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EVALUATION OF FORMULATION OF NOVEL DRUG DELIVERYSYSTEM- A REVIEW

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Abstract : The purpose of this study was to evaluate different novel drug delivery system (NDDS) i,e liposome , noisome, nanoparticle etc. . The NDDS are compared by their physiochemical characteristics, storage stability, surface charge. The diameter and surface charge of the NDDSs are comparable with previously reported injectable nanocarriers. The NDDSs showed good encapsulation efficiency and drug loading. Moreover, the NDDSs were stable during storage and in fetal bovine serum for extended periods, showed low complement consumption and were non-toxic to high concentrations. Due to less pronounced burst effect and extended release characteristics, the nano capsules could be favorable approaches for achieving prolonged pharmacological activity of AG using injectable NDDS. To perform drug polymer compatibility FT-IR studies were carried out and observed that there was no interaction between the APl and excipients.Prepared formulations are characterized by vesicle size, shape, surface charge, entrapment efficiency, drug content and invitro drug release studies. The vesicle size, size distribution and zeta potential of the optimized formulation is found to be 65.6 nm and zeta potential is found to be -1.5mV.Size distribution curve confirms the normal size distribution of the vesicles. The % entrapment efficiency of vesicles formulations were found to be in the range of 54.18±0.59 to 92.71±0.56 and optimized formulation is found to be 92.71±0.56 and drug content of noisome formulations. Thus the novel drug delivery systems (NDDS)are carriers which maintain the drug concentration in therapeutic range for longer period of time and also, in addition, may deliver the content to the site of action if so desired as per requirements.
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IndexTerms **- NDDS, delivery system, stability, efficiency**

1. INTRODUCTION

A novel drug delivery system (NDDS) as an innovative approach that combines novel concepts, development, formulation, and particular ways to effectively deliver pharmaceutical drugs to the body as needed to achieve their desired effects. It include targeting site within the body, improves drug potency, control drug release with prolonged pharmacological effect. It involves the development of novel, better and safer drugs with long half-life and large therapeutic index. Some drugs have an optimum concentration range within which maximum benefit is derived, and concentrations above or below this range can be toxic or produce no therapeutic benefit at all.

On the other hand, quite limited progress has been made in the effectiveness of treating severe diseases, which emphasize a growing need for a multidisciplinary strategy to deliver therapies to targeted tissues. For regulating the pharmacokinetics, pharmacodynamics, non-specific toxicity, immunogenicity, biorecognition, and efficacy of medications were developed . These novel techniques, also known as drug delivery systems (DDS), are founded on interdisciplinary methodologies that combine polymer science, pharmaceutics, bioconjugate chemistry, and molecular biology. Various drug delivery and drug targeting systems are now being developed to reduce drug degradation and loss, to prevent adverse reactions, increase medication bioavailability, and to improve the percentage of the drug accumulating in the necessary zone.

Fig no1: Drug delivery system

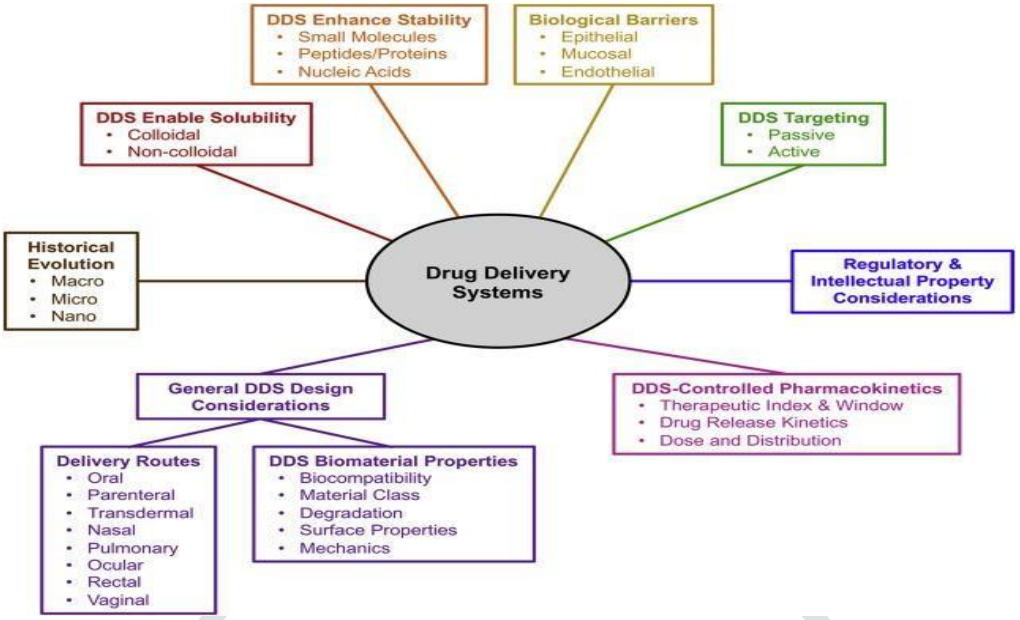
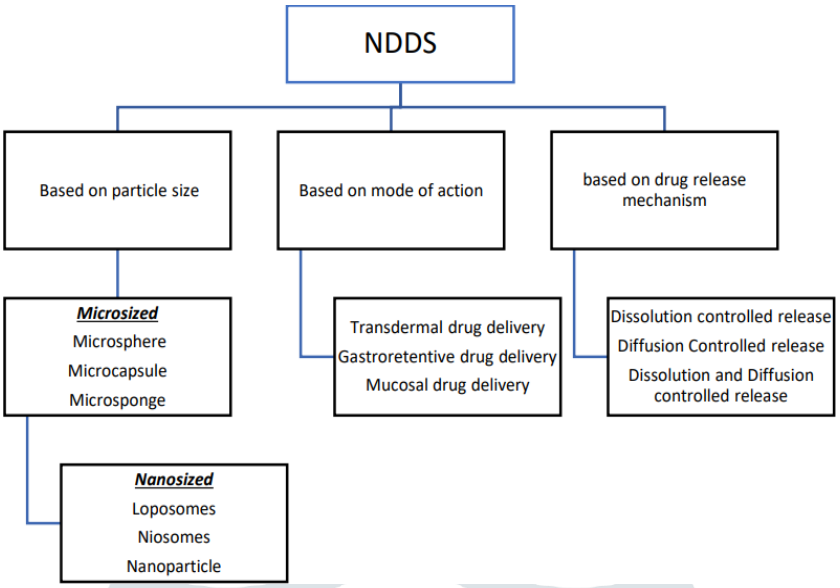


Fig 2- Classification of NDDS



2. EVALUATION PARAMETER OF THE FORMULATION

These review focus on various evaluation parameter to formulate different novel drugdelivery system such as physical characterization include particle size, particle shape, homogeneity, drug loading, drug entrapment efficiency, swelling index, bulk density etc.

a. *Particle Size*

In order to study the micromeritic properties of powdered drugs and excipients, particle size determination is a technique used to determine the appearance, shape, size, and distribution of the particles. Depending on the test specimen's characteristics and the measurement goal, optical microscopy isused.

To maximise cellular absorption and therapeutic index, various lipidic nanocarrier types have been used as drug delivery systems for diagnostic and targeted nanotherapy (using active or passive targeting mechanisms) . It is possible to manufacture and process nanocarriers to have different compositions, sizes, charges, and lamellarities. To regulate the size and size distribution of various drug carrier systems, methods like extrusion, sonication, homogenization, and/or freeze-thawing are used . Continuous physicochemical advancements in the creation of lipid-based nanocarriers may have significant effects on cellular absorption, internalisation, and bioavailability of the medicinal substance that is encapsulated. A highly important characteristic of lipidic nanocarriers is particle size, which influences cellular adhesion, biodistribution, drug release profile, stability, and encapsulationeffectiveness.[1]

Solid colloidal nanoparticles with drug encapsulation have a size range of 10 to 1000 nm.Based on their size and polymeric composition, they are able to target drug to specified sites in the body, and have also shown potential for sustained drug delivery. With drug loading, an increase in size of particles by few nanometers was observed. Nosignificant change was observed in the particle size, particle size distribution and zeta potential withincrease in drug loading from 5% to 30%; however, aslight increase in the particle size and its distributionwas observed with 50% and 75% loading. [2]

The key components that comprise nanoparticle systems are particle size and size distribution. They determined the nanoparticle system's in vivo distribution, biological metabolism, toxicity, and targeting capacity. Additionally, they have an impact on the stability, drug loading, and drug release of nanoparticles. Currently, photon-correlation spectroscopy or dynamic light scattering are the more expedient and commonplace methods of detecting particle size. Typically, scanning or transmission electron microscopy (SEM or TEM) is used to confirm the results of photon-correlation spectroscopy.[3]

A particle is generally considered to be the smallest discrete unit. A particle may be aliquid or semisolid droplet ;a single crystal or polycrystalline; amorphous or anagglomerate. Thisdegreeofassociationmaybedescribedby the following terms.

Lamellar-Stacked plates.Aggregate-Massofadheredparticles.Agglomerate-Fusedor cemented particles. Conglomerate - Mixture of two or more types of particles.Spherulite - Radical cluster. Drusy- Particle covered with tiny particles. Particle condition may be described by the following terms Edges -Angular, rounded, smooth, sharp, fractured. Optical - Color (using proper color balancing filters), transparent, translucent, opaque. Defects - Occlusions, inclusions. Surface characteristics may be described as: Cracked
- Partial split, break, or fissure. Smooth - Free of irregularities, roughness, or projections. Porous-Having opening or passage ways. Rough-Bumpy,uneven,not smooth.[4]

b. *Homogeneity*

Homogeneity is defined as the state in which the drug molecule are evenly distributed through out the formulation. It is determined by FTIRspectrophotometer and NMR spectrophotometer. The sample is scanned over thereasonofwavelength 4000 to 400 nm.

FTIR

Nanodiamond one of the nanoparticle , is loaded with pharmaceutical drugs where the homogeneity is measured with the help of FTIR. Additionally, the nanodiamond-amlodipine conjugates is apparently distinctive FTIR bands of amlodipine and nanodiamond.[5]

FTIR Analysis Techniques:

There are several FTIR analysis sampling techniques that can be used to understand a material's structure and identify the material, each with their own proficiency:

Attenuated Total Reflectance – ATR spectroscopy only requires that the sample comes into contact with the ATR crystal.

Specular Reflectance–SR typically occurs with glossy samples, such as glass and crystal.

Reflection-Absorption – RA works with thin samples such as residues and paints Transmission – TR passes IR (radiation) through gas, liquid or solid samples and measure show well the sample absorbs that infrared radiation.
Photoacoustic – PAS can be difficult, but not impossible. Infrared absorptions are converted to heat inside the sample, creating the photoacousticsignal.[6]

c. *DrugLoading*

In the context of nanomedicine and nanotechnology-based drug delivery systems (NDDS), drug loading refers to the process of incorporating therapeutic agents (drugs) into the carrier or delivery system. NDDS typically consist of nanoscale particles, such as liposomes, polymeric nanoparticles, or dendrimers, which can encapsulate or conjugate drugs for targeted delivery and controlled release.

The drug loading process involves the physical or chemical association of the drug with the carrier system. Physical encapsulation relies on the entrapment of drugs within the carrier structure, while chemical conjugation involves the covalent attachment of drugs to the carrier surface. The choice of drug loading method depends on the properties of the carrier and drug, as well as the desired release kinetics and therapeuticobjectives.

The drug loading efficiency refers to the amount of drug that is successfully incorporated into the carrier system, expressed as a percentage of the total drug used in the formulation. It is an important parameter as it determines the drug payload, which directly influences the therapeutic efficacy and dosage of the NDDS. High drug loading efficiency is desirable to maximize the drug concentration within the delivery system, thereby increasing the therapeutic effect while minimizing the required dose.

Optimizing drug loading in NDDS involves various factors such as the physicochemical properties of the drug and carrier, the method of drug incorporation, and the formulation parameters. These factors can impact the loading efficiency, stability, release profile, and overall performance of the NDDS. Therefore, careful consideration and optimization of drug loading parameters are crucial in the development of effective and efficient nanomedicine-based drug delivery systems.[7]

d. *Drug EntrapmentEfficiency*

These systems are designed to enhance the therapeutic effectiveness and safety of drugs by delivering them to the target site in a controlled manner. Drug entrapment in NDDS refers to the process of capturing or encapsulating a drug within the delivery system.When developing NDDS, scientists and researchers employ various techniques to encapsulate drugs. The goal is to protect the drug from degradation, improve its stability, and control its release profile. Here are a few common methods used for drug entrapment in NDDS: Microencapsulatio, Liposomes, Nanoparticles, Nanocapsules, Dendrimers.

The choice of the method depends on various factors, including the properties of the drug, the desired release profile, and the targeted site of action. By encapsulating drugs within NDDS, researchers aim to improve drug stability, enhance bioavailability, reduce side effects, and achieve more precise and effective drug delivery.

METHOD-Using 10 ml of phosphate buffer (pH 6.6) containing 0.1% (v/v) Tween 80 to wash away the medication from the surface-associated microspheres loaded with 25 mg of propranolol allowed researchers to assess the incorporation efficiency. After being digested for 12 hours at room temperature in 10 ml of 0.1 M HCl (2520), the medicine was then released from the microspheres. A spectrophotometric measurement at 219 nm was used to determine the amount of medication present.

Overall percentage entrapment efficiency = percentage of surface associated drug + percentage of entrapped drug was the formula used to calculate the percentage**.**[8]

e. *Swelling Index*

The term "swelling index" typically refers to a characteristic of certain drug delivery systems, particularly hydrogels or swelling-based systems.Swelling index in NDDS refers to the ability of a hydrogel or swelling-based drug delivery system to absorb and retain fluids, typically water or biological fluids. It is a measure of the extent to which the system swells upon contact with the fluid, and it is often expressed as a percentage.

The swelling index is an important parameter in the design and evaluation of drug delivery systems, as it can impact the release kinetics and performance of the system. By controlling the swelling index, researchers can regulate the rate of drug release, optimize the drug delivery profile, and enhance therapeutic efficacy.

In summary, in the context of NDDS, the swelling index refers to the ability of a hydrogel or swelling-based drug delivery system to absorb and retain fluids, influencing the release of drugs from the system.

METHOD- Swelling studies were conducted using the Vankel Dissolution Apparatus. Pre- weighted tablets were immersed in 500 mL of the medium (deionized water, DIW; simulated gastric solution, 0.1N HCl) and maintained for 8 h at 37.0 ± 0.5°C. At predetermined time intervals (0, 0.5, 2, 4, 6, and 8 h), the swollen tablets were removed from the solution, immediately wiped with a paper towel to remove surface droplets, and weighed. The swelling index (S_w) was calculated according to the following equation:

Swelling index(Sw)=Wt−W0/Wt

where W_0 is the initial weight of the dry tablet and W_t is the weight of the swollen tablet at time t. Data are presented as the mean±standard deviation (SD) from three samples per formulation.[9]

f. Bulk Density

Bulk density refers to the mass of a powdered or granular substance divided by its bulk volume, usually expressed in grams per milliliter (g/mL) or grams per cubic centimeter (g/cm³). It is a measure of how closely the particles are packed together within a given volume.

Bulk density is an important parameter in the formulation and characterization of NDDS, as it can influence various aspects of drug delivery, such as flow properties, compressibility, and dissolution behavior. Different bulk densities can affect the manufacturing processes, dosage form design, and ultimately the drug release kinetics.

To determine the bulk density of a substance, a known mass of the material is poured into a graduated cylinder or a bulk density apparatus, and the volume occupied by the material is measured. The bulk density is then calculated by dividing the mass by the volume.

It's worth noting that the specific method of measuring bulk density may vary depending on the nature of the material and the instrument used. The choice of method should be appropriate for the NDDS formulation being studied or developed.

METHOD-Using a funnel, a sample of microspheres that had been precisely weighed was slowly added to a graduated cylinder with a capacity of 10 ml. Typically, the initial volume was noted. If necessary, carefully level the microspheres without compacting them, and then read the unsettled apparent volume V0 to the closest graded unit. Determine the bulk density in grammes per cubic centimetre.

Df=M/V0

Where Df is bulk density, M is weight of samples in grams and V0 is volumes of sample in cm3[10]

g. *Tapped Density*

Tapped density refers to a measurement that characterizes the packing properties of a powdered material. It is an important parameter in the development and manufacturing of solid dosage forms such as tablets and capsules.

Tapped density is determined by measuring the bulk density of a powder after it has been subjected to a specific tapping procedure. The tapping procedure involves mechanically tapping or vibrating a container or cylinder filled with the powder to settle the particles and reduce void spaces.

The tapped density is expressed as the mass of the powder divided by the volume occupied after tapping. It is typically reported in units of grams per milliliter (g/mL) or grams per cubic centimeter (g/cm³).Tapped density provides information about the powder's flow properties,

compressibility, and ability to fill a specific volume uniformly. It is a critical parameter in dosage form development because it affects the weight and content uniformity of tablets or capsules, as well as the powder's ability to flow and fill die cavities during manufacturing processes.

By measuring the tapped density, pharmaceutical scientists can optimize formulation and manufacturing processes to ensure consistent drug delivery and dosage accuracy.

By dividing a powder's mass by the tapped volume in cm3, the tapped density can be determine. A graduated cylinder with a 10 ml capacity is carefully filled with the microsphere sample. At 2- second intervals, a cylinder was dropped 100 times from a height of 1 inch onto a hard wood surface. The tapped density of each formulation was then calculated by dividing the sample weight in gm by the final tapped volume of the sample contained in the cylinder, which is expressed in cm3. It was determined using theequation

D=M/Vp

Where Do is bulk density, M is weight of samples in grams and Vp is final tapped volumes of granules in cm^3[11]

h. *Spreadability*

Spreadability refers to the ability of a topical formulation, such as creams, gels, or ointments, to spread smoothly and evenly over the skin surface. It is an important characteristic to consider when designing formulations for topical application.

Spreadability is influenced by various factors, including the rheological properties of the formulation, such as viscosity and consistency, as well as the interactions between the formulation components and the skin surface. The ideal spreadability ensures that the formulation can be easily and uniformly applied, providing efficient coverage of the affectedarea.

Several methods can be used to evaluate spreadability, including the use of spreadability testers or texture analyzers. These instruments measure parameters such as the diameter of the spread, the force required for spreading, and the rate of spreading.

METHOD-Due to its simplicity and relative affordability, the parallel-plate approach (also known as the slide and drag method) is an extensively used technique . Two identically sized glass slides are used in the instrumentation; one is fixed to the wooden block and the other is mobile and coupled to a pulley at one end to assess spreadability. A stationary glass slide will hold the dosage form, which will then be pressed between two mobile glass slides. To evenly divide the formulation between two slides and get rid of any air bubbles, the formulation is squeezedhard.

When the upper slide separates from the lower slide, the known weights are added to the pulley. The time needed to slip off is noted, and spreadability is determined using the following equation

S=ML/T

where S, M, L, and T stand for spreadability, weight bound to the top slide, slide length, and time required to separate the slides, respectively.[12]

i. *Extrudability*

Extrudability in the context of New Drug Delivery Systems (NDDS) refers to the ability of a formulation to undergo extrusion or be expelled through a small opening or nozzle. It is a critical characteristic for formulations that are intended for extrusion-based drug delivery systems such as transdermal patches, topical gels, or injectable depot formulations.

Extrudability is influenced by the rheological properties of the formulation, including viscosity, shear thinning behavior, and elasticity. These properties determine the flow behavior of the formulation when subjected to the applied pressure during the extrusion process.

Formulations with good extrudability exhibit a smooth and consistent flow through the extrusion device or applicator, ensuring controlled and predictable delivery of the drug. On the other hand, formulations with poor extrudability may exhibit resistance to flow, clogging of the extrusion device, or uneven expulsion, leading to dosage variability and compromised performance.

METHOD-This test involves filling a tube with the formulation, forcing it out, and measuring the amount of force needed to push the formulation out. The formulation will extrude from the filled aluminium tubes that have been pressed with a finger. The weight on the aluminium collapsible tube loaded with dosage form causes it to extrude the dosage at least 0.5 cm ribbon in 10 seconds. The weight applied is expressed in gm. Calculate the average of the results from the same experiment after three repetitions. To determine the extrudability it is calculated as follows:

Applied weight (g)/Area (cm) slides for extruding from tubes.[13]

j. *Viscosity*

Viscosity in the context of New Drug Delivery Systems (NDDS) refers to the measure of a formulation's resistance to flow. It is a fundamental property that characterizes the thickness or stickiness of a liquid or semi-solid formulation. Viscosity plays a crucial role in the development and performance of various dosage forms, including oral suspensions, topical creams, gels, and injectable solutions.

Viscosity is influenced by the internal friction between the molecules or particles present in the formulation. It is typically measured in units of centipoise (cP) or Pascal-seconds (Pa·s). Higher viscosity indicates greater resistance to flow, while lower viscosity indicates easier flow.

The viscosity of an NDDS formulation impacts several aspects of drug delivery, including:Administration and Dosage, Flow and Spreading, Stability

Viscosity testing can be conducted using various instruments, such as viscometers or rheometers, which measure the force required to move a liquid or the flow behavior under controlled conditions. This information helps in selecting appropriate formulation components and evaluating the impact of viscosity on drug delivery and product performance.

METHOD-At 25°C, the viscosity of the formulations (gel) was measured in cps using a Brookfield viscometer with spindle number S-96 rotating at 1 rpm. Each formulation was measured three times, with the average values being calculated.[14]

k. *CompatibilityStudy*

A compatibility study in the context of New Drug Delivery Systems (NDDS) refers to an investigation conducted to assess the compatibility between different components or materials used in the formulation. It is a critical step in the development of NDDS to ensure that the components of the formulation are compatible with each other and do not lead to any adverse interactions or degradation.

During a compatibility study, various factors are evaluated, including chemical compatibility, physical compatibility, and stability. The study aims to identify any potential incompatibilities that could impact the quality, efficacy, or safety of the NDDS formulation.

l. *pH*

pH in the context of Novel Drug Delivery Systems (NDDS) refers to the measurement of the acidity or alkalinity of a formulation. It is a fundamental parameter that plays a crucial role in the stability, efficacy, and safety of various pharmaceutical.

The pH of various nanogel formulations was determined by using digital pH meter. **.** pH is the critical factor for all formulation because it has an impact on the solubility of the molecule, determine the stability of the formulations.

Significant:

1. Influence on drugdissolution
2. Solubility ofdrug
3. DrugRelease
4. Drugstability
5. Interstinalpermeability[15]

m. *Stability*

Stability studies are an important part of the drug development process. They are used to predictthe shelf life of a drug product and determine proper storage conditions [16]. Stability studiesshould include testing of those attributes of the drug substance that are susceptible to changeduring storage and are likely to influence quality, safety, and/or efficacy .
Novel Drug Delivery System (NDDS) is a new approach that combines innovative development,formulations, new technologies, novel methodologies for delivering pharmaceutical compounds inthe body as needed to safely achieve its desired pharmacological effects .NDDS can minimizeproblems by enhancing efficacy, safety, patient compliance and product shelf life

n. *Carr'sIndex*

Carr's Index, also known as the Carr Index, is a parameter used to assess the flowability and compressibility of powdered materials, including those used in New Drug Delivery Systems (NDDS). It is a measure of the powder's ability to be compacted or flow under certain conditions.[17]

The Carr's Index is calculated using the following formula:

Carr's Index (%) = [(Tapped Density - Bulk Density) / Tapped Density] × 100 where:

Tapped Density refers to the density of the powder after it has been subjected to tapping or vibration to settle the particles.(18)

Bulk Density refers to the density of the powder in its loose, untapped state.

Carr's Index provides an indication of the cohesiveness and flowability of the powder. A low Carr's Index value indicates good flowability, meaning the powder particles have minimal cohesion and can flow freely. Conversely, a high Carr's Index value suggests poor flowability, indicating greater particle cohesion and difficulty in flow.

o. *Hausner ratio*

Hausner ratio of microspheres was calculated according to equation given below Hausner ratio: =Vf/V

where Where V0 is bulk density and Vf is Tapped density**.**[19]

p. *PermeabilityMeasurement*

Permeability measurement in the context of Novel Drug Delivery Systems (NDDS) refers to the assessment of a formulation's ability to allow the transport or diffusion of a drug molecule across biological barriers or membranes. It plays a crucial role in understanding and optimizing the drug release, absorption, and targeting characteristics of NDDS.

In NDDS, permeability measurement is conducted to evaluate the transport of drugs across various barriers, including biological membranes, tissues, or specific target sites. The measurement helps determine the rate and extent of drug permeation, providing valuable information for formulation optimization, bioavailability prediction, and therapeutic efficacy.

CONCLUSION

The goal of any drug delivery system is to provide the therapeutic amount of drug to the proper site in the body also to achieve and maintain the drug concentration in the body. Various formulation parameters of drug delivery and permeation enhancers where optimized to get thin, stable and permeableproduct.

The FTIR of drug excipient and formulation showed that there is no extra peaks that indicates incompatibility of the drug.

The physiochemical parameters such as appearance, solubility were performed by suitable method. The analytical profile of drug was evaluated for determination of absorption maximum and % purity of thedrug.

Compatibility of the drug was done by performing DSC study it was concluded that there was no interaction between the drug and polymer. All formulation were evaluated for the % yield, entrapment efficacy, particle size, SEM, TEM and in vitro drug releaseprofile. On comparing the major criteria such as drug content in vitro drug release profile, the formulation was selected as the best formulation as it showed high % yieldand it also show good sustained release of drug.

Based on the in vitro released characteristics, entrapment efficacy, shelf life of the formulation was found best formulation. According to the stability study it was fond that there was no variation in the % yield, entrapment efficacy, drug loading and invitrodrug release profile of the selected formulation.

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