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Article

Curcumin Inspired Designing and Organocatalytic Synthesis of New Chalcone Analogs

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ABSTRACT

Natural products have long been a source of therapeutic agents. This study focuses on the natural product-inspired design and synthesis of new chalcone derivatives using eco-friendly protocols in organic synthesis. The molecular hybridization approach is adopted for designing the new chalcone derivatives by combining the Curcumin pharmacophoric group and chalcone functionality. The Organocatalytic synthetic route has been developed for the synthesis of Chalcone derivatives by using piperidine as an organocatalyst. The synthesized molecules were fully characterized by spectroscopic and spectrometric data. Emphasis is placed on the green chemistry approach to minimize environmental impact and preparation of pharmacologically important molecules. The synthesized compounds were further found to be antimicrobial and antifungal agents. This research highlights the potential of natural products in drug discovery, particularly in the development of new treatments for various diseases.

Key words: Chalcone, Curcumin, Hybrid molecule, Organocatalysis, Piperidine.

1. INTRODUCTION

Curcumin is an active constituent of the traditional Indian herb turmeric and is regarded as one of the key components for inducing the biological significance of the molecule. The molecular hybridization rational is considered to be one of the very effective tools in medicinal chemistry for designing new molecules of Enhanced therapeutic index. The structural features of compounds governing the biological behavior of molecules are selected. This specific tool has been utilized in our laboratory to design compounds with more than one Pharmacophores. In the designing of the desired molecule, the 1,3-diketo moiety was selected from Curcumin as shown in the Figure 1. The specifically altered benzaldehyde analog consisting of piperidine and pyrrolidine rings was used. We plan to achieve the preparation of our designed molecule through the synthesis of Chalcone derivatives by reacting the dehydroacetic acid molecule and substituted benzaldehyde derivatives. The reaction was speeded up by using organocatalysis and a catalytic quantity of piperidine was used as organocatalyst.

Chalcones functionality is one of the most reactive and pharmacologically significant moiety due to: (1) The ease of preparation of this specific structure, (2) the most expanded substrate variation (3) Straightforward and simple methods of isolation, (3) its stability toward moisture and air makes it safe to store, (4) the better solubility in most of the organic solvents, (5) easy characterization by spectroscopic tools, (6) enhanced biological potential, and (7) Increased complexity of the system. All these properties present in this magical molecule provide them as a professional target for synthetic as well as medicinal chemists.

The first two properties mentioned above enabled synthetic chemists to join the molecules of desired importance using this link of chalcones. Synthetic medicinal chemists can utilize this chemistry to fabricate newly designed molecules having novel pharmacophores. Apart from the bioactive groups in Chalcones the conjugated carbonyl system of chalcones is well known for enhancing the bioactivity in the molecule. It is believed that the electrophilic unsaturated system in Chalcones bears the capability of forming non-bonding interactions with donor atoms in biomolecules. This specific binding capacity of chalcones makes them enable to act as bioactive molecules. This capacity of molecules can be enhanced or altered by changing the aromatic systems present in the chalcone moiety in a desired way.

A synthetic medicinal chemist finds endless opportunities to modification of chalcone moiety in the designed manner by carefully selecting the groups attached in the aromatic system of the parent molecules. A thorough study of the literature reveals that a number of different ways have been adopted by synthetic chemists in order to modify the chalcone moiety in different parts. Hence, we concluded that designing and proposing a new protocol for the synthesis of Chalcones derivatives will surely open new windows in discovering new bioactive molecules in a rapid manner. We tried to compile the various methods adopted for the construction of specific chalcone derivatives. We included the reports describing the preparation of new moieties with advanced levels of biological application against various targets.

2. EXPERIMENTAL

2.1. General Procedure for Synthesis of Chalcone Analogs (3-15)

Chalcone analogs (3-15) were synthesized through aldol condensation of substituted benzaldehyde and dehydroacetic acid. In dry

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chloroform, substituted benzaldehyde (1.0 mmol) and dehydroacetic acid (1.0 mmol) in the presence of catalytic pyrrolidine (20 mol %) was taken. The reaction was stirred at room temperature for an appropriate period of time, leading to the generation of chalcone. The progress of the reaction was monitored by TLC. After completion of the reaction solvent was evaporated under the reduced pressure and residue was extracted with ethyl acetate and water. The organic layer was separated and dried over anhydrous Na2SO4 and filtered. The filtrate was evaporated under a vacuum on a rotary evaporator. The solid residue left was recrystallized from ethanol.

2.2. Analytical Data for Compounds (3-22)

2.2.1. 3-cinnamoyl-4-hydroxy-6-methyl-2H-pyran-2-one (3)

White solid; mp 148°C; νmax(KBr) 3424, 3083, 1725, 1626, 1326, 1236 cm^{-1}; 1H NMR (CDCl3, 300 MHz): δ 10.12 (s, 1H); 8.36 (d, 1H, J=15.75Hz); 8.01 (d, 1H, J=15Hz); 7.27–7.69 (m, 2H), 7.45–7.42 (m, 3H), 5.98 (s, 1H); 2.30 (s, 3H); 13C NMR (CDCl3, 75 MHz): δ 191.0, 182.4, 166.5, 162.1, 150.5, 148.6, 131.6, 129.8, 127.5, 123.21 120.6, 116.1, 111.4, 103.1, 98.9, 20.7.; MS (ES): m/z (%) = 257 (100) [M+1]+; Ana. calcd. for C15H12O4: C, 70.31; H, 4.72; Found: C, 70.28; H, 4.69%.

2.2.2. (E)-4-hydroxy-3-(3-(4-methoxyphenyl)acryloyl)-6-methyl-2H-pyran-2-one (4)

Yellow solid; mp 130°C; νmax(KBr) Ir 3419, 3087, 1717, 1642, 1348, 1254 cm^{-1}; 1H NMR (CDCl3, 300 MHz): δ 10.08 (s, 1H); 9.89 (s, 1H); 7.86 (d, 2H, J=8.9Hz), 7.03 (d, 2H, J=8.7Hz), 5.9 (s, 1H), 6.97–6.88 (m, 2H), 3.98 (s, 3H), 2.28 (s, 3H); 13C NMR (CDCl3, 75 MHz): δ 190.6, 183.7, 166.4, 161.6, 150.5, 147.2, 137.4, 120.4, 115.6, 111.6, 104.1, 98.7, 55.6, 20.4; MS (ES): m/z (%) = 287 (100) [M+1]+; Ana. calcd. for C16H14O5: C, 67.13; H, 4.93; Found: C, 67.08; H, 4.89%.

2.2.3. (E)-4-hydroxy-3-(3-(3-methoxyphenyl)acryloyl)-6-methyl-2H-pyran-2-one (5)

Yellow solid; mp 135°C; νmax(KBr) 3421, 3072, 1719, 1659, 1328, 1212 cm-1; 1H NMR (CDCl3, 300 MHz): δ 10.08 (s, 1H); 8.22 (d, 2H, J=14Hz), 7.97 (d, 2H, J=14Hz), 6.98-6.94 (m, 2H); 5.96 (s, 1H); 3.98 (s, 3H), 2.28 (s, 3H); 13C NMR (CDCl3, 75 MHz): δ 190.7, 182.6, 167.4, 161.2, 151.2, 148.6, 131.4, 127.4, 123.1, 121.3, 116.2, 111.6, 103.2, 97.8, 21.4.; MS (ES): m/z (%) = 287 (100) [M+1]+; Ana. calcd. for C16H14O5: C, 67.13; H, 4.93; Found: C, 67.09; H, 4.90%.

2.2.4. (E)-3-(3-(3,4-dimethoxyphenyl yloyl)-4-hydroxy-6-methyl-2H-pyran-2-one (6)

Yellow solid; mp 145°C; νmax(KBr) 3466, 3112, 1722, 1629, 1316, 1252 cm^{-1}; 1H NMR (CDCl3, 300 MHz): δ 10.11 (s, 1H); 8.23 (d, 1H, J= 15Hz), 7.97 (d, 1H, J= 15.7Hz) 7.49-7.22 (m, 2H); 7.01–6.89 (m, 2H), 5.96 (s, 1H); 3.86 (s, 6H), 2.38 (s, 3H); 13C NMR (CDCl3, 75 MHz): δ 191.0, 181.4, 167.4, 162.1, 151.4, 148.6, 132.8, 127.7, 123.2, 121.0, 116.1, 112.5, 103.1, 98.9, 56.4, 21.3.; MS (ES): m/z (%) = 317 (100) [M+1]+; Ana. calcd. for C17H16O6: C, 64.55; H, 5.10; Found: C, 64.51; H, 5.06%.

2.2.5. (E)-4-hydroxy-6-methyl-3-(3-(4-nitrophenyl)acryloyl)-2H-pyran-2-one (7)

Creamish solid; mp 182°C; νmax(KBr) Ir 3697, 3020, 2924, 1725, 1596, 1216 cm^{-1}; 1H NMR (CDCl3, 300 MHz): δ 10.13 (s, 1H); 8.40–8.34 (m, 2H); 8.26 (d, 1H, J=12.4Hz), 8.09 (d, 1H, J=12.4Hz), 7.98–7.94 (m, 2H); 5.98 (s, 1H); 2.28 (s, 3H); 13C NMR (CDCl3, 75 MHz): δ 191.1, 183.7, 167.4, 161.6, 152.8, 148.4, 131.6, 122.7, 114.2, 112.7, 103.2, 98.9, 20.5; MS (ES): m/z (%) = 302 (100) [M+1]+; Ana. calcd. for C15H11NO6 C, 59.80; H, 3.68; Found: C, 59.75; H, 3.63%.

2.2.6. (E)-4-hydroxy-6-methyl-3-(3-(2-nitrophenyl)acryloyl)-2H-pyran-2-one (8)

Yellow solid; mp 176°C; νmax(KBr) 3571, 3032, 1719, 1636, 1218 cm^{-1}; 1H NMR (CDCl3, 300 MHz): δ 10.16 (s, 1H), 8.43-8.35 (m, 2H), 8.28 (d, 1H, J= 12Hz), 8.10-8.06 (m, 2H), 7.58 (d, 1H, J= 12Hz); 6.00 (s, 1H); 2.29 (s, 3H); 13C NMR (CDCl3, 75 MHz): δ 13C NMR: δ 191.1, 182.6, 167.5, 161.2, 150.4, 148.6, 134.8, 127.7, 123.2, 120.4, 116.1, 111.7, 103.2, 98.9, 21.3.; MS (ES): m/z (%) = 302 (100) [M+1]+; Ana. calcd. for C15H11NO6: C, 59.80; H, 3.68; N, 4.65 Found: C, 59.74; H, 3.66; N, 4.67%.

2.2.7. (E)-3-(3-(4-(dimethylamino)phenyl)acryloyl)-4-hydroxy-6-methyl-2H-pyran-2-one (9)

Dark maroon solid; mp 180°C; νmax(KBr) 3516, 3116, 1724, 1669, 1326, 1218 cm^{-1}; 1H NMR (CDCl3, 300 MHz): δ 10.08 (1H, s), 8.22 (d, 1H, J= 15Hz), 8.11 (d, 1H, J= 15Hz), 8.90 (d, 2H, J= 9Hz,), 6.72 (d, 2H, J= 9Hz), 5.98 (s, 1H), 3.09 (s, 6H); 2.27 (s, 3H); 13C NMR (CDCl3, 75 MHz): δ 191.3, 183.9, 167.4, 161.6, 152.7, 148.3, 131.8, 122.7, 116.4, 111.7, 103.2, 98.9, 40.1, 20.5; MS (ES): m/z (%) = 300 (100) [M+1]+; Ana. calcd. for C17H17NO4: C, 68.21; H, 5.72; N, 4.68; Found: C, 68.18; H, 5.67; N, 4.71%.

2.2.8. (E)-3-(3-(3-chlorophenyl)acryloyl)-4-hydroxy-6-methyl-2H-pyran-2-one (10)

Light yellow solid; mp 170°C; νmax(KBr) 3518, 3087, 1720, 1621, 1328, 1248 cm^{-1}; 1H NMR (CDCl3, 300 MHz): δ 9.87 (s, 1H), 8.30 (d, 1H, J= 14Hz), 8.12 (d, 1H, J= 14Hz), 7.94–7.67 (m, 3H), 7.63–7.55 (m, 1H), 5.98 (s, 1H), 2.28 (s, 3H); 13C NMR (CDCl3, 75 MHz): δ 190.1, 181.4, 167.5, 161.2, 150.4, 147.6, 134.8, 127.7, 122.2, 120.8, 116.3, 112.7, 103.2, 98.7, 21.1.; MS (ES): m/z (%) = 291 (100) [M+1]+; Ana. calcd. for C15H11ClO4 C, 61.98; H, 3.81; Found: C, 61.91; H, 3.84%.

2.2.9. (E)-3-(3-(4-chlorophenyl)acryloyl)-4-hydroxy-6-methyl-2H-pyran-2-one (11)

Light brown solid; mp 166°C; νmax(KBr) 3452, 3152, 1721, 1665, 1327, 1242 cm-1; 1H NMR (CDCl3, 300 MHz): δ 10.15 (s, 1H); 8.26 (d, 1H, J= 16Hz), 7.95 (d, 1H, J= 16Hz), 7.51–7.18 (m, 2H); 6.99–6.78 (m, 2H), 5.98 (s, 1H); 2.31 (s, 3H); 13C NMR (CDCl3, 75 MHz): δ 190.8, 183.9, 166.3, 161.6, 151.5, 147.2, 138.4, 121.7, 116.4, 112.6, 103.1, 98.9, 20.4; MS (ES): m/z (%) = 291 (100) [M+1]+; Ana. calcd. for C15H11O4: C, 61.98; H, 3.81; Found: C, 61.94; H, 3.79%.

2.2.10. (E)-3-(3-(2-chlorophenyl)acryloyl)-4-hydroxy-6-methyl-2H-pyran-2-one (12)

yellow solid; mp 188°C; νmax(KBr) 3517, 3084, 1720, 1626, 1328, 1248 cm^{-1}; 1H NMR (CDCl3, 300 MHz): δ 9.83 (s, 1H), 8.30–8.11 (m, 2H), 7.97–7.66 (m, 3H), 7.61–7.55 (m, 1H), 5.96 (s, 1H), 2.27 (s, 3H); 13C NMR (CDCl3, 75 MHz): δ 190.4, 181.6, 167.9, 161.6, 150.1, 147.3, 134.5, 127.2, 122.2, 120.1, 116.3, 112.7, 103.2, 98.7, 21.4.; MS (ES): m/z (%) = 291 (100) [M+1]+; Ana. calcd. for C15H11ClO4 C, 61.98; H, 3.81; Found: C, 61.94; H, 3.86%.

2.2.11. (E)-4-hydroxy-3-(3-(3-hydroxy-4-methoxyphenyl) acryloyl)-6-methyl-2H-pyran-2-one (13)

Yellow solid; mp 175°C; νmax(KBr) 3355, 3100, 1711, 1600, 1424, 1275 cm^{-1}; 1H NMR (CDCl3, 300 MHz): δ 10.08 (s, 1H), 8.21 (d, 1H, J= 15.6Hz), 7.11 (d, 1H, J= 15.6Hz), 7.28–7.22 (m, 3H), 6.77 (d, 1H, J= 8.1Hz), 5.96 (s, 1H), 3.98 (s, 3H), 2.28 (s, 3H). 13C NMR (CDCl3, 75 MHz): δ 191.1, 181.3, 167.4, 162.1, 151.4, 148.6, 132.8, 126.7, 123.1, 121.2, 116.4, 112.3, 103.1, 98.7, 56.4, 21.2; MS (ES): m/z (%) = 303 (100) [M+1]+; Ana. calcd. for C16H14O46 C, 63.57; H, 4.67; Found: C, 63.53; H, 4.63%.

2.2.12. (E)-3-(3-(4-(benzyloxy)phenyl)acryloyl)-4-hydroxy-6-methyl-2H-pyran-2-one (14)

Yellow solid; mp 171°C; νmax(KBr) 3436, 3021, 1724, 1635, 1343, 1217 cm^{-1}; 1H NMR (CDCl3, 300 MHz): δ 10.18 (s, 1H), 8.19 (d, 2H, J= 15.6Hz), 7.68 (d, 2H, J= 8.7Hz), 7.43-7.41 (m, 5H), 7.42-7.03 (m, 1H), 7.01 (d, 1H, J= 8.7Hz), 5.95 (s, 1H); 5.11 (s, 2H), 2.27 (s, 3H); 13C NMR (CDCl3, 75 MHz): δ; MS (ES): m/z (%) = 363 (100)

[M+1]+; Ana. calcd. for C22H18O5 C, 72.92; H, 5.01; Found: C, 72.89; H, 4.98%.

2.2.13. (E)-4-hydroxy-3-(3-(3-hydroxyphenyl)acryloyl)-6-methyl-2H-pyran-2-one (15)

Orange solid; mp 195°C; νmax(KBr) 3536, 3172, 1722, 1657, 1378, 1220 cm^{-1}; 1H NMR (CDCl3, 300 MHz): δ 10.04 (s, 1H), 8.31 (d, 1H, J= 15.8Hz), 7.89 (d, 1H, J= 15.8Hz), 7.62 (d, 2H, J= 6.68Hz), 7.39 (d, 1H, J= 6.9Hz), 5.97 (s, 1H), 2.29 (s, 3H); 13C NMR (CDCl3, 75 MHz): δ 191.3, 182.2, 167.5, 161.2, 150.1, 148.4, 134.6, 127.7, 123.2, 121.4, 116.1, 112.7, 103.1, 98.9, 21.1.; MS (ES): m/z (%) = 273 (100) [M+1]+; Ana. calcd. for C15H12O5 C, 66.17; H, 4.44; Found: C, 66.12; H, 4.38%.

2.2.14. (E)-4-hydroxy-3-(3-(4-hydroxyphenyl)acryloyl)-6-methyl-2H-pyran-2-one (16)

Bright yellow solid; mp 167°C; νmax(KBr) 3541, 3167, 1724, 1658, 1346, 1268 cm^{-1}; 1H NMR (CDCl3, 300 MHz): δ 10.04 (s, 1H), 8.39 (d, 1H, J= 16Hz), 7.92 (d, 1H, J= 16Hz), 7.76 (d, 2H, J= 7.81Hz), 7.51 (d, 2H, J= 7.78Hz), 5.98 (s, 1H), 2.28 (s, 3H); 13C NMR (CDCl3, 75 MHz): δ 190.3, 181.2, 166.5, 162.1, 151.3, 147.2, 129.6, 126.4, 123.2, 111.5, 103.1, 97.6, 21.0.; MS (ES): m/z (%) = 273 (100) [M+1]+; Ana. calcd. for C15H12O5 C, 66.17; H, 4.44; Found: C, 66.12; H, 4.41%.

2.2.15. (E)-4-hydroxy-3-(3-(4-hydroxyphenyl)acryloyl)-6-methyl-2H-pyran-2-one (17)

Bright yellow solid; mp 149°C; νmax(KBr) 3541, 3167, 1724, 1658, 1346, 1268 cm-1; 1H NMR (CDCl3, 300 MHz): δ 10.04 (s, 1H), 8.39 (d, 1H, J= 16Hz), 7.92 (d, 1H, J= 16Hz), 7.76 (d, 2H, J= 7.81Hz), 7.51(d, 1H, J= 7.78Hz), 5.98 (s, 1H), 2.28 (s, 3H); 13C NMR (CDCl3, 75 MHz): δ 190.3, 181.2, 166.5, 162.1, 151.3, 147.2, 129.6, 126.4, 123.2, 111.5, 103.1, 97.6, 21.0.; MS (ES): m/z (%) = 273 (100) [M+1]+; Ana. calcd. for C15H12O5 C, 66.17; H, 4.44; Found: C, 66.12; H, 4.41%.

3. RESULTS AND DISCUSSION

Entry	Catalyst	Reaction Time (hrs.)	Yield (%)
1	Piperidine	4	92
2	Pyrrolidine	5	88
3	Proline	6	85
4	Morpholine	6	80
5	Triethylamine	8	75
6	Imidazole	8	78

The organocatalyzed synthesis of chalcone derivatives was successfully achieved using a variety of substituted aromatic aldehydes and acetophenones under mild conditions. The reactions were conducted in the presence of a catalytic amount of an organic base, typically proline or a similar amino acid derivative, which facilitated the aldol condensation reaction. The selection of an appropriate catalyst is crucial for the efficiency and selectivity of the organocatalyzed synthesis of chalcone derivatives. In this study, various organic bases were evaluated for their catalytic performance, including piperidine, pyrrolidine, proline, morpholine, triethylamine, and imidazole. The catalytic efficiency of these bases was assessed by conducting the reaction between benzaldehyde and acetophenone under identical conditions. The yields and reaction times were compared to determine the most effective catalyst.

Table 1 summarizes the yields and reaction times for the synthesis of chalcone using different organic bases.

The data presented in Table 2 and the graphical representation in Figure 3 clearly indicate that piperidine was the most effective catalyst among the tested bases, providing the highest yield of 92% within the shortest reaction time of 4 h.

The superior performance of piperidine can be attributed to its strong nucleophilicity and ability to facilitate the enamine formation more efficiently than the other bases. Pyrrolidine and proline also demonstrated good catalytic activity, with yields of 88% and 85%, respectively. The slightly longer reaction times for these catalysts suggest that while they are effective, they are not as efficient as piperidine under the given conditions. Morpholine, triethylamine, and imidazole exhibited lower yields and longer reaction times, indicating that they are less suitable for this reaction. The reduced catalytic efficiency of these bases could be due to their relatively weaker nucleophilicity and steric hindrance, which may impede the formation of the enamine intermediate or destabilize the transition state.

Once we lade our decision to use piperidine as an organocatalyst for the chalcone synthesis we shifted the efforts toward the preparation of other chalcone derivatives. Table 1 Summarize the yields and reaction times for the synthesis of various chalcone derivatives. The results indicate that the reaction proceeded efficiently with high yields ranging from 78% to 92% within a reaction time of 4–8 h, depending on the nature of the substituents on the aromatic ring. A total of 17 derivatives were synthesized by applying our developed protocol. A few substrates were designed to enhance the biological potential in the molecule by converting the 4-hydroxy benzaldehyde derivatives into aminoalkyl analogs. The piperidine, pyrrolidine, and morpholine analogs were prepared.

Table 1: summarizes the yields and reaction times for the synthesis of chalcone using different organic bases.

Entry	Catalyst	Reaction Time (hrs.)	Yield (%)
1	Piperidine	4	92
2	Pyrrolidine	5	88
3	Proline	6	85
4	Morpholine	6	80
5	Triethylamine	8	75
6	Imidazole	8	78

Table 2: Synthesis of different Chalcone derivatives

Compound	R^1	R^2	R^3	R^4	Yield(%)	Time
3	H	H	H	H	88	8
4	H	H	OCH_3	H	91	8
5	H	OCH^3	H	H	90	8
6	H	OCH^3	OCH_3	H	90	8
7	H	H	NO_2	H	89	6
8	NO^2	H	H	H	83	10
9	H	H	N, N-$(CH_3)^2$	H	92	7
10	H	Cl	H	H	91	7
11	H	H	Cl	H	92	8
12	H	Cl	H	3-Cl	90	8
13	H	OH	OCH_3	H	86	10
14	H	H	OCH_2Ph	H	87	8
15	H	OH	H	H	84	8
16	H	H	OH	H	82	6
17	H	H	F	H	94	9

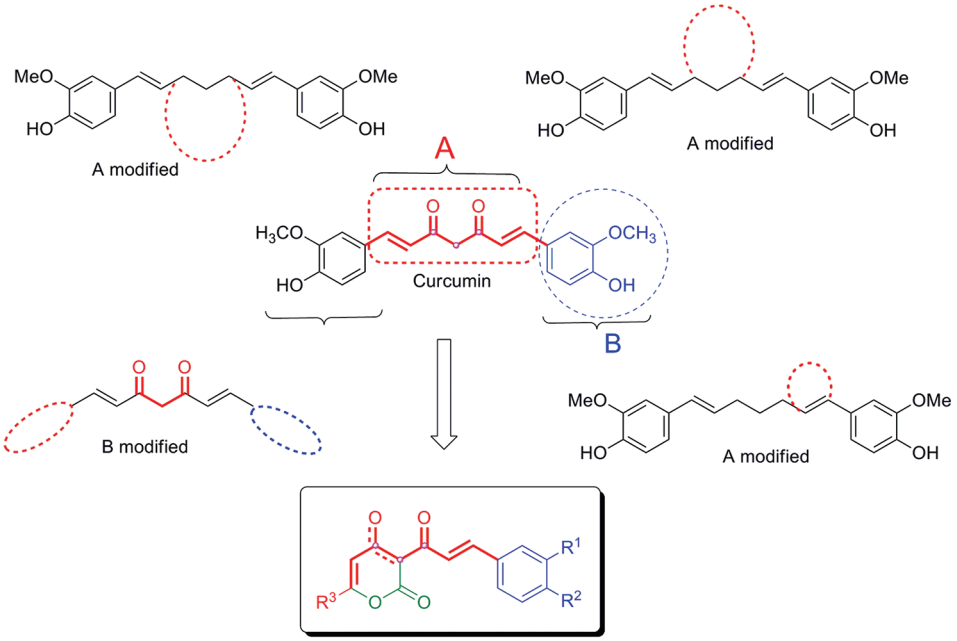


Figure 1: Various ways of modification of the original Curcumin nucleus.

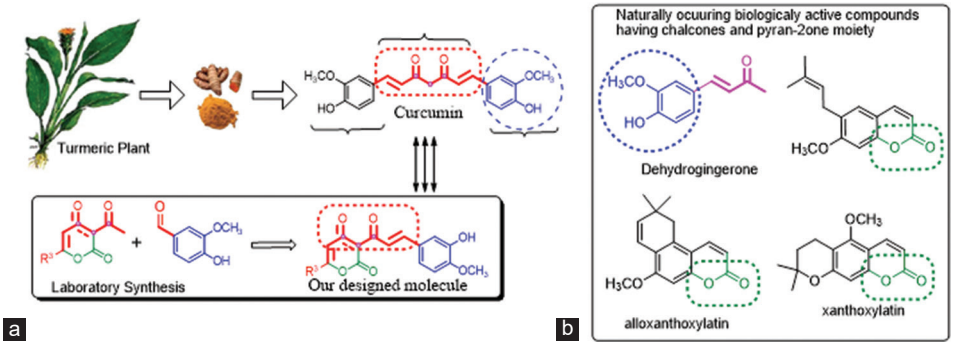


Figure 2: (a and b) Designing of new curcumin-based chalcone derivatives.

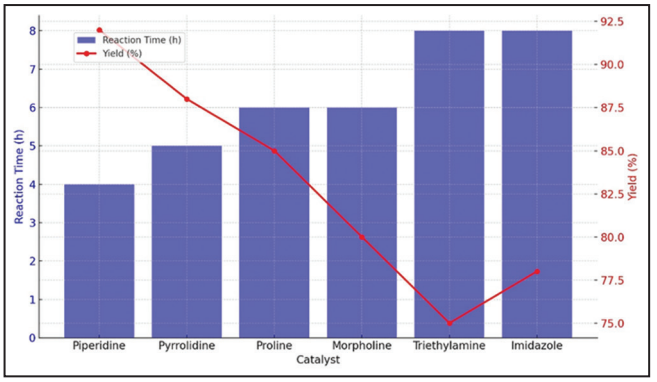
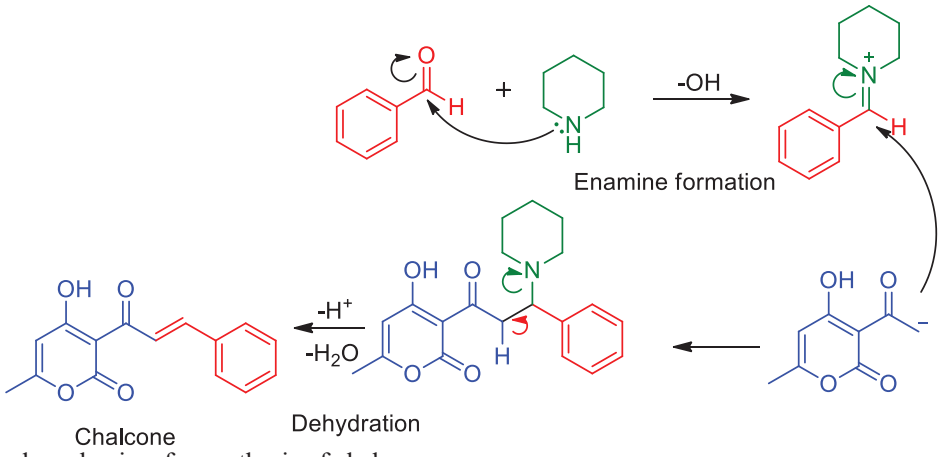


Figure 3: Representation of catalytic efficiency of different organocatalysts employed in the reaction.

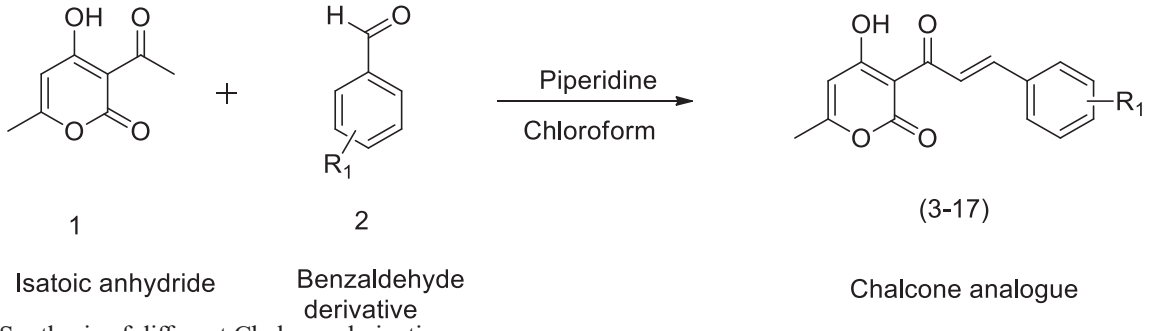
The proposed mechanism for the organocatalyzed synthesis of chalcone derivatives involves the initial activation of the aldehyde by the catalyst, leading to the formation of an enamine intermediate. This intermediate then undergoes nucleophilic addition to the carbonyl group of the acetophenone, followed by dehydration to yield the corresponding chalcone.

Proline, in particular, was found to be highly effective due to its bifunctional nature, providing both nucleophilic and acidic sites necessary for the reaction. The synthesized chalcone derivatives were characterized using various spectroscopic techniques, including NMR, IR, and mass spectrometry. The representative 1H NMR spectrum of chalcone displays characteristic signals for the α,β-unsaturated carbonyl system. The peaks at δ 7.20–7.80 ppm correspond to the aromatic protons, while the vinylic protons appear at δ 7.50–7.60 ppm. The IR spectrum of the same chalcone, highlights the stretching vibrations of the carbonyl group at 1650 cm^{-1} and the C=C double bond at 1600 cm^{-1}. The mass spectrum further confirmed the molecular weight of the product, with a prominent peak at m/z corresponding to the molecular ion.

Thus we have reported here the synthesis of 21 substituted natural product-inspired chalcone type analogs consisting of curcumin nucleus [Scheme **1**]. Analogs were synthesized bearing different functional groups at the phenyl ring and in an attempt to optimize the anticancer activity and potentially gain insight into the structure-activity relationship of 3-cinnamoyl-4-hydroxy-6-methyl-2H-pyran-2-one (compound **3-17**) and its derivatives. The reaction scheme for the synthesis of the designed analogue is shown schematically in Figure **2**. Compounds (**3-17**) were synthesized from dehydroacetic acid (**1**) and substituted benzaldehydes (**2**) through condensation reaction using pyridine as a base. Both the reactants were mixed in anhydrous chloroform and the reaction was allowed to reflux for an appropriate time period up to completion



AQ2 **Figure 4:** The proposed mechanism for synthesis of chalcone.



Scheme 1: Synthesis of different Chalcone derivatives.

of the reaction. After completion of reaction desired products were isolated by only filtration. No chromatography is required for publication.

4. CONCLUSION

In the present work, we have demonstrated the designing of new structurally important chalcone derivatives and proposed a sustainable way for their preparation. By applying the oragnocatalytic methodology we have prepared a 15-membered library of new chalcone derivatives. The synthesized molecules were further characterized using spectroscopic and spectrometric data. The effect of substitution on benzaldehyde molecule on the reactivity is investigated. The developed protocol presents an alternative methodology for the synthesis of chalcone analogs. The molecule prepared in the present work could be of great importance in future drug discovery projects.

5. ACKNOWLEDGMENT

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6. CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

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