RESEARCH ARTICLE

FORMULATION AND EVALUATION OF LACTIC ACID BACILLUS AND ZINC SULPHATE FAST DISPERSIBLE TABLETS

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ABSTRACT:

The aim of the present work is to formulate fast dispersible tablets of lactic acid bacillus & Zinc sulphate. In this study, different formulations of fast dispersible tablets were prepared using various excipients & super disintegrants. Different concentrations of crospovidone, cross carmellose sodium & sodium starch glycolate were used as super disintegrants in the formulation of fast dissolution tablet. The powder mass was evaluated for flow properties. All these formulations were prepared by wet granulation method. The tablets were evaluated for hardness, thickness, weight variation, friability, wetting time, disintegration time, and water absorption ratio. Tablets containing crospovidone showed shorter disintegration time i.e. less than 30 sec, comparaed to cross carmellose sodium & sodium starch glycolate hence better patient compliance & effective therapy.
Key words: Lactic Acid Bacillus, Zinc Sulphate, Fast dispersible tablets, Super disintegrants.

INTRODUCTION

The tablet is the most commonly used oral dosage form. It is also quite complex in nature. The biggest problem is overcoming the reduction in effective surface area produced during the compression process. One may start with the drug in a very fine powder, but then proceeds to compress it into a single dosage unit. Many pharmaceutical dosages are administered in the form of pills, granules, powders and liquids. Generally a pill design is for swallowing intact or chewing to deliver a precise dosage of medication to patients. The pills, which include tablets and capsules, are able to retain their shapes under moderate pressure. However, some patients particularly pediatric and geriatric have difficulty swallowing or chewing solid dosage forms. Many pediatric and geriatric patients are unwilling to take these solid preparations due to fear of choking[1]. In order to assist these patients, several fast-dispersible drug delivery systems[2] have been developed for oral administration. They dissolve in saliva & do not require water for swallowing. Oral disintegrating tablets are also called as 'mouth dissolving tablets', 'orodispersible tablets', quick disintegrating tablets, rapid dissolving tablets, porous tablets and rapimelts[3]. Various techniques are used in manufacturing of ODT[4], includes Freeze-Drying or Lyophilization, Tablet Molding, Spray Drying, Sublimation, Direct Compression, Cotton Candy Process, Mass-Extrusion.

The main objective of this study was to formulate & evaluate fast dispersible tablets of zinc sulphate and lactic acid bacillus combination. The combination of zinc sulphate and lactic acid bacillus is used for treatment of diarrhoea.

These dosage forms are designed in such a way that, they disperse in patient's mouth up on contact with saliva within seconds without aid of water. The drug after entering into the intestine will become metabolically active & it will replace the bacteria which are damaged. After that spores will produce lactic acid which is helpful in killing the pathogenic microbes.

METHODOLOGY

Materials:

lactic acid bacillus was obtained from Unisankyo, Hyderabad ,sodium starch glycolate, Starch, Sodium CMC, Ethylcellulose , Zinc sulphate & Dicalcium Phosphate was purchased from S.D. Fine Chemicals Mumbai., Crospovidone & cross carmellose sodium were gifted by Alembic Ltd, Mannitol, Talc & Magnesium stearate was purchased from Merk India Ltd, Mumbai.

Method of preparation:

We prepared the 3 types of granules one is zinc sulphate granules, another one is placebo granules and last one lactic acid granules. All the three types are wet granulation method. 12 formulations were prepared using different concentrations of crospovidone (CP), cross carmellose sodium (CCS) & sodium starch glycolate (SSG) and coaded F1 to F12 as showed in table 1.

Zinc sulphate granules

Zinc sulphate granules are prepared by mixing zinc sulphate powder with the ethylcellulose solution (dissolved in methylene chloride) with added aspartame & lemon flavour to it by octagonal blender. The resultant wet mass was passed through sieve no 30 and dried it at 50°c for one hour.

Placebo of granules

Prepared starch paste using water and kept aside. Then sifted Dicalcium phosphate, Mannitol, super disintegrant and mixed for 10min.Added the paste to the dry mix blend by passing through sieve no 40 and dried. The dried granules were passed through the sieve no.30 to get desired granules.

Preparation of Lactic acid granules

Lactic acid was mixed with soaked sodium CMC, then passed through sieve no 16 and dried it 40°c for one hour.

Compression

Mixed the above three types of granules with talc and magnesium stearate for lubrication. Then granules are punched with 16 stage rotatary punching machine (Cadmach).

Table 1: Tablet Compositions for Fast dispersible tablets

INGREDIENTS (mg)	F_1	F_2	F_3	F_4	F_5	F_6	F_7	F_8	F_9	F_{10}	F_{11}	F_{12}
Lactic acid bacillus	20.5	20.5	20.5	20.5	20.5	20.5	20.5	20.5	20.5	20.5	20.5	20.5
Zinc sulphate	61	61	61	61	61	61	61	61	61	61	61	61
DCP	139	134.75	130.5	126.25	139	134.7	130.5	126.2	139	130.5	122	113.5
Mannitol	150	150	150	150	150	150	150	150	150	150	150	150
CP	8.5	12.75	17	21.25	--	--	--	--	--	--	--	--
CCS	--	--	--	--	8.5	12.75	17	21.25	--	--	--	--
SSG	--	--	--	--	--	--	--	--	8.5	17	25.5	34
Starch	15	15	15	15	15	15	15	15	15	15	15	15
Ethylcellulose	4	4	4	4	4	4	4	4	4	4	4	4
Aspartame	10	10	10	10	10	10	10	10	10	10	10	10
Lemon flavour	10	10	10	10	10	10	10	10	10	10	10	10
Talc	4	4	4	4	4	4	4	4	4	4	4	4
Magnesium stearate	3	3	3	3	3	3	3	3	3	3	3	3
Total weight (mg)	425	425	425	425	425	425	425	425	425	425	425	425

Evaluation of flow properties

Angle of Repose[5]

Angle of repose (Θ) was determined using fixed funnel method. The blend was poured through a funnel that can be raised vertically until a maximum cone height (h) was obtained. Radius of the heap ® was measured and the angle of repose (q) was calculated using the formula. Values are shown in table 2.

Bulk Density[6]

Apparent bulk density was determined by pouring the blend into a graduated cylinder. The bulk volume (V_h) and weight of the powder (M) was determined. The bulk density was calculated using the formula. Values are shown in table 2.

Tapped Density[7]

The measuring cylinder containing a known mass of blend was tapped for a fixed time. The minimum volume (V_1) occupied in the cylinder and the weight (M) of the blend was measured. The tapped density was calculated using the formula. Values are shown in table 2.

Compressibility Index[8]

The simplest way for measurement of free flow of powder is compressibility, a indication of the ease with which a material can be induced to flow is given by compressibility index (I) which is calculated as follows:

Where V_b is the bulk volume and V_1 is tapped volume. The value below 15% indicates a powder with usually gives rise to good flow characteristics, where as above 25% indicates poor flowability. Values are shown in table 2.

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Hausner's Ratio[9]

Hausner's ratio is an indirect index of ease of powder flow. It is calculated by the following formula

Where P_t tapped density and P_b is bulk density. Lower Hausner's ratio (<1.25) indicates better flow properties than higher ones. Values are shown in table 2.

Table 2: Physical parameters for the final blend

Formulations	F_1	F_2	F_3	F_4	F_5	F_6	F_7	F_8	F_9	F_{10}	F_{11}	F_{12}
Bulk density (gm/cc)	0.454	0.286	0.512	0.256	0.29	0.252	0.26	0.261	0.512	0.29	0.25	0.28
Tapped density (gm/cc)	0.526	0.323	0.588	0.333	0.282	0.278	0.28	0.295	0.588	0.33	0.27	0.32
Carr's index (%)	13.6	11.4	12.9	10.2	9.21	9.3	7.1	13.2	12.9	10.2	9.3	11.4
Hausner ratio	1.15	1.12	1.14	1.14	1.1	1.1	1.07	1.13	1.2	1.2	1.1	1.12
Angleof repose (°)	27.2	28.3	29.1	29.7	28.6	27.7	29.4	28.7	28.5	27.9	27.7	28.3

Evaluation of tablets

Different quality control tests were performed for all the FDT formulations to check whether these have met the specifications given in USP.

Weight variation test [10]

20 tablets were randomly selected from each formulation and their average weight was calculated using digital balance. Individual weight of each tablet was also calculated using the same and compared with the average weight. Values are shown in table 3.

Thickness measurement [10]

Randomly 10 tablets were taken from each formulation and their thickness was measured using a digital screw gauge, the individual tablet was placed between two anvils of the screw guage and sliding knob was rotated until the tablet was tightly fitted. The digital reading displayed was noted. Values are shown in table 3

Hardness [10]

The tablet hardness of different formulations was measured using the Monsanto hardness tester the tester consists of a barrel containing a compressible spring held between two plungers. The lower plunger was placed in contact with the tablet, and a zero was taken. The upper plunger was then forced against the 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 the force. The force of fracture is recorded, and the zero force reading is deducted from it. Generally, a minimum hardness of 3-5 kg is considered acceptable for tablets. Values are shown in table 3

Friability[10]

This test is performed using a laboratory friability tester known as Roche Friabilator.10 tablets were weighed and placed in a plastic chambered friabilator attached to a motor, which revolves at a speed of 25 rpm, dropping the tablets from a distance of 6 inches with each revolution. The tablets were subjected to 100 revolutions for 4 minutes. After the process, these tablets were dedusted and reweighed. Percentage loss of tablet weight was calculated. Values are shown in table 3 and fig 1.

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Table 3: Physical parameters of the compressed tablets

Formulations	F_1	F_2	F_3	F_4	F_5	F_6	F_7	F_8	F_9	F_{10}	F_{11}	F_{12}
Hardness (kg/cm^2)	4.1	3.2	3.5	3.6	3.9	4.0	3.6	3.4	3.3	4	3.6	3.5
Thickness (nm)	2.36	2.45	2.28	2.55	2.32	2.22	2.49	2.23	2.21	2.42	2.22	2.32
Friability (%)	0.44	0.51	0.46	0.48	0.50	0.49	0.42	0.53	0.51	0.45	0.46	0.41
Weight variation (mg)	425.4 ±4.03	424.8 ±2.79	423.7 ±4.71	425.2 ±3.52	426.7 ±4.92	424.2 ±5.25	425.8 ±3.77	426.6 ±7.03	425.6 ±2.71	426.4 ±2.52	424.6 ±7.03	425.2 ±2.52

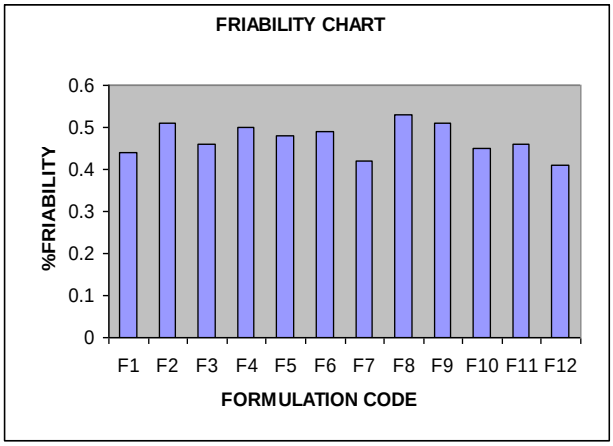

Figure 1: Graphical representation of friability of different ODT formulations

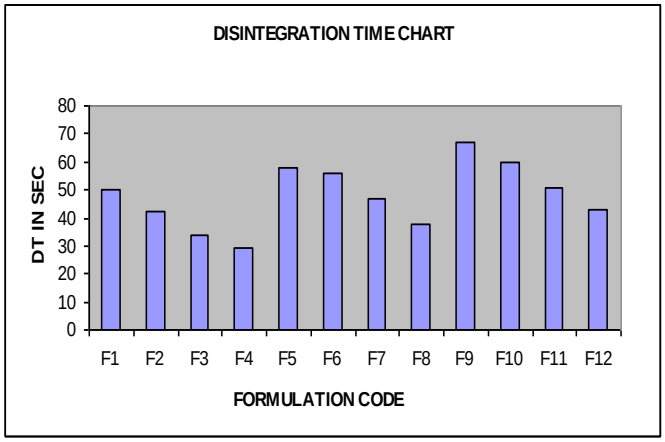

Fig 2: Graphical representation of disintegration time of different ODT formulations

Table 4: Disintegration time and assay for ODT formulations

Formulations	F_1	F_2	F_3	F_4	F_5	F_6	F_7	F_8	F_9	F_{10}	F_{11}	F_{12}
Disintegration time (sec)	50	42	34	29	58	56	47	38	67	60	51	43
Assay(million spores)	475	476	474	480	478	480	474	478	480	472	476	478

Disintegration Time[10]

Disintegration time was also measured using a modified disintegration method (n=6). For this purpose, a petridish (10 cm diameter) was filled with 10 ml of water. The tablet was carefully put in the center of the petridish and the time for the tablet to completely disintegrate into fine particles was noted using a stop watch. Values are shown in table 4 and fig 2.

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Assay

Take 10 tablets then transfer the tablets into 250ml flask add DM water & shake well up to dissolve the tablets filter it & collect the powder then dry it. Transfer the dried powder into homogenizer, add exactly 200ml of phosphate buffer of pH 7.2 and mix well, for 10min. Take 1ml from the above solution & add into 9ml of phosphate buffer in a test tube. Mix well using cyclomixer & dilute it further stepwise through a series of test tubes, containing 9ml of phosphate buffer by an appropriate decimal dilution method. Final dilution should be 200×107.Cool immediately to about 45°c.Pipette accurately 1 ml from above solution & add into each of 2 sterile Petri dishes. Add about 15ml of glucose yeast extract medium previously sterilized, molted& coded to 45°c to 50°c to each of 2 Petri dishes. Incubate the plates at 37°-40°c for 72 hours& count the number of colonies in each plate. Values are shown in table 4.

Wetting time and Water absorption ratio[11]

Five circular tissue papers were placed in a petri dish with a 10-cm diameter. Ten milliliters of water containing Eosin, a water-soluble dye, was added to the petri dish. The dye solution is used to identify the complete wetting of the tablet surface. A tablet was carefully placed on the surface of tissue paper in the petri dish at room temperature. The time required for water to reach the upper surface of the tablets and completely wet them was noted as the wetting time. To check for reproducibility, the measurements were carried out in replicates (n=6). The wetting time was recorded using a stopwatch.

The weight of the tablet before keeping in the petri dish was noted (W_b) using digital balance. The wetted tablet from the petri dish was taken and reweighed (W_a) using the same. The Water absorption ratio, R, was determined according to the following equation:

$R = 100 (Wa - W_b) / W_b$

Where W_b and W_a are the weight before and after water absorption respectively. Values are shown in table 5

Table 5: Wetting time and water absorption ratio for ODT formulations

Formulations	F_1	F_2	F_3	F_4	F_5	F_6	F_7	F_8	F_9	F_{10}	F_{11}	F_{12}
Wetting time (sec)	56-58	46-47	39-40	37-38	65-66	62-63	55-56	44-46	73-72	68-69	59-60	49-50
Water absorption ratio	96.5	102	108	115	119	126	132	140	122	136	142	146

Stability studies [12,13,14]

In view of potential utility of the formulation, stability studies were carried out at 40˚c & 75% RH for 3 months to asses their long term stability. The protocols of stability studies were in compliance with the guidelines in the WHO document for stability testing of products intended for the global market. After storage, the formulation was subjected to a weight variation, hardness, thickness, friability, disintegration time, wetting time, assay. Below table showed that physical parameters of the optimized formulation F_4 tablets, before &after storage in accelerated stability conditions. Values are shown in table 6.

RESULTS & DISCUSSION

For each designed formulation, blend of drug and excipients was prepared and evaluated for micromeritic properties shown in Table2. Bulk density was found to be between 0.252 and 0.512gm/cm^3 and tapped density between 0.270 and 0.588 gm/cm^3 for all Formulations. From density data % compressibility was calculated and was found to be between

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7.1% and 13.6%. Angle of repose was found to be in the range of 27° and 29° .Hausner's ratio was found below 1.15. The results of evaluations of Different batches of FDTs were shown in Table no.3. Tablets produced were of hardness (3.2-4.1 kg/cm ^{2}) and friability loss (0.4-0.5%) indicated that tablets had a good mechanical resistance which may not break during handling on machines. Weight variation results are compliance with USP specification. . As shown in table 4 the Disintegration time (DT) of tablets was found to be in the range of 29 to 67 secs. DT is considered to be one of the important criteria in selecting the best formulation. The wetting time of formulations was found to be in the range of 37 to 74 sec. The water absorbance ratio was found to be from 96 to 146. Crospovidone (CP) is achieved in shorter time compared to CCS, SSG. Among all formulations F4 had shown a shorter DT. In assay million spores of LAB was found to be within the range as shown in table 4. Stability studies performed on batch F4 formulation for 3 months at 40^{o}c & 75% RH. That shows no remarkable changes in the physical properties of the tablets as well as no remarkable changes in drug content as indicated in table 6

Table 6: Accelerated stability studies of formulation (F_4) FDT

Parameters	Initial	One month	Two month	Three month
Tablet weight(mg)	425.2±3.52	425.2	425.2	425.2
Hardness(kg/cm2)	3.6	3.6	3.6	3.6
Disintegration time(sec)	29	29	28	29
Thickness(mm)	2.55	2.55	2.56	2.57
Friability	0.48	0.48	0.48	0.47
Wetting time(sec)	37-38	37	37	37

CONCLUSION

In this study, the three different super disintegrate were used. crospovidone showed better performance in disintegration time when compare to cross carmellose sodium and sodium starch glycolate in case of lactic acid bacillus. The formulation of F_4 (CP 21.25 mg) was found to be best among lactic acid bacillus fast dispersible tablets formulations which were prepared by wet granulation method because it has exhibited faster disintegration time (29 sec)when compare to other formulations. Future possibilities for improvements in Rapid disintegrating and drug delivery are bright, but the technology is still relatively new. Several drug delivery technologies that can be leveraged on improving drug therapy from these dosage form

REFERENCES:

1. Parakh SR, Gothoskar AV: A review of mouth dissolving tablet technologies, 2003, 27(11): 92-98.
2. Bhowmik D, An Overview: Fast dissolving tablet. J Chem Pharm Res, 2009,1(1): 163-177.
3. Avani R. Gosai, Sanjay B. Patil. Formulation & evaluation of Ondansetron hydrochloride by direct compression using super disintegrants**.** Indian J Pharm Sci**,** (1) 1:106-112**.** .
4. Milind PW**.** Fast dispersible tablets of Aceclofenac using different superdisintegrants.Int J Pharm & Pharm Sci , 2001, 2 (1):154-157.
5. Sinha VR; Agarwal MK; Kumria RC, Drug Deliv., 2005, 2, 1-8.
6. Martin A. Diffusion and Dissolution. In: Physical pharmacy. 3rd ed. Philadelphia: Lea and Febiger; 1983. p. 399-444.
7. Fiese EF, Hagen TA. Preformulation. In: Lachman L, Lieberman HA, Kanig JL. Editors. The theory and practice of industrial pharmacy. 3rd ed. Mumbai: Varghese Publishing House; 1987. p. 182-184.
8. Ansel HC, Popovich NG, Allen LV. Pharmaceutical dosage forms and drug delivery system. 8th ed. New Delhi. B.I. Waverly Pvt. Ltd., 1995; p. 189-94, 235-36.

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9. Staniforth JN, Aulton ME. Powder flow In: Aulton's Pharmaceutics: the design and manufacturing of medicines. 3rd ed. Hungary: Harcourt publisher ltd.; 2007. p. 175-79.
10. Banker GS, Anderson NR. In: Lachman L, Lieberman HA, Kanig JL. The Theory and Practice of Industrial Pharmacy. 3rd ed. Mumbai: Varghese Publishing House; 1987. p. 293-99.
11. Sreenivas SA, Gadad AP, Patil MB. Formulation and Evaluation of Ondasetron hydrochloride directly compressed mouth disintegrating tablets. Indian Drugs 2006; 43: 35-37.
12. Swamy PA, Areefulla SH, Shrisand SB, Gandra S, Prashanth B, Orodispersible tablets of meloxicam using superdisintegrant blends for improvedefficiency. Ind. J. Pharm. Sci., 2007, 69(6):836-840.
13. Malke S, Shidhaye S, Kadam VJ, Formulation and evaluation of oxcarbazepine fast dissolving tablets, Ind. J. Pharm. Sci, 2007, 69(2): 211-214.
14. Patel MM, Patel DM, Fast dissolving valdecoxib tablets containing solid dispersion of valdecoxib, Ind. J. Pharm. Sci, 2006, 68 (2): 222-226.

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