ISSN 0975 - 6299 Vol 2 / Issue 4 / Oct - Dec 2011

International Journal of Pharma and Bio Sciences

RESEARCH ARTICLE PHARMACEUTICS

DESIGN AND DEVELOPMENT OF TABLETS CONTAINING HIGH AMOUNT OF POLYHERBAL AQUEOUS EXTRACT WITH IMPROVED DISINTEGRATION TIME

VIJAYA SRR[1*], ANITHAKUMARI[2], RAMESH RV[2] AND SELVAKUMAR DURAIPANDI[3]

[1*]Ultra College of Pharmacy, Annanagar, Madurai, 625020, India
[2]N Ramavarier Ayurveda Foundation, Vilachery Main Road, Madurai, 625004, India
[3]School of Pharmacy, Taylors University Lakeside, Subang Jaya, 47500, Malaysia

VIJAYA SRR
Ultra College of Pharmacy, Annanagar, Madurai, 625020, India

***Corresponding author**

ABSTRACT

The polyherbal decoction, Gulugulutitakam is known for the treatment of various inflammatory conditions. For the ease of administration, this dosage form has been converted into tablets containing high amount of dry extract but it has the disadvantage of longer disintegration and dissolution parameters. In our attempt to develop tablets with improved disintegration and dissolution time, we have prepared eight formulations of varying concentrations of dry extract with different excipient blends. Super disintegrants (Cros carmellose sodium, Crospovidone, sodium starch glycolate), Diluents (Dibasic calcium phosphate) were used in the formulation of tablets. We have performed the pre-compression evaluations like Angle of repose, Carr's index and Hausner ratio to study the powder blend characteristics. We have evaluated the tablet characteristics via Friability, Hardness and Disintegration time. It was concluded that the threshold level of dry extract should be kept at 700mg/g of tablet for excipient blend of super disintegrants SSG, CCS and CP in equal parts for faster disintegration of tablets.

KEYWORDS

polyherbal, tablets, formulation, gulgulutitakam

INTRODUCTION

Poly herbal dry extracts mainly due to their hygroscopic nature, increase the tablet hardness and prolong the disintegration time. Tablets containing high doses, which often required eliciting the therapeutic action, are impossible due to their poor tabletting properties. The problem associated with this is due to multiple factors such as inconsistent botanical ingredients, moisture content and hygroscopicity, which in turn affects the powder characteristics. The direct compression of dry extract with disintegrating agents is often preferred to make herbal tablets, but have the disadvantage of prolonged disintegration time. The binding agents are not preferred since the silica loaded dry extract itself has very good compactibility and adding binders to the dry extract increases the hardness and prolong the disintegration time to the greater extent. Granulation of the dry extract either by non-aqueous wet granulation or by slugging is often preferred for producing improved flowability and compactibility. The use of lubricants during the direct compression of herbal dry extracts increases the disintegration time.[2] The tablets with high amount of magnesium stearate incorporated into the granules had shorter disintegration times than the tablets containing powdered mixture alone.[2, 3] The poly herbal dry extract makes this process very difficult due to complex nature of the powder characteristics. The Ayurveda and siddha, the Indian system of medicine, prescribes poly herbal aqueous extract (Kashayams) for various ailments and are well documented. For the ease of administration these dosage forms have been converted into tablets containing not less than 850mg of the dry extract but having the disadvantage of longer disintegration and dissolution parameters. The aim of the present investigation is to develop tablets containing high amount of poly herbal extract with acceptable disintegration time with reference to Ayurvedic Pharmacopoeia of India and to optimize the right excipient mixture for the standardization of the tabletting process and to study the effect of concentration dry extract in different excipient blends to optimize the threshold level of the dry extract in tablets.

MATERIALS AND METHODS

Materials

The polyherbal extract (PHE) is selected from the ayurvedic Kashayams namely Gulgulutitakam Kashayam used in various inflammatory conditions, contains *Piper longum* (Long piper), *Trichosanthes cucumerina, Curucma longa* (Turmeric), *Acorus calamus* (Sweet fig), *Cyperus rotundus* (Nutgrass), *Cyclea peltata*(Glaucous leaf), *Apium raveolens* (Cellary seed), *Piper nigrum*(Black pepper), *Cedrus deodara* (Deodar)*Alpinia galangal*(Greater galangal), *Commiphora mukul* (Gum-gugul, Indian Bdellium), *Azadirachta indica* (Neem tree), *Embelia ribes,* (False Black Pepper), *Solanum melongena* (Brinjal), *Adhatoda vasica* (Vasak), *Rubia cordifolia* (Indian Maddar), *Celestrus paniculatus* (Climbing staff tree), *Zingiber officinale* (Ginger), *Alpinia galangal* (Greater galangal), *Scindapsus officinalis* (Elephant piper), *Semicarpus anacardium* (Marking nut), *Peucedanum graveolens* (Indian dill), *Holarrhena antidysenterica* (Conessi bark) *Plumbago zeylanica* (Leadwort), *Picrorhiza kurroa*

(Hellebore), *Saussurea lappa* (Costus) *Cuminum cyminum* (Cumin seed), *Piper retrofractum* (Cubeb) and obtained from AVN Ayurveda Formulations Private Limited, India.

All plant materials were powdered well to a desired particle size and extracted with distilled water (1:8, w/v) to make polyherbal decoction. The total solid was adjusted to contain 17g per 100ml so that each 5ml contains 850 mg of the active botanical ingredients. The extract thus produced is mixed with Colloidal silicon dioxide (Aerosil) 0.8g per litre to reduce hygroscopic properties. Then the extract is concentrated over vacuum evaporator and dried using Vacuum tray drier, at a temperature of 70ºC for 4hrs. Appropriate amount of dry extract have been taken for the formulations containing various concentrations to optimize the threshold level of dry extract to be taken for a tablet with requisite quality.

Excipients

Microcrystalline cellulose, Crospovidone, Cross-linked carmellose sodium, Sodium starch glycolate, Colloidal silicon dioxide (Aerosil), Magnesium stearate, Polyvinyl pyrolidine, Poly ethylene glycol (PEG 400), Poly ethylene glycol (PEG 6000) were used to prepare desired excipient blends.

Methods - Slugging and Granulation

Slugs of 1 g were produced at a compression force of 2-5 Kg/cm^2 using a single-punch tablet press. The slugs were crushed in a dry granulator to obtain granules with a desired particle size. The resulting material was passed through an oscillating granulator using a sieve. The granulate fraction between 10 and 40 mesh was chosen for tablet optimization. The non-aqueous wet granulation using PVP in isopropyl alcohol (1%) was employed for making the granules before adding the excipient blends to the dry extract to increase the granule characteristics required to produce a quality tablet. Evaluation of mixed blends was carried out for all the formulations for angle of repose, bulk density, tapped density, % compressibility and flowability.

Preparation of Tablets

Tablets were prepared from each formulation described in Table-1.The granule proportion was kept constant at 85% wt/wt. The different formulations were prepared by mixing the appropriate excipients in a double cone blender for 10 minutes.

Analysis of TabletsDisintegration time

Disintegration time was measured according to the European Pharmacopoeia without disks. (Disintegration tester, Electro lab) Six Tablets randomly selected from each batch were used for the test. The disintegration medium was distilled water maintained at 37ºC.[4]

Friability

Tablet friability was measured as the percentage of weight loss of 20 tablets randomly selected from each batch tumbled in friability apparatus (Thermonic). After 5 minutes of rotation at 25 rpm, the dust of tablet was removed and the percentage of weight loss calculated.[4]

Tablet Hardness

Twenty tablets randomly selected from each batch were used for the test. Erweka automatic hardness tester type TBH 20 was employed.

RESULT AND DISCUSSION

The recommended dose of poly herbal decoction according to Ayurveda and siddha is 15ml at a time twice daily for producing required therapeutic response. When converting this decoction into a tablet form, this dosage regimen should not be altered. Thus, a tablet containing as high as 850mg of the dry extract is required and little portion is only left for the excipient blend. This excipient blend should be

selected in such a way that the tablet is formed with requisite qualities. We have performed the pre-compression evaluations like Angle of repose, Carr's index and Hausner ratio to study the powder blend characteristics. The results of this study were presented in table 1 &2.

From the study it was observed that regardless of concentration of dry poly herbal extract the disintegration time of the tablets varied unsystematically because of the nature of the powder. It was also observed that the concentration of MCC did not alter the disintegration time considerably. Likewise increasing the strength of the super disintegrant Crospovidone did not alter the DT considerably but blend of equal portions of SSG, CCS and CP at the dose level of 700mg/g of the tablet brought down the DT considerably. Addition of CP alone to the dry extract reduced the DT of the tablet appreciably when compared to the tablets containing lower amount of the dry poly herbal extract.

Table 1

Pre-compression parameters of formulations

Formulations	Bulk Density (gm/cc)	Tapped Density (gm/cc)	Angle of repose	carr's index	Hausner index
I	0.63	0.78	31.7	19.23	1.24
II	0.66	0.82	32.6	19.51	1.24
III	0.65	0.81	33.2	19.75	1.25
IV	0.54	0.64	32.7	15.63	1.19
V	0.67	0.83	33.6	19.28	1.24
VI	0.62	0.74	34.6	16.22	1.19
VII	0.53	0.63	31.2	15.87	1.19
VIII	0.69	0.84	31.8	17.86	1.22

Coating of the dry extract powder with PEG 400 and PEG 6000 before making the granules did not influence the DT considerably. Finally it was concluded that the threshold level of dry extract should be kept at 700mg/g of tablet for excipient blend of super disintegrants SSG, CCS and CP in equal parts for faster disintegration of tablets. If the dry extract is kept at higher dose, it eventually increases the disintegration time regardless of different excipient blends. To bring the DT of tablets containing high dose of polyherbal extracts within the limits of pharmacopoeial standards further research has to be performed with which newer technologies for disintegration will be envisaged.

Table: 2

Tablet formulations and their post compression evaluations

Excipients(G)	I	II	III	IV	V	VI	VII	VIII
Powder	500	600	700	700	750	800	800	850
Aerosil	18	22	25	25	27	30	30	31
Microcrystalline cellulose	280	196	73	-	-	-	-	-
Polyvinyl pyrolidine	-	-	-	1	-	-	-	-

PEG (400)	-	-	-	-	-	-	1	-
PEG (6000)	-	-	-	-	-	-	-	25
Sodium Starch Glycolate	100	100	100	92	-	85	60	-
Cros Carmellose Sodium	100	100	100	92	-	84	55	92
Crospovidone	-	-	-	90	223	-	55	-
Magnesium Stearate	2	2	2	-	-	2	-	2
Disintegration Time (min)	**27**	**32**	**49**	**13**	**36**	**41**	**51**	**46**
Hardness (kg/cm^2)	**2 to 4**	**1 to 3**	**1 to 2**	**1 to 2**	**1 to 2**	**1 to 2**	**2 to 3**	**2 to3**
Friability (%)	**0.54**	**0.23**	**0.36**	**0.73**	**0.79**	**0.59**	**0.87**	**0.65**

REFERENCE

1. De Souza TP, Bassani VL, González Ortega G, Dalla Costa TCT, Petrovick PR. Influence of adjuvants on the dissolution profile of tablets containing high doses of spray-dried extract of Maytenus ilicifolia. Pharmazie., 56, 730-733. (2001)
2. Rocksloh K, Rapp FR, Abu Abed S, et al. Optimization of crushing strength and disintegration time of a high-dose plant extract tablet by neural networks. Drug Dev Ind Pharm., 25, 1015-1025, (1999)
3. Von Eggelkraut-Gottanka SG, Abu Abed S, Müller W, Schmidt PC. Roller compaction and tabletting of St. John's wort plant dry extract using a gap width and force controlled roller compactor, I: granulation and tabletting of eight different extract batches. Pharm Dev Technol., 7, 433-445. (2002)
4. The Ayurvedic Pharmacopoeia of India, Part-I, Volume I-VII, Department of Ayush, Ministry of Health, Government of India, (2010)
5. European Pharmacopoeia Supplement. Strasbourg, France: Council of Europe, (2001).
6. Bi Y, Sunada H, Danjo K, Yonezawa Y. Evaluation of rapidly disintegrating tablet prepared by a direct compression method. Drug Dev. Ind. Pharm., 25, 571-580, (1999)
7. Kornblum S, Stopak S. A new tablet disintegrating agent: Cross linked polyvinyl pyrrolidone. J Am Pharm Assoc, 41(2), 229-272, (2001)
8. Ansel, H.C. and Allen, L.V., Pharmaceutical dosage forms and drug delivery systems, 7th edition, Lippincott, 347-56, (2000)