Introduction

Heterocyclic compounds are widely distributed in nature and are essential to life in various ways, particularly these compounds are important because of the wide variety of physiological activities associated with this class of substances. Heterocyclic rings are present in several compounds. Most of the members of vitamins B-complex, antibiotics, chlorophyll, haemin, amino acid, enzymes, plant pigments, dye stuff, genetic material DNA etc.

The glorious importance of heterocycles in natural product chemistry and pharmacology constantly drive the search for new methods for the construction of heterocyclic molecules containingazole unit such as pyrazoles and isoxazoles. These pyrazole and isoxazoles were prepared from chalcones which are important intermediate products and they also possess biological and pharmacological applications (Dhar, 1981). The substituted azole unit is an essential pharmacophore of number of antifungal (Chevreuil et al., 2007), antibacterial (Solanki and wadodkar, 2003) and various biological activities (Gautam, 2013; Patel, 2017; Dongre, 2017; Ali, 2011). Therefore considering the antifungal and antibacterial potential of azole derivatives (Sharma and Sharma, 2010), we would like to report herein the synthesis of chloro-substituted isoxazolines derivatives which are found to be potential antibacterial agents.

Objectives: The chemistry of chalcones has generated intensive scientific studies throughout the world. Especially interest has been focused on the synthesis and biodynamic activities of isoxazoline derivatives. In recent year numerous isoxazoline derivatives have been synthesized for their anticancer, anti-inflammatory, cytotoxic, antiviral activities. The reaction of substituted chalcones with hydroxylamine hydrochloride in presence of acetic acid gave isoxazoline derivatives.

Material and methods: The five membered oxygen and Nitrogen containing compounds exhibited antioxidant, analgesic, antibacterial, antifungal activities. Therefore the attempt have been made to synthesize chloro-substituted isoxazolines by the reaction of different substituted chalcones with hydroxylamine hydrochloride in presence of few drops of acetic acid. All the synthesized compounds confirmed by TLC and spectral analysis and also screened for their antibacterial activity.

Results: The novel chloro-substituted isoxazolines showed good to moderate antibacterial activity against Gram+ve and Gram –ve bacterial strains tested.

Conclusion: These compounds containing chloro, bromo, iodo groups were found showed potent antibacterial, antifungal activities. These findings promoted us to to synthesize novel chloro-substituted isoxazolines derivatives which are found to be potential antibacterial agents.

Keywords: Chalcones, hydroxylamine hydrochloride, isoxazolines, antibacterial activity

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General procedure for synthesis of Isoxazolines

A mixture of substituted chalcones (0.01 mol) and hydroxyamine hydrochloride (0.02 mol) in 20 ml ethanol was refluxed for 5-6 hr in presence of 2-3 drops of acetic acid. After completion of the reaction the reaction mixture was cooled and poured into ice cold water. The resultant solid product (5a-5f) was filtered, washed with sufficient cold water, dried and purified by recrystallization from ethanol.

Results and discussion

All the synthesized compounds (5a-5f) have been characterized by their M.P., Elemental analysis, IR, 1H NMR and mass spectra.

4-chloro-2-(5-(3-ethoxy-4-hydroxyphenyl)-4,5-dihydroisoxazol-3-yl) naphthalene-1-ol (5a):
M.F: C19H18ClNO, M.Wt: 383.82, M.P: 190°C, Elemental analysis (%): C-65.71, H-4.73, N-3.65, Cl-9.24, IR (Cm): 3414(OH), 1498 (C=N), 1382 (C-O), HNMR (300 MHz CDCl3) ppm: 1.32 (t, 3H, CH3), 4.09 (q, 2H, O-CH2), 3.60 (dd, 1H, CH3), 3.85 (dd, 1H, CH3), 5.93 (dd, 1H, CH3), 6.75-8.63 (m, 8H, Ar-H), 13.10 (s, 2H, OH).

4-chloro-2-(5-(5-chloro-2methoxyphenyl) -4,5-dihydroisoxazol-3yl) naphthalene-1-ol (5c):
M.F: C19H15ClNO2, M.Wt: 388, M.P: 191°C, Elemental analysis (%): C-61.87, H-3.89, N-3.61, Cl-18.26, IR (Cm): 3380(OH), 1506 (C=N), 1385 (C-O), HNMR (300 MHz CDCl3) ppm: 3.83 (s, 3H, OCH3), 3.60 (dd, 1H, CH3), 3.84 (dd, 1H, CH3), 5.93 (dd, 1H, CH3), 6.86-8.63 (m, 8H, Ar-H), 12.10 (s, 1H, OH).

Antibacterial activity

All the newly synthesized compounds were screened in vitro antibacterial activity. The antibacterial activity was evaluated against 24 hr culture of different bacterial strains such as E-coli, S. typhi (Gram –ve) and P. aeruginosa, S. aureus (Gram +ve) at a concentration of 50 µg ml-1. The cultures were diluted with 5% of autoclaved saline and the final volume was adjusted to a concentration of approximately 105-106 CFU ml-1. The synthesized compounds were diluted with acetone for the antibacterial biological assay for agar disc diffusion method. The liquid form of test compound was soaked on to a disc (5mm) and then allowed to air dry, such that the disc became completely saturated with the test compound. The saturated...
chemical discs were introduced onto the upper layer of medium evenly loaded with the bacteria and incubated at 37°C for 24 to 48 hrs for better inhibition of bacteria. The zones of inhibition were measured after 24 to 48 hrs. All the experiments were performed in triplicate and the results are expressed as zone of inhibition in mm. The zone of inhibition of the synthesized compounds (5a-f) was compared with zone of inhibition of standard antibiotics Ofloxacin (50 μg mL⁻¹).

From the screening studies (Table 1), it is evident that the synthesized isoxazoline derivatives 5a, 5b, 5c and 5d showed good antibacterial activity against all the tested organisms. It was further observed that the electron rich (5c) with one –OMe and two -Cl substituent, showed best activity near to that of standard drug. This observation leads to conclusion that electron rich isoxazolines showed higher activity against bacterial strain tested.

**Conclusion**

In the present work, we synthesized some novel isoxazoline derivatives from different substituted chalcones and hydroxylamine hydrochloride. The newly synthesized compounds were obtained in good yield and confirmed by spectral analysis. Ofloxacin is used as standard drug for antibacterial activity. The antibacterial data revealed that all compounds showed good to moderate activity compared to standard drug.

**Conflict of interest**

There is no conflict of interest in the present study.

**References**


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**Table 1. Antibacterial activity (zone of inhibition mm) of compounds (5a-5f)**

<table>
<thead>
<tr>
<th>Compounds</th>
<th>Diameter of zone of inhibition (mm)</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>P. aeruginosa</td>
</tr>
<tr>
<td>5a</td>
<td>23</td>
</tr>
<tr>
<td>5b</td>
<td>25</td>
</tr>
<tr>
<td>5c</td>
<td>26</td>
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<td>5d</td>
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<td>5e</td>
<td>19</td>
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<tr>
<td>5f</td>
<td>19</td>
</tr>
<tr>
<td>Standard</td>
<td>27</td>
</tr>
<tr>
<td>DMSO</td>
<td>-</td>
</tr>
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Positive control (Standard ): Ofloxacin; Negetive control: DMSO