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Sythesis and biological evolution of trizole derivatives

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ABSTRACT

1,2,4-Triazole derivatives have consistently attracted scientific and practical interest because of their widely varying chemical properties, synthetic versatility, and pharmacological activities, such as antibacterial, antifungal, anti tubercular, analgesic, anti-inflammatory, anticancer, anticonvulsant, antiviral, insecticidal, and antidepressant antiviral properties. Moreover, the 1,2,4-triazole compounds carrying sulfone moiety or imine bond have been reported as antibacterial and antifungal, antihypertensive, analgesic, anti-inflammatory, or anti tumoral agents. The synthsised triazole compounds 5-(4-nitrostyryl)-5-(benzylideneamino)-1, 2, 4-triazolidine-3-one, 5-(hydroxy styryl)-5-(benzylideneamino)-1, 2, 4-triazolidine-3-one were biologically evaluated for antibacterial, antifungal, antihelmintic activity. The synthsised triazole compounds shows good anti bacterial, anti fungal activity, against standard drugs like chloramphenicol, tetracycline, fluconazole. In the present study, as a part of our ongoing research, we designed and synthesized new hybrid molecules containing different pharmacophores in a single structure.

INTRODUCTION

Triazole belongs to one of the most widely used class of antifungal drugs known as azoles, based on their common feature, an imidazole or triazole ring. The first compound in this class was discovered by the Janssen group in the late 1960s. Triazole refers to either one of a pair of isomeric chemical compounds with molecular formula $C_2H_3N_3$, having a five-membered ring of two carbon atoms and three nitrogen atoms. The azoles act through inhibition of lanosterol-14a-demethylase (CYP51), a key enzyme involves in the biosynthesis of ergosterol a major component of fungal cell membranes. This enzyme catalyses the oxidative removal of a specific methyl group from lanosterol through a cytochrome-P450-dependent mechanism. The azoles act through coordination to the heme group, preventing coordination of the oxygen required to initiate oxidation. 1,2,4-Triazole is one of a pair of isomeric chemical compounds with molecular formula $C_2H_3N_3$,called triazoles, which have a five-membered ring of two carbon atoms and three nitrogen atoms.1, 2, 4-Triazoles can be prepared using the Einhorn-Brunner reaction

or the Pellizzari reaction. The Einhorn-Brunner reaction is the chemical reaction of imides with alkyl hydrazines to form a mixture of isomeric 1, 2, 4-triazoles. The Pellizzari reaction is the chemical reaction of an amide and a hydrazide to form a 1, 2, 4-triazole.

Anti-inflammatory activity

The synthesis of 3-[1-(4-(2-methylpropyl)phenyl)ethyl]-1,2,4-triazole-5-thione and its condensed derivatives 6-benzylidenethiazolo[3,2-b]-1,2,4-triazole-5(6H)-ones are described. The structures of the compounds were elucidated by spectral and elemental analysis. In the pharmacological studies, anti-inflammatory activities of these compounds have been screened. In gastric ulceration studies the synthesized compounds were generally found to be safe at a 200 mg/kg dose level. The synthesis of different acylated 1, 2, 4 - triazole-3-acetates with the objective of discovering novel and potent anti-inflammatory agents. Structures of the synthesized compounds were elucidated by spectral and elemental analyses. The obtained compounds were evaluated for their anti-inflammatory activites as well as gastric ulcerogenic effects and acute toxicity.

Anti mycobacterial activity

Series of 3-benzylsulfanyl derivatives of 1,2,4-triazole and 4-methyl-1,2,4-triazole were synthesized by alkylation of starting triazole-3-thiol with appropriately substituted benzyl halide. All members of the set were evaluated for in vitro antimycobacterial activity against Mycobacterium tuberculosis, M. avium, and two strains of M. kansasii. The activities were expressed as the minimum inhibitory concentration. The compounds exhibited only a moderate or slight antimycobacterial activity. Minimum inhibitory concentrations fall into a range of 32- >1000 μmol/l. The most active substances bear two nitro groups or a thioamide group on the benzyl moiety. As regards the cytotoxicity effect, the evaluated compounds can be considered as moderately toxic.

Antimicrobial activity

Glucosidation of some 4-amino- and 4-arylideneamino-5-(pyridin-3-yl)-2,4-dihydro-[1,2,4]- triazole-3-thiones with 2,3,4,6-tetra-O-acetyl-a-D-glucopyranosyl bromide followed by chromatographic separation gave the corresponding N- and S-b-D-glucosides. The structure of these two regiosiomers was established chemically and spectroscopically. Deamination as well as deacetylation of some selected nucleosides have been achieved. Antimicrobial screening of 14 selected compounds resulted in their activity against Aspergillus fumigatus, Penicillium italicum, Syncephalastrum racemosum, Candida albicans, Staphylococcus aureus, Pseudomonas aeruginosa, Bacillus subtilis, and Escherichia coli. Ethyl 5-(2-furyl)-4-ethyl-1,2,4-triazole-3-mercaptoacetate, 5-(2-furyl)-4-ethyl-1,2,4-triazole-3- mercaptoacetic acid hydrazide and a series of new N-alkylidene/arylidene-5-(2-furyl)-4-ethyl-1,2,4-triazole-3-mercaptoacetic acid hydrazides were synthesized and evaluated for in vitro antibacterial activity against Staphylococcus aureus ATCC 6538, Staphylococcus epidermis ATCC 12228, Klebsiella pneumoniae ATCC 4352, Pseudomonas aeruginosa ATCC 1539, Escherichia coli ATCC 8739, Shigella flexneri, Salmonella typhi, Proteus mirabilis and antifungal activity against Candida albicans ATCC 10231 using the disk diffusion andmicrodilution methods. The in vitro antimycobacterial activity of the new compounds against Mycobacterium tuberculosis H37Rv was evaluated employing the BACTEC 460 radiometric system. The highest inhibition observed was 61% at 6.25 g/ml

Anticonvulsant activity

Novelcompounds3-{[(substitutedphenyl)methyl]thio}-4-alkyl/aryl-5 (4aminophenyl)-4H-1,2,4-triazoles and several related Schiff's bases, 3-{[(substituted phenyl)-methyl]thio}-4-alkyl/aryl-5-{[[(substitutedphenyl/5-nitro-2-furyl)methylene]amino]-phenyl}-4H- 1,2,4-triazoles were synthesized for evaluation of their biological properties. Structures of the synthesized compounds were confirmed by the use of their spectral data besides elemental analysis. All compounds were evaluated for their anticonvulsant activity by maximal electroshock (MES), subcutaneous pentylenetetrazole (scPTZ) and neurotoxicity (NT) screens. A number of triazole derivatives, exhibited protection after intraperitoneal administration at the dose of 100 and 300mg/kg in one or both models employed. Some of the tested compounds showed marginal

activity against M. tuberculosis H37 Rv. A series of 4-(4-alkoxylphenyl)-3-ethyl-4H-1,2,4-triazole derivatives was synthesized as open- chain analogues of 7-alkoxyl-4,5 dihydro[1,2,4]triazolo[4,3-a]quinolines. Their anticonvulsant activities were evaluated by the maximal electroshock test (MES test) and their neurotoxicity was evaluated by the rotarod neurotoxicity test (Tox). MES test showed that 3-ethyl-4-(4- octyloxyphenyl)-4H-1,2,4-triazole 3q was found to be the most potent with ED50 value of 8.3 mg/kg and protective index (PI = TD50/ED50) value of 5.5, but compound 3r, 3-ethyl-4-(4- octyloxyphenyl)-4H-1,2,4-triazole, exhibited better PI value of 9.3, which was much greater than PI value of the prototype drug phenytoin. For explanation of the possible mechanism of action, the compound 3r was tested in pentylene tetrazole test, isoniazid test, thiosemicarbazide test, 3- mercaptopropionic acid and strychnine test.

Analgesic Activity

A series of 1,3,4-oxadiazole/thiadiazole and 1,2,4-triazole derivatives of biphenyl-4-yloxy acetic acid were synthesized in order to obtain new compounds with potential anti-inflammatory activity, analgesic activity and lower ulcerogenic potential. All compounds were evaluated for their anti-inflammatory activity by the carrageenan induced rat paw oedema test method. The compounds possessing potent anti-inflammatory activity were further tested for their analgesic, ulcerogenic and antioxidant activities. These compounds showed significant analgesic effect and at an equimolar oral doses relative to flurbiprofen were also found to be non-gastrotoxic in rats. (81.81%) than the reference drug (79.54%), low ulcerogenic potential and protective effect on lipid peroxidation.

Cytotoxic activity

Novel derivatives of 4,5-substituted-1,2,4-triazole-thiones and 2,5-substituted-1,3,4-thiadiazoles were synthesized and evaluated for their cytotoxicity. The biological study indicated that compounds 4-ethyl-5-(4,5,6,7-tetrahydro-1benzothien-2-yl)-2,4-dihydro-3H-1,2,4-triazole-3-thione,N-ethyl-5-(4,5,6,7-tetrahydro-1-benzothien-2-yl)-1,3,4-thiadiazol-2-amine,4-amino-5-(4,5,6,7-tetrahydro-1-benzothien-2-yl)-2,4-dihydro-3H-1,2,4-triazole-3-thione and 4-amino-5-(5-phenylthien-2-yl)-2,4-dihydro-3H-1,2,4-triazole-3-thione possessed high cytotoxicity in vitro against thymocytes. The corresponding IC50 values were 0.46 mM, 5.2 _ 10_6 mM, 0.012 mM and 1.0 _ 10_6 mM. The tested compounds showed a general stimulation effect on B-cells' response.

Antioxidant activity

Some 4-benzyl-idenamino-4,5-dihydro1H-1,2,4-triazol-5-one derivatives were prepared and investigated for their antioxidant activity also the pKa in Non aqueous solvent is also determined. Triazole refers to either one of a pair of isomeric chemical compounds with molecular formula C 2 H 3 N 3 , having a five-membered ring of two carbon atoms and three nitrogen atoms. The two isomers are, the triazole antifungal drugs include fluconazole, isavuconazole, itraconazole, voriconazole, pramiconazole and posaconazole. The triazole plant protection fungicides include epoxiconazole, triadimenol, propiconazole, metconazole, cyproconazole, tebuconazole, flusilazole and paclobutrazol. 1,2,3-Triazole is one of a pair of isomeric chemical compounds with molecular formula C 2 H 3 N 3 , called triazoles, which have a five-membered ring of two carbon atoms and three nitrogen atoms. 1,2,3-Triazole is a basic aromatic heterocycle. Substituted 1,2,3-triazoles can be produced using the azide alkyne Huisgen cycloaddition in which an azide and an alkyne undergo a 1,3-dipolar cycloaddition reaction. It is a surprisingly stable structure compared to other organic compounds with three adjacent nitrogen atoms. However, flash vacuum pyrolysis at 500 °C leads to loss of molecular nitrogen (N 2) to produce aziridine. Certain triazoles are relatively easy to cleave due to so-called ring-chain tautomerism. One manifestation is found in the Dimroth rearrangement. 1,2,3-Triazole finds use in research as a building block for more complex chemical compounds, such as pharmaceutical drugs like tazobactam.

LITERATURE REVIEW

Mamata khatak et., al., In the last few decades, the chemistry of 1,2,4-triazoles and their fused heterocyclic derivatives has received considerable attention owing to their synthetic and effective biological activities such as anti-

inflammatory, CNS stimulants sedatives, antianxiety, antimicrobial agents and antimycotic activity such as fluconazole, intraconazole, voriconazole. Also, there are known drugs in market containing the 1,2,4-triazole group e.g. Triazolam, Alprazolam, Etizolam and Furacylin. Present antitubercular drugs are more toxic and multiple drug therapy is required. So it is important to find out the analogues with good antitubercular activity. Microwave heating has attracted the attention of investigators in synthesis of drugs to shorten the length of reactions significantly, to increase their selectivity, and to increase the product yields, which is particularly important in the case of high-temperature processes that take a long time. This review includes the Microwave synthesis of 1,2,4- triazoles and its reported derivatives.

Wakale et.,al., Several five membered aromatic systems having hetero atoms at symmetrical positions such as triazoles have been studied extensively owing to their interesting biological activities. The five membered triazole ring exists in two tautomeric forms i.e. 1, 2, 3-triazole and 1, 2, 4-triazole. The prototype of 1,2,4- triazoles are 1H-1, 2, 4- triazole and 4H-1, 2, 4-triazole collectively known as s-triazoles The s-triazole derivatives possess wide spectrum of biological activities such as antibacterial, antifungal, antitubercular, anticancer, anticonvulsant, antidepressants, analgesic, anti-inflammatory, antioxidant, antiviral, antihelmintic antitumor, hypoglycemic activities. This diversity in the biological response profile has attracted the attention of many researchers to explore this skeleton to its multiple potential against several activities. This review contains various pharmacological activities of triazole in one place and it is also the milestone for the new research towards this moiety.

Pandaya surendra et., al., Azoles belong to very important class of Antimicrobial drugs. Triazoles is very important azole which exists in two isomeric forms namely 1,2,3-triazoles and 1,2,4-triazoles. The review article covers the different approaches to synthesize triazoles having different substitution and their different biological activity. This review article can be useful to synthesize new compounds having triazole nucleolus.

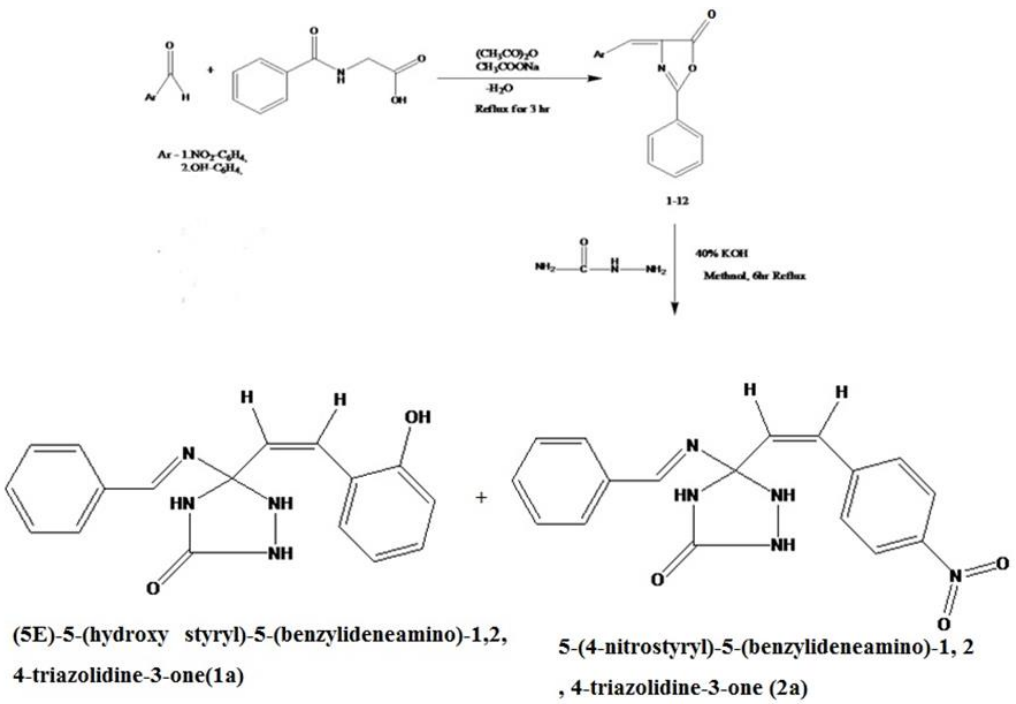
Priyanka et., al., Triazole is a five membered heterocyclic system consisting of two carbon atoms and three nitrogen atoms shows wide range of biological activities. Triazoles can be synthesized using Einhorn-Brunner reaction or the Pellizzari reaction from acyl hydrazides. Triazoles posses wide spectrum of biological activities like including antibacterial, antifungal, antiviral, anti-inflammatory, anticonvulsant, antidepressant, antihypertensive, analgesic, and hypoglycemic properties. The present reviews attempted to gather the various developments in synthesis and biological activities of triazole derivatives.

MATERIAL AND METHODS

Materials

Hippuric acid – (LOBA-B.NO-G228507), Acetic anhydride – (FISHER'S SCIENTIFIC-B.NO-92757004-2), Sodium Acetate – (FINAR-B.NO-19095780), semicarbazide –(LOBA-B.NO-S057310), Methanol (SD FINE-CHEMLIMITED-B.NO-IOZA-0502-0409-13), Charcoal – (QUALINGENS-BNO-17335406-S), Ethanol – (CSS-B.NO-110605), Aldehydes:4-Nitro benzaldehyde – (LOBA-B.NO-SG48351208), Agar –agar – (LOBA-B.NO-V0324/1),Peptone – (HIMEDIA – RM667-500G), Beef extract – (HIMEDIA – RM002-500G), Sodium chloride – (SD FINE-CHEMLIMITED- B.NO-H12A/1611/2301/13), Dextrose – ((LOBA-B.NO-SL37611202), Disodium hydrogen phosphate – (FINAR- B.NO-19105845), Potassium Ferric cyanide – (FINAR- B.NO-18042046), Trichloro acetic acid – (MERCK- B.NO-MD9M590220, Ferric chloride – (LOBA-B.NO-SL26831111), Ascorbic acid – (LOBA-B.NO-SL44911205), Gum Acacia – ((LOBA-B.NO-V0324/1), DMSO – ((LOBA-B.NO-LMO4231309)

From the literature review we have planned to design N-substituted 1, 2, 4-triazoles by the following procedure. Methods: General Procedure for the Synthesis of Compounds (1a-2a) The compounds were synthesized as per the scheme as shown in Fig 1



Scheme 1: synthesis of various 1, 2, 4 triazolidin-3-one derivatives

Step-1: Synthesis of 4-benzylidene-2-phenyloxazol-5(4H)-one

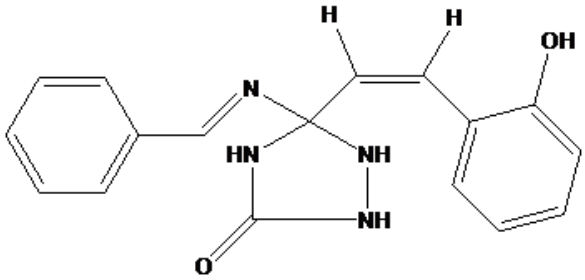
Oxazolin-5-ones were prepared by condensation of 0.01 moles of Hippuric Acid with 0.02 moles of aromatic aldehydes in presence of 0.075 moles of Acetic Anhydride and 0.025 moles of Sodium Acetate .To this 2ml of water was added and the reaction mixture was refluxed for 3 hrs. The reaction mixture was cooled; precipitate was filtered, dried, recrystallized from methanol and confirmed by thin layer chromatography and melting point.

Step-2: Synthesis of 5-(hydroxy styryl)-5-(benzylideneamino)-1, 2, 4-triazolidine-3-one

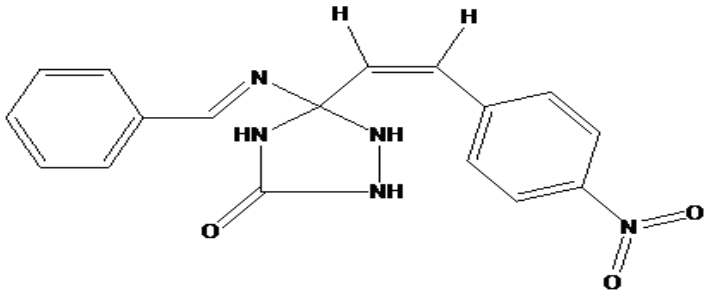
The product from step1 condensed with equimoles (0.001moles) of semicarbazide in presence of methanol and a few drops of 40% KOH refluxed for 6hrs, cooled; the product formed was filtered, dried and recrystallized from methanol. The progress and the purity of the reaction were confirmed by thin layer chromatography and melting point. The procedure was illustrated under scheme 1.

Physical and spectral characterisation

(5E)-5-(hydroxy styryl)-5-(benzylideneamino)-1, 2, 4-triazolidine-3-one (1a)



Molecular formula: $C_{17}H_{16}N_4O_2$
Molecular weight: 308
Melting point: 243^0C
5-(4-nitrostyryl)-5-(benzylideneamino)-1, 2, 4-triazolidine-3-one (2a)



Molecular formula: $C_{17}H_{15}N_5O_3$
Molecular weight: 337
Melting point: 228 ^{0}C

BIOLOGICAL EVALUTION

The synthesized compounds were biologically evaluated for Antibacterial, Anti fungal and Antihelmintic activity

Antibacterial activity

All the synthesized compounds 1a-2a were examined for invitro antibacterial activity against an assortment of two gram-positive bacteria *Staphylococcus aureus* and *Bacillus subtilis* and one Gram-negative bacteria *Escherichia coli* by diffusion method. Tetracycline and Chloramphenicol were used as an internal standard. Nutrient agar (Hi-media) was dissolved and distributed in 25 ml quantities in boiling tubes and were sterilised in an autoclave at 121^{o}C (15Lbs /sq.in) for 20 minutes. The medium was inoculated at one percent level using 18 hours old cultures of the test organism mentioned above aseptically into sterile petri dishes and allowed to set at room temperature for about 30 minutes. In a size of 4 inches petri dishes, five cups of 8mm diameter at equal distance were made in each plate. In the cups the test solutions of different concentrations were added and in another plate cups were made for standard and control. The plates thus prepared were left for 90 minutes in a refrigerator for diffusion. After incubation for 16 hours at 37^{o}C the plates were examined for inhibition zones. The experiment was performed in duplicate and the average diameter of the zones of inhibition measured is recorded .the results were represented in Table 1

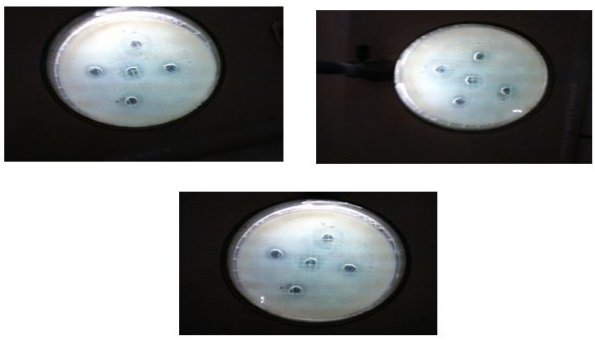


Fig 1: Anti bacterial activity

Antifungal activity

The antifungal activity of compounds were assayed against three different strains of *Aspergilus Niger* Potato dextrose agar (Hi- media) was dissolved and distributed in 25 ml quantities in 100ml conical flasks and were sterilized in an autoclave at 121^{0}C (15lbs/sq.in) for 20 minutes. The medium was inoculated at one percent level

using 18hr old cultures of organisms mentioned above aseptically in to sterile petridish and allowed to set at room temperature for about 30 minutes. . In a size of 4 inches petridish 5 cups of 8mm diameter at equal distance were made in Petri plate with a sterile borer. The solutions of test and standard at concentrations (250µg/ml, 200µg/ml, 150µg/ml, 100µg/ml and 50µg/ml) were added to respective cup aseptically and labelled accordingly. DMF as control did not show any inhibition. The plates were left for 90 minutes in refrigerator for diffusion. After incubation for 24 hrs at $37^0 \pm 1^0$ c. The plates were examined for incubation inhibition zones. The experiments were performed in duplicate and the average diameters of the zones of inhibition were summarized in **table 2**

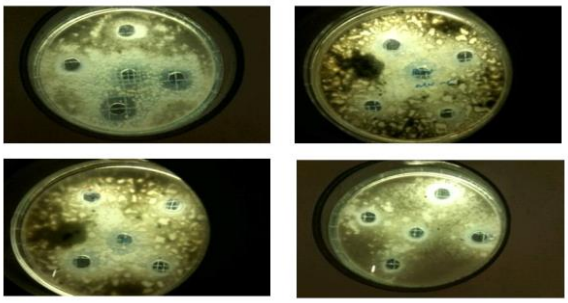


Fig 2: Anti fugal activity of aspergillums niger, pencillium chrysogenum, pencillium notatum

Antihelmenthic activity

Indian adult earthworms of the genus and species, *Pheritima posthuma* (family: Megascolecidae), were used to study the antihelmintic activity. The earthworms were collected from the water logged areas of soils in Vijayawada, Andhra Pradesh, India 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 all experiment protocols. The earthworms resembled the intestinal roundworm parasites of human beings both anatomically and physiologically and hence were used to study the antihelmintic activity.

1% Gum acacia solution prepared in normal saline, different concentrations was prepared by usingthis solution. Sample were taken petriplates and adult healthy earth warms (n=6) were introduced in to them. Observations were made for the time taken to paralyze and time taken for death of the organism. Paralysis was said to occur when the worms do not review even in normal saline. Death was concluded when worms lost their motility followed by fading away of the body colour.

Fig 3: Anti helmenthic activity

RESULTS AND DISCUSSIONS

Antibacterial activity

The synthesized compounds (1a-2a) were screened for anti bacterial activity studies at concentration of 50µg/ml and 100µg/ml, 150µg/ml, 200µg/ml, 250µg/ml using dimethyl formamide solution control against bacterial organisums like bacillus subtilis, staphylococcus aureus, pseudomonas aeruginosa, by disc diffusion method using nutrient agar medium here tetracycline, chloramphenicol as standard drugs in concentration of 50µg/ml and 100µg/ml, 150µg/ml, 200µg/ml, 250µg/ml against gram positive, gram negative organisms. In a table 1 indicate thiazole derivatives like 5-(4-nitrostyryl)-5-(benzylideneamino)-1, 2, 4-triazolidine-3-one, 5-(hydroxy styryl)-5-(benzylideneamino)-1, 2, 4-triazolidine-3-one shows good anti bacterial activity.

Table 1 Anti bacterial activity of bacillus subtilis, staphylococcus aureus, pseudomonas aeruginosa & Proteusvulgaris

Zone of inhibition (Diameter in Cm)										
Compound	**Bacillus subtilis**					**Staphylococcus aureus**				
	50 µ/ml	**100 µ/ml**	**150 µ/ml**	**200 µ/ml**	**250 µ/ml**	**50 µ/ml**	**100 µ/ml**	**150 µ/ml**	**200 µ/ml**	**250 µ/ml**
1a	1.1	1.2	1.3	1.4	1.6	1.1	1.5	1.5	1.6	1.7
2a	0.9	1	1.1	1.2	1.3	1	1.1	1.2	1.2	1.4
Tetracycline	1.9	2	2	2.1	2.2	2	2.1	2.2	2.3	2.3
Chloramphenicol	2	2.1	2.2	2.3	2.4	1.9	2	2.1	2.2	2.3
Compound	**Pseudomonas aeruginosa**					**Proteusvulgaris**				
	50 µ/ml	**100 µ/ml**	**150 µ/ml**	**200 µ/ml**	**250 µ/ml**	**50 µ/ml**	**100 µ/ml**	**150 µ/ml**	**200 µ/ml**	**250 µ/ml**
1a	1.1	1.2	1.4	1.6	1.7	0.9	1.1	1.2	1.4	1.6
2a	1	1.1	1.3	1.4	1.6	1	1.2	1.2	1.3	1.5
Tetracycline	1.9	2	2.1	2.1	2.2	1.9	2	2.1	2.2	2.3
Chloramphenicol	2	2.1	2.2	2.3	2.4	1.9	2	2.1	2.2	2.3

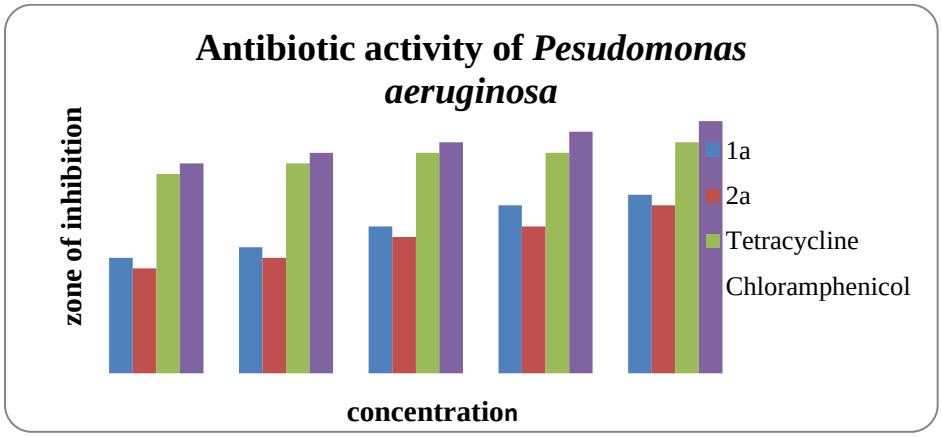


Fig: 4 Antibiotic activity of Pesudomonas aeruginosa

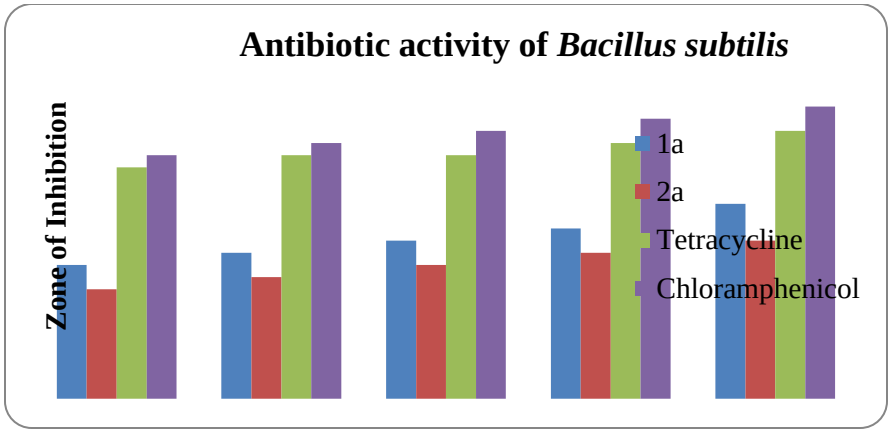


Fig: 5 Antibiotic activity of Bacillus subtilis

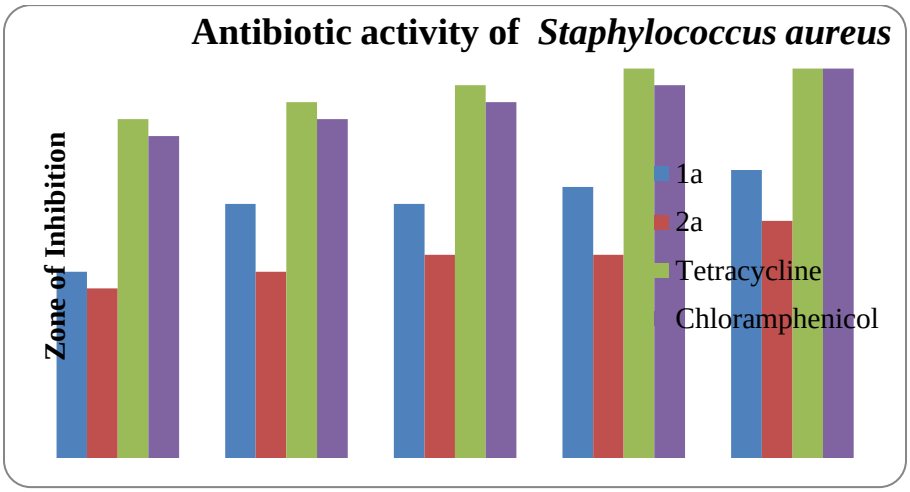


Fig: 6 Antibiotic activity of Staphylococcus aureus

Antifungal activity

The synthesized compounds (1a-2a) were screened for anti bacterial activity studies at concentration of 50µg/ml and 100µg/ml, 150µg/ml, 200µg/ml, 250µg/ml using dimethyl formamide solution control against bacterial organisums like aspergillums niger, pencillium chrysogenum, pencillium notatum by disc diffusion method using nutrient agar medium here fluconazole as standard drugs in concentration of 50µg/ml and 100µg/ml, 150µg/ml, 200µg/ml, 250µg/ml against fugal organisms.

In a table 1 indicate thiazole derivatives like 5-(4-nitrostyryl)-5-(benzylideneamino)-1, 2, 4-triazolidine-3-one, 5-(hydroxy styryl)-5-(benzylideneamino)-1, 2, 4-triazolidine-3-one shows good anti fugal activity.

Table: 2 anti fungal activity of aspergillums niger, pencillium chrysogenum, pencillium notatum

Zone of inhibition (Diameter In Cm)															
Compound	**Aspergillums Niger**					**Pencillium chrysogenum**					**Pencillium notatum**				
	50 µ/ml	**100 µ/ml**	**150 µ/ml**	**200 µ/ml**	**250 µ/ml**	**50 µ/ml**	**100 µ/ml**	**150 µ/ml**	**200 µ/ml**	**250 µ/ml**	**50 µ/ml**	**100 µ/ml**	**150 µ/ml**	**200 µ/ml**	**250 µ/ml**
1a	1	1.1	1.2	1.2	1.3	0.9	1	1	1.1	1.1	1	1.1	1.1	1.2	1.3
2a	1	1.1	1.2	1.2	1.3	1	1.1	1.2	2	2.1	1	1.1	1.2	1.2	1.3
Fluconazole	1.6	1.7	1.8	1.9	2.0	1.5	1.6	1.8	1.9	2.0	1.7	1.8	1.9	2.0	2.1

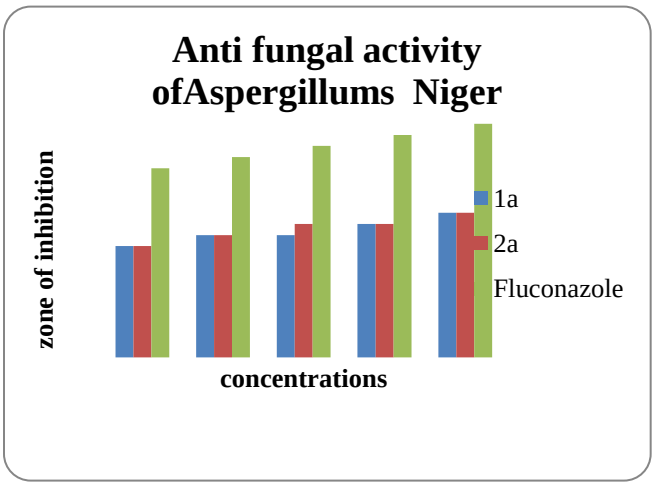


Fig:7Anti fungal activity of Aspergillums niger

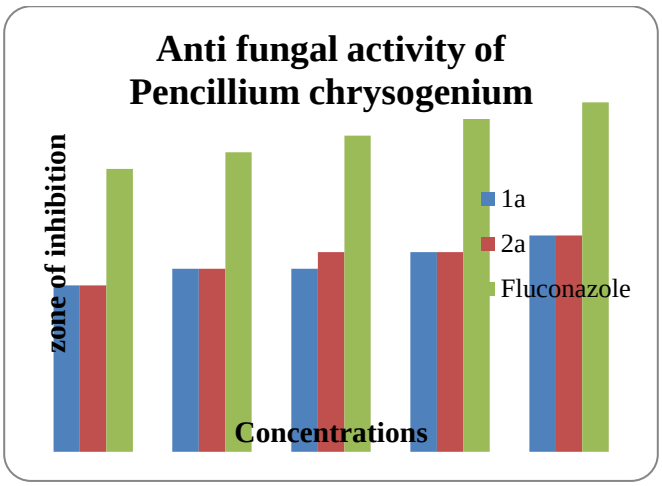


Fig: 8 Anti fungal activity of Pencillium chrysogenium

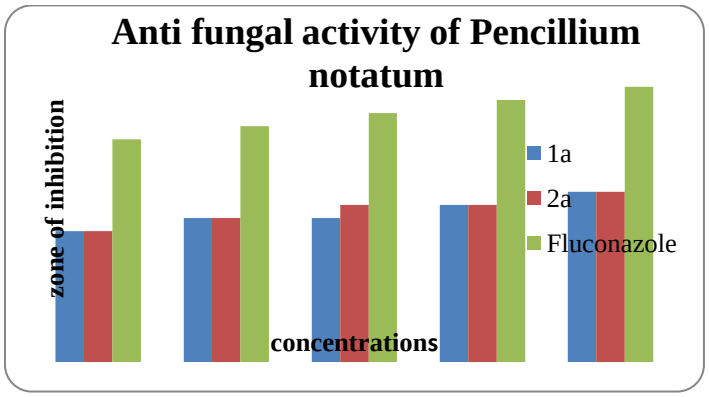


Fig: 9 Antifungal activity of Pencillium notatum

Antihelmenthic activity

The synthesised compounds screen for anti helmenthic activity observed in earth worms. The synthsised compounds like 5-(4-nitrostyryl)-5-(benzylideneamino)-1, 2, 4-triazolidine-3-one, 5-(hydroxy styryl)-5-(benzylideneamino)-1, 2, 4-triazolidine-3-one solutions prepared in the concentration of 50mg/ml against standard solution of albendazole in the concentration of 50mg/ml to note down the paralysis time, death time in minutes. The synthsised compounds show good anti helmenthic activity against standard drug albendezole.

Table 3: Antihelmintic activity of novel N-substituted 1,2,4 triazolidin-3-one derivatives

S. No	Compounds	Dose	Paralysis time in minutes	Death time in minutes
			MEAN±S.M	MEAN±S.M
1	1a	50mg/ml	4 ± 0.5	5.13±0.416
2	2a	50mg/ml	3.6±0.529	5.1±0.36
3	Control	Normal saline	-------	------
4	Albendazole	50mg/ml	11±1	21.5±2.1

CONCLUSION

The synthsised triazole compounds 5-(4-nitrostyryl)-5-(benzylideneamino)-1, 2, 4-triazolidine-3-one, 5-(hydroxy styryl)-5-(benzylideneamino)-1, 2, 4-triazolidine-3-one shows good anti bacterial, anti fungal activity, against standard drus like chloramphenical, tetracycline, fluconazole, Anti helmenthic activity done by invitro studies from these results compounds have excellent helmenthic activity compared to control saline solution. From these compounds 5-(4-nitrostyryl)-5-(benzylideneamino)-1, 2, 4-triazolidine-3-one, 5-(hydroxy styryl)-5-(benzylideneamino)-1, 2, 4-triazolidine-3-one have excellent anti helmenthic activity.

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