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# Synthesis of some new hydrazones of sugar as an antitubercular agent

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**ABSTRACT**

*A series of the new derivatives of hydrazones of sugars have been synthesized by acid catalyzed condensation of substituted phenyl hydrazine with corresponding sugars. The compounds have been characterized by IR, NMR and spectral analysis. All the synthesized compounds are evaluated for antimicrobial activity.*

**Keywords:** sugars, phenyl hydrazine, antimicrobial.

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## INTRODUCTION

Carbohydrates participate in various vital processes, showing important physiological and biological activities. In a recent review, Becker and coworkers [1] emphasized that the introduction of pharmacophores into sugar templates that possess dense stereochemical information is an excellent strategy for the development of bioactive compounds with rich structural diversity. Free reducing sugars (hemiacetal), which are often available from natural sources, react with α-heteroatom nucleophile hydrazide to give cyclic pyranoside adducts in predominantly β-anomeric form or the open chain hydrazone tautomer [2–5]. In fact, this intrinsic chemoselective condensation reactivity of carbohydrates has been skillfully employed in numerous applications, including biotin labeling [6–8], formation of glycoarrays [9–11], glycan capture for structural and functional glycomics [12–14], and the generation of glycopeptide analogues [15,16].

Hydrazones containing an azometine (Schiff base) –NHN=CH– group possess various bioactivities such as antimicrobial, anticonvulsant, analgesic, antiinflammatory, antiplatelet, antitubercular and antitumoral activities [17]. A very famous example is the isonicotinic acid hydrazide (isoniazid) which showed very high inhibitory activity towards *Mycobacterium tuberculosis* H37Rv *in vivo*. Researchers synthesized isoniazid- hydrazones derivatives that were reported to have inhibitory activity in mice infected with various strains of *M. tuberculosis* and also showed less toxicity in these mice than isoniazid [18] because of the blockage of –NH2 group. These findings further support the growing importance of the synthesis of hydrazide-hydrazones compounds [19].

As part of our ongoing research program focused upon the synthesis of biologically active molecules, here in the present context, we carry the work based on incorporation of hydrazide moiety in some sugars by using 3-chlorophenyl hydrazine and 4-chlorophenyl hydrazine. The synthesized compounds are screanned for antimicrobial activitie were we found that some of the synthesized compounds shows significant antimicrobial activities.

## MATERIALS AND METHODS

### Chemistry

All reagents were obtained from commercial suppliers and used without further purification. Reaction progress was monitored through thin layer chromatography (TLC) on pre-coated Merck alu-foil plate (silica gel 60F-254, 0.25 mm thickness) visualized by iodine vapors. Melting points were determined by open capillary method and are uncorrected. IR spectra were recorded (in KBr pallets) on SCHIMADZU spectrophotometer.1H NMR spectra were recorded on an Avance/Bruker 300/400 MHz spectrophotometer using TMS as an internal standard. All NMR Spectra were obtained in DMSO d6/deuterated chloroform (CDCl3); chemical shifts are reported in parts per million, and coupling constant in hertz (Hz). Multiplicities are reported as follows: s (singlet), d (doublet), t (triplet), m (multiplet). The mass spectra were recorded on GC–MS SHIMDZU (Q2010 PLUS) in EImode spectrometer and mass values are reported in m/z.

### General procedure of Hydrazones of Aldoses (D1-8)

To a solution of 3–Chloro Phenyl hydrazine (5mm) in ethanol (15ml) was added Aldose (5mm) and acetic acid (0.1ml) the mixture was heated under reflux for 30 min. The yellowish white solid that separated was filtered washed with ethanol and recrystalize from ethanol.

### Microbiology

The anti-bacterial activity of the synthesized compounds was tested against four gram + ve bacteria (*Staphylococcus aureus* ATCC 9144, *Staphylococcus epidermidis* ATCC 155, *Micrococcus luteus* ATCC 4698 and *Bacillus cereus* ATCC 11778) and three gram – ve bacteria (*Escherichia coli* ATCC 25922 *Pseudomonas aeruginosa* ATCC and *Klebsiella pneumoniae* ATCC 11298) using nutrient agar medium (Hi-Media Laboratories, India). The antifungal activities of the compounds were tested against two fungi namely *Aspergillus niger* ATCC 9029 and *Aspergillus fumigatus* ATCC using sabouraud dextrose agar medium (Hi-Media Laboratories,India).

***Paper disc diffusion technique*:** The sterilized78 (autoclaved at 120°C for 30min) medium (40 50°C) was inoculated (1mL/100mL of medium) with the suspension (105 cfu mL-1) of the micro-organism (matched to McFarland barium sulphate standard) and poured into a petridish to give a depth of 3-4 mm. The paper impregnated with the test compounds (100 µg/disc) was placed on the solidified medium. The plates were pre-incubated for 1 hr at room temperature and incubated at 37°C for 24 and 48 hrs for anti-bacterial and anti-fungal activities, respectively. Ciprofloxacin (100 µg/disc) and Fluconazole (100 µg/disc) were used as standard for anti-bacterial and anti-fungal activities, respectively. The observed zone of inhibition is presented in Table-2.

**Table 1: Spectral Data of selected compounds**

| Compounds | Spectral Data |
|---|---|
| D1 | IR (KBr): 3578 (O-H Stretching), 3368 (N-H Stretching), 3030 (Ar-H Stretching), 2985 (C-H Stretching)1610 (C=N), cm-1; 1H NMR (300 MHz, DMSO-d6): δ 8.12 (s, 1H, -NH), 7.4 (s, 1H,), 7.33-6.28 (m, 4H, Ar-H), 4.79 (S, 1H, $–CH_2$), 3.91 (S, 1H,-OH), 3.68-3.33 (m, 4H,-OH), 3.11-2.89 (m, 4H,) ppm; Mass (m/z), 304 (M+ ion). |
| D2 | IR (KBr): 3560 (O-H Stretching), 3370 (N-H Stretching), 3035 (Ar-H Stretching), 2980(C-H Stretching)1612 (C=N), cm-1; 1H NMR (300 MHz, DMSO-d6): δ 8.15 (s, 1H, -NH), 7.53 (s, 1H,), 7.23-6.38 (m, 4H, Ar-H), 4.65 (S, 1H, $–CH_2$), 3.81 (S, 1H,-OH), 3.53-3.21 (m, 4H,-OH), 3.03-2.69 (m, 4H,) ppm; Mass (m/z), 304 (M+ ion). |
| D3 | IR (KBr): 3540 (O-H Stretching), 3349 (N-H Stretching), 3027 (Ar-H Stretching), 2977 (C-H Stretching)1608 (C=N), cm-1; 1H NMR (300 MHz, DMSO-d6): δ 7.91 (s, 1H, -NH), 7.2 (s, 1H,), 7.10-6.11 (m, 4H, Ar-H), 4.82 (S, 1H, $–CH_2$), 3.74 (S, 1H,-OH), 3.48-3.19 (m, 4H,-OH), 2.97-2.68 (m, 4H,) ppm; Mass (m/z), 304 (M+ ion). |
| D4 | IR (KBr): 3590 (O-H Stretching), 3375 (N-H Stretching), 3035 (Ar-H Stretching), 2990(C-H Stretching)1620 (C=N), cm-1; 1H NMR (300 MHz, DMSO-d6): δ 8.22 (s, 1H, -NH), 7.6 (s, 1H,), 7.40-6.35 (m, 4H, Ar-H), 4.82 (S, 1H, $–CH_2$), 3.93 (S, 1H,-OH), 3.74-3.41 (m, 4H,-OH), 3.24-2.92 (m, 4H,) ppm; Mass (m/z), 304 (M+ ion). |
| D5 | IR (KBr): 3578 (O-H Stretching), 3368 (N-H Stretching), 3030 (Ar-H Stretching), 2985 (C-H Stretching)1610 (C=N), cm-1; 1H NMR (300 MHz, DMSO-d6): δ 8.12 (s, 1H, -NH), 7.4 (s, 1H,), 7.33-6.28 (m, 4H, Ar-H), 4.79 (S, 1H, $–CH_2$), 3.91 (S, 1H,-OH), 3.68-3.33 (m, 4H,-OH), 3.11-2.89 (m, 4H,) ppm; Mass (m/z), 304 (M+ ion). |
| D6 | IR (KBr): 3560 (O-H Stretching), 3370 (N-H Stretching), 3035 (Ar-H Stretching), 2980(C-H Stretching)1612 (C=N), cm-1; 1H NMR (300 MHz, DMSO-d6): δ 8.15 (s, 1H, -NH), 7.53 (s, 1H,), 7.23-6.38 (m, 4H, Ar-H), 4.65 (S, 1H, $–CH_2$), 3.81 (S, 1H,-OH), 3.53-3.21 (m, 4H,-OH), 3.03-2.69 (m, 4H,) ppm; Mass (m/z), 304 (M+ ion). |
| D7 | IR (KBr): 3540 (O-H Stretching), 3349 (N-H Stretching), 3027 (Ar-H Stretching), 2977 (C-H Stretching)1608 (C=N), cm-1; 1H NMR (300 MHz, DMSO-d6): δ 7.91 (s, 1H, -NH), 7.2 (s, 1H,), 7.10-6.11 (m, 4H, Ar-H), 4.82 (S, 1H, $–CH_2$), 3.74 (S, 1H,-OH), 3.48-3.19 (m, 4H,-OH), 2.97-2.68 (m, 4H,) ppm; Mass (m/z), 304 (M+ ion). |
| D8 | IR (KBr): 3590 (O-H Stretching), 3375 (N-H Stretching), 3035 (Ar-H Stretching), 2990(C-H Stretching)1620 (C=N), cm-1; 1H NMR (300 MHz, DMSO-d6): δ 8.22 (s, 1H, -NH), 7.6 (s, 1H,), 7.40-6.35 (m, 4H, Ar-H), 4.82 (S, 1H, $–CH_2$), 3.93 (S, 1H,-OH), 3.74-3.41 (m, 4H,-OH), 3.24-2.92 (m, 4H,) Ppm; Mass (m/z), 304 (M+ ion). |

## RESULTS AND DISCUSSION

The derivatives of Aldose hydrazones i.e (D1-8) were synthesized by the reported method as shown in Scheme. Hydrazones of aldoses from 3–Chloro Phenyl Hydrazine and 4–Chloro Phenyl Hydrazine was prepared by adding the substituted Chloro Phenyl Hydrazine in ethanol to respective sugar in the presence of acetic acid to gives hydrazones of sugars.

**Fig. 1: Reaction of sugar hydrazones**

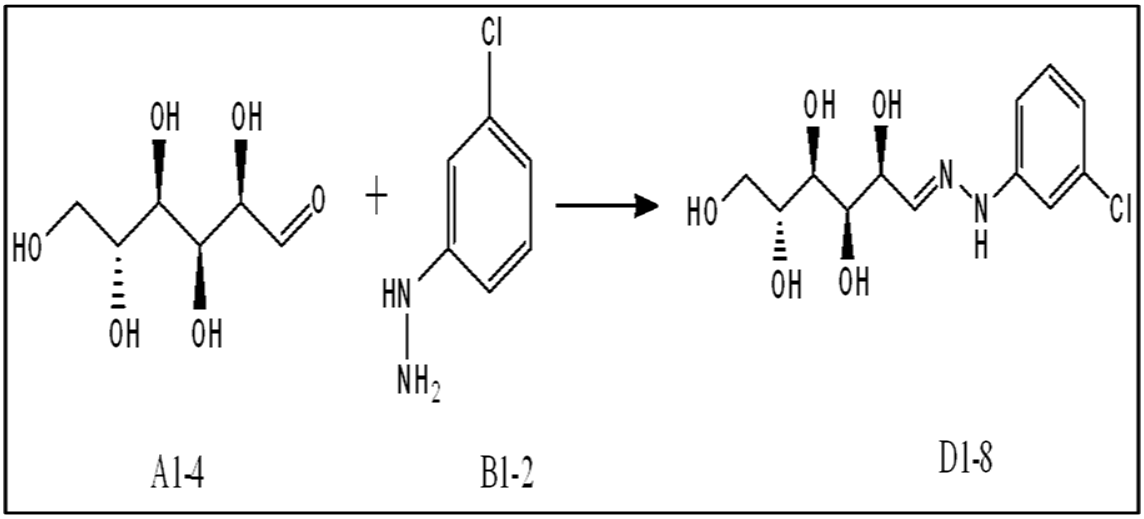
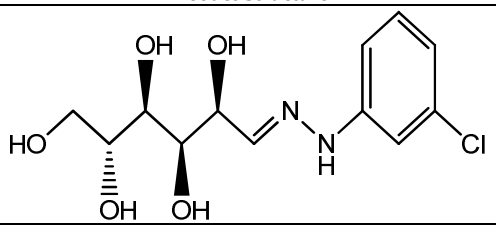
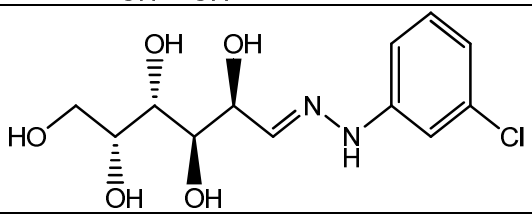
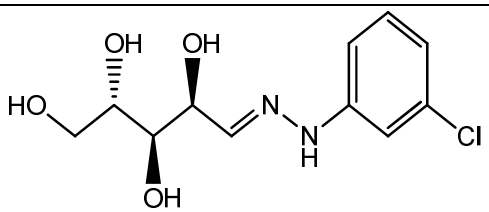
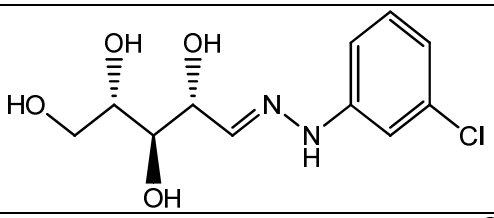
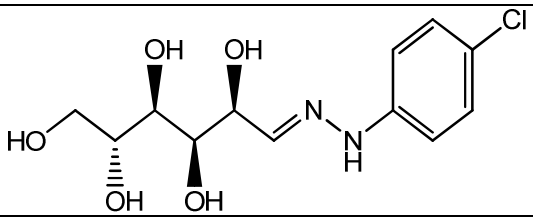
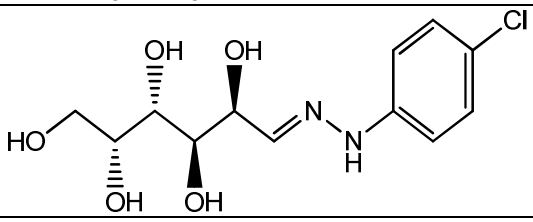
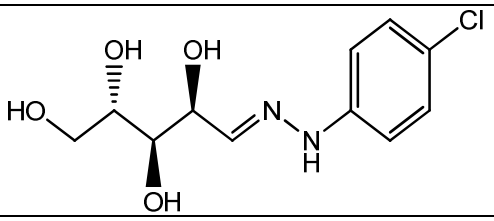
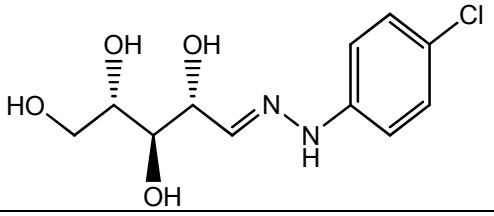



**Table 2: Physical data of synthesized compounds (D1-D8)**

| Sr. N0. | Product | Product Structure | Yields in % | MP in °C |
|---|---|---|---|---|
| 1 | D1 |  | 80 | 180-182 |
| 2 | D2 |  | 84 | 175-177 |
| 3 | D3 |  | 79 | 210-213 |

| | | | | |
|---|---|---|---|---|
| 4 | D4 |  | 75 | 220-222 |
| 5 | D5 |  | 83 | 195-198 |
| 6 | D6 |  | 80 | 245-248 |
| 7 | D7 |  | 82 | 288-291 |
| 8 | D8 |  | 85 | 240-243 |

The structures of the synthesized compounds were elucidated through analytical and on the basis of spectral data. The 1H NMR spectrum showed the presence of singlets at δ 2.2-7.6 ppm for NH proton and presences of multilpates in aromatic region shows introduction of aromatic nucleus. The IR spectrum exhibited sharp band at 3350-3370 for N-H and a characteristic band at 1610-1620 cm-1 for -C=N stre. The clears disappearance of -C=O band of aldehyde at 1720 cm-1 confirms the condensation of sugar with corresponding phenylhydrazine.

**Table 1. Antimycobacterial activity results of the synthesized compounds (3a-3p)**

| Compound | **Invitro activity - zone of inhibition (in mm)** | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | Gram + ve bacteria | | Gram - ve bacteria | | | | Fungi | | |
| | *S.aureus* | *S.epidermidis* | *M.luteus* | *B.cereus* | *E.coli* | *P.aeuriginosa* | *K.pneumoniae* | *A.niger* | *A.fumigatus* |
| D1 | 5 | 7 | 6 | 5 | 3 | 4 | 3 | 8 | **7** |
| D2 | 9 | 11 | 8 | 7 | 6 | 4 | 5 | 10 | **12** |
| D3 | 8 | 9 | 9 | 6 | 5 | 6 | 5 | 12 | **8** |
| D4 | 10 | 12 | 10 | 8 | 5 | 4 | 7 | 13 | **10** |
| D5 | 7 | 10 | 9 | 7 | 6 | 8 | 8 | 11 | **9** |
| D6 | 15 | 18 | 16 | 15 | 12 | 10 | 13 | 19 | **15** |
| D7 | 12 | 10 | 13 | 11 | 9 | 8 | 10 | 15 | **13** |
| D8 | 10 | 12 | 11 | 09 | 8 | 9 | 8 | 14 | **12** |

## CONCLUSION

In the present study a serious of hydrazones of sugar derivatives were synthesized and screened for their antimicrobacterial activities. The structure of the compounds were established on the basis of satisfactory spectral analysis. Some of the synthesized compound showed inhibitory activity against gram + and Gram –ve bacteria in primary screening assays especially compound D2, D4, D6, D7 and D8 possess significant anti-bacterial and anti-fungal activity when compared to standard drug (Ciprofloxacin and Fluconazole for anti-bacterial and anti-fungal respectively). In conclusion, the present study highlights the importance of hydrazone of sugars features responsible for the antimicrobial activities and therefore may serve as a lead molecule for further modification to obtain clinically useful novel entities.

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## REFERENCES

[1] Meutermans W, Le GT, Becker B, *Chem. Med. Chem*, **2006**, *1*, 1164.
[2] Takeda Y, *Carbohydr. Res*,**1979**, *77*, 9.
[3] Bendiak B, *Carbohydr. Res*, **1997**, *304*, 85.
[4] Peri F, Dumy P, Mutter M, *Tetrahedron*, **1998**, *54*, 12269.
[5] Gudmundsdottir AV, Paul CE, Nitz M, *Carbohydr Res*, **2009**, *344*, 278.
[6] Mahal LK, Yarema KJ, Bertozzi CR, *Science*, **1997**, *276*, 1125.
[7] Leteux C, Childs RA, Chai W, Stoll MS, Kogelberg H, Feizi T, *Glycobiology*, **1998**, *8*, 227.
[8] Lee JH, Baker TJ, Mahal LK, Zabner J, Bertozzi CR, Wiemer DF, Welsh, M.J. *J. Biol. Chem*, **1999**, *274*, 21878.
[9] Lee M, Shin I, *Org. Lett*, **2005**, *7*, 4269.
[10] Park S, Lee MR, Shin I, *Bioconjug. Chem*, **2009**, *20*, 155.
[11] Godula K, Bertozzi CR, *J. Am. Chem. Soc*, **2010**, *132*, 9963.
[12] Zhao Y, Kent SBH, Chait BT, *Proc. Natl. Acad. Sci. USA*, **1997**, *94*, 1629.
[13] Furukawa J, Shinohara Y, Kuramoto H, Miura Y, Shimaoka H, Kurogochi M, Nakano M, Nishimura SI, *Anal. Chem*, **2008**, *80*, 1094.
[14] Bohorov O, Andersson-Sand H, Hoffmann J, Blixt O, *Glycobiology*, **2006**, *16*, 21C.
[15] Rodriguez EC, Marcaurelle LA, Bertozzi CR, *J. Org. Chem*, **1998**, *63*, 7134.
[16] Peluso S, Imperiali B, *Tetrahedron Lett*, **2001**, *42*, 2085.
[17] Rollas S, Kucukguzel SG, *Molecules*, **2007**, *12*, 1910.
[18] Sah PPT, Peoples SA, *J. Am. Pharm. Assoc*, **1954**, *43*, 513.
[19] Yu Y, Kalinowski DS, Kovacevic Z, Siafakas AR, Jansson PJ, Stefani C, Lovejoy DB, Sharpe PC, Bernhardt PV, Richardson DR, *J. Med. Chem*, **2009**, *52*, 5271.