Standardization of the finished product: *Habbe Irqun Nisa* - A Unani anti-inflammatory formulation

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Abstract

Background:

Habb (Pill) is one of the important dosage forms of Unani system of medicine. A number of effective formulations are manufactured in form of *Habb* because of its various advantages. Out of these, *Habbe Irqun Nisa* (HI) is a popular anti-inflammatory formulation used in the treatment of *Warame Mafasil* (arthritis) and *Irqun Nisa* (sciatica). Nowadays, with increased incidence of these diseases many non-steroidal anti-inflammatory drugs (NSAIDs) are being used in their treatment. Owing to the adverse effects of these drugs, the use of herbal medicines is seen as a better alternative. The basic requirement for the development of Unani system of Medicine is the standardization of single and compound drugs. HI is mentioned in National Formulary of Unani Medicne and selected for the present study.

Materials and Methods:

HI was prepared manually with the powder of crude drugs, passed through sieve no. 100 and mixed with 1% w/w of gum acacia in mucilage form. It was then dried at 60°C for 90 min and then tested for its standardization on different physicochemical parameters, e.g. organoleptic properties, pH values, moisture content, ash values, friability, hardness, weight variation, disintegration time, and thin layer chromatography (TLC).

Results and Conclusion:

The data evolved from this study will make it a validated product and will help in the quality control of other finished products in future research.

KEY WORDS: Anti-inflammatory, *Habb*, standardization, *Unani* system of medicine

INTRODUCTION

Habb (pill) is an ancient dosage form of Unani system of medicine invented by *Hakeem Seelon*.[1] Numbers of Unani formulations are prepared in the form of *Habb* and, out of these numerous *Huboob* (plural of *Habb*), *Habbe Irqun Nisa* (HI) is a very common and popular formulation that is mentioned in *Qarabadeene Azam* and National Formulary of Unani Medicine

(NFUM).[2,3] It consists of three crude drugs namely *Sibr*, *Post Halela Zard*, and *Suranjan Shirin*.[2,3] These plant drugs have various pharmacological activities. *Sibr* (dried juice of *Aloe barbadensis*) has analgesic,[4] anti-inflammatory,[4] and hepatotonic activity.[5] Post Halela Zard (dried pericarp of Terminalia chebula) has astringent,[6,7,8] diuretic,[5,9] and laxative[5,9] activity and it is also useful in gout and rheumatism.[5,9] *Suranjan Shirin* (dried corns of *Colchicum autumnale*) has analgesic[10] and anti-inflammatory activity,[5,10] and it is used in gout and rheumatism as well.[5,10] Apart from the pharmacological actions of its ingredients, HI as a compound formulation, is used as *muqawwie asab* (nervine tonic), *mulaiyin* (laxative), and *mohallile waram* (anti-inflammatory) and is also indicated in the treatment of *irqun nisa* (sciatica), *niqras* (gout), and *wajaul mafasil* (arthralgia).[2] It is a popular anti-inflammatory formulation of Unani system of medicine, but no quality control studies have been performed on it as yet. The rising popularity of herbal products, both as food and food supplements and as phytotherapeutic drugs, has given rise to many reports describing adverse health effects, variable quality, efficacy and contents of herbal products.[11] Thus, it has become essential to develop reliable, specific, and sensitive quality control methods using a combination of classical and modern methods of analysis. Standardization is essential for ensuring the quality control of the herbal drugs.[12] All the above mentioned factors that possibly act as drawbacks in the acceptance of the Unani formulations have necessitated the urgency for their standardization. This work was undertaken with the objective of evaluation and physicochemical standardization of a classical Unani anti-inflammatory formulation—HI.

MATERIALS AND METHODS

Preparation of Habbe Irqun Nisa

The method mentioned in NFUM was followed for the preparation of HI. The ingredients, *Sibr* (*Aloe barbadensis*), *Zard* (*Terminalia Chebula*), *Suranjan Shirin* (*Colchicum autumnale*) were taken in equal quantities of 5 g each, as mentioned in NFUM [Table 1].[2] The ingredients were procured from a crude drug dealer in Bangalore, and all of them were identified by an expert. Total 16 batches (each batch was prepared with 15 g of powder) of HI were prepared with different conditions, i.e., binder, particle size, time of drying, and temperature of drying. All 16 batches of HI were evaluated for hardness, friability, and disintegration time. The batch with minimum friability, hardness nearest to the standard value, and minimum disintegration time as per pharmacopoeias was selected as the final batch. All crude drugs of the selected final batch were ground into a powder with the help of an electric grinder and passed through sieve no. 100 to get powder of particle size of ≤ 150 μm.[13] *Loabe Samaghe Arabi* (gum acacia mucilage as binder) was prepared as per Pharmacopoeia of India, briefly, 4 ounces of gum acacia in small pieces was taken and added in 6 fluid ounces of water in a beaker, and the mixture was stirred frequently till the gum dissolved.[14] HI was prepared manually repeatedly for performing different tests with 15 g of the powder as sample in the laboratory of Department of Ilmul Saidla, NIUM, Bangalore as per the instructions given in NFUM.[2] After their preparation, they were dried in a hot air oven at the temperature of 60°C for a duration of 90 min.

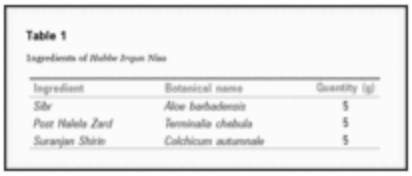

Table 1

Ingredients of *Habbe Irqun Nisa*

Ingredient	Botanical name	Quantity (g)
Sibr	*Aloe barbadensis*	5
Post Halela Zard	*Terminalia chebula*	5
Suranjan Shirin	*Colchicum autumnale*	5

Method of preparation of *Habbe Irqun Nisa* pills

HI was manually prepared in the form of pills (circular in shape). The powders of all ingredients of HI (15 g) were made into *lubdi* (dough) of proper consistency by adding sufficient quantity of *Loabe Samaghe Arabi gum acacia* (1% w/w). *Loabe Samaghe Arabi* was prepared by mixing 0.15 gm of *Samaghe Arabi* in 2.5 ml of DDW and this prepared Loab was mixed with 15 gm of powder. The *lubdi* was rolled by fingers into suitable size sticks. The sticks were measured by vernier calliper to maintain uniformity of size, and the thickness of sticks was kept as 6 mm. The sticks were cut manually into equal pieces with the help of a sharp knife to get small pieces of the desired size and weight. All the pieces were measured and weighed for consistency in size and weight. The cut pieces were rounded between the fingers to form *Huboob* (*pills*). The pills were placed in a hot air oven and dried. Loss of weight was equal in all pills after drying.

Standardization studies

1. The physicochemical studies carried out included the following parameters:
    - Organoleptic characters like appearance, color, smell, texture, taste
    - pH in 1% and 10% solution
    - Moisture content by toluene distillation method
    - Loss of weight on drying at 105°C for 5 hour
    - Ash values
    - Extractive values
    - Water and alcohol soluble matter
    - Total alkaloidal estimation
    - Weight variation test
    - Uniformity of diameter
    - Hardness test
    - Friability
    - Disintegration time.
2. Thin layer chromatography (TLC).

Physicochemical parameters

The prepared pills were evaluated for organoleptic characters based on the method described by Siddiqui *et al*.,[15] pH value of 1% solution and pH value of 10% solution,[16] moisture content,[17,18] loss of weight on drying at 105°C,[16,18] total ash, water soluble ash, acid insoluble ash,[18,19,20] successive and non-successive extractive values,[16] and alcohol and water soluble matter.[20] Alkaloidal estimation was done based on the method described by

Sutharsingh *et al*.[21] Twenty pills were randomly selected and their average weight was determined. The pills were also weighed individually. The deviation from the average weight in each case was calculated and expressed as percentage. The pills meet the test if no more than two pills were outside the percentage limit of 7.5%.[22] Uniformity of diameter was ensured by picking three pills randomly and the diameter being measured individually by using a Vernier calliper and expressed in millimeter.[23] Three pills were taken and they were individually tested for hardness by the Monsanto hardness tester in terms of kg/cm.[22,24] Friability of the pills was determined using Friability test apparatus (Roche's Friabilator) and expressed in percentage.[22,25] The rate of disintegration was measured by a disintegration-testing apparatus manufactured as per USP using double distilled water as media maintained at 37°C. Each of the six pills were placed separately in the six cylinders of the two-basket rack assemblies of the disintegration apparatus. Particles of the pills were noted by naked eye and time was noted when all the particles were passed out through the sieve of cylinder. Digital apparatus was used having inbuilt thermometer to measure the temperature.[22,24]

Thin layer chromatography

TLC was carried out on TLC pre-coated aluminium plates, silica gel 60 F 254 (layer thickness 0.25 mm) for alcoholic extract of HI in n-hexane: acetone (7.6:2.4) as the mobile phase.[26]

The alcoholic extract of HI was prepared by the hot extraction method, i.e., soxhlet extraction method. The HI was ground and converted into coarse powder, 10 g of this powder and 200 ml of ethanol was taken in the ratio of 1:20. The whole process was allowed to run until the solution in the siphon tube of the extraction chamber of the soxhlet extractor became colorless. It took about 5 hours to complete the procedure. Proper spotting was only possible by using concentrated liquid, otherwise the spots are very light Therefore the liquid mixture was filtered and allowed to get slightly concentrated by heating on the water bath.

The Rf values of the spots were calculated by the following formula.

$$R_F \text{ value} = \frac{\text{Distance traveled by the spot}}{\text{Distance traveled by the solvent}}$$

RESULTS

The organoleptic characteristics, i.e., appearance, color, smell, texture, and taste of HI were found to be spherical pill-like, dark brown, pleasant and sweet, hard, and slight bitter and astringent, respectively, as given [Figure 1] and [Table 2]. Average weight was found to be 244.8 ± 2.12 mg [Table 3]. Average diameter was 7.00 ± 0.00 mm [Table 4]. Average hardness of pills was 4.33 ± 0.33 kg/cm [Table 5]. Friability was found to be 0.18 ± 0.04% [Table 6]. pH was found to be 4.78 ± 0.01 in 1% aqueous solution and 4.35 ± 0.01 in 10% aqueous solution [Table 7]. Moisture content was 8.17 ± 0.17% w/w [Table 8]. Loss of weight on drying was 11.50 ± 0.10% w/w [Table 9]. Total ash, acid insoluble ash, and water soluble ash of HI were found to be 4.59 ± 0.31%, 2.06 ± 0.09%, and 2.68 ± 0.06% w/w, respectively, [Table 10]. Alcohol and water soluble content were found to be 5.95 ± 0.15% and 46.00 ± 0.19% w/w, respectively[Table 11].

Non-successive extractive values were found to be 40.51 ± 0.28% and 25.39 ± 0.12% w/w with water and alcohol, respectively [Table 12]. Successive extractive values were found to be 0.07 ± 0.00%, 0.46 ± 0.03%, and 22.67 ± 0.18% w/w with petroleum ether, chloroform and alcohol, respectively [Table 13]. Disintegration time was 32.67 ± 0.88 min [Table 14]. Total alkaloidal estimation was 0.59 ± 0.00% w/w [Table 15]. In TLC two spots were found in HI and their Rf Values were found to be 0.42 and 0.72 [Figure 2] [Table 16].

Figure 1
Sample of *Habbe Irqun Nisa* prepared in the laboratory of Department of *Ilmul Saidla*

Table 2

Organoleptic description of Habbe Irqun Nisa

Appearance	Pill
Color	Dark brown
Smell	Pleasant and sweet
Texture	Hard
Taste	Slightly bitter and astringent

Table 2
Organoleptic description of *Habbe Irqun Nisa*

Table 3

Weight variation of Habbe Irqun Nisa

Serial no.	Weight of individual Habb (mg)	Difference in weight of individual Habb and average weight of Habb (mg)	Weight variation (%)
1	255	12.03	4.95
2	239	3.97	1.63
3	246	3.03	1.24
4	228	14.97	6.16
5	259	16.03	6.59
6	257	14.03	5.77
7	239	3.97	1.63
8	244	1.03	0.42

Table 3
Weight variation of *Habbe Irqun Nisa*

Table 4

Diameter of Habbe Irqun Nisa

Serial no.	Diameter of pill (mm)
1	7.0
2	7.0
3	7.0
Mean ± SEM	7.0 ± 0.00

Table 4
Diameter of *Habbe Irqun Nisa*

Table 5

Hardness of Habbe Irqun Nisa

Serial no.	Hardness (kg/cm)
1	5
2	4
3	4
Mean ± SEM	4.33 ± 0.33

Table 5
Hardness of *Habbe Irqun Nisa*

Table 6

Friability of *Habbe Irqun Nisa*

Serial no.	Friability (%)
1	0.14
2	0.14
3	0.25
Mean ± SEM	0.18 ± 0.04

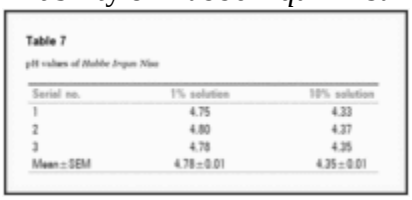

Table 7

pH values of *Habbe Irqun Nisa*

Serial no.	1% solution	10% solution
1	4.75	4.33
2	4.80	4.37
3	4.78	4.35
Mean ± SEM	4.78 ± 0.01	4.35 ± 0.01

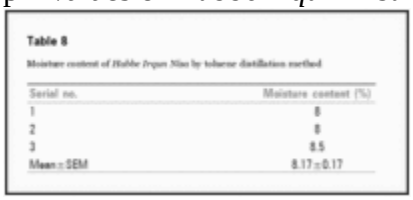

Table 8

Moisture content of *Habbe Irqun Nisa* by toluene distillation method

Serial no.	Moisture content (%)
1	8
2	8
3	8.5
Mean ± SEM	8.17 ± 0.17

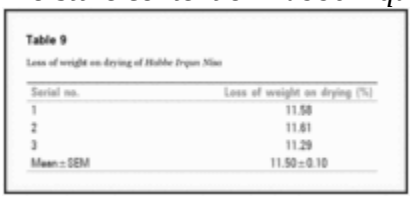

Table 9

Loss of weight on drying of *Habbe Irqun Nisa*

Serial no.	Loss of weight on drying (%)
1	11.58
2	11.61
3	11.29
Mean ± SEM	11.50 ± 0.10

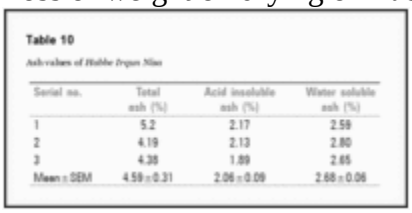

Table 10

Ash values of *Habbe Irqun Nisa*

Serial no.	Total ash (%)	Acid insoluble ash (%)	Water soluble ash (%)
1	5.2	2.17	2.59
2	4.19	2.13	2.80
3	4.38	1.89	2.65
Mean ± SEM	4.59 ± 0.31	2.06 ± 0.09	2.68 ± 0.06

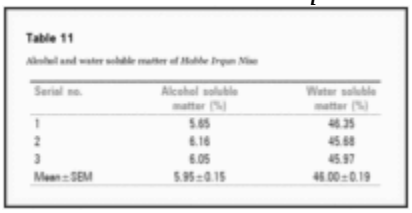

Table 11

Alcohol and water soluble matter of *Habbe Irqun Nisa*

Serial no.	Alcohol soluble matter (%)	Water soluble matter (%)
1	5.65	46.35
2	6.16	45.68
3	6.05	45.97
Mean ± SEM	5.95 ± 0.15	46.00 ± 0.19

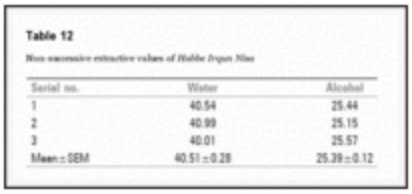

Table 12

Non-successive extractive values of *Habbe Irqun Nisa*

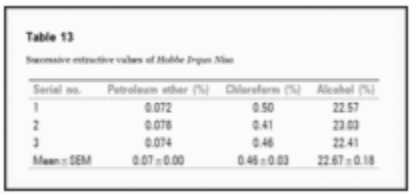

Table 13

Successive extractive values of *Habbe Irqun Nisa*

Table 14

Disintegration time of *Habbe Irqun Nisa*

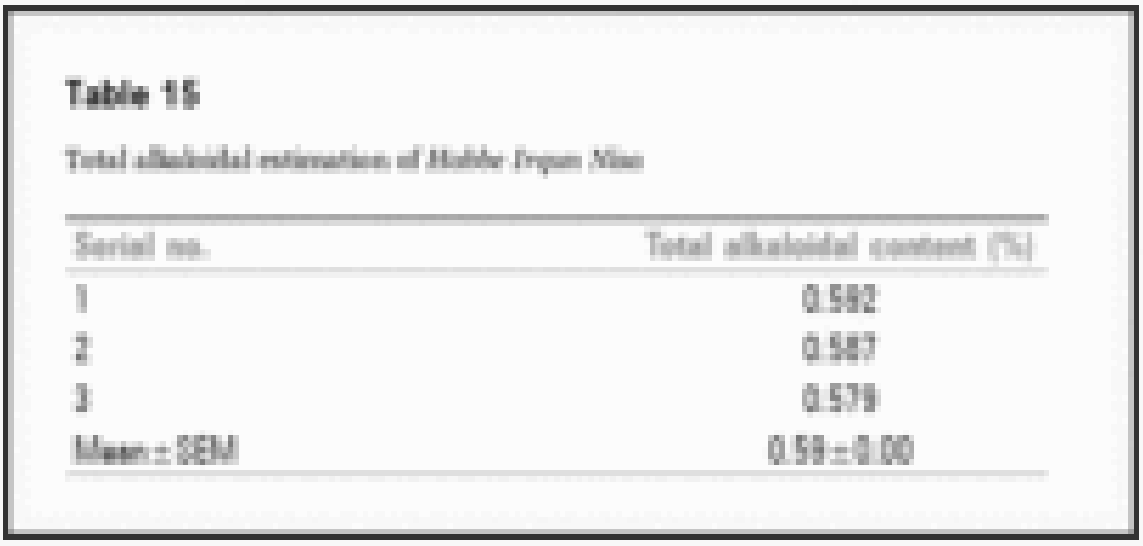

Table 15

Total alkaloidal estimation of *Habbe Irqun Nisa*

Figure 2
Thin layer chromatography of *Habbe Irqun Nisa*

Table 16
TLC of *Habbe Irqun Nisa*

Extract	Solvent	No. of spots	R_f value	Color
Ethanol	n-hexane: acetone (7.6:2.4)	2	0.42 and 0.72	Dark yellow and light yellow

TLC=Thin layer chromatography

DISCUSSION

Organoleptic properties can be used for rapid identification of the drug and these help to determine the quality of drugs.[22] The organoleptic characteristics, i.e. appearance, color, smell, texture, and taste of HI, were found to be spherical pill-like, dark brown, pleasant and sweet, hard, bitter, and astringent, respectively.

pH value of the drug is also an important parameter. Drugs that are weak acids are better absorbed from the stomach than from the upper intestine.[27] It was found to be 4.78 ± 0.01 in 1% aqueous solution and 4.35 ± 0.01 in 10% aqueous solution and both were weakly acidic.

The moisture content indicates the quality of the drug and also its efficacy.[28] Excessive moisture content becomes an ideal medium for the growth of different types of bacteria as well as fungi, which subsequently reduce the purity of the drug. The percentage of moisture content

was found to be 8.17 ± 0.17%. Moisture may vary in same drug due to different climatic conditions and quantity of moisture is different in same climatic condition in different drugs. Presence of 8.17% of moisture is acceptable and it is the standard fixed for future batches, if prepared, in the same climatic condition.

Loss of weight on drying at 105°C is done to determine the amount of water, all or a part of the water of crystallization or volatile matter in the sample, which is removed during drying,[29] and it was found to be 11.50 ± 0.10%.

The ash value of the drug is an important parameter for the detection of impurities and adulteration. Hence, ash value determination furnishes a basis of determining the identity and purity of the drug and gives information related to its adulteration with inorganic matter.[17] The mean percentage values of the total ash, acid insoluble ash, and water soluble ash of HI were found to be 4.59 ± 0.31%, 2.06 ± 0.09%, and 2.68 ± 0.06%, respectively. These are the ash values of compound formulation made up of several ingredients. References or Data regarding the ash values of compound formulation are not available by which the confirmation of purity or impurity is possible. Hence on the basis of Ash value of compound formulation, it cannot be concluded that this drug is pure or impure, unless or otherwise all the ingredients of compound formulation have been properly checked. In this preparation, first identity and purity of all the ingredients was confirmed by various parameters and after confirmation compound drug was prepared. Ash Value of the compound drug only indicates the presence of this much ash in this particular drug which may be helpful for future batches.

Extractive values in the different solvents are based on the quantities of different chemical constituents that are soluble in them. It is an important test to check the quality of the drug and any variation in the chemical constituents leads to a change in the extractive values.[28] The mean percentage of the non-successive extractive values of HI were found to be 40.51 ± 0.28% and 25.39 ± 0.12% with water and alcohol, respectively, and successive extractive values were found to be 0.07 ± 0.00%, 0.46 ± 0.03%, and 22.67 ± 0.18% with petroleum ether, chloroform, and alcohol, respectively. This is the standard fixed of Habbe Irqun Nisa for future references.

Water and Alcohol soluble matter. In some cases, the amount of drug soluble in a given solvent is an index of its purity, e.g., acacia must yield not more than 1% of water insoluble residue to meet the official requirement.[17] The mean percentage of alcohol and water soluble content were found to be 5.95 ± 0.15% and 46.00 ± 0.19%, respectively. There is no range of extractive values, these values indicates the amount of soluble constituents in particular drug in the given solvent. If reference of extractive value of a particular drug in a given solvent is available, then it can be say that this value is under, over or within the range by comparing the reference value. Above data shows the extractive values of compound formulation and these values may be taken as standard values for future batches.

Estimation of quantity of alkaloids A slight deficiency of alkaloid in a preparation may cause a marked decrease in physiological effect; on the other hand, a slight excess may cause toxic effects when the preparation is administered. It therefore follows that the accurate estimation of the quantity of alkaloids present in a medicinal substance is an important subdivision of pharmaceutical analysis.[17] The mean value of total alkaloidal estimation was found to be 0.59

± 0.00%. Literature of all the ingredients shows that there is no any toxic alkaloid present in the ingredients. So it can be concluded that this range is acceptable.

Weight variation test is done to help ensure that a pill contains the proper amount of drug that helps to maintain the good quality and good efficacy of the pill.[22] Only one pill was found to be out of the limit of ±7.5%. Hence, the percentage weight variation of the laboratory samples was found to be within the prescribed pharamacopoeial limits of ±7.5%.[22] The mean weight value was found to be 244.8 ± 2.12 mg.

Uniformity of diameter of the circular hand-made pills was also measured. The mean value of the diameter was found to be 7.00 ± 0.00 mm.

Hardness test is done to determine the force needed to fracture or break the specimen along its diameter.[30] The mean value of the hardness was found to be 4.33 ± 0.33 kg/cm, which is above 4 kg/cm, the minimum acceptable hardness for uncoated tablets.[24]

Friability test is done to find out the possible reduction in the weight of solid dosage forms as a result of mechanical erosion during handling.[30] The mean percentage of friability was found to be 0.18 ± 0.04%, which is very good in comparison to the maximum permissible limit of 1%.[22]

Disintegration test is done to determine whether tablets, capsules, and pills disintegrate within the prescribed time when placed in a liquid medium at the experimental conditions.[29] The mean value was found to be 32.67 ± 0.88 min and is close to the 30 min mentioned as a limit for the uncoated tablets.[22,24]

TLC is one of the important parameter used for detecting adulteration for judging the quality of the drugs. Two spots were found in HI and their Rf values were found to be 0.42 and 0.72, respectively. As confirmatory test for identification and purity of all the ingredients was also done before preparing the compound formulation, therefore, it is clear that this preparation was made by all pure ingredients. Rf values only indicates that, if any one, will prepare this formulation with the same ingredients, the Rf Values should be same.

Footnotes

Source of Support: Nil.

Conflict of Interest: None declared.

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