

**SYNTHESIS, CHARACTERIZATION AND BIOLOGICAL EVALUATION OF SOME
NEW PYRIMIDINE ANALOGUES**Prabhudev S. M.*¹, Yasmeen B.¹, Kishore Singh C.¹, H. J. Kallur¹, Samina Sultana¹¹Department of Pharmaceutical Chemistry, R.M.E.S's College of Pharmacy, Balaji Nagar, Old Jewargi Road, Kalaburagi-585102, Karnataka, India.***Corresponding Author: Dr. Prabhudev S. M.**

Department of Pharmaceutical Chemistry, R.M.E.S's College of Pharmacy, Balaji Nagar, Old Jewargi Road, Kalaburagi-585102, Karnataka, India.

Article Received on 08/03/2020

Article Revised on 29/03/2020

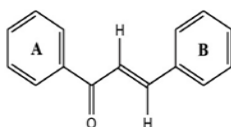
Article Accepted on 19/04/2020

ABSTRACT

In the present study, we focused on the environment-friendly processes used for the preparation of pyrimidine derivatives with pharmacological properties. In this regard, microwave heating is used as the alternative energy sources to synthesize a series of pyrimidine derivatives by the condensation of chalcones with urea under basic conditions. Chalcones were synthesized by Claisen-Schmidt condensation of acetophenone with various substituted benzaldehyde in the presence of ethanolic potassium hydroxide solution. The synthesized pyrimidine derivatives were characterized by IR, ¹H NMR, Mass Spectra and CHN analyses confirmed the structure of the prepared compounds. The newly synthesized pyrimidine derivatives were screened for their antimicrobial & anthelmintic activity.

KEYWORDS: Pyrimidine, Chalcone, Condensation, antimicrobial, anthelmintic activity.**INTRODUCTION**

Chalcones are α , β -unsaturated ketones consisting of two aromatic rings such as ring A and B. Both rings are interconnected by a highly electrophilic three carbon α , β -unsaturated carbonyl system that assumes linear or planar structure.



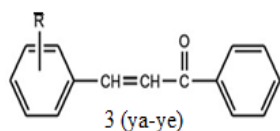
They possess conjugated double bonds and a completely delocalized π -electron system on both benzene rings. Chemically, chalcone is 1, 3-diphenyl- 2-propene-1-one. These are coloured compounds due to presence of the chromophore, ketoethylenic group ($-\text{CO}-\text{CH}=\text{CH}-$) in their structure. Chalcones are synthesized by claisen-schmidt condensation of ketone with different aromatic aldehydes by strong bases (NaOH/ KOH) or acid catalyzed followed by dehydration process. The presence of reactive α,β -unsaturated keto group in chalcones is found to be responsible for producing their biological activity. Chalcone derivatives are considered as key starting materials for the syntheses of different classes of heterocyclic compounds such as pyrazolines, oxazoles, isoxazoles, thiophenes and pyrimidines, etc. Among the heterocyclic compounds, Pyrimidine derivatives are valuable heteroaromatic compounds because of their wide spectrum of pharmacological applications such as antimalarial, anthelmintic, anticancer, antimicrobial, anti-convulsion and anti-inflammatory activities.

MATERIALS AND METHODS

All chemicals were of synthetic grade (S. D. Fine. Chem. Ltd. Mumbai, India). Both conventional and microwave synthesis was carried out to compare reaction time and yield of product. The microwave irradiated synthesis was performed in scientific microwave oven, Catalyst System (operating between 140-700 W). All the reactions were carried out at power level-2, which corresponds to 210 W. The synthesized products were recrystallized from ethanol as a solvent. Melting points were determined in open capillary tubes, expressed in ⁰C and are uncorrected. The time required for completion of the reaction and the purity of the compounds were checked by ascending TLC using pre-coated Silica gel-G plates and spots were observed by exposure to iodine vapours or by UV light at 254 and 366 nm. The compounds were characterized by using IR, ¹H NMR, Mass spectral and Elemental analysis. The IR spectra of the compounds were recorded on Shimadzu IR Affinity FT-IR using KBr discs and the values are expressed in cm^{-1} . The ¹H NMR spectra were recorded on a Bruker AC 400 MHz spectrometer using TMS as the internal standard in DMSO-d₆. The multiplicities of the signals are denoted with the symbols s, d, t and m for singlet, doublet, triplet and multiplet, respectively. The LCMS spectra were recorded on Waters Micromass Q-ToF Micro (70 eV), a hybrid quadrupole time of flight mass spectrometer. Elemental analyses of the newly synthesized compounds were carried out on Carlo Erba 1108 analyzer.

EXPERIMENTAL**Synthesis of Pyrimidine derivatives**

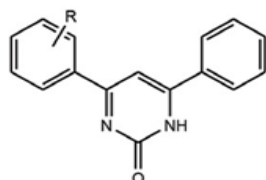
1. Synthesis of Chalcones (3ya-3ye):



R= H, 3-NO₂, 4-NO₂, 2-OH, 4-OH

Substituted benzaldehydes (1ya-1ye) (0.01 mol) and acetophenone (2) (0.01 mol, 1.2 g) were mixed and dissolved in ethanol (10 ml). To this, 40% aqueous solution of potassium hydroxide (10 ml) was added slowly with constant stirring. The reaction mixture was stirred continuously for 3 h at room temperature. The completion of reaction was confirmed by monitoring TLC using silica gel-G. After completion of the reaction, the reaction mixture was kept in refrigerator overnight. The product was filtered and washed with cold water till the washings were neutral to litmus, if necessary acidified with dilute HCl. The product was dried and recrystallized from rectified spirit to get pale yellow colored solid chalcones (3ya-3ye).

2. Syntheses of 4-(substituted-phenyl)-6-phenyl - pyrimidin-2(1h)-one (4ya-4ye)



R= H, 3-NO₂, 4-NO₂, 2-OH, 4-OH

Conventional Synthesis

A mixture of chalcone (3ya-ye) (0.01 mol), urea (0.01 mol, 0.6 g) were dissolved in ethanol (10 mL, 95%). To this, 40% aqueous potassium hydroxide solution (10 ml) was added slowly with constant stirring. The reaction mixture was allowed to reflux on water bath for 4 h. In between TLC was monitored to check the completion of reaction. After completion of reaction, the reaction mixture was cooled to room temperature and then poured into ice cold water and neutralized by adding dilute HCl. The precipitate (4ya-4ye) obtained was filtered, washed with water and dried. The product was recrystallized from rectified spirit. Conventional synthesis (yield 58-65%). All the synthesized compounds were soluble in methanol, ethanol, and dimethyl sulphoxide and insoluble in nonpolar solvents. The structures of prepared pyrimidine derivatives have been elucidated by spectroscopic data and elemental analysis.

Microwave Synthesis

A mixture of chalcone (3ya-3ye) (0.01 mol), urea (0.01 mol, 0.6 g) were dissolved in ethanol (10 ml, 95%). To this, 40% aqueous potassium hydroxide solution (10 ml) was added slowly with constant stirring. The reaction mixture was placed in microwave and irradiated at power level-2 (210 W) for 7-10 min. In between, TLC was monitored to check the completion of reaction condition. After completion of reaction, the reaction mixture was cooled to room temperature and then poured into ice cold water and neutralized by adding dilute HCl. The precipitate obtained was filtered, washed with water and dried. The product (4ya-4ye) was recrystallized from rectified spirit.

Table 1: Elemental Analysis of Titled Compound (4ya-4ye).

Compound Code	Molecular formula	Elemental Analysis (%)							
		Calculated				Found			
		C	H	N	O	C	H	N	O
4ya	C ₁₆ H ₁₂ N ₂ O	77.40	4.87	11.28	6.44	77.33	4.85	11.23	6.43
4yb	C ₁₆ H ₁₁ N ₃ O ₃	65.53	3.78	14.33	16.37	65.20	3.69	14.36	16.39
4yc	C ₁₆ H ₁₁ N ₃ O ₃	65.53	3.78	14.33	16.37	65.80	3.79	14.30	16.38
4yd	C ₁₆ H ₁₂ N ₂ O ₂	72.72	4.58	10.60	12.11	72.18	4.71	10.63	12.09
4ye	C ₁₆ H ₁₂ N ₂ O ₂	72.72	4.58	10.60	12.11	72.90	4.54	10.58	12.10

Table 2: Physical Characterization Data and Comparison between Conventional and Microwave Assisted Synthesis of Pyrimidine Derivatives (4ya-4ye).

Comp. Code	Structure (R)	Rf Value	M.P. (0C)	Conventional Method			Microwave Assisted Method			
				Time (h)	Energy (Temp. 0C)	Yield (%)	Time (min.)	Energy (Power. Watt)	Yield (%)	Atom Economy
4ya	H	0.64	88-91	3	98-100	60.65	7	210	78.48	65.52 %
4yb	3-NO ₂	0.66	201-204	4	98-100	60.85	9	210	82.73	71.47%
4yc	4-NO ₂	0.68	176-179	4	98-100	62.85	8	210	82.33	69.35%
4yd	2-OH	0.56	197-200	4	98-100	65.31	10	210	86.82	73.83%
4ye	4-OH	0.50	185-190	3	98-100	62.56	9	210	81.66	68.28%

The synthesized compounds were analyzed by their physical and chromatographic parameters. Further analysis by IR, NMR, and Mass spectroscopy was carried out to interpret the structure of the above synthesized compounds. The mobile phase selected for TLC study was n-hexane: ethyl acetate (70:30). The spectra of chalcones show usually a peak, near $1638\text{--}1670\text{ cm}^{-1}$, characteristic of α,β unsaturated carbonyl group. The α -H and β -H of chalcones resonate at δ 6.7-7.4 and δ 7.3-7.7 as two doublets ($J=17\text{ H}$) in the ^1H NMR spectra. The IR spectrum of pyrimidine derivatives (4ya-4ye) showed absorption at δ max $2961\text{--}2991\text{ cm}^{-1}$ (Ar-C-H), 1601 and 1610 cm^{-1} (Ar- NO_2), $1638\text{--}1670$ (C=O Str), 3168--

3316 cm^{-1} (pyrimidine-NH Str.), $3293\text{--}3302\text{ cm}^{-1}$ (Ar-OH) respectively. In the ^1H NMR spectrum, the proton of the -CH and -NH of pyrimidine nucleus resonated as a sharp singlet at δ 3.61 and 8.24 respectively. The aromatic protons were seen as a multiple at δ 6.74-8.02. The mass spectra of the pyrimidine derivatives exhibited molecular ion peak corresponding to their molecular formula. Compound 4ya and 4yb showed molecular ion peak at m/z 250 and 295 respectively. All the synthesized compounds showed significant anthelmintic activity. Among the tested compounds, 4ye showed potential anthelmintic activity 27 ± 0.66 and 35 ± 0.76 min for paralysis and death respectively as compared to the standard drug.

Characterization

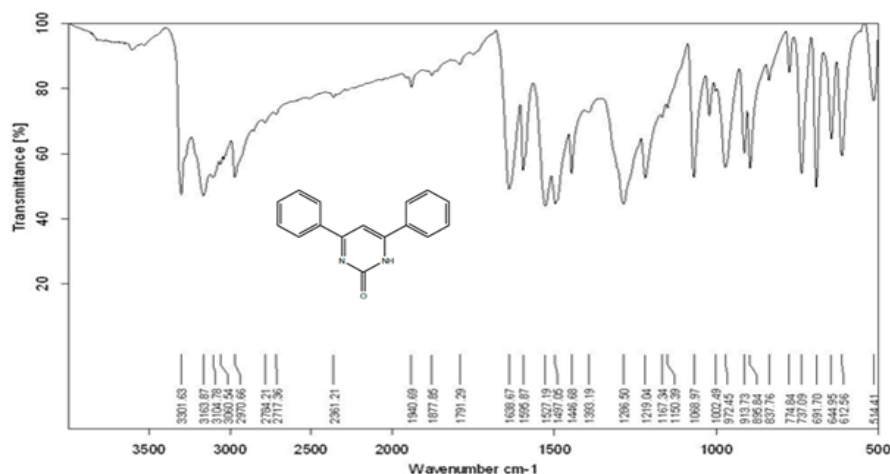


Figure No. 1: IR Spectra of 4, 6-di-phenyl-pyrimidin-2(1H)-one (4ya).

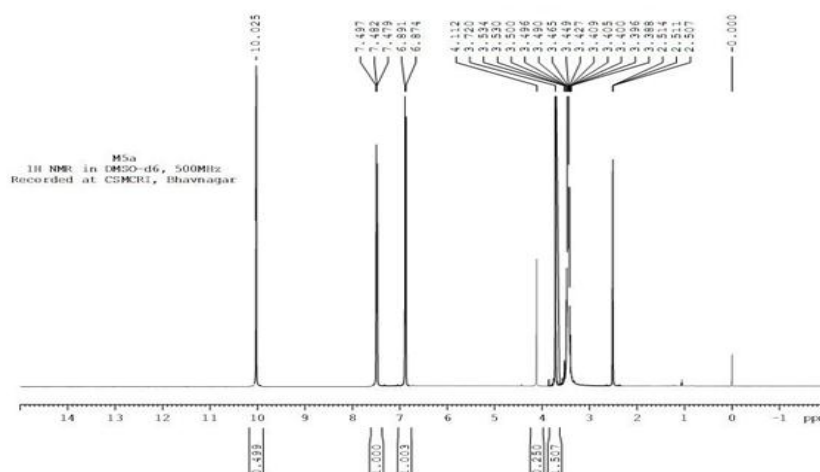


Figure No. 2: ^1H NMR Spectra of (4ya).

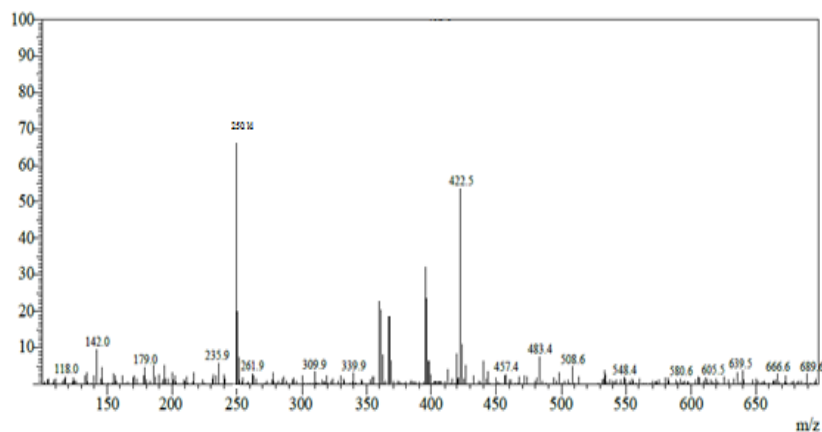


Figure No. 3: Mass Spectra of (4ya).

MS, m/z (%): Found for $C_{16}H_{12}N_2O$: 250.14. Molecular weight of the compound is 248 & the mass spectral data nearly matching the same as 250.14 m/z it shows that $M^+ + 1$ peak.

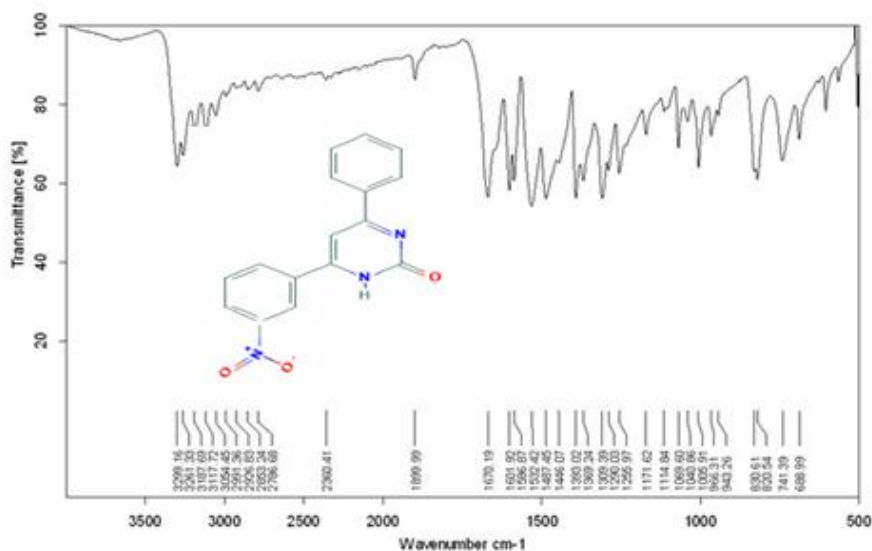


Figure No. 4: IR Spectra of 4-(3-nitro-phenyl)-6-phenyl-pyrimidin-2(1H)-one (4yb).

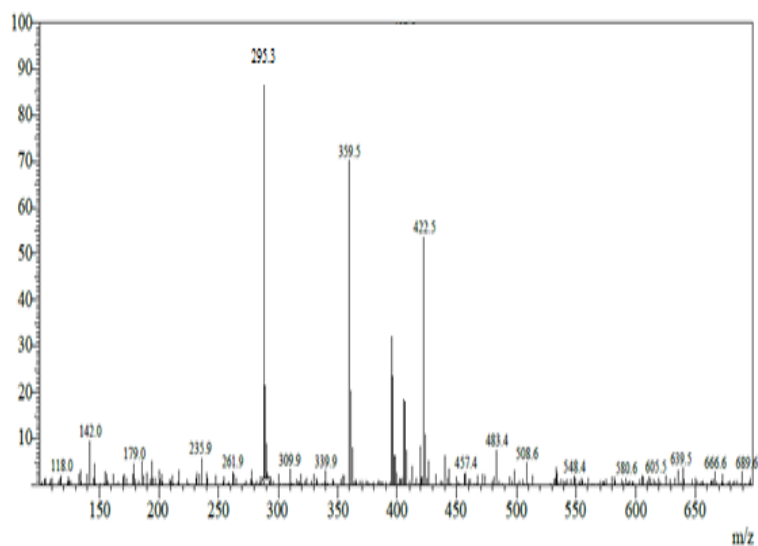


Figure No 5: Mass Spectra of (4yb).

MS, m/z (%): Found for C₁₆H₁₁N₃O₃: 295.3. Molecular weight of the compound is 293.4 & the mass spectral data nearly matching the same as 295.3 m/z it shows that M⁺+1 peak.

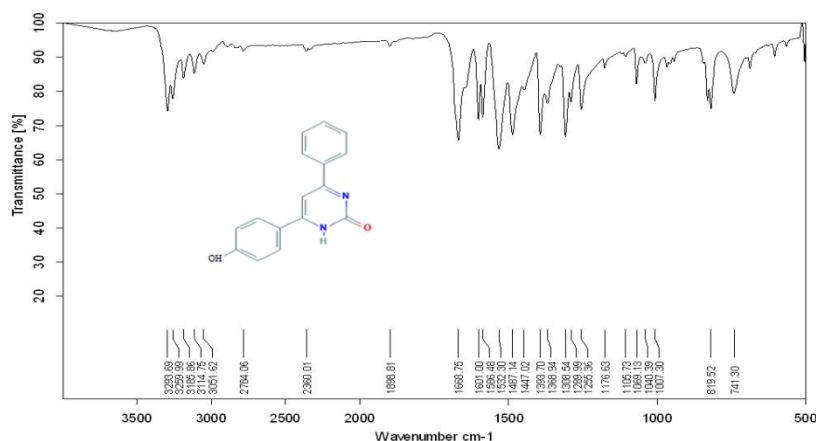


Figure No. 6: IR Spectra of 4-(4-hydroxy-phenyl)-6-phenyl-pyrimidin-2(1H) - one (4ye).

BIOLOGICAL EVALUATION ANTIBACTERIAL AND ANTIFUNGAL EVALUATION MATERIAL AND METHODS

Test samples

Pyrimidine Derivatives synthesized by conventional method are used for screening purpose. The test samples were dissolved in dimethylsulphoxide (DMSO) and the corresponding concentrations were expressed in terms of µg of compound per ml of solvent (µg/ml).

Test organisms

Clinically isolated four bacterial strains namely *Staphylococcus aureus*, *Bacillus subtilis*, *E. coli*, *Pseudomonas aeruginosa* and three different fungal strains namely, *Aspergillus niger*, and *Candida albicans* were collected from Department of Microbiology, M. R. Medical College, Gulbarga, India. The bacterial strains were grown in Mac Conkey agar plates at 37 °C and maintained on nutrient agar slants, while fungi were grown at 30 °C and maintained in Sabouraud glucose agar slants.

SCREENING FOR ANTIMICROBIAL ACTIVITY

The test was performed by disc diffusion assay as per NCCLS, 1993. The nutrient agar plates containing an inoculum size of 10⁶ cfu / ml for bacteria and 2×10⁵ spores for fungi on Sabouraud glucose agar plates were

used. Previously prepared compound impregnated disc (6mm in diameter) at the concentrations of 200 µg/ml for bacterial and 200 µg/ml for fungal strains were placed aseptically on sensitivity plates with appropriate controls Ciprofloxacin (200 µg/ml) and Griseofulvin (200 µg/ml) were used as standard antibacterial and antifungal antibiotics respectively. Plates were incubated at 37 °C for 24 hours for bacteria and 30 °C for 72 hours for fungal inoculums. Sensitivity was recorded by measuring the clean zone of growth inhibition on agar surface around the disc.

Determination of Minimum Inhibitory Concentration (MIC) by broth dilution method

MIC was determined by broth dilution method for each of the test organism. To 0.5 ml of varying concentrations of the compounds (0-200 µg/ml for bacterial strains and 0-200 µg/ml for fungal strains), 2ml of nutrient broth was added and then a loopful of test organism was introduced into the tubes. The procedures were repeated on the test organisms using standard antibiotics Ciprofloxacin and Griseofulvin. A tube containing nutrient broth only seeded with the test organisms served as control. Tubes containing bacterial cultures were then incubated at 37 °C for 24 hours for bacteria and 30 °C for 72 hours for fungal spores. After incubation the tubes were examined for microbial growth by observing the turbidity through spectroscopic method.

Table No 3: Antibacterial Activity of Synthesized Compounds.

Sl. No	Compound code (200 µg/ml)	<i>S. aureus</i> (mm)	<i>B. subtilis</i> (mm)	<i>E. coli</i> (mm)	<i>P. aeruginosa</i> (mm)
1	4ya	15.85 ± 0.10	13.29 ± 0.34	13.38 ± 0.01	12.19 ± 0.88
2	4yb	14.68 ± 0.34	13.90 ± 0.25	14.57 ± 0.48	13.02 ± 0.00
3	4yc	13.42 ± 0.20	13.44 ± 0.08	14.80 ± 0.01	13.65 ± 0.00
4	4yd	12.33 ± 0.65	12.00 ± 0.00	12.21 ± 0.30	14.66 ± 0.10
5	4ye	13.00 ± 0.23	14.72 ± 0.55	13.38 ± 0.07	15.33 ± 0.07
6	3ya	11.30 ± 0.23	11.21 ± 0.66	10.44 ± 0.40	12.12 ± 0.22
7	Ciprofloxacin	16.90 ± 0.10	14.95 ± 0.14	15.00 ± 0.09	17.00 ± 0.11

All values are expressed as mean ± S.E.M. of three replications

Table No 4: Antifungal Activity of Synthesized Compounds.

Sl. No	Compound code (200 µg/ml)	<i>A. niger</i> (mm)	<i>C.albicas</i> (mm)
1	4ya	12.21±0.34	12.39 ±0.00
2	4yb	11.06 ±0.07	09.88 ±0.23
3	4yc	14.18 ± 0.88	10.18 ±0.78
4	4yd	12.08 ±0.59	10.00 ±0.43
5	4ye	15.43 ±0.88	13.88 ± 0.88
6	3ya	10.23 ±0.08	10.38 ±0.02
7	GRISEOFULVIN	16.50 ±0.99	14.00 ±0.14

All values are expressed as mean ± S.E.M. of three replications

Table No 5: MIC of Synthesized Compounds for Bacterial strains.

Sl. No	Compound code (200 µg/ml)	<i>aphylococcus aureus</i>	<i>Bacillus subtilis</i>	<i>E. coli</i>	<i>Pseudomonas aeruginosa</i>
1	4ya	20	30	100	20
2	4yb	80	50	-	60
3	4yc	30	40	60	30
4	4yd	60	80	80	50
5	4ye	40	30	10	40
6	3ya	40	40	30	-
7	CIPROFLOXACIN	10	-	20	20

Table No 6: MIC of Synthesized compounds for fungal strains.

Sl. No	Compound code (200 µg/ml)	<i>A. niger</i>	<i>C. albicans</i>
1	4ya	50	40
2	4yb	60	90
3	4yc	10	40
4	4yd	60	80
5	4ye	30	60
6	3ya	60	20
7	Griseofulvin	10	20

From the data of the Table No 5 and Table No 6 of antibacterial and antifungal activity it is clearly concluded that the synthesized compounds are significant and moderate antibacterial and antifungal agents. The substituted Pyrimidine moieties are already known for different biological activities. Here we have synthesized some Pyrimidine analogues combining with different substituted aromatic system with view to get a good antibacterial and antifungal agents with less toxic and side effects. As per the results of screening it is clearly indicated that the compounds 4ya, 4yb, 4yc, 4yd and 4ye have shown significant antibacterial and compounds 4ya, 4yb, 4yc, 4yd and 4ye has shown significant antifungal activity with the standard drugs. This is because of the presence of different groups like –NO₂, -OH at the 4th positions of phenyl nucleus which is attached to Pyrimidine molecule. From the above results one can establish that the synthesized substituted Pyrimidine molecule can be rich source for the exploitation. Therefore in search of new generation of the active compounds, it may be worthwhile to explore the possibility in this area by introducing different functional groups or by cyclization as substitutions. Which may results into better pharmacological agents? The objective of the present work is to synthesize some

Pyrimidine derivatives and to study their antibacterial, antifungal activity, and antimicrobial activity thus an attempt has been made in this direction. As expected Pyrimidine derivatives exhibited significant and moderately antibacterial, antifungal activity and antimicrobial activity when compared with standard drugs respectively. Therefore further a detailed study of toxicity is necessary. There is no such a thing as completely safe drug. Drugs are powerful tools, which alter physiological processes for the better or for the worse. A society that wishes to benefit from them will not achieve all the benefits open to it, if it ignores the fact and seeks for impossible standards of harmlessness. Further the detailed structural activity relationship studies are required along with the molecular manipulation i.e. molecular modeling may give better drugs. Molecules prepared for the biological testing do not always turn out as potential new drugs, but may be intended to serve as models for evaluation of hypothesis.

ANTHELMINTIC ACTIVITY

Helminthiasis is a macroparasitic disease found in humans due to parasitic worms such as Nematodes or Cestodes which are present in skin, liver, brain, lungs, lymph, eye, muscles etc. of the body. The marketed

anthelmintic drugs are used to expel such parasitic worms from the body by either stunning or killing them without causing any significant damage to the host cell. Pyrimidine derived drugs such as pyrantel and morantel are commonly used as anthelmintic agents which has broad spectrum activity. Indian adult earthworms were selected to study the anthelmintic activity. The earthworms were collected from the water logged areas of soils in Kalaburagi, Karnataka, India. Earthworms were

washed with normal saline to remove all the fecal matter and waste surrounding their body. The earth worms (*Pheritima posthuma*) 5-8 cm in length and 0.2-0.3 cm width weighing 0.8-3.04 g were used for experimental protocols. As the earthworms are resembled anatomically and physiologically with the intestinal roundworm parasites of human beings, hence they were selected to study the anthelmintic activity.

Table No 7: Anthelmintic activity of titled compounds.

Sl.No	Compounds	Dose	Paralysis time (Minute)	Death time (Minute)
			Mean±S.E.M	Mean±S.E.M
1	4ya	100mg/mL	20±0.5	32±0.41
2	4yb	100mg/mL	25±0.529	32±0.36
3	4yc	100mg/mL	30± 0.763	35±0.61
4	4yd	100mg/mL	27±0.76	32±0.8
5	4ye	100mg/mL	27±0.66	35±0.76
6	3ya	100mg/mL	20±1.2	22±0.78
7	Control (Normal saline)	-----	-----	-----
8	Albendazole	100mg/mL	20±1.1	21±2.1

PROCEDURE

Gum acacia solution (1%) was prepared by using normal saline. Test solutions (100mg/ml) were prepared by using Gum acacia solution. Samples were taken in petriplates and adult healthy earth worms (n=6) were introduced into petriplates. Observations were made for the time taken to

paralyze and time taken for death of the earthworms. Paralysis was said to occur when the worms do not revive even in normal saline. Death was concluded when worms lost their motility followed by fading away of the body color and the values are summarized in Table 7 and in figure 7.

Effect of Pyrimidine Derivatives on *Pheritima Posthuma* (Earth Worms)

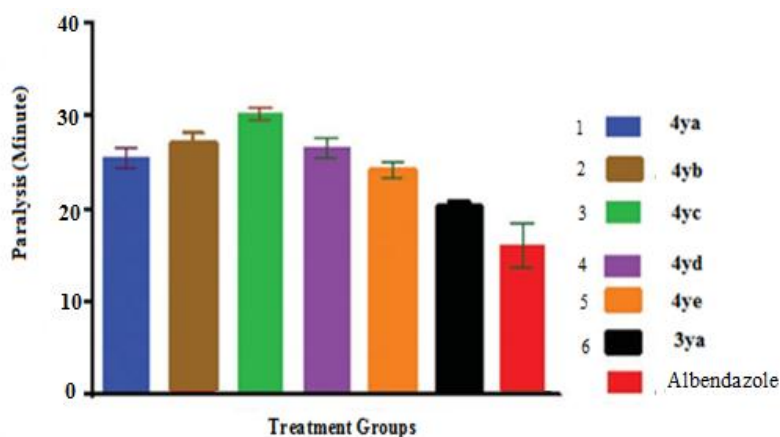


Figure No. 7: Anthelmintic activity (Paralysis time) of titled compounds.

RESULTS AND DISCUSSION

The chalcones were prepared by the Claisen Schmidt condensation of acetophenone with various substituted benzaldehyde (1ya-1ye) in the presence of ethanolic potassium hydroxide solution. Both conventional as well as microwave assisted methods followed to prepare a series of pyrimidine derivatives via chalcones by the treatment of chalcones with urea in basic media. The prepared compounds along with their reaction time period and

percentage yields were given in Table 2. It was found that the microwave assisted method is energetically favorable which requires less time with enhanced reaction rates and provides better yields (78-85%) with pure product as compared to the standard marketed miraculous drug.

CONCLUSION

In an attempt to develop new class of anthelmintic agents, a series of pyrimidine derivatives were efficiently synthesized with good yield and purity in less reaction time by microwave irradiated method as compared to conventional heating technique. Microwave irradiated synthesis is an invaluable technology which made the chemical reaction simple, rapid and eco-friendly to get the cleaner products. By the help of microwave synthesis, the yield of product was increased from 60 upto 86 % as compared to conventional synthesis which signifies the utility of green chemistry approach. Some of the synthesized compounds showed significant anthelmintic activity. Compound 4ye with electron withdrawing groups was found to be highly potent among the series. Thus, the quest to explore many more modifications on chalcone and pyrimidine moiety needs to be continued.

ACKNOWLEDGEMENT

I express my sincere gratitude and honest thanks to Department of Pharmaceutical Chemistry, R.M.E.S's College of Pharmacy, Gulbarga. has provided necessary facilities to carry out the work. I greatly acknowledge to my colleague's for their support and kind Co-operation.

REFERENCES

- Patil CB, Mahajan SK, Katti SA. Chalcone: A Versatile Molecule. *J Pharm Sci and Res.*, 2009; 1(3): 11-22.
- Nidhi S, Ahmad S, Alam MS. Biological Potentials of Chalcone: A Review. *Int J of Pharm and Biolog Arch.*, 2012; 3(6): 1298-303.
- Trivedi AR, Dodiya DK, Ravat NR, Shah VH. Synthesis and biological evaluation of some new pyrimidines via novel chalcone series. *ARKIVOC.* 2008; 11(1): 131-41.
- Kachroo M, Panda R, Yadav Y. Synthesis and biological activities of some new pyrimidine derivatives from chalcones. *Der Pharma Chemica.*, 2014; 6(2): 352-9.
- Ahmed MA. Synthesis, characterization and antibacterial activity of (E) +Chalcone derivatives. *Eur. J. Chem.*, 2013; 4(3): 207-10.
- Jyothi MV, Prasad YR, Venkatesh P, Reddy MS. Synthesis and Antimicrobial Activity of Some Novel Chalcones of 3-acetyl Pyridine and their Pyrimidine Derivatives. *Chem. Sci. Trans.*, 2012; 1(3): 716-22.
- Jin C, Liang Y, He H, Fu H. Synthesis and antitumor activity of novel chalcone derivatives. *Biomedicine and Pharma.*, 2013; 67(3): 215-7.
- Kachroo M, Panda R, Yadav Y. Synthesis and biological activities of some new pyrimidine derivatives from chalcones. *Pharm. Chem.*, 2014; 6(2): 352-9.
- Dudhe R, Sharma PK, Verma PK. Synthesis and biological activities of some new pyrimidine derivatives from chalcones. *Int J Res Dev Pharm Life Sci.*, 2015; 4: 1.
- Verma A., Sahu L, Chaudhary N, Dutta T, Dewangan D, Tripathi DK. A Review: pyrimidine their chemistry and pharmacological potentials. *Asian Journal of Biochemical and Pharmaceutical Research*, 2012; 1(2): 1-15.
- Arikkatt SD, Baldwin MV, Joseph J, Chandran M, Bhat AR, Kumar K. Pyrimidine derivatives and its biological potential-A review. *Int J of Org and Bio org Chem.*, 2014; 4(1): 1-5.
- Dansena H, Dhongade HJ, Chandrakar K. Pharmacological potentials of pyrimidine derivative: A Review. *Asian J Pharm Clin Res.*, 2015; 8(4): 171-7.
- Kaur N, Aggarwal AK, Sharma N, Choudhary B. Synthesis and *in-vitro* antimicrobial Activity of pyrimidine derivatives. *Int J of Pharm Sci and Drug Res.*, 2012; 4(3): 199-204.
- Mohana KN, Basavapatna N, Mallesha L. Synthesis and biological activity of some pyrimidine derivatives. *Drug Invent.*, 2013; 5(3): 216-22.
- Gupta YK, Gupta V, Singh S. Synthesis, characterization and antimicrobial activity of pyrimidine based derivatives. *J Pharm Res.*, 2013; 7(6): 491-5.
- Hussaina MMM, Bhat KI, Revanasiddappa BC, Bharathi DR. Synthesis and biological evaluation of some novel 2-mercapto pyrimidines. *Int J Pharm Sci.*, 2013; 5(2): 471-3.
- Bansal S, Chaudharya AN, Kothiyal P. Microwave assisted synthesis and antibacterial activity of pyrimidine derivatives. *Int J Pharm Pharm Sci.*, 2014; 5(1): 346-8.
- Madhavi A, Surati SJ, Desai KR. A brief review: Microwave assisted organic reaction, *Arch. Appl Sci Res.*, 2012; 4(1): 645-61.
- Ravichandran R, Karthikeyan E. Microwave synthesis-A potential tool for green chemistry. *Int J Chem Tech Res.*, 2011; 3(1): 466-70.
- Anastas P, Eghbali N. Green chemistry: principles and practice. *Chem Soc Rev.*, 2010; 39(1): 301-12.
- Sheldon RA. Fundamentals of green chemistry: efficiency in reaction design. *Chem Soc Rev.*, 2012; 41(4): 1437-51.
- Kappe CO, Dallinger D. The impact of microwave synthesis on drug discovery. *Nature Rev. Drug Discov.*, 2006; 5(1): 51-63.
- Gedye R, Smith F, Westaway K, Ali H, Baldisera L, La-berger L, *et al.* The use of microwave ovens for rapid organic synthesis. *Tetrahedron Lett.*, 1986; 27(3): 279-82.
- Kappe CO. Controlled microwave heating in modern organic synthesis. *Angew. Chem. Int Ed.*, 2004; 43(46): 6250-84.
- Dunn PJ. The importance of green chemistry in process research and development. *Chem Soc Rev.*, 2012; 41(4): 1452-61.