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Guest Editorial

Macromolecules Applied to Pharmaceutical Chemistry

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Macromolecular and polymer science have evolved significantly over the past few years, with remarkable advances in many areas such as polymeric drugs, self-assembly systems, implant materials, drug delivery systems and controlled drug release. These areas have now become well established in the realm of multidisciplinary technology and science. An increasing number of applications of macromolecules have required a covalent attachment of the polymers to a wide range of substrates, including low-molecular weight drugs, affinity ligands, proteins, oligonucleotides, micro-and nanoparticles. Ten contributions from renowned scientists who have embarked on research programs in the exciting area of the application of macromolecules in pharmaceutical chemistry are included in this interdisciplinary Special Issue of *Molecules*.

The first article in this issue, by T. Coviello, A. Palleschi, M. Grassi, P. Matricardi, G. Bocchinfuso and F. Alhaique, deals with the use of scleroglucan and some derivatives in the field of pharmaceutics and in particular, for the formulation of modified-release dosage forms. A novel hydrogel obtained from this polysaccharide and borate ions is described, and a deep attention is devoted to the mechanisms involved in drug release from the tested dosage forms.

In the next article H. Eliyahu, Y. Barenholz and A.J. Domb describe recent developments in nucleic acid delivery and its many applications in basic science, biotechnology, and medicine. Non-viral gene delivery vectors, termed "self-assembled" systems, are based on cationic molecules, which form spontaneous complexes with negatively charged nucleic acids. A transition from *in vitro* to *in vivo* gene delivery is also presented, with an emphasis on the obstacles to achieving successful transfection *in vivo*.

The third paper, written by F. Delie and M.J. Blanco-Prieto, covers recent progress in the design and preparation of polymeric oral formulations. Biotechnology has produced highly potent new molecules such as peptides, proteins and nucleic acids. Due to their sensitivity to chemical and enzymatic hydrolysis as well as a poor cellular uptake, their oral bioavailability remains very low. The

most common manufacturing methods for polymeric particles and the physiology of particle absorption from the GI tract, and the use of polymeric particulate systems to improve the oral absorption of insulin are discussed.

Next, F. Aulenta, M. Drew, A. Foster, W. Hayes, S. Rannard, D. Thornthwaite and T. Youngs assess the relevance of enzymes as powerful tools in organic synthesis that are able to catalyse a wide variety of selective chemical transformations. However, the use of these natural catalysts in the synthesis and the post-synthetic modification of dendrimers and hyperbranched molecules is an application of chemistry yet to be explored extensively. Two hydrolytic enzymes, a lipase from *Candida Cylindracea* and a cutinase from *Fusarium Solani pisii,* were investigated in the selective cleavage of ester groups situated on the peripheral layer of two families of branched polyamides.

In the fifth article, R. Quesnel and P. Hildgen report on the importance of biodegradable polymers applied to drug carriers and controlled release systems. The authors propose an efficient synthetic method for a polyester-polyethylene multiblock copolymer where the polyester blocks alternate with polyethylene oxide blocks to form a repetitive sequence. The copolymers shown here offer the basic characteristics required for the microencapsulation of a drug.

Next, V. Nadeau and P. Hildgen explore the different routes towards the synthesis of novel biodegradable charged polymers to be used in DNA complexation for genetic delivery in different diseases. Also, atomic force microscopy (AFM) is described as a powerful tool for semi-quantitative and qualitative measurements of the molecular shape and distribution of non-oriented or oriented polymer films.

The seventh article, written by C. Elvira, A. Gallardo, J. San Roman, and A. Cifuentes, explores polymer-drugs conjugates used as drug delivery systems (DDS) attending to their chemical conjugation. The classification of this type of DDS is based on the conjugation sites of the reactive groups (i.e., via end groups or pendant polymer groups). Advantages and limitations of these types of DDS are discussed through representative examples of recently developed polymer-drug and polymer-protein conjugates.

J. Irache, M. Huici, M. Konecny, S. Espuelas, M. Campanero and P. Arbos offer in the next paper a comprehensive discussion about biodegradable nanoparticles with bioadhesive properties for the oral delivery of poorly available drugs. Nanoparticles administered by the oral route may interact with the gastrointestinal surface and develop adhesive bonds with different components of the mucosa. The bioadhesive potential of Gantrez nanoparticles fluorescently labeled with rhodamine B isothiocyanate is summarized.

A review on the application of biodegradable polymers to drug delivery systems by J. Park, M. Ye and K. Park follows. The majority of biodegradable polymers have been used in the form of microparticles, from which the incorporated drug is released to the environment in a controlled manner. This review discusses both the conventional and newer technologies for the micro-encapsulation of drugs using biodegradable polymers. In addition, the characteristics and degradation behavior of biodegradable polymers which are currently used in drug delivery are discussed.

Finally, H. Shibata, Snakagawa and Y. Tsutsumi present their work on the optimization of protein therapies by polymer-conjugation as an effective DDS and present their protein-drug system designed to promote disease proteomic based drug development for protein therapies and to overcome the clinical difficulties of using proteins as effective and safe drugs, due to their very low stability and pleiotropic actions *in vivo*.

I am sincerely grateful to the contributing authors for their outstanding cooperation and valuable support in putting this issue together. All are experts in their respective fields and I am honored that each of them not only agreed to participate, but also clearly devoted a great deal of time and diligence to their efforts. Special thanks are also due to all the peer reviewers for their valuable comments, criticisms, and suggestions.

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