Synthesis and Study of Some Amino Acid Derivatives as New Non-Steroidal Anti-Inflammatory / Analgesic Drugs

A Thesis Submitted
By

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Abstract

The thesis contained four chapters, chapter one show the nature of inflammation and relationship with metabolism of unsaturated fatty acid, and the factors effect on it. Types of non steroidal anti-inflammatory and analgesic drugs were illustrated, chemical classification and side effects. The chapter explained biochemical activity of amino acid derivatives, amino acid reactions which used to prepare the compounds.

Chapter two: thirty amino acids derivatives were prepared in different methods. First histidine derivatives like ethyl ester and acetyl or propanoyl group was added on α-amino group. Second tryptophan derivatives as methylene group were added as schiff base or adding benzoyl group as amid. Third lysine and valine derivatives as methylene or benzal group were added as schiff bases or benzoyl group was added as amid. Forth tyrosine derivatives as aldehyde group were added to the benzene ring of tyrosine then p-nitroaniline as schiff base. Fifth N-methylated amino acids derivatives methyl group was added to α-amino group of unusual amino acids as furfuryl alanine; N,N-dimethyl-p-amino phenylalanine and N-acetyl-p-amino phenylalanine. Sixth imidazole derivatives by the reactions of the following amino acids: histidine, aspargine, tyrosine, tryptophan and glycine with triethylorthoformate and amino acid glycine to give derivative of amino acid which contains imidazole ring in alpha position.

Chapter three explained the identification of the prepared compounds by CHNS analysis, FT-IR, H NMR, and GCMS. The results certified the chemical structures of the prepared compounds.

Chapter four explained the result and discussion of anti-inflammatory and anti-nociceptive activity which studied by two different tests the hot plate test and writhing test for analgesic activity, and two tests for anti-inflammatory activity they are formalin induced inflammation test and carrageenan induced inflammation test. Aspirin and diclofenac sodium (voltarine) were used as stander drugs in all tests.

The histidine derivatives were found out, has potent activity as anti-inflammatory and anti-nociceptive, lysine and valine derivatives have moderate activity, tyrosine derivatives have weak activity. The N-methylated amino acids have potent anti-inflammatory and potent anti-nociceptive too. Imidazole amino acids derivatives have good activity too. The active compounds were tested to acute toxicity and fond that they are safety to the dose 5 g/kg orally in mice without any mortality. Knowledge the LD_{50} of aspirin and diclofenac sodium were 1.1 and 0.390 g/kg orally in mice respectively.