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Development of Solid Lipid Nanoparticles (SLNs) for Poorly Soluble Drugs

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ABSTRACT
In recent years, nanotechnology has significantly impacted various technological domains, especially drug delivery systems. As modern drug delivery techniques evolve, Solid Lipid Nanoparticles (SLNs) have emerged as a promising platform in the fields of biotechnology, hiomedical engineering, and nanomedicine for their potential in healthcare and diagnostics. SLNs address critical challenges in drug formulation, particularly the poor solubility and bioavailability of many newly developed drugs.Lipid-based nanoparticles have shown great promise in overcoming these limitations. Compared to other colloidal carriers, lipid nanoparticles are biocompatible. Biodegradable, and mainly composed of components generally recognized as safe (GRAS). Since their emergence in the early 1990s, SLNs have demonstrated their capability to surpass the shortcomings of traditional drug delivery systems.
Many effective pharmaceutical formulations fail in clinical practice due to low absorption, high metabolism, wide systemic distribution, and poor bioavailability especially in the case of BCS Class II and IV drugs, peptides, and proteins. Instead of developing new drugs from scratch, repurposing existing drugsusing carriers like SLNs proves to be more cost-effective and efficient.
SLNs consist of solid lipids such as triglycerides, waxes, and glyceride blends that remain solid at room and body temperature. They also contain surfactants and co-surfactants (0.5%-5%) for stabilization. The unique nanoscale size of SLNs (typically 50-200 nm) allows for reduced toxicity, sustained release, and protection against enzymatic degradation, Furthermore, their surfaces can be functionalized with ligands or polymers for targeted delivery, and both hydrophilic and lipophilic drugs can be efficiently incorporated into their matrices.Due to these attributes, SLNs offer a powerful and flexible nanocarrier system with applications in various therapeutic areas, especially for drugs with poor water solubility.

Keywords: Solid Lipid Nanoparticles (SL.Ns), Poorly Soluble Drugs. Drug Delivery Systems, Nanotechnology, Lipid-Based Nanocarriers, Bioavailability Enhancement Controlled Release, Biopharmaceutical Classification System (BCS), Cyclosporine A

I. INTRODUCTION

In recent years, nanotechnology has had a big impact on various technical areas, including drug delivery systems. Modem drug delivery technology is developing quickly. For a deeper understanding and connection with biotechnology, biomedical engineering, and nanotechnology, solid lipid nanoparticles (SLNs) have expanded their use in healthcare and diagnosis[1] Formulation scientists are dealing with challenges in improving the solubility and bioavailability of newly developed drugs. Lipid nanoparticles have proven to be a successful way to solve these solubility and bioavailability problems. Nanotechnological applications in medicine [2] compared to other colloidal carriers, lipids are biocompatible, biodegradable, and mostly consist of physiological components that are generally considered safe (GRAS). Insoluble drug delivery strategies: review of recent advances and business prospects [3] SLNs as a colloidal carrier have shown their potential by overcoming the limitations of other carriers since the carly 1990s, [4] Several effective formulations have not been. Successful in treatment, resulting in a higher rejection rate of APIs by the FDA. Factors that lead to treatment failure include low absorption and rapid metabolism, widespread drug distribution leading to insufficient drug concentration (e. g., peptides, proteins), BCS class II and IV drugs (excluding IV aqueous injectable solutions), and

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unpredictable bioavailability. [5] To improve the success rate of treatment, rather thar developing or focusing on a new molecule, it is more cost-effective to make suitabla modifications to an existing drug molecule using a colloidal carrier like SLNs. The structure of SLNs (Figure 1) is made of lipid, which may include triglycerides, glyceride blends, or waxes that are solid at both room temperature and body. Temperature. [6]SLNs also contain various surfactants and co-surfactants to improve stability within a concentration range of 0. 5% to 5%. Commonly used lipids are listedIn Table 1.

Because of the presence of solid lipid and submicron-sized nanoparticles, SLNs show lower toxicity and can achieve sustained release.[7] The reticuloendothelial system. Does not immediately take up particles, especially those between 50-200 nm, allowing them to bypass liver and spleen filtration, SLNs also offer the benefit of controlled and targeted release because the surface of solid lipid can be easily modified with appropriate ligands and polymers. [8] Adding active compounds into the solid matrix of SLNs provides stability against chemical degradation and environmental factors, (Both hydrophilic and lipophilic drugs can be easily incorporated into the matrix of solid liquid.

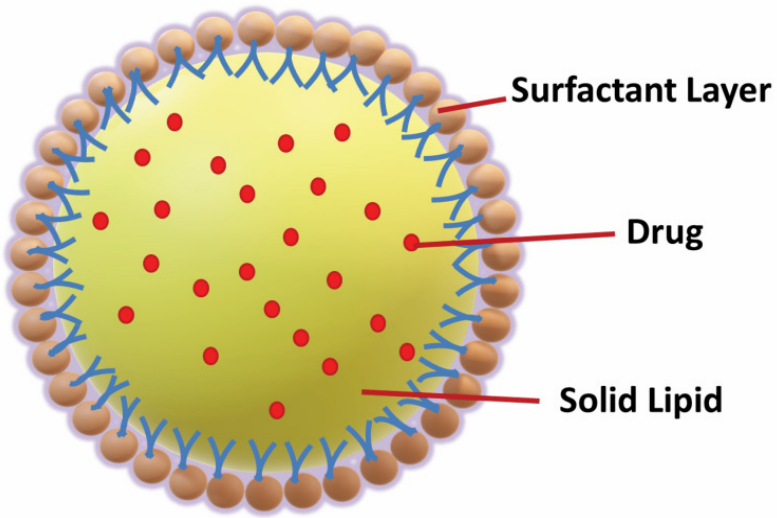

Figure No. 01 Schematic figure of solid lipid nanoparticles.

1.1

1.2 Advantages of polymeric nanoparticles:

- Increases the concentration of medicines between cells by improving permeability and the retention effect.
- Protects the drugs inside from breaking down.
- Reduces how often medicine needs to be taken.
- Allows for controlled and steady release of the drug over time.

International Journal of Pharmaceutical Research and Applications
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- Enhancing the solubility of drugs that don't mix well with water.
- By wrapping the drug and delivering it to specific areas of the body, the harmful effects on the whole body can be reduced.
- The drug becomes more effective in treating the condition.
- It's possible to combine both water-friendly and water-repellent drugs into one polymer-based structure.
- The drug spreads better in the body and stays longer in the bloodstream.
- The drug can be given through different ways like swallowing, sniffing.
- Injecting, applying on the skin, or putting into the eye.
- Nanoparticles are more stable than liposomes, which makes them better for precise targeting in the body.
- Patients are more likely to follow the treatment plan.
- For each dose, the body's response to the drug is stronger.
- The harmful side effects and unwanted reactions from the drug are less likely to happen.
- Nanoparticles made into amorphous spheres dissolve better than those that are crystalline, which helps improve the drug's ability to mix with water and its overall effectiveness in the body.

II. MATERIALS AND METHODS

2.1 Materials

Stearic acid, trilaurin, triphalmitin and sodium taurocholate were bought from Sigma-Aldrich (Dorset, UK), Lutrol F127 was kindly provided by BASF (Ludwigshafen, Germany). Cyclosporine was purchased from Spectrum Chemicals (New Brunswick, US). All other chemicals and solvents used were of analytical and high performance. Liquid chromatography grade.

2.2 SLN Preparation

In short, the samples [9] were either made of empty lipids or loaded with CyA. They were first heated to a temperature above the melting point of the lipid while CyA was dissolved in the melted lipid. This process was adapted by zurMühlen et al. 12, known as the hot homogenization process. In this method, the drug is dissolved in the lipid at a temperature 10-15°C above the melting point. The drug-containing melt was then. Dispersed in a hot surfactant solution and mixed using an Ultra Turrax T25 homogenizer (IKA-WERKE GMBH, Staufen, Gennany) to create a pre-emulsion. The resulting dispersion was then transferred and homogenized in a Micro DeBee (South Easton,USA) high pressure homogenizer at 350-750 bars and 60-75°C for 3 cycles. The hotnanodispersions were allowed to cool down, allowing the lipid to crystallize and formlipid nanoparticles with a solid matrix.

2.3 Particle Size Analysis and Zeta Potential.

The particle size distribution and zeta potential of the created preparations were measured using dynamic light scattering (PCS) with a Malvern ZetasizerNanoZS (Malvern, UK). The NanoZS can measure particle sizes in the range of 0.6 mm to 6µm

2.4 Lyophilization of CyA SLNs

The CyA SLNs formulations were filled into glass vials and placed in a Dewar flask filled with liquid nitrogen. Once the dispersion was fully frozen, it was removed and lyophilized. A Lyovac GT2 (FinnaquaSantasalo-Sohleberg GmbH, Hürth, Germany) was used to lyophilize the samples at -35°C and a pressure of 5 Pa for 48 hours.

2.5 HPLC Analysis

The amount of CyA in all samples was determined using HPLC[10]. A Beckman Gold (Fullerton, CA, USA) system with a UV detector (model No. 168) was used for HPLC analysis (Software 32 Karat 5. 0). The injection volume was 100 . Chromatography was run using a Macherey-Nagel Lichrosphere 100 RP, 5x3 mm×25 cm column and a Beckman, ultrasphere (ODS), 54.6 mm×4, 5 cm pre-column with a mobile phase. Consisting of 40% acetonitrile, 30% methanol, and 30% water at a flow rate of 1. 5 ml/min and a detection wavelength of 214 nm. The column temperature was maintained at 70°C using a Kontron oven 480 (Kontron Instruments, Rotkreutz, Switzerland). The retention time of CyA was 5, 6 minutes. A CyA calibration curve (correlation coefficient of 0. 9997) was used for analysis, covering concentrations from 5 to 100 µg/ml,

2.6 X-Ray Powder Diffraction (XRD)

Samples, including pure and loaded CyA and empty SLN formulations, were analyzed using a Bruker D8 Advance (Coventry, UK) diffmetometer to assess the solid state of CyA. The samples were exposed to Ni-filtered Cu K radiation at 40 kV and 30 mA. The samples were scanned from 10° to 35° of diffraction angle (20) at a

International Journal of Pharmaceutical Research and Applications
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scanning speed of 1s.

2.7 Differential Scanning Calorimetry (DSC)

DSC measurements for pure and loaded CyA, as well as empty SLN formulations, were performed on a Pyris-1 calorimeter (Perkin-Elmer, Massachusetts, USA) Approximately 3-5 mg of samples were accurately weighed into standard aluminum pans. An empty pan was used as reference. The samples were heated from room temperature to 200°C at a scan rate of 10°C/min. All DSC curves were normalized to a sample mass of 1 g. The DSC scans were carried out under an inert nitrogen. Atmosphere.

2.8 Atomic Force Microscopy (AFM)

For AFM experiments, the samples were diluted 100 times with water (Millipore, 18. 2 M2 cm) and then 5 µl of the SLN dispersion was dropped onto freshly cleaved mica plates (G250-2 Mica sheets 1"x1"x0. 006"; Agar Scientific Ltd, Essex, UK). The samples were air-dried under vacuum for 24 hours at 25°C. Images were obtained by scanning the mica surface in air under ambient conditions using a.TheVeecoMultiMode system with NanoScope IIID Controller scanning probeMicroscope (Digital Instruments, Santa Barbara, CA, USA: Veeco software, version 5. 31r1) was used in tapping mode. Atomic force microscopy (AFM) measurements. Were performed using soft silicon probes (FESP; nominal length 225 micrometers, width 28 micrometers, tip radius 8 nanometers, resonant frequency 75 kHz, spring constant 2.8 Nar^{1}; Vecco Instruments SAS, Dourdan, France). AFM scans were taken at a resolution of 512x512 pixels, and were repeated twice on fresh mica. (five areas per mica). Typical scanning parameters included a tapping frequency of 74 kHz, integral and proportional gains of 0. 3 and 0.5 respectively, a set point of 0.4-0. 9 volts, and a scanning speed of 0,5-1,0 Hz.

2.9 Determination of Encapsulation Efficiency (E.E.%)

The amount of cyclosporine A (CyA) in the nanoparticles was determined using high-performance liquid chromatography (HPLC) as described earlier. The method followed a similar approach to Jaiswal et al, Briefly, the free CyA content in the nanosuspension was determined by centrifuging 1 ml of nanosuspension at 20,000 rpm for 30 minutes at 25°C. Two hundred microliters of the clear supernatant was extracted with 800 microliters of acetonitrile. After centrifuging again for 20 minutes at 20,000 rpm, 100 microliters were injected into the HPLC system. The total drug concentration in the nanosuspension was measured by extracting 100 microliters of the suspension with 900 microliters of acetonitrile. Quantification of lipids was done using the Bartlett assay. The drug loading and encapsulation efficiency (E. E.%) were calculated using equations (1) and (2). The amount of CyA in the nanoparticles was determined by subtracting the free drug concentration from the total drug concentration.Drug loading (Amount of CyA in nanoparticles/Amount of nanoparticles) x 100 (1) Encapsulation efficiency (Drug loading/ Theoretical drug loading) × 100 (2)

2.10. Release of CyA

The release of CyA from the nanosized powder was studied using a USP/Ph. Eur. Paddle dissolution apparatus (Dissolution Tester, Series DT80, GmbH, Heusenstamm, Germany). All release studies were conducted under sink conditions with a total drug amount of 4 mg. The loaded SLN powder was added to 900 ml of phosphate buffer pH 7.4 (USP 25) at 37°C, and the paddle was set to 100 rpm. At predetermined sampling times (30, 60, 150, and 300 minutes), 5 ml aliquots were taken and filtered through a 0. 1-micron filter (MillexDurapore, Millipore). The removed fluid was immediately replaced with an equal volume of fresh dissolution medium. Stability of CyA in saturated solutions was assessed over 24 hours with no signs of degradation detected. By HPLC analysis.

2.11. Cytotoxicity Studies

Cytotoxicity studies were conducted to evaluate the viability of intestinal Caco-2 cells using the MTT assay, which measures mitochondrial activity. The assay is based on the ability of viable cells to convert thiazolyl blue tetrazolium bromide into blue formazan crystals within their mitochondria. Cells were seeded at a concentration of 5 10 cells/mL/well in 24-well plates and incubated with SLNs at increasing concentrations. For 24 hours. The first three wells were incubated without the formulation. Dimethyl sulfoxide (DMSO) at 0.5 mL/well served as a positive control for cell death.

After 24 hours of incubation, 100 microliters of MTT solution (concentration 5 mg/mL) was added to each well, and the cells were incubated for 2 hours at 37°C. The blue formazan salts were dissolved in 100 microliters of acidified isopropanol (0. 33 ml. HCl in 100 mL. isopropanol)

International Journal of Pharmaceutical Research and Applications
Volume 10, Issue 5 Sept - Oct 2025, pp: 518-528 www.ijprajournal.com ISSN: 2456-4494

and transferred to 96-well plates. The absorbance was measured using a microplate reader (Bio-Tec, Bad Friedrichshall, Germany) at a wavelength of 490 nm. Cell viability was calculated by comparing the number of viable cells in the formulation-treated wells to those in the non-formulation-treated wells.

III. POORLY SOLUBLE DRUGS: CHALLENGES & AMP; IMPORTANCE

Oral delivery of drugs is still the most common and easiest way to give medicineBecause it's easy to use, people are more likely to take it, and it's cheaper [11] But one big problem with this method is that many active ingredients in medicines don't dissolve well in water. Research shows that about 40 to 60% of new drugs being developed have poor water solubility. These drugs often don't get absorbed well, have low levels in the body, and their effects can change a lot from person to person. This can lead to the medicine not working properly or needing higher doses, which can cause more side effects [12]

3.1 Biopharmaceutical Classification System (BCS)

The Biopharmaceutical Classification System puts drugs into four groups based on howWell they dissolve in water and how easily they pass through the body:

Class I: Dissolves well and moves through the body easily

Class II: Doesn't dissolve well but moves through the body easily

Class III: Dissolves well but doesn't move through the body easily

Class IV: Doesn't dissolve well and doesn't move through the body easily Most drugs that don't dissolve well are in Class II or Class IV. For these, the main goal is to improve how well they dissolve and how fast they break down in the stomach so they can be better absorbed when taken by mouth [13]

3.2Challenges with Poorly Soluble Drugs

a. Slow Dissolution:

When a drug doesn't dissolve well in water, it takes longer to break down, which slows down how quickly it enters the blood, especially when taken by mouth [14]

b. Unpredictable Absorption:

The way poorly soluble drugs are absorbed can vary a lot depending on what a person eats, the acidity or alkalinity of the stomach, and how active the stomach is.[15]

c. Need for Higher Doses:

To make sure the drug works, people might need to take more of it, which can increase the risk of harmful side effects.[16]

D. Poor Targeting:

Because these drugs don't dissolve well, they might not reach the parts of the body they're supposed to act on. This makes it hard to get enough medicine where it's needed.

3.3 Need for Solubility Enhancement.

- Making poorly soluble drugs dissolve better and break down faster is very important because it helps:
- Improve how much of the drug gets into the body
- Reduce the amount needed and how often it has to be taken
- Make the medicine work better
- Make it easier to create oral forms of the drug

Different methods like making the drug smaller, changing it into a salt form, mixing it with other substances, using special molecules like cyclodextrins, making lipid-based drugs, and using nanotechnology have been tried. Among these, Solid Lipid Nanoparticles (SLNs) stand out as a promising and practical solution [17].

3.4 Importance of Lipid-Based Nanocarriers

SLNs are special because they wrap lipophilic drugs inside a solid lipid structure, which makes them appear more soluble and protects them from breaking down in the stomach. Their small size helps them dissolve more easily and get absorbed by the intestines, possibly avoiding the liver's first-pass effect[18]

IV. LIPID BASED NANOPARTICLES DRUG DELIVERY SYSTEM

Lipid-based drug delivery systems are showing great promise because lipids are well-known for helping drugs be absorbed through the mouth. They can also be made into small particles with different shapes. These systems include a wide variety of products, ranging from simple oil solutions to more complex mixtures that include

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oils, surfactants, co-surfactants, and co-solvents. When using lipids to deliver drugs orally, the drug is usually dissolved in a mixture of two or more ingredients, like triglyceride oils, partial glycerides, surfactants, or co-surfactants. For drugs that are not very soluble in water and are more soluble in fats, lipid-based delivery systems are becoming more popular. The better absorption of these lipid-based drug forms may be due to several factors, [19] The main reason is usually that these systems help avoid the slow dissolving process that causes poor absorption of fat-soluble drugs from solid forms. Ideally, the lipid-based formulation keeps the drug dissolved as it moves through the digestive system. Traditional lipid-based systems, like emulsions, aren't effective for solving the issues faced by fat-soluble drugs, such as poor solubility, low stability, and difficulties in patient compliance. The need for new delivery systems has led to the creation of novel lipid-based carriers. Among various approaches, using lipid and surfactant-based formulations has gained attention because it has proven effective in improving the oral absorption of drugs that aren't very soluble in water. There are two main types of lipid nanoparticles: solid lipid nanoparticles and nanostructured lipid carriers, which are the second generation of lipid nanoparticles. These two types differ based on their composition and structure of the lipid matrix.[20]

V. DRUG LOADING MODEL AND RELEASE PATTERN FROM SINS

According to the different ways SLNs are made, as explained by Müller et al, three kinds of SLNs are mentioned for including drugs. [21]SLNs are made up of natural lipids and have a size between 50 and 1000 nanometers. At room temperature, they are solid, which helps keep the drugs inside them from moving around too much, which is important for controlled release [22], The way drugs come out of nanoparticles, depends on the size of the particles and how the drugs are trapped inside the SLNs. The release of drugs can also be influenced by things like how the drug solution interacts with the lipid structure. The release pattem of drugs from SLNs can change based on temperature. Chen and others tested how doxorubicin, which is loaded into cholesterol-PEG coated SLNs, releases under different pH levels, They found that doxorubicin released faster at pH 4. 7 compared to pH 7. 4. The reason was that the negative charge on the lipid core, lauric acid, reacted with the positive charge on doxorubicin, reducing the electrostatic attraction and increasing release in the acidic environment of cancer cells(4), A burst release is often seen with SLNs. However, increasing the size of the particles can help reduce this burst release and lead to a longer release period ZurMühlen and others used tetracaine, etomidate, and prednisolone as examples. They found that tetracaine and etomidate SLNs released all the drug within less than a minute due to their large surface area and drug coating, while prednisolone SLNs showed prolonged release over five weeks. This difference is due to the chemical behavior of the lipid matrix, such as cholesterol and compritol, where burst release was 83. 8% and controlled release was 37. 1%. Olbrich and Muller noted that lipase enzymes need a lipid interface to work[23] To adjust the release and increase stability, it's important to use the right stabIlizers and surfactants. Surface modification with water-loving carriers like PEG can help SLNs avoid being targeted by lipase enzymes. Savla and others have said that drugs with a Log P value of high melting points are not good candidates for lipid systems, Lipid-based syst are great for very lipophilic drugs (Log P >5) that fall into BCS Class-11. Chen and others also suggested that for lipid formulations, the drug should have low water solubility (less than 10 mcg/ml), high Log P value, good solubility in oils and lipids. A relatively low melting point, and good chemical stability. However, there are not enough studies on drugs with Log P values between 2 and 5.

VI. TYPES OF SLNS

Lipid nanoparticles come in two main types: Nanostructured lipid carriers (NLC) are made up of a mix of solid and liquid materials at room temperature, while solid lipid nanoparticles (SLNs) are made of solid lipids when the temperature is between 20 and. 28 degrees Celsius (Fig. 2). SLNs have some issues, like a tendency to become gel-like, hold a lot of water, have less ability to pack drugs, experience more movement during phase changes, and show variations in their structure. These problems can lead to drug loss, make it hard to optimize their performance, and complicate the preparation process in some cases. NLCs are considered the next generation of lipid nanoparticles and are designed to fix these problems with SLNs. Depending on where the drug is placed inside the structure, SLNs can be grouped into three main types: (1) the homogeneous matrix model, where the drug is evenly spread through the lipid. Material; (2) the drug-enriched shell model, where the drug is concentrated in the outer liquid

International Journal of Pharmaceutical Research and Applications
Volume 10, Issue 5 Sept - Oct 2025, pp: 518-528 www.ijprajournal.com ISSN: 2456-4494

layer; and (3) the drug-enriched core model, where the drug is grouped together in the central liquid part [24].

The position of the drug inside the solid lipid nanoparticles (SL.Ns) affects how quickly it is released. Types 1 and 3 of SLNs are good for controlled release, while type 2 is better for a quick release. SLNs are made in a way that helps keep the drug release steady, which means people don't have to take the medication as often and it can work better [25].

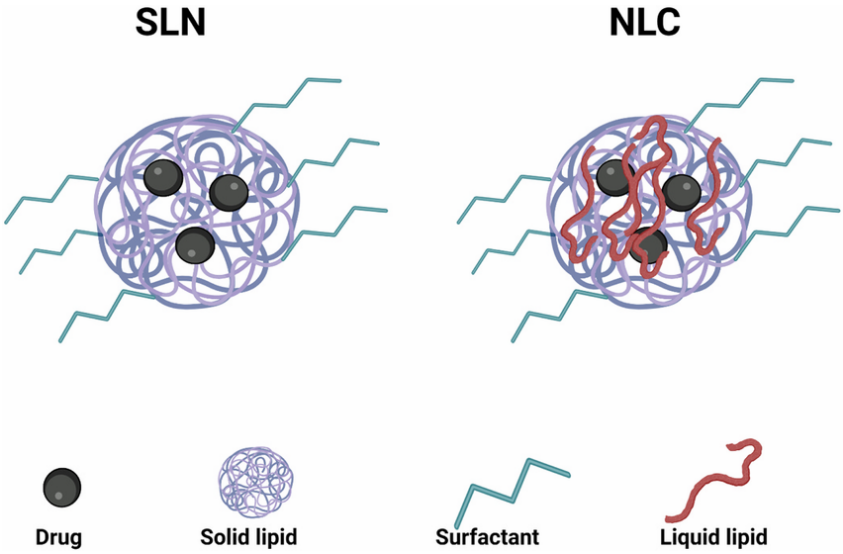


Figure No. Schematic illustration of a SLN and NLC

Several factors are important when making SL.Ns, like their size, the solid state of the lipid core, how it's crystallized, the spread of particle sizes, the charge on the surface, how well the drug is trapped inside, and how much drug is loaded. [26].When it comes to fighting bacteria, the charge on the surface of the bacteria plays a part in how well the SLNs interact with them. So, SLNs can work differently with different types of bacteria to deliver the drug effectively. Since most bacteria have a negative charge, it's thought that SLNs with a positive charge could be more effective in killing them. [27]Studies have shown that cationic SLNs, which have a positive charge, stick to bacteria more quickly and work better in killing them because of their lipid structure.The lipid core inside the SLNs is also key in getting the drug to work inside the cells. It seems that using tripalmitin as the lipid core is the most efficient for delivering the drug inside cells. [28].

However, some research suggests that attaching antibiotics to anionic SLNs, which have a negative charge, can also make the drug work better. [29] Additionally, it's been found that SLNs with a negative charge are taken up more easily by macrophage cells. [30]

VII. APPLICATION OF SLNS IN NANOTECHNOLOGY

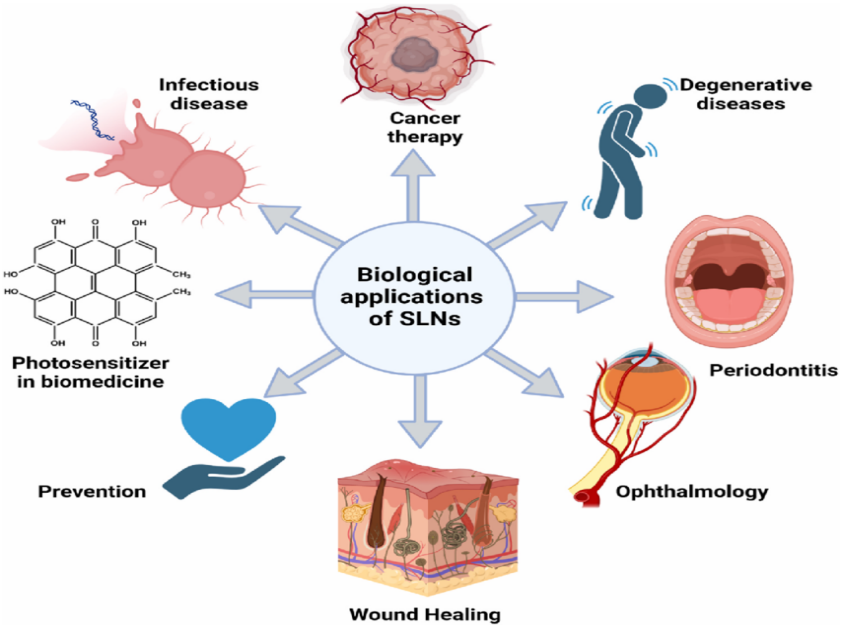
Tissue engineering, cell-based biosensors, high-power microarrays, targeted drug. Administration, and regenerative medicine are just a few of the areas where medical nanotechnology is used [31].changing the nanostructures, the functions of these technologies can vary, helping with the treatment, prevention, and diagnosis of diseases. Many medical nanotechnology methods are used to detect illnesses, give medicines, and spread hormones in cases of chronic diseases and problems with the body's systems. In living organisms, more advanced tools, such as nano-bots, act like tiny surgeons [32]. These molecules act like smart machines, as they can be altered and programmed to deal with specific illnesses and offer positive results. They may also be equipped with sensors. That help them understand their

International Journal of Pharmaceutical Research and Applications
Volume 10, Issue 5 Sept - Oct 2025, pp: 518-528 www.ijprajournal.com ISSN: 2456-4494

surroundings and make decisions. For targeted drug

7.1. The use of SLN in degenerative diseases

Curcumin has a protective effect on the nervous system in Parkinson's disease. Prabhu and his team created a microneedle that contains curcumin wrapped in SLN to improve how well the body absorbs curcumin. The SLN was made using a method called micro-emulsion, with ingredients like glyceryl monostearate and tween 80. The SLN was then put into a microneedle array through micro-molding. The microneedle patch was tested for any skin inflammation. The results showed that curcumin-SLN microneedles were safe for the body and could be used to deliver curcumin, which might help reduce the symptoms of Parkinson's disease [33].



7.2. The use of SLN in cancer treatment

A type of SLN that contains magnetic materials and the drug doxorubicin can deliver this medication to breast cancer cells. Soltani and others developed an SLN made of iron oxide coated with stearic acid and tripalmitin. Doxorubicin was added to the SLN using a technique that involved emulsification, dispersion, and ultrasound. The magnetic properties of the SLN helped control how the drug was released. Also, the doxorubicin inside the SLN was not too harmful to the tumor cells in culture. So, this magnetic SLN was effective in delivering doxorubicin to breast cancer cells [34] . The SLN was made from precirol, tween 80, and the drug molecules. The created SLN improved how well the drug passed through the mouth lining and helped fight infection for one day after treatment, which was helpful in managing periodontitis [35].

7.3. The use of SL.N in ophthalmology

In a study, a carrier made of PEGylated material that contained latanoprost was used to improve the performance of contact lenses. The PEGylated SLN containing latanoprost (LP-PSLNs) had a spherical shape, with a size of 105-132 nm and a zeta potential of 29. 1 to 26.7 mV. The LP-PSLN helped reduce the bulging, stickiness, and discomfort of the contact lens compared to non-PEGylated SLN and regular

International Journal of Pharmaceutical Research and Applications
Volume 10, Issue 5 Sept - Oct 2025, pp: 518-528 www.ijprajournal.com ISSN: 2456-4494

contact lenses [36].

7.4. The use of SI.N in wound healing.

A study used SLN that contained simvastatin, a drug that is not water-soluble, for wound healing. The SLN-simvastatin helped increase the solubility of the drug and released it slowly over three days. In this research, the SLN was combined with a hydrogel to make a suitable platform for wound healing. This platform needed certain properties like porosity, flexibility, elasticity, and the ability to manage wound exudate. The SLN-hydrogel was tested in the lab and showed no signs of toxicity or inflammation. In an animal model, the wound healed completely within eleven days,and the healing was ten times better than using iodopovidone disinfectant [37].

7.5. The use of SL.N in aging prevention

Pereira and colleagues made a SLN that contained three natural oils with antioxidanm properties extracted from sugarcane epigallocatechingallate, resveratrol, and myriectin. This SLN at a concentration of 50 µg/ml was safe to use in cosmetics. The developed SL.N had a better protective effect against oxidative stress in skin cells,which could help prevent aging [38]

7.6. The use of SL.N as a photosensitizer in biomedicin

Polymethine dyes are useful in medical diagnosis and treatment, but they are not stable or soluble in water. SLN can prevent these dyes from clumping in water and keep their original properties. SLN containing benzoindolenine rings can increase the solubility and stability of the dyes in water. This process helps the dyes be taken up by cells and work inside them more effectively. Also, SLN with the dye showed better light sensitivity than standard dyes, as tested in a lab for phototoxicity [39].

7.7. The use of SLN in infectious diseases

Shah and others improved an SLN-encapsulated form of levofloxacin to treatTuberculosis.

The SLN had a particle size less than 300 nm and a median mass acrodynamic diameter less than 5 µm. The drug was released over 12 hours in a simulated lung fluid. The best version of the SLN had a size of 79, 70 nm and a median mass aerodynamic diameter of 3. 71 µm. The SLN was made using emulsification, solvent evaporation, and lyophilization methods.

The prepared SLNs had a minimum inhibitory value of 0.7 µg/ml against the free drug, with a minimum inhibitory concentration of 1.0 µg/ml. However, the correct dosage for use in humans and the drug's behavior in the body, like how it is absorbed and works, still need to be studied [40].

International Journal of Pharmaceutical Research and Applications
Volume 10, Issue 5 Sept - Oct 2025, pp: 518-528 www.ijprajournal.com ISSN: 2456-4494

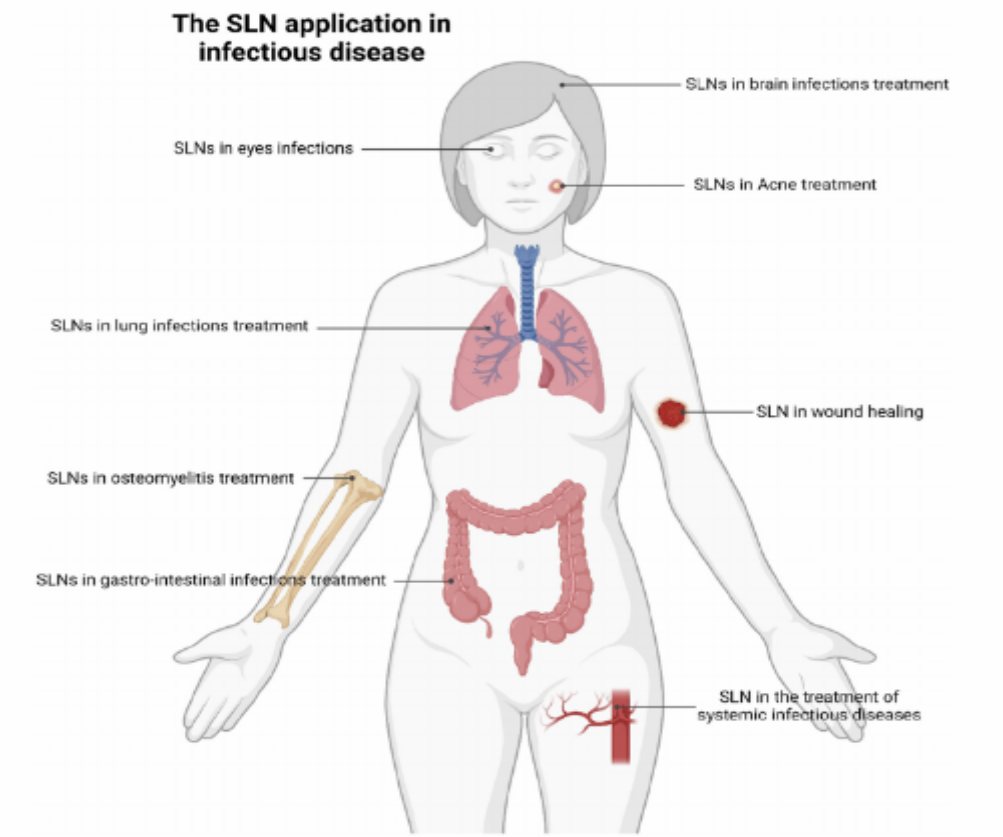


Figure 1. The solid lipid nanoparticles application in infectious disease

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