



FORMULATION AND EVALUATION OF EXTENDED RELEASE SPHEROIDS FOR ANTIDEPRESSANT DRUG BY MUPS

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The extended release spheroids was Formulated using Ethyl Cellulose, Povidone and Triacetin as a Coating material and evaluated the effect of change in weight build up on drug release profile. Optimization of extended release coating by 19% build up of EC/PVP-K30 of formulation (F4), in which the formulation is formulated by Reservoir system and the drug release depends on coating thickness of EC/PVP-K30. As concentration of coating weight buildup increases. which increases the thickness of coating on the reservoir system hence release retarded and transformed into an extended release system.

Keywords: Antidepressants, Weight build Up, Extended Release, Thickness

INTRODUCTION

Major goal behind the project is to improved efficacy as well as pharmacological response to be achieved by formulation and evaluation of extended release dosage form. Pharmacokinetics parameters of extended release pellets altered by means of weight build up a method that ultimately affects changes in bioavailability. Amount of drug is released at a controlled rate (maintenance dose, DM) to maintain the said blood levels for some desirable period of time.^{1,2} in this Experimental Work special emphasis has been given to increase the surface area of MUPS by increase in thickness of coating layer for the individual pellets

Pellets are defined as geometrical agglomerates obtained from diverse starting materials (sucrose, starch, microcrystalline cellulose, etc) and can be produced by different process conditions.²

Above study was designed to develop a better efficacious formulation for drugs having short biological half life and low bioavailability. The dosage form may also improve solubility in water results improve pharmacological action.

METHOD AND MATERIAL EMPLOYED

Material:- The drug Duloxetine HCL was obtained from Alembic Ltd. Hypromellose, ethyl cellulose (ethocel 45 cps) were procure from the Dow Chemicals. Isopropyl alcohol (IPA), Methylene chloride was obtained from Deepak Fertilizer; Microcrystalline cellulose (Avicel PH

102) was procured from Fmc Bio.Poly. Triacetin collected from Merck and Purified Talc was obtained from Barretts Minerals.

A) Method Employed for Preparation of Core Pellets and Coating

PREPARATION OF CORE PELLETS:

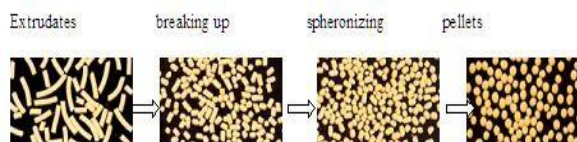
Drug Mixing and Wet Massing: During the Pellets Preparation, dry powder mixture was prepared by mixing drug, excipient in a rapid mixer granulator (Ganson Pvt. Ltd. 100L, USA) at slow impeller speed for about 15 min. The blend was granulated using purified water as granulating fluid. Additional purified water, if required was incorporated during granulation to obtain wet mass suitable for extrusion and obtaining the quality pellets in terms of roundness.

Extrusion / Spheronization: The wet mass was extruded through a screen extruder (EXDC(R) JS 60G, Fuji Paudal Co. Ltd., Japan) equipped with a standard screen 1.0 mm diameter aperture and the rolls rotating at 40-60 RPM. The extruded were transferred to a spheronizer (QJ-400TG, Fuji Paudal Co. Ltd., Japan) equipped with a crosshatch plate 1mm and processed at 15-250 rpm for 1-2 min. followed by 850-950 rpm for 1-5 min.

Drying and Sifting: The resultant pellets were dried in a fluidized bed dryer (100L, Pam-Glatt Pvt. Ltd., Germany) with an inlet temp. at 55-65°C till loss of drying achieved NMT 3.0%. The dried pellets were sifted through BSS 12 (1405 microns) and retentions were discarded.

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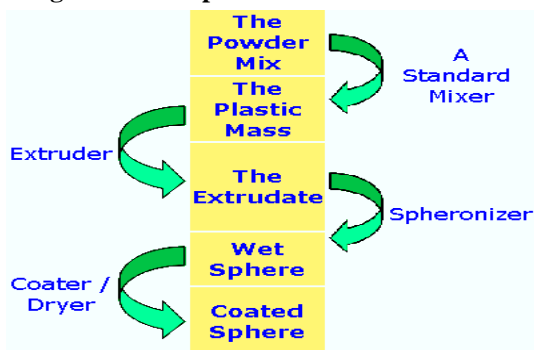


Method employed for Coating of Core spheroids

Preparation of Coating Solution for spraying on Core spheroids

Extended Release coating of Core Spheroids

Sifting of Coated Spheroids



Overview of the Formulation of ER Pellets^{1 and 2}

1) Increasing thickness of MUPS by Employing the Coating Solution :

FORMULATIONS					
Coating solution required for 50 kg spheroids	F1 (16%)	F2 (17%)	F3 (18%)	F4 (19%)	F5 (20%)
	200L	212.5L	225L	237.5L	250 L

EVALUATION OF COATED SPHEROIDS

1) The ER coated spheroids were firstly evaluated for sufficient flow properties, using various characteristics parameters such as

- Bulk Density
- Tapped density
- Compressibility index
- Hausner ratio

W(g)	(V0)	(V)	BD	TD	CI	HR
50.0	67.0	60.0	0.75	0.83	10.4	1.12
50.0	66.8	60.0	0.75	0.83	10.2	1.11
50.0	67.0	60.1	0.75	0.83	10.3	1.11
Avg	66.9	180.1	0.75±	0.83	10.3±	1.11
±S.D	±0.12	±0.06	0.0	±0.0	0.13	±0.0

W= Weight of drug taken, V0 = Initial volume, V= Final volume

2) *IN VITRO* DRUG RELEASE OF FORMULATED FORMULATIONS

The in-vitro dissolution studies were carried out using USP 24 dissolution apparatus Test was carried out for a total period of 24 hours.

2) Percentage drug release of all formulations

% cumulative drug Release						
Time	Innovator	F1	F2	F3	F4	F5
1hr	9	12	10	7	6	4
4hrs	49	69	60	53	48	40
12hrs	89	93	87	81	78	63
24hrs	101	101	99	95	91	74

The result shows that dissolution depends on particle size and surface area. Greater the particle size less is the surface area and less will be the dissolution. Effect of change in weight build up with increase in thickness of coating layer on drug release profile.

RESULT & DISCUSSION

Based on the literature search and reference product review, prototype development initiated with preparation of core spheroids by extrusion/spheronization technique followed by coating the spheroids with an extended release rate controlling polymer by employing Wurster Coater

Optimization of extended release coating builds up 19% build up of EC/PVP-K30 of formulation (F4), in which the formulation is formulated by Reservoir system and the drug release depends on coating thickness of EC/PVP-K30 as concentration of coating weight buildup increases it increases the thickness of coating on the reservoir system hence release retarded and transformed into an Extended release system which shows The result better to that of Innovator and meets up the requirements of extended release system. The pellets were analyzed for the parameters such as bulk density, tapped density, compressibility index, Hausner's ratio and the results were found within the limits

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Received 14th September 2014

Revised 21st September 2014

Accepted 26th September 2014

J. App. Pharm. Res., 2 (4); 2014: 24 – 26