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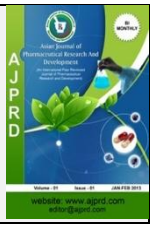

Open Access Research Article

Comparison Effect of Natural and Synthetic Superdisintigrants In Fast Dissolving Tablet Formulation

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A B S T R A C T

The main object of the recent and present study is to develop the oral fast disintegrating tablets of levolfloxacin HCL using natural and synthetic disintegrants in order to find out the difference in drug release from the dosage form levofloxacin is an antibiotic which is used to treat number bacterial infection including , pneumonia ,urinary tract infections,chronicprostatitis and some type of gastroenteritis.we prepared levofloxacin HCL superdisintegranting tablet to treat bacterial infections.we studied the use of natural and synthetic disintrgrants in the preparation of levofloxacin tablet. The present study comprise all information of superdisintigrants including its type , mechanism ,selection criteria ,ideal properties incorporation method and advantage which are being used in the formulation to provide the safer ,effective drug delivary with patients compliance.

Keywords: Levofloxacin HCL, Fenugreek, Crosscarmellose sodium, Cross povidone , Sodium starch glycolate.

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INTRODUCTION

Disintegrates are substances or mixture of substances or mixture of substances added to the drug formulation that facilitate the breakup or disintegration of tablet or capsule content into smaller particles that dissolve more rapidly.

Superdisintigrants are generally used at a low concentration in the solid dosage form typically 1-10% by weight relative to total weigh of the dosage unit[1].

Example -Superdisintigrants contain a particulate agglomerate of co- processed starch or cellulose and a sufficient amount of an augmenting agent to increase the compatibility. The augmented superdisintigrants of a solid dosage from when incorpolatedin sufficient quantity.

Researchers these days are looking for a new, safe and effective disintegrating new, safe and effective disintegrating agents which can disintegrate tablet rapidly Even at a tablet crushing strength of greater than 3.5kg .On analyzing the behavior of disintegration time in the oral cavity as well as wetting time by surface free energy we came to know that for a faster wetting a molecule should have high polar component of surface free energy and the agents which meet these special requirements are called as superdisintigrants. Superdisintigrants are another version of super –absorbing materialwith tailor made swelling properties.

Advantages and disadvantages of superdisintigrants-

Advantages-

- Superdisintigrants have tendency on wetting causing rapid disintegration.
- It have no lump formulation on disintegration .
- Compatible with commonly used therapeutic agent.
- Provide good mechanical strength to the tablet facilitating easy.
- Administered without water anywhere, anytime.
- Beneficial in cases such as motion sickness, coughing, where an ultrarapidon set of action required.

Disadvantage-

- More hygroscopic may be problem with moisture sensitive drugs.
- Some are anionic and may cause some slight invitrobinding with cationic drug.
- Most fast dissolving tablet lack the mechanical strength compared to traditional tablet. Many products are light in weight and fragile requiring them to be individually packaged.
- Patients should be advised not to push these tablets through the foil film ,but instead, peel the film back to release the fast dissolving tablet[2].

Mechanism of action of disintegrates-

The tablet breaks to primary particles by one or more of the mechanism listed below-

By capillary action- Replaces the air adsorbed on the particles, which weakens and breaks the tablet into fine particles.

By swelling- Perhaps the most widely accepted general mechanism action for tablet into disintigrant is swelling which creates pressure leads to disintigrants.

Due to release of gases-The tablet disintigrants due to generation of pressure within the tablet.

Due to repulsion- The electric repulsive forces between particles are the mechanism of disintegration and water is required for it.

Factor Affecting Superdisintigrants

Effect of filters.
Effect of binder
Effect of lubricants
Effect of surfactant[2]

SURFACTANT	REMAKS
Sodium lauryl sulfate	Good various drug
Polysorbate20	Good
Polysorbate80	Good
Tweens	Poor

Types of Superdisintigrants

The superdisintigrants can be classified into two categories on the basis of their availability.

1. Natural Superdisintegrants.
2. Synthetic Superdisintegrants

Natural superdisintigrates–These super disintergrating agents are natural in origin are natural in origin and are preferred over synthetic substances because they are comparatively cheaper, non-irritating and non-toxic in nature. The natural materials are like gums and mucilage have been extensively used in the field of drug delivery for easy availability, cost effectiveness, eco friendliness and compatible due natural origin. There are several gums mucilage available which have super disintegrating activity[3].

Plantagoovata Seed Mucilage (Isapgula) - Isapghula consists of dried seeds of the plant Plantagoovata and it contains mucilage which is present in the epidermis of the seeds. The seeds of Plantagoovata were soaked in distilled water for 48 hrs and then boiled for few minutes for complete release of mucilage into water. The material was squeezed through muslin cloth for filtering and separating out the marc. Then, an equal volume of acetone was added to the filtrate so as to precipitate the mucilage. The separated mucilage was dried in oven at temperature less than 60°C. The mucilage of Plantagoovata is a recent innovation for its superdisintegration property when compared with Crospovidone. It shows faster disintegration time than the superdisintegrant Crosspovidone[4].

Lepidiumsativum Mucilage – Lepidiumsativum (family: Cruciferae) is known as asaliyo and is widely used as herbal medicine in India. It is widely available in market and has very low cost. Parts used are leaves, root, oil, seeds etc. Seeds contain higher amount of mucilage, dimericimidazole alkaloids lepidine B, C, D, E and F and two new monomericimidazole alkaloids semilepidinoside A and B. Mucilage of Lepidiumsativum has various characteristic like binding, disintegrating, gelling etc[4].

Synthetic superdisintigrants- A group of super disintegrants including cross camellose sodium starch glycolate most of these alleviatemost of these problems. Use of the super disintegrates in fast dispersible tablets is possible as tablet shows optimum Physical properties.

Sodium Starch Glycolate: (Explotab, Primogel) - Sodium starch glycolate is widely used in oral pharmaceuticals as a disintegrant in capsule and tablet formulations. It is recommended to use in tablets prepared by either direct-compression or wet-granulation processes. The recommended concentration in a formulation is 2-8%, with the optimum concentration about 4% although in many cases 2% is sufficient. Disintegration occurs by rapid uptake of water followed by rapid and enormous swelling. The disintegrant efficiency of sodium starch glycolate is unimpaired in the presence of hydrophobic excipients, such as lubricants unlike many other disintegrants. Increasing the tablet compression pressure also appears to have no effect on disintegration time. These are modified starches with dramatic disintegrating properties and are swell in water to the extent of 10-20 percent and the modified starches increase in volume by 200-300 percent in water[5].

Selection Criteria for Superdisintigrants

Although superdisintigrants primarily affect the rate of disintigrants but when used at high levels it can also affect mouth feel, tablet hardness and friability hence various ideal factors to be considered[5].

MATERIALS AND METHODS

Materials:

LevofloxacinHCl was taken as model drug and Fenugreek Seed Mucilage was taken as a natural superdisintegrant. All other chemicals and reagent were of analytical grade. A UV-Visible spectrophotometer (Systronics, double beam UV-vis spectrophotometer) was used for drug analysis[6].

Methods:

Preparation of Fenugreek Seed Mucilage:

Fenugreek seeds (150 g) were soaked in double distilled water at room temperature and then boiled with sufficient amount of distilled water under stirring condition in a water bath until slurry was prepared. Then the slurry was cooled and kept in refrigerator overnight to settle out insoluble materials. The upper clear solution was decanted off and centrifuged at 1000 rpm for 30 minutes. The supernatant was separated and concentrated at 50-55º C on a water bath to a third of its original volume. Solution was cooled down to room temperature and was poured into thrice volume of acetone by continuous stirring. The precipitate was washed repeatedly with acetone and dried[7].

Table 1: Formulation Table of Formulation Using Natural Disintegrant[15]

Preparation Code	Drug (mg)	Fenugreek Seed Mucilage (%)	Lactose (mg)	Primogel (%)	Mannitol (mg)	Ethanol (ml)	Magnesium (%)	Talc (%)
N1	150	8	32	8	148	q.s	2	2
N2	150	12	24	12	160	q.s	2	2
N3	150	4	40	4	148	q.s	2	2
N4	150	12	16	12	156	q.s	2	2
N5	150	8	32	8	148	q.s	2	2

Table 2: Formulation Table of Formulation using Synthetic Disintegrant[16]

Preparation Code	Drug (mg)	Cross carmellose Sodium (%)	Sodium starch Glycolate (%)	Cross povidone (%)	Micro crystalline Cellulose (mg)	Magnesium (%)	Talc (%)
S1	150	4	-	2	190	2	2
S2	150	2	4	-	190	2	2
S3	150	8	8	4	176	2	2
S4	150	4	-	8	184	2	2
S5	150	-	2	2	192	2	2

Pre-compression Parameters:

The granules prepared initially were evaluated for flow properties such as bulk density, true

density, Car's index, Hausner's ratio, angle of repose.

Bulk density: Bulk density is the ratio of the total mass of powder to the bulk volume of

powder. It is measured by pouring the weighed powder (passed through a standard sieve #20) into a measuring cylinder and the initial volume (bulk volume) was noted. From this, the bulk density is calculated. Tapped density is the ratio of the total mass of powder to the tapped volume of powder. It was measured by pouring the weighed powder into a measuring cylinder and then it was subjected to 500 tapings from a height of 2 inches. The volume was measured, tapped density is calculated. Three determinations were done for each formula[7].

Bulk density = mass/bulk volume

Hausner's Ratio and Compressibility index or Carr's index (%)

Hausner's ratio is the ratio of tapped density to bulk density. It was measured by pouring the weighed powder into a measuring cylinder and the initial volume was noted and then it was subjected to 500 tapings from a height of 2 inches. Hauser's ratio was calculated by noted tapped density and poured density values[8].

Hausner's ratio= Tapped density/bulk density

Carr's index: Carr's index was calculated as 100 times the ratio of the difference between tapped density and bulk density to the tapped density. It was measured by calculated tapped density and poured density values. Determinations were carried out in triplicate.

Carr's index = [Tapped density-Bulk density]/Tapped density ×100

Angle of repose: It is defined as the maximum angle possible between the surface of a pile of powder and the horizontal plane; it was measured by pouring the weighed powder mixture into the funnel which was fixed to stand at a definite height (h). The drug excipient blend was allowed to flow through the Funnel freely onto the surface and placed on a graph sheet. Then the height and diameter of the heap formed were noted, the angle of repose was calculated. Three determinations were performed.

θ= tan-1 h/r[8]

Post compression parameters:

Hardness: Hardness or tablet crushing strength is the force required to break a tablet in a diametric compression. Hardness of the tablet was determined using the Pfizer hardness tester. A tablet was placed between two anvils of the hardness tester, and force was applied to the anvils, and the crushing strength that caused the tablet to break was recorded. The hardness was computed by deducting the initial pressure from the final pressure. Three tablets were randomly picked up from each formulation and the mean and standard deviation values were calculated[13].

Weight variation: This test was carried out according to Indian Pharmacopoeia. Twenty tablets were selected at the random and average weight was determined. Then individual tablets were weighed and the individual weight was compared with an average weight[12].

Thickness: Three tablets were selected randomly from each batch and thickness was measured by using Vernier Calipers. The tablet was placed between two arms of Vernier Calipers and thickness was measured[9].

Friability: The Roche friability test apparatus was used to determine the friability of the tablets. This device chamber revolves at 25 rpm. About 10 tablets were selected

randomly, de-dusted and weighed. Then they were placed in a drum and rotated for 100 times over a period of 4 minutes. Then tablets were deducted to remove loose dust and were reweighed. The percentage loss in weight was calculated and taken as a measure of friability.

% Friability= [Winitial– Wfinal]/Winitial×100

Rapidly Disintegrating Property: To evaluate the tablets for their rapid disintegration properties, following tests were carried out[10].

Wetting time: Five circular tissue papers of 10 cm diameter were placed in a Petri dish with a 10 cm diameter. 10 mm of water-containing methylene blue, a water-soluble dye, was added to Petri dish.A tablet was carefully placed on the surface of the tissue paper. The time required for water to reach upper surface of the tablet is noted as a wetting time.

Modified disintegration test: The standard procedure of performing disintegration test for these dosage forms has several limitations and they do not suffice the measurement of very short disintegration times. The disintegration time for ODT needs to be modified as disintegration is required without water, thus the test should mimic disintegration in salivary contents. For this purpose, a Petri dish (10cm diameter) was filled with 10 ml of water. The tablet was carefully put in the centre of Petri dish and the time for the tablet to completely disintegrate into fine particles was noted[11].

***In-vitro* dispersion time:** Tablet was added to 10 ml of phosphate buffer solution, pH 6.8 at

37+0.5ºC, Time required for complete dispersion of a tablet was measured.

Wetting time: A small piece of tissue paper was folded twice and placed in a small petri dish (internal diameter 5 cm) containing 6 ml of water. A pre-weighed tablet was put on the paper and the time required for complete wetting was measured, the wetted tablet was then weighed. The water uptake characteristic allows the evaluation of both the intrinsic swelling and the wet ability of the superdisintegrating agents' water uptake were performed at room temperature. Three tablets from each formulation were performed and standard deviation was also determined[12].

***In-vitro* drug Release studies:**

In-vitro dissolution of melt in mouth tablets of LevofloxacinHCl was studied in USP type-II dissolution apparatus employing a paddle stirrer at 50 rpm. 900 ml of pH1.2 buffer solution was used as dissolution medium. The temperature of dissolution medium was maintained at 37±0.5ºC throughout the experiment. One tablet was used in each test. Samples of dissolution medium (5ml) were withdrawn by means of syringe fitted with pre-filter at known intervals of time and analyzed for drug release by measuring the absorbance at 293nm.The volume withdrawn at each time interval was replaced with the fresh quantity of dissolution medium. The dissolution studies were carried out in triplicate. A cumulative percent drug released was calculated and plotted against time[12].

Dissolution test parameters for melt in the mouth tablets of Levofloxacin hydrochloride

Medium: 900 ml of 0.1N hydrochloric acid

Rpm: 50

Time: 5, 10,15,20,25 min.

Apparatus: Paddle

λmax: 293nm

Temperature: 37 ˚C ± 0.5˚C[17]

RESULTS AND DISCUSSIONS

The preformulation studies revealed that the granules of LevofloxacinHCl exhibited good flow properties, and the infrared spectrum of the drug as well as the individual excipinents showed that there was no interaction between the peaks, which indicates that the polymers selected for the preparation of FDT were suitable and stable. As the percentage weight variation was within the pharmacopoeial limits of ±7.5%. It is related to tooling of the compression machine, head pressure, machine speed and flow properties of the powder.

Inconsistent powder or granulate density and particle size distribution are common sources of weight variation during compression. In all the formulations, hardness test indicated good mechanical strength, as the hardness of the FDTs was found in the range of 3.0 to 4.4 kg/cm2.High hardness values increase the disintegration time and reduced dissolution values. By exploiting the correlation between hardness, disintegration, dissolution, friability, percentage defective and weight variation, improves the quality of the tablets.

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