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RESEARCH ARTICLE OPEN ACCESS

Synthesis and Spectral Charectarization of Oxazole/Thiazole Derivatives and Their Biological Potent Activities

Mr. P Venugopal, Dr. T.Payani and Prof.K.B.Chandrasehar
Department of Chemistry, JNTUA, Ananthapuram A.P
(India).

ABSTRACT

The Oxazoles, thaiazoles, oxadiazoles, thiazolidinones, Benzimidazoles, 1,2,4 triazoles, pyrimidine and pyridine their nucleus has a annulment Biological activities as Aneasthetic, antimalarial, antibacterial, antifungal etc. Oxazoles/thaiazoles. The Nucleus of thiazole are prosingdifferentbiologicalactivities and useful in the hospitalization as anaesthetic, hypertrophy, cardiac, malarial, bactericidal, antidepressant, cancer, anti biotic and antifungal activity. The main study of the method of this work is the effect of three methoxygroup reaction inthecoursewithsubstituted the nucleus ofoxazole/thiazole and on the activities as Aneasthetic, antimalarial, antibacterial, antifungal antibioticsothesynthesized derivatives.The derivative compoundswere explorationagainst plasmodium group for the antimalarial examination.B.subtilis Staphylococcusaureus,E.coli, and P.A eruginosa, for antibacterial study and against Aspergillus Niger ,C. Albicans, for antifungalactivity and anti-bodices in medicine and aneasthetic in some their activities for the cancer treatment.

KEYWORDS:- Oxazole, Thiazole,trimethoxybenzaldehyde,Aneasthetic, antimalarial, Antifungal,a n t i b i o t i c Antibacterialactivity, Benzimidazoles,.

INTRODUCTION

The progressin pharmacology, Organic and the medicinalchemistry hasovercome of the applicationof modernbiochemistry to its issues. The study and design of medicinal agents has initially on the Overall chemical structure of synthetic and natural compounds having confirmed in the biological action.

The chemical synthesis of Oxazoles and thiozoles are effect of their changes in biological responses is used to the relationship in structural activity.

In the chemical synthesis is basically modifications of the primarystructure of the compound and the consequenceeffect of changein the response of biological activity and used to structure activity relationship.These relationships a reguide in the new drugs in the modern synthesis,design of new agents of similar biological activity. and very useful, effective result as are the development interpretation of the structural feature.

At present themethod of action which leads to acomprehension of drug activity by the approaching the attempt by related as per the drug physio chemical properties or result in thedevelopment of advanced effective drug.

The investigating studies and application of Medicinal and organicchemisty[1] are very large interesting andoutstandinglyuseful of nitrogen and Sulphur molecules.The differentbranches oforganic, nitrogen Sulphur hetero cyclic and combination of chemistry, the heterocyclic compounds of oxazole, Thiozoles, pyrimidine, oxadiazoles,thiadiazoles,pyridine, tetralin occupyimportant place in the

process.

The Oxazoles and thiozoles arevery important inthe Anastatic, anti-malarial, antibacterial, antifungal drugs in the pressing by increased conspicuous ofthesystemicspreading offungalinfections in immunosuppressed patients.They are being used asantifungal[2-8] ,antituberculosis[9],CNS[10-15],antispasmodic[16-17],antimalarialandantibacterialactivities.
The Oxazoles and thiozoles derivatives are mainly preparation by the phenyl nucleus and compounds with phenolic group,1,3 ,4, Oxadiazoles and thaiazoles.which have the anti-fungalactivities [18-20].1,2,4 triazoles derivatives [21] triazoles ofgallic acid [22] the substituted phenyl semi carbazide& quinazolinone, benzylidene /oxaquinazolin[23]of the heterocyclicderivatives[24] shows the biologically potent[25] antibacterialand antifungalactivities.

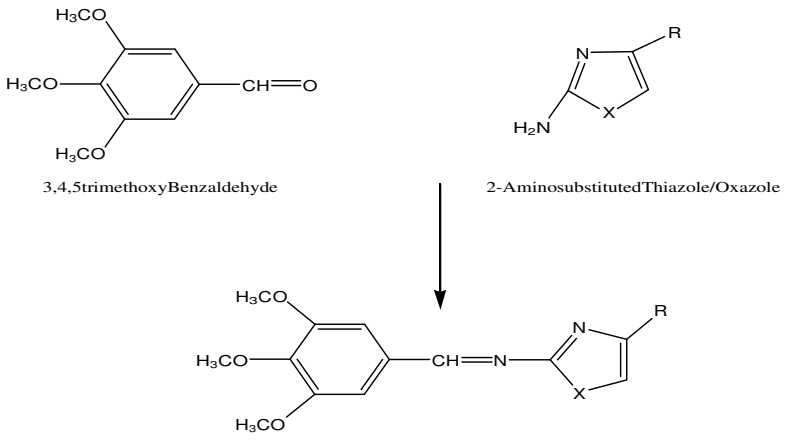
Thiazolidine derivatives [26]1,3,4 oxadiazoles [27],1,2,4disubstituted thiazoles [28],and mixed oxazole's /Thiazoles of heterocycle asthe biologically potent antibacterial, anti-malarial, aneasthetic, antibiotic and antifungalactivities.

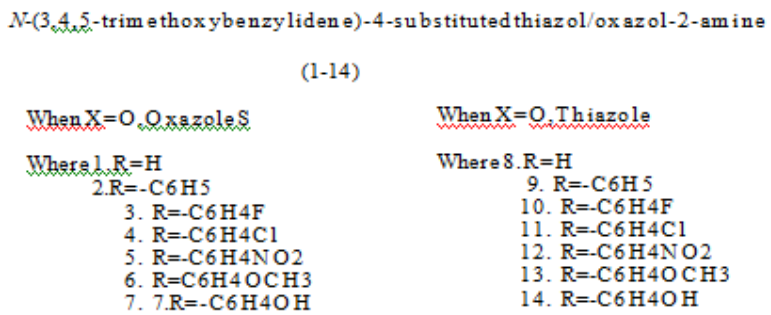
The presenceofhydroxyl, methoxy, groups compounds of Imines are to possess biological activity theparent compound have the phenylnucleus is very use full for the increasing the biologicalactivity. Furanose having thePyrimidine derivatives [29] and pyrimidine substituted derivatives [30] hasactive to possessforantifungal, anticancer,antioxidant activities.

Literaturereveal reviews that tetrazoles derivatives [31], Pyrrole derivatives [32], pyrazine heterocycles [33],azolesandazinederivativesoftertiary butyl carbazate[34], pyranopyrazolederivatives[35],chalcones have the heterocycliccompoundsderivatives[36,37],6-chloropyridazinethiones of heterocycliccompoundsderivatives[38],Schiff base derivative[39], 3-indolylthiophenesubstituted derivatives forpotential antimalarial,antimicrobial and antifungalactivities[40].

The plenty of work has been done on oxazole&thiazole nucleus with potential biological potential activitieslikeAneasthetic, anti-malarial, antibacterial, antifungal anti-inflammatory,antidiuretic,antiviral antibiotic, anticancerand antioxidant activities.The present work shown the effect of carbonphenyl compound withthree methoxy group on their actionswithoxazole/thiazole substitutednucleusand the antifungal,antibacterial, anti-inflammatory biological activities oftheproduced products.

Theliteraturefacts and studyinthepresent process of workshows in the condensation of 4`-(p-subst/unsubst)-phenyloxazole/ thiazole / 3,4,5trimethoxybenzaldehyde [41]with2-aminothiazoleand evaluated for biologicallypotent antimalarial,antibacterial & antifungal activityaccordingto scheme 1.





Picture-1

METHODs AND MATERIALS

The mixture of compound melting points is identified in open capillary tubes. Perkin Elmer FT-IRspectrophotometer (model RX-1) model of spectra instrument were used for the put down for compound spectra. DMSO-d6 solvent spectra recorded in the PMR spectra in room temperature and TMS as refer to IR spectra of the solvent were identified and documentation in the solid state with the method of KBrpellet. PerkinElmerModel 32 NMR spectrometer at 300MHz at CDRILucknow for the record of NMR Spectra of the compound.

TLC for the monitored of reaction. The required 2-Amino-4-[p-subst/unsubst] phenyl oxazole's /thiazoles and 3,4,5 trimethoxybenzaldehyde[41] were prepare and produced by different know methods.Each onecompound has been described in sequel on procedure in different steps. The compound's analyzed Data are follows in Table 1.

Table-1PhysicalDataofCompounds

CompdNo.	Natureof Ar-NH_2	Yield (%)	M.P(°C)	MolecularFormula
1	2-Amino-oxazole	**88**	**135**	$C_{13}H_{14}N_2O_4$
2	2-Amino-4-phenyloxazole	**80**	**138**	$C_{19}H_{18}N_2O_4$
3	2-Amino-4-(p-fluoro)phenyloxazole	**76**	**171**	$C_{19}H_{17}N_2O_4F$
4	2-Amino-4-(p-chloro)phenyloxazole	**77**	**158**	$C_{19}H_{17}N_2O_4Cl$
5	2-Amino-4-(p-nitro)phenyloxazole	**79**	**184**	$C_{19}H_{17}N_3O_6$
6	2-Amino-4-(p-methoxy)phenyloxazole	**81**	**169**	$C_{20}H_{20}N_2O_5$
7	2-Amino-4-(p-Hydroxy)phenyloxazole	**80**	**172**	$C_{19}H_{18}N_2O_5$
8	2-Amino- thiazole	**83**	**143**	$C_{13}H_{14}N_2SO_3$
9	2-Amino-4-phenylthiazole	**85**	**151**	$C_{19}H_{18}N_2SO_3$
10	2-Amino-4-(p-fluoro)phenylthiazole	**83**	**174**	$C_{19}H_{17}N_2SO_3F$
11	2-Amino-4-(p-chloro)phenylthiazole	**82**	**162**	$C_{19}H_{17}N_2SO_3Cl$
12	2-Amino-4-(p-nitro)phenyloxazole	**79**	**191**	$C_{19}H_{17}N_2O_6$
13	2-Amino-4-(p-Hydroxy)phenylthiazole	**74**	**166**	$C_{19}H_{18}N_2O_4S$
14	2-Amino-4-(p-methoxy)phenylthiazole	**74**	**172**	$C_{20}H_{20}N_2SO_4$

The Synthesis process ofN-(3, 4, 5 tri methoxy Benzylidene)-4-subst/unsbst oxazole/thiazol-2-aminePreparation

2-amino-4-phenylthiazole(2.50gm,0.1mol) and3,4,5trimethoxybenzaldehyde(39.0gm,0.1mol)were taken in R.B flask (500ml) of benzene (200ml) with Dean &Stark apparatus for filter. The compound ofmixture was

refluxed in (3.4 gm, 0.1mol) till water wasdivided and separate out in the plates.Thecrudeproduct of compound was received after the cooled temperature the total product wasrecrystallizefrom ethanolto get crystalswhite product of N-(3, 4, 5 tri methoxy Benzylidene)-4-subst/un-sbst oxazole**/thiazol**-2-amine.

Yield: 93%, M.P 158°C. IR (KBr): 1112cm^{-1} (on to C=S), 1605-1580cm^{-1}(azomethine proton),1605 cm^{-1}& 1255 cm^{-1}(onC=N&C-N), PMR: δ 3.96 (9H, due to methoxy protons),δ 7.2(s,2H), δ9.80 (s,1H), δ7.6 (Ar-H, m, 5H), δ6.6(s, CH)δ 8.4 (singlet, on azomethine proton),

The Synthesis process of2-Amino-4-phenylOxazole

Amixture of compound preparing from urea (1.2 mmol) and PEG (0.5mL)and2-bromo-1-phenylethanone (1.2 mmol), atroom temperature withstirred untilcompletionofthe reaction process(The thinlayerchromatography for monitor).4ml of water extracted with ethyl acetate (3X15ml) for using of wash of the mixture; the organicphase of compound was separated, thenthe useof a hydroussodiumsulphate, for dried over the product and filtered. The complete solvent wasremoved under vacuum process.Silica gel column chromatography using ethyl acetate-petroleum ether equal sharefor theuse of purification of thecrude reaction product. Thesolution of PEG400 andH_2O wasconcentrated. After extraction withethylacetate,

B.P.:112-115^{0}C, IR(KBr):cm-^{1} 3435, 2979,1626,1389.1HNMR:(300MHz,CDCl3):
δ7.53–7.48(m,ArH,2H,),7.08(m,ArH1H,), 6.76(s,1H,oxazole),
5.17 (brs, 2H,NH2),7.34–7.29(m,ArH,2H,).

The Synthesis process of 2-Amino-Thiazole

A solution preparing from 100 ml of warm water include of 38 gm of thiourea in 500ml three Conical flask titrated with dropping funnel, reflux condenser and instrumental stirrer.142 gm of α, β-Di chloroethyl ether is added and the total compound is heated for 2 hours under instinctive reflux with stirring. Two layers of compound gradually merged withthe reaction process. Added solid state of sufficient NaOH inthe cold solution toreceive the salt position of liberate 2-Amino Thiazole. The product dissolve with adding of Ether and after the sometime etheris evaporated. With the addition of ethanol to received recrystallized product of 2-Amino Thiazole.

M.P.: 89^{0}C - 90^{0}C.Yield: 94%, IR(KBr):1260 cm-^{1}(on C-N), 695 cm-^{1}(onC-S-C),
1616&1536cm-^{1}(on C=N)PMR:δ 6.8 (s, 1H,on-CH), δ7.2 (s, 1H, -CH), δ11.5(d, 2H).

The Synthesis process of2-Amino-4-phenylThiazole

Amixtureof compound preparing from thiourea(15.2gm,0.2mol)acetopheneone(12.0gm,0.1mol),andiodine(25.4gm, 0.1mol) was heat ebon a steam bath for 10 hours.The totalcrude reaction the compound of mixture was repeatedly extracted with ether in cooled stage and unreacted acetopheneoneand iodinewere removed in that stage. They're issued product was dissolved in worm water and to remove sulphur and other impurities by filtered.Themoderatelycooled solution and madeconc.Ammonia.2-amino-4-phenyl thiazole with alkaline, thuscollected of precipitated and with the addition of diluted ethanol to received recrystallized product as long colourless needles.

M.P:148^{0}C.IR(KBr):1260 cm-^{1}(C-N),695 cm-^{1}(C-S-C),1618&1538cm-^{1}(C=N)

PMR:δ6.8 (s, 1H,on-CH), δ7.6 (m, 5H,Aromatic), δ11.36 (d, 2H,NH_2).

Similarly,2-Amino-4-p-nitro/chloro/fluoro/methoxy/hydroxylphenyloxazoles /thiazoleswereprepared. [42-44]

DISCUSSIONS ANDRESULTS

Antifungal Screening andAntibacterial activities

The complexes of synthesizedcompoundswere partitionfortheirAntifungal, ThingsagainstAspergillusNiger C.albicans, ,Antimalarial activities against plasmodium malaria and related parasites. to againstP.Aeruginosa,B.subtilis(gram+vebacteria),Staphylococcusaureus,E.coli(gram-vebacteria).The biologically potent activities of the compounds were tested in cup plate method of test, using a 3 mm diameters of sterile corkborer.As Wells were made in separated petri dish using 0.2 ml of standard control sterile syringe injection process and test into the cups. After injection at theroom temperature in the petri dishes for continuous of complete one day. In the equal diffusion of the agentin seeded Nagar. The Petry dishes evolution atthe 36±0.5 °C for one day.After the completion of one dayof evolution period in millimeter was contrastwith particular of standard drug. 100 µgm/ml of ketoconazole Drugwas used for fungi.100 µgm/ml of Doxycycline Drug wasused for malaria and 100 µgm/ml of Ampicillin Drugwas used for fungi.The zone of evolution was measured in millimeter to approximate the strength of the synthesized compounds as given inTable2.

Table2:ResultsofthenewlysynthesizedCompounds as Antifungal,Antibacterial & anti-malarialActivityin the Screening

Evolution**Zone(mm)**								
Comp'dn o.	**Fungi**		**Gram -veBacteria**		**Gram+ veBacteria**		malarial	
	A.niger	**C.albicans**	**P.Aeruginosa**	Pl.malaria	**S.aureus**	**B.subtilis**	Pl.malaria	Pl.malaria
1	9	8	10	08	9	7	11	12
2	8	7	10	11	14	11	10	9
3	15	16	18	17	20	22	09	11
4	18	20	17	17	18	14	12	14
5	19	18	13	15	16	10	08	10
6	11	09	15	16	16	17	12	11
7	12	14	16	14	20	18	17	18
8	14	15	11	06	13	16	16	19
9	12	12	18	16	8	10	15	14
10	11	10	13	12	15	16	18	16
11	18	17	09	11	17	18	20	18
12	14	16	10	11	13	14	10	12
Ketoconazole	19	21	-	-			-	-
Ampicillin	-	-	18	16	21	23		
Doxycycline	-	-	-	-			20	18

a) inhibition measured in mm for Antifungal strains

1. <12mm: minimum activity
2. 12-16 mm: medium activity
3. >16 mm: maximum activity

b) Inhibitionmeasuredin mmforAntibacterialstrains

1 <12mm: minimum activity

2. 12-16 mm: medium activity

3. >16 mm: maximum activity

c) inhibition measuredinmm forAntimalarial strains

1. <12mm: minimum activity
2. 12-16 mm: medium activity
3. >16 mm: maximum activity

The evaluation of the Data in the above Table 2,The Strains were also evaluated for Antifungal activity AspergillusNiger, C.Albicans, and initiate that strains No 4,5,11 &12 showed maximum inhibition of all the two above strains.The serial No 3,7,8 &9 samples are showed medium activity of the two above strains and strains No 1,2,6 &10 showed the minimum or least activity both theAntifungals.
The strain containing anti-bacterial gram -ve and Gram +ve bacteria, we concluded that strains No 3,4,6,7,9& 11 showed maximum inhibition of all the four strains P.Aeruginosa, E.coli ,Staphylococcus aureus, B.subtilis, &strain No 2,5,6,8,9,10 & 12 showed medium activity of all the fourstrainsnumber No.1or 2 showsminimum activityof all the four strains.the antibacterial measured data the strain containing fluoro, methoxy &hydroxylgroups at para positions exhibitedverygoodactivity in bothof thestrains.

The Strains were also evaluated for antimalarial activity against P.malaria,P.vivox and initiate that strains No 7,8,10 &11 showed maximum inhibition of all the two above strains.The serial No1,4,6,9 &12 samples are showed medium activity of the two above strains andstrains No 2,3&5 showed the minimum or least activity both the antimalarials.

CONCLUSIONS

From the above antifungal, antimalarial &antibacterial &screening measurements of data the synthesized compounds containing fluoro&nitro group atpara state ofpositions exhibited very good biologicalactivity against all the strains i.e.withdrawing of electrongroup exhibitedinhibition maximum in the strains.

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