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*Research Article*

# Synthesis and antimicrobial activity of some newer semicarbazone analogues

**Prachi Agrawal[1] & G. Jeyabalan[2]***

*[1]Sunrise University, Alwar, Rajasthan, India*
*[2]Alwar Pharmacy College, Alwar, Rajasthan, India*

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**ABSTRACT**

On the basis of literature review Semicarbazones have been potent in activities such as antifungal, antibacterial, antituberculosis, anticancerous etc. Till date various works has been done however still there is tremendous opportunities which can be explored. So, we planned for the synthesis of Semicarbazone derivaties and checking their antimicrobial activities. Biological activity was determined for all 19 synthesized compounds against bacteria (gram positive and gram negative) by MIC(Minimum Inhibitory Concentration) method.

## Introduction

The discovery, development, and clinical use of antibiotics during the 20th century have decreased substantially the morbidity and mortality from bacterial infections. The antibiotic era began with the therapeutic application of sulphonamide drugs in the 1930s, followed by a "golden" period of discovery from approximately 1945 to 1970, when a number of structurally diverse, highly effective agents were discovered and developed [1]. The currently available antibiotics includes β-lactums (Penicillin and Cephalosporins), Aminoglycosides, Tetracyclines, Chloramphenicol, Macrolids, lincosamides, Sulfonamides, Sulfones, Quinolones/ Fluoroquinolones, Metronidazole, Nitrofurantoin, Fucidin and Vancomycin. All these agent causes severe to moderate side effects. Moreover, since the 1980s the introduction of new agents for clinical use has declined, reflecting both the challenge of identifying new drug classes and a declining commitment to antibacterial drug discovery by the pharmaceutical industry [2]. The same period with a reduced rate of introduction of new agents has been accompanied by an alarming increase in bacterial resistance to existing agents, resulting in the emergence of a serious threat to global public health [3]. Resistance to current clinically available antibiotics is now major setback in the treatment of infectious disease [4]. Recently in India there was a report of some newer resistant superbugs or MDR (multi drug resistance) causing intense economic loss in medical tourism [5]. These are making medications less effective in both prophylactic and treatment of infections [6]. Antimicrobial resistance is now growing problem in world and causes millions of deaths every years [7]. There have been increasing public calls for global collective action to address the threat. The resistance problem demands that a renewed effort be made to seek antibacterial agents effective against pathogenic bacteria resistant to current antibiotics. All these factors are pressing the needs to develop some newer antimicrobial agents having different structural scaffold acting through different mechanisms. Semicarbazones belong to an important structural class, which have valuable and diverse biological properties. Semicarbazones are extensively used as synthetic intermediates [8]. They have been used to synthesize various heterocyclic compounds which have wide ranges of pharmacological activities, for example anticonvulsant [9], antibacterial [10], antifungal [11], antitubercular [12] and anticancer [13] activities. Keeping all these in mind we have designed and synthesise some newer semicarbazone derivatives as potential antimicrobial agents.

## Experimental

### Instrumentation

The entire chemical reagents which are used in the study are procured locally. The completion of reaction is monitored by thin layer chromatography (TLC) using chloroform-methanol (9:1) as the solvent system. The products were purified by recrystallisation with absolute ethanol and purity of the compounds was checked by thin layer chromatography (TLC) using silica gel G plates (Merck). The spot was developed in iodine chamber or viewed under UV lamp. Melting points were determined in an open capillary using melting point apparatus and are uncorrected. The proton magnetic

***Corresponding Author: G.Jeyabalan,** Sunrise University, Alwar, Rajasthan, India

resonance(1H NMR) spectra were recorded on a Brucker 300 MHz instrument in DMSOd6 using tetramethylsilane as an internal standard. The infrared spectra of compounds were recorded in KBr on a Bio-Rad FTIR Spectrophotometer.

General procedure for the synthesis of (2E)-2-(substitutedbenzylidene)-N-(3-chloro-4-methoxyphenyl) hydrazinecarboxamide (3a–s). Synthesis of semicarbazones were carried out by the earlier reported procedure. A mixture of semicarbazide (0.01 mole) and aldehydes or ketones (0.01 mole) were refluxed in presence of sodium acetate and HCl (2 ml) in alcohol. The completion of reactions was monitored by TLC using benzene: acetone (7:3) as the mobile phase.

***(2E)-2-(2-chlorobenzylidene)-N-(3-chloro-4-methoxy phenyl)hydrazinecarboxamide*** (**3a**). Yield 74%; m.p. 175; IR (KBr) $cm^{-1}$: 3375 (N-H), 1675(C=O), 1534 (C=N); 1H; NMR (DMSO-$d_6$) δ ppm: 3.83 (s, 3H, $OCH_3$), 6.89–7.85(m, 7H, aromatic), 7.64 (s, 1H, N=CH), 9.00 (s, 1H, Ar–NH), 10.62 (s, 1H, CONH); MS: m/z, M+ 338; Anal. Calcd for $C_{15}H_{13}Cl_2N_3O_2$ : C 53.27 ; H 3.87 ; Cl 20.97 ; N 12.43 ; O 9.46 Found: C 53.17 ; H 3.88 ; N 12.45 ; O 9.48.

***(2E)-2-(4-chlorobenzylidene)-N-(3-chloro-4-methoxy phenyl)hydrazinecarboxamide*** **(3b)**
Yield 71%; m.p. 188 _C, IR (KBr) $cm^{-1}$: 3405 (N-H), 1701 (C=O), 1540 (C=N) ; 1H NMR (DMSO-d6) δ ppm3.81 (s, 3H, $OCH_3$), 6.84–7.82(m, 7H, aromatic), 7.61 (s, 1H, N=CH), 8.99 (s, 1H, Ar–NH), 10.60(s, 1H, CONH) ; MS: m/z, M+ 325 ; Anal. Calcd for $C_{15}H_{13}Cl_2N_3O_2$ : C 53.27 ; H 3.87 ; Cl 20.97 ; N 12.43 ; O 9.46. Found: C 53.17 ; H 3.88 ; N 12.45 ; O 9.48.

***(2E)-N-(3-chloro-4-methoxyphenyl)-2-(2-nitrobenzyl idene)hydrazinecarboxamide*** **(3c)**
Yield 74%; m.p. 217 _C, IR (KBr) $cm^{-1}$: 3406 (N-H), 1695(C=O), 1531 (C=N) ; 1H NMR (DMSO-d6) δ ppm 3.79 (s, 3H, $OCH_3$), 6.82–7.80(m, 7H, aromatic), 7.59 (s, 1H, N=CH), 8.98 (s, 1H, Ar–NH), 10.59(s, 1H, CONH); MS: m/z, M+ 348.74 Anal. Calcd for $C_{15}H_{13}ClN_4O_4$ : C 51.66 ; H 3.76 ; Cl 10.17 ; N 16.07 ; O 18.35. Found: C 51.62 ; H 3.77 ; N 12.47 ; O 9.49.

***(2E)-N-(3-chloro-4-methoxyphenyl)-2-(4-nitro benzylidene)hydrazine carboxamide*** **(3d)**
Yield 66%; m.p. 197 _C, IR (KBr) $cm^{-1}$: 3408 (N-H), 1699 (C=O), 1536 (C=N); 1H NMR (DMSO-d6) δ ppm 3.80 (s, 3H, $OCH_3$), 6.83–7.81(m, 7H, aromatic), 7.62 (s, 1H, N=CH), 8.99(s, 1H, Ar–NH), 10.60(s, 1H, CONH); MS: m/z, M+ 348.74, Anal. Calcd for $C_{15}H_{13}ClN_4O_4$ : C 51.66 ; H 3.76 ; Cl 10.17 ; N 16.07 ; O 18.35. Found: C 51.62 ; H 3.77 ; N 12.47 ; O 9.49.

***(2E)-N-(3-chloro-4-methoxyphenyl)-2-(2-hydroxy benzylidene)hydrazinecarboxamide*** **(3e)**
Yield 56%; m.p. 171_C, IR (KBr) $cm^{-1}$: 3380 (N-H), 1681 (C=O), 1541 (C=N) ; (DMSO-d60) δ ppm 3.81 (s, 3H, $OCH_3$), 6.84–7.82(m, 7H, aromatic), 7.63 (s, 1H, N=CH), 9.00(s, 1H, Ar–NH), 10.61(s, 1H, CONH) ; MS: m/z, M+ 319.74 ; Anal. Calcd for $C_{15}H_{14}ClN_3O_3$ : C 56.35 ; H 4.41 ; Cl 11.09 ; N 13.14 ; O 15.01. Found: C 56.36 ; H 4.43 ; Cl 11.08 ; N 13.16 ; O 15.02.

***(2E)-N-(3-chloro-4-methoxyphenyl)-2-(4-hydroxyl benzylidene)hydrazinecarboxamide*** **(3f)** Yield 65%; m.p. 201 _C, IR (KBr) $cm^{-1}$: 3385 (N-H), 1685 (C=O), 1546 (C=N) ; (DMSO-d6); δ ppm 3.83 (s, 3H, $OCH_3$), 6.86–7.84(m, 7H, aromatic), 7.65 (s, 1H, N=CH), 9.02(s, 1H, Ar–NH), 10.63(s, 1H, CONH) ; MS: m/z, M+ 319.74 ; Anal. Calcd for $C_{15}H_{14}ClN_3O_3$ : C 56.35 ; H 4.41 ; Cl 11.09 ; N 13.14 ; O 15.01. Found: C 56.36 ; H 4.43 ; Cl 11.08 ; N 13.16 ; O 15.02.

***(2E)-N-(3-chloro-4-methoxyphenyl)-2-(4-methoxy benzylidene)hydrazinecarboxamide*** **(3g)**
Yield 69%; m.p. 144 _C, IR (KBr) $cm^{-1}$: 3375 (N-H), 1682 (C=O), 1541 (C=N) ; (DMSO-d6); δ ppm : 3.83 (s, 3H, $OCH_3$), 6.86–7.84(m, 7H, aromatic), 7.65 (s, 1H, N=CH), 9.02(s, 1H, Ar–NH), 10.63(s, 1H, CONH); MS: m/z, M+ 333.76; Anal. Calcd for $C_{16}H_{16}ClN_3O_3$ : C 57.58 ; H 4.83 ; Cl 10.62 ; N 12.59 ; O 14.38. Found: C 57.59 ; H 4.44 ; Cl 11.09 ; N 13.17 ; O 15.03.

***(2E)-N-(3-chloro-4-methoxyphenyl)-2-(3,4-dimethoxy benzylidene) hydrazinecarboxamide*** **(3h)** Yield 67%; m.p. 200 _C, IR (KBr) $cm^{-1}$: 3365 (N-H), 1693 (C=O), 1551 (C=N) ; (DMSO-d6) δ ppm : 3.84 (s, 3H, $OCH_3$), 6.87–7.85(m, 6H, aromatic), 7.66 (s, 1H, N=CH), 9.03(s, 1H, Ar–NH), 10.64(s, 1H, CONH); MS: m/z, M+ 363.79 ; Anal. Calcd for $C_{17}H_{18}ClN_3O_4$ : C 56.13 ; H 4.99 ; Cl 9.75 ; N 11.55 ; O 17.59. Found: C 56.14 ; H 4.98 ; Cl 11.56 ; N 11.56 ; O 17.60.

***(2E)-N-(3-chloro-4-methoxyphenyl)-2-[4-(dimethyl amino)benzylidene]hydrazinecarboxamide*** **(3i)** Yield 66%; m.p. 179 _C, IR (KBr) $cm^{-1}$: 3375 (N-H), 1683 (C=O), 1581 (C=N); (DMSO-d6) δ ppm : 3.85 (s, 3H, $OCH_3$), 6.88–7.86(m, 7H, aromatic), 7.67 (s, 1H, N=CH), 9.04(s, 1H, Ar–NH), 10.65(s, 1H, CONH); MS: m/z M+ 346.81; Anal. Calcd for $C_{17}H_{19}ClN_4O_2$ : C 58.87 ; H 5.52 ; Cl 10.22 ; N 16.15 ; O 9.23. Found: C 58.88 ; H 5.53; Cl 10.23 ; N 16.16 ; O 9.22.

***(2E)-N-(3-chloro-4-methoxyphenyl)-2-[1-(2,4-dichlorophenyl)ethylidene]hydrazinecarbox-amide*** **(3j)** Yield 64%; m.p.145 _C, IR (KBr) $cm^{-1}$: 3370 (N-H), 1683 (C=O),1543 (C=N); (DMSO-d6) δ ppm : 3.85 (s, 3H, $OCH_3$), 6.88–7.86(m, 6H, aromatic), 7.67 (s, 1H, N=CH), 9.04(s, 1H, Ar–NH), 10.65(s, 1H, CONH); MS: m/z, M+ 386.66; Anal. Calcd for $C_{16}H_{14}Cl_3N_3O_2$ : C 49.70 ; H 3.65 ; Cl 27.51 ; N 10.87 ; O 8.28. Found: C 49.71 ; H 3.66 ; Cl 27.52 ; N 10.88 ; O 8.29.

***(2E)-N-(3-chloro-4-methoxyphenyl)-2-[1-(4-hydroxy phenyl)ethylidene]hydrazinecarbox-amide*****(3k)** Yield 63%; m.p. 178 _C, IR (KBr) $cm^{-1}$: 3381(N-H), 1681(C=O), 1553(C=N); (DMSO-d6) δ ppm : 3.86 (s, 3H, $OCH_3$), 6.87–7.87(m, 7H, aromatic), 7.68(s, 1H, N=CH), 9.05(s, 1H, Ar–NH), 10.66(s, 1H, CONH) ; MS: m/z, M+ 333.76; Anal. Calcd for $C_{16}H_{16}ClN_3O_3$ : C 57.58 ; H 4.83 ; Cl 10.62 ; N 12.59 ; O 14.38. Found: C 57.59 ; H 3.27 ; Cl 28.57 ; N 11.28 ; O 8.61.

***(2E)-N-(3-chloro-4-methoxyphenyl)-2-[1-(4-methoxyphenyl)ethylidene]hydrazinecarbox-amide*(3l)** Yield 72%; m.p.132 _C, IR (KBr) $cm^{-1}$: 3378 (N-H), 1691 (C=O), 1533 (N=C); (DMSO-d6); δ ppm : 3.85 (s, 3H, $OCH_3$), 6.86–7.86(m, 7H, aromatic), 7.69(s, 1H, N=CH), 9.05(s, 1H, Ar–NH), 10.67(s, 1H, CONH) ; MS: m/z, (M+) 347.796 ; Anal. Calcd for $C_{17}H_{18}ClN_3O_3$ : C 57.58 ; H 4.83 ; Cl 10.62 ; N 12.59 ; O 14.38. Found: C 58.71 ; H 5.22 ; Cl 10.19 ; N 12.08 ; O 13.80.

***(2E)-N-(3-chloro-4-methoxyphenyl)-2-[1-(4-chloro phenyl)ethylidene]hydrazinecarbox-amide*(3m)** Yield 68%; m.p.265 _C, IR (KBr) $cm^{-1}$: 3374 (N-H), 1674 (C=O), 1546(C=N); (DMSO-d6) δ ppm : 3.86 (s, 3H, $OCH_3$), 6.87–7.87(m, 7H, aromatic), 7.70(s, 1H, N=CH), 9.06(s, 1H, Ar–NH), 10.68(s, 1H, CONH); MS: m/z, M+ 352.21; Anal. Calcd for $C_{16}H_{15}Cl2N_3O_2$.: C 54.56 ; H 4.29 ; Cl 20.13 ; N 11.93 ; O 9.09.Found: C 54.57 ; H 4.30 ; Cl 20.14 ; N 11.94 ; O 9.10.

***(2E)-N-(3-chloro-4-methoxyphenyl)-2-[1-(4-nitrophenyl)ethylidene]hydrazinecarboxamide*(3n)**Yield 68%; m.p. 182 _C, IR (KBr) $cm^{-1}$: 3365 (N-H), 1684 (C=O), 1555 (C=N); (DMSO-d6) δ ppm : 3.87 (s, 3H, $OCH_3$), 6.88–7.88(m, 7H, aromatic), 7.71(s, 1H, N=CH), 9.07(s, 1H, Ar–NH), 10.69(s, 1H, CONH); MS: m/z, M+ 362.77; Anal. Calcd for $C_{16}H_{15}ClN_4O_4$ : C 52.97 ; H 4.17; Cl 9.77 N 15.44 O 17.64 Found: C 57.96 ; H 4.16 ; Cl 9.78 ; N 15.43 ; O 17.65.

***(2E)-N-(3-chloro-4-methoxyphenyl)-2-[1-(4-methyl phenyl)ethylidene]hydrazinecarboxamide* (3o)**Yield 70%; m.p. 174 _C, IR (KBr) $cm^{-1}$: 3374 (N-H), 1680 (C=O), 1584 (C=N); (DMSO-d6) δ ppm : 3.87 (s, 3H, $OCH_3$), 6.88–7.88(m, 7H, aromatic), 7.71(s, 1H, N=CH), 9.07(s, 1H, Ar–NH), 10.69(s, 1H, CONH); MS: m/z, M+ 331.79; Anal. Calcd for $C_{17}H_{18}ClN_3O_2$ : C 61.54 ; H 5.47 ; Cl ; 10.69 N ; 12.66 ; O 9.64 Found: C 61.55 H ; 5.48 ; Cl 10.71; N 12.67 ; O 9.65.

***(2E)-2-(4-chlorobenzylidene)-N-(2-methoxyphenyl) hydrazinecarboxamide* (3p)**

Yield 70%; m.p. 178 _C, IR (KBr) $cm^{-1}$: 3382 (N-H), 1690 (C=O), 1550(C=N); (DMSO-d6) δ ppm : 3.88 (s, 3H, $OCH_3$), 6.89–7.89(m, 8H, aromatic), 7.72(s, 1H, N=CH), 9.08(s, 1H, Ar–NH), 10.70(s, 1H, CONH); MS: m/z, (M+) 303.74; Anal. Calcd for $C_{15}H_{14}ClN_3O_2$ : C 59.31 ; H 4.65 ; Cl 11.67 ; N 13.83 ; O 10.53 Found: C 59.28 ; H 4.66 ; Cl 11.68 ; N 13.84 ; O 10.54.

***(2E)-N-(2-methoxyphenyl)-2-(4-nitrobenzylidene) hydrazinecarboxamide* (3q)**

Yield 69%; m.p. 157 _C, IR (KBr) $cm^{-1}$: 3388 (N-H), 1695 (C=O), 1560(C=N); (DMSO-d6) δ ppm : 3.89 (s, 3H, $OCH_3$), 6.90–7.91(m, 8H, aromatic), 7.73(s, 1H, N=CH), 9.09(s, 1H, Ar–NH), 10.71(s, 1H, CONH); MS: m/z, (M+) 314.29 ; Anal. Calcd for $C_{15}H_{14}ClN_4O_4$ : C 57.32 ; H 4.49 ; N 17.83 ; O 20.36 Found: C 57.33 ; H 4.49 ; N 17.84 ; O 20.37.

***(2E)-2-(2,4-dichlorobenzylidene)-N-(2-methoxy phenyl)hydrazinecarboxamide*(3r)**

Yield 67%; m.p. 181 _C, IR (KBr) $cm^{-1}$: 3388 (N-H), 1695 (C=O), 1555(C=N); (DMSO-d6) δ ppm : 3.87 (s, 3H, $OCH_3$), 6.91–7.91(m, 7H, aromatic), 7.72(s, 1H, N=CH), 9.08(s, 1H, Ar–NH), 10.70(s, 1H, CONH); MS: m/z, (M+) 338.18; Anal. Calcd for $C_{15}H_{13}Cl_2N_3O_2$ : C 53.27 ; H 3.87 ; Cl 20.97 ; N 12.43 ; O 9.46 Found: C 53.28 ; H 3.88 ; Cl 20.98 ; N 12.44 ; O 9.47.

***(2E)-2-(2-chlorobenzylidene)-N-(2methoxyphenyl) hydrazinecarboxamide* (3s)**

Yield 68%; m.p. 142 _C, IR (KBr) $cm^{-1}$: 3398 (N-H), 1705 (C=O), 1564(C=N); (DMSO-d6) δ ppm : 3.91 (s, 3H, $OCH_3$), 6.90–7.91(m, 8H, aromatic), 7.75(s, 1H, N=CH), 9.11(s, 1H, Ar–NH), 10.73(s1H,CONH); MS: m/z, (M+) 303.74; Anal. Calcd for $C_{15}H_{14}ClN_3O_2$ C : 59.31 H ; 4.65 ; Cl 11.67 ; N 13.83 ; O 10.53 Found: C 59.32 ; H 4.66 ; Cl 11.68 ; N 13.84 ; O 10.54.

## Results and discussion

### Chemistry

The titled compounds (**3a-s**) were synthesised by following the synthetic protocols as mentioned in Scheme 1. 3-chloro-4-methoxy aniline was reacted with sodium cyanate to get 1-(3-chloro-4-methoxyphenyl)urea (**1**) and then it was refluxed with hydrazine hydrate to get semicarabazide (**2**). Reaction of compound **2** with different aldehydes and ketones resulted in the formation of semicarbazone derivatives. The yields of the titled compounds were ranging from 64% to 75% after recrystallization with absolute ethanol. The purity of the compounds was checked by TLC using eluants benzene: aceton (7:3) and elemental analyses. Both the analytical and spectral data (IR, 1H NMR) of all the synthesized compounds were in full agreement with the proposed structures. In general, infra red spectra (IR) revealed N-H, C=O, and C=N at 3365–3408, 1674–1710, and 1541–1546 $cm^{-1}$, respectively. The 1H NMR spectra showed a singlet at δ 3.79–3.91 ppm corresponding to $OCH_3$ group; multiplet at δ 6.82–7.91 ppm corresponding to aromatic protons; singlet at δ 8.99–9.11 ppm corresponding to Ar–NH; singlet at δ 7.59– 7.75 ppm corresponding to N=CH; singlet at δ 10.59–10.73 ppm corresponding to CONH. The elemental analysis results were within ±0.4% of the theoretical values.

**Table 1: Compounds and their characteristics**

| S.No. | Comp. No. | R | $R^1$ | $R^2$ | M.P.(°C) | Yield% | $R_f$ | Log p | Mol. Wt. |
|---|---|---|---|---|---|---|---|---|---|
| **1.** | 3a. | 3-Chloro-4-methoxy- | H | 2-Chlorophenyl- | 175 | 73 | 0.79 | 4.91 | 338.189 |
| **2.** | 3b. | 3-Chloro-4-methoxy- | H | 4-Chlorophenyl- | 188 | 73 | 0.74 | 4.97 | 338.189 |
| **3.** | 3c. | 3-Chloro-4-methoxy- | H | 2-nitrophenyl- | 216 | 73 | 0.73 | 4.32 | 348.742 |
| **4.** | 3d. | 3-Chloro-4-methoxy- | H | 4-nitrophenyl- | 196 | 65 | 0.70 | 4.14 | 348.74 |
| **5.** | 3e. | 3-Chloro-4-methoxy- | H | 2-Hydroxyphenyl- | 170 | 55 | 0.71 | 4.19 | 319.743 |
| **6.** | 3f. | 3-Chloro-4-methoxy- | H | 4-Hydroxyphenyl- | 200 | 64 | 0.76 | 3.97 | 319.743 |
| **7.** | 3g. | 3-Chloro-4-methoxy- | H | 4-Methoxyphenyl- | 145 | 68 | 0.69 | 4.34 | 333.770 |
| **8.** | 3h. | 3-Chloro-4-methoxy- | H | 3,4-dimethoxyphenyl- | 188 | 66 | 0.68 | 4.34 | 363.780 |
| **9.** | 3i. | 3-Chloro-4-methoxy- | H | 4-N,N-Dimethylaminophenyl- | 178 | 65 | 0.75 | 4.39 | 346.811 |
| **10.** | 3j. | 3-Chloro-4-methoxy- | $CH_3$ | 2,4-Dichlorophenyl- | 145 | 64 | 0.56 | 4.68 | 386.660 |
| **11.** | 3k. | 3-Chloro-4-methoxy- | $CH_3$ | 4-hydroxyphenyl | 178 | 63 | 0.77 | 3.37 | 333.770 |
| **12.** | 3l. | 3-Chloro-4-methoxy- | $CH_3$ | 4-Methoxyphenyl- | 133 | 70 | 0.69 | 3.90 | 347.796 |
| **13.** | 3m. | 3-Chloro-4-methoxy- | $CH_3$ | 4-Chlorophenyl- | 265 | 67 | 0.78 | 4.50 | 352.215 |
| **14.** | 3n. | 3-Chloro-4-methoxy- | $CH_3$ | 4-Nitrophenyl | 182 | 67 | 0.67 | 3.69 | 362.768 |
| **15.** | 3o. | 3-Chloro-4-methoxy- | $CH_3$ | 4-Methylphenyl | 173 | 70 | 0.68 | 4.19 | 331.796 |
| **16.** | 3p. | 2-methoxy- | H | 4-Chlorophenyl | 178 | 69 | 0.60 | 4.18 | 303.743 |
| **17.** | 3q. | 2-methoxy- | H | 4-Nitrophenyl | 158 | 69 | 0.61 | 3.35 | 314.296 |
| **18.** | 3r. | 2-methoxy- | H | 2,4-Dichlorophenyl- | 182 | 66 | 0.73 | 4.88 | 338.188 |
| **19.** | 3s. | 2-methoxy- | H | 2-Chlorophenyl | 140 | 69 | 0.57 | 4.12 | 303.743 |

**Antimicrobial activity:** Synthesized compounds were screened for Antimicrobial activities by MIC ( Minimum Inhibitory Concentration ) method as follows :

**Biological Activity**: **Procedure**

**Preparation of inoculum**: Three Gram positive (*S.aureus, S.pneumonia* and *Bacillus subtilis*), three Gram negative (*E.coli, Klebsiella* and *Shigella*) and two fungal cultures were taken for the study. The microbial cultures were periodically subcultured in mueller hinton broth in case of bacterial cultures and in sabouraud dextrose broth in case of fungal cultures. For the study the cultures were grown overnight in the respective medium.

**Preparation of test sample:** Different concentrations of the test samples were dissolved in dimethyl sulphoxide. Various concentrations of the test solutions were made in DMSO, like 1000 µg/ml, 750 µg/ml, 500 µg/ml, 250 µg/ml and 100 µg/ml. Standard was also dissolved in DMSO prior to use.All the glassware used for the experiments were sterilized by placing in a hot air oven at 160 °C for 2 hours and used after reaching the room temperature.

**Experimental**: For each set of experiments six test tubes were sterilized and labelled appropriately. To each set of appropriately labelled test tubes 2 ml of sterile Mueller hinton broth was added. To this 1 ml of the sample dilution was added and was inoculated with the test microorganism. One tube was set as a control with 2 ml of medium, 1 ml of standard solution (Ciprofloxacin for anti bacterial studies and ketoconazole for anti fungal studies) and the inoculums. All the process was carried out in an aseptic manner in an aseptic chamber. The test tubes were then incubated at 37 °C for 18 to 24 hours in case for anti bacterial studies.

**Table 2: Organism and their concentration**

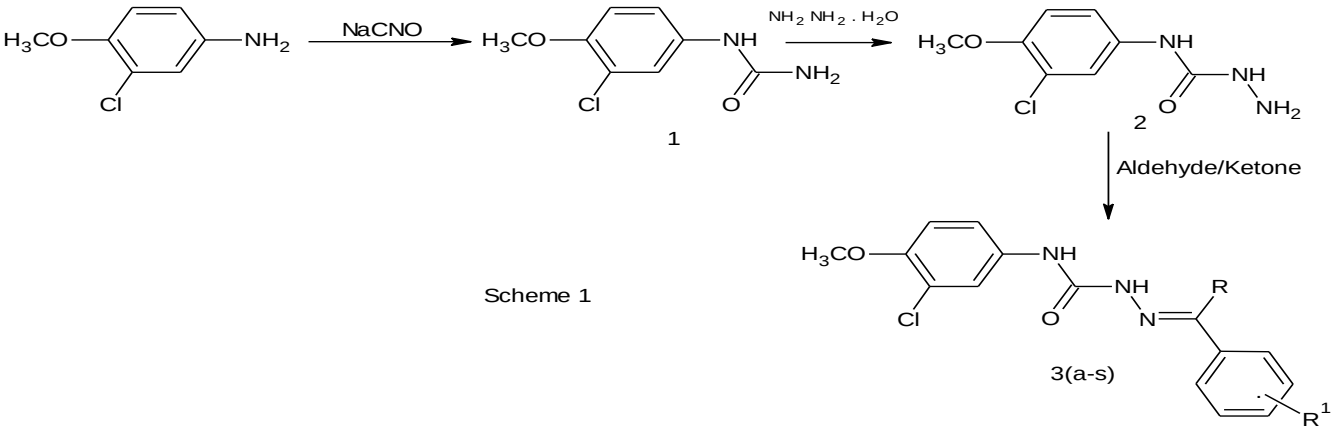
| PR4,PR13,PR16,PR17,PR18 | | Concentration | | | | | | |
|---|---|---|---|---|---|---|---|---|
| **S.no.** | Organism | 1000 mcg | 750 mcg | 500 mcg | 250 mcg | 100 mcg | NB | STANDARD |
| **1** | ***BacillusSubtilis*** | - | - | - | + | + | + | - |
| **2** | ***E.Coli*** | - | - | - | + | + | + | - |
| **3** | ***Klebsiella*** | - | - | - | + | + | + | - |
| **4** | ***S. aureus*** | - | - | - | + | + | + | - |
| **5** | ***S. pneumonia*** | - | - | - | + | + | + | - |
| **6** | ***Shigella*** | - | - | - | + | + | + | - |

After the incubation period is over, the test tubes are checked for growth of micro organisms. The presence of turbidity indicates the growth or in other words the inability of the test compound to show any inhibitory effect against the test micro organisms. If there is no turbidity, that indicated the inhibitory effect of the test compound against the tested microbes.

- 52 derivatives were selected for synthesis after a thorough study of literature on Semicarbazones and 19 compounds (PR1-PR19) were finalised for the research from CADD studies .
- All the 19 compounds were analysed physically and spectrally for chemical and structural evaluation.
- A series (PR1 – PR19) of semicarbazone derivatives were subjected for the prediction of molecular properties before antimicrobial screening.
- The compound PR1, PR3, PR5, PR6, PR7, PR8, PR9, PR10, PR11, PR12, PR15 and PR 19 does not have any inhibitory effect on the tested micro organisms. All the three Gram positive and Gram negative organisms tested were not inhibited in the tested concentration of the test compound.
- The standard ciprofloxacin has completely inhibited the growth of the test organism in all instances.
- Synthesized Compound PR2 and PR14 have Minimum inhibitory Concentration (MIC) at 750µg/l.
- Synthesized Compound PR4 , PR13, PR16, PR17 and PR18 has Minimum inhibitory Concentration(MIC) at 500µg/l.

**Conclusion**

A series (3a-s)of semicarbazone derivatives were subjected for the prediction of molecular properties before antimicrobial screening. All the 16 compounds followed the Lipinski ‘‘Rule of Five’’. The syntheses of semicarbazone derivatives were governed by treating aniline with sodium cyanate to obtain phenyl urea (2) which was then refluxed with hydrazine hydrate in ethanol to obtain 3-chloro-4-fluorophenyl semicarbazides (3) followed by condensation with appropriate aldehydes or ketones in the presence of ethanol and sodium acetate furnished the titled compounds (3a–s).




Scheme 1

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