The Synthesis of New Phenytoin Derivative and the Study of Its Inhibition Activity to Cyclooxygenase-2 (COX-2)

Abstract

Inflammation is the complex biological response to a protective attempt to remove the injurious stimuli, most strongly implicated are prostaglandins (PGs), leukotrienes (LTs), histamine, bradykinin, platelet activity factor (PAF) and interleukins. The Phenytoin is a drug used for the treatment of antiepileptic. Phenytoin acts to suppress the abnormal brain activity seen in seizure by reducing electrical conductance among brain cells by stabilizing the inactive state of voltage gated sodium channels, Phenytoin (5,5-diphenylimidazolidine-2,4-dione) were prepared from benzil and urea with sodium hydroxide in absolute ethanol. The derivative of phenytoin was prepared from a histidine acidifies with hydrochloric acid in absolute ethanol and phenytoin to give phenytoin-3-histdine IUPAC name is (S)-3-(2-amino-3-(1H-imidazol-4-yl) propanoyl)-5,5-diphenylimidazolidine-2,4-dione. The identifications were performed by measuring the melting point, the Fourier transform infra red (FT-IR) spectra and elemental analysis (CHN). The Carrageenan induced inflammation model was used to determine the anti-inflammatory activity. The Inflammations were induced by sub-plantar injection of homogenous suspension of (1%) carrageenan in water. The Phenytoin derivative (with histidine) has significant ($p<0.001$) anti-inflammatory activity. The presence of imidazole ring in the compound (as in phenytoin and histidine) increased the activity. So it resembles some of the non-steroidal anti-inflammatory drugs in its structure. It was predicted that the phenytoin derivative will act as an anti-inflammatory agent, through the inhibition of biosynthesis of prostaglandins and inhibitor for cyclooxygenase-2 enzyme (COX-2).