

Development of standard operating procedures of Habbe Shifa: A polyherbal Unani formulation

Asira Tarannum, Shariq Shamsi, Roohi Zaman

Department of Ilmul Saidla (Unani Pharmacy), National Institute of Unani Medicine, Bangalore, Karnataka, India

ABSTRACT

Background: Unani medicines are being used since antiquity. However, in spite of their efficacy, they have been widely criticized due to lack of standardization and poor quality presentation. For this reason, application of good manufacturing practices and development of standard operating procedures (SOPs) in the manufacture of herbal medicines became an essential tool to assure their quality. **Objectives:** Therefore, the objective of the study was to develop the SOP of Habbe Shifa (HS) regarding the particle size (PS), binder, temperature of drying, and duration of drying. **Materials and Methods:** In this study, 24 batches of HS were prepared according to the instructions given in formulary to develop SOP. Three particle sizes (i.e., 80, 100, and 120 No. Mesh sieve), were taken for preparation of pills. Water and Samaghe Arabi (Gum Acacia mucilage [GAM]) were used as binder for preparing the lubdi (mass) in different batches. Different temperature and duration of drying were used to dry the pills in hot air oven to get satisfactory results. All the batches were assessed three times for hardness, friability, and disintegration time and mean regarded as standard parameter value. **Results and Conclusion:** The batch with 150 μm PS (100 mesh sieve), 5% w/w GAM used as a binder, dried at 90°C for 120 min showed hardness 3.50 ± 0.00 kg/cm, friability $0.02 \pm 0.003\%$, and disintegration time 25.00 ± 0.57 min, which showed most appropriate result among all batches and considered as final batch. Its SOP may be used for future reference which can help in setting up regulatory limit to assure the quality of Unani medicines.

Key words: Binder, duration of drying, particle size, standard operating procedures, temperature of drying

INTRODUCTION

Herbal medicines are prepared from materials of herbal origin, which are often obtained from varied geographical and/or commercial sources. As a result, it may not always be possible to ascertain the conditions to which they may have been subjected. In addition, they may vary in composition and properties. Furthermore, the procedures and techniques used in the manufacture and quality control of herbal medicines are often substantially

different from those employed for conventional pharmaceutical products. Because of complex nature of naturally grown medicinal plants, often variable nature of cultivated ones, contamination with toxic medicinal plants and the number and small quantity of defined active ingredients, the production and primary processing has a direct influence on the quality of herbal medicines.^[1]

Although World Health Organization has developed guidelines for the quality control of herbal drugs, which provide a detailed description of the techniques and measures required for the appropriate cultivation and collection of medicinal plants, there is still a lacuna between this available knowledge and implementation. Herbal medicines have been used for thousands of years, basic research programmes need to be focused on the quality assurance. To overcome contaminations from pesticide residues and heavy metals, there should be control measures to implement necessary standard operating procedures (SOP) at source.^[2]

The Unani (Greco-Arab) system of medicine has been practiced since ancient times for the treatment of range of diseases. Buqrat's (Hippocrate), the father of medicine, medical principles of the doctor-patient relationship are still followed today.^[3] Unani medicines are being used since

Address for correspondence:

Dr. Asira Tarannum, 1403, Katra Shahanshah, Farash Khana, Delhi - 110 006, India.

E-mail: dr.asira@gmail.com

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centuries but until now no scientific methods have been adopted to develop SOPs for preparation of Unani dosage forms. It is very important to develop SOPs for producing good quality Unani drugs. In spite of their efficacy, they have been widely criticized due to lack of standardization and poor quality presentation. Lack of quality standards and problems in preparing or testing the Unani drugs are the main hurdles experienced by both patients and physicians.

The concept of SOPs is a part of good manufacturing practices (GMP) and it is commonly used in pharmaceutical industry. SOP is an authorized written procedure giving instructions for performing operations not necessarily specific to a given product or material (e.g., equipment operation, maintenance and cleaning; validation; cleaning of premises and environmental control; and sampling and inspection). Certain SOPs may be used to supplement product-specific master and batch production documentation.^[1] The introduction of SOPs in the community pharmacies will bring many benefits and provide an opportunity to demonstrate professionalism and responsibilities. Pharmacists should make SOPs to cover different activities/functions that are carried out in their premises, taking into consideration the laws and regulations, and these are always kept in mind while writing and following SOPs.^[4]

Habb (Pill) is one of the earliest solid unit dosage forms and invented by ancient Unani physicians. Habbe Shifa (HS) is an important pharmacopoeial Unani formulation which is widely used in the treatment of *Humma* (fever), *Iya* (fatigue), *Tashannuje rewi* (pulmonary spasm), *Zeequn Nafas* (asthma), and opium de-addiction.^[5-7] Therefore, in this study, SOP of HS regarding the particle size (PS), binder, temperature of drying, and duration of drying were developed.

MATERIALS AND METHODS

Ingredients of habbe shifa

The ingredients of HS as per National Formulary of Unani Medicine (NFUM) are Tukhme dhatura (seeds of *Datura stramonium*), Rewandchini (roots of *Rheum emodi*), Zanjabeel or Sonth (roots of *Zingiber officinale*), and Samaghe Arabi (gum of *Acacia arabica*).^[6]

Procurement of raw drugs

The ingredients of HS were procured from the registered crude drug dealer, Bangalore, and all the crude drugs were identified and authenticated by the botanist of National Institute of Unani Medicine (NIUM), Bangalore. Voucher specimens of all the ingredients were deposited in the Drug Museum of NIUM for future reference (under Voucher Number 01/SA/Res/2012).

Preparation of powders of different particle size

All crude drugs were grounded with the help of an electric grinder and passed through sieve No. 80, 100, and 120 to get powders of different dimensions (less than or equal to 177, 150, and 125 μm , respectively)^[8,9] for preparing different batches of HS with different particle size (PS) to develop SOP regarding PS.

Preparation of loabe samaghe arabi GAM

As per NFUM, various binders can be used for preparation of Huboob (pills). Thus, two different binders were taken in study, i.e., Loabe Samaghe Arabi (GAM) and water for preparation of different batches of HS GAM was prepared as per Pharmacopoeia of India by following method.^[10]

Gum Acacia in small pieces, four ounces (1 ounce = 28.34 g), and water six fluid ounces were taken. The gum and water were put in a beaker and stirred frequently until the gum is dissolved.

Preparation of huboob (Pills)

Totally, 24 batches of HS were prepared under varied conditions according to the instructions prescribed in NFUM. Twelve batches were prepared in which double distilled water (DDW) was used as rabeta (binder) and other twelve batches were prepared in which Loabe Samaghe Arabi (5% w/w) was used as rabeta (binder) with variation in PS, temperature of drying, and duration of drying. Each batch was prepared as follows:

- The powders of all ingredients of HS (17.5 g in each batch) were made into lubdi (mass) of sufficient consistency by adding sufficient quantity of DDW (10 mL) or Loabe Samaghe Arabi (5% w/w) in different batches
- The lubdi was rolled into suitable size sticks by fingers. The thickness of the sticks was measured by vernier calliper; to maintain the uniformity, the thickness of sticks was kept 7 mm
- The sticks were cut into equal pieces with the help of a knife to get the pills of desired size and weight
- The cut pieces were rounded between the fingers to shape the huboob of required size
- The pills were kept in hot air oven and dried in it at different conditions, i.e., 80°C for 100 min, 80°C for 120 min, 90°C for 100 min, and 90°C for 120 min [Table 1].

Assessment of all batches

Each batch was assessed 3 times for hardness, friability, and disintegration time and mean regarded as standard parameter value.

Hardness test

Hardness of pills was evaluated by Monsanto hardness tester (Shital Scientific Industries, Mumbai). Hardness was

Table 1: Batches of Habbe Shifa

Batch no.	Method of preparation				
	Sieve no.	Particle size	Binder	Temp. of drying	Duration of (µm) (°C) drying (min)
1	80	177	DDW	80	100
2	80	177	DDW	80	120
3	80	177	DDW	90	100
4	80	177	DDW	90	120
5	80	177	GAM	80	100
6	80	177	GAM	80	120
7	80	177	GAM	90	100
8	80	177	GAM	90	120
9	100	150	DDW	80	100
10	100	150	DDW	80	120
11	100	150	DDW	90	100
12	100	150	DDW	90	120
13	100	150	GAM	80	100
14	100	150	GAM	80	120
15	100	150	GAM	90	100
16	100	150	GAM	90	120
17	120	125	DDW	80	100
18	120	125	DDW	80	120
19	120	125	DDW	90	100
20	120	125	DDW	90	120
21	120	125	GAM	80	100
22	120	125	GAM	80	120
23	120	125	GAM	90	100
24	120	125	GAM	90	120

DDW=Double distilled water, GAM=Gum acacia mucilage

performed on three tablets in all instances, and the average values were recorded.^[11]

Friability test

Friability of the pills was determined using Roche's Friability test apparatus also called Friabilator (Labinda Tab Friability Tester, Mumbai). The friability (f) is calculated by the formula:

$$f = \left(1 - \frac{W}{W_0} \right) \times 100$$

where W is the weight of the pills before the test and W_0 is the weight of the pills after the test. The procedure was repeated three times and the mean value was calculated.^[11,12]

Determination of disintegration time

The rate of disintegration was measured by a double six-cylinder basket rack assembly, disintegration-testing apparatus (TAB machines disintegration tester model Tablet Density – 20S) as per United States Pharmacopoeia (USP) using the two media. (the aqueous as well as acidic media). Simulated gastric fluid (pH about 1.2) was prepared without enzyme by dissolving 1 g of NaCl in 500 mL of deionized water, adding 7 mL of concentrated HCL, and diluting the volume to 1,000 mL with water. For measurement in aqueous medium, DDW was taken.^[11,13]

RESULTS

SOP for manufacturing process of HS was developed by assessing each batch three times for hardness, friability, and disintegration time and mean regarded as standard parameter value. The results of all batches are given in Table 2. The batch with PS 150 µm (100 mesh sieve), in which 5% w/w GAM used as a binder, dried at 90°C for 120 min, showed hardness 3.50 ± 0.00 kg/cm, friability $0.02 \pm 0.003\%$, and disintegration time 25.00 ± 0.57 min, showed most appropriate result among all the batches and was selected as a final batch and all of its conditions regarding PS, binder, temperature, and duration of drying were considered as its SOP.

DISCUSSION

Unani medicines are effective but the standardization of these formulations is essential in order to assess the quality of drugs. The development of SOPs is an essential tool to assure the quality of medicines.

PS plays an important role in dissolution of drug. Dissolution rate is directly proportional to the surface area of the drug. Since the surface area increases with the decrease in PS, higher dissolution rate may be achieved

Table 2: Results of all batches of Habbe Shifa

B.no.	Method of preparation				Hardness (kg/cm) mean±SEM	Friability (%) mean±SEM	Disintegration time (min) mean±SEM
	Particle size (µm)	Binder	Temp of during (°C)	Duration of during (min)			
1	177	DDW	80	100	2.33±0.16	0.30±0.03	16.66±0.33
2	177	DDW	80	120	2.33±0.16	0.12±0.02	17.33±0.66
3	177	DDW	90	100	2.33±0.16	0.13±0.0117	33±0.66
4	177	DDW	90	120	2.50±0.00	0.07±0.04	17.66±0.33
5	177	GAM	80	100	2.33±0.16	0.03±0.003	17.00±0.57
6	177	GAM	80	120	2.50±0.00	0.06±0.03	18.00±0.00
7	177	GAM	90	100	2.66±0.16	0.03±0.003	18.33±0.33
8	177	GAM	90	120	3.00±0.00	0.03±0.003	18.00±0.57
9	150	DDW	80	100	2.50±0.00	0.14±0.006	17.66±0.66
10	150	DDW	80	120	2.66±0.16	0.11±0.006	17.66±0.66
11	150	DDW	90	100	3.00±0.00	0.03±0.006	19.66±0.33
12	150	DDW	90	120	3.16±0.16	0.11±0.006	21.00±0.00
13	150	GAM	80	100	3.00±0.00	0.11±0.006	22.33±0.33
14	150	GAM	80	120	3.16±0.16	0.12±0.008	22.00±0.57
15	150	GAM	90	100	3.33±0.16	0.04±0.008	23.33±0.33
16	150	GAM	90	120	3.50±0.00	0.02±0.003	25.00±0.57
17	125	DDW	80	100	3.16±0.16	0.06±0.005	24.66±0.66
18	125	DDW	80	120	3.00±0.00	0.05±0.008	25.66±0.33
19	125	DDW	90	100	3.16±0.16	0.05±0.003	26.33±0.33
20	125	DDW	90	120	3.33±0.16	0.04±0.003	26.33±0.33
21	125	GAM	80	100	3.33±0.16	0.04±0.005	26.00±0.57
22	125	GAM	80	120	3.33±0.16	0.03±0.003	27.00±1.00
23	125	GAM	90	100	3.50±0.00	0.03±0.006	29.00±0.57
24	125	GAM	90	120	3.50±0.00	0.03±0.003	29.33±0.33

DDW=Double distilled water, GAM=Gum acacia mucilage

through the reduction of PS.^[8] Binder, temperature, and duration of drying also play an important role in friability, hardness, and disintegration time of pills or tablets. The hardness and friability are important parameters for determining the mechanical strength of pills. These two parameters evaluate the ability of the pill or tablet to withstand abrasion in packaging, handling, and shipping.^[8] Drying is most commonly used in pharmaceutical manufacturing as a unit process in the preparation of different dosage forms. Drying helps in preservation of drugs by minimizing mould and bacterial growth in moisture laden material.^[11] Unfortunately, the operation of drying is taken for granted and SOPs regarding the temperature of drying and duration of drying are not developed in the preparation of huboob (Pills) or any other dosage form.

Hardness is a measure of resistance of a solid dosage form to mechanical deforming. The resistance of the tablet or pill to shipping, abrasion or breakage under conditions of storage, transportation, and handling before usage depend on its hardness.^[8] Friability is also another important measure of tablet's strength. Conventional compressed tablets that lose 0.5-1% of their weight are generally considered acceptable.^[11] Disintegration test is used to determine whether tablet or pill disintegrate within

the prescribed time when placed in a liquid medium at the experimental conditions.^[14] This test is useful as a quality assurance tool for conventional (non-sustained release) dosage forms. Uncoated USP tablets have disintegration time standards as low as 5 min, but the majority of tablets have a maximum disintegration time of 30 min.^[11]

Twenty-four batches, which were prepared with different PS, showed variable results because the surface area of drug particles, which is an important parameter that influences drug dissolution, and in turn drug absorption. Smaller particles with greater surface area dissolve more rapidly than larger particles, even though both have the same intrinsic solubility.^[11] It was observed that reducing the PS increases the disintegration time because reducing the PS while maintaining a constant solid content causes a colloidal system to have a higher particle density. When PS decreases, the average interparticle distance also decreases significantly. Since the magnitude of interparticle forces depends inversely upon separation distance, the force exerted on a given particle by all particles is greater if the average interparticle distance is small. Conversely, at low particle density, the average interparticle distance is relatively large so that the particles are less influenced by each other.^[11] Therefore, when PS decreases, the interparticle distance decrease and interparticle forces

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increases and pills take more time to disintegrate on reduction of PS. Thus, the batch with minimum friability under the range of 1%, hardness nearest to the standard value (standard value is 4 kg/cm), and considerable disintegration time (under stated standard duration of 30 min) was selected as a final batch.

CONCLUSION

It can be concluded that the procedure used to prepare the final batch, i.e., 150 µm PS (100 mesh sieve), 5% w/w GAM used as a binder, dried at 90°C for 120 min may be taken as the SOP for future references in regard to the process standardization and GMP of the pill and it may also help in further studies for establishing regulatory limit to assure the quality of Unani medicine.

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REFERENCES

1. Anonymous. WHO guidelines on good manufacturing practices (GMP) for herbal medicines. Geneva: World Health Organization; 2007. p. 2-3.
2. Aneesh TP, Hisham M, Sekhar MS, Madhu M, Deepa TV. International market scenario of traditional Indian herbal drugs – India declining. *Int J Green Pharm* 2009;3:184-90.
3. Mayer D. A brief history of medicine and statistics. *Essential Evidence-Based Medicine*. 1st ed. Cambridge University Press;

2004. p. 3.
4. Anonymous. Standard Operating Procedures (SOPs) in Community Pharmacies Article Review. *Pharmaceutical Newsletter*, Sultanate of Oman, Ministry of Health 2007;15:1-3.
5. Arzani HM. *Amraz-e-Sar.Qarabadeene Quadri*. New Delhi: Ejaz publishing House; 1998. p. 26.
6. Anonymous. *Compound Formulation – Huboob & Aqras. National Formulary of Unani Medicine*. (English ed). Part I. New Delhi: Ministry of Health and Family Welfare; 2006. p. 31.
7. Said HM. *Huboob. Hamdard Pharmacopeia of Eastern Medicine*. Delhi: Sri Satguru Publications; 1997. p. 106.
8. Anonymous. Chapter 35. Dissolution, Chapter 37. Powder, Chapter 45. Oral Solid Dosage Form. *Remington; The Science and Practice of Pharmacy*. 21st ed., Vol. 1. B.I Publications Pvt. Ltd, Delhi; 2006. p. 675, 710, 916-918.
9. Anonymous. *Indian Pharmacopoeia*. Vol. 1. Ghaziabad: Indian Pharmacopoeia Commission; 2007. p. 20.
10. Waring EJ. *Vegetable Materia Medica. Pharmacopoeia of India*. Delhi: Asiatic Publishing House; 2010. p. 62.
11. Lachman L, Lieberman HA, Kanig JL. Chapter 221-Biopharmaceutics, Chapter 47, Chapter 115 - Basic chemical principles related to suspension and emulsion dosage form, Chapter 297 – 301. *Tablets. The Theory and Practice of Industrial Pharmacy*. 3rd ed. Mumbai: Varghese Publishing House; 2008. p. 47, 115, 221, 297-301.
12. Vijaya KS, Mishra DN. Rapidly disintegration oral tablets of Meloxicam. *Indian Drugs* 2006;43:117-21.
13. Anonymous. *Food and Drug Regulations*. U.S.A: Minister of Health; 1989.
14. Anonymous. *The United States Pharmacopoeia (USP 32) NF 27*. Vol. I. Washington DC: The USP Convention, Rockville; 2009. p. 262.

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