Research Article

STUDY OF EFFECT OF SUPER DISINTEGRANTS IN FORMULATION OF METRONIDAZOLE ORO DISPERSIBLE TABLETS

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ABSTRACT

To obviate the problems associated with conventional dosage forms, Mouth Dissolving Tablets (MDTs) have been developed having good hardness, dose uniformity, easy administration and serves as the first choice of dosage form for pediatrics, geriatrics and travelling patients. Poor water solubility and metallic taste are the major problems associated with Metronidazole. Moreover, it is a better choice for periodontal diseases. In the present work an attempt was made to prepare MDTs of Metronidazole using super disintegrants like Cross- povidone (CPV), Pre gelatinized starch (PGS) and Sodium Starch Glycolate (SSG) in different concentrations. Metronidazole Oro Dispersible Tablets (ODTs) were prepared by Direct Compression technique. The tablets were tested for various parameters like Wetting time and *In vitro* Dispersion time in addition to physico chemical parameters. The tablets weighed 400 mg with hardness of 3.1 kg/cm^2. *In vitro* dispersion time and Wetting time was found to be high for tablets containing Pre gelatinized starch. The effect of the disintegrants on Wetting time and *in vitro* dispersion time was in the order of CPV < SSG < PGS and the efficiency of super disintegrants was in the order of CPV > SSG > PGS. From over all observations, F2 containing 5% w/w of Cross-povidone was considered to be the best formulation among all the formulations.

Keywords: Metronidazole, Oro dispersible tablets, Wetting Time and *In vitro* dispersion time.

INTRODUCTION

Conventional tablets and Capsules are now a days facing the problems likes dysphagia, resulting in the high incidence of non compliance and making the therapy ineffective. This problem is arising from 50% of the population. To obviate the problems associated with conventional dosage forms, mouth dissolving tablets have been developed having good hardness, dose uniformity, easy administration and serves as the first choice of dosage form for pediatrics, geriatrics and travelling patients. The MDTs were developed with an aim of having sufficient hardness, integrity and faster disintegration without water. Drugs for treating diseases like cancer, diabetes, heart diseases, and GI diseases are suitable candidates for formulating MDTs. The choice of excipients and the method of formulation seriously affects the wetting time and mechanical integrity of the MDTs. mouth dissolving tablets are also known as, Oro dispersible tablets, melt-in-mouth tablets, fast dissolving tablets, rapimelts, porous tablets and quick dissolving tablets.[1-3]

Metronidazole is, 1-(β-hydroxyethyl)- 2-methyl-5-nitroimidazole, antiprotozoal and antibacterial agent which exerts its action by inhibiting nucleic acid synthesis (add a reference). It is effective against diseases like Amebiasis, Pseudomembranous Colitis, Surgical Prophylaxis, Trichomoniasis, Crohn's Disease, Dracunculiasis, Giardiasis, Helicobacter pylori Infection, Pelvic Inflammatory Disease, Deep Neck Infection, Bacterial Vaginosis, Aspiration Pneumonia, Bacteremia, Meningitis, Diverticulitis, Intraabdominal Infection, Peritonitis, Endocarditis, Joint Infection, Osteomyelitis, Pneumonia, Soft Tissue Infection, Bacterial Infection, Amebiasis, Pseudomembranous Colitis, Trichomoniasis, Dracunculiasis, Giardiasis and Bacterial Vaginosis.[4]

Poor water solubility and metallic taste are the major problems associated with Metronidazole .More over; it is a better choice for periodontal diseases. Hence it was selected as a model drug. In the present work an attempt was made to prepare MDTs of Metronidazole using super disintegrants like Cross-povidone (CPV), Pre gelatinized starch (PGS) and Sodium Starch Glycolate (SSG) in different concentrations.

MATERIALS AND METHODS

Materials

Metronidazole drug was purchased from Search Chemicals, Mumbai. Chitosan was purchased from Himedia, New Delhi. Sodium Saccharin, Sodium starch glycolate, CPV, Pregelatinized starch, Magnesium stearate and Talc were purchased from Qualichems, New Delhi and the other reagents used were of analytical grade.

Method of preparation

Metronidazole Oro dispersible tablets were formulated as per the formulations given in table 1. All the ingredients were weighed accurately. Drug was mixed with required quantity of all ingredients by blender. This blend was directly compressed into tablets using 9 mm flat-face round tooling on a Rimek-I rotary tablet compression machine. Compression force was adjusted to obtain tablets with hardness in range of 3 to 4 kg/cm^2. Tablets weighed 400mg, and were round flat-face.

Evaluation of tablets

Uniformity of weight

Average weight of the tablet was calculated by weighing 20 tablets individually and all together. The percent weight deviation of each tablet was computed as per official method.[5-7]

Friability

Previously weighed 10 tablets were taken in a friabilator and the friability was checked at 25 rpm for 4 minutes. Then the tablets were dusted and reweighed. The percentage of powder eroded during 4 minutes was recorded.[5,6]

Hardness test

Hardness of tablets was tested using Pfizer Hardness tester. In all cases mean± SD of three replicate determinations were taken in calculation.[5,7]

Drug content uniformity of the tablets

The drug content was determined by analyzing sample equivalent to 10 mg of drug in to simulated saliva and absorbance was taken against the blank at 320.5 nm using double beam UV- Visible Spectrophotometer.[8]

Wetting time

The method reported by Yunixia *et al.*, was followed to measure tablet-wetting time. A piece of tissue paper folded twice was placed in a small petridish (ID = 6.5 cm) containing 6 ml of simulated saliva pH 6.8, a tablet was put on the paper, and the time for complete wetting was measured. Three trials for each batch were performed and standard deviation was also determined.[8,9]

In vitro Dispersion Time

In-vitro Dispersion Time was measured by dropping a tablet in a measuring cylinder containing 6 ml of pH 6.8 (simulated saliva fluid). Three tablets from each formulation were randomly selected and *in-vitro* dispersion time was performed.[8,9]

Table 1: Composition of Formulations of Metronidazole ODTs

Ingredients	Unit formula (mg/tablet)					
	F1	F2	F3	F4	F5	F6
Metronidazole	250	250	250	250	250	250
Crospovidone	20	30	-	-	-	-
Sodium Starch Glycolate	-	-	20	30	-	-
Pre gelatinized starch	-	-	-	-	20	30
Chitosan	10	10	10	10	10	10
Mannitol	101	91	101	91	101	91
Sodium Saccharin	10	10	10	10	10	10
Menthol	3	3	3	3	3	3
Magnesium stearate	3	3	3	3	3	3
Talc	3	3	3	3	3	3
Total weight	400	400	400	400	400	400

Table 2: Results of Pre-Compression Parameters

Formulation Code	Angle of Repose (θ)	Bulk Density (gm/ml)	Tapped Density (gm/ ml)	Carr's Compressibility Index (I_C)	Hausner's Ratio (H_R)
F1	26.23	0.561	0.608	1.08	7.73
F2	24.19	0.577	0.617	1.06	6.48
F3	25.40	0.621	0.689	1.11	9.86
F4	26.12	0.583	0.662	1.13	11.93
F5	27.49	0.609	0.697	1.14	12.62
F6	24.18	0.585	0.655	1.12	10.68

Table 3: Results of Physicochemical Parameters

Formulation Code	Weight Variation	Hardness (Kg/cm^2)± SD	Friability (%)± SD	Drug Content (%)± SD	Wetting Time (sec) ± SD	*In vitro* Dispersion time (sec) ± SD
F1	Passes	3.34±0.23	0.235±0.03	99.62±0.25	18.43±0.23	7.25±0.39
F2	Passes	3.42±0.38	0.218±0.02	99.10±0.28	16.29±0.17	6.34±0.57
F3	Passes	3.03±0.14	0.322±0.01	98.43±0.46	45.22±0.29	26.42±0.43
F4	Passes	3.15±0.63	0.524±0.01	98.96±0.67	39.46±0.54	24.33±0.21
F5	Passes	3.98±0.48	0.228±0.04	97.44±0.79	110.28±0.88	70.48±0.29
F6	Passes	3.74±0.21	0.196±0.03	98.15±0.36	102.03±0.47	65.21±0.22

RESULTS AND DISCUSSION

Pre- compression parameters

The powder of formulations was evaluated for bulk density, tapped density, compressibility index and Hausner's ratio. The results of bulk density & tapped density were shown good flow properties of powder. This was further supported by lower compressibility index value. The results were reported in the table 2.

Physicochemical parameters

All prepared formulations were subjected for weight variation study and results given in table 3. The deviation from the average weight was found to be within the prescribed official limits. Hardness of tablets was found to be in the range of 3 to 4 Kg/cm^2 given in the table 3. The friability of all tablets was found to be in range of 0.10-0.53 which is less than 1% that showed good mechanical strength.

Drug content of the tablets was within the range of 97.44% to 99.62% in all formulations. Wetting time was 16-18 seconds for tablets containing Crospovidone (F1 & F2), 39-46 seconds for the tablets containing Sodium Starch Glycolate (F3 & F4) and 102- 110 seconds for the formulations containing Pre gelatinized starch (F5 & F6). *In vitro* dispersion time was found to be 7 seconds for F1 & F2, 25 seconds for F3 & F4 and 65 to 70 seconds for F5 & F6 formulations. *In vitro* dispersion time and Wetting time was found to be high for tablets containing Pre gelatinized starch.

DISCUSSION

It has been observed that the selected super disintegrants were found to be suitable in formulating Oro dispersible tablets of Metronidazole. The maximum permissible concentration ranges of CPV, SSG and Pre gelatinized starch in ODTs were 2-5%, 2-8% and 1-20% respectively. The mechanism of action of SSG and Pre gelatinized starch was swelling mechanism. By swelling in contact with water, the adhesiveness of other ingredients in a tablet is increased so as to break the tablet. The mechanism of action of CPV was swelling and Wicking mechanism. In wicking mechanism, the super disintegrant impart their action through porosity and capillary action.[10]

The effect of these disintegrants on Wetting time and *in vitro* dispersion time was in the order of CPV < SSG < PGS. This shows that the efficiency of super disintegrants was in the order of CPV > SSG > PGS. From over all observations, F2 containing 5% w/w of Crospovidone was considered to be the best formulation among all the formulations.

CONCLUSION

Oro dispersible tablets of Metronidazole were successfully prepared by direct compression technique using selected super disintegrants for better therapy and patient compliance. The relative efficiency of these disintegrants was found to be in the order of CPV > SSG > PGS. Further research is to be done in this field to develop novel technologies in preparation of ODTs of drugs belonging to various classes. Extensive research is to be done in identification and evaluation of new super disintegrants belonging to natural and synthetic origin.

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Mr.Vishnumurthy Vummaneni graduated from Jawaharlal Nehru Technological University, Kakinada and is presently pursuing his Post Graduation from Amity University, Noida, where he is specializing in Pharmaceutics. His areas of interests include Novel Drug Delivery Systems. His Master thesis perfectly depicts his area of interest and is titled "Formulation development and Optimization of Liposomes containing herbal drug". He has many accolades under his hat, some of which include; University rank holder in Graduation and authored 7 articles which are published in various peer reviewed International Journals.