Functionalization of well-defined polyacrylates with TEMPO and PEG moieties for the modification of hemoglobin-based oxygen carriers for the treatment of traumatic brain injuries

Ommiya Alomainy
Georgia Southern University, USA

Hemoglobin, the active component in the red blood cell, carries and delivers oxygen throughout the body via the four heme subunits of the protein. Each heme group contains a central iron ion that readily binds with oxygen for transport. Injuries that result in significant blood loss, such as traumatic brain injuries (TBI) combined with hemorrhaging, thus impede the cardiovascular system's ability to oxygenate the injured tissues, posing serious health concerns. The development of Hemoglobin-Based Oxygen Carriers (HBOCs) though holds promise as a treatment for such injuries by exploiting the oxygen transport mechanisms of cell-free hemoglobin to restore oxygen flow throughout the body. Utilizing cell-free hemoglobin eliminates the immunogenic complications associated with blood transfusions and also allows for the hemoglobin molecules to infiltrate swollen brain tissue. However, lacking the homeostatic control mechanisms of the red blood cell, these HBOCs have been found to scavenge nitric oxide and oversupply oxygen in arterioles, inflating blood pressure and causing oxidative damage resulting in inflammation and severe vasoconstriction.

The latest generation of HBOCs, Polynitroxyl Pegylated Hemoglobin (PNPH), are attached with 2,2,6,6-tetramethylpiperidine-1-oxidyl (TEMPO), polyethylene glycol (PEG) and a cysteine-binding group (maleimide). These functional groups reduce the oxidative effects and mediate the oxygen delivery of the hemoglobin to the injured brain tissues. While treatment using PNPH has been approved by the phase-III clinical trials, the current synthesis involves a costly multistep procedure not conducive for large scale manufacturing of a potential treatment. This current research aims to develop a new synthetic strategy of functional polymers that reduces synthesis steps of PNPH. Primarily, a more efficient and practical synthetic strategy will be developed by conjugating acrylate monomers with the functional groups to attach to the hemoglobin molecule. The synthetic strategy is based on Reversible Addition-Fragmentation chain Transfer (RAFT) polymerization of an acrylate monomer containing a reactive amino functionality which can be modified to bind the desired TEMPO, PEG and hemoglobin binding moiety. The polymerization will allow the control of the molecular weight and thus the number of binding sites. Additionally, this will allow us to control the functional group density and loading when the polymer would be attached to the hemoglobin. The resulting PNPH should then be synthesized more efficiently and cost effectively for the enhanced treatment of severe TBI.

X-ray irradiation-induced changes in (PVA–PEG–Ag) polymer nanocomposite films

M M Abutalib
King Abdulaziz University, Saudi Arabia

The effects of X-ray irradiation on the structural, thermal and optical properties of polyvinyl alcohol–polyethylene glycol–silver (PVA–PEG–Ag) nanocomposites have been investigated. The samples of nanocomposites were prepared by adding Ag nanoparticles with 5 wt.% to the (PVA–PEG) blend. The films of 0.05 mm thickness were prepared by the casting method. These films were irradiated with X-ray doses ranging from 20 to 200 kGy. The resultant effect of X-ray irradiation on the structural properties of PVA–PEG–Ag has been investigated using X-ray diffraction and Fourier transform infrared spectroscopy. Also, thermal property studies were carried out using thermogravimetric analysis. Further, the transmission of the PVA–PEG–Ag samples and any color changes were studied. Fourier transform infrared spectroscopy measurements showed that the crosslinking is the dominant mechanism at the dose range 50–200 kGy. This led to a more compact structure of PVA–PEG–Ag samples, which resulted in an improvement in its thermal stability with an increase in the activation energy of thermal decomposition. Moreover, the color intensity ΔE was greatly increased with an increase in the dose, and was accompanied by a significant increase in the yellow color component.