Malaysian Journal of Analytical Sciences (MJAS)
Published by Malaysian Analytical Sciences Society

MICROWAVE-ASSISTED AND CONVENTIONAL SYNTHESIS OF HALOGENATED COUMARIN-AZO DERIVATIVES AND STRUCTURAL-ACTIVITY RELATIONSHIP STUDY FOR ANTIMICROBIAL POTENTIAL

(Sintesis Berbantukan Gelombang Mikro dan Konvensional Derivatif Coumarin-Azo Berhalogen dan Kajian Hubungan Struktur-Aktiviti untuk Potensi Antimikrob)

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Received: 21 September 2022; Accepted: 18 December 2022; Published: 19 April 2023

Abstract

Untreatable bacterial infectious diseases have become a leading cause of mortality due to the emergence of drug-resistant bacteria. The search for a new effective pharmaceutical drug can be time-consuming and expensive. Therefore, structural chemical modification of natural product-based compounds with known biological properties for potential drug candidates has gained a great interest among researchers. Microwave-assisted synthesis is quickly becoming the method of choice in modern organic synthesis for drug discovery due to benefits such as higher yield and shorter reaction time. In this study, a series of coumarin derivatives have been synthesized by incorporating halogenated azo moieties in the molecular network *via* diazo-coupling, Knoevenagel condensation, and hydrolysis reactions. Microwave-assisted organic synthesis reaction has produced overall higher yields of products (74-94 %) in 6-17 mins compared to the conventional reflux method (56-85 %) in 6-18 h. The structural activity relationship of all compounds was initially evaluated *via in silico* (molecular docking) for potential antimicrobial properties against *Escherichia coli* and *Staphylococcus aureus*. The synthesized compound gave a higher binding affinity (-6.3 to -8.9 kcal/mol) compared to ampicillin (-6.7 to -7.3 kcal/mol) and coumarin (-6.0 to -6.2 kcal/mol). *In vitro* evaluation (agar well diffusion), nevertheless, gave weak to no bacterial inhibition activity. This study is significant in searching for potential drug precursors to benefit mankind.

Keywords: diazo, docking, *In silico*, Knoevenagel, microwave

Abstrak

Penyakit berjangkit bakteria yang tidak dirawat disebabkan oleh kemunculan bakteria kerintangan ubat telah menjadi punca utama kematian. Proses pencarian ubat farmaseutikal baharu yang efektif boleh mengambil masa yang lama dan memerlukan kos yang tinggi. Oleh itu, pengubahsuaian struktur kimia sebatian yang berasaskan produk semula jadi dengan sifat biologi yang diketahui sebagai calon ubat yang berpotensi telah menarik minat dikalangan para penyelidik. Kaedah sintesis berbantukan gelombang mikro dengan cepatnya telah menjadi kaedah pilihan dalam sintesis organik moden untuk pencarian ubat berpotensi kerana kelebihannya seperti mampu menghasilkan produk yang lebih tinggi dan mengurangkan masa tindak balas. Dalam kajian ini, siri derivatif kumarin telah disintesis dengan menggabungkan moieti azo halogen dalam rangkaian molekul melalui tindak balas gandingan