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Research Article

Development and Characterization of Chalcone Derivatives Using 4-Hydroxyacetophenone and Anti-bacterial Activity against Two Pathogenic Bacterial Isolates From Women with Acute Urinary Tract Infections

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Abstract

In this work, the synthesis of a series of chalcone analogs with 4-hydroxyacetophenone as skeleton is interesting. Compounds Chalcone derivatives 1, 2 and 3 were prepared by the condensation of 4-hydroxyacetophenone with N,N-dimethylaminobenzaldehyde,3-methoxy4-hydroxybenzaldehyde,4-bromobenzaldehyde, respectively. The melting points of the synthesized compounds were determined and Fourier Transform Infrared (FT-IR) spectroscopy was carried out. The reaction was monitored by TLC using benzene:methanol (4:1) as a solvent system to keep track of the order and measurement of the progress. The antibacterial activity of the chalcone derivatives was tested against two multidrug-resistant aerobic pathogenic bacteria obtained from women with urinary tract infections. The resistant strains included both gram negative (*Acinetobacter baumannii*) and gram positive (*Streptococcus pyogenes*) bacteria. The activity was evaluated at four selected tested concentrations (25, 50, 100, and 150mg/ml) of each compound. Compound 3 showed the best antibacterial activity among other derivatives tested at 150 mg/mL concentration; inhibition zone diameters were attained at 20.450 ± 0.541 mm against *Acinetobacter baumannii* and 18.978 ± 0.600 mm against *Streptococcus pyogenes*.

1. Introduction

Chalcones are a class of α,β-unsaturated ketones containing two aromatic rings connected by a three-carbon enone bridge. Due to the simple chemical structure, ease of synthesis and great diversity of chemistry, chalcones have drawn tremendous interest in organic as well as medicinal chemistry [1]. These are not only central intermediates in the preparation of various heterocyclic systems, but also biologically active agents with wide pharmacological profiles. The substitution on the aromatic rings is known to significantly alter the physical, chemical, and biological properties of chalcones [2].

One of the most widely used procedure for chalcone synthesis is Claisen–Schmidt condensation reaction that involves base-catalysed condensation of an aromatic aldehyde with an aromatic ketone [3]. In aromatic ketones, 4-hydroxyacetophenone is often employed as a substrate because of its reactive carbonyl group and hydroxyl substituent which may lead to intermolecular interactions and biological activities. Coumarin forming reaction as well as the properties of chalcone derivatives are greatly influent by the electronic effect of electron-donating or electron-withdrawing substituents on benzaldehyde [4].

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Interest has been developed in the past few years to investigate chalcone derivatives as antimicrobial candidates. The reason of this interest is mainly due to the growing presence of multidrug-resistant pathogenic microorganisms that are considered a serious concern for public health [5]. Urinary tract infections are the most frequently diagnosed bacterial infections, especially in women and characterised by infections with multidrug resistant bacteria [6]. These include the Gram-positive bacteria *Streptococcus pyogenes*, and the Gram-negative bacterium *Acinetobacter baumannii*, which are each remarkable in their capacity to develop routes towards resistance, rendering them increasingly difficult to treat [7].

Thus, finding new antimicrobials with more potent activities and/or new modes of action has been a high priority [8]. Derivatives of chalcone have been recommended as promising alternatives in such replacements, because they can interact with other antimicrobial cell walls and cell membrane enzymes [4-9]. Functional groups, such as hydroxyl, methoxy, amino and halogen functions substituent on the aromatic rings of the compound could play a enhancing role to increase antibacterial activity by increasing lipophilicity membrane-permeability binding affinity toward biological targets [9].

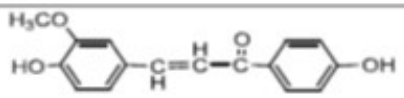
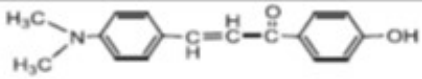
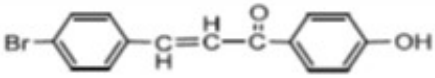
Besides in vitro testing of their biological activity, adequate characterization of the synthesized compounds is necessary for verifying their chemical structures and purity [10]. Various methods are used to verify the identity of new compounds, they include melting point determination, Fourier Transform Infrared (FT-IR) spectroscopy and thin layer chromatography (TLC). Such analysis methods are useful in determining functional groups, integrity of the molecule and extent of reaction at the time synthesis [11].

According to these considerations, the aim of this study is to develop a range of chalcone derivatives from 4-hydroxyacetophenone and chosen benzaldehyde derivatives. The synthesized compounds are rigorously characterized employing standard physicochemical techniques and further tested for their antibacterial activity against selected urinary tract infections causing multidrugresistant pathogens. The purpose of this work is to join in the continuing researches for new chalcone-based compounds with possible antibacterial application and to try to correlate structure-biological properties.

2. Methods

4-Hydroxyacetophenone (0.01 mol) and aromatic aldehyde (0.01 mol) were dissolved in ethanol (30 mL), with continuous stirring. The reaction mixture was then dropwise added with 40% NaOH solution in H_2O. The reaction was continued for 24 h at 25 °C and after the completion, collected precipitate separated through filtering, washed properly with diethyl ether and purified via recrystallization from alcohol. The progress and the completion of the reaction were monitored by thin layer chromatography (TLC) using benzene:methanol as eluent (4:1) [12]. The compounds 1, 2 and showed 3 in Table 1.

Table 1: Compounds 1, 2 and 3 and their steps synthesis in this study

Comp. No.	Structural Formula	Yiled %	Color	M.P. °C	Rf
1		79	Dark Brown	269	0.69
2		85	Brown	284	0.82
3		75	Orange	261	0.73

Antibacterial Activity Testing

Anti-biological testing of three synthesized derivative compounds (1, 2, and 3) was conducted in order to investigate their biological activity against two aerobic bacteria pathogens that were multidrug resistant and were isolated from women with acute urinary infections. *Acinetobacter baumannii* and *Streptococcus pyogenes* were examined, respectively.

Antibacterial activity was screened by agar well diffusion assay. The surface of Mueller–Hinton agar plates were inoculated with *Acinetobacter baumannii* and *Streptococcus pyogenes* having an optical density at 0.5 McFarland turbidity standard [13]. Four stock solutions (25, 50, 100 and 150 mg/mL) were obtained from each crude derivative product. Four wells were bored into the agar with a cork-borer and 50 µL of each concentration was placed in the appropriate wells. The plates were incubated at 37° C for 24 hr. Experiments were repeated in triplicate. Inhibition zone diameters (mm) around the wells were recorded [14].

3. Results and Discussion

In the current study, the prepared chalcone derivatives (compounds 1, 2 and 3) were characterized and confirmed by their chemical structure through melting point determination and FT-IR spectral analysis. The characteristic absorption bands in the FT-IR spectra of synthesized compounds indicated a proper construction of chalcone cores. The bands found at the region of 3050–3072 cm^{-1} were attributed to stretching

vibrations of the olefinic (=C–H) group. Strong absorption bands at the range 1650 to 1674 cm^{-1} are assigned for carbonyl (C=O) stretching vibrations. The absorption bands between 1507–1557 cm^{-1} are attributed to the stretching vibrations of α,β-unsaturated (CH=CH) group.

The emergence of those diagnostic bands could manifest that chalcone compounds are formed. The other most important and characteristic IR absorption bands for the synthesized compounds are presented in Table 2, and the corresponding FT-IR spectra are shown in Figures 1, 2 and 3.

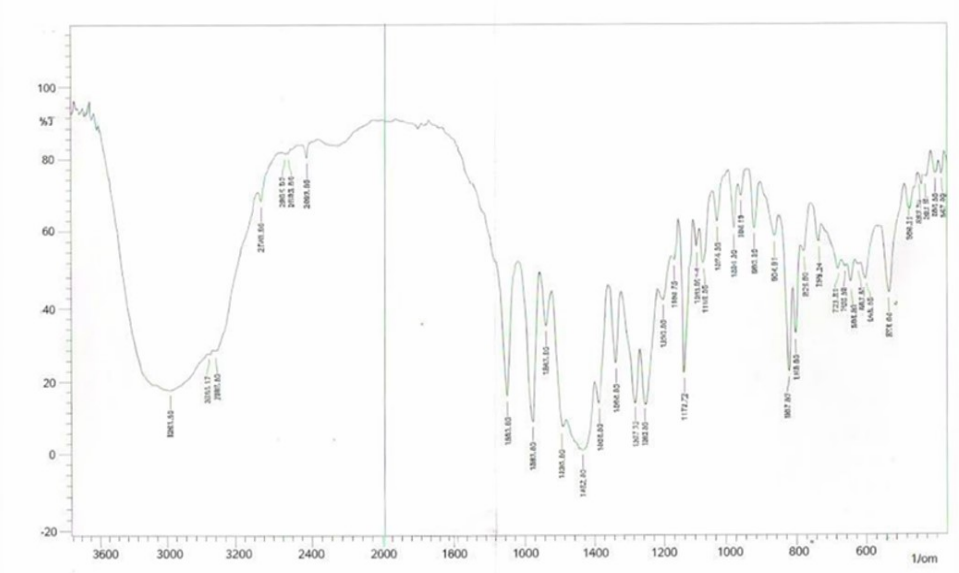


Figure 1: Chemical structure and FT-IR of Compound 1

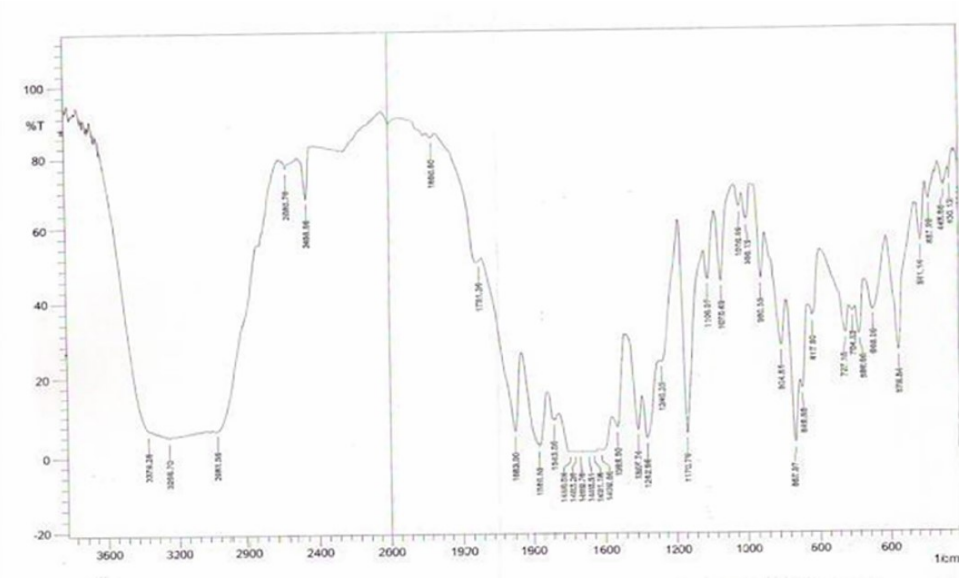


Figure 2: Chemical structure and FT-IR of Compound 2

Table 2: Chalcones derivatives and Some physical properties

Comp No.	V(=C-H)str.	V(CH=O)str.	V(CH=CH)str.	V(C=C)str.Ar	V Ar(C-H) bending
1	3030	1653	1581	1541	779
2	2981	1653	1585	1543	725
3	3030	1726	1583	1543	766

Compounds effects against pathogenic bacteria

The results of the present study reveal that all the processed derivative compounds (1, 2 and 3) exerted significant antibacterial activity against both strains of multidrug-resistant aerobic pathogenic bacteria at different tested concentrations. Of all the tested compounds, 3 with a concentration of 150 mg/mL exhibited the best antibacterial activities against *Acinetobacter baumannii* and *Streptococcus pyogenes* with inhibition zone diameter of 20.450 ± 0.541 mm and 18.978 ± 0.600 mm, respectively Table 3.

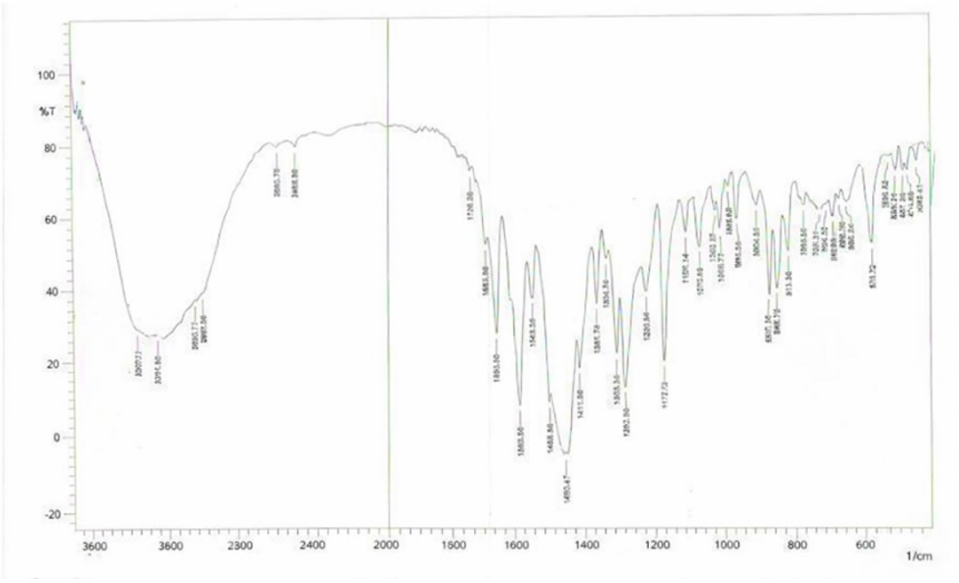


Figure 3: Chemical structure and FT-IR of Compound 3

Table 3: Determination of diameters to evaluate the antibacterial effect of three derivatives compounds against multidrug-resistance *Acinetobacter baumannii* and *Streptococcus pyogenes*

Derivative compounds	Multidrug resistance bacteria			
	Acinetobacter baumannii		*Streptococcus pyogenes*	
	Concentration (mg/mL)	M ± SE (mm)	Concentration (mg/mL)	M ± SE (mm)
1	25	7.122 ± 0.205	50	6.124 ± 0.231
	50	8.236 ± 0.651	100	6.981 ± 0.541
	100	10.900 ± 0.324	150	7.129 ± 0.987
	150	11.452 ± 0.652	200	9.215 ± 0.652
2	25	11.950 ± 0.547	50	9.254 ± 0.841
	50	12.300 ± 0.741	100	10.581 ± 0.954
	100	12.841 ± 0.452	150	11.654 ± 0.652
	150	14.222 ± 0.623	200	11.517 ± 0.765
3	25	14.541 ± 0.985	50	13.652 ± 0.652
	50	15.102 ± 0.314	100	13.950 ± 0.568
	100	17.980 ± 0.574	150	16.987 ± 0.200
	150	20.450 ± 0.541	200	18.978 ± 0.600

4. Conclusion

All of these synthesized compounds are stable by resonance, having a high melting point also on the other hand it will be another strong evidence in relation to stability. The derivative compound 3 (150 mg/ml) exhibited the most potent inhibition against *Acinetobacter baumannii* and *Streptococcus pyogenes* with inhibition zone diameters 20.450 ± 0.541, 18.978 ± 0.600, respectively.

Article Information

Disclaimer (Artificial Intelligence): The author(s) hereby declare that NO generative AI technologies such as Large Language Models (ChatGPT, COPILOT, etc.), and text-to-image generators have been used during writing or editing of manuscripts.

Competing Interests: Authors have declared that no competing interests exist.

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