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A Comprehensive Review on immediate release Tablet

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ABSTRACT

Among all the dosage forms immediate release tablets is one of the mostly widely using dosage forms, especially for children's because of their nervous system and muscular system is not well developed as compare to adults. and in case of adult patients who is suffering from Parkinson's disorder or hand tremors. Few solid dosage forms like capsules and tablets are present days facing the problems like difficulty in swallowing (dysphagia), resulting in many incidences of non-compliance and making the therapy ineffective. Most preferred route of administration for various drugs are oral dosageforms and oral route having certain limitations like first-pass metabolism, psychiatric patients, bedridden and uncooperative patients.IDTs are dissolving quickly in saliva without any need of water. Iimediatrly dissolving tablets are dissolved in salivain very less time span which is less than 60 sec., and that are real immediately - dissolving tablets.IDTs formulations contain super disintegrants to increase the disintegration rate of a tablet in the buccal cavity.IDTs have advantages such as they are easily manufactured,having accurate dose, good chemical and physical stability and an ideal alternative for children and adult patients.IDTs have quick disintegration rate, absorb faster so, in vitro drug release time improve and this property of drugs (dosage form) increase bioavailability.IDT formulations have the certain merits of both conventional tablet formulation and liquid dosage form. There are several technologies that are spray drying, cotton candy process, sublimation, melt granulation, direct compression freezes drying/lyophilization, phase transition process, mass extrusion, etc. have been developed for manufacturing of IDTs. This review contain brief information about IDTs including definition, advantages, needs or requirements of IDTs, salient features of IDTs, limitations, different challenges to developing IDT, marketed formulations of Immediate tablets, etc.

KEYWORDS : immediate release tablets, Super-disintegrants, Mouth dissolving tablets.

I. INTRODUCTION:

Formulation of drugs into a presentable form is the basic requirement and need of today. The dosage form is a mean of drug delivery system,used for the application of the drug to a living body. Various type of dosage forms are available such as tablets, syrups, suspensions, suppositories, injections, transdermal and patches having a different type of drug delivery mechanisms. These classical/ modern dosage forms have some advantages and disadvantages. Therefore, the development of an ideal drug delivery system is a big challenge to the pharmacist in the presence scenario. In order to get the required effect, the drug should be delivered to its site of action at such concentration and rate to achieve the highest therapeutic effect and lower adverse effect. For the development of a suitable dosage form a thorough study about the physicochemical principles that governs a specific formulation of a drug should be subjected [1].

Oral routes of drug administration have wide acceptability of up to 5060% of total dosage forms. Solid dosage forms are popular because of their easy route of administration, accurate dosage, self-medication, pain avoidance and most important factor and that is the patient compliance. The most popular using solid dosage forms are being capsules and tablets; and having one of the most important drawback of this dosage forms for some patients is their difficulty to swallow. Swallowing of oral dosage forms is mostly done by the drinkingwater. Sometimes people are not able to swallowing conventional dosage forms such as tablet when water is not available, in the case of the motion sickness (kinetosis) and sudden episodes of coughing during the common cold, allergic condition and bronchitis. For these reason, tablets that can rapidly dissolve or disintegrate in the oral cavity have attracted a great deal of attention [2].The problem of swallowing is a common phenomenon in a geriatric patient due to fear of choking, hand tremors, dysphasia and in young individuals due to

underdeveloped muscular and nervous systems and in schizophrenic patients which leads to poor patient compliance. Near about one-third of the population (mainly childrens and adults) has swallowing problems, which results in poor compliance with oral tablet drug therapy which leads to reduced overall therapy effectiveness. Due to this reason, tablets that can rapidly dissolve or disintegrate in the oral cavity have attracted a great deal of attention [3].

United States Food and Drug Administration (USFDA) describe Immediate tablet (FDT) as "a solid dosage form containing a medicinal substance or active ingredient which dissolves rapidly usually within a time of seconds when placed upon the tongue" [3].Immediate drug delivery systems were firstly developed in the late 1970s as an alternative to conventional dosage forms for the paediatric and geriatric patient. These tablets are dissolve or disintegrate rapidly in the saliva generally less than time span of 60 seconds [5]. To deliver these medical needs, pharmaceutical technicians have developed a novel oral dosage forms known as orally disintegrating (dispersible) tablets (ODTs) or Fast disintegrating (dissolving) tablets (IDTs) or mouth melting tablets (MMTs) or mouth dissolving tablets(MDTs),rapid release tablets which disintegrate rapidly in saliva, usually in a time span of seconds,without the need to take water.

Recently market study was conductedand its indicate that more than half of the patient population prefersIDTs over the other dosage forms. We can formulate mouth dissolving tablets mainly by two techniques first use of super disintegrants like Croscarmellose sodium, sodium starch glycolate and crospovidone. Another method is maximising pore structure of the tablets which is done by freeze drying and vacuum drying [5]. In amongst methods, direct compression is mostly used because of its effortlessness, quick procedure and cost-effectiveness [1].There is increase in bioavailability of some drugs may be due to absorption of drugs in oral cavity and also due to pregastric absorption of saliva containing dispersed drugs that pass down into the stomach. Moreover, the amount of drug that is subjected to first pass metabolism is reduced as compared to standard tablets [5].

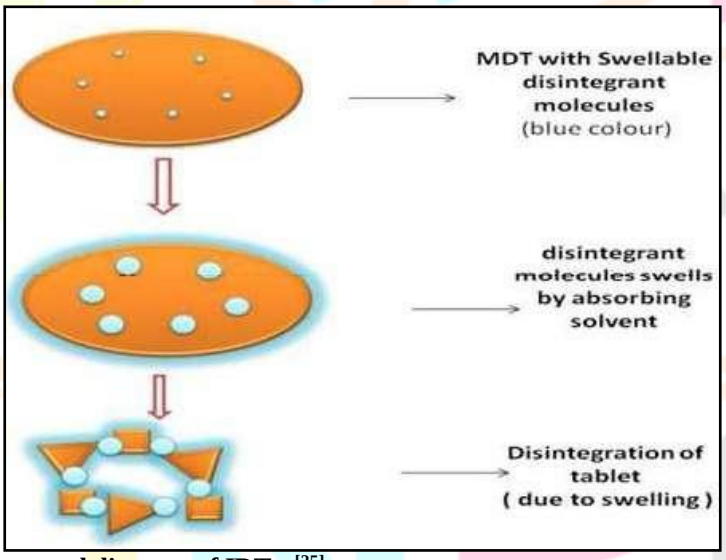

Fig. 1: Conceptual diagram of IDTs. [25]

Requirements of Immediate tablets

Patient factors [3]

Suitability of Immediate tablets is for those patients (particularly pediatric and geriatric patients) who having the difficulties to swallow traditional tablets and capsules with an 8-oz glass of water. These include the following:

- Patients who cant swallow or chewing solid dosage forms.
- Patients in compliance due to fear of choking.
- Elder patients who are facing the problem of depression who may not be able to swallow the solid dosage forms
- An eight-year-old patient with allergies desires a more convenient dosage form than antihistamine syrup.

- A middle-aged patient undergoing radiation therapy for breast cancer may be too nauseous to swallow her H2-blocker.
- A schizophrenic patient who may use to try to hide a conventional tablet under his or her tongue to avoid their daily dose of an atypical antipsychotic.
- A patient with persistent nausea, who may be a journey, or has little or no access to water.

Effectiveness factor [5]

Increase in bioavailability rate and faster onset of action are a major claim of these formulations. Dispersion in saliva in oral cavity causes pregastric absorption from some formulate ions in those cases where drug dissolves quickly. Buccal, pharyngeal and gastric regions are all areas of absorption for many drugs. First pass metabolism is avoided by pre gastric absorptionand can be a great advantage in drugs that undergoes hepatic metabolism. Beyond that, safety profiles may be improved for drugs that produce significant amounts of toxic metabolites mediated by first-pass liver metabolism and gastric metabolism, and for drugs that have a substantial fract ion of absorption in the oral cavity and pre- gastric segments of GIT.

Manufacturing and marketing factors [11]

As a drug nears the end of its patent life, it is easy for pharmaceutical manufacturers to develop a given drug entity in a new improved dosage form. A newly developeddosage form allows a manufacturer to extend the market exclusivity, unique product differentiation and extend the patent protection. For examples, Eisai Inc. launched Aricept IDT, a line extension of donepezil for Alzheimer's disease, in Japan in 2004and in the U. S. in 2005 Ranbaxy filed a generic challenge in USA in response to given drug.

Advantages of Immediate tablets [6, 7]

- Without water we can swallow the tablet.
- IDTs can be easily administered to paediatric, elderly and mentally disabled patients.
- Accurate dosing as compared to liquids.
- Drug can be dissolved and absorbed fastly, offering rapid onset of action.
- Bioavailability of drugs is increased10as some drugs are absorbed from mouth, pharynx and esophagus through saliva passing down into the stomach.
- In terms of administration as well as transportation it is advantageous over liquid medication.
- There is reduction in first pass metabolism,thus offering improved bioavailability and thus reduced dose and side effects.
- offering improved safety.
- ◦Suitable for sustained/controlled release actives.
- Allows high drug loading.

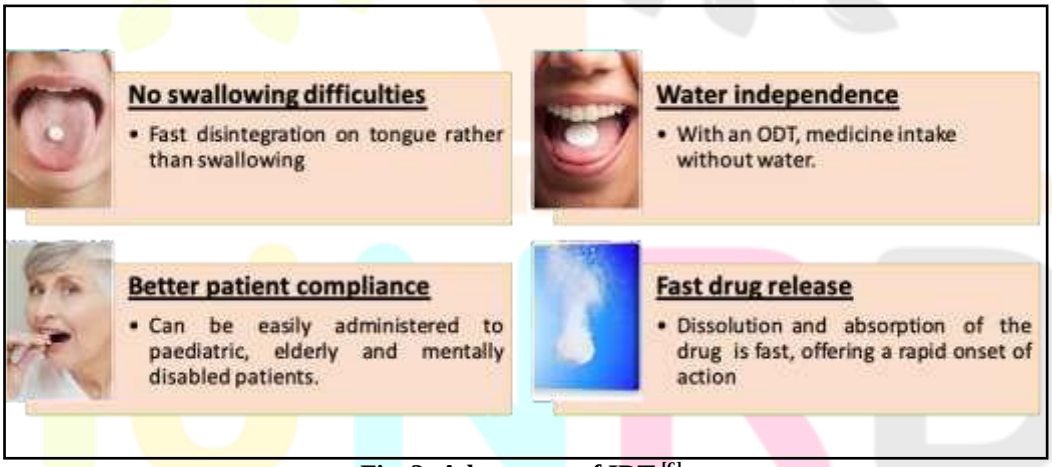

Fig. 2: Advantages of IDT [6]

Limitations of IDTs [4, 5]

- The major disadvantages of IDTs is related to the mechanical strength of tablets.
- FDT are having very porous and soft molded metrics or compressed in a tablet which having low compression, Due to which tablets are friable and brittle which difficult to handle.
- Bad tastes drugs are difficult to formulate as IDT; special precaution should have to be taken before formulate such kind of drug.

- Several IDT are hygroscopic cannot maintain physical integrity under normal condition from humidity which requires specialized package.
- Candidate which having the dryness in saliva production may not be good candidates for these tablet formulations.
- Overall bioavailability is the rate of absorption from the saliva solution.
- •Drug and dosage form stability.
- Ease of Administration to the patient who cannot swallow, such as the elderly, stroke victims, bedridden patients, a patient affected by renal failure and patient who refuse to swallow such as paediatric, geriatric and psychiatric patients.
- No need of water to swallow the dosage form, which is a highly convenient feature for patients who are travelling and do not have immediate access to water.
- Rapid dissolution and absorption of the drug, which will produce the quick onset of action.
- Some drugs are absorbed from the mouth, pharynx and oesophagus as the saliva passes down into the stomach. In such cases, the bioavailability of the drug is increased.
- Pre-gastric absorption can result in improved bioavailability and as a result it reduces the dosage;
- If there is reduction in unwanted effect then they might be due to of improve clinical performance.
- Good mouth feels property helps to change the perception of medication as a bitter pill particularly in the child patient.
- The risk of choking or suffocation during oral administration of conventional formulation due to physical obstruction is avoided, thus safety improves.
- Having business opportunity like product differentiation, product promotion, patent extensions and life cycle management.
- Beneficial in cases such as motion sickness, sudden episodes of allergic attack or coughing, where an ultra-rapid onset of action required.
- Due to increased bioavailability, particularly in cases of insoluble and hydrophobic drugs, due to rapid disintegration and dissolution of these tablets. Stability for a longer duration of time, since the drug remains in solid dosage form till it is consumed. So, it combines the advantage of the solid dosage form in stability and liquid dosage form in bioavailability.
- Easily adaptable and amenable to existing processing and packaging machineries.
- Allow high drug loading, Cost effective.

Challenges to develop IDTs [3, 10]

Palatability

Most of the drugs are unpalatable, IDTs usually contain the medicament in a taste-masked form. IDTs after administration, it disintegrates or dissolves in oral cavities of patient, hence releasing the active ingredients which come in contact with the taste buds. theirfore, taste-masking of the drugs becomes critical to patient compliance [3, 11].

Mechanical strength and disintegration time

In order to allow IDTs to disintegrate in the oral cavity, they can be made of either very porous and soft-molded matrix or compressed into tablets with very low compression force, due to which tablet make friable and/or brittle, difficult to handle, and often requiring specialized peel-off blister packing that may add to the cost. There are only 2 technologies like wow tab and durasolv can produce tablets that are sufficiently hard and durable to allow them to be packaged in multi-dose bottles.

Hygroscopicity

Several orally disintegrating dosage forms are hygroscopic and cannot maintain physical integrity under normal conditions of temperature and humidity [3, 11] Hence, they need protection from humidity which calls for specialized product packaging [3].

Amount of drug

The application of technologies used for IDTs is limited by the amount of drug that can be incorporated into each and every unit dose. In lyophilized dosage forms, the the level of drug dose must be less than 400 mg for insoluble drugs and 60 mg for soluble drugs. this parameter is particularly challenging when formulating a immediate dissolving oral films or wafers [3].

Aqueous solubility

Water-soluble drugs pose various formulation challenges because they form eutectic mixtures, which result in freezing-point depression and the formation of a glassy solid that may collapse upon drying because of loss of supporting structure during the sublimation process [3, 5, 11] Such collapse sometimes can be prevented by usingvarious matrix-forming excipients such as mannitolthat can induce crystallinity and hence, impart rigidity to the amorphous composite [3].

Size of tablet

The rate of administration of a tablet depends on its size. It has been reported that the simple size of tablet to swallow is 7-8 mm while the simple size to handle was one larger than 8 mm. Therefore, the tablet size that is both easy to take and easy to handle is difficult to achieve [3, 5].

Mouth feel

IDTs are not disintegrate into larger particles in the oral cavity. The diffn particles which are generated after disintegration of theIDTs should be as small as possible. Addition of diffn flavours and cooling agents like menthol improve the mouth feel [5].

Sensitivity to environmental conditions

IDTs should exhibit low sensitivity to environment conditions such as like humidity and temperature as most of the materials used inIDTs are meant to dissolve in minimum quantity of water[5].

Criteria for excipient used in formulation ofIDTs [5, 10-13]

- Their individual properties should not affect the IDTs.
- It must be able to disintegrate quickly.
- It should not have any interaction with drug and other excipients.
- At the time of binder selection(a single or combination of binders) care must be taken in the final integrity and stability of the product.
- The melting point of the excipients used should be in the range of 30-35 °C.
- It should not interfere in the efficacy and organoleptic properties of the product.
- The nature of binder may be in liquid, semi-solid, solid or polymeric in nature.

Excipients used inIDT preparation [5, 13-20]

Among the further excipient like one super disintegrant, a diluent, a lubricant and optionally a swelling agent, a permeabilizing agent, sweeteners and flavouring agentsIDTs should contain at least one.

Table 1: Name and weight percentage of various excipients inIDTs [1, 15]

Sr. No.	Name of excipient	% used
1	Super disintegrants	1-15 %
2	Binders	5-10 %
3	Antistatic agent	0-10 %
4	Diluents	0-85 %

As day's passes, demand for the faster disintegrating formulation is increased. So, the pharmacist needs to formulate disintegrants i.e. super disintegrants which are effective at low concentration and have greater disintegrating efficiency, and they are more effective intragranular. The act of these super disintegrant is done by swelling and due to swelling pressure exerted in the outer direction or radial direction, it causes the tablet to burst or the acceleratedabsorption of water which leads to an enormous increase in the volume of granules to promote disintegration.

- **Factors which are used to considered for selection of super disintegrants [5, 16, 23]**

➢ **Disintegration**

The disintegrant must quickly absorb saliva into the tablet to generate the volume expansion and hydrostatic pressure necessary to provide rapid disintegration in the mouth.

➢ **Compatibility**

It is desirable to haveIDT with acceptablehardness and less friability at a given compression force to produce robust tablets that avoid the need to use specialised packaging while maximising production speed.

➢ **Mouthfeel**

Large particles can result in a gritty feeling in the mouth. Thus, small particles are preferred. If the tablet forms a gel-like consistency on contact with water, however, it produces a gummy texture that many consumers find objectionable.

➢ **Flow**

In typical tablet formulation, super disintegrants are used to be need atleast 2-5 wt % of the tablet formulation. Disintegrant level can be significantly higher with IDT formulation [16].

Table 2: List of super disintegrants [5, 23]

S.no	supredisintegrant	Mechanism of action	Specific properties
1	Croscarmellose sodium	Swell 4-8 fold in <10s Swelling and wicking action	Effective in low concentration ,high swelling Capacity cross-linking of carboxyl ester group
2	Crospovidone	Combination of swelling and wicking action swell 7-12 folded in <30 s	The effective concentration is 1-3% rapidly disperses and swells in water
3	Cross-linked alginic acid	Hydrophilic colloidal sub-tance which has high sorption capacity	The combination of swelling and wicking action causes disintegration.
4	Gellan gum	Strong swelling properties upon contact with water	Anionic polysaccharide of linear tetera saccharides ,good super disintegrant
5	Sodium starch glycolate	Strong swelling properties upon contact with water swell 7-12 folds in <30s	Rapid absorption of water result in swelling upto 6 % high concentration cause gelling
6	Soy polysaccharide	Rapid dissolving	Does not contain starch and sugar so can be used in products meant for diabetics
7	Xanthan gum	Extensive swelling properties for faster disintegration	High hydrophilicity and low gelling tendency ,low water suliblity

- **Bulking materials [7, 23]**

Bulking materials are important in the development of Immediate tablets. They contribute in the functions of a diluent, filler and cost reducer. Bulking agents helps to improve the texture of the tablets that consequently enhances the disintegration in the mouth, besides adding volume and reducing the concentration of the active in the formulation. The bulking agents whichis used for this dosage form should be more sugar- based such as mannitol, polydextrose, lactosederivatives such as directly compressible lactose (DCL) and starch hydrolysate for higher aqueous solubility and good sensory perception. Mannitol especially has high aqueous solubility and goodsensation perception, as it provides a cooling effect which is due to its negative heat of solution. Bulking agents are added in the range of 10% to about 90% by weight of their final composition. The decreasing order of brittleness of excipients is ranked as microcrystalline cellulose>alpha lactose monohydrate>spray-dried lactose>anhydrous beta lactose>anhydrous alpha lactose>> dicalcium phosphate dihydrate. The most commonly used sugar-based excipients are especially bulking agents (like dextrose, fructose, lactitol, maltitol, maltose, mannitol, sorbitol, starch hydrolysate, polydextrose and xylitol) which exhibit high aqueous solubility and sweetness contributed in taste masking property and provide pleasant mouth feel.

- **Sugar based excipients can be of types on the basis of moulding and dissolution rate:**
- Type 1 saccharides: (lactose and mannitol) which exhibits low moldability but high dissolution rate.
- Type 2 saccharides: (maltose and maltitol) which exhibit high moldability but low dissolution rate.

- **Emulsifying agents [5, 23]**

Emulsifying agents are significantly used for formulating Immediate tablets as they help in quick disintegration and drug release without the need for chewing, swallowing or drinking water.

Also, emulsifying agents stabilize the immiscible blends and increase bioavailability. A variety of emulsifying agents for Immediate tablet formulations include alkyl sulfates, propylene glycol esters, lecithin, sucrose esters and others. These can be added in the range of 0.05% to about 15% by weight of the final formulation.

- **Lubricants** [5, 12]

Though not essential excipients, these can aid in making the tablets more palatable after they disintegrate in the mouth. Lubricants reduces grittiness and help in the drug transit process from the oral to the stomach.

- **Flavours (taste masking agents) and Sweeteners [5, 23]**

Flavours and taste masking agents make the products more palatable and for patients. The incorporation of these ingredients assists in overcoming bitterness and undesirable tastes of some actives. Natural and synthetic flavours can be used to enhance the organoleptic characteristic of Immediate tablets. A wide range of sweeteners including sugar, dextrose and fructose, as well as non-nutritive sweeteners such as aspartame, sodium saccharin, sugar alcohols and sucralose are available. The addition of sweeteners increase a pleasant taste as well as bulk to the formulation.

Techniques for preparing Immediate tablets
Conventional technologies
Various conventional manufacturing techniques for FDDDS

Freeze-drying or lyophilization [2]

It is a pharmaceutical process whichallows the drying of heat sensitive drugs and biological substances under low temperature by the application of vacuum to remove water by sublimation. Drugs are dissolved or dispersed in aqueous solution of a carrier, transferred to preforme a blister packs and subjected to nitrogen flush to freeze out, after that placed in the refrigerator to complete the process. Characteristicsof lyophilization techniques are as, they possess high porosity and specific surface area, and gets dissolve quickly in mouth presenting high drug bioavailability. The main drawback of this system is having high cost, time-consuming procedure and fragility, making conventional packing inappropriate for packing this dosage form and stability issues are under stress condition.

Advantages

The major advantage of using this technique is that the tablets produced by this technique have very low disintegration time and have great mouthfeel due to fast melting effect.

Moulding method [19]

Tablets are used to designed by using hydrophilic ingredients, with the aim to get maximum drug dissolution. Mass of powder is wetted with hydroalcoholic solvent and compressed into a dosage form. The solvent system is then allowed to evaporate. Taste of drug particles is developing by spray congealing the molten mixture of hydrogenated cottonseed oil, sodium carbonate, lecithin, polyethene glycol which is an having an active ingredient into lactose based tablet triturate. Characteristics of moulding method are, veryporous as solvents are removed by drying leaving porous mass which promotes rapid dissolution.

Melt granulation [24, 25]

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 a conventional granulation is that no water or organic solvents is required. Since there is no drying step, the process is less time consuming and requires less energy than wet granulation. This technique useful to enhance the dissolution rate of poorly water-soluble drugs, such as griseofulvin.

Mass-extrusion [24, 25]

In this mixed ingredients are softened by using water soluble ingredient i.e. polyethene glycol, using methanol as solvent, after passing through an extruder to form thin cylinders. Which is further get sliced with a heated blade to form small tablets. Characteristics of this method is these products can be used to mask bitter tasting drugs making small granules thus enhancing oral bioavailability.

Sublimation [18]

Rapid disintegration and dissolution factor is acquiring by formulating into porous mass by incorporating inert solid ingredients that volatilize rapidly like urea, camphor ammonium carbonate, ammonium bicarbonate and hexamethylene-tetramine. They were mixed with other ingredients and compressed. The volatile material is evolved by reduced pressure and applying slight temperature leaving the mass in porous form.

Characteristics of sublimation method are, they are porous in nature, solvents like cyclohexane and benzene can be used.

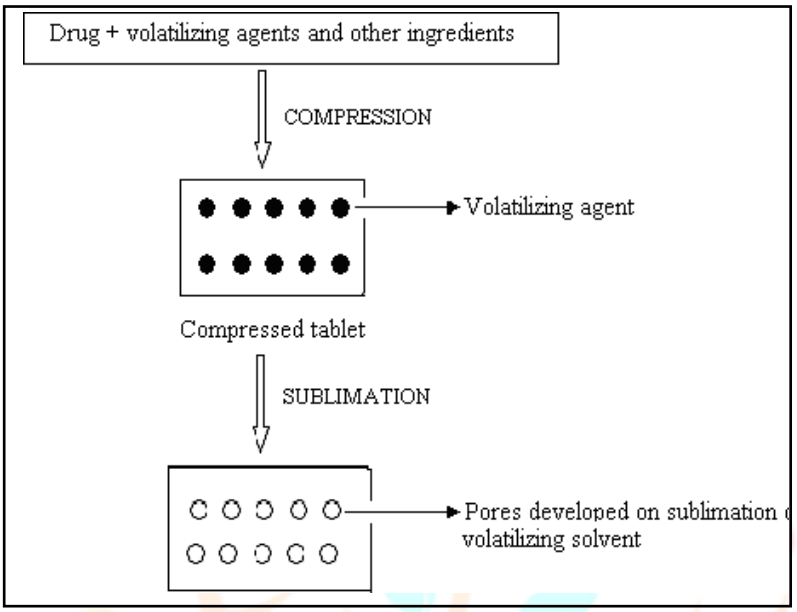

Fig. 3: Schematic diagram of sublimation techniques for preparing Immediate tablets [24]

Direct compression [4]

The disintegrant addition technology (direct compression) is the mostly preferred technique to manufacture the tablets due to having certain advantages:

- High doses can be included and final weight of the tablet can exceed that of other methods.
- The easiest way to manufacture the tablets.
- Conventional equipment and generally available excipients are used.
- A limited no. of processing steps are involved.
- Cost effectiveness.

Tablet size and hardness affect the disintegrant efficacy. Hard and greater tablets have more disintegration time than normally required. Very smooth and small tablets have low mechanical strength. So, an minimum kind and concentration of disintegrant should be chosen to achieve quick disintegration and high dissolution rates. Above the critical concentration level, however, disintegration time remains near about constant or even increases.

Fig. 4: Process of direct compression [25]

Table 3: general requirements, advantages and limitations of direct compression [25]

Sr.no	Ideal Requirement	Advantage	Limitation
1	Flowability	Cost effective production	Segregation
2	compressibility	Better stability of API	Variation in functionality
3	Dilution potential	Faster dissolution	Low dilution potential
4	Reworkability	Less wear and tear of punches	Reworkability
5	Stability	Simple validation	Poor compressibility of

Cotton candy process [5]

This process is so named as it utilises a unique spinning mechanism to produce a floss-like crystalline structure, which mimics cotton candy. This process involves the formation of Matrix of polysaccharides or saccharides by the simultaneous action of flash melting and spinning. The matrix which is formed is partially recrystallized to have improved flow properties and compressibility. This candy floss matrix is after that milled and blended with active ingredients and excipients and subsequently compressed toIDTs. However, other polysaccharides such as poly maltodextrins and polydextrose can be transformed into fibers at 30-40% lower temperature than sucrose. This modification permits the safely incorporation of thermolabile drugs into the formulation. The tablets manufactured by this process are highly porous in nature and offer very pleasant mouth feel due to fast solubilization of sugars in the presence of saliva.

Spray-drying [21]

Using the above method, ingredients are integrated by using hydrolyzed and nonhydrolyzed gelatins as supporting agents, mannitol as bulking agent, sodium starch glycolate or crosscarmellose sodium as disintegrating and an acidic material (e. g. citric acid) and or alkali material (e. g. sodium bicarbonate) to enhance disintegration and dissolution. Characteristics of the spray-drying method is this method gives rapid dissolution (within 20 seconds) when dosage form gets in contact with the aqueous medium.

Phase transition process [25]

This processes for the disintegration ofIDTs by phase transition of sugar alcohols using erythritol (melting point 122 °C), xylitol (93-95 °C), trehalose (97 °C), and mannitol (166 °C). Tablets are produced by compressing a powder which containing two sugar alcohols with high and low melting points and subsequent heating at a temperature between their melting points. Before the heating process, the tablets do not have sufficient hardness because of low compatibility. The tablet hardness was increased after heating, due to the increase of interparticle bonds or the bonding surface area in tablets induced by phase transition of lower melting point sugar alcohol.

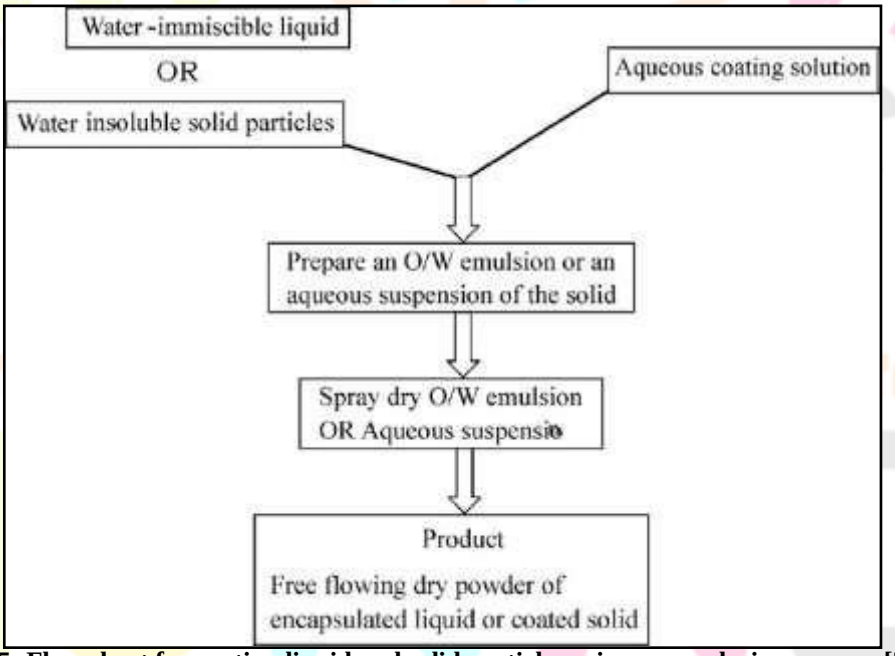

Fig. 5: Flow chart for coating liquid and solid particles using spray-drying process [24]

Nanoionization [25, 27-29]

A newly developed nanomelt technology involves a reduction in the particle size of the drug to nano size by milling the drug using a proprietary wet-milling technique. The nanocrystals of the drug are stabilized against the agglomeration by surface adsorption on selected stabilizers, which are then incorporated into MDTs. This technique is especially advantageous for poorly water soluble drugs. Other advantages of this technology contains fast disintegration/dissolution of nanoparticles leading to increased absorption and hence higher bioavailability and reduction in dose, cost effective manufacturing process, conventional packagingdue to exceptional durability and a greater range of doses (up to 200 mg drug per unit).

Oral disintegrating or Immediate thin films [25-29]

It is a new frontier in quick release tablet that provides a very convenient means of taking medications and supplements. In given technique, a non-aqueous solution is prepared containing water soluble film forming polymer (pullulan, carboxymethylcellulose, hydroxypropyl methyl cellulose, hydroxyl ethyl cellulose, hydroxyl propyl cellulose, polyvinyl pyrrolidone, polyvinyl alcohol or sodium alginate, etc.), drug and other taste masking agents, which is allowed to form a filmafter evaporation of solvent. In the case of a bitterdrug, resin adsorbate or coated microparticles ofthe drug can be incorporated into the film. Thisfilm, when placed in the mouth, melts or dissolves rapidly, releasing the drug in solution or suspension form. The features of this system include paper-thin films of size less than 2×2 inches, dissolution in 5 sec, instant drug delivery and flavoured aftertaste.

Patented technologies for Immediate tablets

Immediate characteristic ofIDTs is generally attributed to fast penetration of water into tablet matrix resulting in its fast disintegration. Several technologies have been developed on the basis of formulation aspects and different processes and patented by several pharmaceutical companies. Patented technology is described below: [30]

Zydis technology [30]

Zydis formulation is a special freeze-dried tablet in which drug is physically entrapped or dissolved within the given matrix of Immediate carrier material. When zydis units are kept into the mouth, the freeze-dried structure disintegrates instantaneously and does not require water to aid swallowing. The zydis matrix is mainly composed of many materials designed to achieve a number of objectives. To give the strength and resilience during handling, polymers such as gelatin, dextran or alginates are incorporated. These given form a glossy amorphous structure, which imparts strength.

II. LIMITATIONS

- •The amount of drug could be incorporated should generally be less than 400 mg for insoluble drugs and less that 60 mg for soluble drugs.
- The particle size of the insoluble drugs should not be less than 50 µm and not more than 200 µm to prevent sedimentation during processing.

Advantages

- Buccal pharyngeal and gastric regions are all areas of absorption from this formulation. Any pre-gastric absorption avoids the first-pass metabolism and can be an advantage in drugs that undergo a great deal of hepatic metabolism.
- The Zydis formulation is self-preserving because the final water concentration in freeze-dried product is too low to allow for microbial growth.
- Patients who have difficulty swallowing oral medication due to dysphagia, stroke or medical conditions such as gastroesophageal reflux disease, multiple sclerosis or Parkinson's disease.

Disadvantages

- This process of freeze-drying is a relatively expensive manufacturing process.
- The formulation is very lightweight and fragile, and therefore should not be stored in backpacks or the bottom of purses.
- It has poor stability at higher temperatures and humidities.
- A drug which is insoluble in water can be incorporated only up to 400 mg per tablet or less. On the other hand water, the soluble drug can be incorporated only up to 60 mg.

Orasolv technology [5, 10]

Orasolv technology has been developed by CIMA labs. In this system, the active medicament is taste masked. It also contains the effervescent disintegrating agent. Tablets are made by direct compression technique at certain low compression force in order to minimise oral dissolution time. Tablet machine and Conventional blenders is used to produce the tablets. The tablets which are produced by this technique are soft and friable and

packaged in specially designed pick and place system.

Advantages [30]

Taste-masking is two-fold, quick dissolution. This technology has been used for drug strengths in the range of 1 mg to 750 mg. Depending on formulation and tablet size, the disintegration time of the tablet can be designed in the range of 10 to 40 seconds.

Disadvantages [30]

They are sensitive to moisture due to the presence of the effervescent system and must be packaged appropriately. Low mechanical strength.

Durasolv technology [4, 5]

Durasolv is the patented technology of CIMA labs. The tablets made by this technology composed of a drug, fillers and lubricant. Tablets are prepared by using this conventional tableting equipment and having a good rigidity. These can be packed into conventional packaging system like that of blisters. Durasolv is an another appropriate technology for products requiring low amounts of active ingredients.

Advantages [30]

DuraSolv technology is good for thetablets having a low amount (125 mcg to 500 mg) of active ingredients and tablets are compressed to the greater hardness of 15-100 N, resulting in a more durable ODT. As a result, this technology enables packaging flexibility; and then tablets can be bottled and blistered.

Disadvantages [30]

The technology is not compatible with larger doses of active ingredients because the formulation is subjected to high pressure during compaction. The coating of drug powder in Durasolv may become fractured during compaction, exposing the bitter tasting drugs to the patient taste buds.

Wow tab technology [4, 5, 30-31]

This, tab technology is patented by Yamanouchi Pharmaceutical Co. WOW means "Without Water". In this process, a combination of low moldability saccharides and high moldability saccharides is used to obtain a rapidly melting strong tablet. The combination of their high and low moldability is used to produce tablets of adequate hardness.

Advantages

Adequate dissolution rate and hardness. Wow, tab product can be packed in both into the conventional bottle and blister packs.

Disadvantages

No significant change in bioavailability.

Flash dose technology [4, 23, 30]

Flash dose technology has been patented by Fuisz. Nurofen melts let, a new form of the Ibuprofen as melt-in-mouth tablets, they are prepared using flash dose technology is the first commercial product launched by Biovail Corporation. Flash dose tablets consist of the self-binding shear form matrix termed as floss. Shearform matrices are then prepared by flash heat processing.

Advantages

High surface area for dissolution

Disadvantage

- High temperature is required to melt the matrix can limit the use of heat-sensitive drugs, sensitive to moisture and humidity.
- The dosage form can accommodate only up to 600 mg of drug.
- Tablets which are produced are highly friable, soft and moisture sensitive. Therefore specialised packing is required.

Pharmabust technology [5, 12]

Pharmaburst technology is being patented by SPI pharma. The tablets which are manufactured by this process involves a dry blend of agiven drug, flavors, and also a lubricant then followed by compression into tablets which then dissolve within 30-40 seconds. Tablets which are manufactured by this methodology have sufficient strength can be packed in blister packs and bottles.

Flashtab technology [38, 39]

The flashtab technology is yet another fast-dissolving/disintegrating tablet formulation. Prographarm laboratories have patented the flashtab technology. It utilizes the most of the same excipients as in conventional compressed tablets. A disintegrating agent and also a swelling agent are used in a combined form with the coated drug particles in this formulation to produce a tablet that disintegrates in the mouth in less than one minute.

Oraquick technology [30-33]

K. V. S. Pharmaceuticals have a patentover this technology. It utilizes the taste masking microsphere technology called as micromask, which provides superior mouth feel over taste masking alternatives, significant mechanical strength, and quick disintegration/ dissolution of

the product. Any kind of solvents are not utilized by taste masking process. Hence it leads to superiorand fast efficient production.

Advantages
Faster and efficient production, appropriate for heat-sensitive drugs

Dispersible tablet technology [5]

Lek in Yugoslavia was issued patents for dispersible tablets of dihydroergotoxine and cimetidine, which were then claimed to disintegrate in less than 1 minute when they are in contact with water at room temperature. Dihydroergotoxine in its base form is poorly soluble in water. An improved dissolution rate of this dihydroergotoxine methanesulphonate was observed with the dispersible tablets containing 0.8-10%, preferably about 4% by weight, of organic acids. One of the essential excipients in the cimetidine formulate ion a disintegrating agent. It provides a rapid swelling and/or good wetting capability to the tablets and hence a quick disintegration. The disintegrating agents include starch or modified starches, microcrystalline cellulose, alginic acid, cross–linked sodium carboxymethylcellulose, and cyclodextrin polymers. A combination of two or more disintegrating agents produced better disintegration results.

Advatab technology [39]

Advatab tablets disintegrate rapidly in the mouth, typically in less than 30 seconds, to allow for convenient oral drug administration without water. These tablets are specially suited to those patients who experience difficulty in swallowing capsules and tablets. Advatab is distinct thanIDT technologies as it can be combined with the Eurand's complimentary particle technologies like its world leading Microcaps® taste masking technology and its Diffucaps®, controlled release technology.

Nanocrystal technology [5, 12, 30]

For rapid dissolving tablets, elan's proprietary nanocrystal technology can enable formulation and improve compound activity and final product characteristics. Decreasing particle size increases the surface area, which leads to an increase in dissolution rate. This can be accomplished predictably and efficiently using nanocrystal technology. Nanocrystal particles are readily 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.

Nanocrystal Immediate technology provides for

- Pharmacokinetic benefits of orally administered nanoparticles (<2 microns) in the form of a rapidly disintegrating tablet matrix.
- Product differentiation based upon a combination of proprietary and patent protected technology elements.
- Cost-effective manufacturing processes that utilize conventional, scalable unit operations.

Frosta technology (Akina) [5, 12, 13]

This technology is patented by Akina. Frosta technology utilizes the core concept of formulating the plastic granules and compressing at low pressure to produces the strong tablets with high porosity. The process involves mixing the porous plastic material with water penetration enhancer and followed by granulating with a binder.

Table 4: Patents on diffierent Immediate drug delivery system orI D T s. [4, 6, 7, 40]

S.NO	AUTHOR	DRUG	METHOD/PLYMER	INTERFERENCE
1	Lee et aL(2013)	megestrol	Spray drying	Quicker dissolve and mask the taste of drug.
2	Szamost et aL(2013)	Phenyl propanolamine Lamina HCL	Direct compression	melt at 37.c and low compression force.
3	Constantine (2011)	Ondasetron	Polyethylene glycol	Used of the bioactive agent and treatment of dysphagia.
4	Singh et Al (2006)	Nimesulide	Sodium starch glycolate	Dissolve or disintegrate in digestive organ.
5	Aggarwal et aL(2005)	Galanthamine	Direct compression	Used in Alzheimer disease.

6	Callihan et aL(2005)	Aspirine	Direct compression	Mannose provide rapid disintegration and dissolution.
7	Szamost et aL(2013)	Ibuprofen	Direct compression	Provide excellent mouth feel.
8	Khawla et aL(2013)	Ibuprofen	Melt extrusion	Very low compression force.
9	Callihan et aL(2013)	Caffeine	Direct compression	Rapid dissolution.
10	John et aL (2013)	Active substance	Freeze drying	Rapid disintegration.
11	Abu-lzzakawla et aL(2013)	Iboprofen	Direct compression	Low melting point of compound use.
12	William et aL(2013)	efavirenz	Wet granulation	Used in HIV.
13	Gilis et aL(2013)	Galanthamine HBr	Direct compression	Used in treatment of Alzheimer dementia.
14	Warner Lambert Co.et aL(2012)	Active substance	Direct compression	Used low density granules.
15	Makino et aL(2012)	Active substance	Compression molding	High adequate strength disintegration and dissolving rate.

Table 5: Work which is done on Immediate drug delivery system orIDTs: [3, 4, 40]

s.no	Author	Drug	Method /polymer	inference
1	Durgabhavani te aL (2016)	valsartan	Vaccume drying technique	Improve disintegration time
2	Karia et aL (2015)	Olmesartan medozoinil	Co-processed excipient technique	Better in vitro drug release
3	Subbaiah et aL (2015)	Amoxicillin trihydratevand potassium clavunate	Direct compression	Improve disintegration time and in vitro drug release
4	Munde et aL (2015)	Lansoprazole	Direct compression	Improve in vitro drug release.
5	Metkari et aL (2014)	Carbamazepine	Direct comp.using solid dispersion	Good dissolution profile with short disintegration time.
6	Babu et aL (2014)	Carbamazepine	Direct compression	In vitro drug release increased.
7	Arunachalam et aL (2013)	Levofloxacin	Direct compression	Improve disintegration time.
8	Valera et aL (2013)	Amoxicillin trihydratevand potassium clavunate	Dry granulation method	Improve in vitro drug release.
9	Rawat et aL (2013)	Pioglitazone hydrocloride	Direct compression	Improved patient compliance.
10	Saroha et aL (2013)	Amoxicillin trihydrate	Direct compression	Better disintegration rate.

11	Bhati et aL (2013)	Metoclopramide hydrochloride	Direct compression	Improve patient compliance in pediatric and geriatric.
12	Layer et aL (2013)	Risperiodone	Granulation methodSolvent evaporation method	Enhanced dissolution and increase bioavailability.
13	Singh et aL (2013)	Amoxicillin trihydrate and potassium clavunate	Wet Granulation method	Improve in vitro drug release .
14	Rao et aL (2012)	fosinopril	Sublimation method	Increase rate of dissolution and bioavailability.
15	Rao et aL (2012)	fosinopril	Direct compression	Used in treatment of various cardiovascular disorder.
16	Bhupati et aL (2012)	Terbutaline sulphate	Direct compression	Maintain therapeutic concentration and enhance and bioavailability.

The technology can be used for almost any drugs including market place and extension of patent term of innovator. The clinical studies that shows theIDTs can improve patient compliance, provide a rapid onset time of action, and increase bioavailability. Considering the many benefits ofIDTs, it is only a matter of time until a majority of oral formulations are prepared inIDT forms.

Lyo (Pharmalyoc) [5, 12, 13]

Oil in water emulsion is prepared and placed directly into blister cavities followed by freeze-drying. Non-homogeneity during freeze-drying is avoided by incorporating inert filler to increase the viscosity finally the sedimentation. A high proportion of filler reduces the porosity of tablets due to which disintegration is lowered.

Sheaform technology [5]

The technology is based on the preparation of floss that is also known as, shear from matrix, which is produced by subjecting a feed

Stock which containing a sugar carrier by flash heat processing. In this process, the sugar is simultaneously subjected to centrifugal force and then to a temperature gradient, which raises the temperature of the mass to create an internal, flow condition, which permits part of it to move with respect of the given mass. The floss so produced is amorphous in nature, hence it is further chopped and recrystallized by various techniques.

Marketed products of Immediate tablets

The commercialised products ofIDT which are available in the market are given in table no. 6 and 7.

Table 6: Different Immediate tablets products available in Indian market [2-8]

Sr.no	Brand (trade) name	Active drug	Manufacturer/company
1	Acepod-O	cefpodoxime	ABL Lifecare, India
2	Acufix DT-TAB	cefixime	Macleods, India
3	Alepam	Amoxycillin trihydrate and potassium clavulanata	Scoshia remedy, India
4	Bigecef DT-TAB	Cefuroxime	Bestochem ,India
5	Clonazepam ODT	clonazepam	Par pharmaceutical
6	Dompan	Pantoprazole and	Medley pharmaceutical,

		domperidone	India
7	Mosid-MT	Mosapride citrate	Torrent pharmaceuticals, Ahmedabad, India
8	Minoclav DT-TAB	Amoxycillin trihydrate and potassium clavulanata	Minova life sciences,India
9	Nulev	Hyoscyamine sulfate	Schwarz pharma, India
10	Nimulid MDT	nimesulide	Panacea Biotech ,New delhi, India
11	Numoxylin CV DT	Amoxycillin trihydrate and potassium clavulanata	Gepach international, india
12	Zyrof meltab	Rofecoxib	Zydus cadila, India
13	Romilast	montelukast	Ranbaxy labs Ltd,New Delhi, India
14	Torrox MT	Rofecoxib	Torrent pharmaceuticals, ahemadabad, india
15	valus	Valdecoxib	Glenmark , India

Table 7: Different Immediate tablets products available in international market [2-6]

SR.NO	Brand (trade) name	Active drug	Manufacture/company
1	Benadryl Fastmelt	diphenhydramine and psudoephedrine	Warner-Lambert ,NY,USA
2	Claritin redi tab	Loratadine	Schering- plough corp. USA
3	Domperidone Ebb	Domperidone	Ebb medical ,Sweden
4	Domperon	Domperidone	Astra pharma ,Bangladesh
5	Feldene fast melt	Piroxicam	Pfizer Inc, NY, U.S.A
6	Febrectol	Paracetamol	Prographarm,chateauneuf, France
7	Gaster D	Famotidine	Yamanouchi
8	Impodium Istant melt	Loperamide HCL	Janssen, UK
9	Maxalt MLT	Rizatriptan	Merk and co. nj. USA
10	Nasea OD	Ramosetoron HCL	Yamanouchi

III. CONCLUSION

Immediate 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 paediatric patients. Immediate tablets are designed to dissolve or disintegrate quickly in the salivagenerally within less than 60 seconds (range of 5-
60 seconds). Immediate 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 ofIDTs has increased fabulously over the last decade.IDTs need to be formulated for psychotic patients, bedridden, geriatric, paediatric patients, for those patients who may not have access to water, patients who are busy in traveling.IDTs formulations formulated by some of these conventional and patent technologies andIDTs have sufficient mechanical strength, quick disintegration/dissolution in the buccal cavity without water. The newer technologies utilized for the formulation of theIDTs that provide more effective dosage forms with more advantages and minimal disadvantages.

CONFLICT OF INTERESTS

Declare none

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