# RAFT MEDIATED POLY(N-VINYLPYRROLIDONE) AS A POLYMERIC MODIFIER IN SELF-ASSEMBLING DRUG DELIVERY SYSTEMS USING THIAZOLIDINE CHEMISTRY

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## ABSTRACT

The feasibility of using polymer-protein conjugates in the biomedical field and more specifically as drug delivery systems (DDS) is being investigated. Such systems may be achieved via drug delivery vehicles where amphiphilic conjugates have the ability to self assemble into three-dimensional structures in aqueous media, where the hydrophobic core can be loaded with a drug. Alternatively this can be accomplished by covalently linking bioactive proteins to water-soluble synthetic polymers. The therapeutic effectiveness is enhanced by reducing tissue distribution as well as by increasing the plasma half-life, when compared to the native protein. Poly(*N*-vinylpyrrolidone) (PVP) is a non-toxic, water-soluble polymer, which has been identified as a possible polymeric modifier for bioactive proteins as it has shown an increase in their mean residence time (MRT) after *in vivo* injection as well as a minimum extent of tissue distribution compared to other hydrophilic polymers[1]. Thus, the design of PVP-based polymer-protein conjugates was explored. We first established the conjugation chemistry between PVP and a model hydrophobic polypeptide (poly (γ -benzyl-L-glutamate)) which is a mimic of our target anti-tumour protein based drugs. Aldehyde end-functionalised PVP polymer of various molecular weights were derived from xanthate mediated reversible addition-fragmentation chain transfer (RAFT) polymerization of *N*-vinylpyrrolidone (VP) and successfully conjugated with the cysteine terminated poly (γ -benzyl-L-glutamate)[2] ($M_n$ = 11,000 g/mol, PDI < *1.2*) to form amphiphilic copolymers with a thiazolidine linkage (figure 1). The amphiphilic conjugate formed micelles in water which were observed by cryo-TEM and also characterised by dynamic light scattering. Such nanostructures are promising candidates for therapeutic applications. They can be used as drug delivery vehicles for hydrophobic drugs, or they have the ability to transport conjugated hydrophobic protein-based drugs in their cores within the human body environment.

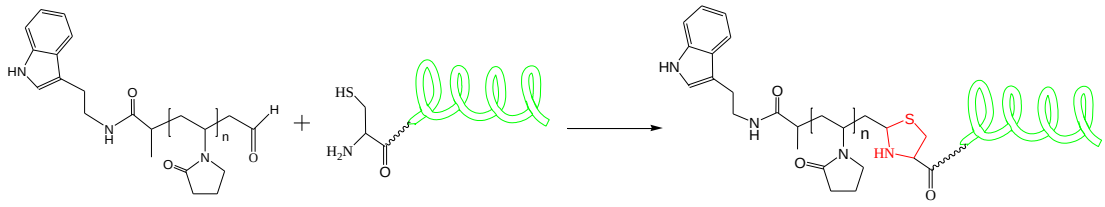


**Figure 1** **Aldehyde end-functional PVP conjugated with the polypeptide, PBG via a thiazolidine linkage.**

References:

1 Kaneda, Y.; Tsutsumi, Y.; Yoshioka, Y.; Kamada, H.; Yamamoto, Y.; Kodaira, H.; Tsunoda, S.-i.; Okamoto, T.; Mukai, Y.; Shibata, H.; Nakagawa, S.; Mayumi, T. *Biomaterials* **2004**, *25*, 3259-3266.

2 Habraken, G. J. M.; Koning, C. E.; Heuts, J. P. A.; Heise, A. *Chemical Communications* **2009**, 3612-3614.