Pharmacokinetics of Intramuscularly Administered Thermoresponsive Polyacrylamides

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Abstract

Polymer solutions with lower critical solution temperature (LCST) undergo a phase separation when heated above their cloud point temperature (T_{CP}). These thermoresponsive polymers have numerous promising medicinal applications, such as *in situ* depot-forming radiotherapy (brachytherapy), controlled drug-release, immuno-radiotherapy, injectable thermogelling for tissue engineering and cell culture and magnetic resonance imaging (MRI), among others. Yet, despite extensive research on medicinal applications of thermoresponsive polymers, their fate after their administration remains largely unknown.

Thus, in our study, we synthesized and thoroughly characterized four different thermoresponsive polyacrylamides, namely poly(*N*-(2,2-difluoroethyl)acrylamide), poly(*N*-isopropylacrylamide), poly(*N*,*N*-diethylacrylamide) and poly(*N*-acryloylpyrrolidine) under physiologically relevant conditions. Subsequently, we determined their biodistribution kinetics in mice and proposed a data-based pharmacological model to describe their *in vivo* behaviour, correlating their physico-chemical properties with their pharmacokinetics. Overall, our findings may be used to tailor their properties to meet the demands of their medicinal applications.

Key words: polyacrylamides, thermoresponsive, pharmacokinetics, *in vivo*, polymers, biodistribution, fluorescence