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Editorial

New Thermosensitive Nanocomposite Hydrogels for Intravitreal Administration

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Topical, periocular and intraocular administration of drugs to the eye is often inefficient and potentially unsafe, particularly in the case of the intravitreal route. Recently, significant efforts are in progress aimed to develop new sustained release drug delivery systems (DDS) able to improve drug ocular bioavailability and duration of action, thus reducing the dosing frequency and invasiveness of the posterior segment treatments.

Indeed, posterior segment diseases are the most frequent cause of visual impairment and they are likely to become more and more important with the rapid growth of the ageing population. If left untreated, they might lead to permanent loss of vision [1].

Among the novel drug delivery systems [2] such as nanomicelles, nanoparticles, liposomes, dendrimers, implants, contact lenses, nanosuspensions, microneedles, and injectable in situ thermoresponsive hydrogels [3], the last one have recently been deeply investigated. They are liquid at room temperature and gel-like at body temperature, can be injected in a liquid form to the vitreous cavity through a small gauge needle, becoming a solid gel that releases the entrapped drug when it is exposed to the intravitreal temperature. Recognized as an efficacious drug delivery platform to the posterior segment, they are based on natural polymers such as polysaccharides (cellulose, chitosan and xyloglucan) and proteins (gelatin) as well as synthetic ones such as N-isopropylacrylamide (NIPAAm), poly(ethylene oxide)–b-poly(propyleneoxide)–b-poly(ethylene oxide) (PEO–PPO–PEO), poly(ethylene glycol) (PEG)-biodegradable polyester copolymers and 2-(dimethylamino) ethyl methacrylate (DMAEMA) [4].

Recently, sustained-release drug delivery systems, defined as thermosensitive nanocomposites hydrogels [5], have been proposed for intravitreal administration, based on nanoformulations, such as polymeric micro- and nanoparticles (Mps/MPs), nanostructured lipid carriers (NLC), micelles, liposomes suspended in thermoresponsive gels. Their entrapment in a gel matrix provides an additional diffusion barrier, when compared with free MPs/NPs, allowing the long-term drug release, especially for macromolecules, minimizing burst effect, resulting in long-term zero order kinetics. Moreover, composite nanosystems can protect macromolecules from enzymatic degradation and help in improving the biological half-life. Several drugs, such as such as antisense oligonucleotides [6], retinoids [7], loteprednol etabonate [8], triamcinolone acetonide, anti VEGF agents (ranibizumab, bevacizumab or aflibercept) [9], doxorubicin [10] have been entrapped in thermosensitive nanocomposite hydrogels, whose physicochemical characteristics and release patterns depended on their chemical structure, molecular weight, block arrangements.

A further development of thermosensitive nanosystems lies on the development of composite hydrogels containing solid lipid nanoparticles (SLN), chitosan-coated SLN, nano and microemulsions (μE). Lipid-based nanocarriers are among the most biocompatible and versatile means for ocular delivery [11], as they can improve the therapeutic efficiency, compliance and safety of ocular drugs; generally they present more physiological features as compared with polymeric ones. SLN are formed by a solid lipid matrix surrounded by a layer of surfactants in an aqueous dispersion. The drug entrapment capability of both SLN and μE dispersed in the hydrogel will endow the system with sustained release characteristics, which opens a new transom for the treatment of ocular disorders where a slow drug release is required. The innovative preparation method of SLN called "cold dilution of microemulsion" [13] is just under evaluation to develop SLN of trilaurin as lipid matrix and chitosan-coated SLN, with morphological and physico-chemical features suitable to intravitreal administration.

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