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ACOMPREHENSIVE REVIEW ON AN ORODISPERSIBLE TABLETS USING NATURAL SUPERDISINTEGRANTS

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ABSTRACTS

Orodispersible tablets are the Novel Solid Dosages forms which disintegrates or dissolves with no need of water. It is a good choice of drug delivery for paediatric and geriatric patients because it troubleshoots the problem of dysphagia i.e. difficulty in swallowing which is seen in many elderly patients. The superdisintegrants are those agents which helps to improve the disintegration of tablets. Natural superdisintegrants are obtained from natural as well as synthetic origin from which the natural form are widely used due to its easily availability, inexpensive and non-toxic in nature. The objective of this article is to highlights the various kind of natural superdisintegrants like poly saccharides, mango peel pectin, etc., the types of superdisintegrants, mechanism of superdisintegrants and methodology used in preparation of orodispersible tablet are discussed.

Key Words: orodispersible, superdisintegrants, natural superdisintegrants, disintegration.

INTRODUCTION

The pharmaceutical industry has made itself of a significant importance for making it as a major contribution in the healthcare industry for improving the quality of life [1]. Among the novel drug delivery, oral routes is most preferred route by medical practitioner and manufacturer due to highest acceptability of patients, ease of ingestion, pain avoidance, and versality [2]. A Novel drug delivery system has developed in oral delivery called as orodispersible tablets who has difficulty in swallowing (Dysphagia) in all age groups, especially paediatric and geriatric patients, patients suffering with nausea, vomiting and motion sickness [3,4].

The tablet will get disintegrated quickly in the mouth within few seconds when it comes in contact with saliva. Disintegrants are the substance which incorporated the break-up of the compressed mass into the primary particles in order to facilitate the dissolution or release of the active ingredients when in comes in contact with water. They help for the moisture penetration and dispersion of the tablet. Now-a-days super-disintegrants are developed to enhance the disintegration processes [5].

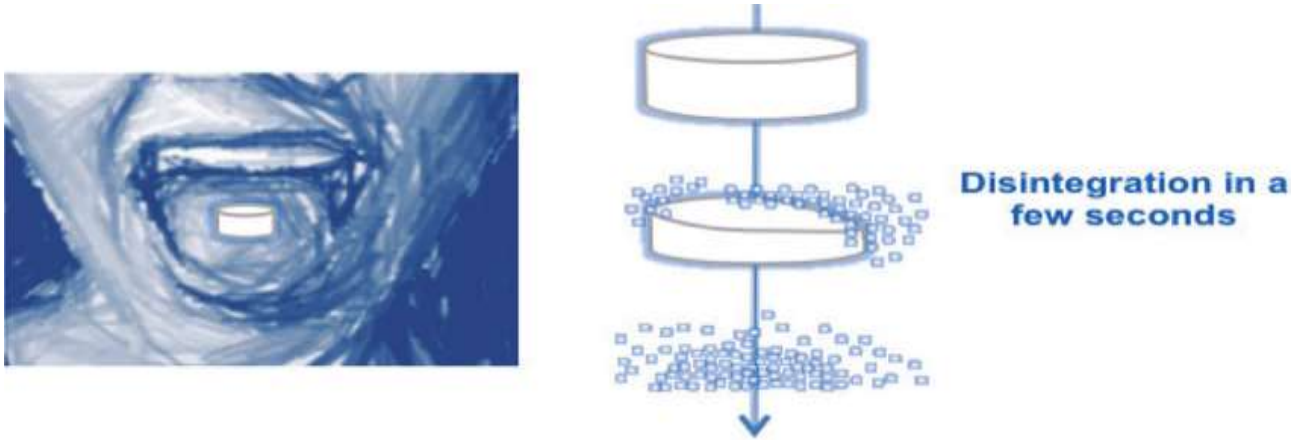

Figure no. 1 Diagram showing the administration of orodispersible tablet

The basic approach in development of ODTs is the use of superdisintegrants, which provide prompt disintegration of tablet after putting on a tongue, thereby releasing the drug on a saliva. Various methods are adopted for manufacturing with the aim of giving fast disintegration to the dosage good agreeable mouth-feelings [6].

Orodispersible tablets also called as 'Mouth dissolving tablet', 'Rapi-melts tablets', 'Melt -in-mouth', 'Orally disintegrating tablet', 'Fast dissolving drug delivery', 'Porous tablets', 'Quick dissolving tablets', etc. Recently ODT Terminology has been approved by United States Pharmacopoeia, British Pharmacopoeia and centre for Drug Evaluation and Research (CDER) [7].

Ideal properties of ODTs

1) It does not require any water or liquid to swallow.
2) It is easy to convey.
3) It rapidly dissolves and disintegrates in saliva within a second.
4) It has a pleasant taste and mouth feel.
5) It is easily transportable and mobile.
6) It is able to manufacture in a simple conventional method with low cost [8]

Advantages of ODTs

1) Allows high drug loading.
2) Provides rapid onset of action, ODTs tablets show rapid disintegration of tablets and rapid absorption.
3) Alternation to liquid dosages forms.
4) Formulation is cleared from the oesophagus especially in the supine position without lodging or sticking to it when swallowed, thus offering improved safety.
5) Cost effective.
6) No risk of chocking.
7) New business opportunities; line extension, exclusively of product promotion and patient life extension [9].

Disadvantages of ODTS

1) They are hygroscopic in nature so they should be kept in dry place.
2) It needs particular packaging for well stabilization and safety of stable product.
3) Dose uniformity in a technical challenge [6].

Table- 1 A list of Marketed Orodispersible tablets products

Product	Generic Name	Company
Abilify®	Aripiprazole	Otsuka America Pharmaceutical, Inc
Imodium® Instant Melts/ Imodium® Lingual/ Imodium® Quick Dissolve	Loperamide HCl	Johnson and Johnson
Klonopin® Wafers	Clonazepam	Roche
Motilium®	Domperidone	Johnson and Johnson
Maxalt-MLT®	Rizatriptan benzoate	Merek
Zelapar	Selegiline HCl	Elan and Amarin Corporation
Zofran® ODT	Ondansetron HCl	GlaxoSmithKline

Zubrin	Tepoxalin	Schering Corporation
Paralyoc	Paracetamol	Teva
Proxalyoc	Piroxicam	Teva
Allegra	Fexofenadine	Aventis Pharmaceuticals
Kemstra	Baclofen	Schwarz Pharma
Niravam	Alprazolam	Schwarz Pharma
Gaster® D	Famotidine	Yamanouchi
Nasea® OD	Ramosetoron HCl	Yamanouchi
Paracetamol Flashtab	Paracetamol	Ranbaxy
Fluoxetine® ODT	Fluoxetine	Biovail
Hyoscyamine Sulphate ODT	Hyoscyamine sulphate	Perrigo
Fluxid™	Famotidine	Azur Pharma
Nurofen® Flashtab	Ibuprofen	Boots Healthcare

Ingredients used for preparation of orodispersible tablets

1. **Flavours**
   Flavours and taste-masking agents make the products more palatable and pleasing for patients. The addition of these ingredients assists in overcoming bitterness and undesirable tastes of some active ingredients. For examples- peppermint flavours, flavour oils and clove
   oil, bay oil, anise oil, etc. Aspartame, sugar derivatives are used as sweeteners

2. **Fillers**
   Selection of fillers also had an important role in deciding the disintegration time. Examples are mannitol, sorbitol, xylitol, calcium carbonate, magnesium carbonate.

3. **Surface active agents**
   The presence of esterase or bile salts (sodium doecyl sulphate, sodium lauryl sulphate, polyoxy ethylene Sorbiton fatty acid esters) like surface active agents plays a role in drug release.

4. **Lubricants**
   Lubricants remove grittiness and assist in the drug transport mechanism from the mouth down into the stomach. Some examples are stearic acid, magnesium stearate, zinc state, calcium state, talc, polyethylene.

5. **Binders**
   Binders are added to tablet to add cohesiveness to powders, thus providing the necessary bonding to form granules, which under compaction from a cohesive mass or a compact which is referred to as a tablet. Examples-polyvinyl pyrrolidone, polyvinyl alcohol, hydroxypropyl methylcellulose.

6. **Colour**
   Sunset yellow, Amaranth, etc. [10]

7. **Superdisintegrants**
   The most important ingredients for oral disintegrating tablets are super-disintegrants, which play a major role in the disintegration and dissolution of ODT. As the superdisintegrants can be easily available, less expensive and direct compressible, use of superdisintegrants is more suggestible and profitable method to prepare ODTs as compared to other patented technologies.

Selection of Superdisintegrants

- Particle size should be small.
- Compatible with other excipients and drug.
- Produce good mouth feel to the patients.
- Should have good flow property.
- Should be non-toxic.
- Effective in less quantity.
- Should have good hydration capacity [11].

Types of superdisintegrants

1) Synthetic superdisintegrants

They are frequently used in tablet formulation to improve the rate and extent of tablet disintegration thereby increasing the rate of drug dissolution. For examples- Croscarmellose sodium, sodium starch glycolate, crosspovidone.

2) Natural superdisintegrants

These superdisintegrants agents are natural in origin and are preferred over synthetic substances because they are comparatively cheaper, abundantly available, non-irritating ang non-toxic in nature. For examples- gellan gum, locust bean gum, gaur gum, mango peel pectin, etc [10]. They are:

a) **Gellan Gum-** gellan gum is a linear anionic polysaccharide, biodegradable polymer which produced from the microbe *Pseudomonas elodea*. It consists a linear tetra-saccharide repeat like structure and used as a tablet disintegrant. Gellan polymers also consists of a monosaccharide α-L-rhamnose, β-D-glucuronic acid and β-D-glucose in a molar ratio of 1:1:2 which are linked together to form a primary structure. Due to its high hydrophilic nature, it shows the instantaneous swelling characteristics of gellan gum when it comes in contact of water. In a study, the complete disintegration of tablet was observed within 4 minutes with gellam gum concentration of 4% w/w and 90% of drug dissolved within 23 minutes [12].

b) **Locust been gum-** it is also known as Carob been gum. It is a galactomannan vegetable gum extracted from the seeds of *Ceratonia siliqua*. The gum is a white to yellowish-white, odourless powder and insoluble in most organic solvents i.e ethanol and partially soluble in water. It is utilized as a gelling and thickening agent in the food industry as a bio-adhesive and it enhances the solubility [13].

c) **Gaur Gum-** Gaur gum is obtained from the endosperm of the seed of the gaur plant, *Cyamopsia Tetragonaloba (L) Taub*. It is also a galactomannan which are commonly used in cosmetics, food products as well as in pharmaceutical formulation. The molecular weight of gaur gum is approximately 50,000- 8,000,000. Gaur gum has also been examined for use in colonic drug delivery [14].

d) **Mango peel pectin-** mango peel consists of 20-25% of mango processing waste that was found to be a good source for the extraction of pectin of good quality and suitable for the preparation of film and acceptability jelly. Dried mango peel powder is also used for extracting pectin. Rather mango peel pectin cannot be used but due to its good swelling index and good solubility in biological fluids, it can be used to prepare fast dispersible fluids [15].

e) **Plantago ovata seed mucilage (Ispaghula)-** Ispaghula mucilage consists of epidermis of the dried seeds of *Plantago ovata*. They possess a variety of pharmaceutical properties including binding, disintegrating, suspending, emulsifying and sustaining properties at different proportion in different pharmaceutical dosage forms. It shows faster disintegration time than the crosspovidone [16].

Table no-2 Representing various mucilage and their application in pharmaceutical dosage forms [16-20]

Mucilage (used as superdisintegrants)	Drug	Approach used	Pharmaceutical application
Fenugreek Seed Mucilage	Metformin HCl	Conventional direct compression	Disintegrating agent
Plantago ovata seed mucilage	Prochlorperazine maleate	Direct compression	Binding, Disintegrating, Suspending, Emulsifying agent
Ocimum basilicum seed mucilage	Metoprolol tartrate	Wet granulation	Disintegrating agent
Lepidium sativum mucilage	Promethazine HCl	Direct compression	Binding, Disintegrating, Gelling agent
Hibiscus rosa-sinensis mucilage	Amlodipine besylate	Direct compression	Disintegrating agent
Ocimum basilicum seed mucilage	Paracetamol	Direct compression	Disintegrating

Cydonia vulgaris pers, seed mucilage	Paracetamol	Direct compression	Disintegrating agent
Plantago ovata mucilage	Ciprofloxacin	Compression method	Disintegration, Swelling and gelling agent

Mechanism of action of superdisintegrants

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

- Swelling
- Porosity and capillary action (Wicking)
- Combination of Wetting
- Deformation
- Enzymatic reaction
- Particle repulsive force/ electrostatic repulsion
- Chemical reaction

a. Swelling

Swelling is most widely accepted general mechanism of action for tablet disintegration. Those tablets having high porosity shows poor disintegration due to lack of adequate swelling force were as tablet with low porosity have sufficient swelling force. If the packing fraction is very high, fluid is unable to penetrate into the tablet and the disintegration of tablet is slow down again [21].

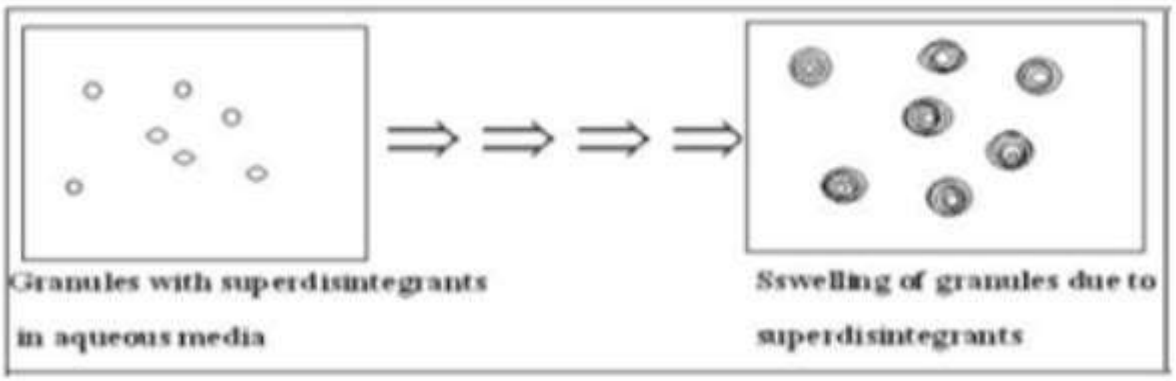

Figure no. 2 Diagram representing the swelling effect on granules

b. Porosity and capillary action (Wicking)

Capillary action is the first step for disintegration. When we put the tablet into a 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 depends on the hydrophilicity of the drug or excipients and on tableting condition.

For this type of disintegrants, it is very necessary to maintain the porous structure and low interfacial tension towards aqueous fluid that help in disintegration of tablet by creating a hydrophilic network around the drug particles [21].

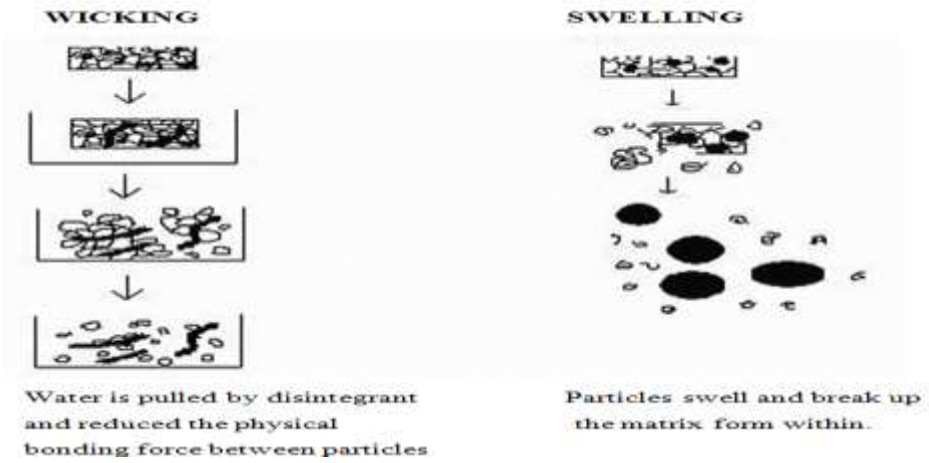

Figure no. 3 Diagram representing the swelling and wicking mechanism of superdisintegrants

c. Combination of action

The combination of swelling and wicking mechanism causes the breakdown of tablet into fine particles [21].

d. Heat of wetting

For this mechanism, disintegrants should have exothermic properties. When the disintegrant comes in contact with aqueous medium or get wetted, a capillary air expansion may occur which lead to localised stress this in turn leads of the disintegration of tablet.

e. Deformation

During the compression of tablet, the disintegrated particles get deformed and deformed particles turn into normal structure when they come in contact with water or liquid. During the compression of tablet, the granules were extensively deformed that improved the swelling capacity of starch. Increasing in size of deformed particles cause the breakdown of the tablet.

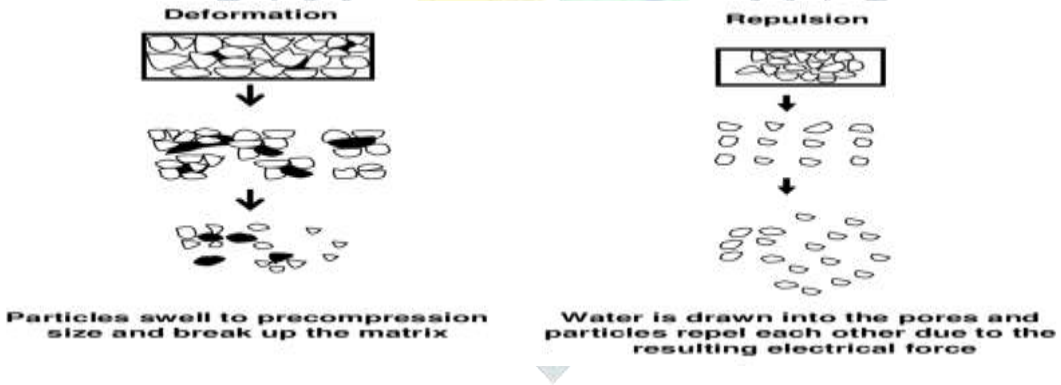

Figure no. 4 Diagram representing the deformation and repulsive action of disintegrants

f. Particle repulsive force

Guyot-Hermann has proposed a particle repulsion theory based on observation that non-swelling particle also cause disintegration of tablets. The electric repulsion forces between particles are the mechanism of disintegration and water is required for it. Researcher found that repulsion is secondary to wicking.

g. Enzymatic reaction

Enzymes which present in our body also acts as disintegrants. The enzymes dearth the binding action of binder and helps in disintegration. Pressure exerted in the outer direction due to swelling cause the tablet to burst or the accelerated absorption of water leads to an enormous increase in the volume of granules to promote disintegration.

h. Chemical reaction

When tartaric acid and citric acid reacts with alkali carbonates and bicarbonates in water, carbon dioxides internally liberate in water which causes the tablet disintegrates rapidly. Due to formation of pressure within tablet, it gets disintegrate. Liberation of carbon dioxide gas highly effect on disintegrants which are highly sensitive [22].

Table no- 3 A list of natural superdisintegrants and their properties

Natural superdisintegrants	Commercially available brands	Mechanism of action
Gallen Gum	kilcogel®	Swelling
Locust been gum	CESAGUM®	Swelling and capillary action
Gaur gum	Gum karaya, Agar	Swelling
Mango peel pectin	Dried mango powder	Swelling and have good solubility
Plantago ovata seed mucilage	Isapghula husk	Swelling
Soy polysaccharides	Emcosoy®	Swelling
Chitin and chitosan	Chitin	Swelling
Banana powder	Kalans, TATTVAM	swelling
Xanthum gum	Xanthum gum	Swelling property

Methodology of orodisperdible tablet

There are several methods for the preparation of orodispersible tablets but the prepared products vary in their properties depending on the method of preparation. The properties in which they vary are mechanical strength of the tablets, swallowability, and bioavailability, drug dissolution in saliva, stability and to same extent taste. Various process for manufacturing of orodispersible tablet are discussed below: -

- Molding methods
- Compaction methods
- Spray-drying methods
- Freeze-drying methods
- Melt granulation
- Phase transition process
- Sublimation

a) Freeze drying or lyophilization

This process includes the removal of solvent from a frozen suspension or a solution of drug with structure forming additives. Freeze drying of drug along with additives imparts glossy amorphous structure resulting in highly porous and lightweight product [23].

b) Compaction method

Conventional methods for the preparation of tablets such as dry granulation, wet granulation and direct compression are also exist for the preparation of orodispersible tablets.

i) **Direct compression**

It is an easiest way to manufacture tablets. Crosspovidone, croscarmellose sodium, sodium alginate, acrylic acids derivatives are used as superdisintegrants for the preparation of orodispersible tablet which provide fast disintegration of tablet into fine particle [24].

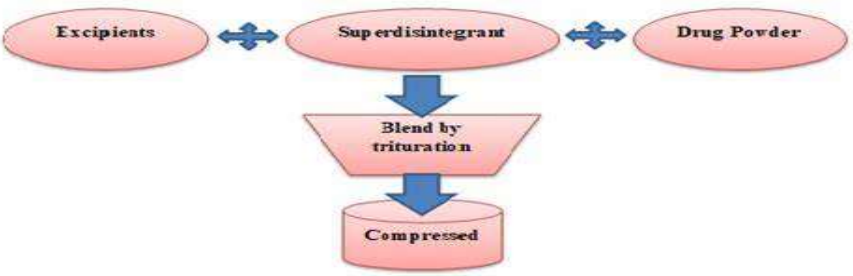

Figure no. 5 Diagram representing the step involved in direct compression method

c) Spray-drying method

In this method, hydrolysed and non-hydrolysed gelatin were used as supporting matrix. Sodium starch glycolate or croscarmellose sodium used as superdisintegrants. Sometimes in order to increase the disintegration and dissolution, acidic substances (citric acid) or alkali substances (sodium bicarbonate) are used. This technology produces highly porous and fine powders as processing solvent is evaporated during process [25, 26].

d) Melt granulation

Powders are efficiently agglomerated by a meltable binder. No water or organic solvents is needed. For this, propose high shear mixers are utilized. Product temperature is raised above the melting point by a heating jacket or by the heat of friction generated by impeller blades. A hydrophilic waxy binder (Superpolystate©, PEG-6-stearate) are used. So, it will not only act as a binder but will also help as the disintegration [24].

e) Sublimation

In this process, subliming material camphor is used. It was sublimed in vacuum at 80ºC for 30 minutes after preparation of tablets. In conventional types, sometimes rapid disintegration does not occur. Therefore, in order to improve the porosity, volatile substance camphor is added in the preparation, which get sublimed from the formed tablet [27]

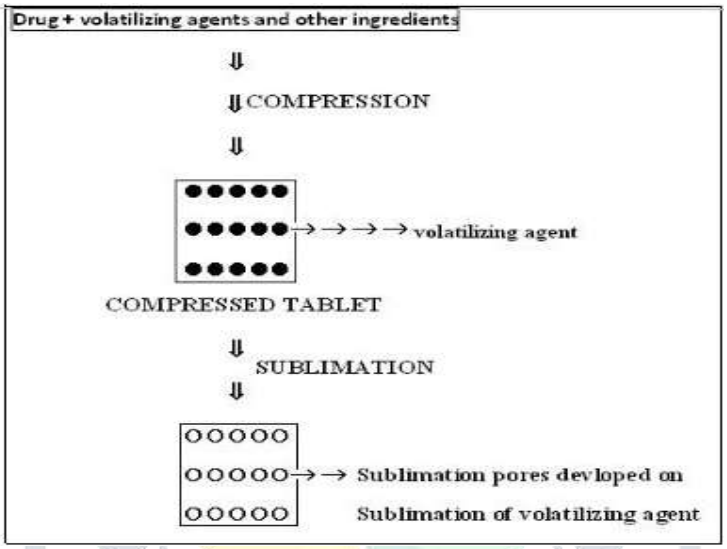

Figure no.6 Diagram representing the sublimation technique

f) Phase transition process

in this process, compress powder containing erythritol and xylitol and then heating at about 93ºC for 15 minutes. After heating the median pore size and tablet hardness was increased. Heating process enhances the bonding among particles leads to sufficient hardness of tablets [28].

Table no.4 patented technology for preparation of ODTs

S.No.	Technology	Technology patented/ developed by	Process involved	Drugs used (Brand name)
1	WOWTAB	Yamanuchi Pharmaceutical Company	Compression tablets	Famotidine (Gaster D)
2	Flashtab	Prographarm laboratories	Conventional technique like Coacervation, microencapsulation and Extrusion spheronisation	Ibuprofen (Nurofen Flastab)
3	Adva Tab	Kyowa Hakko Kogyo	Microcaps and diffuscap CR Technology	Adva Tab cetirizine, Adva Tab Paracetamol
4	Quick Solv	Jansen Pharmaceutical	Lyophilization	Cisapride monohydrate (propulsid Quicksolv)
5	Zydis	R.P. Scherer Inc	Lyophilizing or Freeze-drying method	Loratadine (Claritin Reditab)
6	Durasolv	CIMA Labs	Molding method	Hyoscyamine sulfate (NuLev)

7	Orasolv	CIMA Labs	Direct Compression	Paracetamol (Tempra Quicklets)
8	Flash Dose	Fuisz Nurofen Meltlet	Flash heat processing	Tramadol HCl (Relivia Flash dose)
9	Ziplets	Eurand	Molding method	Ibuprofen (Cibalgina Due Fast)

Conclusion

Orodispersible tablets is one of the most acceptable technique of Novel Drug Delivery System which provide patient compliance. Orodispersible tablet target the patients who are generally patients with dysphagia, children and elderly. Different types of superdisintegrants are used for the formulation of orodispersible tablet which provide better and fast disintegration. Natural superdisinterdintegrants are preferred over synthetic superdisintegrants due to its non-toxic in nature, easily available in low cost, used in low concentration and naturally extracted which provides natural supplements as well. They are also used to improve the efficacy of solid dosages form.

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