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CHALLENGES IN NANOTECHNOLOGY DRUG DELIVERY SYSTEMS - STATE OF ART TECHNOLOGIES

A. Deevan Paul*, P. Nagaraj, E. Reshma, T. Mahesh, Y. Divyasree

SVU College of Pharmaceutical Sciences, SV University, Tirupati (India)

Abstract:

The potential challenges to solve the poor solubility, limited chemical stability in vitro and in vivo after administration (i.e. short half-life), poor bioavailability and potentially strong side effects requiring drug enrichment at the site of action (targeting). This review describes the use of nanoparticulate carriers, developed in our research group, as one solution to overcome the dosage forms. The performance of ODTs depends on the technology used in their manufacture. The orally disintegrating property of these tablets is attributable to the quick ingress of water into the tablet matrix, which creates porous structure and results in rapid disintegration. Hence, the basic approaches to develop ODTs include maximizing the porous structure of the tablet matrix, incorporating the appropriate disintegrating agent and using highly water-soluble excipients in the formulation. Fast disintegrating tablets have better patient acceptance, compliance and possibly will tender enhanced biopharmaceutical properties, superior efficacy, and enhanced safety compared to conventional oral dosage forms. The perspective for such dosage forms is promising because of the accessibility of new technologies combined with strong market/patient acceptance.

Keywords: *Oro dispersible tablets, Bioavailability, Conventional films, Disintegrating time.*

Corresponding author:

A. Deevan Paul,
SVU College of Pharmaceutical Sciences,
SV University,
Tirupati,Andhra Pradesh,
E- mail: deevan4@gmail.com

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INTRODUCTION:

An orally disintegrating tablet (ODT) is defined as a solid dosage form that dissolves or disintegrates quickly in the oral cavity without the need for administration of water. The ODTs as uncoated tablets intended to be placed in the mouth where they disperse rapidly before being swallowed and as tablets which should disintegrate within 3min(1). Orally disintegrating tablets are claimed to be a better solution than conventional solid oral dosage forms (tablets and capsules) as the latter create problems for pediatric, geriatric, bedridden, nauseous or non-complient patients (2). After meeting saliva ODTs disintegrate immediately and produce a suspension that can be easily swallowed by the patient (3). The active ingredients in solution are more rapidly absorbed through the pre-gastric route from the mouth, pharynx and esophagus and through gastrointestinal epithelium to produce the desired effect (4). ODTs are preferred for people suffering from dysphagia, institutional psychiatric patients as well as hospitalized patients suffering from a variety of disorders such as stroke, thyroid disorder, Parkinson's disease and other neurological disorders like multiple sclerosis and cerebral palsy. Dysphagia is a condition marked by the difficulty in swallowing and it has been reported that about 35 % of the general population, in addition to 30–40 % of elderly institutionalized patients and 18–22 % of all persons in long- -term care facilities, suffer from dysphagia (5). ODTs have also been found to be the dosage form of choice for patients suffering from nausea, vomiting or motion sickness.

The use of nanoparticles as a drug-delivery approach for various difficult-to-formulate reagents is not a new concept. In pharmaceutics, nanoparticles are typically defined as a discrete internal phase consisting of an active pharmaceutical ingredient having physical dimensions, less than 1 micron in an external phase. Also, nanoparticles can be designed to form de novo when exposed to the appropriate biological fluid. The inability to achieve high drug loading, the cost of ingredients and processing, and the restricted number of suitable excipients have either to limit the broader use of these formulation approaches. which focuses on poorly water-soluble drugs, has addressed many of these major concerns and has successfully expanded the scope and use of nanoparticulates or nanosuspensions to include the oral, inhalation, intravenous, subcutaneous (SubQ) and intramuscular (IM), and ocular routes of delivery (6).

Nanoparticles represent a very promising carrier system for the targeting of anti-cancer agents to tumors as they exhibit a significant tendency to accumulate in many tumors after intravenous injection. The development of appropriate vehicles to deliver new macromolecules coming out of the biotech industry is a challenge for pharmaceutical scientists. In many cases peptides are quite efficiently bound to nanoparticles (7).

TECHNOLOGIES USED FOR DEVELOPING ORALLY DISINTEGRATING TABLETS

Lyophilization/freeze-drying:

The principle of the lyophilization technique is drying carried out at low temperature under conditions involving removal of water by sublimation. In this technique, the material is initially frozen below –18 °C and then reducing the pressure of the system and giving the necessary heat allows the sublimation process. This technique is extremely useful for heat sensitive drugs and biological. Here, the drug is physically entrapped in a water-soluble matrix, which is then freeze-dried to give a product that is highly porous and has a large surface area. Due to the porous nature of the product, the liquid medium penetrates the interior surface of the tablet thereby enhancing its disintegration. The tablets prepared by lyophilization disintegrate rapidly in less than 5s due to quick penetration of saliva in pores when placed in the oral cavity. The lyophilization process gives a glassy amorphous structure to the bulking agent and sometimes to the drug. In the lyophilization process, the API is dissolved or dispersed in an aqueous solution of a water-soluble excipients, such as gelatin, mannitol, starch or hydrophilic gum and the resultant mixture is poured onto the blister film (8).

In the lyophilization process, the API is dissolved or dispersed in an aqueous solution of water-soluble excipients, such as gelatin, mannitol, starch or hydrophilic gum and the resultant mixture is poured onto the blister film. The filled blisters are passed through a cryogenic freezing process, specially designed to control the ultimate size of ice crystals. These frozen units are then transferred to large-scale freeze dryers for the sublimation process, where the remaining moisture is removed from the tablets. Finally, the freeze-dried open blisters are sealed *via* a heat-seal process to ensure stability and to protect the product from varying environmental conditions. The main advantage of lyophilization is elimination of the adverse effect of heat on the pharmaceutical product as APIs are not exposed to the elevated temperature. The ideal drug candidate for formulating ODTs by lyophilization is a tasteless, water insoluble drug with particle size preferentially smaller than 50 mm. Particle size plays an important role as larger particles than the mentioned ones might produce sedimentation problems during manufacturing (9). Water insoluble drugs are generally preferred

because incomplete freezing or collapse may occur with water soluble drugs at low eutectic freezing temperature. (10) used a mixture of mannitol and natural gum such as acacia gum, guar gum, xanthan gum or tragacanth as carrier material for preparation of an open matrix network structure. The mannitol concentration in stable ODT was reported to be at least 50 % (*m*/*m*) and the natural gum concentration of the solid dosage form was about 0.07 to 3.2 % (*m*/*m*). This study revealed an improvement in the properties of ODTs when the open matrix structure comprised mainly mannitol.

Molding:

ODTs prepared by molding, also known as solid dispersion, disintegrate within 5 to 15 s. Compression molding and heat molding is the two approaches to preparing ODTs by the molding technique. Compression molding involves moistening of the powder blend with a hydro-alcoholic solvent, followed by compression into mold plates to form a wetted mass. The wetted mass is then air-dried to remove the solvent. The compression force involved in compression molding is lower than that used for conventional tablet and hence molded tablets are less compact than conventional compressed tablets and a possess highly porous structure, which in turn increases disintegration and dissolution rates. In the heat molding process for the preparation of ODTs, molten mass containing a dispersed drug and/or dissolved drug is used (11). The disintegration time and dissolution rate of ODTs prepared using molding depend upon the dissolution or dispersion type of the drug. Hence, it can be said that the ODTs preparation using the molding process is easy and convenient at an industrial scale although cannot achieve disintegration time compared to that of lyophilized forms. The molded tablets typically do not possess great mechanical strength and can break during handling or when blister packs are opened. However, the addition of binders (acacia, polyvinyl pyrrolidone, PEG) gives sufficient consistency to the formulation and prevents tablet breaking (12).

Cotton candy process:

Cotton candy process utilizes a unique spinning mechanism to produce floss of crystalline structure. The process involves formation of a matrix of saccharides or polysaccharides by simultaneous flash melting and spinning. This results into formation of the candy floss matrix, which is then milled and blended with active ingredients and excipients and subsequently compressed into ODTs. To improve the flow properties and compressibility, the candy floss matrix may sometimes partially recrystallize, which imparts good mechanical strength and can accumulate a large quantity of drug. However, this process is not suitable for thermolabile drugs (13).

Compaction:

In the compaction process, a mixture of particulate matter is fed to a compression device which promotes agglomeration due to pressure. Continuous sheets of solid material or solid forms such as briquettes or tablets are produced. Compaction processes range from confined compression devices such as tableting to continuous devices such as roll presses, briquetting machines and extrusion. The following different techniques are based on the compaction mechanism.

Crystalline transition process*:*

ODTs are prepared by crystalline transition through compressing two saccharides having high and low compressibility/mold ability indices and are then subjected to the conditioning process (14). Transition from the amorphous to crystalline state is intentionally done by the conditioning process after tablet compression to achieve sufficient hardness and fast disintegration time. Fluidized bed granulator is commonly used for the crystalline transition process.

Phase transition:

The manufacturing ODTs using phase transition of sugar alcohol (SA). This method was mainly dependent upon the melting point of SA. The process involves compressing the powder containing two SAs of high and low melting points and subsequently heating the compressed mass at the temperature between their melting points. However, in case of talc, oral disintegration time did not change with an increase in hardness. Among the three lubricants studied, *i.e.*, magnesium stearate, sodium stearyl fumarate and talc, talc was recommended as the most desirable lubricant for preparation of ODTs by phase transition of SA (16) .

Sublimation:

Conventional tablets with high water-soluble ingredients fail to disintegrate rapidly because of their low porosity and this suggests that the presence of a highly porous particle structure in the tablet matrix is an important factor for fast disintegration of ODT. In the sublimation process, volatile substances like camphor, ammonium carbonate, ammonium bicarbonate, benzoic acid, hexamethonium tetramine, naphthalene, phthalic anhydride, urea and urethane were used along with other excipients. Solvents such as cyclohexane/benzene were sometimes also used for further enhancement in the porous matrix formation. Volatilization of these materials eliminates the complicated process associated with

the lyophilization process, that is, sublimation of frozen water.

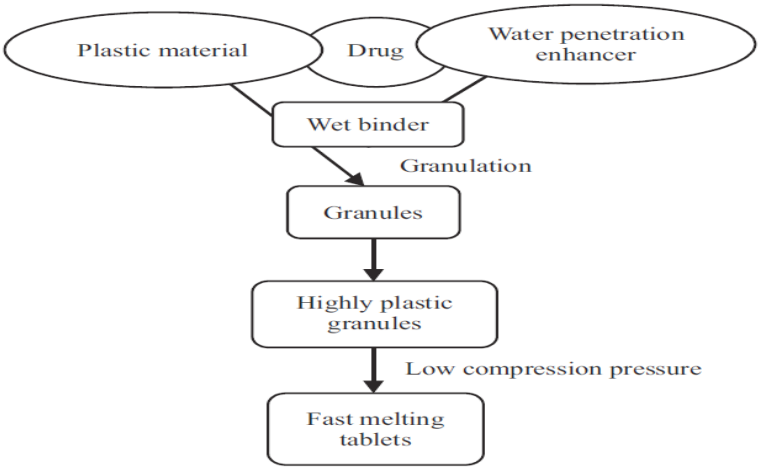
Conventional methods:

Different conventional methods such as direct compression, wet granulation and dry granulation are used in the preparation of ODTs. The relationship between disintegration time in the mouth and stationary time of upper punch displacement (STP) was studied using a tableting process analyzer. As the value of bulk density increased, STP became longer and disintegration time in the mouth was shorter. A formulation with bulk density greater than 0.5 g mL^{-1} with the chosen compression force of 5kN produced a tablet which gave a disintegration time of less than 60 s. Also, the hardness of the tablet was found to be greater than 3 kg if at least one compressible excipients was used in the formulation. (17).

Direct compression method:

Few drugs can be directly compressed into tablets of acceptable quality with good flow properties and stability under pressure. This technique is now applied to the preparation of ODTs if good tablet disintegrants, superdisintegrants and sugar-based excipients are available. Disintegration of the tablets prepared by direct compression depends upon the single or combined effect of disintegrants, water soluble excipients and effervescent agents. Superdisintegrants are a family of disintegrants that are superior to the traditional disintegrants in promoting the tablets to disintegrate into their primary particles when placed in an aqueous environment and are efficient at concentrations as low as 2–5 %.

The commonly used superdisintegrants in ODTs are summarized in Table.



SUPERDISINTEGRANTS EMPLOYED IN ODTS

Superdisintegrant	Chemical structure	Physical properties	Mechanism Of action
Crospovidone (Kollidon CL, Polyplasdone XL	Synthetic homopolymer of cross-linked *N*-vinyl-2-pyrrolidone	Water insoluble, spongy in nature so gives a porous tablet, smoother mouth feel	Capillary action absorbs water leading to swelling
Croscarmellose sodium (Ac-Di-Sol®, Nymce ZSX®, Primellose®, Solutab®, Vivasol®)	Crosslinked form of sodium CMC	Swells in two dimensions, swells 4–8 folds in < 10 s	Swelling
Sodium starch glycolate (Explotab®, Primogel®, Vivastar P)	Sodium salt of carboxymethyl ether of starch	Swells in three dimensions and at high concentration, serves as sustained-release matrix, Insoluble in organic solvents, disperse in cold water	Water uptake followed by rapid and Enormous swelling
Sodium alginate (Kelcosol, Keltone, Protanal)	Sodium salts of alginic acid	Hygroscopic in nature and slowly soluble in water	Swelling

Soypolysaccharides	Natural polysaccharide	Does not contain any starch or sugar	Wicking
ECG-505 (carmellose calcium)	Calcium salt of CMC	Disintegration time 80 s	Swelling
Ion exchange resin (Indion 414, Indion 234, Tulsion 234, Tulsion 344, Amberlite IPR 88)			Swelling
Gas evolving disintegrants (citric acid, tartaric acid, sodium bicarbonate)	Effervescence substance	Evolution of CO2 after contact with fluid	In contact with water liberates CO2 that disrupts the tablet

Wet granulation method:

A new method for fast melting tablets formed by wet granulation based on highly plastic granules. If a plastic material is polymeric, then it is essential to prevent formation of a viscous layer of the material at tablet surface when it dissolves in aqueous medium. One way of making such tablets is to mix the plastic material with water penetration enhancers at certain ratios and compress them at low pressure. These results in plastic deformation of plastic materials, creating intimate contact among the particles required for forming bonds between the particles. In this process, the plastic particles are separated by water penetration enhancing particles, which prevent formation of a viscous layer on the tablet surface. Highly plastic granules were produced by the wet granulation method.

Nanoparticles are solid colloidal particles ranging in size from 10 nm to 1000 nm. They consist of macromolecular materials in which the active principle is dissolved, entrapped or encapsulated, and/or to which the active principle is absorbed or attached. Nanoparticles have been studied extensively as particulate carriers in several pharmaceutical and medical fields. The group of Speiser initiated the research in the 1970s. They were initially devised as carriers for vaccines and anticancer drugs. Nanoparticulate technology is progressing through the development of new approaches in the field of drug delivery.

APPLICATIONS OF NANOPARTICLES

Nanoparticles, in general, can be used to provide targeted (cellular/tissue) delivery of drugs, to sustain drug effect in target tissue, to improve oral bioavailability to solubilize drugs for intra-vascular delivery and to improve the stability of therapeutic agents against enzymatic degradation. Nanoparticles formulated as amorphous spheres show higher solubility than standard crystalline formulations, thus improving the poor aqueous solubility of the drug and hence its bioavailability. Nanoparticles can be formulated as injections consisting of spherical amorphous particles which do not aggregate, hence they can be safely administered by the intravenous route. Since no co-solvent is used to solubilize the drug, the overall toxicity of the formulation is reduced. Nanoparticles represent a very promising carrier system for the targeting of anti-cancer agents to tumors as they exhibit a significant tendency to accumulate in a number of tumors after intravenous injection. The first anticancer drug bound to nanoparticles was actinomycin D. Over the last 20 years, considerable progress has been made in the preparation of well-characterized nanoparticle formulations loaded with a variety of anticancer agents. Nano capsules may have the potential to deliver drugs to the lymph node through tissue spaces by local administration. The cosmetic applications of nanoparticles are currently under investigation. A cosmetic product containing nanocapsules of vitamin E, Primordiale1 has recently been launched (18).

TECHNOLOGIES USED FOR DEVELOPING NANOPARTICULATE DRUG DELIVERY SYSTEMS

Polymeric nanoparticles:

Polymeric nanoparticles as drug delivery systems usually exhibit a long shelf life and a good stability on storage. Nanoparticles are superior to liposomes in targeting them to specific organs or tissues by adsorbing and coating their surface with different substances Polymeric nanoparticles are solid colloidal particles consisting of non-biodegradable synthetic polymers or biodegradable macromolecular materials of synthetic, semisynthetic or natural origin. According to the process used for the preparation of nanoparticles, nanospheres or nanocapsules can be obtained. Nanocapsules are vesicular systems in which the drug is confined to a cavity surrounded by a unique polymeric membrane. Nanospheres are matrix systems in which the drug is

dispersed throughout the particles. Although both types of active ingredients may be incorporated, most often they are hydrophilic in the case of nanospheres and lipophilic in the case of nanocapsules. Polymeric nanoparticles including nanospheres and nanocapsules can be prepared according to numerous methods.

The major disadvantages of polymeric nanoparticles are their relatively slow biodegradability, which might cause systemic toxicity. Apart from polymer accumulation on repeated administration, toxic metabolites may be formed during the biotransformation of polymeric carriers, for example, formaldehyde as a metabolite of polycyanoacrylates. The formation of larger polymer particles and lumps cannot be avoided totally in large scale production of nanoparticles. The system also suffers from the lack of a cost-effective large scale production method yielding a product of a quality being acceptable by the regulatory authorities. Also polymeric nanoparticles possess limited drug loading capacity.

Solid lipid nanoparticles (SLN):

Solid lipid nanoparticles have been developed as alternative delivery system to conventional polymeric nanoparticles. The solid lipid nanoparticles (SLN) are sub-micron colloidal carriers (50–1000 nm) which are composed of a physiological lipid, dispersed in water or in an aqueous surfactant solution. Solid lipid nanoparticles combine advantages of polymeric nanoparticles, fat emulsions and liposomes, and avoid some of their disadvantages. They are biodegradable, biocompatible and non-toxic. The possibility of large scale production of SLN is an important feature.

Advantages of SLN are:

1. Avoidance of coalescence leads to enhanced physical stability.
2. Reduced mobility of incorporated drug molecules leads to reduction of drug leakage.
3. Static interface solid/liquid facilitates surface modification.

The drug release can be controlled by varying the carrier matrices as well as by the choice of emulsifier. Besides parenteral administration, solid lipid nanoparticles are also suitable for other routes of administration and might be an interesting carrier system for the per oral administration of poorly water-soluble drugs with low per oral bioavailability. An advantage of the emulsified lipid particles might be their improved wet ability in gastrointestinal fluids.

This problem has been overcome by the new generation of solid lipid nanoparticles, the so called nanostructured lipid carriers (NLC). These particles are characterized as forming on purpose an imperfect lipid particle matrix. This matrix gives much more room to incorporate drugs, the drug loading is increased. To achieve this, spatially very different lipid molecules are used for particle production. The "old" SLN are made from a solid lipid and subsequent melting and homogenization. The NLC are made by mixing a solid lipid with a liquid lipid (oil), these lipid molecules are spatially so different that they form imperfect matrices. Of course, the blend needs to be chosen in a way that after homogenization and cooling the blend solidifies and is solid at body temperature.

Nanosuspensions (drug nanoparticles) for many decades' drug carriers have represented the only group of colloidal drug administration systems. Nowadays a fundamentally different group of dispersions i.e. nanosuspensions (drug nanoparticles) are also under investigation. Pharmaceutical nanosuspensions are usually very finely dispersed solid drug particles in an aqueous vehicle for both oral and topical use or for parenteral and pulmonary administration. The next development was transformation of a micronized drug powder into drug nanoparticles. In a nanosuspension, the overall bioavailability is improved by an increase in surface area and saturation solubility via particle size reduction. The drug microparticles are ground to nanoparticles in between the moving milling pearls. Preparation of DissoCubes involves dispersion of drug powder in a surfactant solution by a high-speed stirrer. First, the particle size is reduced in a jet mill. The obtained macro-suspension is passed through a high-speed homogenizer leading to the formation of a nanosuspension. The cavitation forces experienced are sufficient to disintegrate drug microparticles to nanoparticles. The Table compares features of NanoCrystals and DissoCubes(19).

NEW DEVELOPMENTS IN DRUG NANOCRYSTALS

DissoCubes are prepared by homogenizing drug powder dispersed in pure water. This is based on the fact that it was believed that cavitation is the major force to disintegrate large particles to drug nanocrystals. To obtain cavitation one needs to have a liquid with a high vapour pressure, i.e. water. Cavitation should not be present or only present at a very limited extent when homogenizing in liquids with a low vapour pressure, e.g. liquid oils (MCT) or liquid PEG. Recently, a new patent application was filed describing the production of drug NanoCrystals in non-aqueous media. In addition, it is also claimed to produce drug NanoCrystals in mixtures of water with water-miscible liquids (e.g. production in isotonic dispersions of glycerol-water).

Drug NanoCrystals are produced in melted PEG, the obtained nanosuspension is then filled straight away as liquid at 70 _C in hard gealtin or HPMC capsules. Cooling forms a solid matrix in the capsule which contains the drug nanocrystals in a finely dispersed form. In addition, stock dispersions of water-sensitive drugs can be prepared. Such a stock suspension in e.g. glycerol can then be diluted prior to parenteral administration using sterile water to yield on isotonic suspension

The major advantages of nanosuspension technology are its general applicability to most drugs and its simplicity. Interesting special features of nanosuspensions are

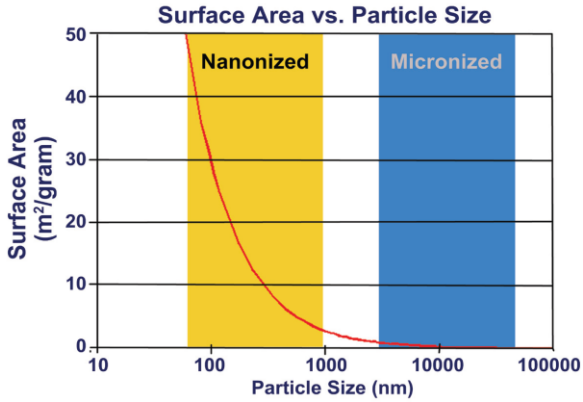
a. Increase in saturation solubility and consequently an increase in the dissolution rate of the drug.
b. Increase in adhesive nature, thus resulting in enhanced bioavailability.
c. Increasing the amorphous fraction in the particles, leading to a potential change in the crystalline structure and higher solubility.
d. Absence of ostwald ripening, producing physical longterm stability as an aqueous suspension.
e. Possibility of surface-modification of nanosuspensions for site specific delivery.
f. Possibility of large-scale production, the pre-requisite for the introduction of a delivery system to the market.

DRUG NANO PARTICLES TOWARDS SOLUBILITY CHALLENGE

It is estimated that ~40% of active substances identified through combinatorial screening programs are difficult to formulate as a result of their lack of significant solubility in water. In one sense, this is understandable. If a molecule must penetrate a biological membrane to be absorbed, the molecule generally must possess some hydrophobic or lipophilic characteristics. The classical approach to deal with this issue is to generate various salts of a poorly water-soluble molecule so as to improve solubility while retaining biological activity. The problem is that, frequently, these approaches are not successful, and the molecule is abandoned early on in its development process or the product is launched with suboptimal properties including poor bioavailability, lack of fed/fasted equivalence, lack of optimal dosing, presence of extra excipients that pose limitations with respect to dose escalation, and ultimately, poor patient compliance. When these types of situations arise, a nanoparticles formulation approach has proven to be very useful and invaluable in all stages of the drug development and has opened opportunities for revitalizing marketed products with suboptimal delivery.

NANOPARTICLE FORMULATIONS

No matter what approach is taken to generate drug nanoparticles, in comparison to particulates greater than 1 micron, surface area is increased. This increase in surface area and surface interactions can be positively used to enhance the dissolution rate and provide a platform for controlling the pharmacokinetic properties of the dosage form. However, unless properly dampened, this tremendous increase in surface energy can cause the nanometer-sized drug particles to spontaneously aggregate into a more thermodynamically stable state. It should be emphasized that surface stabilization does not necessarily involve chemical grafting of the surface stabilizer to the molecule. Stabilization is typically driven by the mere adsorption of the stabilizer to the surface of the poorly water-soluble compound.



For instance, if a poorly water-soluble compound is an acid or a base, the pH of the fluid phase can be adjusted so as to minimize ionization; that is, acids would be processed under more acidic conditions, and free bases would be processed at a higher pH.

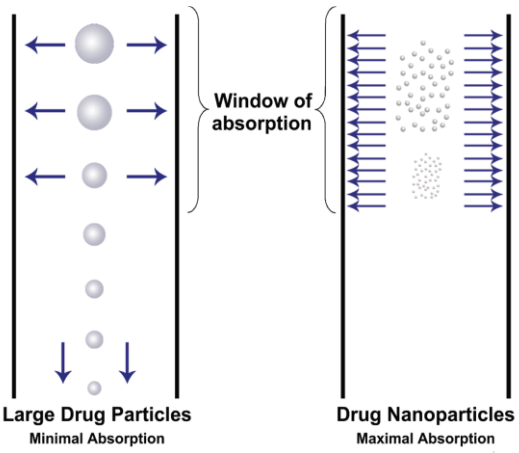
Nanoparticle dispersions generated using NanoCrystal technology consist of drug and stabilizer, and most commonly, the fluid phase is water. These dispersions are processed using a high-energy media mill with highly cross-linked polystyrene which provides a highly durable milling media resulting inefficient processing of crude drug crystals to homogenous nanoparticle–nanocrystalline dispersion with a particle size approximately 1 micron or less. The key characteristics of NanoCrystal formulations for poorly water-soluble molecules are

1) The versatility of the approach: suitable for many different classes of compounds, provided the aqueous solubility is less than 10 mg/ml.
2) The potential to achieve formulations with high drug loading: 300 mg/g or (30% w/w).

3) A drug-to-stabilizer ratio on a weight basis typically 10:1 or lower: 30% drug to 3% or lower stabilizer concentration.
4) Usefulness for all routes of administration: oral, pulmonary, intravenous, IM and ophthalmic.
5) The ability to be readily post processed into most commonly used dosage forms: tablets, capsules and sterile products.

NANOPARTICLES:
IMPROVED PERFORMANCE

The activity of a compound depends on its ability to dissolve and interact with the relevant biological target, either through dissolution and absorption or dissolution and receptor interaction. The poor bioavailability of poorly water-soluble molecules that are not permeation-rate limited can be attributed to dissolution- rate kinetics. The dissolution rate is directly proportional to the surface area of the drug, according to the Noyes-Whitney model for dissolution kinetics. Drug crystals reduced in size from 10 microns to 100-nm particles generate a 100-fold increase in surface-area-to-volume ratio. If the bioavailability of a poorly water-soluble compound is dissolution- rate limited, approaches that afford delivery using nanometer-sized particles of drug improve bioavailability by enhancing dissolution. This maximizes the amount of soluble drug that is free to be absorbed. This is especially true for poorly water-soluble compounds absorbed at a defined region of the gastrointestinal tract(20).



CONCLUSION:

Nanotechnology is the engineering and manufacturing of materials at the atomic and molecular scale. In its strictest definition from the National Nanotechnology Initiative, nanotechnology refers to structures roughly in the 1−100 nm size regime in at least one dimension. Despite this size restriction, nanotechnology commonly refers to structures that are up to several hundred nanometers in size and that are developed by top-down or bottom-up engineering of individual components. Herein, we focus on the application of nanotechnology to drug delivery and highlight several areas of opportunity where current and emerging nanotechnologies could enable entirely novel classes of therapeutics. Orodispersable tablets have better patient acceptance, compliance and possibly will tender enhanced biopharmaceutical properties, superior efficacy, and enhanced safety compared to conventional oral dosage forms.

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