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Effect of Temperature and pH on the Drug Release Rate from a Polymer Conjugate System

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Abstract

Hydroximide and A^-methylhydroxamic acid of poly(ethylene-altmaleic anhydride) (average MW 100-500k) were used as a carrier for a new drug delivery system. The synthesis of the hydroximide and *N*methylhydroxamic acid of poly(ethylene-alt-maleic anhydride) were carried out by chemical modification of poly(ethylene-alt-maleic anhydride) with hydroxylamine and *N*-methyl hydroxylamine, respectively, in *N,N'*-dimethylformamide at room temperature to yield water soluble copolymer. Ketoprofen was reacted with hydroximide and *N*-methylhydroxamic acid derivatives of poly(ethylene-alt-maleic anhydride) using dicyclohexylcarbodiimide as condensating agent at -5°C to yield waterinsoluble ketoprofen conjugates. All products were characterized by elemental analysis, FTIR and 1HNMR spectra. The *in-vitro* ketoprofen release was carried out by UV spectrophotometer at λ,max =260 nm. The results demonstrated the effectiveness of hydroximide and *N*-methylhydroxamic acid of polyCethylene-alt-maleic anhydride) as a drug delivery system. The release rates were studied at various pH's and temperatures. The copolymer-drug adducts released the drug very slowly at the low pH found in the stomach thus protecting the drug from the action of high concentrations of digestive acids. These results showed the usefulness of hydroxamic acid polymer-drug conjugates as a new drug delivery system for drugs to be targeted to sites in the GI system.