Synthesis, structural studies and screening for antimicrobial activity of *N*-glucosylated bisdithiazolidines [1, 4-Bis (3- tetra-*O*-acetyl β-D-glucopyranosylimino-5-aryl-1, 2, 4-dithiazolidin-4'yl)-benzene.]

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***Abstract*— *N*-Glucosylated bisdithiazolidines [1, 4-Bis (3- tetra-*O*-acetyl β-D-glucopyranosylimino-5-aryl-1,2,4-dithiazolidin-4'yl)-benzene.] have been prepared by the interaction of 1,4-(3,3'-bis-tetra-*O*-acetyl β-D-glucopyranosyl-thiocarbamido)benzene(1) and N- aryl-S-chloro isothiocarbamoyl chloride (2).The intermediate1 ,4-(3,3'-bis-tetra-*O*-acetyl-β-D-glucopyranosyl-thiocarbamido) benzene was prepared by refluxing tetra-*O*-acetyl β-D-glucopyranosyl isothiocyanate with p-phenylene diamine in chloroform. The synthesized compounds were characterized by analytical, IR, NMR and mass spectral studies and were screened for their antibacterial and antifungal activities.**

Keywords*— *N-Glucosylated bisdithiazolidines, 1, 4-(3,3'-bis-tetra-O-acetyl β-D-glucopyranosyl-thiocarbamido)benzene.

1.INTRODUCTION

The disulphide (-S-S -) linkage in dithiazolidnes is considered responsible for its varied biological and physiological activities [1-13]. Dithiazolidines are also reported as heterocyclic inhibitors for prevention of mild steel corrosion[14]. Looking at the importance of dithiazolidines, we are reporting the synthesis, structural and biological studies of *N*-Glucosylated bisdithiazolidines [1,4-Bis (3- tetra-*O*-acetyl β-D-glucopyranosylimino-5-aryl-1,2,4-dithiazolidin-4'yl)-benzene.] .

2.Experimental:

Melting points determined by using electro thermal apparatus are uncorrected. FT-IR spectra were recorded using KBr disk on Perkin Elmer FT-IR KBR spectrophotometer.

^{1}H NMR spectra were recorded on Bruker avance-II 400 NMR spectrometer at 400 MHz. The spectra were recorded using TMS as internal standard and chemical shifts were reported relative to it in parts of chromatography on Merck Silica Gel 60 F_{254} plates with detection by UV light and spots were visualized by iodine vapours. The compounds were screened for their antibacterial and antifungal activities by the agar diffusion method.

I) Preparation of the intermediate1,4-(3,3'-bis-tetra-*O*-acetyl β-D-glucopyranosyl-thiocarbamido) benzene (1):

The 1,4-(3,3'-bis-tetra-*O*-acetyl β-D-glucopyranosyl -thiocarbamido)benzene was prepared by the reaction of 2,3,4,6 tetra-*O*-acetyl β-D-glucopyranosyl isothiocyanate (TAGNCS)[15-17] 1.9450 g (0.0050mole) and p-phenylene diamine 0.27g (0.0025mole) by refluxing them for 4 hours in chloroform. After the completion of reaction, the reaction mixture was cooled, the solvent was distilled off to give granular solid (1).It was crystallized from ethanol to afford cream coloured crystals. Yield 95 %, mp 175^o C.

II) Preparation of *N*-glucosylated aryl bisdithiazolidines (3).

The intermediate1,4-(3,3'-bis- tetra-*O*-acetyl β-D-glucopyranosyl-thiocarbamido)benzene 1g (0.0020 mole) and *N*-aryl-S-chloro-isothiocarbamoyl chloride ($RNCSCl_2$)[18] in 10 ml benzene 0.824 to 0.96 g (0.0040mole) were refluxed for 5 hr. The reaction proceeded with the evolution of hydrogen chloride gas detected by moist blue litmus. The reaction was carried until the evolution of hydrogen chloride completely ceased. A granular solid was separated when the solvent benzene was removed by vacuum distillation.

III) Anti-bacterial: Details of materials used and procedure followed are as reported earlier. [19, 21]

IV) Anti-fungal:

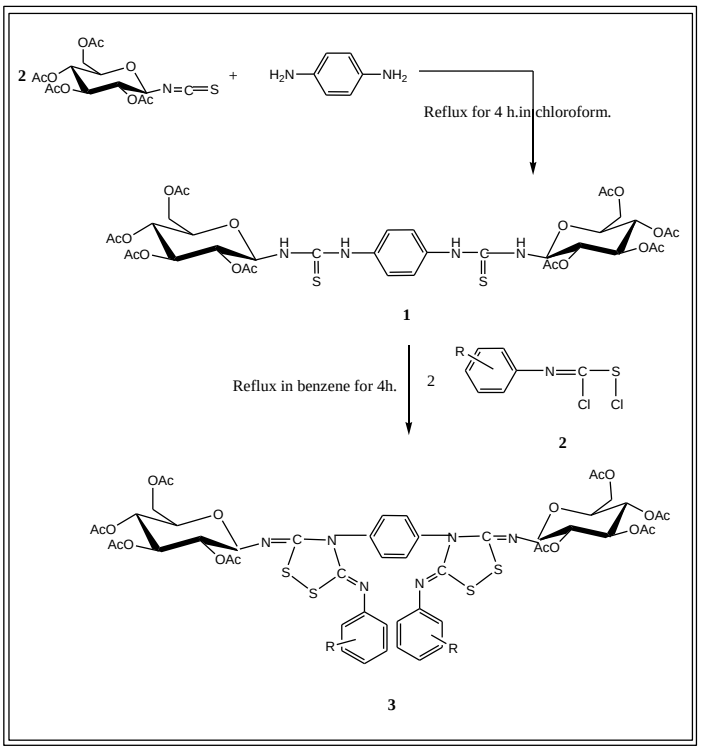
Details of materials used and procedure are as reported earlier. [20, 21]

3. Results and Discussion

The intermediate 1,4-(3,3'-bis-tetra-*O*-acetyl β-D-glucopyranosyl-thiocarbamido)benzene was prepared by the reaction of TAGNCS,1.9450 g (0.0050mole) and p-phenylene diamine 0.27g (0.0025mole) by refluxing them for 4 hours in chloroform. After the completion of reaction, the reaction mixture was cooled, the solvent was distilled off to give granular solid (1). It was crystallized from ethanol to afford cream coloured crystals.

The intermediate 1g (0.0020mole) and respective $RNCSCl_2$ in 10 ml benzene, 0.824 to 0.96 g (0.0040 mole) were refluxed for 5 hr. The reaction proceeded with the evolution of hydrogen chloride gas detected by moist blue litmus. The reaction was carried until the evolution of hydrogen chloride completely ceased. The solvent benzene was removed by vacuum distillation, when a granular solid was separated. It was crystallized from ethanol to afford crystals of ***N***-glucosylated aryl bisdithiazolidines.

Reaction Scheme



Where, R in 2, 3 a)-CH_3(m), b)-CH_3(o) , c)-CH_3(p), d)- H , e) -Cl (p), f) –OCH_3 (o), g)–OCH_3 (p) , h) -Cl (o).

The *N*-glucosylated bisdithiazolidines were prepared by the reaction shown above and in good yields products were isolated

Table A: SYNTHESIS OF N-GLUCOSYLATED BISDITHIAZOLIDINES

Reactants: Intermediate1,4-(3,3'-bis-tetra-*O*-acetyl β-D-glucopyranosyl-thiocarbamido) benzene (1) And $RNCSCl_2$ (2)

R in $RNCSCl_2$ (2)	*N*-glucosylated bisdithiazolidines (3)	Yield %	mp °C	Elemental analysis Found (cal) (%) N S
m-tolyl (2a)	*N*-glucosylated m-tolyl bisdithiazolidines (3a).	95.5%	169	6.72 10.31 (6.77) (10.33)
o-tolyl (2b)	*N*-glucosylated o-tolyl bisdithiazolidines(3b).	94.4%	92	6.73 10.29 (6.77) (10.33)
p-tolyl (2c)	*N*-glucosylated p-tolyl bisdithiazolidines(3c).	95.2%	183	6.70 10.28 (6.77) (10.33)
Phenyl (2d)	*N*-glucosylated phenyl bisdithiazolidines (3d).	93.6%	195	6.85 10.51 (6.93) (10.57)
p-chlorophenyl (2e)	*N*-glucosylated p-chlorophenyl bisdithiazolidines (3e).	96.4%	175	6.50 9.97 (6.55) (10.00)
o-anisyl (2f)	*N*-glucosylated o-anisyl bisdithiazolidines(3f).	96.2%	115	6.55 10.02 (6.60) (10.07)
p-anisyl (2g)	*N*-glucosylated p-anisyl bisdithiazolidines (3g).	97.4%	190	6.58 10.03 (6.60) (10.07)
o-chloro phenyl (2h)	*N*-glucosylated o-chlorophenyl-bisdithiazolidines (3h).	80%	125	6.52 9.98 (6.55) (10.00)

1,4-(3,3'-bis-tetra-*O*-acetyl β-D-glucopyranosyl-thiocarbamido) benzene (1)

IR (KBr) ν max cm^{-1}: 3325(N-H),3100(C-H aromatic), 1751(C=O), 1613(C=N), 1537(C=C aromatic),1300(C-N),1228(C=S),1047(C-O),898 (Glucosidic C-H deformation β-anomer) ; ^{1}H NMR ($CDCl_3$) δ ppm: 7.43-6.66(Ar-H), 5.90 (Ar-H),5.38-4.19(the pyranosyl ring protons), 4.01-3.94(NH), 2.10-1.92(acetyl protons) C^{13}-NMR($CDCl_3$)δ ppm :169.69-169(CO), 149-117(Aromatic Ring Carbon), 83.13(Anomeric Ring C),79.01-61.54 (glucosyl ring carbons), 20.43-20.22(Me-CO) ; MS(m/z): 887 (M+1).The molecular formula C_{36} $H_{46}O_{18}N_4$ S_2.

***N*-glucosylated m-tolyl bisdithiazolidines(3a).**

IR (KBr) ν max cm^{-1}:3100(C-Haromatic), 1754(C=O),1613(C=N),1592(C=C aromatic),1300(C-N),1300(C-O),898(Glucosidic C-H deformation β-anomer), 648(C-S) ; ^{1}H NMR ($CDCl_3$) δ ppm: 7.30-6.85(Ar-H), 5.75-3.83(the pyranosyl ring protons), 2.06-2.38(Ar-CH_3), 2.02(acetyl protons) ; MS(m/z): 1180 (M^+).The molecular formula $C_{52}H_{56}O_{18}N_6S_4$.

***N*-glucosylated o-tolyl bisdithiazolidines (3b).**

IR(KBr) ν max cm^{-1}:3059(C-H aromatic) ,1750(C=O),1611(C=N),1515(C=C aromatic),1300(C-N),1038(C-O),897(Glucosidic C-H deformation β-anomer),758(C-S) ; ^{1}H NMR ($CDCl_3$) δ ppm: 7.36-6.73(Ar-H), 5.34-3.74(the pyranosyl ring protons), 2.38-2.31(Ar-CH_3), 2.02(acetyl protons) ; C^{13}-NMR($CDCl_3$) δ ppm :170.63-169.48(CO),147.33(Ring carbon),138.81-125.95(Ar-Carbons),87.80-61.93 (glucosyl ring carbons),20.83-18.39(Me-CO),17.70and 17.60(Ar-CH_3) ; MS(m/z): 1181 (M+1).The molecular formula $C_{52}H_{56}O_{18}N_6S_4$.

***N*-glucosylated phenyl bisdithiazolidines (3d).**

IR (KBr) ν max cm^{-1}:3059(C-H aromatic), 1751(C=O),1623(C=N),1536(C=C aromatic) ,1300(C-N),1228(C-O),891(Glucosidic C-

H deformation β-anomer),758(C-S) ; ^{1}H NMR ($CDCl_3$) δ ppm: 7.36-6.73(Ar-H), 5.35-3.76(the pyranosyl ring protons), 2.02(acetyl protons) ; C^{13}-NMR($CDCl_3$) δ ppm :171.28-169.57(CO),127.64(Ring carbon),138.81-125.95(Ar-Carbons),83.09-61.77 (glucosyl ring carbons),20.79-20.55(Me-CO),; MS(m/z): 1153 (M+1).The molecular formula $C_{51}H_{54}O_{18}N_6S_4$.

Biological Screening of *N*-glucosylated bisdithiazolidines

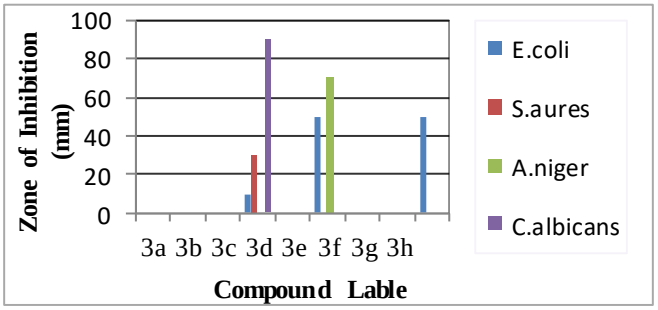
The compounds *N*-glucosylated bisdithiazolidines exhibited low to moderate antibacterial (Table 2) and fairly good antifungal activity (Table3).Inhibition Zone record of compounds revealed that compounds 3e and 3h were sensitive against E.coli while 3c showed moderate sensitivity. All the compounds showed nearly same activity against S.aureus except 3c with moderate activity. Compound 3e exhibited significant activity against A.niger while compound 3c exhibited significant activity against C.albicans.

Table B: ANTIBACTERIAL ACTIVITY OF N-GLUCOSYLATED BISDITHIAZOLIDINES

Table C: ANTIFUNGAL ACTIVITY OF N-GLUCOSYLATED BISDITHIAZOLIDINES Table B: ANTIBACTERIAL ACTIVITY OF N-GLUCOSYLATED BISDITHIAZOLIDINES

(In table B and C, diameter of inhibition zone is in mm) (Concentration 500 μ g/ml)

Graph showing antimicrobial activity of *N*-glucosylated bisdithiazolidines



4. Conclusions

This research work provides a new protocol for the synthesis of bisdithiazolidine with carbohydrate moiety on exocyclic nitrogen following an interaction of 1,4-(3,3'-bis-tetra-*O*-acetyl β-D-glucopyranosyl-thiocarbamido)benzene and *N*-aryl-S-chloro-isothiocarbamoyl chloride. The method provides high yields of bisdithiazolidines in efficient way and procedure involved is simple and easy to follow for the isolation of bioactive novel bisdithiazolidines.

Acknowledgement

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Organism	3a	3b	3c	3d	3e	3f	3g	3h
E.coli	-	-	+ (10mm)	-	+++ (50mm)	-	+++ (50mm)	-
S.aureus	-	-	++ (30mm)	-	-	-	-	-

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Organism	3a	3b	3c	3d	3e	3f	3g	3h
A.niger	-	-	-	-	+++ (70mm)	-	-	-
C.albicans	-	-	+++ (90mm)	-	-	-	-	-

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