

Synthesis, Characterization and evaluation of Carbamazepine and Valproic acid polymeric Adducts as controlled release prodrugs.

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Abstract:

The present study represents the conjugation of carbamazepine and valproic acid with polymers to prepare polymeric prodrugs as controlled release drug systems. This approach may lead to minimizing their side effects and /or adjusting their physical chemical properties.

Most of the current research work in this field of study is concerned with the physical methods for preparation of the controlled release drugs. A limited number of chemical methods have considered the use of prodrugs as controlled release systems.

The present study involves the chemical attachment of carbamazepine and valproic acid with several polymers:

Poly(vinyl alcohol)(PVA), Chitosan, poly(ethylene glycol) (PEG), dimethylurea and poly(methylolacryl amide) has been used. The chemical attachment of drugs to polymers was performed by either esterification methods and / or using MDI as spacer arm between the drug and the polymeric chain. The chemical bonding involved the formation of urea and / or

urethane interlinkage groups between the polymeric chains and the drug molecules.

In all the methods, the drug is attached to a preformed polymer backbone via biodegradable chemical bonds like ester, amide, urea, and urethane.

All the prepared polymers and polymer carrying drugs were characterized by Infra Red spectroscopy, chemical methods that include determination of functional group and by differential scanning calorimetry.

The IR and DSC studies confirm the bonding of the drugs to the related polymers via comparison with the IR spectra and DSC thermograms of the starting materials and the products.

The polymer-drug conjugates were prepared using equimolar quantities of the polymer with either drug.

The stability studies of the polymer-drug conjugates were carried out using different pH values (3, 5 and 8). The rate of hydrolysis was determined using spectrophotometric technique adopting standard drugs.

The obtained results showed that the polymer-drug conjugates undergo hydrolysis, releasing the bond drugs. The chemical modification of these drugs has resulted in a remarkable effect on the solubility of the drugs and their physical chemical properties. However, the development of such systems requires further extensive evaluation such as in vivo studies.