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DEVELOPMENT AND IN VITRO EVALUATION OF FAST DISINTEGRATING TABLET OF MEFENAMIC ACID USING SUBLIMATION TECHNIQUE

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ABSTRACT

The purpose of this research was to improve Fast disintegration time of mefenamic acid tablets by using sublimation methods and determine existence of tablet. Rapid orally disintegrating tablets of mefenamic acid were successfully prepared by direct compression, which is the simplest, and most cost-effective technique to prepare tablets with good physical properties and minimum stability issues, and sublimation technique, using either camphor or menthol as the subliming agent. Further ten batches (TF1-TF10) were prepared by using camphor or menthol,0.1N NaOH, 0.1N HCl and PBS in different All the formulations were evaluated for weight variation, hardness, friability, drug content, in vitro disintegration time, wetting time, in vitro dissolution. The percentages of drug dissolved from FDTs TF10 after 20 minutes were 98.98±0.03, indicate that the process used to prepare the FDTs greatly enhanced the extent and rate of dissolution of mefenamic acid.

Keywords: Fast disintegration Tablet, Mefenamic acid, Bioavailability, Sublimation Methods.

INTRODUCTION

Solid dosage forms are popular because of low cost, ease of administration, accurate dosage self-medication, pain avoidance and the most importantly the patient compliance. The most popular solid dosage forms are being tablets and capsules[1]. However, in case of dyspepsia of geriatric patients, the underdeveloped muscular and nervous system in young individuals and incase of uncooperative patient, many problems is occur but swallowing is common phenomenon which leads to poor patient compliance. To improve these drawbacks fast dissolving tablets or orally disintegrating tablets has immersed as alternative oral dosage forms [2].

The FDT technology, which makes tablets dissolve or disintegrate in the mouth without additional water intake. The FDT formulation is defined by the Food and Drug Administration (FDA) as "a solid dosage

form containing medical substances whish disintegrates rapidly, usually within a seconds, when placed upon the tongue[3]. "According to European Pharmacopoeia, "the FDT should disperse/disintegrate in less than three minutes [1, 4]. Fast dissolving tablets are also called as mouth-dissolving tablets, melt-in mouth tablets, Orodispersible tablets, rapid melts, porous tablets, quick dissolving etc[1]. The basic approach in development of FDT is the use of super disintegrates, which provide instantaneous disintegration of tablet after putting on tongue, their by release the drug in saliva[5]. The fast dissolving tablets are rapidly dissolved or disintegrate by the use of super disintegrates.

Oral routes of drug administration have wide acceptance up to 50- 60% of total dosage forms. Solid dosage forms are popular because of ease of administration, accurate dosage, self-medication, pain avoidance and most importantly the patient compliance. The most popular solid dosage forms are being tablets and capsules; one important drawback of this dosage forms for some patients is the difficulty to swallow. Drinking water plays an important role in the swallowing of oral dosage forms. Often times people experience inconvenience in swallowing conventional dosage forms such as tablet when water is not available, in the case of the motion sickness (kinetosis) and sudden episodes of coughing during the common cold, allergic condition and bronchitis. For these reason, tablets that can rapidly dissolve or disintegrate in the oral cavity have attracted a great deal of attention [2]. The problem of swallowing is a common phenomenon in a geriatric patient due to fear of choking, hand tremors, dysphasia and in young individuals due to underdeveloped muscular and nervous systems and in schizophrenic patients which leads to poor patient compliance. Approximately one-third of the population (mainly paediatric and geriatric) has swallowing difficulties, resulting in poor compliance with oral tablet drug therapy which leads to reduced overall therapy effectiveness. For these reason, tablets that can rapidly dissolve or disintegrate in the oral cavity have attracted a great deal of attention[6].

MATERIAL AND METHODS

Preparation of Mefenamic acid containing fast disintegrating tablets using sublimation technique

Mefenamic acid RODTs were prepared by sublimation technique. Ingredients of each formulation (except magnesium stearate) were sieved through 600μm screen, geometrically mixed, lubricated with magnesium stearate (previouslysievedthrough250μmscreen) the compressed into 500mg (mg) tablets, using a 7 mm, rounded, flat punch, equipped in a single punch tablet press (Korsch XP1, Germany) with fixed pressure to obtain a tablet hardness in a range from 3 to 5 kilopond (Kp). Tablets were kept at 60 °C for 12 h in a vacuum oven (Binder VDL 53, GmbH, Germany) to ensure complete sublimation, which was verified by weight loss comparison with TF1 and TF6, which didn't contain subliming agents and were subjected to the same conditions of vacuum drying[7].

Table1.Composition of different drug loaded Mefenamic acid containing fast disintegrating tablets by using sublimation technique

S.no	Formulation	Mefenamic acid(mg)	Ac-Di-sol(%w/w)	Aerosil 200 (%w/w)	Menthol(%w/w)	Camphor (%w/w)	Mannitol	Magnesiumstearate
1.	TF1	250	25	50	0	0	75	100
2.	TF2	250	25	50	25	0	50	100
3.	TF3	250	25	50	50	0	25	100
4.	TF4	250	25	50	0	25	50	100
5.	TF5	250	25	50	0	50	25	100
6.	TF6	250	50	50	0	0	50	100
7.	TF7	250	50	50	25	0	25	100
8.	TF8	250	50	50	50	0	0	100
9.	TF9	250	50	50	0	25	125	100
10.	TF10	250	50	50	0	50	100	100

In-vitro characterization of Mefenamic acid containing fast disintegrating tablets using sublimation technique

Weight variation of tablet

Twenty tablets were randomly taken from each batch and the weight of their average weight was determined. Then individual tablet was taken and its weight was calculated. That individual weight was compared with average weight. The weights were measured using weighing balance[8].

Hardness

The tablet hardness was evaluated using a TA.XT plus texture analyser (UK) equipped with a computer software Exponent Stable Micro Systems (Ver 5.1.1.0). A 2-mm flat surface probe was equipped on the texture analyser with a load of 100g. The penetration force applied on the sample which penetrated a 2-mm depth into the sample was defined as the hardness of the tablet [8].

Thickness

The thickness of each FDT formulation was measured using a micrometre at the centre. Ten samples of each FDT formulation were measured[9].

Friability test

Ten FDTs were used for the friability test using a friabilator. The FDTs were weighed and the initial total weight of ten tablets was determined by Analytical balance. After 100 rotations at 25 rpm, the FDTs were removed from the friability tester and again weighed [10].

In-vitro disintegration time test

The disintegration time test determines whether tablets disintegrate within a prescribed time when placed in a liquid medium under experimental conditions. The in vitro disintegration time of the FDTs formulations was determined using a disintegration tester with 0.1N HCl at 37.0 ± 0.5°C. The disintegration time is defined as the time taken for FDT to completely dissolve and pass through the screen at the bottom of each tube of the disintegration tester, such that no solid residue remaining on the screen. A total of 6 FDTs were run for each formulation [11].

Percentage Drug Content

The Drug Content was determined using the UV-Visible spectroscopy method. One FDT was dissolved in a 100 ml volumetric flask with methanol. The solution was subjected to sonication for 30 min. 1 ml of the stock solution was drawn out and was diluted with methanol to 10ml in a volumetric flask and analysed using UV visible spectroscopy[12].

FT-IR spectrum:

Fourier transform infrared spectroscopy of different compounds was performed for identification of that particular compound. FT-IR Spectroscopy of pure drug, final optimized formulation was done using KBr pellets. Various peaks in FT-IR Spectrum were interpreted for identification of different group in the structure of pure drug and optimized formulation. FT-IR Spectroscopy can also be used to investigate and predict any physicochemical interactions between different components**.**

In vitro Dissolution

The dissolution studies were carried out on the optimum FDT formulation (250 mg Mefenamic acid). Drug dissolution study was carried out in 900ml of 0.1M HCl(pH 1.0 ± 0.1) at 37.0 ± 0.5°C, using USP basket method at a stirring speed of100 rpm at present time intervals of 1 min, 3min, 5min, 10min, 15min, 20min, 25min, 30min. 1 ml of samples were withdrawn and immediately replaced with an equal volume of fresh dissolution medium. The samples were filtered through 0.45lm membrane filter and the amount of drug released was determined using the UV-visible spectroscopy [13,14,15].

RESULTS AND DISCUSSION:

Rapid orally disintegrating tablets of Mefenamic acid were successfully prepared by direct compression, which is the simplest and most cost effective technique to prepare tablets with good physical properties and minimum stability issues, and sublimation technique, using either camphor or menthol as the subliming agent. Complete sublimation, of menthol or camphor, was confirmed by comparing average weight loss, after sublimation, with the original weight of incorporated subliming agents in each formulation, against TF1 and TF6 which didn't contain any subliming agents**.**

Tablets were obtained of uniform weight variations as per pharmacopoeial specifications. The average weight of all tablets was found to be in a range of 500.04±0.010to500.39±0.037. Weight of tablet of each batch is as given below table 2. The drug content was found in the range of 97.28±0.071 to 99.89±0.098% and the hardness of the tablets between 3.374±0.05 to 4.224±0.017, the tablet thickness of all formulation was uniform and it was found to be in the range of 4.05±0.022 to 4.37±0.079mm, friability of the all batch tablets were found below 1% indicating a good mechanical resistance of tablets. Disintegration time of all formulation was uniform and it was found to be in the range of 15.24±0.059 to 128±0.69 sec. The percentages of drug dissolved from FDTs TF10 after 20 minutes were98.98±0.03, indicate that the process used to prepare the FDTs greatly enhanced the extent and rate of dissolution of Mefenamic acid from the prepared tablets. All results were reported in table 2.

Table 2: In-vitro characterization of Mefenamic acid containing fast disintegrating tablets using sublimation technique

Formulations	Average weight of tablet (mg)	Hardness (kp)	Thickness (mm)	% Friability	Disintegration time (Sec)	% drug content
TF1	500.25±0.058	4.224±0.017	4.12±0.096	0.18±0.008	128±0.69	98.56±0.058
TF2	500.14±0.036	3.752±0.015	4.10±0.025	0.24±0.005	59.37±0.55	99.30±0.037
TF3	500.01±0.027	3.595±0.029	4.28±0.0.057	0.59±0.001	48.21±0.37	98.10±0.091
TF4	500.17±0.064	3.648±0.081	4.21±0.069	0.41±0.003	39.57±0.52	97.28±0.071
TF5	500.25±0.010	3.427±0.035	4.05±0.022	0.92±0.007	30.10±0.48	99.10±0.058
TF6	500.10±0.028	4.108±0.049	4.17±0.031	0.14±0.009	90.88±0.22	99.87±0.025
TF7	500.39±0.037	3.610±0.051	4.25±0.077	0.56±0.010	31.66±0.10	98.27±0.041
TF8	500.21±0.059	3.591±0.084	4.20±0.022	0.67±0.011	29.47±0.98	99.10±0.007
TF9	500.04±0.010	3.520±0.038	4.37±0.079	0.64±0.005	24.88±0.87	98.74±0.035
TF10	500.11±0.058	3.374±0.05	4.20±0.001	0.77±0.003	15.24±0.059	99.89±0.098

N=3

FT-IR spectral analysis

FT-IR analysis measures the selective absorption of light by the vibration modes of specific chemical bonds in the sample. The FT-IR spectrum of pure drug and optimized formulation is shown in figure no 1.

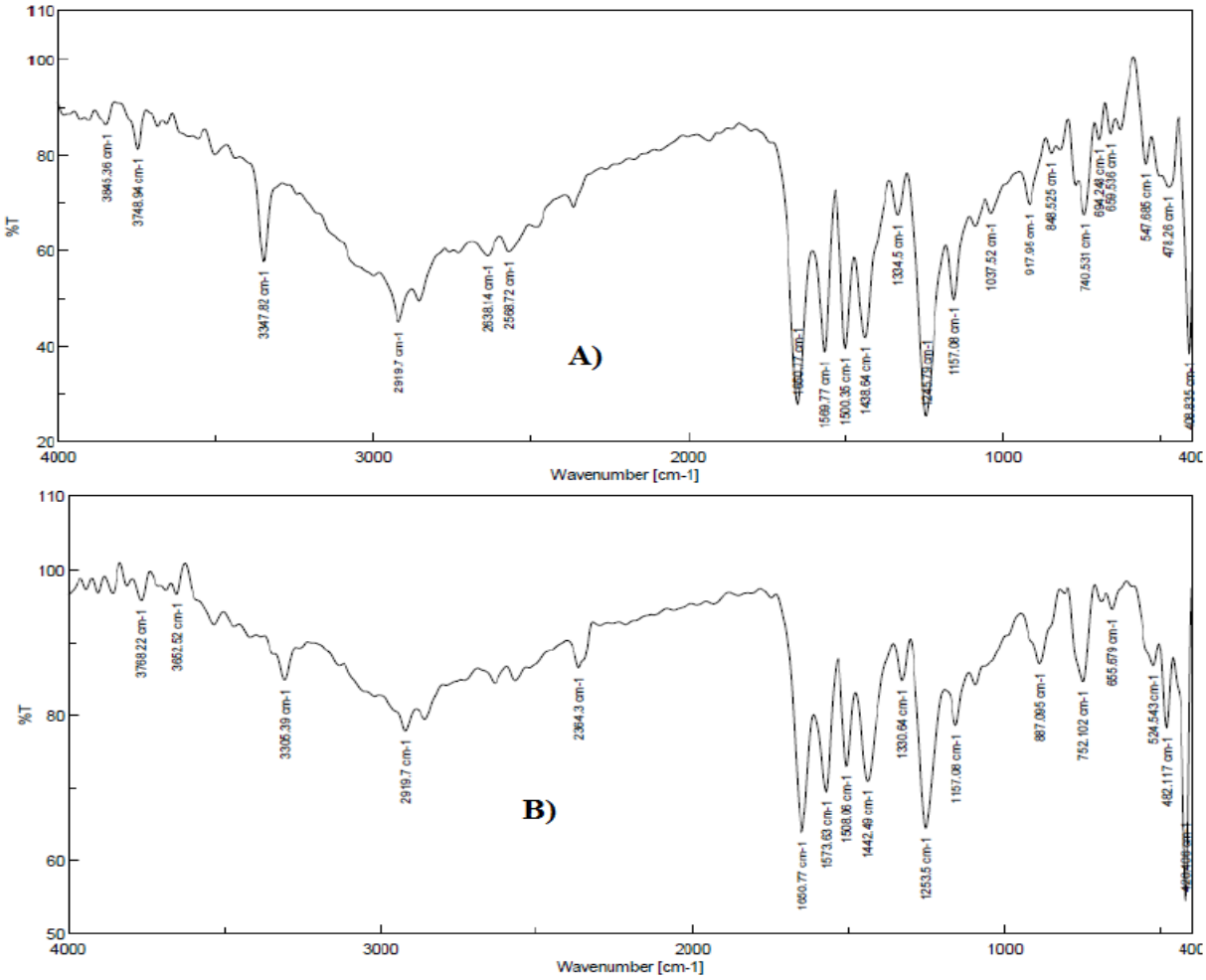

Figure 1. FTIR Spectrum of A) Mefenamic acid B) Optimized formulation

On the basis of above in vitro evaluation parameter formulation code TF10 was selected for further evaluation. The percentages of drug dissolved from FDTs TF10 after 20 minutes were 98.98±0.03, indicate that the process used to prepare the FDTs greatly enhanced the extent and rate of dissolution of Mefenamic acid from the prepared tablets.

Table No.3: Percentage dissolution of formulation TF10

S.No.	Time(min)	Percentage drug release of TF10
1.	0	00
2.	1	1.29±0.57
3.	3	38.59±0.79
4.	5	71.10±0.28
5.	10	95.67±0.99
6.	15	98.67±0.82
7.	20	98.98±0.03
8.	25	98.47±0.57
9.	30	98.36±0.68

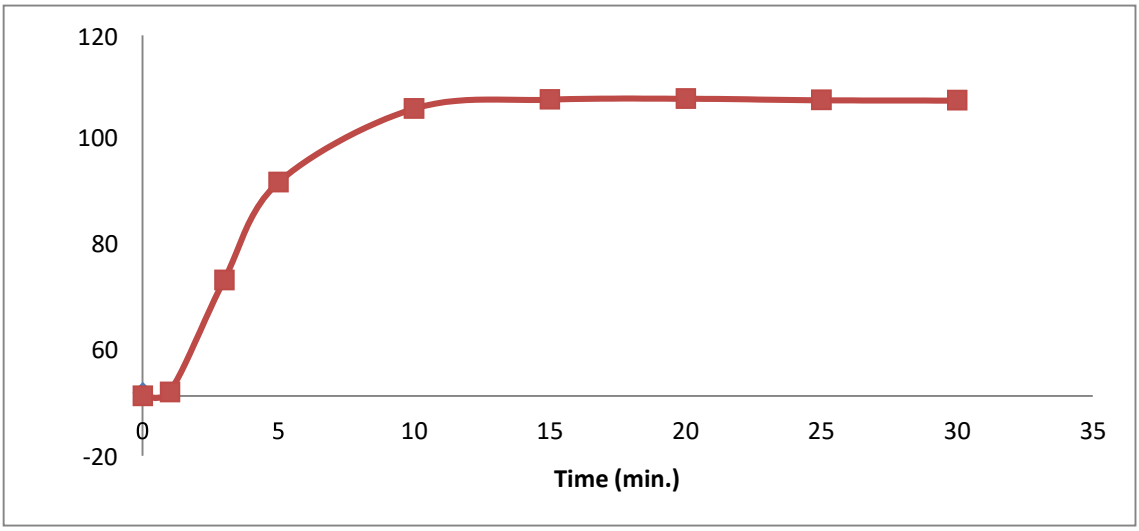

Figure 2: Percentage dissolution of drug release of formulation TF10

CONCLUSION:

The conventional immediate release tablets have some limitation as dosage form such as frequent side effects and non compliance of the patients towards dosage regimen. In order to overcome such problems, the Mefenamic acid is now-a-days available as controlled release dosage form. The dissolution of a drug can also be influenced by disintegration time of the tablets. Faster disintegration of tablets delivers a fine suspension of drug particles resulting in a higher surface area and faster dissolution. Thus these tablets undergo rapid dissolution within seconds and faster action within minutes. Melting point of mefenamic acid bulk powder form was found to be range of 229.14±1.04-232.098±0.69°C. Partition coefficient of

mefenamic acid in n-octanol-water system was found to be 4.15± 0.027 described the lipophilic nature of the drug in bulk api. Rapid orally disintegrating tablets of mefenamic acid were successfully prepared by direct compression, The average weight of all tablets was found to be in a range of 500.04±0.010to500.39±0.037. The hardness of fast dissolving tablet containing mefenamic acid of all batches was found to be in a range of 3.374±0.05 to 4.224±0.017 the tablet thickness of all formulation was uniform and it was found to be in the range of 4.05±0.022 to 4.37±0.079mm.

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