

## SYNTHESIS AND ANTIBACTERIAL SCREENING OF FEW NEW 5-MEMBERED HETEROCYCLIC SUGAR HYDRAZONES

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### ABSTRACT

**Objective:** The aim of this study is to synthesize, characterize, and screen some new 5-membered heterocyclic sugar hydrazones for their antibacterial activities.

**Methods:** A library of sugar hydrazones containing 2-benzofuryl, 2-thiophenyl, and 2-pyrrolyl motifs were synthesized. Structures of the newly synthesized compounds were deduced based on spectral data and elemental analyses.

**Results:** Antibacterial activity was screened against Gram-positive and Gram-negative bacterial strains. Results were compared to gentamicin. Compound 6a exhibited most potent antibacterial activity against all the tested strains.

**Conclusion:** 2-benzofuryl derivatives were observed to be good antibacterials.

**Keywords:** Benzofuran, Thiophene, Pyrrole, Antibacterial, Sugar.

### INTRODUCTION

Hydrazones are closely associated to imines but are not abundantly present in biological molecules. Hydrazones with an azometine -NHN=CH- proton are synthesized by heating substituted hydrazides with aldehydes/ketones in solvents such as methanol, ethanol, isopropanol, butanol, and glacial acetic acid [1]. Hydrazones are not only good intermediates [2] but are also reported to be valuable organic compounds in their own right [3]. Hydrazones exhibit a broad spectrum of activities including antimicrobial [4-7], antitumor [8-11], anti-inflammatory [12], anticonvulsant [12-14], antiplatelet [15], antidepressant [15], and antimycobacterial [16-18] activities. Literature also reveals the importance of hydrazones blended with sugars [19-21]. Carbohydrates are the abundantly present class of biomolecules, performing vital functions of life [22]. Carbohydrate derivatives are the synthons for drug synthesis [23] and asymmetric catalysis [24].

As a part of our continued work in the chemistry of 5-membered heterocycles [25-28], we wanted to synthesize sugar hydrazones of 1-(4-fluorophenyl)-1,3-dihydro-2-benzofuran-5-carbohydrazide [29]. This carbohydrazide is the derivative of 1-(4-fluorophenyl)-1,3-dihydroisobenzofuran-5-carbonitrile, an intermediate in the synthesis of the well-known antidepressant citalopram [30,31]. Perhaps, due to the steric hindrance of the bulky benzofuran moiety, there was no condensation between this hydrazide and the monosaccharides. However, sugar molecules were successfully introduced to other heterocyclic systems such as benzofuran, thiophene, and pyrrole. In hydrazones, there is blockage of -NH<sub>2</sub> group of hydrazides, making them less toxic [32]. Besides, the free sugar moiety enhances the antimicrobial properties [33,34]. Monosaccharides are the constitutional parts of nucleotides, complex lipids (glycolipids), and proteins (glycoproteins). Due to the properties inherent to this class of molecules, carbohydrates have been used to prepare bioactive materials [35] and better-targeted drugs [36]. They help in functionalization of hydrophobic materials [37]. Exploring the biological significance of sugar hydrazones, we herein report the antibacterial screening of few 5-membered heterocyclic sugar hydrazones formed by a simple approach.

### METHODS

#### Chemistry

Fourier transform infrared (FT-IR) spectra in KBr pellets were recorded on a Shimadzu 8300 FT-IR spectrometer. <sup>1</sup>H and <sup>13</sup>C NMR spectra (400 and 100 MHz) were recorded on a Bruker AM spectrometer in DMSO-*d*<sub>6</sub> solution with TMS as internal standard. ESI mass spectra were recorded on an Agilent 6520 ESIQTOF instrument at ionization potential of 110 V and acetonitrile as solvent. Elemental analyses were performed on a Vario-EL instrument. The melting points were determined on a Thomas Hoover apparatus and are uncorrected. Reactions were monitored by thin layer chromatography (TLC) using 0.25 mm silica gel plates (60F254, Merck). Visualization was made with ultraviolet light (UV. R-340). Reagents were obtained commercially and used as received.

#### General procedure for the synthesis of heterocyclic carbohydrazides (3-5) [29]

##### General procedure for the synthesis of sugar hydrazones (6a-8d)

An equimolar mixture of heterocyclic hydrazide (3-5) and respective monosaccharides was dissolved in ethanol (1 ml) and refluxed for 30 minutes. Completion of reaction was indicated by TLC (chloroform-ethyl acetate, 1:1). The solid compound formed (6a-8d) on cooling the reaction mass was filtered off, washed with ethanol, dried, and recrystallized from methanol.

#### N'-[(1Z)-2,3,4,5,6-pentahydroxyhexylidene]-1-benzofuran-2-carbohydrazone (6a)

IR (KBr) ( $\nu_{\max}$ , cm<sup>-1</sup>): 3460 (OH), 1658 (C=O), 1596 (C=N), 1454 (C=C); <sup>1</sup>H NMR (400 MHz, DMSO *d*<sub>6</sub>):  $\delta_{\text{H}}$  (ppm) 10.26 (1H, s, NH), 7.78 (1H, d, *J*=7.6 Hz, H Benzofuran), 7.67 (2H, d, *J*=8.4 Hz, H Benzofuran), 7.64 (1H, s, CH=N), 7.49-7.46 (1H, t, *J*=7.2 Hz, H Benzofuran), 7.36-7.32 (1H, t, *J*=7.6 Hz, H Benzofuran), 5.97 (1H, s, OH), 5.12 (1H, s, OH), 5.00 (1H, s, OH), 4.96 (1H, s, OH), 4.39 (1H, s, OH), 3.91 (1H, s, CH), 3.70 (1H, s, CH), 3.48 (1H, s, CH), 3.22 (1H, s, CH), 3.15 (1H, s, CH), 3.02 (1H, s, CH); <sup>13</sup>C NMR (100 MHz, DMSO *d*<sub>6</sub>):  $\delta_{\text{C}}$  158.2, 154.7, 148.1, 127.4, 127.3, 124.2, 123.2, 112.3, 110.4, 91.3, 78.4, 77.1, 71.8, 70.8, 61.8; MS (*m/z*): 339 [M+H]<sup>+</sup>, 209, 115; Anal. Calcd. for C<sub>15</sub>H<sub>18</sub>N<sub>2</sub>O<sub>7</sub>: C, 53.25; H, 5.36; N, 8.28. Found: C, 53.29; H, 5.30; N, 8.22.

**N'-[(1Z)-2,3,4,5,6-pentahydroxyhexylidene]-1-benzofuran-2-carbohydrazone (6b)**

IR (KBr) ( $\nu_{\max}$ ,  $\text{cm}^{-1}$ ): 3412 (OH), 1649 (C=O), 1591 (C=N), 1452 (C=C);  $^1\text{H}$  NMR (400 MHz, DMSO  $d_6$ ):  $\delta_{\text{H}}$  (ppm) 11.89 (1H, s, NH), 7.90 (1H, s, H Benzofuran), 7.82 (1H, s, H Benzofuran), 7.81 (1H, s, H Benzofuran), 7.70 (1H, s, CH=N), 7.50 (1H, s, H Benzofuran), 7.36 (1H, s, H Benzofuran), 5.03 (1H, s, OH), 4.57 (1H, s, OH), 4.46 (3H, s, OH), 4.23 (2H, s, CH), 3.74 (1H, s, CH), 3.56 (3H, s, CH);  $^{13}\text{C}$  NMR (100 MHz, DMSO  $d_6$ ):  $\delta_{157.2, 154.1, 148.9, 127.6, 127.2, 124.4, 123.7, 112.9, 110.0, 91.8, 78.2, 77.6, 71.3, 70.9, 62.1$ ; Anal. Calcd. for  $\text{C}_{15}\text{H}_{18}\text{N}_2\text{O}_7$ : C, 53.25; H, 5.36; N, 8.28. Found: C, 53.20; H, 5.31; N, 8.25.

**N'-[(1Z)-2,3,4,5-tetrahydroxypentylidene]-1-benzofuran-2-carbohydrazone (6c)**

IR (KBr) ( $\nu_{\max}$ ,  $\text{cm}^{-1}$ ): 3411 (OH), 1625 (C=O), 1589 (C=N), 1472 (C=C);  $^1\text{H}$  NMR (400 MHz, DMSO  $d_6$ ):  $\delta_{\text{H}}$  (ppm) 10.34 (1H, s, NH), 7.78 (1H, d,  $J=7.6$  Hz, H Benzofuran), 7.66 (1H, d,  $J=8.0$  Hz, H Benzofuran), 7.63 (1H, s, CH=N), 7.49-7.45 (1H, t,  $J=7.2$  Hz, H Benzofuran), 7.36-7.32 (1H, t,  $J=7.2$  Hz, H Benzofuran), 5.94 (1H, s, OH), 5.12 (1H, s, OH), 5.05 (1H, s, OH), 4.99 (2H, s, OH), 3.90 (1H, s, CH), 3.74 (1H, s, CH), 3.27 (1H, s, CH), 3.19 (1H, s, CH), 3.03 (1H, s, CH);  $^{13}\text{C}$  NMR (100 MHz, DMSO  $d_6$ ):  $\delta_{157.9, 154.1, 148.5, 127.8, 126.1, 124.3, 123.5, 112.2, 110.6, 92.3, 75.4, 71.6, 70.1, 66.2}$ ; Anal. Calcd. for  $\text{C}_{14}\text{H}_{16}\text{N}_2\text{O}_6$ : C, 54.54; H, 5.23; N, 9.09. Found: C, 54.57; H, 5.26; N, 9.02.

**N'-[(1Z)-2,3,4,5-tetrahydroxypentylidene]-1-benzofuran-2-carbohydrazone (6d)**

IR (KBr) ( $\nu_{\max}$ ,  $\text{cm}^{-1}$ ): 3402 (OH), 1666 (C=O), 1566 (C=N), 1450 (C=C);  $^1\text{H}$  NMR (400 MHz, DMSO  $d_6$ ):  $\delta_{\text{H}}$  (ppm) 10.34 (1H, s, NH), 7.78 (1H, d,  $J=7.6$  Hz, H Benzofuran), 7.66 (1H, d,  $J=8.0$  Hz, H Benzofuran), 7.63 (1H, s, CH=N), 7.49-7.45 (1H, t,  $J=7.2$  Hz, H Benzofuran), 7.36-7.32 (1H, t,  $J=7.2$  Hz, H Benzofuran), 5.94 (1H, s, OH), 5.12 (1H, s, OH), 5.05 (1H, s, OH), 4.99 (2H, s, OH), 3.90 (1H, s, CH), 3.74 (1H, s, CH), 3.27 (1H, s, CH), 3.19 (1H, s, CH), 3.03 (1H, s, CH);  $^{13}\text{C}$  NMR (100 MHz, DMSO  $d_6$ ):  $\delta_{158.2, 154.7, 148.1, 127.4, 127.3, 124.2, 123.4, 112.2, 110.1, 92.0, 76.9, 71.6, 70.2, 67.2}$ ; Anal. Calcd. for  $\text{C}_{14}\text{H}_{16}\text{N}_2\text{O}_6$ : C, 54.54; H, 5.23; N, 9.09. Found: C, 54.58; H, 5.21; N, 9.11.

**N'-[(1Z)-2,3,4,5,6-pentahydroxyhexylidene]-thiophene-2-carbohydrazone (7a)**

IR (KBr) ( $\nu_{\max}$ ,  $\text{cm}^{-1}$ ): 3486 (OH), 1632 (C=O), 1591 (C=N), 1426 (C=C);  $^1\text{H}$  NMR (400 MHz, DMSO  $d_6$ ):  $\delta_{\text{H}}$  (ppm) 11.13 (1H, s, NH); 7.90 (2H, d,  $J=4.8$ , H Thiophene); 7.52 (1H, s, CH=N), 7.24 (1H, t,  $J=4.0$ , H Thiophene); 5.91 (1H, s, OH), 5.18 (1H, s, OH), 5.08 (1H, s, OH), 4.89 (1H, s, OH), 4.41 (1H, s, OH), 3.91 (1H, s, CH), 3.72 (1H, s, CH), 3.21 (1H, s, CH), 3.26 (1H, s, CH), 3.05 (1H, s, CH), 3.00 (1H, s, CH);  $^{13}\text{C}$  NMR (100 MHz, DMSO  $d_6$ ):  $\delta_{161.8, 138.0, 131.6, 129.0, 128.5, 91.4, 78.5, 77.0, 71.7, 70.8, 61.7}$ ; Anal. Calcd. for  $\text{C}_{11}\text{H}_{16}\text{N}_2\text{O}_6\text{S}$ : C, 43.41; H, 5.30; N, 9.21. Found: C, 43.39; H, 5.35; N, 9.26.

**N'-[(1Z)-2,3,4,5,6-pentahydroxyhexylidene]-thiophene-2-carbohydrazone (7b)**

IR (KBr) ( $\nu_{\max}$ ,  $\text{cm}^{-1}$ ): 3460 (OH), 1658 (C=O), 1596 (C=N), 1454 (C=C);  $^1\text{H}$  NMR (400 MHz, DMSO  $d_6$ ):  $\delta_{\text{H}}$  (ppm) 11.09 (1H, s, NH); 7.91 (2H, d,  $J=4.6$ , H Thiophene); 7.52 (1H, s, CH=N), 7.27 (1H, t,  $J=4.0$ , H Thiophene); 5.89 (1H, s, OH), 5.18 (1H, s, OH), 5.16 (1H, s, OH), 4.91 (1H, s, OH), 4.43 (1H, s, OH), 3.91 (1H, s, CH), 3.70 (1H, s, CH), 3.58 (1H, s, CH), 3.20 (1H, s, CH), 3.11 (1H, s, CH), 3.02 (1H, s, CH);  $^{13}\text{C}$  NMR (100 MHz, DMSO  $d_6$ ):  $\delta_{160.2, 140.2, 131.9, 129.4, 128.1, 91.2, 78.8, 76.2, 71.9, 70.5, 62.1}$ ; Anal. Calcd. for  $\text{C}_{11}\text{H}_{16}\text{N}_2\text{O}_6\text{S}$ : C, 43.41; H, 5.30; N, 9.21. Found: C, 43.49; H, 5.32; N, 9.18.

**N'-[(1Z)-2,3,4,5-tetrahydroxypentylidene]-thiophene-2-carbohydrazone (7c)**

IR (KBr) ( $\nu_{\max}$ ,  $\text{cm}^{-1}$ ): 3487 (OH), 1647 (C=O), 1593 (C=N), 1446 (C=C);  $^1\text{H}$  NMR (400 MHz, DMSO  $d_6$ ):  $\delta_{\text{H}}$  (ppm) 11.03 (1H, s, NH); 7.93 (2H, d,  $J=4.8$ , H Thiophene); 7.43 (1H, s, CH=N), 7.21 (1H, t,  $J=4.0$ , H Thiophene); 5.90 (1H, s, OH), 5.31 (1H, s, OH), 5.08 (1H, s, OH), 4.83 (1H, s, OH), 3.86 (1H, s, CH), 3.73 (1H, s, CH), 3.36 (1H, s, CH), 3.12 (1H, s, CH),

3.05 (1H, s, CH);  $^{13}\text{C}$  NMR (100 MHz, DMSO  $d_6$ ):  $\delta_{160.7, 139.8, 131.7, 129.5, 128.0, 91.3, 78.4, 76.0, 71.4, 62.4}$ ; Anal. Calcd. for  $\text{C}_{10}\text{H}_{14}\text{N}_2\text{O}_5\text{S}$ : C, 43.79; H, 5.14; N, 10.21. Found: C, 43.77; H, 5.10; N, 10.26.

**N'-[(1Z)-2,3,4,5-tetrahydroxypentylidene]-thiophene-2-carbohydrazone (7d)**

IR (KBr) ( $\nu_{\max}$ ,  $\text{cm}^{-1}$ ): 3412 (OH), 1682 (C=O), 1566 (C=N), 1452 (C=C);  $^1\text{H}$  NMR (400 MHz, DMSO  $d_6$ ):  $\delta_{\text{H}}$  (ppm) 10.91 (1H, s, NH); 7.90 (2H, d,  $J=4.8$ , H Thiophene); 7.51 (1H, s, CH=N), 7.31 (1H, t,  $J=4.0$ , H Thiophene); 5.94 (1H, s, OH), 5.46 (1H, s, OH), 5.18 (1H, s, OH), 4.74 (1H, s, OH), 3.82 (1H, s, CH), 3.63 (1H, s, CH), 3.36 (1H, s, CH), 3.13 (1H, s, CH), 3.05 (1H, s, CH);  $^{13}\text{C}$  NMR (100 MHz, DMSO  $d_6$ ):  $\delta_{160.3, 139.0, 131.4, 129.2, 127.4, 90.7, 78.6, 76.0, 71.4, 62.2}$ ; Anal. Calcd. for  $\text{C}_{10}\text{H}_{14}\text{N}_2\text{O}_5\text{S}$ : C, 43.79; H, 5.14; N, 10.21. Found: C, 43.71; H, 5.17; N, 10.18.

**N'-[(1Z)-2,3,4,5-tetrahydroxypentylidene]-1H-pyrrole-2-carbohydrazone (8a)**

IR (KBr) ( $\nu_{\max}$ ,  $\text{cm}^{-1}$ ): 3414 (OH), 3142 (NH), 1673 (C=O), 1561 (C=N), 1451 (C=C);  $^1\text{H}$  NMR (400 MHz, DMSO  $d_6$ ):  $\delta_{\text{H}}$  (ppm) 11.13 (1H, s, NH); 10.11 (1H, s, Pyrrole NH); 7.52 (1H, s, CH=N), 7.17 (2H, d,  $J=4.8$ , H Pyrrole); 6.98 (1H, t,  $J=4.0$ , H Pyrrole); 5.93 (1H, s, OH), 5.26 (1H, s, OH), 5.07 (1H, s, OH), 4.97 (1H, s, OH), 4.52 (1H, s, OH), 3.95 (1H, s, CH), 3.69 (1H, s, CH), 3.53 (1H, s, CH), 3.21 (1H, s, CH), 3.07 (1H, s, CH), 3.01 (1H, s, CH);  $^{13}\text{C}$  NMR (100 MHz, DMSO  $d_6$ ):  $\delta_{157.2, 146.1, 130.2, 118.7, 108.5, 91.7, 78.8, 77.6, 71.2, 70.1, 61.9}$ ; Anal. Calcd. for  $\text{C}_{11}\text{H}_{17}\text{N}_3\text{O}_6$ : C, 45.99; H, 5.96; N, 14.63. Found: C, 45.91; H, 5.99; N, 14.60.

**N'-[(1Z)-2,3,4,5-tetrahydroxypentylidene]-1H-pyrrole-2-carbohydrazone (8b)**

IR (KBr) ( $\nu_{\max}$ ,  $\text{cm}^{-1}$ ): 3419 (OH), 3140 (NH), 1642 (C=O), 1559 (C=N), 1456 (C=C);  $^1\text{H}$  NMR (400 MHz, DMSO  $d_6$ ):  $\delta_{\text{H}}$  (ppm) 10.88 (1H, s, NH); 10.06 (1H, s, Pyrrole NH); 7.61 (1H, s, CH=N), 7.22 (2H, d,  $J=4.8$ , H Pyrrole); 6.82 (1H, t,  $J=4.0$ , H Pyrrole); 5.88 (1H, s, OH), 5.43 (1H, s, OH), 5.25 (1H, s, OH), 5.01 (1H, s, OH), 4.78 (1H, s, OH), 4.05 (1H, s, CH), 3.99 (1H, s, CH), 3.52 (1H, s, CH), 3.23 (1H, s, CH), 3.10 (1H, s, CH), 3.03 (1H, s, CH);  $^{13}\text{C}$  NMR (100 MHz, DMSO  $d_6$ ):  $\delta_{154.7, 148.1, 129.5, 118.9, 108.6, 91.7, 78.7, 77.0, 71.3, 70.1, 62.3}$ ; Anal. Calcd. for  $\text{C}_{11}\text{H}_{17}\text{N}_3\text{O}_6$ : C, 45.99; H, 5.96; N, 14.63. Found: C, 45.93; H, 5.97; N, 14.66.

**N'-[(1Z)-2,3,4,5-tetrahydroxypentylidene]-1H-pyrrole-2-carbohydrazone (8c)**

IR (KBr) ( $\nu_{\max}$ ,  $\text{cm}^{-1}$ ): 3422 (OH), 3141 (NH), 1640 (C=O), 1542 (C=N), 1459 (C=C);  $^1\text{H}$  NMR (400 MHz, DMSO  $d_6$ ):  $\delta_{\text{H}}$  (ppm) 11.01 (1H, s, NH); 10.52 (1H, s, Pyrrole NH); 7.41 (1H, s, CH=N), 7.29 (2H, d,  $J=4.5$ , H Pyrrole); 6.99 (1H, t,  $J=4.0$ , H Pyrrole); 5.88 (1H, s, OH), 5.42 (1H, s, OH), 5.18 (1H, s, OH), 4.99 (1H, s, OH), 4.31 (1H, s, CH), 3.99 (1H, s, CH), 3.42 (1H, s, CH), 3.19 (1H, s, CH), 3.07 (1H, s, CH);  $^{13}\text{C}$  NMR (100 MHz, DMSO  $d_6$ ):  $\delta_{160.3, 140.5, 129.1, 119.5, 108.2, 91.9, 79.0, 76.8, 71.2, 64.8}$ ; Anal. Calcd. for  $\text{C}_{10}\text{H}_{15}\text{N}_3\text{O}_5$ : C, 46.69; H, 5.88; N, 16.33. Found: C, 46.67; H, 5.80; N, 16.38.

**N'-[(1Z)-2,3,4,5-tetrahydroxypentylidene]-1H-pyrrole-2-carbohydrazone (8d)**

IR (KBr) ( $\nu_{\max}$ ,  $\text{cm}^{-1}$ ): 3418 (OH), 3251 (NH), 1644 (C=O), 1539 (C=N), 1460 (C=C);  $^1\text{H}$  NMR (400 MHz, DMSO  $d_6$ ):  $\delta_{\text{H}}$  (ppm) 11.07 (1H, s, NH); 10.69 (1H, s, Pyrrole NH); 7.44 (1H, s, CH=N), 7.30 (2H, d,  $J=4.8$ , H Pyrrole); 6.84 (1H, t,  $J=4.0$ , H Pyrrole); 5.89 (1H, s, OH), 5.46 (1H, s, OH), 5.15 (1H, s, OH), 4.81 (1H, s, OH), 4.42 (1H, s, CH), 3.96 (1H, s, CH), 3.61 (1H, s, CH), 3.28 (1H, s, CH), 3.11 (1H, s, CH);  $^{13}\text{C}$  NMR (100 MHz, DMSO  $d_6$ ):  $\delta_{159.7, 142.7, 129.6, 119.1, 108.8, 91.1, 78.6, 76.4, 71.2, 63.5}$ ; Anal. Calcd. for  $\text{C}_{10}\text{H}_{15}\text{N}_3\text{O}_5$ : C, 46.69; H, 5.88; N, 16.33. Found: C, 46.63; H, 5.82; N, 16.39.

**Antibacterial studies**

Synthesized compounds were screened for their antibacterial activity by disc diffusion method [26] under NCCLS document M62-A7 protocols. Four bacterial strains, *Escherichia coli* NCIM 2574, *Pseudomonas aeruginosa* NCIM 2036, *Streptococcus aureus* NCIM 2079, and *Bacillus subtilis* NCIM 2063 were maintained on Muller-Hinton agar medium.

Gentamicin was the standard antibacterial drug. A 10 mg/ml solution of compounds was prepared in dimethyl sulfoxide for the screening.

As per M62-A7 protocols, broth dilution test by doubling dilution of the antibiotics was carried out to examine the minimum inhibitory concentration of the promising compound 6a. The antibacterial assay was performed in Mueller-Hinton broth with the minimum inhibitory concentration (MIC) for microbes observed between 250 mg/ml and 7.81 mg/ml. Gentamicin (1 mg/ml) was the standard antibacterial drug with DMSO as a solvent control.

## RESULTS AND DISCUSSION

### Synthesis and characterization

The synthetic pathway for 5-membered sugar hydrazones (6a-8d) is as per Scheme 1. The target compounds were synthesized by the reaction between heterocyclic hydrazides (3-5) and different monosaccharides in ethanolic solution. Structures of the compounds were confirmed on the basis of NMR, IR, mass and elemental analyses. The FT-IR spectra of sugar hydrazones showed characteristic stretching bands of OH, C=O, and C=N groups in the regions of 3200-3500/cm, 1528-1670/cm, and 1532-1596/cm, respectively. <sup>1</sup>H NMR spectra had a sharp singlet around  $\delta$  10.0-11.0 ppm for the single NH of the hydrazones. A singlet around  $\delta$  7.6 ppm was for CH=N proton. CH proton of the monosaccharides appeared at  $\delta$  3.02-4.2 ppm and sugar OH at  $\delta$  4.3-5.9 ppm. <sup>13</sup>C NMR spectra of sugar hydrazones had the salient signal for C=N in the range of  $\delta$  148-138 ppm confirming the hydrazone formation. The carbons of the sugar backbone lie in the region of  $\delta$  60-78 ppm with C=O occurring around  $\delta$  150-160 ppm. The mass spectrum of 6a showed molecular ion peak at  $m/z=339$  (M+1), which is in agreement with its formula weight, i.e., 338. Table 1 stands for the physical data of synthesized compounds.

### Biology

The disc diffusion testing for the antibacterial activities of the target compounds was observed as provided in Table 2. Compound 6a, a blend of benzofuran-2-carbohydrazide and glucose, showed significant inhibition against all the tested bacteria. 2-benzofuryl derivatives of monosaccharides showed good inhibition against the selected bacterial strains. 2-thiophenyl and 2-pyrrolyl derivatives of monosaccharides

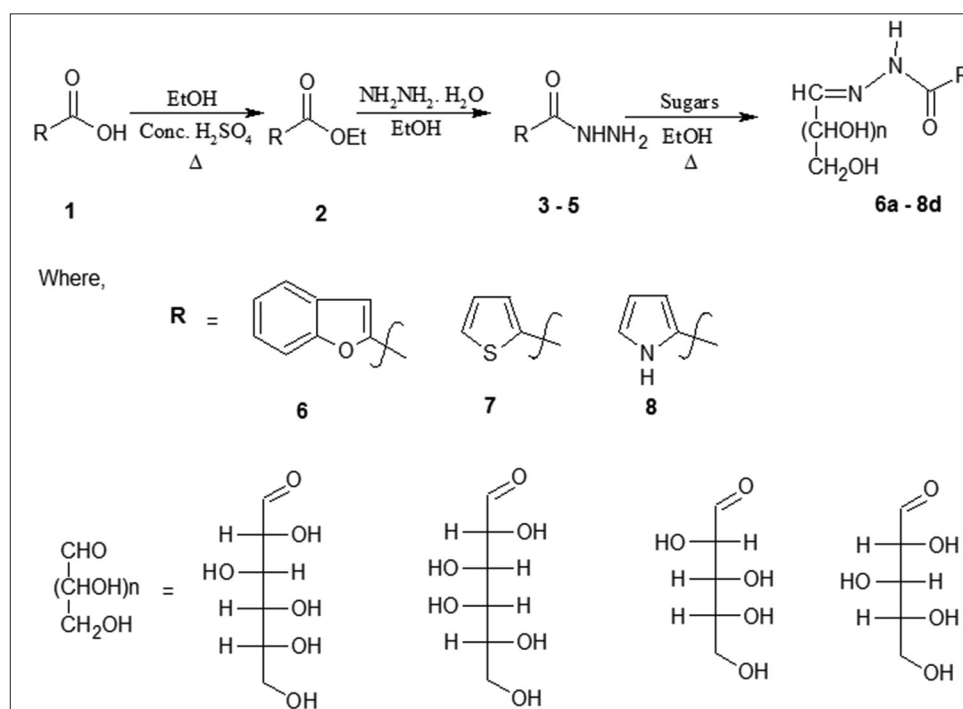
Table 1: Physical data of synthesized compounds (6a-8d)

Product	R <sub>f</sub>	Mp (°C)	Yield (%)
6a	0.30	208-210	82
6b	0.28	202-204	85
6c	0.21	216-218	79
6d	0.24	196-198	81
7a	0.26	194-196	70
7b	0.26	174-176	73
7c	0.28	202-204	76
7d	0.25	166-168	74
8a	0.18	184-186	72
8b	0.16	200-202	76
8c	0.18	166-168	78
8d	0.14	170-172	72

Table 2: Inhibitory zone (diameter) mm of synthesized compounds against tested bacterial strains by disc diffusion method\*

Compound	<i>B. subtilis</i>	<i>S. aureus</i>	<i>E. coli</i>	<i>P. aeruginosa</i>
6a	28	25	19	15
6b	26	23	19	13
6c	23	18	15	11
6d	21	16	14	10
7a	25	22	-	-
7b	21	19	-	-
7c	18	12	-	-
7d	15	12	-	-
8a	19	17	-	-
8b	20	12	-	-
8c	20	14	-	-
8d	16	12	-	-
Gentamicin	27	26	22	18

\*Synthesized compound taken was 10 ml of 10 mg/ml and gentamicin (10 mg per disc) was the positive reference standard antibiotic disc. *B. subtilis*: *Bacillus subtilis*, *S. aureus*: *Staphylococcus aureus*, *E. coli*: *Escherichia coli*, *P. aeruginosa*: *Pseudomonas aeruginosa*



Scheme 1: Synthesis of sugar hydrazones (6a-8d)

showed average activities. In general, good inhibition was observed against Gram-positive bacteria than the Gram-negative ones. MIC observed for 6a was  $62.5 \text{ mg/ml} \leq \text{MIC} < 31.25 \text{ mg/ml}$  for Gram-positive bacteria and  $125.0 \text{ mg/ml} \leq \text{MIC} < 62.5 \text{ mg/ml}$  for Gram-negative bacteria.

## CONCLUSIONS

In the present work, a series of new sugar derived 5-membered heterocyclic hydrazones were synthesized in good yields and characterized by spectral studies. The title compounds were screened for their antibacterial activities against *B. subtilis*, *S. aureus*, *E. coli*, and *P. aeruginosa* by disc diffusion method. A potent compound 6a was tested further for its MIC by serial dilution method.

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