IJNRD.ORG ISSN : 2456-4184
INTERNATIONAL JOURNAL OF NOVEL RESEARCH AND DEVELOPMENT (IJNRD) | IJNRD.ORG
An International Open Access, Peer-reviewed, Refereed Journal

SOLID LIPID NANOPARTICLES: A PROMISING APPROACH TO ENHANCE THE BIOAVAILABILITY OF ANTIHYPERTENSIVE DRUGS

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Abstract: The pharmaceutical industry is interested in SLNs because they are promising drug delivery systems that can increase bioavailability. With so many emerging uses in research and medicine, SLNs are a rapidly developing area of nanotechnology. Because of their small size, lipid-based nanoparticles have special qualities that enable the development of new treatments. A new paradigm in drug delivery is made possible by the encapsulation of medications in nano-carriers, which allows for improved secondary and tertiary level targeting. This review explores the potential of SLNs in enhancing the bioavailability of antihypertensive drugs, discusses the mechanisms of bioavailability enhancement, and reviews the current formulations and clinical implications of SLN-based delivery systems for hypertension treatment.

Keywords: Antihypertensive, Drug delivery, Nanoparticles, Bioavailability

I. INTRODUCTION

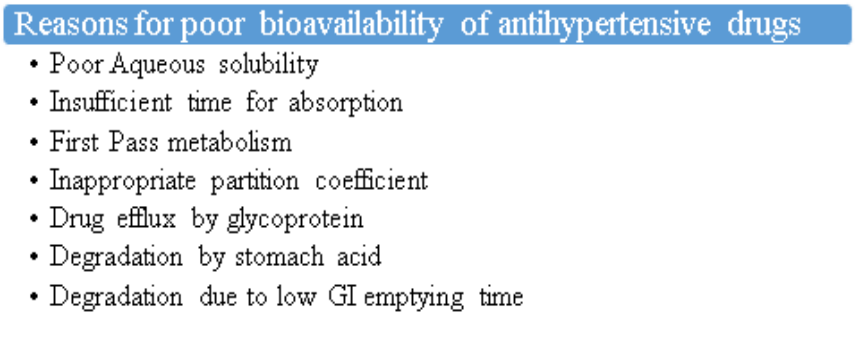
Hypertension is a chronic disorder and is also a risk factor for many other diseases like cardiovascular disease, ischemic heart disease, stroke etc., and is affected globally [1]. High blood pressure is one of the most serious and preventable risk to the health of individual as well as to the society [2]. The most convenient method of administration of antihypertensive drugs is oral delivery. Poor oral bioavailability prevents several medications from achieving the minimal effective concentration necessary for therapeutic action [3]. Many of the antihypertensives are poorly water soluble, which leads to reduction in oral bioavailability.

Efforts to address hypertension globally involve implementing preventive measures, promoting lifestyle modifications, and providing effective treatment options. Antihypertensive are crucial in controlling BP and tumbling the jeopardy of complications. Conversely, the efficacy of these drugs can be hindered by their stumpy solubility, deprived stability, and partial bioavailability[4]
Solid lipid nanoparticles (SLNs) are developed as colloidal carrier systems for delivery of water-soluble drugs and for successful correction of dynamic therapy [5]. A recent report demonstrated that SLNs form a dynamic drug delivery system that is diverse and adaptable. This system has increased potential for improving drug stability and controlling drug release from the matrix over time. Moreover, packaging drugs in SLNs aids in resisting proteolytic degradation before the drugs reach their target sites [6].

As a result, there is a necessary for modern remedy delivery systems that can augment the bioavailability of antihypertensive agents, improving their curative conclusion. Solid lipid nanoparticles (SLNs) have come

into sight as promising carriers for drug delivery, offering rewards like augmented solubility, shielding from degradation, sustained discharge, and targeted delivery.[7]

Fig. 01 reasons for poor bioavailability of antihypertensive drugs



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II) Advantages of SLNs in Enhancing Drug Bioavailability

SLNs offer multiple benefits for improving the bioavailability of antihypertensive drugs:

1. **Improved Solubility**: SLNs solubilize poorly water-soluble drugs in their lipid matrix, resulting in increased dissolution rates and improved bioavailability [8]
2. **Controlled Drug Release:** Liposomes engineered to proffer controlled drug release silhouette. By varying the lipid composition or incorporating specialized delivery systems, like pH-sensitive or temperature-sensitive liposome's discharge of drugs can be correctly regulated.[9]
3. **Reduced First-Pass Metabolism**: By facilitating direct absorption into the bloodstream, SLNs help bypass the first-pass metabolism in the liver, enhancing the systemic bioavailability of the drug [10].
4. **Biocompatibility and Safety:** Liposomes are compiled of biocompatible lipids that are well-tolerated and secure for use. They are generally non-toxic, non-immunogenic, and biodegradable, minimizing the risk of adverse effects.[11]

III) Mechanisms of Bioavailability Enhancement

The bioavailability of antihypertensive drugs can be enhanced by SLNs through several mechanisms:

1. **Solubility Improvement**: Lipophilic antihypertensive drugs tend to have low aqueous solubility, which limits their absorption. Encapsulation in SLNs increases the solubility of these drugs by dispersing them in the lipid matrix, which enhances their dissolution rate in gastrointestinal fluids [12].
2. **Increased Permeability**: SLNs improve the permeability of drugs through biological membranes, such as the intestinal mucosa, by facilitating drug diffusion across the membrane and reducing the efflux by P-glycoprotein [13].
3. **Sustained Drug Release**: The solid lipid core of SLNs provides a controlled release profile, which not only prolongs the therapeutic effect but also minimizes fluctuations in plasma drug concentrations, leading to reduced side effects and better overall drug management [14].
4. **Protection from Degradation**: SLNs can protect the encapsulated drug from environmental factors such as oxidation, hydrolysis, and photodegradation, thus improving the stability and shelf-life of sensitive drugs [15].

5. **Bypassing First-Pass Metabolism**: The nanoparticle size and lipid composition of SLNs enable drugs to be absorbed directly into the lymphatic system or through the intestinal wall, bypassing the first-pass metabolism in the liver and thus increasing bioavailability [16].

IV) Methods of Preparation for SLNS

SLNs can be prepared using assorted techniques to accomplish diverse particle sizes, drug encapsulation efficiencies, plus release profiles. Here are some commonly employed methods –

1.High-Pressure Homogenization (HPH):

High-pressure homogenization (HPH) has been used as a reliable technique for the preparation of SLN. Several manufacturers produce homogenizers of diverse sizes at a reasonable cost. The particles of the submicron range are obtained at elevated shear stress and cavitation compulsion. Nanoemulsions for parenteral nutrition are produced by HPH. HPH pushes the liquid at high pressures (100–2,000 bar) through a narrow space (range of few microns). The fluid moves faster over a short distance with high velocity. With homogenization, even the high lipid concentration could be transformed into nanodispersions. [17]

Hot and cold homogenization techniques are the means for the manufacturing of SLN. A preparatory step involves in both the cases. Lipid matrix used in this process is extracted from the physiological lipids which reduce the risk of acute and chronic toxicity.
It is a customary format for SLN preparation. Here, the lipid phase is melted and homogenized under high pressure with an aqueous phase containing a surfactant. The resulting coarse emulsion is then processed through multiple cycles of forceful homogenization to condense the particle size and acquire SLNs. [18]

2.Ultrasonication or high speed homogenization: SLN were also developed by high speed stirring or sonication[19,20]. A most advantages are that, equipments that are used here are very common in every lab. The problem of this method is broader particle size distribution ranging into micrometer range. This lead physical instability likes particle growth upon storage. Potential metal contamination due to ultrasonication is also a big problem in this method. So for making a stable formulation, studies have been performed by various research groups that high speed stirring and ultrasonication are used combined and performed at high temperature.

3.Microemulsion Templating: : It employs an impulsive arrangement of a microemulsion system comprising a lipid phase, surfactants, and co-surfactants. SLNs form by dispersing the microemulsion in a nonsolvent or altering the temperature to tempt lipid precipitation.[21]

4.Solvent Evaporation/Emulsion-Solvent Evaporation: Lipid liquefied in organic solvent. The organic phase is emulsified by an aqueous phase containing a preservative. Succeeding vanishing of the organic solvent upshot in the building of SLNs.[22]

5.Spray drying : It is another procedure to lyophilization for the modification of an aqueous dispersion into a drug. It is an economical method when compared to lyophilization. There is a chance of particle gathering due to the elevated temperature, shear forces, and incomplete melting of the particle recommended that the lipids with a boiling point higher than 70°C should be selected for spray drying. The best result was procured by spray drying with SLN concentration of 1% in a solution of trehalose in water or 20% trehalose in ethanol–water mixtures (10/90 v/v).[23,24]

V)Mechanisms of Enhanced Bioavailability

The mechanisms of enhanced bioavailability of antihypertensive drugs by SLNs are multifaceted. SLNs have been shown to increase the solubility of poorly soluble drugs, reduce their particle size, and enhance their permeability across biological membranes [25]. Additionally, SLNs have been shown to protect drugs from degradation and metabolism, leading to increased bioavailability [26].

Enhanced bioavailability

For treating cardiovascular (CV)-related diseases, SLNs have been used orally, to enhance drug plasma concentration and prolong circulation duration. These features are important for attaining better therapeutic benefits. Under refrigeration at room temperature, the optimized SLNs were stable for 3 months [27]

A 2.2-fold increase in the oral bioavailability of SLNs was given by the pharmacokinetic study as compared with nisoldipine suspension. For hypertension and heart failure remission, a prodrug of candesartan called candesartan cilexetil and an angiotensin-2 type-I receptor antagonist is employed. Using dynasan as the solid–lipid, oral bioavailability was increased more than 2.8-fold by SLNs after inclusion of candesartan cilexetil [28]

An antihypertensive drug called carvedilol has a low oral bioavailability of 20% because of the first-pass effect. SLNs were developed with N-carboxymethyl chitosan coating which improved oral delivery while protecting carvedilol in an acidic environment [29]

Conclusion

SLNs have demonstrated considerable potential in increasing the bioavailability of antihypertensive medications, but additional research is necessary to refine formulation techniques and address existing challenges. Future investigations should concentrate on improving the stability of SLNs, creating scalable production methods, and discovering innovative lipid materials that enhance encapsulation efficiency.

Moreover, integrating SLNs with other drug delivery systems, such as nanostructured lipid carriers (NLCs), could provide even greater enhancements in drug delivery effectiveness and therapeutic results.

In conclusion, SLNs have emerged as a promising approach to enhance the bioavailability and permeability make them an desirable choice for poorly soluble drugs. The potential of SLNs to improve the bioavailability of antihypertensive medications requires more investigation.

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