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Research Article

FORMULATION AND EVALUATION OF DISPERSIBLE TABLETS OF AMOXICILLIN TRIHYDRATE AND DICLOXACILLIN SODIUM

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ABSTRACT
In the present work attempts were made to prepare dispersible tablets of Amoxicillin trihydrate and Dicloxacillin sodium by direct compression technique to enhance patient compliance. The three superdisintegrents used in the study were Crosscarmellose sodium, Crospovidone and Sodium starch glycolate. Tablet batches having superdisintegrents at different concentrations (20,30 and 60 gm) level were prepared. The prepared batches of tablets were evaluated for uniformity of weight, thickness, hardness, friability, disintegration test and *invitro* – dissolution study. Tablet containing combination of Crosscarmellose sodium and Crospovidone showed excellent invitro disintegration time and drug release as compared to other formulations.
KEYWORDS: Amoxicillin trihydrate, Dicloxacillin sodium, Invitro evaluation, Superdisintegrents.

INTRODUCTION

Tablet is the most widely used dosage form because of its convenience in terms of self administration, compactness and ease in manufacturing. For the past one decade, there has been an enhanced demand for more patient – friendly and compliant dosage forms. As a result, the demand for developing new technologies has been increasing annually [1]. Many patients find it difficult to swallow tablets and hard gelatin capsules and thus do not comply with prescription. This results in high incidence of noncompliance and ineffective therapy [2]. The proper choice of superdisintegrant and its consistency of performance ar e of critical importance to the formulation development of fast dispersible tablets [3].

Amoxicillin is a penicillin antibiotic. Amoxicillin is used to treat many different types of infections caused by bacteria, such as ear infections, bladder infections, pneumonia, gonorrhea, and E. coli or salmonella infection. Amoxicillin is also sometimes used together with another antibiotic called clarithromycin (Biaxin) to treat stomach ulcers caused by Helicobacter pylori infection. This combination is sometimes used with a stomach acid reducer called lansoprazole Prevacid**.** This drug acts by inhibiting the synthesis of bacterial cell walls. It inhibits cross linkage between the linear peptidoglycan polymer chains that make up a major component of the cell walls of both Gram-positive and Gram-negative bacteria. It has two ionizable groups in the physiological range (the amino group in alpha-position to the amide carbonyl group and the carboxyl group) [4].

Dicloxacillin exerts a bactericidal action against penicillin-susceptible microorganisms during the state of active multiplication. All penicillins inhibit the biosynthesis of the bacterial cell wall. By binding to specific penicillin-binding proteins (PBPs) located inside the bacterial cell wall, dicloxacillin inhibits the third and last stage of bacterial cell wall synthesis. Cell lysis is then mediated by bacterial cell wall autolytic enzymes such as autolysins; it is possible that dicloxacillin interferes with an autolysin inhibitor [5].

The objective of the present study is to develop dispersible tablets of Amoxicillin trihydrate and Dicloxacillin sodium and to study the effect of functionality differences of superdisintegrants on the tablet properties.

MATERIALS AND METHODS

Amoxicillin trihydrate and Dicloxacillin sodium was a gift from Micro Labs PVT LTd. The superdisintegrents used was analytical grade from Micro Labs PVT LTd . All the other chemicals used were of analatycal grade.

Preparation of dispersible tablets of Amoxicillin trihydrate and Dicloxacillin sodium

Dispersible tablets containing 150mg Amoxicillin trihydrate and 157mg Dicloxacillin sodium were prepared by direct compression method and various formula used in the formulation are shown in table 1. Each formulation having different ratios for superdisintegrents, are mixed uniformly. The prepared powder blend was evaluated for various parameters like bulk density, tapped density, angle of repose, compressibility index and Hausner ratio. After evaluation of powder blend the tablets were compressed with a rotary punch-tableting machine (Rimek Mini Press- 1) using 12.5 mm normal plain punches.

Evaluation of powder blends [6-9]

Bulk density

Apparent bulk density (b) was determined by placing presieved drug excipients blend into a graduated cylinder and measuring the volume (Vb) and weight (M) as it is .

$$b = M/Vb$$

Tapped density

The measuring cylinder containing a known mass of blend was tapped for a fixed number of taps. The minimum volume (Vt) occupied in the cylinder and the weight (M) of the blend was measured. The tapped density (t) was calculated using following formula.

$$t = M/ Vt$$

Angle of repose

Angle of repose (ø) was determined using funnel method. The blend was poured through a funnel that can be raised vertically until a maximum cone height (h) was obtained. The radius of the heap (r) was measured and angle of repose was calculated.

$$ø = \tan^{-1} h/r$$

Compressibility index

The simplest way of measurement of free flow property of powder is compressibility, an indication of the ease with which a material can be induced to flow is given by % compressibility which is calculated as follows:

C = (t b) / t x 100

t - Tapped density, b - Untapped bulk density

Hausner s ratio

Hausner s ratio is an index of ease of powder flow; it is calculated by following formula.

Hausner s ratio = t\ b

t - Tapped density, b -Untapped bulk density

Evaluation of Dispersible tablets of Amoxicillin trihydrate and Dicloxacillin sodium [10-12]

Weight variation test

Weight variation test was done by weighing 20 tablets individually, by using digital weighing balance Calculating the average weight and comparing the individual tablet weight to the average weight.

Tablet thickness

The thickness was measured by placing tablet between two arms of the Varnier calipers. 5 tablets were taken and their thickness was measured.

Tablet hardness

The tablet hardness, which is the force required to break a tablet in a diametr ic compression force. The hardness tester used in the study was Monsanto hardness tester, which applies force to the tablet diametrically with the help of an inbuilt spring.

Tablet friability

The friability of the tablets was measured in a Roche friabilator (Camp-bell Electronics, Mumbai). Tablets of a known weight (W_o) or a sample of 20 tablets are dedusted in a dr um for a fixed time (100 r evolutions) and weighed (W) again. Percentage friability was calculated from the loss in weight as given in equation as below. The weight loss should not be more than 1 % . Determination was made in triplicate.

% Friability = 100 (Wo -W) / Wo

In-vitro disintegration time

This test was carried out at 25 ± 2°C in 900 ml of distilled water. Six tablets were taken and one tablet was introduced in each tube, disc was placed and basket rack was positioned in 1 liter beaker containing water 25 ± 2°C and apparatus operated for 3 min with no palable mass and the disintegration time in seconds was noted (Indian pharmacopoeia 2007).

In-vitro dissolution study

Amoxicillin trihydrate:

Dissolution studies of all tablets were performed using dissolution tester USP II (Paddle type, TDL-08L, Electrolab, India). Tablets were added to the 900 ml of 0.1 N HCl at 37°C ± 0.5°C, which was stirred with a rotating paddle at 75 rpm. At time intervals of 15 minutes, 1ml samples were withdrawn and equal volume of fresh medium prewarmed at the same temperature was replaced in to the dissolution medium after each sampling to maintain its constant volume throughout the test. Assay carried out using U.V. spectrophotometer (UV 1700 shimadzu /Visible double beam spectrophotometer, Japan) at254nm.

Dicloxacillin sodium:

Dissolution studies of all tablets were performed using dissolution tester USP II (Paddle type, TDL-08L, Electrolab, India). Tablets were added to the 900 ml of phosphate buffer at 37°C ± 0.5°C, which was stirred with a rotating paddle at 75 rpm. At time intervals of 15 minutes, 1ml samples were withdrawn and equal volume of fresh medium prewarmed at the same temperature was replaced in to the dissolution medium after each sampling to maintain its constant volume throughout the test. Assay carried out using U.V. spectrophotometer (UV 1700 shimadzu /Visible double beam spectrophotometer, Japan) at225nm.

RESULTS AND DISCUSSION

For each designed formulation, blend of drug and excipients was prepared and evaluated for micromeritics properties. All the precompression parameters were shown in table 2. Bulk density was found to be between 0.461 and 0.555 gm/mi and tapped density between 0.588 and 0.75 gm/ml for all formulations. Hausner s ratio was found below 1.9 and carr's compressibility index between 18.33 – 33.84. The angle of repose is known to be a measure of flowability and the angle of repose of all formulations was found between 13.38 – 24.14.

The evaluated physical parameters for all the batches were shown in table 3. The weight variation of all the tablets was within the ranges of 599 - 614 mg. The thickness of the tablets were within the range of 4.16 – 4.3. The hardness of the tablets was within the range of 61.2 – 114.8 newton. The friability of all tablets below 1% and the disintegration time was found to be 1 minute for the batch having the combination of Crosscarmellose and Crospovidone. The drug release varies with different in the ratio of superdisintegrants. Out of nine formulations F4 shows best drug release 90.45% for Amoxicillin trihydrate and 90.40% for Dicloxacillin sodium in 40 minutes. Fig.1 showing the release profile for Amoxicillin trihydrate and Fig. 2 for Dicloxacillin sodium.

CONCLUSION

The present study shows that Amoxicillin and Dicloxacillin combination can be made into dispersible tablet dosage form by direct compression technique. The invitro study shows formulation 4 (F4) which is formulated by using superdisintegrents croscarellose and crospovidone is well suited to dispersible tablet formulation due to the disintegration time of just 1 minute. This optimized dispersible tablet formula can be used for further investigations.

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Table 1: Formula for dispersible tablets of amoxicillin and dicloxacillin

Ingredient Name	Amoxicillin trihydrate	Dicloxacillin Sodium	Micro crystalline cellulose	Aspartame	Banana flavour	Vnilla flavour	Aerosil	Magnesium stearate	Croscarmellose sodium	Crospovidone	Sodium starch glycolate
F1	300	314	463	20	10	10	20	3	60		
F2	300	314	463	20	10	10	20	3		60	
F3	300	314	463	20	10	10	20	3			60
F4	300	314	463	20	10	10	20	3	30	30	
F5	300	314	463	20	10	10	20	3	30		30
F6	300	314	463	20	10	10	20	3		30	30
F7	300	314	463	20	10	10	20	3	20	20	20

Table 2: Pre compression parameters data for Amoxicillin trihydrate and Diclxacillin sodium powder blend

Sr. No.	Angle of repose	Bulk density (gm / ml)	Tapped density (gm/ml)	Haussner ratio	Carr's index (%)
1	24.10	0.555	0.75	1.463	31.666
2	17.25	0.545	0.75	1.375	27.272
3	25.25	0.461	0.697	1.511	33.846
4	13.38	0.476	0.588	1.224	18.333
5	19.98	0.491	0.666	1.35	25.925
6	15.25	0.5	0.612	1.311	23.729
7	14.74	0.476	0.588	1.235	19.047

Table 3: Evaluation of Dispersible tablets of Amoxicillin trihydrate and Dicloxacillin sodium

Formulation Parameters		F1	F2	F3	F4	F5	F6	F7
Weight variation		607	607	607	607	607	607	607
Thickness		4.22	4.22	4.22	4.22	4.22	4.22	4.22
Hardness		62	62	62	62	62	62	62
Friability		0.099	0.099	0.099	0.099	0.099	0.099	0.099
Disintegration time		2.45	2.45	2.45	2.45	2.45	2.45	2.45
% drug release	Amoxicillin	86.12	87.93	59.76	90.45	86.49	88.59	90.24
	Dicloxacillin	85.25	85.32	55.67	90.40	85.54	88.29	88.24

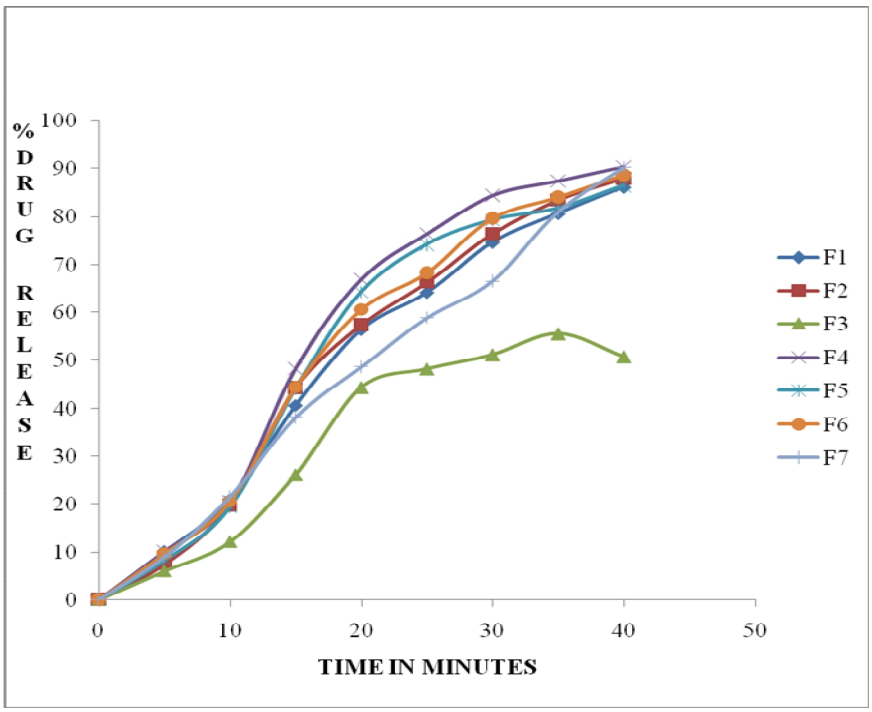

Fig.1 IN VITRO DISSOLUTION PLOT OFAMOXICILLIN TRIHYDRATE

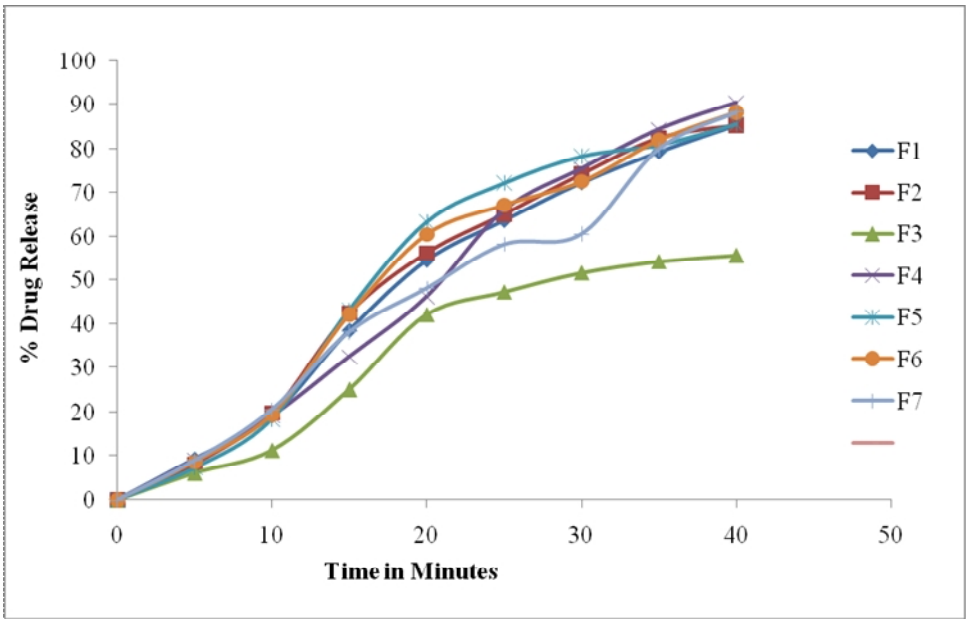

Fig.2 IN-VITRO DISSOLUTION PLOT OF DICLOXACILLIN SODIUM

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