Section A-Research paper
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Gastrorententive delivery of Orlistat pellets - Micro particulate formulation and characterization by extrusion & spheronization

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Abstract

Multi particulate system has undergone a great change in past decade with a significant role in novel approaches achieving drug delivery within time. Much research was done in Pelletization process over the implementation and advanced techniques. It was found to be the technology enlightenment over accurate delivery. It delivers large pharmaceutical applications over the benefits of distinguished loading size of pharmaceutical ingredients specifically to APIs, distribution in minimum size and in-expensive to help in Targeted site delivery and to improve the drugs bioavailability. The present research aimed with the extrusion-spheronization processing formulation of the modified release gastro retentive orlistat micro particles of the pellets were subjected to dissolution. The drug release studies revealed that the formulated pellet produced desire effect.

Key words: Extrusion spheronization, Orlistat micropellets, Gastroretentive micropellets, Orlistat GRDDS.

Research drug delivery systems is explored comparatively to attain maximum therapeutic effect while minimizing the adverse effects. Microparticulation is one of technique to render the drug as a sustained and controlled delivery over a longer period. They can visually explained as a small solid mass or droplet dressed up with natural and synthetic polymers of attributed concentration to vary their thickness and degree of or shell.

Microparticule drug delivery system lays the focus due to its characteristic technical advancements by comparing to the conventional dosage forms by benefiting over the efficacy improvement, adverse reaction reduction and ease of patient compliance.

In this research, we aimed to formulate agglomeration process by making the wet mass of fine powders/granules or in the combination of API and excipients and passing through the extruder to form extrudes. The extrudes were further shaped as required size of spheroids by spheronizer and dried to form orlistat micro particle pellets.

A remarkable progress is achieved by using the melt extrusion, Extrusion and spheronization methods as a technique for novel drug delivery of drugs which offers the control drug delivery for oral solid and topicals by using their current technological advancements.

Materials and Methods

Orlistat was received from Biocon Ltd. as a gift sample. Ac-di-sol SD 711, Eudragit RSPO, Eudragit 30 D and Eudragit L 100 – 55 were purchased from Evonik and SD fine chemicals and drugs. The raw materials used are of Pharma grade and all other chemicals were obtained from Chemie Pvt. Ltd. All the reagents and chemicals used for the study are of Analytical grade.

Formulation development of gastro retentive orlistat pellets by extrusion and spheronization technique.

Orlistat granulated with other polymeric coating material solution. The wet mass was extruded through 5mm die. The formed extrudes were passed through 2 mm checkered plate groove die to form uniform spheroids, dried and uniformly sized to be with 20 mesh passed pellets are lubricated and are filled in Size “0” Hard Gelatin capsules.

Table 1. Composition of various formulations of gastro retentive orlistat pellets by extrusion and spheronization technique.

INGREDIENT	FUNCTION	AMOUNT IN CAPSULE (mg)							
		T1		T2		T3		T4	
		IR	SR	IR	SR	IR	SR	IR	SR
Orlistat	Active	40	80	40	80	40	80	40	80

MCC 101	Filler/Binder	10	10	10	10	10	10	10	10
DCP Anhydrous	Diluent	5	10	8	10	8	10	8	10
Ac-di-sol SD 711	Disintegrant	2.5	-	-	2.5	-	2.5	-	2.5
Magnesium stearate	Lubricant	2.5	2.5	2	2.5	2	2.5	2	2.5
Eudragit RSPO	Polymer	-	-	-	15	-	5	-	5
MCC 112	Filler	-	2.5	-	5	-	5	-	5
Eudragit 30D	Polymer	-	-	-	15	-	20	-	10
Eudragit L100-55	Polymer	-	35	-	-	-	5	-	15
Average Fill weight (mg)		60	140	60	140	60	140	60	140

Characterisation of pellets formulated by Extrusion and spheronization technique are evaluated for the following

- Particle size determination sieve method
- Weight variation testing
- Drug Content
- Dissolution study
- Stability Studies

Trial T4 was evaluated for accelerated stability testing as per the ICH guidelines. The study was conducted for accelerated conditions 40^{o}C & 75% RH up to 6 months period.

Results and discussion

Formulation of pellets

Gastroretentive Oristat pellets were prepared by using extrusion and spheronizer using various modified release polymers of Eudragit grades such as L100-55, 30 D and RSPO. Four formulations were prepared by modifying the concentration of the polymers to obtain the desired release. Trail formulation T4 was found to produce a definite microparticles.

Table 2. Characterisation of pellets formulated byExtrusion and spheronization

Pellet Characterization	Observations			
	T1	T2	T3	T4

Particle size analysis (Pellet)	0.2 to 0.5 mm	0.2 to 0.4mm	0.3 to 0.6mm	0.2to 0.5mm
Weight variation	+/-1% w/w	+/-1% w/w	+/-1% w/w	+/-1% w/w
Drug content	99.5% -99.9%	98.4% - 98.8%	99.9%-101.2%	98.9% -99.4%

The formulated pellets possessed particle size of 0.2 to 0.6 mm diameter. Weight variation and drug content results were significant with the monograph standards. The results are mentioned in table 2.

Table 3. In vitro dissolution study

TIME IN HOURS	Medium	DRUG RELEASE (%)			
	0.1N Hcl	T1	T2	T3	T4
1		12.0	14.0	13.4	12.6
2		20.8	21.4	22.4	24.6
3		39.4	36.4	37.8	38.5
4		56.0	51.5	67.2	51.5
5		66.3	61.4	73.9	61.4
6	pH 7.2 phosphate buffer	80.3	73.9	82.4	76.2
7		85.0	82.4	88.5	80.3
8		87.6	88.5	92.4	85.0
9		91.2	92.4	94.3	87.6
10		92.0	94.3	96.5	91.2
11		96.0	96.5	98.2	92.0
12		98.5	98.2	99.4	96.0

Drug release was found to show about 44.8 % at 5th hour in gastric pH and 98.1 % at 12 hours in pH 7.2. The drug release was found to be extended up to 12 hours and the results were represented in the table 3 and figure 1.

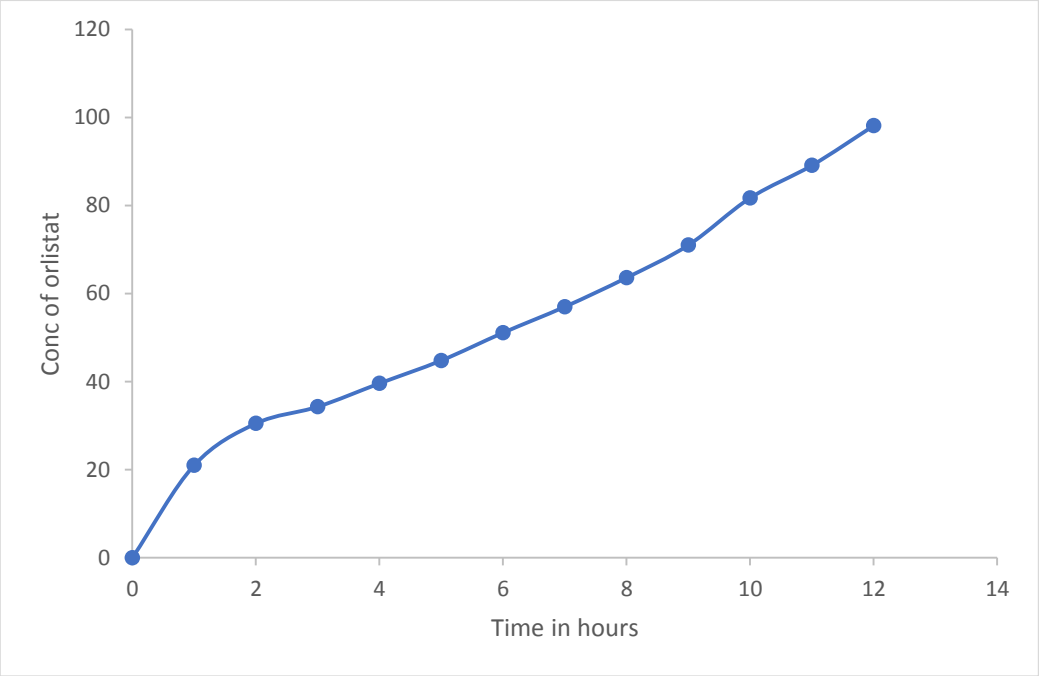

Figure 1. Dissolution profile of orlistat pellets at pH 1.2 and 7.4

Table 4. Accelerated stability testing of GRDDS pellets of orlistat

S.No	PARAMETERS	SPECIFICATION	OBSERVATIONS			
			Initial	Month - 1	Month - 3	Month - 6
01.	Description	Yellow to brownish yellow colored micro granules & Tablet filled in hard gelatin capsules	Complies	Complies	Complies	Complies
02.	Assay (%)	98% –101.5% of the Label claim	100.1%	99.84%	99.77%	99.56%
03.	Related substances (%)	Total Impurity NMT5.0	1.02	1.10	1.18	1.27

04.	Moisture content	NMT 2.0%	0.52%	0.66%	0.71%	0.79%

The stability results are represented in Table 4. The results of the accelerated stability showed no significant change in the physical appearance, drug content, related substances and moisture content. The optimised formulation showed good stability as per the ICH guidelines.

Conclusion

The formulation made by extrusion and spehonization technology for Orlistat has met the objectives of the present study and it is concluded that this floating formulation orlistat may hold promise for further commercialization and to reach the market.

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