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RESEARCH ARTICLE

Effect of Polymers on Amoxicillin Release from Matrix Tablets

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ABSTRACT

Sustained Release Matrix Tablets of Amoxicillin were prepared by using Different Rate controlling polymers like Sodium Alginate, Chitosan, Guar Gum and Eudragit L100. Developed total four formulations by using Direct Compression method. The prepared sustained release matrix tablets were evaluated for different evaluation tests like weight variation, Hardness, thickness, friability, Content Uniformity and Invitro release studies. Out of all the four formulations F4 containing eudragit L 100 showed 100 % drug release within 10 hours with sustained. So, Eudragit L100 was selected as best formulation based on the evaluation tests.

Keywords: Matrix tablets, sustained release dosage forms, Amoxicillin, Eudragit L100.

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CONTENTS

1. Introduction

Sustained Release dosage forms are most convenient dosage forms to improve the bioavailability of drugs. These dosage forms delay the release of drug by matrix formation there by allowing the drug to get soluble and absorbed completely from intestinal mucosa. These dosage forms are prepared by using rate retarding polymers which form network like matrix upon hydration.[2] The drugs which are sensitive to gastric environment can also be protected by formulating as matrix type dosage forms because of their ability to withstand the acidic environment. To get a successful sustained release product, the drug must be released from the dosage form at a predetermined rate and dissolve in the gastrointestinal fluids.[1] The formulations of

sustained-release drug delivery systems wish to achieve desired release rates, decrease the number of daily administrations, improve compliance and minimize side-effects. Among all the formulations of sustained release, matrix tablets are useful because of many advantages.[3]

In Present work Amoxicillin used as a model Drug, which is an Antibiotic, formulated into sustained Release Matrix tablets using different natural and synthetic polymers like Hydroxy Propyl Methyl Cellulose, Eudragit L-100, Sodium Alginate, Chitosan, Micro Crystalline Cellulose as Diluent, Magnesium Stearate as Lubricant and Talc as Glidant[5,13].

2. Materials and Methods

Amoxicillin was obtained from Sura Labs, Hyderabad, Eudragit L 100, HPMC were obtained from Yarrow Chemicals, Mumbai,Chitosan and Sodium alginate were obtained from Monsanto Chemicals, Micro Crystalline Cellulose Purchased from NR Chem Mumbai and Magnesium stearate Was purchased from Accord Labs, Hyderabad.

Methodology

Pre formulation studies[15,16]:

Standard graph of amoxicillin :

In 0.1 N HCl : 100 mg of drug was taken into 100ml volumetric flask and is dissolved in few amount of HCl and it was made up to mark with 0.1N HCL and it was named as stock -1 which gives 1000µg/ml.and then taken 10 ml from stock-1 into100 ml volumetric flask and dilute it with medium and label it as stock-2 which gives 100µg/ml. From stock-2 0.2 ml was taken into 10 ml volumetric flask and diluted up to mark with 0.1N HCl and labelled as 2 µg/ml solution and similarly prepred different concentrations like 4, 6, 8 and 10 was µg/ml and absorbance was determined at 217 nm.

In pH 7.4 phosphate buffer : First 100 mg of drug was taken and is dissolved in few amount of pH 7.4 phosphate buffer in 100 ml volumetric flask, after it has been completely dissolved it was made up to mark with pH 7.4 phosphate buffer and it was named as stock -1 which gives 1000µg/ml.and then after take 10 ml from stock-1 in to100 ml volumetric flask and dilute it with pH 7.4 phosphate buffer (medium) and label it as stock-2 which gives 100µg/ml. From stock-2, 2 ml was taken in 10 ml volumetric flask and diluted up to mark with pH 7.4 phosphate buffer and labelled as 2 µg/ml solution and similarly prepred different concentrations like 4, 6, 8 and 10 was µg/ml and absorbance was determined at 217 nm.

Formulation of Tablets:

Weighed required quantity of amoxicillin and transferred it in to a polybag ,and Eudragit L100 is added as rate controlling polymer and MCC is added as diluents and mixed for 10 min, and finally before compression magnesium stearate and talc was added for powder blend and mixed together, and compressed in to tablets by using four station rotary tablet punching machine. Simultaneously with HPMC, Chitosan, Sodium alginate, different formulation were prepared[11,12].

Determination of Flow Properties:

a) Angle of Repose[6,7]:

The angle of repose is determine by allowing mass of powdered to flow freely through an orifice from a certain height and form a conical heap on the horizontal surface. The angle of repose is determined by the formula[22]

$$\tan\theta = h/r \text{ or } \theta = \tan^{-1} h/r$$

where, θ is the angle of repose,
h is the hight of the heap of powder and
r is the radius of the base of the heap of powder.

b) Compressibility Index[15]:

$$C = 100(1 - B/T)$$

Where, B is the freely settled bulk density of the granules, T is the tapped bulk density of the granules.

c) Hausners ratio[19]:

Hausners ratio is the measure of the propensity of a powder to be compressed.

d)Bulk Density[24, 25]:

Bulk density of a powder is defined as the ratio of the mass of the powder and its bulk volume. For bulk density determination a weigh quantity of the powder material is introduce into a graduated measuring cylinder and volume of powder is determine.

Bulk Density = Mass of the powder/ Bulk volume

Units: g/cm^3

e) Tapped Density[27]:

For determination of the bulk density, a weigh quantity of the granular powder is introduced into a graduated measuring cylinder and is tapped mechanically either manually or using a tapping device till a constant volume is obtain.

Tapped density = Mass of the granular powder/ Tapped volume of granule.

Post Compression Charecterization

a. Weight Variation Test[26,28]:

The weight of tablet is measured to ensure that the tablets contain the proper amount of drug.

1. The weight variation test is run by weighing 20 tablets individually.
2. Calculated the average weight.
3. Compared the individual tablet weights with the average weight.

b. Friability [10]:

This test evaluates ability of tablet to with abrasion and edge damage during packing, handling and shipping. Friability is measured by the help of Roche friabilator. A number of pre weigh (10) tablet is placed in plastic chamber that revolves at 25 rpm for 4 min (or) 100 revolutions. The tablet are then de-dusted and reweighed. The friability is calculated by the formula. Acceptance limit of friability is: 0.5 –1%.

$$F = (1 - w/w^*)\ 100$$

Where,
W* is the original wt. of tablet
W is the final wt. of tablet after test.

c. Hardness Test[30 ,21]:

Tablet requires a certain amount of hardness to with stand mechanical shock of handling in manufacture, packaging and shipping. Hardness is measured with the help of hardness tester like:Monsanto tester, Pfizer tester, Strong cob tester.

Hardness is measured with the help of Monsanto tester. The tester consists of a barrel containing a compressed spring held between two plungers. The lower plunger is then forced against a spring by turning a threaded bolt until the tablet fractures. As the spring is compressed, a pointer rides along a gauge in the barrel to indicate thither force. The force of fracture is record and the zero force reading is deducted from it[23]. Hardness is measured in kg/ cm sq^2

d. Content uniformity[18]:

Using UV Visible spectrophotometer found the amount of the drug using the calibration curve method.

The variation in percentage of medicament per tablet is due to the following reasons:

1. Weighing of materials before granulation.
2. During the process of granulation.
3. Variation in the weight of an individual.

Dissolution Test[29]:

Selected Amoxicilline matrix tablets from F-1 formulation and place it in a Type-1 dissolution apparatus containing 900 ml of 0.1 N HCL .with an RPM of 70 and which is maintained at a temp of 37±5ºc up to 2 hrs and after that the medium was replaced with pH 7.4 phosphate buffer and continued the dissolution up to 10 hrs by withdrawing samples at different time intervals at 0.5hr, 1hr, 2hrs, 4hrs, 6hrs, 8 and 10hrs by replacing with same ml of medium, and absorbance for the collected samples using UV Visible spectrophotometer at a wave length of 217 nm; and from the absorbance percentage drug release was calculated and a graph was plotted by taking time on X-axis and percentage drug release on Y-axis.

3. Results and Discussion

Evaluation of powder blends for precompression parameters:

The bulk density of granules were found to be in the range 0.37 to 0.50 w/v. The tapped density of granules was found to be in the range of 0.62 to 0.43 w/v. The flow characteristics of granules were assessed by determining their angle of repose which is found to be in the range of 280 to 320 and compressibility index was found to be in the range of 11.6 to 21. The hausners ratio was found to be in the range of 1.12 to1.27.

Post Compression Parameters:

The prepared tablets were evaluated for their weight variation, hardness, friability, drug content uniformity. Tablet hardness was found to be in the range of 5.1 to 5.6kg/cm^3. Friability values which are also affected by the hardness of the tablets in the range of 0.10 to 0.68.

The drug content was found to be in the range of 95.85 to 99.23%

In vitro drug release of prepared tablets:

The percentage drug release of Amoxicillin matrix tablets was found to be 102 % for F1 and F4 formulations with in 10 hrs. F3 and F2 formulations showed 100 % drug release in 8 hrs. Based on all the evaluations F4 formulation containing Eudragit showed sustained Drug Release.

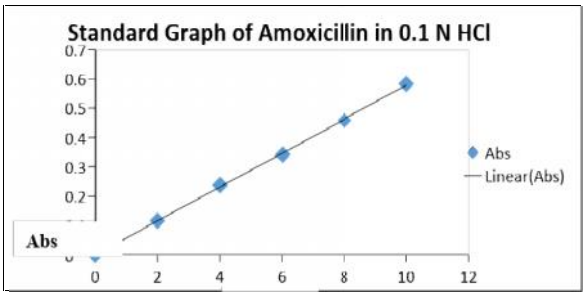

Figure 1: Standard graphs of amoxicillin in 0.1 N HCl

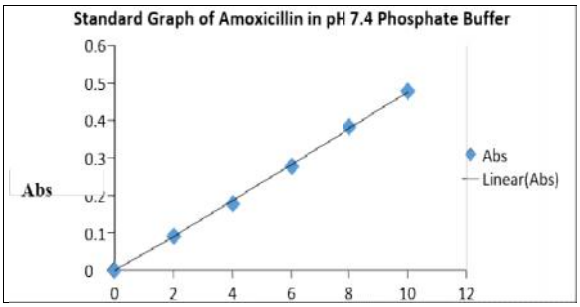

Figure 2: Standard graph of amoxicillin in pH 7.4 phosphate buffer

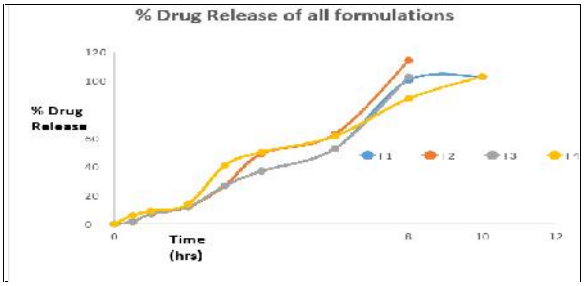

Figure 3: Percentage Drug Release of Prepared Amoxicillin Matrix Tablet

4. Conclusion

It was concluded that the Amoxicillin Sustained Release Matrix Tablets prepared with Eudragit showed more retarded drug release with sustained action within 10 hours. So, F3 formulation was selected as optimized formulation based on all the evaluation tests. Eudragit L100 is useful for more retardation of drug release by increasing the concentration.

Table 1: Composition of Amoxicillin Matrix Tablets

Ingredients	F1	F2	F3	F4
Amoxicillin	250	250	250	250
Sodium Alginate	125	-	-	-
HPMC	-	125	-	-
Chitosan	-	-	125	-
Eudragit L100	-	-	-	125
MCC	105	105	105	105

Mg stereate	10	10	10	10
Talc	10	10	10	10

Table 2: Relationship between angle of repose and flowability

Angle of repose	Flowability
<25	Excellent
25-30	Good
30-40	Passable
>40	very poor

Table 3: Relationship between compressibility and flowability

Compressibility	Flow ability
5-15	Excellent
12-16	Good
18-21	Fair passable
23-35	Poor

Table 4: Tapped density/bulk density

Hausner's ratio	Flow ability
>1.25	Poor
<1.25	excellent

Table 5: Weight variation limits

Average weight of the tablet (mg)	Maximum % difference
130 or less	10%
130 – 324	7.5%
More than 324	5%

Table 6: Standard graph of amoxicillin 0.1N HCl and pH 7.4 phosphate buffer by using UV spectroscopy

Concentation (mcg/ml)	Absorbance	Absorbance in pH 7.4 phosphate buffer
0	**0**	**0**
2	0.117	0.092
4	0.238	0.178
6	0.342	0.278
8	0.458	0.384
10	0.583	0.479

Table 7: Physical Properties of powder blends

Formulation	Bulk density (g/ml)	Tapped density (g/ml)	Compressability index (%)	Hausners ratio	Angle of repose (Ɵ)
F1	0.40	0.45	11.11	1.12	29^0.3'
F2	0.37	0.47	21.2	1.25	28^0.3'
F3	0.38	0.43	11.6	1.13	28^0.7'
F4	0.50	0.62	20.0	1.27	32^0.4

Table 8: Physical properties of prepared tablets

Formulation	Weight variation test (mg)	Hardness test (kg/cm^3)	Friability test (%)	Drug content (%)
F1	498.6	5.1	0.30	98.23
F2	500.3	5.2	0.10	95.85
F3	502.8	5.4	0.68	97.85
F4	501.4	5.6	0.26	99.23

Table 9: Cumulative % drug release of all the formulations

Time (hrs)	% Drug Release			
	F1	**F2**	**F3**	**F4**
0	0	0	0	0
0.5	1.52	1.52	1.52	5.94
1	7.07	7.07	7.07	9.09
2	11.68	11.68	11.68	13.71
3	26.65	26.65	26.65	40.80
4	37.01	49.01	37.01	50.15s
6	52.67	62.78	52.67	61.39
8	100.42	114.06	102.69	87.54
10	102.69	-	-	102.95

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