

REVIEW ARTICLE

ORAL DISINTIRATING TABLET OF ANTIHYPERTENSIVE DRUG

Lalji V Amipara*, MM Gupta¹

Department of Pharmaceutics, Jaipur College of Pharmacy, Jaipur (Rajasthan) India

Corresponding Author's Email id: lvamipara88@gmail.com, Contact no. +919426435262

Received 15 Dec 2012; Review Completed 01 Jan 2013; Accepted 08 Jan 2013, Available online 15 Jan 2013

ABSTRACT:

Hypertension is very dangerous problem. It may occur any time to elder patients so drugs are available for all the times and administered by patients are very easy mode. Normally all drugs are administered by oral route with water or some other liquid vehicles. At the time of emergency (for hypertension patients) water may get or not. So, to overcome these problems, tablets are to be developed and administered without need of water. The purpose of this research was to develop oral disintegrating tablets (ODT) of low bitter hypertensive drugs like Drugx using taste enhancers as a taste masking agents. ODT of Drugx were prepared using different superdisintegrants by direct compression method. Mannitol was used as a diluent. Aspartame and Acesulfame Potassium were used for unpleasant taste masked from the Drugx by co sifting and serial of blending with other excipients. The mixed final blend was then compressed into tablets. The formulations were evaluated for weight variation, hardness, friability, wetting time, disintegrating time, dissolution, taste evaluation study and in vitro dissolution. All the formulation showed low weight variation with different disintegration time and rapid in vitro dissolution. The results revealed that the tablets containing taste enhancers(40-45% w/w) had a good palatability for the patients.

Keywords: Oral Disintegrating Tablet(ODTs), Superdisintegrants, taste masking, patented technology

INTRODUCTION¹:

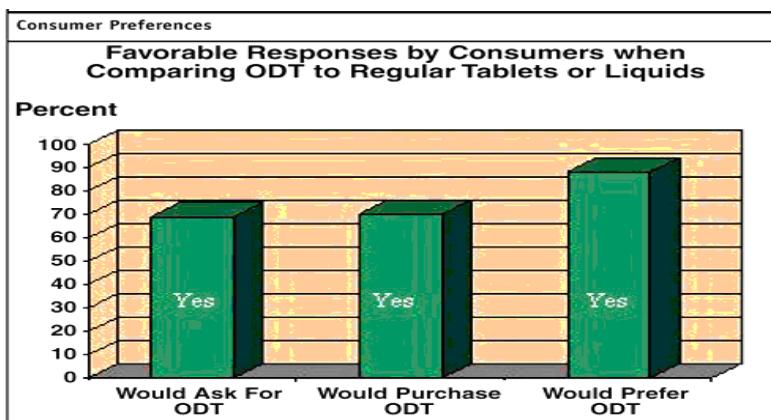
Among the different routes of administration, the oral route of administration continues to be the most preferred route due to various advantages including ease of ingestion, avoidance of pain, versatility and most importantly patient compliance. The important drawback of tablets and capsules dosage forms for pediatric and geriatric patients is being difficulty in swallowing.

Nearly 35% of the general population, especially the elderly patients and children suffer from dysphasia or difficulty in swallowing, which results in high incidence of noncompliance and ineffective therapy. Swallowing problems also are very common in young individuals because of their poorly developed muscular and nervous systems. Other groups who may experience problems in swallowing conventional oral dosage forms are the patients with tremors of extremities, mentally ill, developmentally disabled, non co-operative patients and patients with reduced liquid intake plans or patients suffering from nausea. The swallowing problems are also common in

some cases such as patients with motion sickness, sudden episodes of allergic attack or coughing and due to lack of water.

Recent advances in technology have presented viable dosage alternative for patients who may have difficulty in swallowing tablets or capsules. Traditional tablets and capsules administered with an 8-oz. glass of water may be inconvenient or impractical for some patients.

To overcome these problems, formulators have considerably dedicated their effort to develop novel drug delivery systems (NDDS) which enhance safety and efficacy of drug molecule and to achieve better patient compliance. One such approach is 'Oral dispersible Tablets', which disintegrate or dissolve in saliva and are swallowed without water as tablet disintegrate in mouth, this could enhance the clinical effect of drug through pregastric absorption from the mouth, pharynx, esophagus. This leads to an increase in the bioavailability by avoiding first pass liver metabolism.

Figure 1: Consumer Acceptance for ODT²

The centre for drug evaluation and research states an orally dissolving tablet to be "A dosage form containing medicinal substances, which disintegrates rapidly, usually within a matter of seconds, when placed upon tongue." This system is recognized with other synonyms like fast dissolving tablets; melt in mouth tablets, porous tablets, rapidly disintegrating tablets, quick dissolving, and rapimelt tablets. Despite various nomenclatures the

function and concept of all these Drug Delivery System (DDS) is similar.

Advantages of orally disintegrating tablets are being recognized in both industry and academia. Their growing importance was underlined recently when the European Pharmacopoeia adopted the term Oro-dispersible tablet as a "tablet to be placed in the mouth where it disperses rapidly before swallowing".

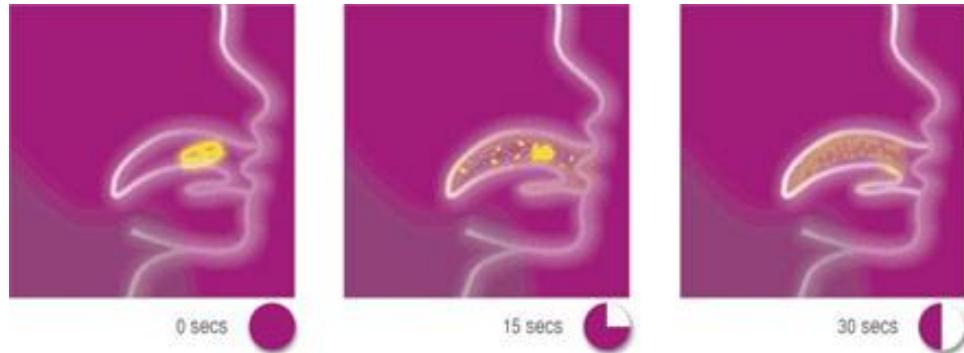


Figure 2: Disintegration of tablet in mouth³

IDEAL CHARACTERISTICS^{4,6}

- They should not require water or other liquid at the time of administration.
- Should easily disintegrate and dissolve.
- Mask or overcome unacceptable taste of drug.
- They should have high drug loading.
- They should have pleasant feel in the mouth.
- They should have negligible or no residue in oral cavity after administration

ADVANTAGES⁵:

- Ease of administration to patients who refuses to swallow a tablet such as pediatrics, geriatric patients and psychiatric patients.
- No need or little water is required to swallow the dosage form which is highly convenient feature for patients who are traveling and do not have access to water.
- Free of risk of suffocation due to physical obstruction when swallowed, thus offering improved safety.
- Rapid disintegration and absorption of drug, which will produce quick onset of action.
- Quick absorption from the gastro intestinal tract improves bioavailability and reduces unwanted effects caused by the drugs and also improves patient compliance¹.

DISADVANTAGES:

- Most fast dissolving tablets lack the mechanical strength common to traditional tablets. Many products are very lightweight and fragile requiring them to be individually packaged.
- Due to the formulation of fast dissolving tablets which are also more susceptible to degradation via temperature and humidity, some of the newest fast dissolving tablet

TECHNIQUES USED IN FDT⁶:

Following technologies have been used by various researchers to prepare fast dissolving tablets:

- Freeze-Drying or Lyophilization
- Tablet Molding
- Spray Drying
- Sublimation
- Direct Compression
- Dry granulation
- Cotton Candy Process
- Mass-Extrusion

1. Freeze-Drying or Lyophilization⁶:

Freeze drying is the process in which water is sublimed from the product after it is frozen. This technique creates an amorphous porous structure that can dissolve rapidly. Commonly used excipients with their uses and examples employed in manufacturing of fast dissolving tablets using Freeze-drying are listed on next page. A typical procedure involved in the manufacturing of fast dissolving tablets using this technique is mentioned here. The active drug is dissolved or dispersed in an aqueous solution of a carrier/polymer. The mixture is dosed by weight and poured in the wells of the preformed blister packs. The trays holding the blister packs are passed through liquid nitrogen freezing tunnel to freeze the drug solution or dispersion. Then the frozen blister packs are placed in refrigerated cabinets to continue the freeze-drying. After freeze-drying the aluminum foil backing is applied on a blister-sealing machine. Finally the blisters are packaged and shipped.

The freeze-drying technique has demonstrated improved absorption and increase in bioavailability. The Zydis formulations consist of a drug physically trapped in a water-soluble matrix (saccharine mixture and polymer), which is freeze dried to produce a product that dissolves rapidly when placed in mouth. The ideal candidate for Zydis technology should be chemically stable and water

insoluble and particle size preferably less than 50 micron. Water soluble drugs might form eutectic mixtures and not freeze adequately, so dose is limited to 60 mg and the maximum drug limit is 400 mg for water insoluble drug as large particle sizes might present sedimentation problems during manufacture.

The major disadvantages of lyophilization technique are that it is expensive and time consuming; fragility makes conventional packaging unsuitable for these products and poor stability under stressed conditions.

2. Tablet Moulding^{4,6}:

The preparation of fast dissolving tablets using molding technology employs water-soluble ingredients so that the tablet dissolves completely and rapidly. The active ingredients in most cases are absorbed through the mucosal lining of the mouth. Molding process is of two types i.e. solvent method and heat method. Solvent method involves moistening the powder blend with a hydro alcoholic solvent followed by compression at low pressures in molded plates to form a wetted mass (compression molding). The solvent is then removed by air-drying. The tablets manufactured in this manner are less compact than compressed tablets and possess a porous structure that hastens dissolution.

The heat molding process involves preparation of a suspension that contains a drug, agar and sugar (e.g. Mannitol or lactose) and pouring the suspension in the blister packaging wells, solidifying the agar at the room temperature to form a jelly and drying at 30°C under vacuum. The mechanical strength of molded tablets is a matter of great concern. Binding agents, which increase the mechanical strength of the tablets, need to be incorporated. Taste masking is an added problem to this technology.

3. Spray Drying⁶:

Spray drying is used in pharmaceutical industries to produce highly porous powders. The processing solvent is evaporated rapidly by spray drying, which renders the product highly porous and thus can be used in manufacturing fast dissolving tablets. In this technique, gelatin can be used as a supporting agent and as a matrix, mannitol as a bulking agent and sodium starch glycolate or croscarmellose sodium or crospovidone are used as superdisintegrants. Tablets manufactured from the spray-dried powder have been reported to disintegrate in less than 20 seconds in aqueous medium.

4. Sublimation:

The key to rapid disintegration of fast dissolving tablets is preparation of a porous structure in the tablet matrix. To generate such a porous matrix, volatile ingredients are incorporated in the formulation that is later subjected to a process of sublimation. Highly volatile ingredients like ammonium bicarbonate, ammonium carbonate, benzoic acid, camphor, naphthalene, urea, urethane and phthalic anhydride may be compressed along with other excipients into a tablet. This volatile material is then removed by sublimation leaving behind a highly porous matrix. Tablets manufactured by this technique have reported to usually disintegrate in 10-20 sec. Even solvents like cyclohexane, benzene can be used as pore forming agents.

Vacuum drying technique has been very often used by researchers to sublime the volatile ingredients and thus maximize the porous structure in the tablet matrix. It is likely that a porous hydrophilic matrix will easily pick up the disintegrating medium and break quickly.

5. Direct Compression:

There was no much attention to the direct compression of pharmaceuticals in the previous days (late 1950s). Now a days great deal of attention has been given to both product and process development. The availability of new materials, new forms of old materials and the invention of new machinery has allowed the production of tablets by simplified and reliable methods. In early 1960's, the introduction of spray dried lactose (1960) and avicel (1964) had changed the tablet manufacturing process and opened avenues of direct compression tableting.

Previously, the word direct compression was used to identify the compression of a single crystalline compound (i.e. sodium chloride, potassium chloride, potassium bromide, etc.) into a compact form without the addition of other substances. Current usage of the term direct compression is used to define the process by which tablets are compressed directly from the powder blends of active ingredient/s and suitable excipients. No pre-treatment of the powder blends by wet or dry granulation is involved.

Direct compression represents the simplest and most cost effective tablet manufacturing technique. This technique can now be applied to preparation of fast dissolving tablets because of the availability of improved excipients especially superdisintegrants and sugar based excipients. Direct compression, using directly compressible excipients is the most commonly used method of preparing fast dissolving tablets. Directly compressible excipients are very coarse and granular in nature and give a coarse dispersion in the mouth with decreased mouth feel and compliance. It is very difficult to prepare fast dissolving tablets with drugs having very low bulk density, higher dose and poor flow property using this technique.

(a) Superdisintegrants:

In many orally disintegrating tablet technologies based on direct compression, the addition of superdisintegrants principally affects the rate of disintegration and hence the dissolution. The presence of other formulation ingredients such as water-soluble excipients and effervescent agents further hastens the process of disintegration. This technique contains coated crystals and micro granules along with the disintegrants. In this technology, two types of granules are used; a disintegrating agent (e.g. modified cellulose- croscarmellose sodium), which has a high swelling force, and a swelling agent (e.g. starch), which has a low swelling force.

Other techniques like effervescent tablets in which disintegration is aided by evolution of carbon dioxide. Saliva activates the effervescent agent, causing the tablet to disintegrate. Care should be observed because effervescent excipients and final product require higher protection against humidity conditions.

(b) Sugar Based Excipients:

This is another approach to manufacture fast dissolving tablets by direct compression. The use of sugar based

excipients especially bulking agents like dextrose, fructose, isomalt, lactitol, lactose, maltitol, maltose, mannitol, sorbitol, starch hydrolysate, polydextrose and xylitol, which display high aqueous solubility and sweetness, and hence impart taste masking property and a pleasing mouth feel.

These excipients under defined manufacturing conditions gives a highly porous structure and friable exterior structure which helps in faster disintegration of fast dissolving tablets, they also provide a satisfactory mouth feel and so suitable for use in preparation of harder fast dissolving tablets by direct compression at low pressure.

There was no much attention to the direct compression of pharmaceuticals in the previous days (late 1950s). Now a days great deal of attention has been given to both product and process development. The availability of new materials, new forms of old materials and the invention of new machinery has allowed the production of tablets by simplified and reliable methods. In early 1960's, the introduction of spray dried lactose (1960) and avicel (1964) had changed the tablet manufacturing process and opened avenues of direct compression tableting.

Previously, the word direct compression was used to identify the compression of a single crystalline compound (i.e. sodium chloride, potassium chloride, potassium bromide, etc.) into a compact form without the addition of other substances. Current usage of the term direct compression is used to define the process by which tablets are compressed directly from the powder blends of active ingredient/s and suitable excipients. No pre-treatment of the powder blends by wet or dry granulation is involved.

6. Dry granulation technique: The fast dissolving tablets has been prepared by means of dry granulation technology, which has the following advantages over other techniques of preparation:

1. It can be used for all types of drugs including moisture sensitive and heat sensitive.
2. It can be used for drugs having very low bulk density
3. It can be used for poorly compressible drugs and drugs having poor flow property.
4. The tablets can be packed into regular bottles, blister, strip pack or sachets.
5. The tablets can be stored in bulk in drums to be packaged subsequently. Moreover conventional tablet packaging feeders can be used for packing purpose. The process of dry granulation is cost effective as it avoids solvents, and the processes of drying like freeze drying, spray drying etc.
6. This reduces overall reduction in capital expenditure (conventional processing, packaging, and storage facilities). These dosage forms may be in the form of tablets, wafers, granules, or granules packed as such along with other pharmaceutically acceptable additives in a suitable package which upon contact with water, saliva or aqueous solution disintegrates within a few seconds.

7. Cotton Candy Process:

The cotton candy process is also known as the "candy floss" process and forms the basis of the technologies such

as Flash Dose (Fuisz Technology). A fast dissolving tablets is formed using a candyfloss or shear form matrix; the matrix is formed from saccharides or polysaccharides processed into amorphous floss by a simultaneous action of flash melting and centrifugal force. The matrix is then cured or partially recrystallised to provide a compound with good flow properties and compressibility. The candyfloss can then be milled and blended with active ingredients and other excipients and subsequently compressed into fast dissolving tablets. However the high processing temperature limits the use of this technology to thermo stable compounds only.

8. Mass Extrusion⁵: This technology involves softening the active blend using the solvent mixture of water-soluble polyethylene glycol and methanol and subsequent 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. The dried cylinder can also be used to coat granules for bitter drugs and thereby achieve taste masking.

NEW ORALLY DISINTEGRATING DOSAGE FORMS⁶:

Oral films and wafers:

Oral films and wafers are the newer technologies in the manufacturing of orally disintegrating dosage forms. They are thin elegant films of edible water-soluble polymers of various sizes and shapes like square, rectangle or disc. The strips may be flexible or brittle, opaque or transparent. They are designed to provide rapid disintegration on the tongue without the need for water. They have the advantage of a large specific surface area for disintegration. One or a combination of the following processes like hot-melt extrusion; solid dispersion extrusion, rolling and solvent casting are used to manufacture these films. A major limitation of these dosage forms is low drug loading capacity and limited taste masking option.

ZYDIS (R.P. Scherer, Inc.):

Zydis, the best known of the fast-dissolving/disintegrating tablet preparations, was the first marketed new technology tablet. The tablet dissolves in the mouth within seconds after placement on the tongue. A Zydis tablet is produced by lyophilizing or freeze-drying the drug in a matrix usually consisting of gelatin. The product is very lightweight and fragile, and must be dispensed in a special blister pack. Patients should be advised not to push the tablets through the foil film, but instead peel the film back to release the tablet. The Zydis product is made to dissolve on the tongue in 2 to 3 seconds. The Zydis formulation is also self-preserving because the final water concentration in the freeze-dried product is too low to allow for microbial growth. The Zydis formulation utilizes flavors and sweeteners to optimize the taste of the dosage form. In addition, it utilizes microencapsulation with specialized polymers or complexation with ion exchange resins to mask the bitter tasting drug. The combination of lyophilization and taste masking creates a product that is both pleasing to the eye and also to the senses of taste and touch. A major claim of the Zydis product is increased bioavailability compared to traditional tablets. Because of its dispersion and dissolution in saliva while still in the

oral cavity, there can be a substantial amount of pregastric absorption from this formulation. Buccal, pharyngeal and gastric regions are all areas of absorption of the Zydis formulation. Any pre-gastric absorption avoids first-pass metabolism and can be an advantage in drugs that undergo a great deal of hepatic metabolism. However, if the amount of swallowed drug varies, there is the potential for inconsistent bioavailability. While the claimed increase in bioavailability is debatable, it is clear that the major advantage of the Zydis formulation is convenience.

There are some disadvantages to the Zydis technology. The process of freeze-drying is a relatively expensive manufacturing process. As mentioned earlier, the Zydis

formulation is very lightweight and fragile, and therefore should not be stored in backpacks or the bottom of purses. Finally, the Zydis formulation has poor stability at higher temperatures and humidities. It readily absorbs water, and is very sensitive to degradation at humidities greater than 65%. If there is any pinhole or minor damage to the package, the patient may find the lyophilized product has collapsed due to absorption of moisture. As with most other drugs, patients should be advised to avoid storing the Zydis technology in the medicine cabinet in the bathroom. Patients should use their Zydis formulation within six months of opening the laminated foil pouch and immediately after opening its individual blister packaging.

Table1: List of Patented Technologies using manufacturing techniques and description

Technology	Basis for technology	Company
Zydis	Lyophilization	R. P. Scherer Inc.
Quicksolv	Lyophilization	Janseen Pharmaceutical
Lyoc	Lyophilization	Farmlyoc
Flashtab	Multiparticulate Compressed Tablets	Ethypharm
Orasolv, Durasolv	Compressed Tablets	Cima Labs Inc.
Rapitab	Compressed Tablets	Schwarz Pharma
Wowtab	Compressed Molded Tablets	Yamanouchi PharmaTechnologies, Inc.
Fastmelt	Molding	Élan Corp.
Ziplets	Molding	Eurand
Flashdose	Cotton-candy process	Fuisz Technology Ltd.

ORASOLV (Cima Labs, Inc.):

Orasolv was Cima's first fast-dissolving/disintegrating dosage form. The Orasolv technology, unlike Zydis, disperses in the saliva with the aid of almost imperceptible effervescence. The Orasolv technology is best described as a fast-dissolving tablet; the tablet matrix dissolves in less than one minute, leaving coated drug powder. The taste masking associated with the Orasolv formulation is two-fold. The unpleasant flavor of a drug is not merely counteracted by sweeteners or flavors; both coating the drug powder and effervescence are means of taste masking in Orasolv. This technology is frequently used to develop over-the-counter formulations. The major disadvantage of the Orasolv formulations is its mechanical strength. The Orasolv tablet has the appearance of a traditional compressed tablet. However, the Orasolv tablets are only lightly compressed, yielding a weaker and more brittle tablet in comparison with conventional tablets. For that reason, Cima developed a special handling and packaging system for Orasolv. An advantage that goes along with the low degree of compaction of Orasolv is that the particle coating used for taste masking is not compromised by fracture during processing. Lyophilization and high

degrees of compression, as utilized in Orasolv primary competitors, may disrupt such a taste masking approach.

DURASOLV (Cima Labs, Inc.):

Durasolv is Cima's second-generation fast-dissolving/disintegrating tablet formulation. Produced in a fashion similar to Orasolv, Durasolv has much higher mechanical strength than its predecessor due to the use of higher compaction pressures during tableting. The Durasolv product is thus produced in a faster and more cost-effective manner. Durasolv is so durable that it can be packaged in either traditional blister packaging or vials. The newest Durasolv formulation, NuLev, is actually dispensed in a conventional stock bottle. Pharmacists are advised to take care when dispensing such Durasolv formulations from stock bottles to ensure they are not exposed to high levels of moisture or humidity. Excess handling of tablets can introduce enough moisture to initiate dissolution of the tablet matrix. One disadvantage of Durasolv is that the technology is not compatible with larger doses of active ingredients, because the formulation is subjected to such high pressures on compaction. Unlike Orasolv, the structural integrity of any taste masking may be compromised with high drug doses. The drug powder coating in Durasolv may become fractured during

compaction, exposing the bitter-tasting drug to a patient's taste buds. Therefore, the Durasolv technology is best suited for formulations including relatively small doses of active compound.

WOWTAB (Yamanouchi Pharma Technologies, Inc.):

The WOWTAB fast-dissolving/disintegrating tablet formulation has been on the Japanese market for a number of years. It has just recently been introduced into the U.S. The WOWTAB technology utilizes sugar and sugar-like (e.g., mannitol) excipients. The two different types of saccharides are combined to obtain a tablet formulation with adequate hardness and fast dissolution rate. Due to its significant hardness, the WOWTAB formulation is a bit more stable to the environment than the Zydus or Orasolv. It is suitable for both conventional bottle and blister packaging. The taste masking technology utilized in the WOWTAB is proprietary, but claims to offer superior mouth feel due to the patented SMOOTHMELT action. The WOWTAB product dissolves quickly in 15 seconds or less. The WOW in WOWTAB signifies the tablet is to be given Without Water. Two WOWTAB formulations currently on the U.S. market are Benadryl Allergy and Sinus FASTMELT and Children's Benadryl Allergy and Cold FASTMELT.

OTHER TECHNOLOGIES:

Flash Dose (Fuisz Technologies), Flashtab (Prographarm Group), and OraQuick (KV Pharmaceutical Co., Inc.) are three formulations on the worldwide market. Biovail Corp. recently announced the filing of an NDA for a FlashDose version of zolpidem tartrate. These technologies are similar to Zydus, WOWTAB, Orasolv and Durasolv in that they dissolve or disperse on the tongue within a minute. However, each also has unique characteristics to differentiate itself from the competition.

FLASHDOSE (Fuisz Technologies, Ltd.): Fuisz Technologies has three oral drug delivery systems that are related to fast dissolution. The first two generations of quick-dissolving tablets, Soft Chew and EZ Chew, require some chewing. However, these paved the way for Fuisz's most recent development, FlashDose. The FlashDose technology utilizes a unique spinning mechanism to produce a floss-like crystalline structure, much like cotton candy. This crystalline sugar can then incorporate the active drug and be compressed into a tablet. This procedure has been patented by Fuisz and is known as Shearform. The final product has a very high surface area for dissolution. It disperses and dissolves quickly once placed onto the tongue. Interestingly, by changing the temperature and other conditions during production, the characteristics of the product can be altered greatly. Instead of a floss-like material, small spheres of saccharides can be produced to carry the drug. The process of making microspheres has been patented by Fuisz, and is

known as CEFORM1 and serves as an alternative method of taste masking.

FLASHTAB (Prographarm Group): The Flashtab technology is yet another fast-dissolving/disintegrating oral tablet formulation. It utilizes most of the same excipients as in conventional compressed tablets. A disintegrating agent and a swelling agent are used in combination with coated drug particles in this formulation to produce a tablet that disintegrates in the mouth in less than one minute.

ORAQUICK (KV Pharmaceutical Co., Inc.):

The OraQuick fast-dissolving/disintegrating tablet formulation utilizes a patented taste masking technology. KV Pharmaceutical claims its microsphere technology, known as Micro Mask, has superior mouth feel over taste-masking alternatives. The taste masking process does not utilize solvents of any kind, and therefore leads to faster and more efficient production. Also, lower heat of production than alternative fast-dissolving/disintegrating technologies makes OraQuick appropriate for heat-sensitive drugs. KV Pharmaceutical also claims that the matrix that surrounds and protects the drug powder in microencapsulated particles is more pliable, meaning tablets can be compressed to achieve significant mechanical strength without disrupting taste masking. OraQuick claims quick dissolution in a matter of seconds, with good taste masking.

1.3 TASTE MASKING WITH ION EXCHANGE RESIN

Drug can be bound to the resin by either repeated exposure of the resin to the drug in a chromatographic column or by prolonged contact of resin with the drug solution. The resin forms insoluble adsorbates or resonates through weak ionic bonding with oppositely charged drugs. The exchange from counter ions from the resin is competitive.

Drug release from the resin depends on the two factors:

1. The ionic environment (i.e., pH and electrolyte concentration) within the gastrointestinal tract
2. The properties of the resin.

Drug molecules attached to the resin are released by exchanging with appropriately charged ions in the gastrointestinal tract, followed by diffusion of free drug molecule out of the resins. The process can be depicted by the following equation 1 and 2 for anion exchange and cation exchange respectively. Where x and y are ions in the GI tract.



Table 4: Flavouring agents used for taste masking

Basic Taste	Masking agents
Sweet	Vanilla, Bubble gum, Grapefruit
Acid	Lemon, Lime, Orange, Cherry, Grapefruit
Metallic	Grape, Marsh, Mellow, Gurana, Berries, Mints
Bitter	Liquorice, Coffee, Chocolate, Mint, Grapefruit, Cherry, Peach, Raspberry, Orange, Lemon, Lime.

1.5 POLYMERS USED FOR TASTE MASKING BY COATING

A number of coating materials such as hydrophilic polymers, lipophilic polymers, celluloses, carbohydrates, etc are employed for taste masking.

Table 3: Polymers used for Taste Masking

Bitter drugs	Polymer used
Artemether	Eudragit E 100
Valdecoxib	Eudragit EPO and hydroxypropylmethylcellulose
Pinaverium bromide	Cellulose or shellac
Propantheline bromide	L-HPC,EC
Ibuprofen	Methacrylic acid co-polymer(Eudragit)
Triprolidine HCL	HPMC
Cefeanel daloxate HCL	PVP,EC,HPMC
Enoxacin	HPMC,HPC,EC
Sparfloxacin	HPMC,HPC,EC, L-HPC
Aspirin	Cellulose acetate latex and triacetine
Famotidine	HEC,HPMC
Amoxicillin trihydrate	MCC,L-HPC
Acetaminophen	Cellulose acetate,HPC/cellulose acetate,Eudragit E100,PVP
Amiprilose HCL	Calcium gluconate, Calcium alginate
Clarithromycine	Carbopol,PVP
Drugx	PEG,EudragitL 100-55
Nizatidine	Eudragit E 100
Cetraxate HCL	Corn starch,Macrogol-6000
Ciprofloxacin	Eudragit NE30 D
Pirenzepine and Oxybutynin	Eudragit E-100,MCC, HPC

Disadvantage:

- The coating of fine particles is usually unsuccessful and Coating of granular particles is readily ruptured by chewing and compression.
- Coating with polymers requires sophisticated instruments.
- In addition, most coatings do not have an acceptable in vivo drug releasing mechanism.

Table 5: Taste masking of Drugx with Taste masking Agent

Bitter drugs	Taste masking agent	Taste masking approach
Drugx	Kyron	Complexation

5.4 Physico-mechanical characterization

5.4.1 Bulk Density:

It refers to packing of particles. Bulk density is used to determine the amount of drug that occupies the volume in g/ml.

Procedure: Weighed quantity (10gm) of Drug X was transferred into 100 ml measuring cylinder without tapping during transfer. The volume occupied by drug was measured. Bulk density was measured by using formula

$$\rho_i = m / V_i$$

Where, m = mass of the blend

V_i = untapped volume

Tapped density:

Weighed quantity (10gm) of drug was taken into a graduated cylinder. Volume occupied by the drug was noted down. Then the cylinder was subjected to 500, 750 & 1250 taps in tap density apparatus (Electro Lab USP II). According to USP, The blend was subjected for 500 taps.

% Volume variation was calculated and subjected for additional 750 taps. % Variation is calculated.

$$\rho_t = m / V_t$$

Where, V_t is tapped volume

5.4.3 Carr's Index (Compressibility):

The compressibility index and Hausner ratio are measures of the property of powder to be compressed. The packing ability of drug was evaluated from change in volume, which is due to rearrangement of packing occurring during tapping. It was indicated as Carr's compressibility index was calculated as follows.

$$\text{Carr's index} = [\text{Tapped density} - \text{Bulk density} / \text{Tapped density}] \times 100$$

5.4.4 Hausner Ratio: It is measurement of frictional resistance of the drug. The ideal range should be 1.2-1.5. It was determined by the ratio of tapped density and bulk density

$$\text{Hausner Ratio} = \text{Tapped density} / \text{Bulk density}$$

5.4.5 Angle of Repose:

It is defined as the maximum angle that can be obtained between the free standing of powder heap and horizontal plane, which is given by the equation:

$$\theta = \tan^{-1} h/r$$

Where, θ = Angle of repose.

h = Height of powder heap.

r = Radius of the powder cone.

CONCLUSION:

The objective of formulation development and evaluation of fast disintegrating tablets of Drugx was being achieved. The effective taste masking was achieved for Drugx by preparation of granules using Dushion P544 (R). These patient compliant tablets that had a good taste and rapidly disintegrated in the mouth are useful and practical for pediatric and geriatric formulation. Thus, we are able to achieve our objective of preparing FDTs of Drugx to increase its dissolution by its faster disintegration.

REFERENCE:

- 1) Adel M A, Semreen M, Mazen KQ. Superdisintegrants for solid dispersion to produce rapidly disintegrating tenoxicam tablets via camphor sublimation. *Pharm Technol* 2005 Jan;68-78.
- 2) Kuchekar B.S., Pattan S.R., Gode R.K., Laware R.B., Nirmal S.A., Parjane S.K.; Merekar A.N., Formulation and evaluation of Norfloxacin Dispersible tablets using Natural substances as Disintegrants, *Journal of Chemical and Pharmaceutical Research*, 2009, 1(1): 336-341.
- 3) Fukami J F, Etsuo Y, Yasuo Y, Katsuhide T. Evaluation of rapidly disintegrating tablets containing glycine and carboxymethylcellulose. *Int J Pharm* 2006;310 (1-2):101-9.
- 4) Fukami J, Ozawa A, Yoshihashi Y, Yonemochi E, Terada K. Development of fast disintegrating compressed tablets using amino acid as disintegration accelerator: Evaluation of wetting and disintegration of tablet on the basis of surface free energy. *Chem Pharm Bull* 2005;53 (12):1536-9.
- 5) Kuno Y, Kojima M, Ando S, Nakagami H. Evaluation of rapidly disintegrating tablets manufactured by phase transition of sugar alcohols. *J Control Release* 2005 Jun; 105 (1-2):16-22.
- 6) Martino PD, Martelli S, Wehrle P. Evaluation of different fast melting disintegrants by means of a central composite design. *Drug Dev Ind Phar* 2005;31 (1):109-210.
- 7) Mishra DN, Bindal M, Singh SK, Vijaya Kumar SG. Spray dried excipient base: a novel technique for the formulation of orally disintegrating tablets. *Chem Pharm Bull* 2006;54 (1):99-102.
- 8) Mizumoto T, Masuda Y, Takeshi Y, Estuo Y, Katsuhide T. Formulation design of a novel fast-disintegrating tablet. *Int J Pharm* 2005;306 (1-2):83-90.
- 9) Moen MD, Keating GM. Sumatriptan fast-disintegrating/rapid-release tablets. *Drugs* 2006;66 (6):883-900.
- 10) Mukesh C. Gohel, Rajesh K. Parikh, Bansari K. Brahmbhatt, and Aarohi R. Shah, Improving the Tablet Characteristics and Dissolution Profile of Ibuprofen by Using a Novel Coprocessed Superdisintegrant: A Technical Note, *AAPS PharmSciTech* 2007; 8 (1) Article 13.