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Formulation And Evaluation Of Fast Disintegrating Tablets Of Loaratidine

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ABSTRACT:

Fast disintegrating tablets have possible advantages over usual dosage forms, with improved patient observance, convenience, bioavailability and rapid onset of action. They are good substitute for drug delivery to geriatric and paediatric patients. They have major advantages of both solid and liquid dosage forms, as they remain solid during storage, which assist in stability of dosage forms and transform into liquid form within few seconds after its administration Thus FDT has great scope for being immediate drug delivery. The Loratidine are used as a model drug in the preparation of formulation. It is generally used for the treatment of Asthma. It is safe well tolerated. The study began with the preformulation characterization of drug which involves determination of melting point and development of suitable analytical method for the estimation of drug. The direct compression approach was used to create fast-dissolving tablets. It was discovered that the disintegration time of medication tablets made via direct compression was between 30 and 40 seconds. The best results were obtained from tablets manufactured with the highest amount of Crospovidone, or F15. According to the dissolving study's findings, almost half of the medication was released in the first five minutes.

Key-words: Loratidine, Fast Disintegrating Tablets, Crospovidone

1.

2. Introduction:

Asthma is a chronic, varied, inflammatory illness that affects the airways.. It is usually characterised by an inflammation or swallowing in the airway (Akinbami et al., 2014). As the condition of the ill person is not good due to which some other indicators possibly will seriously degrade the standard of patient life, which are generally experienced by the asthmatic person or an individual. Due to some restriction of activities, anxieties, embarrassment and the constant concern for their condition. In asthmatic disease condition common warning indicators of cough, tightness in rib cage, wheezing with shortness of inhalation of air.

Factors influencing the pathogenesis of asthma

2.2.1 Risk factors: Our surroundings or environment play a key responsible factor for the development of pathogenesis of atopic asthma. It is to be a usual that asthma reflects exposure to ecological trigger factors in genetically susceptible individuals (Ellwood et al., 2005). There are some primary factors, which are responsible for external environmental exposures that lead to inflammation in airway and cause some allergic symptoms in a person. When a person is exposed to environmental tobacco smoke, common aeroallergens and exposure to viral respiratory infections. In susceptible individuals, these exposures may increase the chance or risk of developing asthma in a person from initial childhood age (Palmer and Cookson, 2000).

2.2.2 Protective factors: It has been investigated from the numerous studies that if a person is early diagnosed with Mycobacterium tuberculosis infection then there is a chance of development of allergic diseases. Apart from mycobacterium tuberculosis some other early respiratory infections like measles and sometimes even respiratory syncytial virus (RSV), may protect against the development of asthma (Stein et al., 1997). It has been suggested by some researcher that, sometimes an environmental condition also play a significant or major role in the development of putative protective factors for allergic diseases like asthma or other respiratory disorder. Although, there are various protective factors are associated but an environmental condition of farmers found to be more amongst the numerous protective factors. Due to following of more traditional lifestyle, they developed tolerance and it did not show any symptoms in a short duration of time, but for long course of time it showed symptoms. In line with the above-mentioned studies, there is one common theory that attempts to describe the increased incidence of occurrence of asthma and other respiratory or lungs related disorders. A theory has been proposed by Strachan in 1989 which is known as Hygiene hypothesis (Strachan, 1989). As per the theory suggested that the development of allergies and asthma in an individual may be prohibited by less exposure to immune stimulants such as viruses, bacteria and endotoxins, during the pregnancy time or childhood age which causes shifting of Th2 cell dominance to Th1 cell dominance (Von et al., 2000). To avoid such condition of asthma, one should live in excessively follow hygienic and healthy environment from the very beginning i.e. from childhood phase only. Precaution or preventions can only truly predispose a person from occurrence of asthma, allergies condition and other respiratory or autoimmune disorders of lungs (Strachan, 1999)

MATERIALS AND METHODS:

Materials:

Loratidine was obtained as a gift sample from Jai Radhe Sales, Ellis Bridge, Ahmedabad, India. Talc, Sodium starch glycollate, Crospovidone, and Magnesium stearate was procured from Loba chemicals Pvt.Ltd. Mumbai, India. Microcrystalline cellulose was purchased from Yarrow chem. Products, Mumbai,India.

METHODS:

Preparation of fast disintegrating tablets:

The direct compression method was used to create fast-dissolving tablets due to its many benefits:

- Easiest way to manufacture tablets.
- High doses can be accommodated.
- Use of conventional equipment

Pre-compression characterization:

The quality of formulated or prepared FDTs

Ingredients(mg)	**F1**	**F2**	**F3**	**F4**	**F5**
Loratidine	18	18	18	18	18
Ac-di-sol	1	2	3	4	5
Sodium starch glycollate	-	-	-	-	-
Crospovidone	-	-	-	-	-
Avicel PH102	55	54	53	52	51
Lactopress	25	25	25	25	25
Mannitol	25	25	25	25	25
Talc	2	2	2	2	2
Magnesium stearate	2	2	2	2	2

mainly depends upon the best quality of physico-chemical properties of the prepared blends. In the literature, it has been reported that there are many process and formulations variables, which are involved in proper and uniform steps of mixing steps. All the variables can affect the characteristics features of obtained blends.

There are various characterization parameters are involved for evaluating the flow property of mixed blends, which includes bulk density of powder, Hausner's ratio, compressibility index, tapped density and angle of repose.

Bulk density: Density in bulk The mass of an untouched powder sample divided by its volume, including the contribution of the interparticulate void volume, is the bulk density (ρb) of the powder.

Method: Bulk density of a powder is determined by pouring the blend into a graduated cylinder. The bulk volume and weight of the powder was determined.

The bulk density was calculated using the formula:

Bulk density = Mass of an untapped powder sample / Bulk volume ρb= M / Vb

Tapped density:

The increased bulk density that results from mechanically tapping a container containing the powder sample is known as the tapped density (ρt). The tapped density is obtained by mechanically tapping a graduated measuring cylinder containing a known mass of powder sample (M) for 100 times The measuring cylinder is mechanically tapped after the initial powder volume is seen, and minimum volume (Vt) values occupied by powder in the graduated cylinder are recorded until little to no more volume change is noticed.

Tapped density = Mass of an untapped powder sample / Tapped volume ρb = M / Vt

Angle of repose (Θ):

It is the maximum angle possible between the surface of a pile of powder and the horizontal plane. It is measured according to the "fixed funnel and freestanding cone method". On a level, horizontal surface, a funnel was clamped with its tip 7 cm above graph paper. The powders were gradually added to the funnel until the apex of the resulting cone barely touched the funnel's tip. The following equation was used to compute the tangent of the angle of repose and obtain the mean diameters of the powder cone bases:

$\tan \Theta = h / r$

where, Θ = angle of repose

h = height of tip of funnel from base

r = radius of base of the heap of the powder

% Compressibility index:

% Compressibility = tapped density - bulk density / tapped density x 100

Hausner ratio:

It is an indirect index of ease of powder flow. It is calculated by the following formula: Hausner ratio = tapped density / bulk density If value obtained is less than 1.25, it indicates powder falls in the category of good flow.

Carr's index (CI):

(Subrahmanyam, 2000, Shariff et al., 2007) The Carr's index is an indication of the compressibility of a powder. It is an indirect measure of bulk density and cohesiveness of material. Relationship between Carr's index (CI) and Hausner ratio is: Hausner ratio = 100/ (100 - Carr'sindex) Also, CI = Initial volume – final volume / final volume X 100 Values below 15% indicate a powder with usually good flow characteristics, whereas those above 25% indicate poor flowability.

Preparation of co-processed disintegrate blends:

For the preparation of ODTs, the blends of coprocessed super disintegrate was prepared by method mentioned in the literature. With reference to the literature, for the preparation of blends Ac-di-sol/SSG and crospovidone into different ratios (1:1, 1:2, 1:3, 2:1, 2:3, 3:1, and 3:2) was weighed accurately. 50 ml of measured isopropyl alcohol was mixed with 10 g of super disintegrates that had been weighed. It was measured, and the beaker's contents were constantly swirled at 50 rpm.

The uniformity of the temperature was maintained between the ranges of 65-700 . It was stirred till most of the isopropyl alcohol evaporated. After complete evaporation of isopropyl alcohol, the wet coherent mass was obtained. The coherent mass was sieved through sieve number 100. After, completion of sieving, it was carried out for drying. The wet mass of blends were dried out in a tray drier at 600 for 20 minutes. This obtained mass was again sieved through sieve no 120. The obtained sieved powder was stored in airtight container. Coprocessed super disintegrant in the ratio of 1:1 was prepared for the preliminary study. It was further evaluated for different parameters.

Evaluation of Tablets:

Drug contents :

For the determination of drug contents, ten tablets were accurately weighed. It was crushed and finely powdered. An amount of the powder equivalent to 100 mg of drug was taken in volumetric flask. It was completely dissolved in 100 ml volumetric flask containing phosphate buffer solution of pH 6.8. It was passed and filter through filter paper. Filtered solution was further diluted with solvent. It was analyzed for drug contents study at wavelength of 271 nm by using UV- visible double beam spectrophotometer (UV 2201 SYSTRONICS).

Size and shape:

(Indian Pharmacopeia, 2007) These include diametric size, shape and thickness. The diameter and thickness was noted down of the prepared tablets. It was measured in micrometer by using digital micrometer.

Tablets hardness :

(Gennaro, 2000) Hardness of the FDTs were measured by using Monsanto tablet hardness tester apparatus. Hardness of the tablets can be defined as the force which required to crush the tablets. It is measured as hardness and in Kg/cm2 .

Weight variation :

(Indian Pharmacopeia, 2007) To carry out the weight variation study, twenty tablets were accurately weighed individually. A digital weighing balance was used for the purpose of weighing. The average weight of twenty tablets was calculated after they were precisely weighed. The weight of a single tablet was contrasted with the mean weight.

Friability:

(Indian Pharmacopeia, 2000) Friability of the FDTs were determined by using Roche Friabilator. In a plastic chamber rotating at 25 rpm, tablets were exposed to the combined effects of shock and abrasions. Every revolution, tablets that were six inches high were dropped. A pre-weighed tablet sample was put in the friabilator to perform the friability test. It was subjected to 100 revolutions. Tablets were dedusted by using soft muslin cloth and reweighed. The friability is given by the formula: % Friability = (Wi – Wf/ Wi) X 100 Where, Wi = initial weight of tablets Wf = final weight of tablets

In- vitro disintegration test:

Using a dissolving instrument, the produced tablets' in-vitro disintegration test was measured. The disintegration test was conducted by placing one pill in each of the basket's tubes.The basket is having the bottom surface made of a stainless-steel screen with mesh size no. 10. It was immersed in water bath at temperature of 37 ± 2ºC. The time required for complete disintegration of the tablet in each tube was determined using a stop watch. It was further complied with the given Pharmacopoeia' standards. As per pharmacopoeia' given standards "dispersible or disintegrating tablets must disintegrate within 3 min

Result and Discussion:

Pre-formulation studies:

Determination of wavelength of maximum

absorbance (λmax value):

Loratidine:

The published value of absorption maximum (λmax) is 231 nm, however the value that was discovered was 229 nm (Zaater et al., 2000).

Drug-excipients compatibility studies:

Drug-excipients compatibility study is important parameters for the development of formulation in its dosage form to increase bioavailability and proper administration of the drug.

FTIR analysis:

from the comparative FTIR spectrum analysis for the excipient and medication powder compatibility investigation. In the FTIR spectrum of the physical mixture, all of the main peaks associated with crospovidone and loratidine were maintained, suggesting that there was no interaction. It can be said that there were no noteworthy.

Bulk density:

Table**:** Bulk density of different formulation change or differences were observed in the FTIR spectra of physical mixtures when compared to FTIR spectra of individual components

Pre-compression characterization:

For the manufacturing of tablets with uniformity, there is a need to maintain the quality of physicochemical properties of blends. As the formulation of tablets, require lots of formulations and process variables.

Formulation Codes	Bulk Density(gm/cc)
F1	0.296±0.01
F2	0.396±0.01
F3	0.371±0.02
F4	0.386±0.00
F5	0.398±0.01

Tapped density:

Table :Tapped density of different formulation

Formulation Codes	Tapped Density(gm/cc)
F1	0.414±0.01
F2	0.425±0.01
F3	0.392±0.00
F4	0.409±0.00
F5	0.427±0.00

Angle of repose *(Θ)*:

Table .Angle of repose as an indication of powder flow properties

Formulation Codes	Angle of Repose(o)
F1	23.34±1.36
F2	25.19±1.22
F3	23.56±1.13
F4	24.44±1.12
F5	25.99±1.09

% Compressibility index:

Table : Compressibility index of different formulation

Formulation Codes	Compressibility Index(%)
F1	6.604±1.33
F2	5.621±1.23
F3	6.076±1.23
F4	5.623±1.22
F5	6.792±1.01

Hausner ratio:

Table: Hausner ratio of different formulation

Formulation Codes	Hausner's Ratio
F1	1.076±0.01
F2	1.065±0.02
F3	1.0125±0.00
F4	1.059±0.01
F5	1.073±0.01

Post-compression characterization:

When the compression of the power blends was done. The produced tablets were assessed for various organoleptic characteristics, including thickness, color, odor, and diameter. Apart from the organoleptic features, it was also carried out for physical characteristics like hardness of the tablets, its percentage of friability, disintegration and dispersion time, wetting time of the ODTs.

Drug contents:

Drug contents of the ODTs was within the range and found to be 95 to 99%, which was within acceptable limits.

Size and shape:

The shape of the prepared tablet was found to be round shape.

Tablets hardness:

Hardness was measured using Monsanto tablet hardness tester. While, mechanical integrity is of chief significance in successful formulations. Hence, the hardness of tablets was determined. It was found to be in the vary

in the range of 4- 5 Kg/cm2 .

Weight variation:

Tablets passes the Variation in weight According to the IP, tablets pass the weight fluctuation test. The percentage weight deviation was almost in the range of 4.0 and 6.1 . This range was well within the given limit of standard limit for uncoated tablets as per Pharmacopoeia. It is well identified to formulation scientists that the tablets with more hardness confirm longer disintegration time.

Friability:

Friability of the tablets was observed between

0.40 and 0.59 %. This range was less than 1%, indicating that the produced tablets had enough mechanical integrity and strength. The results of friability signify that the tablets were mechanically stable in nature. It can withstand rigors of shipping and handling.

In-vitro disintegration test:

For tablets that dissolve quickly, disintegration time is crucial. In the FDTs, the desired disintegrating time is reported to be less than minute. This speedy disintegration assists faster drug absorption and thus promoting increased bioavailability of the drug. In-vitro disintegration time was determined by means of disintegration test apparatus. The disintegration medium was 900 mL of distilled water set aside at 37 ± 0.5ºC and stirred at the speed of 30±2 cycles/min. The time was measured in seconds for complete disintegration of the tablet with no palpable mass remaining in the apparatus. The experiment was carried out in triplicate. The disintegration time for formulations was found to be 30 seconds. The results of disintegration of all the tablets were found to be within prescribed limits and satisfied the criteria.

Dissolution studies:

In-vitro drug release study was performed in phosphate buffer saline pH 6.8. solution using the methodology described (Singh et al., 2015). The USP eight-stage dissolving testing apparatus-2 (paddle method) (Lab, India) was used to determine the release of formulated FDTs. 500 mL of phosphate buffer solution with a pH of 6.8 was used for the dissolving test, which was run at 37 °C and 50 rpm. At predetermined intervals, a sample (5 mL) of the solution was taken out of the dissolution equipment and replaced with new dissolution media. Whatman filter paper was used to filter the samples. Absorbance of these solutions was measured at 243 nm using a double beam UV spectrophotometer (UV-1800 Shimadzu). In- vitro dissolution studies on the promising formulations

(F1-F5) was carried out. The comparative dissolution graph was plotted separately and analyzed for best formulation.

SUMMARY AND CONCLUSION:

1.The study began with the preformulation characterization of drug which involves determination of melting point and development of suitable analytical method for the estimation of drug. When compared to the standard, all of the evaluation parameters were found to be within range.

2.Drug excipients interaction studies carried using FTIR analysis indicated that drug is compatible with the selected formulation excipients. All the drugs and excipients used in preparation of formulation was found to be compatible with each-other.

3.Fast disintegrating tablets were prepared by direct compression method. Preliminary fifteen trial batches of fast disintegrating tablets were prepared in order to select the two factors and their level. On the basis of results of preliminary trial batches, the amount of crospovidone were selected as super disintegrating agent.

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