SHORT COMMENTARY

Finite Networks of Infinite Capabilities: Nanogels

M.G. Buonomenna*

Consiglio Nazionale dei Chimici, Piazza di S. Bernardo, 106, 00187 Roma, Italy

Hydrogels are three-dimensionally cross-linked polymeric networks of natural or synthetic origin swollen by the solvent (i.e. water) in which they are dissolved. The polymers exhibit high water absorbent capacities (over 90% weight of water in the composite). When the size of the hydrogel networks is in the range of nanometers, they are called nanogels. The term “nanogels” was introduced in 1999 by Vinogradov and co-workers [1, 2] to define the swollen chemically cross-linked networks of cationic and neutral polymers such as branched PEG-cl-PEI made from Polyethyleneimine (PEI) and poly(ethylene glycol) (PEG), initially designed for the delivery of antisense oligonucleotides. However, Sunamoto and co-workers [3] six years before described the phenomenon of the self-assembly of cholesterol-modified polysaccharides, which resulted in the formation of swollen hydrogels of nanoscale size. Hydrogels, in general, and nanogels, in particular, are similar to living cells and are unique systems that are distinctly different from rigid nanoparticles, flexible macromolecules, micelles, vesicles and soft components. Living cells contain multiple compartmentalized organelles surrounded by membranes that perform distinct functions to maintain cell physiology. The construction of multi-compartmental systems to perform distinct biochemical reactions in one pot, as in living cellular systems, has attracted the attention of many research groups [4-8]. Compared to Pickering emulsions and functional polymeric micelles which even though opportunely manipulated to form distinguished spatial compartments to optimize incompatible tandem reactions [9, 10] present the challenge of bio-compatibilities, nanogels exhibit reliable mechanical stability and biocompatibility making them not only promising for the construction of multi-compartmental systems, but also widely applicable in the biomedical industry as discussed by Nita et al. [11] in their recent review entitled “Polymeric Nanogels with applicability in the biomedical field”. Compared to comprehensive and specific review articles in the same field [12-16], the review by Nita et al. [11] has the relevant characteristic of focusing on recent patents literature carefully divided according to their domain of applicability: drug delivery systems, inhibition of tumor cells for the release of chemotherapeutic compounds, vaccines, tissue engineering reconstruction, contact lens and contrast agents, imaging and theranostic applications (Fig. 1). Among these biomedical applications, the area of drug delivery systems is vast with many patents compared to the other biomedical subfields because nanogels have proper characteristic to be used as platforms for drug delivery.

Fig. (1). Schematication of the biomedical application of nanogels reported in the patents literature reviewed by Nita et al. [11].

Several methods have been developed to produce structured hydrogels with multiple compartments [17-19] to load different drugs in separate compartments with a programmed, controllable sequential release. Nanogels provide the possibility to introduce chemical functionality at different positions. This issue is specifically addressed by Nita et al [11] in the paragraph on vaccines of therapeutic agents by discussing a patent on the application of a multifunctional biodegradable PEG nanogel that includes a multi-arm polyethylene glycol cross-linking unit covalently bound to at least four multiarm polyethylene glycol nanocarrier units. Many hydrogel systems utilize covalent crosslinking approaches [20], including radical processes initiated by light [21, 22], temperature [23] and pH [24]. In the patents reviewed by Nita et al. [11] the approach is that of covalent crosslinking. Even though these covalently cross-linked hydrogels form robust, though and elastic materials as reported in the patents, however, they can be limited by the irreversibility of their crosslinks. The research on this issue is very active as demonstrated by the recent paper by Appel et al [25] which reports a new paradigm for the fabrication of self-assembled hydrogels with shear-thinning (viscous flow under shear stress) and self-healing properties (rapid recovery when the applied stress is relaxed). Mouldable hydrogels with such characteristics provide attractive alternatives to

*Address correspondence to this author at the Consiglio Nazionale dei Chimici, Piazza di S. Bernardo, 106, 00187 Roma, Italy; Tel: +39 0984496702; Fax: +39 0984496655; E-mail: mg.buonomenna@chimici.it.
covalent hydrogels for many applications including local drug delivery in the body, cell carriers for tissue engineering, bone fillers or hydraulic fracturing fluids. Shear-thinning and self-healing properties as well as the high shear viscosity low for facile application through high gauge needles, enable minimally invasive implantation in vivo though direct injection or catheter-based delivery [26]. In the systems described in the section of patents on tissue engineering reconstruction reviewed by Nita et al. [11] injectable hydrogels which allow a good tissue-hydrogel interaction in vivo are discussed.

Hydrogels are the main constituent in contact lenses due to their high water content and favourable properties that render them highly compatible with human tissues [27, 28]. Hydrogel contact lenses are not only used for vision correction or cosmetic purposes, but they are also used as drug delivery devices for extended delivery of ophthalmic medications [15]. Novel hydrogels are interesting biomaterials that are used for ophthalmic applications including drug delivery or as replacement corneal membranes. Unfortunately, clinical applications of smart gels are still limited as shown by the few patents on the topic. Developing smart gels that mimic natural systems can advance and broaden their therapeutic uses [29].

The nanogels features of chemical functionality, structural integrity, macromolecular architecture, adaptivity, permeability and deformability in a unique way to include the best of the colloidal, polymeric and surfactants worlds make them interesting not only for biomedical applications, as reported by Nita et al. [11] and in other recent papers [12-16], but also for very different fields such as in sensors, catalysis and separation technology [30]. Indeed they are “finite networks of infinite capabilities” [31].

REFERENCES