Investigation of Aminomethyl Indole Derivatives as Hyaluronidase Inhibitors

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Hyaluronidase inhibitors are of potential therapeutic value for the treatment of a variety of diseases, such as cancer, arthrosis, or bacterial infections. Potent and selective hyaluronidase inhibitors are not known so far, and current approaches to the development of hyaluronidase inhibitors are limited. Elevated levels of hyaluronan (HA) are connected with most malignant tumours. Therefore, the search for drugs modulating the hyaluronidase activity became very important. In the present study, a new series of aminomethyl indole derivatives (AMIDs) were tested for inhibition of bovine testes hyaluronidase (BTH). *In vitro* assays were performed using stains-all at pH 7 and Morgan-Elson reaction at pH 3.5. Among the AMIDs, 3-[(4-methylpiperazin-1-yl)methyl]-5-phenyl-1*H*-indole (**9**) was found to be active with 23% inhibition at 50 μM and pH 7. All the other inhibitors showed less activity at pH 3.5 and pH 7. These activity results demonstrated that compounds with phenyl substitution at position 5 have higher activity. The results confirmed that more lipophilic compounds have better inhibition against the hyaluronidase enzyme.

Key words: Indole Derivatives, Inhibitors of Hyaluronidases, Cancer