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Hyaluronic acid-poloxamer thermosensitive hydrogels studied by Small-Angle Neutron Scattering (SANS) and rheology: from nanostructure to biomedical applications

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Poloxamer (P)-based hydrogels have been used as drug carrier due to its low toxicity and ability to control drug release, mainly due to their ability to self-assemble in micelles and supramolecular structures with different phase organizations in response to physiological temperature and additives such as drugs, salts and other polymers. These features favor their parenteral administration associated to hyaluronic acid (HA) for improving hydrogels mechanical properties and to develop biocompatible formulations. Hydrogels formulations with P407 (15% or 30% w/w), HA (0.5% w/w) and the local anesthetics ropivacaine (RVC) or bupivacaine (BVC) (0.5% w/w), isolated or in binary systems with P338 (P407 15% + P338 15%), were prepared in D2O and measured in V16 SANS (HZB, Berlin-Germany) at 25 °C, 37 °C and 40 °C. For rheological analysis, samples were analyzed against frequency sweep and temperature interval from 10 to 50 °C to determine viscous (G'), elastic (G") moduli and sol-gel transition temperature (Tsol-gel). SANS results revealed all P407 15% systems were organized as lamellar structures, with decreased lattice parameters according to temperature increase. P407 30% and P407 15% + P407 15% samples present cubic and hexagonal structures, indicating both phases organization coexistence. SANS data showed that BVC decreased the lattice parameter in 3 % after incorporation into P407 30%, and 6% in P407 30% + HA at three temperatures. As BVC is more hydrophobic than RVC, it is probably maintained inside micellar hydrophobic core and expelling water molecules, resulting in a stable structure even at 40 °C. For P407 30% samples, HA decreased in 3% the lattice parameter at 25 °C but presented increased particle sizes (10 nm). Possibly, HA hydrophilic chains act as scaffolds around P407 supramolecular aggregates, stabilizing their phase organization. For binary systems, no structural changes were observed, since for P407 15% + P338 15% hydrogels showed similar lattice parameter to P407 30%. Whereby P338 is more hydrophilic than P407, with a longer polyethylene oxide hydrophilic chains, is possible to form highly hydrated gel structure. These structural differences result from the material properties: the presence of drugs RVC or BVC in P407 30% did not shift the Tsol-gel (~22 to 23°C), but increased the G'/G"relationship from 31 to 47-fold, which shows enhanced structural interaction among polymeric chains. HA, on the contrary, reduced the Tsol-gel value until ~21 °C and increased G'/G"to 38-fold when incorporated to P407 30%. P407 15% + P338 15% system displayed high Tsol-gel (~28 °C) and G'/G"(x40) values. Therefore, as it is seen in our work, the addition of additives can promote mechanical and structural changes, enabling the design of the best supramolecular structure and mechanical properties for controlling drug release kinetics.

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Level of Expertise

Student

Speakers Gender

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Do you wish to take part in the poster slam

Yes

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