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ORALLY DISINTEGRATING TABLET: A REVIEW

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ABSTRACT

The main objective behind the orodispersible tablet formulation is patient compliance. Even there is no need of water while consuming this tablets. Due to these dosage forms fast onset is achieved as ODT is dissolved or disintegrated in oral cavity when it comes in contact with saliva. Difficulty in swallowing is problem about tablet and capsules also water is required for their intake, which may not be available while travelling. Those conventional dosage forms are difficult to administer in case of uncooperative patients, geriatric and pediatric patients. Various research fellows have used different superdisintegrats both natural, coprocessed and artificial in different proportions. This review describes in detail need of ODTs, challenges while formulating ODTs, conventional and patented technologies. It also summarises evaluation of ODTs and recent reseach work on ODTs.

INTRODUCTION

Despite many innovations in drug delivery, the oral route remains the most preferred route for the administration of therapeutic agents because of low-cost therapy, accurate dose, self-medication, ease of administration, and non-invasive methods leading to a high level of patient compliance. But in the case of geriatric patients capsules and tablets given with a glass of water may be inconvenient due to aging including hand tremors, dysphagia, hearing, and deterioration in their eyesight, memory.

Solid dosage forms also have significant administration problems in other patient groups, like mentally challenged, children, bedridden and uncooperative patients. Pediatric patients have ingestion problems because of underdeveloped nervous and muscular control.

To overcome the inconvenience faced by the patients the researchers focus on the development of feasible dosage alternatives popularly known as orally disintegrating tablets

(odts). During the past decade, the FDT (fast dissolving tablet) technology, which makes tablets dissolve or disintegrate in the mouth without additional water intake, has drawn a great deal of attention. The technology is also referred to as fast disintegrating tablet, rapid dissolve tablet, fast dispersing tablet, rapid melt tablet, orally disintegrating tablet, and quick disintegrating tablet.[1,2]

DEFINITIONS ACCORDING TO REGULATORY BODIES

US FDA

- A solid dosage form having medicaments that disintegrate rapidly when placed upon the tongue within a matter of seconds
- This tablet should weigh less than 500mg and a disintegration time of fewer than 30 seconds.

EU FDA

- Uncoated tablets should be placed in the mouth where they disintegrate rapidly before they are swallowed and should disintegrate *within3 minutes* when evaluated by the test for disintegration

Challenges In Formulating Fast Dissolving Tablets[5,6,7,8]

Like all other formulations orally disintegrating tablets also have some challenges while formulating, following table summarises challenges along with their possible solution.

Table no. 1: Challenges in formulating fast dissolving tablets.

Sr. No.	Challenge	Description	Solution
1.	Mechanical Strength	Odts must disintegrate in time less than a minute. While achieving so, maintaining good mechanical strength is a challenge. The odts must possess sufficient hardness else the chances of tablet breaking during the transit will increase	Selection of adhesive or binder in an appropriate amount
2.	Disintegration Time	Increasing the hardness will increase the disintegration time. Hence, a good balance between these two parameters is desired	Selection of super disintegrant in sufficient amount
3.	Palatability	Many drugs have an unpleasant taste and taste masking is a must for a better patient compliance	Selection of flavoring agent
4.	Hygroscopicity	Orally disintegrating tablets are hygroscopic and cannot maintain	Cellophane polyethylene laminating paper at 20 µm or 30

		physical integrity at room temperature and humidity	µm thickness and glassine papers are widely used for one-dose packaging.
5.	Amount of drug	Amount of API for lyophilized dosage forms, the dose must be less than 60 mg for soluble drugs and 400 mg for insoluble drugs	
6.	Aqueous solubility	Water-soluble drugs form eutectic mixtures, which leads to the formation of a glassy solid that may break upon drying because of loss of supporting structure during the sublimation process and freezing-point depression	Such collapse sometimes can be prevented by using various matrix-forming excipients such as mannitol that can induce crystallinity and hence, impart rigidity to the amorphous composite

Ideal Properties of Orally Disintegrating Tablets

- No residue in the mouth after oral administration
- Low sensitivity to environmental condition
- Must have sufficient strength
- Mouthfeel should be pleasant
- Insensitive to environmental conditions
- Should disintegrate within seconds
- Less effective by environmental conditions

Drugs Explored For Orally Disintegrating Tablet

There are no particular limitations as long as it is a substance that is used as a pharmaceutically active ingredient.

Analgesics and Anti-inflammatory Agents: Indomethacin, Ketoprofen, Meclofenamic Acid, mefenamic acid, Nabumetone, Naproxen, Oxaprozin, Oxyphenbutazone, Phenylbutazone, Piroxicam, Sulindac, Aloxiprin, Auranofin, Azapropazone, Benorylate, Diflunisal, Etodolac, Fenbufen, Flurbiprofen, Ibuprofen.

Anthelmintics: Cambendazole, Dichlorophen, Iverrnectin, Albendazole, Bephenium Hydroxynaphthoate, Thiabendazole, Mebendazole, Oxarnniquine, Oxfendazole, Oxantel Embonate, Praziquantel, Pyrantel Embonate.

Anti-Arrhythmic Agents: Flecainide Acetate, Amiodarone, Disopyramide, Quinidine Sulphate.

Anti-bacterial Agents: Doxycycline, Erythromycin, Ethionamide, Imipenem, nalidixic acid, Nitrofurantoin, Rifampicin, Spiramycin, Benethamine Penicillin, Cinoxacin, Ciprofloxacin,

Clarithromycin, Clofazimine, Cloxacillin, Demeclocycline Sulphabenzamide, Sulphadoxine, Sulphamerazine, Sulphafurazole, Sulphamethoxazole, Sulphapyridine, Sulphacetamide, Sulphadiazine.

Anti-coagulants: Dicoumarol, Phenindione, Dipyridamole, Nicoumalone.

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

Anti-Epileptics: Carbamazepine, Clonazepam, Methoin, Methylphenobarbitone, Oxcarbazepine, Paramethadione, Phenytoin, Phensuximide, Primidone, Sulthiame, Valproic Acid, Beclamide, Ethotoin., Methsuximide, Phenacemide, Phenobarbitone.

Anti-Fungal Agents:, Econazole Nitrate, Fluconazole, Fiucytosine,Griseofulvin, Itraconazole, Ketoconazole, Miconazole, Terbinafine, Terconazole, Amphotericin, Butoconazole Nitrate, Clotrimazole, Tioconazole, Undecenoic Acid, Natamycin, Nystatin, Sulconazole Nitrate

Anti-Gout Agents: Probenecid, Sulphinpyrazone Allopurinol.

Anti-Hypertensive Agents: Carvedilol, Darodipine, Diltiazem, Diazoxide, Felodipine, Guanabenz Acetate, Benidipine, Indoramin, Minoxidil, Nicardipine, Nifedipine, Nimodipine, Phenoxybenzamine, Prazosin, Reserpine,Amlodipine, Terazosin Isradipine.

Anti-Malarials: Chlorproguanil, Halofantrine, Mefloquine, Pyrimethamine, Quinine Sulphate Amodiaquine, Chloroquine, Proguanil.

Anti-Migraine Agents: Methysergide Maleate, Pizotifen Maleate, Dihydroergotamine Mesylate, Ergotamine Tartrate, Sumatriptan Succinate.

Anti-Muscarinic Agents: Biperiden, Ethopropazine, Hyoscyarnine, Mepenzolate Bromide, Atropine, Benzhexol, Orphenadrine, Oxyphencylcimine, Atropine, Benzhexol, Tropicamide.

Anti-Neoplastic Agents and Immunosuppressants: Amsacrine, Chlorambucil, Cyclosporin, Dacarbazine, Estramustine, Etoposide, Lomustine, Melphalan, Mercaptopurine, Methotrexate, Mitomycin, Azathioprine, Busulphan, Mitotane, Mitoxantrone, Procarbazine, Tamoxifen Citrate, Aminoglutethimide, Testolactone.

Anti -Protozoal Agents: Benznidazole, Clioquinol, Decoquinate, Diiodohydroxyquinoline, Diloxanide Furoate, Dinitolmide, Furzolidone, Metronidazole, Nimorazole, Nitrofurazone, Omidazole, Tinidazole.

Anti-Thyroid Agents: Carbimazole, Propylthiouracil.

Anxiolytic, Sedatives, Hypnotics and Neuroleptics: Barbitone,Temazepam, Bromazepam, Bromperidol, Brotizoiam, Carbromal, Chlordiazepoxide,Bentazeparn Chlormethiazole,

Chlorpromazine, Clobazam,Butobarbitone,Clotiazepam, Clozapine, Diazepam, Droperidol, Ethinamate, Flunanisone, Flunitrazepam,Fluopromazine, Flupenuiixol Decanoate, Fluphenazine Decanoate, Flurazepam, Haloperidol,Lorazepam, Lormetazepam, Medazepam, Meprobamate, Methaqualone, Midazolam,Nitrazepam, Oxazepam, Pentobarbitone, Perphenazine Pimozide, Prochlorperazine, Suipiride Thioridazine, Triazolam,Alprazolam, Amyiobarbitone, Zopiclone.

Cardiac Inotropic Agents: Digitoxin, Enoximone,Digoxin, Lanatoside C, Amrinone, Medigoxin.

Corticosteroids: Betamethasone, Budesonide, Methylprednisolone, Cortisone Acetate, Desoxymethasone, Flunisolide, Dexamethasone, Fludrocortisone Acetate, Flucortolone, Fluticasone Propionate, Hydrocortisone, Prednisolone, Prednisone, Beclomethasone, Triamcinolone.

Diuretics: Amiloride, Bendrofluazide,Metolazone, Bumetanide, Chlorothiazide, Chlorthalidone,Ethacrynic Acid, Frusemide, Spironolactone,Acetazolarnide, Triamterene.

Anti-Parkinsonian Agents: Lysuride Maleate. Gastro-Intestinal Agents: Bisacodyl, Cimetidine, Cisapride, Diphenoxylate, Ondansetron, Domperidone, Famotidine, Loperamide, Mesalazine, Nizatidine, Omeprazole, Ranitidine, Bromocriptine Mesylate, Sulphasalazine.

Histamine H 1-Receptor Antagonists: Astemizole, Cinnarizine, Flunarizine, Loratadine Cyclizine, Cyproheptadine, Dimenhydrinate, Meclozine, Oxatomide, Terfenadine, Acrivastine, Triprolidine.

Lipid Regulating Agents: Bezafibrate, Clofibrate,Fenofibrate, Gemfibrozil,Bezafibrate, Probucol.

Local Anaesthetics: Lidocaine

Anti-Anginal Agents: Glyceryl Trinitrate, Isosorbide Dinitrate, Amyl Nitrate, pentaerythritol tetranitrate.

Nutritional Agents: Betacarotene, Vitamin B 2, Vitamin A, Vitamin D, Vitamin K, Vitamin E.

Opioid Analgesics: Dextropropyoxyphene, Diamorphine, Meptazinol, Dihydrocodeine, Methadone, Nalbuphine, Morphine, Pentazocine.

Proteins, Peptides and Recombinant Drugs: Glucagon, Calcitonin And Synthetic Modifications Thereof, Growth Hormone (Somatotropin), Polypeptides or Their Derivatives, (Preferably With A Molecular Weight from 1000 To300,000), Enkephalins, Insulin (Hexameric/Dimeric/Monomeric Forms), Interferons (especially alpha-2 Interferon For Treatment Of Common Cold).

Sex Hormones: Clomiphene Citrate, Ethinyloestradiol, Medroxyprogesterone Acetate, Stiboestrol, Mestranol, Methyltestosterone, Norethisterone, Norgestrel, Oestradiol, Conjugated Oestrogens, Progesterone, Stanozolol, Testosterone, Danazol, Tibolone.

Stimulants: Dexamphetamine, fenfluramine, dexfenfluramine, mazindol, Amphetamine pemoline

TECHNIQUES FOR PREPARATION OF ODTs

A. Conventional Techniques

1. Lyophilization or Freeze-drying[2]

The process in which solvent is removed from a frozen drug solution or suspension containing structure forming excipients. The formulated tablet possesses a light and porous structure allowing rapid dissolution. The glassy amorphous porous structure of excipients, as well as the drug substance results in enhanced dissolution.

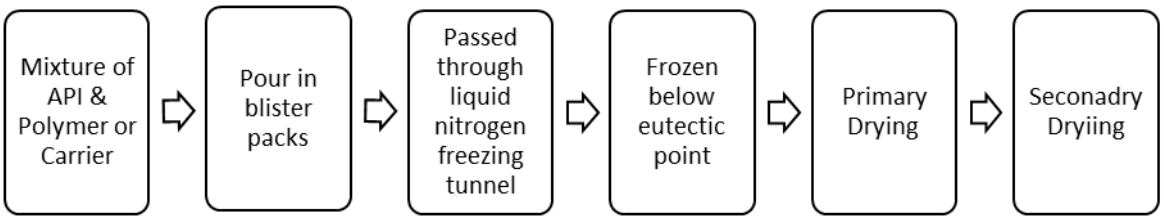

Fig. 1: Manufacture process in Freeze-drying.

Primary drying: To reduce the moisture (4% w/w of dry product).

Secondary drying: To reduce the bound moisture up to the required final volume.

2. Sublimation

The highly porous structure in the tablet matrix results in rapid disintegration of ODT. The conventional tablets containing highly water-soluble ingredients, often fail to disintegrate rapidly because of low porosity. To improve the porosity, volatile substances such as camphor can be incorporated which sublimates from the formed tablet.

Volatizing agents: Camphor, ammonium bicarbonate, naphthalene, urea, urethane, etc. The solvents like cyclohexane, benzene can be used as pore-forming agents.

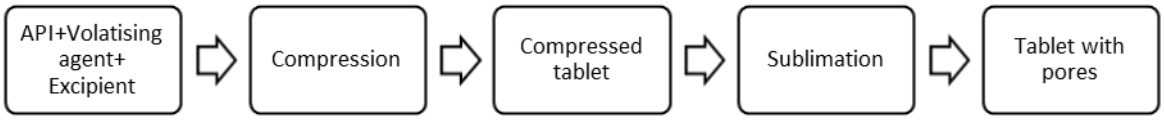

Fig. 2: Manufacture process in Sublimation.

3. Molding

Tablets are formulated using a polymer matrix. The drug can exist as discrete particles or microparticles in the prepared matrix. Tablets produced by molding are a result of solid dispersions.

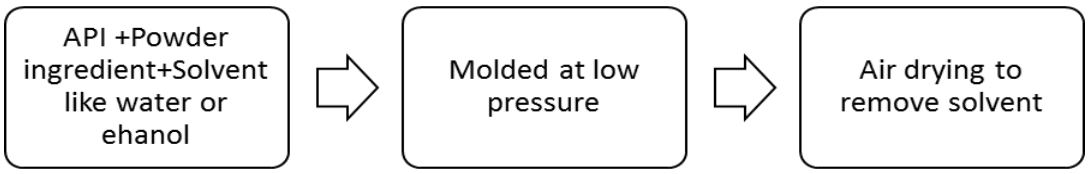

Fig. 3: Manufacture process in molding.

4. Spray Drying

Spray drying techniques produce highly porous and fine powders that dissolve rapidly. The process involves the incorporation of the following ingredients:

Table no. 2: Ingredients in the spray drying process.

Sr. No.	Ingredient	Function
1.	Hydrolysed or nonhydrolysed Gelatin	Supporting agent
2.	Mannitol	Bulking agent
3.	Sodium starch glycolate	Disintegrating agent
4.	Acidic or alkali material	Enhances dissolution and disintegration

The method is suitable to achieve immediate dissolution (<20 sec), but the approach involves high cost and more time for production. The tablet produced is of poor mechanical strength. The product formed here is the free-flowing dry powder of encapsulated liquid or coated solid.

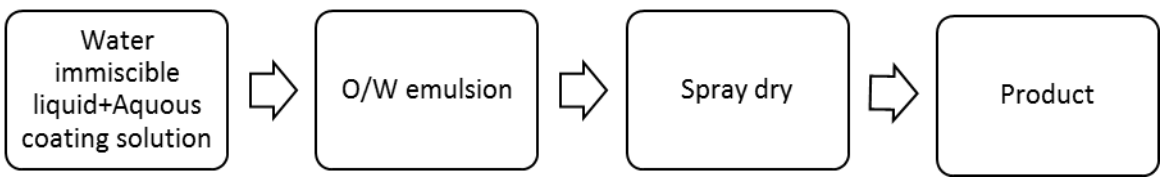

Fig. 4: manufacture process in Spray Drying.

5. Mass Extrusion

The technology involves softening the active blend using the solvent mixture of water-soluble polyethylene glycol and methanol. The softened mass is extruded through a syringe to form a cylinder and cut into even segments using the heated blade to form a tablet. The dried cylinder can also be used to coat granules for bitter drugs and thereby achieving taste masking.

6. Direct Compression

It is the easiest way to manufacture tablets. Conventional equipment, commonly available excipients, and a limited number of processing steps are involved in direct compression. Also, high doses can be accommodated and the final weight of the tablet can easily exceed that of other production methods. The disintegration and solubilization of directly compressed tablets depend on single or combined action of disintegrants, water soluble excipients and effervescent agents used.

7. Melt Granulation

Melt granulation technique is a process by which the pharmaceutical powders are capably agglomerated by a meltable binder. The benefit of this technique compared to conventional granulation is that no water or organic solvents are required. Since there is no drying step, the process is less time-consuming and requires less energy than wet granulation. It is a technique useful to enhance the dissolution rate of poorly water-soluble drugs, such as griseofulvin.

Table no. 3: Advantages and disadvantages of conventional techniques.

Technique	Advantages	Disadvantages
Lyophilization	More rapid dissolution than other available Solid products	High cost of the types of equipment & lack of Physical resistance in blister packs
Sublimation	Tablets dissolve in 10-20 sec. And exhibit Sufficient mechanical strength	
Molding	Disintegrate more rapidly And offer improved taste because the dispersion matrix is, in general, made from water-soluble sugars	Do not possess sufficient mechanical strength. Erosion & breakage occur during handling & opening of blister packages
Spray drying	Rapid disintegration of tablets.	High cost and time of production and produce tablets of very poor mechanical strength.
Mass Extrusion	To mask the bitter taste	

Patented Technologies

Over the past three decades, orally disintegrating tablets (ODTs) have gained considerable attention as a choice over conventional tablets and capsules because of better patient compliance. ODTs are solid unit dosage forms containing medicament(s) which disintegrate rapidly usually in seconds, when placed on the tongue. Products of ODT technologies entered the market in the 1980s, have grown steadily in demand, and their product pipelines are rapidly expanding. New ODT technologies address many pharmaceutical and patient needs, ranging from enhanced life-cycle management to convenient dosing for pediatric, geriatric, and psychiatric patients with dysphasia. This has encouraged both academia and industry to generate new orally disintegrating formulations and technological approaches in this field. [3] Table no contains patented technology, patent holder, the basic technology behind that patent along with available products of that technology in the market, active ingredients in that products along its indication.

Table no. 4: patented technologies.

Patented Technology	Patent Holder	Technology Basis	Active Ingredients	Available Products	oooaaaaUse
Zydus	R.P.Scherer, Inc [Cardinal Health]	Freeze-drying	Fanotidine	Pepcid®ODT	Anti-rheumatic
			Loratidine	Claritin®Reditab	Anti-histaminic
			Ondansetron	Zofran®ODT	**Anti-emetics**
			Selegiline	Zelapartm	
			Rizatriptan benzoate	Maxalt-®MLT	Anti-migraine
			Piroxicam	Feldene Fast Melt	
			Risperidone	Risperdal M-tab	Schizophrenia
			Zubrin (pet drug)	Tepoxalin	Canine NSAID
			Clonazepam	Klonopin Wafer	Sedation
			Loperamide HCl	Imodium Instant Melts	Anti-Diarrheal
Orasolv	Cima Labs Inc,	Direct compression	Mirtazapine	Remeron®soltab	
			Acetaminophen	Tempra Quicklets	Antipyretic
			Mirtazapine	Remeron soltab	Anti-depression
			Various combinations	Triaminc Softchews	Pediatriccold, cough, and allergy
Flash Dose	Biovail(Fuisz Technology, Ltd)	Cotton Candy Process	Tramadol HCl	Relivia Flashdose®	
			Fluoxetine	Fluoxetineodt	Anti-depression
			Zolpidem Tartrate	Zolpidem ODT	Sleep Disorders
			Tramadol HC	Relivia Flashdose®	Analgesics
Durasolv	Cima Labs Inc, Prographarm	Direct Compression	Zolmitriptane	Zolmig®ZMT	Anti-migignaine
			Hyoscyamine Sulfate	Nulev®	Anti-ulcer
			Baclofen	Kemstrotm	Anti-spastic analges
			Loratadine	Alavert	Anti-histaminic
Wowtab	Yamanouchi Pharma Tech, Inc		Famotidine	Gaster	Anti-ulcer
			Ramosetron HCl	Nasea ODT	Anti-emetics

			Diphenhydramine Citrate	Benadryl®Fastmelt	Anti –allergic
Flash tab	Prographarm laboratories	Direct compression	Ibuprofen	Nurofen®Flash Tab	
Oraquick	KV Pharm. Co.Inc	Micromask taste masking	Hyoscyamine sulfate	Hyoscyamine sulfate ODT	Anti-ulcer
Advatab	Eurand International, Dayton OH	Direct compression	Cetrizine	Advatab Cetrizine	
			Paracetamol	Advatab Paracetamol	
Ziplets	Eurand International, Dayton OH	Direct compression	Ibuprofen	Cibalginadue Fast	

EVALUATION OF FAST DISSOLVING TABLETS

1. Weight variation

20 tablets were selected randomly from the lot and weighted individually to check for weight variation. Weight variation specification as per I.P.

Table no. 5: weight variation specification as per I.P.

The average weight of a tablet	% deviation
80mg or less	±10
More than 80 mg but less	±7.5
250mg or more	±5

2. Content uniformity

To evaluate the content of tablet assay is performed and evaluated whether it is within limits. Normally limit is between 85-110%.

3. Hardness

The hardness of the tablet is evaluated by applying force across the diameter until it breaks. Hardness is important as it governs whether the tablet is resistant to chipping, abrasion, or breakage under the condition of storage. It is tested using a Monsanto hardness tester. The force is measured in kg and the hardness is achieved about 3-5 kg/cm2. This tablets have lower hardness compare to conventional tablets.

4. Friability test

Friability can be defined as the loss of weight of tablet in the particular container due to removal of fine particles from the surface. Friability test is performed to check the ability of the tablet to withstand abrasion in handlingpackaging and transport. Roche friabilator is used for checking the friability of the tablets.

5. Thickness

The diameter and thickness of the tablets was measured using a Micrometer screw gauge. It is expressed in mm.

6. Water absorption ratio

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 the time required for complete wetting was measured. The wetted tablet was then weighed. Water absorption ratio (R), was determined using the following equation,

$$R=10\times Wa/Wb$$

Where Wb is the weight of the tablet before water absorption and Wa is the weight of the tablet after water absorption.

7. Disintegration time

The test was carried out in apparatus specified in I.P.-1996. For this distilled water at 37°C ±, 2°C was used as a disintegration media and the time in the second taken for complete disintegration of the tablet with no palatable mass remaining in the apparatus. This test is performed on 6 tablets.

8. Wetting time

A piece of tissue paper (12 cm × 10.75 cm) folded twice was placed in a small Petri dish (ID = 9 cm) containing 6 ml pH 6.8 phosphate buffer, a tablet was placed on the paper and the time taken for complete wetting was noted. Three tablets from each formulation were randomly selected and the average wetting time was noted.

9. Dissolution test

It is a test by which the drug-release profile can be obtained. Here, both the USP dissolution test apparatus can be used. The dissolution of orodispersible tablets is very fast. So, USP 2 Paddle-type apparatus at 50-100 r/minutes is used for dissolution testing. USP Type Ilapparatus have more reproducible results compared to type l.

10. Moisture-uptake studies

This study is performed to assess the stability of the tablets. It is performed in the desiccator over calcium chloride at 37°C for 24 Hr. The tablets were then weighted and exposed to 75% relative humidity, at room temperature for 2 weeks.

One tablet as control (without super disintegrant) was kept to assess the moisture uptake due to other excipients. Tablets are weighed and the percentage increase in weight is recorded.

RECENT RESEARCH

Due to the fast release and fast action of ODTs, scientists are formulating and evaluating different drugs in these dosage forms. For this, they have tested different super disintegrants in different concentrations. The following table contains a summary of different ODTs along with super disintegrants they have used.

Croscarmellose sodium (CCS), Sodium starch glycolate (SSG), and Crosspovidone (CP)

Table 6: Summary of recent research on ODTs.

Sr. No.	Drug	Method	Result	Ingredients	Reference
1.	Diltiazem	Direct compression	Formulation C1(20 mg CCS) showed in vitro disintegration time is 09-11 seconds.	CCS, SSG	[4]
2.	Dexchlorpheniramine(fast dissolving strip)	solvent casting method	360 mg HPMC E15 as a polymer and 1 ml PEG 400 as a plasticizer, offers rapid drug release (100%) at 10 min compared to the Polaramine®	HPMC E15, HPMC K4M, and polyvinyl alcohol (PEG 400 and propylene glycol as plasticizer)	[5]
3.	Fexofenadine	Direct compression	12 % croscarmellose sodium and 14.66 % lactose had the least disintegration time of 32.33 ± 3.23 s	SSG, CCS, Gellan gum	[6]
4.	Metoprolol	Direct compression	4% Moringa gum and 2% SSG, the drug release was found to be 97% within 2 min.	CP, SSG, and CCS were processed with natural disintegrants Moringa gum	[7]
5.	Levocetirizine	Direct compression	SSG (6%) and CP (4.5%) were more effective in enhancing the rate of drug release.	SSG, CCS, CP,	[8]
6.	Donepezil	Wet granulation	high concentration of CP and mixture as the best formulation	HPMC, CCS, CP	[9]
7.	Simvastatin	Solvent dispersion method	Pharmaburst® 500 was better than Ludiflash® concerning dissolution parameters.	Ludiflash®, Pharmaburst® 500, Mannitol (granular), CP.	[10]
8.	Lacosamide	Direct compression method	98% of drug release at the end of 30 min and disintegration time was found to be 25 sec.	dehydrated banana powder (DBP) and Ocimum sanctum powder	[11]
9.	Nifedipine	Direct compression	C1 containing 20 mg CCS have better results.	CCS, lactose	[12]
10.	Nimodipine	Direct compression	superdisintegrants 5 mg, mannitol 30 mg and MCC 61 mg has shown disintegration time of 21 seconds along with 100%	CP, SSG, Co-process (SSG+CP)	[13]

			drug release within 45 min.		
11.	Dabigatran	Direct compression	Tablet containing SSG have better results.	SSG, CP, CCS	[1]
12.	Ibuprofen	Direct compression	The rate of drug release is interfered with by the nature and amount of drug and polymer.	SSG, CP, CCS	[14]
13.	Atenolol	Direct compression	20 mg CCS has better results than its lower conc.	CCS, SSG, Starch DC	[15]
14.	Metaprolol	Direct compression	As the level of super disintegrating agent decreased the drug release rates were found to be increased, a formulation containing CCS as super disintegrant is fulfilling all the parameters satisfactorily.	SSG, CP, CCS	[16]
15.	Aripiprazole	Direct compression	Kyron T-154 possesses a disintegration time of 15 sec, water absorption ratio (77.5 %), and wetting time (22.7 sec) with taste masking property at low concentration.	Kyron T-104, Kyron T-154, and Kyron T-314.	[17]
16.	Aceclofenac	Direct compression	SSG and CCS (1:4) showed disintegration in 18sec and better release up to 66% in 50min.	SSG, CCS.	[18]
17.	Clonazepam	Direct compression	SSG+CCS containing formulation have max. release and stability.	SSG, CP, CCS	[19]
18.	Atorvastatin	Direct compression	Higher conc. of β-cyclodextrin, Hibiscus Rosa- Senesis Mucilage have better results	β-cyclodextrin, Hibiscus Rosa-Senesis Mucilage Microcrystalline cellulose Mannitol	[20]
19.	Tiemonium methylsulfate	Ion exchange resin complexation technique	HPMC can be used as a taste masking agent	MCC, Aspartame (5%) Talc (2%) Povidone K30 (3%) (granules treated with HPMC and alcohol)	[21]

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