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# Melphalan Loaded *In situ* Thermoreversible Injectable Hydrogel of Tri Block Copolymer System

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In the present study, we have investigated the role of thermoreversible injectable hydrogel for the successful administration of a PEGylated anticancer drug. To achieve the objective, a modified PEGylated melphalan (MLPEG) synthesized from a linear methoxy poly (ethylene glycol) (M-PEG) 2000 and 5000, Da with improved solubility was loaded to the thermosensitive Poloxamer 407 (P407) gel to produce an injectable hydrogel (MPX). As far as the safety issues are concern, conjugates at a concentration of 32 µg/ml after 1 h, showed low hemolysis (48.8 ± 1.5%) compared to high hemolysis (81.3 ± 0.5) for MLPEG 5000 and MLPEG 2000, respectively. Therefore, a significant decrease in hemolytic activity was found in case of MLPEG 5000 conjugate compared to MLPEG 2000. The tightening of the PEO chains due to the presence of NaCl salt reduced the initial burst release of the drug from the hydrogel and only 43 % of drug released during 2 hours from MPX-CG hydrogel. Moreover, a lower diffusion coefficient (D) for MPX-CG gel as compared to MPX-7.4 gel ($4.8 \times 10^{-6}$ *vs* $19.7 \times 10^{-6}$ $cm^2$ $min^{-1}$, respectively) showed prolonged release of melphalan from the MPX-CG hydrogel. Administration of the prepared hydrogel via subcutaneous and intramuscular routes, confirms the depot formation, good syringeability and biocompatibility.

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