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Solid Lipid Nanoparticles for the Delivery of Antiviral Agents

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ABSTRACT
Solid lipid nanoparticles are at the forefront of the rapidly emerging field of nanotechnology, with numerous potential uses in medication delivery, clinical treatment, and research, as well as other fields. Effective prevention and reduction of viral transmission are crucial for protecting human and animal health. Antivirals have limited efficacy due to poor solubility, permeability, bioavailability, untargeted release, side effects, and resistance. Nanotechnology-based antiviral delivery systems can effectively address several of these challenges. Antivirals can be placed into nanoparticles made of synthetic or natural materials for delivery. Antiviral delivery techniques derived from natural components, including lipids, phospholipids, surfactants, proteins, and polysaccharides, are gaining attention due to health and environmental concerns. Nanoparticles' composition, shape, size, and interfacial properties can enhance antiviral efficacy and stability. This article reviews recent work on antiviral nanoparticle-based delivery systems and discusses potential future possibilities. The benefits of SLNs include ease of synthesis, low toxicity, high active chemical bioavailability, the capacity to incorporate hydrophilic and lipophilic medicines, and the possibility of large-scale production. This article gives an overview of the SLN preparation methods, the SLN micro and nanostructure properties, and the various parameters impacting sustained release and targeted drug delivery.

Keywords: Nanoparticles, Solid lipid nanoparticles, Drug delivery, Antiviral

I. INTRODUCTION

The field of Novel Drug Delivery Systems is growing at an exponential rate as a result of the extensive knowledge gathered in Biotechnology, Biomedical Engineering, and Nanotechnology. Many modern formulation approaches make use of nanotechnology, which involves the creation of nanosized structures containing the API [1]. The National Nanotechnology Initiative (NNI) defines nanotechnology as the study and application of structures with dimensions ranging from 1 to 100 nm. The overall goal of nanotechnology is the same as that of medicine: to diagnose as correctly and early as feasible and to treat as effectively as possible while minimizing adverse effects through the use of controlled and targeted drug delivery [1-2]. Nanoparticles, solid lipid nanoparticles, nanosuspension, nanoemulsion, and nanocrystals are examples of major drug delivery systems developed employing nanotechnology principles. This page focuses on Solid Lipid Nanoparticles (SLNs). SLNs, which were first introduced in 1991, are a superior alternative to typical colloidal carriers such as emulsions, liposomes, and polymeric micro and nanoparticles [2].

Targeted distribution of a therapeutic molecule to specific organ sites is one of the most complex areas of pharmaceutical research. The development of colloidal delivery systems such as liposomes, micelles, and nanoparticles has opened up new avenues for enhancing medication delivery [2-3]. Nanoparticles, with their unique qualities of small particle size, vast surface area, and the capacity to change surface properties, have significant benefits over alternative delivery systems. Nanoparticles are solid colloidal particles ranging from 10 to 1000 nm (1.0 μm) in size [3]. The active principles are dissolved, entrapped, and adsorbed or attached. Solid lipid nanoparticles (SLN) are aqueous colloidal dispersions composed of solid biodegradable lipids [3-4]. SLNs combine the benefits of numerous colloidal carriers in their class while avoiding the disadvantages, such as physical stability, protection of integrated labile medicines from degradation, regulated release, and great tolerability. SLN formulations for several application routes (parental, oral, dermal, ophthalmic, pulmonary, and rectal) have been created and fully tested in vitro and in vivo [4].

Viruses can enter the body via several pathways, such as the nose, mouth, eyes, and skin [4-5]. This review will cover antiviral platforms for major pathogenic viruses such as HIV, norovirus,

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hepatitis viruses, HPV, HSV, and coronaviruses, which cause significant morbidity and mortality [5].Existing antiviral agents face challenges such as poor solubility, instability during storage or application, low bioavailability, potential side effects or toxicity, and the development of drug-resistant viruses, limiting their effectiveness. Using a pure antiviral medication can pose significant hurdles. Antivirals eaten orally may be damaged by the harsh environment of the gastrointestinal tract (GIT), resulting in lower absorption. Antivirals often have minimal permeability through cell membranes, mucosal layers, skin, and gut epithelial surfaces, limiting their effectiveness. Antivirals' efficacy may be limited due to their fast metabolism and elimination following absorption [5-6].

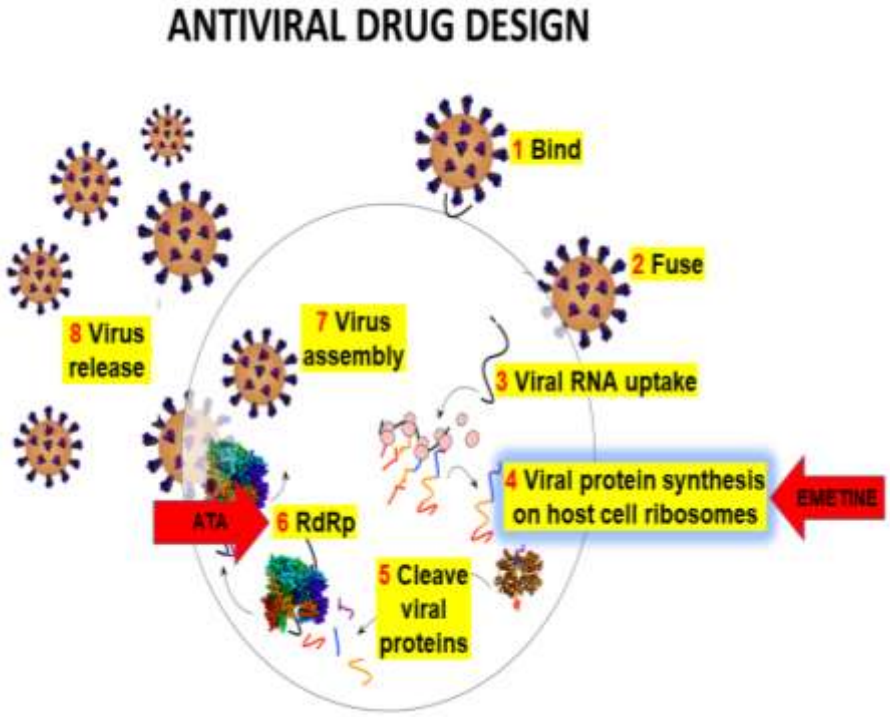

Fig. 1: Antiviral drug design

To address these problems, well-designed delivery systems can encapsulate antiviral drugs, protect them during storage, and deliver them to their intended target, resulting in increased antiviral activity. Nano-enabled delivery systems, containing bioactive compounds within nanoparticles, are ideal for this purpose due to their adaptable compositions, architectures, and functional properties [7]. Nanoparticles in delivery systems can be chemically produced or derived from natural components. Biocompatible components, such as biopolymers, lipids, phospholipids, and biosurfactants, are increasingly being used to create nanoparticles due to their diverse functional characteristics, high biocompatibility, and biodegradability. Nanoparticle-delivery systems have small particle sizes and high specific surface areas, making them useful for applications that require quick digestion, penetration, and absorption [8]. Nanoparticle composition, structure, and interfacial characteristics can enhance bioactive agent dispersion and stability.

Nanoparticles

Nanoparticles are the foundation of Nano technology. Nanoparticles range in size from 1 to 100nm and are composed of metals, metal oxides, organic materials, and carbon [9]. Apart from their substance, nanoparticles vary in dimension, shape, and size. The surface might be uneven, with surface changes, or homogeneous. Some nanoparticles are crystalline or amorphous, having single or many crystals that are either agglomerated or loose [10]. During the process of synthesizing new medications, most drug candidates are insoluble or weakly soluble in water, causing a significant

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setback for the pharmaceutical industry. A drug's complex and massive molecular structure is a major cause of its insoluble nature.

Types of nanoparticles

A. Lipid-Based Nanoparticles

- **Liposomes**

Spherical vesicles made of phospholipid bilayers that can hold both hydrophobic and hydrophilic medicines.

- **Solid Lipid Nanoparticles (SLNs)**

Solid lipid matrices that can encapsulate pharmaceuticals while providing good stability and controlled release.

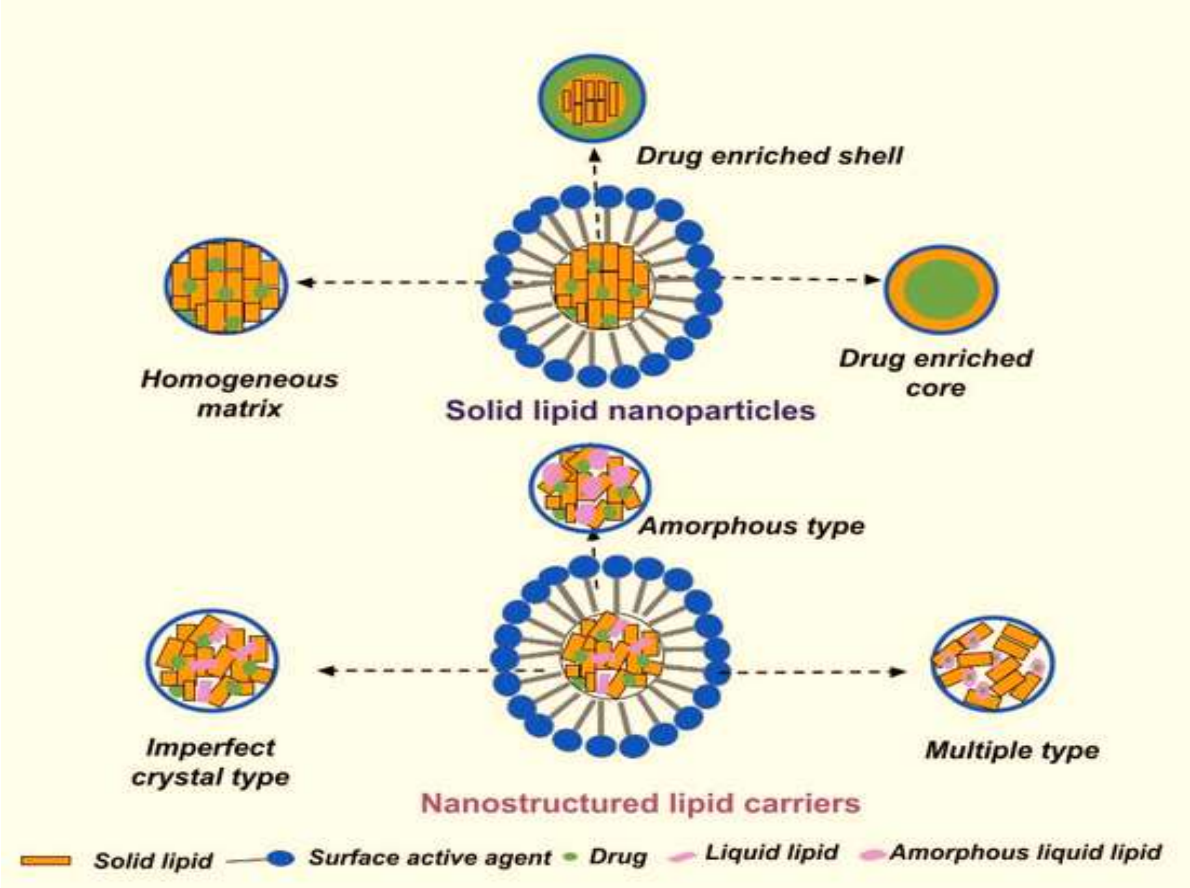

Fig. 2: Difference Between Lipid based Nanoparticles

- **Nanostructured Lipid Carriers (NLCs)**

Similar to SLNs, but with a more complicated lipid structure for better drug loading and controlled release.

B. Polymer-Based Nanoparticles

- **Polymeric Nanoparticles**
  - These nanoparticles, made of biodegradable or non-biodegradable polymers, can be engineered into nanospheres (matrix systems) or nanocapsules (cavity systems).

- **Dendrimers**

Highly branching, tree-like structures that are effective drug carriers due to their exact structure and ability to encapsulate drugs.

- **Polymeric Micelles**

Amphiphilic block copolymers that self-assemble in water to form a core and a shell around hydrophobic medicines.

C. Inorganic Nanoparticles

- **Metal Nanoparticles**

Gold nanoparticles (AuNPs), iron oxide nanoparticles, and silver nanoparticles are used for

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their distinctive optical, magnetic, and sensing capabilities in drug administration and imaging.

- **Quantum Dots (QDs)**

Semiconductor nanocrystals with unique fluorescence characteristics allow for simultaneous medication administration and imaging applications.

- **Carbon Nanomaterials**

Carbon nanotubes (CNTs) and nanohorns are used because of their large surface area and potential for targeted drug delivery.

- **Silica Nanoparticles**

Used as a drug delivery scaffold, with high biocompatibility and controlled release qualities.

D. Hybrid Nanoparticles

- **Lipid-Polymer Hybrid Nanoparticles**

Combine the benefits of lipids and polymers to generate more effective medication delivery systems.

- **Organic-Inorganic Hybrid Nanoparticles**

Combining organic and inorganic nanomaterials, such as cell membrane-coated nanoparticles, can improve targeting and cellular interactions.

Solid Lipid Nanoparticles

In 1991, solid lipid nanoparticles (SLN) were introduced as an alternative to traditional colloidal carriers like emulsions, liposomes, and polymeric nanoparticles. Solid lipid nanoparticles are gaining popularity as a colloidal drug carrier for intravenous applications, offering an alternative to particulate carriers. SLN are sub-micron colloidal carriers (50-1000 nm) made of physiological lipids and dispersed in water or aqueous surfactant solutions. SLN's unique qualities, including tiny size, vast surface area, high drug loading, and phase interaction at the interface, make them interesting for improving pharmaceutical efficacy.

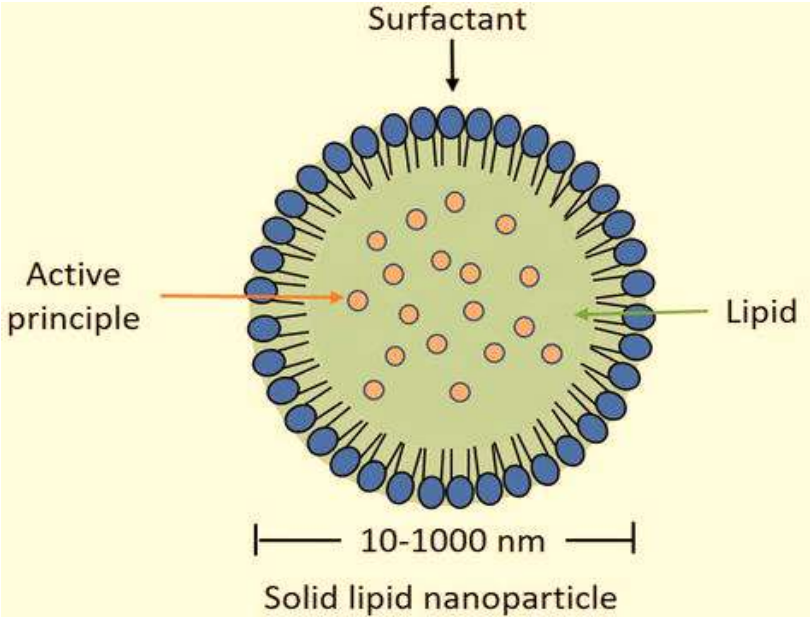

Fig.3: Structure solid lipid nanoparticles.

Solid lipid nanoparticles are a new colloidal carrier method for parenteral nutrition, similar to oil in water emulsions. However, instead of the liquid lipid, a solid lipid is used (Fig. 1). Solid lipid nanoparticles offer numerous benefits, including high biocompatibility, minimal toxicity, effective delivery of lipophilic medicines, and physical stability.

Since their introduction in the early 1990s, solid lipid nanoparticles (SLNs) have proven to be the most effective lipid-based colloidal carriers. This is a typical method for increasing the oral bioavailability of medicines with low water solubility. SLNs are submicron-sized (50-1000 nm) and made up of physiologically tolerable lipid components that are solid at normal temperature.

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A schematic illustration of several particle drug carriers, including emulsions and liposomes.

Types of solid lipid nanoparticles

1. **Aqueous solutions**
   - Drug dissolved in water.
   - Ex., Syrups, drop, injections
2. **Non-aqueous solutions**
   - Solvent other than water is used (oils, alcohol, glycerin)
   - Ex., Vitamin oil injections , tinctures.
3. True solutions:-
   - Clear, homogeneous solutions where solute is completely dissolved.
   - Particles size < 1nm
4. Colloidal solutions:-
   - Particles size between 1-1000 nm.
   - Includes micelles, liposomes, niosomes, nanoemulsion.
5. Supersaturated solutions:-
   - Contain more solute than normally soluble.
   - Improve drug absorption.
6. Micellar solutions:-
   - Drug entrapped in micelles formed by surfactants.
7. Liposomal solutions:-
   - Drug enclosed in lipid bilayer vesicles.
   - Used in cancer therapy.
8. Complexation solutions :-
   - Drug + complexing agent to increase solubility and stability.

Advantages of Solid lipid nanoparticles :-

• SLNs have no bio toxicity because the lipids utilised are biocompatible and biodegradable materials.
• It is possible to make SLNs without employing organic solvents.
• The physical stability of SLNs is high.
• SLNs can be used to achieve both drug targeting and controlled drug release.
• Incorporating active compounds into SLNs can boost their stability.
• Lipophilic and hydrophilic medications may be encapsulated in SLNs.
• Easy to large-scale production.
• Targeted drug delivery.
• Significantly more straightforward to produce compared to biopolymeric nanoparticles.
• • Traditional methods for manufacturing emulsions can be used.
• The raw materials needed are identical to those used in emulsions.
• The level of long-term stability is significant.

Disadvantage of solid lipid nanoparticles:-

• Lipid dispersions have high water content.
• Limited transdermal medication delivery.
• Hydrophilic drug loading capacity is constrained.
• Increase in particle size while being stored.
• The toxicity of lipid nanoparticles on retinal cells has not yet been thoroughly investigated.
• Particle growth and aggregation.
• Particle agglomeration is possible.
• Unforeseeable propensity for gelation.
• Unforeseen kinetics of polymeric phase changes.
• Burst release

Objectives of solid lipid nanoparticles :-

1. To improve bioavailability of poorly water-soluble drugs.
2. To achieve controlled and sustained drug release for a longer duration.
3. To enhance drug stability by protecting drugs from degradation (chemical, photolytic, or enzymatic).
4. To enable targeted drug delivery to specific tissues or cells.
5. To reduce side effects by minimizing drug exposure to non-target tissues.
6. To improve drug loading capacity for both hydrophilic and lipophilic drugs.
7. To provide alternative routes of administration (oral, topical, parenteral, ocular, pulmonary, etc.).
8. To ensure biocompatibility and biodegradability using physiological lipids.
9. To improve patient compliance by reducing dosing frequency.
10. To replace traditional colloidal carriers such as liposome.

Formulation of solid lipid nanoparticles

Lipids are often used as matrix materials in SLNs, with emulsifiers, co-emulsifiers, and water added to the formulation [11]. Charge modifiers, which are agents that increase both the duration of circulation and the ability to target specific locations, are used to meet the stability and targeting requirements. The following is a list of excipients used in the production of solid lipid nanoparticles.

- **Lipid matrix**

The formulation's key ingredients are lipids, which play an important role in influencing an API's stability, release, and encapsulation. One significant issue with SLNs is their limited ability to accommodate hydrophilic drugs, owing to

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partitioning effects that occur during the manufacturing process. Only hydrophilic medicines with high potency and modest doses can be successfully incorporated into the solid lipid matrix [12]. In lipid medication, a surfactant interfacial area stabilizes the lipid drug core, yet the conjugates have a spherical shape. Core lipids include fatty acids, acylglycerols, waxes, and their mixtures. The surface stabilizers include bile salts, cholesterol, phospholipids, and sphingomyelins 12-13]. Ligands improve tissue targeting. Lipid-drug Conjugates can contain both water-loving (hydrophilic) drugs like doxorubicin and tobramycin, as well as fat-loving (lipophilic) drugs like progesterone and cyclosporin A.

- **Surfactants**

Surfactants are used to improve the colloidal stability of particles during the production of classic SLNs. The physical and chemical properties of SLNs vary depending on the composition and concentration of the surfactant [13]. Surfactants provide two crucial functions: dispersing the lipid melt in the aqueous phase and stabilizing lipid nanoparticles in dispersions after cooling. The key considerations for using surfactants in the formulation of solid lipid nanoparticles are their safety and compatibility with other excipients. Surfactants can increase epithelial cell permeability and overcome drug absorption barriers.

- **Co-surfactants**

Differential scanning calorimetry and static light scattering are utilized to investigate the effects of co-surfactants on SLN crystallization patterns and physical durability. According to research, the best co-surfactants are amphiphilic, which means they possess both hydrophobic and hydrophilic qualities [13-14]. These co-surfactants must have considerable hydrophobic areas and be very soluble in water. This allows them to have a ready supply of molecules to stabilize surfaces.

- **Emulsifiers**

The choice of emulsifier has a considerable impact on the quality of solid lipid nanoparticles. Increasing the emulsifier concentration aids in the lowering of surface tension and particle partitioning during homogenization [15]. As particle size decreases, the exposed surface area increases. Emulsifiers must have the following properties: non-toxicity, compatibility with other excipients, the ability to generate the necessary size with a small amount of material, and the ability to maintain sufficient stability for SLNs by coating their surfaces. They promote the circulation of SLNs by blocking the Reticuloendothelial System and improving medication delivery to the brain. The emulsifiers are phosphatidylcholine 95% (Epikuron 200), soy lecithin (Lipoid S 75 and Lipoid S 100), egg lecithin (Lipoid E 80), poloxamer 188 (Pluronic F 68), poloxamer 407, poloxamine 908, polysorbate 80, Cremophor EL, and Solutol HS.

- **Co-emulsifiers**

The mobility of phospholipid molecules linked to vesicles is constrained. As a result, they are unable to quickly encapsulate newly created surfaces, whereas solid lipids undergo recrystallisation. When an emulsifier is suddenly removed from the particle's surface, particle aggregation and an increase in the size of SLNs occur due to the limited mobility of phospholipid molecules [16]. To counteract this, co-emulsifiers such glycocholate (an ionic chemical) and tyloxapol (a nonionic polymer) are utilized. Tyloxapol, taurocholate sodium salt, sodium dodecyl sulfate, sodium glycocholate, sodium oleate, cholesteryl hemisuccinate, and butanol are some of them.

- **Cryoprotectants**

Cryoprotectants are commonly used during the lyophilization process to decrease or eliminate solute or suspended material aggregation. These compounds include trehalose, glucose, mannose, maltose, lactose, sorbitol, mannitol, glycine, Polyvinylpyrrolidone (PVP), Polyvinyl Alcohol (PVA), and gelatin [16-17].

- **Charge modifiers**

Surface modifiers, such as hydrophilic polymers, can reduce lipid nanoparticle uptake by the reticuloendothelial system. These include: stearylamine, dicetyl phosphate, dipalmitoylphosphatidylcholine (DPPC), dimyristoylphosphatidylglycerol (DMPG), polyethylene glycol, and poloxamer.

Methods of Preparation of Solid Lipid Nanoparticles

SLN preparedness strategy includes high shear homogenization, ultrasonication, microemulsion-based SLN planning, supercritical liquid invention, splash drying, dissolvable emulsification/vanishing, dissolvable infusion

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method, and dissolvable emulsification-dissemination [18]. Recently, this method has been used to plan lipid nanoparticles. This process is based on the precipitation of lipids that have broken down in organization. In this method, dissolvables are removed, and lipids accelerate at the same time. Dissolvable ejection is fundamental and can be accomplished through refining or other techniques if evacuation is not possible under the given conditions. The lipid nanoparticles are arranged after the water-immiscible natural dissolvable has vanished. Partical size is determined by a variety of factors, including the amount to be infused, the grouping of lipids, temperature, mixing, the type of natural dissolvable, and the emulsifier [19]. SLNs are formed from lipid, emulsifier, and water/dissolvable using several ways and are listed below.

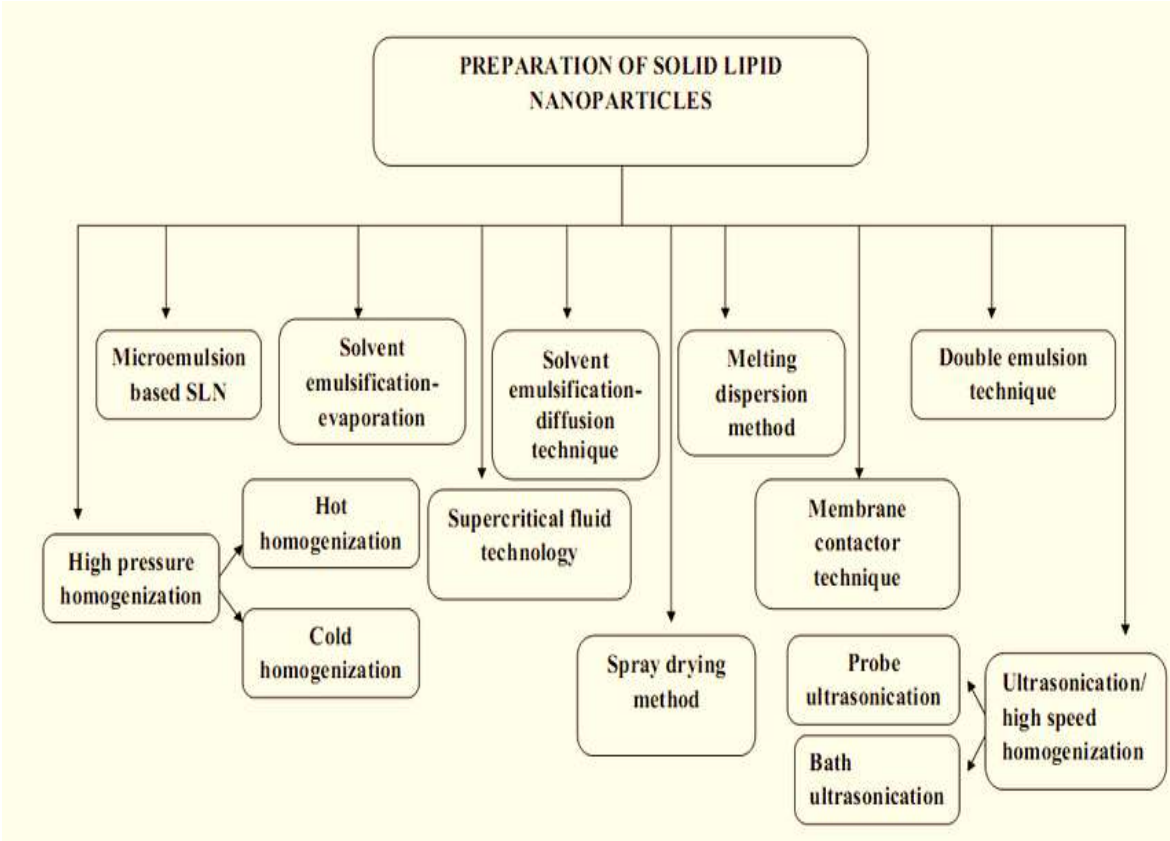

Fig. 4: Various methods of preparation of SLN

- **High Pressure Homoginizer**

HPH is a reliable procedure for preparing SLN. Several manufacturers offer cost-effective homogenizers of various sizes. Particles in the submicron range are obtained with high shear stress and cavitation compulsion. HPH produces nanoemulsions for parenteral feeding. HPH uses high pressures (100-2,000 bar) to drive liquid into a tight space (within a few microns).

The fluid travels quickly over a short distance at high velocity.

Homogenization transforms even high lipid concentrations into nanodispersions.

- **Ultrasonication**

Eldem et al. (1991) reported that SLN can also be created through high-speed stirring or sonication. This method's impediments are common across all laboratories. The technique's biggest negative is its broader particle size distribution, which might lead to physical instability (Svilenov and Tzachev, 2009). This approach has significant challenges, including particle increase during storage and metal decay [20]. Extensive study has shown that combining high-speed stirring with ultrasonication at high temperatures results in consistent formulations.

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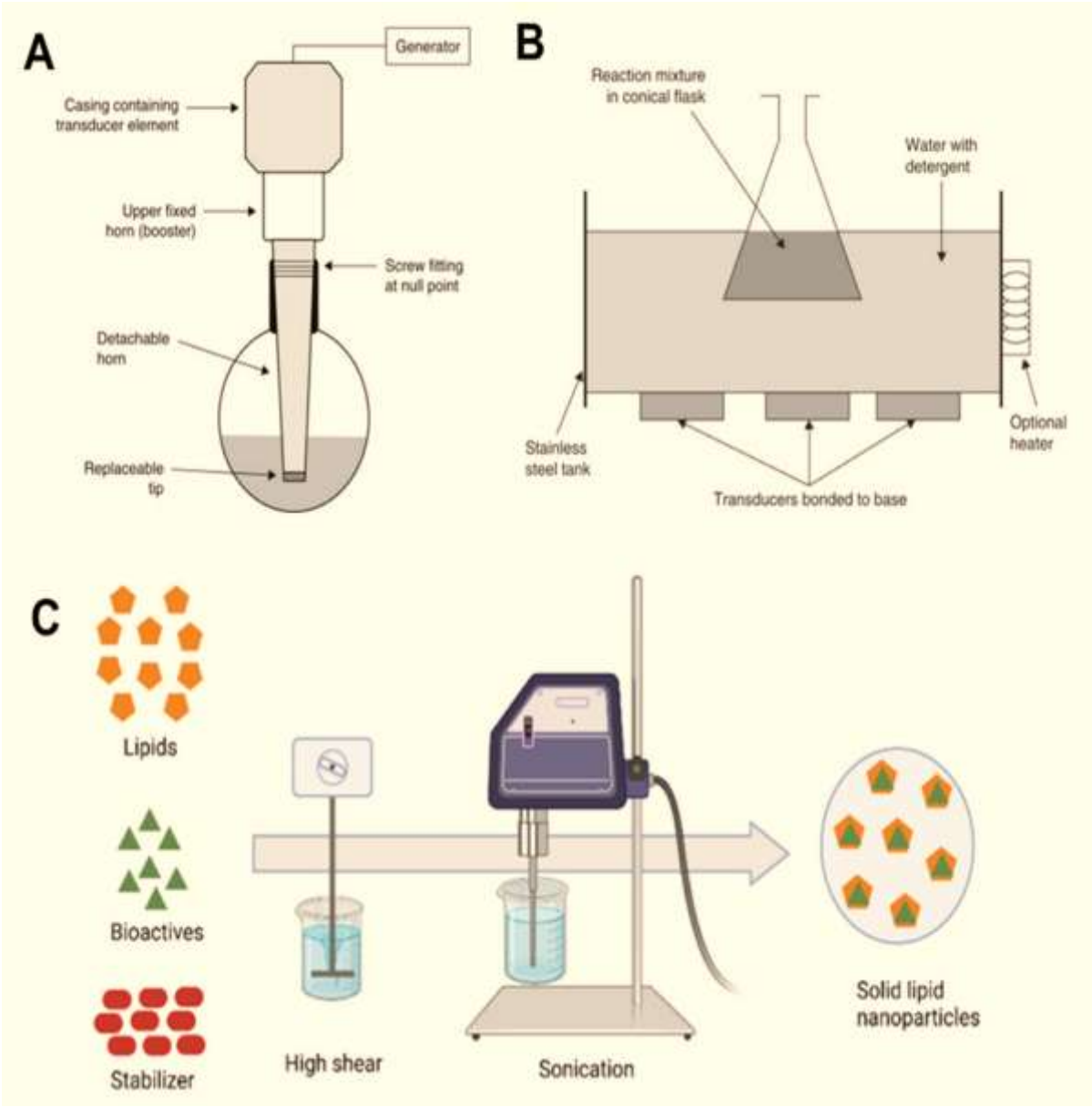

Fig. 5: Basic methods used to prepare Slid lipid nanoparticles

- **Solvent emulsification–evaporation**

This method involves dissolving lipophilic materials and hydrophobic drugs in water-immiscible organic solvents such cyclohexane, toluene, and chloroform. The mixture is homogenized at high speed to form an aqueous phase. The coarse emulsion is quickly passed through a microfluidizer. Ramteke et al. (2012) employed a rotary evaporator with mechanical agitation at room temperature and reduced pressure to evaporate the organic solvent. This strategy mostly relies on avoiding heat stress. Fig. 6 shows the possibilities of including extremely thermolabile medicines. The downside is that the organic solvent used may react with medication molecules.

- **Supercritical fluid**

This is a sophisticated way for producing SLNs. The supercritical fluid has unique thermophysical properties that can be fine-tuned with small pressure adjustments. Chen et al. (2006) and Kaiser et al. (2001) reported solvent-free processing. As pressure increases, fluid density and liquefaction capacity increase while velocity remains constant. ScF is a material that exceeds its

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pressure and critical temperature. At these conditions, the fluid exhibits unique features such as liquid-like density, gas-like viscosity, and greater diffusivities (intermediate between liquid and gas), resulting in a faster mass transfer rate.

- **Microemulsion**

Gasco and colleagues developed SLN preparations by lowering the concentration of microemulsions (Akanksha et al., 2012). Microemulsions are biphasic, with both internal and exterior media. The combination comprises of a low melting fatty acid (e.g., stearic acid), an emulsifier (e.g., polysorbate 20, polysorbate 60, or soy phosphatidylcholine), coemulsifiers (e.g., butanol and sodium mono cetyl phosphate), and water. In cold water (2°C-3°C), the heated microemulsion diffuses. The diluting process can be rectified by combining microemulsions. Gasco (1997) and Ramteke et al. (2012) found that this approach requires no additional energy to achieve submicron size.

- **Spray Drying**

Similar to lyophilization, this process modifies an aqueous dispersion into a medication. In comparison to lyophilization, this process is more cost-effective. Particle collection may occur due to high temperatures, shear stresses, and partial melting (Jawahar et al., 2012). According to Freitas et al. (1998), lipids with a boiling point above 70°C are ideal for spray drying. Spray drying using a 1% SLN solution in water or 20% trehalose in ethanol-water mixes (10/90 v/v) yielded the greatest results.

Evaluation of solid lipid nanoparticles

- **Electron Microscopy of Solid Lipid Nanoparticles:**

Transmission electron microscopy revealed solid lipid nanoparticles. SLN tests were weakened tenfold and then put on a gold plate. The mounted plates were dried and examined under a transmission electron microscope without using any stain [21]. The CCD camera and delicate image framework were used in conjunction with the transmission electron magnifying apparatus to visualize SLN.

- **Zeta potential of Solid Lipid Nanoparticles:**

Zeta potential of SLN definitions were dictated by Zeta sizer. Tests were fittingly weakened with deionized water to get 50 and 200 Kcps for the estimations. Tests were put in the cubit accessible for instrument and zeta potential measured specifically .

Fig. 6: Particles size analyzer

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- **Particle Size and Polydispersity Index of Solid Lipid Nanoparticles:**

The normal particle size and polydispersity files of SLN details were measured using a Zeta sizer DTS (Malvern Instrument, UK). The SLN scattering specimens were weakened using deionized water. The results of normal particle size and polydispersity records were obtained from an instrumental-based calculation system [22].

- **Encapsulation Efficiency of Solid Lipid Nanoparticles :**

The amount of testosterone encapsulated in solid lipid nanoparticles was calculated to represent productivity. Dialysis was performed on solid lipid nanoparticles. Dialyzing medium consisted of 30 milliliters of 30% v/v PEG 400 in a phosphate cushion (pH-6) configuration. Dialysis of solid lipid nanoparticles was carried out for two hours. One hundred mg of dialyzed solid lipid nanoparticles were extracted from the dialysis pack and analyzed for drug content by supercritical fluid chromatography (HPLC) at 254 nm (Shimadzu, Japan). The samples were attenuated and separated using Millipore film channels (0.2 µm).

- **Viscosity of Solid Lipid Nanoparticles :**

The viscosity of testosterone-containing solid lipid nanoparticles was evaluated using a Brookfield viscometer (DV-E viscometer, Brookfield, USA) with shaft no. 63 at 30 r/m in the surrounding conditions. The shaft speed no. 63 was set in the viscometer nob, and the maximum torque was measured before checking the viscosity. The viscosity of testosterone-containing solid lipid nanoparticles was evaluated using a computerized viscometer.

- **In Vitro Release Study of Solid Lipid Nanoparticles:**

The viscosity of solid lipid nanoparticles was determined using a Brookfield viscometer (DV-E viscometer, Brookfield, USA) with shaft number 63 at 30 r/m in ambient circumstances. Before checking the viscosity, the shaft speed was adjusted to 63 on the viscometer nob, and the maximum torque was measured. A computerized viscometer was used to determine the viscosity of solid lipid nanoparticles.

Applications of solid liquid nanoparticles

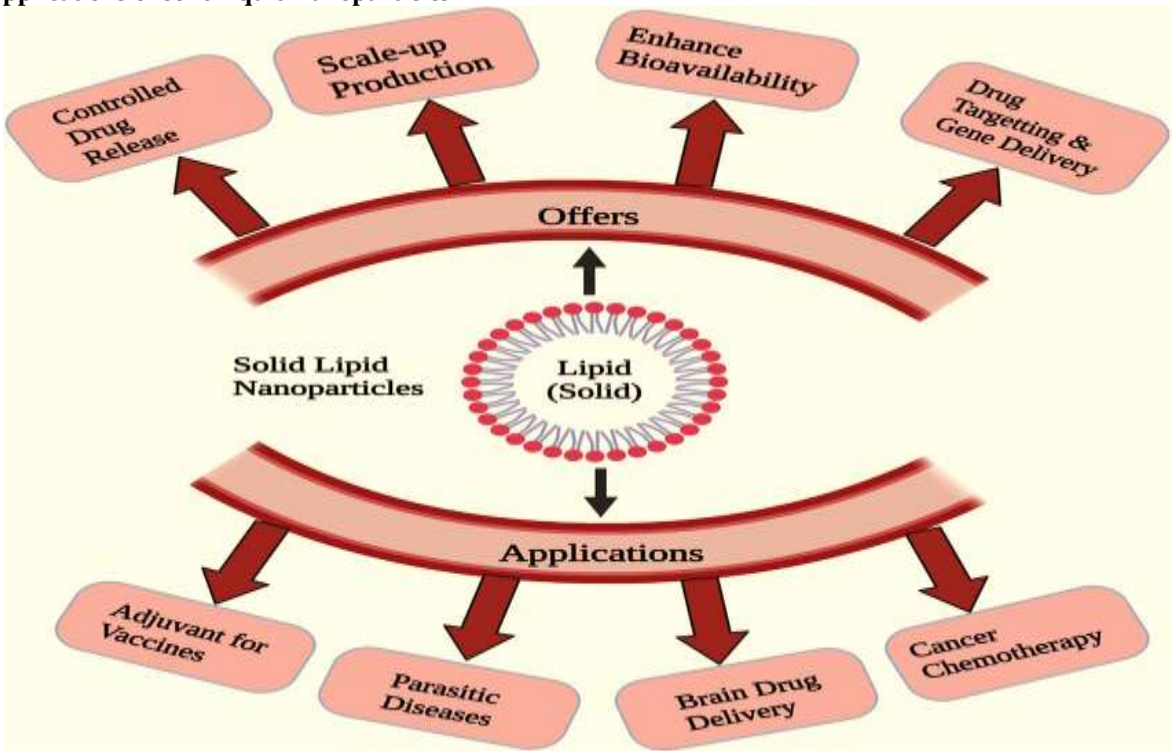

Fig. 7: Applications of Solid lipid nanoparticles

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- **Cancer Therapy**

SLNs can overcome multidrug resistance and deliver therapeutic agents directly to tumors, improving cancer treatment efficacy.

- **Infectious Diseases**

They are used to deliver antibiotics and other drugs to infection sites, enhancing their distribution and therapeutic effect.

- **Central Nervous System (CNS) Disorders**

SLNs are explored for treating neurodegenerative diseases and brain cancers due to their ability to cross the blood-brain barrier.

- **Diabetes Management**

SLNs offer improved pharmacokinetics and modified drug release, which is beneficial for managing conditions like diabetes.

- **Topical and Transdermal Delivery**

SLNs can enhance the skin penetration and localized delivery of drugs for inflammatory and skin conditions, including nonsteroidal anti-inflammatory drugs (NSAIDs).

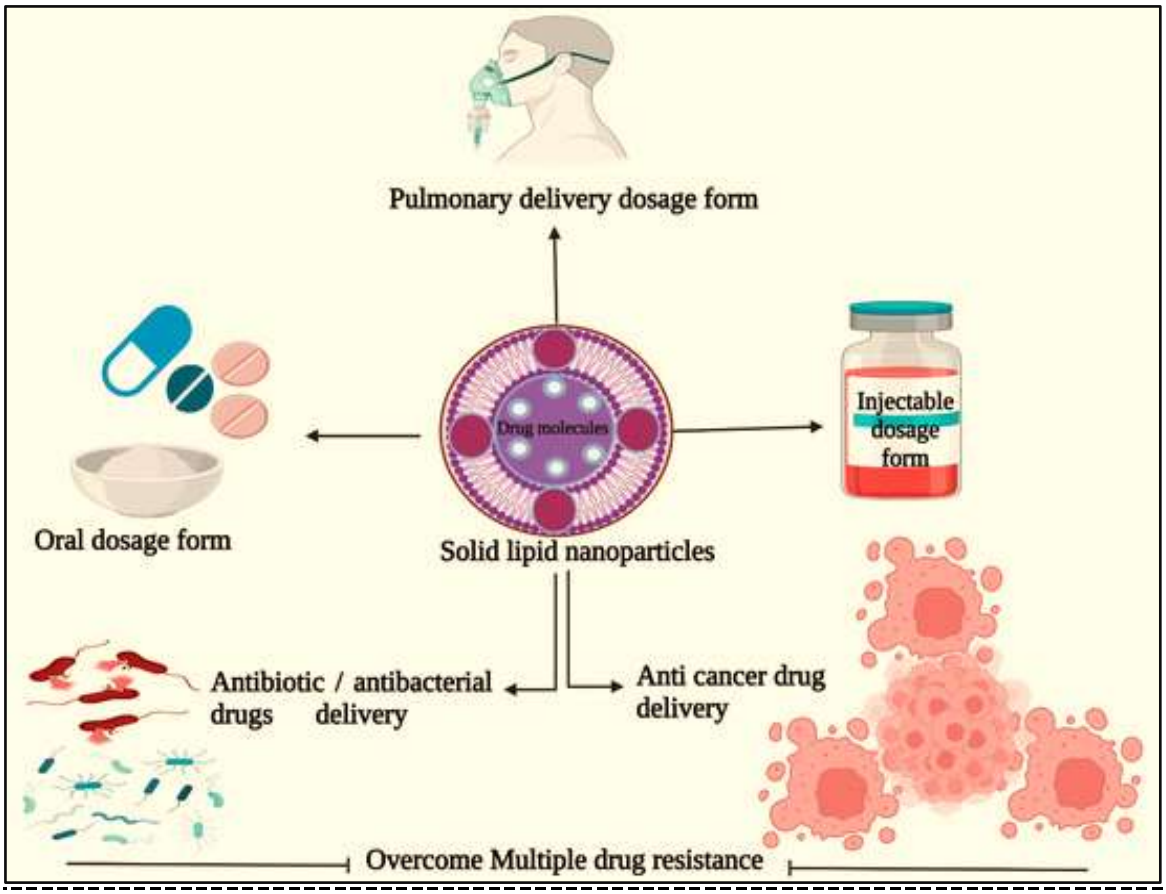

Fig. 8: Benefits of SLN in various routes of drug delivery.

- **Oral Delivery**

SLNs can improve the oral bioavailability of poorly soluble drugs by increasing their dissolution and residence time in the gut. They can increase the bioavailability of compounds that are poorly absorbed when taken orally.

- **Drug delivery**

SLNs are used to deliver hydrophobic drugs, improve their solubility and bioavailability, and provide controlled and sustained release.

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- **Targeted drug delivery**

They can be engineered to target specific tissues or organs, such as the brain or tumors, to enhance treatment efficacy.

II. FUTURE PROSPECTIVES

Antiviral agents are drugs approved in the USA by the Food and Drug Administration (FDA) for the treatment or control of viral infections. The development of antiviral agents is not trivial as viral replication is intricately linked with the host cell that any antiviral drug that interferes even to a lesser extent with host cell factors may be toxic to the host depending on the duration and dosage used. Available antiviral agents mainly target stages in the viral life cycle. The target stages in the viral life cycle are; viral attachment to host cell, uncoating, synthesis of viral mRNA, translation of mRNA, replication of viral RNA and DNA, maturation of new viral proteins, budding, release of newly synthesized virus, and free virus in body fluids. Antiviral agents used to treat viral diseases are currently limited, and at least half of the available agents are for the treatment of human immunodeficiency virus (HIV) infections. Other Future prospectives of SLN:-

- **Customized and personalized medicine:** Future SLN-based systems will be tailored to a patient's specific genetic and metabolic profile. The design of nanoparticles will be optimized using artificial intelligence (AI) to predict the most effective formulations for an individual's therapy.
- **Active and precise targeting:** Ongoing research is heavily focused on developing surface-modified "stealth" SLNs. These are designed to bypass the immune system's rapid clearance and accumulate at specific disease sites, such as tumors or inflamed tissues, through the use of targeting ligands or antibodies.
- **Responsive drug release:** The next generation of NDDS is smart and responsive. These systems release their drug payload only when triggered by specific internal or external stimuli, such as changes in pH, temperature, or enzyme activity within a diseased area.
- **Combination therapies:** Future nanocarriers will be designed to deliver multiple therapeutic agents simultaneously. This can allow for a synergistic effect that is greater than the sum of individual drug effects, leading to more potent treatments, particularly for complex diseases like cancer.
- **Gene and nucleic acid delivery:** Building on the success of lipid nanoparticle (LNP)-based mRNA vaccines, future SLNs will be adapted for gene-editing technologies like CRISPR-Cas9. This will enable the precise correction of genetic mutations for treating rare genetic disorders.
- **Treatment of infectious diseases:** SLNs are highly effective carriers for antibiotics and antitubercular drugs such as rifampicin and isoniazid. This is particularly relevant in India, where there is a significant burden of infectious diseases, including drug-resistant tuberculosis.
- **Cancer therapy:** SLNs can be engineered to target tumors, potentially reducing the severe side effects of conventional chemotherapy. Researchers in India and elsewhere are developing SLNs for breast, lung, and prostate cancer therapies.
- **Targeted brain drug delivery:** The blood-brain barrier (BBB) prevents many drugs from reaching the brain. SLNs are a promising technology to cross this barrier for treating neurological disorders like Alzheimer's and Parkinson's disease, as well as brain tumors.
- **Improved oral drug bioavailability:** For many poorly soluble drugs, SLNs can significantly enhance oral bioavailability. This improves therapeutic efficacy and patient compliance, an important factor for managing chronic diseases.
- **Cosmeceuticals and dermatology:** In India's growing cosmetics market, SLNs are used in skin-care products and sunscreens for enhanced stability and effective delivery of active ingredients.
- **Herbal and nutraceutical delivery:** Indian researchers are focusing on using SLNs to improve the delivery and bioavailability of natural compounds and plant extracts (phyto-bioactive compounds), such as curcumin.

III. CONCLUSION

Lipid nanoparticulate delivery systems can improve the efficacy of antiviral agents by overcoming physicochemical and biological barriers like low solubility, poor stability, matrix interactions, low bioavailability, untargeted release, unwanted side effects, and resistance development. There are various delivery mechanisms available for this purpose, including micelles, microemulsions, nanooliposomes, nanoemulsions, solid lipid nanoparticles, biopolymer nanoparticles,

and biopolymer nanogels. Each distribution mechanism has unique advantages and disadvantages for specific purposes. Choosing the best option and optimizing its formulation is crucial. Currently, researchers often choose a familiar delivery method and examine its potential, rather than identifying the most appropriate one. There is a dearth of comprehensive studies comparing different delivery systems for a certain application to determine the best appropriate one. Standardized testing procedures for antiviral medicines against specific viruses utilizing various delivery modalities will greatly improve this field. These strategies can be used to compare the advantages of various systems.

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