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### Synthesis and Investigation of Anti-Bacterial Activity of N-(3-aminophenyl)-N'-(prop-2-en-1-yl) Thiourea Compound

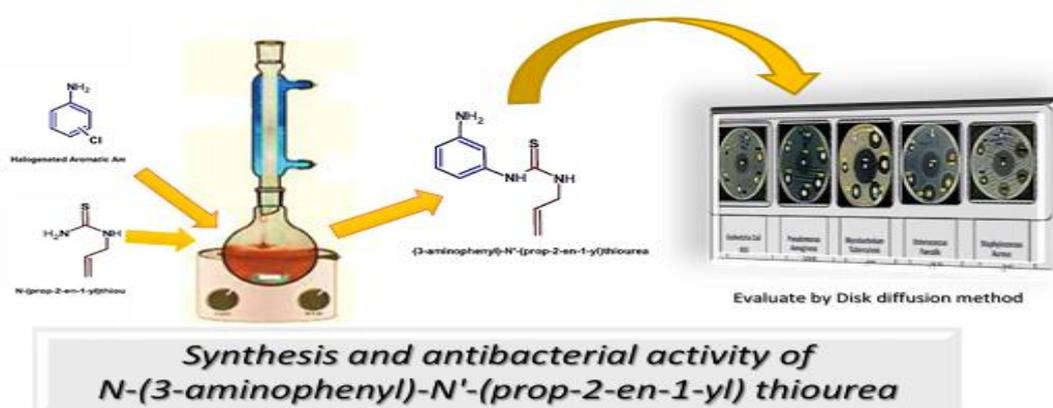
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Peer Review Information	Abstract
<p>Submission: 07 Feb 2023</p> <p>Revision: 20 Feb 2023</p> <p>Acceptance: 11 March 2023</p> <p><b>Keywords</b></p> <p>Antibacterial activity, Disk diffusion method, Thiourea, Aromatic amines</p>	<p>N-(3-aminophenyl)-N'-(prop-2-en-1-yl) thioureas was synthesized from halogenated aromatic amines reflux with N-prop-2-en-1-yl thioureas in isopropanol. Synthesized compound was characterized using FT-IR, NMR, Mass spectra and CHNS-elemental and Chemical analysis. Further, antibacterial activity of compound was examined against gram-positive and gram-negative bacteria strains such as Escherichia Coil, Pseudomonas Aeruginosa, Mycobacterium Tuberculosis, Enterococcus Faecalis, and Staphylococcus Aureusin by using disk diffusion method. Susceptibility of bacterial strains against compound was tested with standard antibiotic ciprofloxacin. Outcome of test displayed good antibacterial activity against Pseudomonas Aeruginosa, Mycobacterium Tuberculosis, Staphylococcus Aureusin than Escherichia Coil and Enterococcus Faecalis bacterial strain.</p>

#### Graphical Abstract:



#### Introduction

Heterocyclic compounds play an important part in organic chemistry and drug discovery because of their broad scope of properties, which distinguishes them from other cyclic molecules. A significant component of the chemical and biological studies are heterocyclic molecules. In

biological structures, heterocyclic molecules play a vital role. Additionally, a wide range of pharmacological potential medicines, including those with antibacterial, anti-cancer, antiviral, anti-inflammatory, antimicrobial, antifungal, and antidiabetic characteristics, incorporate heterocyclic compounds. Synthesis,

identification, and pharmacological research on thiourea derivatives have attracted a great deal of attention during the previous several years. Nencki synthesized thiourea for the first time in 1873, and which is a new family of chemical compounds. This class of compounds has chemical reactivity and biological characteristics due to thiourea linkage (NH-CS-NH) and produces a variety of organometallic complexes and displayed an extensive range of biological activities<sup>1-5</sup>. One well-known class of good ligands for transition metals is thiourea. These ligands' easy synthesis from generally available and inexpensive starting materials is one of their intriguing features. It has been discovered that these stable compounds exhibit unparalleled coordination chemistry and more unpredictable coordination action. The thiourea moieties can be employed as H-bond donors in a variety of receptor designs. Gelatin generation is also made possible by this specific H-bonding ability. Consequently, the anion sensors frequently thiourea binding sites. Parallel-oriented hydrogen bonds (H-bonds) are formed by hydrogen atoms on the N-atoms in the thiourea groups. Thiourea derivatives are widely used in forensic chemistry, agricultural science, and medicinal products<sup>5-9</sup>.

One significant class of medications that have transformed the treatment of viruses and bacteria is antibiotics. Antibiotics are among the most important supplies in the pharmaceutical sector worldwide because of their significant therapeutic effectiveness.

Additionally, the usage of antibiotics has increased in a number of connected industries. However, bacterial diseases' normal biological functions are different and complicated. For scientists to deal with resistant strains of organisms that were formerly susceptible to an older antibiotic, the production of safer and newer antibiotics has become important. This is because the growing use of antibiotics has resulted in microbial resistance<sup>10-13</sup>.

Thioureas are useful molecules having an assortment of biological applications. These are employed in the sectors of agriculture, manufacturing, metallurgical analysis, and medicinal. The primary biological applications of thioureas consist of the treatment of infectious

diseases, antioxidants, antimicrobial substances, anti-inflammatory, anti-thyroid, anti-epileptic, anti-hypertensive, rodenticide, anti-cancer, DNA binder, and urease inhibitors. Thiourea complexes have applications as antibacterial agents and precursors<sup>14-17</sup>. In this research article new molecule of thiourea was synthesized by conventional method and investigation of its biological implication were studied against gram positive and gram negative bacterial strains in vivo.

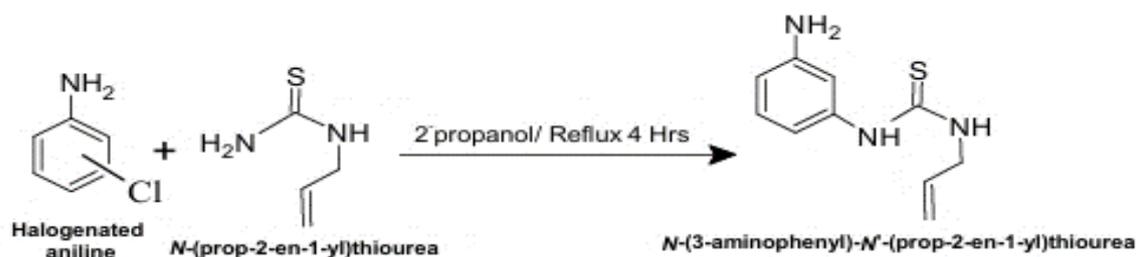
## Methods And Materials

### a) General:

Analytical-grade compounds are used. The melting points are uncorrected and were measured on an open capillary tube. Thin-layer chromatography (TLC) in a hexane:ethyl acetate (10:1) solvent solution was used to monitor the reaction's progress. FTIR Perkin Elmer (400 MHz) Spectrophotometer KBr disc was used to record IR spectra. The Bruker Avance (500 MHz) NMR Spectrometer was used to record <sup>1</sup>H NMR spectra using CDCl<sub>3</sub> solvent and TMS as an internal standard; the Waters Corporation (Alliance II-2795) micro mass spectrometer was used to record LCMS spectra; and the Thermo Scientific (Flash 2000) elemental analyzer was used to perform CHNS analysis.

### b) Synthesis of N-(3-aminophenyl)-N'-(prop-2-en-1-yl)thiourea:

Halogenated aromatic amines reflux with N-prop-2en-1-yl thiourea in presence of alcohol gives the aromatic thiourea compound. The shielding amino group was initially treated with Halogenated aromatic amines (5 mmol) and di-tert-butyl dicarbonate (BOC), followed by reflux with N-prop-2en-1-yl thiourea (5 mmol) in the presence of isopropanol for about 6 hours. Ultimately, deprotection of BOC under acidic conditions (4M HCl in methanol) get N-(3-aminophenyl)-N'-(prop-2-en-1-yl) thiourea, which is then washed with cold water and dried. Ethyl alcohol was used to further recrystallize. Employing single spot TLC in a mobile phase of hexane-ethyl acetate (10:1 volume ratio) to track the reaction's progress and melting point was measured on an open capillary tube.



**c) Spectral analysis:****M.F.** C<sub>10</sub>H<sub>13</sub>N<sub>3</sub>S, M.P. 76-78 °C**I.R. (KBr pellets, v/cm<sup>-1</sup>):** (N-H<sub>stret</sub>) 3282, (Ar-H) 2979, (Ar C=C), 1688, (broad stret.) 1711, (C-N) 1153, (C=S) 623,**<sup>1</sup>H NMR (500MHz, CDCl<sub>3</sub>, δ in ppm):** 6.56 (s, 1H, Ar-H), 7.02 (d, 1H, Ar-H), 7.19 (dt, 1H, Ar-H), 7.28 (d, 1H, Ar-H), 7.53 (s, 1H, N-H)**<sup>13</sup>C NMR (500MHz, CDCl<sub>3</sub>, δ in ppm):** 77.03 (CDCl<sub>3</sub>), 116.40, 118.53, 123.02, 129.90, 134.73, 139.58 (Ar-C), 152.44 (C=S)**CHNS Analysis:** C, H, N, S (%) calc. 57.94, 6.32, 20.27, 15.47, found 58.39, 5.89, 6.18, and 0.051;**Mass:** m/z=207.08, M.W. = 207.23**d) Disk diffusion test:**

The antibacterial activity was checked by using disk diffusion method (Kirby Bauer method). The MHA plates were inoculated by spreading with compound 100 µl of bacterial culture strains *E. coli* (MTCC-452), *P. aeruginosa* (MTCC3541), *M. tuberculosis* (MTCC-300), *E. Faecalis* (MTCC-439), *S.aureus* (MTCC-740) (adjusted to 0.5 McFarl and Unit Approx cell density (1.5 X 10<sup>8</sup> CFU/mL) and followed by placing the discs containing different concentration (0 to 1000 µg/ml). 10 % of the compound was taken and serially diluted to achieve the required amount to be loaded on the disc. One disc in each plate was loaded with solvent (DMSO) alone which served as vehicle control and Ciprofloxacin disc (10µg) were taken as positive control. The plates were incubated at 37 °C for 24 hrs. A clear zone created around the disc were measured and recorded. All tests were performed in triplicates and the average was taken as the final reading.

**Results and Discussion**

N-(3-aminophenyl)-N'-(prop-2-en-1-yl) thioureas was successfully synthesized and FT-IR, NMR, Mass spectra and CHNS-elemental and Chemical analysis confirmed the formation of the compound. FTIR spectra of this thiourea compound showed expected frequencies of ν (N-H<sub>stret</sub>), ν (Ar-H), ν (Ar C=C), ν (broad stret.), ν (C-N), ν (C=S) at 3282, 2979, 1688, 1711, 1153, 623 cm<sup>-1</sup> respectively, <sup>1</sup>H NMR spectra of aromatic protons gave four peaks between 6.56 to 7.28 ppm and <sup>13</sup>C NMR spectra clearly indicate presence of thioureas C=S showed chemical shift at 152.44 ppm. Elemental analysis of C, H, N, S % calculated values 57.94, 6.32, 20.27, 15.47 were exactly matched with observed values 58.39, 5.89, 6.18, and 0.051. The mass spectrum of compound showed molecular ion peak at m/z=207.08 and which was correspond to molar mass of 207.23 C<sub>10</sub>H<sub>13</sub>N<sub>3</sub>S.

Synthesized compound was screened for their antibacterial activity against bacterial strain *E. coli*, *P. aeruginosa*, *M. tuberculosis*, *E. Faecalis* and *S. aureus*. Susceptibility of bacterial strains against compound was tested with standard antibiotic ciprofloxacin. N-(3-aminophenyl)-N'-(prop-2-en-1-yl) thiourea compound solution put on at conc. 0 to 1000 µg/ml on an agar plate shown an antibacterial activity presenting zone of inhibition in the range of 5 to 15.8 mm. It was observed that *P. aeruginosa*, *M. tuberculosis* and *S. aureus* bacterial strain inhibited by tested compound and displayed maximum zone of inhibition 15.8, 13 and 11 mm. This compound also showed lower zone of inhibition 5 and 8.2 mm against bacterial strain *E. coli*, *S. aureus* at the maximum dose of 1000 µg, as compared to the positive control's 23.67 mm inhibition zone at a dose of 10 µg.

**Figure 1: Zone of Inhibition (mm) at 0 to 1000 µg of Compound N-(3-aminophenyl)-N'-(prop-2-en-1-yl) thiourea against standard antibiotic (Ciprofloxacin) 50 µg and different bacterial strain shown on following disc**

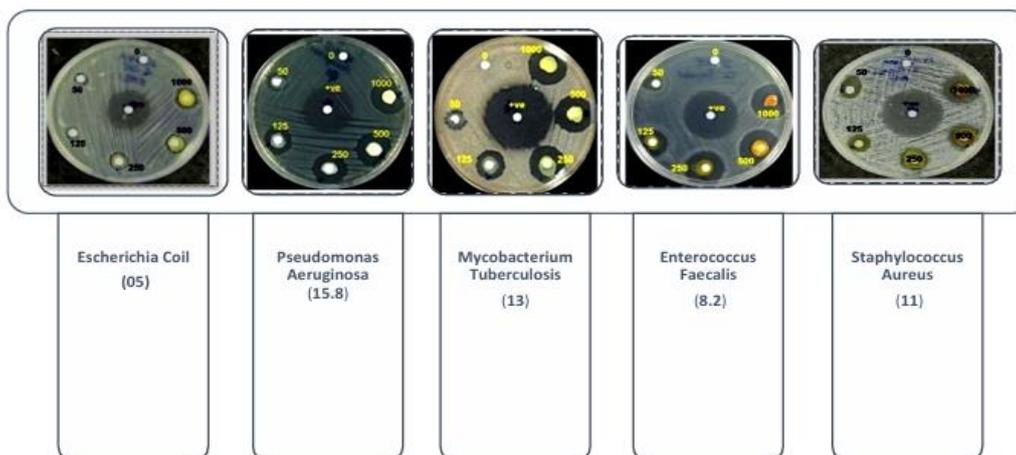
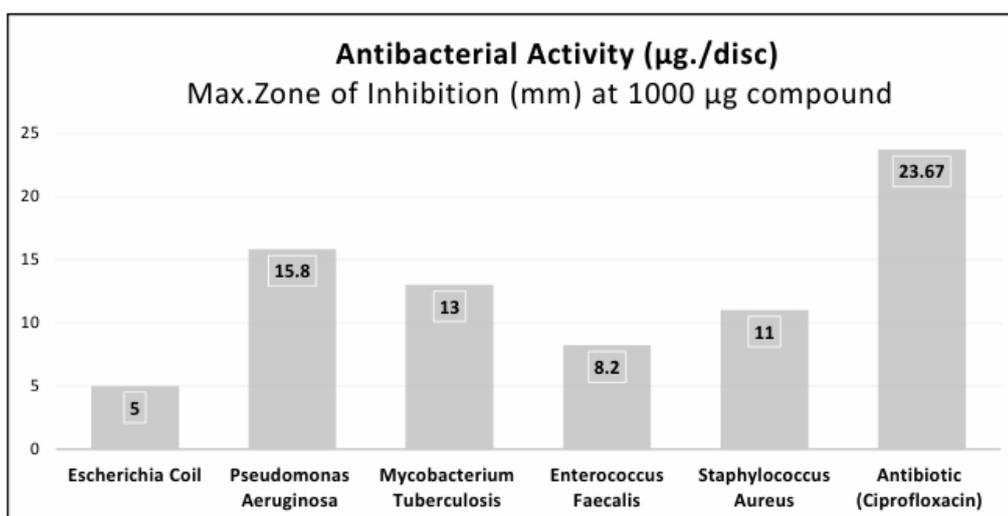


Figure 2: Max. Zone of Inhibition (mm) at 1000 µg compound against different bacterial strains



### Conclusion

In conclusion, N-(3-aminophenyl)-N'-(prop-2-en-1-yl) thioureas was successfully synthesized and confirmed by FT-IR, NMR, Mass spectra and CHNS-elemental and Chemical analysis. The antibacterial activity of thiourea compound was studied against bacteria strains like Escherichia Coil, Pseudomonas Aeruginosa, Mycobacterium Tuberculosis, Enterococcus Faecalis, and Staphylococcus Aureus by using disk diffusion method. Thiourea Compound displayed good antibacterial activity against Pseudomonas Aeruginosa, Mycobacterium Tuberculosis, Staphylococcus Aureus with zone of inhibition 15.8, 13, 11 as compared to Escherichia Coil and Enterococcus Faecalis bacterial strains with zone of inhibition 5, 8.2. This compound has potent antibacterial active due to presence of bioactive thiourea moiety in structure of the molecule.

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**Ethical Approval:** This has not been published elsewhere and is not currently under consideration for publication elsewhere. This study does not involve experiments on animals or human subjects.

**Conflict of interest:** The authors declare that they have no conflict of interest.

**Informed consent:** Written informed consent was obtained from all individual participants included in the study.

**Data and materials availability:** All data associated with this study are present in the paper.

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