INTERNATIONAL JOURNAL OF DRUG DELIVERY AND NANOTECHNOLOGY
VOL. 1 ISSUE 1, 2015; 65 – 69 ; http://ijddn.sbtjournals.com
SBT JOURNALS

RESEARCH ARTICLE

FORMULATION AND EVALUATION OF FAST DISSOLVING TABLET OF IBUPROFEN BY SUBLIMATION METHOD

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Date Received: 4th October 2015; Date Accepted: 18th October 2015 Date published: 19th October 2015
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Abstract: The aim of the proposed work was to formulate and characterize fast dissolving tablets of Ibuprofen for rapid dissolution, which may produce rapid onset of action. In this work, fast dissolving tablets of Ibuprofen were prepared by sublimation method with a view to enhance patient compliance. Sodium starch glycolate in different concentration was used as super-disintegrant, and Ammonium carbonate (20 -30 % w/w) was used as subliming agent. The prepared batches of tablets were evaluated for Physico-chemical properties, wetting time, *in-vitro* disintegration and *in-vitro* drug release. Among the prepared formulations, the formulation (F4) containing 4% w/w of sodium starch glycolate and 25% w/w of ammonium carbonate as a subliming agent was found to be promising with disintegration time of 28 seconds, wetting time of 18 seconds and percentage of drug release of 99.5% for 30 mins. So we can conclude F4 is the best formulation when compared to all other formulations.

Keywords: Sublimation, Super disintegrant, Fast dissolving, Ibuprofen

INTRODUCTION:

Many patients especially children, old people bedridden, or mentally disabled find difficulty in swallowing tablets and hard gelatin capsules, resulting in non-compliance and ineffective therapy[1]. In recent time, a variety of new pharmaceutical research have been conducted by scientists to develop new dosage forms for patients considering safety of life, ease of medication. One such approach leads to development of fast dissolving/disintegrating tablets[2,3].

Fast dissolving dosage forms can be disintegrated, dissolved or suspended by saliva in the mouth Some drugs are absorbed from mouth, pharynx and esophagus as the saliva passes down into the stomach and in such cases bioavailability of the drug is increased: pre-gastric absorption can result in improved bioavailability and as result of reduced dosage, improved clinical performance through a reduction of unwanted effects. These dosage forms dissolve or disintegrate in the oral cavity within a minute without the need of water or chewing[4]. The objective of this study was to achieve better patient compliance, solve the problem of difficulty in swallowing and enhance onset of action by developing fast disintegrating tablets of Aceclofenac. The effect of concentration of different super-disintegrants such as crospovidone and sodium starch glycolate on the tablet properties, disintegration time and in-vitro drug release was also considered.

MATERIALS AND METHODS

Ibuprofen was obtained as gift sample from fourrts india Pvt, Ltd. Ammonium chloride and SSG was procured from chandan co chemicals**.** All other chemicals of analytical grade were purchased from commercial sources.

PREPARATION OF IBUPROFEN

Various formulation of fast disintegrating tablets of Ibuprofen were prepared by using sublimation method. sodium starch glycolate is used as a super disintegrating agent in varying concentration and Ammonium carbonate (20 -30 % w/w) was used as subliming agent. Accurately weighed quantity of Ibuprofen, subliming agent, Hydroxy propyl methyl cellulose super disintegrating agent , aspartame and mannitol were mixed and passed through the sieve no # 44. Finally magnesium stearate and talc were added as lubricating agent. The powder mixture was compressed into tablet. After compression tablets were heated in a hot air oven at 60°c until constant weight was obtained to ensure the complete removal of volatilizable component[5]

EVALUATION OF PRE-COMPRESSION PARAMETERS OF POWDER

PERCENTAGE COMPRESSIBILITY:

Compressibility is the ability of powder to decrease in volume under pressure. Compressibility is a measure that is obtained from density determinations.

% compressibility = (tapped density- bulk density/tapped density) ×100.

Compressibility measures give idea about flow property of the granules as per carr"sindex.

HAUSNER RATIO: Hausner ratio is a number that is correlated to the flowability of a powder or granular material. It is calculated by the formula

Hausner ratio = tapped density/bulk density

ANGLE OF REPOSE: It is the maximum angle between the surface of a pile of powder and horizontal plane. It is usually determined by fixed funnel method and is the measure of the flowability of powder/granules.

EVALUATION OF POST –COMPRESSION PARAMETERS OF TABLET

THICKNESS:
Dimension of the tablets was measured by using a calibrated dial caliper five tablets of each formulation were picked out randomly and its thickness was measured individually.

WEIGHT VARIATION:
The procedure described in Indian pharmacopoeia (IP, 1996) was employed to determine the weight variation of the tablets. Ten tablets were randomly selected from each batch and weighed on an electronic balance and mean weight was taken. Each tablet was then weighed individually and standard deviation in weight was calculated for each batch.

Table 1: Formulation

s.no	Ingredients (mg)	F1	F2	F3	F4	F5	F6
1	Drug	100	100	100	100	100	100
2	Ammonium carbonate	50	50	50	50	40	60
3	HPMC	4	8	-	-	-	-
4	Sodium starch glycolate	-	-	4	8	8	8
5	Aspartame	4	4	4	4	4	4
6	Mannitol	36	32	36	32	40	22
7	Magnesium stereate	2	2	2	2	4	2
8	Talc	4	4	4	4	4	4
	Total	200 mg	200 mg	200 mg	200 mg	200 mg	200 mg

HARDNESS:
Five tablets were randomly selected from each batch and harness of tablets was determined by using Monsanto hardness tester. The mean values and standard deviation for each batch were calculated.

FRIABILITY:
Friability indiacates the tablets to withstand mechanical shocks while handling. Friability of the tablets were determined using roche friabilator 10 tablets weighed (W initial) and placed into the friabilator. The friabilator was operated at 25 rpm for 4 minutes or run up to 100 revolutions and then the tablets were weighed again (W final). The loss in tablets weight due to abrasion or fracture was the measure of tablet friability. Percent friability (F) was calculated by using the formula.

$$F = \frac{W_{(initial)} - W_{(final)} \times 100}{W_{(initial)}}$$

DRUG CONTENT UNIFORMITY:
Three were tablets powdered and weigh accurately equivalent to 100 mg of ibuprofen and transferred into 100 ml volumetric flask. Then 10 ml of phosphate buffer 7.4 added and shaken for 10 minutes. Then, the volume was made up to 100 ml with methanol. Subsequently, the solution in the volumetric flask was suitably diluted and

analyzed for drug contact at 232 nm using UV-spectro photometer (shimadzu 1700. Japan).

DISINTEGRATION TEST:

The disintegration time was determined by using USP tablet disintegration test apparatus place six tablets in six baskets. The time in seconds taken for complete disintegration of the tablets until no mass remaining in the apparatus was measured. The readings were shown in the table2.

WETTING TIME[6]:

The wetting time and capillarity of the oral dispersible tablets were measured by a conventional method. The tablet was placed in a petridish containing 6.5 cm diameter containing 10ml water taken time for complete wetting of tablets were recorded in the table 2.

***IN – VITRO* DRUG RELEASE STUDIES[7]:**

The *in- vitro* drug release studies of Ibuprofen tablets were carried out using USP dissolution test apparatus type- II (paddle type) in 900 ml of dissolution medium (phosphate buffer pH 7.4) at 37± 0.5°C temperature and rotated at 50 rpm. In this test, single tablet from 5ml samples were withdrawn at 5, 10, 15, 20, 25, 30 minutes time interval and immediately replaced with an equal volume of fresh medium. Samples were suitably diluted and analyzed by using UV- spectrophotometer at 232nm. All thetests were carried out in triplicate.

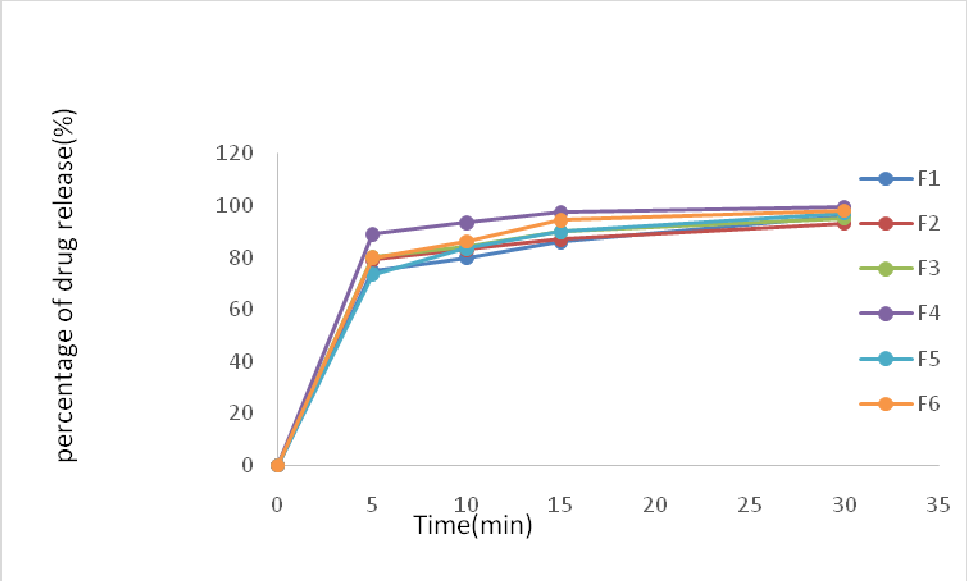
Table 2: Evaluation of prepared fast dissolving tablets

S.No	Parameters	F1	F2	F3	F4	F5	F6
1	Thickness (mm^2)	2.091	2.108	2.091	2.034	2.034	7.21
2	Weight variation	196±3.2	198±2.0	201±1.7	200±1.0	204±4.3	202±1.92
3	Hardness (kg/cm^2)	3.08±0.1	3.22±0.1	3.5±0.21	3.45 ±0.1	3.04±0.1	3.26±0.0
4	Friability (%)	0.60	0.78	0.94	0.96	0.91	0.56
5	Drug content uniformity (%)	96.74±0.62	97.26±0.25	96.68±0.59	98.03±0.28	96.70±0.68	100.00±0.56
6	Disintegration test (seconds)	45±3.21	50±1.54	31±1.64	20.95±	36.26±1	40.85±0
7	Wetting time (seconds)	19.54±3.15	24.69±1.74	20.41±0.52	18.00±1.14	22.45±1.89	30.57±0.98

Table 3: *In-vitro* dissolution study of prepared fast dissolving tablets

S.NO	TIME (MIN)	F1 (%)	F2 (%)	F3 (%)	F4 (%)	F5 (%)	F6 (%)
1	5	75.6±0.1	79.25±0.9	80.4±0.6	89±0.5	73.6±0.8	80±0.5
2	10	80±0.02	83.18±0.5	84.550.36	93.5±0.2	83.5±0.01	86.3±0.4
3	15	84.55±0.4	87.26±0.25	90.08±0.4	97.3±0.22	90±0.42	94.4±0.21
4	20	88.12±0.6	89.22±0.14	91.28±0.04	97.86±0.35	93.04±0.4	95.64±0.3
5	25	92.18±0.3	91.15±0.08	93.67±0.52	98.85±0.84	95.96±0.2	97.08±0.12
6	30	92.84±0.44	93.56±0.04	95±0.26	99.5±0.34	97.08±0.6	98.16±0.5

Fig.1: In-vitro dissolution drug release profile of prepared fast dissolving tablets graph



Discussion

Fast dissolving tablets of Ibuprofen were prepared by sublimation method employing sodium starch glycolate as super disintegrant in different ratio along with Ammonium carbonate as a subliming agent. As the tablet powder mixture was free flowing, tablets produced were of uniform weight with acceptable weight variation. In the range of 196 to 204 mg. Drug content was found between 96% to 100% in all the tablet formulations. Which indicates the drug content is uniform in all batches. Wetting time which are important criteria for understanding the capacity of disintegrants to swell in pressure of little amount. The results were found to in the range 18 to 32 seconds respectively shown in the table 2. The most important parameter that needs to to optimized in the development of fast disintegrating tablets is the disintegration time of tablets. It is observed that the disintegration time of the tablets had no effect of HPMC. It indicates that increase level of sodium starch glycolate had a positive effect on the disintegration of the tablets. At different levels formation of viscous gel layer by sodium starch glycolate might have formed a thick barrier to the further penetration of the disintegration medium and hinder the disintegration or leakage of tablets containing sodium starch glycolate. Thus, these result suggest that the disintegration times can be decreased by using of disintegrants (sodium starch glycolate) up to some extent. The formulations show disintegration time in the range of 20-45 seconds. *In vitro* drug release studies were carried out in pH 7.4 phosphate buffer and the dissolution profile depicted in fig.1 and the percentage readings are mentioned in the table 3 & Fig 1. It was found that formulation F4 with 4% SSG and 25% ammonium carbonate shows higher percentage of drug release about 99.5% within 30 min when compared to other formulations.

CONCLUSION

From the work it was concluded that the formulation F4 containing 4% w/w of sodium starch glycolate along 25% w/w of ammonium carbonate as a subiming agent was found to be promising and has shown as in disintegration time of 20 seconds wetting time of 18 seconds and drug release of 99.5% at the end of 30 min. so, we concluded F4 is the best formulation when compared to all other formulations. Further *in-vivo* studies on animals have to be performed.

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