REVIEW ARTICLE

Industrial approach of process validation of Bharjana (frying) process WSR to *Eranda Bhrishta Haritaki*: An experimental observation

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Abstract

Eranda Bhrishta Haritaki (EBH) is popularly used Ayurvedic medicine indicate in the management of *Vatavyadhi*, *Amavata* (rheumatoid arthritis), *Grudhrasi* (sciatica) which lacks of documentation of parameters of standardization, especially in process standardization. In the present study, few economic, desirable parameters of its Standard Manufacturing Process at industrial level are identified and observed. Randomized observations of two major (½ quintal each referring to large scale) and 18 sub-batches of EBH of pharmacy department, Gujarat Ayurved University, Jamnagar, Gujarat were made. Immature *Haritaki* was classified as per parameters quoted in *Bhavaprakasha* and formulation EBH prepared from it was divided into 2 groups as per heating pattern (increasing degree of heating from Group A and B) and subdivided into three subgroup on the basis of its size and studied their quality parameters. Percentage of yield in weight in two batch and three sub-batches 74%, 83.62%, 82.05%, and 71.20%, 83.80%, and 78.40%, respectively. The maximum yield is found in medium size *Haritaki*. In physiochemical parameter, there was no major changes was observed except Ash value. The study concludes if proportion of standard ingredients, batch size, equipment, duration and pattern of frying and frequency of stirring is kept constant the procedure can be validated by proper regulation of heat.

Key words: *Eranda Bhrishta Haritaki, Gandharva Haritaki, Haritaki, Treminaliachebula,* Castor oil

INTRODUCTION

Ayurvedic medicine implies knowledge and practice of herbal healing for the prevention, diagnosis, and elimination of physical, mental, or social imbalance. The cost for health care are rising at an alarming rate throughout the world, at the same time, the world market for phytopharmcaeutical is growing steadily pharmaceutical standardization of *Rasaushadhis* (herbo-metallic and herbo-mineral preparations) can be defined with the number of processes, involved in the production of a drug. The standard protocols mentioned in the classics,[1] which may be applied to the present manufacturing scientific pharmaceutical ambience, such as quality of raw materials[2] to be taken for the process. The process standardization protocols are such as temperature, time space, instruments, and heating devices. along with purification protocols like number of levigation,[3] *Swedana* (steam heating)[4] etc. and the finished drug protocol[5] such as color, and fineness. Validation[6] of the method of preparation is to be performed by manufacturing the same product by similar method and instrumentation, for any number of times, with standard raw material getting output of same product with specification of parameters. Comparative pharmaceutical standardization supports in understanding the difference between two manufacturing process. It also helps to know the reason behind the different preparative process of single formulation.

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Ancient Ayurvedic Pharmaceutics mostly dealt with small scale production as there medicines were prepared by Vaidya himself. A slight modifications in the procedures were also found in different traditions of medicine preparations. In today's era, patients are being attracted towards Ayurveda, thus, large scale production is needed which can be achieved through industrial scale production. The range of operating parameters may defer in production at small scale and at the industrial level. *Eranda Bhrishta Haritaki* (EBH), synonymously known as *Gandharva Haritaki* is popular Ayurvedic formulation indicated in the management of pain in *Amavata* (rheumatoid arthritis), *Grudhrasi* (sciatica), *Ardita* (facial paralysis).[7] The formulation also therapeutically used as per the indication of single drugs it consists, that is, *Haritaki (Terminalia chebula)* and *Eranda (Ricinus communis)* castor oil. The formulation is used for *Anulomana* (Carminative) *Vruddhi, Vatavyadhi, Ajirna* (indigestion),[8,9] etc. An average utilization of EBH at Gujarat Ayurved University Jamnagar is approximately a quintal per month. Due to large scale production, easy availability and method of preparation, there is need to establish the standard manufacturing procedure and their quality parameters for the EBH formulations so as to minimize batch to batch variation and to maintain their quality and therapeutic efficacy.

Aim and Objective

1. To identify and document desired, recordable parameters for process validation of Bharjana (frying) on industrial level WSR to EBH.
2. To document some industrially applicable, economic, sensitive, and quality parameters of standardization of EBH for industrial level production.

MATERIALS AND METHODS

The study was carried out as random process monitoring of industrial manufacture of EBH at Pharmacy Department and modified laboratorial methods at the Department of RS & BK, IPGT & RA, GAU, Jamnagar. Immature *Haritaki* was identified and randomly selected and fried in Erand taila (castor oil). After frying, fried *Haritaki* was powered and sieved through 100 mesh size. The duration of heating and size play a major role for the preparation of EBH. For the standardization purpose, two batches were planned on the basis of the size of immature *Haritaki* and the time duration of heating. Immature *Haritaki* was divided into three sub-batches on the basis of their size as small, medium, and big. The average size of small, medium, and big *Haritaki* is 0.8775 cm, 1.516 cm, and 1.9 cm, respectively. The two batches A and B are planned on the basis the heating time duration. In Batch A, the time duration and frequency of heating are less in comparison to Batch B. Percent distribution of raw immature (Bal/Chhoti) *Haritaki* at Pharmacy of GAU, Jamnagar on the basis of floatability, size, shape, color, and ridges was noted as these parameters are used for the classification of *Haritaki* in Ayurvedic classics. Dimensions of vessels, the quantity of ingredients, duration of heating, temperature inside the pan during frying, physicochemical parameters of ingredients before and after experiment were recorded. A total of 470 kg of raw, immature *Haritaki* was processed for frying in two Batches A, and B. Among batch A and B, three sub-batches are divided on the basis of their size, and each sub-batches are again divided into three batches for the development of SMP and validation.

Observations of total 3 batches and randomly selected sub-batches by 3 different operators were evaluated. In batch "A", the sub-batch size and % of castor oil, duration of heating was less as that of batch "B", whereas in batch "C" batch size was in between A and B and proportion of ingredients was same as that of batch "B" but duration and frequency of heating was more and intensity of heating was comparatively low.

OBSERVATION AND RESULTS

As per material and method, we prepare the three batches of EBH. In this batches, the distribution of *Bala* (raw immature) *Haritaki* and Its average dimensions was depicted in Table 1. In this size of small *Haritaki* in 3 batches was found to be 0.877, 0.928, 0.983 cm respectively, medium *Haritaki* in 3 batches was found to be 1.516, 1.781, 1.821 cm respectively and big size *Haritaki* in 3 batches was found to be 1.9, 11.78, 2.5 cm respectively. The distribution of *Haritaki* (*T. chebula* L.). As per floatability character depicted in Table 2. The percentage of floatable *Haritaki* was found to be 72.64% and non floatable was found to be 28.64%. The observation during process of EBH of both the batches are depicted in Tables 3 and 4. In both the table we observe the *Haritaki* qty. in kg, castor oil in ml, temp of bottom of the vessel, temp on upper surface, duration of heating in min, EBH powder percentage yield. The organoleptic character of EBH was depicted in Table 5. The physicochemical parameters of EBH powder such as ash value, water soluble

Table 1: Distribution of *Bala* (raw immature) *Haritaki* and its average dimensions

Size of *Haritaki*	Batch I (cm)	Batch II (cm)	Batch III (cm)
Small	0.877	0.928	0.983
Medium	1.516	1.781	1.821
Big	1.9	11.78	2.5

Table 2: Distribution of *Haritaki* (*Terminalia chebula* L.) As per floatability character

Characteristics of *Haritaki*	Floatable	Non floatable
Percentage	72.64%	28.86%

Table 3: Observation during process of EBH of Batch A

Batch A	Subbatch	*Haritaki* qty. in kg	Castor oil in ml	Temp of bottom of the vessel	Temp on upper surface	Duration of heating in min	EBH powder	Percentage yield
Small	EBHS1	2.5	250	102	82	20	1.95	78
	EBHS2	2.5	250	101	84	20	1.90	76
	EBHS3	2.5	250	99	86	20	1.85	74
Average		2.5	250	100.66	84	20	1.85	74
Medium	EBHM1	5.68	568	100	83	40	4.70	82.74
	EBHM2	5.68	568	102	85	40	4.80	82.50
	EBHM3	5.68	568	98	86	40	4.75	83.62
Average		5.68	568	100	84.66	40	4.75	83.62
Big	EBHB1	3.01	301	101	82	50	2.45	81.39
	EBHB2	3.01	301	103	86	50	2.46	81.72
	EBHB3	3.01	301	104	85	50	2.50	83.05
Average		3.01	301	102.66	84.33	50	2.47	82.05

Table 4: Observation during process of EBH of Batch B

Batch B	Subbatch	*Haritaki* qty in kg	Castor oil in ml	Temp of bottom of the vessel	Temp on upper surface	Duration of heating in min	EBH powder	Percentage yield
Small	EBHS1	2.5	250	100	82	30	1.80	72
	EBHS2	2.5	250	102	85	30	1.85	74
	EBHS3	2.5	250	103	84	30	1.70	68
Average		2.5	250	101.66	83.66	30	1.78	71.20
Medium	EBHM1	5.68	568	102	86	45	4.75	83.62
	EBHM2	5.68	568	105	84	45	4.80	84.50
	EBHM3	5.68	568	103	81	45	4.75	83.62
Average		5.68	568	103.33	83.66	45	4.76	83.80
Big	EBHB1	3.01	301	100	84	60	2.34	77.74
	EBHB2	3.01	301	99	85	60	2.36	78.40
	EBHB3	3.01	301	102	87	60	2.40	79.73
Average		3.01	301	100.33	85.33	60	2.36	78.40

Table 5: Organoleptic character of EBH

Parameters	Before frying	After frying	Powder EBH
Color	Grayish black	Grayish black	Grayish black
Odor	Characteristics	Characteristics	Characteristics
Taste	Astringent	Astringent	Astringent
Touch	Smooth	Smooth	Smooth

EBH: *Eranda Bhrishta Haritaki*

extractives value, alcohol soluble extractives value, petroleum soluble extractives value, % reduction in bulk density was depicted in Table 6. The specification of equipments such as iron vessel dimensions, iron pan dimensions depicted in Table 7. In this we followed the parameters such as capacity of vessels, diameter at top, height of the vessels etc. The average percentage of EBH powder was pass through different sieve are depicted in Table 8. In this different size of sieves are used such as 200, 100, 72, 40. Their are several parameters for monitoring physical response to frying are depicted in

Table 6: Physicochemical parameters of EBH powder

Batch	Subbatch	Ash value	Water soluble extractives values	Alcohol soluble extractives values	Petroleum soluble extractives value	% Reduction in bulk density
A	EBHS	1.47	54.43	53.05	2.3	50
	EBHM	2.08	54.50	52.95	2.5	54
	EBHB	1.63	54.75	53.50	2.6	55
Average		1.72	54.56	53.16	2.466	53
B	EBHS	1.53	54.55	53.65	2.4	52
	EBHM	2.10	55.05	53.85	2.6	54
	EBHB	1.70	54.75	53.75	2.3	55
Average		1.77	54.78	53.75	2.43	53.66

EBH: *Eranda Bhrishta Haritaki*

Table 7: Specification of equipment

Specification of vessel	Iron vessel dimensions	Iron pan dimensions (cm)
Capacity	75 l	-
Diameter at top	60 cm	2.5
Height	60 cm	100

Table 8: Average percentage of EBH powder pass through different sieve

Batch	Mesh size	Average percentage of pass through
A	200	11.04
	100	55.8
	72	81.72
	40	95.38
B	200	11.40
	100	56.26
	72	80.45
	40	94.50

EBH: *Eranda Bhrishta Haritaki*

Table 9. The morphological changes and their probable causes for fluctuation in % of groups was depicted in Table 10.

DISCUSSION

Haritaki is attributed with many qualities like act as Deepan (Appetizer*), Pachan (*Digestive*), Anuloman* (Carminative), *Rasayan (Rejuvenator), Chakshushya* (in Eyes disorder) *Medya* (Intellect *promoting), Prajasthapnan* (help in implantation)[10] etc. Ideal *Haritaki* to be used in formulations is the one which floats on water.[11] However, due to the large demand of the drug in various formulations sometimes pharmacy uses sinked ones also in formulations. The percentage distribution of *Haritaki* according to its density is depicted in Table 1. *Eranda* possess *Vatahara, Vrishya,*[12] *Rechana* (Purgative) properties.[13] EBH is a widely used formulation in the management of *Vatavyadhi, Sandhivat* (arthritis), *Ajeerna* (indigestion) and *Anaurexia* (aruchi) induced diseases.[11] *Bhavaprakasha* has mentioned varieties of *Haritaki* fruits[14] on the basis of maturity and weight parameters as *Bala, Rangari,* and *Survari Haritaki*.[8] In the above experiment, in spite of the observed difference in two batches and three sub batches, which was due to uniformity in sub-batch size, duration, and frequency of stirring, rate of frying, sample of raw, immature *Haritaki*, there was reproducibility of monitored parameters of standardization in the same batch prepared by same worker. In laboratory experiments, all *Haritaki* fruits started increasing in bulk at once and achieved maximum bulk suddenly after average 20, 40 and 50 min at 100°C, 100.66°C, and 102.66°C, respectively, in Batch A while in Batch B the duration of heating in three different sub-batches are 30, 45, and 60 min at 101.66°C, 103.33°C, and 100.33°C, respectively. Intensity and duration of heating are not directly proportional to swelling of fruits. Observations on parameters of standardization and classification of product on the basis of heating pattern within the subgroups were reproducible. With the reduction in heating intensity and increment in duration of heating and frequency of stirring increases in subgroups as the increasing the size of *Haritaki*. The yield in two Batches A and B and also in sub-batches was average 74%, 83.62%, 82.05%, and 71.20%, 83.80%, and 78.40%, respectively. It was possible to yield near a homogeneous product with more precision at industrial level, even though, the raw sample is non-uniform. Percentage yield is more in medium size *Haritaki* as they give less residue after sieving.

Further, if proportion of standard ingredients, batch size, equipment, duration of frying, duration, pattern, and frequency of stirring are kept constant, the procedure can be validated with just regulation of heating pattern, which can be done by means of sand bath and or thermal oil jacketed iron pan. Since, the stirring is more laborious, uneconomic and varies from subject to subject hence it can be overcome by means of regulated mechanical stirrer. Probable causes and effective factors for fluctuation in the percentage of groups after heating is depicted in Table 6.

Table 9: Parameters for monitoring physical response to frying

Group	Small	Medium	Big
Degree of frying	++	++	++
Parameters for monitoring physical response to frying			
Ridges	Least, almost 100%	Less (very poorly differentiable or nil)	Prominent (very poorly differentiable or nil) ++++ almost 100%
Blackness/blackish spots	Less prominent, 0-20% surface area covered or ill-defined brownish discoloration over<50% surface area	Prominent, 20-45% surface area covered, or marked generalized brownish discoloration	More prominent, 50-75% surface area covered, or marked generalized brownish discoloration
Weight/heaviness	Less	Medium	More
Increment in size (swelling)	<20% of expected	<80% of expected	More than 80% of expected
Average weight loss	Slightly less	Less	Less or more

Table 10: Morphological changes and their probable causes for fluctuation in % of groups

Method of frying	Observed effect	Probable cause
Desirable heating pattern followed in current study	Increment in % of Group 2 and 3	Slow heating and at optimum intensity
	Increase in % of Group 1	Less degree of frying (intensity and duration of heating)
	Increase in % of Group 1	More degree of frying (intensity and duration of heating)
	Medium burnt with black spots (>50% surface area) along with wrinkles	Increased intensity of heating with less stirring
Undesirable	More blackening with persistent ridges-Major change in weight loss and increment in size was in between 195°C and 210°C	More intensity of heating less frequent stirring

Average values of parameters of standardization of EBH are depicted in Table 6. % raw *Haritaki*. There were no remarkable changes observed in all the sub-batches except ash value which is high as compared to other sub-batches which may be due to more absorbance of castor oil in medium size immature *Haritaki*. The qualitative test showed that tannin was found to be present in all the group.

CONCLUSION

Medium size *Haritaki* (average size 0.928-11.78 cm) is give more yield of 83.62% and 83.80% in two batches A and B as compared to other three sub-batches.

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REFERENCES

1. Sharma HP, editor. Rasa Yoga Sagar. 4th ed., Vol. II. Varanasi: Krishnadas Academy; 1998. p. 563-5.
2. Kulkarni DA, editor. Vagbhattacharya. Rasa Ratna Samuchchaya. Reprint. New Delhi: Meharchand Laxmandas Publication; 1998. p. 64.
3. Bhatta KG. In: Tripathi ID, editor. Rasendra Sara Sangraha. 2nd ed. Varanasi: Chaukhamba Orientallia; 1998. p. 48-9.
4. Nityanath P, Ratnakar R, Mishra S, editors. Vadikhanda Ridhhikhanda. 2nd ed., Vol. 3. Varanasi: Chaukhamba Publishers; 2003. p. 35.
5. Shastri K, editor. Sadananda Sharma, Rasa Tarangini. 11th ed. New Delhi: Motilal Banarsidas Publication; 2000. p. 257-8.
6. Murthi S, editor. Sharangadhara. Sharangadhara Samhita. Reprint. Varanasi: Chaukhamba Orientallia, Madhyama Khanda; 2009. p. 145.
7. Shah NC. Bharat Bhaishyajya Ratnakar. 1st ed., Vol I-Vol V. New Delhi: B. Jain Publishers; 2005.
8. Shastry H. Rasatarangini. 11th ed. Reprint 2000.

New Delhi: Motilalbanarasidas Publication; 1979. p. 678.
9. Mishra S, editor. Kaviraj Govind Das Sen, Bhaishajya Ratnavali. Reprint 2011. Varanasi: Chaukhambhasurabharati Prakashan; 2011.
10. Chunekar KC. Bhavprakash Nighantu of Bhavmishra. Varanasi Reprint Edition 2015. Varanasi: Chaukhamba Bharati Academy, Haritakyadi Varga; 2007. p. 5.
11. Dwivedi V. Bhaaprakasha Nighantuhu. 9th ed. Reprint 2007. New Delhi: Motilal Banarasidas Pubication; 2007. p. 7.
12. Caraka, Samhita C, Bhagwandas, Sharma RK, editors. Sutra Sthan. 3rd ed. Ch. 25. Varanasi: Chaukhamba Sanskrit Series Office; 2003. p. 448.
13. Sushruta. Sushruta Samhita (Nibhandasangraha Commentary of Dalhanacharya and Nyayapanijaka Commentary of Gayadasa). In: Trikamji, editor. 1st ed., Vol. 45. Varanasi: Chaukhamba Sanskrit Samsthan, Sutra Sthana; 2007. p. 114, 369.
14. Chunekar KC. Bhavprakash Nighantu of Bhavmishra. Varanasi Reprint Edition 2015. Vol. 8. Varanasi: Chaukhamba Bharati Academy, Haritakyadi Varga; 2010. p. 3.

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