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A REVIEW ON MOUTH DISSOLVING TABLET TECHNIQUES

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ABSTRACT

The objective of this paper was to review the information about mouth dissolving tablets prepared by solid dispersion technique. Mouth dissolving tablets are being increasingly recognized in the market because of their potential benefits over conventional tablets. Solid dispersion is an innovative technique to improve solubility of drug moieties with low solubility profile. Formulation of solid dispersion as mouth dissolving tablet not only improves dissolution characteristics of drug but also provides ease of administration and quicker action. Various techniques used for the preparation of mouth dissolving tablet and solid dispersion are described in this article. Furthermore, the various characterization parameters used for mouth dissolving tablets formulated by solid dispersion technique are discussed.

KEY WORDS: Mouth dissolving tablets, solid dispersion, characterization, advantages.

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INTRODUCTION

There has been exploration of different routes for administration of therapeutic moiety. But, amongst the various routes the oral route is preferred route for drug administration, so about 50% of pharmaceuticals are administered orally. Tablet is the most widely preferred oral solid dosage form. But one-third of the world population mainly the geriatric and pediatric patient experience difficulty in swallowing and do not take medicines as prescribed resulting in patient incompliance and in-effective therapy. For such patients mouth dissolving tablets (MDTs) have emerged as an alternative which is potentially safer and convenient as compared to conventional tablets and capsules[1]. A solid dosage form that dissolves or disintegrates rapidly in oral cavity, resulting in solution or suspension without the need of water is known as MDT. These are newer types of tablets that disintegrate/dissolve/disperse in saliva within few seconds. MDT was introduced in 1980s since then they have gained popularity in market with increased consumer acceptance and their product pipeline is expanding continuously[2]. Various terminologies used to describe an MDT by various researchers and inventor companies are melt in mouth tablet (MMT); fast-melting tablet (FMT); fast-dissolving/ disintegrating tablet (FDT); orally disintegrating tablet (ODT); rapidly disintegrating tablet (RDT); and orodispersible tablet (OT)[3]. The US Food and Drug Administration's (USFDA) Center for Drug Evaluation and Research developed the following definition for an MDT as a new dosage form in 1998: "A solid dosage form containing medicinal substances, which disintegrates rapidly, usually within a matter of seconds, when placed upon the tongue"[4].

MDT can also be formulated for its local action or for its absorption from buccal and oesophageal mucosa. In such cases first pass metabolism is avoided and consequently increasing of bioavailability of drug and reducing undesirable metabolites[1].

NEED TO DEVELOP MOUTH DISSOLVING TABLET

Need of patients

MDT aims to develop non-invasive delivery systems that can be used for patients having swallowing problems like in case of geriatrics and pediatrics patients and those who prefer readily administered dosage form.

Need of industry

The current needs of industry to provide improved solubility, stability, bioavailability enhancement, along with safety and compliance.

Need of market

Up to 2008, 18 crucial products with sales of more than $ 37 bn have lost their patent protection. By 2010, three hundred drugs are going to lose patent as the patent of a drug entity comes near to end, it becomes necessary to formulate it into new and improved form and to extend market exclusion [5, 3].

CHARACTERISTICS OF MDT

MDTs are required to disintegrate, disperse or dissolve in saliva without the need of water. An ideal MDT should fulfill following criteria[6].

a) It should not require water for oral administration.
b) It should be insensitive to environmental conditions such as humidity and temperature.
c) It should not leave any residue in the mouth after disintegration.
d) It should have sufficient hardness to withstand the rigors during manufacturing processes and post manufacturing handling.
e) It should be adaptable to current processing and packaging machinery.
f) It should allow high drug loading.
g) It should have pleasant mouth feel.
h) It should be cost effective.

ADVANTAGES OF MDTS

They have the twofold advantage of both liquid pharmaceutical forms and conventional tablets, i.e. ease of administration and swallowing, and precision of dosage. The benefits of MDTs can be illustrated as follows[7, 8].

a. Administration to the patients who can not swallow, such as the elderly, stroke victims, bedridden patients, patients affected by renal failure & patients who refuse to swallow such as pediatric, geriatric & psychiatric patients.
b. Achieve increased bioavailability/rapid absorption through pregastric absorption of drugs from mouth, pharynx & oesophagus as saliva passes down.
c. Rapid drug therapy intervention.
d. Convenient for administration and provides patient compliance for disabled, bedridden patients and for travelers and busy people, who do not always have access to water.
e. Good mouth feel property helps to change the perception of medication as bitter pill particularly in pediatric patients. The risk of chocking or suffocation during oral administration of conventional formulations due to physical obstruction is avoided, thus providing improved safety.
f. New business opportunity like product differentiation, product promotion, patent extension and life cycle management.

CHALLENGES TO DEVELOP MDTS

Along with this various challenges encountered during development of MDT are as follows:

Rapid disintegration

MDT is required to disintegrate rapidly in matter of seconds.

Taste and mouth feel characteristics

Approved Sweeteners and flavors are typically included to achieve a palatable formulation, but additional taste masking strategies may also be required such as ion exchange resin and active pharmaceutical ingredient encapsulation.

Avoid increase in size

The tablet size of the MDT need to be monitored and is kept small to maintain the characteristic of rapid disintegration.

Sufficient mechanical strength

Another challenge is to have sufficient mechanical strength the MDTs are potentially less robust than conventional oral solid dosage forms, to achieve rapid disintegration.

Good package design

Packaging requirements need to be considered early in the development process to protect MDTs from moisture and other environmental hazards[4].

FORMULATION ASPECTS IN DEVELOPING MDTS

The MDTs formed vary in various properties[9] such as,

Taste and mouth feel

MDTs should have good taste and mouth feel property without feeling of grittiness. Taste of nauseous drugs can be improved by use of flavors and sweeteners, complexation with ion-exchange resin and Microencapsulation of drug with suitable polymer.

Mechanical strength of tablets

MDTs should have appropriate mechanical strength to withstand the handling and transportation.

Drug dissolution in saliva

The drug should get solubilization in saliva so that, it can cross the mucosal lining and finally reach to the systemic circulation.

Swallowability

MDTs should have good swallowability as it is for those patients who have swallowing problem.

Bioavailability

Those drugs which have low bioavailability are good candidates to formulate MDTs because of bypass of first metabolism, no degradation of drug by gastric juice and enzymes present in gastro-intestinal (GI) tract.

Stability

Another factor of consideration is stability of drug in the formulation with the excipient used and process opted for formulation.

MDTS VS OTHER DOSAGE FORMS

MDT offer advantage over other dosage forms such as effervescent tablets, dry syrups, chewing gums or chewable tablets[10], which are commonly used to enhance patient compliance.

The conventional tablets are often difficult to swallow and therefore cause hanging effect in throat whereas MDTs have no such effect as it gets dissolved in the oral cavity, when placed on tongue.

Administering effervescent tablets or granules and dry syrups involves intake of water.

Elderly patients cannot chew large pieces of gum or tablets. Even sometimes bitter or unpleasant taste of the drug in the dosage form results, if the taste-masking coating ruptures during mastication.

Though MDT has so many advantages over conventional oral solid dosage form but it has some short comings. Manufacturing of MDT requires either expensive processing technique producing fragile tablets that requires costly specialized packaging or the use of conventional tabletting procedures which give longer disintegration time than desired which still requires specialized packaging.

POTENTIAL CANDIDATES FOR MDT

Drugs from various categories are used as candidate for MDT and as such there no specific limitation as long as it is used as active pharmaceutical ingredient (API). The ideal characteristics of a drug to be used as a candidate for MDT includes,

a. stable in water and saliva,
b. potential drugs requiring lower dose less than 20 mg,
c. small to moderate molecular weight,
d. partially non-ionized at the oral cavities pH,
e. able to diffuse and partition into the epithelium of the upper GI tract, and
f. able to permeate oral mucosal tissue.

Whereas the drug which have short biological half-life, requiring frequent dosing, having very bitter taste and those requiring controlled or sustained release are not acceptable as vital candidates[11]. The potential candidates for MDT are listed in Table 1.

EXCIPIENTS USED FOR MDTS

For selection of excipients a thorough understanding of chemistry of excipients is necessary so as to avoid any interaction of active principle with the excipients. The ingredients used are of food grade and helps to impart desired organoleptic properties and product efficacy. Following are the excipients used for preparation of MDT:

Super Disintegrates

Superdisintegrant primarily affects the rate of disintegration, when used at high levels it can also affect mouth feel, tablet hardness, and friability. Factors such as disintegration, compatibility, mouth feel and flow are considered for selecting a superdisintegrant. Depending on the level and characteristics of the API and the desired release profile, the levels of superdisintegrant used can be 10–20 wt % of the formulation, and it can be higher or lower in some cases[12]. Examples of superdisintegrants include crospovidone, microcrystalline cellulose, sodium starch glycolate, sodium carboxy methyl cellulose, pregelatinzed starch, calcium carboxy methyl cellulose, and modified corn starch.

Binders

Proper selection of a binder or combination of binders is essential to maintain integrity and stability of the tablet and to achieve desired sensory and melting characteristics. Binding agents may be liquid, semi-solid, and solid or mixtures of varying molecular weights i.e. Polyethylene glycol. Fats such as cocoa butter and hydrogenated vegetable oils can also be used.

Bulking Agents

It improves the textural characteristic that in turn enhances disintegration in mouth. Recommended bulking agents for this delivery system should be more sugar-based such as mannitol, polydextrose, lactitol and starch hydrolysate for higher aqueous solubility and good sensory perception. Lactitol in particular has high aqueous solubility and good sensory perception. The examples of bulking agents include calcium carbonate, magnesium carbonate, calcium phosphate, calcium sulfate, pregelatinzed starch, magnesium trisilicate, and aluminium hydroxide. Bulking agents are added in the range of 10% to about 90 % by weight of the final composition.

Lubricants

It assists in making tablets palatable and provides quicker disintegration. It removes grittiness and assists in drug transport mechanism from mouth down to stomach. Examples of lubricants include stearic acid, magnesium stearate, zinc stearate, calcium stearates, talc, polyethylene glycol, liquid paraffin, magnesium lauryl sulfate, and colloidal silicon dioxide.

Flavors & Sweeteners

Flavors 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. Both

natural and synthetic flavors can be used to improve the organoleptic characteristic of fast-melting tablets. Examples include peppermint oil, clove oil, bay oil, anise oil, eucalyptus oil, thyme oil, and oil of bitter almonds. Flavoring agents include vanilla, citrus oils and fruit essences. A wide range of sweeteners are available including sugar, dextrose and fructose, as well as non-nutritive sweeteners such as aspartame, sugar alcohols and sucralose. The addition of sweeteners contributes a pleasant taste as well as bulk to the composition[13, 11].

VARIOUS APPROACHES FOR PREPARATION OF MDTS

Following are the approaches applied to manufacture MDTs:

Disintegrant Addition

Disintegrant addition technique is one popular technique for formulating fast-dissolving tablets because of its easy implementation and cost-effectiveness. The basic principle involved in formulating fast-dissolving tablets by disintegrant addition technique is addition of superdisintegrants in optimum concentration so as to achieve rapid disintegration along with the good mouth feel. Examples of superdisintegrants include Avicel PH 102, Avicel PH-M06, Crospovidone, Croscarmellose sodium etc[14, 15, 16].

Molding

In this method, molded tablets are prepared by using water-soluble ingredients so that the tablets dissolve completely and rapidly. The powder blend is moistened with a hydro-alcoholic solvent and is molded into tablets under pressure lower than that used in conventional tablet compression. The solvent is then removed by air-drying. These possess porous structure that enhances dissolution. Molded tablets can also be prepared by heat molding process, which involves setting of molten mass that contains a dispersed drug. Molding technology results in tablets with an appropriate dissolution time, even though they are characterized by poor mechanical properties[10].

Sublimation

Inert solid ingredients that sublime readily (e.g. urea, ammonium bicarbonate, hexamethylene tetramine, camphor etc.) were added to the other tablet ingredients and the mixture is compressed into tablets. The volatile materials were then removed via sublimation, which generates porous structures. Additionally, several solvents (e.g. cyclohexane, benzene) can be also used as pore forming agents. Mane *et al.*[17] formulated the highly porous MDTs of Domperidone, by using meltable binder polyethylene glycol-4000, a diluent mannitol and a subliming agent camphor/ ammonium carbonate.

Mass-Extrusion

This technology involves softening the active blend using the solvent mixture of water-soluble polyethylene glycol, methanol and expulsion of softened mass through the extruder or syringe to get a cylinder of the product into even segments using heated blade to form tablets. Dandag *et al.*[18] prepared fast disintegrating domperidone tablets by using sodium starch glycolate, Eudragit E-100, low substituted hydroxypropylcellulose (HPC) and lactose.

Direct Compression

It is the easiest way to manufacture tablets. Directly compressed tablet's disintegration and solubilization depends on single or combined action of disintegrants, water-soluble excipients and effervescent agent. Schiermeier and Schmidt[19] used direct compression to prepare rapidly dispersing tablets containing ibuprofen while seeking to minimize gastric irritation of the drug and to improve palatability. Direct compression involves a reduced number of operations and has a relatively low cost; however, the active principle and the excipients are often in high concentrations. So, water-soluble and/or effervescent disintegrants must be used. Koizumi *et al.*[20] developed meclizine tablet direct compression method using mannitol and camphor, which resulted in tablets with high porosity and dissolves rapidly in saliva. These compressed tablets which have high porosity (approximately 30%) rapidly dissolved within 15 s in saliva in the mouth. Gilis *et al.*[21] prepared fast-dissolving tablet of galanthamine hydrobromide for oral administration in the ratio (1:1) with a pharmaceutically acceptable carrier, which comprises of spray-dried mixture of lactose monohydrate and microcrystalline cellulose (75:25) as a diluents, and a disintegrant; by using direct compression method.

Bi *et al.*[22] and Watanabe *et al.*[23] used microcrystalline cellulose (MCC) and low substituted HPC to manufacture rapidly disintegrating tablets in the ratios of MCC to HPC, 8:2 to 9:1.

Cotton Candy Process

This process utilizes a unique spinning mechanism to produce floss-like crystalline structure, which mimic cotton candy. Cotton candy process involves formation of matrix of polysaccharides or saccharides by simultaneous action of flash melting and spinning. The matrix formed is partially recrystallized to have improved flow properties and compressibility. This candy floss matrix is then milled and blended with active ingredients and excipients and subsequently compressed to MDT. This process can accommodate high doses of drug and offers improved mechanical strength. However, high-process temperature limits the use of this process[24].

Some marketed preparations of mouth dissolving tablets available in Indian and international market are given in **Table 2 and 3**, respectively.

EVALUATION OF MDT

MDT are subjected to all the parameters as that for conventional tablets such as general characteristics, uniformity of weight, drug content of tablets, hardness, friability (limits are bound within limits 0.1-0.9 %). But along with it certain specific evaluation parameters for MDT are performed which are as follows:

Modified Disintegration Time

The time for disintegration of MDTs is generally less than three minute and actual disintegration time that patient can experience ranges from 15-90 seconds. The standard procedure of performing disintegration test for these dosage forms has several limitations and they do not suffice the measurement of very short disintegration times. The disintegration time for mouth dissolves tablet needs to be modified as disintegration is required without water, thus the test should mimic disintegration in salivary contents. For this purpose, a petridish (10 cm diameter) was filled with 10 ml of water. The tablet was carefully put in the center of petridish and the time for the tablet to completely disintegrate into fine particles was noted[25].

Wetting Time

Wetting time of the MDT is another important parameter, which needs to be assessed to give an insight into the disintegration properties of the tablets; a lower wetting time implies a quicker disintegration of the tablet. The wetting time of the tablets can be measured using a simple procedure. Five circular tissue papers of 10 cm diameter were placed in a petridish with 10 cm diameter and 10 ml of water was filled into the petridish. A tablet was carefully placed on the surface of the tissue paper. The time required for water to reach upper surface of the tablet was noted as a wetting time[25].

Absorption Ratio

For measuring water absorption ratio the weight of the tablet before keeping in the petridish is noted (W_b).The wetted tablet from the petridish is taken and reweighed (W_a). The water absorption ratio, R can be then determined according to the following equation:

$$R = 100(W_a - W_b)/W_b$$

***In Vitro* Dispersion Time**

In vitro dispersion time is measured by dropping a tablet in a beaker containing 50 ml of Sorrenson's buffer pH 6.8 and *in vitro* dispersion time is determined.

***In Vivo* Disintegration Time**

The time required for complete disintegration of a tablet in the oral cavity is determined by administering the formulation to 10 healthy volunteers at an interval of 24-h.

Dissolution Study

The dissolution study is performed by use of USP II (Paddle speed of 50 rpm) apparatus which is most suitable for MDT. USP monographs dissolution conditions should be followed in addition 0.1 N HCl, pH 4.5 and 6.8 buffers should be evaluated for orally disintegrating tablets[11].

***In Vivo* Oral Absorption Test**

Each formulation is administered to 10 healthy volunteers (21-25 years old), and the tablet is to be kept in oral cavity till disintegration. The subjects are then required to rinse their mouth with an aliquot of distilled water. The rinsed water is then subjected to quantitative assay as prescribed for the drug in official books. The amount of drug absorbed through oral mucosa is calculated by subtracting the remaining amount of drug from initial concentration[26].

Stability Study

The stability studies for MDTs are carried out as prescribed by ICH Q1A guidelines for accelerated studies; the tablets were stored at 40±1°C/75% ± 5% RH for 4 weeks. The tablets were withdrawn afterwards and analyzed for the physical characterization (visual defects, hardness, friability, disintegration, dissolution etc.) and drug content.

MARKET POTENTIAL OF MDT

The market of MDT is promising. Recent market survey indicates that more than half of the patient prefers MDT to other dosage forms and in near future most of the consumers will ask their doctors for MDT purchase MDT or prefer MDT to regular tablets, capsules or liquids. The global market for MDT in the year 2004 was estimated as $ 2.4 billion, which was increased to $ 3.0 billion in the year 2006 and would surely increase in coming future because of its rapid acceptance by consumers and pharmaceutical companies[4]. The Zydis MDTs operational in 2007 and commercial production from the site is anticipated in 2009 pending associated regulatory filings. In August 2007, Catalent reported that ALK-Abelló will fund a new production line for current and future tablet-based allergy products at Catalent's Swindon facility. Commercial production on the new line is expected to begin in 2010. The market success of MDTs is evident from the fact that about 50 products are formulated in this dosage form for various purposes as schizophrenia, migraine, nausea, pain, allergies, Parkinson's disease, Alzheimer's disease, diarrhea, hypertension, anxiety and erectile dysfunction[3].

CONCLUSION

In today's market world consumer satisfaction is most important consideration and industries are trying continuously to achieve this objective. About one-third of the World's population mainly contributed by pediatric and geriatric patient faces the problem of swallowing and for them MDT has came out to be as an alternative which not only provides ease of administration but rapid action, low dose and decrease in side effects too. So, it is a patient oriented dosage form.

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Table 1: Potential Candidates for MDT

S. No.	Category	Drugs as candidate
1.	Analgesics and Anti-inflammatory Agents	Aloxiprin, Auranofin, Azapropazone, Benorilate, Diflunisal, Etodolac, Fenbufen, Fenoprofen, Flurbiprofen, Ibuprofen, Indomethacin, Ketoprofen, Meclofenamic Acid, Mefenamic Acid, Nabumetone, Naproxen, Oxaprozin, Oxyphenbutazone, Phenylbutazone, Piroxicam, Sulindac.
2.	Anthelmintics	Albendazole, Bephenium hydroxynaphthoate, Cambendazole, Dichlorophen, Ivermectin, Mebendazole, Oxarnniquine, Oxfendazole, Oxantel embonate, Praziquantel, Pyrantel embonate, Thiabendazole.
3.	Anti-Arrhythmic Agents	Amiodarone, Disopyramide, Flecainide Acetate, Quinidine Sulphate
4.	Anti-bacterial Agents	Benethamine Penicillin, Cinoxacin, Ciprofloxacin, Clarithromycin, Clofazimine, Cloxacillin, Demeclocycline, Doxycycline, Erythromycin, Ethionamide, Imipenem, Nalidixic Acid, Nitrofurantoin, Rifampicin, Spiramycin, Sulphabenzamide, Sulphadoxine, Sulphamerazine, Sulphacetamide, Sulphadiazine, Sulphafurazole,

		Sulphamethoxazole, Sulphapyridine, Tetracycline.
5.	Anti-coagulants	Dicoumarol, Dipyridamole, Nicoumalone, Phenindione.
6.	Anti-Depressants	Amoxapine, Ciclazindol, Maprotiline, Mianserin, Nortriptyline, Trazodone, Trimipramine Maleate, Acetohexamide
7.	Anti-Epileptics	Beclamide, Carbamazepine, Clonazepam, Ethotoin, Methoin, Methsuximide, Methylphenobarbitone, Oxcarbazepine, Paramethadione, Phenacemide, Phenobarbitone, Phenytoin, Phensuximide, Primidone, Sulthiame, Valproic Acid.
8.	Anti-Fungal Agents	Amphotericin, Butoconazole nitrate, Clotrimazole, Econazole Nitrate, Fluconazole, Flucytosine, Griseofulvin, Itraconazole, Ketoconazole, Miconazole, Natamycin, Nystatin, Sulconazole nitrate, Terbinafine, Terconazole, Tioconazole, Undecenoic Acid
9.	Anti-Gout Agents	Allopurinol, Probenecid, Sulphinpyrazone
10.	Anti-Hypertensive Agents	Amlodipine, Carvedilol, Benidipine, Darodipine, Diltiazem, Diazoxide, Felodipine, Guanabenz Acetate, Indoramin, Isradipine, Minoxidil, Nicardipine, Nifedipine, Nimodipine, Phenoxybenzamine, Prazosin, Reserpine, Terazosin
11.	Anti-Malarials	Amodiaquine, Chloroquine, Chlorproguanil, Halofantrine, Mefloquine, Proguanil, Pyrimethamine, Quinine Sulphate.
12.	Anti- Migraine Agents	Dihydroergotamine Mesylate, Ergotamine Tartrate, Methysergide Maleate, Pizotifen Maleate, Sumatriptan
13.	Anti-Muscarinic Agents	Atropine, Benzhexol, Biperiden, Ethopropazine, Hyoscine Butyl Bromide, Hyoscyarnine, Mepenzolate Bromide, Orphenadrine, Oxyphenonium, Tropicamide.
14.	Anti-Neoplastic Agents and Immuno-suppressants	Aminoglutethimide, Amsacrine, Azathioprine, Busulphan, Chlorambucil, Cyclosporin, Dacarbazine, Estramustine, Etoposide, Lomustine, Melphalan, Mercaptopurine, Methotrexate, Mitomycin, Mitotane, Mitozantrone, Procarbazine, Tamoxifen Citrate.
15.	Anti Protozoal Agents	Benznidazole, Clioquinol, Decoquinate, Diiodohydroxyquinoline, Diloxanide Furoate, Dinitolmide, Furzolidone, Metronidazole, Nimorazole, Nitrofurazone, Omidazole, Tinidazole.
16.	Anti-Thyroid Agents	Carbimazole, Propylthiouracil.
17.	Anxiolytic, Sedatives, Hypnotics And Neuroleptics	Alprazolam, Amylobarbitone, Barbitone, Bentazepam, Bromazepam, Bromperidol, Brotizolam, Butobarbitone, Carbromal, Chlordiazepoxide, Chlormethiazole, Chlorpromazine, Clobazam, Clotiazepam, Clozapine, Diazepam, Droperidol, Ethinamate, Flunanisone, Flunitrazepam, Fluopromazine, Flupentixol Decanoate, Fluphenazine Decanoate, Flurazepam, Haloperidol, Lorazepam, Lormetazepam, Meprobamate, Methaqualone, Midazolam, Nitrazepam, Oxazepam, Pentobarbitone, Perphenazine Pimozide, Prochlorperazine, Suipiride, Temazepam, Thioridazine.
18.	B-$_2$ blockers	Acebutolol, Alprenolol, Atenolol, Labetalol, Metoptolol, Nadolol, Oxprenolol, Pindolol, Propranolol
19.	Cardiac Inotropic Agents	Amiodarone, Digitoxin, Digoxin, Enoximone, Lanatoside C.
20.	Corticosteroids	Beclomethasone, Betamethasone, Budesonide, Cortisone Acetate, Desoxymethasone, Dexamethasone, Fludrocortisone Acetate, Flunisolide, Flucortolone, Fluticasone Propionate, Hydrocortisone, Methylprednisolone, Prednisolone, Prednisone, Triamcinolone.
21.	Diuretics	Acetazolamide, Amiloride, Bendrofluazide, Bumetanide, Chlorothiazide, Chlorthalidone, Ethacrynic Acid, Frusemide.
22.	Enzymes	All the Enzymes
23.	Anti-Parkinsonian Agents	Bromocriptine Mesylate, Lysuride Maleate.
24.	Gastro-Intestinal Agents	Bisacodyl, Cimetidine, Cisapride, Diphenoxylate, Domperidone, Famotidine, Loperamide, Mesalazine, Nizatidine, Omeprazole, Ondansetron, Ranitidine, Sulphasalazine.

25.	Histamine H,-Receptor Antagonists	Acrivastine, Astemizole, Cinnarizine, Cyclizine, Cyproheptadine, Dimenhydrinate, Flunarizine, Loratadine, Meclozine, Oxatomide.
26.	Lipid Regulating Agents	Bezafibrate, Clofibrate,Fenofibrate, Gemfibrozil, Probucol.
27.	Local Anaesthetics	Lidocaine
28.	Neuro -Muscular Agents	Pyridostigmine
29.	Nitrates And Other Anti-Anginal Agents	Amyl Nitrate, Glyceryl Trinitrate, Isosorbide Dinitrate, Isosorbide Mononitrate, Pentaerythritol Tetranitrate
30.	Nutritional Agents	Betacarotene, Vitamin A, Vitamin B_2 , Vitamin D, Vitamin E, Vitamin K
31.	Opioid Analgesics	Codeine, Dextropropyoxyphene, Diamorphine, Dihydrocodeine, Meptazinol, Methadone, Morphine, Nalbuphine, Pentazocine
32.	Oral Vaccines	Influenza, Tuberculosis, Meningitis, Hepatitis, Whooping Cough, Polio, Tetanus, Diphtheria, Malaria, Cholera, Herpes, Typhoid, HIV, Aids, Measles, Lyme Disease, Travellers Diarrhea, Hepatitis A, B and C, Otitis Media, Dengue Fever, Rabies, Parainfluenza, Rubella, Yellow Fever, Dysentery, Legionnaires Disease, Toxoplasmosis, Q-Fever, Haemorrhegic Fever, Argentina Haemorrhagic Fever, Caries, Chagas Disease, Urinary Tract Infection caused By E.Coli, Pneumoccoccal Disease, Mumps, Chikungunya.
33.	Proteins, Peptides and Recombinant Drugs	Insulin (Hexameric/Dimeric/Monomeric forms), Glucagon, Growth Hormone (Somatotropin), Polypeptides or their derivatives, (preferably with molecular weight from 1000 to 300,000), Calcitonins and Synthetic modifications thereof, enkephalins, Interferons (especially α-2 interferon for treatment of common colds).
34.	Sex Hormones	Clomiphene Citrate, Danazol, Ethinyloestradiol, Medroxyprogesterone Acetate, Mestranol, Methyltestosterone, Norethisterone, Norgestrel, Oestradiol, Conjugated Oestrogens, Progesterone, Stanozolol, Stilboestrol, Testosterone, Tibolone

Table 2: Mouth Dissolving Tablets Available In Indian Market

Brand name	Active ingredient	Company
Domray MD	Domperidone	Ray Remedies Mumbai.
Velrid MD	Domperidone	Shreyam Health care Mumbai.
Vomidon	Domperidone	Olcare Lab Rajkot.
Zotacet MD	Cetrizine HCl	Zota Pharma Surat
Olenex Instab	Olanzepine	Ranbaxy Laboratories New Delhi
Manza RDT	Olanzepine	Mano Pharma Chennai.
Romilast	Montelukast	Ranbaxy Laboratories New Delhi
Torrox MT	Rofecoxib	Torrent Pharma Ahmedabad
Ziflam	Rofecoxib	Kopran Pharma, Mumbai
Doloroff	Rofecoxib	Indoco Remedies Mumbai
Rofaday MT	Rofecoxib	Lupin Labs Mumbai
Dolib MD	Rofecoxib	Panacaea Biotech Ltd New Delhi
Orthoref MD	Rofecoxib	Biochem Pharma Pvt. Ltd. Mumbai
Rbcox-25 MD	Rofecoxib	Shalman Pharma, Vadodara.
Roffec MD	Rofecoxib	Excare Lab, Surendranagar, Guj.
Roftab MD	Rofecoxib	Olcare Lab Rajkot.
Zofex-25 MD	Rofecoxib	Zota Pharma Surat.
Valus	Valdecoxib	Glenmark Pharma. Ltd. Mumbai
Nency MD	Nimesulide	Zenon Health care, Ahmedabad
Nexus MD	Nimesulide	Lexus Organics, Ahmedabad
Nimex MD	Nimesulide	Zota Pharma Surat
Nisure-MD	Nimesulide	Panacea Biotech Ltd, New Delhi
Olnim –MD	Nimesulide	Olcare Lab Rajkot
Sulbid	Nimesulide	Alpic remedies Ahemedabad
Nimpain MD	Nimesulide	Prompt Cure Pharma N. Delhi
Mosid MD	Mosapride	Torrent Pharma. Ltd. Ahmedabad

Table 3: Orally Disintegrating Tablet Products Available In International Market

Brand name	Active ingredient	Company
Zomig ZMT and Repimelt	Zolmitriptan	Astra Zeneca London UK
Alavert	Loratadine	Wyeth Consumer Health New York
Cibalginadue Fast	Ibuprofen	Novartis Consumer Health Switezerland
Hyoscyamine Sulphate ODT	Hyoscyamine Sulphate	Ethex Corporation France
Nulev	Hyoscyamine Sulphate	Schwarz Pharma Monheim Germany
Nurofen Flash Tab	Ibuprofen	Boots Health care Sanghai China
Kemstro	Baclofen	Schwarz Pharma Monheim Germany
Fluoxetine ODT	Fluoxetine	Bioavail Pharma. Canada
Benadryl Fastmelt	Diphenhydramine	Pfizer Ltd. New York
Zolpidem ODT	Zolpidem tartrate	Bioavail Pharma. Canada
Nasea ODT	Ramosetoron	Yamanouchi Tokyo, Japan
Ralivia Flash Dose	Tramadol HCl	Bioavail Pharma. Canada
Gaster D	Famotidine	Yamanouchi Tokyo, Japan
Excedrin Quick Tabs	Acetaaminophen	Bristol-Myers Squibb New York
Claritin RediTabs	Loratidine	Sching Corporation NJ, USA
Remeron SolTab	Mirtazepine	Organon Inc. USA
Feldene Melt	Piroxicam	Pfizer Ltd. NJ, USA
Tempra Quicklet –tempra Firs Tabs	Acetaminophen	Bristol-Myers Squibb New York
Maxalt-MLT	Rizatriptan benzoate	Merck Ltd. NJ, USA
Propulsid Quicksolv	Cisapride monohydrate	Janssen Pharma. Belgium
Pepcid ODT	Famotidine	Merck Ltd. NJ, USA
Imodium instant melts	Loperamide HCl	Janssen Pharma. Belgium
Zyprexa	Olanzapine	Eli Lilly and company, USA
Childrens Dimetapp ND	Loratadine	Wyeth ConsumerHealth care New York
Zofran ODT	Ondansetron	Glaxo Smith Kline UK
Klonopin Wafers	Clonaxepam	Roche Pharma, NJ USA
Risperidal M-Tab	Risperidone	Janssen Pharma. Belgium
Zelapar	Selegiline	Elan/Amarin Corporation London,UK
Zubrin (Pet drug)	Tepoxaline	Schering Corporation Geneva USA
Aricept ODT	Donepzil HCl	Eisai and Pfizer New York
Fazalco	Clonazapine	Alamo Pharmaceuticals NJ USA
Permax	Pergolide	Amarin Corporation London, UK
Febrectol	Paracetamol	Prographarm Thymerais France
Benadryl Fast melt	Diphenhydramine and Pseudoephedrine	Warner Lambert NJ USA