Mouth Dissolving Tablets: An innovative deviation in drug delivery system

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Abstract
The main aim of novel drug delivery system is to develop a dosage form which is easy to administer, free from side effects, exhibit immediate release and offer enhanced bioavailability for better patient compliance. To achieve such results oral drug delivery system, preferably, tablets are the most widely accepted dosage forms which offer numerous advantages. Beside those advantages, Dysphagia is the most common disadvantage of conventional tablets which is associated with number of conditions like sudden exposure of allergies, mental disability, motion sickness, unconsciousness, unavailability of water etc. To get rid from these problems several innovative drug delivery systems have been developed like Mouth Dissolving Tablets (MDT’s) which dissolve in saliva within a few seconds, when put on tongue. These tablets can be administered anywhere and anytime, without the need of water and are thus quite suitable for children, elderly and mentally disabled patients.

Keywords: Mouth Dissolving Tablets, Manufacturing techniques, patented technologies.

INTRODUCTION
Drug Delivery Systems (DDS) are a unit strategic tool for increasing markets/indications, extending product life cycles and generating opportunities. It build a major contribution to international pharmaceutical sales through market segmentation which is continuously move on and also scientists acquired a better understanding of the physicochemical and biochemical parameters related to their performance. Despite of incredible advancements in drug delivery, the oral route is considered to be the perfect route for the administration of therapeutic agents because of low cost of therapy, easily administered, accurate dosage, self-medication, non invasive leading to high levels of patient compliance. Tablets and Capsules are the widely used oral dosage forms.

But one important drawback of such dosage forms is ‘Dysphagia’ which means difficulty in swallowing. This is seen to bother nearly 35% of the general population and is also associated with a number of conditions like:

a. Parkinsonism
b. Motion sickness
c. Unconsciousness
d. Elderly patients
e. Children
f. Mentally disabled persons
g. Unavailability of water.

Improved patient compliance is demanded in this modern era. Therefore demand for the new technologies is also increasing. To develop a chemical entity, there is need of lot of money, hard work and sufficient time. So focus is rather being laid on the development of new drug delivery systems for already existing medication, with enhanced efficacy and bioavailability, reducing the dose and dosing frequency to minimize the side effects.

It is always the desire of a scientist or a dosage form designer to augment the safety of a drug molecule while maintaining its therapeutic efficacy. Recent advances in Novel Drug Delivery Systems (NDDS) wish for the same by formulating a dosage form, which is easy to be administered so as to achieve better patient compliance. Researchers have put in their best efforts to develop a Fast Dissolving Drug Delivery System i.e. Mouth Dissolving Tablet. These are also called melt in mouth tablets, repremels, porous tablets, oro-dispersible, quick dissolving or rapid disintegrating tablets, fast dissolving, rapid dissolve, fast Absorption system, Orosolv, Zydis etc. Most fast delivery system films must include taste masking substances which masks the taste of the active ingredient which is then swallowed by the patient along with the soluble and insoluble excipients.

Mouth dissolving tablet (MDT)
These dosage forms rapidly disintegrate and dissolve to release the drug when they come in contact with saliva, thus there is no need of water during administration, an attribute that makes them highly suitable for pediatric and geriatric patients. A mouth dissolving tablet dissolves in the oral cavity within 15 s to 3 min and mainly contains certain super disintegrants.

Ideal properties of MDT
Mouth Dissolving Tablet should:

a. Easily dissolve or disintegrate in salivary fluid within a few seconds.
b. Have a gratifying taste.
c. Leave negligible or no residue in the mouth when administered.
d. Be portable and easy to transport.
e. Manufacturing procedure is simple and within low budget.
f. exhibit low sensitivity to environmental conditions like temperature, humidity etc.

MDT Advantages of MDT

a. Do not require water to swallow the tablet.
b. It can be easily administered to pediatric, elderly and mentally disabled patients.
c. Accurate dosing as compared to liquids.
d. Rapid onset of action as dissolution and absorption of drug is fast.
e. Advantageous over liquid medication in terms of administration as well as transportation.
f. First pass metabolism is reduced, thus offering improved bioavailability and thus reduced dose and side effects.
g. Free of risk of suffocation due to physical obstruction when swallowed, thus offering improved safety.
h. Suitable for sustained/controlled release actives.10
i. Allows high drug loading.11

![Fig. 1: Advantages of MDT](image)

**Limitations of Mouth Dissolving Tablets:**
a. Mechanical strength of final product.
b. Drug and dosage form stability.
c. Mouth feel.
d. The tablets may leave unpleasant taste or grittiness in mouth if not formulated properly.
e. Dissolution rate of formulated drug in saliva.
f. Swallow ability.
g. Rate of absorption of drug from the saliva fluids.
h. Overall bioavailability.
i. Decreased saliva production leads to dryness of mouth which may not be good candidates for these tablet formulations.

**FORMULATION OF MDTs:** 12,13,14,15

**Drug:** The ideal characteristics of a drug for dissolution in the mouth and pre gastric absorption from MDTs include:
a. Free from bitter taste.
b. Dose lower than 20 mg.
c. Small to Moderate molecular weight.
d. Good solubility in saliva.
e. Ability to permeate through oral mucosal tissue.

**Bulking materials:** Bulking materials are significant in the formulation of mouth dissolving tablets. These improve the textural characteristics that successively enhance the disintegration in the mouth, besides this adding bulk material also reduces the concentration of the active material in the composition. The suggested bulking agents for this delivery system ought be more sugar-based such as mannitol, polydextrose, lactitol, DCL (direct compressible lactose) and starch hydrolystate for higher aqueous solubility and good sensory perception. From these Mannitol in particular has high aqueous solubility and good sensory perception. Bulking agents are incorporated in the range 10 percent to 90 percent by weight of the final composition.

**Emulsifying agents:** Emulsifying agents are important excipients for formulating these tablets, they aid in rapid disintegration and drug release without chewing, swallowing or drinking water. Incorporating emulsifying agents is useful tool in stabilizing the immiscible blends and enhancing bioavailability. A wide range of emulsifiers are present for fast-tablet formulation, including alkyl sulfates, propylene glycol esters, lecithin, sucrose esters and others. These agents are added in the range of 0.05 percent to about 15 percent by weight of the final composition.

**Lubricants:** Lubricants, although not an essential excipient, but can make these tablets more palatable after they disintegrate in the mouth. Lubricants remove grittiness and assist in the drug transport mechanism from the mouth down into the stomach e.g. Magnesium Stearate.

**Flavours and sweeteners:** Flavours and taste-masking agents make the products more appetizing for patients. These are added to overcome bitterness and undesirable tastes of some active ingredients. Both natural and synthetic flavours can be used to boost the organoleptic characteristic of these tablets. Formulators can choose a wide range of sweetening agents including sugar, dextrose and fructose, as well as non-nutritive sweeteners such as aspartame, sodium saccharin, sugar alcohols and sucralose.

The addition of these agents contributes a pleasant taste as well as bulk to the composition.

**Superdisintegrants:** Use of disintegrants is the basic approach in development of MDTs. Disintegrants play a vital role in the disintegration and dissolution of MDT. It is essential to choose a suitable disintegrant in a suitable concentration so as to ensure fast disintegration and high dissolution rates.16 The quick action is due to combined effect of swelling and water absorption by the formulation. Due to swelling of superdisintegrants, the wetted surface of the carrier increases, this promotes the wettability and dispersibility of the system, thus enhancing the disintegration and dissolution.17, 18 The desired concentration of the superdisintegrant can be selected according to critical concentration of disintegrant. Below this concentration, the tablet disintegration time is inversely proportional to the concentration of the superdisintegrant, whereas if concentration of superdisintegrant is above critical concentration, the disintegration time remains almost constant or even increases.

Sodium starch glycolate, croscarmellose sodium, Crospovidone, Microcrystalline cellulose, Pregelatinised starch are some of examples of disintegrants.

**Mechanism of action of disintegrants:** 19, 20

The tablet breaks to primary particles by one or more of the mechanisms listed below:
a. By capillary action
b. By swelling
c. Because of heat of wetting
d. Due to release of gases
e. By enzymatic action
f. Due to disintegrating particle/particle repulsive forces
g. Due to deformation

**a. Porosity and capillary action (Wicking)**

Disintegration by capillary action is always the first step. When we put the tablet into suitable aqueous medium, the medium penetrates into the tablet and replaces the air adsorbed on the particles, which weakens the intermolecular bond and breaks the tablet into fine particles. Water uptake by tablet depends upon
hydrophilicity of the drug /excipient and on tableting conditions.
For these types of disintegrants, maintenance of porous structure and low interfacial tension towards aqueous fluid is necessary which helps in disintegration by creating a hydrophilic network around the drug particles.

b. Swelling
The most widely accepted general mechanism of action for tablet disintegration is swelling. Tablets with high porosity show poor disintegration due to lack of adequate swelling force. On the other hand, sufficient swelling force is exerted in the tablet with low porosity. It is worthwhile to note that if the packing fraction is very high, fluid is unable to penetrate in the tablet and disintegration is again slows down.

c. Because of heat of wetting (air expansion)
When disintegrants with exothermic properties gets wetted, localized stress is generated due to capillary air expansion, which helps in disintegration of tablet. This explanation, however, is limited to only a few types of disintegrants and cannot describe the action of most modern disintegrating agents.

d. Due to release of gases
Carbon dioxide released within tablets on wetting due to interaction between bicarbonate and carbonate with citric acid or tartaric acid.
The tablet disintegrates due to generation of pressure within the tablet. This effervescent mixture is used when pharmacist needs to formulate very rapidly dissolving tablets or fast disintegrating tablet. As these disintegrants are highly sensitive to small changes in humidity level and temperature, strict control of environment is required during manufacturing of the tablets. The effervescent blend is either added immediately prior to compression or can be added in to two separate fraction of formulation.

e. By enzymatic reaction
Here, enzymes present in the body act as disintegrants. These enzymes destroy the binding action of binder and helps in disintegration.
Actually due to swelling, pressure exerted in the outer direction or radial direction, it causes tablet to burst or the accelerated absorption of water leading to an enormous increase in the volume of granules to promote disintegration.

f. Due to disintegrating particle/particle repulsive forces
Another mechanism of disintegrants attempts to explain the swelling of tablet is made with non swellable disintegrants. Guyot-Hermann has proposed a particle repulsion theory based on the observation that non swelling particle also cause disintegration of tablets. The electric repulsive forces between particles are the mechanism of disintegration and water is required for it.
Researchers found that repulsion is secondary to wicking.

g. Due to deformation
During tablet compression, disintegrated particles get deformed and these deformed particles get into their normal structure when they come in contact with aqueous media or water. Occasionally, the swelling capacity of starch was improved when granules were extensively deformed during compression. This increase in size of the deformed particles produces a breakup of the tablet.

Fig.2: Disintegration of Tablet by Wicking and Swelling

Fig. 3: Disintegration by Deformation and Repulsion

Approaches for preparation of MDTs:
Various technologies used in the manufacture of Mouth Dissolving Tablets include:
a. Freeze-drying or lyophilization
b. Sublimation
c. Spray drying
d. Moulding
e. Mass extrusion
f. Direct compression

Patented Technologies for Mouth Dissolving Tablets
a. Zydis Technology
b. Durasolv Technology
c. Orasolv Technology
d. Flash Dose Technology
e. Wowtab Technology
f. Flashtab Technology
g. Nanocrystal Technology

Freeze drying:
The tablets formulated by freeze-drying or lyophilization are very porous in nature and disintegrate or dissolve fastly when come in contact with saliva. This process involved the sublimation of water from product after freezing. First of all, the product is frozen to bring it below its eutectic point. Then primary drying is carried out to minimize the
moisture to around 4% w/w of dry product. Finally, secondary drying is done to decrease the bound moisture to the required volume. Due to lyophilization, bulking agent and sometimes drug gain glossy amorphous structure and thus dissolution is enhanced. A tablet that rapidly disintegrates in aqueous solution comprises of a partially collapsed matrix network that has been vacuum dried above the collapsed temperature of the matrix. The matrix is dried partially below its equilibrium freezing point. Vacuum drying the tablet above its collapse temperature, instead of freeze drying below its collapse temperature provides a process for producing tablets with enhanced structural integrity, while rapidly disintegrating in normal amounts of saliva.

However this technique is not widely employed because of high cost of equipment and processing. Lack of physical resistance in standard blister packs is another vital disadvantage.

**Sublimation:**
In this process there is addition of inert volatile substances like urea, urethane, naphthalene, camphor, etc to other excipients and then compression of blend into tablet. Removal of volatile material by sublimation creates pores in tablet structure, due to which tablet solubilizes when comes in contact with saliva. Additionally several solvents like cyclohexane, benzene etc may also be used as pore forming agents. Highly porous structure and good mechanical strength MDTs have been developed by this method.

**Spray drying:**
A highly porous and fine powder is prepared by spray drying an aqueous composition containing support matrix and other components. This is then mixed with active ingredient and compressed into tablet. Allen and Wang used this technique to prepare mouth-dissolving tablets, which disintegrated within 20 s.

**Moulding:**
In this technology, water-soluble ingredients are used so that tablet disintegrate and dissolve rapidly. The powder blend is firstly moistened with a hydro alcoholic solvent and is molded in to tablet using compression pressure which must be lower than used in conventional tablets compression. The solvent is then removed by air-drying. Molded tablets have a porous structure that increases dissolution. Less mechanical strength and poor taste masking are the two major problems with molding. However, by using binding agents such as sucrose, acacia or poly vinyl pyrrolidone can increase the mechanical strength of the tablet.

Various moulding techniques which can be used to prepare mouth-dissolving tablets are as under:

a. Compression moulding: The powder mixture wetted with a solvent like ethanol/water previously is compressed into mould plates to form a wetted mass.

b. Heat moulding: A molten matrix in which drug is dissolved or dispersed can be directly moulded into Mouth dissolving tablets.

c. No vacuum lyophilization: This process involves evaporation of solvent from a drug solution or suspension at a standard pressure.

**Mass extrusion:**
In this technique, a blend of active drug and other ingredients is softened using solvent mixture of water soluble polyethylene glycol, methanol and then the softened mass is extruded through the extruder or syringe to get a cylinder of product, which is finally cut into even segments with the help of heated blades to get tablets. The dried cylinder can be used to coat the granules of bitter tasting drugs.

**Direct compression:**
This is the most preferred technique for the formulation of MDTs due to certain advantages:

a. High doses can be accommodated and final weight of the tablet can exceed that of other methods.

b. Easy way to formulate the tablets.

c. Standard equipments and commonly available excipients are used.

d. A few numbers of processing steps are involved.

e. Cost-effectiveness.

In this method, tablets are compressed directly from the mixture of the drug and excipients without any preliminary treatment. The mixture to be compressed must have adequate flow properties and binds under pressure. Type of disintegrant and its proportion in formulation are of prime importance. The other factors which might be considered are particle size distribution, contact angle, pore size distribution, tablet hardness and water absorption capacity. This technology is cost effective and easy to implement at industrial level.
Patented Technologies for preparation of MDT: 29, 30

Following are some commercially useful technologies for MDTs are:

**Zydis technology**

Zydis is a unique freeze-dried oral solid dosage form that can be swallowed without water as it dissolves instantly on tongue in less than 5 seconds. The drug is physically trapped in a soluble matrix, and then freeze-dried to produce a product that rapidly dissolves. The matrix contains water soluble saccharides and polymer (gelatin, dextran, alginates) to provide quick dissolution and to allow adequate physical strength to withstand handling. Water is utilize during the process to produce porous units for rapid disintegration. Various gums are used to eliminate the sedimentation problem of dispersed drugs. Glycine is employed to prevent the shrinkage of zydis unit throughout the process and in long-term storage. As the zydis dosage form is fragile in physical strength, unit is contained in peelable blister pack, which permits removal of product without damaging it.

**Orasolv technology:**

CIMA labs have developed Orasolv technology. The system essentially makes tablets that contain taste masked active ingredients and effervescent disintegrating agent which on contact with saliva, rapidly disintegrates and releases the taste mask active ingredient. The tablets made by direct compression at very small compression force in order to minimize oral dissolution time. The tablets so produced are soft and friable and are packaged specially designed pick and place system. The taste masking related with Orasolv formulation is two folds. The unpleasant flavour of a drug is not merely prevented by sweeteners or flavours; coating the drug powder and effervescence are means of taste masking in Orasolv.

**Durasolv technology:**

Durasolv is CIMA’s second generation fast dissolving tablet formulation. Produced in a similar fashion to that of Orasolv, Durasolv has much higher mechanical strength than its predecessor due to the use of higher compaction produced during tabletting. The Durasolv product is thus formulated in a faster and more cost effective manner. One disadvantage of Durasolv is that the technology is not suitable for larger doses of active ingredients, because formulation is subjected to high pressures on compaction.

**Wowtab technology:**

Yamanuchi pharmaceutical company patented this technology. ‘wow’ means ‘without water’. The active ingredients may contain up to 50% w/w of the tablet. In this technique, saccharides of both low and high mouldability are used to prepare the granules. Mouldability is the capacity of a compound to be compressed. Highly mouldable substance has high compressibility and thus shows slow dissolution. The combination of high and low mouldability is used to produce tablets of adequate hardness. Active ingredients are mixed with low mouldability saccharides and then granulated with high mouldability saccharides and then compressed into tablet. The Wowtab product dissolves quickly in 15 s or less. Wowtab product can be packed in both into conventional bottle and blister packs.

**FlashDose Technology:**

Fuisz has patented the FlashDose technology. The FlashDose technology utilizes a special spinning mechanism to produce floss like crystalline structure, much like cotton candy. This crystalline sugar can then incorporate the active drug and be compressed into a tablet. FlashDose tablet consists of self-binding Shearform matrix termed “floss”. The procedure has been patented by Fuisz and known as “Shearform”. By changing the temperature and other conditions during production, the characteristics of the product can be altered greatly. Instead of floss-like material, small spheres of saccharide can be produced to carry the drug. The procedure of making microspheres has been patented by Fuisz and known as “Ceform”.

**FlashTab technology:**

Prographarm labs have a patent over this technology. In this technique, microgranules of the taste-masked active drug are used. These may be prepared by using conventional techniques like coacervation, microencapsulation, and extrusion-spheronisation. All these processes utilize conventional tabletting technology. These taste-masked micro crystals of active drug, disintegrating agent, a swelling agent and other excipients like soluble diluents etc are compressed to form a multiparticulate tablet that disintegrates rapidly.

**Nanocrystal technology:**

For MDT, Elan's proprietary Nanocrystal technology will modify formulation and improve compound activity and final product characteristics. Decreasing particle size will increases the surface area, which results in increase in dissolution rate. This can be fulfill predictably and efficiently using Nanocrystal technology. NanoCrystal particles are small particles of drug substance, typically less than 1000 nanometers (nm) in diameter, which are produced by milling the drug substance using a proprietary wet milling technique. The resultant product is remarkably vigorous, but yet dissolves in very small quantities of water in seconds. This approach is especially interesting when working with highly potent or hazardous materials because it avoids manufacturing operations (e.g., granulation, blending, and tableting) that generate large quantities of aerosolized powder and present much higher risk of exposure. The freeze-drying approach also enables small quantities of drug to be converted into Orodispersable dosage forms because manufacturing losses are negligible.

**EVALUATION PARAMETERS:**

31, 32, 33

**Weight variation test:** Take 20 tablets randomly and their individual weights & the average weight is determined. The deviation of each individual tablet from that of the average weight is calculated and compared with the standard values given in Pharmacopoeia. The % weight variation of each individual tablet is calculated by the given formula:

\[
\% \text{Weight Variation} = \frac{\text{Individual weight of each tablet} - \text{Average weight of 20 tablets}}{\text{Average weight of 20 tablets}} \times 100
\]
**Hardness test:** Hardness of the tablets was measured by using hardness testers like Monsanto hardness tester, Pfizer hardness tester etc. The pressure need to break the tablets is measured as a function of hardness (kg/ cm²). The values obtained must meet the standard that is in the range of 4.0 to 4.2 kg/cm².

**Friability:** Friability is to measure the extent of tablet breakage during physical stress conditions like Packing, transportation etc. 6 tablets selected randomly is evaluated for friability using Roche friabilator at 25 rpm for 4 minutes. The % weight loss is calculated by measuring the total weight of 6 tablets before and after operation. Formula for calculating the % weight loss is given below:

\[
\% \text{ Weight loss} = \left( \frac{\text{Total weight of tablets before test} - \text{Total weight of tablets after test}}{\text{Total weight of tablets before test}} \right) \times 100
\]

**Friability**

**Wetting time:** Wetting time and water absorption ratio are the significant parameters for mouth dissolving tablets. The following method is employed for calculating the wetting time of the tablet. A piece of filter paper (circularly cut) is placed in a Petri plate containing water soluble dye solution. Testing tablet is placed on that paper and the time required for complete wetting of the tablet is determined.

\[
\text{Wetting time} = T_f - T_a
\]

Fig 6: Wetting time of Mouth dissolving tablet. The time taken for appearance of dye colour on tablet is wetting time.

**Water absorption ratio:** Similar to the procedure followed in determination of wetting time. However, here the initial weight and the final weight (after complete wetting) of tablet is calculated and the water absorption ratio is calculated by given formula:

\[
R = \frac{W_a - W_b}{W_b} \times 100
\]

Where, R is water absorption ratio, Wa and Wb are the weights of tablet before and after wetting respectively.

\[
\text{Water Absorption Ratio } (R) = \left( \frac{(W_a - W_b) \times 100}{W_b} \right)
\]

Fig 7: Calculation of water absorption ratio for MDTs. Difference between initial and final weights of tablet is noted Water absorption.

**Disintegration time:** Disintegration time for randomly selected 6 tablets is measured using disintegration test apparatus. The resulting disintegration time is calculated and compared with standards.

**In vitro dissolution studies:** Randomly selected 6 tablets is subjected to drug release studies using USP dissolution apparatus, in dissolution medium volume of 900 ml is used and a temperature of 37±0.5°C will be maintained. 5 ml of the sample is collected in every 5 minutes interval and replace with same quantity of buffer solution for 30 minutes. The samples are then filtered and suitably diluted and the drug assay is performed using UV spectrophotometer or HPLC system. The results are then compared with standard values.

**Taste or mouth feel:** Healthy human volunteers are used for evaluation of mouth feel of the tablet. One tablet is evaluated for its mouth feel. A panel of 5 members evaluates the mouth feel by time intensity method. Sample equivalent to 40 mg is placed in mouth for 10 seconds and the opinion is rated by giving different score values. (0: good, 1: tasteless, 2: slightly bitter, 3: bitter, 4: awful).

**Stability studies:** Various stability studies like accelerated stability study, intermediate and long term stability studies are done during preformulation. The sample is subjected to higher temperature or humidity or both, to know their impact on the stability of mouth dissolving tablet.

**Uniformity of dispersion:** Randomly selected 2 tablets are kept in 100 ml water and stirred for two minutes. The dispersion is passed through 22 meshes. If no residue remains on the screen then the tablets pass the test.

**Drugs to be promising in corporate in Mouth dissolving tablets:** There are no particular limitations as long as it is a substance which is used as a pharmaceutical active ingredient. Analgesics and Anti-inflammatory Agents: Aloxiprin, Auranofin, Azapropazone, Benorylate, Diflunisal, Etodolac, Fenbufen, Fenoprofen Calcium, Flurbiprofen, Ibuprofen, Indomethacin, Ketoprofen, Meclofenamic Acid, Mefenamic Acid, Nalidixic Acid, Norfloxacin, Oxyphenbutazone, Phenylbutazone, Piroxicam, Sulindac.

Antihelmintics: Albendazole, Bephenium Hydroxynaphthoate, Cambendazole, Dichlorophen, Ivermectin, Mebendazole, Oxamnique, Oxfendazole, Oxantel Embonate, Praziquantel, Pyrantel Embonate, Thiabendazole.


**Anti-Gout Agents:** Allopurinol, Probencid and Sulphinpyrazone.

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

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

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

**Anti-Neoplastic Agents and Immunosuppressant:** Aminoglutethimide, Amsacrine, Azathioprine, Busulfan, Chlorambucil, Cyclosporin, Dacarbazine, Estramustine, Etosside, Lomustine, Melphalan, Mercaptopurine, Methotrexate, Mitomycin, Mitotane, Mitozantrone, Procarbazine, Tamoxifen Citrate, Testolactone.

**Anti-Thyroid Agents:** Carbimazole, Propylthiouracil.

**Nutritional Agents:** Betacarotene, Vitamin A, Vitamin B2, Vitamin D, Vitamin E, Vitamin K.

**Proteins, Peptides and Recombinant Drugs:** Insulin (Hexamer/Dimeric/Monomeric Forms), Glucagon, Growth Hormone (Somatotropin), Polypeptides or Their Derivatives, (Preferably With a Molecular Weight from 1000 to 300,000), Calcitonins and Synthetic Modifications, Enoxaparin, Interferons (Especially Alpha-2 Interferon for Treatment of Common Colds).

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

**CONCLUSION:**

Mouth dissolving tablets are innovative dosage forms developed and specially designed to overcome some of the problems that seen in conventional solid dosage form i.e. difficulty in swallowing of the tablet in geriatric and pediatric patients. Fast dissolving tablets are designed to dissolve or disintegrate quickly in the saliva generally within less than 60 seconds (range of 5-60 seconds). Fast dissolving tablets have better patient compliance and acceptance may improve biopharmaceutical properties, bioavailability improved efficacy, convenience, and better safety compared with conventional oral dosage forms. The popularity of MDTs has increased fabulously over the last decade. MDTs need to be formulated for psychotic patients, bedridden, geriatric, pediatric patients, for those patients who may not have access to water, patients who are busy in traveling. MDTs formulations formulated by some of these conventional and patent technologies and MDTs have sufficient mechanical strength, quick disintegration/dissolution in the buccal cavity without water. The newer technologies utilized for the formulation of the MDTs that provide more effective dosage forms with more advantages and minimal disadvantages. st dissolving tablets are innovative dosage forms developed and specially designed to overcome some of the problems that seen in conventional solid dosage form i.e. difficulty in swallowing of the tablet in geriatric and pediatric patients. Fast dissolving tablets are designed to dissolve or disintegrate quickly in the saliva generally within less than 60 seconds (range of 5-60 seconds). Fast dissolving tablets have better patient compliance and acceptance may improve biopharmaceutical properties, bioavailability improved efficacy, convenience, and better safety compared with conventional oral dosage forms. The popularity of MDTs has increased fabulously over the last decade. MDTs need to be formulated for psychotic patients, bedridden, geriatric, pediatric patients, for those patients who may not have access to water, patients who are busy in traveling. MDTs formulations formulated by some of these conventional and patent technologies and MDTs have sufficient mechanical strength, quick disintegration/dissolution in the buccal cavity without water. The newer technologies utilized for the formulation of the MDTs that provide more effective
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