REVIEW ARTICLE

Solid Lipid Nanoparticles: Drug Delivery Systems for Enhancing the Bioavailability of Antihypertensives

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ABSTRACT

The pharmaceutical industry focuses the SLNs as promising drug deliverance methods for improving bioavailability. SLNs are a swiftly budding field of nanotechnology amid plentiful budding applications in medicine and research. Lipid-based nanoparticles possess unique properties due to their small size, allowing novel therapeutics to be developed. The encapsulation of drugs within nano-carriers presents a new paradigm in drug delivery, enabling enhanced targeting at secondary and tertiary levels. Consequently, SLNs have garnered significant attention from researchers for their site-specific drug delivery. This review enlightens on the responsibilities of SLN for improving the pharmacokinetics of poorly soluble antihypertensive drugs. Profound investigations confirmed SLNs have latent to transfigure antihypertensives through enhanced oral delivery.

Keywords: liposomes, Antihypertensive, Drug delivery, Nanoparticles, Nioavailability

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INTRODUCTION

Hypertension- a chronic medical circumstance characterized by elevated BP persistently above the customary range. It is a significant universal well-being alarm with a major risk factor for cardiovascular diseases. It affects millions of people worldwide and substantially impacts fatality, illness, and healthcare costs.[1]

According to the WHO, hypertension is estimated to impinge on more than 1.13 billion individuals globally, accounting for approximately 20% of deaths worldwide. This number is projected to continue due to numerous factors, including aging, sedentary lifestyles, unhealthy diets, and increasing pervasiveness of obesity.[2]

The global burden of hypertension is distributed unevenly across different regions and countries. While it is prevalent in urbanized and budding nations, stumpy and middle-income countries bear a bigger saddle due to limited access to healthcare possessions and inadequate control measures. Additionally, hypertension often remains undiagnosed or inadequately managed, foremost to stern complications and unpleasant health outcomes.[3]

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]

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.[5]

SLNs have materialized as hopeful nanotechnology-based drug delivery systems with ample applications. These lipid-based nanoparticles offer unique advantages like improved drug solubility, enhanced stability, controlled release, and prospective for targeted delivery. SLNs achieved noteworthy consideration by their adaptability, biocompatibility, and capability to encapsulate moieties, including weakly soluble compounds. SLNs are a type of colloidal carrier ranging in flanked by 10 and 1000 nm and categorized as nanoparticles (Figure 1).[6-15]

Rationale for Using Nano-Carriers

The use of nano-carriers offers several rationales and advantages for delivering therapeutic agents effectively. Here are some key rationales for using nano-carriers:

- Enhanced Drug Stability: Nano-carriers provide protection to encapsulated drugs, shielding them from degradation and enzymatic metabolism, thereby enhancing drug stability during storage and administration.[16]
- Improved Solubility and Bioavailability: Nano-carriers can augment the solubility of weakly soluble drugs, foremost to enhanced dissolution and absorption. This, in turn,

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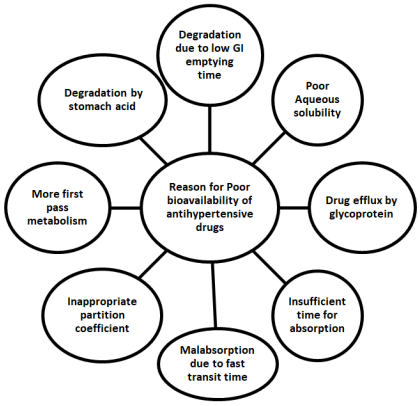

Figure 1: Reasons for poor bioavailability of oral antihypertensive drugs

boosts bioavailability and therapeutic efficacy.[17]

- Nano-carriers can be engineered to make available controlled & sustained drug release profiles, allowing for extended drug action, reduced dosing frequency, and improved patient compliance.[18]
- Targeted Drug Delivery: Nano-carriers functionalized by ligands or surface modifications to enable targeted drug delivery to specific cells, tissues, or organs. This targeted approach increases drug concentration at the desired spot, minimizing off-target consequences and enhancing therapeutic product.[19]
- Protection from Clearance and Elimination: Nano-carriers can shield drugs from rapid clearance from the reticuloendothelial system and extend circulation time, increasing drug revelation and budding effectiveness.[20]

Solid Lipid Nanoparticles (SLN)

SLNs are a colloidal carter process amid particle sizes ranging 10-1000 nm. Over time, SLNs materialized as a versatile proxy to liposomes for drug delivery rationale. The victorious utilization hinges on their capability to pierce diverse anatomical blockades, achieve controlled release of their cargo, and ensure safety at the nanoscale. However, the limited availability of approved and cost-effective polymers has hindered the widespread adoption of nanoparticles in clinical medicine.[21-23]

Advantages of SLN in the Pharmaceutical Industry

These lipid-based vesicles have gained noteworthy consideration for drug delivery because of their inimitable properties and impending profit. Here are some advantages:

- **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.[24]
- **Drug Encapsulation:** Liposomes provide a suitable environment for encapsulating various drugs, including hydrophilic and hydrophobic compounds. This versatility allows the liberation of diverse therapeutic agents, improving stability and solubility.[25]
- **Targeted Drug Delivery:** Liposomes tailored amid ligands or antibodies to pull off targeted drug liberation. These facade adjustments facilitate specific recognition and binding to target cells or tissues, enhancing drug concentration at the longing site with plummeting off-target effects.[26]
- **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.[27]
- **Protection and Stability:** Liposomes offer protection to encapsulated drugs, shielding them from degradation by enzymes or harsh environmental conditions. This protection enhances the stability of sensitive drugs, allowing for improved storage and extended shelf life.[28]

Disadvantages of Liposomes in the Pharmaceutical Industry

While liposomes offer various advantages as drug delivery systems, they also have some limitations and disadvantages that need to be considered in the pharmaceutical industry. Here are some disadvantages of liposomes:

- **Physical and Chemical Stability:** Liposomes can undergo physical changes amid aggregation, blend, and seepage of encapsulated drugs, leading to reduced stability and compromised drug efficacy over time.[29]
- **Size and Polydispersity:** Liposomes often exhibit a broad size distribution, with a range of vesicle sizes. This polydispersity can affect their biodistribution, targeting efficiency, and therapeutic outcomes.[30]
- **Limited Drug Loading Capacity:** Liposomes have limited remedy loading competence, especially for hydrophilic drugs, due to their hydrophobic lipid bilayer structure. This can result in lower drug encapsulation efficiency and require higher doses for therapeutic efficacy.[31]
- **Manufacturing Complexity and Cost:** The production of liposomes can be technically demanding and require specialized equipment, making the manufacturing process more complex and costly compared to conventional drug formulations.[32]
- **Batch-to-Batch Variability:** Liposome formulations can exhibit this in terms of size, stability, and drug encapsulation efficiency. This variability can impact the reproducibility and consistency of drug delivery, necessitating rigorous quality control measures.[33]

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 -

- **High-Pressure Homogenization (HPH):** 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.[34]

- **Ultrasonication:** It involves the application of high-frequency ultrasound waves to disperse the lipid phase in an aqueous medium having surfactant—the energy generated by ultrasound shaping of tiny lipid droplets, which congeal into SLNs upon cooling.[35]
- **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.[36]
- **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.[37]
- **Hot Homogenization:** It involves the scattering of the lipid and drug (if present) in a molten state in an aqueous surfactant. The mixture is then homogenized under high shear to ease the particle size, followed by chilling to solidify the SLNs.[38]

Sln of Antihypertensive Drugs

- Suresh, P.K., *et al.* explored the prospective of SLNs in improving the bioavailability and therapeutic outcome of antihypertensive. It tinted the reward of SLNs, like enhanced drug constancy and controlled release, in the context of antihypertensive therapy.[39]
- Mendoza-Muñoz N *et al.* focused on and discussed the various formulation strategies employed, including lipid selection, surfactant incorporation, and surface modification, to augment the oral bioavailability and therapeutic worth.[40]
- Shidhaye SS *et al.* gave a comprehensive review highlighting the potential of SLNs as effective carriers for managing hypertension. It discussed the formulation approaches and characterization techniques in advancing SLN-based antihypertensive DDS.[41]
- Khurana, R.K. *et al.* endow with an overview of the application of SLNs in delivering antihypertensive drugs. It discussed the benefits of SLNs in controlled drug release, improved drug stability, and targeted delivery, emphasizing their latent as an effectual delivery system for antihypertensive therapy.[42]
- Mishra V. *et al.* covered various aspects of SAN as an emerging drug delivery system. They discussed the formulation techniques, characterization methods, and potential applications of SLNs, including their use in delivering antihypertensive drugs.[43]
- Suvarna G. *et al.* (2015) explained the enhancement of oral bioavailability of rosuvastatin calcium (RC) with low bioavailability. SLNs were developed and characterized for zeta potential, entrapment efficiency, and drug content and size.[44] NLCs of ND were developed using sizzling homogenization-ultrasonication with oleic acid and trimyristate as liquid and solid lipids, respectively. They exhibited prolonged drug release and absorption compared to SLNs and a suspension.[45]
- The oral bioavailability of candesartan cilexetil (CC) increased by SLNs loaded with CC developed using various lipid components and surfactants. They exhibited improved physical stability and sustained release.[46-48]
- Veerabrahma *et al.*[49] developed SLN (LD-SLNs) loaded with lacidipine (LD) to enhance its oral bioavailability. He utilized a two-step method involving hot homogenization and ultrasonication to prepare LD-loaded solid lipid nanoparticles (LD-SLNs). The findings suggested that LD-SLNs can serve as an effective lipid-based carrier system for enhancing the oral bioavailability of LD.
- To enhance the oral bioavailability of the highly lipophilic antihypertensive drug nimodipine (NMD), Chalikwar *et al.*[50] developed nimodipine-loaded solid lipid nanoparticles (NMDSLNs) using factorial design. Here, the SLN delivery system was employed to enhance the oral bioavailability of olmesartan medoxomil (OM).
- Nooli *et al.*[51] observed a 2.32-fold increase in the oral bioavailability of OM in male Sprague Dawley rats compared to the plain drug solution. Veerabrahma *et al.*[52] reported a 7.21-fold improvement compared to OM coarse suspension and a 3.52-fold improvement compared to the nano-suspension formulation. Pandya *et al.*[53] examined OM-SLNs and demonstrated a 2.3-fold enhancement in oral bioavailability match up to the existing one.
- Havanoor *et al.*[54] and Thirupathi *et al.*[55] developed isradipine-loaded solid lipid nanoparticles (SLNs) and observed a noteworthy decline in signify systolic BP for 12 hours. These studies emphasize the budding of SLNs as long-circulating nano-carriers, offering improved oral bioavailability and prolonged drug residence time.

CONCLUSION

The utility of SLNs as drug delivery systems holds immense latent for enhancing the bioavailability and curative worth of antihypertensive agents. Through various formulation strategies, SLNs offer numerous recompenses like enhanced drug stability, controlled release, and targeted delivery. The comprehensive review of literature on SLNs for antihypertensive drug delivery has shed light on the following key conclusions:

- **Enhanced Bioavailability:** SLNs have confirmed the skill to pick up the bioavailability of poorly soluble antihypertensive drugs. Encapsulation of drugs within SLNs enhances their solubility, thereby facilitating their absorption and increasing systemic exposure.
- **Controlled Drug Release:** SLNs provide controlled and sustained drug release, ensuring a prolonged therapeutic effect. By modifying the lipid composition or incorporating specialized delivery systems, the release profile of antihypertensive agents can be tailored to achieve optimal therapeutic outcomes.
- **Targeted Delivery:** SLNs can be surface-amended with ligands or antibodies to facilitate targeted delivery to

specific sites. This enables increased drug concentration at the desired location, reducing off-target effects and enhancing therapeutic efficacy.

- **Improved Drug Stability:** SLNs protect encapsulated antihypertensive drugs from degradation, offering improved stability and prolonged shelf life. This is particularly important for drugs with limited stability or sensitivity to environmental factors.
- **Potential for Combination Therapy:** SLNs permit for the co-delivery of manifold antihypertensive or combinations, enabling synergistic curative effects and simplified treatment regimens. This opens avenues for personalized medicine and improved patient compliance.

FUTURE PERSPECTIVES

- **Optimization of Formulation Parameters:** Auxiliary investigation is required to optimize various formulation parameters such as lipid composition, surfactant selection, and particle dimension to enhance drug loading efficiency and improve therapeutic outcomes.
- **Advanced Characterization Techniques:** Developing advanced characterization techniques will offer deeper insights into the physicochemical properties of SLNs and their role in drug discharge and steadiness. This knowledge will aid in the design of more efficient SLN formulations.
- **Combination with Targeting Strategies:** Combining SLNs with targeting strategies, such as ligand conjugation or stimuli-responsive systems, can further enhance the site-specific delivery of antihypertensive drugs, maximizing therapeutic potential while curtailing ADR.
- ***In-vitro* and *In-vivo* Evaluation:** For safety, efficiency, and pharmacokinetic profiles of SLN-based antihypertensive drug delivery systems. This will contribute to a healthier understanding of the therapeutic prospective and conduct clinical translation.
- **Clinical Translation and Commercialization:** The successful clinical translation and commercialization of SLN-based antihypertensive drug delivery systems require rigorous evaluation of their safety, efficacy, and cost-effectiveness. Collaborations between academia, industry, and regulatory bodies are crucial to surmount related to large-scale creation and regulatory compliance.

In summary, the comprehensive review highlights the significant likelihood of solid lipid nanoparticles for enhancing antihypertensive agents' bioavailability and therapeutic effectiveness. Continued investigation and improvement efforts in this pasture grasp undertake advancement of antihypertensive therapy, ultimately benefiting patients with hypertension worldwide.

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