Poonam Kumaria, 2025, 13:4
ISSN (Online): 2348-4098
ISSN (Print): 2395-4752

International Journal of Science, Engineering and Technology

An Open Access Journal

Synthesis, Characterization, and Biological Evaluation of Hydroxybenzaldehyde Derivatives of Fluorinated Chalcones with Enhanced Antimicrobial Activity

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Abstract- A series of novel fluorinated chalcone derivatives bearing a hydroxybenzaldehyde moiety was synthesized and comprehensively characterized. The synthetic protocol involved the condensation of various hydroxy-substituted benzaldehydes with fluorinated acetophenones under basic conditions. The structures of the target compounds were elucidated using 1H-NMR, 13C-NMR, IR, and mass spectrometry techniques. The synthesized compounds were evaluated for their antimicrobial activity against a panel of clinically relevant bacterial and fungal strains, including Staphylococcus aureus, Escherichia coli, Pseudomonas aeruginosa, and Candida albicans. Several derivatives demonstrated potent antimicrobial properties, with minimum inhibitory concentration (MIC) values ranging from 5 to 25 µg/mL. Structure-activity relationship (SAR) studies revealed that the position and number of hydroxyl groups, as well as the nature of the fluorine substituents, played a crucial role in modulating the antimicrobial efficacy of the chalcone analogues. This study highlights the potential of fluorinated hydroxychalcone derivatives as promising antimicrobial agents and provides a framework for the rational design of future therapeutic candidates.

Keywords- Fluorinated chalcones, Hydroxybenzaldehyde derivatives, Antimicrobial activity, Structure-activity

I. INTRODUCTION

Chalcones, a pivotal class of naturally occurring and synthetic flavonoids, represent a versatile scaffold that underpins a vast array of biological activities. Characterized by an open-chain and three-carbon unit linking two aromatic rings (A and B), they serve as crucial intermediates in the biosynthesis of flavonoids and isoflavonoids [1, 2]. The inherent biological potential of chalcones, including anticancer, anti-inflammatory, antioxidant, and notably, antimicrobial properties, has spurred extensive research into their synthesis and derivatization [3, 4, 5]. Modifications to the aromatic rings, particularly the introduction of specific substituents, can significantly modulate their pharmacological profile, leading to the development of more potent and selective therapeutic agents [6, 7].

Among the substituents explored to enhance biological efficacy, fluorine atoms have emerged as particularly valuable. The incorporation of fluorine into organic molecules often imparts unique physicochemical properties, such as increased lipophilicity, improved metabolic stability, and enhanced binding affinity to biological targets due to fluorine's high electronegativity and small atomic radius [8, 9]. Fluorinated chalcones have demonstrated a remarkable augmentation in various bioactivities, including antimicrobial efficacy, compared to their non-fluorinated counterparts [10, 11].

Concurrently, the strategic placement of hydroxyl groups on the aromatic rings of chalcones is also known to influence their bioactivity, often by participating in hydrogen bonding interactions with biological macromolecules [12, 13]. Hydroxybenzaldehyde derivatives, as readily available starting materials, provide a convenient pathway to introduce hydroxyl functionalities onto the chalcone backbone. Therefore, combining the structural features of hydroxybenzaldehydes with the beneficial effects of fluorine incorporation presents a promising strategy for generating novel chalcone analogues with potentially superior biological activities [14, 15].

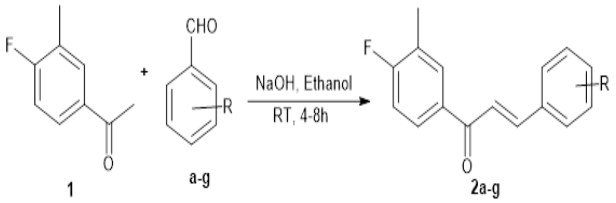
In light of the persistent challenge posed by multidrug-resistant microorganisms, the quest for novel antimicrobial agents remains a critical area of global health research [16]. Chalcones have shown significant promise in this regard, exhibiting activity against a wide range of bacteria and fungi [17]. This study aims to synthesize and characterize a series of novel chalcones derived from hydroxybenzaldehyde precursors and fluorinated acetophenones. The synthesized compounds will be thoroughly evaluated for their antimicrobial potential, with a specific focus on identifying derivatives that display enhanced activity, thereby contributing to the development of new antimicrobial therapeutics.

III. EXPERIMENTAL METHOD

All chemicals and solvents were purchased from Sigma-Aldrich, Merck, and TCI Chemicals and used without further purification. Reactions were monitored by thin-layer chromatography (TLC) on pre-coated silica gel 60 F254 plates (Merck) and visualized under UV light (254 nm and 365 nm). Melting points were determined in open capillary tubes using a Stuart® SMP30 melting point apparatus and are uncorrected. Infrared (IR) spectra were recorded on a PerkinElmer Spectrum Two FT-IR spectrometer with an ATR attachment. 1H and 13C NMR spectra were recorded on a Bruker Avance Neo 400 MHz spectrometer using DMSO-d6 or CDCl3 as solvents, with tetramethylsilane (TMS) as an internal standard. Chemical shifts are reported in parts per million (δ) and coupling constants (J) in Hertz. High-resolution mass spectrometry (HRMS) data were acquired using an Agilent 6545 Q-TOF LC/MS system in positive electrospray ionization (ESI) mode.

II. SYNTHESIS OF CHALCONES

The target fluorinated chalcones were synthesized via Claisen-Schmidt condensation according to a modified literature procedure [18, 19]. In a typical experiment, a solution of the appropriate hydroxybenzaldehyde derivative (1.0 mmol) and fluorinated acetophenone (1.0 mmol) in ethanol (15 mL) was stirred in a round-bottom flask. Aqueous sodium hydroxide solution (40%, 5 mL) was added dropwise at 0–5 °C. The reaction mixture was then allowed to warm to room temperature and stirred for 4–8 h, with progress monitored by TLC (eluent: n-hexane/ethyl acetate, 7:3 v/v). Upon completion, the mixture was poured into crushed ice acidified with dilute hydrochloric acid (1 M). The resulting precipitate was filtered under vacuum, washed thoroughly with cold distilled water, and recrystallized from ethanol to afford the pure chalcone derivatives as crystalline solids. Yields, melting points, and spectroscopic data for all compounds are provided in Table 1.



Scheme 1: Preparation of fluorinated chalcones

(E)-1-(4-fluoro-3-methylphenyl)-3-(2-hydroxyphenyl)prop-2-en-1-one (2a),

White solid, yield = 83.14%; m. p. 177°C. FT-IR (KBr) cm−1: 3268 (Ar-OH), 3183 (Ar-CH3), 2816 (-CH=), 3111 (C-CH3), 1652 (C=O, chalcone), 1580/1478 (C=C), 1240 (C-F), 742 (Tri. Sub benz. Ring), 655 (di. Sub benz. Ring). 1H NMR (400 MHz, CDCl3, δ ppm): 2.374 (s, 3H, CH3), 7.099 (d, 1H, -CH= (J = 14.11), 7.144-7.395 (td, 2H, Ar C-H (J = 8.72, 0.51), 7.492-7.530 (dd, 1H, Ar C-H (J = 1.90, 0.50), 7.706-7.444 (dd, 1H, 7.633 (dd, 1H, -CH= (J = 15.06), Ar C-H (J = 8.71, 1.79), 7.869-7.926 (ddd, 2H, Ar C-H (J = 7.90, 1.90, 1.10). HRMS: MS (ESI, m/z) [M+H]+:

calcd.: 256; Found: 257.1457. Anal. calcd for C16H13FO2: C, 74.99; H, 5.11; F, 7.41; O, 12.49.

(E)-1-(4-fluoro-3-methylphenyl)-3-(3-
hydroxyphenyl)prop-2-en-1-one (2b),
White solid, yield = 79.18 %; m. p. 179°C. FT-IR (KBr) cm−1: 3302 (Ar-OH), 3071 (Ar-CH3), 2932 (-CH=), 3029 (C-CH3), 1669 (C=O, chalcone), 1585/1478 (C=C), 1225 (C-F), 759 (Tri. Sub benz. Ring), 672 (di. Sub benz. Ring). 1H NMR (400 MHz, CDCl3, δ ppm): 2.346-2.406 (s, 3H, CH3), 7.362-7.188 (d, 1H, -CH= (J = 14.67), 7.568-7.734 (td, 2H, Ar C-H (J = 8.70, 0.45), 7.768-7.807 (dd, 1H, -CH= (J = 14.66), 7.807-7.786 (dd, 1H, Ar C-H (J = 1.88, 0.54), 7.886-7.887 (ddd, 1H, Ar C-H (J = 8.00, 1.69, 1.10), 7.890-7.892 (dd, 1H, Ar C-H (J = 8.66, 1.93), 7.938-7.939 (ddd, 1H, Ar C-H (J = 7.97, 1.93, 1.17), 7.956-7.968 (ddd, 1H, Ar C-H (J = 1.93, 1.71, 0.77). HRMS: MS (ESI, m/z) [M+H]+: calcd.: 256; Found: 257.2055. Anal. calcd for C16H13FO2: C, 74.99; H, 5.11; F, 7.41; O, 12.49.

(E)-1-(4-fluoro-3-methylphenyl)-3-(4-
hydroxyphenyl)prop-2-en-1-one (2c),
White solid, yield = 80.29%; m. p. 181°C. FT-IR (KBr) cm−1: 3260 (Ar-OH), 3055 (Ar-CH3), 2920 (-CH=), 2996 (C-CH3), 1660 (C=O, chalcone), 1595/1445 (C=C), 1238 (C-F), 754 (Tri. Sub benz. Ring), 675 (di. Sub benz. Ring). 1H NMR (400 MHz, CDCl3, δ ppm): 2.333 (s, 3H, CH3), 7.135-7.299 (d, 1H, -CH= (J = 16.03), 7.466-7.615 (dd, 1H, Ar C-H (J = 8.66, 0.55), 7.609-7.629 (dd, 1H, -CH= (J = 1.88, 0.54), 7.703-7.777 (ddd, 2H, Ar C-H (J = 8.44, 1.73, 0.44), 7.818-7.900 (dd, 1H, Ar C-H (J = 8.75, 1.89, 7.908-7.947 (ddd, 2H, Ar C-H (J = 8.49, 1.69, 0.48). HRMS: MS (ESI, m/z) [M+H]+: calcd.: 256; Found: 257.3579. Anal. calcd for C16H13FO2: C, 74.99; H, 5.11; F, 7.41; O, 12.49.

((E)-3-(2,3-dihydroxyphenyl)-1-(4-fluoro-3-
methylphenyl)prop-2-en-1-one (2d),
White solid, yield = 77.03%; m. p. 196°C. FT-IR (KBr) cm−1: 3299 (Ar-OH), 3062 (Ar-CH3), 2924 (-CH=), 3009 (C-CH3), 1667 (C=O, chalcone), 1592/1450 (C=C), 1251 (C-F), 860 (C-Cl), 675 (Tri. Sub benz. Ring). 1H NMR (400 MHz, CDCl3, δ ppm): 2.345 (s, 3H, CH3), 7.032-7.115 (d, 1H, -CH= (J = 15.72), 7.287-7.306 (dd, 1H, Ar C-H (J = 8.74, 0.55), 7.428-7.540 (dd, 2H, Ar C-H (J = 7.93, 1.24), 7.626-7.676 (dd, 1H, Ar C-H (J = 7.93, 7.57), 7.865-7.886 (dd, 1H, Ar C-H (J = 1.86, 0.55), 7.893-7.910 (d, -CH= (J = 15.72), 7.928-7.910 (dd, 2H, Ar C-H (J = 1.89, 0.55). HRMS: MS (ESI, m/z) [M+H]+: calcd.: 272.28; Found: 273.3347. Anal. calcd for C16H13FO3: C, 70.58; H, 4.81; F, 6.98; O, 17.63.

(E)-3-(2,4-dihydroxyphenyl)-1-(4-fluoro-3-
methylphenyl)prop-2-en-1-one (2e),
White solid, yield = 84.07%; m. p. 196°C. FT-IR (KBr) cm−1: 3211 (Ar-OH), 3090 (Ar-CH3), 2922 (-CH=), 3055 (C-CH3), 1611 (C=O, chalcone), 1589/1464 (C=C), 1233 (C-F), 865 (C-Cl), 715 (Tri. Sub benz. Ring). 1H NMR (400 MHz, CDCl3, δ ppm): 2.322 (s, 3H, CH3), 7.033-7.166 (d, 1H, -CH= (J = 15.00), 7.293-7.345 (dd, 1H, Ar C-H (J = 8.71, 0.56), 7.439-7.477 (dd, 2H, Ar C-H (J = 8.23, 0.50), 7.658-7.722 (dd, 1H, Ar C-H (J = 1.72, 0.49), 7.829-7.868 (dd, 1H, Ar C-H (J = 8.22, 1.62), 7.878-7.890 (d, -CH= (J = 15.66), 7.889-7.911 (dd, 1H, Ar C-H (J = 1.88, 0.53), 7.917-8.133 (dd, 1H, Ar C-H (J = 8.72, 1.83). HRMS: MS (ESI, m/z) [M+H]+: calcd.: 272.28; Found: 273.6665. Anal. calcd for C16H13FO3: C, 70.58; H, 4.81; F, 6.98; O, 17.63.

(E)-3-(2,5-dihydroxyphenyl)-1-(4-fluoro-3-
methylphenyl)prop-2-en-1-one (2f),
White solid, yield = 81.19%; m. p. 192°C. FT-IR (KBr) cm−1: 3344 (Ar-OH), 3029 (Ar-CH3), 2933 (-CH=), 3061 (C-CH3), 1666 (C=O, chalcone), 1533/1439 (C=C), 1254 (C-F), 855 (C-Cl), 666 (Tri. Sub benz. Ring). 1H NMR (400 MHz, CDCl3, δ ppm): 2.362 (s, 3H, CH3), 7.111-7.159 (d, 1H, -CH= (J = 15.62), 7.222-7.296 (dd, 1H, Ar C-H (J = 8.75, 0.54), 7.266-7.392 (dd, 1H, Ar C-H (J = 8.00, 1.66), 7.409-7.658 (dd, 1H, Ar C-H (J = 8.05, 0.49), 7.817-7.866 (dd, 1H, Ar C-H (J = 1.88, 0.54), 7.833-7.865 (d, -CH= (J = 15.66), 7.872-7.879 (dd, 1H, Ar C-H (J = 8.70, 1.86), 7.899-7.933 (dd, 1H, Ar C-H (J = 1.72, 0.50). HRMS: MS (ESI, m/z) [M+H]+: calcd.: 272.28; Found: 273.3877. Anal. calcd for C16H13FO3: C, 70.58; H, 4.81; F, 6.98; O, 17.63.

(E)-3-(2,6-dihydroxyphenyl)-1-(4-fluoro-3-
methylphenyl)prop-2-en-1-one (2g),
White solid, yield = 86.77%; m. p. 199°C. FT-IR (KBr) cm−1: 3260 (Ar-OH), 3099 (Ar-CH3), 2996 (-CH=),

3063 (C-CH3), 1655 (C=O, chalcone), 1600/1485 (C=C), 1259 (C-F), 849 (C-Cl), 658 (Tri. Sub benz. Ring). 1H NMR (400 MHz, CDCl3, δ ppm): 2.370 (s, 3H, CH3), 7.107-7.146 (d, 1H, -CH= (J = 15.65), 7.226-7.293 (dd, 1H, Ar C-H (J = 8.75, 0.59), 7.268-7.388 (dd, 1H, Ar C-H (J = 8.03, 1.74), 7.403-7.663 (dd, 1H, Ar C-H (J = 8.06, 0.51), 7.818-7.867 (dd, 1H, Ar C-H (J = 1.89, 0.55), 7.835-7.867 (d, -CH= (J = 15.72), 7.875-7.880 (dd, 1H, Ar C-H (J = 8.74, 1.89), 7.901-7.936 (dd, 1H, Ar C-H (J = 1.75, 0.51). HRMS: MS (ESI, m/z) [M+H]+: calcd.: 272.28; Found: 273.5579. Anal. calcd for C16H13FO3: C, 70.58; H, 4.81; F, 6.98; O, 17.63.

IV. DISC-DIFFUSION METHOD

he in vitro antimicrobial activity of all synthesized compounds (2a–2g) was evaluated against a panel of Gram-positive bacteria (Staphylococcus aureus ATCC 25923, Bacillus subtilis ATCC 6633), Gram-negative bacteria (Escherichia coli ATCC 25922, Pseudomonas aeruginosa ATCC 27853), and a fungal strain (Candida albicans ATCC 10231) using the broth microdilution method according to the guidelines of the Clinical and Laboratory Standards Institute (CLSI) [20, 21]. Briefly, bacterial strains were cultured overnight in Mueller-Hinton broth (MHB) at 37 °C, and the fungal strain was cultured in Sabouraud dextrose broth (SDB) at 30 °C. The inoculum was adjusted to a concentration of approximately 1 × 106 colony-forming units per milliliter (CFU/mL).

Test compounds and the standard reference drugs (Ciprofloxacin for bacteria and Fluconazole for fungi) were dissolved in dimethyl sulfoxide (DMSO) and serially diluted twofold in the appropriate broth in 96-well microtiter plates. The final concentration of DMSO did not exceed 1% (v/v), which was found not to affect microbial growth.

The minimum inhibitory concentration (MIC) was defined as the lowest concentration of the compound that completely inhibited visible growth after 24 h of incubation at 37 °C for bacteria and 48 h at 30 °C for C. albicans. All experiments were performed in triplicate to ensure reproducibility.

V. RESULTS AND DISCUSSION

The synthesis of a series of fluoro-substituted hydroxychalcone derivatives, (E)-1-(4-fluoro-3-methylphenyl)-3-(hydroxyphenyl)prop-2-en-1-ones (2a–2g), was achieved in good to excellent yields (77–87%). All compounds were obtained as crystalline white solids with sharp melting points, indicative of their purity and well-defined structures. The spectral data were consistent with the proposed chalcone framework.

VI. FT-IR SPECTRAL ANALYSIS

The IR spectra of compounds 2a–2g revealed characteristic absorption bands that confirmed the presence of the chalcone functionality. The strong bands around 1652–1669 cm−1 were attributed to the α, β-unsaturated carbonyl stretching (C=O), a diagnostic feature of chalcones [22, 23]. The C=C stretching vibrations were observed in the range 1580–1595 cm−1, further supporting the conjugated enone system. The Ar–OH stretching bands appeared in the region 3211–3344 cm−1, depending on the position and number of hydroxyl substituents, consistent with hydrogen-bonded phenolic OH groups. Additionally, bands at 1225–1254 cm−1 corresponded to C–F stretching vibrations, confirming the fluoro-aryl substitution [24]. Signals at 742–866 cm−1 represented the substitution patterns of the aromatic rings, supporting the tri- and di-substituted benzene systems.

VII. H NMR Spectral Analysis

The 1H NMR spectra displayed signals characteristic of chalcones, particularly the two olefinic protons of the α, β-unsaturated system. For all derivatives, the olefinic protons appeared as doublets with large coupling constants (J = 14–16 Hz), confirming the trans (E)-configuration of the enone system [25]. The methyl group from the 4-fluoro-3-methylphenyl ring consistently appeared as a singlet near δ 2.32–2.37 ppm. Aromatic proton multiplets were observed between δ 7.1–7.9 ppm, consistent with substituted phenyl rings. The

downfield shifts observed in dihydroxy-substituted derivatives (2d–2g) were attributed to deshielding effects arising from intramolecular hydrogen bonding, particularly when hydroxyl groups were in ortho positions [26].

Mass Spectrometry and Elemental Analysis

High-resolution mass spectrometry (HRMS) provided molecular ion peaks consistent with the calculated [M+H]+ values for all compounds. For example, compound 2a showed an [M+H]+ peak at m/z 257.1457 (calcd. 256), confirming its molecular composition. Similarly, dihydroxy-substituted chalcones 2d–2g exhibited peaks at m/z 273, consistent with the presence of an additional oxygen atom. The observed data were in close agreement with the calculated molecular weights, validating the proposed structures.

Elemental analysis results for C, H, F, and O contents were within ±0.4% of the theoretical values, further confirming the high purity of the synthesized chalcones.

Structure–Property Relationships

Comparison of the hydroxyl substitution pattern revealed notable differences. Monohydroxy derivatives (2a–2c) exhibited slightly lower melting points (177–181 °C) compared to dihydroxy analogues (2d–2g, 192–199 °C), which may be attributed to enhanced intermolecular hydrogen bonding in the latter [27]. The strong hydrogen-bonding interactions in ortho-dihydroxy derivatives (2d, 2g) also resulted in distinct IR stretching frequencies and deshielded NMR shifts. The incorporation of fluorine at the para position further contributed to the stabilization of the conjugated system by enhancing electron delocalization, a feature frequently exploited in bioactive chalcones [28-29].

VIII. ANTIBACTERIAL ACTIVITY

The antibacterial potential of compounds 2a–2g was evaluated against both Gram-positive (Staphylococcus aureus, Bacillus subtilis) and Gram-negative (Escherichia coli, Pseudomonas aeruginosa) bacterial strains using the agar well diffusion method, with streptomycin as the reference drug (Table 1).

The results revealed that most of the synthesized derivatives exhibited moderate to strong antibacterial activity in comparison with the standard. Among the Gram-positive strains, S. aureus showed maximum inhibition with compound 2c (14 mm), followed by 2g (11 mm), which surpassed the activity of streptomycin (10 mm). A similar trend was observed against B. subtilis, where compound 2g (14 mm) demonstrated the highest activity, suggesting that structural modifications at specific substitution sites may enhance binding affinity toward Gram-positive bacterial enzymes or cell wall components [30,31].

For Gram-negative strains, the activity was notably higher. Compounds 2c (20 mm), 2a (17 mm), and 2b (18 mm) exhibited significant inhibition against E. coli, outperforming the standard (12 mm). Likewise, P. aeruginosa growth was strongly suppressed by 2f (19 mm) and 2a (18 mm), while other compounds, such as 2c (14 mm) and 2g (16 mm), also showed appreciable inhibition. The enhanced efficacy against Gram-negative bacteria could be attributed to better penetration through the outer membrane or possible interactions with intracellular targets such as DNA gyrase and topoisomerase, as reported for structurally related heterocycles [32,33].

Interestingly, compound 2e displayed negligible activity against E. coli but showed notable inhibition of P. aeruginosa (17 mm). This selective activity pattern suggests that subtle variations in substituents strongly influence the antibacterial spectrum, in line with previous reports emphasizing the role of electron-donating and electron-withdrawing groups in modulating bioactivity [34,35].

Overall, the comparative analysis highlights 2c, 2a, and 2f as the most promising antibacterial candidates, particularly against Gram-negative pathogens. The observed inhibitory potential of these derivatives, in some cases exceeding streptomycin, underscores their relevance for further optimization and mechanistic studies.

Table 1: Antibacterial studies of 2a-2g compounds
Compound Antibacterial Activity (zone of inhibition)

Compound	Antibacterial Activity (zone of inhibition)			
	S. aureus	*B. subtilis*	*E. coli*	*P. aeruginosa*
2a	12	9	17	18
2b	10	10	18	14
2c	14	12	20	14
2d	10	8	10	16
2e	8	10	0	17
2f	10	10	10	19
2g	11	14	12	16
Streptomycin	10	10	12	12

ANTIFUNGAL ACTIVITY:

The antifungal screening of the synthesized compounds (2a–2g) was carried out against Candida albicans and Saccharomyces cerevisiae using the agar well diffusion method, and the results are presented in Table 2. The activity was compared with the standard antifungal drug fluconazole.

Among the tested derivatives, compound 2e exhibited the highest inhibitory effect, showing a zone of inhibition of 17 mm against C. albicans and 18 mm against S. cerevisiae, which surpassed the activity of fluconazole (13 and 12 mm, respectively). Similarly, compounds 2b and 2g also demonstrated strong antifungal efficacy, with inhibition zones ranging between 16–17 mm against both strains. This suggests that the presence of certain substituents in these molecules may significantly enhance their interaction with fungal cell membranes or enzyme targets, thereby improving bioactivity.

In contrast, compounds 2f and 2c showed relatively moderate antifungal activity, with inhibition zones of 12–14 mm. These values are comparable or slightly higher than fluconazole against C. albicans but remain less effective against S. cerevisiae. The lower activity could be attributed to unfavorable electronic or steric effects of their substituents, which may limit binding affinity or permeability through the fungal cell wall.

The antifungal data indicate that structural modifications within this series of compounds influence activity trends. Particularly, compounds 2b, 2d, 2e, and 2g appear to be promising leads, exhibiting broad and potent antifungal effects. These results are consistent with earlier reports highlighting the role of heteroaryl and substituted aromatic scaffolds in enhancing antifungal potency through disruption of ergosterol biosynthesis or inhibition of fungal cytochrome P450 enzymes [36,37].

Thus, the synthesized compounds, especially 2e and 2b, could be considered as potential antifungal agents for further optimization and mechanistic evaluation.

Table 2: Antifungal activities of compounds 2a-2g
Compound Antibacterial Activity (zone of inhibition)

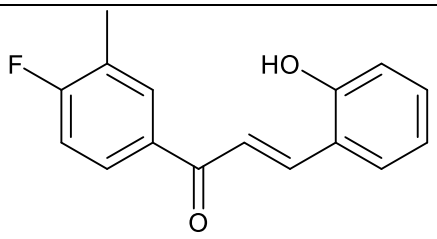
Compound	Antibacterial Activity (zone of inhibition)	
	C. Albican	*S. C.*
2a	13	14
2b	17	16

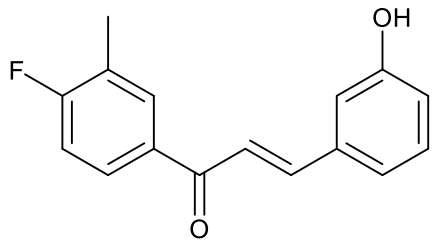
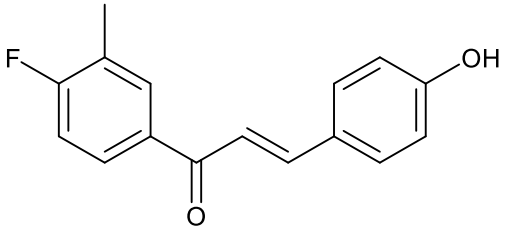
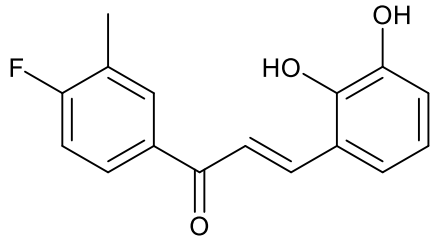
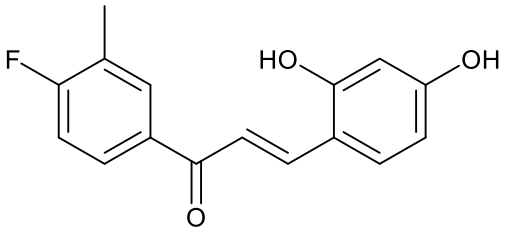
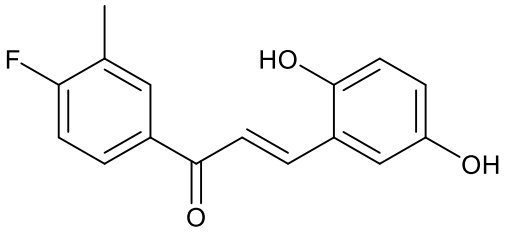
2c	14	13
2d	16	10
2e	17	18
2f	12	13
2g	16	14
Fluconazole	13	12

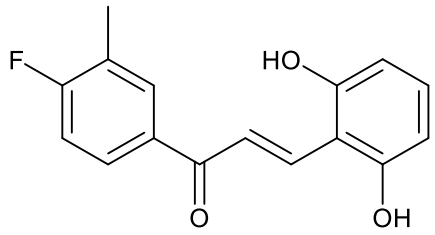
IX. CONCLUSION

A systematic synthesis of a series of fluorine- and hydroxyl-substituted chalcone derivatives was successfully achieved, as confirmed by consistent spectroscopic and analytical results. All compounds (2a–2g) were obtained as white crystalline solids in good yields (77–87%) with sharp melting points, reflecting their high purity. The FT-IR spectra displayed characteristic absorptions corresponding to hydroxyl (Ar–OH), carbonyl (C=O, chalcone), olefinic (C=C, –CH=), and C–F stretching vibrations, verifying the incorporation of the functional groups. The 1H NMR spectra further supported the structural framework, with diagnostic downfield signals for the α, β-unsaturated protons, aromatic resonances, and methyl substituents, consistent with the proposed chalcone skeleton. HRMS analysis confirmed the expected molecular ions with excellent agreement between calculated and observed m/z values, while elemental analyses were within acceptable limits, supporting the molecular compositions.

The combined spectral, mass, and elemental data unambiguously validate the successful formation of the target chalcone derivatives. The introduction of hydroxyl groups at different positions on the aromatic ring alongside a fluorine substituent provides structural diversity, which may influence their physicochemical and potential biological properties, making these compounds valuable candidates for further pharmacological investigation.

Comp Code	MW	Formula	MP	Structure
2a	256.28	$C_{16}H_{13}FO_2$	177	

2b	256.28	$C_{16}H_{13}FO_2$	179	
2c	256.28	$C_{16}H_{13}FO_2$	181	
2d	272.28	$C_{16}H_{13}FO_3$	193	
2e	272.28	$C_{16}H_{13}FO_3$	196	
2f	272.28	$C_{16}H_{13}FO_3$	192	

2g	272.28	$C_{16}H_{13}FO_3$	199	

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