Pharmacokinetics and Analgesic Effect of Ketorolac Floating Delivery System

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Abstract:

Objectives: The efficacy of ketorolac tromethamine (KT) floating alginate beads as a drug delivery system for better control of KT release was investigated. The formulation with the highest drug loading, entrapment efficiency, swelling, buoyancy, and in vitro release would be selected for further in vivo analgesic effect in the mice and pharmacokinetics study in rats compared to the tablet dosage form. Methods: KT floating alginate beads were prepared by extrusion congealing technique. KT in plasma samples was analyzed using a UPLC MS/MS assay. Results: The percentage yield, drug loading and encapsulation efficiency were increased proportionally with the hydroxypropylmethyl cellulose (HPMC) polymer amount in the KT floating beads. A reverse relationship was observed between HPMC amount in the beads and the KT in vitro release rate. F3-floating beads were selected, due to its better in vitro results (continued floating for >8 h) than others. A longer analgesic effect was observed for F3 in fed mice as compared to the tablets. After F3 administration to rats, the Cmax (2.2±0.3 µg/ml) was achieved at ~2 h and the decline in KT concentration was slower. F3 showed a significant increase in the AUC (1.89 fold) in rats as compared to the tablets. Conclusion: KT was successfully formulated as floating beads with prolonged in vitro release extended to a better in vivo characteristic with higher bioavailability in rats. KT in floating beads shows a superior analgesic effect over tablets, especially in fed mice.

Keywords:

Floating alginate beads; GRDFS; UPLC MS/MS; hydroxypropylmethyl cellulose; ketorolac tromethamine; pharmacokinetics

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