ROLE OF NATURAL SUPERDISINTEGRAN TS IN FAST DISSOLVING TABLET TECHNOLOGY

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ABSTRACT

Now a day fast dissolving technology has a nice applicability in case of patient care. Because this type of formulation can disintegrate within few seconds and release their active ingredient very fast and onset of action can be achieved in few minutes. Mostly superdisintigrants are added to the formulations to break up the tablet into small particle that can rapidly dissolve. Many synthetic substances like Sodium Starch Glycolate, Micro Crystalline cellulose, Ac-Di-Sol, Cross providone, Kyron T314 have been used as a disintegrating agent in the tablet formulation. Mucilage and gums have been used since ancient times for their medicinal uses. Mucilage of natural origin is preferred over synthetic and semi synthetic agent because they are cheaper, abundantly available, nontoxic and non-irritating in nature. *Lepidium sativum* (family: Cruciferae) is known as asaliyo and widely used as herbal medicine in India. Mucilage of *Lepidium Sativum* has various characteristics like binding, disintegrating, gelling etc. Hence in the present study, a method is developed to isolate the mucilage from seeds and its use to develop the fast dissolvig tablet. The disintegration property of FDTs was compared with widely used superdisintigrants like Sodium starch glycolate (SSG), Kyron T314, Ac Di Sol.

KEYWORDS : FDT ,technique ,evaluation, disintegrants, superdisintegrants , FDT etc...

INTRODUCTION

A fast dissolving drug delivery system (FDDDS) can be defined as a dosage form for oral administration, which when placed in mouth, rapidly disintegrates or dissolves and can be swallowed in the form of liquid. FDDTs disintegrate and/or dissolve rapidly in the saliva without the need for water. Some tablets are designed to dissolve in saliva remarkably fast, within a few seconds, and are true fast-dissolving tablets. The target populations for these new fast-dissolving/disintegrating dosage forms have generally been pediatrics, geriatric, and bedridden or developmentally disabled patients. Patients with persistent nausea, who are travelling, or who have little or no access to water are also good candidates for FDDTs.

Advantages and disadvantages of Fast Dissolving Drug Delivery System-

(a) Advantages

Fast dissolving technology offers, Improved compliance, No water needed., No chewing needed., Better taste., Improved stability., Suitable for controlled/sustained release actives., Ability to provide advantages of liquid medication in the form of solid preparation., Adaptable and amenable to existing processing and packaging machinery., Allows high drug loading & Cost- effective.

(b) Disadvantages:

It should not expose to high levels of moisture or humidity.;Excess handling of tablets can introduce enough moisture to initiate dissolution of the tablet matrix.;Patients taking Zydis formulations should use them within six months of opening the laminated foil pouch and immediately after opening its individual blister packaging.;They are more susceptible to degradation via temperature and humidity.;Patients with dryness of the mouth due to decreased saliva production may not be good candidates for these tablet formulations. Although no water is needed to allow the drug to disperse quickly and efficiently, most technologies utilize the body's own salivation.;Decreased volume of saliva may slow the rate of dissolution/disintegration and decrease the bioavailability of the product.

Salient features of Fast Dissolving Drug Delivery System

Ease of administration for patients who are mentally ill, disabled and uncooperative.

Requires no water.

Quick disintegration and dissolution of the dosage form.

Overcomes unacceptable taste of the drugs.

Can be designed to leave minimal or no residue in the mouth after administration and also to provide a pleasant mouth feel.

Allows high drug loading.

Ability to provide advantages of liquid medication in the form of solid preparation.

Technologies used in the manufacture of FDT

The performance of FDT depends on the technology used in their manufacture. The orally disintegrating property of the tablet is attributable to a quick ingress of water into the tablet matrix, which creates porous structure and results in rapid disintegration. Hence, the basic approaches to develop FDT include maximizing the porous structure of the tablet matrix, incorporating the appropriate disintegrating agent & using highly water soluble excipient in the formulation. Following technologies have been used by various researchers to prepare FDT: -

- Direct Compression
- Wet granulation method
- Tablet Moulding
- Spray Drying
- Sublimation
- Freeze-Drying or Lyophilisation
- Cotton Candy Process
- Mass-Extrusion

Evaluation of Fast Dissolving Tablet

Tablets from all the formulation were subjected to following quality control test.

General Appearance

The general appearance of a tablet, its visual identity and over all "elegance" is essential for consumer acceptance. Include in are tablet's size, shape, colour, presence or absence of an odour, taste, surface texture, physical flaws and consistency and legibility of any identifying marking.

Size and Shape

- The size and shape of the tablet can be dimensionally described, monitored and controlled.

Tablet thickness

- Tablet thickness is an important characteristic in reproducing appearance and also in counting by using filling equipment. Some filling equipment utilizes the uniform thickness of the tablets as a counting mechanism. Ten tablets were taken and their thickness was recorded using micrometer.

Uniformity of weight

- I.P. procedure for uniformity of weight was followed, twenty tablets were taken and their weight was determined individually and collectively on a digital weighing balance. The average weight of one tablet was determined from the collective weight. The weight variation test would be a satisfactory method of determining the drug content uniformity.

Table 2.1: Tablet uniformity of weight	
Average weight of tablet	**Maximum percentage difference allowed**
130 or less	10
130-324	7.5
More than 324	5

Tablet hardness

Hardness of tablet is defined as the force applied across the diameter of the tablet in the order to break the tablet. The resistance of the tablet to chipping, abrasion or breakage under condition of storage transformation and handling before usage depends on its hardness. Hardness of the tablet of each formulation was determined using Monsanto Hardness tester.

Friability

It is measured of mechanical strength of tablets. Roche friabalator was used to determine the friability by following procedure. A pre weighed tablet was placed in the friabalator. Friabalator consist of a plastic-chamber that revolves at 25 rpm, dropping those tablets at a distance of 6 inches with each revolution. The tablets were rotated in the friabalator for at least 4 minutes. At the end of test tablets were de-dusted and reweighed, the loss in the weight of tablet is the measure of friability and is expressed in percentage as

- %Friability = Loss in weight / Initial weight x 100

7. In Vitro Disintegration test

The test was carried out on 6 tablets using the apparatus specified in I.P.-1996. distilled water at 37°C ± 2°C was used as a disintegration media and the time in second taken for complete disintegration of the tablet with no palable mass remaining in the apparatus was measured in seconds.

Wetting time

Wetting time of dosage form is related with the contact angle. Wetting time of the ODT is another important parameter, which needs to be assessed to give an insight into the disintegration properties of the tablets; a lower wetting time implies a

quicker disintegration of the tablet. The wetting time of the tablets can be measured using a simple procedure. Five circular tissue papers of 10 cm diameter are placed in a petridish with a 10 cm diameter. Ten millimeters of water-containing Eosin, a water-soluble dye, is added to petridish. A tablet is 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.

9. Moisture uptake

Moisture uptake studies for ODT should be conducted to have an insight into the stability of the formulation. Ten tablets from each formulation were kept in desiccators over calcium chloride at 37˚C for 24 h. The tablets were then weight and exposed to 75% RH, at room temperature for two weeks. Required humidity was achieved by keeping saturated sodium chloride solution at the bottom of the desiccators for three days. One tablet as control (without superdisintegrant) was kept to assess the moisture uptake due to other excipients. Tablets were weighed and the percentage increase in weight was recorded.

DISINTEGRANTS

Disintegrant and superdisintegrants are substances routinely included in the tablet formulations to aid in the break-up of the compacted mass into the primary particles to facilitate the dissolution or release of the active ingredients when it is put into a fluid environment. They endorse moisture penetration and dispersion of the tablet matrix. The major function of disintegrant is to oppose the efficiency of the tablet binder and physical forces that act under compression to structure the tablet.

Ideal properties of Superdisintegrants

- 1. It should have poor solubility.
- 2. Poor gel formation.
- 3. Have good hydration capacity.
- 4. It must have good flow properties.
- 5. No tendency to form complexes with the drugs.
- 6. It should have good mouth feel.

Types of Superdisintegrants:

The Superdisintegrants can be classified into two categories on the basis of their availability:

1. Natural Superdisintegrants
2. Synthetic Superdisintegrants

Natural Superdisintegrants

Plant *Lepidium sativum* - Biological source: Mucilage is isolated from the seeds of *Lepidium sativum* (family: cruciferae) known as asaliyo and widely used as herbal medicine in India..

Geographical source: The drug is commercially cultivated in Ethiopia, India mainly in north Gujarat.

Family: *Curciferace/Brassicaceae*

Cultivation

An easily grown plant, it succeeds in most soils. For the best results, however, it requires a moist soil and also some shade

during the summer to prevent it running straight to seed Garden cress is often cultivated as a sprouted seed, there are some named varieties. It is the cress of 'mustard and cress'. A very easy and fast crop, it can be ready within 7 days from sowing the seed. It can also be grown outdoors as full grown plants and can provide fresh leaves for the salad bowl all year round from successional sowings. Plants can be overwintered outdoors to provide edible leaves all year round, though they will require some protection if temperatures fall below -5°C. This plant is cultivated in Ethiopia for the edible oil from its seed.

(Plant of lepidium sativum)

(Mature seed of lepidium sativum)

Propagation

Seed - if you want a succession of young leaves then it is possible to sow the seed in situ every 3 weeks in succession from early spring to early autumn. Germination is very rapid, usually taking place in less than a week. When sowing seed for use in mustard and cress, the seed is soaked for about 12 hours in warm water and then placed in a humid position. Traditionally, it is sown in a tray on a thin layer of soil, or on some moist blotting paper, and the tray is placed in a warm dark place for a few days to encourage rapid and rather etiolated growth. The seedlings can then be placed in a lighter position for a couple

more days to turn green before being eaten. The cress seed should be sown about 3 - 4 days before the mustard for them both to be ready at the same time.

Chemical constitute

Parts used are leaves, root, oil, seeds etc. Seeds contain higher amount of mucilage, dimeric imidazole alkaloids lepidine B, C, D, E and F and two new monomeric imidazole alkaloids semilepidinoside A and B.

Action

Used in asthma, bronchial affections and bleeding piles. Seeds—lactagogue, diuretic, and emmenagogue. Used for treating skin disorders, fever, amoebic dysentery and asthma. Leaf stimulant, antiscorbutic, diuretic. Roots are used in secondary syphilis and in tenesmus.

The seeds are a good source of iron, but its bioavailability is poor (5.4% of total iron). They are used for rapid healing of bone fractures. The ethanolic extract of seeds significantly increased collagen synthesis and its deposition at bone fracture portion in the treated rats. The tensile strength of the broken tibiae also increased. The seeds contain an alkaloid (0.19%), glucotropaeolin, sinapin (choline ester of sinapic acid), sinapic acid, mucilaginous matter (5%) and uric acid (0.108 g/kg). The seed oil exhibits pronounced oestrogenic activity. The seed mucilage allays the irritation of the mucous membrane of intestines in dysentery and diarrhoea.

Dosage: Seed—3-6 g powder.

Gellan Gum

Gellan gum is obtained from Pseudomonos elodea. It is a linear anionic polysaccharide biodegradable polymer consisting of a linear tetrasaccharide repeat structure and is used as a food additive. Gellan gum as a superdisintegrant and the efficiency of gum is compared with other conventional disintegrants such as dried corn starch, explotab, avicel (pH 102), Ac di-sol and Kollido.The disintegration of tablet might be due to the instantaneous swelling characteristics of gellan gum when it comes into contact with water and owing to its high hydrophilic nature.

The complete disintegration of tablet is observed within 4 minutes with gellan gum concentration of 4 percent w/w and 90 percent of drug dissolved within 23 minutes. Ac-di-sol and Kollidone CL shows very similar pattern of disintegration and in vitro dissolution rates. With the same concentration tablet with explotab show 36 minutes for 90% of drug release and with starch show 220 minutes. From this result gellan gum has been proved itself as a superdisintegrant.

Synthetic Superdisintegrants-

Sodium Starch Glycolate

Non-proprietary Names

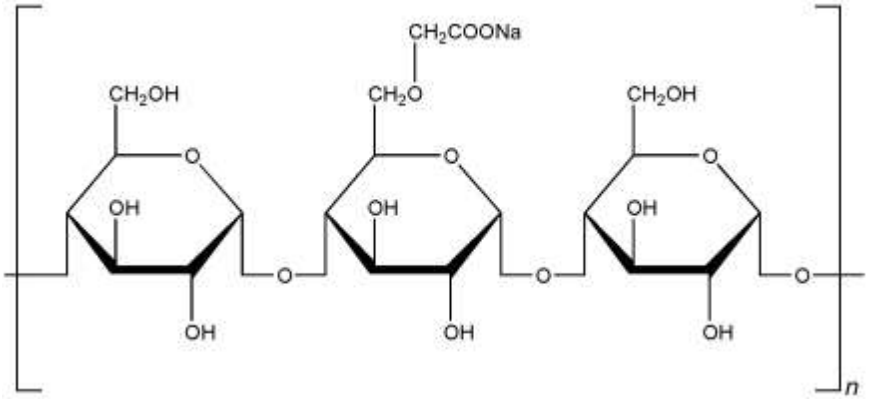
- BP: Sodium starch glycolate
- Ph.Eur: Carboxy methyl amylum natricum
- USPNF: Sodium starch glycolate

Synonyms

Carboxy methyl starch, sodium salt; *Explosol*; Explotab; *Glycolys*; Primojel; starch

Carboxy methyl ether, sodium salt; *Tablo*; Vivastar P.

Structural Formula



(Chemical structure of sodium starch glycolate)

Functional Category

Tablet and capsule disintegrant.

Applications in Pharmaceutical Formulation or Technology

Sodium starch glycolate is widely used in oral pharmaceuticals as a disintegrants in capsule and tablet formulations. It is commonly used in tablets prepared by either direct compression or wet-granulation processes. The usual concentration employed in a formulation is between 2% and 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.

Typical properties of sodium starch glycolate:

Physical properties of sodium starch glycolate	
Properties	**Value**
Bulk density	0.756 gm/cm^3
Tapped density	0.945 gm/cm^3
True density	1.443 gm/cm^3
Melting point	It does not melts but chares at 200°C

Stability and Storage condition:

Tablets prepared with sodium starch glycolate have good storage properties. Sodium starch glycolate is stable and should be stored in a well-closed container in order to protect it from wide variations of humidity and temperature, which may cause caking. The physical properties of sodium starch glycolate remain unchanged for up to 3–5 years if it is stored at moderate temperatures and humidity.

Incompatibilities:

Sodium starch glycolate is incompatible with ascorbic acids.

Cros carmellose sodium

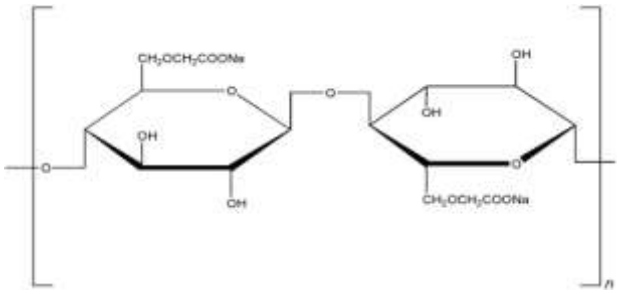
Non-proprietary Names

- BP: Croscarmellose sodium
- PhEur: Carmellosum natricum conexum
- USPNF: Croscarmellose sodium

Synonyms

Ac-Di-Sol; cross linked carboxy methylcellulose sodium; *Explocel*; modified cellulose gum; Nymcel ZSX; *Pharmacel XL*; Primellose; *Solutab*; Vivasol.

Structural Formula



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(Chemical structure of croscarmellose sodium)

Functional Category

Tablet and capsule disintegrant.

Applications in Pharmaceutical Formulation or Technology

Croscarmellose sodium is used in oral pharmaceutical formulations as a disintegrant for capsules, tablets, and granules. In tablet formulations, croscarmellose sodium may be used in both direct-compression and wet-granulation processes. When used in wet granulations, the croscarmellose sodium should be added in both the wet and dry stages of the process (intra- and extra granularly) so that the wicking and swelling ability of the disintegrant is best utilized. Croscarmellose sodium at concentrations up to 5% w/w may be used as a tablet disintegrant, although normally 2% w/w is used in tablets prepared by direct compression and 3% w/w in tablets prepared by a wet-granulation process.

Typical properties of cross- carmellose sodium:

Physical properties of croscarmellose sodium	
Properties	**Value**
Bulk density	0.529 g/cm^3
Tapped density	0.819 g/cm^3
True density	1.543 g/cm^3
Melting point	It does not melts but chares at 200ºC

Stability and Storage condition

Croscarmellose sodium is a stable though hygroscopic material. A model tablet formulation prepared by direct compression, with croscarmellose sodium as a disintegrant, showed no significant difference in drug dissolution after storage at 30°C for 14 months. Croscarmellose sodium should be stored in a well-closed container in a cool, dry place.

Incompatibilities

The efficacy of disintegrant, such as croscarmellose sodium, may be slightly reduced in tablet formulations prepared by either the wet-granulation or direct-compression process that contain hygroscopic excipient such as sorbitol. Croscarmellose sodium is not compatible with strong acids or with soluble salts of iron and some other metals such as aluminum, mercury, and zinc.

REFERENCES

Allen LV, Wang B. Rapidly Dissolving Tablets. US Patent No. 5,807,576; 1998.

Allen LV, Wang B. Method of making a rapidly dissolving tablet. US Patent No. 5 Bi Y. Preparation and evaluation of a compressed tablet rapidly disintegrating in the oral cavity. Chem. Pharm. Bull. 1996; 44 (11):2121-2127.

Chang RK, Guo X, Burnside B, Couch R. Fast-dissolving tablets. Pharm Technol. 2000; 24(6):52-58,635,210; 1997

Gohel MC., Parikh RK, BrahmbhattBK, ShahAR. Preparation and Assessment of Novel Co processed Superdisintegrant Consisting of Crospovidone and Sodium Starch Glycolate: A Technical Note. AAPS Pharm Sci Tech. 2007; 8 (1): E1-6.

Chougule D, Ghodke D, ShahRR, Ghaste R. Fast Dissolving Tablets: An Overview. 2010.

Mangal M, Thakral S, Goswami M, Ghai P. Superdisintegrants: An Updated Review. International Journal of Pharmacy and Pharmaceutical Science Research 2012; 2(2):26-35.

Deshmkh H, Nagesh C, Murade A & Usgaunkar S. Superdisintegrants: A Recent Investigation and Current Approach. Asian J. Pharm. Tech.2012 ;(2):19-25

DM Patel, DG Prajapati, NM Patel, Seed mucilage from *Ocimum americanum* linn. as disintegrant in tablets: Separation and evaluation, IJPS Year : 2007, Volume : 69, Issue : 3, Page : 431-435

Guest RT. Croscarmellose sodium, In: Handbook of Pharmaceutical Excipients; **Rowe RC, Sheskey PJ, Weller PJ**. Published by Pharmaceutical Press & American Association, 2003, 4th edition, 181-184.

Miller RW. Sodium starch glycolate, In: Handbook of Pharmaceutical Excipients; Rowe RC, Sheskey PJ, Weller PJ. Published by Pharmaceutical Press & American Association, 2003, 4th edition, 185-189.

Watanabe Y. New compressed tabletrapidly disintegrating in saliva in the mouth using crystalline cellulose and a disintegrant. Biol. Pharm. Bull. 1995; 18 (9):1308-1310.