Original Research Article

Formulation and evaluation of fast dissolving tablet-bilastine

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Abstract
In the present, study to establish Fast dissolving tablets of Bilastine by using different ratio of superdisintegrants. The tablets were prepared by using two superdisintegrants(croscarmellose sodium, sodium starch glycolate) in different composition. Development of Fast dissolving tablets of Bilastine were designed to give rapid onset of action and help those patients who have difficulty in swallowing the drug . The present study aims to improve patient compliance, reduce the condition of dysphagia and also reduces the multiple dosing. Tablets were evaluated by different parameters such as Weight variation, Tablet hardness, Friability ,Mouth feel ,Wetting time, Water absorption ratio, In vitro drug release study, In vitro disintegration time, Drug content uniformity, Accelerated stability testing. The present study concludes that fast dissolving tablets of Bilastine with different composition of superdisintrgants shows rapid disintregation time as well as dissolution profile which represents rapid onset of action of the formulation.

Key Words: Bilastine, Fast dissolving tablets, NSAIDs.

Introduction

Due to simplicity of self-administration, compactness and manufacturing facilities, the tablet is the most commonly used dosage type. However, some patients have trouble obtaining tablets and pills, especially for children and the elderly. About 50% of the populace is impacted by this, with the rate of non-compliance and contagious treatment being high.

In order to solve such problems, quickly destroyed or oral tablets emerged as alternate dosage forms. They are also called swift breakdown, easy dissolution, rapid disintegration and dissolution of mouth, mouth or mouth freezing, tablets which are orally otherwise or orally disintegrating.

The US Pharmacopoeia (USP), Centre for formulation development and Study (CDER) recently approved Orally Disintegrating (OD) tablet technology. USFDA Described OD tablet as **"a strong type of dosage that contains a drug that disintegrates quickly and is usually placed on the tongue in a matter of seconds."**

Requirements of Fast Disintegrating Tablets

1. It should not require oral water, but it will disintegrate / dissolve in the mouth after few seconds.
2. Have a mouth-feel good.
3. Get a taste masking property acceptable.
4. Will be more difficult and friable.
5. After oral administration, leave a little if any residue in the mouth.
6. Displays low environmental sensitivity such as temperature and humidity[1]

Quick dissolving drug delivery system salient feature

1. The patient who cannot swallow will be readily treated, like the elderly, victims of the stroke, bedridden patients, patients with renal disease and patients who refuse to swallow, for instance, patients with infancy, geriatric and mentoring patients.
2. The dose type is highly comfortable for patients who fly and have no urgent exposure to drink, without any of the need requiring water to sip.
3. Fast break down and product absorption culminating in a rapid onset of operation.
4. Such medications are taken from your mouth, pharynx and esophagus as the fluid falls through your stomach. The bioavailability of medicines is greatly increased in such cases.
5. Good mouth sensation tends to improve the presence of drugs in adult patients as bitter pills.

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Disadvantages of FDTs

1. FDT is in the natural environment hygroscopic and it should be kept dry.
2. Most time it has mouth sensation.
3. It also reveals the properties in fragile, ebullient granules.
4. For the proper stability and protection of a stable product FDT requires specific packaging.

MECHANISMS OF FDTs

FDTs include the following mechanisms for attaining the intended rapidly dissolving property:

1. Water should penetrate the tablet matrix rapidly to allow rapid disintegration or the tablet to dissolve instantly.
2. Includes a good The disintegrating agent or coformer in the tablet form is highly water-soluble.
3. The tablet is separated into smaller particle form, and a cure or suspension of the medication ultimately happens in several pathways.The processes -

- High swellability of disintegration
- Chemical reaction
- Capillary action[4]

Fast Dissolving Tablet (FDT) manufacturing Techniques

some commercially available fast-dissolving proprietary technologies.

1. Conventional Technologies
2. Patented Technologies

1. Sublimation

- A process where water travels through the fluid state straight from the solid state to the steam state.
- In the preparation, volatile ingredients are integrated, sublimated afterwards, creating a highly porous surface.
- Using additives such as Urethane, Urea, Ammonium Carbonate, Bicarbonate Ammonium, TetramineHexamethylene, Benzoic Acid, Phthalic Anhydride, Naphtalene and Camphor.

2. Cotton Candy Process or its Modifications

- The "candy floss" cycle is also considered to shape the base of the Flash dose system.
- The method includes formulation of the saccharide matrix or the polysaccharides which, by flash melting and centrifugal force, is converted into amorphous floss.
- The matrix is then cured or partly recrypted to create an ODT with active ingredients as well as with other excipients. However, the high temperature of manufacturing often restricts thermal substances to the application of this equipment.

3. Tablet Molding

The method of molding process produces an improved dissolution of the porous material. Two methods require the preparation of molded tablets:

a) Solvent Molding, and
b) Heat Molding

a) **Solvent Molding**: A hydro-alcoholic solution moistens the polish mix and is shaped in tablets. Air drying removes solution
b) **Heat Molding:** Drug suspension (Agar, Sugar), which is solvent in hot form in the appropriate agent. This is molded and later suction-dried to solidify at room temperature. The tablets are mechanically low

4. Melt Granulation

- Drugs are spread in a Super Polystate At the melting point, hydrophilic waxy binder, stable then.
- Super polystate is a waxed substance of 33-37 ° C and 33-37 ° C Hydrophilic-lipophilic balance (HLB) of 9.
- Super Polystate not only acts as a binder, it also enhances the toughness of tablets, disintegrating the tablets quickly and rapidly, as they melt in the mouth. resolves without any traces.

5. Mass extrusion

- A soft mass contains a medical drug, water-soluble polyethylene glycol and methanol combination.
- This soft mass is then extruded to build uniform liquid type cylinders using an extruder or syringe[6]

B.Technologies not Employing Heating Process:

1. Direct Compression

- The method is easier, more appropriate, quicker..
- The production method uses traditional tablets and excipients with improved movement, separation properties and improved compression properties.
- Form & proportion of the disintegrating agents are of key importance in the formulation.
- Particle size distribution, touch angle, allocation of pore lengths, strength of the pill and absorption potential of water are also regarded

2. Freeze-drying/ Lyophilization/Gelsication

- Drugs are found in water-soluble matrix of balanced mixture
- Polymer and Saccharides.
- This matrix is freeze dried.
- The matrix comprises other excipients such as reinforcing chemicals, precipitating chemicals, preservatives, nutrients, colours or tastes, in order to improve product products..
- This creates an amorphous and porous material that readily dissolves, accelerates absorption and increases bioavailability.

3. Spray-drying

- This is to mix a widely dispersed material with enough heated air to achieve evaporation and deshydration..
- The feed is sprayed into a moist filtered air current that provides the evaporation fuel and transfers the dry commodity to the collector.
- A sprayed mixture of tablet compounds, such as diluents, disintegrant & binder is combined with the active substance.
- It creates extremely brittle, small powders as the solution is easily evaporated[7].

METHODOLOGY

Prepared by Direct Compression Method

The following steps involved in preparation of FDTs:-

All components shown in Table 9 have been transmitted via mesh # 60.

Both of the ingredients were then put into a pestle motor for five min.

The excipients were compressed using a single tablet pounder press with 10 mm flat surface punching unit, with a low pound of 250 mg for each tablet. The punch was compressed with 10 mm flat surface punching..

About 50 tablets have been compressed for both formulations.

RESULT

A. Preformulation

A.1. Organoleptic Properties:-

Table14: Colour, odour and taste of both drugs

S. No.	Properties	Drugs
		Bilastine
1	Colour	White
2	Odour	Odourless
3	Taste	Mild Bitter

A.2. Solubility analysis:-

Table15: Solublity analysis of drugs

S. No.	Solvent	Solubility
		Bilastine
1	Water	Very sparingly *soluble*
2	Ethanol	Very soluble
3	Ether	Slightly soluble

A.3. Identification Of Bilastine by:-

I. Determination of melting point :-

The Thiele tube technique or capillary process for the calculation of liquid melting point In this analysis, paraffin was used.

Melting point of the drugs

Melting Point
Bilastine
210°c

Note:-The melting point of the drug compile with the official value

II. Determination of absorption maxima by UV Spectroscopy:-

The double beam UV spectroscopy method was used to estimate the concentration of drug in the system.

(a) For Bilastine--Absorption maximum was determined by taking 10mg of Bilastine dissolve in 10ml of distilled water in a 10 ml volumetric flask, from this solution 1ml is pipetted out and add to another 10ml of volumetric flask which gives the concentration of 100µg/ml.

Now from this stock solution 1ml solution was added to the10ml of volumetric flask, and this In the range of 200-400 nm in the systronic solution was tested -2202 double beam spectrophotometer, which exhibits maximum absorption at 213nm this was the official meaning in compliance.

A.4. Preparation of the Regular Bilastine Calibration Curve

Calibration curve of Bilastine-

Table17: Concentration & Bilastine test curve absorbance values

Serial no	Concentration (µg/ml)	Absorbance
1	**0**	**0**
2	**10**	**0.164**
3	**20**	**0.275**
4	**30**	**0.392**
5	**40**	**0.506**
6	**50**	**0.638**

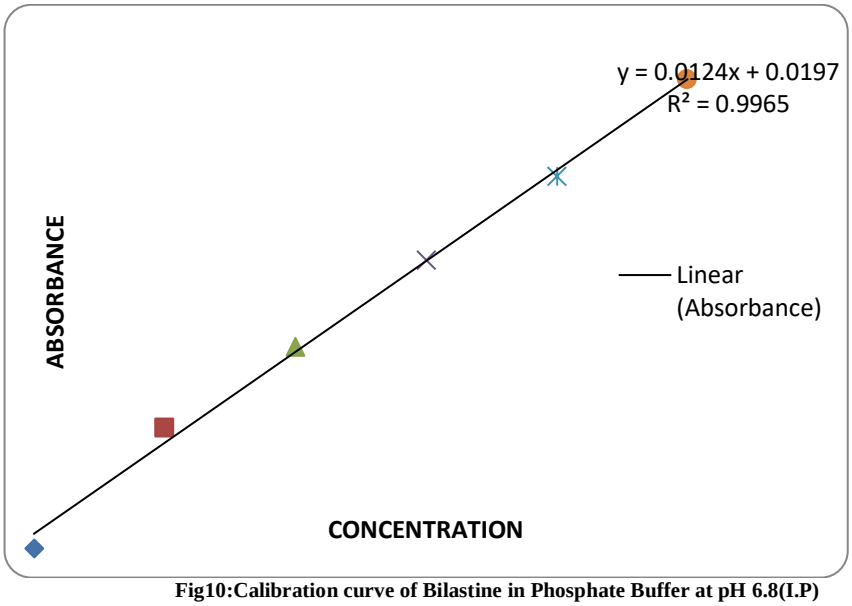


Fig10:Calibration curve of Bilastine in Phosphate Buffer at pH 6.8(I.P)

B. EVALUATION

B.1 .Pre compression parameters:-

Bulk density,tappeddensity,carr's index, hausner ratio & angle of repose values of the formulations

Formulations	Bulk density (g\cm3)	Tapped density(g\cm3)	Carr's index(%)	Hausner ratio	Angle of repose (θ)
F1	0.478	0.668	28.44	1.397	35° 50'
F2	0.470	0.667	29.53	1.419	31° 32'
F3	0.471	0.678	30.53	1.439	30° 52'
F4	0.477	0.651	26.72	1.364	30° 82'
F5	0.415	0.551	24.68	1.327	31° 22'

Note- Among the five formulation the F5 got good flow properties due to its least value of carr's index as well as hausner ratio that of other formulations.

Formulation Code	Hardness (kg/cm^2) (n=3)	Friability (%) (n=3)	Weight Variation (mg) (n=20)	Drug Content Uniformity (%) (n=3)
				Bilastine
F_1	4.13± 0.240	0.25	250.21± 1.15	98.50±0.90
F_2	4.17 ± 0.351	0.30	249.95± 0.58	99.22±0.55

F_3	4.35 ± 0.361	0.45	248.32± 1.11	100.02±0.32
F_4	4.22 ± 0.407	0.61	250.10± 0.35	100.21±0.13
F_5	3.95 ± 0.285	0.55	250.01± 0.09	100.51±0.40

B.2. Post compression parameters:-

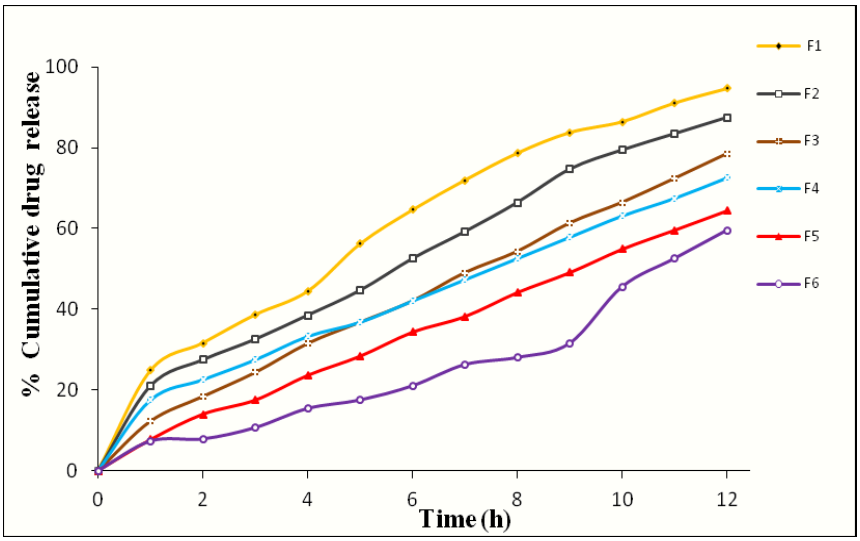
friability, Hardness, weight variation & drug content consistency values of the formulation Wetting time ,absorption ratio, disintegration time & mouth feel of the formulations

Formulation	Wetting Time (s)	Absorption ratio (%)	Disintegration Time (s)	Mouth Feel
F_1	75	80.21	50.12±2.34	good palatable
F_2	60	87.34	58.01±1.22	good palatable
F_3	55	90.51	48.11±0.98	good palatable
F_4	45	88.12	39.56±1.11	good palatable
F_5	25	86.81	26.34±2.14	good palatable

Note: All the above parameters meets the official acceptance according to I.P .

Dissolution profile of the formulations

Sl no.	Time(hr)	F1±SD	F2±SD	F3±SD	F4±SD	F5±SD
1.	0	0	0	0	0	0
2.	1	24.815 ± 0.62	20.97 ± 0.10	12.23 ± 0.60	17.47 ± 0.09	7.68 ± 0.50
3.	2	31.64 ± 0.49	27.44 ± 0.20	18.35 ± 0.62	22.52 ± 0.14	13.98 ± 0.54
4.	3	38.65 ± 0.69	32.53 ± 0.10	24.30 ± 0.60	27.45 ± 0.06	17.48 ± 0.60
5.	4	44.44 ± 0.68	38.49 ± 0.04	31.48 ± 0.61	33.24 ± 0.12	23.61 ± 0.68
6.	5	56.17 ± 0.67	44.62 ± 0.26	36.74 ± 0.56	36.75 ± 0.10	28.34 ± 0.60
7.	6	64.59 ± 0.60	52.51 ± 0.41	42.01 ± 0.59	42.01 ± 0.24	34.30 ± 0.58
8.	7	71.96 ± 0.67	59.18 ± 0.16	49.02 ± 0.57	47.28 ± 0.09	38.16 ± 0.60
9.	8	78.65 ± 0.52	66.38 ± 0.07	54.29 ± 0.61	52.55 ± 0.27	44.12 ± 0.69
10.	9	83.76 ± 0.68	74.63 ± 0.16	61.31 ± 0.63	57.82 ± 0.14	49.04 ± 0.73
11.	10	86.42 ± 0.56	79.39 ± 0.16	66.41 ± 0.61	63.09 ± 0.14	54.84 ± 0.66
12.	11	91.08 ± 0.59	83.41 ± 0.36	72.35 ± 0.62	67.46 ± 0.06	59.56 ± 0.56
13.	12	94.64 ± 0.53	87.43 ± 0.15	78.47 ± 0.59	72.53 ± 0.09	64.35 ± 0.66



The differences in mean of % cumulative drug release between batch series 'F1-F5'were significant (p < 0.0001).

Stability Studies for Formulation(F5) Stored at 40^0C/75% RH.

Weight shift, hardness, coldness, time of disintegration and weather in ASS

Tested after time (days)	Weight Variation (mg)	Hardness (kg/cm2)	Disintegration Time (s)	Friability (%)	Wetting time (s)
0	250.01± 0.09	3.95 ± 0.285	26.34±2.14	0.55	25
10	250.55± 0.12	4.01±0.225	27.12±1.15	0.74	27
20	249.82± 0.85	4.32±0.551	28.44±0.14	0.62	30
30	250.35± 0.24	4.58±0.112	26.54±1.12	0.58	26

CONCLUSION

- Following conclusions are made from the results obtained by various evaluation parameters:-
- The peaks characteristic of the FTIR formulation blend have maintained the peaks in the pure medication, that is to assume there is no contact with excipients and Bilastine and Excipients.

- The F_5 had strong flow properties of the 5 formulations owing to its lower value of the carr index and the household ratios of other formulations.
- All formulations displayed a rest angle of 30 which shows positive that the angle of rest was marginally higher over 30 indicating equal flow..
- The tablets without chipping, capping and sticking have been found to be solid by direct compression..
- Time of disintegration is the most critical parameter for quick-dissolve tablets. In this analysis all tablets have been broken down within 58.01 seconds to satisfy the official specifications for dispersible tablets (allow 3 minutes). Formulation F_5 revealed 26.34seconds of disintegration.
- Within the period of 3.95 – 4.35kg / cm^2 the toughness of the tablets was observed
- There was a good sign of strong mechanical resistance in tablets less than 1 percent for all formulations.
- **There was a drug element in the field of the two drugs —:-**

For Bilastine- 98.50-100.51%

- THE F_5 formulation showed a strong water absorption ratio of about 86,81%, suggesting stronger and faster swelling potential with limited amounts of water of superdisintegrants.
- The formula F5 has a wetting period of 25 seconds that allows mouth dispersal simpler.
- A complete drug was release within 60 minutes through dissolution analysis of formula F5.
- The stability tests carried out in the streamlined formulation (F5) have shown that there are no major changes occur after keeping the formulation in excessive stressed condition.

To sum up,

The formulation (F_5) which has a 1:1 ratio of two superdisintegrants (croscarmelose sodium & sodium starch glycolate) shows best release in least time (only 60min). So it is called as aoptimized formulation.

This optimized formulation ($F_{5)}$ shows best disintegration time 26.34 sec than that of other formulations.

Conflict of Interest: Nil
Source of support: Nil

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