Synthesis and Biological Evaluation of a Novel Quinone Derivative as a Potential Therapeutic Agent

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Abstract:

Quinone derivatives have demonstrated promising biological activities and therapeutic potential in various disease conditions. This research article presents the synthesis, characterization, and biological evaluation of a novel quinone derivative, aiming to explore its potential as a therapeutic agent. The synthetic route involves a series of chemical transformations starting from readily available precursors, resulting in the formation of the target compound. The synthesized quinone derivative was characterized using spectroscopic techniques, such as nuclear magnetic resonance (NMR) spectroscopy. Furthermore, the compound's biological activity was evaluated using a range of in vitro including antimicrobial activity and it was in range of 18-28 mm, and evaluation of its antioxidant potential which is found to be Log IC_{50} i.e., 1.054. The results indicate that the novel quinone derivative exhibits significant biological activity, highlighting its potential as a lead compound for further optimization and development as a therapeutic agent.

Keyword:

Quinone, Anticancer, Antimicrobial, NMR spectroscopy, Diels-Alder reaction,

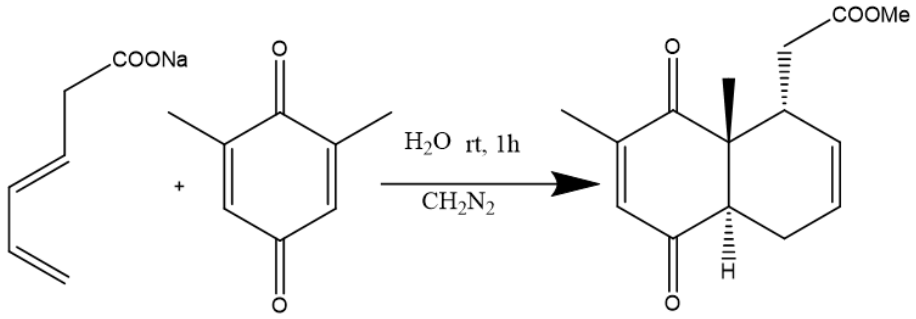
Introduction:

Quinone derivatives are a diverse class of organic compounds known for their biological activities, including anticancer, antimicrobial, and antioxidant properties [1,2]. These compounds possess a characteristic quinone core structure, which contributes to their reactivity and biological effects. The modification of the quinone scaffold has been extensively studied to enhance the potency and selectivity of these compounds as therapeutic agents [3]. In this study, we report the synthesis and evaluation of a novel quinone derivative designed to explore its biological potential and pave the way for the development of new therapeutic strategies [4,5]. Quinones are a class of organic compounds that contain a cyclic dione structure. These compounds have attracted significant research interest due to their diverse chemical properties and potential applications in various fields, including materials science, medicine, and energy storage. In recent years, there have been several exciting developments and research advancements in the field of novel quinones. These advancements have expanded our understanding of the fundamental chemistry and unique characteristics of quinones, paving the way for their practical utilization in various domains. One area of research focuses on the synthesis and characterization of novel quinone derivatives with enhanced properties [6]. Researchers have explored different strategies to modify the quinone structure, introducing various functional groups or altering the substitution patterns to fine-tune their chemical reactivity and physical properties. These modifications can lead to improved stability, solubility, redox activity, and other desirable features, making quinones more versatile for different applications.

Methods:

The Diels-Alder reaction involving a dienecarboxylate and a quinone dienophile was carried out using water as the solvent. The reaction proceeded with a yield of 75% within 1 hour, resulting

in the formation of the product shown in the scheme. Initially, a cis adduct was formed, but it equilibrated to the more stable trans form. Water, known for its environmental friendliness and abundance in nature, has gained significant attention among organic chemists as a solvent for organic reactions. Early studies by Breslow demonstrated the use of water as a solvent, highlighting its ability to enhance the rate of Diels-Alder reactions. This has sparked a growing interest in utilizing water as a solvent for various organic reactions, particularly in cases where the reactants are insoluble in water."



methyl 2-((1*R*,4a*R*,8a*R*)-7,8a-dimethyl-5,8-dioxo-1,4,4a,5,8,8a-hexahydronaphthalen-1-yl)acetate

Characterization through NMR:

The synthesized quinone derivative was characterized using various spectroscopic techniques to confirm its structure and purity. NMR spectroscopy provided valuable information about the compound's connectivity and functional groups. Nuclear Magnetic Resonance (NMR) spectroscopy is a powerful analytical technique used to determine the structure, composition, and dynamics of molecules. It is based on the principle that atomic nuclei with an odd number of protons or neutrons possess a property called spin, which creates a magnetic moment. When these nuclei are placed in a magnetic field and exposed to radiofrequency radiation, they can absorb energy and undergo a transition between different energy states. The sample under investigation is typically dissolved in a suitable solvent and placed in an NMR tube, which is

then inserted into the NMR spectrometer. The solvent taken was DMSO and the concentration and amount of sample was 0.5mg per ml.

Antimicrobial activity

The antimicrobial study in a laboratory setting involved the use of the microbroth dilution method to test the effectiveness of the compounds against specific organisms. The method used was previously described. To begin the experiment, bacterial cultures were introduced into Mueller Hinton Broth medium from Biocorp, Warsaw, Poland, and incubated at 37°C with vigorous shaking at 200 rpm for 24 hours [7]. Bacterial cell suspensions with an initial inoculum of 5×105 in Mueller-Hinton liquid medium were then exposed to varying concentrations (ranging from 0.001 to 2 mg/mL) of the compounds being examined for a duration of 24 hours at 37°C. Simultaneously, standard antibiotics including caspofungin, amphotericin B, chloramphenicol, and streptomycin (used as a positive control) were tested against the bacterial pathogens. The minimum inhibitory concentration (MIC) was determined as the lowest concentration of the compound that prevented visible growth of the microorganism. Each experiment was repeated three times for accuracy and consistency

Antioxidant activity

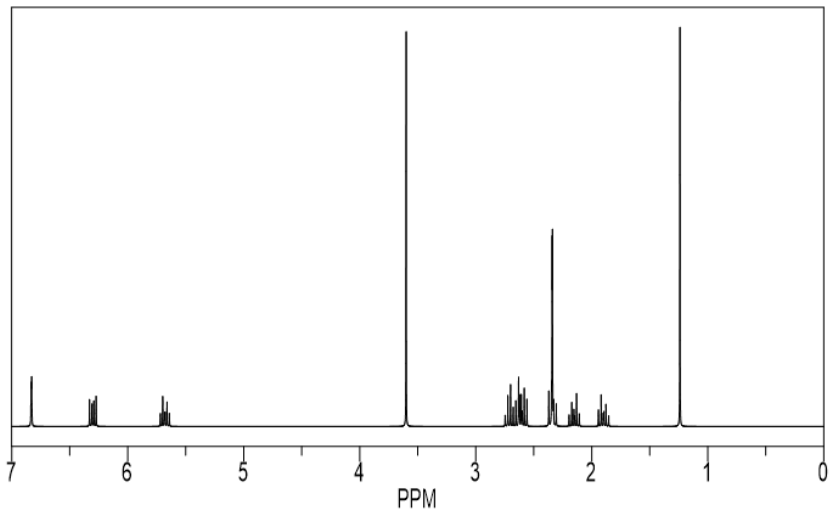
The DPPH assay was performed following the procedure To summarize the method, 90 µL of DPPH solution was combined with 180 µL of test solutions at various concentrations (0.5, 1.0, 1.5, 2.0, 2.5 mg/mL) and the standard solution. The reaction mixture was thoroughly mixed and incubated at 25°C for 15 minutes. Subsequently, the absorbance of the mixture was measured at 510 nm using a Plate reader [8]. A control reaction was also conducted without the test sample. To determine the percentage of inhibition, the absorbance values obtained from the test samples

were compared to the control reaction. The formula for calculating the percentage of inhibition is as follows:

% inhibition = [(Absorbance control - Absorbance sample) / Absorbance control] x 100

The IC50 values, which represent the concentration required to scavenge 50% of the DPPH radicals, were determined by performing a nonlinear regression analysis using a sigmoidal dose-response curve fitting method

Results and Discussion:



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Protocol of the H-1 NMR Prediction (Lib=SU Solvent=DMSO 300 MHz):

Node     Shift    Base + Inc.   Comment (ppm rel. to TMS)

CH  5.90              5.59      cyclohexene
                         0.31      general corrections
CH  5.65              5.59      cyclohexene
                         0.06      general corrections
CH  2.71              1.96      cyclohexene
                         0.22      1 beta -C=O from methine
                        -0.10      1 beta -C from methine
                         0.63      1 beta -C(=O)OR from methine
CH2 2.15,1.905000        1.96      cyclohexene
                         0.07      1 beta -C(=O)C=C from methylene
CH3 3.60              0.86      methyl
                         2.81      1 alpha -OC(=O)
                        -0.07      general corrections
CH2 2.59,2.335000        1.37      methylene
                         0.92      1 alpha -C(=O)O-C
                         0.00      1 beta -C=C
                        -0.06      1 beta -C
                         0.23      general corrections
CH3 2.34              0.86      methyl
                         1.07      1 alpha -C(C(=O)R)=C
                         0.41      general corrections
CH3 1.24              0.86      methyl
                         0.25      1 beta -C(=O)C=C
                         0.10      2 beta -CC
                         0.03      general corrections
H   2.63              1.65      cyclohexene
                         0.86      1 alpha -C=O from methine
                         0.22      1 beta -C=O from methine
                        -0.10      1 beta -C from methine
H   6.83              5.25      1-ethylene
                         0.74      1 -C(=O)-R trans
                        -0.22      1 -C cis
                         1.06      1 -C(=O)-R gem


1H NMR Coupling Constant Prediction

shift   atom index  coupling partner, constant and vector

5.90        9
                     8  10.9  H-C=C-H
                    10   6.2  H-C(sp2)-C-H
5.65        8
                     9  10.9  H-C=C-H
                     7   6.2  H-C(sp2)-CH-H
2.71       10
                     9   7.0  H-C-C-H
                    15   7.0  H-C-CH-H
2.03        7 diastereotopic -12.4  H-C-H
                     8   7.0  H-CH-C-H
                    14   7.0  H-CH-C-H
3.60       20
2.46       15 diastereotopic -12.4  H-C-H
                    10   7.0  H-CH-C-H
2.34       13
                    21  -1.0  H-CH2>C=C<H
1.24       16
2.63       14
                     7   7.0  H-C-CH-H
6.83       21
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Antimicrobial activity

The prepared derivative showed moderate to high microbial activity in all tested microorganisms with zone diameters of 8-30 mm compared to the zone diameters (18-26 mm) of the control antibiotic disk [Chloramphenicol (C30)] for the tested microorganisms The results obtained from the biological evaluation demonstrated that the novel quinone derivative exhibits significant biological activity. The compound also exhibited antimicrobial activity against a broad spectrum

of bacterial highlighting its potential for combating infectious diseases. Moreover, its antioxidant activity suggested a possible role in reducing oxidative stress-related conditions. The results of each assay were discussed in detail, emphasizing the structure-activity relationship and potential mechanisms of action.

Microbes	**Zone diameter(mm)**	**Positive control**	**Negative control**
S. aureus	25	27	-
S. epidermidis	28	26	-
E. faecalis	13	19	-
B. cereus	17	26	-
P. vulgaris	19	18	-
C. albicans	19	27	-

Antioxidant activity:

DPPH assay of synthesized compound-

Parameter	**Values**
Log IC_{50}	**1.054**
IC_{50}	**13.65**

Conclusion:

In conclusion, this research article presents the synthesis, characterization, and biological evaluation of a novel quinone derivative. The compound demonstrated promising biological activity like antimicrobial, and antioxidant effects. These findings highlight the compound's potential as a lead molecule for further optimization and development as a therapeutic agent.

Future studies should focus on elucidating the compound's mechanism of action, conducting in vivo studies, and optimizing its pharmacokinetic properties to determine its suitability for clinical applications. The novel quinone derivative holds promise as a valuable addition to the existing repertoire of therapeutic agents and may contribute to the development of novel treatment strategies for various diseases

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