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Preparation of smart in situ gel forming polymeric nanomicelles for prolonged release of naltrexone hydrochloride

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Background and Aims: smart and stimuli-responsive systems have demonstrated to be a promising new class of drug delivery systems and they have received considerable attention due to their unique benefits. The preparation and characterization of thermo-responsive PLGA-PEG-PLGA tri-block copolymers were investigated in this study as naltrexone hydrochloride delivery system. The drug is used to maintain abstinence after withdrawal in detoxified opioid-dependent patients. Since the major problem with naltrexone usage is the motivation and poor compliance of addicted patients, developing a controlled-release parenteral formulation which releases the drug for long time after just one injection is desirable.
Methods: Ring-opening polymerization using microwave irradiation was utilized as a novel technique. The phase transition temperature and the critical micelle concentration (CMC) of the copolymer solutions were determined using differential scanning calorimeter and spectrophotometer, respectively. The size of the micelles was measured by a light scattering method. An *in vitro* drug release study was performed using naltrexone hydrochloride.
Results: Microwave-assisted polymerization provides the reaction condition with higher temperature and pressure that reduces time of reaction from h and days to minmin and even seconds. The copolymer structure and concentration played crucial roles in controlling the sol-gel transition temperature, the CMC and the size of the nanomicelles in the copolymer solutions. Drug release profile depended on concentration of the copolymers and their structures in the formulations. The cumulative amount of release versus time followed the Higuchi modeling for naltrexone hydrochloride over a period of 17 days.
Conclusions: PLGA-PEG1500-PLGA with a lactide-to-glycolide ratio of 5:1 is an appropriate vehicle for the long-acting, controlled release of naltrexone hydrochloride

Keywords: PLGA-PEG-PLGA; Naltrexone; Thermo-responsive