Synthesis of ω-functional telechelic PVP conjugates of Tyrocidine for cancer drug delivery.

This study describes the synthesis of self-assembled cancer drug delivery constructs of ω-functional Poly(*N*-Vinylpyrrolidone) (PVP) functionalised by therapeutic payload in the form of membrane disruptive peptides termed tyrocidines. Three polymer systems of telechelic ω-functional PVP were synthesised via reversible addition fragmentation chain transfer (RAFT) mediated polymerisation of *N*-Vinylpyrrolidone (NVP) ($M_{n,\,SEC}$ = 2004, $\boldsymbol{Đ}$ = 1.17), ($M_{n,\,SEC}$ = 3939, $\boldsymbol{Đ}$ = 1.18), and ($M_{n,\,SEC}$ = 5502, $\boldsymbol{Đ}$ = 1.17). Post polymerisation, the labile ω-xanthate chain end was converted into thiol and disulphide functionalities through aminolysis. Tyrocidine (Trc) was obtained from tyrothricin, which was cultured from *Bacillus aneurinolyticus*. The resultant complex mixture of non-ribosomally produced cyclic decapeptides (tyrothricin) was purified to obtain a preparation of mainly Trc. Tyrocidine was modified on the position 7 of the cyclic structure to yield the acrylate derivative of tyrocidine. PVP and acrylate modified Trc were successfully conjugated via thiol-ene Michael addition and subsequently self-assembled into micelles whose sizes were determined by dynamic light scattering (DLS) and transmission electron microscopy (TEM). The constructs' ability to release Trc at endosomal pH 5.5 was determined by UPLC-MS and haemolysis assays performed. Finally the activity studies were performed on LNCap human prostate cancer cell lines.