Indian Journal of Traditional Knowledge
Vol 22(1), January 2023, pp 57-62
DOI: 10.56042/ijtk.v22i1.51840

An open label hepatoprotective activity of *Jawārish bisbāsā* in central obesity patients

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Received 30 June 2021; revised 20 September 2022; accepted 14 October 2022

Liver plays a major role in metabolism and excretion of xenobiotics. Liver dysfunction is a major health problem that challenges health care professionals, pharmaceutical industry and drug regulatory agencies. The most common symptoms are fatigue and discomfort in abdomen while in patients who are obese with BMI > 25, about one third have metabolic syndromes. The present clinical research was conducted in Regional Research Institute of Unani Medicine, Aligarh. The patients under trial were selected from GOPD of institute for obesity and it was observed that out of total registered patients' approx 28% have elevated liver enzymes from its normal range without any sign and symptom of hepatitis etc. Total 23 patients were selected from the study whose liver enzymes (SGOT, SGPT and ALP) were high at the baseline. Unani pharmacopoeial drug *Jawārish bisbāsā* 7 g daily was prescribed with lukewarm water in the morning and evening empty stomach for 8 weeks. At the end of study the result were compared with base line. It was observed that *Jawārish bisbāsā* significantly reduced the liver enzymes, e.g. SGOT, SGPT, Alkaline Phosphatase in comparison to baseline values. It may be concluded that *Jawārish bisbāsā* showed hepatoprotective effect in this clinical study.

Keywords: Clinical validation, Hepatoprotective, *Jawārish bisbāsā*, Unani medicine

IPC Code: Int Cl.[23]: A61K 36/00, A61K 9/00, A61P 1/16

Liver is one of the largest exocrine gland of human body and the chief site for intense metabolism and excretion. It has a surprising role in the maintenance, performance and regulating homeostasis of the body. It is involved with almost all the biochemical pathways to growth, immunity, nutrients, energy requirement and reproduction. The major functions of the liver are metabolism of food, detoxification, secretion of bile and storage of vitamin and metabolism of drugs. Thus, to maintain a healthy liver is a crucial factor for overall health and well-being. However, when it is continuously and variedly exposed to environmental toxins, chemicals like CCl_4, drug habits, alcohol, infections and autoimmune disorders, prescribed (antibiotics, chemotherapeutic agents) cum over-the-counter drugs can eventually lead to various liver ailments like hepatitis, cirrhosis and alcoholic liver disease[1-3].

Abnormal liver enzyme levels may signal liver damage or alteration in bile flow. Liver enzyme alteration may be either the accompanying biochemical picture in a patient with symptoms or signs suggestive of liver disease or an isolated, unexpected finding in a patient who has undergone a wide range of laboratory tests for a non-hepatic disease or for minor, vague complaints. The latter situation is a common clinical scenario today because of the routine incorporation of hepatic tests in automated blood chemistry panels[4].

Unani System of Medicine (USM) believes that the metabolism plays an important role for keeping an individual healthy. Most of the diseases are generated from the malfunctioning of digestives organs. Liver is the chief organ for metabolism of our food and drugs, all the medicine are metabolizes in the liver. Unani physicians emphasize on the metabolism and keep the liver as one of the vital organ for life. That is why they advocated keep the liver healthy for good health[5-10]. Unani classical literature is full of mono and poly-herbal hepatoprotective[11], cardioprotective[12], nephroprotective[13-16], neuroprotective[17-18], antihyperlipedemic[19], antileshmanial[20-21], antipsoriatic[22], lithotriptic[23] and antidiabetic[24] preparations. Therefore, many Unani single plant origin drugs are tested for its

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potential antioxidant and hepatoprotective liver damage in experimental animal model[25]. Simultaneously Unani medicine gives good results in RCT on various dieases[26].

The Central Council for Research in Unani Medicine (CCRUM) is an apex autonomous research organization, functioning under the Ministry of AYUSH, Government of India. The research programme of the CCRUM comprises of clinical research including RCT and validating the Unani medicines and therapies, which have been in use for centuries[27]. RRIUM, Aligarh is one of the important clinical research institutes, more than fifteen validation of pharmacopoeial programme are running at the centre[28].

Jawārish bisbāsā is a classical Unani Pharmacopeial formulation indicated for *zof-e-mida* (functional dyspepsia) *zof-e-hazm* (indigestion), *bawaseer-i-amya* (non bleeding piles), *nafakh-s-shikam* (flatulence) and *ghasyan* (nausea) due its action *muqawwi-e-mida* (gastrotonic), *kasir-e-riyah* (carminative) *daf-e-qai* (antiemetic)[29]. In experimental study, it was found safe in 90 days repeated oral dose toxicity on Wistar albino rats[30].

Objectives of the study

To observe the hepatoprotective activity of Unani pharmacopeial formulation *Jawārish bisbāsā* in central obesity patients.

Materials and Methods

A clinical validation study on *Jawārish bisbāsā* in cases of central obesity was conducted at RRIUM, Aligarh. In this clinical validation study total 173 patients were screened, out of which 129 were enrolled in the study. Total 49 cases were dropout for various reasons in achieveing the target of 80 complete cases[31]. Total 23 patients from the completed 80 cases of above said clinical validation study were selected whose SGOT, SGPT, Serum Alkaline Phosphatase were high but not a significant for any pathological condition. All the patients were having high levels of liver markers but not of limit to develop any clinical sign and symptoms of hepatotoxicity. As per the mentioned protocol, patients with the raised liver enzymes to 2.5 folds to the normal limit was allowed to enroll in the study. In enrolled cases, total 23 patients have raised liver enzymes but less than 2.5 folds of their normal values.

Ethical clearance and consent

The study was cleared by Institutional Ethics committee F.No. 5-11/2011-12/RRI/ALG/Tech/150 and registered under CTRI with REF/2018/08/021125AU at RRIUM, Aligarh. At the time of registration of human subjects a written consent was taken before enrolment in the study. All the human subjects were informed in advance regarding the test drug (*Jawārish bisbāsā*), dosage, time of intake, number of follow-ups, laboratory investigations and diet chart.

Type and location of study

An open label non comparative clinical validation study was conducted on central obesity patients at GOPD of RRIUM, Aligarh.

Duration of treatment

Duration of treatment was 8 weeks.

Test drug, route of administration and dose

The test drug (a pharmacopoieal preparation*)* *Jawārish bisbāsā* was given to all the patients 7 g twice a day with lukewarm water in empty stomach in the morning and evening for 8 weeks with fortnightly follow-up. The laboratory investigation was done at baseline, on first follow-up and at the end of the study. In the present presentation serological raised liver markers were taken and analyses for the hepatoprotective activity.

Statistical analysis

The values of different biochemical investigations were compared from Baseline to last follow-up. Results were statistically evaluated by applying Student's paired t test. The result was expressed as the Mean±SD. The data were analysed on Statistical Analysis System (SAS) (version 9.4) and Ms Excel 2019.

Results and Discussion

The study population comprised between 20-50 years of age. However the maximum incidence was found to be between 30-40 years of age followed by 20-30 years and than above 40 years of age. In age group of 20 to 30, years the male patients are more than the females. While in age group of 30-40 years females patients are more in comparison to male and in age group of more than forty years the male are more in comparison to female as shown in Fig. 1.

In this observation 61% patients were non vegetarians 35% were taking mixed diet and only 4% were vegetarians. This shows that the liver enzymes were high in non-vegetarians and mixed diet group as compared to vegetarian group as shown in Fig. 2.

According to religious status it is observed that 32% were Hindu and 68% were Muslim in the total sample size of study as shown in Fig. 3.

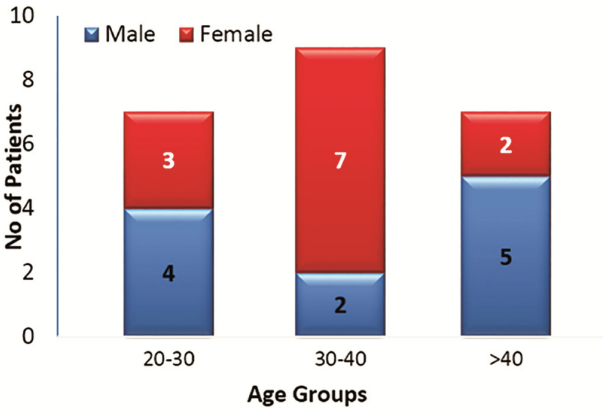

Fig. 1 — Age and sex wise distribution of patients

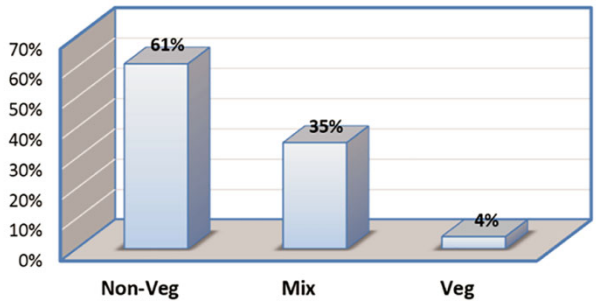

Fig. 2 — Distribution of patients according to their dietary status

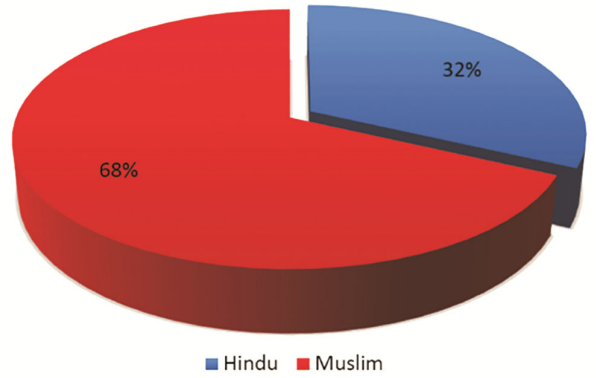

Fig. 3 — Religion wise distribution of patients

Temperament of an individual is an important aspect according to Unani philosophy. Physicians take into consideration for examination and prescription for any disease[5]. It is observed that maximum patients were from *Damvi* (Sanguine) temperament followed by *Balghami* (phlegmatic), *Safaravi* (bilious) and *Saudavi* (melancholic) 43%, 39%, 13% & 4% respectively as shown in Fig. 4.

It is observed that maximum were homemaker then service class followed by student and labour community 30%, 17% & 9% respectively. Whereas business class community were only 4% as shown in Fig. 5.

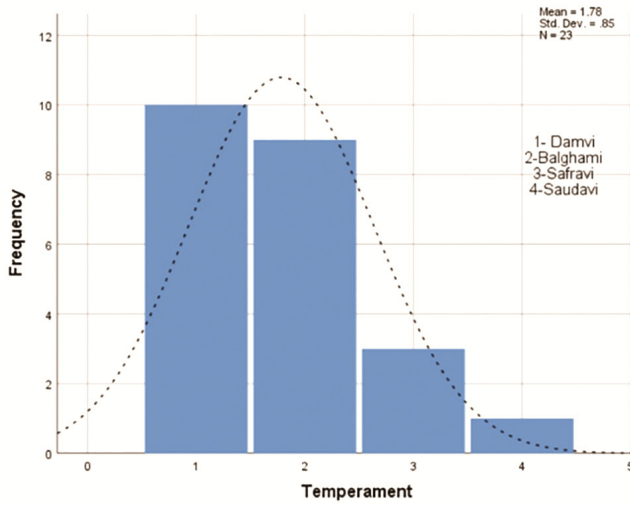

Fig. 4 — Distribution of patients according to temperament

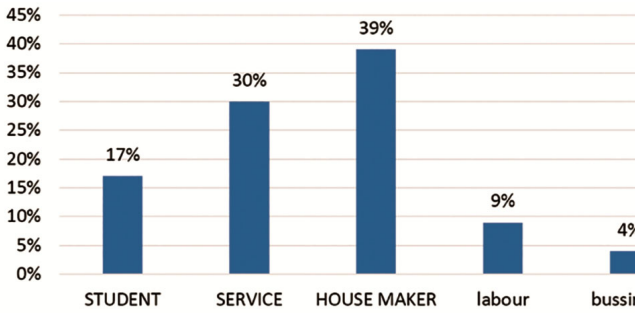

Fig. 5 — Distribution of patients according to occupation

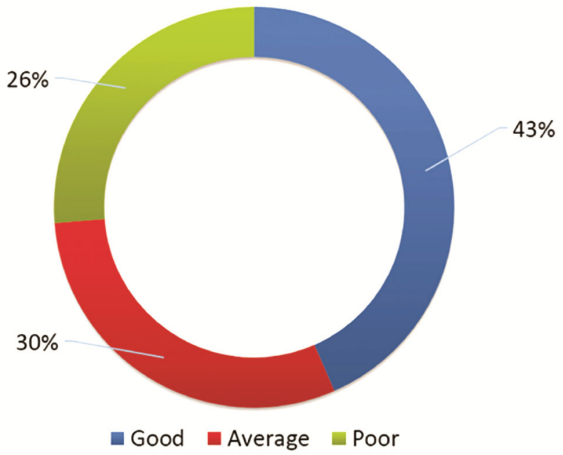

Fig. 6 — Distribution of patients according to socio-economic status

All patients were observed for their socio-economic status and it was observed that maximum patients from good socio-economic status followed by average and poor 43%, 30% and 26% respectively as shown in Fig. 6.

Table 1 — Effect of *Jawārish bisbāsā* on liver enzymes

Name of Parameter	Mean ± S.D. AT Baseline	1st Follow-up	After Treatment	95% Confidence Interval of the difference (BL vs AT)	Changes	t-statistics	p-value
SGOT IU/L	58.52±15.12	42.63±17.17	29.82±2.19	28.71 (20.76, 36.65)	↓	7.49	<0.001*
SGPT IU/L	67.01±23.16	51.78±22.67	40.52±20.85	26.47 (19.74, 33.21)	↓	8.15	<0.001*
ALP IU/L	130.66±29.79	90.67±34.58	85.72±25.41	44.93 (31.92, 57.95)	↓	7.16	<0.001*
S.BILI mg/dl	0.91±0.33	0.56±0.25	0.52±0.27	0.39 (0.26, 0.52)	↓	6.4	<0.001*

*Statistically significant

All the liver parameters were analyses at 95% confidence interval of difference from baseline to end of the study. As it is evident from the above tables that the mean serum bilirubin was 0.91 mg/dL before starting the treatment and after the treatment of 8 weeks with *Jawārish bisbāsā* there was change in decrease of 64% (0.56 mg/dL) in comparison to the base line. The mean SGOT was 58.52 IU/L at baseline and become 29.82 IU/L at the end of the study. Similarly mean SGPT was 67.01 IU/L at baseline and it become 40.52 IU/L after 8 weeks of treatment with the test drug. The ALP (Serum Alkaline Phosphatase) also reduces in compression to base line from 130.66 IU/L to 44.93 IU/L. All the changes from baseline to the end of the study are statistically significant of $p<0.001$. The changes in all the liver parameters showed that the drug is hepatoprotective as shown in Table 1.

This decrease in liver enzymes in comparison to baseline levels may be due to the ingredients of *Jawārish bisbāsā* mentioned as in Unani classical literature *mutayyab-e-dehan* (mouth freshener), *kasir-e-riyah* (carminative), *hazim* (digestive), *daf-e-qai wa gasyan* (anti emetic), *muqawwi-e-qalb* (cardiotonic), *moharrik-e-qalb* (cardiac stimulant), *daf-e-taffun* (antiseptic), *munaffis-e-balgham* (expectorant), *moharrik* (stimulant), *mushtahi* (appetizer), *muqawwi-e-deimagh wa asaab* (nervine tonic), *mudir-e-baul* (diuretics), *mudir-e-haiz* (emonogogue), *Mukhaddir* (sedative), *musakkin* (analgesic), *tiryaq-e-samoom* (antidote)[32-35]. The ingredient of *Jawārish bisbāsā* such as *Heel kalan* (*Amomum subulatum*)[36], *Bisbasa* (*Myristica fragrans* Houtt.)[37] *Saleekha* (*Cinnamomum cassia* Blume.)[38] *Heel Khurd* (*Elettaria cardamomum* (L) Maton)[39] *Zanjabeel* (*Zingiber officinale* Rosc.)[40] *Daarchini* (*Cinnamomum zeylanicum* Blume.)[41] *Asaaroon* (*Asarum europaeum* Linn.) *Filfil siyah* (*Piper nigrum* Linn.)[42] *Qaranfal* (*Syzygium aromaticum* (L.) Merr.)[43] showed hepatoprotective activity in different animal models. All these experiments proved the claims of Unani scholars as mentioned in literature.

The improvement in liver enzymes in comparison to baseline to end of the study may be due the complex effect as action mentioned in Unani classical literature and the hepatoprotective activity showed in different experimental models. This is the first ever claim of hepatoprotection of *Jawārish bisbāsā* in any clinical study.

Conclusion

On the basis of above results and discussion it can be concluded that *Jawārish bisbāsā* is effective in decreasing the liver enzymes markers in human studies. It is the first study for claiming its hepatoprotoective effect in clinical trial for *Jawārish bisbāsā* in a human subject treating for central obesity. *Jawārish bisbāsā* in a sugar based preparation of unani pharmacopeia. According to a survey of WHO India is going to be capital of diabetes mellitus and every fifth Indian will have type II DM in the near future[44]. Due to this problem unani scientists may think on alterative dosage form for different disease. Earlier some dosage form of classical unani formulations have been modified and found safe in safety evaluation[45]. It may be suggested a full-proof hepatoprotective research may be done on large sample size especially for hepatoprotection in hepatotoxic cases. Therefore, it can be concluded that the *Jawārish bisbāsā* can be safely used for the management of hepatitis however a study on larger sample size is required to elucidate the other pharmacological action and probable mechanism of action of *Jawārish bisbāsā*.

Acknowledgement

The authors are thankful to laboratory staff of the institute for technical support.

Conflicts of Interest

There are no conflicts of interest.

Author's Contributions

All the authors have made an ample role to the idea of the article, acquisition, analysis and interpretation of the data for the script.

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