

Orally Disintegrating Tablets: A Review

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ABSTRACT

Orally disintegrating tablets is one of the most chosen routes of administration of drugs. The desire of improved palatability in orally administered drugs has provoked the development of numerous formulations with improved performance and acceptability. Orally disintegrating tablets are the emerging trend in novel drug delivery system and has increasing demand during the last few decades. This can be achieved by decreasing the disintegrating time which in turn increases the dissolution rate. Difficulty in swallowing (Dysphagia) is common all age groups especially in geriatrics and paediatrics. Hence, there is need for development of appropriate dosage form. A novel orodispersible tablet was investigated in this study as most desirable and user-friendly dosage form for all age groups. Apart from the conventional methods of manufacturing this review also provides information about the unique technologies like freeze drying, spray drying, sublimation, cotton candy process. This article also focuses on the patented technologies of manufacturing along with the types of superdisintegrants and their advantages. This type of drug delivery offers immediate release and increased bioavailability.

Keywords: Orally disintegrating tablets, Increased bioavailability, Dysphagia, palatability, patented technologies.

INTRODUCTION:

The development of an orally disintegrating tablets (ODT's) has been enormously increased because it has substantial impact on the patient compliance. Due to society, which is becoming increasingly aged, the development of an appropriate dosage form for the aged patients is obligatory. Due to various changes in physiological functions of geriatric patients, they face difficulty in swallowing of conventional dosage form like capsules, tablets. The most desirable formulation for use by the geriatric patients is the one which is easier to swallow and easy to handle. Taking all these necessities into deliberation attempts have been made in order to develop an Orally disintegrating tablet [1]. It has been reported that dysphagia which means difficulty in swallowing is communal among the age groups including paediatric, geriatric population and also in patients with nausea, motion sickness, vomiting complications. ODT's when are designed with good taste and flavour increases the acceptability of even the bitter drugs. Orally disintegrating tablets are also called as quick disintegrating, fast dissolving, mouth melts, fast disintegrating tablets and rapi melts.

UNITED STATES OF FOOD & DRUG ADMINISTRATION (FDA) defined ODT's as "A solid dosage form containing medicinal substance or active ingredient which disintegrates rapidly usually within a matter of seconds when placed upon the tongue". According to **EUROPEAN PHARMACOPOEIA** (4.1 2002) ODT's are solid single unit dosage form that are placed in the mouth, allowed to disperse in saliva and then swallowed without the need of water [2]. ODT's are mostly suitable for geriatrics, paediatrics and travelling patients [3]. These also increases the bioavailability of poorly water-soluble drug through enhancing the dissolution profile of the drug. As the ODT's gets disintegrated within the matter of seconds on the tongue so, there is need to improve the taste of the bitter drugs by masking the taste of the drug. This can be done by incorporating the additives such as taste masking agents such as aspartame, mannitol etc also flavours.

Nonetheless, these additives were found to be not so operative in complete taste masking of the bitter drugs. Therefore, recent advances in the technology was been reported which involve complexation, freeze-drying, microencapsulation, fluidized-bed coating and supercritical fluids for taste masking the bitter drugs [4]. There are different methods to develop an ODT's such as:

- i. Lyophilization and moulding techniques which produce ODT's that disintegrate with about 30sec, but they have low physical resistance and high friability.
- ii. Direct compression technique which produce tablets which are less friable but disintegrates on longer time [5].

❖ **Ideal properties of Orally disintegrating tablets:**

1. It should require no water for administration.
2. It should get easily dispersed/dissolved in saliva within seconds.
3. It should leave no residue in mouth.
4. It should have pleasant taste.
5. It should be easy to transport.
6. It should be able to manufacture in simple conventional technique.
7. Cost effective.
8. It should be less sensitive to environment.

❖ **Advantages:**

1. Ease of administration to patients who cannot swallow, patients who should not swallow and patients who refuses to swallow such as paediatrics, geriatrics and mentally retarded patients.
2. It has fast action when it is administered by the patient, it melts upon meeting saliva, it gets rapidly absorbed in oral cavity therefore produces fast action.
3. ODT's do not require water to swallow which can be taken anywhere and at any time, they are convenient for travelling patients who do not have access to water.
4. They are very convenient for paediatrics, geriatric and dysphagic patients.
5. These are less sensitive to environmental condition; hence they are stable.
6. They are cost effective, which means they does not require costly ingredients.
7. No water is needed.
8. No chewing is needed.
9. Improved compliance.
10. It also allows high drug loading.
11. It leaves minimum residue in mouth.
12. It is best option for the patients with oesophageal problems.

❖ **Disadvantages:**

1. Insufficient mechanical strength therefore careful handling is required.
2. These tablets will leave unpleasant taste in mouth if they are not formulated properly.

❖ **Challenges to develop ODT's**

1. Tablet size should be low.
2. Rapid disintegration of tablet.
3. Have enough mechanical strength.
4. Minimum or no residue in mouth.
5. Protection against moisture.
6. Compatible with taste masking [6-8].

❖ **Potential drug candidates for ODT's:**

- There are several factors to be considered while selecting an appropriate drug for development of ODT's.
- These include:
 - i. Ability to permeate in oral mucosa.
 - ii. It should have good solubility in water and saliva.
 - iii. It should be free from bitter taste.
 - iv. The dose should be lower than 20mg.
 - v. Small to moderate molecular weight.

- vi. It should be partially non-ionized at oral cavity's pH.
- Whereas some of the drugs which are unsuitable for delivery as an orally disintegrating dosage form such as:
 - i. Drugs with short half-life and frequent dosing.
 - ii. Drug with bitter taste or unacceptable taste.
 - iii. Drugs which require controlled or sustained release [9].

❖ **Drug candidates suitable for Orally disintegrating drug delivery:**

1. Analgesic and Anti-Inflammatory agents:

Aloxiprin, Auranofin, Azapropazone, Benorylate, Diflunisal, Ketorolac Tromethamine, Etodolac, Fenbufen, Fenoprofen, Calcium, Flurbiprofen, Ibuprofen, Indomethacin, Ketoprofen, Meclofenamic Acid, Mefenamic acid, Nabumetone, Naproxen, Oxaprozin, Oxyphenbutazone, Phenylbutazone, Piroxicam, Sulindac, Rofecoxib[10].

2. Anti-helminthic:

Albendazole, Bephenium Hydroxynaphthoate, Cambendazole, Dichlophen, Mebendazole, Oxfendazole, Oxantel Embonate, Pyrantel Embonate, Thiabendazole [10].

3. Anti- Arrhythmic:

Amiodarone, Disopyramide, Flecainide Acetate, Quinidine Sulphate [10].

4. Anti-Asthmatic:

Salbutamol Sulphate for respiratory disorders for paediatrics. [11].

5. Anti-Bacterial Agents:

Benethamine Penicillin, Cinoxacin, Ciprofloxacin, Clarithromycin, Clofazimine, Cloxacillin, Demeclocycline, Doxycycline, Erythromycin, Ethionamide, Imipenem, Nalidixic Acid, Nitrofurantoin, Rifampicin, Spiramycin, Sulphabenzamide, Sulphadoxine, Sulphamerazine, Sulphacetamide, Sulphamethoxazole, Sulphapyridine, Tetracycline, Trimethoprim.

Kamal Saroha et al Formulated and evaluated fast disintegrating tablets of amoxicillin trihydrate using synthetic disintegrants[12].

6. Anti-Coagulant

Dicoumarol, Dipyridamole, Nicoumalone, Phenindione.

7. Anti-Depressants:

Amoxapine, Ciclazindol, Maprotiline, Mianserin, Nortriptyline, Trazodone, Trimipramine Maleate, Acetohexamide, Chlorpropamide, Glibenclamide, Gliclazide, Glipizide, Tolazamide, Tolbutamide.

Danish Kurien et al successfully formulated and evaluated Fast dissolving tablets of Escitalopram oxalate by hydroxy propyl beta cyclodextrin[13]

8. Anti- Diabetics:

Glipizide, Tolazamide, Tolbutamide Acetohexamide, Chlorpropamide, Glibenclamide, Gliclazide.

Gnana Chaitanya et al prepared and evaluated oral fast disintegrating tablet formulations of Sitagliptin phosphate using the superdisintegrants for various parameters[14].

9. Anti-Emetics:

Basawaraj S, Patil et al attempted to prepare fast dissolving tablets of Granisetron Hydrochloride by sublimation technique [15].

10. Anti-Epileptics:

Beclamide, Carbamazepine, Clonazepam, Ethotoin, Methoin, Methsuximide, Methylphenobarbitone, Oxcarbazepine, Paramethdione, Phenacemide, Phenobarbitone, Phenytoin, Phensuximide, Primidone, Sulthiame, Valproic acid [10].

11. Anti-Fungal Agents:

Amphotericin, Butoconazole Nitrate, Clotrimazole, Econazole Nitrate, Fluconazole, Griseofulvin, Itraconazole, Ketoconazole, Miconazole, Natamycin, Nystatin, Sulconazole nitrate, Terbinafine, Terconazole, Tioconazole.

12. Anti-Gout agents:

Allopurinol, Probenecid, Sulphinpyrazone.

13. Antihistamine:

Acrivastine, Astemizole, Cinnarizine, Cyclizine, Cyproheptadine HCL, Dimenhydrinate, Flunarizine HCL, Loratadine, Meclozine HCL, Oxatomide, Terfenadine, Triprolidine.

14. Anti-Hypertensive:

Amlodipine, Carvedilol, Benidipine, Diltiazem, Diazoxide, Felodipine, Indoramine, Isradipine, Nifedipine, Nimodipine, Phenoxybenzamine, Prazosin, Reserpine.

Valsartan[16]

15. Anti- Malarial:

Amodiquine, Cloroquine, Chlorproguanil, Halofantrine, Mefloquine, Proguanil, Pyrimethamine, Quinine sulphate.

16. Anti- Migraine agents:

Dihydroergotamine Mesylate, Ergotamine Tartrate, Methysergide Maleate, Pizotifen Maleate, Sumatriptan Succinate.

17. Anti-Neoplastic agents and immunosuppressants:

Aminoglutethimide, Amsacrine, Azathiopne, Busulphan, Chlorambucil, Cyclosporin, Dacarbazine, Estramustine, Etoposide, Lomustine, Melphalan, Mercaptopurine, Mitomycin, Procarbazine, Tamoxifen Citrate, Testolactone.

18. Anxiolytics, Sedatives, Hypnotics & Neuroleptics:

Alprazolam, Amyiobarbitone, Barbitone, Bentazeparn, Bromazepam, Brotizoiam, Butobarbitone, Carbromal, Chlordiazepoxide, Clozapine, Diazepam, Ethinamate, Flunanisone, Lorazepam, Lormetazepam, Methaqualone, Oxazepam, Pentobarbitone, Prochlorperazine, Suipiride, Temazepam, Thioridazine, Triazolam, Zopiclone[10].

19. Diuretics:

Acetazolarnide, Amiloride, Bendrifluazide, Bumetanide, Chlorothiazide, Chlorthalidone, ethacrynic Acid, Frusemide, Metolazone, Spironolactone, Triamterene.

20. Anti-Parkinsonian agents:

Bromocriptine mesylate, Lysuride Maleate.

21. Local anaesthetics:

Lidocaine.

22. Gastro-intestinal agents:

Bisacodyl, Cimetidine, Cisapride, Diphenoxylate, Domperidone, Famotidine, Loperamide, Mesalazine, Nizatidine, Omeprazole, Ondansetron, Ranitidine, Sulphasalazine.

23. Nutritional agents:

Betacarotene, vitamin A, vitamin B2, vitamin D, vitamin E, vitamin K.

24. Stimulants:

Amphetamine, Dexamphetamine, Dexfenfluramine, Fenfluramine, Mazindol, Pemoline.

25. Anti-Thyroid Agents:

Carbimazole, Propylthiouracil.

❖ METHODS USED FOR PREPARATION OF ODT's:**1. Melt granulation:**

- In this process, the pharmaceutical powder is agglomerated by a meltable binder.
- The advantage of this method when compared to other conventional techniques is that no water (or) organic solvent are required.
- This process is less time consuming because there is no drying step involved and uses less energy than wet granulation.
- It is useful to increase the dissolution rate of poorly water-soluble drugs such as griseofulvin.
- This method uses hydrophilic waxy binder (superpolystate, PEG-6-stearate) for enough mechanical strength.
- Superpolystate is a waxy material with melting point of 33-37°C and HLB value of 9.
- It not only act as a binder but also enhance the physical resistance of tablets and also disintegrates rapidly and solubilizes rapidly leaving no residue in mouth[3].

2. Effervescent method:

- This method involves mixing of sodium bicarbonate and tartaric acid of concentration 12%(w/w) along with superdisintegrants such as pregelatinized starch, SSG, CP and CS.
- Initially the sodium bicarbonate along with tartaric acid were preheated at a temp of about 80°C to eliminate all the absorbed (or) residual moisture from it and then it is completely mixed in the motor. Finally, these blends were compressed into tablets[17].

3. Cotton candy process:

- It is one of the unique methods which utilizes shear form technology which is used in preparation of a matrix which is known as FLOSS.
- The fibrous nature of this is similar as that of cotton candy fibres.
- This FLOSS is generally made of saccharides such as sucrose, lactose, fructose and dextrose at temp ranging between 180-260°F.

4. Direct compression method:

- it is one of the simplest and most convenient technique in manufacturing of ODT's.
- In this technique the pure drug along with the required excipients such as lubricating agents, superdisintegrants, bulking agents, diluents, sweeteners and flavouring agents are used as it is a ODT in which the taste masking of bitter drugs plays an important role[18].

5. Tablet moulding:

- Solid dispersion means the tablets produced by moulding technique.
- In this technique the drug is existed as discrete particles which is dispersed in matrix.
- It is dissolved totally in carrier which is in molten state in order to produce solid solution [19].

6. Sublimation:

- Presence of porous structure in tablet matrix is the key for rapid disintegration in orodispersible tablets.
- Conventional tablets which contain low porosity of matrix often fail to dissolve(or) disintegrate rapidly. Therefore, in order to produce porous matrix, a volatile ingredient is used which are the subjected to process of sublimation.

- Sublimation, it is a process in which water passes directly from solid state to vapour state without converting into liquid state. This process involves addition of volatile substance like urea, urethane, naphthalene, camphor, menthol to the excipients and then compressing it into a tablet.
- Removal of this volatile constituents by means of sublimation creates pores in the tablet structure, which help rapid dispersion when it meets saliva.

7. Phase transition:

- In this method the ODT's are produced by compressing powder which contains erythritol which has melting point of about 122°C and xylitol which has melting point of about 93-95°C and then it is heated at 93°C for about 15min. This heating leads to increase in pore size of tablets as well as hardness is also increased [20].

8. Freeze drying:

- It is the process in which water is sublimed from the product immediately after it is frozen.
- Due to this it creates porous structure that can dissolve(or) disperse rapidly.

9. Mass extrusion:

- In this technique the softening of the active blend is done by using the solvent mixture of water-soluble polyethylene glycol, methanol and expulsion of softened mass through the extruder (or) syringe to form tablet [21].

❖ PATENTED TECHNOLOGIES:

1. Zydis technology:

It is one of the unique techniques to obtain freeze dried tablet in which the drug is physically entrapped in fast dissolving carrier material. When these zydis units are put into mouth, the freeze-dried structure disintegrates instantly which does not require water to swallow. In this technique in order to provide strength to the tablets during handling polymers such as gelatin, dextran is used. Saccharides such as mannitol(or) sorbitol are incorporated to obtain crystallinity, elegance and hardness.

2. Durasolv technology:

It is patented technology of CIMA labs. In this, the tablets which are made contain drug, filler and lubricating agent. It is as similar as conventional techniques in case of tableting or packaging systems like blisters, strips. It is the best technology for potent drugs.

3. Orosolv technology:

It is CIMA's first orodispersible dosage form. In this technique it contains disintegrants and the active ingredient is taste masked. The disintegration of ODT's in mouth is caused by the action of effervescent agent which is activated by saliva. Concentration effervescent disintegration pair is an acid source (citric acid, tartaric acid, malic acid, fumaric, adipic) and a carbonate source (sodium bicarbonate, sodium carbonate, potassium bicarbonate and potassium carbonate, magnesium carbonate)

4. Wow's tab technology:

Wow's tab technology which means tablet without water. This technology uses sugar and sugar like excipients. Two types of saccharides like good binding property (maltose, mannitol, sorbitol and oligosaccharides) and low moldability (glucose, lactose, mannitol, xylitol) are combined. Due to significant hardness of the Wow tab technology is more stable than Zydis and Orosolv. Erythritol was found to be the best sugar for this type of formulation which shows rapid disintegration and is unaffected by hardness.

5. Oraquick technology:

This technique generally uses patented taste masking technology. It does not utilize any kind of solvents which ultimately lead to faster and more efficient production [22].

6. Flash tab technology:

This technology utilizes almost all excipients like conventional compressed tablets. The excipients used in this technique comprise two groups of components: disintegrating agents such as CMC or insoluble reticulate PVP and swelling agents such as CMC, starch, carboxymethylated starch, MCC and directly compressible sugars.

7. Quick-Dis technology:

Lavipharm laboratories Inc has invented an ideal intraoral fast dissolving drug delivery system, trademarked Quick-dis™, is Lavipharm proprietary patented technology. This film is placed on the

tongue which rapidly releases the active agent for local/systemic absorption. The dissolving time is around 30sec for quick disTM film with thickness of 2mm. 50% released within 30sec and 95% within 1 minute (Dobetti, 2001 and Rish, 2004) [23].

➤ **Table1: List of Orally disintegrating tablet products available in Indian Market**

S. No	Brand name	Active Ingredient	Company
1	Domray MD	Domperidone	Ray remedies
2	Velrid MD	Domperidone	Shreyamhealth care
3	Vomidon MD	Domperidone	Olcare lab
4	Zotacet MD	Cetirizine HCl	Zota pharma
5	Olanex Instab	Olanzapine	Ranbaxy
6	Manza RTD	Olanzapine	Mano pharma(orchid)
7	Romilast	Montelukast	Ranbaxy
8	Torrox MT	Rofecoxib	Torrent
9	Ziflam	Rofecoxib	Kopran
10	Doloroff	Rofecoxib	Indoco
11	Rofaday MT	Rofecoxib	Lupin
12	Dolib MT	Rofecoxib	Panacea
13	Orthoref MD	Rofecoxib	Biochem
14	Rbcox-25 MD	Rofecoxib	Shalman pharma
15	Roffec MD	Rofecoxib	Excare lab
16	Roftab MD	Rofecoxib	Olcare lab
17	Zofex-25 MD	Rofecoxib	Zota pharma
18	Valus	Valdecoxib	Glenmark
19	Nency MD	Nimesulide	Zenon health care
20	Nexus MD	Nimesulide	Lexus
21	Nimex MD	Nimesulide	Menox health care
22	Nimez- MD	Nimesulide	Zota pharma
23	Nisure MD	Nimesulide	Suzen pharma
24	Nimulid- MD	Nimesulide	Panacea
25	Olnim- MD	Nimesulide	Olcare lab
26	Sulbid-Md	Nimesulide	Alpic remedies
27	Topmide	Nimesulid	Antigen health care
28	Nimpain MD	Nimesulide	Prompt cure pharma
29	Mosid MT	Mosapride	Torrent

➤ **Table2: List of orally disintegrating tablet products available in International Market**

S.No	Brand name	Active ingredient	Company
1	Zomig ZMT and rapimelt	Zolmitriptan	Astra Zeneca
2	Alavert	Loratadine	Wyeth consumer healthcare
3	Cibalginadue FAST	Ibuprofen	Novartis consumer health care
4	Hyoscyamine sulfate ODT	Hyoscyamine sulfate	ETHEX corporation
5	Nulev	Hyoscyamine sulfate	Schwarz pharma
6	Nurofen flash tab	Ibuprofen	Boots health care
7	Kemstro	Baclofen	Schwarz pharma
8	Fluoxetine ODT	Fluoxetine	Bioavail
9	Benadryl fastmelt	Diphenhydramine	Pfizer
10	Zolpidem ODT	Zolpidem Tartrate	Bioavail
11	Nasea OD	Ramosetoron	Yamanouchi
12	Ralivia flash dose	Tramadol HCl	Bioavail
13	Gaster D	Famotidine	Yamanouchi
14	Excedrin quick tab	Acetaminophen	Bristol-Myers squibb
15	Claritin Redi tabs	Loratadine	Sching corporation
16	Remeron Sol Tab	Mirtazapine	Organon Inc

17	Feldene Melt	Piroxicam	Pfizer
18	Tempra Quicklet-Tempra Firs Tabs	Acetaminophen	Bristol-Myers squibb
19	Maxalt-MLT	Rizatriptan benzoate	Merck
20	Propulsid Quicksolv	Cisapride monohydrate	Janssen
21	Pepcid ODT	Famotidine	Merck
22	Imodium Instant melts	Loperamide HCl	Janssen
23	Zyprexa	Olanzapine	Eli lilly
24	Childrens Dimetapp ND	Loratadine	Wyeth consumer healthcare
25	Zofran ODT	Ondansetron	Glaxo smith kline
26	KlonopinODT	Clonaxepam	Roche
27	Risperidal M-Tab	Risperidone	Janssen
28	Zelapar	Selegiline	Elan corporation
29	Zubrin	Tepoxaline	Schering corporation
30	Aricept ODT	Donepezil HCl	Eisai and Pfizer
31	Fazalco	Clonzapine	Alamo pharmaceuticals
32	Permax	Pergolide	Amarin corporation
33	Febrectol	Paracetamol	Prographarm
34	Benadryl Fast melt	Diphenhydramine and pseudoephedrine	Warner lambert

❖ Approaches for taste masking

Orally disintegrating tablets which when disintegrates in mouth produces either positive or negative taste in the mouth. Most of the drugs are bitter or unpleasant in taste, in this case taste masking plays an important role to mask the unpleasant taste of the drug.

This bitterness of the drug can be reduced by various approaches which include addition of sweeteners and flavours, encapsulating the drug into microparticles and adjusting the pH.

➤ Addition of sweeteners and flavours:

In order to mask the bitterness of the tablet various sweeteners and flavours are added. Usually sugar based excipients are used as they are highly water soluble and dissolve quickly in the saliva. Mannitol is the most widely used sweetener in formulating ODT's. Aspartame and citric acid is used along with the flavours such as mint flavour, orange flavour, strawberry flavour to produce better mouth feel[25].

➤ Encapsulating or coating of drug:

Some of the drugs cannot be masked by sweeteners or flavours in such cases alternative methods of taste masking is done by encapsulating or coating the drug[26].

Various techniques include:

- i. CIMA's taste masking technique [27].
- ii. Phase separation technique for taste masked microcapsules [28].
- iii. Microcaps process for microencapsulation [29].
- iv. Extrusion method.
- v. Flash tab technology.
- vi. Blending with cyclodextrin [30].
- vii. Coating crystals, granules and pellets with aqueous dispersion of methacrylic acid polymers.

❖ SUPERDISINTEGRANTS:

- Superdisintegrants provides improved compressibility, compatibility and have no negative impact on the mechanical strength of formulations containing high dose drugs.
- Superdisintegrants are selected on the basis of following properties:

1. For good mouth feel small particle size is preferred in order to produce patient compliance.
2. It should have good flow property.
3. It should possess rapid disintegration.

➤ **Mechanism of action of superdisintegrants:**

Superdisintegrants acts by various mechanisms which includes:

1. Capillary action.
2. Swelling.
3. Heat of wetting.
4. Due to release of gases.
5. Enzymatic action.
6. Due to disintegrating particle/particle repulsive forces.
7. Due to deformation.
8. Chemical reaction.

➤ **Types of superdisintegrants:**

1. Natural superdisintegrants.
2. Synthetic superdisintegrants.

1) Natural superdisintegrants:

The superdisintegrants which are natural in origin and these are preferred over synthetic because they are economical, non-irritating and non-toxic in nature. There are several gums and mucilage's which have super-disintegrating activity.

➤ **Advantages of Natural Super-Disintegrants:**

- i. Biodegradable
- ii. Biocompatible and non-toxic.
- iii. Low cost.
- iv. Environmentally friendly processing.
- v. Local availability.
- vi. Patient tolerance as well as public acceptance.

➤ **Some of the FDA approved Natural Superdisintegrants:**

i. Plantago ovata seed mucilage(ispaghula)

It contains mucilage in the epidermis of the seeds. For this the seeds were soaked in water for 48hrs and then boiled for about few minutes. This was squeezed using muslin cloth. To the obtained filtrate the equal amount of acetone was added to precipitate the mucilage. The mucilage obtained was dried in oven at 50°C. When compared to synthetic superdisintegrants like Crosspovidone it showed rapid disintegration[31].

ii. Fenugreek seed mucilage:

As fenugreek seeds contains high percentage of mucilage it can be a best option to be used as natural superdisintegrants. Mucilage which means a natural gummy substance present in the coatings of seeds. These fenugreek seeds does not dissolve in water but forms a tacky mass when exposed to fluids. These seeds swells up and become slick when exposed to fluids[32].

iii. Guar gum:

Guar gum is commonly used in cosmetics, food products and also in pharmaceutical formulations. Guar gum has high molecular weight (approx. 50,000-8,000,000) polysaccharides composed of galactomannans and this is obtained from the endosperm of the seed of guar gum plant. It is also used as stabilizer, thickener and emulsifier which is approved in most areas of the world(eg.EU,USA,JAPAN and Australia)[33].

iv. Gum karaya:

Gum karaya occurs as a partially acetylated derivative. It is a dried exudation of sterculiaurenstree(family-sterculiaceae)[34].

- v. **Mango peel pectin:**
For this dried mango peel is used for extracting pectin. It is not as promising superdisintegrant as others but due to its good swelling index and solubility in biological fluids it can be used to prepare orally disintegrating tablets[35].
- vi. **Lepidium sativum mucilage:**
(family-Cruciferae)
It is widely used as herbal medicine in India. It is easily available in India and it is also economical. Parts such as leaves, roots, oil, seeds. Most widely seed are used because it contains higher amount of mucilage in it. Mucilage of it has various characteristics like binding, disintegrating, gelling etc [36,37].
- vii. **Aloe vera:**
Aloe vera belongs to the family Liliaceae. Aloe vera is also used in fast disintegrating tablets[38].
- viii. **Hibiscus Rosa sinensis linn Mucilage:**
It belongs to Malvaceae family. The dried hibiscus leaves powder is used as superdisintegrant. Extraction of mucilage can be done by maceration and precipitation by soaking the dried powder in water and then filtering to remove marc. To the filtrate equal amounts of acetone is added to precipitate the mucilage. The obtained mucilage is dried in oven at 50°C[39,40].
- ix. **Chitosan:**
Chitosan is a natural polymer obtained by deacetylation of chitin which is the second most abundant polysaccharides in nature after cellulose. It has the superdisintegrant property which can be used in fast disintegrating tablets. Chitosan engulf water when in contact with aqueous media and burst due to exerted by their capillary action thereby impart instantaneous disintegration of the dosage form and resulting in the formation of a uniform dispersion in the surrounding media leading to rapid and complete absorption of the drug[41].
- 2) **Synthetic Superdisintegrants:**
These are frequently used in tablet formulation to improve the rate and extent of tablet disintegration thereby increasing the rate of drug dissolution. The most widely used synthetic superdisintegrants are:
- Cross-linked polyvinylpyrrolidone (Crosspovidone).
 - Sodium starch glycolate.
 - Modified cellulose (Croscarmellose sodium).
 - Low substitute hydroxypropyl cellulose(L-HPC)[42].

❖ Table3: Natural polymers used in the fast dissolving tablets[43].

S.No	Natural polymer	Marketed drug	Disintegration time	Concentration used
1	Chitin and chitosan	Cinnarizine	60sec	3% w/w
2	Guar gum	Glipizide	30sec	1% w/w
3	Gum karaya	Amlodipine, Granisetron hydrochloride	17.10sec	4% w/w
4	Agar and treated agar	Theophylline	20sec	1-2% w/w
5	Fenugreek seed mucilage	Metformin hydrochloride	15.6sec	4% w/w
6	Soy polysaccharide	Lornoxicam	12sec	8% w/w
7	Gellan gum	Metronidazole	155sec	4% w/w
8	Mango peel pectin	Aceclofenac	11.59sec	0.1-4% w/w
9	Lepidium sativum mucilage	Nimesulide	17sec	5-15% w/w
10	Plantago ovata seed mucilage	Granisetron HCl	17.10sec	5% w/w

11	Aegle marmelos gum	Aceclofenac	8-18min	6% w/w
12	Locust bean gum	Nimesulide	13sec	10% w/w
13	Lepidium sativum	Nimesulide	17sec	10% w/w
14	Mangifera Indica gum	Metformin Hcl, paracetamol	3-8min	6% w/w
15	Hibiscus rosa-sinensis mucilage	Aceclofenac	20sec	6% w/w
16	Dehydrated banana powder	Ondansetron Hcl, gabapentin	15-36sec	6% w/w

➤ Current regulatory status of these Disintegrants

All these superdisintegrants are approved by US Food and Drug Administration (FDA). The FDA recognizes these polymers as GRAS (generally recognized as safe). The Gellan gum meets all the standards and the purity criteria issued in different regions of world or internationally, such as the Food Chemicals Codex and JECFA, the US Pharmacopoeia and the European Directives. So, these superdisintegrants are completely safe and can be used safely[43].

❖ Evaluation of ODT's

- 1. Hardness:** Hardness can be measured using Pfizer hardness tester. The test is performed according to IP specifications.
- 2. Thickness:** Hardness can be measured using Vernier callipers. The test is performed to IP specifications.
- 3. Friability:** Friability of the tablets can be determined using Roche friabilator and expressed in percentage (%).
- 4. Wetting time:** Wetting time of dosage form is related with the contact angle. It is another important parameter, which needs to be assessed to give an insight into the disintegration properties of the tablet. It can be done by placing the two-fold circular tissue paper on the Petri dish containing 10ml of 6.8 phosphate buffer. The time required for the fluid to reach the upper surface of the tablet was noted.
- 5. In-vitro disintegration time:** The invitro disintegration time was determined using the disintegration apparatus. One tablet was placed in each tube and this tube was immersed in the beaker containing 6.8 phosphate buffer (which correlate the pH of saliva). Time taken for complete disintegration of tablet with no palatable mass remaining in the apparatus was measured in seconds.
- 6. Dissolution test:** The dissolution methods for ODT's is identical to the conventional tablets when the ODT's does not utilize taste masking. The drugs may have dissolution conditions as in USP monograph. 0.1N HCl, pH 4.5 and pH 6.8 phosphate buffers should be used for evaluation of ODT's. USP II paddle is most common and suitable choice for dissolution test of ODT's. Since the dissolution of ODT's is very fast when using USP monograph conditions hence slow paddle speeds may be utilized to obtain comparative profile.
- 7. Weight variation:** Weight variation is done according to the IP specifications[44].

❖ Packaging of ODT's:

In Manufacturing process, Packaging is one of the most important aspect. The products which are obtained by various technologies such as Zydis, Lyoc, Quicksolv and Nanocrystal by using Lyophilization process are porous in nature, have less mechanical strength, sensitive to moisture and may degrade at higher humidity conditions. Therefore, these products require special packaging. Zydis units are generally packed in peelable backing foil. For Orasolv tablets, a special packaging unit called Paksolv is utilized, which is a dome shaped blister and prevents the vertical movement of the tablet within the depression and protects the tablets from breaking during storage and transport. Some of the tablets obtained from Durasolv, WOW tab, Pharmaburst oraquick, Zipllets technologies have sufficient mechanical strength to withstand the transport and handling shock. Hence, they are generally packaged in blisters and bottles [24].

- ❖ **Future Perspective:** As there is unremitting innovation in the pharmaceutical excipients one can expect the emerge of more novel technologies for ODT's in forthcoming days. These innovations may include modification of formulation composition and processing in order to accomplish new performance end points or may unite new technological advances with traditional pharmaceutical processing techniques to produce novel Orally disintegrating dosage forms. It is admissible to expect that future trends in innovations of drug delivery systems will continue to bring different technological disciplines to create novel technologies. It has been shown in table 4[45].

Table4: ODT's under development

Product	Manufacturer	Active Ingredient	Category
Citalopram ODT	Biovail	Citalopram	SSRIs
Metoclopramide Zydus	Salix pharmaceuticals	Metoclopramide	Dopamine receptor agonist
Reglan ODT	Schwarz Pharma	Metoclopramide	Dopamine receptor agonist
Tramadol ODT	Biovail	Tramadol	Opioid analgesic
Zolpidem ODT	Biovail	Zolpidem	Non benzodiazepine Hypnotics

Conclusion:

The ODTs have many advantages over Conventional dosage forms with the improved patient compliance, bioavailability and with rapid onset of action. ODTs formulations have good mechanical strength, quick disintegration or dissolution in mouth without water. These ODTs are most prominently beneficial for the paediatrics and geriatrics. They have substantial advantages over conventional dosage forms like they remain solid during storage which aid in stability of the dosage form and transmute into liquid form within few seconds after their administration. Thus, ODTs may be developed for most of the drugs in near future.

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