

**EVALUATION OF EFFICACY OF UNANI PHARMACOPOEIAL FORMULATION
DABIDULWARD IN TASHHAMUL KABID (NAFLD) - A PRELIMINARY STUDY****¹Maqbool Ahmad Khan, ^{1*}Najmus Sehar, ¹Mohammad Naime and ²Jamal Akhtar**¹Central Research Institute of Unani Medicine (CRIUM), Lucknow, U.P., India.²Central Council for Research in Unani Medicine (CCRUM), New Delhi, India.***Corresponding Author: Najmus Sehar**

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ABSTRACT

Fatty liver is acknowledged as fatty liver disease or hepatic steatosis. It is a reversible condition wherein large vacuoles of triglyceride fat accumulate in liver cells via the process of steatosis (i.e. abnormal retention of lipids within a cell). It is normal to have some fat in liver but in the condition of fatty liver more than 5-10% of liver weight is fat. NAFLD is a spectrum of liver disease that ranges from simple fatty infiltration of the liver parenchyma (steatosis) to fat with inflammation (nonalcoholic steatohepatitis; NASH). The term Tashhamul Kabid is used for fatty liver disease in Unani System of Medicine. The objective of the present study was to evaluate the efficacy and safety of Unani pharmacopoeial formulation 'Majoon Dabidulward' in the treatment of NAFLD. Patients were advised to take orally 7 grams of Majoon Dabidulward with water twice daily before the meal for 21 days. After treatment, it was observed that associated symptoms of fatty liver including abdominal tenderness, nausea, anorexia, general weakness and ultrasonography report were significantly reduced ($p < 0.05$). The percentage reduction in abdominal tenderness, nausea, anorexia, general weakness and report of ultrasonography were 42.98%, 81.57%, 73.68%, 47.38% and 30.70% respectively as compared to base line. No adverse effect of the drug was found. Highly significant improvements in all associate symptoms of the fatty liver suggest that the results are really due to the therapy. On the ground of above result, it can be concluded that Majoon Dabidulward is very effective and safe in the treatment of Tashhamul Kabid.

KEYWORDS: Kabid; Unani medicine; Fatty Liver; NAFLD; Dabidulward.**INTRODUCTION**

Fatty liver is acknowledged as fatty liver disease or hepatic steatosis. It is a reversible condition wherein large vacuoles of triglyceride fat accumulate in liver cells via the process of steatosis (i.e. abnormal retention of lipids within a cell). It is normal to have some fat in liver but in the condition of fatty liver more than 5-10 % of liver weight is fat. Fatty liver disease is classified into alcoholic fatty liver disease and Nonalcoholic fatty liver disease.^[1] NAFLD is a spectrum of liver disease that ranges from simple fatty infiltration of the liver parenchyma (steatosis) to fat with inflammation (nonalcoholic steatohepatitis; NASH) and ultimately cirrhosis occurring in absence of excessive alcohol consumption (upper threshold of 30 g/day for men and 20 g/day for women).^[2] The true extent of associated morbidity is not well defined; however, in one study, NASH was found associated with a greater than ten-fold increased risk of liver-related death (2.8% vs. 0.2%) and a doubling of cardiovascular risk over a mean follow up of 13.7 years.^[3]

NAFLD is a significant health problem worldwide, which affects 20%-30% of the adult population. NAFLD can progress to non-alcoholic steatosis hepatitis (NASH).^[4] It is strongly associated with obesity, dyslipidemia, insulin resistance and type-2, non- insulin dependent diabetes mellitus and so many considered to be the hepatic manifestations of the metabolic syndrome. Increasingly sedentary life style and changing dietary patterns means that the prevalence of obesity and insulin resistance is increased, making NAFLD, the leading cause of liver dysfunction in the Nonalcoholic, viral hepatitis-negative population in Europe and North America.

According to Unani concept, Fatty liver may be literally termed as Tashhamul Kabid. There is no specific description of fatty liver in Unani classical literature but features described by eminent Unani scholars under the heading of Amraze jigar (liver disorder) due to Su' mijaz haar ((impaired hot temperament) and Su' mijaz barid (impaired cold temperament) in various Unani classical text resemble with sign and symptoms of fatty liver.^[5,6,7]

The clinical features of the disease is feeling of uncomfortable heat, excessive thirst, bitter taste, anorexia, vomiting, diarrhea, itching, heaviness at right hypochondrium and inability to sleep on right side.^[7,8,9,10,11] According to Unani scholars, Kabid (liver) is one of the fundamental organ responsible for the metabolic activities mainly synthesis of Akhlaat. The normal mijaz (temperament) of liver is hot and moist.^[6,9,12,13] Due to erratic dietary habits and excessive fat consumption, its Mijaz is altered to barid, which is incompatible to the liver, thereby allowing to accretion of morbid matter in the form of fat which disturb normal functioning of liver resulting in Su'mizaj barid. Sometimes, the temperament of liver may become haar (hot) due to excessive intake of hot foods, drinks, drugs and alcohol etc., which interrupts the normal functioning of liver resulting in Su'mizaj haar kabid.^[5,9,13,14]

Various single as well as compound Unani formulations used by Unani Physicians, since long times are found effective in the treatment of Tashhamul kabid (NAFLD) but they need to be validated on scientific parameters in

order to generate data for their safety and efficacy. Unani Pharmacopoeial formulation Majoon Dabidulward is effective and safe in the treatment of fatty liver disease. The Unani drugs used in the treatment of Amraz-e jiger (*liver disorder*) is also described in the National Formulary of Unani Medicine and Unani Pharmacopeia of India. Therefore, the present clinical study has been planned to evaluate the safety and efficacy of Unani Pharmacopoeial formulation – *Majoon Dabidulward* in the treatment of *Tashhamul Kabid*.

MATERIAL AND METHOD

Study drug

The study drug Majoon Dabidulward is a poly herbal Unani Formulation, having drug of plants origin except luk-e maghsool (Table 1).

Study drug details

The following is composition of Majoon Dabidulward.^[15]

Table 1: Composition of Majoon Dabidulward.

S. No.	Unani Name	Scientific Name	Weight
1.	Sumbuluttib	Nordostachys jatamansi	10 g
2.	Mastagi	Pistacia lentiscus	10 g
3.	Zafran	Crocus sativus	10 g
4.	Tabasheer	Bambuse arudinace	10 g
5.	Darchini	Cinnamomum verum	10 g
6.	Izkhar	Cymbopogon jwarancusa	10g
7.	Asaroon	Asarum europaeum	10 g
8.	Qust Shreein	Saussurea lappa	10 g
9.	Gul-e-Ghafis	Gentiana Olivieri Griseb	10 g
10.	Tukhm-e-Kasoos	Cusuta reflexa	10 g
11.	Majeeth	Rubia cordifolia	10 g
12.	Luk-e Maghsool	Coccus lacca	10g
13.	Tukhm-e-Kasni	Cichorium intybus	10 g
14.	Tukh-e-Karafs	Apium graveolens Linn	10g
15.	Zarawand Taweel	Aristolochia rotunda	10g
16.	Habbe-e-Balsan	Balanites aegyptiaca	10g
17.	Ood Hindi	Aquilaria agallocha	10g
18.	Qaranfal	Eugenia Aromatica	10g
19.	Heel Khurd	Elettaria cardamomum	10g
20.	Gul-e-Surkh	Rosa	200g
21.	Asal or Qand Safaid	Saccharum offinarum	Q S

Study Design

An open-label, pilot clinical study.

Place of Study

The present study, which was approved by the Institutional Ethics Committee (IEC), was carried out on the patients of Tashhamul Kabid (Fatty liver) in General Out Patients Department of Central Research Institute of Unani Medicine, Lucknow from March 2019 to October 2019. All selected patients had given written consent before their enrollment for this study.

Selection Criteria

Inclusion Criteria

- Patients of either sex in the age group of 18 to 65 years
- Diagnosed case of fatty liver through ultrasonography.
- Patients not taking any other drugs for the treatment of fatty liver

Exclusion Criteria (Any of the following)

- Inflammatory Bowel Disease e.g. ulcerative colitis, *Crohn's* Disease
- Palpable abdominal mass
- History of Zollinger Ellison syndrome
- History of sudden weight loss
- History of long-term medication
- Known cases of cancer, anemia/ hematemesis/ melaena
- Known cases of severe hepatic, renal or cardiac ailments
- Diabetes Mellitus
- H/o addiction (tobacco chewing, smoking, alcohol, drugs)
- Pregnancy and lactation

Selection of Patients

The patients who met the inclusion / exclusion criteria and had Ultra Sonography report for abdominal discomfort and heaviness with presence of associated symptoms of Tashhamul Kabid (NAFLD) like nausea, abdominal tenderness, anorexia, general weakness, were selected for their treatment with Majoon Dabidulward.

Treatment Details

All selected patients as per the inclusion / exclusion criteria were treated with Majoon Dabidulward in the dose of 7 grams twice daily for 21 days.

Clinical Evaluation

The effects of Majoon Dabidulward were assessed on objective and subjective parameters of Tashhamul Kabid. Ultra Sonography report of patients were of Grade 1, Grade 2 and Grade 3 fatty liver. The clinical parameters of the disease like nausea, abdominal tenderness, anorexia and general weakness, which were differing in severity (such as absent, mild, moderate or severe) from patient to patient, were graded as absent =0, mild= 1, moderate=2, severe=3 for appropriate assessment and

statistical evaluation of the efficacy of Unani compound formulation. The temperaments of the patients were also assessed as per details given in Unani classical literature.

Safety Assessment

The safety was assessed by monitoring adverse events as reported by the patients or elicited by the investigator by clinical as well as laboratory investigations before and after treatment.

Statistical Analysis

All data were statistically analyzed by applying paired 't' test to evaluate the efficacy and safety of the drugs. Probability level of less than 5% was considered as statistically significant.

OSERVATIONS

19 subjects were selected for the study. Demographic characteristics of the patients, who were divided into various treatment groups to observe the prevalence of the disease are given in Table-2 . It was observed that high incidence of the disease was found in people of age groups 21-30. Among the 19 selected patients, 06 (31.58 %) were male and 13 (68.42%) were female and patients with vegetarian and non-vegetarian dietary habits were 03 (15.79%) and 16 (84.21%) respectively. It was observed that prevalence of the disease was relatively high among the female and people having non vegetarian dietary habits.

It was observed that incidence of disease was relatively lower in high income group, high in middle income group and nil in low income group. It was also observed that the incidence of the disease was higher among the people, who adopted sedentary life styles. Incidence of the disease was also found high among the people having irregular bowel habits. It was observed that prevalence of the disease was highest i.e. 13 (68.42%) in urban areas but lowest i.e. 01 (5.26) in rural areas.

Table 2: Demographic characteristics of the patients.

Total No. of Patients = 19,		Mean age of patients =
Characteristics	Treatment Groups	No. of Patients (%)
Age-group (in years)	21-30	07 (36.84)
	31-40	05 (26.32)
	41-50	03 (15.79)
	51-60	04 (21.05)
Gender	Male	06 (31.58)
	Female	13 (68.42)
Dietary Habits	Non-Vegetarian	16 (84.21)
	Vegetarian	03 (15.79)
Socio-economic Status	Lower income group	--
	Middle Income Group	17 (89.47)
	High Income Group	02 (10.53)
Education levels	Illiterate	04 (21.05)
	Primary	02 (10.53)
	Middle	02 (10.53)
	High School	--

	Inter mediate	03 (15.78)
	Graduate	06 (31.58)
	Post Graduate	02 (10.53)
Geographical Distribution	Urban	13 (68.42)
	Semi-Urban	05 (26.32)
	Rural	01 (5.26)
Mizaj (Temperament)	Safravi	08 (42.11)
	Saudawi	--
	Balghami	08 (42.11)
	Damvi	03 (15.78)
Look-wise	Well	17 (89.47)
	Unwell	02 (10.53)
Built type	Fatty	06 (31.58)
	Thin	03 (15.79)
	Normal	10 (52.63)
Life styles	Active	07 (68.42)
	Moderate	03 (26.32)
	Sedentary	09 (5.26)
Medical History	Regular Bowel Syndrome	07 (36.84)
	Irregular Bowel Syndrome	12 (63.16)

RESULT AND DISCUSSION

After treatment of Tashhamul Kabid (NAFLD) with Unani Pharmacopoeial formulation 'Majoon Dabidulward', it was found that clinical parameters of Tashhamul Kabid including abdominal tenderness, nausea, anorexia, general weakness and objective parameters of Ultra sonography report were significantly reduced by 42.98 %, 81.57%, 73.68%, 47.36% and 30.70% respectively as compared to base line finding (Table-3).

Our study demonstrated that people of all age groups have risk of Tashhamul Kabid (NAFLD). The prevalence of Tashhamul Kabid (NAFLD) is higher among the people having non vegetarian dietary habits. This finding of the study is supported by the study of Tina H et al, that vegetarians had less severe fibrosis than non-vegetarians. Vegetarian diets are associated with a lower risk of fatty liver.^[16]

The present study also demonstrated that people living sedentary life styles are the most affected people by this disease. As, the physical activity has beneficial effects on NAFLD by improving hepatic injury, hepatic fat, and histologic features of NAFLD, independent of weight loss therefore people living sedentary life are the most affected people. Physical activity supervision is the preferable method in the management of NAFLD patients.^[17]

The distribution of patients according to temperament have also been classified because in Unani Tibb, temperament is a notion of primary importance, through a difficult theory as it indicates the properties of an organ and human body as a whole. Temperament of a person represents its physical constitution and tendencies. It is believed in Unani Tibb that imbalance in temperament

predisposes human body to various diseases by producing a biotic imbalance within body. Causes of initial imbalance in temperament lies in more subtle elements of life like air, water, food, rest, activity, work, evacuation of wastes and sleep etc. and temperament acts as a guiding force for maintenance and preservation of individuals' health.^[18] Gastro Intestinal symptoms and bowel habits are common in liver cirrhosis as compare to healthy control. To determine the relation of bowel habits (Bowel Syndrome) with fatty liver, patients have been classified into regular and irregular bowel habits. The prevalence of the disease was relatively high in patients with irregular bowel habits. This observation is very closed to study of Antonella et al^[19] that Non-alcoholic fatty liver disease (NAFLD) and irritable bowel syndrome (IBS) are two very common diseases in the general population. There are no studies that highlight a direct link between NAFLD and IBS, but some recent reports have found an interesting correlation between obesity and IBS. Some Common mechanisms are involved in many of the local and systemic manifestation of NAFLD, leading to an increased cardiovascular risk, and IBS, which leads to microbial dysbiosis, impaired intestinal barrier and altered intestinal motility. It is not known, when considering local and systemic inflammation/immune system activation, which one has greater important in NAFLD and IBS pathogenesis.^[19]

After completion of the present study, it was found that the severity of associated symptoms of the Tashhamul Kabid (NAFLD) including abdominal tenderness, nausea, anorexia, general weakness and objective parameter of Ultra sonography report in the patients were significantly reduced by 42.98 %, 81.57%, 73.68%, 47.36% and 30.70% respectively as compared to base line. After treatment, highly significant ($p < 0.001$) reduction in Mean+/- SD scores of the associated symptoms of the disease including abdominal tenderness,

nausea, anorexia, general and weakness as compare to base line and also significant decrease in objective parameters of ultrasonography reports as compare to base-line, suggests that significant improvement in the associated symptoms of NAFLD in the patients was really due to therapy of the disease by the Unani Pharmacopoeial formulation. Reduction in severity and intensity of the associated symptoms of Fatty liver was on the ground of the treatment of the disease by the poly herbal Unani formulation 'Majoon Dabidulward', which is a unique Unani classical formulation and is used by Unani physicians since long times. The ingredients of the Unani classical formulation have mulatife, muarrique, Mudir-e-bol, mulallile awram and carminative effects. The ingredient Sumbul-ut-teeb (*Nardostachys jatamansi*

dc) has muqawwi, muharrik, daffe taffun and laxative effect. Mastagi (*Pistacia lobniscus* Linn) has pleasant smell, kasir-e-riyah (carminative) and hadhim (digestive) effects. Zafraan (*crocus sativus*) is hot and dry in temperament and act internally as daff-e taffun (antiseptic), muhallile awram (anti-inflammatory). Tabasheer (*Bambusa arundinacea*) has anti-inflammatory and anti-ulcer activity.

The present study has some limitations that it was a preliminary study and the sample size were very small. The study period of 21 days is also short period for observation of the improvement in grade of fatty liver. The further study of large sample size and for longer period of time is suggested.

Table 3: Efficacy of Majoon Dabidulward on the Clinical parameters of Tashhamul Kabid (NAFLD).

Parameters	(Mean ± SD) BT	(Mean ± SD) AT	Severity Reduction Percentage	P. Value	Results
Abdominal Tenderness	(1.63±0.68)	(1.00±0.75)	42.98 %	0.00001	significant at p<0.05
Nausea	(0.89±0.46)	(0.05±0.23)	81.57 %	<0.00001	significant at p<0.05
Anorexia	(1.05±0.62)	(0.16±0.37)	73.68 %	<0.00001	significant at p<0.05
General Weakness	(0.84±0.37)	(0.42±0.51)	47.36 %	0.003	significant at p<0.05
Ultra sonographic scores	(1.53 ±0.70)	(1.15 ± 0.90)	30.70 %	0.002	significant at p<0.05

CONCLUSION

On the ground of above observation, it can be concluded that Unani Pharmacopoeial Formulation Majoon Dabidulward is clinically effective and safe in the treatment of Tashhamul Kabid (NAFLD) and hence it can be prescribed to the patients.

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