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[Research article]

Formulation And Evaluation Of Mouth Dissolving Tablets In Mirtazapine

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ABSTRACT

The present study was undertaken with an aim to development of formulation and evaluation of mouth dissolving tablets in mirtazapine. Mirtazapine, Gelatin, Cross Caramellose Sodium, Mannitol, aerosil, magnesium stearate, aspartame, mango flavor and microcrystalline cellulose were used for the preparation of tablets. The tablets were prepared by wet granulation method and evaluated for tablets thickness, weight variation, tablet hardness, friability, and in vitro drug release. Formulation F6 can be considered as an ideal or optimized formulation for mouth dissolving tablets of mirtazapine. It can be concluded that mouth dissolving tablet of mirtazapine. Can be successfully formulated and improving its bio availability.

Keywords: Mirtazapine, cross caramellose sodium, wet granulation method.

INTRODUCTION

Mouth dissolving tablets as a novel dosage form, have several characteristics to distinguish them from the more traditional dosage forms. These tablets in increased bioavailability compared to traditional tablets[1]. Because of dispersion in saliva while still in the oral cavity, there can be pregastric absorption from some formulation in those cases where the drug dissolving quickly and that the substances are rapidly absorbed via the blood vessels of the tongue rather than via the digestive tract[1,2]. A middle aged women undergoing radiation therapy for breast cancer may be too nauseous to swallow her H_2-blocker. Mouth dissolving/fast dissolving tablets are a perfect fit for all of these patients[2]. It is easy of administration for the disabled, uncooperative, pediatric, geriatric, bedridden and mentally ill patients with no water intake and no patient compliance[3]. Mirtazapine is a tetracyclic antidepressant. It is contra indicated in patients with hyper sensitivity to drug, co administration with MAO inhibitors is contra indicated Mirtazapine and its active metabolite cytochrome P450 isoenzyme involved are CYP 2 D6 and CYP1 A2and CYP 3A4 the N-desmethyl metabolite is pharmacologically active[4,5].

MATERIALS AND METHODS

Materials

Mirtazapine, cross caramellose sodium, mannitol, gelatin, Aerosil, Magnesium stearate, aspartame, micro crystalline cellulose and mango flavour were obtained from Cassel Research Laboratories, Chennai.

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Methods

Preparations of Mirtazapine mouth dissolving tablets

Tablets were made by wet granulation method. Mirtazapine was mixed with the required quantities of gelatin, cross caramellose sodium, mannitol, Aerosil, Aspartame and micro crystalline cellulose by geometric mixing. The powder blends was then lubricated with magnesium stearate and mango flavor mixed. Finally, the mixture was compressed on a rotary tablet machine (Fluidpack Mc-200) using standard 5mm standard flat-face punches to get 140mg weights of tablets. Composition of all formulation is given in table –1.

Evaluation of Tablets

Evaluation of powder blend

The powder blends of all formulation were evaluated for Bulk density[6], Tapped density[7], compressibility index and angle of repose[9].

Evaluation of tablet properties

The prepared tablets were tasted for weight variation, Hardness (Monsanto hardness tester), Thickness (Vernier caliper), friability (Electrolab EF-1W) and drug content.

Dissolving property

The tablets were placed in a 100 ml beaker containing distilled water. Dissolving time of fabricated mouth dissolving tablets of batch F 06 was less than 20 secs, which complies with the requirements for disintegration of mouth dissolving tablets.

In vitro Drug Release Study

The release rate of Mirtazapine mouth dissolving tablets was determined using USP X 1V type 2 (paddle type) dissolution tester. The dissolution test was performed in triplicate, using 900ml of 0.1NHCl at 37±0.5 c at 100 rpm for 3 hours. A 5 ml sample was withdrawn from the dissolution apparatus at specified time points and the samples were replaced with fresh dissolution medium. The samples were filtered through a 0.45µm membrane filter and diluted if necessary. Absorbances of these solutions were measured at 294 nm using UV-visible spectrophotometer.

RESULTS AND DISCUSSION

The compatibility study was carried out for chemical characteristics of combination such as drug to excipients used in the formulation drug excipients compatibility done. The powder blend of six formulations (F01 –F06) was evaluated for angle of repose, bulk density, tapped density, showed the pre-compressed blend has good flow property.(Table:2) The physical evaluation parameters and drug content were also tested for the tablets (Table: 3). The total weight of each formulation was maintained constant; the weight variation of the tablets were within the permissible limits of 7.5%, as specified for tablet weighing less than 325 mg. weight of the tablet was fixed at 140mg and the weight variation for every batch was tested and found within the acceptable limits. Hardness of the tablet was fixed 3kg/cm^2 and was maintained for all the batches.

Tablet thickness was also used to assess the quality of tablets. Under uniform conditions of manufacture, the total weight of tablet and thickness were linearly related. The thickness of tablet ranged from 2.96 to 3.21 mm and linearly correlated with the weight of the tablets. Friability test of all the formulations was found satisfactory showing enough resistance to the mechanical shock and abrasion. Drug content uniformity in all formulations was calculated and the presence of active ingredient ranged from 98.78 – 101.01 % (the amount drug released limits NLT 98.5 – NMT 101%) .[5,7]

In vitro dissolution studies of all formulations are depicted in table 5. Formulation F_1, F2, F3, F4, F5 and F_6 prepared with mirtazapine were done in 0.1 NHCl and the drug release from formulations F_6 was 99.16% in 25 min. formulation F_6 showed the desired drug release profile and dissolution for desired period of time within 30 secs, for this reason it was considered as best formulation among all the six formulations. (Figure- 1).

Stability studies of mouth dissolving tablets (F_6) were carried out at 45°c for one month. Evaluation of these tablets indicates that there was no change in the weight, thickness, hardness and degreased in the drug content of the tablets loaded for stability. The dissolution profile of the stability loaded tablets show that there was slight change in the release rate, but the amount of drug released 98.52% was within

limits. (NLT 98.5% of NMT 101%). The results as shown in table 6.

Mouth dissolving tablets of mirtazapine formulation F_6 showed improve its bioavailability and better drug release in comparison to the other formulation, the extent of if drug release was found to be 99.16 % at the desired time 20 secs and drug –excipients interactions was observed. Hence it was concluded that formulation F_6 can be taken as an ideal or optimized formulation of mouth dissolving tablets for 20 secs.

Table: 1 Formulation of month dissolving tablet of mirtazapine

Ingredients (mg/tablet)	F1	F2	F3	F4	F5	F6
Mirtazapine	15	15	15	15	15	15
Gelatin	2	4	4	2	2	2
Cross Caramellose sodium	2	16	4	16	6	6
Mannitol	20	20	20	20	20	20
Aerosil	2	2	2	2	2	2
Magnesium Stearate	1	2	2	2	2	2
Aspartame	1	1	1	1	1	1
Mango flavour	4	4	4	4	4	4
Sodium starch Glycolate	-	-	-	-	4	-
Microcrystalline cellulose	93	76	88	78	84	88

Table: 2 Physical evaluation

Formulation	Angle of repose	Bulk density	Tapped density
F1	25.89	0.496	0.585
F2	23.75	0.473	0.496
F3	24.34	0.431	0.590
F4	24.89	0.495	0.641
F5	25.65	0.523	0.648
F6	26.09	0.570	0.657

Table: 3 Physical evaluation parameters and drug content

Formulation	Weight variation(mg)	Thickness(mm)	Hardness (kg/cm2)	Friability(%)	Diameter(mm)	Drug content(%)
F1	139±1.3	3.15	2.1-2.6	0.72	7.21	91.73
F2	141.2±0.6	3.21	2.0-2.5	0.80	7.23	98.64
F3	140.1±0.9	2.96	2.56-2.90	0.67	7.20	98.80
F4	139.3±1.7	3.10	2.7-3.10	0.70	7.19	99.65
F5	140.1±1.3	3.18	2.74-2.95	0.54	7.22	99.48
F6	140.4±1.5	3.21	2.78-3.0	0.51	7.15	99.54

Table: 4 In vitro dissolution studies: cumulative percent drug release of formulation

Sampling time (min)	F1	F2	F3	F4	F5	F6
5	85.3	87.62	88.60	86.14	86.43	87.04
10	90.05	89.93	91.17	92.32	91.07	92.58
15	98.94	97.54	98.53	98.23	99.14	98.57
20	98.96	99.85	98.04	98.96	99.43	99.85

Table: 5 *Invitro* dissolution studies: cumulative percent drug release of formulation after storage for one month at 45° C

Sampling time(min)	F1	2	F3	F4	F5	F6
5	84.20	85.72	85.05	86.14	85.95	86.42
10	89.45	90.13	91.37	93.82	92.27	93.08
15	97.54	98.21	97.72	98.12	97.65	37.68
20	98.61	99.02	98.86	98.73	98.57	98.65

Figure: 1 Cumulative % drug release from Mouth Dissolving Tablets (F_1 - F_6)

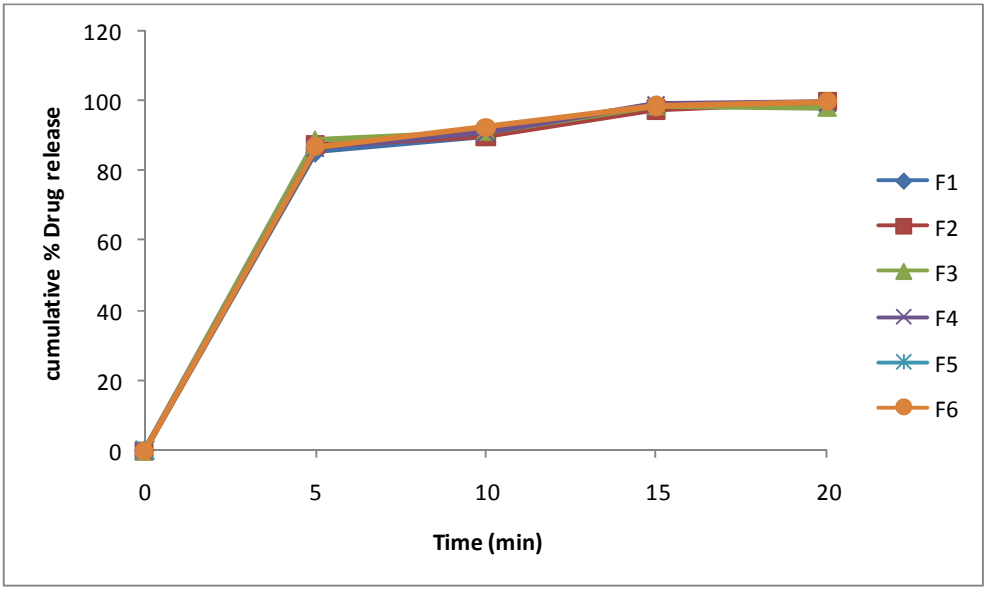
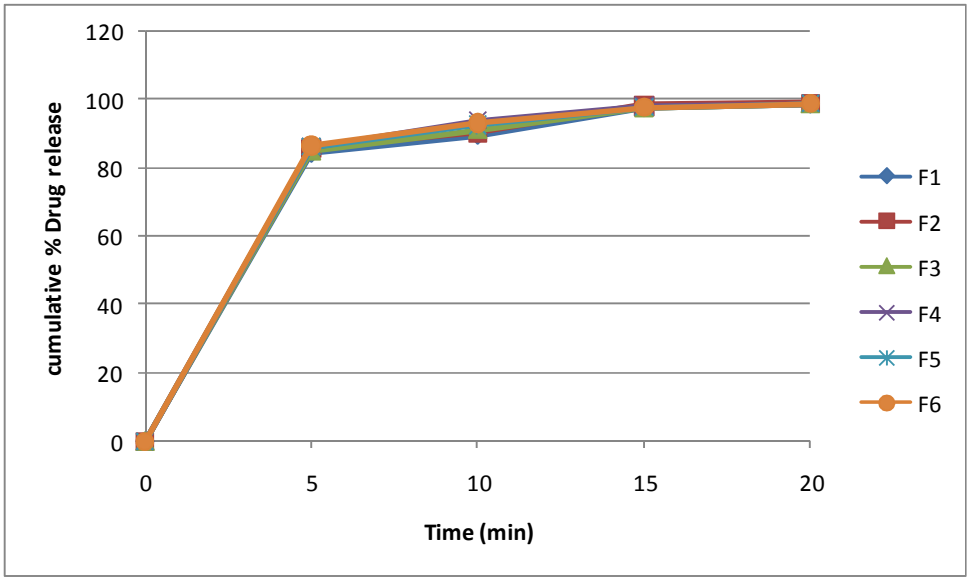


Figure: 2 Cumulative percent drug release of formulation after storage for one month at 45° C (F_1 – F_6)



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