UNIVERSITI TEKNOLOGI MARA

SYNTHESIS AND BIOLOGICAL ACTIVITIES OF DIARYLPENTANOIDS AND THEIR PYRAZOLINE ANALOGUES

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Candidate's Declaration

I declare that the work in this thesis was carried out in accordance with the regulations of Universiti Teknologi MARA. It is original and is the result of my own work, unless otherwise indicated or acknowledged as referenced work. This topic has not been submitted to any other academic institution or non-acedemic institution for any other degree or qualification.

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Abstract

Diarylpentanoid is structurally similar to curcumin **3**, a constituent of the rhizome of *Curcuma longa* L. (turmeric) which is known to possess various pharmaceutical properties. Interestingly diarylpentanoids have been reported to be more active than curcumin. They are also precursors towards the synthesis of nitrogen-containing five-membered heterocyclic compounds called pyrazoline which are reported to possess important pharmacological activities. In this study, 13 diarylpentanoids were successfully synthesized by the reaction between various substituted benzaldehyde with cyclic ketone in the presence of base (NaOH) in EtOH via microwave-assisted (73-92% in 10-60 s) and conventional methods (17-90% in 30-120 min) through Claisen-Schmidt reaction (cross aldol condensation). Microwave-assisted method has been found to be a very efficient method which dramatically reduces reaction time and significantly improved yields as compared to conventional method. Diarylpentanoids **43** and **49** were selected as representatives of precursor bearing electron-withdrawing and electron-donating group, respectively in the synthesis of their pyrazoline analogues. Compound **64** and **65** were obtained in 87-99% using microwave-assisted method. In all reactions, it was found that compounds bearing halogen substituents undergo reaction at a faster rate than those bearing methoxy substituents. Compounds **43**, **49**, **64** and **65** were evaluated for their antiinflammatory potential with Griess assay and their immunomodulatory potential by employing the T cell proliferation and chemiluminescence assays. In the Griess assay, only compound **65** was found to increase the inhibition of nitric oxide (NO) production of macrophages (RAW 264.7 cell lines) from 5.80-28.97% (with respect to compound **49**) while compound **43** was found to induce the NO production. Pyrazoline analogues **64** and **65** were found to increase the suppression of T cell proliferation as compared to the precursors **43** and **49** from 50.40-96.30% and 18.10-98.30%, respectively. Compounds **64** and **65** also increase the inhibition of reactive oxygen species (ROS) production in human blood from 8.70-28.10 % and 9.50-31.50 %, respectively.

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