ONLINE ISSN :3007-309X
PRINT ISSN :3007-3081

Journal Of Medical & Health Science Review

PREPARATION AND ASSESSMENT OF POLYHERBAL POWDER FOR THE TREATMENT OF FATTY LIVER

Aimen Jabbar[1*], Rai Muhammad Amir[1b], Shahzadi Uzma Khan[1c], Nagamana Fiaz[1d]

[1a,1b,1c,1d]Institute of Food and Nutritional Sciences, Pir Mehr Ali Shah Arid Agriculture University, Rawalpindi

ARTICLE INFO

Keywords

Polyherbal powder, Lipid profile, Antioxidant capacity, Milk thistle

Corresponding Author: Aimen Jabbar, Institute of Food and Nutritional Sciences, Pir Mehr Ali Shah Arid Agriculture University, Rawalpindi,

Email:aimenjabbar99@gmail.com

ABSTRACT

Non-alcoholic fatty liver disease (NAFLD) is a condition in which surplus fat builds up in liver but this fat buildup is not related to alcohol abuse. Metabolic syndromes such as insulin resistance, dyslipidemia, type II diabetic disease and obesity are also companied with NAFLD. Present study examined the effects of polyherbal powder supplementation on lipid profile, liver enzymes, glycemic status and body mass index. In this randomized, placebo-controlled trail, 30 participants with diagnosed NAFLD were chosen randomly. Participants were randomly subdivided into three groups; control group received only modified diet therapy, group A received modified diet therapy with 5grams of polyherbal powder, group B received 10grams of polyherbal powder. Serum alanine transaminase (ALT), high density lipoproteins (HDL) and low-density lipoproteins (LDL). All the obtained data was statistically analyzed. The polyherbal powder showed significant reduction in all measured parameters. Group B showed significant reductions in Serum ALT as well as lipid profile (p value < 0.05). The results of current study showed that polyherbal powder could be a preferable option for the treatment of NAFLD patients as compared to the hepatoprotective drugs as well as antimetabolic disorders agents. Herbal therapy might be an optimal option if combined with change in lifestyle and proper nutrition and diet intake.

1. INTRODUCTION

Non-alcoholic fatty liver disease (NAFLD) is becoming one of the most common progressive diseases worldwide with approximately 25% globally and 14% in Pakistan (Ali et al., 2021). NAFLD is a condition in which surplus fat builds up in liver but this fat buildup is not related to alcohol abuse. Metabolic syndromes such as insulin resistance, dyslipidemia, type II diabetic disease as well as obesity are also companied with NAFLD (Muthiah, et al., 2020). Prevalence of NAFLD in diabetic patients ranges from 47.3% to 63.7% and is seen in 80% of obese people (Powell et al., 2021). Nonalcoholic steatohepatitis (NASH), an aggressive form of fatty liver disease characterized by liver inflammation, can result in severe scarring (cirrhosis) as well as liver failure in some patients with NAFLD. This damage is comparable to the harm caused by consumption of excessive alcohol. NAFLD management is particularly difficult to diagnose and treat due to the complex causes of the pathogenesis. Patients with NAFLD who are initially asymptomatic may disregard their health problems, and it will eventually proceed to NASH before manifestation. Healthy weight loss through caloric restriction is an effective treatment against NAFLD. Modifying lifestyle and improving healthy eating habits are still considered one of the most important tactics for preventing NAFLD progression, but some people find it difficult to follow long term lifestyle modification. Thus, developing therapeutic agents and using them as an intervention has gained much more attention in past years specifically because of their higher efficacy against NAFLD as well as lower risk of side effects (Pan et al., 2019). If proper management of NAFLD is not done, it can lead to further serious inflammation and degeneration of hepatic cells thus leading to an irreversible damage to hepatic cells. It may result in the development of hepatocellular carcinoma (Liang et al., 2021). Using nutraceuticals for lipid lowering therapies is of great use. Several simultaneous pathways contribute to the lipid-lowering impact. Increased antioxidant and anti-inflammatory capabilities of dietary supplements may result from similar simultaneous actions. Good outcomes have been demonstrated when taken in conjunction with exercise. Consequently, in present study efforts are done to treat NAFLD with polyherbal powder. The main aim of this research is to determine the potential involvement of herbs in the treatment of NAFLD.

2. MATERIALS AND METHOD

2.1 Study population

The study population included 20 – 60 years old non-alcoholic fatty liver disease (NAFLD). Data was collected from the referred patients to the Outpatient Department (gastroenterology/hepatology) of tertiary hospitals/clinics. The inclusion criteria were diagnosed patients of NAFLD (Grade 1-3). No use of any hypolipidemic or hypoglycemic

medications prior or during the study. The exclusion criteria were pregnant or lactating mothers, smoking, presence of thyroid, pulmonary, coronary or renal disease. All the eligible patients were provided with written informed consent form.

2.2 Study design and randomization

Current study was 4 months, randomized, placebo-controlled trail. 30 participants with diagnosed NAFLD were chosen randomly. Participants were randomly subdivided into three groups; control, group A and group B. 10 participants were placed in each group.

2.3 Intervention

Control group received only modified diet therapy, group A received modified diet therapy with 5grams of polyherbal powder, group B received 10grams of polyherbal powder.

2.4 Supplement preparation

The ingredients based on their hepatoprotective properties were procured from local market of district Rawalpindi in dried form. Later these were shifted to Institute of Food and Nutritional Science, PMAS Arid Agriculture University, Rawalpindi. Polyherbal powder was prepared according to the desired concentrations of ingredients. *Silybum marianum* (milk thistle), *Cichorium intybus* (chicory), *Curcuma longa* (turmeric), *Zingiber officinale* (ginger), *Nigella sativa* (black cumin), *Cinnamomum verum* (cinnamon) and *Glycyrrhiza glabra* (licorice) will be used for the formulation of polyherbal powder. All these herbs were air dried and ground in fine powder form and mixed in desired proportion.

2.5 Analytical procedures

Dietary history, physical examination, clinical data and lab reports were noted at baseline. Diet history was collected by using predesigned questionnaires. These questionnaires were used to analyze the nutritional status and dietary habits of patients. 24-hour dietary recall was taken and analyzed for this purpose. Body weight was measured in accordance to the standard procedures such as patient was in fasting state, without shoes and light clothing using weighing scale. Height was measured using height measuring bar and patient was without shoes. Using height and weight data, BMI was calculated. For patient selection South Asian standards for BMI were preferred. All subjects were screened at both random and pre-selected hospitals. Selected patients were evaluated for basic laboratory tests such as ALP viral load, ALT and cholesterol.

2.6 Statistical Analysis

Demographic data as well as clinical data were statistically analyzed by using descriptive statistics which include mean value, standard deviation. Comparison of all quantitative variables at baseline and after the study within every group was done using paired

t test. Values reported in results are based on Mean ± SD. Also, p value of < 0.05 was considered the statistical significance level.

3. RESULTS

3.1 Human study design

The present research was based entirely on human study and lasted for 4 months. Prior to the initiation of present study, 30 patients were selected randomly after conducting survey between the age limit of 20 to 60 years. Table 3 shows the baseline characteristics of patients. Patients were allocated in 3 groups based on the dose of polyherbal powder.

Table 1: Baseline characteristics of participants

Variables		Control group	Experimental group		*P* value
			Group A	Group B	
Dose of polyherbal powder		0 grams	5 grams	10 grams	
Number of patients		N = 10	N = 10	N = 10	
Age		41.6± 10.16*	40.4 ± 7.16*	45.1 ± 11.4*	0.000
Gender (n)	**Male**	6 (58.82%)	6 (50%)	7 (64.70%)	0.0003
	Female	4 (41.17%)	4 (50%)	3 (35.29%)	
Weight		87.3 ± 5.14*	86.4 ± 6.02*	83.4 ± 6.5*	0.001
BMI		30.57 ± 1.0*	30.45 ± 1.32*	34.47 ± 1.78*	0.000

* Mean ± SD, *p* value < 0.05 = significant

There was no significant difference between the weight and BMI of all three groups (*p* value > 0.05). Physical activity showed no significant difference in all three groups at baseline. Anthropometric indices are shown in Table 4. At baseline there was no significant difference among all three groups (*p* value > 0.05) but at the end of the study the weight was reduced significantly in the experimental group B (*p* value <0.001) with dose of 10g polyherbal powder.

Table 2: Anthropometric indices and glycaemic status of the participants before and after the intervention

Variables	Experimental group B	p value	Experimental group A	p value	Placebo group	P value
Body weight (kg)						
Before	83.53 ± 6.35	< 0.001	82.81 ± 7.28	0.004	85.94 ± 7.15	0.003
After	76.06 ± 5.29		77.31 ± 7.35		81.71 ± 7.12	
BMI (kg/m^2)						

Before	29.124 ± 1.91	<0.001	29.687 ± 1.91	0.005	30.047 ± 1.67	0.011
After	26.582 ± 1.41		27.763 ± 1.69		28.576 ± 1.73	

* BMI = Body Mass Index,

* Mean ± SD, *p* value < 0.05 = significant

Table 3: Lipid profile of the participants before and after the intervention

Variables	Intervention group B	p value	Intervention group A	p value	Placebo group	P value
ALT (U/L)						
Before	76.10 ± 6.19	< 0.001	65.70 ± 7.38	0.011	62 ± 5.27	0.005
After	49 ± 4.45		59 ± 8.76		53.20 ± 7.61	
ALP (U/L)						
Before	107.70 ± 7.17	<0.001	102.30 ± 6.62	<0.001	104 ± 6.99	0.014
After	72.70 ± 7.30		75.70 ± 5.62		84.40 ± 5.32	
Cholesterol (mg/dL)						
Before	243.70 ± 8.14	<0.001	239.20 ± 6.94	0.001	247 ± 7.04	0.004
After	108.6 ± 8.69		207.50 ± 4.43		208.90 ± 4.84	
LDL – c (mg/dL)						
Before	152 ± 9.26	0.003	147.40 ± 6.60	0.002	137.50 ± 6.82	0.034
After	114 ± 8.67		128 ± 4.11		128.50 ± 6.08	
HDL – c (mg/dL)						
Before	32.70 ± 2.75	<0.001	36.90 ± 4.82	0.008	36.60 ± 4.40	0.028
After	53.31 ± 9.10		48.60 ± 3.72		41.80 ± 2.39	

* ALT = Serum Alanine Transaminase, ALP = Serum Alkaline Phosphate, HDL = High Density Lipoproteins, LDL = Low Density Lipoproteins

* Mean ± SD, *p* value < 0.05 = significant

It is clear from the Table 4 and 5. that experimental group B showed the highest results as compared to experimental group A and control group. All these results confirm the efficacy of polyherbal powder. Cholesterol levels, ALT and ALP levels before and after the study are mentioned in Table 5. Cholesterol levels as well as ALT levels reduced significantly in experimental group B as compared to control group (< 0.001).

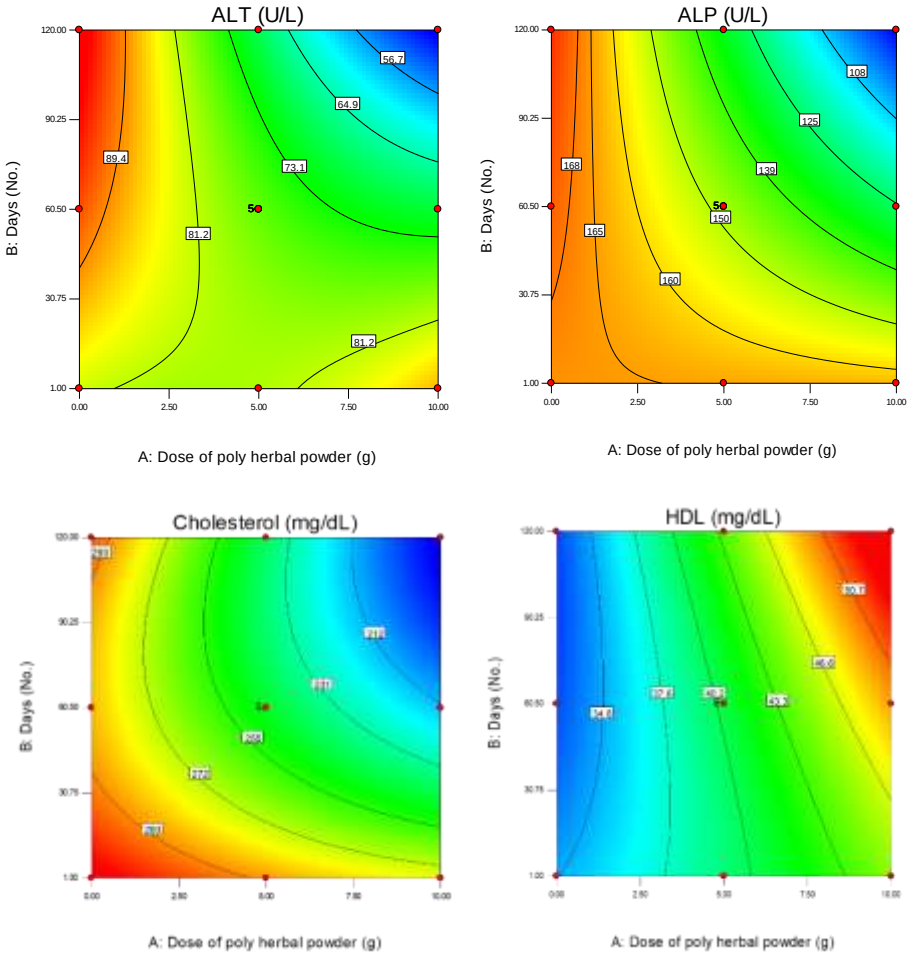

Figure 1: Contour plot showing the effects of each independent variable on ALT (U/L), ALP (U/L), Cholesterol (mg/dL), HDL (mg/dL)

The contour plot in Figure 1 was formed to examine the interaction effects of the dose polyherbal powder and number of days on serum ALT (U/L), ALP (U/L), Cholesterol (mg/dL) and HDL (mg/dL). The contour's convexity indicated the presence of interaction effects among both of the independent variables. Furthermore, the polyherbal powder dose and parameter levels were seen to be in sync with similar increases in dose (g). This interaction was even more visible as the number of days increased, and so the plot very clearly exemplified the nature of the connection.

4. DISCUSSION

In the current study, after consumption of 10grams of polyherbal powder, significant changes in weight and BMI in the experimental group B were seen. Mean differences of serum ALT, ALP, HDL, LDL as well as BMI in group B was significantly reduced in contrast to control group. Previous studies showed positive impact of herbs on lipid profile, serum ALT, ALP, and BMI. Studies have indicated that silymarin significantly lowers the enzymes levels such

as alanine aminotransferase (ALT) and aspartate aminotransferase (AST), which are regarded to be helpful in treating individuals with liver disease (De Avelar et al., 2017). An essential biologically active substance called silybin is obtained from silymarin, a standardized milk thistle extract (*Silybum marianum*). Silybin has a number of pharmacological actions, including anti-hepatic fibrosis, anti-inflammatory, and anti-lipid peroxidation activities (Hackett et al., 2012). Jigrine, an Indian medicine used to treat various liver disorders, contains chicory seed as one of its key constituents. It is also stated that chicory water-soluble extract is a promising option for the treatment of many liver illnesses. Recent studies, for example, show that chicory extract has a substantial hepatoprotective effect against dexamethasone-induced liver damage (Soliman et al., 2016). Apart for the study by Ghaffari (2019), which examined the effects of turmeric supplementation and chicory seeds on individuals with NAFLD, there are no controlled trials (RCTs). In this study, patients who consumed chicory and chicory plus turmeric saw reductions in waist circumference, weight, and body mass index when compared to placebo (Ghaffari et al., 2019). Leal (2019) supported the effectiveness of ginger in improving antioxidant profile and lowering lipid peroxidation. Lower propagation of liver disease was reported in animals treated with ginger (Leal et al., 2019). Ginger's hypotriglyceridemic impact is attributed to an increase in lipoprotein lipase enzymatic activity, which may result in the hydrolysis of circulating TG and a decrease in blood TG (Arablou et al., 2014). *Curcuma longa* (turmeric), curcumin, also plays vital role in lowering the progression of NAFLD among patients. It decreases the production of Reactive Oxygen Species (ROS) and improves inflammation of liver tissues. According to a Food and Drug Administration (FDA) assessment, curcumin supplementation is typically classified as a safe alternative medication, with no significant adverse events observed (Mansour-Ghanaei et al., 2019). In high doses (>1000 mg/day) and for specified durations, curcumin has also been found to potentially have beneficial effects on raised liver enzymes. It has the potential to improve liver function in NAFLD patients. There are evidences that it may also help with body mass index (BMI) and insulin in NAFLD patients (Rahmani et al., 2016). Cinnamon is used as a cough suppressant, anti-arthritic, antifungal, antibacterial, anti-inflammatory, antioxidant, and to treat pain and dental problems in traditional medicine. It has also been demonstrated that it can be used as a safe and inexpensive treatment to manage body weight, insulin resistance, lipid profile, and blood pressure (Mollazadeh & Hosseinzadeh, 2016). Askari (2014) investigated cinnamon's antioxidant effects in a blinded research on NAFLD patients. When compared to a placebo group, taking 1500mg of cinnamon for 12 weeks lowered AST, ALT, and insulin resistance (Askari et al., 2014). Numerous pharmacological studies have

demonstrated that GA has an extensive range of pharmacological functions, such as anti-allergic, anti-inflammatory, and antiviral properties. Studies imply that GA can improve liver pathology and dyslipidemia in NAFLD mice. GA decreased excessive macrophage infiltration and hepatocyte death caused by a high-fat, high-sugar diet. Several studies have demonstrated that GA can improve autophagy in macrophages (Fan et al., 2022). In a clinical study containing 66 NAFLD patients, a daily 2 g capsule of aqueous licorice root extract containing 20% glycyrrhizic acid, corresponding to 400 mg acid, was found to significantly lower levels hepatic transaminases activity which includes ALT and AST (Rostamizadeh, & Mazloom, 2019).

5. CONCLUSION

The results of current study showed that polyherbal powder could be a preferable option for the treatment of NAFLD patients as compared to the hepatoprotective drugs as well as antimetabolic disorders agents. Herbal therapy might be an optimal option if combined with change in lifestyle and proper nutrition and diet intake. In conclusion, current study proved that daily intake of 10 grams of polyherbal powder for 4 months had positive impact on BMI. ALT, ALP, lipid profile in NAFLD and hypercholesterolemia patients.

REFERENCES

Ali, A., Amin, M., Ahmed, M., Taj, A., Aasim, M., & Tabrez, E. (2021). Frequency of non-alcoholic fatty liver disease (NAFLD) and its associated risk factors among type-2 diabetics. *Pakistan Journal of Medical Sciences*, *38*(1), 28-33.

Arablou, T., Aryaeian, N., Valizadeh, M., Sharifi, F., Hosseini, A., & Djalali, M. (2014). The effect of ginger consumption on glycemic status, lipid profile and some inflammatory markers in patients with type 2 diabetes mellitus. *International journal of food sciences and nutrition*, *65*(4), 515-520.

Askari, F., Rashidkhani, B., & Hekmatdoost, A. (2014). Cinnamon may have therapeutic benefits on lipid profile, liver enzymes, insulin resistance, and high-sensitivity C-reactive protein in nonalcoholic fatty liver disease patients. *Nutrition research*, *34*(2), 143-148.

De Avelar, C. R., Pereira, E. M., De Farias Costa, P. R., De Jesus, R. P., & De Oliveira, L. P. (2017). Effect of silymarin on biochemical indicators in patients with liver disease: Systematic review with meta-analysis. *World Journal of Gastroenterology*, *23*(27), 5004-5006.

Fan, Y., Dong, W., Wang, Y., Zhu, S., Chai, R., Xu, Z., Zhang, X., Yan, L., & Bian, Y. (2022). Glycyrrhetinic acid regulates impaired macrophage autophagic flux in the treatment of non-alcoholic fatty liver disease. *Frontiers in Immunology*, *13*(1), 1-16.

Ghaffari, A., Rafraf, M., Navekar, R., Sepehri, B., Asghari-Jafarabadi, M., & Ghavami, S. M. (2019). Turmeric and chicory seed have beneficial effects on obesity markers and lipid profile in non-alcoholic fatty liver disease (NAFLD). *International Journal for Vitamin and Nutrition Research*, *89*(6), 293–302.

Hackett, E., Twedt, D., & Gustafson, D. (2012). Milk Thistle and its derivative compounds: A review of opportunities for treatment of liver disease. *Journal of Veterinary Internal Medicine, 27(*1), 10-16.

Leal, D., Fontes, G., Vila, J., Freitas, R., Campos, M., Carvalho, C., Pizziolo, V., & Diaz, M. (2019). *Zingiber officinale* formulation reduces hepatic injury and weight gain in rats fed an unhealthy diet. *Anais Da Academia Brasileira De Ciências, 91*(4), 1-11.

Liang, Z., Chen, X., Shi, J., Hu, H., Xue, Y., & Ung, C. (2021). Efficacy and safety of traditional Chinese medicines for non-alcoholic fatty liver disease: a systematic literature review of randomized controlled trials. *Chinese Medicine, 16*(1), 1-38.

Mansour-Ghanaei, F., Pourmasoumi, M., Hadi, A., & Joukar, F. (2019). Efficacy of curcumin/turmeric on liver enzymes in patients with non-alcoholic fatty liver disease: a systematic review of randomized controlled trials. *Integrative medicine research, 8*(1), 57-61.

Mollazadeh, H., & Hosseinzadeh, H. (2016). Cinnamon effects on metabolic syndrome: a review based on its mechanisms. *Iranian journal of basic medical sciences, 19*(12), 1258-1262.

Muthiah, M., Cheng Han, N., & Sanyal, A. (2021). A clinical overview of non-alcoholic fatty liver disease: A guide to diagnosis, the clinical features, and complications – What the non-specialist needs to know. *Diabetes, Obesity and Metabolism, 24*(2), 3-14.

Pan, M., Deng, Y., Zheng, C., Nie, H., Tang, K., Zhang, Y., & Yang, Q. (2019). Chinese herbal medicine formula shenling baizhu san ameliorates high-fat diet-induced NAFLD in rats by modulating hepatic microRNA expression profiles. *Evidence-Based Complementary and Alternative Medicine, 2019*(1), 1-14.

Powell, E. E., Wong, V. W. S., & Rinella, M. (2021). Non-alcoholic fatty liver disease. *The Lancet, 397*(10290), 2212-2224.

Rahmani, S., Asgary, S., Askari, G., Keshvari, M., Hatamipour, M., Feizi, A., & Sahebkar, A. (2016). Treatment of non-alcoholic fatty liver disease with curcumin: A randomized placebo-controlled trial. *Phytotherapy Research, 30*(9), 1540-1548.

Rostamizadeh, P., & Mazloom, Z. (2019). The effect of licorice and probiotics on nonalcoholic fatty liver disease (NAFLD): A systematic review. *International Journal of Nutrition Sciences, 4*(4), 163-169.

Soliman, H. A., El-Desouky, M. A., Hozayen, W. G., Ahmed, R. R., & Khaliefa, A. K. (2016). Hepatoprotective effects of parsley, basil, and chicory aqueous extracts against dexamethasone-induced in experimental rats. *Journal of Intercultural Ethnopharmacology*, 5(1), 65-69.