AMERICAN JOURNAL OF PHARMTECH RESEARCH

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Synthesis, Characterization and Biological Activities of Some Novel Heterocyclic Chalcone Derivatives

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ABSTRACT

Chalcones are a category of compounds consisting of two aryl rings linked by an α,β-unsaturated ketone moiety. The synthesized compounds CEA and CMA were evaluated for antimicrobial activity by disc diffusion method. The antibacterial and antifungal activity was evaluated against *Moraxella, Enterobacter, Pseudomonas aeruginosa* (bacterial strains), *Candida albicans, A.niger and Trichophyton* (fungal strains) using *Erythromycin* (for bacteria) and *Ciprofloxacin* (for fungi) as the standard drugs. The structure of synthesized compounds has been elucidated by IR, ^{1}H, ^{13}C NMR and elemental analysis.

Keywords: Chalcone, antibacterial, antifungal, Nystatin and ciprofloxacin.

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Received 24 November 2014, Accepted 2 December 2014

Please cite this article as: Nasser JA, *et al*., Synthesis, Characterization and Biological Activities of Some Novel Heterocyclic Chalcones Derivatives. American Journal of PharmTech Research 2014.

INTRODUCTION

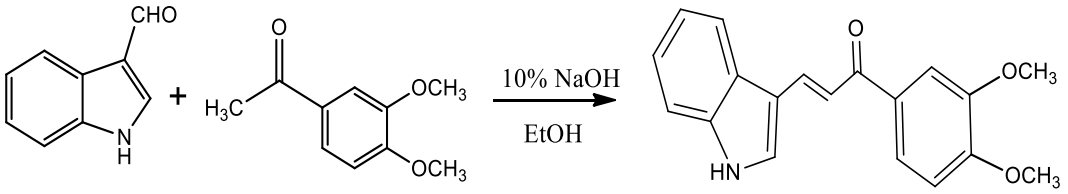
Chalcone can be prepared in a number of ways the simplest being aldolic condensation between benzaldehydes and acetophenones[1]. This method allows for the rapid synthesis of several chalcones using common inexpensive reagents and was used to prepare a library of 154 synthetic chalcones with different substitutions that were subsequently screened for activity against bacterial and fungal strain. The compounds with the backbone of chalcones have been reported to possess various biological activities such as antimicrobial[2], anti-inflammatory[3], analgesic[4], antiulcerative[5], antimalarial[6], antidiabactics[7], antidepressant[8], anticonvulsant[9], anticancer[10] and antioxidant[11] activities. Antibacterial and antifungal activity of chalcones has been investigated by a number of researchers[12]. Considering the above observation and in connection to previous publication involving the synthesis of new biological active heterocyclic. I hope to report here in the synthesis of new substituted Indolyl derivatives.

MATERIALS AND METHOD

The melting point of the compounds was determined in open capillaries, using Eligo digital melting point apparatus and expressed in degree Celsius and the values were uncorrected. IR spectra of the compounds were recorded on Shimadzu 8201 spectrophotometer using KBr and the values are expressed in 4000-400 cm^{-1}. ^{1}H and ^{13}C NMR spectra were recorded on Bruker AV 400 MHz Spectrophotometer using TMS as an internal standard and the values are expressed in δ ppm. All the solvents used were analytical grade. The purity of the compound was checked by TLC using silica gel plates.

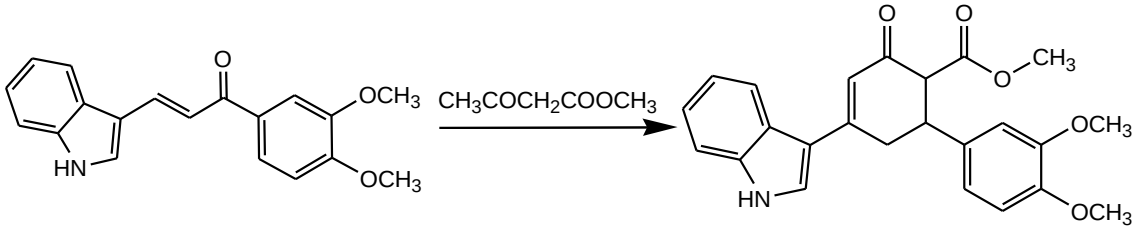
General Method of Preparation of Chalcone

2,3-dimethoxy acetophenone and Indole–3–carboldehyde were commercially purchased (Aldrich) and used as received. HPLC–grade organic solvents were used for the TLC. Equimolar quantity of 2,3-dimethoxy-acetophenone (0.01 mol) and Indole–3–caboldehyde (0.01 mol) were dissolved in 20 ml of ethanol was cooled to 5-10^{0}C in an ice bath. The reaction mixture was magnetically stirred for 3h. In the cold solution, 10 ml of 10% Sodium hydroxide solution was added drop wise. A flocculants precipitate was formed. The precipitate was filtered and washed with cold water and recrystallise from ethanol. The reaction mixture was purified by TLC on a silica gel column (n-hexane: acetone, 7:3).



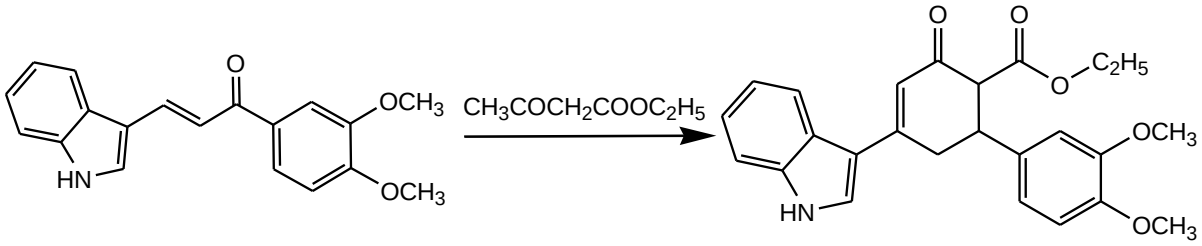
Preparation Of 6-(3, 4-Dimethoxy-Phenyl)-4-(1h-Indol-3-Yl)-2-Oxo-Cyclohex-3-Enecarboxylic Acid Methyl Ester

A mixture of 1-(3, 4-Dimethoxy-phenyl)-3-(1H-indol-3-yl)-propenone (0.001mol) and methylacetoacetate (0.001 mol) in ethanol was refluxed for 4 h in 10-15 mL of ethanol in the presence of 0.8 mL 10% NaOH. The reaction mixture was cooled and poured into 50 mL of ice cold water. The precipitate was collected by filtration and purified by recrystalization from ethanol. The progress of the reaction was monitored by TLC (3:10, methanol: chloroform) the obtained solid was crystallized from Et OH. Yield 70%, Colour- brown.



Preparation of 6-(3,4-Dimethoxy-phenyl)-4-(1H-indol-3-yl)-2-oxo-cyclohex-3-enecarboxylic acid ethyl ester

A mixture of 1-(3,4-Dimethoxy-phenyl)-3-(1H-indol-3-yl)-propenone (0.001mol) and ethylacetoacetate (0.001 mol) in ethanol was refluxed for 6h in 10-15 mL of ethanol in the presence of 10% 10 mL NaOH. The reaction mixture was cooled and poured into 50 mL of ice cold water. The precipitate was collected by filtration and purified by recrystallization from ethanol. The progress of the reaction was monitored by TLC (3:10, methanol: chloroform) the obtained solid was crystallized from EtOH. Yield 70%, Colour- brown.



RESULTS AND DISCUSSION

The results are obtained from various spectral data are results discussed below.

6-(3, 4-Dimethoxy-phenyl)-4-(1H-indol-3-yl)-2-oxo-cyclohex-3-enecarboxylic acid methyl ester (CMA): m.p. 121^{0}C. IR (KBr) cm^{-1}: 3167(N-H_{Str}), 1332(C-N_{Str}), 1633(C=C_{Str}), 2927(C-

H_{Str}), 638-788(C-H_{def}), 1633(C=N_{Str}), and 1726 (ester C-O_{Str}). ^{1}H NMR (DMSO)ppm: 7.0-8.2(Aromatic), 3.3(C-OCH_3), 2.5(CH_2) and 11.5(N-H).^{13}HNMR (DMSO)ppm: 106-134(Aromatic), 39(CH_3), 124(CH), 38(CH_2) and 39(C-OCH_2).

6-(3,4-Dimethoxy-phenyl)-4-(1H-indol-3-yl)-2-oxo-cyclohex-3-enecarboxylic acid ethyl ester (CEA): m.p. 110^{0}C. IR (KBr) cm^{-1}: 3107(N-H_{Str}), 1494(C-N_{Str}), 1523(C=C_{Str}), 2926(C-H_{Str}), 638-788(C-H_{def}), 1635(C=N_{Str}), and 1724 (ester C-O_{Str}). ^{1}H NMR (DMSO)ppm: 7.1-8.2(Aromatic), 3.3(C-OCH_3), 2.5(CH_2) and 12(N-H). ^{13}H NMR (DMSO)ppm: 112-123(Aromatic), 39(CH_3), 124(CH), 38(CH_2) and 39(C-OCH_3).

BIOLOGICAL EVALUATION

Antimicrobial activity

The antimicrobial activity of synthesized compounds was carried out using agar well diffusion method. The bacterial strains were collected from different infectious status of patients who had not administered any antibacterial and antifungal drugs for at least 2 weeks with the suggestions of an authorized physician, in Eumic analytical Lab and Research Institute, Tiruchirappalli, Tamilnadu state, India. The *in vitro* antimicrobial activity was carried out against 24 h culture of three bacterial strains *Moraxella, Enterobacter* and *Pseudomonas aeruginosa.* Three fungal strains were *Candida albicans, A.niger* and *Trichophyton*. The compounds were tested at 25, 50, 75 and 100µg/mL differend concentration against both bacterial and fungal strains. DMSO was used as a vehicle. *Erythromycin* and *Ciprofloxacin* were used as standard drugs for comparison of antibacterial and antifungal activities respectively. The zone of inhibition was compared with standard drug after 24 h of incubation at 37^{o}C for antibacterial activity and 8 h at 37^{o}C for antifungal activity.

Table–1: Bacterial and fungal activities of CMA

Organism CMA	**DMSO Extract added and Zone of inhibition (mm/ml)**				
	Control	25 µl	50 µl	75 µl	100 µl
Moraxella	11	12	15	17	19
Enterobacter	25	15	19	22	26
Pseudomonas aeruginosa	25	12	15	16	20
Candida albicans	13	13	15	18	20
A.niger	20	12	15	18	25
Trichophyton	10	12	15	20	24

Table–2: Bacterial and fungal activities of CEA

Organism CEA	**DMSO Extract added and Zone of inhibition (mm/ml)**				
	Control	25 µl	50 µl	75 µl	100 µl
Moraxella	10	12	14	16	20
Enterobacter	09	15	20	25	30

Pseudomonas aeruginosa	20	11	15	18	20
Candida albicans	10	11	12	14	16
A.niger	22	12	14	15	17
Trichophyton	09	11	13	15	18

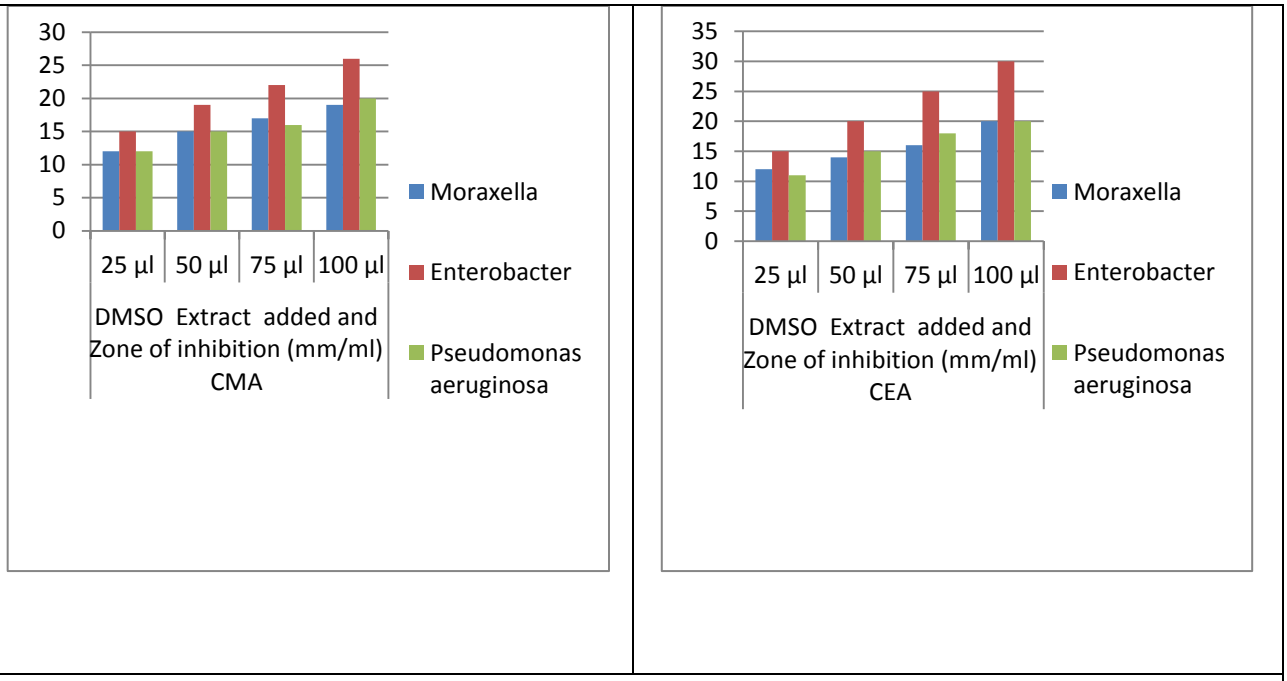


Figure-1: Graphical representation of antibacterial activity CMA and CEA

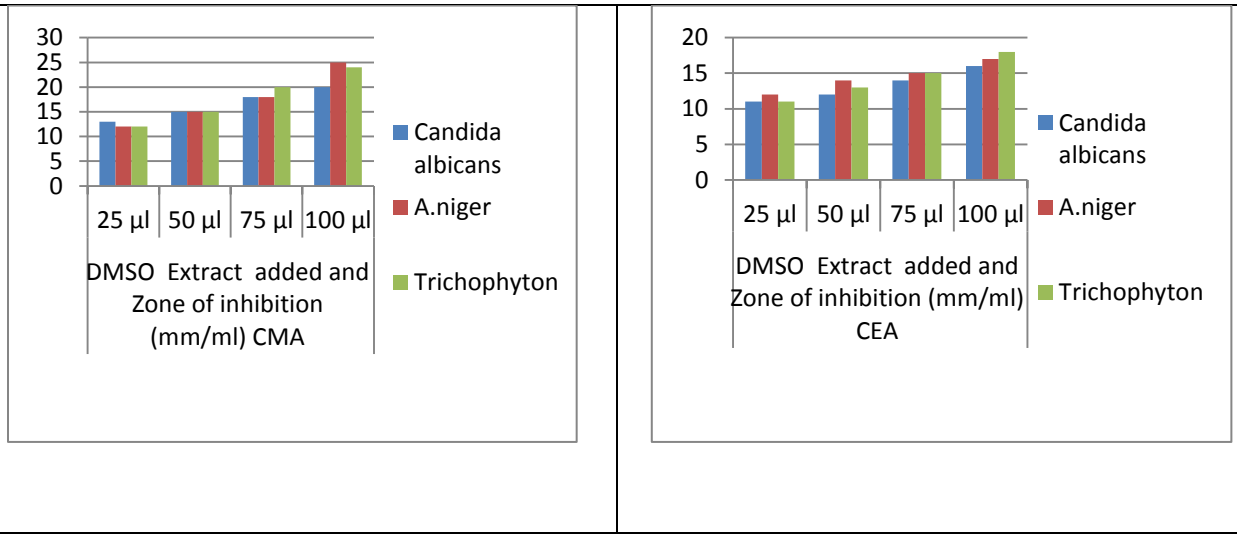


Figure-2: Graphical representation of antifungal activity CMA and CEA

CONCLUSION

A series of Chalcone derivatives were successfully synthesized and characterized spectroscopically by IR, ^{1}H and ^{13}C-NMR. All the synthesized products were screened for their *in - vitro* antibacterial and antifungal properties. The experimental results revealed that all compounds

displayed moderate to good antibacterial and antifungal activity with reference to the standard against the tested organisms.

ACKNOWLEDGEMENT

The authors are thankful to the Principal and Management of Jamal Mohamed College, Thiruchirappalli, Tamilnadu, India.

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