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RESEARCH ARTICLE

Formulations and Evaluations of *Sitopaladi Churna Pellets* by Pelletization Technique to Improve Patient Compliance

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ABSTRACT

The aim of this research work was conversion of Sitopaladi churnas into stable, palatable and patient acceptable pellets to swallow conveniently by direct pelletization techniques using disc pelletizer. In present times, the pelletization technologies are giving much attention as they represent an efficient pathway for manufacture of new drug delivery system. It has good advantage over the conventional dosage form. Pelletization technique help in the formation of pellets having a diameter 0.5 -1.5 mm. The Sitopaladi pellets are prepared by using seven different binding agents such as Avicel, PVPK30, Methyl cellulose (MC), Hydroxyl Propyl Methyl Cellulose (HPMC), starch granules, calcium carbonate and microcrystalline cellulose (MCC). Simultaneously Crosscarmellose sodium was used as disintegrating agent. Propyl and Methyl parabens served as preservatives. Magnesium stearate and talc are used as lubricants. Mannitol is a cooling agent. Aerosil functions as anticaking agent which can stabilize the formulation. The Sitopaladi churna pellet formulation S1-S7 were optimized on the basis of acceptable flow properties of pellets. Developed Sitopaladi churna pellets were tested for post preparation evaluation such as, Carr's index, Angle of Repose, Tapped Bulk density, swelling properties, friability, Disintegration test and particle size distribution were carried, hence S1, S3, S4, S5, S7 formulations showed better particle size distribution compare to other formulations due to drug release kinetics of these formulations are good. S6 formulation showed increase the degree of swelling due to its composition of $CaCO_3$ it acts as a gas evolving disintegrant reacts with the 0.1N HCl used as media for the evaluation of swelling property. Hence increase in the pH of the swelling media due to rapid absorption of water and swell leading to an enormous increase in volume of pellets. The disintegration time of all the formulation of Sitopaladi Pellets are disintegrate at within 15 minutes except S6, are disintegrate at within 5 minutes were observed.

KEYWORDS

Sitopaladi Churna, Binders, Disc Pelletizer, Evaluation studies of Pellets

INTRODUCTION

Herbal medicines are being used by nearly about 80% of the world population. such herbal medicines that are easily available, cheaper, time tested. Primarily in developing countries for primary health care[2].

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Assessing the current status of health care system in adequacies of synthetic drugs is likely to be more glaring in the coming years. It has been reported that there has been an alarming increase in number of diseases and disorders caused by synthetic drugs prompting a switch over to traditional herbal medicine. Ayurveda is a traditional Indian Medicinal System practiced for thousands of years. Considerable research on

pharmacognosy, chemistry, pharmacology and clinical therapeutics has been carried out on ayurvedic medicinal plants. The polyherbal formulations described in Ayurveda have been the basis of treatment of various human diseases .Selection of scientific and systematic approach for the biological evaluation of herbal formulations based on their use in the traditional systems of medicine forms the basis for an ideal approach in the development of new drugs from plants[1].

In the light of above background, the present study aimed at improves the patient compliance by using various techniques such as direct pelletization methods. Because polyherbal formulations are very hygroscopic, astringent, bitter and pungent taste and also stick to the tounge and oral cavity due to polyherbal powders are inherent adhesive nature. Polyherbal formulation of ' SITOPALADI" is an Ayurvedic herb consists of (i) Vaushalochan, a silicious material (Bambusa aurundinacea) (ii) Pippali/long pepper (piper longum) (iii) Dalachini (Cinnammomum Zeylanicum) (iv) Elachi/Cardamomom seeds (Elettaria cardamomom) and (V) Sarkra (sugar).These five beneficial composition of Sitopaladi formulations are used as remedy for cough congestion, bronchitis, trachytis, sinus headache, respiratory allergy, seasonal sneezing, wheezing and excess mucous[2].

Historically, the word pellet has been used by a number of industries to describe a variety of agglomerates produced from diverse raw materials. In the pharmaceutical industry, pellets can be defined as agglomerates of fine powders or granules of bulk drugs and excipients. They consist of small, free-flowing, spherical or semi-spherical solid units, typically from about 0.5 mm to 1.5 mm, and are intended usually for oral administration. The pelletized products can improve the safety and efficacy of the active agent [3].

Pellets offer a great flexibility in pharmaceutical solid dosage form design and development. They flow freely and pack easily without significant difficulties, resulting in uniform and reproducible fill weight of capsules and tablets[3]. Variety of techniques is available for pellet manufacturing. Layering processes have been used over the years. Those processes have some limitations such as non-uniformity in the size of the pellets and less drug loading. In recent year's extrusion-spheronization, cryopelletization, freeze pelletization and hot melt extrusion have been used to produce spherical pellets[3]

Advantages of Pellets

- ✓ They can be divided into desired dosage strength without process or formulation changes.
- ✓ When pellets containing the active ingredient are in the form of suspension, capsules, or disintegrating tablets, they offer significant therapeutic advantages over single unit dosage forms.
- ✓ They can also be blended to deliver incompatible bioactive agents.
- ✓ They can also be used to provide different release profile at the same or different sites in the gastrointestinal tract.
- ✓ Pellets offer high degree of flexibility in the design and development of oral dosage form like suspension, sachet, tablet and capsule (shown in figure 1)
- ✓ Pellets disperse freely in GI tract, maximize drug absorption, and minimize local irritation of the mucosa by certain irritant drugs.
- ✓ Improved flow characteristics: Spheres have excellent flow properties which can be used in automated processes or in processes where exact dosing is required.
- ✓ Coating: The easiest shape to coat is the sphere due to the absence of edges. It is also the most economical one to coat as no extra coating material is required to fill irregularities in the surface of the granules.
- ✓ Density increase: Both the true and the bulk density of granules are increased by spheronizing. This can improve the process and the packaging.

- ✓ Hardness and friability: Hardness and friability depend on the internal cohesive forces and surface characteristics. Spheronization increases the hardness and reduces the friability of granules. This will reduce the amount of fines generated during handling or transportation

Bitter Taste Masking By Pelletization Technique

Pellets for herbal preparation application are defined as spherical, free-flowing granules with a narrow size distribution (between 500- 1500 μm). The pelletization process consists of the agglomerates of fine powders of the herbs and excipients including the taste masking, into spherical units[4].

MATERIAL AND METHODS

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

Figure 1: Pulverizer

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.

Figure 2: Planetary mixer

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

Ingredient	Qty (gm)	Moisture content	Tapped Bulk Density	Angle of Repose
Sarkara	192	1.52%	0.78	$36^{0}52$
Vaushalochan	96	0.15%	0.89	$31^{0}70$
Pippali	48	0.07%	0.52	$41^{0}69$
Ela	24	0.18%	0.85	$30^{0}62$
Tvak	12	0.12%	0.50	$38^{0}65$

Then all the ingredients are mixed by using planetary mill.

Determination of Physicochemical Properties[5]

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 =

$$\frac{W1-W2}{w1} \times 100$$

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 ºC 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).

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.

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 ºC. The weight of the insoluble matter is subtracted from the weight of the ash; the difference in weight represents the water soluble ash.

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

a= weight residue after incineration.

y= weight of Sitopaladi churna used.

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, shaked 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 105ºC, to constant weight and weighed. Calculated the percentage of alcohol soluble extraction.

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

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

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 Pellets

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 Sitopaladi Churna into Pellets

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 above mixture is subjected to convert into pellets by using Disc pelletizer. Disc pelletizer works on the principle of direct pelletization. In direct pelletization process the powders mixtures along with all excipients are directly poured into pelletizer powders is moistened with binding solution and get converted into pellets.

Figure 3: Pelletizer

Evaluation of Pre-Compression Parameters of Pellets[6]

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,

$$Db = M / Vo$$

Where, Db= Bulk density (gm/cc).

M = the mass of powder (gm).

V_O = bulk volume of powder (cc).

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,

$$F = \frac{W(\text{intia}) - W(\text{final})}{W(\text{inital})} \times 100$$

Where,

F = Percentage friability

W_{init} = Initial weight before friability test.

W_{fin} = Final weight after friability test.

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 ^{0}C / 75 ± 5% RH for 90 days. The samples were withdrawn at intervals of fifteen days and checked for physical changes.

Particle Size Distribution

Particle size distribution was determined using mechanical sieve shaker. 10 g of the pellets were sifted through a series of sieves (16, 22, 44 and 100 mesh). The machine was operated for 5 minutes and percentage retained on respective sieves was calculated. The average particle size was determined[39]

Figure 4: Mechanical sieve shaker

Swelling Property

Swelling property was determined for each formulation batch. A weighed amount of pellets (10 g) were placed in a 100 ml measuring cylinder containing pH 1.2 media. Initial volume (Vo) of pellet was noted and change in physical volume was observed (Vt) at regular interval for 6 hr[15]. The degree of swelling was calculated using following formula[7]:

Degree of Swelling = Vt -Vo/Vo

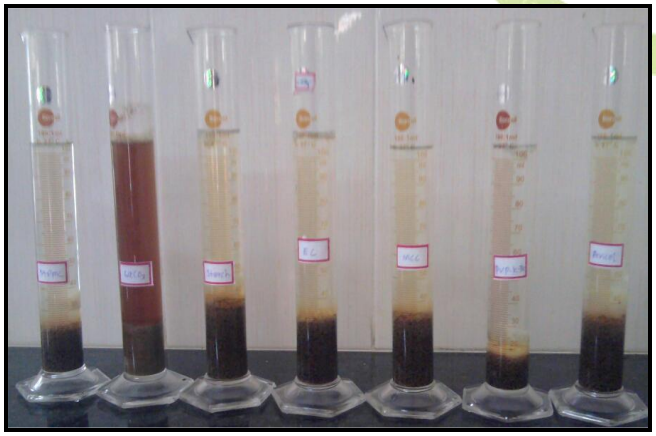

Figure 5: Different formulations of pellets of degree of swelling property

Disintegration Test

Disintegration test for two prepared pellets was done as per procedure mentioned in I.P. phosphate buffer pH 6.8 is taken as disintegration medium.

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 $30^0$62" to $40^0$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	22.02
Water Soluble ash	01.45
Acid insoluble ash	04.2
Water soluble extract	36.22
Alcohol soluble extract	16.1

In order to convert the *Sitopaladi churna* into Pellets 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 Pelletization techniques by using disc Pelletizer to get Stable Patients acceptable Pellets.

Table 3: Formulations of Sitopaladi Churna Pellets by Pelletization Technique 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 (CaCO3)	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 Pellets

Formulation Code	**Moisture Content**	**Sample**	**Angle of Repose**	**Tapped Bulk Density**	**Compressibility Index**
S1	-----	Bulk	41°16″	0.714	26.30
	0.1	Pellets	28°02″	0.588	05.26
S2	-----	Bulk	35°52″	0.606	23.50
	0.08	Pellets	27°14″	0.588	04.16
S3	-----	Bulk	43°13″	0.689	23.60
	0.06	Pellets	25°01″	0.555	10.00
S4	-----	Bulk	39°62″	0.740	20.50
	0.06	Pellets	27°75″	0.645	07.70
S5	-----	Bulk	41°25″	0.758	30.60
	0.05	Pellets	29°41″	0.625	6.50
S6	-----	Bulk	42°33″	0.833	20.00
	0.04	Pellets	25°18″	0.800	7.31
S7	-----	Bulk	39°79″	0.660	33.30
	0.06	Pellets	27°14″	0.606	11.76

Formulations containing 5% of binding agent could not produce slugs with sufficient hardness and roundness whereas formulations containing 10 % of binding agent could produce Pellets. However, in case of formulation S7 containing 10 % of binding agent (MCC) could not produce Pellets but formulation containing 20 % of MCC were able to produce the Pellets. The obtained Pellets are then subjected to Evaluation of Quality control properties like friability, disintegration and particle size distribution, swelling Property.

Figure 6: Images of Prepared Pellets of Sitopaladi Churna

Properties of different blends of *Sitopaladi churna* formulations (bulk) and their Pellets obtained by Pelletization Technique and their results are mentioned in the Table 4. A perusal of Table 4 indicates angle of repose of Pellets was reduced compared to their corresponding bulk in all the formulations (S1 to S7). For example angle of repose bulk of formulation S1 was 41º16″ after converting into Pellets it was reduced to 28º02″. This indicates the flow properties of powder blend had been improved by converting into Pellets. While similar results are observed comparing compressibility index values for bulk and Pellets i.e. compressibility index values of formulations (S1 to S7) were decreased for Pellets while comparison with bulk. Compressibility index values of bulk of S1 formulation was 26.30% after converting into Pellets it was reduced to 05.26%. Decrease in compressibility index values indicates the good flow of Pellets prepared. Among seven binding agents used in formulation, based on angle of repose and compressibility index values cellulose (S3), HPMC (S4), starch granules (S5) and calcium carbonate (S6), MCC (S7) produced good flowable Pellets comparatively.

Table 5: Evaluation of Particle size distribution of Sitopaladi Pellets S-1 to S7

Formulation Code	Retained Particles				Percent Retained Particles				Percent passed particles			
	16	22	44	60	16	22	44	60	16	22	44	60
S1	10.9	6.2	2.2	0.7	54.5	31	11	3.5	45.5	69	89	96.5
S2	10.5	4.5	3.8	1.2	52.5	22.5	19	6	47.5	77.5	81	94
S3	11.0	5.0	3.2	0.8	55	25	16	4	45	75	84	96
S4	11.2	4.8	3.8	0.2	56	24	19	1	44	76	81	99
S5	11.9	4.2	3.1	0.8	59.5	21	15.5	2.5	40.5	79	84.5	96
S6	10.1	4.2	3.2	2.0	50.5	21.0	16	10	49.5	79	84	90
S7	11.4	4.2	3.9	0.5	57	21	19.5	2.5	43	79	80.5	97.5

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.

Evaluation of Particle size distribution of developed sitopaladi formulation of Pellets were carried out by Mechanical sieve shaker, and results are obtained as given in Table 5.

Table 6: Evaluation of swelling property of Sitopaladi Pellets (S-1 to S- 7)

Formulation Code	Time in, degree of swelling			
	2hrs	4hrs	6hrs	8hrs
S1	0.025	0.045	0.0075	0.1
S2	0.033	0.066	0.1	0.166
S3	0.022	0.055	0.068	0.090
S4	0.05	0.05	0.075	0.1
S5	0.02	0.055	0.083	0.11
S6	0.13	0.181	0.204	0.25
S7	0.026	0.078	0.078	0.10

Friability and Disintegration time of developed Pellets are within the range as mentioned in Normal values of the Friability and disintegration time parameters. However, disintegration times for developed Pellets were less ranging from 4.6 to 13.10 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.

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Table 7: Evaluation of Physical properties of Triphala Pellets (T-1 to T- 7)

Formul^{n} Code	S1	S2	S3	S4	S5	S6	S7
Friability (%)	0.4	0.6	0.2	0.7	0.3	0.6	0.7
Disintegration time (min)	12.9	13.4	11.9	12.2	13.1	4.6	13.1

CONCLUSION

The present study confirms the feasibility of use of Pelletization Technique method to convert *Sitopaladi churna* into Pellets dosage form, in order to improve the properties of the *Sitopaladi churna* and also offers more advantages than granulation process. Among the binding agents used PVP K-30 10%, HPMC 10 %, Starch 10 %, $CaCO_3$ 10%, methylcellulose 10% and MCC 20% were produced a Pellets with suitable hardness and good flow properties. Therefore, suitable formulation strategy can overcome the unacceptability of *Sitopaladi churna* by consumers.

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