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Research Article

EFFECT OF *ZANJABĪL* (*ZINGIBER OFFICINALE*) IN NON-ALCOHOLIC FATTY LIVER DISEASE- A RANDOMIZED CONTROLLED TRIAL

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ABSTRACT

Non Alcoholic Fatty Liver Disease (NAFLD) is a reversible condition of the liver, wherein large vacuoles of triglyceride fat accumulates in liver cells via the process of steatosis, despite any evidence of excessive alcohol consumption. In view of present scenario of high prevalence and limited treatment options, this study was conducted to assess the effect of *Murabba-i- Zanjabīl* in NAFLD. Present study was designed as a randomized placebo controlled trial with 30 patients in test group and 10 patients in control group. Participants in test group were administered with *Murabba-i- Zanjabīl,* 5 gm twice daily, 30 minutes before food for 45 days and those in control group were given 1 capsule of 500 mg each containing wheat flour twice daily, 30 minutes before food for 45 days. All the participants were asked to follow up at every 15 days for assessment of subjective parameters. Objective parameter was assessed before and after the trial period. On statistical analysis the test formulation showed significant reduction in scores ($p<0.05$) for most of the parameters on both inter and intra group analysis, while the reduction in control group was not found to be statistically significant (p.0.05). This study lays out that *Murabbā-i Zanjabīl* in a dose of 5gm twice daily given for 45 days is more effective than placebo in treating NAFLD. There was no adverse effect reported during the trial. It was thus concluded that *Murabbā-i Zanjabīl* is effective and safe in therapeutic management of NAFLD.

KEYWORDS: *Su'-i Mizāj Kabid Bārid,* Non-Alcoholic Fatty Liver Disease, NAFLD, *Murabbā-i Zanjabīl,* Unani Medicine.

INTRODUCTION

Non Alcoholic Fatty Liver Disease (NAFLD) is a reversible condition of the liver, wherein large vacuoles of triglyceride fat accumulates in liver cells via the process of steatosis (abnormal retention of lipids within a cell), despite any evidence of excessive alcohol consumption.[1] In the developed countries NAFLD is reported to be the most common liver disorder, with a worldwide prevalence of 6%-35% and 25%-26% in Europe. In Asian countries the pooled prevalence of NAFLD is estimated to be 27.4% (95% CI 23.3%-31.9%). It occurs in all age groups including children, with highest prevalence between 40 to 49 years of age and equal distribution among males and females.

For a significant amount of time fatty infiltration of liver was not thought to be of much clinical significance. However it was acknowledged that similar to alcohol induced liver disease obese and diabetic patients may also show pathological changes in liver. But these problems were given importance after it was established that NAFLD exists as a spectrum of diseases ranging from simple steatosis without any evidence of cell injury to non-alcoholic steatohepatitis, which has the potential to progress to cirrhosis. NAFLD has a close relationship with obesity, insulin resistance and dyslipidemia. Majority of the patients with fatty liver also present with insulin resistance and metabolic syndrome, accompanied with central or visceral obesity. With the obesity emerging as a worldwide epidemic, a great amount of research is in progress.[2]

The patients may remain asymptomatic during the initial phase of the disease. Most patients have an accidental diagnosis of the disease when they undergo imaging for some other problem. Patients may sometimes also be symptomatic and present with features of dull ache/ heaviness in right hypochondrium, anorexia, nausea, vomiting and dyspepsia. Hepatomegaly is present in up to 75% of patients, but stigmata of chronic liver disease are uncommon.[2,3]

Laboratory studies may show mildly elevated aminotransferase and alkaline phosphatase levels; however laboratory values may be normal in up to 80% of people with fatty liver. Biopsy remaining the gold standard for diagnosis, imaging also provides a clear picture of the disease when other diseases like viral hepatitis, autoimmune liver disease, Wilson's disease, hemochromatosis and α_1 antitrypsin deficiency are excluded.[2,4,5,6]

Unani physicians have described liver as one of the principal organs of the body (*Aaza e raeesa*).[7] It is the primary source of natural faculties (*Quwwate Tabiya*), where the functions of digestion, concoction, absorption and excretion are performed.[8,9] Normally mizaj of liver is hot and moist,[9-12] which can get converted to cold due to mutable dietary habits, consumption of fatty and cold food in abundance etc., thereby allowing excessive accumulation of fat in liver parenchyma (*Tashhamul kabid*). This alteration in mizaj (*Su'-i Mizāj Kabid Bārid)* results in alteration in liver functioning which ultimately leads to formation of *Akhlate Raddiya* (abnormal humors).[11,13,14] One of the basic modalities of treatment, recommended by Unani physician for *Su'-I Mizāj Kabid Bārid* is *Ilājbi'lZid*, by using the drugs of opposite temperament than the disease. *Zanajbīl (Zingiberofficinale)*, having *Mizāj* as *HārYābis*, [15-21] has been in practice of ancient Unani physicians to treat *Su'-I Mizāj Kabid Bārid*. Various Unani physicians like *Ibn-i Sīna (Al-Qānūnfi'l-Tib),*[14] *Hakīm Najmal-Ghani (Khazāinal-Advia),*[16] *Ibn-i Baiṭār (Kitāb al-Mukhtārātfi'l-Tib),*[22] *Hakīm Muhammad A'zam Khan (Muhīt-I A'zam)*[15] has mentioned *Zanjabīl* to be *Muqawwi-I Jigar,* and to be effective in *Baroodat e jigar*in the form of *Murabbā* (Pickle). *Ibn-i Baitār* also recommended *Murabbā-I Sonth* to be a remedy for *Su'-I Mizāj Kabid Bārid.*[22]

Materials and Methods

Study Design

The study was carried out as an open label placebo controlled trial in the department of Moalajat of National Institute of Unani Medicine Hospital, Bengaluru, for duration of one year, i.e. from January 2018 to January 2019. Before the commencement of the trial, the study protocol was drafted and submitted to the institutional ethical committee for approval. The study was approved by the Ethics committee of NIUM, Bengaluru under IEC number NIUM/IEC/2016-17/004/Moal/04, and dated 18.05.2017. The trial was registered by the Clinical Trial Registry of India under clinical trial registration number CTRI/2018/01/011531.

Study Participants

A total of 180 patients were screened for the study. 106 patients were selected based on ultrasonography scan. Out of these, 56 patients denied participation in the study. 50 patients were investigated for study participation out of which 10 patients did not meet the inclusion criteria and only 40 were included in the study. 30 patients fulfilling the inclusion criteria were randomly assigned to the test group while 10 to the control group (Fig.1). The patients enrolled were clinically assessed by history taking and clinical examination of all the systems and other required parameters. All the information was recorded in the case record form designed for the study. Patients were then enrolled in the study after taking written informed consent. All the patients were given a diet chart to be followed during the trial period and a compliance chart that was to be filled by the patient himself to ensure patient compliance of drug, diet and exercise.

Randomization

Subject allocation was done by simple randomization technique using a computer generated random allocation table.

Inclusion and Exclusion Criteria

The patients from the OPD/IPD of NIUM hospital, diagnosed as having fatty liver grade I and II based on the ultrasonography report and without any history of alcohol intake were enrolled in the study. Patients with/ without clinical signs and symptoms like Anorexia, Nausea, Dyspepsia, Fatigue, Dull ache/ Heaviness in right hypochondriac region and Hepatomegaly, of either gender between 18-60 years of age, non-alcoholic and diagnosed with fatty liver grade I or II on an ultrasonogram were included in the study. Those diagnosed with fatty liver grade III and positive viral hepatitis markers were excluded from the study. Moreover, patients suffering from any sort of systemic illness and pregnant and lactating women were also not taken to be the participants. Patients with a positive HbsAg and increased random blood sugar were also excluded.

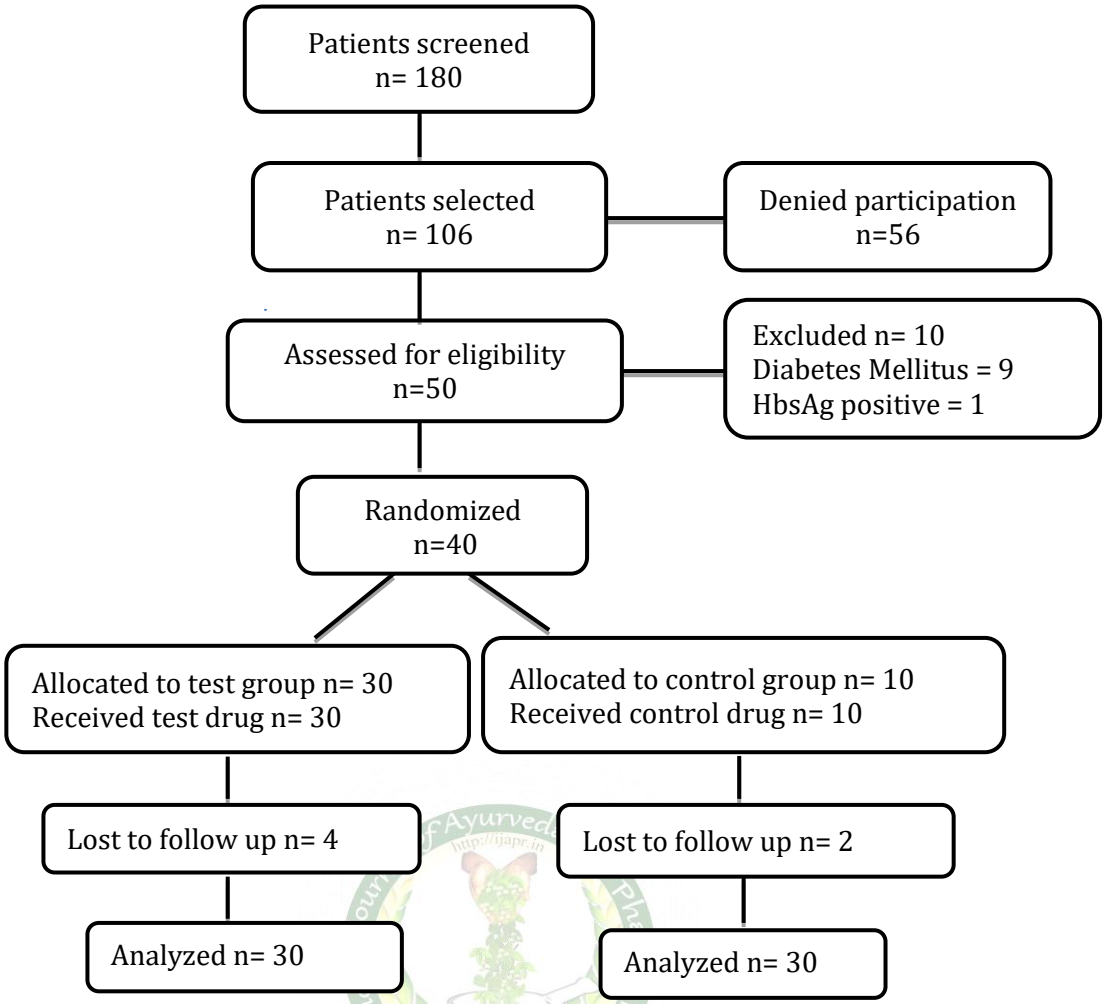

Fig.1: Consort Flow Diagram

Measurements

All the patients, either presenting with the symptoms or accidentally diagnosed with fatty liver in ultrasonogram done for some other purpose, were evaluated for the complaints of dull ache/ heaviness in right hypochondriac region, anorexia, nausea and dyspepsia in the general OPD (Moalajat)/IPD. Patients, who were known cases of diabetes mellitus, were diagnosed with grade III fatty liver or alcoholics were excluded from the study. In each patient complete physical examination was done including presenting complaints, past history, family history, general physical examination and systemic examination. Height and weight of the patients was measured and their BMI was calculated according to the formula BMI= Weight in KG/ Height in M^2. Then the patients underwent biochemical and pathological investigations like Hb%, TLC, DLC, ESR, SGOT (AST), SGPT (ALT), Alkaline Phosphatase, Blood urea, Serum Creatinine, Blood Sugar (Random) and HbsAg to exclude any systemic illness.

Preparation

For preparation of *Murabba-i- Zanjabīl,* Fresh ginger was first peeled and then boiled in water until it became soft. After that *Qiwam* (Syrup) of sugar was made with quantity equal to that of ginger and then soften ginger was put in it and left overnight. If *qiwam* became dilute the next day, it was boiled again without the soften ginger in it to vaporize excess water content. If on the third day again *Qiwam* appears to be dilute then it is again boiled.[23-26]

Intervention

Patients in the test group were administered *Murabba-i- Zanjabīl* in a dose of 5gm twice a day, 30 minutes before meals, orally and those in control group were given wheat flour capsules of 500 mg each, 1 capsule twice a day, 30 minutes before meals. After enrolment in the study patients were asked to visit the hospital after every 15 days for a period of 45 days (3 visits after first visit). During each visit patients were assessed for the progression or regression of subjective symptoms. Grading of fatty liver by ultrasonogram was done before and after the study.

Dietary advice and lifestyle modification

Patients in both groups were asked to follow the diet chart provided at the time of first visit and were asked to do 30-45 minutes of brisk walking daily in morning and evening. They were also given a compliance chart to record whether they followed all the dos and don'ts daily or not.

Outcome Measurements

Efficacy assessment was done on the basis of improvement in subjective and objective parameters. Objective parameter (i.e. fatty liver grade) was assessed by ultrasonography while an arbitrary assessment scale was adopted for the assessment of subjective parameters (i.e. dull ache/heaviness in the right upper quadrant, Anorexia, Nausea, Dyspepsia).

S No	Nature	Grade	Score	Nature of severity
1	No	-	0	No symptoms
2	Mild	+	1	Mild Symptoms but not enough to require remedial therapy to carry out daily routine
3	Moderate	++	2	Moderate symptoms which interfere with daily routine and require remedial therapy to continue to work
4	Severe	+++	3	Severe symptoms which do not allow daily activities

Safety assessment was done on Clinical symptoms and reporting of side effects, if any, and Laboratory Investigations such as Hematological assessment (Hb%, TLC, DLC, ESR), Biochemical assessment (SGOT (AST), SGPT (ALT), Alkaline Phosphatase, Blood urea, Serum Creatinine).

Statistical Analysis

Descriptive and inferential statistical analysis has been carried out in the present study. Results on continuous measurements are presented on Mean ± SD (Min-Max) and results on categorical measurements are presented in Number (%). Significance is assessed at 5 % level of significance. The following assumptions on data is made-

1. Dependent variables should be normally distributed,
2. Samples drawn from the population should be random,
3. Cases of the samples should be independent

Student t test (two tailed, independent) has been used to find the significance of study parameters on continuous scale between two groups (Inter group analysis) on metric parameters. Leven`s test for homogeneity of variance has been performed to assess the homogeneity of variance. Student t test (two tailed, dependent) has been used to find the significance of study parameters on continuous scale within each group. Chi-square/ Fisher Exact test has been used to find the significance of study parameters on categorical scale between two or more groups, Non-parametric setting for Qualitative data analysis. Paired Proportion test has been used to find the significance of proportion in paired data. Smaller percentage of Improvement becomes significant at lower tail compared to higher tail. E.g. Improvement from 10% to 20% is difficult than the Improvement from 80% to 90%

Results

There was no difference in the demographic characteristics between the two groups depicting homogeneity (Table 1). Difference in improvement between test and control groups for Dull ache/ heaviness in right hypochondrium was highly significant with p value <0.001. Also the improvement in test and control group individually was statistically significant (Table 2). In Anorexia there was a significant improvement reported in the test group (p<0.001) while the improvement in the control group was not statistically significant (p= 0.267). On analyzing between test group and control group the difference between the test and control group result was statistically significant (p=0.002) (Table 3).Both the test and control group did not show statistically significant improvement in Nausea but comparing the two groups the p value was 0.058 implying suggestive significance at second and third follow ups (Table 4). Statistically significant improvement was observed in dyspepsia in test group (p<0.001) and not in control group (p= 0.285). Analyzing between groups improvement was highly significant in the test group as compared to the placebo with a p value of <0.001 at second and final follow up (Table 5). The difference in fatty liver grading between the two groups was statistically significant with a p value of 0.002 before and after intervention (Table 6). There was no significant difference between safety profile before and after the treatment except for hemoglobin percentage and erythrocyte sedimentation rate (ESR) (Table 7). No adverse events were noted during the study.

DISCUSSION

The result on hypochondriac dullness and pain is in accordance with the study conducted by Attilio Giacosa et al where a combination of ginger and artichoke is reported to bring about a significance decrease in abdominal pain after 4

weeks of administration.[27] Efficacy of ginger in relieving pain has been compared to some NSAIDs where ginger extract was found to be equally effective as compared to ibuprofen in relieving pain.[28] This effect is due to the anti-inflammatory and analgesic property of ginger.[29] Experimental studies have shown that ginger constituents inhibit a key pathway in inflammatory process i.e. aracidonic acid metabolism. Also, it acts as inhibitor of prostaglandins and leukotriene synthesis by suppressing cyclooxygenase and lipooxygenase pathways.[29-31] Zingerone, a bioactive component of ginger has been suggested to reduce lipopolysaccharide (LPS) induced inflammation in mice by inhibiting infiltration of inflammatory cells and suppressing LPS induced NF-κβ activities in cells.[32] Also in vitro studies have been carried out on 6-, 8-, 10- gingerol and 6- shogaol isolated from ginger rhizome.[33]

Anorexia results due to delayed gastric emptying developing in patients a feeling of satiety thereby decreasing the feeling of hunger. Giacaso et al studied the effect of 100 mg ginger extract on gastrointestinal motility and reported a significant increase in gastrointestinal motility as compared to the placebo.[34] Wu et al. reported that ginger stimulates antral contractions thereby accelerating gastric emptying.[35] Other studies on functional dyspepsia have also shown similar effects without affecting gut hormones.[36]

Antiemesis through ginger could be explained by several mechanisms. 6-gingerol accelerates gastrointestinal transport; it also has been reported to exhibit anti hydroxyl tryptamine activity in isolated guinea pig ileum.[37] This finding is annealed by the fact that 6-gingerol effectively prevented cyclophosphamide induced vomiting in animal model.[38] Another constituent of ginger galanolactone is shown to be a competitive antagonist at ileal 5-HT_3 receptors.[39] The effect of ginger on nausea observed in this study was not found in concordance with the result of previous studies which have shown ginger to be significantly effective in all types of nausea vomiting, i.e. pregnancy induced nausea vomiting, post-operative nausea vomiting and chemotherapy induced nausea vomiting.[27,34,36,38] The reason for this observation could be the small sample size of the study with a very little occurrence of nausea in patients with NAFLD.

Owing to its carminative activity, ginger decreases the pressure on lower esophageal sphincter and impedes intestinal cramping thus relieving dyspepsia.[36] In previous randomized placebo controlled trials similar results have been noticed where ginger was reported to be more effective as compared to placebo in treating dyspepsia.[27,40] Ginger is also known to exhibit spasmolytic action thus increasing the gastric emptying rates without having any effect on gut hormones, ultimately improving the symptoms of dyspepsia.[41]

In a placebo controlled randomized trial conducted by Rahimlou et al, 44 patients with NAFLD were administered with 2g ginger or placebo per day for 12 weeks with similar dietary modification and physical activity in each group. The result showed a significance decrease in hepatic steatosis.[42] In this study also similar effect has been observed.

Table 1: Baseline Characteristics

	Test Group (n=30) No. (%)	Control Group (n=10) No. (%)	p-value
Age in Years			
Mean ± SD	40.53 ± 8.63	44.1±7.83	P=0.2552[a]
Gender			
Female	14 (46.7%)	7 (70%)	
Male	16 (53.3%)	3 (30%)	P=0.201[c]
Occupation			
Business	6 (20%)	1 (10%)	P=0.457[b]
Employee	6 (20%)	3 (30%)	
House wife	11 (36.7%)	6 (60%)	
Labour	6 (20%)	0 (0%)	
Unemployed	1 (3.3%)	0 (0%)	
Marital Status			
Married	25 (83.3%)	10 (100%)	P=0.667[b]
Unmarried	5 (16.7%)	0 (0%)	

Socio Economic Status			
Lower	1 (3.3%)	2 (20%)	P=0.220[b]
Lower Middle	6 (20%)	2 (20%)	
Upper	1 (3.3%)	0 (0%)	
Upper Lower	15 (50%)	6 (60%)	
Upper Middle	7 (23.3%)	0 (0%)	
BMI			
Mean±SD	28.08±3.51	30.50±4.59	P=0.090[a]
Diet distribution			
Mixed	27 (90%)	10 (100%)	P=0.560[b]
Vegetarian	3 (10%)	0 (0%)	

a=Student's *t*-test b=Fisher exact test c=Chi-square test

Table 2: Dull Ache/Heaviness

Dull Ache/ Heaviness	Baseline	1st follow up	2nd follow up	3rd follow up	% difference
Group TG (n=30)					
0	2 (6.7%)	7 (23.3%)	24 (80%)	30 (100%)	93.3%
1	11 (36.7%)	21 (70%)	6 (20%)	0 (0%)	-36.7%
2	15 (50%)	2 (6.7%)	0 (0%)	0 (0%)	-50.0%
3	2 (6.7%)	0 (0%)	0 (0%)	0 (0%)	-6.7%
Group CG (n=10)					
0	3 (30%)	3 (30%)	4 (40%)	5 (50%)	20.0%
1	1 (10%)	3 (30%)	3 (30%)	4 (40%)	30.0%
2	6 (60%)	4 (40%)	3 (30%)	1 (10%)	-50.0%
3	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0.0%
P value	0.129	0.205	0.009**	<0.001**	-

Chi-Square/Fisher Exact Test

Group TG: P<0.001**, Significant, paired proportion test, 93.3% Improvement

Group CG: P<0.001**, Significant, paired proportion test, 50.0% improvement

Table 3: Anorexia

Anorexia	Baseline	1st follow up	2nd follow up	3rd follow up	% difference
Group TG (n=30)					
0	15 (50%)	26 (86.7%)	30 (100%)	30 (100%)	50.0%
1	13 (43.3%)	4 (13.3%)	0 (0%)	0 (0%)	-43.3%
2	2 (6.7%)	0 (0%)	0 (0%)	0 (0%)	-6.7%
3	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0.0%
Group CG (n=10)					
0	4 (40%)	5 (50%)	6 (60%)	6 (60%)	20.0%
1	6 (60%)	5 (50%)	4 (40%)	4 (40%)	-20.0%
2	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0.0%
3	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0.0%
P value	0.840	0.029*	0.002**	0.002**	-

Chi-Square/Fisher Exact Test

Group TG: P<0.001**, Significant, paired proportion test, 50.0% Improvement

Group CG: P=0.267, Not Significant, paired proportion test, 20.0% improvement

Table 4: Nausea

Nausea	Baseline	1st follow up	2nd follow up	3rd follow up	% difference
Group TG (n=30)					
0	22 (73.3%)	29 (96.7%)	30 (100%)	30 (100%)	26.7%
1	6 (20%)	1 (3.3%)	0 (0%)	0 (0%)	-20.0%
2	2 (6.7%)	0 (0%)	0 (0%)	0 (0%)	-6.7%
Group CG (n=10)					
0	8 (80%)	8 (80%)	8 (80%)	8 (80%)	0.0%
1	2 (20%)	2 (20%)	2 (20%)	2 (20%)	0.0%
2	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0.0%
P value	1.000	0.149	0.058+	0.058+	-

Chi-Square/Fisher Exact Test

Group TG: P=0.133, Not Significant, paired proportion test, 26.7% Improvement

Group CG: P=1.000, Not Significant, paired proportion test, 0.00% improvement

Table 5: Dyspepsia

Dyspepsia	Baseline	1st follow up	2nd follow up	3rd follow up	% difference
Group TG (n=30)					
0	8 (26.7%)	15 (50%)	28 (93.3%)	29 (96.7%)	70.0%
1	4 (13.3%)	15 (50%)	2 (6.7%)	1 (3.3%)	-10.0%
2	18 (60%)	0 (0%)	0 (0%)	0 (0%)	-60.0%
Group CG (n=10)					
0	4 (40%)	4 (40%)	4 (40%)	4 (40%)	0.0%
1	1 (10%)	2 (20%)	2 (20%)	2 (20%)	10.0%
2	5 (50%)	4 (40%)	4 (40%)	4 (40%)	-10.0%
P value	0.869	0.004**	<0.001**	<0.001**	-

Chi-Square/Fisher Exact Test

Group TG: P<0.001**, Significant, paired proportion test, 70.0% Improvement

Group CG: P=0.285, Not Significant, paired proportion test, 10.0% improvement

Table 6: Fatty liver grading

Fatty liver grading	Before Treatment	After Treatment	% difference
Group TG (n=30)			
0	0 (0%)	17 (56.7%)	56.7%
1	26 (86.7%)	13 (43.3%)	-43.4%
2	4 (13.3%)	0 (0%)	-13.3%
Group CG (n=10)			
0	0 (0%)	0 (0%)	0.0%
1	10 (100%)	10 (100%)	0.0%
2	0 (0%)	0 (0%)	0.0%
P value	0.556	0.002**	-

Chi-Square/Fisher Exact Test

Group TG: P<0.001**, Significant, paired proportion test, 56.7% Improvement

Group CG: P=1.000, Not Significant, paired proportion test, 0.0% improvement

Table 7: safety profile

	Test Group	Control Group	Total	P value
Hemoglobin (g/dl)				
Before Treatment	13.22±1.99	13.18±1.58	13.21±1.88	0.954
After Treatment	13.76±1.84	13.50±1.27	13.70±1.70	0.678
Difference	-0.543	-0.320	-0.488	-
P value	0.031*	0.595	0.038*	-
TLC (Cells/cumm)				
Before Treatment	7109.33±1729.62	7090.00±3061.75	7104.50±2094.73	0.980
After Treatment	6772.67±1569.47	7620.00±1868.93	6984.50±1666.06	0.167
Difference	336.667	-530.000	120.000	-
P value	0.191	0.587	0.691	-
Polymorphs				
Before Treatment	60.24±8.18	60.40±9.17	60.28±8.32	0.959
After Treatment	58.64±8.41	61.00±9.39	59.23±8.60	0.460
Difference	1.600	-0.600	1.050	-
P value	0.250	0.855	0.418	-
Eosinophils				
Before Treatment	4.77±1.25	4.10±1.45	4.60±1.32	0.168
After Treatment	4.87±1.25	3.70±1.25	4.58±1.34	0.015*
Difference	-0.100	0.400	0.025	-
P value	0.703	0.399	0.912	-
Basophils				
Before Treatment	0.06±0.23	0.00±0.00	0.05±0.20	0.418
After Treatment	0.06±0.23	0.00±0.00	0.05±0.20	0.418
Difference	-	-	-	-
P value	-	-	-	-
Monocytes				
Before Treatment	4.14±1.78	3.50±1.65	3.98±1.75	0.322
After Treatment	4.37±1.73	3.60±1.58	4.18±1.71	0.219
Difference	-0.233	-0.100	-0.200	-
P value	0.428	0.832	0.416	-
ESR (mm/1hr)				
Before Treatment	31.63±21.95	29.80±22.76	31.18±21.88	0.822
After Treatment	20.67±17.82	26.10±22.55	22.03±18.95	0.439
Difference	10.967	3.700	9.150	-
P value	0.001**	0.687	0.007**	-

Variables	Test Group	Control Group	Total	P value
Serum Creatinine (mg/dl)				
Before Treatment	0.84±0.14	0.80±0.07	0.83±0.12	0.388
After Treatment	0.85±0.12	0.84±0.12	0.85±0.12	0.848
Difference	-0.009	-0.040	-0.017	-
P value	0.637	0.269	0.320	-
Blood Urea (mg/dl)				
Before Treatment	26.28±7.33	25.30±5.81	26.04±6.93	0.702
After Treatment	25.55±7.71	28.60±7.17	26.31±7.61	0.278

Difference	0.733	-3.300	-0.275	-
P value	0.438	0.227	0.778	-
Serum Bilirubin (mg/dl)				
Before Treatment	0.66±0.22	0.67±0.21	0.66±0.22	0.856
After Treatment	0.72±0.27	0.62±0.20	0.69±0.26	0.283
Difference	-0.061	0.056	-0.032	-
P value	0.239	0.548	0.478	-
AST (IU/L)				
Before Treatment	28.70±14.02	25.00±6.75	27.78±12.62	0.429
After Treatment	26.03±8.80	28.80±7.89	26.73±8.57	0.384
Difference	2.667	-3.800	1.050	-
P value	0.263	0.234	0.591	-
ALT (IU/L)				
Before Treatment	31.23±13.97	27.30±11.15	30.25±13.30	0.425
After Treatment	30.03±12.25	29.90±10.16	30.00±11.63	0.975
Difference	1.200	-2.600	0.250	-
P value	0.673	0.405	0.912	-
Alkaline Phosphatase (IU/L)				
Before Treatment	216.90±65.25	238.60±35.73	222.33±59.59	0.325
After Treatment	213.37±65.82	246.30±43.72	221.60±62.22	0.150
Difference	3.533	-7.700	0.725	-
P value	0.606	0.538	0.902	-

Future recommendations

Further controlled clinical trials including blinding and more comprehensive study designs with large sample size and life style modification and diet regulation as control are needed. Since ginger was reported to be heptatonic it can also be given as an adjuvant with drugs that are known to be hepatotoxic. Moreover, further studies can be conducted using ginger including grade III fatty liver as well.

CONCLUSION

After 45 days of treatment the subjective symptoms namely dull ache /heaviness in right hypochondrium, anorexia, nausea, dyspepsia and objective symptom i.e. fatty liver grade were found to have significant reduction in score. It was thus concluded that *Murabbā-i Zanjabīl* in a dose of 5gm twice daily given for 45 days is more effective than placebo in treating NAFLD.

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