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SYNTHESIS CHARACTERIZATION AND BIOLOGICAL EVALUATION OF NOVEL 5-((3-((2-(4-PHENYLTHIAZOLE-2-YL)HYDRAZONO)METHYL)-1H-INDOL-1-YL)METHYL)-1,3,4-OXADIAZOLE-2(3H)-THIONE

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Abstract: The article is aimed to synthesize,characterize and screening the biological activity of a series of Synthesis of 5-((3-((2-(4-phenylthiazole-2-yl)hydrazono)methyl)-1H-indol-1-yl)methyl)-1,3,4-oxadiazole-2(3H)-thione 4(a-f). Indole-3-carbaldehyde and chloroethylacetate were dissolved in DMF. To this reaction mixture anhydrous K_2CO_3 was added and the reaction mixture was stirred at room temperature(35^0C) for 8 hours .To afford 2-(3-formyl-1H-indol-1-yl)acetate**.** To this reaction mixture added thiosemicarbazide,MeoH and three drops of acetic acid is added and then heated on a steam bath for 5-6 hrs.Compound(1)Ethyl2-(3-((2-carbamoylhydrazono)methyl)-1H-indol-1-yl)acetate was obtained. Compound(1) is converted into2-((1-(2-Hydrazinyl-2-oxoethyl)-1H-indol-3-yl)methylene)hydrazine carboxamide(2).To this reaction potassium hydraxyde and carbon disulphide in presence of ethanol to obtained 2-((1-((5-thioxo-4,5-dihydro-1,3,4-oxadiazole-2-yl) methyl)-1H-indol-3-yl)methylene) hydrazine carboxamide(3).By the condensation of α-halo substituted ketones to this reaction mixture obtained 5-((3-((2-(4-phenylthiazole-2-yl)hydrazono)methyl)-1H-indol-1-yl)methyl)-1,3,4-oxadiazole-2(3H)-thione(4).The structure of these newly synthesized compounds were characterised by ^{1}H NMR,^{13}CNMR ,Mass ,IR, and elemental analysis. The antimicriobial activity of the novel compounds was screened by agar discdiffusion method.

Keywords;- Antibacterial activity,Antifungal activity,DMF,Indole, Thiosemi carbazide,

INDRODUCTION

Hetero cyclic compounds represents an important class of biological molecules.The hetero cyclic molecules which posses indole,1,3,4oxadiazole and phenyl thiazole moieties exhibit wide range of biological activities.Indoles are one of the most important alkaloids molecules found extensively in biological systems, which play vital role in many of the biochemical process. Indole ring constitutes an important basic skelton and development of the drug.The classical indole drugs are indomethacin and indoxole. Indole derivetives found to posses high which includes,antibacterial,analgesic,antipyretic,antifungal,antiinflamatory,anthelmintic,cardiovascular,anticonvalsant and selective COX-2 inhibitary activities .

Five membered heterocyclic compounds possess interesting biological activity. Among them the compounds bearing 1,3,4-oxadiazole nucleus have wide applications in medicinal chemistry.

These compounds also have been reported to have significant anti-inflammatory [1],antifungal [2], antibacterial [3], antiviral [4], and anticancer [5]activities. Heterocyclic compounds like fluconazole [6, 7], itraconazole [8], ravuconazole [9],voriconazole [10, 11]and posaconazole [12],were used as therapeutically important medicines. The biological studies on sulphones indicate that they can be used in chemotherapy and agriculture, Ex: sulphones like chlorothiazide and hydrochlorothiazide were used as diuretics. Sulphonal, trional and tetranal were used as sedatives and hypnotics. Dapsone [13] was used as potential drug against leprosy and it is also proved to be a potent prophylactic agent.

MATERIALS AND METHODS

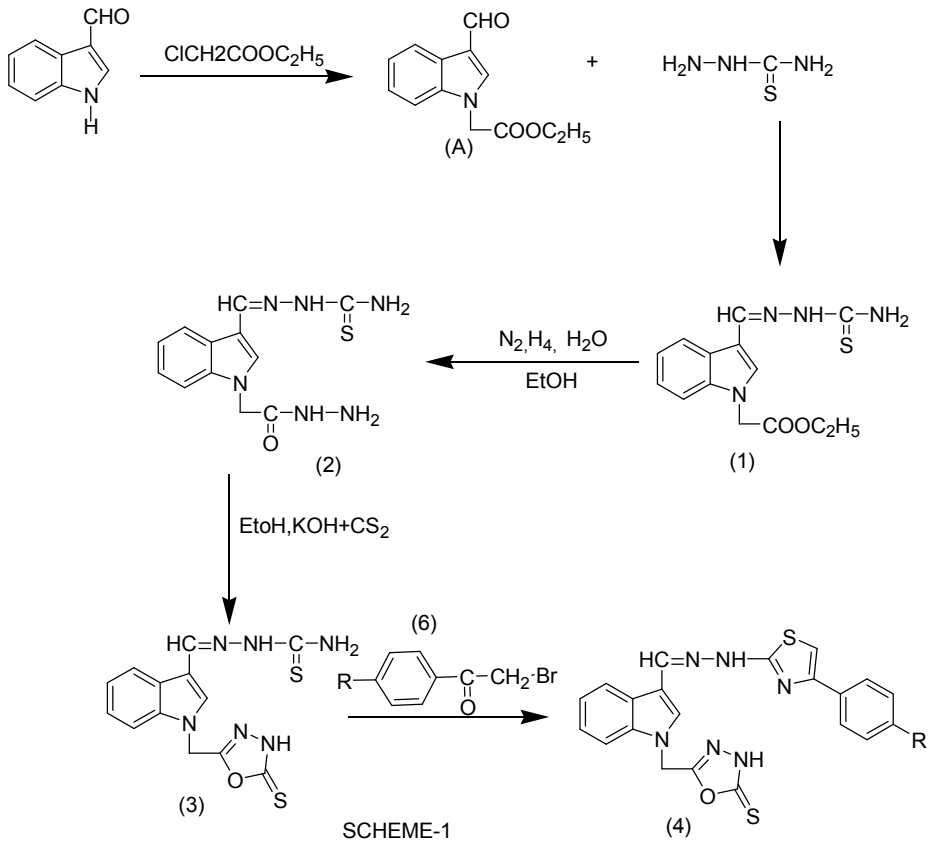
Melting points were determined on open capillaries using a cintex melting point apparatus .T.L.C. analysis were performed on precoatedsilicagel (E-Merck Kieselgel 60 F_{254}) plates and visualisation was done by exposing to iodine vapour .Solvent were purified by standard procedures before use .Column chromatography was conducted by using Silica gel with different solvent systems as elutes .IR Spectra were recorded KBr on perkin –elmer spectrum BX series FTIR spectrometer.H^1-NMR spectrum were recorded on varian zemini 300MHz and 200MHz spectrometers using TMS as internal standard(chemical shifts in & ppm) C^{13}NMR spectra were recorded on a brucker 75MHz spectrometer . mass spectra were scanned on a varian MATCH -7 and jeol JMSD-300 mass spectrometer at 70 ev.elemental analysis were carried out on carloerba 106 and perkin –analyser . all the chemicals used in the present investigation were perchased from Aldrich chemicals ;U.S.A. indole- 3-carbaldehyde was prepared by a reported methode

EXPERIMENTAL SECTION:

Ehyl2-(3-formyl-1H-indol-1-yl)acetate(A):A mixture of indole-3-carbaldehyde,anhydrous K_2CO_3, chloroethyl acetate and DMF were stirred at room temperature for 8 hours. The reaction mixture was diluted with ice cold water. The separated solid was identified as Ethyl2-(3-formyl-1H-indol-1-yl)acetate.

Ethyl2-(3-((2-carbamoylhydrazono)methyl)-1H-indol-1-yl)acetate(1):

To a solution indole-3-aldehyde (10mM) and thiosemicarbazide (0.19gr,10mM) in methanol (20ml) few drops of aceticacid were added and the mixture refluxed for 5hrs.After the solution was cooled at roomtemperarure and poured into ice cold water and the solution was neutralized with solid $NaHCO_3$.The separated solid was filtered and dried to obtain crude product of indole-3-carbaldehyde.The crude product obtained recrystalised from hot MeoH to give pure indole-3-thiosemicarbazone.



SCHEME-1

compd	4(a)	4(b)	4(c)	4(d)	4(e)	4(f)
R	-H	$-CH_3$	$-OCH_3$	-Cl	$-NO_2$	$-CF_3$

2-((1-(2-Hydrazinyl-2-oxoethyl)-1H-indol-3-yl)methylene)hydrazine carboxamide(2):
A solution of 3(a) (0.01mol) and hydrazine hydrate (0.015mol) in ethanol (20ml) was refluxed for 5 hours. The reaction mixture was cooled and poured into ice cold water with stirring. The separated solid was filtered, washed with water and recrystalised from ethanol to afford 2-((1-(2-Hydrazinyl-2-oxoethyl)-1H-indol-3-yl)methylene)hydrazine carboxamide(2).
The IR(KBr) spectrum of 2-((1-(2-Hydrazinyl-2-oxoethyl)-1H-indol-3-yl)methylene)hydrazine carboxamide(2)was recorded in the range 4000-667cm^{-1} and the absorption signals were found at 3198(-NH),3045(ν-Ar-H), 2975 and 2958 (ν aliphatic CH_2 andCH_3), 1755 (ν CO of ester group), 1640(C=N) , and 1195(ν C-O-C of ester group), 1170(C=S).

^{1}HNMR Spectra (δ_{PPm}): The ^{1}HNMR spectra of 2-((1-(2-Hydrazinyl-2-oxoethyl)-1H-indol-3-yl)methylene)hydrazine carboxamide(2) was recorded in DMSO-d6 solvent. The NMR signal of 2-((1-(2-Hydrazinyl-2-oxoethyl)-1H-indol-3-yl)methylene)hydrazine carboxamide(2) was found at $\delta_{PPm,}$ 1.33 (t,3H, J=13.2Hz, CH_3 of ethyl group), 4.11 (q, 2H, J=13.2Hz, CH_2 of ethyl group), 4.36 (s,2H N-CH_2-C =O), 4.78(s, 2H, N-CH_2 group) ,4.95 (s,1 H,-N-NH) and6.92 - 7.56 (m, 5H, C_8H_5N indole nucleus), 11.19(s,1H,-NH),14.7(s,1H,thiol-thione tautomeric proton SH).

2-((1-((5-thioxo-4,5-dihydro-1,3,4-oxadiazole-2-yl) methyl)-1H-indol-3- yl)methylene) hydrazine carboxamide(3):

A mixture of 2 (19.9g,0.1mol),KOH(5.5g,0.1mol)ethanol(100ml) and carbon disulphide (6.02 ml,0.1mol) taken in a round bottomed flask fitted with a water cooled condenser was refluxed on a water bath till the evolution of hydrogen sulphide ceased. The excess of alcohol was removed by distillation. The reaction mixture was cooled to room temperature and the contents were poured to ice cold water and neutralized with dil.HCl.The solid precipitated was filtered, washed thoroughly with water and dried .The product was further purified by recrystallization from ethanol-dioxane mixture to give 3(a) yield 59%,m.p.229-230.

The IR(KBr) spectrum of 2-((1-((5-thioxo-4,5-dihydro-1,3,4-oxadiazole-2-yl) methyl)-1H-indol-3-yl)methylene) hydrazine carboxamide(3) was recorded in the range 4000-667cm^{-1} and the absorption signals were found at 1626 (C=N),1180 (-C-O-C-),1156 (C=S),670(C-S-C),3185(-NH).

^{1}HNMR Spectra (δ_{PPm}): The ^{1}HNMR spectra of 2-((1-((5-thioxo-4,5-dihydro-1,3,4-oxadiazole-2-yl) methyl)-1H-indol-3-yl)methylene) hydrazine carboxamide(3) was recorded in DMSO-d6 solvent. The NMR signal of 2-((1-((5-thioxo-4,5-dihydro-1,3,4-oxadiazole-2-yl) methyl)-1H-indol-3-yl)methylene) hydrazine carboxamide(3) was found at $\delta_{PPm,}$ 5.45(s,2H,-CH_2thiaoxazole attached to indole ring),7.08-8.35(complex,m,6H,four aryl protons of the indole ring,one α-proton of the indolyl ring,one aldehydimine proton),7.20-8.28(complex,m,1H,one proton of the thiazolylring),11.195(s,1H,-NH),14.75(s,1H,thiol-thione tautomeric proton SH).

5-((3-((2-(4-phenylthiazole-2-yl)hydrazono)methyl)-1H-indol-1-yl)methyl)-1,3,4-oxadiazole-2(3H)-thione(4):

To a mixture of 3(a) (2.18 gr,) and K_2CO_3 (0.69gr,) in methanol (20ml) was approximate α-halo ketones (chloro aceto phenone , cloro acetone) 10mM and the mixture stirred at roomtemperature for 30min.At the end of this period, the solution was poured into ice cold water and neutralized with dil AcoH. The separated solid was filtered and dried to obtain crude().The crude compound obtained above,was recrystalised from hot MeOH to obtain pure 4(a).

IR spedtra ; The IR(KBr) spectrum of 5-((3-((2-(4-phenylthiazole-2-yl)hydrazono)methyl)-1H-indol-1-yl)methyl)-1,3,4-oxadiazole-2(3H)-thione 4(a) was recorded in the range 4000-667cm^{-1} and the absorption signals were found at, 1626 (C=N),1180 (-C-O-C-),1156 (C=S),670(C-S-C),3185(-NH),

NMR spectra ;5.42(s,2H,-CH_2thiaoxazole attached to indole ring),7.05-8.30(complex,m,6H,four aryl protons of the indole ring,one α-proton of the indolyl ring,one aldehydimine proton),7.18-8.26(complex,m,6H,one proton of the thiazolylring, five phenyl protons),11.189(s,1H,-NH),14.7(s,1H,thiol-thione tautomeric proton SH).

RESULTS AND DISCUSSION

The target compounds were synthesized via the route as shown in Scheme above. The synthon required for thesynthesis of the target molecules indole-3-carbaldehyde was prepared by a reported method.Filtered and recrystallized from ethanol. These reactions are summarised in the scheme-1.Yields were moderate to affair(55-70%). The purity of the compounds was monitered by TLC.

Synthesis of 2-(3-formyl-1H-indol-1-yl)acetate(A)

An equimolar mixture of indole-3-carbaldehyde and chloro ethyl acetate were dissolved in dimethyl formamide solvent and to this reaction mixture anhydrous K_2CO_3 was added and the reaction mixture was stirred at room temperature(35^0C) for 8 hours and the progress of the reaction was monitered by TLC using cyclohexane and ethylacetate solvent mixture (7:3) as eluent the reaction mixture was kept over night.After completion of the reaction the solvent was evaporated on rota-evaporater. The gummy solid was seperated and it was recrystalised from -2-propanol-petrolium ether(80^0c)solvent mixture.The crystaline solid was found to be -2-(3-formyl-1H-indol-1-yl)acetate. with a yield of 75% and mp 143-145^0C.The indole-3-carbaldehyde used in the present studies was purchased from aldrich company and was used without any forther purification. Yield 75%,m.p.:143-145^0C

The IR(KBr) spectrum of 2-(3- formyl-1H-indol-1-yl) acetate (A)was recorded in the range 4000-667cm^{-1} and the absorption signals where found at 3032(ν-Ar-H), 2980 and 2960 (ν aliphatic CH_2 andCH_3), 1760 (ν CO of ester group), and 1182(ν C-O-C of ester group).

^{1}HNMR Spectra (δ_{PPm}): The ^{1}HNMR spectra of 2-(3- formyl-1H-indol-1-yl) acetate(A) was recorded in DMSO-d6 solvent. The NMR signal of 2-(3- formyl-1H-indol-1-yl) acetate was found at $\delta_{PPm,}$ 1.29 (t,3H, J=13.2Hz, CH_3 of ethyl group), 4.13 (q, 2H, J=13.2Hz, CH_2 of ethyl group), 4.78(s, 2H, N-CH_2 group) and
6.92 , 7.58 (m, 10H, C_8H_5N indole nucleus).

Syntheis of Ethyl2-(3-((2-carbamoylhydrazono)methyl)-1H-indol-1-yl)acetate(1);

Equimolar quantity of hydrazinecarbothioamide and ethyl-2-(-3-formyl-1H-indol-1-yl)acetate(A) were dissolved in absolute alcohol, to this three drops of aceticacid was added then heated on a steam bath for 5-6hrs at 100^0C. The progress of the reaction was monitored by cyclohyxane: ethyacetate (7:3) solvent mixture as an eluent. The reaction mixture was kept over night at room temperature. The solvent was evaporated on rotoevoparator. The semi solid was dried and recrystallized from warm absolute alcohol. The separated solid was identified as Ethyl2-(3-((2-carbamoylhydrazono)methyl)-1H-indol-1-yl)acetate(3).The yield of (1) was found to be 75% with mp with 154-156^oC. The similar procedure was adopted for the synthesis of 4(b-f) from 2-(3-formyl-1H-indol-1-yl)acetate(2) and hydrazinecarbothioamide3(a-f). The structures of (1)were established by IR, ^{1}H-NMR. The analytical data of (1) was shown in the table.

The IR(KBr) spectrum of Ethyl2-(3-((2-carbamoylhydrazono)methyl)-1H-indol-1-yl)acetate(1) was recorded in the range 4000-667cm^{-1} and the absorption signals where found at 3185(-NH),3032(ν-Ar-H), 2980 and 2960 (ν aliphatic CH_2 andCH_3), 1760 (ν CO of ester group), 1629(C=N) , and 1185(ν C-O-C of ester group), 1158(C=S).

^{1}HNMR Spectra (δ_{PPm}): The ^{1}HNMR spectra of Ethyl2-(3-((2-carbamoylhydrazono)methyl)-1H-indol-1-yl)acetate(1) was recorded in DMSO-d6 solvent. The NMR signal of Ethyl2-(3-((2-carbamoylhydrazono)methyl)-1H-indol-1-yl)acetate(1) was found at $\delta_{PPm,}$ 1.31 (t,3H, J=13.2Hz, CH_3 of ethyl group), 4.15 (q, 2H, J=13.2Hz, CH_2 of ethyl group), 4.80(s, 2H, N-CH_2 group) and6.94 - 7.59 (m, 5H, C_8H_5N indole nucleus), 11.189(s,1H,-NH),14.7(s,1H,thiol-thione tautomeric proton SH).

Syntheis of 2-((1-(2-Hydrazinyl-2-oxoethyl)-1H-indol-3-yl)methylene) hydrazine carboxamide(2).

A solution of (1) and hydrazine hydrate in ethanol was refluxed for 5 hrs . The progress of the rection was monitered by TLC with acetone . ethyl acetate (7:3) as mobile phase .The rection mixtured was cooled poured on ice cold water with stirring . The seperated solid was filtered , washed with water re crystalized from ethanol to affered 2-((1-(2-Hydrazinyl-2-oxoethyl)-1H-indol-3-yl)methylene)hydrazine carboxamide(2).

The structures of these newly synthesized compounds (2) were charecterized by their elimental analysis and spectral data

A solution of (1) and hydrazine hydrate in ethanol was refluxed for 5hrs.The reaction mixrure was cooled and poured in to ice cold water with stirring. The separated solid was filtered, washed with water and recrystalised from ethanol to afford2-((1-(2-Hydrazinyl-2-oxoethyl)-1H-indol-3-yl)methylene)hydrazine carboxamide(2).

.The structures of this newly synthesized compounds were charecterised by ^{1}H-NMR and IR spectral data.

The IR(KBr) spectrum of 2-((1-(2-Hydrazinyl-2-oxoethyl)-1H-indol-3-yl)methylene)hydrazine carboxamide(2)was recorded in the range 4000-667cm^{-1} and the absorption signals were found at 3198(-NH),3045(ν-Ar-H)**,** 2975 and 2958 (ν aliphatic CH_2 andCH_3), 1755 (ν CO of ester group), 1640(C=N) , and 1195(ν C-O-C of ester group), 1170(C=S).

^{1}HNMR Spectra (δ_{PPm}): The ^{1}HNMR spectra of 2-((1-(2-Hydrazinyl-2-oxoethyl)-1H-indol-3-yl)methylene)hydrazine carboxamide(2) was recorded in DMSO-d6 solvent. The NMR signal of 2-((1-(2-Hydrazinyl-2-oxoethyl)-1H-indol-3-yl)methylene)hydrazine carboxamide(2) was found at $\delta_{PPm,}$ 1.33 (t,3H, J=13.2Hz, CH_3 of ethyl group), 4.11 (q, 2H, J=13.2Hz, CH_2 of ethyl group), 4.36 (s,2H N-CH_2-C =O), 4.78(s, 2H, N-CH_2 group) ,4.95 (s,1 H,-N-NH) and6.92 - 7.56 (m, 5H, C_8H_5N indole nucleus), 11.19(s,1H,-NH),14.7(s,1H,thiol-thione tautomeric proton SH).

Syntheis of 2-((1-((5-thioxo-4,5-dihydro-1,3,4-oxadiazole-2-yl) methyl)-1H-indol-3-yl)methylene) hydrazine carboxamide(3).

2-((1-(2-Hydrazinyl-2-oxoethyl)-1H-indol-3-yl)methylene)hydrazine carboxamide(2) with a mixture of KOH,EtOHand carbondisulphide afford the corresponding of 2-((1-((5-thioxo-4,5-dihydro-1,3,4-oxadiazole-2-yl) methyl)-1H-indol-3-yl)methylene) hydrazine carboxamide (3) in very good yields.In a typical example a mixture of 2-((1-(2-Hydrazinyl-2-oxoethyl)-1H-indol-3-yl)methylene)hydrazine carboxamide(2) with a mixture of KOH,EtOHand carbondisulphide refluxed on a waterbath till the evaluation of hydrogensulphide ceased. After usual work up the corresponding 2-((1-((5-thioxo-4,5-dihydro-1,3,4-oxadiazole-2-yl) methyl)-1H-indol-3-yl)methylene) hydrazine carboxamide 3(a) was obtained in 84% yield with mp 227^{0}C

The above reaction of (2) with a mixture of KOH,C_2H_5OH and carbondisulpnide has been extended (3).

.The structures of this newly synthesized compounds were charecterised by ^{1}H-NMR and IR spectral data.

The IR(KBr) spectrum of 2-((1-((5-thioxo-4,5-dihydro-1,3,4-oxadiazole-2-yl) methyl)-1H-indol-3-yl)methylene) hydrazine carboxamide(3) was recorded in the range 4000-667cm^{-1} and the absorption signals were found at 1626 (C=N),1180 (-C-O-C-),1156 (C=S),670(C-S-C),3185(-NH).

^{1}HNMR Spectra (δ_{PPm}): The ^{1}HNMR spectra of 2-((1-((5-thioxo-4,5-dihydro-1,3,4-oxadiazole-2-yl) methyl)-1H-indol-3-yl)methylene) hydrazine carboxamide(3) was recorded in DMSO-d6 solvent. The NMR signal of 2-((1-((5-thioxo-4,5-dihydro-1,3,4-oxadiazole-2-yl) methyl)-1H-indol-3-yl)methylene) hydrazine carboxamide(3) was found at $\delta_{PPm,}$ 5.45(s,2H,-CH_2thiaoxazole attached to indole ring),7.08-8.35(complex,m,6H,four aryl protons of the indole ring,one α-proton of the indolyl ring,one aldehydimine proton),7.20-8.28(complex,m,1H,one proton of the thiazolylring),11.195(s,1H,-NH),14.75(s,1H,thiol-thione tautomeric proton SH).

Syntheis of 5-((3-((2-(4-phenylthiazole-2-yl)hydrazono)methyl)-1H-indol-1-yl)methyl)-1,3,4-oxadiazole-2(3H)-thione(4);

A mixture of 2-((1-((5-thioxo-4,5-dihydro-1,3,4-oxadiazole-2-yl) methyl)-1H-indol-3-yl)methylene) hydrazine carboxamide (3) and K_2CO_3 in methanol was added approximately α-halo ketones(bromo aceto phenone) and this mixture stirred at room temperature for 30min.At the end of this period the solution was poured into ice cold water and neutarlised with dilute acetic acid.The separated solid was filtered and neutralized with dilute acetic acid.The separated solid was filtered and dried to obtain crude.5-((3-((2-(4-phenylthiazole-2-yl)hydrazono)methyl)-1H-indol-1-yl)methyl)-1,3,4-oxadiazole-2(3H)-thione 4(a). The crude compound obtained above was recrystalised from hot methyl alcohol to obtain pure 4(a)compound.The reaction process leading to the synthesis of 5-((3-((2-(4-phenylthiazole-2-yl)hydrazono)methyl)-1H-indol-1-yl)methyl)-1,3,4-oxadiazole-2(3H)-thione 4(a-f) and their analytical data given in the tables.

The structures of this newly synthesized compounds 4(a-f) were charecterised by H-NMR and IR spectral data.

NMR spectra ;5.42(s,2H,-CH_2thiaoxazole attached to indole ring),7.05-8.30(complex,m,6H,four aryl protons of the indole ring,one α-proton of the indolyl ring,one aldehydimine proton),7.18-8.26(complex,m,6H,one proton of the thiazolylring, five phenyl protons),11.189(s,1H,-NH),14.7(s,1H,thiol-thione tautomeric proton SH).

IR spedtra ; The IR(KBr) spectrum of 5-((3-((2-(4-phenylthiazole-2-yl)hydrazono)methyl)-1H-indol-1-yl)methyl)-1,3,4-oxadiazole-2(3H)-thione 4(a) was recorded in the range 4000-667cm^{-1} and the absorption signals were found at, 1626 (C=N),1180 (-C-O-C-),1156 (C=S),670(C-S-C),3185(-NH),

Spectral Analysis: IRspectra

OMPOUND	R	ν_{max} in cm^{-1}				
		C=N	C-O-C	C-S-C	C=S	NH
4(a)	H	1625	1180	670	1156	3185
4(b)	CH_3	1620	1175	665	1150	3180
4(c)	OCH_3C	1615	1170	660	1145	3175
4(d)	Cl	1630	1185	675	1160	3190
4(e)	NO_2	1635	1190	680	1165	3195
4(f)	CF_3	1640	1195	685	1170	3200

compound	R	^{1}HNMR (DMSO-d_6) (δ_{PPm})
4a	H	5.42(s,2H,-CH_2 thiaoxzoe attached to indole ring),4.05-8.30(complex,m,6H,four aryl protons of the indole ring,oneα-proton of the indolylring, one aldehydimine proton),7.18-8.26(complex m, 6H,one proton of the thiazolyl ring,five phenyl protons),11.189(s,1H,-NH),14.7(s,1H,thiol-thione tautomeric proton SH).
4b	CH_3	2.14(s,3H,-CH_3 attached to phenyl ring),5.42(s,2H,-CH_2 thiaoxzoe attached to indole ring),4.05-8.30(complex,m,6H,four aryl protons of the indole ring,oneα-proton of the indolylring, one aldehydimine proton),7.18-8.26(complex m, 5H,one proton of the thiazolyl ring,four phenyl protons),11.189(s,1H,-NH),14.7(s,1H,thiol-thione tautomeric proton SH).
4c	OCH_3	2.08 (s,3H,-OCH_3 attached to phenyl ring),5.42(s,2H,-CH_2 thiaoxzoe attached to indole ring),4.05-8.30(complex,m,6H,four aryl protons of the indole ring,oneα-proton of the indolylring, one aldehydimine proton),7.18-8.26(complex m, 5H,one proton of the thiazolyl ring,four phenyl protons),11.189(s,1H,-NH),14.7(s,1H,thiol-thione tautomeric proton SH).
4d	Cl	5.45 (s,2H,-CH_2 thiaoxzoe attached to indole ring),4.10-8.35(complex,m,6H,four aryl protons of the indole ring,oneα-proton of the indolylring, one aldehydimine proton),7.20-8.30(complex m, 6H,one proton of the thiazolyl ring,five phenyl protons),11.190(s,1H,-NH),14.8(s,1H,thiol-thione tautomeric proton SH).
4e	NO_2	5.48 (s,2H,-CH_2 thiaoxzoe attached to indole ring),4.20-8.40(complex,m,6H,four aryl protons of the indole ring,oneα-proton of the indolylring, one aldehydimine proton),7.25-8.40(complex m, 6H,one proton of the thiazolyl ring,five phenyl protons),11.200(s,1H,-NH),14.9(s,1H,thiol-thione tautomeric proton SH).
4f	CF_3	5.50(s,2H,-CH_2 thiaoxzoe attached to indole ring),4.30-8.50(complex,m,6H,four aryl protons of the indole ring,oneα-proton of the indolylring, one aldehydimine proton),7.30-8.45(complex m, 6H,one proton of the thiazolyl ring,five phenyl protons),11.225(s,1H,-NH),14.99(s,1H,thiol-thione tautomeric proton SH).

Characterization of above compound

COMPOUND	YIELD	M.P.O^{0}C	% of Analysis					
			C		H		N	
			Calcd	FOUND	Calcd	FOUND	Calcd	FOUND
4a	58%	185	58.33	57.31	3.70	3.73	19.44	19.43
4b	55%	190	59.19	59.17	4.06	4.03	18.83	18.82
4c	53%	180	57.14	57.13	3.89	3.92	18.17	18.18
4d	52%	182	53.73	53.68	54.07	54.01	18.02	18.00
4e	56%	185	52.83	52.82	3.14	3.17	20.53	20.54
4f	51%	180	52.80	52.79	3.00	3.02	16.80	16.79

Anti-Bacterial Activity

The anti bacterial activity of synthesized compounds was studied by the disc diffusion method against the following pathogenic organisms. The gram-positive bacteria screened were staphylococcus aureus NCCS 2079 . The gram negative bacteria screened were Escherichia coli NCCS 2065 and pseudomonas aeruginosa NCCS 2200.

The synthesized compounds were used at the concentration of250 µglml and 500µglml using DMSO as a solvent the Ciprofloxacin 10µglml disc was used as a standard .(Himedia,Laboratories Ltd, Mumbai).

The test results presented in the table -1,suggest that 4b,4d,4e exhibit high activity against the tesed bacteria, the rest of the compounds were found to be moderate active against the tested microorganisms.

Antifungal activity

The antifungal activity of synthesized compounds were studied by disc diffusion method against the organisms of Penicillium and Trichophton.

Compounds were treatd at the concentrations of 500µglm and 1000µglml using DMSO as solvent. The standard used was Cyclopiroxolamine 50µglml against both organisms.The test results were presented in the table-2.

TABLE.- Antibacterial activity by disc diffusion method of indolelinked 1,3,4oxadiazole 4(a.f)

Compound	Zone of inhibition (mm)			
	E.Coli	Pseudomonas aeruginosa	Staphylococcus aureus	Streptococcus pyogene
4a	10	12	13	17
4b	12	15	12	12

4c	11	13	13	13
4d	13	16	17	11
4e	14	12	15	15
4f	12	13	14	11
Ciprofloxacin	17	21	21	23

Table-;2 Antifungal activity by disc diffusion method for indole linked1,3,4oxadiazole 4(a-f).

Compound	Zone of inhibition (mm)	
	Aspergillus niger	Helminthosporium oryzae
4a	12	10
4b	11	13
4c	09	12
4d	12	11
4e	11	07
4f	09	08
Griseofulvin	15	14

Conclusions:

1. Further more the substitution with phenyl group having a chloro group at p-position showed better activities.
2. The tetrazoles showed better antibactirial and antifungal activities.
3. thiazoles and its derivatives were found to play a
4. n important role in medicinalchemistry as herbicidal, fungicidal, bacterial, anti-inflammatory.

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