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Perspective

Physicochemical Characteristics of PEG-Polypeptides and Indomethacin-Encapsulated HIP Micelles

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DESCRIPTION

Micelles, nano-sized molecular aggregates, have gained significant attention in drug delivery due to their ability to enhance the solubility, stability and bioavailability of poorly soluble drugs. Among various micelle formulations, the combination of Polyethylene Glycol (PEG) with polypeptides for drug encapsulation has been particularly potential. This article focuses on the physicochemical characteristics of PEG-polypeptide micelles and explores the encapsulation of Indomethacin (IND), a Non-Steroidal Anti-Inflammatory Drug (NSAID), within Hydrophobic Interaction-Driven (HIP) micelles. This approach is increasingly utilized for controlled and targeted drug release, improving therapeutic outcomes.

Introduction to PEG-polypeptide micelles

PEG is a widely used polymer in drug delivery due to its biocompatibility, water solubility and low immunogenicity. When PEG is combined with polypeptides, the resulting copolymers form self-assembling micellar structures in aqueous solutions. The PEG block contributes to the hydrophilicity of the micelle, forming the outer shell, while the polypeptide block, which can be engineered to be hydrophobic or hydrophilic, forms the core or interacts with hydrophobic drugs. This architecture is advantageous for drug delivery because it allows for the encapsulation of hydrophobic drugs in the micellar core, increasing their solubility and stability.

Polypeptides, due to their structural diversity, offer additional tunability. By modifying the amino acid sequences or side chains, the mechanical strength, degradability and stimuli responsiveness of the micelles can be adjusted. This versatility makes PEG-polypeptide micelles ideal for tailoring drug delivery systems to specific therapeutic needs.

Physicochemical properties of PEG-polypeptide micelles

The physicochemical characteristics of PEG-polypeptide micelles are vital in determining their drug encapsulation efficiency, release kinetics and overall performance in drug delivery. Main properties include size, surface charge (zeta potential), Critical Micelle Concentration (CMC) and stability.

Size and morphology: The size of micelles typically ranges between 10 nm to 100 nm. This nano-size is critical for Enhanced Permeability and Retention (EPR) effect, enabling the micelles to preferentially accumulate in tumor tissues or sites of inflammation. PEG-polypeptide micelles often exhibit a spherical morphology, although their shape can be modified based on the length and composition of the polypeptide chains. Dynamic Light Scattering (DLS) and Transmission Electron Microscopy (TEM) are commonly used to characterize micelle size and morphology. The PEGylation of the micelles contributes to a stealth effect, preventing recognition and clearance by the Reticuloendothelial System (RES), thus increasing their circulation time in the bloodstream.

Critical Micelle Concentration (CMC): CMC is a critical parameter that defines the concentration at which micelles form in solution. PEG-polypeptide micelles have relatively low CMC values, making them stable in dilute conditions such as those encountered in physiological environments. The low CMC ensures that micelles do not dissociate easily upon dilution, thereby maintaining their drug-carrying capacity throughout circulation.

Surface charge (zeta potential): The surface charge of micelles influences their interaction with biological membranes and their stability in biological fluids. PEG-polypeptide micelles can be engineered to have neutral, positive, or negative surface charges, depending on the desired interaction with the biological environment. A neutral or slightly negative zeta potential is often preferred to reduce opsonization and subsequent clearance by immune cells, thereby enhancing circulation time.

Stability: The stability of PEG-polypeptide micelles is important for their performance as drug carriers. Stability refers to the micelles' ability to retain their structural integrity and encapsulated drug during storage and circulation. PEG provides steric stabilization, preventing micelle aggregation, while polypeptide segments can be

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designed to degrade in response to specific stimuli such as pH or enzymes, allowing for controlled drug release.

Indomethacin (IND) encapsulation in HIP micelles

Indomethacin (IND) is a widely used NSAID with potent anti-inflammatory, analgesic and antipyretic effects. However, IND's poor water solubility and potential gastrointestinal side effects limit its clinical application. Encapsulating IND within PEG-polypeptide micelles offers a potential strategy to overcome these limitations.

The encapsulation of IND into PEG-polypeptide micelles is driven by hydrophobic interactions between the drug and the hydrophobic core of the micelle. This process increases the solubility of IND and protects it from degradation in the biological environment, potentially reducing side effects and enhancing therapeutic efficacy.

Encapsulation efficiency and drug loading capacity: The Encapsulation Efficiency (EE) refers to the percentage of the drug successfully encapsulated within the micelles, while the Drug Loading Capacity (DLC) represents the amount of drug relative to the total weight of the micelles. In PEG-polypeptide micelles, these parameters can be optimized by adjusting the hydrophobicity of the polypeptide block or the drug-to-polymer ratio. High EE and DLC are desirable for minimizing the amount of carrier material required and maximizing the therapeutic dose.

Release kinetics: The release profile of IND from PEG-polypeptide micelles is typically characterized by an initial burst release followed by a sustained release phase. The burst release occurs due to the desorption of loosely bound drug from the micellar surface, while the sustained release results from the diffusion of the drug from the micelle core. The rate of release can be modulated by altering the composition of the polypeptide block, introducing stimuli-responsive elements, or adjusting the micelle's size.

Advantages of IND-encapsulated HIP micelles

Encapsulating IND in PEG-polypeptide micelles offers several advantages, including enhanced solubility, controlled release and reduced toxicity. The PEG coating increases the micelles' circulation time, while the polypeptide core can be engineered for stimuli-responsive degradation, allowing for site-specific drug release. This reduces the potential for gastrointestinal side effects commonly associated with IND and improves its bioavailability at the target site.

CONCLUSION

PEG-polypeptide micelles represent a versatile and effective platform for drug delivery, particularly for hydrophobic drugs like Indomethacin. Their favorable physicochemical properties, including size, stability, low CMC and tunable release profiles, make them ideal for enhancing the solubility, bioavailability and therapeutic efficacy of encapsulated drugs. As research in this area continues, PEG-polypeptide-based systems are likely to become increasingly prevalent in clinical applications, suggesting improved outcomes in drug delivery and disease treatment.