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Pegylation and *in vitro* characterization of naloxone

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Background and Aims: Naloxone is a non-specific, competitive opioid receptor antagonist with short plasma half-life (1hr) used for the treatment of opioid-overdose-induced respiratory depression and detoxification of opioid-dependent patients. We aim to produce and evaluate a prolonged release form of naloxone by pegylation technique.
Methods: mPEG2000 and 5000 became acidic in the site of hydroxyl groups on polymer structure and Hydroxyl conversion to carboxylic group was confirmed by FTIR. The carboxylic group was activated by N-Hydroxysuccinimide (NHS), Dicyclohexylcarbodiimide (DCC) and Triethylamine (TEA) and bound to naloxone with different molar ratios. The pegylated drug conjugates (PEG-NLX) were purified by chromatography and desalted by ultrafiltration technique and then freeze-dried. At last the conjugates were characterized by FTIR and 1H NMR and stability was determined in different pH values.
Results: The appearance of a wide and short peak instead of a relatively sharp and strong peak in around 3400 cm-1 confirmed the conversion of hydroxyl to carboxyl group in mPEG polymers. The HPLC results showed that pegylation reaction efficiency was identical at different pegylation ratios (Average 60%) . Appearance of strong peaks at about 1100 cm-1 (C-O etheric related to PEG) and around 1700cm-1 (esteric carbonyl) in FTIR spectrum of PEG-NLX and strong peak at 3.6ppm in 1H NMR (ethylene protons of mPEG) confirmed successful drug-polymer conjugation. The Results of stability study showed that the conjugates had enough stability at acidic pH values and could sustainedly release the drug at pH 7.4.
Conclusions: Opioeid antagonist naloxone was pegylated and the conjugate characterization was performed successfully. The pegylated drug had enough solubility and stability in pH 7.4 and could release drug in a sustained manner in order to develope an injectable sustained release dosage form of drug.

Keywords: Naloxone; Pegylation; Invitro characterization; Sustained release