Diclofenac nanomicelles: Synthesis and anti-inflammatory activity

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Abstract:

Diclofenac is the most well-known globally non-steroidal anti-inflammatory drug (NSAIDs), Diclofenac produces analgesic, antipyretic, and anti-inflammatory effects and is widely used for the treatment of moderate pain and inflammation, its absorption may be influenced by gastric emptying rate and mechanical agitation in the stomach, and it has low solubility and low dissolution profile, so in this study we try to develop a novel drug delivery system of diclofenac derivative which have amphiphilic structure that is capable to self assemble to form nanomicelles which will be more water soluble with high efficiency of loading capacity that will work as a sustained release system. By using different polymers (triethylene glycol TEG, polyethylene glycol PEG 400, PEG 600) presenting the hydrophilic chain, linking the chain with the hydrophobic drug (Diclofenac). We successfully synthesize the diclofenac derivatives and their characterization using Nuclear Magnatic Resonance (NMR), then formation of the nanomicelles of the amphiphilic derivative and their characterization by atomic force microscopy (AFM)obtaining a spherical shape of the micelles with average diameters of 200nm for Dic-PEG400-Dic, 80-140nm for Dic-PEG600-Dic. The critical micelle concentration (cmc) has been calculated using Pyrene method obtaining cmc 2.7 x 10^{-5}mg/ml for Dic-PEG400-DicAnd 1 x 10^{-4}mg/ml forDic-PEG600-Dic. We also study the in vitro diclofenac release profile by esterase enzyme PLE,Quantitative analysis showed that conversion of free

Diclofenac was completed within 35 hrs. After 24 hrs, ≈95% was released from Dic-PEG400-Dic derivative micelles. More than 85% of Dic-PEG600-Dic derivative was converted within 30 hours. Then we determined the anti-inflammatory activity by testing TNF-α production in LPS-stimulated Balb/c mice.diclofenac derivative dose-dependently and significantly suppressed TNF production after a 5mg/kg dose were given. After 1.5 hr, 3hr, 6hr, 24 and 48 hr the derivative reduce the TNF level in a proportion of 51.3± 28.1, 46.2± 2.2, 44.8 ± 10.8, 38.6 ± 27.7 and 66.7 ± 34.2 respectively, while diclofenac reduced the TNF level after 1.5 hr, 3hr, 6hr, 24, and 48 hr in a proportion of 37.7 ± .6, 36 ± 1.6, 38.8 ± 20.3, 46.8 ± 13.5 and 49.7± 10 .9 respectively.Dic-PEG400-Dic micelles have stronger anti-inflammatoryeffect and lasted for a longer period than diclofenac only.we conclude thatthe diclofenac derivative (micelles) will have more water solubility with high efficiency of loading capacity than that of the diclofenac alone, that will work as a sustained release system.