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A Review on Recent patents on Fast Dissolving Drug Delivery System

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Introduction

Recent developments in technology have presented viable dosage alternatives for patients who may have difficulty swallowing tablets or liquids. Traditional tablets and capsules administered with an 8-oz. glass of water may be inconvenient or impractical for some patients. For example, a very elderly patient may not be able to swallow a daily dose of antidepressant. An eight-year-old with allergies could use a more convenient dosage form than an antihistamine syrup. A schizophrenic patient in the institutional setting can hide a conventional tablet under his or her tongue to avoid their daily dose of an atypical antipsychotic. A middle-aged woman undergoing radiation therapy for breast cancer may be too nauseous to swallow her H2-blocker. Fast-dissolving/disintegrating tablets (FDDTs) are a perfect fit for all of these patients.

FDDTs disintegrate and/or dissolve rapidly in the saliva without the need for water. Some tablets are designed to dissolve in saliva remarkably fast, within a few seconds, and are true fast-dissolving tablets. Others contain agents to enhance the rate of tablet disintegration in the oral cavity, and are more appropriately termed fast-disintegrating tablets, as they may take up to a minute to completely disintegrate

A fast-dissolving drug delivery system, in most cases, is a tablet that dissolves or disintrigrants in the oral cavity without the need of water or chewing. Most fast-dissolving delivery system films must include substances to mask the taste of the active ingredient. This masked active ingredient is then swallowed by the patient's saliva along with the soluble and insoluble excipients.These are also called melt-in-mouth tablets, repimelts, porous tablets, oro-dispersible, quick dissolving or rapid disintegrating tablets2

The target populations for these new fast-dissolving/disintegrating dosage forms have generally been pediatric, geriatric, and bedridden or developmentally disabled patients. Patients with persistent nausea, who are traveling, or who have little or no access to water are also good candidates for FDDTs.[1]

Salient Features of Fast Dissolving Drug Delivery System

- Ease of administration to patients who refuse to swallow a tablet, such as paediatric and geriatric patients and, psychiatric patients.
- Convenience of administration and accurate dosing as compared to liquids.
- No need of water to swallow the dosage from, which is highly convenient feature for patients who are traveling and do not have immediate access to water.
- Good mouth feels properly of MDDS helps to change the basic view of medication as "bitter pill", particularly for paediatric patients.
- Rapid dissolution of drug and absorption which may produce rapid, onset of action.
- Some drugs are absorbed from the month pharynx and oesophagus as the saliva passes down into the stomach, in such cases bioavailability of drugs is increased.
- Ability to provide advantages of liquid medication in the form of solid preparation.
- Pregastric absorption can result in improved bioavailability and as a result of reduced dosage, improved clinical performance through a reduction of unwanted effects. [2]

Requirements of Fast Dissolving Tablets

An ideal FDT should

- Have a pleasing mouth feel.
- Require no water for oral administration, yet dissolve / disperse/ disintegrate in mouth in a matter of seconds.
- Have an acceptable taste masking property.
- Be harder and less friable

- Exhibit low sensitivity to environmental conditions (temperature and humidity).
- Allow the manufacture of tablet using conventional processing and packaging equipments.
- Advantages of FDT
- Leave minimal or no residue in mouth after administration
- Rapid drug therapy intervention.
- Good mouth feel property helps to change the perception of medication as bitter pill particularly in pediatric patients.
- Administration to the patients who can not swallow, such as the elderly, stroke victims, bedridden patients, patients affected by renal failure & patients who refuse to swallow such as pediatric, geriatric & psychiatric patients.
- Achieve increased bioavailability/rapid absorption through pregastric absorption of drugs from mouth, pharynx & oesophagus as saliva passes down.
- Convenient for administration and patient compliant for disabled, bedridden patients and for travelers and busy people, who do not always have access to water.
- The risk of chocking or suffocation during oral administration of conventional formulations due to physical obstruction is avoided, thus providing improved safety.
- New business opportunity like product differentiation, product promotion, patent extension and life cycle management. [2]

Methodology Employed For FDT Formulations[3] Melt granulation

Melt granulation technique is a process by which pharmaceutical powders are efficiently agglomerated by a meltable binder. The advantage of this technique compared to a conventional granulation is that no water or organic solvents is needed. Because there is no drying step, the process is less time consuming and uses less energy than wet granulation. It is a useful technique to enhance the dissolution rate of poorly water-soluble drugs, such as griseofulvin.This approach to prepare FDT with sufficient mechanical integrity, involves the use of a hydrophilic waxy binder (Superpolystate©, PEG-6-stearate). Superpolystate© is a waxy material with a melting point of 33–37°C and a HLB value of . So it will not only act as a binder and increase the physical resistance of tablets but will also help the disintegration of the tablets as it melts in the mouth and solublises rapidly leaving no residues.

Phase transition process

It is concluded that a combination of low and high melting point sugar alcohols, as well as a phase transition in the manufacturing process, are important for making FDTs without any special apparatus. FDT were produced by compressing powder containing erythritol (melting point: 122 °C) and xylitol (melting point: 93 95 °C), and then heating at about 93 °C for 15 min. After heating, the median pore size of the tablets was increased and tablet hardness was also increased. The increase of tablet hardness with heating and storage did not depend on the crystal state of the lower melting point sugar alcohol.

Sublimation

In this method a subliming material like camphor, is removed by sublimation from compressed tablets and high porosity is achieved due to the formation of many pores where camphor particles previously existed in the compressed tablets prior to sublimation of the camphor. A high porosity was achieved due to the formation of many pores where camphor particles previously existed in the compressed mannitol tablets prior to sublimation of the camphor. These compressed tablets which have high porosity (approximately 30%) rapidly dissolved within 15 seconds in saliva. Granules containing nimusulide, camphor, crospovidone, and lactose were prepared by wet granulation technique. Camphor was sublimed from the dried granules by vacuum exposure. Conventional methods like dry granulation, wet granulation and direct compression with highly soluble excipients, super disintegrants and/or effervescent systems can also be used.

Three-dimensional Printing (3DP)

Three-dimensional printing (3DP) is a rapid prototyping (RP) technology. Prototyping involves constructing specific layers that uses powder processing and liquid binding materials. A novel fast dissolving drug delivery device (DDD) with loose powders in it was fabricated using the three dimensional printing (3DP) process. Based on computer-aided design models, the DDD containing the drug acetaminophen were prepared automatically by 3DP system.10 It was found that rapidly disintegrating oral tablets with proper hardness can be prepared using TAG. The rapid disintegration of the TAG tablets seemed due to the rapid water penetration into the tablet resulting from the large pore size and large overall pore volume.

Mass Extrusion

This technology involves softening of 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.

Spray Drying

Maximum drug release and minimum disintegration time were observed with Kollidon CL excipient base as compared to tablets prepared by direct compression, showing the superiority of the spray dried excipient base technique over direct compression technique.

Cotton Candy Process

This process is so named as it utilizes a unique spinning mechanism to produce floss-like crystalline structure, which mimic cotton candy. Cotton candy process involves formation of matrix of polysaccharides or saccharides by simultaneous action of flash melting and

spinning. The matrix formed is partially recrystallized to have improved flow properties and compressibility. This candy floss matrix is then milled and blended with active ingredients and excipients and subsequently compressed to ODT. This process can accommodate larger drug doses and offers improved mechanical strength. However, high-process temperature limits the use of this process.

Molding

The molding technology results in tablets with an appropriate dissolution time, even though they are characterized by poor mechanical properties (hardness).

Lyophilization or Freeze-Drying

Freeze-drying allows immediate dissolution of the tablets because of their high porosity, and enhances drug stability, especially for moisture-sensitive substances; on the other hand, a porous network is associated with low physical resistance and high friability. Special packaging is required in some cases

Patented Technologies for Fast Dissolving Tablets[3]

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.5 Thirteen products are currently available using Zydis technology.4 In the U.S., they include: Claritin Reditab, Dimetapp Quick Dissolve, Feldene Melt, Maxalt-MLT, Pepcid RPD, Zofran ODT and Zyprexa Zydis. On the worldwide market, other Zydis formulations are available for oxazepam, lorazepam, loperamide, and enalapril.

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.3 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.

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-disintegrating 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's primary competitors, may disrupt such a taste masking approach.

The OraSolv technology is utilized in six marketed products: four Triaminic Softchew formulations, Tempra FirsTabs, and Remeron SolTab.

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. DuraSolv is currently available in two products: NuLev and Zomig ZMT.

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 Zydis 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 mouthfeel 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 With Out Water. Two WOWTAB formulations currently on the U.S. market are Benadryl Allergy & Sinus FASTMELT and Children's Benadryl Allergy & Cold FASTMELT.

OTHER TECHNOLOGIES NOT YET ON THE U.S. MARKET

FlashDose (Fuisz Technologies, Ltd.), Flashtab (Prographarm Group), and OraQuick (KV Pharmaceutical Co., Inc.) are three formulations on the worldwide market which will likely reach the United States in the near future. Biovail Corp. recently announced the filing of an NDA for a FlashDose version of zolpidem tartrate. These technologies are similar to Zydis, 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 under 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 MicroMask, has superior mouthfeel 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/disinte-grating 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. There are no products using the OraQuick technology currently on the market, but KV Pharmaceutical has products in development such as analgesics, scheduled drugs, cough and cold, psychotropics, and anti-infectives.

ADVANTOL™ 200

Advantol™ 200 is a directly compressible excipient system offering "Soft-Melt" functionality and specially

formulated for nutraceutical applications. SPI Pharma's Advantol platform uses proprietary co-processing technology. Advantol requires no special manufacturing equipment or tooling. Advantol formulations utilize a standard rotary tablet press with standard tooling under normal tableting temperature and humidity conditions to make robust "soft-melt" tablets.

FROSTA TECHNOLOGY

Akina patents this technology. It utilizes the concept of formulating plastic granules and compressing them at low pressure to produce strong tablets with high porosity. Plastic granules composed of porous and plastic material, water penetration enhancer, and binder. The process involves mixing the porous plastic material with water penetration enhancer followed by granulating with binder. The tablets obtained have excellent hardness and rapid disintegration time ranging from 15 to 30 sec depending on size of tablet.

ADVATAB

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 especially suited to those patients that experience difficulty in swallowing capsules and tablets. AdvaTab is distinct from other ODT technologies as it can be combined with Eurand's complimentary particle technologies like its world leading Microcaps® taste-masking technology and its Diffucaps® , controlled release technology. The pairing of AdvaTab with Microcaps creates products that offer the dual advantage of a patient preferred dosage form, together with a superior taste and smooth mouth feel. This is a critical advantage as the unpleasant taste of drugs is a significant restriction in the application of other ODT technologies.

PATENTS ON FAST DISSOLVING TECHNOLOGY

Ahmed, Salah U.Gorukanti, et al received US patent for Ondansetron orally disintegrating tablets. The present invention provides a non-effervescent, solid orally disintegrating dosage form adapted for oral administration to a mammal, such as a human, of ondansetron composition having at least one hydrophilic component comprising a first-waterdispersible component, a component having a --CHOH functional group and a water-insoluble component, optionally a lubricant and optionally a sweetener. Useful dosage forms include ondansetron orally disintegrating tablets. In some embodiments, the dosage forms provide for greater than 75 percent dissolution at thirty minutes when measured in a medium of 500 mL of 0.01 N HCl and a paddle speed of 50 rpm. In some embodiments, the dosage forms provide for greater than 95 percent dissolution at fiveminutes, when measured in a medium of 500 mL of 0.01 N HCl and a paddle speed of 50 rpm. A representative dosage form comprises ondansetron, microcrystalline cellulose, aspartame, crospovidone, mannitol, colloidal silicon dioxide, magnesium stearate,sodium stearyl fumarate and xylitol. In addition, the present invention provides a non-effervescent tablet comprising the ondansetron composition. The dosage forms can be used for the treatment of emesis such as nausea and vomiting caused by cancerchemotherapy and radiation or mental disorders. Finally, a process of forming an ondansetron disintegrating tablet is disclosed.[4]

Shimizu, Toshihiro Morimoto(2008), et al patented Orally disintegrable tablets in which an orally disintegrable tablet which comprises (i) fine granules having an average particle diameter of 400 μm or less, which fine granules comprise a composition coated by an enteric coating layer, said composition having 10 weight % or more of an acid-labile physiologically active substance and (ii) an additive, has superior disintegrability or dissolution in the oral cavity so that it can be used for treatment or prevention of various diseases, as an orally disintegrable tablet capable of being administered to the aged or children and easily administered without water. Also, because the tablet of the this invention contains fine granules having the average particle diameter such that it will not impart roughness in mouth, it can be administered easily without discomfort at the administration.[5]

Moreau, Marinette et al(2008) filled US patent application for Methods for Obtaining a Fast Dissolving Imidapril Powder in which they developed a method which is advantageously economical, simple and quick, and makes it possible to use equipment known and widespread in the pharmaceutical industry. The method makes it possible to obtain an Imidapril powder which can be directly packaged and which has good stability when stored. And thus it is possible to obtain Imidapril in a particular physical condition and, more notably, a new crystalline condition, whatever the initial physical condition of the Imidapril used, by spraying a Imidapril solution onto an excipient in a granulator, for instance, a fluidized bed granulator, and by drying the resulting Imidapril powder. Such new crystalline condition makes it possible to obtain a powder having a high dissolution rate, at least comparable not to say increased with respect to the dissolution rates described in the prior art for the known formulations of Imidapril. Thus, it provide a method for preparing a fast dissolving Imidapril powder comprising at least the steps of spraying a solution of Imidapril onto at least one excipient in a granulator, preferably a fluidized air bed granulator or a fluidized inert gas bed granulator and drying the powder thus obtained.[6]

Nakatani, Manabu Yokoyama et al (2008) filled US patent application for bilayer tablet comprising telmisartan and diuretic. The invention relates to a bilayer pharmaceutical tablet comprising a first layer containing 3 to 50 wt. % of telmisartan dispersed in a dissolving tablet matrix comprising (a) a basic agent in a molar ratio of basic agent: telmisartan=1:1 to 10:1, (b) a surfactant or

emulsifier in an amount of about 1 to 20 wt. % of the final composition,(c) 25 to 70 wt. % of a water-soluble diluent, and(d) optionally 0 to 20 wt. % of further excipients and/or adjuvants,and a second tablet layer containing a diuretic in a disintegrating tablet matrix. The bilayer tablet according to the this invention provides a largely pH-independent dissolution of the poorly water-soluble telmisartan, thereby facilitating dissolution of the drug at a physiological pH level, and also provides for immediate release of the diuretic from the fast disintegrating matrix. At the same time, the bilayer tablet structure overcomes the stability problem caused by the incompatibility of diuretics like HCTZ with basic constituents of the telmisartan formulation.[7]

Withiam, Michael C. et al (2007) filled US patent application for Rapidly dissolving tablets comprising low surface area titanium dioxide. This invention pertains to the ability to provide rapidly disintegrating tablets through the inclusion of a titanium dioxide material in combination with other common tablet components. Such a titanium dioxide material must exhibit a sufficiently low surface area in order to boost the ability of the tablet to separate quickly when introduced into a user's mouth cavity. Such a tablet is dimensionally stable prior to use (low friability) and, when immersed in water the tablet disintegrates therein in less than about 60 seconds. Such an inventive tablet provides an effective quick dissolving result while also exhibiting low friability such that the product is highly acceptable to the user aesthetically as well. Without the low surface area calcium phosphate material, the resultant tablet would not exhibit the same degree of quick dissolution.[8]

Fu, Yourong Jeong et al(2006) received US patent for Mannose-based fast dissolving tablets in which Fast-dissolving pharmaceutical tablets comprising mannose are described. The mannose component imparts both structure-forming and fast-dissolution properties to the tablets. Granulation of tablet components and humidification forms strong liquid bridges at the surface interfaces of mannose particles, which leads to strengthened tablets. The mannose particles, however, remain porous following compression so that contact with moisture, e.g., saliva in the mouth, leads rapidly to tablet disintegration and dissolution.[9]

Yousef, Abdul Razzaq et al (2005) received US patent for Instant dissolving tablet composition for loratidine and desloratidine in which tablet formulation of loratidine and desloratidine, non-sedating antihistaminic agents, that allows fast dissolution of tablets in the mouth allowing administration of these drugs without the aid of water. The formulation has pleasing taste and texture. A pharmaceutical composition for oral administration comprising of an anti-allergic effective amount of loratadine in a pharmaceutically acceptable carrier medium consisting essentially of a proprietary disintegrant, PHARMABURST, an amount of lubricant talc, an amount of lubricant sodium stearyl fumarate, an amount of lubricant magnesium stearate, an amount of lubricant silicon dioxide, an amount of sweetening agent acesulfate potassium, an amount of flavor anise dry flavor, and an amount of flavor mint dry sufficient to provide dissolution of at least about 80% by weight of the pharmaceutical composition in about 45 minutes.[10]

Wang, Wen-Che et al (2005) received US patent for Fast dissolving tablet and method of preparing fast dissolving tablet. The fast dissolving tablet comprises a pharmaceutically active ingredient, a starch, a hydrophilic polymer, a surfactant, and excipients. A method of preparing the fast dissolving tablet is also disclosed. A method of preparing a fast dissolving tablet, comprising: providing a first solution comprising a hydrophilic polymer and a starch; providing a second solution comprising a pharmaceutically active ingredient and a surfactant; blending the first and second solutions to form a plurality of granule powders by a granulating; blending the granule powders and excipients; and performing a compression-molding process to form the tablet.[11]

Kohlrausch et al (2005) received US patent for Multilayer tablet in which tablet comprises a first layer formulated for instant release of the angiotensin II receptor antagonist telmisartan from a dissolving tablet matrix, a second layer formulated for instant release of the angiotensin converting enzyme inhibitor ramipril and optionally a diuretic from a disintegrating tablet matrix, and, optionally, a third layer formulated for instant release of a diuretic like hydrochlorothiazide from a fast disintegrating tablet matrix. In accordance with the invention problems associated with the preparation of a fixed dose combination drug comprising telmisartan, ramipril and, optionally, a diuretic can best be handled by means of a multilayer pharmaceutical tablet comprising a first layer of telmisartan, preferably in substantially amorphous form, in a dissolving tablet matrix and a second layer of ramipril alone or ramipril together with a diuretic such as HCTZ in a disintegrating tablet matrix. Alternatively, the tablet may contain a third layer comprising the diuretic in a disintegrating tablet matrix. The tablet according to the present invention provides a largely pH-independent dissolution of the poorly water-soluble telmisartan, thereby facilitating dissolution of the drug at a physiological pH level, and adequate stability and drug release of ramipril. In combination with a diuretic it provides for instant release of the diuretic from a fast disintegrating matrix. The tablet structure also overcomes the stability problem caused by the incompatibility of diuretics like HCTZ with basic constituents of telmisartan formulations and the stability problem caused by the incompatibility of ramipril with basic constituents of telmisartan.[12]

Purdy, David F et al (2005) received US patent for Dual layer tablet, method of making and use thereof in which A method for treating a recirculating water system which comprises introducing into said water system a multifunctional, multilayer tablet, wherein the multilayer tablet comprises a fast dissolving layer and a slow dissolving layer, wherein said fast dissolving layer releases a combination of active ingredients including a

member selected from the group consisting of lithium hypochlorite, calcium hypochlorite, trichloroisocyanuric acid (TCCA), anhydrous sodium dichloroisocyanurate, sodium persulfate, potassium persulfate, potassium monopersulfate, sodium monopersulfate, and mixtures thereof, and at least one of a clarifier, chelating agent, sequesterant, algaestat, water softener, algaecide, corrosion inhibitor, scale inhibitor, flocculent, disintegrant, dispersant, colorant, dissolution control agent, fragrance, or surfactant and, wherein said slow dissolving layer includes a member selected from the group consisting of trichloroisocyanuric acid (TCCA), calcium hypochlorite, 1,3-dichloro-5,5-dimethylhydantoin (DCDMH), 1,3-dibromo-5,5-dimethylhydantoin (DBDMH), 1-bromo-3-chloro-5,5-dimethylhydantoin (BCDMH), 1,3-dichloro-5-ethyl-5-methylhydantoin (DCEMH), 1,3-dibromo-5-ethyl-5-methylhydantoin (DBEMH), 1-bromo-3-chloro-5-methyl-5-ethylhydantoin (BCEMH), and mixtures thereof, and at least one of a clarifier, chelating agent, sequesterant, algaestat, water softener, algaecide, corrosion inhibitor, scale inhibitor, flocculent, disintegrant, dispersant, colorant, dissolution control agent or surfactant.[13]

Danilovski, Aleksandar et al (2005) received US patent for Single dose fast dissolving azithromycin The present disclosure related to a method of treating an infection by oral administration of a single dose of a fast dissolving form of azithromycin. The disclosure also relates to a method of reducing the adverse effects arsing from treatment of a subject having an infection by administering a single dose of a fast dissolving form of azithromycin. As used herein, with reference to the azithromycin dosage forms, the term "fast dissolving" denotes an azithromycin dosage form in which at least about 20% by weight of the azithromycin contained in the dosage form is dissolved within 5 minutes at pH 3.0 or higher. Preferably, at least about 20% by weight of the fast dissolving azithromycin dissolves within 5 minutes at pH 3.0, at least about 50% by weight dissolves within 10 minutes at pH 6.0 and at least about 60% by weight dissolves within 20 minutes at pH 6.8. The dosage forms described herein are effectively immediate release dosage form and a dose that is administered only once over the whole anti-infective treatment period.[14]

Fu, Yourong Pai, Chaul Min et al (2005) received US patent for Highly plastic granules for making fast melting tablets in which A fast-melting pharmaceutical tablet comprises a porous, plastic substance, a water penetration enhancer and a binder. One or more drugs can be incorporated into the formulation at different stages of the process so as to afford a pharmaceutically active tablet. Methods of making the pharmaceutical tablet entail combining the porous, plastic material, the water penetration enhancing agent, and the binder so as to form highly plastic granules, which are compressed into tablets. The resulting tablets dissolve rapidly in the mouth and have good hardness with low brittleness. The tablets are particularly valuable to those who have difficulty swallowing conventional pills.[15]

Abu-Izza, Khawla A. et al (2004) received US patent for Fast dissolving tablet. The present invention relates to processes for the preparation of tablets which dissolve rapidly in the mouth and provide an excellent mouthfeel. The tablets of the invention comprise a compound which melts at about 37° C. or lower, have a low hardness, high stability and generally comprise few insoluble disintegrants which may cause a gritty or chalky sensation in the mouth. Convenient and economically feasible processes by which the tablets of the invention may be produced are also provided.The present invention advantageously provides compositions and methods for preparing a fast dissolving tablet of low hardness but good physical stability that can be made at very low compression force.Thus, the invention provides a tablet comprising a low melting point compound that melts or softens at or below 37° C., a water soluble excipient, and an active ingredient. Preferably, the low melting point compound comprises from about 2.5% to about 20% (wt/wt) of the composition (e.g., 2.5, 5, 7.5, 10, 12, 14, 16, 18, or 20% (wt/wt)). Preferably the tablet has a hardness of about 3 kP or less, more preferably about 2 kP or less, and still more preferably about 1 kP or less. Preferably, the minimum hardness of the tablet is about 0.1 kP, although lower values, including 0.05 kP, are possible. The invention further provides a method of producing a tablet composition. The method comprises combining an active agent with a fast dissolving granulation. The fast dissolving granulation comprises a low melting point compound and a water soluble excipient. Preferably, the low melting compound is present in an amount that will yield values of about 2.5% to about 20% (wt/wt) in a final tablet composition (e.g., 2.5, 5, 7.5, 10, 12, 14, 16, 18, or 20% (wt/wt)).[16]

Sparks, Robert E. et al (2003) received US patent for Method of producing porous tablets with improved dissolution properties in which A method of producing a fast-dissolving pharmaceutical delivery device of moderate strength. The delivery device is a fully formed tablet composed of readily available sugars, strength polymers and a volatilizable excipient along with an active ingredient and optional flavorings. The tablet as made will disintegrate in an aqueous medium such as saliva in under 15 seconds, making mastication unnecessary or at least requiring only one or two bites on the tablet. Essential to the invention is the easily obtainable particle size ranges of the sugars and the volatilizable excipient which promotes optimum release and tablet strength. The invention also allows for effective taste masking of the active ingredient with standard particle coating techniques.[17]

Thombre, Avinash G. et al (2002) received US patent for Rapidly disintegrating and fast-dissolving solid dosage form which is Described are non-friable, rapidly disintegrating, fast-dissolving solid dosage forms that are produced from pharmaceutically acceptable steam extruded polymers. The solid dosage forms dissolve in

the mouth and are particularly useful for subjects that require or desire oral medication but have difficulty swallowing standard oral dosage forms such as tablets or in subjects suffering from emesis. The solid dosage forms are also useful for rapid drug delivery as vaginal or rectal suppositories or for oral delivery of veterinary drugs.[18]

Liu, Fang-yu. et al (2002) received US patent for Water soluble polymer-based rapidly dissolving tablets and production processes thereof. The invention provides for novel compressed tablets capable of rapidly disintegrating in aqueous solutions, comprising at least one non-saccharide water soluble polymer, which are free of organic solvent residues, and methods of making such pharmaceuticals. A process for producing a pharmaceutical tablet, comprising the following steps: (a) granulating a formulation comprising a water soluble polyvinylpyrrolidone and at least one active ingredient together, wherein no organic solvents are included in the formulation, and wherein a saccharide of low moldability is included in the formulation; (b) compressing the product of the granulation into a tablet form; (c) humidifying the tablet by exposing the product of step (b) to an aerated environment at least about 50% to 100% relative humidity; and (d) drying the tablet, wherein the hardness of the tablet is between about 0.5 kilopounds to about 12.0 kilopounds, and further wherein the tablet has an in vivo disintegration time of about 1 second to about 40 seconds, and further wherein the tablet comprises an effective amount of the polyvinylpyrrolidone to achieve said in vivo disintegration time and said hardness factor.[19]

Khankari, Rajendra K. et al (2001) received US patent for Rapidly dissolving robust dosage form The invention relates to a hard, compressed, rapidly dissolvable dosage form adapted for direct oral dosing. The dosage form includes an active ingredient and a matrix. The matrix is composed of at least a nondirect compression filler and a lubricant. The dosage form is adapted to rapidly dissolve in the mouth of a patient and thereby liberate the active ingredient. Preferably, the dosage form has a friability of about 2% or less when tested according to the U.S.P. The dosage form also preferably has a hardness of 15-50 Newtons ("N"). It is desirable that the dosage form dissolve in about 90 seconds or less in the patient's mouth. It is also often desirable that the dosage form include at least one particle. The particle would the active ingredient and a protective material. These particles can include rapid release particles and or sustained release particles. In a particularly preferred formulation in accordance with the present invention there is provided a hard, compressed, rapidly dissolving tablet adapted for direct oral dosing. The tablet includes particles made of an active ingredient and a protective material. These particles are provided in an amount of between about 0.01 and about 75% by weight based on the weight of the tablet. The tablet also includes a matrix made from a nondirect compression filler, a wicking agent, and a hydrophobic lubricant. The tablet matrix comprises at least about 60% rapidly water-soluble ingredients based on the total weight of the matrix material. The tablet has a hardness of between about 15 and about 50 Newtons, a friability of less than 2% when measured by U.S.P. and is adapted to dissolve spontaneously in the mouth of a patient in less than about 60 seconds and thereby liberate said particles and be capable of being stored in bulk. The dosage forms described above are able to dissolve rapidly in the mouth of the patient, with a minimum of grit or other organoleptically unpleasant species. Moreover, because the dosage forms are hard and have low friability they can be handled and packaged like other, nonrapidly dissolving dosage form[20]

Allen, Loyd V. et al (2001) received US patent for Particulate support matrix for making a rapidly dissolving dosage form. According to one aspect of the invention, there is provided a particulate matrix comprising a first polymeric component having a predetermined net charge when in solution, a second polymeric (solubilizing) component having a predetermined net charge when in solution of the same sign as the net charge of the first polymeric component, and a bulking agent, characterized in that the second polymeric component has a solubility in aqueous solution greater than that of the first polymeric component. According to another aspect of the invention, there is provided a rapidly dissolving pharmaceutical dosage form comprising: a particulate support matrix comprising a first polymeric component having a predetermined net charge when in solution, a second polymeric component having a predetermined net charge when in solution of the same sign as the net charge of the first polymeric component, and a bulking agent, and wherein the second polymeric component has a solubility in aqueous solution greater than that of the first polymeric component; and a pharmaceutical ingredient mixed with the particulate support matrix. The support matrix is generally substantially completely disintegrable within less than about 20 seconds when the dosage form is introduced into an aqueous environment so as to release the pharmaceutical ingredient to the aqueous environment.[21]

Herreid, Richard M. et al (2000) received US patent for Method for making fast dissolving bouillon cubes in which method for producing a fast dissolving low fat bouillon cube includes providing a bouillon powder which is free-flowing to a die having a residual of water on a surface. The bouillon powder is compressed at low pressure, thereby forming a fast dissolving bouillon cube. The invention is a method of producing a fast dissolving, low fat bouillon cube which includes providing a bouillon powder. The powder has substantially no water added to it. A compression surface of a punch is cleaned with water, leaving a residue of water on the compression surface. A die is filled with bouillon powder and the bouillon powder within the die is compressed with the compression surface of the punch to form a low density fast dissolving bouillon cube.

In another embodiment, the invention is a method of producing a fast dissolving, low density bouillon cube. The method includes filling a hopper with a free-flowing

bouillon powder. A compression surface of a punch is cleaned with water, thereby leaving a residue of water on the compression surface. The compression surface is movable within a four-sided die. The compression surface extends out of an open top when being cleaned. The compression surface is moved to form a bottom of the die and free-flowing bouillon powder from the hopper is then filled into the die. The compression surface is moved toward the top of the die, thereby compressing the powder against a compression member to form a low density, fast dissolving bouillon cube.In another embodiment, The cube is formed by applying a residue coating of water to an inside surface of a die, the inside surface defining a portion of a cavity formed by the die. The cavity of the die is filled with a free-flowing bouillon powder. A force of less than 3,000 pounds per square inch is applied to the powder, thereby forming a low density, fast dissolving bouillon cube.[22]

References:

1. Robin h. Bogner, r.ph., ph.d., associate professormeghan f. Wilkosz, pharm.d. (cand.)University of connecticutschool of pharmacy,storrs, ct,fast dissolving tqablets,us pharmacist,13/09/2002
2. Shailesh sharma, new generation of tablet: fast dissolving tablet,pharmainfo.net, vol. 6 issue 1, 2008
3. Dinesh bhandari, recent trends - fast dissolving tablets.,pharmainfo.net, vol. 6 issue 6, 2008
4. Ahmed, salah u. Gorukanti, sudhir r. Chowdhury, tahseen a., ondansetron orally disintegrating tablets, us patent 7390503,_june 24, 2008
5. Shimizu, toshihiro morimoto
6. Moreau, marinette ,grellety, sebastien, methods for obtaining a fast dissolving imidapril powder, us patent application 20080167358,_july 10, 2008
7. Nakatani, manabu,yokoyama, kazutoshi sawada, takeshi, bilayer tablet comprising telmisartan and diuretic, us patent application 20080113023,_may 15, 2008
8. withiam, michael c.,mehra, dev k.,cornelius, john m, rapidly dissolving tablets comprising low surface area calcium phosphates, us patent application 20070196477,_august 23, 2007
9. Fu, yourong ,jeong, seong hoon,kim, jeanny,callihan, jacqueline a park, kinampai, chaul minpark, sang yeobseomoon, mannose-based fast dissolving tablets, us patent application 20060134195,june 22, 2006
10. Yousef, abdul razzaq,zaman, quamar, instant dissolving tablet composition for loratidine and desloratidine, us patent application 20050214365,_september 29, 2005
11. wang, wen-che,chen, hui-yu,yang, chih-chiang, fast dissolving tablet and method of preparing the same, us patent application 20050196438,september 8, 2005
12. Nakatani, manabu,yokoyama, kazutoshisawada, takeshi, bilayer tablet comprising telmisartan and diuretic, us patent application 20080113023,_may 15, 2008
13. Davis f purbi,dual layer tablets-method of using and therof,us patent no-6863830,march 8,2005.
14. Danilovski, aleksandar, zdravka, knezevic, single dose fast dissolving azithromycin, us patent application 20050026851,_february 3, 2005
15. Fu, yourong,pai, chaul minpark, sang yeob,seomoon, gun,park, kinam, highly plastic granules for making fast melting tablets, us patent application 20050013857,_january 20, 2005
16. Abu-izza, khawla a.li, vincent h.look, jee l.parr, graham d.schineller, matthew k., fast dissolving tablet, us patent 6733781,_may 11, 2004
17. Robert e sparks,irvin c jacobs,method of produsing porous tablets with improved dissolution properties,patent no-us 6544552,april 8 2003,
18. Thombre g, avinash,rapidly disintegrating and fast dissolving solid dosage form,patent no-6494899, december 24,2002
19. Liu, fang-yu,he, min michael,nyshadham, janaki ram,sharma,kuldeepak,chu, james shunnan,fix, joseph a. Water soluble polymer-based rapidly dissolving tablets and production processes thereof, us patent 6465009,_october 15, 2002
20. Khankari, rajendra k.,hontz, john,chastain, sara j,katzner, leo, rapidly dissolving robust dosage form us patent 6024981_february 15, 2000
21. Allen, loyd v,wang, bingnan, particulate support matrix for making a rapidly dissolving dosage form us patent 6177104,january 23, 2001
22. Herreid, richard m.,lippert, vernon e., method for making fast dissolving bouillon cubes, us patent 6126979,october 3, 2000

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