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SYNTHESIS, CHARACTERIZATION AND ANTIMICROBIAL ACTIVITY OF CHALCONES, PYRAZOLINES AND PYRIMIDINE DERIVATIVES

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ABSTRACT

A new series of chalcones and their derivatives like pyrazolines, aminopyrimidine, and thiazine have been synthesized. All the synthesized compounds were characterized by spectroscopic methods and screened for their antimicrobial activity they show moderate antimicrobial activity.

KEYWORDS: chalcones, pyrazolines, thiazines, Anti-microbial activity.

INTRODUCTION

Chalcone is α, β unsaturated carbonyl compound in which two aromatic rings joined by three carbons (α, β unsaturated carbonyl system).[1] The Presence of α, β unsaturated carbonyl group is responsible for various biological activities like antimicrobial, antifungal, antibacterial[2-3], anti-inflammatory[4], antimalarial[5] anti-tubercular[6] antidiabetic[7] antileishmanial.[8]

Commonly chalcone can be synthesized by aldol and Claisen-Schimdt reaction of substituted benzaldehyde with substituted acetophenone under basic condition. There are many more methods that have been reported for the synthesis of chalcones.

Chalcone act as the central core for the synthesis of various heterocycles like pyrazolines, oxazolines, thiazine, amino pyrimidine, etc. which shows promising biological activity.

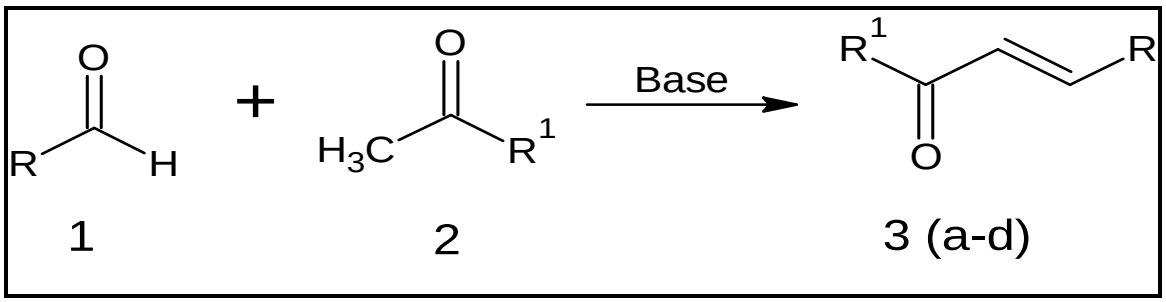
In this article we report the synthesis of chalcone derivatives and heterocyclic compound namely pyrazolines, aminopyrimidine, thiazine studies their biological activity.

Experimental details

The melting point of the synthesized compound was determined in open capillary tubes and are uncorrected. Compounds synthesized and structure confirmed by IR and ^{1}H NMR spectroscopy. Infrared spectra were recorded on schimadzu FT-IR spectrophotometer.^{1}H NMR spectra recorded on a Bruker AM-500 spectrometer with tetramethylsilane as an internal standard.

a) The general method for synthesis of chalcone.[9-11]

An equimolar mixture of (0.01 mole) substituted acetophenone/ketone and substituted benzaldehyde was dissolved in ethanol in 50 ml in the presence of 40% NaOH for 3 to 4 hr. on the magnetic stirrer. After the completion of the reaction mixture was cooled, diluted with cold-water and acidified with 1:1 HCI. The product was filtered, dried, and recrystallized.



Scheme 1: Synthesis of Chalcone.

Table 1: Substituted benzaldehyde and substituted ketone.

Sr.No.	R	R^1
3a	4-Isopropyl phenyl	4-Ethyl-phenyl
3b	4-Isopropyl phenyl	4-fluorophenyl
3c	4-Isopropyl phenyl	4-Chlorophenyl
3d	3,4,5-trimethoxy phenyl	Isobutyl

(2*E*)-1-(4-ethylphenyl)-3-[4-(propan-2-yl) phenyl] prop-2-en-1-one (3a)

IR (KBr ν cm^{-1}): (C=O) 1625 cm^{-1} , (C=C) 1552-1584 cm^{-1}, aromatic(C-H) 3116 cm^{-1}

^{1}H NMR ($CDCl_3$) δ ppm: 1.2 (d, 6H),2.9(m,1H), 1.3 (t,3H), 2.2(quartet 2H),7.8 (d ,1H J= 16 Hz), 7.4 (d,1H J=16Hz) ,6.9 (d,2H), 7.8(d 2H), 7.5(d 2H), 7.7(d,2H)

(2*E*)-1-(4-fluorophenyl)-3-[4-(propan-2-yl) phenyl] prop-2-en-1-one (3b)

IR (KBr ν cm^{-1})): (C=O) 1654 cm^{-1}, (C=C) 1554-1593 cm^{-1}, aromatic(C-H) 2963 $cm^{-1,}$ (C-F) 640cm^{-1}, ^{1}H NMR ($CDCl_3$) **δ** ppm: 1.2 (d, 6H), 2.6(m, 1H), 7.4 (d, 1H J= 16Hz), 7.76 (d, 1H J=16Hz), 7.4 (d, 2H), 7.76(t 2H), 7.34(d 2H), 7.42(d, 2H)

(2*E*)-1-(4-chlorophenyl)-3-[4-(propan-2-yl) phenyl] prop-2-en-1-one (3c)

IR (KBr ν cm^{-1})): (C=O) 1625 cm^{-1}, (C=C) 1540-1583 cm^{-1}, aromatic(C-H) 2943 $cm^{-1,}$ (C-Cl) 550cm^{-11}H NMR ($CDCl_3$) **δ** ppm: 1.2 (d, 6H), 2.6(m, 1H), 7.4 (d, 1H J= 15.5 Hz), 7.76 (d, 1H J=15.5 Hz), 7.4 (d, 2H), 7.5(d 2H), 7.34(d 2H), 7.42(d, 2H)

(1*E*)-5-methyl-1-(3, 4, 5-trimethoxyphenyl) hex-1-en-3-one (3d)

IR (KBr ν cm^{-1})): (C=O) 1635 cm^{-1}, (C=C) 1556-1591 cm^{-1}, aromatic(C-H) 3031 $cm^{-1,}$ (C-O) 1105 cm^{-1} ^{1}H NMR ($CDCl_3$) **δ** ppm: 1.1(d 6H), 1.4(m 1H), 2.6 (d, 2H) 7.3 (d, 1H J= 16 Hz), 7.72 (d, 1H J=16 Hz), 7.2 (s, 2H)

b) General method for synthesis of heterocyclic derivative[10-12]

I) Synthesis of 4-(2-methylpropyl)-6-(3, 4, 5-trimethoxyphenyl) pyrimidin-2-amine (4a)

To the mixture of chalcone (0.01 mol), guanidine hydrochloride (0.02mol) was added and potassium hydroxide (40%) in ethanol (30 ml) was heated under reflux on oil bath after 8 hrs. Reaction was completed. The reaction mixture poured into ice water and precipitate was formed, filtered the product and recrystallized from ethanol.

IR (KBr, ν cm^{-1}) 3410 cm^{-1}(N-H str.), 2956(=C-H str.), 1648 cm^{-1}(C=N str.), 1060 cm^{-1}(C-O-C str.) ^{1}H NMR ($CDCl_3$) **δ** ppm: 0.96(d,6H),1.95(m,1H),2.0(d,2H),3.85(s,9H),6.5(s, 2H), 4.6(bs,1H), 6.8 (bs,1H), 5.06(s,1H),7.6(s,1H)

II) Spectra of compound II 4-(2-methylpropyl)-6-(3, 4, 5-trimethoxyphenyl)-3, 4-dihydropyrimidine-2(1*H*)-thione (4b)

To the mixture of chalcone (0.01 mol), thiourea (0.02mol) was added and potassium hydroxide (40%) in ethanol (30 ml) was heated under reflux on an oil bath. Progress of the reaction is monitored by TLC, after 8 hrs. The reaction was complete. The reaction mixture poured into ice water and precipitate was formed, filtered the product, and recrystallized from ethanol.

IR (KBr *v* cm^{-1}) 2956(=C-H str.), 1550-1611 cm^{-1}(C=C str.) 1136 cm-1(C=S str.) 1648 cm^{-1}(C=N str.), 1060cm^{-1}(C-O-C str.) ^{1}HNMR($CDCl_3$)δppm 0.96(d,6H),1.95(m,1H), 2.0(d,2H), 3.85(s,9H) ,6.5(s, 2H), 4.6(bs,1H), 6.8(bs,1H), 5.06(s,1H),7.6(s,1H)

III) Synthesis of Pyrazolines[13]

To the mixture of chalcone (0.01 mol), hydrazine hydrate /phenyl hydrazine (0.02mol) was added in glacial acetic acid (30 ml) was heated under reflux on an oil bath, after 10 hrs. The reaction was complete. The reaction mixture poured into ice water and precipitate was formed, filtered the product, and purified by column chromatography.

3-(4-ethylphenyl)-1-phenyl-5-[4-(propan-2-yl) phenyl]-4, 5-dihydro-1*H*-pyrazole (5a)

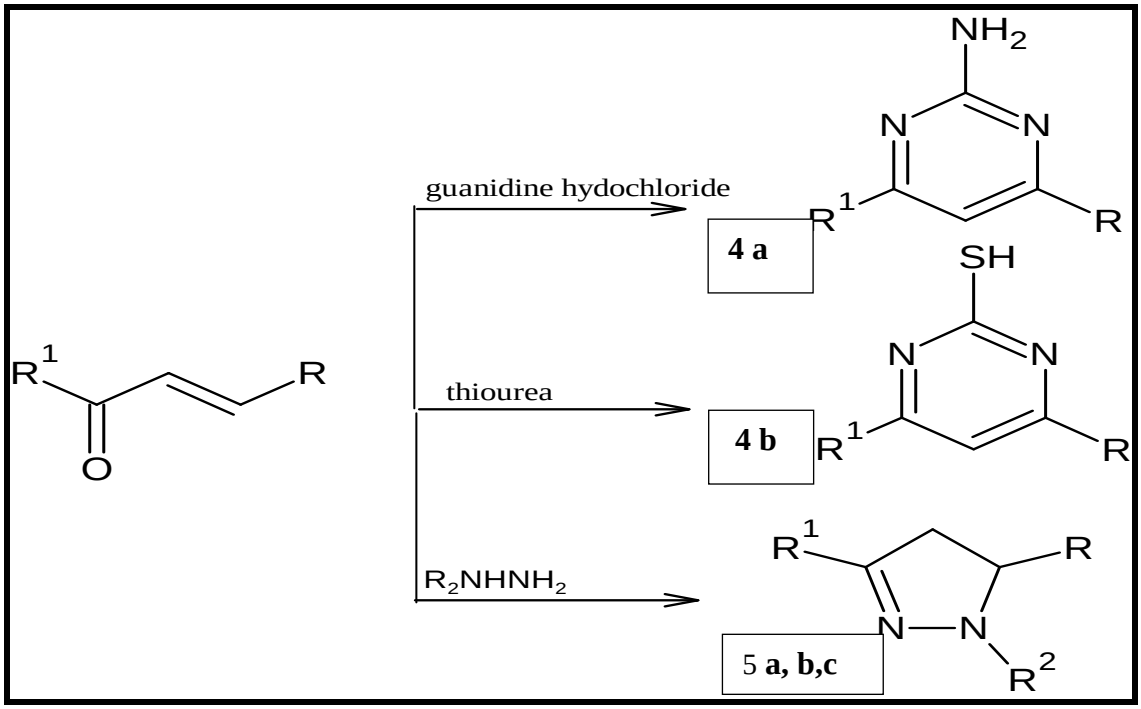
IR (KBr *v* cm^{-1}) 3066 cm^{-1}(aromatic C-H), 2936(aliphatic C-H) 1664 cm^{-1} (C=N), 1550-1594 cm^{-1} (aromatic C=C), 1429 cm^{-1} (aliphatic C-C) ^{1}H NMR (CDCl3) **δ** ppm 1.28 (d 6H), 2.58(m,1 H),1.28 (t,3 H),2.69(m 2H) ,3.67(dd,1 H),3.04((dd,1H),7.23 -7.16 (m,5H), 7.1-7.26 (m 4H), 7.83(d,2H),6.77(d,2H)

3-(4-chlorophenyl)-1-phenyl-5-[4-(propan-2-yl) phenyl]-4, 5-dihydro-1*H*-pyrazole (5b)

IR (KBr *v* cm^{-1}) 3084 cm^{-1}(aromatic C-H), 2924(aliphatic C-H) 1668cm^{-1} (C=N), 1596cm^{-1} (aromatic C=C), 1429 cm^{-1} (aliphatic C-C) ^{1}H (CDCl3) NMR **δ** ppm 1.28 (d 6H), 2.58(m,1 H),1.28 (t,3 H),2.69(m 2H) ,3.82(dd,1 H),3.14((dd,1H),7.191-7.151(m,5H), 7.2-7.37 (m 4H), 7.83(d,2H),6.77(d,2H)

3-(4-fluorophenyl)-5-[4-(propan-2-yl) phenyl]-1*H*-pyrazole (5c)

IR (KBr *v* cm^{-1}) 3444(NH), 3072cm^{-1}(aromatic C-H), 2856(aliphatic C-H) 1686cm^{-1} (C=N), 1540-1592 cm^{-1} (aromatic C=C), 1387cm^{-1} (aliphatic C-C) ^{1}H NMR(CDCl3) **δ** ppm 1.28 (d 6H), 2.58(m, 1 H), 7.25 (s, 1H), 7.3 (d 2H), 7.6 (d, 2H), 7.4(d,2H),8.4(t,2H).



Scheme 2: Synthesis of Chalcone.

Table 2: Substituted pyrazolines.

Sr.No.	R	R^1	R^2
4a	3,4,5-trimethoxy phenyl	Isobutyl	--
4b	3,4,5-trimethoxy phenyl	Isobutyl	--
5a	4-isopropyl phenyl	4-ethyl-phenyl	Phenyl
5b	4-isopropyl phenyl	4-fluorophenyl	Hydrogen
5c	4-isopropyl phenyl	4-chlorophenyl	Phenyl

Biological study

All the synthesized compounds were evaluated for antimicrobial activity (by disc diffusion method) against various bacterial strains like Escheria coli, staphylococcus aureus, Bacillus subtilis, and salmonella Typhi and antifungal activity against Aspergillusflavus, Trichodermaviridae and candida albicans.

Table 3: Antimicrobial activity of synthesized compounds.

Product	Bacteria				Fungi			
Ec		Bs	St	Sa	An	Af	Pc	Ca
4a	10(25)	09(25)	10(25)	09(25)	08(25)	11(25)	08(25)	09(25)
4b	08(25)	06(25)	08(50)	07(50)	10(25)	10(25)	08(25)	10 (25)
5a	09(25)	06(25)	09(25)	06(25)	10(25)	12(25)	08(25)	09(25)
5b	12(25)	08(25)	07(25)	08(50)	11(25)	08(25)	06(25)	10 (25)
5c	08(25)	08(25)	07(25)	10(25)	10(25)	10(25)	09(25)	10 (25)
Penicillin	15(25)	17(25)	13(25)	13(25)	NA	NA	NA	NA
Nystatin	NA	NA	NA	NA	16(25)	14(25)	13(25)	13(25)

Zone of inhibition expressed in mm.

The zone of inhibition is expressed in mm.

Ec-*Escherichia coli*, An-*Aspergillus niger*,

Sa-*Staphylococcus aureus*, Af-*Aspergillus flavus*,

Bs- *Bacillus subtillis*, Pc- *p.crosogenum*,

St-*Salmonella Typhi*, Ca- *Candida albicans*,

-- No activity, NA-Not Applicable

CONCLUSION

We have been successfully synthesized chalcones and their derivatives mainly pyrazolines, aminopyrimidine, and thiazine and characterized by IR, ^{1}H NMR spectroscopy. All the synthesized compounds were subjected to anti-bacterial and anti-fungal activity, they show moderate activity.

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Conflict of interest

The authors declare no conflict of interest.

REFERENCES

1. Prasad YR, Rao AL and Rambabu R.Synthesis and Antimicrobial Activity of some Chalcone Derivatives. E-Journal of Chemistry, 2008; 5(3): 461-466.
2. Dimmock JR, Elias DW, Beazely MA, Kandepu NM. Bioactivities of chalcones. Curr. Med Chem, 1999; 6: 1125–49. [PubMed]
3. Go ML, Wu X, Liu XL. Chalcones: an update on cytotoxic and chemoprotective properties. Curr Med Chem, 2005; 12: 483–99. [PubMed]
4. Israf, D.; Khaizurin, T.; Syahida, A.; Lajis, N.; Khozirah, S. Cardamonin inhibits COX and iNOS expression via inhibition of p65NF-_B nuclear translocation and I_-B phosphorylation in RAW 264.7 macrophage cells. Mol. Immunol, 2007; 44: 673–679. [CrossRef] [PubMed]

5. Singh, P.; Anand, A.; Kumar, V. Recent developments in biological activities of chalcones: A mini-review. *Eur. J. Med. Chem*, 2014; *85*: 758-777.
6. Gaonkar, S.; U N, V. Synthesis and pharmacological properties of chalcones: a review. *Res. Chem. Intermed*, 2017; *43*: 6043-6077.
7. Mahapatra, D.K.; Asati, V.; Bharti, S.K. Chalcones, and their therapeutic targets for the management of diabetes: Structural and pharmacological perspectives. *Eur. J. Med. Chem*, 2015; *92*: 839- 865.
8. Mahapatra, D.K.; Bharti, S.K.; Asati, V. Chalcone scaffolds as anti-infective agents: Structural and molecular target perspectives. *Eur. J. Med. Chem*, 2015; *101:* 496-524.
9. Vishal D Joshi, Mahendra D Kshirsgar and Sarita Singhal, *Int J Chem Tech Res*, 2012; 4(3): 971-975.
10. Sadgir, N.V., Dhonnar, S.L., Jagdale, B.S. *et al.* Synthesis, spectroscopic characterization, XRD crystal structure, DFT and antimicrobial study of (2E)-3-(2,6-dichlorophenyl)-1-(4-methoxyphenyl)-prop-2-en-1-one. *SN Appl. Sci*, 2020; 2: 1376. https://doi.org/10.1007/s42452-020-2923-9
11. Sadgir N. V, Dhonnar S. L, Jagdaleb B, Waghmare B, Sadgird C, Synthesis, Spectroscopic characterization, Quantum Chemical studyand antimicrobial study of (2E) -3-(2, 6-dichlorophenyl) -1-(4-Fluoro) -prop-2-en-1-one.Mat. Sci. Res. India, 17(3).
12. Chern J H, Shia K S, Hsu A H, Chia-Liang T, Chung-Chi L, Yen-Chun L, Chih- Shiang C, Sung-Nien T and Shin-Ru S, *Biorg Med Chem Lett*, 2004; 14: 2519-2525.
13. Agarwal A, Srivastawa K, Puri S K, Sinha S and Chauhan P M S, *Biorg Med Chem Lett*, 2005; 15: 4923-4926.
14. Chandra N, Ramesh A, Goyal N, Suryawanshi S N and Gupta S, *Eur J Med Chem*, 2005; 40(6): 552-556.
15. Ahmed Abdul Hassan AI-Kadhimi, Ahmed K AI-Khayate, Mohammed G ALDulyme, The F Scientific Conference the collage of Sciences, 2013.
16. Avila HP, Smania EF, Monache FD, Smania A. Structure-activity relationship of antibacterial chalcones. Bioorg Med Chem, 2008; 16: 9790–4.
17. Matos M.J., Vazquez-Rodriguez S., Uriarte E., Santana L. Potential pharmacological uses of chalcones: a patent review (from June 2011 – 2014) Expert Opin. Ther. Pat, 2015; 25: 351–366. [PubMed]