EUROPEAN JOURNAL OF BIOMEDICAL AND PHARMACEUTICAL SCIENCES
http://www.ejbps.com

ISSN 2349-8870
Volume: 11
Issue: 10
175-180
Year: 2024

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

Chhaya D. Badnakhe*[1]

[1]Department of Chemistry, Dr. Manorama and Prof. H.S. Pundkar, Arts, Commerce and Science College, Balapur, Dist. Akola.

***Corresponding Author: Dr. Chhaya D. Badnakhe**

Department of Chemistry, Dr.Manorama and Prof. H.S. Pundkar, Arts, Commerce and Science College, Balapur, Dist. Akola.

Article Received on 01/08/2024 **Article Revised on 22/08/2024** **Article Accepted on 11/09/2024**

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-(heptan-1-one)-2- amino-1,3-thiazole (J) has been screened. The compounds J was synthesized from 1-(2'-hydroxy-3',5'-dichlorophenyl)-2-bromo-1,3-nonanedione (a_4) by the action of thiourea. 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, 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. 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] Chalcones and their analogues having α, β-unsaturated carbonyl system are very versatile substrates for the evolution of various reactions and physiologically active compounds.

In the present study, various 5-phenyl-2-hydroxy-chlorosubstituted-2-amino-1,3 thiazole has been synthesized from 1,3 propanediones by using thiourea. Nanotechnology has the potential to change the entire scenario of the current agricultural and food industry with the help of new tools developed for the treatment of plant diseases, rapid detection of pathogens using nanobased kits, improving the ability of plants to absorb nutrients etc. Nanobiosensors and other smart delivery systems will also help the agricultural industry to fight against different crop pathogens.

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 Breast & liver cancer[12], cancer & HIV[13], brain cancer[14], inhibiting tumour growth.[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, enhancing the ability of plants to absorb nutrients by use of advanced technologies like nanocapsulation of elderberry extract using outer membrane of living cells[16], cosmetic technology[17], vitro-dissolution[18], enhancing cell efficiency of photovoltaic cell.[19] In the present study, the chlorosubstituted 1,3-thiazine (J) 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.

Experimental

All the glasswares used in the present work were of pyrex quality. Melting points were determined in hot paraffin bath and are uncorrected. The purity of compounds was monitored on silica gel coated TLC

plate. IR spectra were recorded on Perkin-Elmer spectrophotometer in KBr pelletes, H^1 NMR spectra on spectrophotometer in $CDCl_3$ with TMS as internal standard. UV spectra were recorded in nujol medium. The analytical data of the titled compounds 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 20^0C. 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-hexylchalcone (a)

2-Hydroxy-3,5-dichloroacetophenone (0.01 mol) dissolved in ethanol (50 ml) treated with heptanaldehyde (0.1 M) at its boiling temperature. Aqueous sodium hydroxide solution [40%, 40 ml] was added dropwise and the the mixture was stirred mechanically at room temperature for about 1 hour. It is then kept for 6 to 8 hours followed by decomposition with ice cold HCl [1:1]. The yellow granules thus obtained were filtered, washed with 10% $NaHCO_3$ solution and finally crystallized from ethanol-acetic acid solvent mixture to get the compound (a).

Preparation of 1-(2'-hydroxy-3'-5'-dichlorophenyl)-2,3-dibromononan-1-one (a_1)

2'-Hydroxy-3',5'-dichlorophenyl-4-hexylchalcone (a) (0.01 M) was suspended in bromine–glacial acid reagent [25% w/v] [6.4 ml]. The reagent was added dropwise with constant stirring. After complete addition of reagent 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 (**a_1**).

Preparation of 2-(4"-hexyl)- 6,8-dichloroflavone (a_2)

1-(2'-Hydroxy-3',5'-dichlorophenyl)-2,3-dibromo-nonan-1-one (a_1) (0.01 mol) was dissolved in ethanol (25 ml). To this, aqueous solution of KOH (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 (a_2).

Preparation of 1-(2'-hydroxy-3',5'-dichlorophenyl)-1,3-nonanedione (a_3)

2-(4"-Hexyl)-6,8-dichloroflavone (a_2) (0.01 mol) was dissolved in ethanol (25 ml). To this, aqueous solution of HCl (25 ml) was added. The reaction mixture was then refluxed for one hour, cooled and diluted with water. The solid product, thus obtained, filtered and crystallized from ethanol to get the compound (a_3).

Preparation of 1-(2'-hydroxy-3',5'-dichlorophenyl)-2-bromo-1,3-nonanedione (a_4)

1-(2'-Hydroxy-3',5'-dichlorophenyl)-1,3-nonanedione (a_3) (0.01 mol) was dissolved in a mixture of ethanol (10 ml) and dioxane (10 ml). To this, calculated amount of liquid bromine (0.5 ml) was added. The product was not separated even after standing for one hour. It was then diluted with water and washed with water several times and extracted with ether. The solvent was removed under reduced pressure to get the white solid of the compound (a_4).

Preparation of 5-(2'-hydroxy-3',5'-dichlorophenyl)-4-(heptan-1-one)-2- amino-1,3-thiazole (J)

1-(2'-Hydroxy-3',5'-dichlorophenyl)-2-bromo-1,3-nonanedione (a_4) (0.01 mol) and thiourea (0.01 mol) were dissolved in ethanol (25 ml). To this, aqueous KOH solution (0.01 mol) was added. The reaction mixture was then refluxed for three hours, cooled, diluted with water and acidified with conc HCl. The product, thus separated, was filtered and crystallized from ethanol to get the compound (J).

The newly synthesized compound was characterised on the basis of elemental analysis, molecular determination, UV, IR, NMR. spectral data.

The UV, IR, and NMR spectral data

Compound (J)

UV : Spectrum No. 1

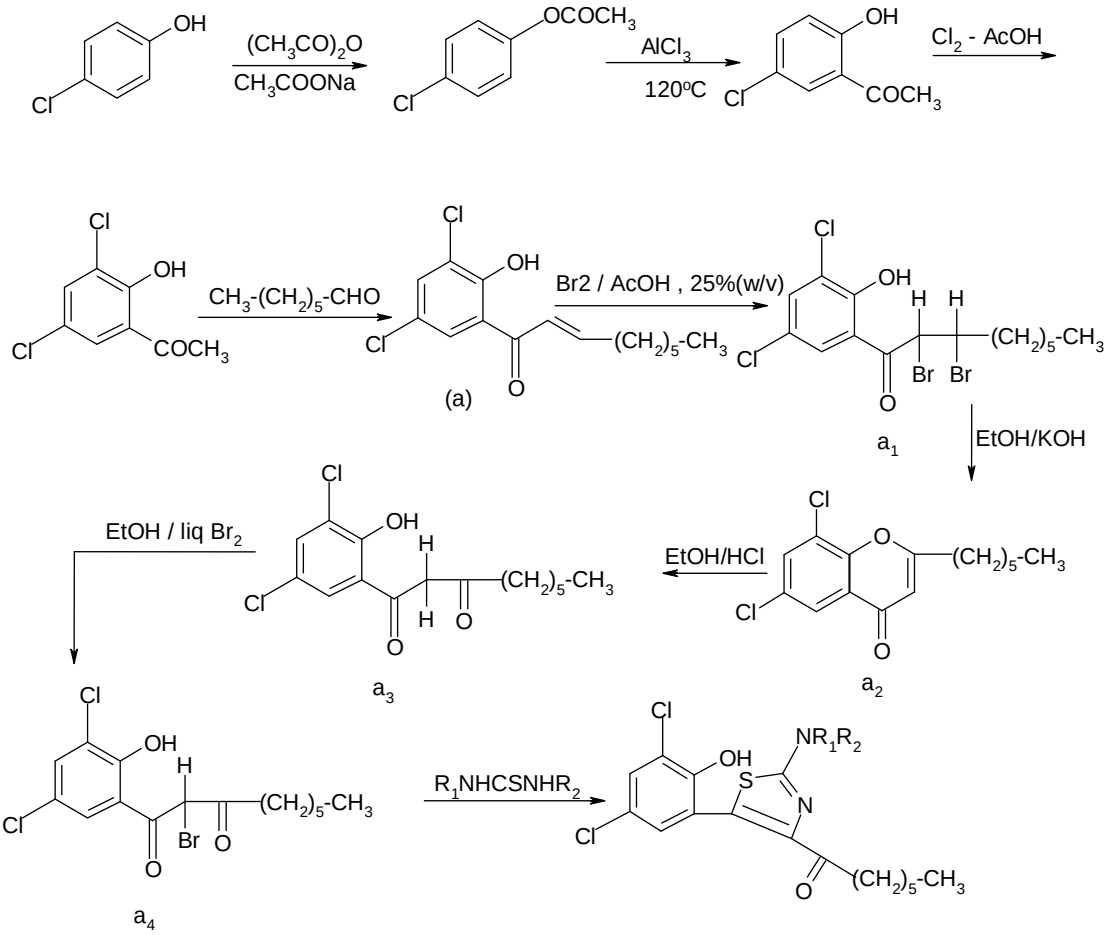
The UV-Vis spectrum of the compound (J) reported in dioxane showed λ_{max} value 410 nm corresponding to $n \rightarrow \pi*$ transition.

IR (KBr) :- Spectrum No. 2

3036.60 cm^{-1}(-OH phenolic), 2955.55 cm^{-1} (aliphatic -C-H stretching), 3208.58 cm^{-1} (aromatic -C-H stretching), 3797.72 cm^{-1} (-N-H stretching), 1228.56 cm^{-1} (-C=N-stretching), 756.57 cm^{-1} (-C-Cl stretching in aliphatic), 1073.66 cm^{-1} (C-Cl stretching in aromatic).

PMR :- Spectrum No. 3

∂ 5.2 (hump, 2H, (-N-**H**) ; ∂ 6.7 (d, 1H, -CH=C-**H**-) ; ∂ 6.8 (d, 1H, -C**H**=C-H-) ; ∂ 7.0 to 7.8 (m, 2H, Ar-**H**) ; ∂ offset, (region not observed, observed, O-**H**)



Scheme

Where
1) R_1 = -H,
2) R_2 = -H,

Preparation of nanoparticles of the titled compounds
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 solution. This solution was taken in a beaker and the probe of the sonapras 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 compounds 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.

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

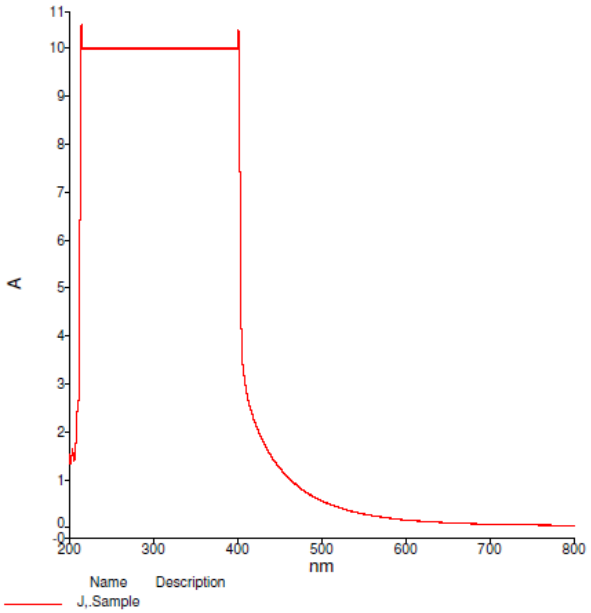
Where,
D = The average crystalline size.
0.94 = The particle shape factor which depends on the shape and size of the particle.
λ = is the wavelength.
β = is the full width at half maximum [FWHM] of the selected diffraction peaks (β = 0.545)
θ = is the Bragg's angle obtained from 2θ values which was corresponding to the maximum intensity peak in XRD pattern (θ = 0.7501 rad).

EXPERIMENTAL DETAILS AND DISCUSSION OF RESULTS
All the newly synthesised compound (J) and it's 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 µm gentamycine as a standard. DMF was used as solvent control using agar

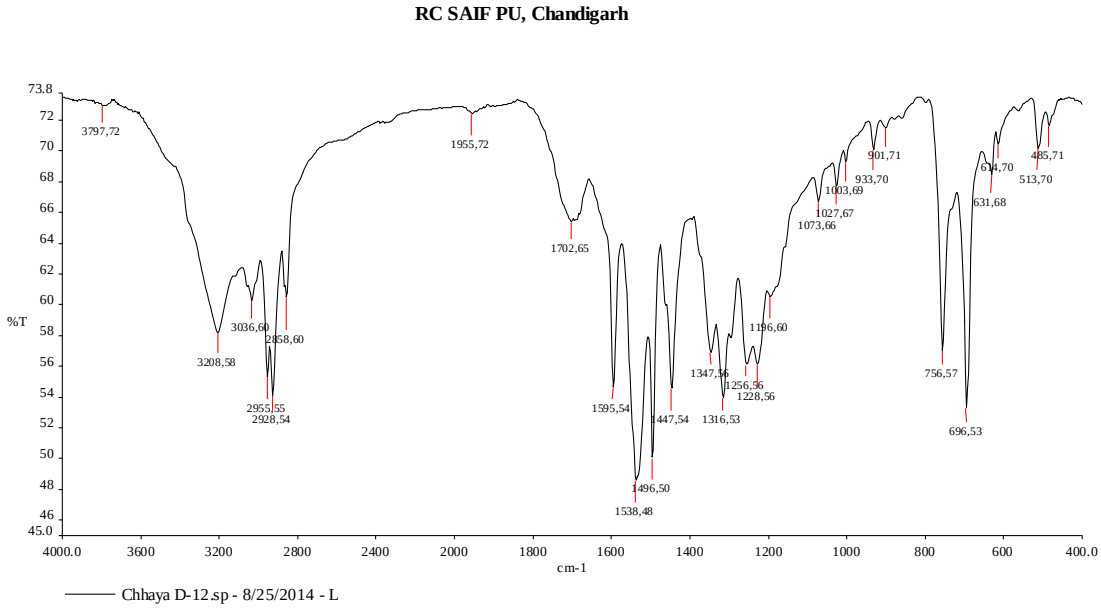
plate techniques. The zones of inhibition formed were measured in mm and are shown in table -2.

Table 1: Characterisation data of newly synthesized compounds.

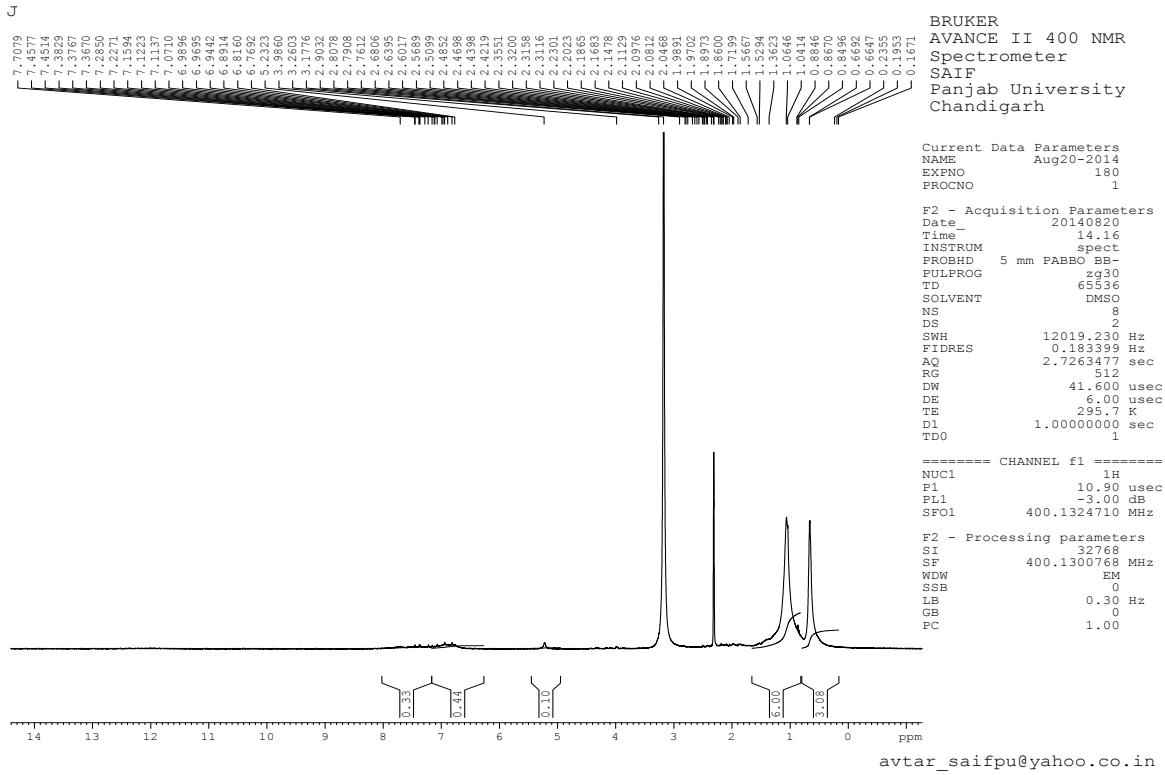
Compounds	Molecular formula	M.P. in ^{0}C	% of yield	% of element					
				C	H	N	S	Cl	Br
	$C_8H_6O_2Cl_2$	54	80	47.90/48	2.95/3			34.15/34.58	
a	$C_{15}H_{18}O_2Cl_2$	103	70	52.20/53.35	53.10/53.21			23.25/23.27	
a_1	$C_{15}H_{18}O_2Cl_2Br_2$	67	50	39.01/39.04	3.85/3.90			15.20/15.40	34.18/34.70
a_2	$C_{15}H_{16}O_2Cl_2$	73	50	60.10/60.20	5.25/5.35			23.70/23.74	
a_3	$C_{15}H_{18}O_3Cl_2$	118	60	56.60/56.78	5.60/5.67			22.33/22.39	
a_4	$C_{15}H_{17}O_3Cl_2Br$	84	50	45.40/45.45	4.20/4.29			17.90/17.92	20.15/20.20
J	$C_{16}H_{20}O_2N_2Cl_2S$	96	60	51.10/51.20	5.30/5.33	7.40/7.46	8.50/8.53	18.90/18.93	



Spectrum No. 1.



Spectrum No. 2.



Spectrum No. 3.

Table 2: Antibacterial Activities of Synthesised New Compounds.

Zones of inhibition (mm)				
Compounds	**Staphylococcus aureus typhi**	**Streptococcus sp.**	**Pseudomonas sp.**	**Solmonella**
A	14	12	14	14
J	14	15	15	14

RESULT AND DISCUSSION

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

ACKNOWLEDGEMENTS

The authors are thankful to Dr. D.H. Pundkar, Principal, Dr.Manorama & Prof.H. S.Pundkar, Arts, Commerce & Science College, Balapur, Dr. B.B. Wankhade, Principal, Malkapur Vidnyan Mahavidyalaya, Malkapur, and Shri Shankarlal Khandelwal College, Akola for providing help in carrying out the antibacterial activities & for providing necessary facilities to carry out the research work.

REFERENCES

1. Baviskar B, Patel S., Baviskr B., Khadabadi S.S., Shiradkar M, Design and synthesis of some novel chalcones as Potent Antimicrobial Agent *Asian J. Research Chem*., 2008; 1.
2. Saravanan G., Alagarsamy V., Pavitra T.G.V., Kumar C.G., Savithri Y., Naresh L., Avinash P. Synthesis, characterisation and antimicrobial activities of novel thiazole derivatives. *International Journal of Pharma and Bio – Sciences,* 2010; 1(3): 1-8.
3. Vicini P. Geronikaki A, Anastasia K, Incer ti M, Zani F. Synthesis and Antimicrobial activity of novel-2-thiazolyl-imino-5-arylidene-4- thiazolidonones *Bio. org. Med. Chem*., 2006; 14: 3859-3864.
4. Pathan S., Alagwadi K., Bhat A., Reddy V., Patthan J., Khade A., Bhat K., *Ind. Drugs,* 2007; 45(7): 532-535.
5. Patthan S., Reddy V., Manvi F., Desai B,, Bhat A., *Ind. J. Chem*., 2006; 45B: 1778-1781.
6. Andreni A., Granajola M., Leoni A., Locatelli A., Morigi R., Rambaldi M., Eur. *J. Med. Chem.*, 2001; 36: 743-746.
7. Azam, A., A.S. Ahmed, M. Oves, M.S. Khan and A.Memic, Size-dependent antimicrobial properties of CuO nanoparticles against *Gram positive and Gram negative* bacterial strains. *Int. J. Nanomed*., 2012; 7: 3527-3535.
8. Jayaseelan C., A.A. Rahuman, A.V. Kirthi, S. Marimuthu and T. Santoshkumar. Novel microbial route to synthesize ZnO nanoparticles using *Aeromonas hydrophila* and their activity against pathogenic bacteria and fungi. *Spectrochimica Acta A*: Mol. Biomol. Spectrosc., 2012; 90: 78-84.
9. Singh, D., A. Kumar, A.K. Singh and H.S. Tripathi, Induction of resistance in field pea against rust disease through various chemicals/micronutrients

and their impact on growth and yield. *Plant Pathol. J*., 2013; 12: 36-49.
10. 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.
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. Andrel L. Gartel, University of Illinois, USA/*Pharmaceutica*, 2013.
13. Chun-Mao Lin and Tan-Yi Lu, *Bentham Science*, ISSN : 2212-4020.
14. Dr. Ho, Nanotech advancements, *Scientific hardness nanotechnology to better diagnose and tract cancer*, 120: 2781-2783; doi 10.1002/Cner.28982.
15. Ming Wang, Mariana Holasia, Kasim Kabirov, Aryamitra Banerjee, *Cell Cycle*, 2012; *11:* 18.
16. Yue Yaun, Xijun Wang Bin Mei, *Dongxin Zhan Scientific Reports*, November 2013; 3: 3523, doi : 10.1038/srep 035 23; 29.
17. D.E. Manolkos and A.P. Markopoulos *Bentham science*, ISSN : 1876-4037, 2015; 7.
18. Umme Hani and H.G. Shivkumar, *Bentham science*, ISSN : 1875-5704, 2015; 12(6).
19. Marina Mazzoni, Andrea lenco, Lorenzo Zani, Gianna Reginato, Massimo Calamante and Cosimo Fortunato, *OSA Publishing*, 2014.