International Journal for Pharmaceutical Research Scholars (IJPRS)

V-5, I-4, 2016 ISSN No: 2277 - 7873

REVIEW ARTICLE

A Review on Optizorb Technology

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Manuscript No: IJPRS/V5/I4/00168, Received On: 31/12/2016, Accepted On: 04/01/2017

ABSTRACT

The article here under emphasizes on how absorption of certain drug can be improved. A novel concept implies when tablets were offered ease of oral administration and increases patient compliance. Technology which allows the tablet to start disintegrating in as little as 5 minutes is called Optizorb Technology. Optizorb disintegration technology is five times faster and shows action more quickly. It gets easily dispersed in stomach and work faster, relief faster. Optizorb technology is based on the use of super-disintegrant such as Alginic acid and Calcium Carbonate that makes it act within five minutes. According to the International Association for the study of pain is defined as "an unpleasant sensory and emotional experience associated with actual or potential tissue damage." Panadol with Optizorb Technology is a Paracetamol based analgesic, using a new disintegrate technology that provides Fast, Suitable, effective relief of Pain and discomfort associated with headache and Migraine. However, Sometimes Standard Paracetamol tablets slowly dissolve and absorb, and can sometimes takes a long time to impart its effects. Panadol with Optizorb technology also relieves fever. Panadol with Optizorb technology contain 3 stages stage.1 disintegration stage – 2. Dissolution stage- 3. Absorption dissolves quickly (in the stomach) due to Super-disintegration which causes the tablet to swell even more, and Speeds up the break up process For pain relief a person can Start to feel in as little as 15 minutes. Panadol with Optizorb technology can still be used by a broad range of people including people with stomach ulcers and breastfeeding mothers.

KEYWORDS

Pain, Optizorb Technology, Panadol, Super Disintegrate, Stomach ulcers, Quick absorption

INTRODUCTION

Fast Release Drug Delivery System

Definition

Immediate release tablets are those which disintegrate rapidly and get dissolved to release the medicaments. Immediate release may be provided for by way of an appropriate pharmaceutically acceptable diluent or carrier, which diluent or carrier does not prolong, to an appreciable extent, the rate of drug release and absorption[1].

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Introduction to Optizorb Technology

Definition

The makers of PANADOL have developed a technology which allows the Paracetamol to be absorbed faster than standard PANADOL tablets - this new technology is called Optizorb. Panadol with Optizorb is a Paracetamol-based analgesic, using a new disintegrate technology to provide fast, suitable, effective relief of pain and discomfort associated. Paracetamol tablets are easy to take, readily available, effective and

suitable for large numbers of people. However, standard Paracetamol tablets are sometimes slow to dissolve and absorb, and can sometimes take a long time to have an effect, associated with:

Headache and Migraine

- Backaches
- Joint and muscle pain
- Period Pain
- Toothaches
- Sore Throat
- Arthritis/Osteoarthritis
- Cold & Flu Symptoms
- people with stomach ulcers

Panadol with Optizorb also relieves fever. Panadol with Optizorb dissolves quickly (in the stomach).[2,3,4]

Constract of Panadol with Optizorb Technology

Unlike standard Paracetamol tablets, PANADOL caplets and tablets with Optizorb.

These include:

1. A naturally occurring substance that makes the tablet act like a sponge so when it reaches the stomach it soaks up water swells then breaks apart.
2. A common ingredient widely used in tablet formulations that, on contact with the stomach acids, releases small amounts of carbon dioxide which helps the tablet break up.
3. A 'super-disintegrate' which causes the tablet to swell even more, and speeds up the break up process.

The science of Optizorb technology allows the tablets to break down fast. For pain relief you can start to feel in as little as 15 minutes. Panadol with Optizorb can still be used by a broad range of people including people with stomach ulcers and breastfeeding mothers.

In human Scintigraphy study the mean time onset of disintegration for Panadol with optizorb formulation was 6.4 minutes.

Panadol with optizorb formulation is 32% greater when compared with standard Panadol with maximum plasma concentration.

Peak plasma levels: 10-60 minutes after administration

Volume of distribution: 1-1.2L/kg

Plasma protein binding: negligible

Time of peak plasma levels was reached twice as fast as 0.27h, 0.32h respectively compared to regular Panadol with 0.67h, 0.65h[2,3,4].

Action of Panadol with Optizorb Technology

Action of Panadol can be explained by 3 major stages. They are

Stage-1 Disintegration- the tablet breaks apart into smaller pieces called granules.

Stage-2 Dissolution- The granules break into particles small enough to dissolve in the stomach.

Stage-3 Absorption- The particles are finally absorbed into the bloodstream – where the medicine can take effect.[2,3,4]

Optizorb in Panadol – Faster Paracetamol Disintegration

Optizorb is the registered trademark for a drug technology that allows fast disintegration of a tablet. However, Optizorb is made of different ingredients.

1. An ingredient that is found commonly in other tablets. This ingredient releases air (in the form of carbon dioxide) so that the tablet becomes effervescent.
2. Another substance that is touted as a super-disintegrate. Again, this ingredient plays a role in ensuring that the tablet dissolves quickly.
3. A substance that is naturally-occurring which absorbs water like a sponge does. As the Paracetamol tablet balloons with the water it absorbs, it dissolves faster.

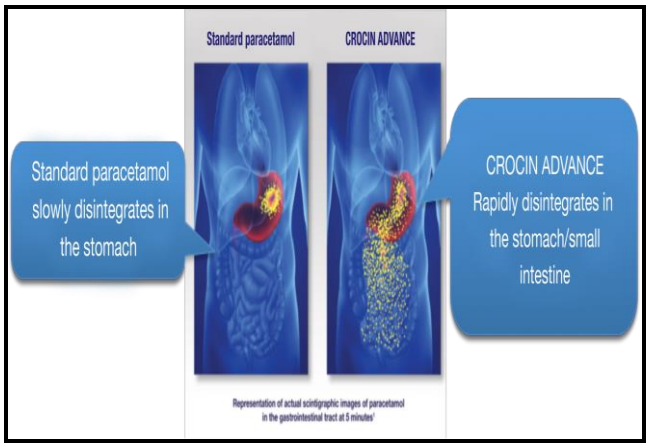

Figure 1: Representation of Paracetamol in GI[3]

Function of Pain Relievers

Majority of capsules and tablets usually contain just one of the following types of pain and fever-relieving ingredients:

- Paracetamol (also called acetaminophen in some countries).
- A non-steroidal anti-inflammatory drug (NSAID), like aspirin, ibuprofen, naproxen or diclofenac.

These analgesics may be combined with other ingredients, such as caffeine and codeine, which increase the pain relieving effects of Paracetamol or NSAIDs. Sometimes, Paracetamol and NSAIDs are combined with cold and flu ingredients, which help to ease symptoms such as congestion and a runny nose. It's important, however, to know that Paracetamol and NSAIDs work in different ways to relieve pain.

Action of Paracetamol and NSAIDS

Both Paracetamol and NSAIDs are effective when it comes to relieving mild-to-moderate pain. But, although they both relieve pain, they work in different ways. Paracetamol is believed to act primarily in the brain and seems to have an effect on many different ways we feel pain. For example, Paracetamol inhibits the production of pain and inflammation-causing chemicals called prostaglandins. Prostaglandins are found throughout the body, but Paracetamol mainly works on those in the brain. Because of this, not only can it effectively relieve pain and fever, but it also has few side effects when taken at recommended doses. Paracetamol also has no effect on inflammation. NSAIDs, such as ibuprofen and aspirin, work differently. They also stop the production of prostaglandins, but they do this throughout the body, not just in the brain. Because of this, NSAIDs can affect prostaglandins that have other important roles in the body. These include prostaglandins that protect the lining of the stomach, and keep the kidneys working properly, our airways open and our blood clotting normally. So, while NSAIDs are good at easing pain by stopping the development of some prostaglandins, they can also have a negative effect on those prostaglandins that are needed to keep our bodies functioning as normal, even at over-the-counter (OTC) doses.[2,3,4]

Optizorb Technology Can have Applied to Following Formulations

Analgesics and Anti-inflammatory Agents

Fenoprofen calcim, flurbiprofen, ibuprofen, indomethacin, ketoprofen, meclofenamic acid, mefenamicacid, nabumetone, naproxen, oxaprozin, oxyphenbutazone, phenylbutazone, piroxicam, sulindac

Anti-bacterial Agents

Nalidixic acid, nitro furantoin, rifampicin, sulphabenzamide, sulphadoxine, sulphamerazine, sulphacetamide, sulphadiazine, sulphafurazole, sulphamethoxazole

Anti-Arrhythmic Agents

Amiodarone HCl, Disopyramide, flecainide acetate, quinidine sulphate

Anti-depressants

Amoxapine, ciclazindol, maprotiline HCl, mianserin HCl, nortriptyline HCl

Anti-hypertensive Agents

Carvedilol, benidipine, darodipine, dilitazem HCl, diazoxide, felodipine, guanabenz acetate

Anti-malarials

Amodiaquine, chloroquine, chlorproguanil HCl, halofantrine HCl, mefloquine HCl, proguanil HCl

Anti-migraine Agents

Dihydroergotamine mesylate, ergotamine tartrate, methysergidemaleate, pizotifen maleate, sumatriptan succinate

Analgesics

Codeine, dextropropyoxyphene, diamorphine, dihydrocodeine, meptazinol, methadone, morphine, nalbuphine, pentazocine[5].

Recent Studies Were Conducted On Formulation and Evaluation of Bisoprolol Fumarate Optizorb Dispersible Tablet to Improve Tablet Disintegration

The present research work was aimed the formulation and evaluation of Optizorb dispersible tablets of bisoprolol fumarate, an antihypertensive agent. The Optizorb technology is based on the use of excipients of Alginic acid and calcium carbonate. Alginic acid absorbs lot of water, swells and leads to decay effect brought about. Calcium carbonate reacts with the stomach acid, within 3 minutes it releases 90% of the active ingredient this compared with only 10-15% in marketed Paracetamol. Optizorb technology is five times faster in tablet disintegration and thus gets to work much more quickly. Dispersible tablets were prepared by wet granulation method by using Alginic acid and calcium carbonate as disintegrant in different concentrations. Compatibility studies of drug and excipients were carried out by using FT- IR spectroscopy and DSC. The formulations were evaluated for precompressional parameters such as bulk density, tapped density, angle of repose, Carr's index and Hausner's ratio. The tablets were evaluated for weight variation, thickness, hardness, friability, drug content, dispersion time, and disintegration time and invitro dissolution study. Invitro dissolution studies were performed by using USP dissolution apparatus type II paddle in 900 ml of 0.1N Hydrochloric acid at 50 rpm. No chemical interaction between drug and excipients was confirmed by FTIR studies. After study of all formulations F9 showed short dispersion time with maximum drug release in 15 min and it contains Alginic acid and calcium carbonate (1:1).

Result

Optizorb dispersible tablets of bisoprolol fumarate were prepared by wet granulation method. From the present work it concludes that the Optizorb technology is based on the use of excipients of Alginic acid and calcium carbonate as disintegrant in different concentrations. Alginic acid absorbs lot of water, swells and leads to decay effect brought about. Calcium carbonate reacts with the stomach acid, within 3 minutes it releases 90% of the active ingredient. Optizorb technology is five times faster and thus gets to work much more quickly. After study of all formulations F9 showed short dispersion time with maximum drug release in 15 min and it contains Alginic acid and calcium carbonate (1:1). FT-IR study reveals that there is no interaction between drug and excipients and can be used for preparation of Optizorb dispersible tablets of bisoprolol fumarate[6].

Advantages of Optizorb Technology

1. Optizorb Technology can be administer to the patients with stomach ulcers and also pregnant women
2. It contain the certain studies which concluded increased bioavailability and proved rapid absorption of drugs through gastric absorption o
3. Optizorb Technology is most convenient for rapid dissolution
4. Optizorb Technology helps to change the perception of medication
5. Drugs have high bioavailability i.e. 100%
6. The risk of chocking or suffocation during oral administration of conventional formulations due to physical obstruction is avoided, thus providing improved safety
7. Optizorb Technology opened new business opportunity like product differentiation, product promotion, patent extension and life cycle management
8. Optizorb Technology drugs produce rapid onset of action

9. No specific packaging required can be packaged in push through blisters
10. Conventional manufacturing equipment
11. Cost effective
12. Good chemical stability as conventional oral solid dosage form
13. New business opportunity like product differentiation, product promotion, patent extension and life style management
14. Allow high drug loading
15. Provides rapid drug delivery from dosage forms
16. Provide instant disintegration and dissolution
17. Rapid drug therapy intervention
18. No chewing needed
19. Adaptable and amenable to existing processing and packaging machinery
20. Improved compliance/added convenience[1]

Disadvantages of Optizorb Technology

1. Drugs with Optizorb Technology are hygroscopic in nature so must be keep in dry place
2. Causes allergic reaction such as skin rashes or itching, sometimes breathing problem , swelling of lips , tongue , throat and face
3. It is also shows the fragile, effervescence granules property
4. Drugs with Optizorb Technology requires special packaging for properly stabilization & safety of stable product
5. Produces carbon dioxide causing bowel problems (1)

Formulation

Panadol Extra with Optizorb

Caplets contain 500 mg of Paracetamol and 65 mg of caffeine as the active ingredients.

They also contain:

- Alginic acid
- Calcium carbonate
- Carnauba wax
- Crospovidone
- Magnesium stearate
- White coloring (Opadry YS- 1R-7003)
- Povidone
- Sodium ethyl hydroxybenzoate
- Sodium methyl hydroxybenzoate
- Starch – pregelatinized maize
- Water – purified[7]

A) Super Disintegrants

Disintegrant 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 when it comes in contact with water in the GIT. They may function by drawing water into the tablet, swelling and causing the tablet to burst apart. Such tablet fragmentation may be critical to the subsequent dissolution of drug and to attainment of satisfactory of drug bioavailability. Starch USP and various starch derivatives are the most common disintegrating agents. Various pregelatinized starches are also employed as disintegrant, usually in 5%conc. The disintegrant of dosage forms are depends upon physical factors of superdisintegrants. They are as follows:

Percentage of disintegrant present in formulations.

- Presence of surfactants.
- Hardening of tablets.
- Nature of drug substances
- Mixing and types of addition.

Ideal Properties of Super- Disintegrants

Good Compressibility and Flow Properties

If the powders have 12-16% compressibility, they are said to be good flow powders. Crospovidone are significantly more compressible than other superdisintegrants.

Poor Solubility

The solubility of the major component in a tablet formulation can affect both the rate and the mechanism of tablet disintegration. Water soluble materials tend to dissolve rather than disintegrate, while insoluble materials generally produce rapidly disintegrating tablets.

Poor Gel Formation Capacity

Gels can delay dissolution as the drug must first diffuse through the gel layer before being released into the body. Sodium starch glycolate is used as superdisintegrants in tablet formulation at a concentration of 4-6%.

Good Hydration Capacity

Drugs or other excipients, which are hydrophobic and could be adsorbed on disintegrant surfaces, advertently influence the extent of hydration and the effectiveness of these disintegrants. Addition of fast disintegration of high hydration capacity reported to minimize this problem, and therefore, enhance dissolution.

Complexation

Anionic disintegrants like croscarmellose sodium and sodium starch glycolate may complex with cationic drug actives and slow dissolution. Crospovidone a non-ionic polymer does not interact with cationic drug actives to retard drug release. The effects of superdisintegrants like croscarmellose sodium, sodium starch glycolate and polyplasdone XL on the dissolution behavior of several cationic drugs with varying water solubility reports that polyplasdone XL had a more rapid dissolution rate for the model cationic drugs, irrespective of their aqueous solubilities.

Method of Incorporation of Super Disintegrant

Superdisintegrants are incorporated by Intragranular

In wet granulation method, the disintegrant is added to other excipients before wetting the powder with the granulating fluid. Thereby, the disintegrant is incorporated within the granules. In dry granulation method, the disintegrant is added to other excipients before compressing the powder between the rollers. In this process the superdisintegrants are blend with other powders and granulation is carried out. Thus the superdisintegrants are incorporated within the granules. In Internal addition method, the disintegrant is mixed with other powders before wetting the powder mixtures with the granulating fluid. Thus the disintegrant is incorporated within the granules.

Extra Granular

This is generally done prior to compression. In both wet and dry granulation method, the superdisintegrants is added to the granules during dry mixing prior to compression.

Intra and Extra Granular

It is also called as internal and external mixing of disintegrants. In this part of superdisintegrants are added to intragranules and a part to extra granules. Superdisintegrant is divided into two portions. One portion is added before granule formation (intra) and remaining portion is added to granules (extra) with mixing prior to compression. This method can be more effective. If both intragranular and extra granular methods are used, extra granular portion break the tablet into granules and the granules further disintegrate by intragranular portion to release the drug substance into solution.

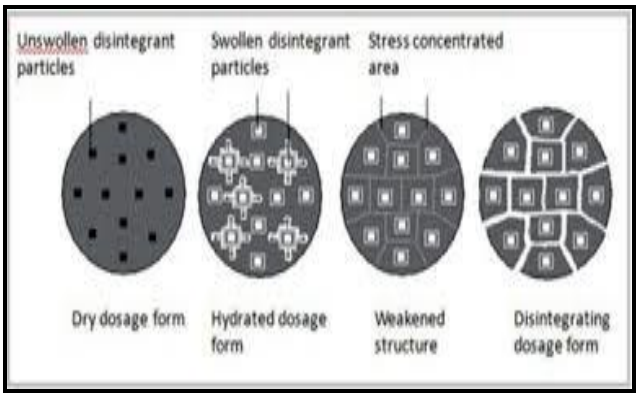

Figure 2: Mechanism of Action of Disintegrants[12]

Mechanism of Action of Super Disintegrant

By Swelling Action

Swelling is believed to be a mechanism in which certain disintegrating agents (such as starch)

impart the disintegrating effect. By swelling in contact with water, the adhesiveness of other ingredients in a tablet is overcome causing the tablet fall apart eg : Sodium starch glycolate.

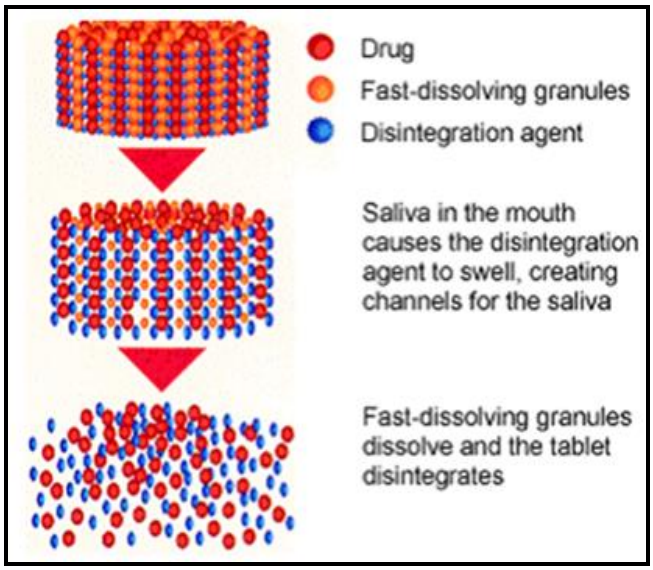

Figure 3: Swelling Action[12]

By Capillary Action / Wicking:

In this mechanism, the disintegrants that do not swell facilitate disintegration by their physical nature of low cohesiveness and compressibility. The disintegrant particles (with low cohesiveness and compressibility) themselves act to enhance porosity and provide these pathways into the tablet. Liquid is drawn up or "wicked" into these pathways through capillary action and rupture the interparticulate bonds causing the tablet to break apart.

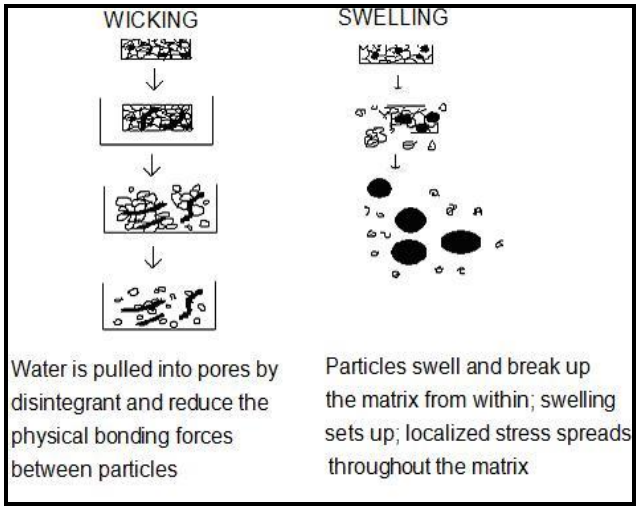

Figure 4: Wicking and Swelling Action[11]

Deformation

Starch such as potato or corn starch is believed to be elastic in nature, but due to high compaction force in case of tableting the elasticity deformed to plasticity with energy rich potential. When these tablets are exposed to aqueous environment, the energy potential of deformed starch grain will be triggered to cause disintegration

By Electrostatic Repulsion

Guyot-Hermannet et al., has proposed a particle repulsion theory based on the observation that non swelling particle also cause disintegration of tablets. The electric repulsive forces between particles are the mechanism of disintegration and water is required for it.

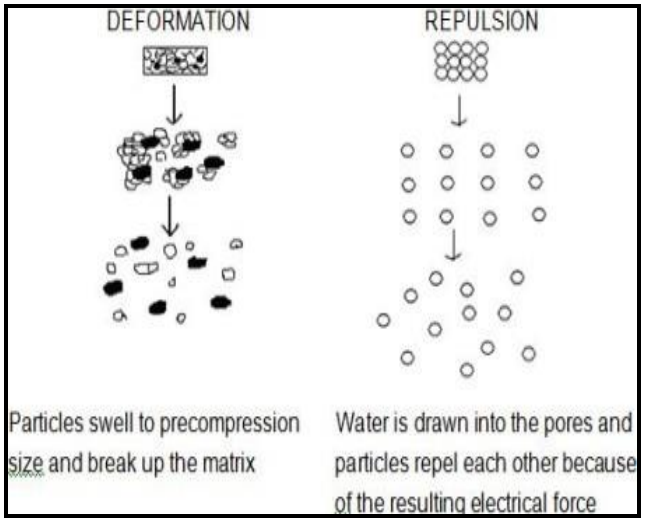

Figure 5: Deformation and Repulsion[11]

Types of Superdisintegrants

Crosscarmellose Sodium

It is modified cellulose and is a cross linked polymer of carboxymethylcellulose. The disintegration rate of Crosscarmellose sodium is higher than that of sodium starch glycolate and the mechanism is also different. The carboxymethyl groups themselves are used to cross link the cellulose chains, process is accomplished by dehydration. The substitution is performed by using Williamson's ether synthesis to give the sodium salt of carboxymethyl cellulose. Thus the crosslinks are carboxyl ester links rather than phosphate ester links as in

Primojel. Cross linking makes it insoluble, hydrophilic, highly absorbent material, resulting in excellent swelling properties and its unique fibrous nature gives it excellent water wicking capabilities. It is used in oral pharmaceutical formulations as a superdisintegrant for capsules, tablets and granules. Concentrations of croscarmellose sodium range between 1-5% w/w, although normally 1-3% w/w is used in tablets prepared by direct compression and 2- 4% w/w in tablets prepared by a wet granulation process. Botzolakis et al. have studied the wicking and swelling properties of pure superdisintegrants from the plugs which are prepared under condition similar to those used in encapsulation of powder mixture into hard gelatin capsules.

Advantages: It uses a combination of swelling and wicking mechanism for disintegration, disintegrates within 2 minutes, easily available and cheap.

Disadvantages: It has lower cross linking density and forms gels when fully hydrated, is poorly compressible and since it is anionic in nature, may form complexes with the cationic drugs.

Sodium Starch Glycolate

It is a cross linked polymer of carboxymethyl starch. It is possible to synthesize sodium starch glycolate from a wide range of native starches but in practice potato starch is used as it gives the product with the best disintegrating properties. The effect of introduction of the large hydrophilic carboxymethyl groups is to disrupt the hydrogen bonding within the polymer structure. This allows water to penetrate the molecule and the polymer becomes cold water soluble. The effect of the cross-linking is to reduce both the water soluble fraction of the polymer and the viscosity of dispersion in water. The mechanism by which disintegration action takes place is rapid absorption of water and swell leading to an enormous increase in volume of granules which result in rapid and uniform disintegration. The natural pre dried starches swell in water to the extent of 10-20 percent and the modified starches increase in volume by 200-300 percent in water. The tablets formulated by using these superdisintegrants are disintegrated in less than two minutes.

***Advantages*:** It absorbs water rapidly and swells in water to the extent of 200-300%, disintegrates within 2 minutes and is easily available and cheaper.

Disadvantages: At high usage level (>8%), disintegration increases due to gelling and its subsequent viscosity producing effects, has lower cross linking density and form gels when fully hydrated, is poorly compressible and since it is anionic in nature, may form complexes with the cationic drugs the gas evolving disintegrant, $CaCO_3$. Sallem et al. (1998), 20 studied the effect of four superdisintegrants on the dissolution of terfenamide tablet containing. The four superdisintegrants improved disintegration and dissolution of the original formulation and their relative efficiency of improvement is in order of Crospovidone> Ac-di-sol> SSG > low substituted HPC.

Cross-Linked Polypyrrolidine (Crospovidone, Polyplasdone, and Xl10)

Crospovidone are synthetic, insoluble, cross-linked homopolymers of N-vinyl-2- pyrrolidone as shown in figure 7. When examined under scanning electron microscope, Crospovidone particles appear as granular and are highly porous. Due to its high crosslink density, Crospovidone swells rapidly in water without gelling. Crospovidone are highly compressible materials as a result of their unique particle morphology. Crospovidone is used as superdisintegrant at low concentration levels (2-5%) in direct compression, wet and dry granulation processes. Rahman et al. (2011),[21] reported that acetaminophen release is faster from tablet formulations containing Crospovidone than sodium starch glycolate (SSG), sodium carboxymethyl cellulose (Na CMC) and is unaffected by the mode of Crospovidone addition. Formulations containing SSG, Na CMC extra granular mode of addition seems to be the best mode of incorporation. Yeli Zhang et al. carried out a study on the functionality and performance of three types of commonly used commercial superdisintegrants

i.e. cross-linked croscarmellose sodium, Crospovidone, and sodium starch glycolate (SSG), in the application of ODTs. For each superdisintegrant, a wide range of disintegrant use levels (0.5–20%) is investigated in commonly used ODT model matrices at different compaction forces (4–12kN). An optimal use level is identified for each superdisintegrant, which is 2% for Ac-Di-Sol, 5% for PVP XL-10, 5% for Kollidon CL-SF, and 5% for Glycols.

Advantages: Crospovidone uses a combination of swelling, wicking and deformation mechanism for rapid disintegration of tablets, swells rapidly in water without forming gel, is highly compressible, unaffected by pH media.

Soy Polysaccharide

It is a natural super disintegrant that does not contain any starch or sugar as and so can be used in nutritional products. Mihirkumar Modh (2009), formulated and evaluated rapidly disintegrating tablets, formulated by direct compression method using aspirin as a model drug containing increasing concentration of superdisintegrants such as Emcosoy STS IP, Ac-Di-Sol, and Explotab. The aspirin tablets containing Emcosoy STS IP has a bursting effect resulting in a dispersion of drug particles facilitating their contact with the medium yielding a faster drug dissolution rate.

Gellan Gum

Gellan gum is a linear anionic polysaccharide biodegradable polymer obtained from Pseudomonas elodea consisting of a linear tetra saccharide repeat structure. Antony et al.[6] studied that the 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 Kollidon CL. 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 superdisintegrants.

Alginates

These are hydrophilic colloidal substances extracted naturally from certain species of Kelp or chemically modified from natural sources like Alginic acid or salt of Alginic acid. They are having higher affinity for water absorption and capable for an excellent disintegrants. They can be successfully used with ascorbic acid, multivitamins formulation. It is a hydrophiliccolloidal substance, which has high sorption capacity. It is also available as salts of sodium and potassium

Chitin/Chitosan-Silica Coprecipitate

Naturally Chitin is extracted from the shell wastes of shrimp, crab, lobster, krill, and squid and used for the production of chitosan by a DE acetylation reaction in alkaline medium. The comparative study of other superdisintegrants with Chitin– silica coprecipitate has proved better function.

Advantages: the good compressibility and the good compact ability properties of chitin–silica allow its use in direct compressions.

Disadvantages: Both chitin and chitosan powders show poor bulk density, thus results in poor flow ability and compressibility, to overcome this they may be coprecipitate with colloidal silicon dioxide to improve their physical properties.

Indion 414

It is ion exchange resin and if used as superdisintegrants, swell on getting hydrated without dissolution and devoid of adhesive tendency cause uniform tablet disintegration. Model drugs belonging to various classes were taste masked and formulated into palatable tablets. Experiments were carried out to evaluate the disintegrating property of Indion 414 in fast disintegrating dosage form like mouth dissolving

tablets they offer better hardness to the tablets on compression. Indion 414 is more effective in hydrophobic formulations, as compared to the conventional disintegrants.

Advantages: 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.

Mucilage of Plantago Ovate Seed Husk (Isapghula)

The mucilage of plantago ovata is a recent innovation for its super disintegration property. It shows faster disintegration time than the superdisintegrant, Crosspovidone.

Modified Polysaccharides

They are biodegradable, directly compressible, having desirable swelling dynamics. The above modified polysaccharides were further used as superdisintegrants in Roxithromycin fast dispersible tablets and compared with conventional tablets containing MCC. The C-TAG and C-TGG have shown better disintegration for their porous nature, better water intake ability and free flowing property than others.27 Agar (AG) and guar gum (GG), natural polysaccharides are treated with water and co grinded further with mannitol which exhibit super disintegration property. These modified polysaccharides may call C-TAG (co grinded treated agar) and C-TGG (co grinded treated guar gum) respectively.

Microcrystalline Cellulose (Avicel)

Avicel concentration of less than 10%, exhibits better disintegration. This mechanism is depending on entry of water to the tablet matrix through capillary pores, which breaks the hydrogen bonding between adjacent bundles of cellulose microcrystals. With more concentration, particularly in oral disintegrating tablet, it shows a tendency to stick to the tongue due to rapid capillary absorption and faster dehydration of the tablet surface. As Avicel has a fast wicking rate for water, hence this in combination with starch makes an excellent and rapid disintegration in OTD formulations.

Others

Although there are many superdisintegrants, which show superior disintegration, the search for newer disintegrants is ongoing and researchers are experimenting with modified natural products, like formalin casein, chitin, chitosan, polymerized agar acrylamide, xylan, smecta, key-jo-clay, crosslinked carboxymethyl guar and modified tapioca starch. Studies have suggested that the water insoluble superdisintegrants show better disintegration property than the slightly water soluble agents, since they do not have a tendency to swell. Superdisintegrants that tend to swell show slight retardation of the disintegration property due to formation of viscous barrier. There is no particular upper limit regarding the amount of superdisintegrant as long as the mechanical properties of the tablet are compatible with its intended use. The superdisintegrant may be used alone or in combination with other superdisintegrant[8].

Table 1: List of Common Disintegrants and Super Disintegrants[8]

Name of excipients	Category	Conc	Stability criteria
Alginic acid	Disintegrants	1-5%	Hydrolyzes slowly at room temperature
Colloidal Silicon Dioxide	Disintegrants	5-10%	Hydroscopic, but do not liquefy upon absorption of water
Cross-povidone	Superdisintegrant	2-5%	As hygroscopic in nature, stored in an air-tight container, in a cool and dry
Methyl	Disintegrants	2-	Slightly hygroscopic

cellulose		10%	, but stable
Micro-crystalline Cellulose	Superdisintegrant	5-15%	Stable at dry and air tight condition
Starch	Superdisintegrant	5-10%	Stable at dry and air tight condition

Evaluation

- Weight variation
- Hardness
- Friability test
- Thickness
- Disintegration test
- Uniformity of dispersion
- Wetting time
- Water absorption ratio
- Moisture uptake studies
- Dissolution test

Weight Variation Test

From each batch twenty tablets are selected at a random and average weight was determined. Then individual tablets were weighed and the individual weight was compared with an average weight, the variation in the weight was expressed in terms of % deviation.

Table 2: Limits of Weight Variation[17]

IP / BP	Limits	USP
80 mg or less	+/- 10%	130mg or less
more than 80mg less than 250 mg	+/- 7.5%	130-324mg
250mg or more	+/- 5%	more than 324mg

Hardness

Ten tablets from each formulation were selected for the hardness and it was determined by using Monsanto hardness tester.

Limits: 5 kilograms minimum and 8 kilograms maximum. i.e. =/- 5 kg/cm^2.

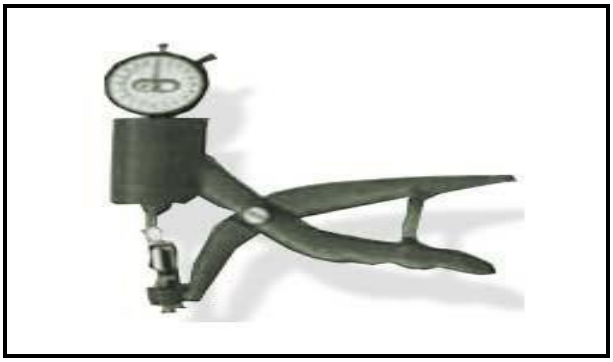

Figure 6: Monsanto Hardness Tester[13]

Friability Test

Figure 7: Roches Friabilator[14]

Friability is related to tablets ability to withstand both shocks and abrasion without crumbling during manufacturing, packing, transportation and consumer handling. Friability can be evaluated by means of friability test apparatus. Acceptable limit was not more than 1.0% of three samples. Method: Accurately weighed 6.5 gm. of tablet and transfer into Friabilator and subjected to 100 revolutions in 4 minutes. DE dusted tablets were reweighed (final wt.).

$$Friability = \frac{Initial\ weight - final\ Weigh}{Initial\ weight} * 100$$

Tablet Friability Apparatus is used for the test. Remove any loose dust from the tablets and

accurately weigh 10 tablets. They are placed in the drum which rotates at 25±1 rpm. Rotate the drum 100 times, and remove the tablets. The sample fails the test, if any of the 10 tablets cracked, cleaved, or broken is present. If the weight loss is more than 1.0%, the test is repeated for twice and the mean of three tests is calculated. The mean not more than 1.0% is considered acceptable.

Thickness

Ten tablets were selected at random from individual formulations and thickness is measured by using Vernier-caliper scale, which permits accurate measurement.

Thickness should be within +/- 5%.

Disintegration Test

The test was carried out on 5 tablets using the Disintegration Test Apparatus. Distilled water at 37oC was used as a disintegration media and the time in second taken for complete disintegration of the tablet by no palatable mass remaining in the apparatus was measured. Disintegration time: Un7coated tablet: 5-30 minutes coated tablet: 1-2 hours.

Figure 8: Disintegration Apparatus

Uniformity of Dispersion

Ten tablets were weighed individually and powdered. The powder equivalent to 20 mg of the active drug was weighed and extracted in water (100ml) and the concentration of drug was determined by measuring absorbance at 222 nm by spectrophotometer.

The Tablet pass the test if 9 of the 10 tablets must contain not less than 85% and not more than 115% of the labeled drug content and the 10th tablet may not contain less than 75% and more than 125% of the labeled content. If these conditions are not met, remaining 20 tablet assayed individually and none may fall outside of the 85 to 115% range.

Wetting Time

A piece of tissue paper folded twice was placed in a small Petri dish containing 6 ml of water. A tablet was put on the paper and time required for complete wetting was measured.

Water Absorption Ratio

A small piece of tissue paper folded twice was placed in a small petri dish containing 6ml of water. A tablet was put on the paper. The wetted tablet was then weighed. Water absorption ratio, R was determined by using following formula

$$R = W_a - W_b / W_a \times 100$$

Here, R = Water absorption ratio Wb = Weight of tablet before water absorption WA = Weight of tablet after water absorption.

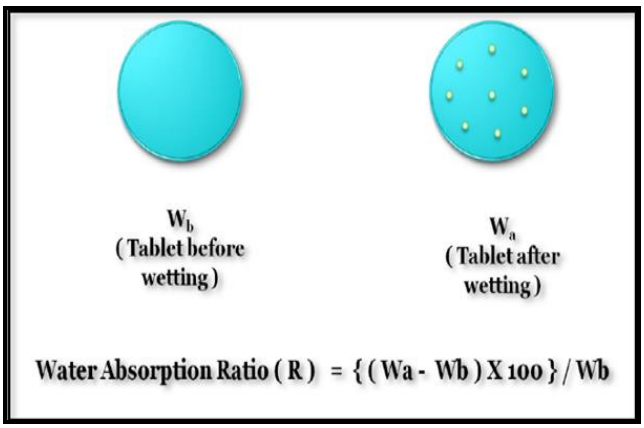

Figure 9: Water Absorption Ratio[10]

Moisture Uptake Studies

Moisture uptake studies for ODT should be conducted to have an insight into the stability of the formulation, as several excipients used are hygroscopic. Ten tablets from each formulation are kept in a desiccator over calcium chloride at 37^0C for 24 h. The tablets are then weighed and

exposed to 75% RH at room temperature for two weeks. The required humidity (75% RH) is achieved by keeping saturated sodium chloride solution at the bottom of the desiccator for three days. One tablet as control (without superdisintegrant) is kept to assess the moisture uptake due to other excipients. Tablets are weighed and the percentage increase in weight is recorded

Dissolution

Figure 10: Dissolution Apparatus[16]

Rate of fast disintegrating can be studied by using USP Type-II apparatus at 50rpm using 900 ml of 0.1N HCl as dissolution medium. Temperature of the dissolution medium was maintained at 370C an aliquot of dissolution medium was withdrawn at every specific time interval and filtered. The absorbance of filtered solution was checked by UV spectrophotometer at 222 nm and concentration of the drug was determined from standard calibration curve.

Table 3: Types of Dissolution Apparatus[17]

	I.P	U.S.P	B.P	E.P
TYPE 1	Paddle apparatus	Basket apparatus	Basket apparatus	Basket apparatus
TYPE 2	Basket apparatus	Paddle apparatus	Paddle apparatus	Paddle apparatus
TYPE 3		Reciprocating cylinder	Flow through cell	Flow through cell
TYPE 4		Flow through cell		
TYPE 5		Paddle over disk		
TYPE 6		Rotating cylinder		
TYPE 7		Reciprocating disk		

Drug Release Kinetics As a model-independent approach, comparison of the time taken for the given proportion of the active drug to be dissolved in the dissolution medium and figures such as T50 and T90 calculated by taking the time points of 50% and 90% of the drug dissolved and another parameter Dissolution Efficiency (DE) suggested by Khan were employed. DE is defined as the area under the dissolution curve up to the time t expressed as a percentage of the area of the rectangle described by 100% dissolution in the same time.

The dissolution efficiency can have a range of values depending on the time interval chosen. In any case constant time intervals should be chosen for comparison. For example, the index DE30 would relate to the dissolution of the drug from a particular formulation after 30 minutes could only be compared with DE30 of other formulations. Summation of the drug dissolution data into a single figure DE enables ready comparison to be made between a large numbers of formulations.

Stability Studies

The purpose of stability testing is provide evidence on how the quality of to a drug substance or drug product varies with time under the influence of a variety of environmental factors such as temperature, humidity and light, enabling recommended storage conditions, re-test periods and shelf-lives. Generally, the observation of the rate at which the product degrades under normal room temperature requires a long time. To avoid this undesirable delay, the principles of accelerated stability studies are adopted.

ICH specifies the length of study and storage conditions.

LONG-TERM TESTING: 25^0C ± 2^0C / 60% RH ± 5% for 12 Months.

ACCELERATED TESTING: 40^0 C ± 2^0 C /75% RH± 5% for 6 Months Stability studies were carried out at 40^0C ± 2^0C /75%RH ± 5% for all the formulations for a period of 3 months.

The selected formulations should be closely packed in amber color bottles and then stored at

$40^0C \pm 2^0C$ /75% RH ± 5% in stability chamber for 3 months and evaluated for their physical appearance, drug content and in-vitro drug release studies at intervals of 1month.[6,9]

Marketed Products

Figure 11: Marketed Products of Paracetamol[3]

Current Market Position

People suffering from regular headaches and over half from muscle aches and pains. There is a need for an effective, safe and fast relief. As one of the leading research-based pharmaceutical and healthcare companies in the world, GlaxoSmithKline (GSK) is stepping up to this challenge in pain medication. Recently, GSK announced the brand entry and launch of Panadol, one of the world's leading Paracetamol-based pain relievers. Panadol has been relieving the pain of people in 85 countries for over 50 years now. In 2013 alone, over 15 billion Panadol tablets were sold worldwide.

"GSK is very important marketplace for a number of reasons, president of Consumer Healthcare for Asia, Pacific and Latin America is the first fastest growing market followed by Philippines the second fastest growing market in Asia with seven percent GDP growth because of the country's overall economic growth, people have become economically able to buy healthcare solutions. GSK has been here in the Philippines for 15 years and we want to grow on that heritage and bring more global brands.

According to JeoffreyYulo, general manager of Consumer Healthcare for GSK Philippines, the company leverages on its deep understanding of the Filipino market and considers it one of Panadol's competitive advantage in the pain medication area. "GSK has a global heritage and the brand is very strong. The key point is that while Paracetamol is Paracetamol, we offer a solution when people say that they want their pain to be relieved right away. In this case fast relief are developed.

Not all Paracetamol are created equal. For one, Panadol has the Optizorb technology with a disintegration system that allows the release of its medicine in as little as five minutes. The pain reliever also has the broad suitability associated with standard Paracetamol, hence, it will not irritate the stomach and can even be taken on an empty stomach or by pregnant women when used as directed.

Total Business

Ex-factory sales for Panadol Optizorb were blown out of the park with 22.7% growth vs. L/Y. Panadol Optizorb consumption for the key 4 week period in market (4WKS from 10/6) was up 28.6%, well ahead of the total at 4.4%. Share +210bps to 11% (share of Everyday Adult Analgesics). WOOLWORTHS: performance was well above the total market with ex-factory sales of sales growth of 33.4% vs. last year. Consumption grew by 36.7%, well above category growth of only 4.3%. This resulted in share gain of 360bps to 16.7%. 550 floor bins were executed in store. The most ever for Panadol. PHARMACY CHANNEL: strong ex-factory sales grew by 56.9%. Consumption grew by 42.7%, with share up 150bps to 5.7%. The stronger growth in pharmacy is rewarding as Panadol Optizorb has struggled to gain traction in the channel due to the strength of generics.[3]

CONCLUSION

Optizorb technology has been developed to provide faster disintegration in the environment so that the active substance is released and absorbed into the blood stream inn the shortest possible time there by to accelerate the onset and action. Optizorb disintegration technology is five times faster and thus gets to work much more quickly .Optizorb formulation have better patient acceptance and compliance and may offer

improved biopharmaceutical properties, improved efficacy, and better safety. Nevertheless formulation challenges such as limited tablet weight, disintegration time, friability, manufacturing technology, and packaging should be considered. The research is still going on. More products need to be commercialized to use this technology properly. Thus ODT may be developed for most of the available drugs in near future.

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