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FORMULATION AND EVALUATION OF DISPERSIBLE TABLET OF AMOXICILLIN TRIHYDRATE

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ABSTRACT

In present study, the oral dispersible tablets of Amoxicillin Trihydrate were prepared by direct compression technique using microcrystalline cellulose (MCC) as direct compressible diluents. Sodium starch glycolate (SSG), Croscarmellulose sodium (CCS) and Crospovidone used as synthetic superdisintegrants. The amoxicillin dispersible tablet powder blends showed satisfactory flow properties. Seven formulations were prepared using different concentrations of superdisintegrants and were investigated for their effect on the disintegration time and dissolution rate of the tablets. Tablets were also evaluated for weight variation, hardness, thickness, friability and % drug content. All the tablets exhibited acceptable pharmaco-technical properties. Tablets prepared with the blend of CCS (15mg) and crospovidone(15mg) exhibited quicker disintegration. According to the present study, it was found that tablets of batch F4 (blend containing CCS & crospovidone (15mg) showed better disintegrating property as well as % drug release (98.78% within 40 min.).

KEYWORDS: Dispersible tablet, dispersibility, dissolution, Amoxicillin Trihydrate.

INTRODUCTION

Oral dispersible tablets have received ever-increasing demand during the last decade and the field has become a rapidly growing area in the pharmaceutical industry.[1] Recent advances in novel drug delivery (NDDS) aims to enhance safety and efficacy of drug molecule by formulating a convenient dosage form for ease of administration and to achieve better

patient compliance.[2] Dispersible tablets are uncoated or film-coated tablets intended to be dispersed in water before administration giving a homogeneous dispersion. The proper choice of disintegrates and its consistency of performance are of critical importance to the formulation development of such tablets. Dispersible tablets are well administered for the paediatric, dysphasic patients, mentally ill, unco-operative and nauseated patients, those with conditions of motion sickness, sudden episodes of allergic attack or coughing.[3]The basic approaches to develop dispersible tablet include maximizing the porous structure of the tablet matrix, incorporating the appropriate disintegrating agent and using highly water soluble excipients in the formulation.[4]

Amoxicillin Trihydrate is a beta-lactum antibiotics are prescribed by doctors for the treatment of mild to moderate infection of ENT (ear, nose and throat), respiratory tract, skin and genitor- urinary tract which should be taken for a minimum time interval of 3-5days.[5] Amoxicillin is 80% absorbed by oral route with good efficacy, safety and limited adverse effect.[6] The objective of the study was to choose the best superdisintegrant by comparative evaluation which gives a disperseable of least disintegration time and good drug release profile.

MATERIALS AND METHOD

Materials

Amoxicillin Trihydrate was procured from commercial market. MCC, croscarmellulose sodium, crospovidone, sodium starch glycolate, vanillin, talc, and magnesium stearate were purchased from S.D Fine Chemicals Ltd., Mumbai.

Methods

Preparaion of Amoxicillin Trihydrate dispersible tablets

Different formulations (F1 to F7) were prepared by direct compression technique. All the ingredients were weighed as specified in the formula (table-1). Drug diluents, lubricant and Disintegrants were passed through sieve # 80. The drug was first mixed homogeneously with diluents and disintegrant in a mortar and pestle and required degree of fineness was attained. Finally magnesium stearate were added and mixed. The resultant blends after micromiritic evaluations were directly compressed using 8mm flat punches with tablet weight 320 mg in a single punch rotatory machine. A batch size of 20 tablets was prepared in each formulation.

Table 1: Formulation of Amoxicillin Trihydrate tablets containing different concentration of superdisintegrants.

Ingredients(mg)	F1	F2	F3	F4	F5	F6	F7
Amoxicillin trihydrate	250	250	250	250	250	250	250
MCC	25	25	25	25	25	25	25
Vanillin	10	10	10	10	10	10	10
Talc	2	2	2	2	2	2	2
Magnesium stearate	5	5	5	5	5	5	5
Croscarmellulose sodium	30	-	-	15	-	15	10
Crospovidone	-	30	-	15	15	-	10
Sodium starch glycolate	-	-	30	-	15	15	10

PRECOMPRESSION EVALUATION OF POWDER BLEND

- **Angle of repose(θ)[7-9]**

The frictional force in a loose powder can be measured by angle of repose. Angle of repose is defined as the maximum angle possible between the surface of a pile of the powder and horizontal plane. It is determined by using fixed funnel method. The granules were poured through a funnel that can be raised vertically until a maximum cone height was obtained. The radius of the heap was measured, as angle of repose was calculated by using formula.

$$\theta = \tan^{-1} (h/r)$$

Where, θ= Angle of repose.

h = Height of pile

r = Radius of the base of pile.

- **Bulk density (Db)**

It is the ratio of total mass of powder to the bulk volume of powder. Bulk density was determined by pouring the powder into graduated cylinder. The bulk volume and mass of the powder was noted. It is expressed in gm/cc and bulk density was calculated by using formula

$$Db = M/Vb$$

Where, M =Mass of powder.

Vb =Bulk volume of the powder.

- **Tapped density (DT)**

It is the ratio of total mass of powder to the tapped volume of powder. The measuring cylinder containing known mass of powder tapped for a fixed time. The maximum volume occupied in the cylinder and weight of the granules was measured. It is expressed in gm/cc, tapped density can be calculated by using formula.

Dt = M/Vt

Where, Dt = Tapped density

M = Mass of powder

Vt =Tapped volume of the powder.

- **Carr's consolidation index**

Specific amount of powder was transferred to measuring cylinder and the initial volume occupied was noted as (Vb) and the content was tapped for 100 times and the volume was noted (Vt). Then calculated the Carr's consolidation index by using the following formula

Carr's consolidation index = (Vt-Vb/Vt) 100

Where, Vb = Bulk volume.

Vt = Tapped volume.

- **Hausner's ratio**

Hausner's ratio is an indirect index of ease of powder flow. Hausner's ratio can be determined by the following equation,

Hausner's ratio = TBD / LBD

Where, TBD =Tapped bulk densities

LBD=Loose bulk densities.

Table 2: Pre-compression evaluation of dispersible tablet blend of Amoxicillin Trihydrate Mean ±SD n=3.

SI.No	Formulation	Angle of repose (ɵ)	Bulk density (g/cc)	Tappeddensity (g/cc)	Carr's index	Hausner's ratio
1	F1	28.45±1.46	0.43±0.01	0.52±0.012	16.22±0.43	1.30±0.010
2	F2	30.58±1.47	0.42±0.02	0.51±0.016	16.84±0.60	1.31±0.034
3	F3	28.95±1.31	0.44±0.03	0.55±0.012	17.16±0.37	1.31±0.011
4	F4	29.61±1.23	0.45±0.01	0.55±0.012	16.46±1.25	1.32±0.030
5	F5	29.28±0.85	0.45±0.00	0.55±0.016	16.72±0.75	1.33±0.034
6	F6	30.86±1.44	0.43±0.00	0.52±0.021	17.22±0.51	1.31±0.032
7	F7	29.17±0.98	0.44±0.30	0.55±0.026	16.43±1.12	1.31±0.028

POST COMPRESSION EVALUATION OF TABLETS[10-11]

Tablets from all the seven formulations were evaluated for its various properties like thickness diameter using digital vernier calipers, hardness by using Monsanto hardness tester, friability by using Roche friabilator and weight variation by using a electronic balance.

Table 3: Post-compression evaluation of dispersible tablet of Amoxicillin Trihydrate.

Sl. No	Formulation	Hardness *(kg/cm2)	Thickness* (mm)	Friability # (%)	**Weight variation	**Drug content
1	F1	5.75±0.27	4.26±0.12	0.600	0.319±0.0038	82.19±0.7
2	F2	6.00±0.31	4.25±0.10	0.632	0.320±0.0020	85.9±0.8
3	F3	5.91±0.20	4.18±0.07	0.613	0.321±0.0022	49.62±0.4
4	F4	6.00±0.31	4.23±0.08	0.650	0.318±0.0021	91.23±0.3
5	F5	6.08±0.37	4.11±0.11	0.525	0.320±0.0021	82.23±0.1
6	F6	6.00±0.31	4.26±0.12	0.587	0.321±0.0023	86.23±0.6
7	F7	5.80±0.31	4.20±0.10	0.687	0.317±0.0023	89.36±0.9

Mean ±SD *n=6, **n=10 and #n=10

- **Dispersibility test**[12]

Two tablets were placed in 100 ml of distilled water and stirred until completely dispersed. A smooth dispersion is produced, which passes through a sieve screen with a nominal mesh aperture of ASTM#22.

- **Disintegration test**[13-14]

One tablet was kept in each tube of the disintegration apparatus, suspended the assembly in the basket containing water and operated with the discs for 4 minutes, unless otherwise stated in the individual monograph. Remove the assembly from the liquid. Dispersible tablet should complete the disintegration within 3 minutes in water temperature 15˚C to 25˚C.

- **% drug content uniformity**

Twenty tablets were powdered, and 250 mg equivalent weight of Amoxicillin Trihydrate in powder was accurately weighed and transferred into a 100 ml volumetric flask. Initially, 50 ml of acidic buffer (pH 1.2) was added and shaken for 10 min. Then, the volume was made up to 100 ml with phosphate buffer. The solution in the volumetric flask was filtered, diluted suitably and analyzed spectrophotometrically at 272 nm. The drug content in each tablet was calculated using the standard calibration curve of Amoxicillin Trihydrate in pH 1.2.

- ***In-vitro* dissolution studies**

Dissolution studies for all the formulated tablets were carried out using USP paddle method at 75 rpm in 900ml of 0.1 N HCL at 37˚C as dissolution media. 5 ml aliquot was withdrawn at the specified time intervals and assayed spectrophotometrically at 272nm. An equal volume of fresh medium, which was prewarmed, was replaced into the dissolution media after each sampling to maintain the constant volume throughout the test.

RESULTS AND DISCUSSION

Characterization of Amoxicillin Trihydrate dispersible powder blend

The formulation showed good flow property and compressibility index. Angle of repose ranged from $28^{\circ}.45^{1}$-$30^{\circ}.86^{1}$, Carr's index ranged from 16-17. The LBD and TBD of the prepared granules ranged from 0.42-0.45 and 0.51-0.55 g/cc respectively, Hausner's ratio was found to be 1.30-1.33. The results of angle of repose indicates good flow property of the granules and the value of carr's index further showed support for the flow property. The result were showed in (Table No. 2).

Characterization of Amoxicillin Trihydrate dispersible tablet

The tablets with weight of 320mg subjected to quality control tests such as weight variation, Hardness, Friability and Thickness (Table No.3). All formulation products lied within the pharmacopoeial requirement within ±7.5 for weight variation. The mean values for hardness was within 5.75-6.08 kg/cm^2 and all formulations exhibits friability within the 0.52- 0.68% during the friability determination. The thickness was found in the range of 4.11 - 4.26 mm.

The results showed good mechanical strength and had uniformity size of the tablets.

Disintegration test and dispersibility test

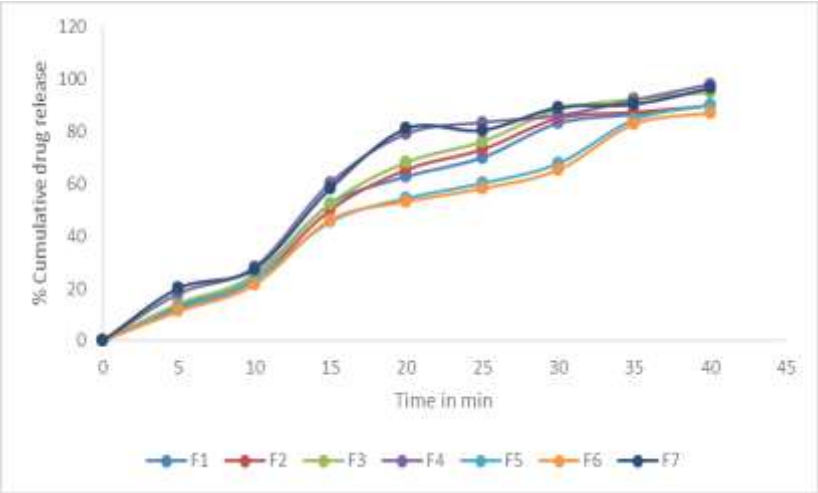
Disintegration is the most important characteristic test of dispersible tablet, among the formulation (F4) formulated with croscarmellulose sodium and crospovidone shows excellent disintegration time of 38 sec. All the formulation passed the dispersibility test.

In-vitro dissolution study

In formulation F1, F2, F3 were formulated with single superdisintegrants, Croscarmellulose sodium, Crospovidone, Sodium starch glycolate and respectively were used along with the drug, the release of the drug from the F1 and F2 was showed satisfactory result. F3 shows better drug release from the formulation. F4 were formulated with crospovidone and croscarmellulose sodium shows an excellent release of the drug from the formulation.

F5 formulated with crospovidone and sodium starch glycolate shows increased drug release. F6 with sodium starch glycolate and croscarmellulose sodium with good release of the drug. The F7 formulated with crospovidone, croscarmellulose sodium and sodium starch glycolate showed satisfactory drug release due to combination of three superdisintegrant agent with low ratio. When comparing to the above formulation, F4 showed excellent drug release. It was

considered as an optimized formulation in this work.



CONCLUSION

The present study shows that Amoxicillin Trihydrate dispersible tablet dosage form formulated by direct compression technique. The *In-vitro* study shows formulation F4 is well suited to dispersible tablet formulation due to the disintegration time of just 38 sec.

Which is formulated by using superdisintegrents croscarmellulose and crospovidone.

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