Original Article

Study The Effect Of Antimicrobial Activity Of Some Synthesize Noval Qunazolino- 2,4,6- Tri - Substituted -S-Triazine Derivatives

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Abstract

Quinazoline and triazine belong to a desirable class of heterocyclic hydrocarbons. As a starting point for the synthesis of triazine, anthranilic acid and substituted anthranilic acid have been used to create a number of synthetic analogues of triazine and quinazolinone. On agar plates, all the produced compounds were screened for their ability to kill off bacteria and fungi using the Saboraud's medium and Nutrient Broth method, respectively. Five gram-positive bacteria, included Staphylococcus aureus, Staphylococcus faecalis, Bacillus substilis, P. vulgaris, and B. pumilus, and two gram-negative bacteria, including Escherichia coli and Proteus vulgaris, were present in the bacterial culture. Agar diffusion was used to create fungal cultures of Saccharomyces cerevisiae, A. nigeria, Candida albicans, and Rhizopus oryzae. Negative bacteria were treated with Ciprofloxacin, and Gram positive bacteria Norfloxacin, Benzyl penicillin, and Clotrimazole was used as an antifungal. The synthetic compounds demonstrated considerable antibacterial and antifungal activity on level with the effects of synthesise compound. The most active of these produced chemicals was compound code A-1.

Keywords: antimicrobial activity, Triazine and Quinazolinone

1. INTRODUCTION

Triazine has a broad range of biological actions, making it extensively utilised in medicine. It has been shown that triazine derivatives exhibit antibacterial[1], antiviral[2], antifungal[3], and herbicidal effects[4]. Additionally, these compounds are utilised to treat HIV infection [5]. It has been proven that 2,4,6-tri-substituted-s-Triazine derivatives have anticancer[6], anticonvulsant[7], antimalarial hypotensive[8], and antiamoebic effects[9]. Although 1,3,5-tirazine derivatives are known to be effective against plant protection, how they are applied depends heavily on how they interact with the environment. The formulation of insecticides in polymers is currently a relatively advantageous method to generate environmentally more bearable effective products with lower toxicity and extended activity[10]. 2,4,6,-triamino-1,3,5-triazine, also referred to as melamine or cyanuramide, is the most popular derivative of 1,3,5,-triazine.

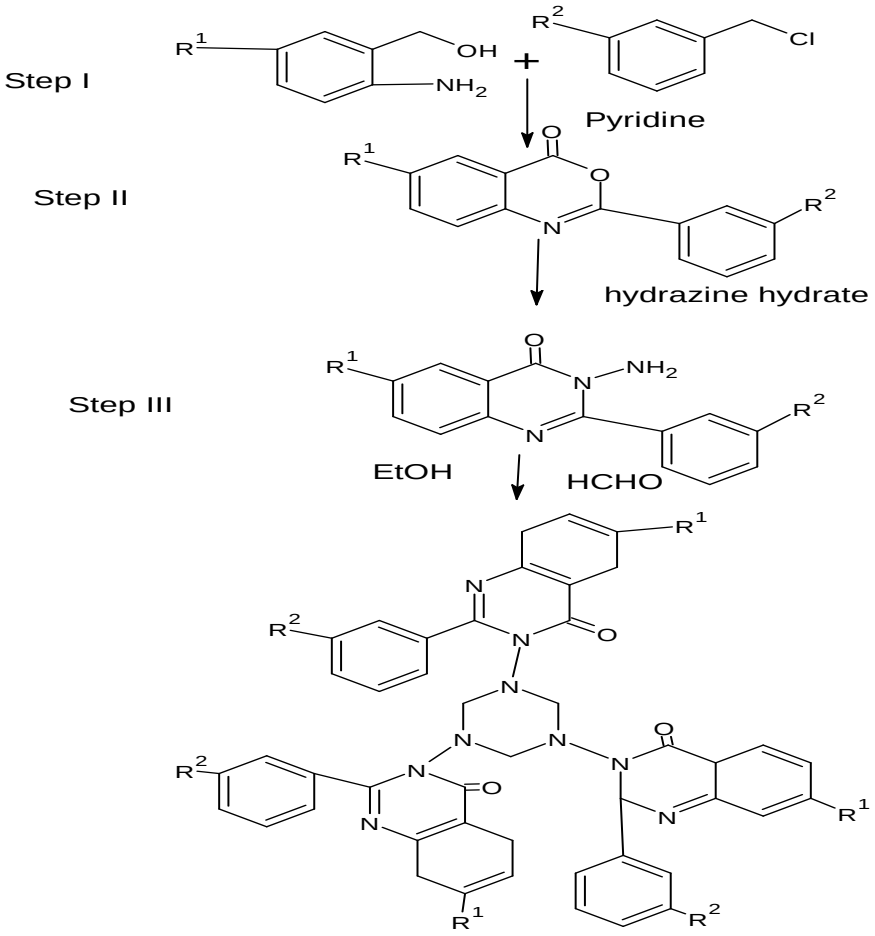
Due to the wide spectrum of biological features possessed by quinazolines and quinazolinones, these classes of fused heterocyclic are of great interest[11]. Other substituted quinazoline and quinazolinone derivatives have a wide range of biological activities, including anticancer[12],

antimicrobial[13],antifungal[14],antiviral[15],antiprotozoan[16],diuretic[17],musclerelaxant[18],antitubercular[19],anti-inflammatory[20], anti-depressant[21], anticonvulsant[22], fungicidal[23], and weedcidal[24], among many others [25-26]. Quinazoline and quinazolinone chemicals are also included in many pharmacological molecules and are utilised to prepare a variety of functional materials for synthetic chemistry.

2. MATERIALS AND METHODS

The synthetic process [27] was used in the current study on -s-Triazine. The process entails the steps listed below.

Reaction Scheme



Step-I Preparation of substituted 4-phenyl-3, 1-bezoxazin-4(3H)-one.

Substituted benzoyl chloride (0.05 mole) was added dropwise to a solution of anthranilic acid or substituted anthranilic acid (0.1 moles) in pyridine (60 mL), stirring the mixture for an hour at a temperature close to 8 0C. At room temperature, the reaction mixture was agitated for a further 4 hours. A solid substance separates out as you stir. With NaHCO3 solution, the entire reaction mixture was neutralised. A light yellow solid (A) was deposited and washed

with water before being recrystallized from ethanol.The melting point was determined by open capillary method using 'Tempo' melting point apparatus and are uncorrected. The melting points were 144^{0}C, 135^{0}C, 141^{0}C, 178^{0}C, 98^{0}C, 194-198^{0}C, 184-188^{0}C, 147^{0}C, 118^{0}C, 178^{0}C, 144^{0}C and 118^{0}C and yeild were 78%, 64.5%,56%,44%,54%,40%,64.6%,68.4%,64.9%,43%,45% and 38% of compounds Ia-l respectively. IR(KBr in cm-1) : 3074.60 (C-H, ArH Str),1759.08 (C=O Str),1681.93 (cyclic C=0 Str),1606.70(C=N Str),1510.46(C=C Str),1446.61 (C-N Str),840.96 (C-H deflaction),1188.15 (C-O Str) 1HNMR (δppm) (CDCl3), 4.530 (s, 3H, -SCH3),7.484-8.090 (m, 8H, Ar-H)

Step-II Synthesis of substituted 2-phenyl-3 amino quinazolin-4(3H)-one

A 0.05mole mixture of (I) and hydrazine hydrate in ethanol was refluxed for three hours until being cooled. Recrystallization of the separated solid (B) from ethanol.

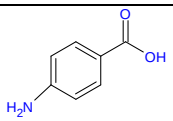
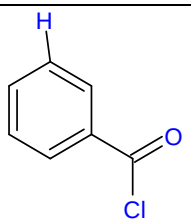
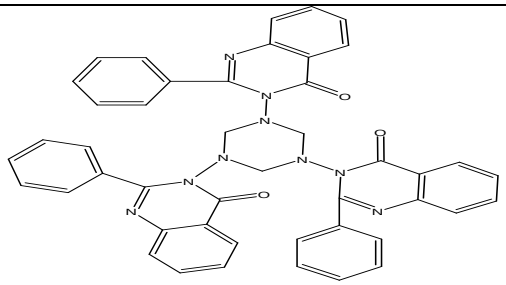
The melting points were 148^{0}C, 145^{0}C, 179^{0}C, 158^{0}C, 179^{0}C, 144^{0}C, 148^{0}C, 140^{0}C, 148^{0}C,143^{0}C,140^{0}Cand176^{0}Candyeildwere76%,75%,50,56%,54%,50%,65%,71%,64%,44.9%,43%,44% and 36% of compounds IIa-l respectively. IR(KBr in cm- 1) : 3068.75 (C-H, ArH Str), 3305.99 (N-H Str),1664.57 (cyclic C=0 Str),1598.99 (C=N Str),1514.14(C=C Str),1450.47(C-N Str),839.57(C-H deflaction) 1HNMR (δppm) (CDCl3), 4.530 (s, 3H, -SCH3),7.484-8.090 (m, 8H, Ar-H)

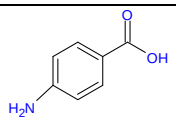
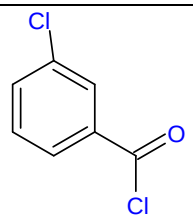
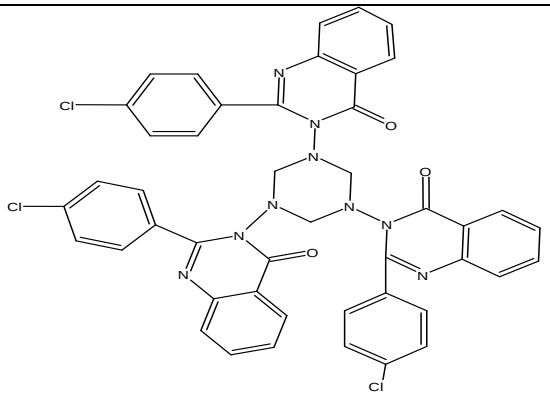
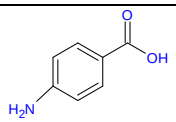
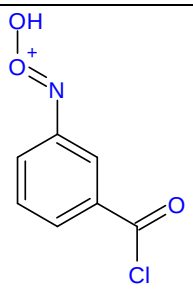
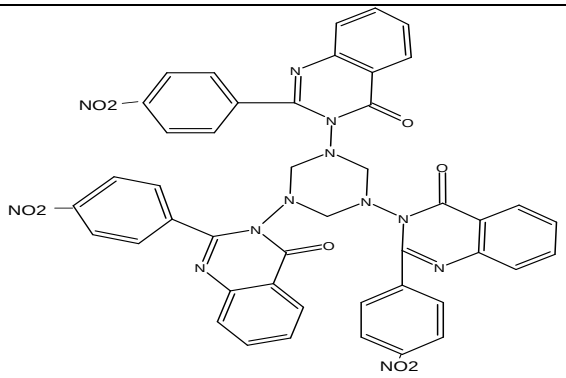
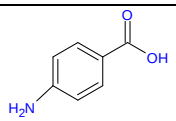
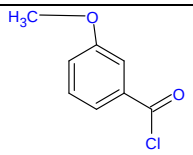
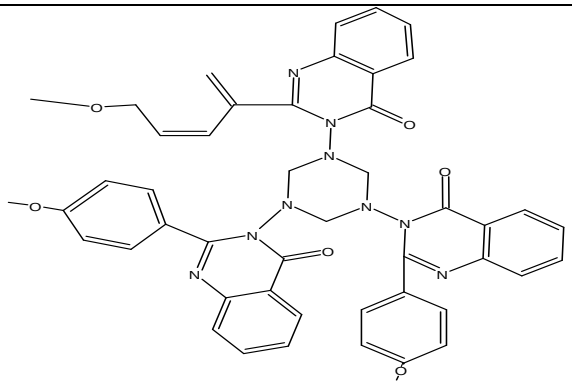
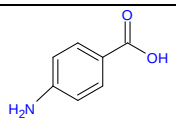
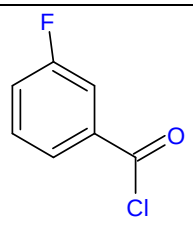
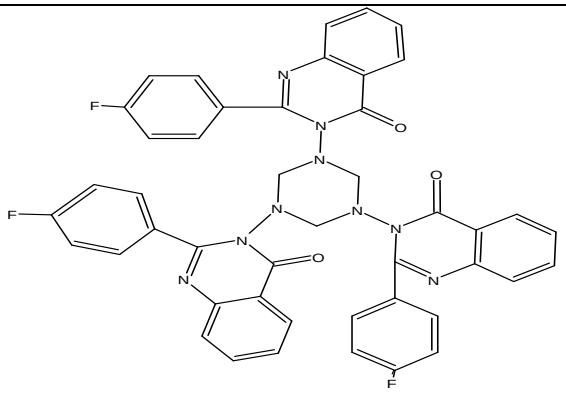
Step-III Synthesis of final product

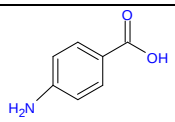
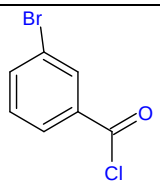
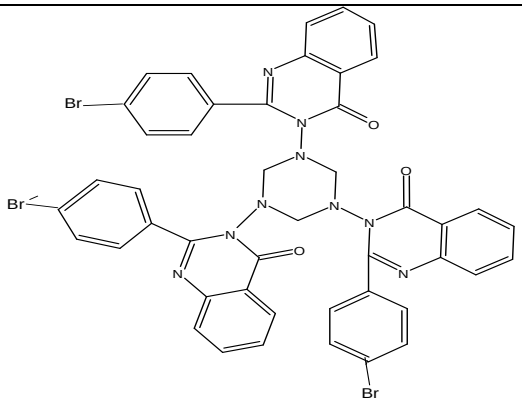
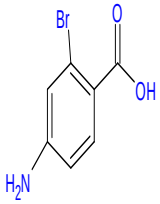
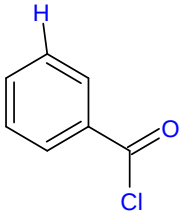
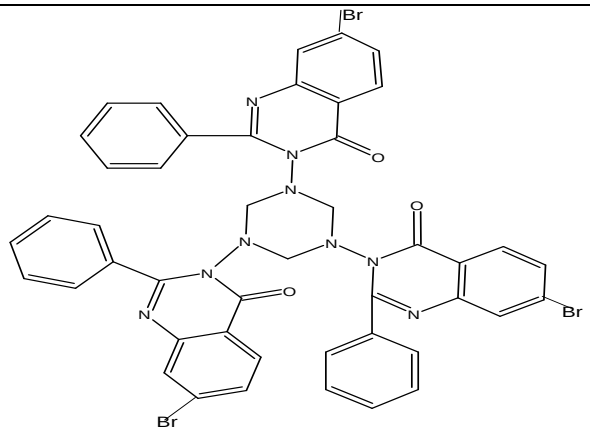
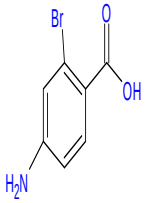
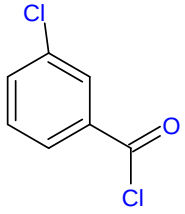
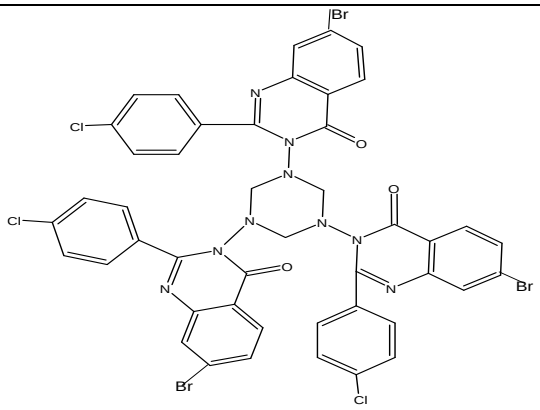
Compound (II) was slowly heated to dissolve in 50 mL of ethanol. Then, at room temperature, 40% aqueous formaldehyde (0.075 mole, 4.85 gm) was slowly added while stirring. The resulting mixture was rapidly stirred for a further half-hour at room temperature then allowed to stand. After being sorted out, the solid was filtered, washed with cold ethanol, and then quickly extracted with boiling petroleum ether (b.p. 80-100 0C). After removing the insoluble high polymer by filtration, the filtrated was cooled in room temperature.

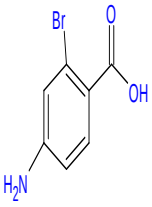
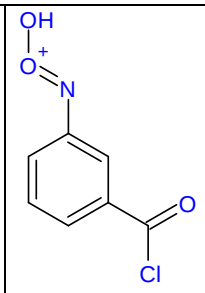
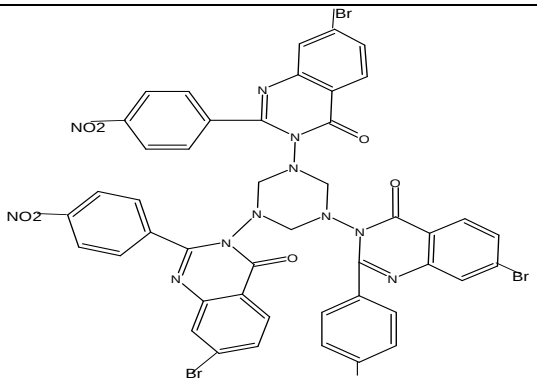
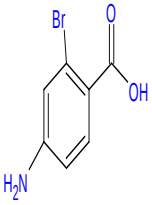
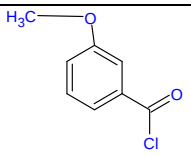
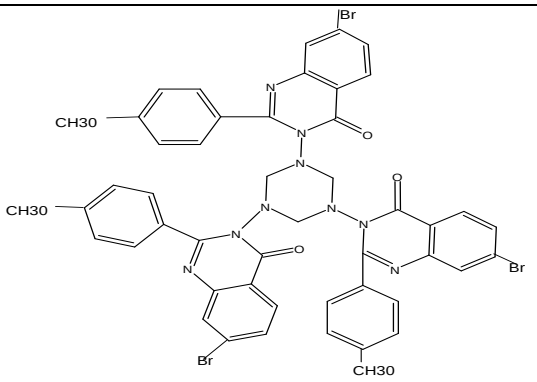
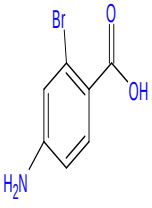
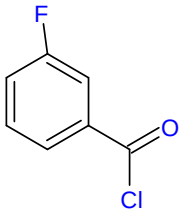
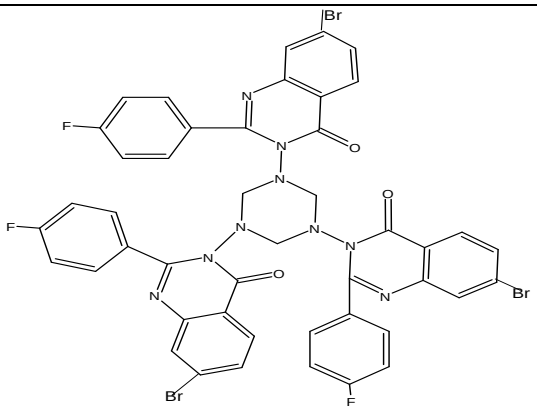
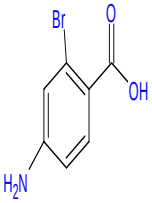
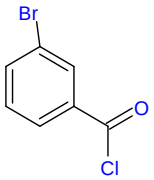
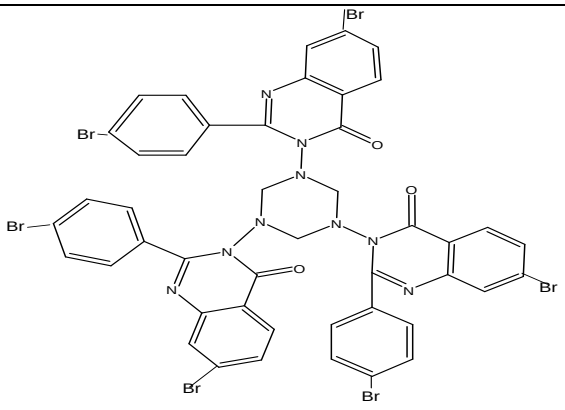
The melting points were 180-184^{0}C, 148^{0}C, 184^{0}C, 148^{0}C, 110^{0}C, 146^{0}C, 138^{0}C, 146^{0}C, 147^{0}C, 137-146^{0}C, 144^{0}C, 148^{0}C, and percentage yield were 37%, 39%, 34%, 44%, 17%,

33%,33%,4349%,34%,47%,34%,puritywere0.19,0.14,0.19,0.34,0.40,0.34,0.51,0.5,0.5,0.47,0.44,0.46 respectively. IR(KBr in cm- 1) : 3068.75 (C-H, ArH Str), 3305.99 (N-H Str),1664.57 (cyclic C=0 Str),1598.99 (C=N Str),1514.14(C=C Str),1450.47(C-N Str),839.57(C-H deflaction) 1HNMR (δppm) (CDCl3), 4.530 (s, 3H, -SCH3),7.484-8.090 (m, 8H, Ar-H) ,3.481 4-alpha-N-C in –s- triazine ring and 7-461- 8.171 Quinazolinone ring.

S NO.	Compound Code	R1 Substituted	R2 Substituted	Synthesized compound
1	A-1			

2	A-2			
3	A-3			
4	A-4			
5	A-5			

6	A-6			
7	B-1			
8	B-2			

9	B-3			
10	B-4			
11	B-5			
12	B-6			

3. DETERMINATION OF ANTIMICROBIAL ACTIVITY

Using the Cup-plate method, the antibacterial and antifungal properties of all the synthesised compounds were tested on agar plates using nutritional broth (antibacterial) and Saboraud's medium (antifungal). [28-30]. By using the Agar diffusion method, five Gram-positive bacteria, including Staphylococcus Aureus, Staphylococcus Faecalis, Bacillus Substilis, Proteus vulgaris, and B. Pumilus, and two Gram-negative bacteria, including Escherichia coli and Proteus vulgaris, were cultured. The fungal cultures included Saccharomyces cerevisiae, A. nigeria, Candida albicans, Ciprofloxacin and fluconazole, which are antibacterial and antifungal drugs, respectively, were the conventional medications employed for the current study21–23. The Concentration of synthetic compounds were taken at concentrations of 50 g/ml and 100 g/ml, respectively. In DMF, each component was completely dissolved. A blank was also carried out using DMF.

Table -I Antibacterial activity of synthesized Triazine derivatives against gram positive bacteria:

COMPOUND	Zone of inhibition in mm									
	Staphylococcus Aureus		Staphylococcus Faecalis		Bacillus Substilis		P. Vulgaris		B. Pumilus	
Concentration	50	100	50	100	50	100	50	100	50	100
A-1	14.84±0.3	14.30±0.8	14.84±0.4	17.84±0.6	14.4±0.3	16.44±0.3	15.64±0.8	17.84±0.7	16.64±0.4	18.84±0.
A-2	8.34±0.5	9.34±0.4	6.34±0.5	7.45±0.5	5.44±0.4	6.45±0.5	6.64±0.5	7.41±0.5	5.16±0.5	6.14±0
A-3	9.34±0.3	10.74±0.6	7.54±0.7	8.64±0.4	6.43±0.5	8.54±0.3	6.35±0.4	7.44±0.6	6.44±0.5	7.13±0
A-4	7.34±0.7	9.44±0.3	8.34±0.1	10.64±0.6	7.34±0.6	9.44±0.7	7.43±0.4	8.36±0.3	6.85±0.4	8.56±0
A-5	6.34±0.4	7.64±0.5	5.64±0.3	6.14±0.3	4.54±0.3	6.56±0.4	6.16±0.5	7.34±0.7	4.46±0.6	6.57±0
A-6	6.34±0.3	6.44±0.4	6.44±0.3	6.34±0.3	6.44±0.3	6.44±0.4	6.14±0.4	6.44±0.3	6.41±0.3	6.17±0
B-1	3.54±0.4	4.64±0.4	6.34±0.4	6.34±0.5	6.34±0.7	6.34±0.7	6.34±0.6	6.34±0.8	6.34±0.3	6.34±0
B-2	10.64±0.7	14.64±0.4	10.44±0.5	13.54±0.7	9.64±0.8	11.44±0.4	10.44±0.7	14.74±0.3	9.44±0.5	11.44±0.
B-3	11.44±0.6	13.74±0.3	11.54±0.8	15.34±0.5	14.34±0.3	14.64±0.7	14.74±0.4	14.34±0.5	13.34±0.3	15.34±0.
B-4	14.74±0.3	14.40±0.8	14.64±0.4	17.74±0.6	14.4±0.5	16.34±0.3	15.44±0.8	17.74±0.7	16.54±0.4	18.74±0.
B-5	08.34±0.8	9.34±0.4	9.65±0.3	11.54±0.8	7.64±0.7	9.54±0.9	8.64±0.4	9.64±0.4	7.44±0.6	8.33±0
B-6	7.34±0.8	8.14±0.7	8.65±0.4	10.44±0.4	6.74±0.4	8.44±0.8	7.47±0.3	8.47±0.7	6.43±0.6	7.43±0

DMSO (Control)	-	-	-	-	-	-				
Norfloxacin	17.44±0.3	19.45±0.5	17.45±0.5	41.54±0.4	16.64±0.3	17.45±0.3	17.64±0.4	40.65±0.4	18.45±0.4	19.33±0.
Benzyl penicillin	18.41±0.4	40.45±0.7	17.44±0.8	40.45±0.6	16.35±0.4	18.45±0.7	16.64±0.6	19.38±0.6	18.45±0.5	40.43±0.

A-1 >B-4>B-3>B-2>A-3>A-2>B-5>B-6>A-4>A-5>A-6>B-1

Table -I

Table - II Antibacterial activity of synthesized -s-Triazine derivatives against gram positive bacteria:

COMPOUND	Zone of inhibition in mm			
	Escherichia coli		Klebsiella Penumoniae	
Concentration	50µg	100µg	50µg	100µg
A-1	14.04±0.44	14.08±0.44	11.04±0.43	13.04±0.44
A-2	07.46±0.45	10.43±0.43	06.46±0.44	08.46±0.45
A-3	07.56±0.47	10.54±0.45	06.56±0.46	08.56±0.46
A-4	08.44±0.43	10.40±0.43	07.44±0.44	09.44±0.47
A-5	04.85±0.48	06.83±0.47	03.85±0.48	06.85±0.45
A-6	04.65±0.43	05.64±0.45	03.65±0.43	06.65±0.43
B-1	06.44±0.43	08.44±0.46	05.44±0.44	07.44±0.43
B-2	06.48±0.43	07.4±0.43	05.48±0.45	07.48±0.44
B-3	05.14±0.47	07.17±0.47	04.14±0.47	06.14±0.44
B-4	09.64±0.44	10.64±0.49	08.64±0.43	10.64±0.44
B-5	10.54±0.46	14.57±0.43	09.54±0.47	11.54±0.48

B-6	05.65±0.43	06.64±0.45	03.65±0.43	06.65±0.43
Ciprofloxacin	17.45±0.36	41.45±0.43	17.64±0.65	40.65±0.46

A-6<A-5<B-3<B-6<B-1<B-2<A-2<A-3<A-4<B-4<B-5<A-1

Table -II

Table - III Anti fungial activity of synthesized Triazine derivatives

COMPOUND	Zone of inhibition in mm							
	Saceharomyces Cerevisiae		A. Niger		C. Albicans		R. Oryzae	
Concentration	50	100	50	100	50	100	50	100
A-1	12.74±0.34	16.40±0.84	9.84±0.43	16.74±0.68	14.4±0.54	18.34±0.36	16.64±0.85	19.84±0.75
A-2	7.34±0.55	7.34±0.45	3.44±0.54	6.45±0.55	4.44±0.44	6.45±0.55	7.64±0.55	9.41±0.55
A-3	8.34±0.33	8.74±0.64	4.54±0.76	7.64±0.44	5.43±0.54	8.54±0.33	7.35±0.43	9.44±0.63
A-4	6.34±0.77	8.44±0.36	5.34±0.13	9.64±0.65	6.34±0.66	9.44±0.46	8.43±0.46	10.36±0.37
A-5	5.34±0.44	6.64±0.53	4.64±0.37	5.14±0.33	4.54±0.33	6.56±0.44	7.16±0.55	9.34±0.74
A-6	5.34±0.37	5.44±0.47	3.44±0.34	5.34±0.36	4.44±0.37	6.44±0.44	7.14±0.46	8.44±0.34
B-1	4.34±0.14	5.74±0.74	3.34±0.57	5.44±0.73	4.44±0.74	6.36±0.46	7.34±0.34	8.43±0.46
B-2	3.34±0.63	4.334±0.67	3.44±0.35	5.44±0.47	4.64±0.65	6.45±0.63	7.44±0.45	8.46±0.83
B-3	4.54±0.45	3.64±0.45	3.64±0.44	5.34±0.54	4.34±0.73	6.34±0.38	7.34±0.63	8.34±0.87
B-4	9.64±0.74	11.64±0.43	7.44±0.53	14.54±0.74	7.64±0.54	11.44±0.44	14.44±0.77	14.74±0.38
B-5	10.44±0.67	14.74±0.37	8.54±0.85	14.34±0.546	10.34±0.36	14.64±0.33	13.74±0.44	16.34±0.53

B-6	11.74±0.34	14.40±0.84	9.64±0.43	16.74±0.68	14.4±0.54	16.34±0.36	16.44±0.85	19.74±0.75
DMSO (Control)	-	-	-	-	-	-		
Ketoconazole	**15** ±0.34	**40**±0.46	**14**±0.34	**19**±0.43	**13**±0.45	**18**±0.69	**18**±0.30	**44**±0.33
Clotrimazole	**16**±0.34	**41**±0.44	**15**±0.45	**40**±0.34	**14**±0.46	**19**±0.65	**18**±0.44	**44**±0.43

A-1>B-6>B-5>B-4>A-3>A-2>A-4>A-5>A-6>B-3>>B-1>B-2

Table –III

4. RESULTS AND DISCUSSION

As can be seen from the table, all of the produced compounds were successful against all Gram positive and Gram negative bacteria as well as two strains of fungus, however compound B-1 was least effective and compound A-1 was most effective when compared to the conventional medicine. The substance A-1 worked best. Two Gram-negative bacteria, Escherichia coli and Proteus vulgaris, five Gram-positive bacteria (Staphylococcus Aureus, Staphylococcus Faecalis, Bacillus Substilis, P. Vulgaris, and B. Pumilus), and two strains of fungus. These substances were created in order to provide better antimicrobial molecules with a high yield and the best antibacterial and antifungal activity.

Methoxy substituted compounds were shown to be more active than Nitro substituted compounds. Comparing the effectiveness of substituted and unsubstituted compounds The presence of two nuclei, Quinozolinone and Triazine, may have contributed to the synthesised compounds' effectiveness against all five Gram-positive bacteria (Staphylococcus Aureus, Staphylococcus Faecalis, Bacillus Substilis, P. vulgaris, and B. Pumilus), two Gram-negative bacteria (Escherichia coli and Proteus vulgaris), and two strains of fungi. Additional research and the proper structural alteration of the title chemical could lead to the development of therapeutically beneficial products.

5. REFERENCES

1. Alagarsami V. Medical Chemistry Textbook; 2016.
2. New 1,2,4-triazine group-containing chalcone derivatives such as Tan X, Su
S, and Chen M:design, synthesis,antibacterialandantiviral activity. RSC Advanced 2019;9(1). Doi: 10.1039/c9ra00618d
3. Lai G.S., Maru J.J. Synthesis strategy of pyrrolo[2,1-f][1,2,4]triazine: the original part of the antiviral drug remdesivir. chemical heterocyclic compound. 2020;56(12).
doi:10.1007/s10593-020-02844-9
4. Morandini A, Spadati E, Leonetti B, et al. Long-acting quaternary ammonium salts of triazines as antimicrobial agents.
RSC Advanced2021;11(45). doi:10.1039/d1ra03455c
5. Barger G., Dale H.H. The chemical structure and sympathomimetic action of amines.
J. Physiol. 1910;41(1-2). doi:10.1113/jphysiol.1910.sp001392
6. Zheng G, Xia J, Chen Z, Yang J, Liu C. A study on the kinetics of thermal decomposition of aluminum sulfate. Phosphorus, sulfur and silicon relatedelments. 2020;195(4).doi:10.1080/10426507.2019.1686377
7. Campbell IB, Macdonald SJF, Procopiou PA.
Medical chemistry looking for drugs in the big pharmas of the past, present and future. Drugs on the disk today. 2018;23(2). doi: 10.1016 / j.Drudis.2017.10.007
8. Morgan E.Vogel's Textbook of Practical Organic Chemistry. 5th edition. try hard. 1990;14(3). Doi: 10.1016/0160-9327(90)90017-l
9. Mishra A., Shaini R.K., Bajpay A.K. A polymeric formulation for releasing an insecticide. In: Controlled Release of Pesticides for Sustainable

Agriculture. ; 2020.
doi:10.1007/978-3-030-23396-9_8

10. Loudon D.D. Chemistry of Heterocyclic Compounds. nature.
1954; 174 (4423). doi:10.1038/174241a0
11.D.J.Connolly, D. Cusack, T. P. O'Sullivan 및 P. J.
Giri, "Synthesis of quinazolinones and quinazolines", Tetrahedron, vol. 61, no. 43, p. 10153–10202, 2005.
12.Abida, P. Nayyar and M. Arpanarana, "An Updated Review: New Quinazoline Derivatives in Clinical Trials", International Journal of Pharmaceutical & Biological Archive, vol. 2, no. 6, p.1651–1657, 2011.
13.Mhaske S.B., N.P.Argade, "Chemistry ofrecentlyisolated natural quinazolinone alkaloids", Tetrahedron, vol. 62, no. 42, p. 9787–9826, 2006.
14. Mahato A.K., Srivastava B., S.Nithya, "Relationship between chemical structure, activity and biological activity of quinazolin-4(3H)-one derivatives", Inventi Rapid: MedChem, vol. 2, no. 1, 2011.
15. Grigg R, Mitchell TRB, Sutthivaiyakit S, Tongpenyai N.
Transition metal catalyzed N-alkylation of amines with alcohols. J Chem Soc Chem Commun. 1981; (12). doi:10.1039/C39810000611
16.Min Y, Zhang X, Zhao H, Qi G. Synthesis of 2,4,6-tri(hydroxylphenylmethylamino)-s-triazine, behavior and mechanism of curing by DGEBA. Acta Polim Sin. 2006; (7). Doi: 10.
3724/sp.j.1105.2006.00855
17.Cascioferro S, Parrino B, Spano V, et al. 1,3,5-Triazines: A Promising
Foundation for AnticancerDrugDevelopment. EurJMedChem. 2017;142.Doi:10.1016/j.ejmech.2017.09.035
18.Schaefer FC, Peters G.A. Synthesis of s-triazine systems. IV. A monosubstituted s-triazine isobtainedbyreaction of striazineandimidate. JOrgChem.1961;26(8). doi:10.1021/jo01066a037
19. Schaefer FC, Peters GA. Synthesis of s-triazine systems.III. Trimerization of the imidate. J Org Chem. 1961; 26(8). Doi: 10.1021/jo01066a036
20. Khattab SN, Abdel Naim SE, El-Sayed M, et al. Design and synthesis of novel s-triazine polymers and their applications as nanoparticle drug delivery systems. New J Chem. 2016;40(11).doi:10.1039/c6nj02539k
21. Nicolau K, Vourloomis D, Winsinger N.BP. The art and science of total synthesis. Angew Chem Int ed. 2000;39.
22.Garcia M.P., Martin M., Oro L.A. Mononuclear and binuclear complexes of rhodium (I) with ligand 3,5-bis(pyridin-2-yl)-1,2,4-triazole. inorganic chemistry. 1992; 191(2). Doi: 10.
1016/S0020-1693(00)93464-9
23. Shivaramu N.J., Nagabhushana K.R., Lakshminarasappa B.N., Singh F. Investigation of ion-induced luminescenceofY2O3:Dy3+ nanophosphorsfromsolgel.2016;169.doi:10.1016/j.jlumin.2015.07.054
24. Eweas AF, Abdallah QMA, Elbadawy MF. Synthesis and biological evaluation of some new derivatives of 2-pyridylquinazoline. CurrChemLett.2021;10(4).doi:10.5267/j.ccl.2021.4.005
25.V. L. F. Armarego, Quinazoline Textbook, 1963.
26. R. Rajput and A. P. Mishra, "An overview of the biological activity of quinazolinones", International Journal of Pharmacy and Pharmaceutical Sciences, vol.
4, no. 2, p. 66–70, 2012.
27. Rghavendra N.M. et al. "Synthesis and biological activity of partially substituted 2-phenyl-quinazolin-4-ones" Asian Journal of Chemistry, Volume 17, Issue 1, pp. 57-65.
28.NB Patel and JC Patel, "Synthesis and antibacterial activity of Schiff's base derived from Quinazoline 4(3H)-one and 2-azetidinone", Arabian Journal of Chemistry, vol.
4, no. 4, p. 403–411, 2011.
29. Bhat HR, Singh UP, Yadav PS, et al.Synthesis, characterization and antimalarial activity of 4-aminoquinoline-1,3,5-triazine hybrid derivatives. Arab J Chem. 2016;9. doi: 10.1016 / j.
Arabic 2011.07.001.
30.Hamama V.S., Ismail M.A., Shaaban S., Zoorob H.Kh. Synthesis and biological evaluation of some new thiazolo[3,2-a][1,3,5]triazine derivatives. honey. chemistry. Res 2012;21(9). Doi: 10.
1007/s00044-011-9783-1.