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Pharmaceutical Standardisation of *Devdarvadyarishta* w.s.r to the Fermenting Vessel

Research Article

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Abstract

Standard operating procedure for pharmaceutical preparation of *Devdarvadyarishta* has been developed in the present research work. A pilot scale study having 3 batches was carried out initially to find out the best possible fermenting vessel among glass jar, porcelain jar and stainless steel vessel and also to investigate for any possible hurdle related with fermentation process as honey and not jaggery is used as sweetening agent in this formulation. Three samples of *Devdarvadyarishta* as per conventional method were prepared in accordance with *Bhaishjya Ratnavali* and process for standard of *Devdarvadyarishta* was set in as a Quality specification for the same. Porcelain jar was found to be the best as per the results of pilot study as evident by alcohol content of 5.73%, 6.25% and 6.10% respectively in glass jar, porcelain jar and stainless steel vessel, the reaction being completed in between 38-47 days. Approximate duration of *Kwatha* formation in all the batches was 9 hours with peak temperature during boiling being maintained at 92^{0}C. In all the three batches, fermentation started on 7th day, 7th day and 9th day, total duration of fermentation was 72 days, 70 days and 75 days, with % loss of 15.78%, 17.76% and 19.07% respectively. Mean % loss observed during preparation was 17.53%.

Key Words: *Devdarvadyarishta, Standardisation, Fermentation, Validation, Sandhana.*

Introduction

In antiquity, experience based experiments were documented in terms of their observation. Today's necessity is to document each and every step in terms of numerical scientific language to establish Ayurveda as the evidence based medical science. This in-depth documentation not only will enable researchers to understand the relationship between the ingredients, processing and different types of operation but also will give immense control over the quality of the final product. A right product is the combination of mainly two components viz. good quality raw material and accurate process. In case of pharmaceutical formulations, the process acquires a great dimension to deliver a product of requisite quality.

Validation literally means to render the process valid after substantiating known process with a scientific ground in order to deliver a particular product. The first step for any kind of validation is to design a well-documented plan of action related to the same, which hereby can be divided in two important components –

1- The equipment validation

2- The process validation

The validation process may be a prospective one or retrospective one; but more specifically for Ayurvedic drug manufacturing is the retrospective and the revalidation. Retrospective process validation is that what we derive from the past experiences.

An elaborate comprehension of the preparation of compound drug with respect to the changes during the processes creates a unique opportunity for formulating the new/existing compounds with improved stability and for superior nutritional, dieting and therapeutic qualities. This arise the necessity to study the preparation of a drug to comprehend the underlying principles, document the findings for further comparison, corroborate the document with therapeutic efficacy and then formulate the resolutions. Considering the above facts, here an attempt is made with following aims and objectives-

- To reveal the best suitable fermenting vessel among glass jar, porcelain jar and stainless steel vessel.

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- To explore a standard "Pharmaceutical Protocol" for preparation of *Devdarvadyarishta* as per the reference of *BhaishjyaRatnavali.*
- To prepare *Devdarvadyarishta* repeatedly for three times to ensure the process validation.

Materials and Methods

Three samples of *Devdarvadyarishta* viz. DVA1, DVA2 and DVA3 was prepared as per *BhaishjyaRatnavali* whose composition is given inTable 1. First of all, a pilot study was conducted to reveal the best suitable fermenting vessel to be taken for main study and to explore a standard "Pharmaceutical Protocol". Three jars were taken for study viz.Glass jar, Porcelain jar and Stainless steel vessel.

Table No 1- Details of the Ingredients of *Devdarvadyarishta*

Dravya	**Drug**	**Amount taken (kg)**			
		Pilot Study	**DVA1**	**DVA2**	**DVA3**
Kwatha Dravya	*Devdaru*	1.2	0.8	0.8	0.8
	Vasa	0.48	0.32	0.32	0.32
	Manjishtha	0.24	0.16	0.16	0.16
	Indrayava	0.24	0.16	0.16	0.16
	Danti	0.24	0.16	0.16	0.16
	Tagara	0.24	0.16	0.16	0.16
	Haridra	0.24	0.16	0.16	0.16
	Daruharidra	0.24	0.16	0.16	0.16
	Rasna	0.24	0.16	0.16	0.16
	Vidanga	0.24	0.16	0.16	0.16
	Mustaka	0.24	0.16	0.16	0.16
	Shirisha	0.24	0.16	0.16	0.16
	Khadira	0.24	0.16	0.16	0.16
	Arjuna	0.24	0.16	0.16	0.16
	Yavani	0.192	0.128	0.128	0.128
	Kutaja	0.192	0.128	0.128	0.128
	Shweta Chandana	0.192	0.128	0.128	0.128
	Guduchi	0.192	0.128	0.128	0.128
	Kutaki	0.192	0.128	0.128	0.128
	Chitraka	0.192	0.128	0.128	0.128
Prakshepa Dravya	*Shunthi*	0.048	0.032	0.032	0.032
	Maricha	0.048	0.032	0.032	0.032
	Pippali	0.048	0.032	0.032	0.032
	Twak	0.096	0.064	0.064	0.064
	Ela	0.096	0.064	0.064	0.064
	Tejpatra	0.096	0.064	0.064	0.064
	Naagkeshar	0.048	0.032	0.032	0.032
	Priyangu	0.096	0.064	0.064	0.064
Sandhana Dravya	*Dhataki*	0.384	0.256	0.256	0.256
Madhura Dravya	*Madhu*	7.2	4.8	4.8	4.8
Drava Dravya	Water	49.2L reduced to 6.15L	33.2L 4.12L	33.2L 4.12L	33.2L 4.12L

For Pilot Study, *Yavakuta*churna (coarse powder mesh size 44) of aforesaid *Kwatha dravyas* was soaked overnight in said quantity of water (approx. 12 hrs) in a stainless steel vessel.Next day, *kwatha* was prepared by heating the vessel on low flame till it was reduced to 1/8th of initial volume of water and was strained with a double layered cotton cloth and measured.The obtained *Kwatha* was divided into 3 groups, mixed with rest of the *dravyas* viz. *Madhura Dravya, Sandhana Dravya* and *Prakshepa Dravya* in three different vessels, stirred properly and kept for fermentation, details being enlisted in Table no. 2.

Main Pharmaceutical Study

Procurement and preparation of raw drugs

The raw drugs except *Madhu* were procured from Shri Hans Ayurveda Bhavan Pvt. Ltd, Haridwar after proper authentication by experts of Dravyaguna Department. All the drugs were cleaned properly as to no physical impurities or adulterants remained and subjected to shade drying up to constant weight obtained.Properly dried drugs were then subjected to size reduction with the help of Pulveriser. *Madhu* (Honey) was procured from local vendor engaged in apiculture and was subjected to chemical tests to confirm its purity.

Preparation of Kwatha

Natural circulation evaporation (*Kwathana*) method was basic principle followed.The *Yavakuta* churna (mesh size 44) of the *Kwathadravyas* was mixed with the mentioned quantity of water in a stainless steel cauldron and was subjected to overnight soaking of 12 hrs to allow the imbibition of the menstrum inside the tissues of the drug so as to escape entrapped air. Next day, constant mild heat was applied to the cauldron with continuous stirring to facilitate the evaporation so as to reduce the volume of the *Kashaya* (Galenical) to 1/8th of the initial volume of water. After desirable reduction in volume, the *Kwatha* was strained with double folded cotton cloth and collected in a separate vessel for further processing.The residue remained above cloth was discarded.

Preparation of *Devdarvadyarishta*

The fermenting vessels (Porcelain Jars) were properly washed with detergent, rinsed well with sufficient quantity of warm water and dried properly to avoid any contamination.Shade dried *Prakshepa Dravya* was processed to fine powder form (mesh size 85), weighed and then mixed well. *Dhataki* flowers were also dried in shade before using in the formulation.After self-cooling of Kwatha, it was poured into well dried fermenting vessels maintaining sufficient air space in them.Aforesaid quantity of *Madhu, Dhataki Pushpa, Prakshepa Dravya* was added in the vessels accordingly and stirred properly till they get wetted completely with the fermenting media.Vessels were closed by respective lids to prevent entry of any contaminant.Assessment of proper initiation of fermentation was done by regular examination on 5th, 7th, 15th, 30th, 45th, 60th day and at every 5 days interval thereafter.After initiation of fermentation, the fermenting vessel was tightly sealed by cloth smeared with mud (*MultaniMitti*).The vessels were placed in a clean area avoiding direct exposure to sunlight, air and variation in the atmospheric temperature. Artificial regulation of the temperature was done with the help of

electric bulbs inside the room.After examination of the completion test of the fermentation as given in Table no. 7-9, the supernatant fluid was decanted in other jar after filtering through a double folded cotton cloth.The residue remained in the bottom of the vessel was discarded. *Arishta* collected was allowed for maturation for a period of 15 days.After maturation, it was again filtered through double folded cotton cloth for separating the suspended particles and getting the clear fluid (*Arishta*) which was then packed in the amber coloured plastic bottles and properly labelled as per rule 161 of Drugs and Cosmetic Act 1940 and rules 1945.

Observations and Results

Table No 2: Practical Details of three samples of *Devdarvadyarishta* (Pilot Study)

Batch Code	I	II	III
Quantity of *Kwatha*	2.05L	2.05L	2.05L
Quantity of Honey	2.4Kg	2.4Kg	2.4Kg
Quantity of *Prakshepa*	0.192Kg	0.192Kg	0.192Kg
Quantity of *SandhanaDravya*	0.128Kg	0.128Kg	0.128Kg
Volume of Wort	3.65L	3.65L	3.65L
Average Yield	2.98L	3.05L	3L
% Loss	18.35%	16.43%	17.08%
Date of Commencement	01-06-14	01-06-14	01-06-14
Onset of Fermentation	7th day	7th day	8th day
Date of Completion	15-07-14	08-07-14	17-07-14
Total Duration of Fermentation	45 days	38 days	47 days
Maturation Period	15 days	15 days	15 days

Table No 3: Practical details of *Kwatha* preparation

Batch code		DVA1	DVA2	DVA3
Date of commencement		2.08. 2014	3.08. 2014	4.08. 2014
Date of completion		2.08. 2014	3.08. 2014	4.08. 2014
Amount of *Kwathya Dravya* (kg)		3.808	3.808	3.808
Quantity of Water (L)		33.200	33.200	33.200
Reduced up to (L)		1/8th	1/8th	1/8th
Temperature ^{0}C	Room temp.	28-30	29-30	27-29
	Peak temp. maintained	84-92	84-92	84-92
	Flame temp	350-380	350-380	350-380
Total yield (L)		4.120	4.120	4.120
Total duration (h)		8:40	8:45	8:55

Table No 4: Equipment specification of *Kwatha* Formation

Sr. No.	Equipment used	Size
1	Stainless steel cauldron	Depth- 16 inch Diameter- 27 inch Circumference- 84 inch Capacity- 50 L
2	Stainless steel ladle	Length- 21.5 inches
3	Gas burner with L.P.G. cylinder	14.5 kg
4	Cotton cloth	1 x 1 meter

Table No 5: Practical details of *Devdarvadyarishta* Preparation

Sr. No.	Parameters	DVA1	DVA2	DVA3
1	*Kwatha* (L)	4.12	4.12	4.12
2	Temperature of *Kwatha* during addition of Honey (^{0}C)	30	31	30
3	Atmospheric Temperature (^{0}C)	28-30	29-30	25-28
4	Quantity of Honey added (kg)	4.8	4.8	4.8
5	Quantity of *SandhanaDravya* added (kg)	0.256	0.256	0.256
6	Quantity of *PrakshepaDravya* added (kg)	0.384	0.384	0.384
7	Wort (L)	7.60	7.60	7.60
8	Final yield (L)	6.40	6.25	6.15
9	% loss	15.78%	17.76%	19.07%
10	Total duration of fermentation	72 days	70 days	75 days

Table No 6: Equipment specification for *Arishta* Formation

Sr. No.	Equipment used	Size
1	Stainless steel ladle	Length- 14.5 inches
2	Porcelain jar	Height- 41 cm Circumference- 81.5 cm Diameter of mouth- 16.5 cm Capacity- 12 L
3	Cotton cloth	1 x 1 meter

Table No 7: Observations of *Devdarvadyarishta* (DVA1) preparation

Sr. No.	Criteria	Before onset of fermentation	After onset of fermentation	After completion of fermentation
1	Date	2.08.2014	9.08.2014	13.10.2014
2	Room temp.	30^{0}C	25^{0}C- 30^{0}C	28^{0}C
3	Effervescence	Absent	Present (7th day)	Absent
4	Bubbling sound	Absent	Present (8th day)	Absent
5	Flocculation	Absent	Absent	Absent
6	Hissing sound	Absent	Present (10th day)	Absent
7	Burning match test	Negative (lighted)	Positive(extinguished)	Negative (lighted)
8	Lime water test	Negative	Slightly positive	Negative
9	Colour	Dark Brown	Dark brown	Reddish brown
10	Smell	Pleasant smell of *Kwatha* and *Prakshepa*	Mild Alcoholic predominantly *Prakshepa* Smell	Alcoholic with *Prakshepa* smell
11	Taste	*Madhura, Katu, Kashaya*	*Madhura, Katu, Kashaya*	*Kashaya* and *Madhura*
12	Consistency	Thicker	Thicker	Slightly Thicker
13	*PrakshepaDravya*	Floating	Floating	Settled down

Table No 8: Observations of *Devdarvadyarishta* (DVA2) preparation

Sr. No.	Criteria	Before onset of fermentation	After onset of fermentation	After completion of fermentation
1	Date	3.08.2014	9.08.2014	12.10.2014
2	Room temp.	30^{0}C	25^{0}C- 30^{0}C	28^{0}C
3	Effervescence	Absent	Present (7th day)	Absent
4	Bubbling sound	Absent	Present (8th day)	Absent
5	Flocculation	Absent	Absent	Absent
6	Hissing sound	Absent	Present (9th day)	Absent
7	Burning match test	Negative (lighted)	Positive (extinguished)	Negative (lighted)
8	Lime water test	Negative	Slightly positive	Negative
9	Colour	Dark Brown	Dark brown	Reddish brown
10	Smell	Pleasant smell of *Kwatha* and *Prakshepa*	Mild Alcoholic predominantly *Prakshepa* Smell	Alcoholic with *Prakshepa* smell
11	Taste	*Madhura, Katu, Kashaya*	*Madhura, Katu, Kashaya*	*Kashaya* and *Madhura*
12	Consistency	Thicker	Thicker	Slightly Thicker
13	*PrakshepaDravya*	Floating	Floating	Settled down

Table No 9- Observations of *Devdarvadyarishta* (DVA3) preparation

Sr. No.	Criteria	Before onset of fermentation	After onset of fermentation	After completion of fermentation
1	Date	4.08.2014	13.08.2014	18.10.2014
2	Room temp.	29^{0}C	25^{0}C- 30^{0}C	26^{0}C
3	Effervescence	Absent	Present (9th day)	Absent
4	Bubbling sound	Absent	Present (10th day)	Absent
5	Flocculation	Absent	Absent	Absent
6	Hissing sound	Absent	Absent	Absent
7	Burning match test	Negative (lighted)	Positive (extinguished)	Negative (lighted)
8	Lime water test	Negative	Negative	Negative
9	Colour	Dark Brown	Dark brown	Reddish brown

10	Smell	Pleasant smell of *Kwatha* and *Prakshepa*	Mild Alcoholic predominantly *Prakshepa* Smell	Alcoholic with *Prakshepa* smell
11	Taste	*Madhura, Katu, Kashaya*	*Madhura, katu, Kashaya*	*Kashaya* and *Madhura*
12	Consistency	Thicker	Thicker	Slightly Thicker
13	*PrakshepaDravya*	Floating	Floating	Settled down

Table No 10- Fermentation chart of *Devdarvadyarishta* preparation

Events during fermentation	DVA1	DVA2	DVA3
Starting day	7th day	7th day	9th day
Completion Day	72	70	75
Maturation Days	15	15	15
Total Duration	87	85	90

Discusssion

For quality assurance of the finished product, it is necessary to evaluate, compare and discuss the data compiled after several times repetition of the same procedure to generate a standard protocol for any formulation. It has been said that honey does not contain sufficient yeast, nor the right kind of yeasts or nutrients to allow rapid fermentation but positive aspect is that the yeast most commonly found in honey (osmophilic yeast - Zygosaccharomyces) grows only in concentrated solutions with more than 50% sugar,(2) so is applicable in the case of *Devdarvadyarishta,* therefore pilot study was conducted initially. As per the observations of pilot study, fermentation started on 7th day in glass and porcelain jar while it started a day after in steel vessel which was evident by slight effervescence and very faint bubbling sound. In most of the cases, fermentation usually starts between 3rd to 5th days when atmospheric conditions are suitable for the same (temp. approx 35^{0}C). But in present study, temperature being around 35^0 C, fermentation started on 7th day, attributable to the high concentration of *MadhuraDravya* i.e. honey which may have restricted the growth of microbes due to its anti-microbial properties(3) initially but later on resulted in good production of alcohol. No fungal growth at all was seen during fermentation period in any of the vessels, but after maturation period, white fungal spots appeared over whole of surface of the liquid in glass jar over a couple of days, but no such growth was observed in other two vessels. Possible reason for this being contamination from outside during collation or vessel may be already contaminated. The completion test comes positive on 38th day in porcelain jar, 45th day in glass jar and 47th day in stainless steel drum. Duration of fermentation was earliest in porcelain jar which may be due to the maintenance of constant temperature inside of porcelain jar in comparison to the other two vessels, in which temperature varies with diurnal variations etc. Also, the average yield as well as the % age content of alcohol (5.73%, 6.25% and 6.10% respectively in glass jar, porcelain jar and stainless steel vessel) was found to be highest in porcelain jar followed by steel vessel and the glass jar. It can be proved on the basis of the study mentioned in Bulletin No. 134, FAO, Agricultural services, as vast variation in temperature is said to be more destructive than the higher or lower consistent range of temperature during the fermentation process and porcelain material shows better insulating properties than that of glass jar and stainless steel vessel. So, Porcelain jar is found to be the best fermenting vessel as compared to the others.

Preparation of *Kwatha*

The net effect of the boiling besides extraction of the aqueous soluble principles, is to render higher molecules/ polysaccharides fit for the microbial action, eliminate the unwanted micro-organisms, coagulate/ precipitate complex proteins, eliminate excess of dissolved oxygen in the solution and reduce the water activity of the drug i.e. the free water available within them which makes the drug susceptible for contaminants.(4)The basic fundamentals told by various *Acharyas* regarding preparation of *Kwatha* stands testimony to the extraction principles established now-a days.(5)

- **Separation of physical impurities-** It was done for maintenance of quality and efficacy.
- **Size reduction-** Yavakuta Churna (Coarse powder-mesh size 44) of *Kwatha Dravyas* was taken so as to facilitate proper extraction of water soluble constituents. Mass transfer theory suggests that the maximum surface area should be obtained by reducing the drug to individual cells, but in practice this is not possible because a prolonged size reduction process is likely to lead to decomposition of constituents or loss of volatile materials and a suspension of extremely fine particles would be very difficult to separate in the final stages. Generally the appropriate degree of size reduction will cause some of the cells of the drug to be broken and to provide a particle size to assist penetration of the solvent and escape of soluble matter.
- **Overnight soaking-** It was to facilitate the imbibition of the menstrum inside the tissues of the drug which allows the entrapped air to escape that can resist the flow of menstrum. The duration of soaking should be decided according to the weather as excess duration may leads to unwanted microbial growth.
- **Application of mild heat-** Mild heating with peak temperature maintained around 92^{0}C was applied for proper extraction and reducing the chances of degradation of the active constituents due to

hydrolysis. As the convection current set up by heating at low temperature for a longer period does not produce sufficient movement of the liquid, hence continuous mechanical stirring is needed to facilitate the natural circulation evaporation. Almost all the batches of *Devdarvadi Kwatha* were prepared in between 8½ - 9 hrs. In the textual reference to prepare *Kwatha* for *Devdarvadyarishta*, water is mentioned to be reduced up to 1/8th that may result in maximum extraction of active constituents.

Preparation of Wort

Honey was added to *Kwatha* at a temp around 30^{0}C along with fine powder of *Prakshepa Dravya, Sandhana Dravya* with proper mixing as the dry superficial agglomeration of the powder added over the liquid may work as the base material for unwanted microbial growth. As the yeast responsible for fermentation in honey can grow in more concentration of sugar(2) and results of pilot study were also found to be promising, therefore all the quantity of honey was added at once rather than batch wise addition.

Sealing of vessel

Yeast cells require sterol for their membrane synthesis which is produced only in the presence of oxygen. Thus both aerobic and anaerobic conditions are required for sterol synthesis and ethanol production respectively which is traditionally provided by non-air tight sealing of the fermentation vessel until first three days so as to prevent any oxygen deficiency and the airtight arrangement thereafter to ensure anaerobic condition. Due to late onset of fermentation in present study, sealing of vessels was done between 7-9 days.(4) It is clearly evident from Table no. 10 that Fermentation started on 7th day in DVA1 and DVA2 while it started on 9th day in DVA3. The completion test came positive on 72nd, 70th and 75th day respectively in DVA1, DVA2, DVA3.

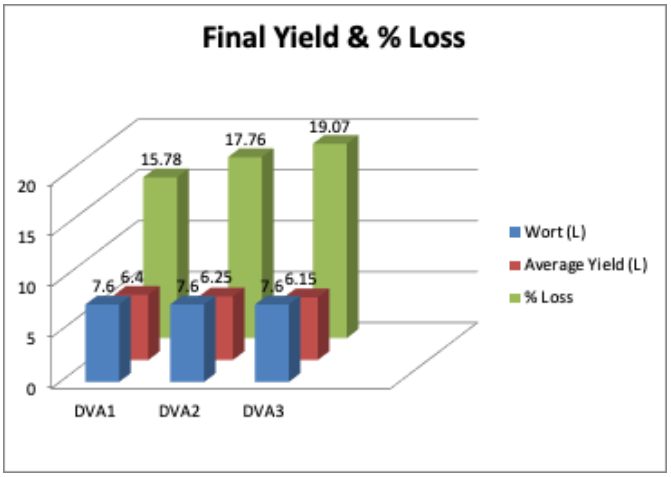

Figure No. 1- Final Yield and % age Loss

Average yield was found to be comparable in all the samples but was highest in Sample I followed by Sample II and III respectively as evident from Figure no. 1.

Conclusion

The accomplishment of pharmaceutical operation of three samples of *Devdarvadyarishta* prepared according to the reference *BhaishajyaRatnavali* 37/237-243 is elaborated detailed in this present research work. Results of pilot study revealed porcelain jar to be the best fermenting vessel and also fermentation occurred well in all the containers as evident by alcohol content of 5.73%, 6.25% and 6.10% respectively in glass jar, porcelain jar and stainless steel vessel, the reaction being completed in between 38-47 days. Approximate duration of *Kwatha* formation in all the batches was 9 hours with peak temperature during boiling being maintained at 92^{0}C. In all the three main pharmaceutical batches, fermentation started on 7th day, 7th day and 9th day, total duration of fermentation was 72 days, 70 days and 75 days, with % loss of 15.78%, 17.76% and 19.07% respectively. Delayed commencement and completion of fermentation occurs in presence of honey but yields a good percentage of alcohol even with higher concentrated solution.

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