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IMMEDIATE RELEASE DRUG DELIVERY SYSTEMS: A CURRENT UPDATE

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ABSTRACT

Instead of tremendous advancements in drug delivery, the oral route remains the most preferred route for the administration of therapeutic agents because of the low cost of therapy and ease of administration that leads to high levels of patient concordance. Incorporating an existing medicine into Newer Drug Delivery System (NDDS) are gaining popularities. One such approach is to formulate Immediate Release Tablet, which dissolve or disintegrate rapidly in saliva without the need of water within few seconds due to action of superdisintegrant in the formulation or other novel manufacturing technique. The demand for orally disintegrating tablets has enormously increased during the last decade over the other oral dosage forms (such as tablets, capsules, dry syrups, chewing gums, chewable tablets etc.) particularly for geriatrics and pediatrics, travelers, dysphasics, psychotics and non-cooperative patients. Considering the advantages of Immediate Release Tablet and its growing demand, an attempt has been made through this article to give an overview of preparation and new methodologies for the Immediate Release Tablet followed currently and in past including some patient information.

INTRODUCTION

The demand for more patient compliant dosage forms is increasing tremendously from the last two decades. As a result, the demand for their technologies is been increasing day by day. Due to the high development cost of a new drug entity, the pharmaceutical companies are focusing on the development of newer drug delivery systems for the existing drug with an improved efficacy and bioavailability together with reduced dosing frequency to minimize side effects [1].

Maximum therapeutically active substances are present in the form of tablet, capsule, and pill or powder dosage forms for oral administration. These dosage forms are to be swallowed so that the pharmaceutically active substance can be absorbed via the gastrointestinal tract [2]. Some time the administration of tablets and capsules with a glass of water become inconvenient or impractical for some patients (e.g. patients with tuberculosis). However, oral dosage forms are difficult to administer in unconscious & non-cooperative patients. Many

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pediatric and geriatric patients are unwilling to take these solid preparations due to fear of choking [3]. It has been found that approximately 25–30 % of the population finds it difficult to swallow an oral dosage form [4]. This disorder is also associated with number of medical conditions including Stroke, Parkinson's disease, head and neck radiation therapy and other neurological disorders including Cerebral Palsy.

Immediate Release Drug Delivery System (IRDDS) has acquired an important position in the market by overcoming previously encountered administration problem and contributing in extension of patient life [1]. IRDDS has the unique property of rapidly disintegrating or dispersing and releasing the drugs as soon as they come in contact with the saliva, thus obviating the requirement of water during administration. The IRDDS usually disintegrates in the oral cavity within 15 seconds to 3 minutes. A major component of success in IRDDS is good taste.

BIOPHARMACEUTICS CLASSIFICATION SYSTEM

The Biopharmaceutics Classification System (BCS) was developed by a collaboration of academic, industrial and government scientists in order to provide guidelines for the development of oral dosage forms. The basic principle behind the classification system is that the absorption of immediate-release dosage forms, orally administered drugs is driven by two properties viz. the solubility of the drug in the gastrointestinal tract and the permeability of the drug across the intestinal epithelial cell barrier. Proper *in vitro* surrogates for these two properties should allow prediction of a drug's absorption *in vivo* from *in vitro* assays [4]. The interest in this classification system stems largely from its application in early drug development and then in the management of product change through its life cycle. In early drug development, knowledge of the class of a particular drug is an important factor influencing the decision to continue or stop its development. Obviously a low solubility/low permeability drug will never be presented as an orally administered product and will probably encounter serious formulation difficulties. A company desiring to produce an oral dosage form will wish to limit its development to those molecules that are highly permeable. Increasingly, these considerations are incorporated from the very earliest phases, with the concept of property-based design being used in combinatorial chemistry to target production of compounds showing optimal properties. In future, the experts predict an increasing shift from the *in vitro* cell-line screening models to absorption studies occurring predominately '*in computro'*, as computer models are developed to link molecular motives to absorption properties [5]. The BCS guidance recommends a strategy for identifying expendable clinical bioequivalence tests and also recommends a class of immediate-release solid oral dosage forms for which bioequivalence may be assessed based on *in vitro* dissolution tests in order to improve the efficiency of drug development and the review process [5].

According to the BCS, drug substances are classified as follows:

Class I - High Permeability, High Solubility
Class II - High Permeability, Low Solubility
Class III - Low Permeability, High Solubility
Class IV - Low Permeability, Low Solubility

Currently, only Class I (highly soluble and highly permeable) drugs are eligible for a biowaiver. This policy is based on research showing systemic exposure to a drug, which is proportional to its rate and extent of absorption, is in turn related to its solubility and permeability, especially when the rate of dissolution is rapid in relation to gastric emptying. There is currently an ongoing exchange of ideas regarding the idea that Class III (high-solubility, low-permeability) compounds should also be eligible for a biowaiver.

The underlying principle is that, once a compound is in solution, its systemic bioavailability is then dependent only on its permeability. If comparable solubilities and rates of dissolution in two different formulations can be revealed, the bioavailability will be comparable. Permeability is based on the chemical structure of a compound. Thus, a compound that has low permeability (Class III) will also have a lower permeability in different formulations. On the other hand, a compound with low permeability is not going to have even lower permeability in a different formulation. Absorption Systems is an active participant in this dialogue, with the FDA and members of the pharmaceutical industry, to extend eligibility for biowaivers beyond Class I to include Class III compounds [5].

IRDDS TECHNOLOGY REVIEW

The concept of IRDDS emerged with intent to provide patients with more convenient means of medication. These rapidly disintegrating and dissolving solid dosage forms release the drug as soon as they come in contact with the saliva, thus bypassing the need of water during drug administration – an

aspect that makes the dosage form highly attractive for the patient groups such as children and the elderly.

Immediate Release Tablet (IRT) offer several advantages over other dosage forms such as effervescent tablets, dry syrups, chewing gums, or chewable tablets, which are commonly used to enhance patient acquiescence. Administering effervescent tablets or granules and dry syrups involve unavoidable preparation that includes intake of water. Elderly patients cannot chew large pieces of gum or tablets and occasionally experience the bitter or objectionable taste of the drug in the dosage form if the taste masking coating ruptures during mastication.

Additional advantages of IRT:

IRT are easy to administer and handle thus leads to better compliance, particularly who can not swallow such as elderly, stroke victims, bed ridden patients, patients affected by renal failure, who refuse to swallow such as pediatric, geriatric and psychiatric patients [6,7]. It provides rapid drug absorption due to pregastric absorption of drug from the mouth, pharynx and oesophagus as saliva passes down which may produce rapid onset of action [6] and it can result in improved bioavailability, as a result of reduced dosage, improved clinical act through a reduction of superfluous effects [8]. IRT improves safety by avoiding the risk of suffocation or choking due to physical obstructions during oral administration of conventional solid dosage form [9]. Superior taste masking capability and good palatability helps to change the basic views of awareness of medication as "bitter pill" particularly in children. It also provides new industrial opportunity like product promotion, patent expansion, life cycle management, and product differentiations [8]. It is suitable for administrations and patient compliance for disabled, for travelers and busy people who do not always have access to water. It has the ability to provide advantages of liquid medications in the form of solid preparation and conveniences of administration and accurate dosing as compared to liquids.

Chronological development in IRT manufacturing technology:

To make certain the tablet's fast dissolving feature, water must quickly egress into the tablet environment to cause rapid disintegration and instantaneous dissolution of the tablet. Maximizing the absorbent structure of the tablet matrix and incorporating an appropriate disintegrating agents or highly water soluble excipient in the tablet formulation are the basic approaches used in current fast dissolving tablet technologies [3, 10, 11]. Basically, the major function disintegrant is to oppose the effectiveness of the tablet binder and the material forces that act under compression to form the tablet. The mechanism by which tablet is broken down into smaller particles and then produces a homogeneous suspension or solution is based on capillary action, high swellability of disintegrants and chemical reaction (release of gases) [11].

Different technologies have been employed for the formulation of IRT so far and each technique has a different system, and the resulting fast dissolving or fast disintegrating dosage form varies on various grounds like mechanical strength of final product, drug and dosage form stability, mouth feel, taste, dissolution rate of the formulation in saliva, swallowability, rate of absorption from the saliva and overall bioavailability. These technologies require specialized equipments and process. The various technologies

Freeze drying / lyophilization:

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. 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 aluminium foil backing is applied on a blister-sealing machine. Finally the blisters are packaged and shipped.

Sublimation:

The key to rapid disintegration for IRT is the presence of a porous organization in the tablet matrix. Conventional compressed tablets that contain highly water-soluble ingredients often dissolve rapidly because of low porosity of the matrix. Hence to generate porous matrix, volatile ingredients are used that are later subjected to a process of sublimation.

According to Heinemann *et al*., Knitsch *et al.*, inert solid ingredients that display high volatility (e.g., ammonium bicarbonate, ammonium carbonate, benzoic acid, camphor,

naphthalene, urea, and urethane) were compressed along with other excipient into a tablet. The volatile material was then removed by sublimation, leaving behind a porous matrix. Solvents such as cyclohexane and benzene were also suggested for the generation of porosity in the matrix [12-14].

Koizumi *et al*. applied sublimation technology to manufacture tablets that rapidly dissolve in saliva using Mannitol as matrix former, and camphor as sublimating agent. The tablets were dissolved in 10-20 s and displayed satisfactory handling properties [15].

Spray drying:

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 developing IRT. In this technique, gelatin can be used as supporting agent and as matrix, mannitol as bulking agent and sodium starch glycolate or cross carmellose or crosspovidone are used as superdisintegrants. Tablets manufactured from the spray-dried powder have been reported to disintegrate in less than 20 seconds in aqueous medium [16].

Mass extrusion:

This expertise involves softening the active blend using the solvent mixture of water-soluble polyethylene glycol and methanol and subsequent eviction 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 accomplish taste masking.

Moulding:

Moulding technique employs water-soluble ingredients so that the tablet dissolves completely and rapidly. The active ingredients usually are absorbed through the mucosal layer of the mouth. Following are the different moulding techniques.

Compression moulding:

It involves moistening the powder blend with a hydroalcoholic solvent followed by pressing it into mould plates to form a wetted mass (compression moulding). The solvent is then removed by air-drying. Such tablets are less compact than compressed tablets and posses a porous arrangement that hastens dissolution.

Heat moulding:

This process uses an agar solution as binder and blister packaging well as mould to manufacture a tablet. The process involves preparing a suspension containing the preparation, agar, and sugar (e.g., mannitol or lactose), followed by pouring the suspension into the blister packaging well, solidifying the agar solution at room temperature to form a jelly, and finally drying under vacuum at approximately 30° C.

No vacuum lyophilization:

Another process used is called no vacuum lyophilization, which involves the evaporation of a solvent from a drug solution or suspension at standard pressure.

Moulded tablets disintegrate more quickly and offer improved taste. These properties are enhanced when tablets with porous structures are produced or when components that are physically modified by the moulding process are used. Compared with lyophilization, tablets produced by the moulding technique are easier to adjust to industrial scale. Unfortunately, moulded tablets typically do not posses great mechanical strength. Erosion and breakage of the moulded tablets often occur during tablet handling and when blister packets were opened.

Cotton candy process:

The cotton candy process is also known as the "candy floss" process. An IRT is formed using a candy floss or shear form matrix, known as "floss", the matrix is formed from saccharides or polysaccharides processed into amorphous floss, which is a fibrous material similar to the cotton candy fibers [17]. The matrix is then cured or partially recrystallised to provide a compound with good flow properties and compressibility. The candy floss can then be milled and blended with active ingredients and compressed into IRT. However the high processing temperature limits the use of this technology to thermostable compounds only.

Direct compression:

It is the simplest and most cost effective tablet manufacturing technique which can now be applied to preparation of IRT because of the availability of improved excipient especially superdisintegrants & sugar based excipient.

Superdisintegrants:

In many orally disintegrating tablet technologies based on direct compression, the addition of superdisintegrants

predominantly affects the rate of disintegration and hence the dissolution. The presence of other formulation ingredients such as water-soluble excipient and effervescent agents further accelerate the process of disintegration.

The introduction of so-called superdisintegrants and a better understanding of their properties have increased the popularity of IRDDS [18]. Focusing on the disintegrant concentration can optimize tablet disintegration time. Below critical disintegrant concentration, tablet disintegration time is inversely proportional to disintegrant concentration. However, above critical concentration level, disintegration time remains approximately constant or even increases [19].

Ethypharm (Saint-Cloud, France) has introduced a technology, which contains coated crystals of drug and microgranules along with disintegrants. In this technology, two types of disintegrants are used; a *disintegrating agent* (e.g. modified cellulose), which has a high swelling force, and a *swelling agent* (e.g. starch), which has a low swelling force [20]. Another concept for rapid disintegration is effervescent tablet. The concept of effervescence is a well-known formulation art utilized in several dosage forms. However, the current technology uses this concept in a modified fashion to achieve fast-disintegrating dosage forms [21]. The microparticulates are prepared by a novel technique involving the dispersion of active ingredients into suitable polymer dispersion together with other excipient such as mannitol and magnesium oxide. Typical polymers include ethyl cellulose, methyl cellulose, and acrylate and methacrylic acid resins. The active material and mannitol are added to the polymeric dispersion under stirring, followed by the addition of magnesium oxide. Mannitol and magnesium oxide added to aid active ingredient release from the polymeric coating and are known as release promoter in current technology. This mixture is dried for one hour at 50°C, delumped, and dried for another hour at the same temperature. The material is then screened (#8 mesh) and dried for one hour at 60°C. The formed microparticles, effervescent agents and other excipient, including flavorants, colorants and lubricants are blended and compressed into tablets at 1.0-2.0 kp hardness [21]. The tablets are fragile with *in-vivo* disintegration time of less than one minute. Because the tablets are very soft, they are packed into foil-foil blisters using a specially designed packaging system. In an attempt to improve the friability of these tablets, a novel method, known as particulate effervescent couple, is developed to prepare the effervescent mixture. In this method the organic acid crystals are coated using a stoichiometrically less amount of base material as compared to the acid. The particle size of the organic acid crystals is carefully chosen to be greater than the base material for uniform coating of base material onto the acid crystals. The coating process is initiated by the addition of a reaction originator, which in this case, purified water. The reaction is allowed to proceed only to an extent of completion of base coating on organic crystals. The required end-point for the reaction termination is determined by measuring carbon di oxide evolution. The resulting effervescent couple can be used in tablet preparation by mixing with polymer-coated active ingredient particulate material and other excipient such as sweeteners, flavorants and lubricants [22].However the major drawback of effervescent excipient is their hygroscopicity (i.e. the ability to absorb atmospheric moisture). Hence, their production requires control of humidity conditions and protection of the final product. This is reflected in the overall cost of the product.

Sugar based excipient:

This is another approach to manufacture IRT by direct compression. The use of sugar based excipient especially bulking agents like dextrose, fructose, isomalt, lactilol, maltilol, maltose, mannitol, sorbitol, starch hydrolysate, polydextrose and xylitol, which display high aqueous solubility and sweetness, and hence impart taste masking property and a pleasing palatability.

Most commercial IRTs have been developed using mannitol as the bulk excipient of choice. Mannitol is tremendously preferred over lactose because of its extremely low hygroscopicity, excellent chemical and physical compatibility, good compressibility and better sweetness. IRT formulators prefer to use a directly compressible mannitol, which enables the preparation of robust tablets that can withstand processing and transportation. Specially textured directly compressible, spray-dried, or granulated mannitol excipients have been designed to meet these needs. These excipient under defined manufacturing conditions gives a highly porous structure and friable exterior structure which helps in faster disintegration of IRT, they also provide a satisfactory mouth feel and so suitable for use in preparation of harder IRT by direct compression at low pressure.

CURRENT TRENDS IN IRDDS

Though several technologies are available for the preparation of IRT or rapid disintegrating tablet, a few have reached commercial marketed products. FDA considers these rapidly dissolving tablets as a new dosage form [1]. Some patented technologies are described here.

Zydis™ technology:

Zydis™ is the first fast dissolving dosage form in the market. Using concept of Gregory *et al*. Scherer has patented the Zydis™ technology [23]. Zydis™, the best known of the fast dissolving/disintegrating tablet preparations. The tablet dissolves in the mouth within seconds after placement on the tongue. 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 microbial growth. This technology is based on the model that it is forming an open matrix network containing the active ingredients. These are freeze-dried products containing water soluble matrix material and drug, which is performed in blister pockets and freeze dried to remove the water by sublimation. The resultant structures are very porous in nature and rapidly disintegrate or dissolve upon contact with saliva. Zydis™ must be produced in blister packs with peelable backing foil, because the units are not strong enough to withstand being pushed through the backing foil of a conventional blister. The use of water as the medium ensures the formulation of porous dosage form. Preservatives may be added in apt concentration to prevent microbial growth in aqueous solutions (during manufacture). Suspending agents and pH-adjusting excipient may be added if necessary. Collapse protectants such as glycine prevent the shrinkage of the Zydis™ units and may be useful additives.

This technology has certain limitations. A water insoluble drug can be incorporated up to 400 mg per tablet or less, on the other hand water soluble drug can be incorporated only up to 60 mg, because water soluble drug might form eutectic mixtures and not freeze adequately, hence the dose is limited to 60 mg. A lyophilized disk is so lightweight and fragile, that it is unsuitable for conventional blister packing. The use of matrix forming agents such as gelatin and sugar based excipients in the formulation could overcome this problem. Freeze-drying is a relatively expensive and time consuming process. Other drawbacks of freeze-drying disks include fragility and poor stability during storage under stressful conditions.

Flash Tab™ technology:

The FlashTab™ technology is yet another Mouth Dissolving Tablet formulation patented by Prographarm group. It utilizes most of the same additives 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 mouth within one minute. This technology utilizes the conventional tabletting technology [24].

OraSolv™ technology:

It is CIMA lab's first fast-generation dissolving formulation. The tablets are prepared by direct compression technique at low compression force in order to minimize oral disintegration and dissolution time. The active medicament is taste masked and dispersed in saliva due to effervescent agent and provides a pleasant sensation of effervescence in mouth of the patient. OraSolv™ technology is an example of slightly effervescent tablet that rapidly dissolves in mouth [25]. This technology utilizes the effervescence materials and taste masked active ingredients and requires only conventional manufacturing process and equipment.

OraSolv™ dosage forms have been developed, containing more than 1000 mg of active load and are capable of combinations of multiple active ingredients in a tablet. The main drawbacks of tablets produced by this technology are soft and friable and hence packaged using an integrated packaging line that uses a specially designed robotic pick and pack system.

DuraSolv™ technology:

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 tabletting. DuraSolv™ tablets are prepared by using conventional tabletting equipment and have good rigidity (friability less than that 2%). The DuraSolv™ product is thus produced in a faster and more cost-effective manner. DuraSolv™ is so durable that it can be packaged in traditional blister packaging, pouches or vials.

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 technique is best suited for formulations including relatively small doses of active compound [26].

WowTab™ technology:

The WowTab™ fast-dissolving/disintegrating tablet formulation has been on the Japanese market for a number of years [27]. Yamanouchi Pharmaceutical Co patents WowTab™ technology. The WOW in WowTab™ signifies the tablet is to be given "*With Out Water*". WowTab™ is an intrabuccally soluble, compressed tablet consisting of granules made with saccharides of low and high mouldability. Mouldability is the capacity of the compound to be compressed. It has just recently been introduced into the U.S. The WowTab™ technology utilizes sugar and sugar like (e.g., mannitol) excipient. It uses a combination of low mouldability saccharides (rapid dissolution) and high mouldability saccharides (good binding property). 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 mouth feel due to the patented SMOOTHMELT action. The WowTab™ product dissolves quickly in 15 seconds or less.

FlashDose™ technology:

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 [28].

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 CEFORM and serves as an alternative method of taste masking.

OraQuick™ technology:

The OraQuick™ fast dissolving tablet formulation utilizes a patented taste masking technology by K. V. Pharmaceuticals Company, who claim that its taste masking technology (Micromask) has superior mouth feel over taste masking alternatives. The taste masking process does not utilize solvents of any kind and therefore leads faster and more efficient production [29].

QuickDis™ technology:

Lavipharm Laboratories Inc. (Lavipharm) has invented an ideal intraoral fast-dissolving drug delivery system, which satisfies the unmet needs of the market. The novel intraoral drug delivery system, trademarked QuickDis™, is Lavipharm's proprietary patented technology and is a thin, flexible, and quick-dissolving film. The film is placed on the top or the floor of the tongue. It is retained at the site of application and rapidly releases the active agent for local and or systemic absorption. This drug delivery system can be provided in various packaging configurations, ranging from unit-dose pouches to multiple-dose blister packages.

The typical disintegration time, which is defined as the time at which the film begins to break when brought into contact with water, is only 5 to 10 seconds for the Quick-Dis™ film with a thickness of 2 mm. The dissolving time, which is defined as the time at which not less than 80% of the tested film is dissolved in aqueous media, is around 30 seconds for QuickDis™ film with a thickness of 2 mm. The typical release profile of an active ingredient exhibited by a QuickDis™ drug delivery system is 50% released within 30 seconds and 95% within 1 minute.

NanoCrystal ™ technology:

For fast 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 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™ Fast dissolving 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 and cost-effective manufacturing processes that utilize conventional, scalable unit operations.

NanoCrystal colloidal dispersions of drug substance are combined with water- soluble GRAS (Generally Regarded As Safe) ingredients, filled into blisters, and lyophilized. The resultant wafers are remarkably robust; yet dissolve in very small quantities of water in seconds. This approach is especially attractive when working with highly potent or hazardous materials because it avoids manufacturing operations (e.g., granulation, blending, and tabletting) that generate large quantities of aerosolized powder and present much higher risk of exposure. The freeze-drying approach also enables small quantities of drug to be converted into IRT dosage forms because manufacturing losses are negligible.

MeltEase™ technology:

MeltEase™ Technology is a newer technology developed by Nutrition Formulators, which allows tablet dissolution in less than five seconds (average 400 mg tablet). This is the best mechanism available to ensure compliance and increase sales in two important markets, children and the elderly for many nutritional supplements at a very marginal development cost in specific formulations, including taste masking and sustained release on certain ingredients.

CONCLUSION

Besides delivering drug to the body, a drug delivery system aim to improve patient concordance and expediency, and IRTs are no exception. The introduction of IRDDS has solved some of the problem encountered in administration of drugs to the pediatric and geriatric patient, which constitutes a large portion of the world's population. The technologies described in this article demonstrate recent advances in formulation development and processing technologies need the effort to achieve more refined drug delivery system. Such products provide opportunity for the product of patent term of innovator. Due to this wide significance of IRT this drug delivery system may lead to better patient compliance and ultimate clinical output. Because of the availability of the technologies and strong patient demand, several products have already been commercialized and the market size for the IRT will surely enlarge further. Thus, looking at the advances and advantages in this therapeutic approach, the pharmaceutical formulator need not to restrict his choice in the development of conventional dosage forms but should also try to develop these IRDDS. Future might witness many more classes of drug developed in the form of IRT.

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NIL

CONFLICT OF INTEREST

The authors declare no conflict of interest

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