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SYNTHESIS AND ANTIMICROBIAL ACTIVITY OF 3, 4-DIHYDRO-4, 6-DIPHENYLPYRIMIDINE-2 (1*H*) -THIONE AND ITS DERIVATIVES

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ABSTRACT

Some new series of pyrimidine and its derivatives were synthesized by reacting different substituted 1, 3-diphenyl prop-2-en-1-one (Chalcones) with urea and thiourea in the presence of ethanolic alkali media, the obtained series of compounds i.e. substituted 3, 4-dihydro-4, 6-diphenylpyrimidine-2 (1H)-thione and 3, 4-dihydro-4, 6-diphenyl pyrimidine-2 (1H)-one respectively which are characterized by physical and spectroscopic data. All newly synthesized compounds were evaluated for their antimicrobial activity.

KEYWORDS

1, 3-diphenyl prop-2-en-1-one, Urea, Thiourea and Chalcones.

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INTRODUCTON

Chalcones are 1, 3-diphenyl prop-2-en-1-one, in which two aromatic rings are linked by a three carbon with α, β- unsaturated carbonyl system as, these are abundant in edible plants and are considered to be precursors of flavonoids and isoflavonoids. The Synthon is synthesized by condensation of aromatic aldehydes with acetophenone by claisen-schmidt condensation reaction[1-3]. Chalcones undergo a variety of chemical reactions which are useful in the synthesis different efficient heterocyclic compounds[4,5]. Like pyrimidine and thiazole derivatives. These derivatives are considered to be important for drugs and agricultural chemicals. They possess several interesting biological activities such as anticancer, anti-inflammatory, antiviral, antihypertensive,

anticonvulsant, antibacterial, antitumor, antifungal activities and so on[6]. On these observations, we are going to synthesize the effective substituted pyrimidine and thiazoles from Chalcones to increases its biological and pharmacological values[7-11].

Treatment of diseases with chemical substances has been known since the fifteenth century. Chemical agents not only provide the structure basis and energy supply of living organism but also regulate their functional activities. The interaction between potent chemical and living system contribute to the understanding of the life process and provide effective method for the treatment, prevention and diagnosis of many diseases. Fighting against diseases with drugs is the endless struggle. The field and scope of medicine is too vast. Various animal experiments have been designed to study the study the effect of drug on living organism and isolated tissue. These gave an insight into where and how a drug act. By knowledge of mode of action of a drug, its effect on various body system and probable adverse effects are important. Thus the search for new drugs with improved antibacterial activity and reduced toxicity is a continuous process. Chalcones are also intermediates in the Auwers synthesis of flavones.

The antibacterial activity[12-18] of synthesized compounds can be determined by screening them against the bacterial species using microbial method.

Generally, two methods used for the determination of antibacterial activity. Diffusion method and Turbidometric method or Tube assay method or dilution method. In Diffusion method, the test solution of substance is inoculated with culture medium. The substance in solution form to be tested is diffuses into agar medium. The concentration of substance in the agar medium decreases with the increase in distance as the substance move away from the interface. Ultimately, equilibrium is attained and the substance concentration becomes uniform throughout whole system. This results into zone of inhibited growth of zones. The diameter of this zone of inhibition reflects the concentration gradient established by diffusion of the substance into agar medium and the sensitivity of microorganisms to the substance. Turbidometric method is based on the growth of microbial culture in homogenous solution of the solute (test substance or antibiotics) in a fluid medium that is favorable to its rapid growth in the absence of solute or antibiotics. Then growth of organism is measured by determining the extinction at particular wavelength. This method has an advantage of a shorter incubation period for the growth of test organism i.e. 3 to 4 hours. This method is not suitable for cloudy or turbid preparation.

Experimental Section

All melting points were determined in open capillary tube and were uncorrected. IR spectra were recorded with potassium bromide pellets technique, ^{1}H NMR spectra were recorded on AVANCE 300 MHz Spectrometer in DMSO using TMS as internal standard. Mass spectra were recorded on a FT VG-7070 H Mass Spectrometer using EI technique at 70 eV. All the reactions were monitored by Thin layer chromatography.

Microbiology

The *in vitro* activities of the synthesized compounds Pyrimidine for tuberculosis inhibition against the *Mycobacterium tuberculosis* H37Rv (ATCC27294) strain were performed using the micro plate alomar blue assay (MABA) 24 method at TAACF. Compounds exhibiting fluorescence are tested in a BACTEC-460 radiometric system25, 26 and/or broth micro dilution assay. The activities are expressed as minimum inhibitory concentration (MIC, μg/mL). Compounds demonstrating at least 90 % inhibition were re-tested at lower concentrations to determine the actual MIC, a value defined as the lowest concentration inhibiting ≈ 90% of the inoculums relative to the control.

MATERIAL AND METHODS

Experimental

General procedure for synthesis of 3, 4-dihydro-4, 6-diphenylpyrimidine-2(1H)-thione and its derivatives

A mixture of [0.01M] of substituted 1, 3-diphenyl prop-2-en-1-one (chalcone) with [0.01M] of thiourea were refluxed in 30 ml ethanol with 10 ml

of 20 % NaOH on water bath for 6 hours. Then the reacting mixture was cooled and poured into crushed ice, then the solid product was precipitate out, then it was filtered, dried and recrystallized from ethanol gives substituted 3,4-dihydro-4, 6-diphenylpyrimidine-2(1H)-thione. The reaction is monitored by TLC. All the compounds are characterized by physical and spectral data

General procedure for synthesis of 3, 4-dihydro-4, 6-diphenylpyrimidine-2(1H)-one and its derivatives

A mixture of [0.01M] of substituted 1, 3-diphenyl prop-2-en-1-one (chalcone) with [0.01M] of urea were refluxed in 30 ml ethanol with 10 ml of 20 % NaOH on water bath for 6 hours. Then the reacting mixture was cooled and poured into crushed ice, then the solid product was precipitate out, then it was filtered, dried and recrystallized from ethanol gives substituted 3, 4-dihydro-4, 6-diphenyl pyrimidine-2(1H)-one. The reaction is monitored by TLC. All the compounds are characterized by physical and spectral data.

Antibacterial activity

For the antibacterial activities against these pathogens N.A. With following composition was used.

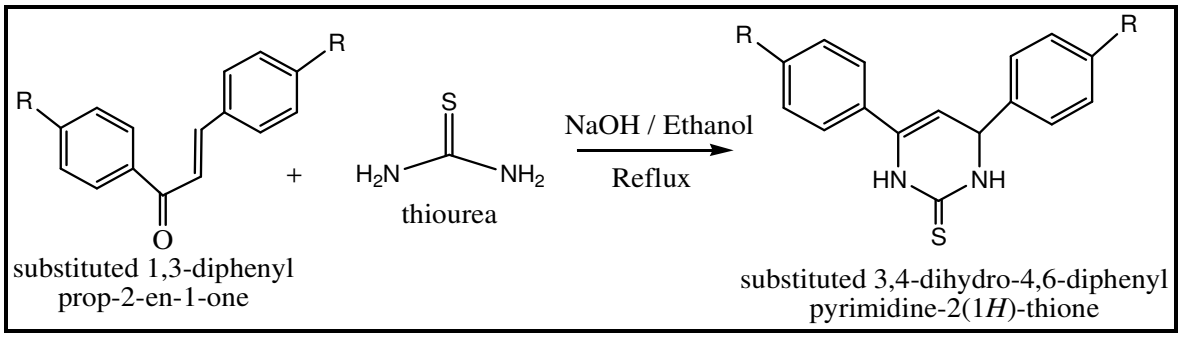
1. Peptone - 5 gm
2. Beef Extarct - 3 gm
3. Yeast Extract - 1.5 gm
4. NaCl - 8 gm
5. Agar -15 gm
6. D/W -1000 ml

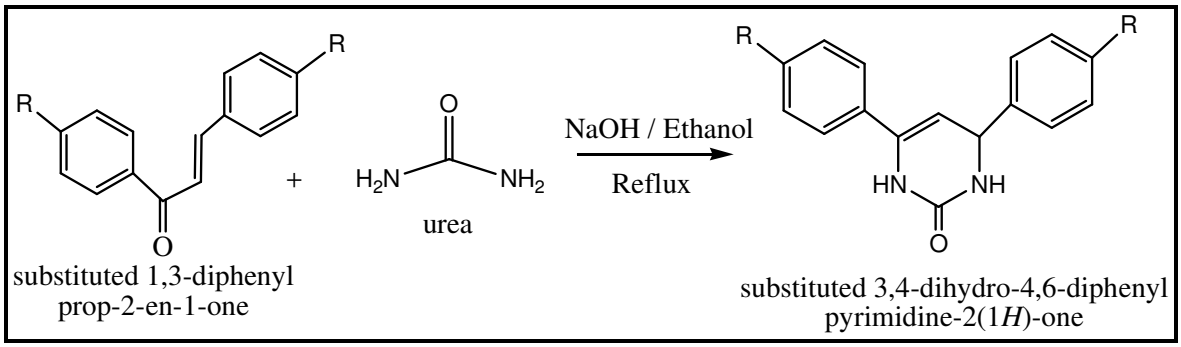
The agar diffusion method was employed for determine the antibacterial activity of the new synthesised comps. All comps. Were tested for antimicrobial activity using the agar diffusion technique on solid media by pour plate method, for bacteria N.A. Sterile 10mn diameter stainless steel cylinders placed on respective plates and boar had made which had been poured with respective compounds. Solution of different compounds at concentration of 200 mg/ml of the compounds were poured in the wells with the help of a sterile micropipette. The plates were thin incubated at 37^0C for 24 hours. The strength of antibacterial activity is reported by measuring the diameter of zone of inhibition in mm and results were standardized against standard antibiotic tetracycline.

RESULTS AND DISCUSSION

All the newly synthesized compounds were screened for antibacterial activity by using cup plate method by taking two standard concentrations i.e. 50 and 100µg/ml over a different bacterial strains. The values obtained is compared with the values produced from the standard drugs like Procaine penicillin, Streptomycin for bacterial strain and the dimethyl formamide (DMF) was used as control for both the strains. Some of the compounds show significant property compared with the standard and other shows moderate.

From the obtained results, it is evident that most of the compounds like BM- 2, 3, 6 and 8 possess very good activity against bacterial strains like *Streptococci, Pseudomonas aeruginisa*, *Staphylococcus arous* and *Escherichia coli* and remaining compounds showed moderate activity against all bacteria.





substituted 1,3-diphenyl prop-2-en-1-one

substituted 3,4-dihydro-4,6-diphenyl pyrimidine-2(1*H*)-one

CONCLUSION

Twenty compounds were screened for their antimicrobial activity against *Mycobacterium tuberculosis* H37Rv using a BACTEC-460 radiometric system. Chalcones and pyrimidines compounds are produces the highest efficiency and exhibited >90% inhibition at 6.25 ≈ µg/ml in the primary screening of these compounds. These newly synthesized compounds exhibited >90% inhibition against *Mycobacterium tuberculosis* at 6.25 µg/ml. This antimicrobial data clearly shows that, due to presence of 2-nitro, 3-nitro and 4-methoxy substitution on chalcone produced remarkable improvements in antibacterial activity.

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CONFLICT OF INTEREST

We declare that we have no conflict of interest.

BIBILIOGRAPHY

1. Chetana B. Patil, Mahajan S K, Suvarna A. Katti. Chalcone: A Versatile Molecule, *J. Pharm. Sci. and Res,* 1(3), 2009, 11-22.
2. Kalirajan R, Sivakumar S U, Jubie S, Gowramma B and Suresh B. Synthesis and Biological evaluation of some heterocyclic derivatives of Chalcones, *International Journal of Chem Tech Research,* 1(1), 2009, 27-34.
3. Rajendra Prasad Y, Praveen Kumar P, Ravi Kumar P and Srinivasa Rao A. Synthesis and Antimicrobial Activity of Some New Chalcones of 2-Acetyl Pyridine, *E-Journal of Chemistry,* 5(1), 2008, 144-148.
4. Ausra Voskiene, Vytautas Mickevicius, and Gema Mikulskieneb. Synthesis and structural characterization of products condensation 4-carboxy-1-(4-styrylcarbonylphenyl)-2- pyrrolidinones with hydrazines, *Arkivoc,* 15, 2007, 303-314.
5. Abdel-Razik H H and Said S B. Enaminonitrile in heterocyclic synthesis: synthesis and reactions of some pyrimidine derivatives, *Chem. Pep,* 58(3), 2004, 209-213.
6. Naik T A and Chikhalia K H. Studies on Synthesis of Pyrimidine Derivatives and their pharmacological evaluation, *E-Journal of Chemistry,* 4(1), 2007, 60-66.
7. Gurubasavaraja Swamy P M and Agasimundin Y S. Synthesis and Antimicrobial Activity of Some Novel Chalcones Containing 3-Hydroxy Benzofuran, *Acta Pharmaceutica Sciencia,* 50(3), 2008, 197-202.
8. Panda S S and Chowdary P V R. Synthesis of novel Indolyl-pyrimidine Antiinflammatory, Antioxidant and Antibacterial Agents, *Indian journal of pharmaceutical sciences,* 70(2), 2008, 208-215.
9. Indian pharmacopoeia controller of publication, *Delhi, India,* 9(1), 1996, 100.

10. Scoog, Lorley. Principles of Instrumental analysis, *Willison Book distributors, Mumbai Cambridge,* 4th Edition, 1971.
11. William Kemp. Infrared spectroscopy, organic spectroscopy, organic spectroscopy, *ELBS with Mc Millain,* 3, 1991, 19-96.
12. Hutchinson I, Chua M, Browne H I, Trapani V, Bradshaw T D, Westwell A D and Stevens M F G. Antitumor benzothiazoles. 14. Synthesis and *in vitro* biological properties of fluorinated 2-(4-aminophenyl) benzothiazoles, *J. Med. Chem,* 44(9), 2001, 1446-1455.
13. Catriona G M, Wells G, Crochard J P, Stone E L, Bradshaw T D, Stevens M F G, Westwell A D. Antitumor benzothiazoles. 26.(1) 2-(3, 4-dimethoxyphenyl)-5-fluorobenzothiazole (GW 610, NSC 721648), a simple fluorinated 2-arylbenzothiazole, shows potent and selective inhibitory activity against lung, colon, and breast cancer cell lines, *J. Med. Chem,* 49(1), 2005, 179-185.
14. Sirockin G and Cullimore S. Practical Microbiology, *Mc Graw Hill Publishing Co. Ltd., Londan,* 1969.
15. Lorian V. Antibiotics in Laboratory Medicine, *William and Wilkins, Baltimore,* 26(8), 1986, 452.
16. Pleczer M J Reid R D and Chan E C S. Microbiology, *Tata Mc Graw Hill Publishing Co. Ltd., London,* 1978.
17. Indian Pharmacopoeia, *Government of India Publication,* Volume 1 and 2, 1st Edition, 1996.
18. Bauer A W, Kirby W M M and Sherris J C. Antibiotic Susceptibility Testing by a Standardized Single Disk Method, *Am. J. Clin. Pathol,* 45(4), 1966, 493-496.

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