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SUPERDISINTEGRANTS: A BIRD'S EYEVIEW

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ABSTRACT

Disintegrants and superdisintegrants are used in tablets and capsules to ensure that these dosage forms are rapidly broken down into the primary particles to facilitate the dissolution or release of active ingredients. Tablets and capsules which need rapid disintegration, the inclusion of right disintegrant is a prerequisite for optimal bioavailability. Superdisintegrants are used to improve the efficacy of the solid dosage forms. This is achieved by decreasing the disintegration time which in turn enhances drug dissolution rate. Superdisintegrants are generally used in low level in the solid dosage form typically 1-10% by weight relative to the total weight of the dosage unit. Tablet disintegration has received considerable attention is an essential step in obtaining fast drug release. The function of the disintegrants is to oppose the efficiency of the tablet binder and physical factors that act under compression to form the tablet. The superdisintegrants act as a hydrophilic carrier for poorly or water insoluble drugs. There are various natural substances like gum karaya, modified starch, and agar have been used in the formulation of fast disintegrating tablets. This review comprises the various kinds of synthetic and natural superdisintegrants which are being used in the formulation to provide safer, effective drug delivery with patient compliance.

INTRODUCTION

Bioavailability of a drug depends on absorption of the drug, which is affected by solubility of the drug in gastrointestinal fluid and permeability of the drug across gastrointestinal membrane. The solubility of a drug mainly depends on physiochemical properties of the drug. The rate of drug dissolution is greatly influenced by disintegration of the tablet[1].

In dosage forms, solid orals gain maximum popularities, about 85%, because of many advantages over others. The therapeutic activity of these formulations is obtained through a typical manner like disintegration followed by dissolution. Hence disintegration has major role for facilitating drug activity and thus gain popularity among other dosage forms[2].

Controlled drug delivery systems are starting their pace in today's pharmaceutical market, but the solid orals particularly tablets are most common and favorable approach with patient compliance as on date. These conventional tablets are intended to be swallowed whole and desired to disintegrate, release the medicaments for dissolution and providing therapeutic efficacy rapidly in the gastrointestinal tract. As disintegration plays a crucial role, so for development of solid orals, formulators are fascinating towards selection of proper disintegrants / superdisintegrants in dosage systems[2]. Disintegrants are substances or mixture of substances added to the drug formulations, which facilitate dispersion or breakup of tablets and contents of capsules into smaller particles for quick dissolution. Superdisintegrants, are those substances, which facilitate the faster disintegration with smaller quantity in contrast to disintegrants[2]. The disintegration of dosage forms are depends upon various physical factors of disintegrants/superdisintegrants. They are as follows:

1. Percentage of disintegrants present in the formulation.
2. Proportion of disintegrants used.
3. Compatibility with other excipients.
4. Presence of surfactants.
5. Hardness of the tablets.
6. Nature of Drug substances.
7. Mixing and types of addition.

They all should possess the following characteristics:

1. Poor water solubility with good hydration capacity
2. Poor gel formation
4. Good flow properties
5. Good compressibility

6. Inert

7. Non-toxic

8. Requirement of least quantity[2].

Superdisintegrants which provide improved compressibility compared to prior art Superdisintegrants and which does not negatively impact the compressibility of the formulations which include high dose drugs, and methods for obtaining the same are disclosed. The Superdisintegrants include a particulate agglomerate of co-processed starch or cellulose and a sufficient amount of an augmenting agent to increase the compatibility of the Superdisintegrants. The augmented Superdisintegrants provides a fast disintegration of a solid dosage form when incorporated in sufficient quantity therein, without untowardly affecting the compatibility of the solid dosage form[3].

SELECTING THE SUPERDISINTEGRANTS[4]

Although the superdisintegrant primarily affects the rate of disintegration, when used at high levels it can also affect mouth feel, tablet hardness, and friability. Thus, several factors must be considered when selecting a superdisintegrant.

Disintegration

The disintegrant must quickly wick saliva into the tablet to generate the volume expansion and hydrostatic pressures necessary to provide rapid disintegration in the mouth.

Compact ability

When manufacturing an ODT, it is desirable to have tablets with acceptable hardness at a given compression force to produce robust tablets that avoid the need to use specialized packaging while maximizing production speed. Thus, a more compactable disintegrant will produce stronger, less-friable tablets.

Mouth feel

To achieve patient compliance, ODTs must provide a palatable experience to the patient. Large particles can result in a gritty feeling in the mouth. Thus, small particles are preferred. If the tablet forms a gel-like consistency on contact with water, however, it produces a gummy texture that many consumers find objectionable.

Flow

As with all direct-compression tablet formulations, attaining good flow and content uniformity is important to achieving the required dosage per unit. In typical tablet formulations, superdisintegrants are used at 2–5 wt % of the tablet formulation. With ODT formulations, disintegrant levels can be significantly higher. At these higher use levels, the

flow properties of the disintegrant are more important because it makes a greater contribution to the flow characteristics of the total blend.

The selection of the optimal disintegrant for a formulation depends on a consideration of the combined effects of all of these factors.

ADVANTAGES OF SUPERDISINTEGRANT

1. Compatible with commonly used therapeutical agents and excipients.
2. Less effect on compressibility and flowability
3. Remarkable tendency on wetting causing rapid disintegration
4. Work equally effective in hydrophilic and hydrophobic formulations.
5. More effective intragranularly
6. Does not stick to the punches and dyes.
7. No lump formation on disintegration
8. Provides good mechanical strength to the tablet facilitating easy packing and transportation.

DISADVANTAGES OF SUPERDISINTEGRANTS

- More hygroscopic (may be a problem with moisture sensitive drugs)
- Some are anionic and may cause slight in-vitro binding with cationic drugs(not a problem in-vivo)

POTENTIAL DISADVANTAGES OF USE OF DISINTEGRANT IN TABLET[5]

formulation, using direct compression as the method of manufacture are –

(1) high concentration needed for optimum disintegrating efficiency

(2) poor disintegration

(3) susceptibility to high compression forces which decrease the efficiency

(4) poor compression properties

(5) decreased disintegrating efficiency in hydrophobic formulations.

A group of superdisintegrants including croscarmellose sodium (*Ac-Di-Sol*), sodium starch glycolate (*Primojel* and *Explotab*) and crospovidone (*Polyplasdone XL*) alleviate most of these problems. Use of the superdisintegrants in fast dispersible tablet is possible as tablet shows optimum physical properties

LIST OF SUPERDISINTEGRANTS

Table 1

EXAMPLE	SUPER-DISINTEGRANTS	MECHANISM OF ACTION	SPECIAL COMMENT
Crosslinked cellulose	Crosscarmellose® Ac-Di-Sol® Primellose® Vivasol®	Swells 4-8 folds in <10 seconds. Swelling and wicking both.	Swelling is in two dimensions. -Direct compression or granulation -Starch free
Crosslinked PVP	Crosspovidone Kollidon Polyplasdone	Swells 7-12 folds in <30 seconds Swells very little and returns to original size after compression but act by capillary action	Swells in three dimensions and high level serve as sustain release matrix Water insoluble and spongy in nature so get porous tablet
Crosslinked starch	Sodium Starch Glycolate	Swells 7-12 folds in <30 seconds	Swells in three dimensions and high level serve as sustain release matrix
Crosslinked alginic acid	Alginic acid NF Satialgine	Rapid swelling in aqueous medium or wicking action	Promote disintegration in both dry or wet granulation
Natural super Disintegrants	Soy polysaccharides Emcosoy	Rapid Dissolving	Does not contain any starch or sugar. Used in nutritional products.
	Calcium Silicate	Wicking action	Highly porous, Optimum concentration is between 20-40%

Table 2[2]

SR. NO	NAME OF EXCIPIENTS	CATEGORY	CONC.	STABILITY CRITERIA
1	Alginic acid	Disintegrants	1-5%	Hydrolyzes slowly at room temperature
2	Colloidal Silicon Dioxide	Disintegrants	5-10%	Hydroscopic , but do not liquefy upon absorption of water
3	Cross-povidone	Superdisintegrants	2-5 %	As hygroscopic in nature, stored in an air-tight container, in a cool and dry place.
4	Methyl cellulose	Disintegrants	2-10%	Slightly hygroscopic, but stable
5	Micro-crystalline cellulose	Superdisintegrants	5-15%	Stable at dry and air tight condition
6	Starch	Superdisintegrants	5-10%	Stable at dry and air tight condition

Table 3[6]

DISINTEGRANTS	CONCENTRATION IN GRANULES(%W/W)	SPECIAL COMMENTS
Starch USP	5-20	Higher amount is required, poorly Compressible
Starch 1500	5-15	-
Avicel®(PH 101, PH 102)	10-20	Lubricant properties and directly Compressible
Solka floc®	5-15	Purified wood cellulose
Alginic acid	1-5	Acts by swelling
Na alginate	2.5-10	Acts by swelling
Explotab®	2-8	Sodium starch glycolate
Polyplasdone®(XL)	0.5-5	Crosslinked PVP
Amberlite® (IPR 88)	0.5-5	Ion exchange resin
Methyl cellulose, Na CMC, HPMC	5-10	-
AC-Di-Sol®	1-3	Direct compression
	2-4	Wet granulation
Carbon dioxide	-	Created insitu in effervescent tablet

MECHANISMS OF SUPERDISINTEGRANTS[6]

There are four major mechanisms for tablets disintegration as follows: (see figure 1)

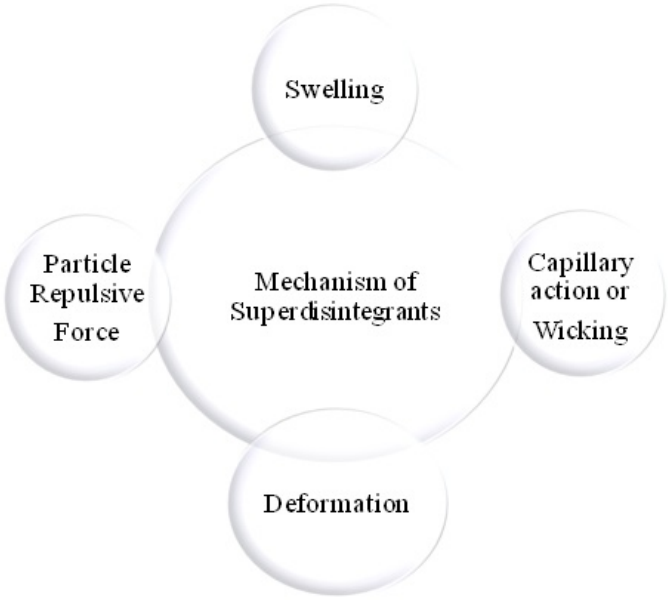
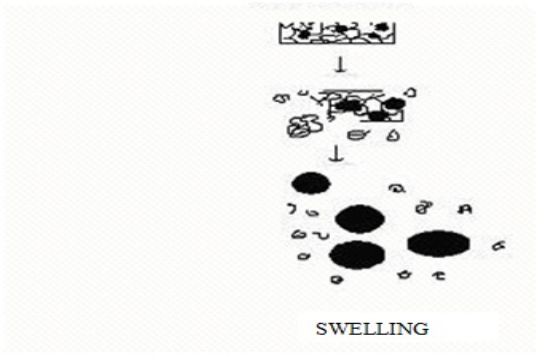


Figure 1

1. Swelling: (see figure 2)

Perhaps the most widely accepted general mechanism of action for tablet disintegration is swelling. Tablets with high porosity show poor disintegration due to lack of adequate swelling force. On the other hand, sufficient swelling force is exerted in the tablet with low porosity. It is worthwhile to note that if the packing fraction is very high, fluid is unable to penetrate in the tablet and disintegration is again slows down.



Particles swell and break up the matrix form within

Figure 2

2. Porosity and capillary action (Wicking): (see figure 3)

Disintegration by capillary action is always the first step. When we put the tablet into suitable aqueous medium, the medium penetrates into the tablet and replaces the air adsorbed on the particles, which weakens the intermolecular bond and breaks the tablet into fine particles. Water uptake by tablet depends upon hydrophilicity of the drug /excipient and on tableting conditions.

For these types of disintegrants maintenance of porous structure and low interfacial tension towards aqueous fluid is necessary which helps in disintegration by creating a hydrophilic network around the drug particles.

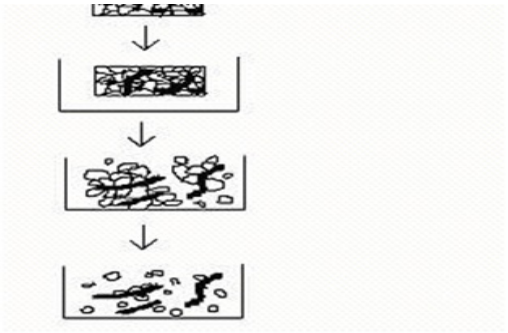


Figure 3

3. Due to disintegrating particle/particle repulsive forces (see figure 4)

Another mechanism of disintegration attempts to explain the swelling of tablet made with 'nonswellable' disintegrants. Guyot-Hermann has proposed a particle repulsion theory based on the observation that nonswelling particle also cause disintegration of tablets. The electric repulsive forces between particles are the mechanism of disintegration and water is required for it. Researchers found that repulsion is secondary to wicking.

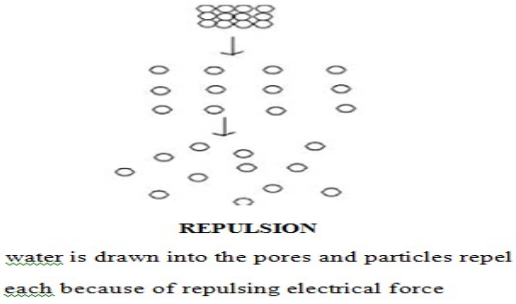


Figure 4

4. Due to deformation (see figure 5)

During tablet compression, disintegrated particles get deformed and these deformed particles get into their normal structure when they come in contact with aqueous media or water. Occasionally, the swelling capacity of starch was improved when granules were extensively deformed during compression. This increase in size of the deformed particles produces a breakup of the tablet. This may be a mechanism of starch and has only recently begun to be studied.

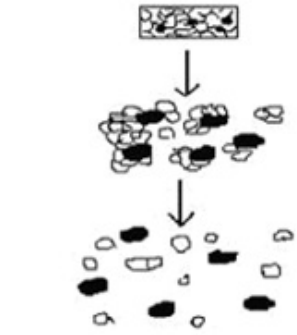


Figure 5

5. Because of heat of wetting (air expansion)

When disintegrants with exothermic properties gets wetted, localized stress is generated due to capillary air expansion, which helps in disintegration of tablet. This explanation, however, is limited to only a few types of disintegrants and cannot describe the action of most modern disintegrating agents.

6. **Due to release of gases**

Carbon dioxide released within tablets on wetting due to interaction between bicarbonate and carbonate with citric acid or tartaric acid. The tablet disintegrates due to generation of pressure within the tablet. This effervescent mixture is used when pharmacist needs to formulate very rapidly dissolving tablets or fast disintegrating tablet. As these disintegrants

are highly sensitive to small changes in humidity level and temperature, strict control of environment is required during manufacturing of the tablets. The effervescent blend is either added immediately prior to compression or can be added in to two separate fraction of formulation.

7. By enzymatic reaction

Here, enzymes presents in the body act as disintegrants. These enzymes destroy the binding action of binder and helps in disintegration.

Table 4[6]

SUPERDISINTEGRANTS	EXAMPLE	MECHANISM OF ACTION	SPECIAL COMMENT
Crosscarmellose® Ac-Di-Sol® Nymce ZSX® Primellose® Solutab® Vivasol® L-HPC	Crosslinked Cellulose	Swells 4-8 folds in < 10 seconds. -Swelling and wicking both.	-Swells in two dimensions. -Direct compression or granulation -Starch free
Crosspovidone Crosspovidon M® Kollidon® Polyplasdone®	Crosslinked PVP	-Swells very little and returns to original size after compression but act by capillary action	Water insoluble and spongy in nature so get porous tablet
Sodium starch glycolate Explotab® Primogel®	Crosslinked Starch	Swells 7-12 folds in < 30 seconds	Swells in three dimensions and high level serve as sustain release matrix
Alginic acid NF Satialgine®	Crosslinked alginic acid	-Rapid swelling in aqueous medium or wicking action	Promote disintegration in both dry or wet granulation
Soy polysaccharides Emcosoy®	Natural super Disintegrant		Does not contain any starch or sugar.
Calcium silicate		Wicking action	-Highly porous, -Optimum concentration is between 20-40%

FACTORS AFFECTING DISINTEGRANT ACTIVITY [7]

- Percentage of disintegrant present in the tablets
- Combination of disintegrants
- Nature of drug substances
- Mixing and screening
- Particle size
- Effect of compression force
- Molecular structure
- Matrix Solubility
- Incorporation In Granulation
- Incorporation In Hard Gelatin Capsules
- Effect Of Reworking
- Effect of fillers
- Effect of binders
- Effect of lubricant
- Effect of surfactant

Surfactants	**Remarks**
Sodium lauryl sulphate	Good-various drugs Poor- various drugs
Polysorbate 20	Good
Polysorbate 40 and 60	Poor
Polysorbate 80	Good
Tweens	Poor
Polyethylene Glycol	Poor

(Good- decrease in disintegrating time, Poor- increase in disintegration time)

METHOD OF INCORPORATION [2]

The incorporation of superdisintegrants in the dosage forms are mainly of three types

1. **Intragranular or during granulation** - In this process the superdisintegrants are blend with other powders and granulation is carried out. Thus the superdisintegrants are incorporated within the granules.
2. **Extragranular or prior to compression** - In this process, the superdisintegrants are mixed with prepared granules before compression.

3. **Incorporation of superdisintegrants at intra and extra granulation steps-** In this process part of superdisintegrants are added to intragranular and a part to extra granules. This method usually produces better results and more complete disintegration than type I and type II.

COMPARATIVE STUDY OF DIFFERENT SUPERDISINTEGRANTS

Superdisintegrants can be obtained from two sources

I. Synthetic

II. Natural

SYNTHETIC SUPERDISINTEGRANTS[8]

1. **Croscarmellose Sodium**

- **Nonproprietary Names**

BP: Croscarmellose Sodium

JP: Croscarmellose Sodium

PhEur: Croscarmellose Sodium

USP-NF: Croscarmellose Sodium

- **Synonyms**

Ac-Di-Sol; carmellosum natricum conexum; crosslinked carboxymethylcellulose sodium; Explocel; modified cellulose gum; Nymcel ZSX; Pharmacel XL; Primellose; Solutab; Vivasol

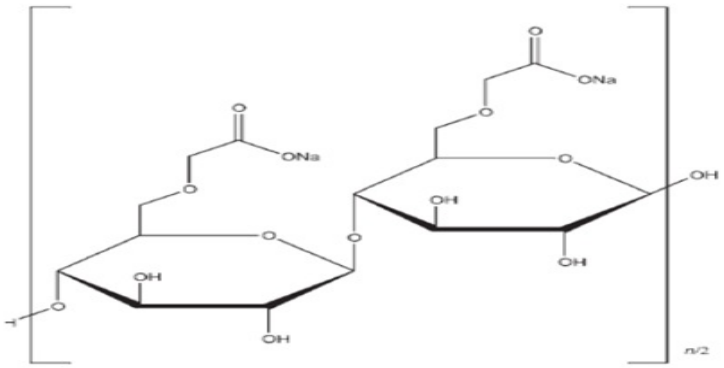
- **Chemical Name and CAS Registry Number**

Cellulose, carboxymethyl ether, sodium salt, crosslinked [74811-65-7]

- **Empirical Formula and Molecular Weight**

Croscarmellose sodium is a crosslinked polymer of carboxymethylcellulose sodium.

- **Structural Formula** (see figure 6)



CROSCARMELLOSE SODIUM

Figure 6

- **Functional Category**

Tablet and capsule disintegrant.

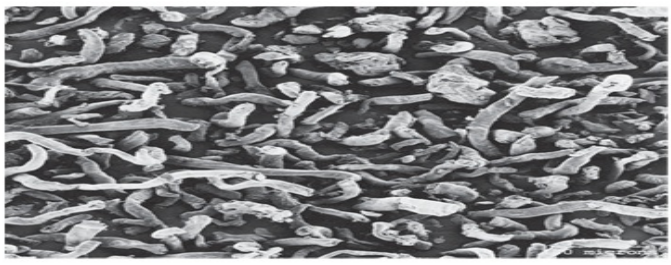
Croscarmellose sodium facilitates rapid disintegration and dissolution at low use levels in tablets, capsules, granules and other dosage forms. It is recognized for superior quality, consistency and stability and it is the standard by which superdisintegrants are compared. Cross linking makes it an insoluble, hydrophilic, highly absorbent material, resulting in excellent swelling properties and its unique fibrous nature gives it excellent water wicking capabilities. It provides superior drug dissolution and drug disintegration characteristics, thus improving the bioavailability of the formulations.

TYPICAL PROPERTIES OF CROSCARMELLOSE SODIUM:

Typical average particle size	NMT 2% 200 mesh NMT10% 325 mesh
PH	5.9-7.0
Degree of substitution	0.63-0.85
Setting volume in ml	10-30
Water soluble substances (%)	NMT 5.5
Loss on drying (%)	NMT 6.0

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 extragranularly) 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. (see figure 7)



SEM of croscarmellose sodium (Ac-Di-Sol); manufacturer: FMC Biopolymer; magnification: 100.

Figure 7

2. Crospovidone

- **Nonproprietary Names**

BP: Crospovidone

PhEur: Crospovidone

USP-NF: Crospovidone

- **Synonyms**

Crospovidonum; Crospopharm; crosslinked povidone; E1202; Kollidon CL; Kollidon CL-M; Polyplasdone XL; Polyplasdone XL-10; polyvinylpolypyrrolidone; PVPP; 1-vinyl-2-pyrrolidinone homopolymer.

- **Chemical Name and CAS Registry Number**

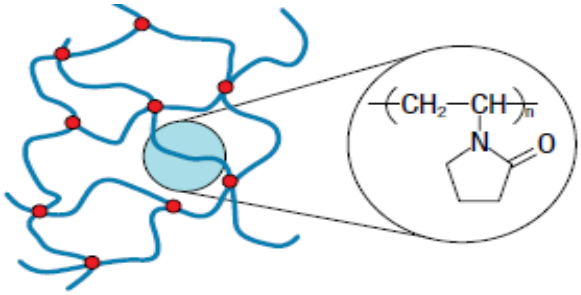
1-Ethenyl-2-pyrrolidinone homopolymer [9003-39-8]

- **Empirical Formula and Molecular Weight**

$(C_6H_9NO)_n$ >1 000 000

The USP32–NF27 describes crospovidone as a water-insoluble synthetic crosslinked homopolymer of N-vinyl-2-pyrrolidinone. An exact determination of the molecular weight has not been established because of the insolubility of the material.

- **Structural Formula** (see figure 8)



CROSPOVIDONE

Figure 8

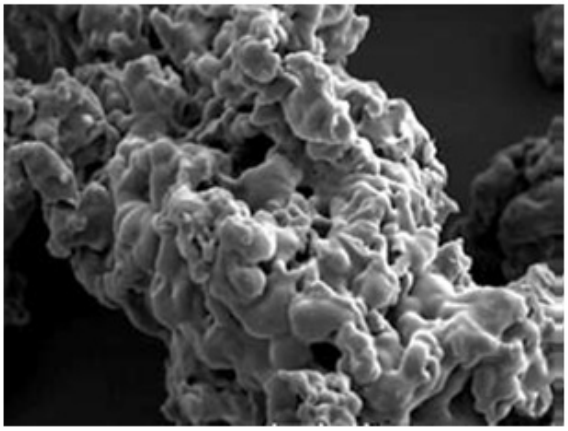
- **Functional Category:** Tablet disintegrant.

Crospovidone is a white to creamy-white, finely divided, free flowing, practically tasteless, odorless or nearly odorless, hygroscopic powder. The insoluble grades of Kollidon (crospovidone) are manufactured by a polymerization process that yields cross linked insoluble polyvinylpyrolidone in the form of 'a popcorn' polymer. The polymerization is performed by using non-aquaous system, no organic solvent are required at any stage. Crospovidone NF is a synthetic, insoluble but rapidly swellable, croslinked homopolymer of N-vinyl-2-pyrolidone.

- **PRODUCT RANGE:**

Polyplasdone XL:

Polymer has the largest average particle size (100-130µ) and provides the fastest disintegration. (see figure 9)

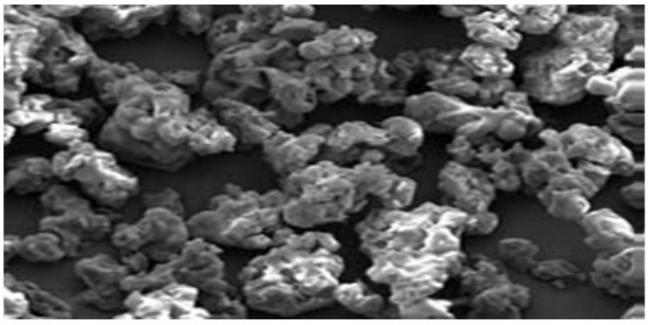


POLYPLASDONE XL

Figure 9

Polyplasdone XL10:

Polymer has a finer average particle size (30-50µ), which enhances content uniformity in the formulation of small tablets (less than 30 mg) and in the intragranular applications while still providing rapid disintegration. (see figure 10)



POLYPLASDONE XL10

Figure 10

Polyplasdone INF 10:

Polymer has the finest average particle size (5-10μ) of the polyplasdone grades and is a highly adsorptive material.

Table 5: FEATURES AND BENEFITS OF VARIOUS GRADES OF CROSPOVIDONE

Features	Benefits
Two particle size for disintegration (Polyplasdone XL & XL-10)	Polyplasdone XL10 superdisintegrant also gives smoother mouth feel in quick dissolve and chewable compared to the other disintegrants with larger particle size
Granular particles	Provides good flow properties during tablet manufacturing.
Porous particle morphology	Swells rapidly and wicks water into the particles and tablet by capillary action, hence providing fast disintegration at low use level. Highly compressible material providing hard non-friable tablets. Excellent for use with poorly compressible drug actives.
Non-gelling	Completely insoluble with relatively high cross linked density. Does not form gels that can impede disintegration, dissolution and drug release. Excellent disintegration performance even after cycles of wetting and drying.

Table 6: PRODUCT SPECIFICATIONS AND TYPICAL PROPERTIES

Properties	Polyplasdone		
	INF-10	XL-10	XL
Appearance	White to off white free flowing powder	White to off white free flowing powder	White to off white free flowing powder
Bulk density(g/cm^3)	0.4	0.3	0.3
Tap density (g/cm^3) (1000 taps)	0.5	0.5	0.4
Specific surface area (m^2/g)	2.0-2.5	1.2-1.4	0.6-0.8
% Adsorptive activity	30-50	-------	------
PH(1g/100ml DI water)	5.0-8.0	5.0-8.0	5.0-8.0
% Moisture	5 maximum	5 maximum	5 maximum
% Ash	0.1maximum	0.1maximum	0.1maximum
Heavy metals (ppm, as lead)	10 maximum	10 maximum	10 maximum

APPLICATIONS IN PHARMACEUTICAL FORMULATION OR TECHNOLOGY

Crospovidone is a water-insoluble tablet disintegrant and dissolution agent used at 2–5% concentration in tablets prepared by direct compression or wet- and dry-granulation methods.

It rapidly exhibits high capillary activity and pronounced hydration capacity, with little tendency to form gels. Studies suggest that the particle size of crospovidone strongly influences disintegration of analgesic tablets. Larger particles provide a faster disintegration than smaller particles. Crospovidone can also be used as a solubility enhancer. With the technique of co-evaporation, crospovidone can be used to enhance the solubility of poorly soluble drugs. The drug is adsorbed on to crospovidone in the presence of a suitable solvent and the solvent is then evaporated. This technique results in faster dissolution rate.

3. **Sodium starch glycolate**

- **Nonproprietary Names**

BP: Sodium Starch Glycolate

PhEur: Sodium Starch Glycolate

USP-NF: Sodium Starch Glycolate

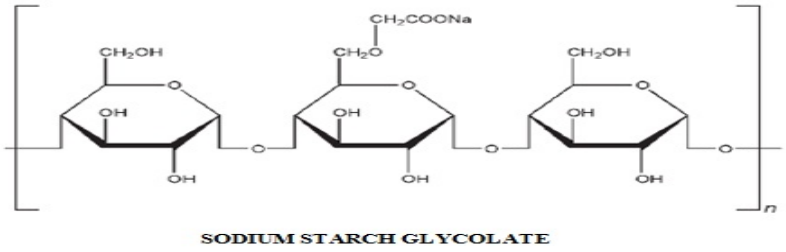
- **Synonyms**

Carboxymethyl starch, sodium salt; carboxymethylamylum natricum; Explosol; Explotab; Glycolys; Primojel; starch carboxymethyl ether, sodium salt; Tablo; Vivastar P.

- **Chemical Name and CAS Registry Number**

Sodium carboxymethyl starch [9063-38-1]

- **Molecular weight:** 500000-1000000
- **Structural formula: (**see figure 11)



SODIUM STARCH GLYCOLATE

Figure 11

- **Functional Category**

Tablet and capsule disintegrant

- **Description**

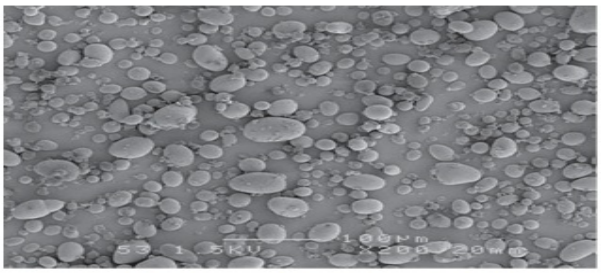
Sodium starch glycolate is a white or almost white free-flowing very hygroscopic powder. The PhEur 6.0 states that when examined under a microscope it is seen to consist of: granules, irregularly shaped, ovoid or pear-shaped, 30–100 mm in size, or rounded, 10–35 mm in size; compound granules consisting of 2–4 components occur occasionally; the granules have an eccentric hilum and clearly visible concentric striations. Between crossed nicol prisms, the granules show a distinct black cross intersecting at the hilum; small crystals are visible at the surface of the granules. The granules show considerable swelling in contact with water.

- **DIFFERENT PRODUCTS OF SODIUM STARCH GLYCOLATE**

1. Primogel (see figure 12)
2. Explotab (see figure 13)
3. Glycolys (see figure 14)
4. Vivastar p (see figure 15)

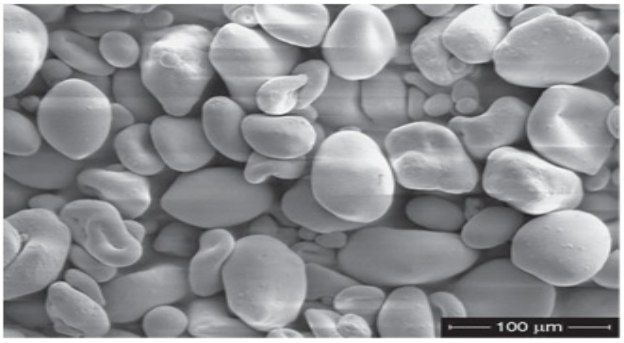
APPLICATIONS IN PHARMACEUTICAL FORMULATION OR TECHNOLOGY

Sodium starch glycolate is widely used in oral pharmaceuticals as a disintegrant 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. Although the effectiveness of many disintegrants is affected by the presence of hydrophobic excipients such as lubricants, the disintegrant efficiency of sodium starch glycolate is unimpaired. Increasing the tablet compression pressure also appears to have no effect on disintegration time. Sodium starch glycolate has also been investigated for use as a suspending vehicle.



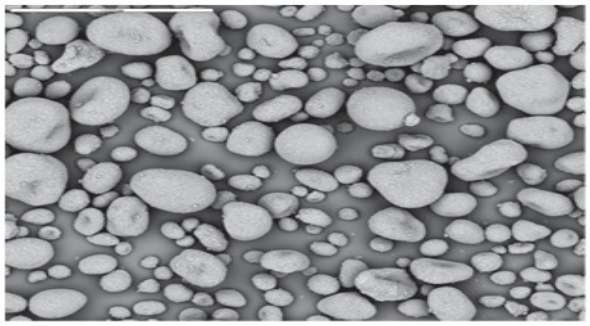
SEM of sodium starch glycolate (Primojel); manufacturer: DMV Fonterra magnification: 200 voltage: 1.5 kV

Figure 12



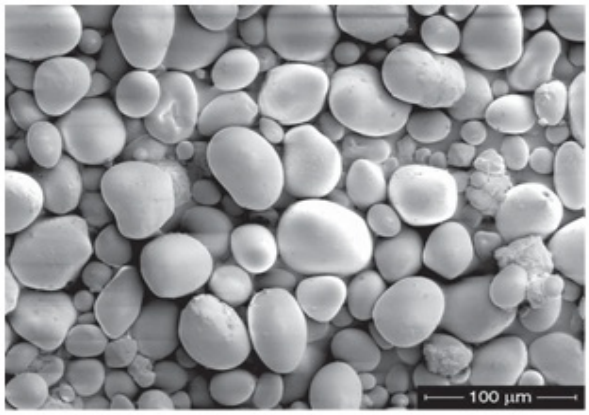
SEM of sodium starch glycolate (Explotab); manufacturer: JRS Pharma; magnification: 300 voltage: 5 kV.

Figure 13



SEM of sodium starch glycolate (Glycolys); manufacturer: Roquettes Fre`res.

Figure 14



SEM of sodium starch glycolate (Vivastar P); manufacturer: JRS Pharma; magnification: 300 x, voltage: 5 kV

Figure 15

4. Indion 414[2]

It is safe for oral consumption, economical and easily available polymer. By nature, it is ion exchange resin and if used as superdisintegrants as compared to conventional ones, swell on getting hydrated without dissolution and devoid of adhesive tendency, cause uniform tablet disintegration. It is chemically cross linked polyacrylic, with a functional group of $-COO^-$ and the standard ionic form is K^+. They do not form lumps, do not stick to tablet press components and are compatible with commonly used active pharmaceutical ingredients as well as other pharmaceutical necessities. They offer better hardness to the tablets on compression. Indion 414 is more effective in hydrophobic formulations, as compared to the conventional disintegrants. For effective disintegration ability in the tablets, concentration of Indion 414 is used in range from 0.5 to 2%.

Table 7: SPECIFICATIONS FOR INDION 414

PARAMETER	SPECIFICATION
Particle size distribution Retained on 100 BSS mesh	1% maximum
Retained on 100 BSS mesh	30% maximum
Moisture content	10% maximum
Sodium content	0.2% maximum
Potassium content	20.6-25.1%
pH of 10% slurry	7-9
Iron content, as Fe	100 ppm maximum
Heavy metals, as Pb	20 ppm maximum
Arsenic content	3 ppm maximum

NATURAL SUPERDISINTEGRANTS[9]

The natural superdisintegrants involve various natural substances like gums, mucilages, and other substances of natural origin which are more effective at lower concentrations with greater disintegrating efficiency and mechanical strength. Some natural substances like gum karaya, modified starch and agar have been used in the formulation of FDT's. Mucilage of natural origin is preferred over semisynthetic and synthetic substances because they are comparatively cheaper, abundantly available, nonirritating and nontoxic in nature. Some natural polymer provides the fast disintegration as synthetic superdisintegrants. Recently some gums and mucilages have been investigated to improve the disintegration processes.

1. *Plantago ovata* seed mucilage

Psyllium or Ispaghula is the common name used for several members of the plant genus Plantago whose seeds are used commercially for the production of mucilage. Mucilage of *plantago ovata* has various characteristics like binding, disintegrating and sustaining properties. In an investigation fast disintegrating tablets of Amlodipine Besylate was prepared by direct compression method using different concentrations of *plantago ovata* mucilage as a natural superdisintegrant. All formulations were evaluated for weight variation, hardness, friability, disintegration time, drug content and dissolution. The optimized formulation shows less in vitro disintegration time 11.69sec with rapid in vitro dissolution within 16 mins. In vitro disintegration time decreases with increase in concentration of natural superdisintegrant. The conclusion is clear that the dried isabgol mucilage as a superdisintergrant in the tablet is suitable for the formulation of fast disintegrating tablet.

In another investigation N. G. Raghavendra Rao et al studied that fast dissolving tablets of poorly soluble drug, carbamazepine showing enhanced dissolution, will lead to improved bioavailability, improved effectiveness and hence better patient compliance by using natural superdisintegrant like *plantago ovata* mucilage. In their study fast dissolving tablets of the carbamazepine was developed by wet granulation method, using different concentrations of natural superdisintegrating agent like *plantago ovata* seed powder and mucilage. Prepared formulations were evaluated for hardness, friability, in vitro disintegration time, wetting time and dissolution test. The formulations prepared with mucilage of *plantago ovata* were showed disintegration time between the ranges 84.58 to 24.74 sec and drug release showed between the ranges of 14 – 16 min. However the formulations prepared with seed powder did not disintegrate in specified limit of time for fast dissolving tablet. The optimized formulations showed 99.71 % drug release within 16 min.

2. *Lepidium sativum* mucilage

Lepidium sativum (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, dimeric imidazole alkaloids lepidine B, C, D, E and F and two new monomeric imidazole alkaloids semilepidinoside A and B. Mucilage of *Lepidium sativum* has various characteristic like binding, disintegrating, gelling etc. The mucilage is extracted from seeds of *Lepidium sativum.*

Recently a study was performed on disintegrating property of *Lepidium sativum* mucilage. Kalpesh K. Mehta et al developed fast dissolving tablets of Nimesulide containing natural *Lepidium sativum* mucilage. The disintegration property of extracted mucilage in FDTs was compared with widely used superdisintegrants like Sodium starch glycolate (SSG), Kyron T314, Ac Di Sol. The prepared FDTs were evaluated for Uniformity of weight, Hardness, Tablet thickness, Percentage friability, Wetting time, *In vitro* disintegration time and *In vitro* dissolution. From the study, it was concluded that higher dissolution of tablet could be obtained when mucilage concentration is 10% and also the mannitol concentration was 10%. Promising optimized batch exhibited better drug dissolution (79.9%) after 30 min than the other tablets. The disintegration and mean dissolution time for this batch was 17 sec and 5.27 sec respectively is better than other tablet prepared from other synthetic disintegrating agent.

3. **Gum karaya**

Gum Karaya is a vegetable gum produced as an exudate by trees of the genus Sterculia. Chemically, gum karaya is an acid polysaccharide composed of the sugars galactose, rhamnose and galacturonic acid. The high viscosity nature of gum limits its uses as binder and disintegrant in the development of conventional dosage form. karaya gum has been investigated for its potential as a tablet disintegrant. The results showed that modified gum karaya produce rapid disintegration of tablets. The optimized formulation showed acceptable physical characteristics. The optimized batch produced complete drug release within 6 minutes. The incorporation of clove oil provided additional properties such as symptomatic relief from nausea and vomiting, good mouth feel and taste masking. Kinetic analysis showed that drug release from optimized formulation was adequately described by first order release kinetics. Gum karaya can be used as an alternative superdisintegrants to commonly available synthetic and semisynthetic superdisintegrants due to their low cost, biocompatibility as well as easily availability.

4. **Soy polysaccharide**

It is a natural superdisintegrant that does not contain any starch or sugar so can be used in nutritional products. Sanyasi R et al evaluated soy polysaccharide (a group of high molecular weight polysaccharides obtained from soy beans) as a disintegrant in tablets made by direct compression using lactose and dicalcium phosphate dihydrate as fillers. A cross-linked sodium carboxy-methyl cellulose and corn starch were used as control disintegrants. Parameters studied were compressibility, friability and disintegration times. Dissolution studies were conducted on tablets containing hydrochlorothiazide as a model drug of low

water solubility. Soy polysacchardie performs well as a disintegrating agent in direct compression formulations with results paralleling those of cross-linked CMC at the 2% level and superior to corn starch at the 8% level. Dissolution rates of the drug from tablets were rapid, particularly at the 5% level and were not adversely affected by aging at room temperatures.

5. **Chitin and chitosan**

Chitin (β-(1→4)-N-acetyl-D-glucosamine) is a natural polysaccharide obtained from crab and shrimp shells. It possesses amino group covalently linked to acetyl group as compared to free amino group in chitosan. Chitosan is produced commercially by deacetylation of chitin, which is the structural element in the exoskeleton of crustaceans (such as crabs and shrimp) and cell walls of fungi. Bruscato et al reported that when chitin was included in the conventional tablets, the tablets disintegrated within 5 to10 min irrespective of solubility of the drug. The disintegration time in the oral cavity as well as wetting time could be analyzed by surface free energy. Chitosan is the best known natural polysaccharide used for its versatile applications in pharmaceutical industry. Mitesh Nagar et al utilized superdisintegrant property of chitosan to develop a fast mouth dissolving tablet by utilizing a novel method of treatment which can replace any other superdisintegrant. The properties of the rapidly dispersible tablet, such as porosity, hardness, disintegration time, wetting time and dissolution time, were investigated accordingly and the formulation was optimized as per 3 level full factorial design and analysed for response surface methodology to decide the best formulation which further evaluated for in-vitro performances. Fast mouth dissolving or OroDispersible tablets (ODTs) of Cinnarizine with acceptable compression parameters and pleasant mouth feel prepared within the optimum region hence Cinnarizine OroDispersible tablets (CODT) upon administration disperse in mouth as soon as in contact with saliva and release the drug content immediately which can be absorbed directly through oral mucosa or can be swallowed without the aid of water hence provide faster and better therapeutics.

STORAGE CONDITIONS FOR SUPERDISINTEGRANTS[8]

They should be stored in a well-closed container in order to protect it from wide variations of humidity and temperature, which may cause caking.

PATENTS

This review article inclined towards the approach of superdisintegrants in various formulations, the innovations, already patented in related field are listed as

1. **Pharmaceutical superdisintegrant** (US20050100600):

Superdisintegrants which provide improved compressibility compared to prior art superdisintegrants. The superdisintegrants include a particulate agglomerate of coprocessed starch or cellulose and a sufficient amount of an augmenting agent to increase the compactibility of the superdisintegrant[10].

2. **Rapidly disintegrating enzyme-containing solid oral dosage compositions** (US20060013807):

Invention relates to rapidly disintegrating solid oral dosage forms having an effective amount of an enzyme and a superdisintegrant. The enzyme lactase is claimed in this patent for solid oral formulations[11].

3. Fast disintegrating tablets (US20050169986): A fast disintegrating tablet comprising Nimesulide and one or more disintegrants. In this research superdisintegrants used are croscarmellose cellulose, crospovidone and sodium starch glycolate[12].

4. Method of producing fast dissolving tablets (US20100074948): A method of producing a fast-melt tablet. The process does not involve any granulation step, thereby making the process more energy efficient and cost effective. The fast dissolving sugar alcohol is selected from the group comprising: mannitol; sorbitol; erythritol; xylitol; lactose; dextrose; and sucrose. The active component is suitably provided in the form of microparticles or microcapsules having an average diameter of less than 125 microns[13].

5. **Disintegrating Loadable Tablets** (US20090186081): A disintegrating loadable tablet product in compressed form. A disintegrant or a mixture of disintegrants has a) porosity of 45% v/v or more, b) a hardness of at least 20 Newton, and c) a loading capacity of at least 30% of a liquid[14].

6. Rapidly disintegrating tablet (US20060115528): The study relates to rapidly disintegrating tablets intended to be used as orodispersible tablets or dispersible tablets. The tablets include silicified microsrystalline cellulose. They are especially suitable for antibiotics. Rapidly disintegrating tablets which contain amoxicillin and clavulanic acid are also described[15].

7. Aminoalkanoylated cellulose as asuperdisintegrants[16]

Inventors: N.H. Aloorkar and M.S. Bhatia

Application no. 2610/MUM/2010A

International classification no. A61K31/00 and A61K9/00

8. Rapidly disintegrating, solid coated dosage form (US331439): Rapidly disintegrating, solid coated dosage form comprising a solid core consisting of at least 60% by weight of an auxiliary mixture, up to 40% by weight of at least one active ingredient, and optionally further auxiliaries, coated with at least one film coating comprising completely or partially hydrolyzed, rapidly water-soluble polyether-vinyl ester graft polymers, methods for the production thereof, and their use[17].

9. Co-Processed Excipient Compositions (US266341) **:** An oral solid dosage form having improved dissolution profile and a method of producing the same are provided. The present invention particularly provides a co-processed excipient composition and a method of producing the same. More particularly, it relates to a co-processed binary mixture of crosslinked polyvinylpyrrolidone and calcium silicate; wherein the weight ratio of crosslinked polyvinylpyrrolidone and calcium silicate is in the range of 1:1 to 20:1. The binary mixture when combined with a poorly soluble drug enhances its dissolution and extent of release[18].

10. Multi-layered orally disintegrating tablet and the manufacture thereof (US052316): The present invention features a tablet containing a first layer and a second layer, wherein: (i) the first layer includes a pharmaceutically active agent and the composition of the first layer is different from the composition of the second layer; (ii) the tablet has a density less than about 0.8 g/cc; and (iii) the tablet disintegrates in the mouth when placed on the tongue in less than about 30 seconds[19].

11. Fine Particle Croscarmellose and Uses Thereof (US970153) **:** The disclosure is directed to fine particle croscarmellose and its use in various compositions such as solid dosage forms. More specifically, the present disclosure relates to fine particle croscarmellose having a median particle size of 5 .mu.m to 36 .mu.m and a volume mean diameter of 40 .mu.m or less. The specific surface area is typically 0.3 m.sup.2/g or more. The fine particle croscarmellose is useful as a disintegrant[20].

12. Pharmaceutical excipient having improved compressibility: A composition, comprising (a) microcrystalline cellulose; and (b) a compressibility augmenting agent which (i) physically restricts the proximity of the interface between adjacent cellulose surfaces; or (ii) inhibits interactions between adjacent cellulose surfaces; or (iii) accomplishes both (i) and (ii) above, is disclosed. The composition is in the form of agglomerated particles of microcrystalline cellulose and the compressibility augmenting agent in intimate association with each other[21].

CONCLUSION

There are many superdisintegrants which show superior disintegration, the search for newer superdisintegrants is ongoing and researchers are experimenting with modified natural products like formaliencasein, chitin, chitosan, polymerized agar acrylamide, xylan, smecta, key-jo-clay, cross linked corboxymethyl guar and modified tapioca starch. Studies have suggested that the water insoluble superdisintegrants show better disintegration property than slightly water insoluble agents, since they do not have a tendency to swell. Superdisintegrants that tend to swell have slight retardation of the disintegration property due to the formation of viscous barrier. There is no particular upper limit regarding the amount of superdisintegrants as long as the mechanical properties of the tablet are compatible with its intended use. The superdisintegrants may be used alone or in combination with the other superdisintegrants. Thus, the overviews of the various types of superdisintegrants witch are available have been discussed. The ease of availability of these agents and the simplicity in the direct compression process suggest that there use would be economic alternative in the preparation of ODT than the sophisticated and patented techniques.

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