Original Article

Some chalcone derivatives as antimicrobial agents: Synthesis and characterization

Ashok Maddheshiya[1], Pooja Chawla[1,2]*

[1]Department of Pharmaceutical Chemistry, B.B.D.N.I.T.M., Lucknow, [2]Department of Pharmaceutical Chemistry, ISF College of Pharmacy, Moga

***Correspondence:**
Pooja Chawla, Department of Pharmaceutical Chemistry, ISF College of Pharmacy, Moga.
E-mail: pvchawla@gmail.com

How to cite this article: Maddheshiya A, Chawla P. Some chalcone derivatives as antimicrobial agents: Synthesis and characterization. Pharmaspire 2019;11(4):128-130.

Source of Support: Nil,
Conflicts of Interest: None declared.

ABSTRACT

Substituted chalcones were synthesized by condensing benzaldehyde derivatives with acetophenone derivatives in dilute ethanolic sodium hydroxide solution at room temperature according to Claisen–Schmidt condensation. In the presence of NaOH/EtOH as a catalyst, various substituted chalcones are synthesized. The reaction is clean with excellent yield. The structures of the synthesized compounds were confirmed by IR and mass spectroscopy.

Keywords: Chalcone, Claisen–Schmidt condensation, aldehydes, antimicrobial

INTRODUCTION

Chalcones are a group of compounds with various substitution patterns on the two aromatic rings of 1, 3-diphenyl-2-propen-1-one. Chalcones constitute an important class of natural products belonging to the flavonoid family and are reported to possess a wide spectrum of biological activities, including antibacterial, antifungal, anti-inflammatory, antitumor, insect antifeedant, analgesic, anti-mutagenic,[1-3] antiplatelet,[4] antiulcerative,[5] antitubercular,[6] immunomodulatory,[7] antihyperglycemic,[8] antimalarial,[9] anticancer,[10] antiviral,[11] antileishmanial,[12] antioxidant,[13] inhibition of chemical mediators release,[14] inhibition of leukotriene B_4,[15] inhibition of tyrosinase,[16] and inhibition of aldose reductase[17] activities. The presence of a reactive α, β-unsaturated ketone function in chalcones was found to be responsible for their antimicrobial activity.

Chemically, they consist of open chain flavonoids in which the two aromatic rings are joined by a three carbon α, β-unsaturated carbonyl system. The presence of a reactive α, β-unsaturated keto function in chalcones is found to be responsible for their antimicrobial activity. In recent years, a variety of chalcones have been reviewed for their cytotoxic, anticancer chemopreventive, and mutagenic as well as antiviral, insecticidal, and enzyme inhibitory properties.[18,19]

Several strategies for the synthesis of these systems, based on the formation of carbon-carbon bond were reported. Among them the direct aldol condensation and Claisen-Schmidt condensation still occupy prominent positions. The main method for the synthesis of chalcones was the classical Claisen-Schmidt condensation in the presence of aqueous alkaline bases,[20] $Ba(OH)_2$,[21] and LiOH microwave irradiation and ultrasound irradiation.[22] They are also obtained through Suzuki reaction,[23] Witting reaction, Friedel-Crafts acylation with cinnamoyl chloride, or photo-Fries rearrangement of phenyl cinnamates. In aldol condensation, the preparation of chalcones requires at least two-steps aldol formation and dehydration. Since aldol addition is reversible, mukaiyama, or Claisen-Schmidt condensation approach of using enol ether has emerged as an alternative pathway. A total of five derivatives were synthesized as shown in Scheme 1, Figure 1 and evaluated for antimicrobial activity. Physical characterisation of compounds is shown in Table 1.

Table 1: Physical characteristics of compounds (a-e).

Compound	R	%Yield	Melting range°C
a	*m*-NO_2	85.27	170–172
b	*p*-F	79.45	172–174
c	*m*-Cl	75.62	179–181
d	*p*-Cl	68.71	175–177
e	*p*-OCH_3	82.66	180–182

Access this article online

Website: www.isfcppharmaspire.com
P-ISSN: 2321-4732
E-ISSN: XXXX-XXXX

Antimicrobial activity

The antimicrobial activity of the synthesized compounds was evaluated using cup-plate method. Ciprofloxacin was used as standard drug. After the application of the inoculum, the plates were incubated for 24 h at temperature 37.5±5°C after that the standard and test samples in appropriate dilutions were applied and incubated for next 24 h at temperature 37.5±5°C, after that zone of inhibition was measured. The outcomes are listed in Table 2.[24]

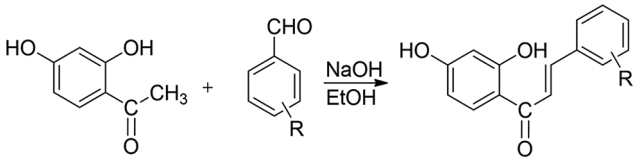
Experimental

The chemicals required were obtained from HiMedia Chem. Ltd, SD-Fine Ltd. and Sigma-Aldrich Pvt. Ltd and were used as such.

Melting points were determined using open capillary tube melting point apparatus and are uncorrected. Reaction progress was monitored by performing thin-layer chromatography on silica gel G plates, using iodine vapors and UV chamber as visualizing agents. After physical characterization, the compounds were subjected to spectral analysis. IR spectra were recorded in KBr on a SHIMADZU FT/IR-5300. The mass spectra were recorded on a JEOL-SX-102 instrument using ESI. Infrared spectra were taken on Perkin-Elmer AX-1 spectrometer and values are expressed in cm^{-1}.

Table 2: Antimicrobial activity

Compounds	Zone of inhibition in mm.			
	S. aureus	*B. subtilis*	*E. coli*	*P. aeruginosa*
A	14	16	17	15
B	19	18	20	22
C	13	14	17	15
D	18	22	17	18
E	19	21	17	20
Ciprofloxacin	28	27	32	29



Scheme 1: Synthetic diagram of 2,4 dihydroxy substituted chalcones

General procedure: Synthesis of substituted chalcones

Stirred the mixture of substituted acetophenone (0.01 mol) and substituted benzaldehyde (a-j) (0.01 mol) in ethanol (30 ml), with continuous stirring 30% NaOH or KOH(15 ml) was added dropwise. The solution was stirred for 2 h and was left over night. The reaction mixture was precipitated by addition of ice cold water. The precipitate thus obtained was the desired product.[25]

a. White amorphous solid: IR (KBr) cm^{-1}: ($^{-}$OH) 3070.46 cm^{-1}, (C=0) 1662.52 cm^{-1}, (C=C) 1608, 1448.44 cm^{-1}, (Ar-NO_2) 1529.45, 1352.01 cm^{-1}. Mass: m/z 285.3 (M^+).
b. White amorphous solid: IR (KBr) cm^{-1}: ($^{-}$OH) 3062.75 cm^{-1}, (C=0) 1660.60 cm^{-1}, (C=C) 1608, 1448.44 cm^{-1}, (Ar-F) 1529.45, 1352.01 cm^{-1}. Mass: m/z 258.4 (M^+).
c. White amorphous solid: IR (KBr) cm^{-1} : (-OH) 3070.46 cm^{-1}, (C=0) 1662.52 cm^{-1}, (C=C) 1606.59, 1477.37 cm^{-1}, (Ar-Cl) 1080.06 cm^{-1}. Mass: m/z 274.8 (M^+).
d. White amorphous solid: (–OH) 3060.82 cm^{-1}, (C=0) 1658.67 cm^{-1},(C=C) 1604.66, 1446.51 cm^{-1}, (Ar-Cl) 1091.63 cm^{-1}. Mass: m/z 274.6 (M^+).
e. Yellow amorphous solid: (-OH) 3060.82 cm^{-1}, (C=0) 1658.67 cm^{-1}, (C=C) 1604.66, 1446.51 cm^{-1}, (Ar-Cl) 1091.63 cm^{-1}. Mass: m/z 270.8 (M^+).

ACKNOWLEDGMENTS

The authors are thankful to management of BBDNITM Lucknow for providing necessary infrastructure.

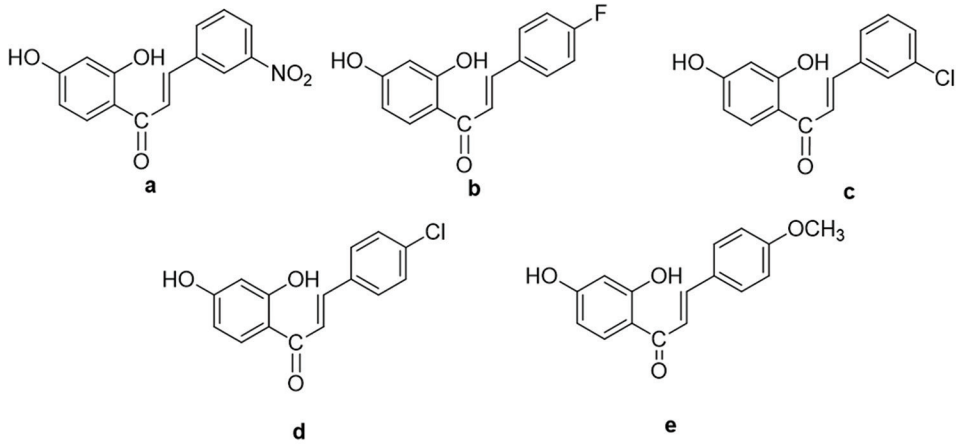


Figure 1: Structures of 2,4 dihydroxy substituted chalcones

CONCLUSION

Structures of the synthesized substituted chalcones were confirmed from their respective IR and mass-spectrometry studies. From the antimicrobial screening, it was observed that all the compounds exhibited activity against all the organisms employed. The compounds b and e, showed good antibacterial activity due to its electron donating properties whereas d showed moderate to good activity because of substitution on *p*-position while a and c showed comparatively lesser activity of all.

REFERENCES

1. Dimmock JR, Elias DW, Beazely MA, Kandepu NM. Synthesis and characterization of 4-hydroxy chalcones using PEG-400 as a recyclable solvent. Curr Med Chem 1999;6:1125-50.
2. Go X, Wu ML, Lui LX. Synthesis and characterization of 4-hydroxy chalcones using PEG-400 as a recyclable solvent. Curr Med Chem 2005;12:483-99.
3. Nowakowka Z. Synthesis and characterization of 4-hydroxy chalcones using PEG-400 as a recyclable solvent. Curr Med Chem 2007;42:125-37.
4. Viana GS, Bandeira MA, Matos F. Synthesis and antiviral activity of unsaturated ketones of thiopene series. J Phytomed 2003;10:189.
5. Mukarami S, Muramatsu M, Aihara H, Otomo S. Synthesis and antimicrobial activity of some chalcone derivatives. Biochem Pharmacol 1991;42:1447.
6. Kumar PM, Basu SK, Mukesh D. Synthetic chalcones as potential anti-inflammatory and cancer chemoprotective agents. Chem Pharm Bull 2007;55:144.
7. Satyanarayana M, Tiwari P, Tripathi K, Srivastava AK, Pratap R. A solid phase synthesis of chalcones by claisen-schmidt condensations. Bioorg Med Chem 2004;12:883.
8. Barford L, Kemp K, Hansen M, Kharazmi A. Synthesis and antimicrobial activity of some chalcone derivatives. Int Immunopharmacol 2002;2:545.
9. Liu M, Wilairat P, Go LM. Synthetic chalcones as potential anti-inflammatory and cancer chemopreventive agents. J Med Chem 2001;44:4443.
10. Francesco E, Salvatore G, Luigi M, Massimo C. Synthesis of chalcone and their derivatives as antimicrobial agents. Phytochemical 2007;68:939.
11. Onyilagna JC, Malhotra B, Elder M, Towers GH. Synthesis of benzimidazolyl chalcone derivatives. J Plant Pathol 1997;19:133.
12. Nielsen SF, Chen M, Theander TG, Kharazmi A, Christensen SB. A solid phase synthesis of chalcones by claisen-schmidt condensations. Bioorg Med Chem Lett 1995;5:449.
13. Miranda CL, Aponso GL, Stevens JF, Deinzer ML, Buhler DR. Synthesis and antimicrobial activity of some chalcone derivatives. Agric Food Chem 2000;48:3876.
14. Ko HH, Tsao LT, Yu KL, Liu CT, Wang JP, Lin CN. Synthesis of chalcone and their derivatives as antimicrobial agents. Bioorg Med Chem 2005;13:433.
15. Deshpande AM, Argade NP, Natu AA, Eckman J. Synthesis and antimicrobial activity of some novel chalcones containing 3-hydroxy benzofuran. Bioorg Med Chem 1999;7:1237.
16. Khatib S, Nerya O, Musa R, Shmnel M, Tamir S, Vaya J. Synthesis and biological evaluation of some heterocyclic derivatives of chalcones. Bioorg Med Chem 2005;13:433.
17. Severi F, Benvenuti S, Costantino L, Vampa G, Melegari M, Antolini L. An efficient and operationally simple synthesis of some new chalcones by using grinding technique. Eur J Med Chem 1998;33:859.
18. Won SJ, Liu CT, Tsao LT, Ko HH, Wang JP, Lin CN. Synthetic chalcones as potential anti-inflammatory and cancer chemoprotective agents. Eur J Med Chem 2005;40:103-12.
19. Yu DC, Panfilova LV, Boreko EI. Synthetic chalcones as potential anti-inflammatory and cancer chemoprotective agents. Pharm Chem 1982;16:103-5.
20. Prasad YR, Rao AL, Rambabu R, Kumar PR. Synthesis and antiviral activity of unsaturated ketones of thiopene series. Orient J Chem 2007;23:927-37.
21. Rao MS, Kotesh J, Narukulla R, Duddeck H. Synthesis and antimicrobial studies of some novel isoxazoline derivatives. Arkivoc 2004;14:96-102.
22. Calvino V, Picallo M, Lopez-Peinado AJ, Martin-Aranda RM, Duran-Valle C. Synthesis and characterization of 2, 4-dihydroxy substituted chalcones using aldol condensation by $socl_2$/EtOH. J Appl Surf Sci 2006;252:6074.
23. Eddarir S, Catelle N, Bakkour Y, Ronlando C. Synthesis, characterization and antimicrobial activity of cu (ii), co (ii) and ni (ii) complexes with O, N, and S donor ligands. Tetrahedron Lett 2003;44:5359-63.
24. Bakkour Y. Theander TG, Kharazmi A, Christensen SB. A solid phase synthesis of chalcones by claisen-schmidt condensations. Bioorg Med Chem 1995;6:449-52.
25. Severi F, Benvenuti S, Costantino L, Francesco E, Salvatore G, Duran-Valle C. Synthesis and biological evaluation of some heterocyclic derivatives of chalcones. Bioorg Med Chem 2008;15:445-9.