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Original Article

Biological evaluation and spectral characterization of 4-hydroxy coumarin analogues

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الملخص

هدف البحث: إن زيادة مقاومة المضادات الحيوية أصبحت في الآونة الأخيرة مشكلة صحية عالمية. صممت هذه الدراسة لتطوير جزيئات فعالة جديدة بأقل تكلفة وأدنى حد من التسمم. درس البحث طريقة تصنيع جديدة بخطوة واحدة لمادة ٣- اريليزو النشطة حيويا واستبدالها بمشتقات الكومارين ومن ثم تقييم عملها الحيوي.

طرق البحث: تم استخدام فئران ويستار من الجنسين أوزانها ١٨٠-٢٠٠ جم، ومن العمر المناسب لتقييم شق الجرح، واستئصال الجرح، والتسمم الحاد. كما تم التفسير الهيكلي للمركبات المصنعة بالفحص الكالوريمتري التفاضلي، والرنين المغناطيسي النووي، والتحليل فوق البنفسجي المرئي، وتحليل العناصر. وتم فحص المركبات المصنعة للتحقق في المختبر من نشاطها كمضادات للميكروبات، ومضادات للأكسدة والتئام الجروح.

النتائج: تم تصنيع سلسلة من المركبات من اقتران خمسة مركبات مختلفة من أملاح أريل ديازونيم بإذابتها في تركيز ١٠٪ من هيدروكسيد الصوديوم. وأظهرت غالبية المركبات خصائص ذات أهمية كمضادات للميكروبات، ومساعدة في التئام الجروح، وكمضادات للأكسدة.

الاستنتاجات: أثبتت الدراسة أن نظائر الأريل ومتغير الأريل للمركب ٤- هيدروكسيد الكومارين معا يمتلكان خصائص ذات أهمية كمضادات للميكروبات، ومساعد في التئام الجروح وكمضادات للأكسدة.

الكلمات المفتاحية: مضادات الميكروبات؛ مضادات الأكسدة؛ التئام الجروح؛ هيدروكسيد كومارين

Abstract

Objective: The development of antibiotic resistance has recently been recognized as a global health problem. This study was designed to develop new potent molecules that are economic and minimally toxic. The research examined a novel one-step synthetic procedure of bioactive 3-arylazo-substituted coumarin derivatives (**4i**–**4v**) and further evaluated their biological actions.

Methods: Male and female Wistar rats of appropriate age weighing 180–200 g were used to assess the wound incision, wound excision, acute toxicity and 1,1-diphenyl-2-picrylhydrazyl (DPPH) models. The synthesized compounds were structurally interpreted with Differential Screening Calorimetry (DSC), FT/IR, 1H Nuclear Magnetic Resonance (NMR), LC-MS, UV-Visible and elemental analysis. The synthesized compounds were screened to investigate their *in vitro* antimicrobial, antioxidant and wound healing activities.

Results: A series of 4-hydroxy-3-(arylazo) coumarin (**4i**–**4v**) analogues were synthesized by coupling five different aryl diazonium salts with 4-HC in the presence of a 10% NaOH solution. The majority of the compounds showed significant antimicrobial, wound healing and antioxidant properties. The most potent compounds identified in the analysis were **4i**v and **4e**.

Conclusion: This study justifies that both aryl and hetero arylazo analogues of 4-hydroxy coumarin possess significant antimicrobial, wound healing and antioxidant properties.

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Keywords: Antimicrobial; Antioxidant; Wound healing; 4-Hydroxy coumarin

Introduction

C-3 aryl-substituted 4-HC is essential for broad biological actions, such as anti-viral,[1] anti-bacterial,[2] anticancer,[3] anticoagulant[1] and antioxidant[4] activities. Heteroarylazo-substituted compounds have been widely used due to their excellent thermal,[5] optical[6] and biological properties includes antibacterial,[7] antiviral[8] and antioxidant[9] activities. The insertion of an aryl/heteroarylazo moiety at the C-3 position of coumarin has been reported to elicit good antimicrobial activity.[10] The 4-hydroxy 3-heteroaryl coumarin moiety is found in many natural and synthetic products and also exerts significant biological actions.[11] In our earlier work, we have reported the synthesis and characterization of several novel bioactive hetero aryl-conjugated 4-HC analogues and investigated their antimicrobial activity against four different bacterial pathogens.[12] Subsequently, we evaluated the antimicrobial, wound healing and antioxidant activities of earlier reported molecules as well as those of recently developed new aryl-conjugated 4-HC analogues against a wide range of bacterial and fungal strains and confirmed their structural characterization.

Materials and Methods

The chemicals used in this study were of synthetic grade and were obtained from Merck specialties Ltd. (Mumbai, India). The synthesized products were structurally confirmed with FT/IR (JASCO FT/IR 4100 Spectrophotometer using KBr disc), ^{1}H NMR (Bruker H^{1}NMR 400 MHZ) using TMS as an internal standard, LC-MS (Shimadzu-Mass spectrometer). differential scanning calorimetry (METTLER TOLEDO STAR^e system at a heating rate of 10 °C min^{-1}, temperature range 30–350 °C using aluminium cans calibrated with indium) and UV spectrophotometry (JASCO V-630 Spectrophotometer). An elemental analysis was carried out with a Perkin Elmer-2400 CHNO/S analyser system. The melting points were determined with the open capillary method (Elico) and are uncorrected.

4-hydroxy-3-(aryl substituted -2-yldiazenyl)-2H-chromen-2-one (**4i–4v**) was synthesized as described previously[12] (Figure 1).

*4-((4-hydroxy-2-oxo-2H-chromen-3-yl) diazenyl) benzenesulfonic acid, (**4i**)*

IR (K Br) cm^{-1}: 3446 (O–H str), 2996 (Ar–H), 1695 (C=O str. lactone carbonyl), 1612 (C=C str. of coumarin), 1510 (–N=N-), 1300, 1134 (SO_2 str.), 1197 (C-Ostr.), 831 (1, 4 disubst. Ar); ^{1}H NMR (DMSO-d_6) δ: 7.81 (d, coumarin H-5,

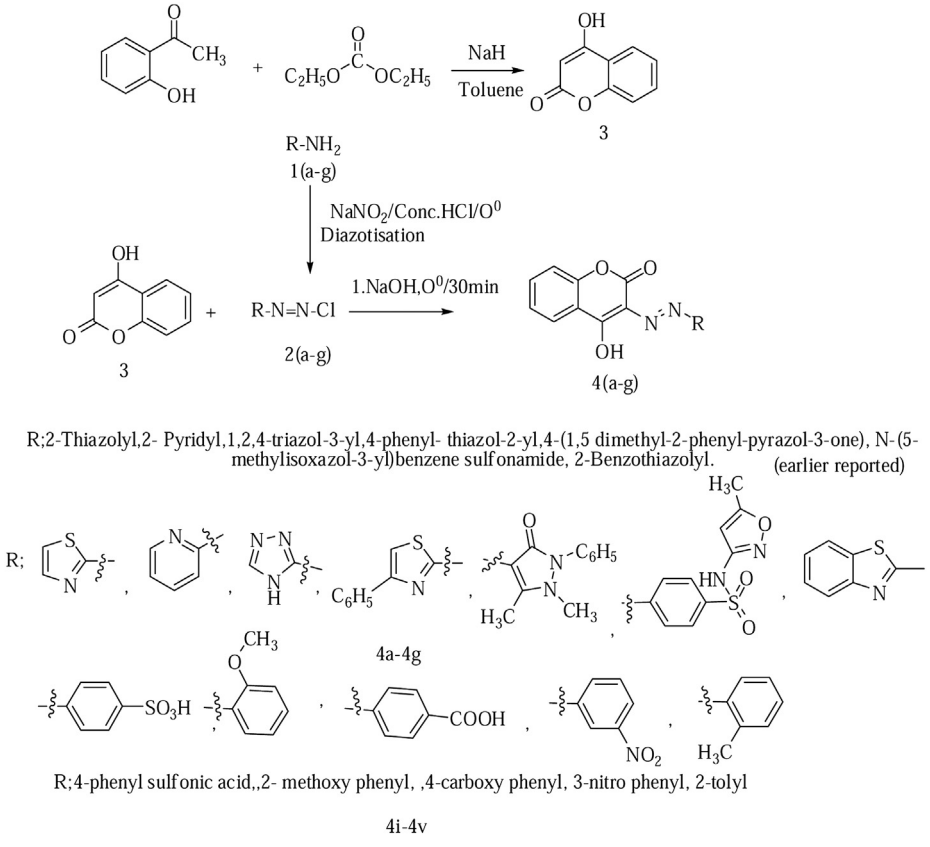

Figure 1: Synthesis of azo derived 4-Hydroxy Coumarin analogues.