



**CONVENTIONAL SYNTHESIS AND ANTIBACTERIAL ASSAY OF NANOPARTICLES
OF SUBSTITUTED ARYL SUBSTITUTED 1,3-THIAZOLE**

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ABSTRACT

The synthesis, spectral analysis and biological activities of 5-phenyl-2-hydroxy-chlorosubstituted-2-amino-1,3-thiazoles have been carried out. In this case 5-(2'-hydroxy-3',5'-dichlorophenyl)-4-(4''-nitrobenzoyl)-2-phenyl-amino-1,3-thiazole (E) has been screened. The compound E was synthesized from 1-(2'-hydroxy-3',5'-dichlorophenyl)-2-bromo-3-(4''-nitrophenyl)-1,3-propanedione (a₄) by the action of phenylthiourea. The nanoparticles of the compound E has been prepared by using ultrasonic technique. The newly synthesized titled compound and it's nanoparticles were screened for their antibacterial activities against some *Gram positive Staphylococcus aureus and Streptococcus sp.* and *Gram negative Pseudomonas sp. and Solmonella typhi* pathogens. All the newly synthesized compounds were found to be active against test pathogens.

KEYWORDS: Chalcone, Thiazole, Phenyl Thiourea, antibacterial assay.

INTRODUCTION

Heterocyclic nucleus plays an important role in medicinal chemistry and it is a key template for the growth of various therapeutic agents. Thiazole is a heterocyclic compound featuring both a nitrogen atom and sulfur atom as part of the aromatic five-membered ring. Thiazoles and related compounds are called 1,3-azoles (nitrogen and one other hetero atom in a five-membered ring). They are isomeric with the 1,2- azoles, the nitrogen and sulphur containing compound being called isothiazoles. Thiazoles are found naturally in the essential vitamins. Molecules that possess sulfur atoms are important in living organisms. Chalcones and their analogues having α , β -unsaturated carbonyl system are very versatile substrates for the evolution of various reactions and physiologically active compounds. The researchers.^[1-6] have reported the synthesis of several thiazoles and also their potent biological activities such as antimicrobial,^[7] antibacterial,^[8] antifungal,^[9] fungicidal,^[10] and insecticidal agent.^[11]

Now a days nanotechnology is a promising field of interdisciplinary research. It opens up a wide array of opportunities in various fields like medicine, pharmaceuticals, electronics and agriculture. Since the physicochemical properties of nanoforms vary greatly, it becomes important to examine the effect of nanoparticles on microorganisms to harness the benefit of this technology in the plant protection especially against

phytopathogens. Previous studies confirmed that metal nanoparticles are effective against pathogens, insects and pests. Hence nanoparticles can be used in the preparation of new formulations like nanomedicines for the diseases like cancer,^[12] translocation of membrane protein,^[13] breast & liver cancer,^[14] cancer & HIV^[15]. Nanotechnology has the potential to revolutionize the different sectors of agriculture and food industry with modern tools for the treatment of diseases, rapid disease detection like intracranial aneurysms,^[16] inhibition tumour growth,^[17] blood, liver & brain cancer,^[18] enhancing cell efficiency & transparency of photovoltaic cell.^[19] In the present study, the chlorosubstituted 1,3-thiazine (E) has been prepared along with its nanoparticles and screened them for their antibacterial activities against some *Gram positive Staphylococcus aureus and Streptococcus sp.* and *Gram negative Pseudomonas sp. and Solmonella typhi* pathogens. All the newly synthesized compounds were found to be active against test pathogens.

MATERIALS AND METHODS

All the glasswares used in the present work were of pyrex quality. Melting point were determined in hot paraffin bath and are uncorrected. The purity of compound was monitored on silica gel coated TLC plate. IR spectra was recorded on Perkin-Elmer spectrophotometer in KBr pellets, ¹H NMR spectra on spectrophotometer in CDCl₃ with TMS as internal

standard. UV spectra was recorded in nujol medium. The analytical data of the titled compound was highly satisfactory. All the chemicals used were of analytical grade. All the solvents used were purified by standard methods. Physical characterisation data of all the compounds is given in Table 1.

2'-Hydroxy-3',5'-Dichloroacetophenone

2-Hydroxy-5-chloroacetophenone was dissolved in acetic acid (5 ml), Sodium acetate (3g) was added to the reaction mixture and then chlorine in acetic acid reagent (40 ml; 7.5 w/v) was added dropwise with stirring. The temperature of the reaction mixture was maintained below 200°C. The mixture was allowed to stand for 30 minutes. It was poured into cold water with stirring. A pale yellow solid then obtained was filtered, dried and crystallized from ethanol to get the compound 2'-hydroxy-3',5'-dichloroacetophenone.

Preparation of 2'-hydroxy-3',5'-dichlorophenyl-4-(4''-nitrophenyl) chalcone (a)

To the boiling solution of the 2-hydroxy-3,5-dichloroacetophenone (0.01 mol) and p-nitrobenzaldehyde (0.01 mol) in ethanol (20 ml) a 40% solution of NaOH was added gradually. The reaction mixture was stirred mechanically at room temperature for 1 hour and kept steady for 6 to 8 hours, followed by decomposition with ice cold HCl (1:1). The yellow granules thus obtained were filtered, washed with 10% NaHCO₃ solution and then crystallized from ethanol-acetic acid mixture to obtain the compound (a).

Preparation of 1-(2'-hydroxy-3',5'-dichlorophenyl)-2,3-dibromo-3-(4''-nitrophenyl)-propan-1-one (a₁):

2'-Hydroxy-3',5'-dichlorophenyl-4-(4''-nitrophenyl) chalcone (a) (0.001 M) was suspended in bromine-glacial acetic acid reagent (25% w/v) (6.4 ml).

The reagent was added dropwise with constant stirring and the reaction mixture was kept at room temperature for about 30 minutes. The solid product, thus separated, was filtered and washed with a little petroleum ether to get the compound (a₁).

Preparation of 2-(4''-nitrophenyl)-6,8-dichloroflavone (a₂):

1-(2'-Hydroxy-3',5'-dichlorophenyl)-2,3-dibromo-3-(4''-nitrophenyl)-propan-1-one (a₁) (0.01 mol) was dissolved in ethanol (25ml). To this, aqueous KOH solution (25 ml) was added. The reaction mixture was refluxed for 1 hour, cooled and diluted with water. The product thus separated was filtered and crystallized from ethanol to get the compound (a₂).

Preparation of 1-(2'-hydroxy-3',5'-dichlorophenyl)-3-(4''-nitrophenyl)-1,3-propanedione (a₃)

2-(4''-Nitrophenyl)-6,8-dichloro-flavone (a₂) (0.01 mol) was dissolved in ethanol (25ml). To this, aqueous solution of HCl (25 ml) was added. The reaction mixture

was then refluxed for 1 hour, cooled, and diluted with water. The product, thus separated, was filtered, and crystallized from ethanol to get the compound (a₃).

Preparation of 1-(2'-hydroxy-3',5'-dichlorophenyl)-2-bromo-3-(4''-nitrophenyl)-1,3-propanedione (a₄)

1-(2'-Hydroxy-3',5'-dichlorophenyl)-3-(4''-nitrophenyl)-1,3-propanedione (a₃) (0.01 mol) was dissolved in a mixture of ethanol and dioxane. To this, calculated amount of liquid bromine was added. The product was not separated even after standing for one hour. It was then diluted with water, washed with water several times and extracted with ether. The solvent was removed under reduced pressure to get the white solid of the compound (a₄).

Preparation of 5-(2'-hydroxy-3',5'-dichlorophenyl)-4-(4''-nitrobenzoyl)-2-phenyl-amino-1,3-thiazole (E)

1-(2'-Hydroxy-3',5'-dichlorophenyl)-2-bromo-3-(4''-nitrophenyl)-1,3-propanedione (a₄) (0.01 mol) and phenyl thiourea (0.01 mol) were dissolved in ethanol. To this, aqueous KOH solution (0.02 mol) was added.

The reaction mixture was refluxed for 3 hours, cooled, diluted with water and acidified with conc. HCl. The product, thus separated, was filtered and crystallized from ethanol to get the compound (E).

The newly synthesized compounds were characterized on the basis of elemental analysis, molecular determination, UV, IR, NMR. spectral data.

The UV, IR, and NMR Spectral Data

Compound (E):

UV: Spectrum No. 4

The UV-Vis spectrum of the compound (E) reported in dioxane showed λ_{max} value 490 nm corresponding to n \rightarrow π^* transition.

IR KBr: Spectrum No. 5

3337.18 cm⁻¹ (O-H phenolic), 2923.20 cm⁻¹ (aliphatic C-H stretching), 3073.17 cm⁻¹ (aromatic C-H stretching), 3925.40 cm⁻¹ (-NH stretching), 1218.9 cm⁻¹ (-C=N-stretching), 769.23 cm⁻¹ [C-Cl stretching in aliphatic], 1053.18 cm⁻¹ [C-Cl stretching in aromatic].

PMR: Spectrum No. 6

δ 3.58 (hump, 1H, =NH); δ 6.64 (d 1H, -CH=C-H-); δ 6.69 (d, 1H, -CH=C-H-); δ 7.1 to 8.3 (m, 11H, Ar-H); δ 12.5 (s, 1H, O-H)

Preparation of Nanoparticles of the Titled Compound

Ultrasonic Processor Sonapros PR-250MP was used to produce nanoparticles of the test compounds. The test compound was dissolved in dioxane to prepare 0.1 M solutions. This solution was taken in a beaker and the probe of the sonapros 250 MP was dipped in solution. This solution was exposed to sonopros MP 250 for 10 minutes separately. The test compound was converted to nanoparticles. The solvent dioxane was evaporated by

conventional heating method. The size of nanoparticles of the test compound was confirmed by X-ray diffraction studies using Benchtop x-ray diffraction (XRD) instrument (Miniflex).

The thin film of the nanoparticles of the test compound was prepared on glass slide. This slide was introduced to the X-ray diffraction instrument to get graphical information which was used for the calculation of the crystal size of test compounds.

Characterisation of Size of Nanoparticles of the Test Compounds

The crystal size of nanoparticles of the test compounds calculated by using Debye-Scherrer equation.

$$D = \frac{0.94 \lambda}{\beta \cdot \cos \theta}$$

Where,

D = The average crystalline size.

0.94 = The particle shape factor which depends on the shape and size of the particle.

λ = is the wavelength.

β = is the full width at half maximum [FWHM] of the selected diffraction peaks ($\beta = 0.545$)

θ = is the Bragg's angle obtained from 2θ values which was corresponding to the maximum intensity peak in XRD pattern ($\theta = 0.7501$ rad).

Table 1: Characterisation Data of Newly Synthesized Compounds.

Compounds	Molecular Formula	M.P. in °C	% of Yield	% of Element C	H	N	S	Cl	Br
	C ₈ H ₆ O ₂ Cl ₂	54	80	47.90/48	2.95/3			34.15/34.58	
a	C ₁₅ H ₉ O ₄ NCI ₂	250	70	53.10/53.25	2.40/2.66	3.98/4.18		21/21.77	
a1	C ₁₅ H ₉ O ₄ NCI ₂ Br ₂	72	70	36.01/36.14	1.78/1.80	2.78/2.81		14.20/14.25	32.08/32.12
a2	C ₁₅ H ₇ O ₄ Cl ₂ N	132	60	53.14/53.57	2.07/2.08	4.13/4.16		21.03/21.13	
a3	C ₁₅ H ₉ O ₅ Cl ₂ N	117	50	50.74/50.84	2.45/2.54	3.90/3.95		20.03/20.05	
a4	C ₁₅ H ₈ O ₅ Cl ₂ BrN	78	60	41.12/41.57	1.78/1.84	3.20/3.23		16.08/16.39	18.34/18.47
E	C ₂₂ H ₁₅ O ₄ N ₃ Cl ₂ S	168	70	54/54.09	3.0/3.07	8.56/8.60	6.50/6.55	14.50/14.54	

Experimental Details and Discussion of Results

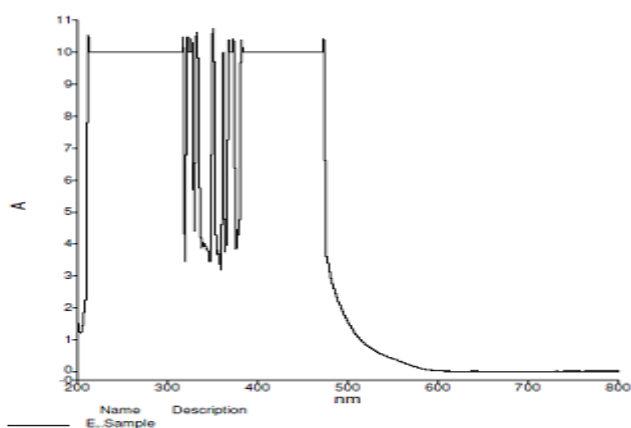
All the newly synthesised compound (E) and its nanoparticles were screened for their antibacterial activity against some Gram positive pathogens viz. *Staphylococcus aureus* and *Streptococcus sp.* and some

Gram negative pathogens viz. *Pseudomonas sp.* and *Solmonella Typhi*. at conc. of 1000 μ m gentamycine as a standard. DMF was used as solvent control using agar plate techniques. The zones of inhibition formed were measured in mm and are shown in table -2.

Table-2: Antibacterial Activities Of Synthesised New Compounds.

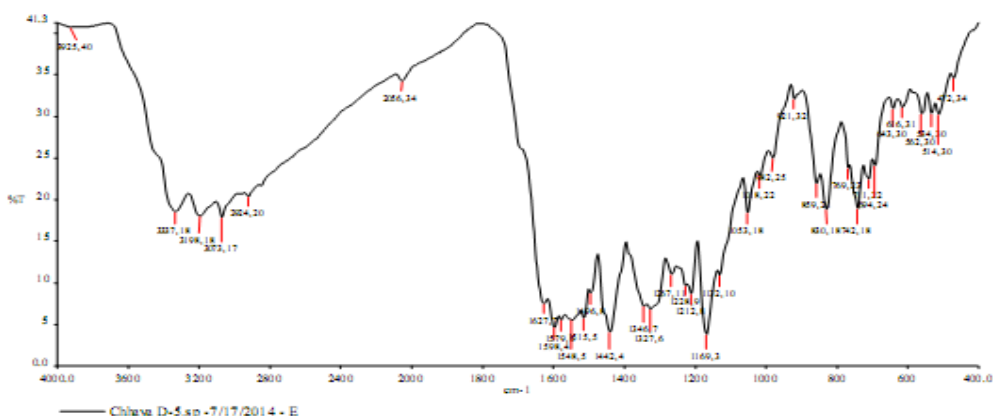
Zones of inhibition (mm)

Compounds	Staphylococcus aureus	Streptococcus sp.	Pseudomonas sp.	Solmonella typhi
a	14	12	14	14
E	14	15	15	14

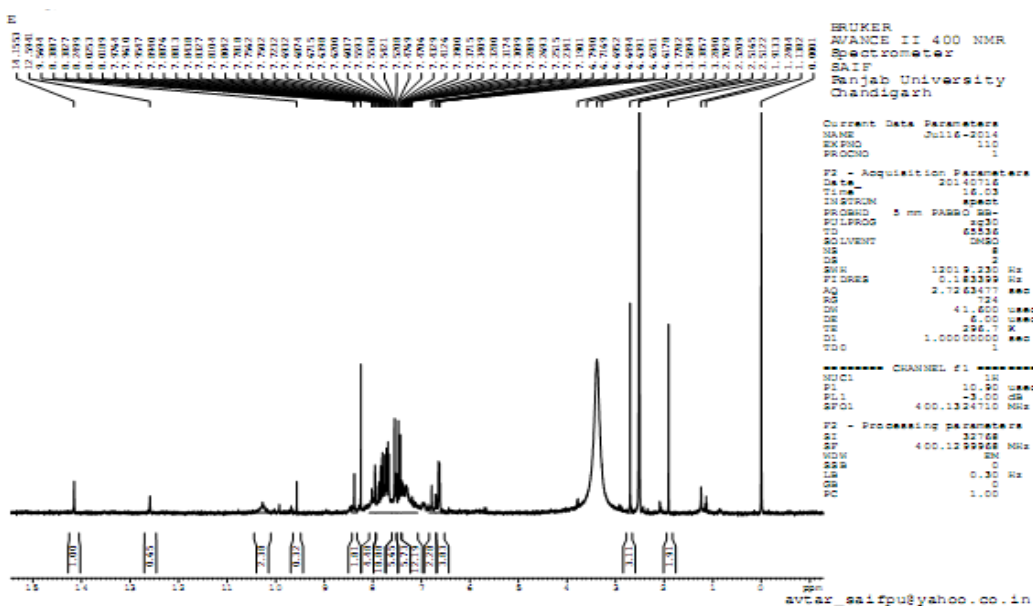


Spectrum No. 4

RC SAIF PU, Chandigarh

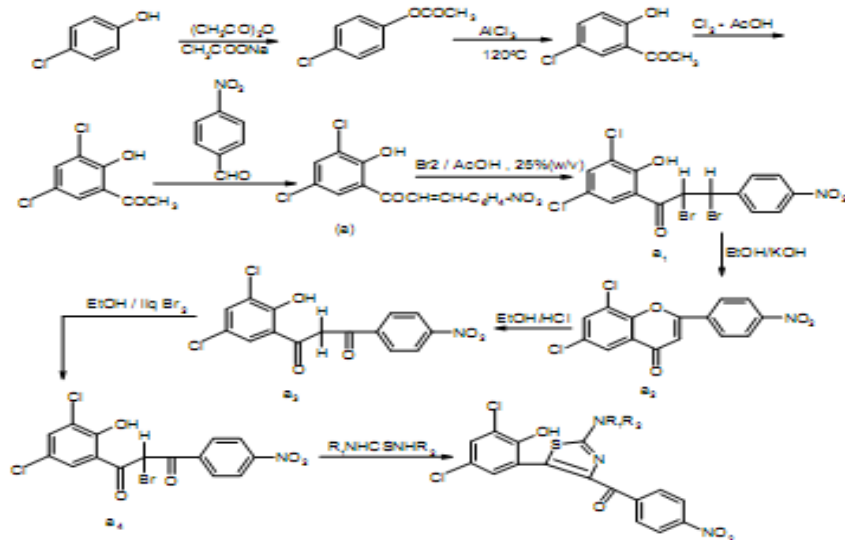


Spectrum No. 5



Spectrum No. 6

Scheme:



Where:

- 1) $\text{R}_1 = -\text{H}, -\text{C}_6\text{H}_5$
- 2) $\text{R}_2 = -\text{H}, -\text{C}_6\text{H}_5$

RESULT AND DISCUSSION

The newly synthesized compound (E) and its nanoparticles were found to be active against test pathogens. However a further detailed study in the light of Medical sciences is advised.

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REFERENCES

1. K. Anilkumar, P.K., K. Shrivastava Rao, Reddana P., *Ind. J. of chem. sec., B*, June 2007; 1033-1037.
2. Kakade B.S., "*Synthesis in heterocyclic compounds Ph.D. Thesis*", Nagpur University, 1983.
3. Seiji Miwatashi, Yasayoshi Arikava, Shigonori Ohkawa, Keiko Ugo-*Chem., Pharm, Bull*, 2008; 56(8): 1126-1137.
4. Airody Vasudeva Adhikari, Karabasanagouda T., Ramgopal Dhanwad and G. Parameshwarappa, *Indian J. of Chem.*, 2008; 47: 144-152.
5. Yasuda, Nobuyuki, Karikome, Michinori, Toda, Takashi, *Chem., Lett.*, 1995; (12): 1141-2.
6. Bhavin Sutariya, Raziya S.K., S. Mohan and S.V. Sombassiva Rao, *Indian J. of Chem*, 2007; 46: 884-887.
7. Khan M.R. and M.S. Jairajpuri, Nematode Infestation in Horticultural Crops, National Scenario. In: Nematode Infestation Part III: Horticultural Crops, Khan M.R. and M.S. Jairajpuri (Eds). *National Academy of Sciences, India*, 2012; 1-30.
8. Guzman, M.G., J. Dille and S. Godet, Synthesis of silver nanoparticles by chemical reduction method and their antibacterial activity-*Int. J. Chem. Biol. Eng.*, 2009; 2: 104-111.
9. Bryaskova, R., D. Pencheva, S. Nnikolov and T. Kantardjiev, Synthesis and comparative study on antimicrobial activity of hybrid materials based on silver nanoparticles (AgNps) stabilized by polyvinylpyrrolidone (PVP). *J. Chem Biol.*, 2011; 4: 185-191.
10. Abd El-Hai, K.M., M.A. El-Metwally, S.M. El-Baz and A.M. Zeid, The use of antioxidants and microelements for controlling damping off caused by *Rhizoctonia solani* and charcoal rot caused by *Macrophomina Phaseoliana* on sunflower. *Plant Pathl. J.*, 2009; 91: 149-161.
11. Teodoro S. Micaela B. David K.W. Novel use of nanosaturated alumina as an insecticide. *Pest Manag Sci.*, 2010; 66(6): 577-579.
12. Piotr Grodzinski, *American cancer society*, 2012; 3. DOI : 10.1002/CnCr. 27766.
13. Yue Yaun, Xijun Wang Bin Mei, *Dongxin Zhan Scientific Reports* 3, Article number: 3523, doi : 10.1038/srep 035 23 ; 29 November, 2013.
14. Andrei L. Gartel, University of Illinois, USA/*Pharmaceutica*, 2013.
15. Chun-Mao Lin and Tan-Yi Lu, *Bentham Science*, ISSN: 2212-4020.
16. Shima Salmasi and Alexander Marcus Sci Falian, *Bentham Science*, ISSN: 1875-533, 2015; 22.
17. Ayman Khedair, Di Chen, Yogesh Patil, Linon Ma, Q. Ping Dou, Malathy P.V. Shekhar, Jayanth Panyom, *Journal of Controlled Release*, 2010; 141(2): 137-144.
18. Dr. Ho, Nanotech advancements, *Scientific hardness nanotechnology to better diagnose and tract cancer*, 120: 2781-2783. doi 10.1002/Cner.28982.
19. Marina Mazzoni, Andrea Ienco, Lorenzo Zani, Gianna Reginato, Massimo Calamante and Cosimo Fortunato, *OSA Publishing*, 2014.