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# Development of (SOPs) standard operating procedure regarding manufacturing processes of Habbe Kafoori

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**Abstract**
**Objectives:** There are no specified Standard Operating Procedures (SOPs) regarding manufacturing processes of most of the Unani compounds mentioned in the books of Unani System of Medicine. It is a need of hour to develop their Standard Operating Procedures for their manufacturing which is essential to maintain the quality control, avoiding batch to batch variation. Therefore present study was designed to develop the SOPs of *Habbe Kafoori* (HK) which is used in "*Hummae Moharraqa* and *Hummae Diqe Mewi*".
**Methods:** Eight batches of HK were prepared according to the general instructions given in the formulary. To develop SOPs of HK; particle size (100 no. mesh sieve) was taken. Binder (Water and Loabe Behidana) were used for preparation of *lubdi*. Different temperature of drying and duration of drying were carried out to dry the pills in hot air oven. Three parameters were taken for development of SOPs includes, hardness test, friability test and disintegration time. All the batches were assessed three times for hardness disintegration time and friability and mean was taken as standard parameter value.
**Results and Conclusion:** The developed SOP of HK is as follows: particle size 100 number mesh sieve, binder mucilage of 1.79% w/w Loabe Behidana and DDW 10 ml, temperature of drying 60°C and duration of drying 30 minutes. Hardness 6.57 ± 0.09 kg/cm and friability 0.09 ± 0.01% which was most appropriate result among all the batches and considered as final batch. The procedures used to prepare the final selected batches among all the batches of the lab samples may be used the SOPs for future references.

**Keywords:** Qarabadeen, standard operating procedures, Habbe Kafoori

## Introduction
India is perhaps the largest producer of medicinal herbs and is rightfully called the "Botanical Garden of the World". India also has a very unique position in the world, where a number of recognized indigenous systems of medicine *viz*. Ayurveda, Siddha, Unani, Homeopathy, Yoga and Naturopathy are being utilized for the health care of people. One reason for the popularity and acceptability is belief that all natural products are safe. The demand for plant based medicines, health products, pharmaceuticals, food supplement, cosmetics etc. are increasing in both developing and developed countries, due to the growing recognition that the natural products are non-toxic, have less side effects [1].
Unani System of Medicine, which is an important part of AYUSH is being practiced since a long time. It is shocking that same formulation prepared by different companies varies and possess different organoleptic properties. There is a need of improvement in manufacturing processes and dispensing of drugs.
WHO has emphasized the need to ensure quality control of medicinal plant products by using modern techniques and by applying suitable parameters and standards.
If proper guidelines/SOPs of manufacturing are followed then there is less or no chance that the compound formulations supplied have different organoleptic properties. If each individual and every Unani pharmaceutical company follow the SOPs of manufacturing processes of compound formulations then prepared medicine from each company must have same characteristics. Since there are no specific SOPs regarding manufacturing procedure available at present. There is a need to develop the SOPs of each and every compound formulation and then to follow these developed SOPs in future. So batch to batch variation in the same company and variation in the same product manufactured by different companies can be avoided.
In view of above discussion there is an urgent need to develop the SOPs of at least all the compound formulations present in the Qarabadeen approved by the Government of India.
Keeping in view of all these factors it becomes evident that development of scientific

protocol such as SOPs of Unani formulations are prerequisite in quality control of single and as well as compound formulations. In order to lay out the SOPs for preparation of Habbe Kafoori, eight batches were prepared at the lab scale by adopting the GMP guide lines.

## Materials and Methods

The method mentioned in NFUM was followed for the preparation of Habbe Kafoori [2, 3].

### Ingredients

| | | | |
|---|---|---|---|
| 1. | Kafoor | (*Cinnamomum camphora*) | 3g |
| 2. | Tabasheer | (*Bambusa arundinacea*) | 5g |
| 3. | Nishasta | (*Triticum sativum*) | 5g |
| 4. | Sandal Safaid | (*Santalum album*) | 5g |
| 5. | Maghze Tukhme Kadu | (*Lagenaria siceraria*) | 5g |
| 6. | Kateera | (*Cochlospermum gossypium*) | 5g |
| 7. | Luabe Behidana | (*Cydonia oblonga*) | Q.S. |

### Procurement of raw drugs

The ingredients of HK (Habbe Kafoori) were procured from the authorized herbalist raw drug dealer in Bangalore, and all the crude drugs were identified by the Guide. Voucher specimens no. 21/IS/Res./2014 was deposited in the drug museum of NIUM. Preliminary evaluation of all the ingredients was done to check the authenticity of ingredients and the results of laboratory investigations were compared with the standard limits.

### Preparation of powders in required particle size

All crude drugs were powdered with the help of an electric grinder and passed through sieve no. 100 to get powders of particle size of dimension less or equal to 150 µm for preparing different batches of HK.

### Preparation of Loab (Mucilage)

As per NFUM various binders such as water, loabe Behidana, Loabe Samaghe Arabi and Loabe Aspaghol are used for the preparation of huboob. Though all the binders have their own importance. Only two binders namely water and loabe behidana were selected for preparation of different batches of HK. Loabe Behidana was prepared by taking 0.5 gm *Tukhme behidana* and adding 20 ml of DDW soaked for overnight and 20 ml of loabe behidana was collected which was used for preparation of Habbe Kafori.

### Preparation of different batches of Habbe Kafoori

Total eight batches of HK (*Habbe Kafoori*) were prepared under different conditions. Four batches were prepared in which DDW (Double Distilled Water) 11 ml was used as rabeta (binder) and other four batches were prepared in which loabe behidana (1.79% w/w) i.e. 0.5 ml of loabe behidana was used as binder in which 10 ml DDW was added for lubdi preparation. Particle size, temperature of drying and duration of drying were different variables adopted in the preparation of different batches. Each batch was prepared as follows

1. Lubdi for four batches of HK were prepared with 28 gm powder and DDW 11 ml and lubdi for another four batches were prepared with 28 gm powder and *Loabe Behidana*(1.79% w/w) and DDW 10 ml.
2. The lubdi was rolled by fingers into suitable size sticks. The sticks were measured by vernier calliper to maintain the uniformity and the thickness of sticks was kept as 10 mm.
3. The sticks were cut manually into equal pieces with the help of a sharp knife to get the small pieces of desired size and weight.
4. The cut pieces were rounded between the fingers to form the Huboob.
5. The pills were kept in hot air oven and dried in it at different conditions i.e. 60 °C for 30 min, 60 °C for 60 min, 70 °C for 30 min and 70°C for 60 min. (Table 1)

**Fig 1:** Sample of Habbe Kafoori

### Development of standard operating procedure (SOP):

All the eight batches of HK were evaluated thrice for hardness, friability and disintegration time. The mean values of these tests were considered as the standard parametric values of the respective batch. Hardness, and friability of the pills were evaluated by Monsanto hardness tester (Shital Scientific Industries, Mumbai), and Roche's friabilator (Labinda Tab Friability Tester, Mumbai) and Disintegration testing apparatus manufactured as per USP respectively. The batch with minimum friability, and hardness nearest to standard value was selected as final batch. Methodology used in the preparation of selected final batch was considered as its Standard Operating Procedure. So, all conditions regarding particle size, binder, temperature of drying and time of drying used in the preparation of final batch was considered as its Standard Operating Procedures.

### Standard operating procedure for manufacturing process of Habbe Kafoori

1. 28 gm accurately weighed powder of the formulation of HK was taken and passed through sieve No. 100 as mentioned in NFUM.
2. *Loabe Behidana* was prepared by mixing 2.5% w/w of *Tukhme Behidana* in 20 ml of DDW, and from this prepared *loab* 0.5 ml was added and 10 ml DDW mixed.
3. The *lubdi* of proper consistency was prepared by mixing 28 gm of drug powder with *loabe behidana* (1.79% w/w).
4. The *lubdi* was rolled with fingers into sticks having uniform diameter of 10 mm. The thickness was maintained by vernier calliper. Stick of this diameter was finally prepared by the stick making machine. Pills of required size were prepared by pill making machine.
5. The Huboob were kept in the clean dry Petri dish and dried in the oven at the temperature of 60°C for 30 minutes.

**Table 1:** SOPs of different batches of Habbe Kafoori Material and methods

| Batch No. | Method of preparation | | | | |
|---|---|---|---|---|---|
| | Sieve No. | Particle size (µm) | Binder | Temperature (°C) | Drying Time (minutes) |
| 1 | 100 | 150 | DDW | 60 | 30 |
| 2 | 100 | 150 | DDW | 60 | 60 |
| 3 | 100 | 150 | DDW | 70 | 30 |
| 4 | 100 | 150 | DDW | 70 | 60 |
| **5** | 100 | 150 | LB+DDW | 60 | 30 |
| 6 | 100 | 150 | LB+DDW | 60 | 60 |
| 7 | 100 | 150 | LB+DDW | 70 | 30 |
| 8 | 100 | 150 | LB+DDW | 70 | 60 |

DDW =Double Distilled Water, LB =Loabe Behidana

**Hardness test**

Three pills were taken and they were individually tested for the hardness by the Monsanto hardness tester in terms of kg/cm. [4, 5]

**Friability test**

Friability of the pills was determined using Friability test apparatus (Roche's Friabilator). This device subjects the pills to the combined effect of abrasions and shock in a plastic chamber revolving at 25 rpm and dropping the pill at a height of 6 inches in each revolution. Pre weighed sample of pills was placed in the friabilator and were subjected to 100 revolutions. Pills were de-dusted using a soft muslin cloth and reweighed. The friability (*f*) was 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 $W_o$ is the weight of the pills after the test [5, 6].

**Disintegration Time**

The rate of disintegration was measured by Disintegration-testing apparatus manufactured as per USP using DDW as the medium at 37 $^0$C. Each of six pills was placed separately in the six cylinders of the two basket rack assemblies of the disintegration apparatus [4, 5].

**Observations and Results**

**Standardization of raw material:** Preliminary evaluation of all the ingredients was also done to check the authenticity of ingredients and the results of laboratory investigations were compared with the standard limits. All the results were found complied with the standard limits. Thereafter authentication and assessment of all the batches were started.

**Assessment of all batches of Habbe Kafoori**

Standard Operating Procedure for manufacturing process of *Habbe Kafoori* was developed by assessing each batch three times for hardness and friability and disintegration time. The batch with minimum friability, hardness nearest to the standard value was selected as final batch. *Habbe Kafoori* was not disintegrated within permissible limit of WHO so it is not considered for the final batch. Results of all batches are tabulated in (Table 2, Figure 1 and 2). Then their results were compared and finally the Batch No. 5 with 150 micron particle size (100 mesh sieve), mucilage of 1.79% w/w *loabe behidana* (binder), dried at 60 °C for 30 minutes was selected as final batch. So, all conditions regarding particle size, binder, temperature of drying and time of drying used in the preparation of final batch were fixed as its Standard Operating Procedures. The mean value of the hardness was found to be 6.57 ± 0.09 kg/cm, friability was found to be 0.09 ± 0.01 (Bold letters in Table 2). Finished product are shown in figure 1.

**Table 2:** Observations of all batches of Habbe Kafoori

| B. No. | Method of Preparation | | | | Hardness (kg/cm) | Friability (%) | Disintegration Time |
|---|---|---|---|---|---|---|---|
| | Sieve Number | Binder | Temp. of Drying (°C) | Duration of Drying (min) | Mean ± SEM | Mean ± SEM | Mean ± SEM |
| 1. | 100 | DDW | 60 | 30 | 7.17 ± 0.02 | 0.09 ± 0.01 | 180 |
| 2. | 100 | DDW | 60 | 60 | 8.07 ± 0.15 | 0.05 ± 0.02 | 180 |
| 3. | 100 | DDW | 70 | 30 | 8.9 ± 0.15 | 0.07 ± 0.02 | 180 |
| 4. | 100 | DDW | 70 | 60 | 10.43 ± 0.35 | 0.05 ± 0.03 | 180 |
| 5. | 100 | LB+DDW | 60 | 30 | 6.57 ± 0.12 | 0.05 ± 0.01 | 180 |
| 6. | 100 | LB+DDW | 60 | 60 | 8.77 ± 0.23 | 0.06 ± 0.02 | 180 |
| 7. | 100 | LB+DDW | 70 | 30 | 9.00 ± 0.12 | 0.05 ± 0.01 | 180 |
| 8. | 100 | LB+DDW | 70 | 60 | 12.47 ± 0.41 | 0.06 ± 0.01 | 180 |

DDW - Double Distilled Water LB – Loabe Behidana

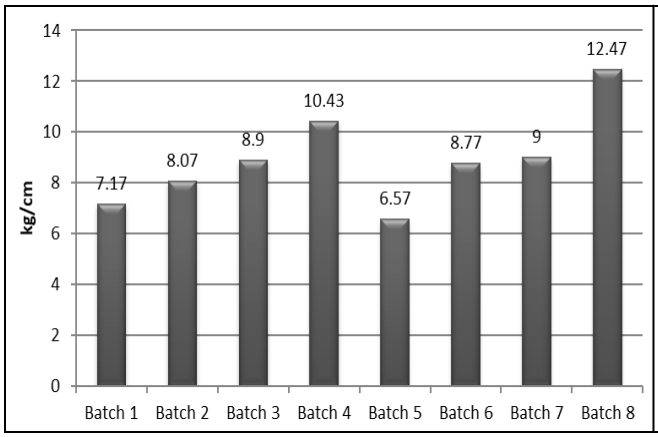


**Fig 2:** Hardness of all batches of Habbe Kafoori

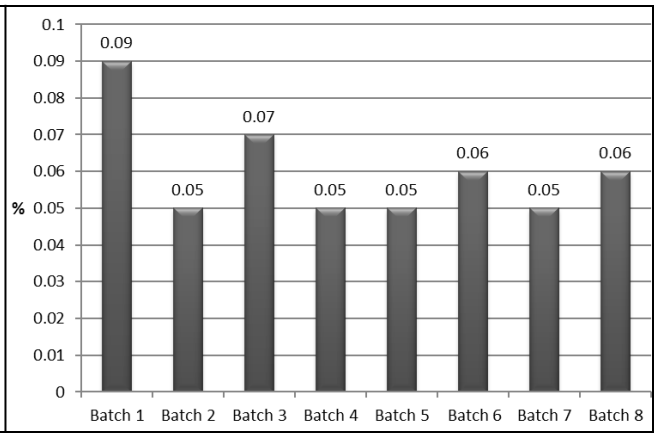


**Fig 3:** Friability of all batches of Habbe Kafoori

## Discussion

Four variables which affects the quality of the Huboob were taken into consideration i.e. binder, particle size, time of drying and temperature of drying.

The first trial was done using 28 gm of powder of particle size (150 µm) was taken and mixed with mucilage of 3.57% Luabe Behidana (binder) but the lubdi was too sticky because some ingredients of HK are mucilaginous, hence the stickiness was increased. Therefore preparation of lubdi was tried with different concentration of mucilage. It was found that proper lubdi was prepared with 1.79% w/w of mucilage and 10 ml of DDW. Small portion of this lubdi was taken and rolled by fingers to form suitable size sticks and to maintain the uniformity in the thickness of sticks, they were measured by the vernier calliper and the thickness of 10 mm was kept and then they were cut with knife. Initially the weight of pills was maintained at 650 mg because the formula contained Kafoor and Sandal which are volatile in nature and comparatively more quantity of water hence there will be loss of weight on drying, so keeping this point in mind the weight of the pills was kept more.

Four batches were prepared using the above composition of concentration of mucilage 1.79% and DDW 10 ml, dried in hot air oven in different variables of temperature and duration. The conditions maintained were 60 $^0$C for 30 min, 60 $^0$C for 60 min, 70 $^0$C for 30 min and 70 $^0$C for 60 min. and batches were finally selected based on the hardness and friability. During testing for disintegration time it was noted that the pills did not disintegrate according to the prescribed time of 30 min. and it was noted that the pills did not disintegrate even at 3 hours in aqueous and acidic medium, so it was decided to delete Kateera from the formula because when the literature for Kateera was reviewed it was found that Kateera does not dissolve in water but it swells and it dissolves in 50% $H_2SO_4$ [7]. Therefore when HK was prepared excluding Kateera from the formulation it was found that the pills disintegrated within 25 min.

Further another four bathes were prepared using water 11 ml as binder and powder 28 gm of 150 µm size and dried under the same condition 60 $^0$C for 30 min, 60 $^0$C for 60 min, 70 $^0$C for 30 min and 70 $^0$C for 60 min.

So, finally eight different batches of Habbe Kafoori were prepared four batches with 1.79% w/w of loabe behidana and 10 ml DDW. The next four batches of Habbe Kafoori were prepared with only DDW 11 ml. All the eight batches of Habbe Kafoori were evaluated for hardness, friability and disintegration but disintegration time test was not considered for the SOP of HK as HK did not disintegrate according to the prescribed time due to reason mentioned above.

Hardness of three huboob from each batch was taken and its mean was considered. Friability test was done thrice from each batch. Finally the batch with the permissible limit of friability under the range of 1%, and hardness nearest to normal range between 4-6 was taken as a final batch and all its conditions regarding particle size, binder, temperature of drying and duration of drying were considered as its SOP.

Standard Operating Procedures (SOPs) of HK was developed on the basis of four different variables (Particle size, Binder, Temperature of Drying and Duration of Drying). Finally the SOPs of Habbe Kafoori developed are as follows (28 gm crude drug powder passed through 100 mesh sieve and kernel of seeds triturated in kharal mixed with mucilage of 1.79% w/w loabe behidana and 10 ml DDW as binder and dried at 60°C for 30 minutes).

Taking this study into account it is also recommended to the regulatory and statutory authorities to exclude Kateera from the formulation due to its failure to disintegrate and dissolve.

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**Conflicts of Interest:** No

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