

CURRENT RESEARCH AND DEVELOPMENT IN BIOTECHNOLOGY ENGINEERING AT IIUM

VOLUME II

Editors:

Ibrahim Ali Noorbatcha
Hamzah Mohd. Salleh
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Raha Ahmad Raus



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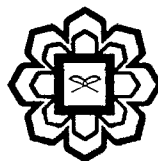
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STRUCTURE ACTIVITY RELATIONS IN PENTACYCLIC TRITERPENOIDS TOWARDS HYALURONIDASE INHIBITORY ACTIVITY

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ABSTRACT

Ursolic acid (UA) **1**, a pentacyclic triterpenoids was isolated in our previous study from *Primatomeris malayana* Ridley. It showed hyaluronidase inhibitory activity at 79.67% compared to apigenin (88.97%) at 100 ug/ml. In an effort to improve the inhibitory activity, seven UA derivatives were design and synthesized with substitution at positions of C-3 and C-28 of UA to give compounds **2-8**. Their structures were confirmed from the spectroscopic data such as NMR 1D and 2D, IR and LCMS/MS. The compounds **1-8** were evaluated for their inhibitory activity on hyaluronidase. Compound **1-4, 7** showed a marked anti-inflammatory effect, with a 50% inhibitory dose (IC₅₀ or ID₅₀) of 103-190 μM. However, the modification of the hydroxyl functional group at one or both positions (C-3, C-28) into other functional groups as in compounds **2-8**, make their inhibitory activity decrease compared to UA. The rank order is : compound **1 > 4 > 2 > 7 > 3 > 6 > 8 > 5**. Our finding could suggest that the free hydroxyl and carboxylic acid group appears to be implicated in the inhibition of hyaluronidase activity.

Keywords: ursolic acid, pentacyclic triterpenoids, hyaluronidase, structure-activity-relationship

INTRODUCTION

Structure activity relationship study (SAR)

In search for a new drug, the number of strategies can be followed. Some research methodologies may be based on random synthesis of new compounds, utilizing combinatorial chemistry techniques, followed by a biological test to select active substances. Similarly, various natural materials such as plants, tissues or body fluids can be screened for biologically active substances. However, a systematic optimization of a lead structure is needed in order to be developed it into a better drug.