

Available online on 15.05.2022 at <http://jddtonline.info>

Journal of Drug Delivery and Therapeutics

Open Access to Pharmaceutical and Medical Research

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Review Article

A Review Article on Dissolution Studies in Novel Drug Delivery System

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Article Info:

Abstract



Article History:

Received 19 March 2022

Reviewed 27 April 2022

Accepted 09 May 2022

Published 15 May 2022

Cite this article as:

Vyshnavi K, Sinduja Y, Adeyemi PG, Ebuka AD, Srija M, Sushma G, A Review Article on Dissolution Studies in Novel Drug Delivery System, Journal of Drug Delivery and Therapeutics. 2022; 12(3):220-225

DOI: <http://dx.doi.org/10.22270/jddt.v12i3.5337>

In present days there is immense advancement in drug delivery despite novel drug delivery has become civilized as pharmaceutical scientists has worked hard over it. However the vocal pathway remnant the excellent pathway is for administration whereas the new drugs achieve the great patient compliance. The dissolution studies in NDDS have limit literature also and to still found locate inside the pharmacopeia. The dissolution studies is highly and commonly recommended for the solid dosage forms now a days it's indeed enlarged to the other pharmaceutical formulations like suspensions, patches etc. The dissolution tactic is indeed an perfect tool such as maintaining batch-batch evaluation tests and also to analyze the drug release in vivo conditions. In sustained release the products that are obtained has several advantages in optimizing bio pharmaceuticals and pharmacokinetics as compared to the conventional drug delivery systems.

Keywords: Dissolution, sustained release, pharmacokinetics

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INTRODUCTION

Dissolution would be described as the act with which a solid substance wants to enter into such a solvent to reveal a solution and seems to be managed even by the affinity here between the solid substance as well as the solvent ¹. The official test described in pharmacopeia is the dissolution. So far and there is really no standard way preferred for within vitro release testing of innovative pharmaceutical dosage forms like nanoparticles, aerosols, microspheres, liposome's, but rather drug eluting stents. EP also provides a one comprehensive information about something like a ruminant instrument for evaluation of chewing gums.

In the pharmaceutical industry the considerable tool in development of drug and quality control is dissolution testing. Initially the dissolution going to test had been formed regarding solid oral dosage forms, immediate release (IR) and then extended to controlled / modified release solid oral dosage forms ². Afterward in recent times it already has broadened to a application of dissolution going to test to either a sort of novel or special dosage forms including such suspensions, chewable tablets, chewing gums, transdermal patches orally disintegrating tablets, suppositories, implants and injectables, micro particulate formulations, semi-solid topical preparations, and liposome's. It is mandatory to refer for the dissolution test for orally administered, IR solid drug products, as the intention is that the drug dissolves rapidly in the test medium ³.

Microspheres:

Microspheres come under the submicron particulate drug delivery systems for these they do have *in-vitro* dissolution method reported inside any pharmacopoeia thus far. Depending on the the ability to discriminate the drug release they may be really used regarding research study as well as financially commercial motive. Just in case of all these microspores the USFDA appearance particularly for such a [Figure 1] approach that could selectively works to help inside this drug release and provide an *in-vitro/in-vivo* correlation ⁴.

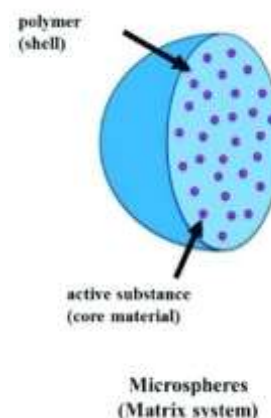


Figure 1: Structure of Microspheres⁵

Nanoparticles:

In medicinal field the nanotechnology has a great importance. Numerous nanoparticulate delivery systems which would include nanosuspensions, nanocrystals, nanoemulsions, but also polymeric nanocarriers lipid nanoparticles, were high to enhance it and pharmacodynamic pharmacokinetic profile or assets sure and therapeutic agents as well as to done in an effective shipping complete special testicles, cells including to cell organelles. Sub-micron colloidal dispersions of pure drug particles are also called as nanosuspensions or nanocrystals. While performing the test regarding the dissolution by taking the samples from the dissolution medium the amount of the drug is expected by using optical characterization methods the drug concentration is determined ⁵.

Because of the efficiency of something like the delivery system would be critically depending just on quality control parameter. And so the assertion of drug release even before nanoparticulate systems it became critical [Figure 2]. The bottle method, is used in *in-vitro* dissolution testing of nanoparticles then these nanoparticles does seem to be provoked through bottle containing dissolution media but rather maintained an definite time must be maintains in the water bath at 37°C. Finally the Samples seem to be turned away out from the dissolution medium as well as differentiated along ultra centrifugation for subsequent analysis ⁶.

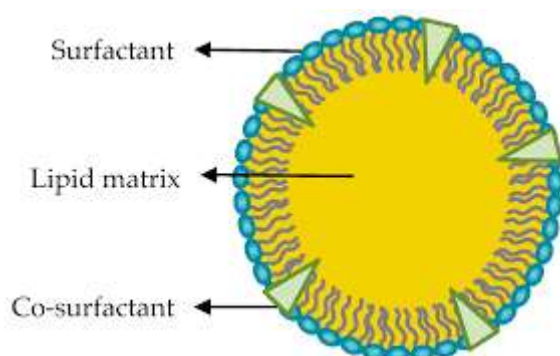


Figure 2: Structure of Nanoparticles ⁸

Liposomes:

Some few standard membrane-free methods can be found are available for this *in-vitro* testing of liposomes has really been demonstrated. Irrespective of the probable phase transitions of the sample viscosity the release profile can be computed. Commonly was using methods seem to be single trace and flipped upside down cup technique. Primarily the Sample has been passed into the cup and through the beginning as well as atmosphere was indeed perforated out. The sample anymore spreads outside or sticks to that the glass based upon that polarity of a sample which again is postponed because of a buoyancy mechanism ⁷.

In case of USP dissolution apparatus - 4 It was established and employed a novel dialysis adapter. The discharge of dexamethasone liposomes through the multiple configurations can also be decisive use these altered instrument [Figure 3]. This system might well be likely to apply regarding *in-vitro* release testing of colloidal disperse systems also including liposome's, nanosuspensions, as well as emulsions ⁸.

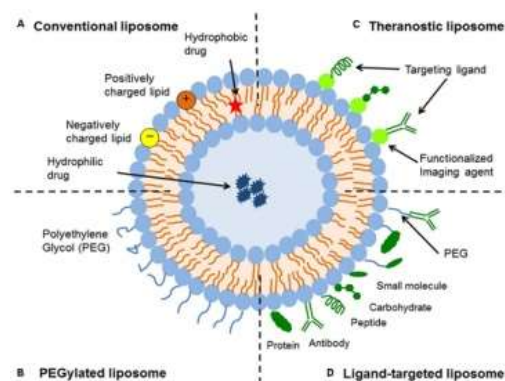


Figure 3: Structure of Liposomes ¹⁰

Design for modulating the release kinetics for novel drug delivery system:

By placing an immediate release rifampicin tablet, gastric floating rifampicin tablet and an enteric coated isoniazid capsule of size 4 a novel dosage forms are formulated. By placing capsule together were put into a hard gelatin capsule of size "00" the novel solid dosage form was formulated finally the formulated novel solid dosage form was evaluated for *in vitro* drug release studies.

Immediate Release

Inside the innovation, parameterization, but also utilization process of pharmaceutical dosage forms, rapid onset as well as controlled-release dosage formulations the mostly had to use techniques were indeed dissolution studies.

In case of *in vitro* release studies to simulate the GI tract conditions, dissolution studies were carried out in acidic media pH1.2 (HCL 0.1N) for 2 hours and then in neutral media pH6.8 (phosphate buffer) for 22 hours. The samples were tested separately in each medium. European pharmacopeia dissolution apparatus 1 was used in order to carry the dissolution testing of coated tablets) at a rotation speed of 50 rpm in 900 ml medium at 37 ± 0.5 °C ⁹.

Sustained Release Drug Delivery System:

Drug release seems to be the method through which a drug leaves the one active pharmaceutical product or active medicament and also is subjected to absorption, distribution, metabolism and excretion, afterward accessible regarding pharmacological action ¹⁰. Recently the NDDS is being replaced by targeted drug delivery system. Among which the some of them have extinct pharmacodynamic actions, which plays a major role in therapeutic action, there are sustained release controlled release dosage forms. Only some of conditions varies the both the dosage forms. Which mainly consider the dosage. As an example slow(Sustained) release tablets were being normally taken a couple of times a day during the one treatment regimen however in conventional dosage forms there was a need to accept 3-4 occasions therapeutic dose in a day.

In-vitro dissolution studies for most of the marketed samples as well as formulated samples were performed by using USP dissolution apparatus II (paddle). Maintained temperature 37 ± 2°C and rotation 100 rpm in 900 ml 0.1 N Hcl for 8 hrs. At predetermined intervals at least 10ml of samples was taken from the dissolution medium and was replaced with same required amount of dissolution media (37 ± 2°C and 100 rpm). In order to maintain the constant volume of the medium. The sample Solution that has been withdrawn from the dissolution medium seemed to be analyzed by using HPLC ¹¹. Based on the concentrations of drugs the percentage of drug that dissolved was calculated. For example the target profile

design parameters of an SR product for metformin hcl were as follows.

- After 1 h: $35 \pm 15 \%$
- After 4 h: $65 \pm 15 \%$
- After 8 h: $100 \pm 15 \%$

Polymeric Drug Delivery Systems

Generally the polymeric drug delivery system has auspicious means the delivering the drugs these polymeric delivery system mainly undergo sol- gel transition after their administration. Either or going to merge of various stimuli by temperature pH change, modulation but rather solvent exchange. Both were the principle justification again for structure of sol- gel transition.

A release of the drug studies has been carried out using the it's plastic dialysis cell like an in situ gel regimens to still be given through it sublingual, conjunctiva rather than oral, ocular or vaginal approaches. Where there are two compartments are present in plastic dialysis cell i.e., donor and acceptor compartment. Which are separated by cellulose layer? The donor compartment was used to introduce with sol form where as receptor compartment used to place the dissolution media which is collected at predetermined intervals of time and replaced with required amount of the fresh media. By using various analytical techniques the drug release in the receptor compartment can be analyzed. The analyzing technique is different for inject able in situ gels, at which formulation has been put into another vials containing receptor media but it is put on such a mixer water bath there as right temperature but also resonance frequency rate. Samples are withdrawn regular intervals but also analyzed ¹².

Fast dissolving drug delivery system

Fast dissolving tablets (FDT) are one of the members in NDDS to achieve the better patient compliance. FDT having more advantages for precise dosage form, simpler and easier portability but rather industrial production excellent physical and chemical stability but also an excellent replacement regarding pediatric and adult patient populations.

FDDT formulation merge additional benefit with both fluid and conventional tablet formulation where also that as well wanting to offer additional benefit through both traditional therapeutic dosage forms. In FDT the Drug dissolution but instead absorption and also clinical onset actually affect or drug bioavailability may very well be substantially greater than just those because after conventional dosage forms [Figure 4]. Current market studies have indicated more than half of the patient population admires prefers fast dissolving tablets both these other dosage forms ¹³.

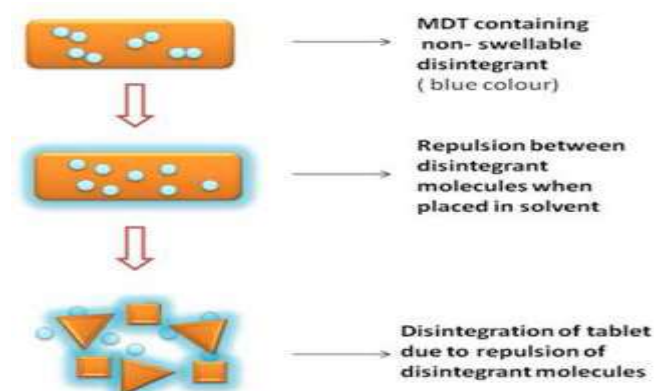


Figure 4: Structure of Fast dissolving Tablets ¹¹

Novel Dissolution test Apparatus for Buccal and Sublingual tablets

Buccal dissolution distinguishes even before G.I. dissolution in regarding ways:

- Smaller volume (of saliva)
- Short residence time (in mouth)
- Solids transfer
- Composition of fluid (saliva composition)
- Incomplete dissolution

In order to perform the dissolution tests for buccal and sublingual tablets the dissolution apparatus must satisfy the above criteria ¹⁴.

Reimagining the *in vitro* dissolution

In present days these dissolution studies are really the most commonly used tools inside this use of process improvement and also in classification, and also of pharmaceutical formulations, either of those IR (immediate release) and CR (controlled release). According to the formulation as well as CMC scientist, they may be invariably are often assigned as for strategy of a product which it obtains a target in vitro dissolution rate that can and will considerably, bring about preferable *in vivo* level of exposure. This same lifecycle regulation team wants to achieve the probability of generating the once-a-day formulation which is bioequivalent to such a B.I.D. (twice a day) or T.I.D. (three times a day) dosing regimen.

We will model and visualize an inside in vitro dissolution of active pharmaceutical ingredients (API) and formulation excipients by using the DDD plus under various experimental conditions in few fractions of time. And start performed decisions which help to improve chances for success.

In present days the rate and extent of drug release can be explained by the various theories and methods. These explanation takes pave among the few developed methods and novel approaches within the provides the appropriate information required except the physicochemical & manufacturing data also the method for dissolution ¹⁶.

Advantages:

It's simple, well defined, intuitive user interface, More effective model, the reports are with high quality and accurate reports.

GUIDELINES

According to the guideline did mention in B.P., it is estimated that all innovative monographs regarding conventional-release capsules and tablets should contain a dissolution necessity but apart from

- The solubility of the active drug is more or somewhat better in water, or dil. Hcl
- The nature drug or dosage forms undergo dissolution test inappropriate dosage forms (for example, liquid-containing capsules, dispersible, effervescent, chewable or soluble tablets) and
- In other justified and authorized circumstances.

The Dissolution tests were the first streamlined to work out an amount as well as extent release of drug from variety of different dosage forms as through Powders, A floating microsphere, Soft gelatin capsules, Aerosol, Immediate release tablets ¹⁷.

Dosage forms for the oral cavity,

- (I) Chewable tablets,
- (II) Buccal /sublingual tablets,
- (III) Medicated chewing gum,
- (IV) Extended-release tablets,
- (V) Transdermal patches
- (VI) Nutritional supplements,

Sink condition

The term sink condition is explained as the concentration of dissolved drug (C) would be less than 20% of something like the saturated concentration C_s , the rate of dissolution is greater compared to normal dissolution because the driving force for dissolution is more at sink conditions. The dissolution test apparatus is a device used to determine the active pharmaceutical ingredient (API) in pharmaceuticals such as tablets, caplets, or capsules for the preparation of any drug according to USP, BP, and IP specifications. It calculates adequate bioavailability and gives the necessary information in the development of solid dosage forms. The dissolution testing will be used as a one actual (official) test besides pharmacopoeias for such assessment of the drug release of Capsule and tablet, etc. Dissolution testing is an important analytical method basically inspected again for the quality control, stability, and review of a batch-to-batch consistency of such product. Before a drug can start acting pharmacologically on the patient in form of solid dosage forms such as tablets or capsules, it should have been first dissolved there in abdomen without first being absorbed into the body. This apparent first step could prove challenging for drug development. The dissolution test apparatus is indeed to give critically important information here on *in-vitro* secretion of medication to anticipate their attitudes *in-vivo*. The oral solid dosage form is still the most frequent method/route of drug administration, the rate at which the drug is released into the body after the dissolution of the dosage form has been swallowed is an important feature of drug development¹⁸.

Overview on types of dissolution test apparatus

There are seven USP- types of dissolution apparatus such as rotating basket type, paddles type, reciprocating cylinders, flow cell type, paddle over the disc, cylinder type, and reciprocating disk type apparatus. These are used in the pharmaceutical industry, research laboratories to provide important *in-vitro* drug release information for both quality control purposes.

Rotating basket (USP Apparatus 1)

It is commonly referred to as a rotating basket since it smoothly rotates and its speed complies with USP recommendations. It consists of a cylindrical basket (capacity of up to 1000 ml) which is held by a motor shaft (made of stainless steel), and the shape is semi-hemispherical to a motor that rotates at a set speed. The sample (tablet/caplet/capsule) is placed in at the bottom. The sample is placed in the basket, which rotates up to 100 rpm in a circular flask filled with dissolution medium. The entire flask is immersed in a constant bath temperature at 37°C. The apparatus-1 is generally preferred for capsules, suppositories, and for dosage forms that float or disintegrate slowly¹⁹.

Paddle type (USP Apparatus 2)

Paddle type is the most widely used dissolution apparatus. It consists of specially coated paddles which reduce the disturbance due to stirring²⁰. The paddle vertically comes in

contact with the bottom of the shaft and is connected dissolving flask with a circular bottom to reduce the turbulence of the dissolution medium. Its operating motor speed is usually at 40 and the operating temperature is 37°C.

Reciprocating cylinder (USP Apparatus 3)

This apparatus is based on the disintegration tester and more suitable for extended-release, chewable tablets. It consists of a set of cylindrical, flat-bottomed glass outer vessels, and a set of glass reciprocating inner cylinders [Figure 5]. Fittings and screens are made of stainless steel and other suitable materials that fit the tops and bottoms of the reciprocating cylinders²¹.

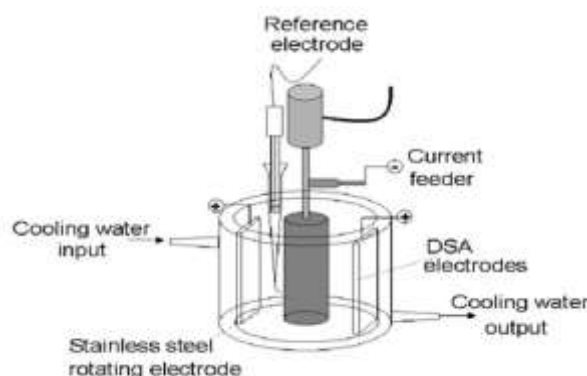


Figure 5: Structure of reciprocating cylinder¹²

Flow-through cell (USP Apparatus 4)

The flow-through method allows the system to be set into two types as an open system and a closed system. It consists of a reservoir for the dissolution medium and a pump that pumps the medium through the test sample-holding cell. The medium is maintained at operating temperature 37°C with flow rates ranging from 4 to 16 ml/min and up to the six samples can evaluate [Figure 6]. The flow through the cell apparatus is used to evaluate modified-release dosage or is typically employed for low-dose medication²².

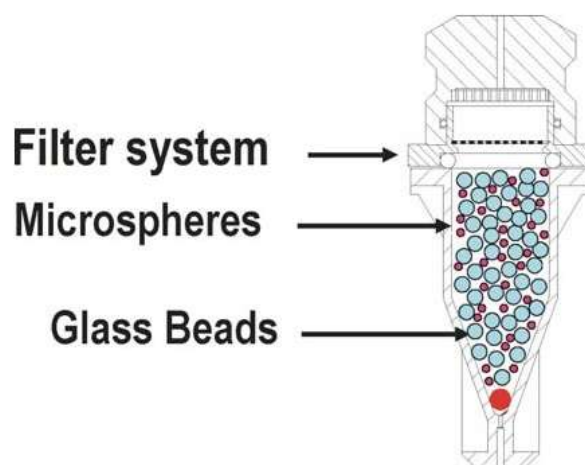


Figure 6: Structure of Flow-through cell¹³

Paddle over the disk (USP Apparatus 5)

It consists of a shaft and a disc assembly that can hold the sample so that the surface can be leveled with a paddle. It is most commonly used for transdermal delivery systems that are attached to a stainless steel disc, which is then placed directly on the bottom of the vessel, under the paddle²³.

Rotating cylinder (USP Apparatus 6)

The cylinder type apparatus is used for testing transdermal patches. It consists of a stainless steel cylinder which is used to hold the sample [Figure 7]. Generally that sample is mounted on to cuprophane. The sample is placed inside the cylinder and will be extracted from the outside into a water bath ²⁴.

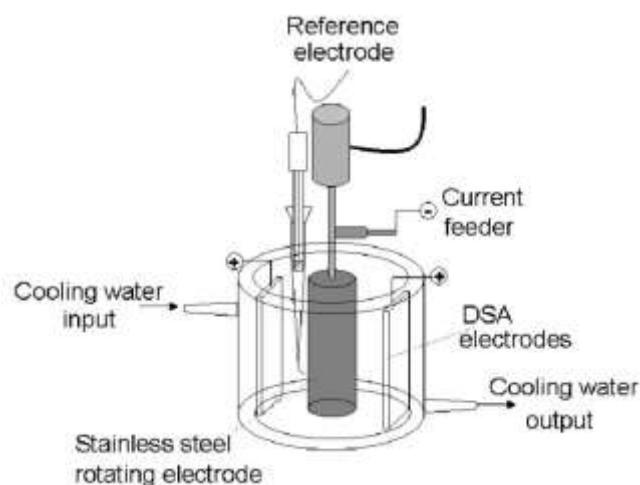


Figure 7: Structure of rotating cylinder ²⁰

Reciprocating disk (USP Apparatus 7)

The reciprocating disc equipment is suitable for small dosages and is ideal for controlled release formulations, and dosage forms that requiring a change of media. It consists of a motor and drives gathering that turns the system perpendicular and also consists of a volumetrically calibrated solution. A flat-bottomed cylinder-shaped vessel with a volume capacity of up to 200 ml is used in this apparatus ²⁵.

CONCLUSION

By using modern production strategies more drugs can really be framed inside this variety of quickly disintegrated tablets ordered list to get more benefits. The fast disintegration tablets have good patient compliance and also better biopharmaceutical properties to fulfill these medical needs. The formulation has developed several types of novel dosage forms. The controlled and sustained release drug products have better patient compliance. The use of compostable or water soluble there in preparation could make its composition greater appropriate as well as excellent drug delivery system.

ACKNOWLEDGEMENTS

The authors are thankful to Dr. Yerikala Ramesh, M.Pharm., Ph.D. Ratnam Institute of Pharmacy, Pidathapolur (V), Muthukur (M) SPSR Nellore – 524 346, Andhra Pradesh, India. Guided to write the review article

Funding support

The author declares that no funding was supported for this study.

Conflict of interest

The author declares there was no conflict of interest for this study.

Contribution of Authors

Authors declare that, the Case Report by the names mentioned in the article and all the liabilities and claims related to the content of the article will be borne by the authors.

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