic explanation for the biochemical and symptomatic benefits seen in this trial. While these mechanisms are supported by classical descriptions and modern pharmacology, confirmation of causality will require future biomarker and imaging studies.

Conclusion

The clinical and mechanistic literature on *Andrographis paniculata* and *Eclipta prostrata* provides a coherent biological explanation for the substantial ALT/AST and lipid improvements observed with KB, acting through complementary metabolic, inflammatory, and antioxidant pathways. These effects plausibly explain the parallel symptomatic improvements. Compared with *dronapushpi*, KB is mechanistically stronger for NAFLD-relevant pathways, though rigorous adjusted analyses, replication, and imaging correlation are required before confirming superiority.

Limitations include reliance on transaminases, which are imperfect surrogates, and the lack of imaging or histology in this trial. Future research should incorporate MRI-PDFF, fibrosis biomarkers, longer-term follow-up, dose-response studies, and head-to-head preclinical comparisons with *Leucas aspera*.

Practical reporting recommendations include presenting within-group mean changes with confidence intervals, between-group adjusted differences, responder analyses, adverse event tables, and, where possible, exploratory mediation analyses linking lipid changes to transaminase declines.

References

1. Harsh Mohan. Textbook of pathology. 4th ed. New Delhi: Jaypee Brothers, 2000.
2. Robert S. Porter, Justin L. Kaplan. Editors. The Merck Manual of Diagnosis and Therapy. 19th Ed. Whitehouse Station, NJ. Merck Sharp & Dohme Corp. 2011
3. Younossi ZM, Koenig AB, Abdelatif D, Fazel Y, Henry L, Wymer M: Global epidemiology of nonalcoholic fatty liver disease-meta-analytic assessment of prevalence, incidence, and outcomes. Hepatology 2016; 64: pp. 73-84.
4. Younossi Z, Anstee QM, Marietti M, Hardy T, Henry L, Eslam M, George J, Bugianesi E. Global burden of NAFLD and NASH: trends, predictions, risk factors and prevention. Nature reviews Gastroenterology & hepatology. 2018 Jan;15(1):11-20.
5. Paik JM, Golabi P, Younossi Y, Mishra A, Younossi ZM: Changes in the global burden of chronic liver diseases from 2012 to 2017: the growing impact of NAFLD. Hepatology 2020; 72: pp. 1605-1616.
6. Duseja A, Singh SP, De A, Madan K, Rao PN, Shukla A, Choudhuri G, Saigal S, Arora A, Anand AC, Das A. Indian national association for study of the liver (INASL) guidance paper on nomenclature, diagnosis and treatment of nonalcoholic fatty liver disease (NAFLD). Journal of clinical and experimental hepatology. 2023 Mar 1;13(2):273-302.
7. Elhence A, Bansal B, Gupta H, Anand A, Singh TP, Goel A. Prevalence of non-alcoholic fatty liver disease in India: a systematic review and meta-analysis. Journal of Clinical and Experimental Hepatology. 2022 May 1;12(3):818-29.
8. Chalmers J, Ban L, Leena KB, Edwards KL, Grove JL, Aithal GP, Shenoy KT. Cohort profile: the Trivandrum non-alcoholic fatty liver disease (NAFLD) cohort. BMJ open. 2019 May 1;9(5):e027244.
9. Neeraj Tandon. Quality Standards of Indian Medicinal Plants. Medicinal Plants Unit, Indian Council of Medical Research. 2011; Vol. 9: 139, 141.
10. Sharma PC., Yelne MB., Dennis TJ. Database on Medicinal Plants Used in Ayurveda. Central Council of Research in Ayurveda & Siddha, Dept. of ISM & H. Min. of Health and Family Welfare, Govt. of India. 2005: 112, 113.
11. Sharma P. C., Yelne M. B., Dennis T.J. Database on Medicinal Plants Used in Ayurveda. Central Council of Research in Ayurveda & Siddha, Dept. of ISM & H Min. of Health and Family Welfare, Govt. of India. 2012:115.
12. Neeraj Tandon, Madhu Sharma. Quality standards of Indian Medicinal Plants. Medicinal plants Unit, Indian Council of Medical Research. 2010;8:55, 61
13. Gupta A. K. Tandon Neeraj. Reviews on Indian Medicinal Plants, Indian Council of Medical Research. 2004;2(30):285.

14. Shukla B, Visen PK, Patnaik GK, Dhawan BN. Choleretic effect of andrographolide in rats and guinea pigs. *Planta medica*. 1992 Apr;58(02):146-9.
15. Zheng ZY. Pharmacokinetic studies on 3H-andrographolide. *Chinese Herbal Med*. 1982;13:33-36.
16. Paul Thomas. Clinical evaluation of Dronapushpi [*Leucas aspera* (Willd.) Link. Link] in Non Alcoholic Fatty Liver Disease (MD dissertation). Thrissur: Kerala University of Health Sciences;2016.
17. Sargdhara. Sargdharasamhitha, Madhyamakhandha. English translation by K.K.Srikantha Murthy; Choukhambha Orientalia. 6th edition. 2006;2/1 – 3:56.
18. Sargdhara. Sargdharasamhitha, Madhyamakhandha. English translation by K.K.Srikantha Murthy; Choukhambha Orientalia. 6th edition. 2006;1/2:52.
19. Svedlund J, Sjödin I, Dotevall G. GSRS-a clinical rating scale for gastrointestinal symptoms in patients with irritable bowel syndrome and peptic ulcer disease. *Dig Dis Sci* (Digestive Diseases and Sciences). 1988;33(1); 129-134.
20. Ran LS, Wu YZ, Gan YW, Wang HL, Wu LJ, Zheng CM, Ming Y, Xiong R, Li YL, Lei SH, Wang X. Andrographolide ameliorates hepatic steatosis by suppressing FATP2-mediated fatty acid uptake in mice with nonalcoholic fatty liver disease. *Journal of Natural Medicines*. 2023 Jan;77(1):73-86.
21. Zhao Y, Peng L, Yang LC, Xu XD, Li WJ, Luo XM, Jin X. Wedelolactone regulates lipid metabolism and improves hepatic steatosis partly by AMPK activation and up-regulation of expression of PPAR α /LPL and LDLR. *PLoS One*. 2015 Jul 13;10(7):e0132720.
22. Hussein NS, Helmy AS, Sherif NM, Ghanem HZ, Ibrahim NA, El Gendy ANG, Abdel-Hamid AZ. Lipidomic analysis reveals the efficiency of *Eclipta prostrata* on diet-induced nonalcoholic fatty liver disease in rats. *J Pharm Biomed Anal*. 2019;165:224–232. doi:10.1016/j.jpba.2018.11.060.
23. Cabrera D, Wree A, Povero D, Solís N, Hernandez A, Pizarro M, Moshage H, Torres J, Feldstein AE, Cabello-Verrugio C, Brandan E. Andrographolide ameliorates inflammation and fibrogenesis and attenuates inflammasome activation in experimental non-alcoholic steatohepatitis. *Scientific reports*. 2017 Jun 14;7(1):3491.
24. Sun W, Yue J, Cui Y, Feng J, He Q, Liang J, You W, Shi H, Sun W, Yi Q. Wedelolactone alleviates inflammation and cartilage degeneration by suppressing the NF- κ B signaling pathway in osteoarthritis. *Int Immunopharmacol*. 2024 Dec 25;143(Pt 1):113359. doi: 10.1016/j.intimp.2024.113359. Epub 2024 Oct 10. PMID: 39388895.
25. Wang W, Chen K, Xia Y, Mo W, Wang F, Dai W, Niu P. The Hepatoprotection by Oleanolic Acid Preconditioning: Focusing on PPAR α Activation. *PPAR Res*. 2018 Apr 2;2018:3180396. doi: 10.1155/2018/3180396. PMID: 29805439; PMCID: PMC5901823..
26. Sophia E. Exploring the Molecular Mechanisms of Andrographolide in Liver Regeneration and Hepatic Fibrosis Prevention. *International Journal of Research in Pharmaceutical Sciences*. March 2025.
27. Shang YX, Shen C, Stub T, Zhu SJ, Qiao SY, Li YQ, Wang RT, Li J, Liu JP. Adverse effects of andrographolide derivative medications compared to the safe use of herbal preparations of *Andrographis paniculata*: results of a systematic review and meta-analysis of clinical studies. *Frontiers in pharmacology*. 2022 Jan 28;13:773282.
28. Prajapati MS, Patel JB, Modi K, Shah MB. *Leucas aspera*: A review. *Pharmacogn Rev*. 2010 Jan;4(7):85–7. doi: 10.4103/0973-7847.65330.
29. Banu S, Bhaskar B, Balasekar P. Hepatoprotective and antioxidant activity of *Leucas aspera* against D-galactosamine induced liver damage in rats. *Pharm Biol*. 2012 Dec;50(12):1592–1595. doi: 10.3109/13880209.2012.685130.
30. Hossan AN, Zaman F, Barman MR, Khatoon S, Zaman M, Khatun F, Mosaib T, Mostafa F, Sintaha M, Jamal F, Rahmatullah M. Antinociceptive activity of *Xanthium indicum* J. Koenig ex Roxb. (Asteraceae) leaves and *Leucas aspera* (Willd.) Link (Lamiaceae) whole plants. *Advances in Natural and Applied Sciences*. 2011 Apr 1;5(2):214-7.
31. Ran LS, Wu YZ, Gan YW, Wang HL, Wu LJ, Zheng CM, Ming Y, Xiong R, Li YL, Lei SH, Wang X. Andrographolide ameliorates hepatic steatosis by suppressing FATP2-mediated fatty acid uptake in mice with nonalcoholic fatty liver disease. *Journal of Natural Medicines*. 2023 Jan;77(1):73-86.
32. Cabrera D, Wree A, Povero D, Solís N, Hernandez A, Pizarro M, Moshage H, Torres J, Feldstein AE, Cabello-Verrugio C, Brandan E. Andrographolide ameliorates inflammation and fibrogenesis and attenuates inflammasome activation in experimental non-alcoholic steatohepatitis. *Scientific reports*. 2017 Jun 14;7(1):3491.
33. Sunil Kumar K, Ratha K, Jaiswal S, Rao MM, Acharya R. Exploring the potential of *Andrographis paniculata* and its bioactive compounds in the management of liver diseases: A comprehensive food chemistry perspective. *Food Chem Adv*. 2024;4:100674. doi:10.1016/j.focha.2024.100674.
34. Zhao Y, Peng L, Yang LC, Xu XD, Li WJ, Luo XM, Jin X. Wedelolactone regulates lipid metabolism and improves hepatic steatosis partly by AMPK activation and up-regulation of expression of PPAR α /LPL and LDLR. *PLoS One*. 2015 Jul 13;10(7):e0132720.
35. Satheesh Naik K, Gurushanthaiah M, Kavimani M, Prabhu K, Lokanadham S. Hepatoprotective role of *Eclipta alba* against high fatty diet treated experimental models—A histopathological study. *Maedica (Buchar)*. 2018;13(3):217–222. doi:10.26574/maedica.2018.13.3.217.
36. Hussein NS, Helmy AS, Sherif NM, Ghanem HZ, Ibrahim NA, El Gendy ANG, Abdel-Hamid AZ. Lipidomic analysis reveals the efficiency of *Eclipta prostrata* on diet-induced nonalcoholic fatty liver disease in rats. *J Pharm Biomed Anal*. 2019;165:224–232. doi:10.1016/j.jpba.2018.11.060.
37. Banu S, Bhaskar B, Balasekar P. Hepatoprotective and antioxidant activity of *Leucas aspera* against D-galactosamine induced liver damage in rats. *Pharm Biol*. 2012;50(12):1592–1595. doi:10.3109/13880209.2012.685130.
38. Sadhu SK, Okuyama E, Fujimoto H, Ishibashi M. Separation of *Leucas aspera*, a medicinal plant of Bangladesh, guided by prostaglandin inhibitory and antioxidant activities. *Chem Pharm Bull (Tokyo)*. 2003;51(5):595–598. doi:10.1248/cpb.51.595.
39. Sadhu SK, Okuyama E, Fujimoto H, Ishibashi M. Diterpenes from *Leucas aspera* inhibiting prostaglandin-induced contractions. *J Nat Prod*. 2006;69(7):988–994. doi:10.1021/np058118m.
40. Chew AL, Jessica JJ, Sasidharan S. Antioxidant and antibacterial

- activity of different parts of *Leucas aspera*. *Asian Pac J Trop Biomed*. 2012;2(3):176–180. doi:10.1016/S2221-1691(12)60037-9.
41. Rahman MA, Islam MS. Antioxidant, antibacterial and cytotoxic effects of the phytochemicals of whole *Leucas aspera* extract. *Asian Pac J Trop Biomed*. 2013;3(4):273–279. doi:10.1016/S2221-1691(13)60062-3.
 42. Sharma PV. *Dravyaguna Vijnana*, Vol. II. Varanasi: Chaukhambha Bharati Academy; 2001. p. 51–55.
 43. Ayurvedic Pharmacopoeia of India. Part I, Vol. II. New Delhi: Ministry of AYUSH, Govt. of India; 2001. p. 103–105.
 44. Sharma PV. *Dravyaguna Vijnana*, Vol. II. Varanasi: Chaukhambha Bharati Academy; 2001. p. 389–393.
 45. Ayurvedic Pharmacopoeia of India. Part I, Vol. V. New Delhi: Ministry of AYUSH, Govt. of India; 2006. p. 19–21.
 46. Zhao Y, Peng L, Yang LC, Xu XD, Li WJ, Luo XM, et al. Wedelolactone regulates lipid metabolism and improves hepatic steatosis partly by AMPK activation and up-regulation of expression of PPAR α /LPL and LDLR. *PLoS One*. 2015;10(7):e0132720. doi:10.1371/journal.pone.0132720.
 47. Cabrera D, Wree A, Povero D, Solís N, Hernandez A, Pizarro M, Moshage H, Torres J, Feldstein AE, Cabello-Verrugio C, Brandan E. Andrographolide ameliorates inflammation and fibrogenesis and attenuates inflammasome activation in experimental non-alcoholic steatohepatitis. *Scientific reports*. 2017 Jun 14;7(1):3491.

§§§