Thermal responsive nanofibers for cancer therapy

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Background: Cancer is one of the leading causes of death worldwide. In 2018 alone, 9.6 million deaths were caused by cancer. Mainstay therapies for cancer include radio and chemotherapies. The latter can be very powerful, but without targeting there is significant off-target toxicity. A stimuli-responsive nanocarrier provides a smart system for various therapeutic applications. Generally, stimuli-responsive systems are able to enhance the release of therapeutic drugs in response to triggering signals (intrinsic or extrinsic). The internal signals include pH, temperature in human body, enzymes, and oxidative stress, whereas external stimuli constitute magnetic field, light, or heat. Meanwhile, the thermal response systems have been researched a lot in the field of electrospinning nanofibers. By using the thermal sensitive polymer, the thermo-responsive behaviour is one of the most essential properties, which can be divided in two types: upper critical solution temperature (UCST) and lower critical solution temperature (LCST). A polymer solution below the LCST is a clear, homogeneous solution while a polymer solution above the LCST appears cloudy (leading to LCST also being referred to as cloudy point). On the contrary, some polymers are soluble above the UCST, and become cloudy below the UCST. These behaviours happens because it is energetically more favourable. In this study, both types of polymers were used to compare the different performances between them in the electrospinning formulation.

Methods: For the multi-responsive systems, pH and temperature-responsive NFs are the most studied. In this study, thermal responsive system had been performed used PNIPAm and copolymer of acrylamide and acrylonitrile (AAm-AN). PNIPAm is a commercially available LCST polymer that is a thermo-responsive polymer, which is one of the most common studied polymers in reference to biomedical applications due to its LCST being very close to body temperature at around 32-34°C and it is fast on-off switching. Meanwhile, the copolymer (AAm-AN) of acrylamide and acrylonitrile, synthesized by random RAFT polymerisation, have been studied as a biocompatible UCST polymer. PNIPAm and AAm-AN were both co-dissolved with PCL as carrier polymer in HFIP to achieve the polymer solution. The formulation all used 1.3ml/h as flow rate and 9.5kv as supplied voltage. The characterisation process including DSC, TGA, XRD, NMR and FTIR had been processed to define the physicochemical properties of these fibres and pure polymers. Furthermore, drug release profile was established, using carmofur as model drug.

Results: As the results, these two thermal sensitives systems, using PNIPAm and copolymer of acrylamide and acrylonitrile with PCL as a carrier polymer, performed uniform fibre diameters and smooth surface geometry. Meanwhile, these fibres had been produced with stable thermal behaviour. According to results of the dissolution test that both LCST and UCST system have shown thermal sensitive properties that the drug release diverse by changing the temperature of the buffer (Phosphate Buffer Saline (PBS) pH 7.4). The AAm-AN/PCL fibres released carmofur faster in 42°C buffer rather than in the 25°C buffer. On the contrary, the PNIPAM/PCL fibres behaved in diverse way that it release faster in 25°C condition which both related to the expected thermal sensitive properties.

Conclusions: To sum up, both PNIPAm and AAm-AN with PCL system can be produced uniformed fibres with good physical properties. In the meantime, the fibres were shown thermal responsive under 43°C buffer which means it can be applied for thermal sensitive application in the future.