Current Pharma Research
ISSN: 2230-7842
CPR 2(2), 2012, 466-470.

Design and Development of Drug Coated Pellets of Erythromycin Base by Using Extruder and Spheronizer.

Gaikwad A.D, *Yadav V.D, Jadhav P. D, Sabale V.U, Gaikwad V. D.
Department of Pharmaceutics, Arvind Gavali College of Pharmacy, Satara, Maharashtra, India.

Abstract
To formulate and Evaluate Enteric Coated Erythromycin Base Pellets. In this study, it is planned to prepare Erythromycin Base Pellets by using Extruder and Spheronizer and to coat the resulting spherules with enteric coating polymer. Erythromycin Base is acid labile and gets degraded in stomach. Conventional enteric coated tablets are available in the market for Erythromycin base which get release the drug in the alkaline media after reaching the small intestine .The transit time required for the tablet to travel from the stomach to the intestine is more than the pellets. The enteric coated tablet of Erythromycin base also releases the drug in the intestine when the enteric coating disintegrates in the alkaline medium of small intestine which also prolongs the onset of action of the drug, whereas the Erythromycin base enteric coated pellets filled in the capsule are released in the stomach after disintegration of the capsule and are easily carried easily and faster to the small intestine due to their narrow particle size distribution and drug is released in intestine after disintegration of the enteric coating , where as these transit time is delayed in case of tablet which also in turn delays the onset of action of the drug. So due to uniform distribution in the gastrointestinal tract resulting in a reduction of peak plasma fluctuations. The reduction of the variation in gastric emptying rates and also the overall transit time for Pellets is also a major advantage over the enteric coated tablet which is the object of this present research topic.

Key Words
Erythromycin, Extruder, Spheronizer.

Introduction[1-4]
Pellets a solid dosage in the shape of a small sphere. Pellets as drug delivery systems offer not only technological advantages, such as better flow properties, less friable dosage form, narrow particle size distribution, ease of coating, and uniform packing, but also therapeutic advantages. Therapeutic advantages include less irritation of the gastrointestinal tract, a lowered risk of side effects associated with dose dumping, and a uniform distribution in the gastrointestinal tract resulting in a reduction of peak plasma fluctuations. The reduction of the variation in gastric emptying rates and the overall transit times is also a major advantage. Pellets can be produced in many different ways: extrusion-spheronization, a 3-step process that has been studied extensively, is used most often. Alternative techniques for producing pellets are the single pot methods, where pellets are produced, dried, and coated in the same equipment. They are 1-stepprocesses that take place in one machine, such as a high-sheer mixer or a rotary processor. Using one machine for the whole process ensure batch- to-batch reproducibility and reduction of production time and cost, and enables automation of the process. Extrusion/spheronization is a multistep process used to make uniformly sized spherical particles. It is used primarily to produce multiparticulates for controlled drug release applications. The major advantage over other methods of producing drug loaded spheres or a pellet is the ability to incorporate high levels of active ingredients without producing excessively large particles (i.e. minimal excipients are necessary).

***Corresponding Author:**
vishal_dy@yahoo.co.in

Material and Methods
Erythromycin, Microcrystalline Cellulose, PEG 400, Sodium Lauryl Sulphate, Colloidal Silicon Dioxide, Hydroxy Propyl Methyl Cellulose was obtained as a gift samples.

Prototype Formulation Development
Procedure
1. Weigh erythromycin Base, Microcrystalline Cellulose, Sodium Lauryl sulphate, Crosscarmellose Sodium and passed through sieve # 40 mesh then mix in polybag.
2. Weigh Hydroxypropyl methyl Cellulose (Methocel E3) and slowly dissolved in

purified water with continuous stirring. Add 2gm of PEG 400 in a binder solution.
3. Granulate the blend in step 01 by using binder solution in step 2.
4. Check the LOD of wet mass.
5. Pass the wet mass through the extruder at optimum speed to obtain uniform extrudes.
6. Load the extrude in spheronizer and rotate the spheronizer at optimum speed to obtain the pellets. (Table no1)

Observation

Extruder

Extrudes formation is mainly depends on the LOD of wet mass. This wet mass is getting crushed between pressing cams, so that the mass is get entered in mesh. Mesh size used is 1.0 mm. This gives formation of Extrudes which are having similar size.

Spheronizer

Pellet Formation is mainly depends on plate rpm speed. At initially Plate rpm speed is 450rpm. According to shape of the pellets, speed of plate was increased. According to the speed of plate, extrudes are get converted into pellets. Lastly, when pellets are formed, speed of plate is decreased. But due to loss of moisture content, pellets of dumble shaped was formed.

Coating of Pellets: Enteric Coating (12.5 %)

Procedure

1. Add 56gm of Eudragit L-30D 55 in 170 ml of water under continuous stirring.
2. Dissolve 1.4 gm of Triethyl Citrate in 11 ml of water.
3. Dissolve 60 mg of Panceau 4R in 10.52 ml of water.
4. Mix the prepared solution in step 1, 2, 3 together in beaker with continuous stirring.
5. Use this solution as enteric coating material for coating of Erythromycin Base Pellets in Fluid Bed Processor (Wurster Chamber).
6. This coating gives 10% build up on Erythromycin Base Pellets. (table no 2)

Total Process Time: 7 hour
Evaluation of Erythromycin Base Pellets
Bulk Density: Mass/Volume: 20/28 = 0.714
Tapped Density: Mass/Tapped Volume: 20/27 = 0.740
Hausner Ratio: Tapped Density/Bulk Density = 0.740/0.714 = 1.0364
Compressibility Index I = 3.58
Total Weight of Capsule: 12566.5 mg
Average Weight: 628.3 mg
Standard Deviation: 12.46206

Disintegration Test

In this test Erythromycin Base Pellets (about 3gm) was kept in filter cloth which was placed in the Disintegration test Apparatus. Erythromycin Base Pellets was placed in 0.1 N HCL for 2hr and then in 6.8 Phosphate Buffer for 20minutes.
Media Used: 0.1 N HCL and 6.8 Phosphate Buffer.
Temperature Condition: 37±2°C
Observation: Erythromycin Base Pellets do not penetrated by 0.1 N HCL i.e. there was no any sign of crack. After 2hrs these pellets was placed in 6.8 Phosphate buffer, which get disintegrated within 16minutes.
Disintegration Time: 2hrs 16 min
Result: Enteric coating test was passed.

Results and Discussion

Analytical Method

Analytical Method suitable to determine content of Erythromycin Base Pellets was developed. Erythromycin Base Pellets are filled in Zero Size Capsule (elongated) and then dissolution Study is performed. That capsules are kept in Basket in 0.1 N HCL for 1hr and then in Phosphate buffer of PH 6.8 for 1hr. Erythromycin Base Pellets Shows Absorption maxima at 410 nm.

Preformulation Study

In preformulation study Erythromycin Base and Excipients where characterized for bulk and tapped density. Result of computed compressibility index and Hausner ratio shows that all material has sufficient compressibility and flow property.

Formulation of Erythromycin Base Pellets

In this formulation, Erythromycin Base is used as API (55.5%), Microcrystalline cellulose as diluent (34.2%), Na Lauryl Sulphate as Surfactant (0.6%), Ac-di-sol as Disintegrant (4.44%), Methocel E-3 as Binder (4%) and PEG 400 (1.11%) as Plasticizer. By using Methocel E-3 and PEG 400, wet mass of Erythromycin Base was prepared. This wet mass was checked for LOD. After coming exact LOD, this wet mass was passed through the Extruder which gives formation of Extrudates. These extrudes was poured in the Spheronizer Plate. By maintaining proper rpm speed extrudes was get converted into round shape pellets (table no 1 and 2).

Coating Process of Erythromycin Base Pellets

Erythromycin Base Pellets was coated by using 12.5% Eudragit L-30- D-55 in Fluid Bed Processor. In the process containing, Eudragit L-30D-55 was used for enteric coating. It includes other ingredients such as Triethyl citrate, Panceau 4R color. In this process, by maintaining proper Atomization, Fluidization, Product temperature (35-40deg) and Inlet temp. Coating process should be completed (Table no 2-4).

Effect of Binder solution

In Erythromycin Base Pellets preparation, Methocel E-3 was used as Binder solution. Methocel E-3 was gives more strength and consistency to the pellets. Methocel E-3 gives strength to the Extrudates, so that they will not break during the rotation in the plate of the Spheronizer.

Discussion of Effect of MCC during the Pellet Formation

Microcrystalline cellulose was used as a diluent in the Erythromycin Base Pellet formation. MCC maintains moisture level and round shape of the pellets. Due to MCC, these extrudes on the Spheronizer plate while increasing speed get converted into round shape pellets. But due to less moisture content, extrudes do not converted into round shaped pellets.

Discussion of Physical Parameter

Bulk Density: Bulk density was determined by using mass by volume ratio.

Tapped Density: Tapped density was determined by using mass by tapped volume ratio.

Hausner ratio: Hauser ratio was determined by using tapped density by bulk density ratio.

Compressibility Index: Compressibility index was determined by using volume before and after tapping ratio.

Particle Size Analysis: Particle size analysis was done by using Sieve Shaker (Table no. 5).

Discussion of Weight Variation Test: In this test 20 capsules are individually weighted and their average weight was determined and compares the average weight to the individual weight of the capsule (Table No. 6).

This batch was taken for 400 Capsules. In this batch 12.5% enteric coating was applied on Erythromycin Base Pellets. In this batch, Pellets formed having doubled shape, due to absorption of moisture in the spheronizer plate. This batch given 79.29% of Drug release and 90.62% Assay (Table no 7&8).

References

1. Gandhi B.G, Badgujar B.P, Kasliwal A.V. *IJPPS, 2011, 3, 96.*
2. Patel H.P, Patel J.K, Patel R.R , Patel M.P. *IJPWR 2010,2,1.*
3. Ghebre-Sellassie, I. in Pharmaceutical Pelletization Technology (Ghebre-Sellassie, I., ed.), 1–13, 1989, Marcel Dekker.
4. Kumar M. A., Lakshmi P.K., Balasubramanium JIPTR 2011,3, 2, 968.

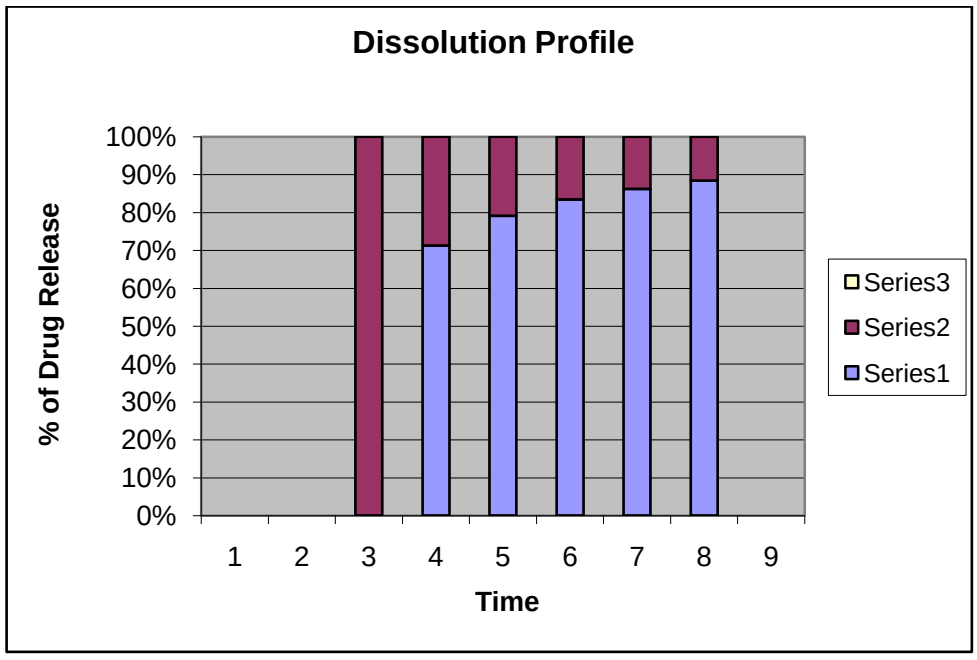

Fig. 1: Dissolution profile.

Table 1: The component of pellets.

Sr. No.	Ingredient	Qty (%)	Qty/Capsule	Qty/Batch (400 Capsule)
1	Erythromycin Base	55.5%	250mg	100gm
2	Microcrystalline Cellulose	34.2%	154mg	61.6mg
3	Sodium Lauryl Sulphate	0.6%	3mg	1.2gm
4	Crosscarmellose Sodium	4.44%	20mg	8gm
5	Methocel E3	4%	18mg	7.2gm
6	Polyethylene glycol 400	1.11%	5mg	2gm
7	Purified Water	q. s.	q. s.	155ml

Table 2: The component of pellets coating.

Sr No.	Ingredient	Quantity taken
1	Eudragit L-30D 55	56gm
2	Triethyl Citrate	1.4gm
3	Panceau 4R colour	3.92mg
4	Purified Water	191.52ml

Table 3: The results of pellets evaluation.

Sr No.	Parameters	Results
1	LOD of wet mass	42.61 % w/w
2	Total weight of Pellets	130.2 gm
3	Amounts of Fines	4.9 gm
4	% of pellets retain on 40 #	96.23 %
5	LOD of Dried Pellets	1.57 %w/w
6	Percentage Yield	72.33 %w/w

Table 4: The results of pellets evaluation.

Sr. No.	Parameter	Limits
1	Inlet temperature	50°C±1 5°C
2	Outlet temperature	To be monitored
3	Bed temperature	36°C± 5°C
4	Spray rate	0.6 to 1.0 rpm
5	Solid Content	18.203 gm

Table 5: The results of Particle Size Analysis.

Sr. No.	Sieve Size	Initial Weight	Final Weight	Difference	% Retention	Cumulative Frequency
1	710 micron	359.2gm	378.9gm	19.7gm	90.36%	90.36
2	600 micron	353.6gm	354.5gm	0.9gm	4.12%	94.48
3	500 micron	334.7gm	335gm	0.3gm	1.37%	95.85
4	355 micron	325.2gm	325.8gm	0.6gm	2.75%	98.6
5	250 micron	319.2gm	319.5gm	0.3gm	1.37%	99.97

Table 6: The results of Weight Variation Test.

Capsule No.	Capsule Weight(mg)	Capsule No.	Capsule Weight(mg)
1	628.9	**11**	639.2
2	616.9	**12**	631.4
3	629.8	**13**	624.4
4	642.4	**14**	630.4
5	643.7	**15**	589.2
6	610.8	**16**	636.1
7	636.1	**17**	622.8
8	637.4	**18**	628.6
9	638.1	**19**	630.4
10	620.4	**20**	629.5

Table 7: The results of Dissolution Study.

Sr. N0.	Sample ID	Absorbance at Wavelength 410 nm	% of Drug Release	Concentration (µg/ml)
1	Blank solution	0.000	------	------
2	Standard Solution	0.437	------	15.3
3	60 min_1 Solution	0.346	78.81%	11.8
4	60min_2 Solution	0.354	80.63%	12.1
5	60min_3 Solution	0.347	79%	11.9
6	60min_4 Solution	0.348	79.26%	11.9
7	60min_5 Solution	0.350	79.72%	12
8	60min_6 Solution	0.344	78.35%	11.8
9	Standard_1 Solution	0.439	------	------

Table 8: The results of Assay.

Sr. No.	Sample ID	Absorbance at 410 nm	% Assay	Concentration (µg/ml)
1	Blank Solution	0.000	-----	------
2	Standard Solution	0.437	-----	15.3
3	First Sample	0.377	90.38%	13
4	Second Sample	0.379	90.86%	13.1

****