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Low Molecular Weight Hydro-and Organo Gelators Used for Medical Applications

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Abstract

Low molecular weight gelators (LMWGs) are molecules capable of forming gels in which they are self-assembled into a physical 3D network of fibers, held together by non-covalent interactions. In this mini-review, the difference between organo- and hydro gelators will be discussed, and their various medical applications.

Keywords: Hydro Gelators; Organo Gelators; Drug Delivery; Tissue Engineering

Abbreviations: LMW: Low Molecular Weight; PAs: Peptide Amphiphiles ; LMWGs: Low Molecular Weight Gelators

Introduction

Gels are formed in organic or aqueous solutions by molecules called gelators. Gelators can be crosslinked polymers (synthetic or biological), or low molecular weight (LMW) molecules that self-assemble into a physical 3D network of fibers, held together by non-covalent interactions like hydrogen bonds, van der Waals forces and π-π-interactions [1,2]. Steric effects, rigidity, and polarity also play an important role in their aggregating tendency [3]. LMW gelators have potential applications involving nanomaterials (such as sensors, molecular electronics, and catalysts) and delivery or modification agents for paints, inks, cleaning agents, cosmetics, drugs, etc. [3,4] . The non-covalent nature of the aggregation process allows a very rapid response to external stimuli and a more efficient tuning of macroscopic properties than in polymeric covalently-assembled hydrogels, consequently the gelating properties of LMW gelators can be easily modulated by modifying the strength of these weak interactions [5]. LMW gelators can be divided into two types according to the medium they operate in, organo gelators and hydro gelators. An organo gelators is a molecule capable of self-organizing into molecular networks (organogels) within organic media such as organic solvents or polymeric melt [6,7]. Upon cooling, the organic gelators spontaneously forms a 3D thermoreversible network of nanofibrils [8]. Hydro gelators form gels in aqueous solutions. Whereas hydrogen bonds are a common driving force in aggregation of organo gelators, hydrophobic forces play a major role in aggregation of hydro gelators in aqueous environments [9]. To achieve gelation, there must be a balance between the tendency of the molecules to dissolve or to aggregate.

Organo Gelators

Though numerous LMW organogel systems have been described, only a few of them have been investigated for biomedical applications, due to toxicity, biocompatibility and absorption issues. Their main use is for transdermal/transmucosal delivery of drugs and injectable parenteral dosage forms [3,10]. One type of LMW organo gelators is glyceryl fatty acid esters used for transdermal delivery of drugs, for example piroxicam (a nonsteroidal anti-inflammatory drug) [11] or levonorgestrel and ethinyl estradiol (contraceptive steroids) [12]. Another type is aromatic amino acids (tyrosine, tryptophan, and phenylalanine) derivatives with aliphatic chains used for the sustained release of the anti-Alzheimer drug rivastigmine [10]. Sorbitan monostearate or molaureate were shown to potentially serve as systems for the controlled release of drugs and antigens and in oral organogel formulations [13].

Hydro Gelators

LMW hydro gelators are usually composed of a hydrophilic moiety and a hydrophobic aromatic group or long hydrocarbon chain. The hydrophilic moieties provide the water compatibility of the molecules, whereas the hydrophobic part is generally providing the main driving force for the self-assembly of the molecules by hydrophobic interactions [1]. In order to obtain effective LMW

hydro gelators, fine-tuning of the balance between the hydrophilic (soluble) and hydrophobic (insoluble) parts is essential. Examples of hydro gelators used for medical applications include derivatives of sugars such as DBS-COOH or DBS-CONHNH [2] used as a drug delivery system for naproxen (a non-steroidal anti-inflammatory drug) by pH mediated drug uptake and release [14,15]. Another class of hydro gelators is peptides of various composition and length, with aliphatic chains or aromatic groups. Those peptides predominantly assume a beta-sheet structure that can further self-assemble spontaneously into fibrils and hydrogels. For example, peptide amphiphiles (PAs) consist of a bio functional peptide head group linked to a hydrophobic alkyl tail to create molecules with distinct hydrophobic and hydrophilic ends, akin to natural lipids.

The hydrophobic tails of PAs promote cellular membrane anchoring and internalization and because of their dynamic structure, individual monomers can escape and insert their tails into other hydrophobic compartments [16]. Charged (ionic) PAs can be used for tissue engineering and regeneration of neural, cardiac, skin, cartilage and bone tissue regeneration. Additional hydro gelators include urea-based, pyridine-based, hydro gelators containing multi/polyhydroxy groups, etc. [2].

Conclusion

To conclude, low molecular weight gelators are gaining more and more interest due to their properties, which are highly process dependent, and therefore it is possible to access materials with very different properties from a single gelators or to control the gelation by modifying the gelators structure [17]. These gels differ from permanently covalently cross-linked polymer gels because the cross-linking is physical and can be reversed, for example, by heating. Those characteristics are the reason for the increasing number of described applications of the LMW gelators.

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