



RESEARCH ARTICLE

**Formulations of *Sitopaladi Churna* Granules and Tablets by Dry Granulation
Technique for Enhancing Patient Compliance**

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ABSTRACT

The objective of this study was to improve the physiochemical properties such as poor flowability, organoleptic characters and stability of *Sitopaladi churna*. Stability is the major concern affect the patient compliance and also dosage form. Granulation is required to overcome all these problems related to *Sitopaladi churna*. Granulation process will improve flow and compression characteristics, reduce segregation, improve content uniformity, and eliminate excessive amounts of fine particles. The present article focus on the dry granulation technology that gives good results based on evaluation of different granule properties, namely the Carr's index, Angle of repose and tapped bulk density. Organoleptic evaluation and stability studies were also evaluated for prepared granules. Finally, the tableting process showed good tablet properties such as weight uniformity, hardness, friability, thickness and disintegration time. These properties were compared with corresponding marketed product. It indicating good compressibility of the prepared granules using different binders and stabilizing agents the selected formulations was stable.

KEYWORDS

Sitopaladi Churna, Binders, Slugging, Granules, Organoleptic Studies, Stability Studies

INTRODUCTION

The term Churna may be applied to the powder prepared by a single drugs or a combination of more drugs. One of the formulations is *Sitopaladi churna* which is very commonly prescribed Ayurvedic medicine for cough. According to *Ashtang Hriday* it consists of a mixture of powder of *Sitopala* (sugar), *Vamasarocana* (*Bambusa arundinaceae* Retz.), fruits of *Pippali* (*Piper longum* Linn.), Seeds of *Ela* (*Amomum subulatum* Roxb.) and *Tvak* (bark of *Cinnamomum Zeylanicum* Blume).¹ It is recipe of traditional Ayurvedic Pharmacopoeia well known and effective in relieving coughs associated with respiratory disorder.²

Dispensing and consumption of churnas (powder) is inconvenient to the patients.³ Churnas are stick to the tongue and oral cavity due to inherent adhesive nature. Patients are showing less interest to take herbal churnas orally because of their astringent, bitter and pungent taste. Churnas being in powder form also suffer stability due to their hygroscopicity.

Determination of stability of herbal drug in formulations is important. The stability is aimed at assuring that the drug/drug product remains within the specifications established to ensure its identity, strength, quality and purity. It can be interpreted as the length of time under specific conditions and storage that a product will remain within the pre-defined limits for all its important characteristics. Each ingredient, whether the therapeutically active or inactive, in

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a dosage form can affect stability. Environmental factors such as temperature, light, air (specifically oxygen, carbon dioxide and water vapors) and humidity can affect stability. Similarly, factors such as particle size, pH, the properties of water and other solvents employed, the nature of container and the presence of other chemicals resulting from contamination or from the intentional mixing of different products can influence stability.⁴ Dry granulation can be achieved either by slugging, using a tablet press. The desired particle size distribution can be adjusted by milling and sieving. The granulation parameters can affect the mechanical (i.e., compression) properties of the granules, which subsequently can influence the tableting behaviour and tablet characteristics. Therefore, the evaluation of granule properties plays an important role in the prediction of tablet characteristics.⁵

Granulation an interesting method to improve the flow property of poorly flowable powders, when associated with a suitable binder and granulation technique. Direct study of the composition of every individual binder bridge formed from soluble materials in the granules is impossible, but their indirect evaluation done by evaluation of tablet property. These data provide additional information towards an understanding of granule formation in a small-scale in academic lab.⁶

The most important point in the evaluation of the stability study of a product is its storage conditions. It should simulate the conditions under which the drug substance or drug product is subjected from manufacturing up to its final application. Storage conditions are derived from real climatic situation. Because most of the chemical reactions follow logarithmic and not linear functions, this characteristic must be taken into consideration while defining the appropriate conditions. Hence, the present packaging and storing technology development are playing a great role in the comparatively longer stability of the raw or finished drug materials. Nowadays, the Ayurvedic industries are also utilizing these technologies

for the packaging and storage of their formulations which ultimately enhances the shelf life of the products.⁷ Hence in the present study, we aimed at conversion of *Sitopaladi churna* into stable, palatable and patient acceptable granules to swallow conveniently by using dry granulation method and suitable formulations strategies. Granules and Tablet were formulated and evaluated appropriately including physical stability studies.

MATERIALS AND METHODS

Materials

Raw Materials

Sitopala (sugar), *Vamasarocana* (*Bambusa arundinaceae* Retz.), fruits of *Pippali* (*Piper longum* Linn.), Seeds of *Ela* (*Amomum subulatum* Roxb.) and *Tvak* (bark of *Cinnamomum Zeylanicum*)

Chemicals

Avicel, pvpk30, methyl cellulose, hydroxyl propyl methyl cellulose, starch granules, calcium carbonate, microcrystalline cellulose, aerosil, croscarmellose sodium, propyl and methyl parabens.

Methods

Procurement of Herbs

Three herbal ingredients of *Sitopaladi churna* were purchased in the local market, Tumkur and the same were authenticated by Prof. K. Siddappa, Department of Botany, Sree Siddaganga College of Arts, Science and Commerce, Tumkur.

Comminution of Herbal Ingredients

All the ingredients of *Sitopaladi churna* were subjected for size reduction using the pulveriser. Obtained powders were passed through sieve no. 60.

Preparation of Churna

Formulation of churna was done as per Ayurvedic Formulary of India, corresponding quantities of each ingredient are shown in the Table 1.

Table 1: Composition and Properties of individual ingredients of *Sitopaladi churna*

Sl. No.	Ingredient	Quantity (gm)	Moisture content	Tapped Bulk Density	Angle of Repose
1	Sarkra	192	1.5%	0.77	35°52''
2	Vaushalochan	96	0.14 %	0.88	32°70''
3	Pippali	48	0.06 %	0.50	40°69''
4	Ela	24	0.16 %	0.83	30°62''
5	Tvak	12	0.10 %	0.50	38°65''

Then all the ingredients are mixed by using planetary mill.

Determination of Physicochemical Properties⁸

a. Determination of Moisture Content by LOD

Each ingredient (1 gm) was taken in petridish individually and noted the weight (W1). Ingredients were dried in a hot air oven at 100 °C for 3 hours. Final weight (W2) was noted and the loss in weight is considered as moisture content.

Moisture content was determined using the formula = $\frac{W1-W2}{W1} \times 100$

b. Determination of Total Ash

About 1 g accurately weighed *Sitopaladi churna* was taken in tared silica dish and incinerated at a temperature not exceeding 450 °C until free from carbon, then cooled and weighed.

$$\text{Total Ash \%} = \left[\frac{Z-X}{Y} \right] \times 100$$

Where,

X=Weight of empty dish.

Y=Weight of *Sitopaladi churna* taken.

Z=Weight of empty dish + ash (after completion of incineration).

c. Determination of Acid Insoluble Ash

To the crucible containing total ash, 25 ml of dilute hydrochloric acid is added. The insoluble matter on an ash less filter paper (Whatman 41) is collected and washed with hot water until the filtrate is neutral. Filter paper containing the insoluble matter is transferred to the original crucible, dried on a hot-plate and ignited to get constant weight in an incinerator. Allowed the residue to cool for 30 minutes and weighed without delay.

$$\text{Acid Insoluble Ash} = \left[\frac{a}{y} \right] \times 100$$

Where, a= weight of acid insoluble residue.

y= weight of *Sitopaladi churna* used.

d. Determination of Water Soluble Ash

Total ash is boiled for 5 minutes with 25 ml of water; insoluble matter is taken on an ash less filter paper, washed with hot water, and ignited for 15 minutes at a temperature not exceeding 450 °C. The weight of the insoluble matter is subtracted from the weight of the ash; the difference in weight represents the water soluble ash.

$$\text{Water Soluble Ash} = \left[\frac{a-b}{y} \right] \times 100$$

Where,

a=weight residue after incineration.

b=weight of water insoluble residue.

y= weight of *Sitopaladi churna* used.

e. Determination of Alcohol Soluble Extraction

Macerated 5 g of the dried *Sitopaladi churna* with 100 ml of alcohol in a closed flask for twenty-four hours, shaken frequently during six hours and allowed to stand for eighteen hours.

Filtered rapidly, taking precautions against loss of solvent, evaporate the filtrate to dryness in a tarred flat bottomed shallow dish, and dried at 105 °C, to constant weight and weighed. Calculated the percentage of alcohol soluble extraction.

f. Determination of Water Soluble Extraction

Procedure followed is similar to determination of alcohol soluble extractive, using chloroform-water instead of alcohol.

Determination of Pre-Compression Parameters of Ingredients

a. Determination of Tapped Bulk Density

Each ingredient (10 gm) was taken in a measuring cylinder and the volume before and after tapping 100 times was noted.

Tapped bulk density was calculated based on the following formula.

Tapped bulk density = weight of the ingredient / Tapped volume

b. Determination of Angle of Repose

Approximately 10 gm of each ingredient was taken and passed through the funnel to obtain a pile of the powder.

The height (h) and radius (r) of the pile of the powder were noted down. The angle of repose (θ) was calculated using the formula

$$(\theta) = \text{Tan}^{-1} (h/r)$$

Formulation of Sitopaladi Churna Granules

Five ingredients of churna were taken as per Ayurvedic Formulary of India, to this disintegrating agent, binding agent, lubricants, preservatives and cooling agent were added.

Method of Preparation of Churna Granules & Tablet

Powders of each ingredient and other excipients were sifted through sieve # 60, weighed and mixed uniformly using the planetary mixer running for 20 minutes.

The mixture is subjected for slugging for converting the powder mixture into slugs. The obtained slugs were passed through the dry granulator to get the granules. Finally tablets were compressed on a 10 station mini rotary tableting machine (Shakti Pharma Tech Pvt. Ltd, Ahmadabad) with flat-shaped punches.

Evaluation of Pre-Compression Parameters of Granules⁹

a. Bulk Density (Db)

It is the ratio of weight of powder to bulk volume. The bulk density depends on particle size distribution, shape and cohesiveness of particles.

Accurately weighed quantity of powder was carefully poured into graduated measuring cylinder through large funnel and volume was measured which is called initial bulk volume. Bulk density is expressed in gm/cc and is given by,

$$\mathbf{D_b = M / V_o}$$

Where, **D_b**= Bulk density (gm/cc).

M = the mass of powder (gm).

V_O= bulk volume of powder (cc).

b. Organoleptic Evaluation of Herbal Churna and Granules Using Human Volunteers

Organoleptic evaluation studies were carried out after obtaining permission from Institutional Ethics Committee for Human Research, Ashwini Ayurvedic Medical College and Research Centre, Tumkur. Volunteers were given *Sitopaladi churna* powder and asked to keep in the oral cavity to evaluate the taste and acceptability. Volunteer rinsed the oral cavity with drinking water and a gap of 30 minutes is given to evaluate developed *Sitopaladi churna* granule.

Evaluation of Post Compression Parameters⁸

a. Thickness

Control of physical dimension of the tablet such as thickness and diameter is essential for consumer acceptance and tablet uniformity. The thickness of the tablet was measured using Vernier callipers. It is measured in mm.

b. Hardness

The Monsanto hardness tester was used to determine the tablet hardness. The tablet was held between a fixed and moving jaw. Scale was adjusted to zero; load was gradually increased until the tablet fractured.

The value of the load at that point gives a measure of hardness of the tablet. Hardness was expressed in kg/cm².

c. Friability (F)

Tablet strength was tested by Roche friabilator. Pre weighed tablets were allowed for 100 revolutions (4 min), taken out and were dedusted. The percentage weight loss was calculated by rewriting the tablets. The percentage of friability was then calculated by,

$$F = \frac{W_{ini} - W_{fin}}{W_{ini}} \times 100$$

Where,

F = Percentage friability

W_{init} = Initial weight before friability test.

W_{fin} = Final weight after friability test.

d. Stability studies

Stability studies of pharmaceutical products were done as per ICH guide lines. These studies are designed to increase the rate of chemical or physical degradation of the drug substance or product by using exaggerated storage conditions.

Selected formulations were placed in a met pet laminates and sealed using sealing machine, stored at different storage conditions at elevated temperatures such as 40 ± 2 °C / 75 ± 5% RH for 90 days. The samples were withdrawn at

intervals of fifteen days and checked for physical changes.

RESULTS AND DISCUSSION

Moisture content, tapped bulk density and angle of repose of individual ingredients of *Sitopaladi churna* is determined and their values are mentioned in Table 1. Angle of repose values ranged from 30°62" to 40°69" for ingredients indicating the fair to possible flow properties of the ingredients. Total ash value, water soluble ash, acid insoluble ash, water soluble extract and alcohol soluble extract of *Sitopaladi churna* are determined and their values are mentioned in Table 2.

Table 2: Physicochemical Properties of *Sitopaladi churna* Without Excipients

Properties	Values
Total ash	22.00
Water soluble ash	01.43
Acid insoluble ash	04.10
Water soluble extract	36.20
Alcohol soluble extract	16.00

In order to convert the *Sitopaladi churna* into granules seven binding agents such as Avicel, PVPK30, methyl cellulose (MC), Hydroxyl propyl methyl cellulose (HPMC), starch granules, calcium carbonate and microcrystalline cellulose (MCC) are used in the trials. Starch granules are prepared in our laboratory by passing the wet mass through sieve no. 14. Croscarmellose sodium is used as disintegrating agent. Propyl and methyl parabens served as preservatives. Magnesium stearate and talc are served as lubricants, mannitol is a cooling agent. Aerosil function as anti-caking agent to stabilize the formulation. Formulations of *Sitopaladi churna* are mentioned in the Table 3.

Mixture blend of *Sitopaladi churna* formulations obtained from planetary mixture subjected for slugging to get slugs by 10 station rotary compression machine.

Table 3: Formulations of Sitopaladi Churna Granules by Dry Granulation to Improve Patient Compliance

Formulation Code	S1	S2	S3	S4	S5	S6	S7
Sitopaladi churna (gm)	250	250	250	250	250	250	250
Binding agent (gm)	25 (Avicel)	25 (PVPK30)	25 (MC)	25 (HPMC)	25 (Starch Granules)	25 (CaCO ₃)	50 (MCC)
Croscarmellose sodium (gm)	5	5	5	5	5	5	5
Propyl paraben (gm)	0.25	0.25	0.25	0.25	0.25	0.25	0.25
Methyl paraben (gm)	0.25	0.25	0.25	0.25	0.25	0.25	0.25
Magnesium stearate (gm)	2.5	2.5	2.5	2.5	2.5	2.5	2.5
Talc (gm)	12.5	12.5	12.5	12.5	12.5	12.5	12.5
Mannitol (gm)	2.5	2.5	2.5	2.5	2.5	2.5	2.5
Aerosil (gm)	5	5	5	5	5	5	5

Table 4: Properties of Sitopaladi Churna Formulations before (Bulk) Converting Into Granules

Formulation Code	Moisture Content	Sample	Angle of Repose	Tapped Bulk Density	Compressibility Index
S1	-----	Bulk	41°16"	0.714	26.30
	0.1	Granules	32°12"	0.588	12.92
S2	-----	Bulk	35°52"	0.769	23.50
	0.08	Granules	29°16"	0.606	10.89
S3	-----	Bulk	43°13"	0.689	23.60
	0.06	Granules	28°80"	0.555	12.25
S4	-----	Bulk	39°62"	0.740	20.50
	0.06	Granules	27°78"	0.645	13.95
S5	-----	Bulk	41°25"	0.758	30.60
	0.05	Granules	29°01"	0.625	29.00
S6	-----	Bulk	42°33"	0.833	20.00
	0.04	Granules	25°17"	0.800	13.87
S7	-----	Bulk	39°79"	0.660	33.30
	0.06	Granules	23°17"	0.606	08.41

Formulations containing 5% of binding agent could not produce slugs with sufficient hardness whereas formulations containing 10 % of binding agent produced slugs of sufficient hardness. However, in case of formulation S7 containing 10 % of binding agent (MCC) could not produce slugs but formulation containing 20 % of MCC were able to produce the slugs. The obtained slugs are then subjected to dry granulator (Cronimach Machinery) to get the granules of *Sitopaladi churna* formulations. (Figure 1)



Figure 1: Photo Showing the Sitopaladi Churna Powder, Slugs and Granules (Left To Right)

Properties of different blends of *Sitopaladi churna* formulations (bulk) and their granules obtained by slugging and use of dry granulator were determined and the results are mentioned in the Table 4. A perusal of Table 4 indicates angle of repose of granules was reduced compared to their corresponding bulk in all the formulations (S1 to S7). For example angle of repose bulk of formulation S1 was $41^{\circ}16''$ after converting into granules it was reduced to $32^{\circ}12''$. This indicates the flow properties of powder blend had been improved by converting into granules. While similar results are observed comparing compressibility index values for bulk and granules i.e. compressibility index values of formulations (S1 to S7) were decreased for granules while comparison with bulk. Compressibility index values of bulk of S1 formulation was 26.30% after converting into granules it was reduced to 12.92%. Decrease in compressibility index values indicates the good flow of granules prepared. Among seven binding agents used in formulation, based on angle of repose and compressibility index values

formulation containing PVP K-30 (S2), methyl cellulose (S3), HPMC (S4), starch granules (S5) and calcium carbonate (S6), MCC (S7) produced good flow able granules comparatively. Starch granules are used as binding agent instead of starch powder with the intention that coarse granules provide more efficient binding site than the powder. The observations showed that sufficient harder granules of *churna* formulations are obtained with the starch granules compared to starch powder as binding agent.

Volunteers of taste evaluation studies reported that *Sitopaladi churna* as such was not acceptable and pungent in taste. But the developed *Sitopaladi churna* granule formulation (S3) was of acceptable with suitable taste. The conversion of granules reduced the effective surface area of the *churna* having pungent taste that come in contact with the tongue upon oral intake. All the volunteers concurrently accepted the taste of *Sitopaladi churna* granule formulation.

Volunteer had mentioned their opinion of organoleptic properties of developed *Sitopaladi churna* granules in sensory evaluation forms. In the volunteer study, for organoleptic evaluation rating used is 1 to 5. As the rating is greater the organoleptic property is most acceptable. As per statistical analysis the developed *Sitopaladi churna* granules (mean 4.47) possess better appearance than marketed *Sitopaladi churna* powder (mean 3.58).

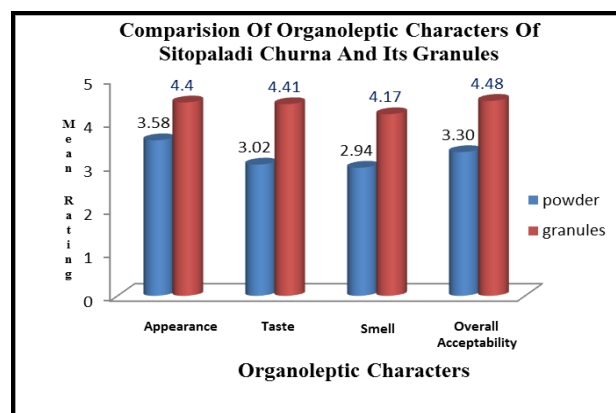


Figure 2: Comparisons of Organoleptic Characters of Sitopaladi Churna and Its Granules

Table 5: Sitopaladi Churna Paired Samples Statistics

		Mean	N	Std. Deviation	Std. Error Mean
Pair 1	Appearance of powder	3.58	39	1.0560	0.1710
	Appearance of granules	4.47	39	0.6422	0.1041
Pair 2	Taste of powder	3.02	39	1.1807	0.1890
	Taste of granules	4.41	39	0.7853	0.1257
Pair 3	Smell of powder	2.94	39	1.2128	0.1942
	Smell of granule	4.17	39	0.8544	0.1368
Pair 4	Overall Acceptability of powder	3.30	39	1.1039	0.1767
	Overall Acceptability of granules	4.48	39	0.7208	0.1154

Table 6: Comparison of Physical Properties of Triphala Tablet Formulation (S-1 to S-7) and Marketed Product

Formulation Code	Marketed product	S1	S2	S3	S4	S5	S6	S7
Thickness (mm)	5.95 ± 0.03	5.78± 0.023	5.82 ± 0.026	5.78 ± 0.012	5.75 ± 0.018	5.72 ± 0.03	5.74 ± 0.031	5.76 ± 0.03
Hardness (kg/cm ²)	4.6 ± 0.4	4.2 ± 0.3	4.1 ± 0.24	4.0 ± 0.21	4.2 ± 0.31	4.3 ± 0.32	4.2 ± 0.28	4.4± 0.25
Friability (%)	0.39	0.25	0.39	0.41	0.41	0.4	0.38	0.42
Weight variation(mg)	565± 15	570± 12	568± 11	565±13	562±10	571±9	559±15	563± 11
Disintegration time (min)	25	12	13	12.5	13.5	15.2	13.5	11.9

Similarly taste and smell of *Sitopaladi churna* granules are better than *Sitopaladi churna* powder. On statistical comparison *Sitopaladi churna* granules (Formulation S3) are overall accepted than marketed product with statistical significance (< 0.001). Feedback from the volunteers (n=39) was collected and subjected to statistical analysis using the SPSS statistical version 16.0 In., Chicago IL as shows in Table 5 and Figure 2.

Hardness, Friability and Weight variation of developed tablets are similar to the marketed product (ZANDU) however, disintegration times for developed tablets were less ranging from 11.9 to 15.2 min, as compared to

disintegration time of marketed product i.e. 25 min (Table 6). Among seven formulations S2, S3, S4, S5, S6 and S7 possess better flow properties, hence these formulations are selected for stability studies. Even after 90 days, and there is no change in the physical appearance and properties of the developed *Sitopaladi churna* granules.

CONCLUSION

The present study confirms the feasibility of use of slugging method to convert *Sitopaladi churna* into granules & Tablet dosage form, in order to improve the properties of the *Sitopaladi churna*. Among the binding agents used PVP K-30 10 %, HPMC 10 %, Starch 10 %, CaCO₃ 10 %, and

methylcellulose 10% and MCC 20% were produced a granules with suitable hardness and good flow properties. Therefore, suitable formulation strategy can overcome the unacceptability of *Sitopaladi churna* by consumers.

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