



## A Green Synthetic Approach For 1-(5-(2-Substituted Phenyl)Thiazol-2-Yl)-3-(4-Substituted Phenyl)Thiourea And Their Antimicrobial Evaluation

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### Abstract:

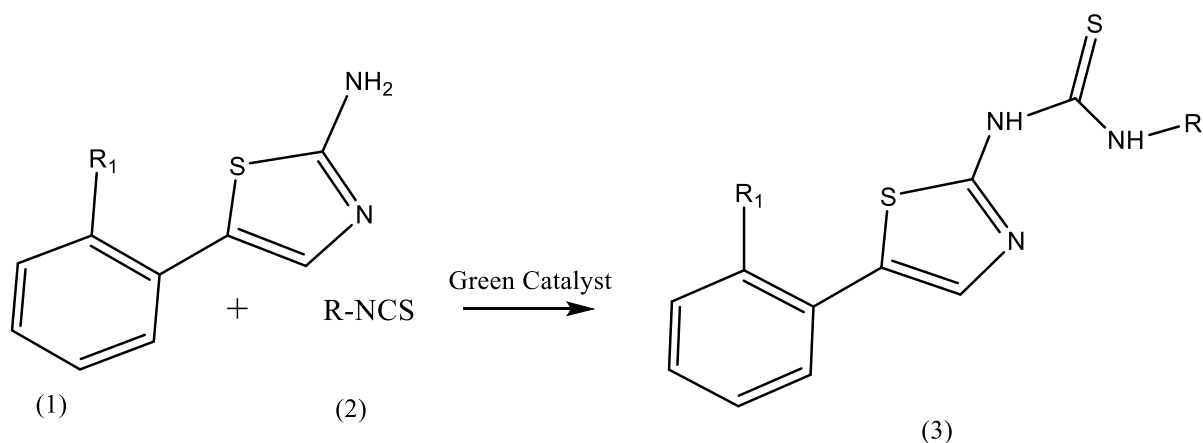
A green synthetic approach for the preparation of 1-(5-(2-Substituted phenyl)thiazol-2-yl)-3-(4-substitutedphenyl)thiourea derivatives by using *Citrullus colocynthis* L. (Sherni) Fruits Juice as eco-friendly and chiefly available green catalyst is presented. Further the antimicrobial activity of several synthesized compounds, was evaluated against selected microbes, including *Staphylococcus aureus*, *Escherichia coli*, *Salmonella Typhi*, and *Pseudomonas aeruginosa*, using the agar well diffusion assay method. The structures of the synthesized compounds were confirmed by elemental analysis, IR, NMR, and Mass spectrometry.

**Keywords:** *Citrullus Colosynthis* L., Sherni, Fruits Juice, Ecofriendly, Antimicrobial.

### Introduction:

Substituted Thioureas, organic compounds containing nitrogen and sulphur, have numerous pharmaceutical and biological applications. Thiourea derivatives are widely used in organic synthesis and have diverse applications in medicine, agriculture, and industry. These compounds typically feature the  $-N=C=S$  group, which has been shown to exhibit toxicity to fungi<sup>1</sup>, insecticidal activity<sup>2-6</sup>, anesthetic properties<sup>7</sup>, and antiviral effects<sup>8</sup>. Additionally, thiocarbamides and their derivatives have significant tuberculostatic activity<sup>9-19</sup> and are utilized in medicinal practices. Despite their usefulness, traditional synthesis methods often involve hazardous catalysts and solvents, which pose risks to both the environment and human health<sup>20-25</sup>. Therefore, there is a need for greener, safer, and more efficient methods for synthesizing thiourea derivatives. In our present research work we were synthesizing the substituted derivative of 1-(5-(2-Substituted

phenyl)thiazol-2-yl)-3-(4-substituted phenyl)thiourea using chief and easily available catalyst such as *Citrullus colocynthis* L.(Sherni) Fruits Juice Scheme-1. ***Citrullus colocynthis* L.** (commonly known as Sherni in India) is a species of plant belonging to the family *Cucurbitaceae*, which is native to the arid and semi-arid regions of Africa and Asia. In India, it is primarily found in dry, desert-like areas such as Rajasthan, Gujarat, Maharashtra and parts of Madhya Pradesh. The fruit is a green, round to oval-shaped melon, which turns yellow when ripe. The fruit has a tough rind and contains numerous seeds.



Where,  
 R=H,o,p,m-tolylgroup,Ph  
 R<sub>1</sub>=Cl, Br, OH

Scheme-1

Green Catalyst=Citrullus colosynthis  
 L.(Sherni) Fruits Juice

### Experimental:

All chemicals used were of analytical grade, purchased from Research Lab Fine Chemical Industry, Mumbai. Melting points were determined using a hot paraffin oil bath. Elemental analysis for carbon, hydrogen, and nitrogen was conducted on a Carlo-Ebra 1106 analyzer. IR spectra were recorded using a Bruker Neo Ltd. spectrometer (4000-400 cm<sup>-1</sup> range). NMR spectra were recorded on a Bruker AC-500F spectrometer with TMS as the internal standard and CDCl<sub>3</sub> as the solvent. Mass spectra were acquired using a Shimadzu 2010S mass spectrometer. The purity of compounds was checked by TLC on silica gel-G plates with a 0.3 mm thickness.

### General Procedure for synthesis:

#### 1.Synthesis of substituted derivatives of 2-amino-4-phenyl thiozole (1)

#### This compound was synthesized by known method

Substituted acetophenone (12 ml), thiourea (15.2 g) and Iodine (25 g) and 60 ml distilled water refluxed for 4hrs. The reaction mixture was cooled and poured on crushed ice to get the solid basify the solid with sodium hydroxide flakes, filter and crystallize from ethanol water (70%)

gave golden coloured fibers of 2-amino-4-phenyl thiazol,m.p. 125<sup>0</sup>c

#### 1-(5-(2-Substituted phenyl)thiazol-2-yl)-3-(4-substituted phenyl)thiourea (3)

Corresponding derivative of 5-(2-substitutedphenyl)thiazol-2-amine (0.01 mole) and particular derivative of isothiocyanate (0.01mole) were taken in RB flask containing 10 ml distilled water medium add 20 ml of *Citrullus colosynthis* L. (Sherni) Fruits Juice as catalyst Refluxed the reaction mixture for 6 hour the white crystalline solid obtained. On cooling the reaction mixture was poured in ice cold water. Filter the products and recrystallised it with ethanol.

#### Synthesis of 1-(5-(2-bromophenyl) thiazol-2-yl)thiourea (3a)

Elemental Analysis: C, 38.22; H, 2.57; Br, 25.43; N, 13.37; S, 20.41 IR (KBr): 3345 cm<sup>-1</sup> (N-H s), 1620 cm<sup>-1</sup> (C=N s), 1302 cm<sup>-1</sup> (C=S s), 765 cm<sup>-1</sup> (C-S s); <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub> + DMSO): 6.90-7.78 ppm (Ar-H), 11.99 ppm (NH), 8.09 ppm (-NH<sub>2</sub>), 6.0 ppm (-CH),

White crystalline solid Chemical Formula: C<sub>10</sub>H<sub>8</sub>BrN<sub>3</sub>S<sub>2</sub>, M. P. 152<sup>0</sup>C-154<sup>0</sup>C.

#### Synthesis of 1-(5-(2-hydroxyphenyl)thiazol-2-yl)thiourea (3b)

Elemental Analysis: C, 47.79; H, 3.61; N, 16.72; O, 6.37; S, 25.51IR (KBr): 3350 cm<sup>-1</sup>

(N-H s), 3580  $\text{cm}^{-1}$  (O-H s), 1580  $\text{cm}^{-1}$  (C=N s), 1310  $\text{cm}^{-1}$  (C=S s), 770  $\text{cm}^{-1}$  (C-S s);  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$  + DMSO): 7.10-7.78 ppm (Ar-H), 12.20 ppm (NH), 10.00 ppm ( $-\text{NH}_2$ ), 10.60 ppm ( $-\text{OH}$ ), 6.20 ppm ( $-\text{CH}$ ), White Crystalline solid, Chemical Formula:  $\text{C}_{10}\text{H}_9\text{N}_3\text{OS}_2$ , M. P. 120 $^\circ\text{C}$ -123 $^\circ\text{C}$ .

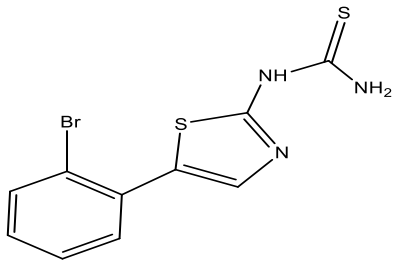
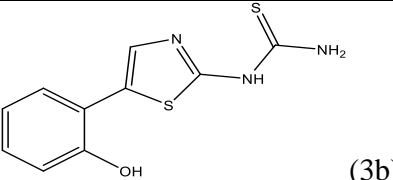
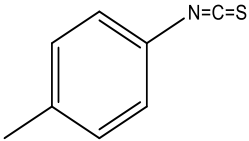
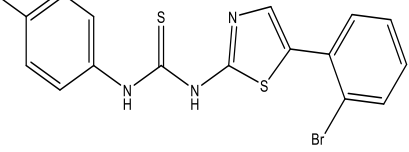
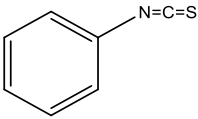
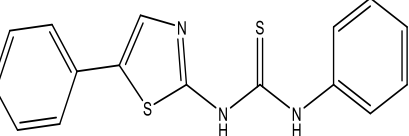
### Synthesis of 1-(5-(2-bromophenyl)thiazol-2-yl)-3-(p-tolyl)thiourea (3c)

Elemental Analysis: C, 50.50; H, 3.49; Br, 19.76; N, 10.39; S, 15.86 IR (KBr): 3401  $\text{cm}^{-1}$  (N-H s), 1598  $\text{cm}^{-1}$  (C=N s), 1330  $\text{cm}^{-1}$  (C=S s), 773  $\text{cm}^{-1}$  (C-S s);  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$  + DMSO): 7.10-7.78 ppm (Ar-H), 12.09 ppm (NH), 11.02 ppm ( $-\text{NH}_2$ ), 6.10 ppm ( $-\text{CH}$ ), 2.40 ppm ( $-\text{CH}_3$ ), Yellow Crystalline solid Chemical Formula:  $\text{C}_{17}\text{H}_{14}\text{BrN}_3\text{S}_2$ , M. P. 162 $^\circ\text{C}$ -165 $^\circ\text{C}$ .

### Results and Discussion:

substituted thioureas, due to their broad range of applications across various fields, have garnered significant attention from researchers and scientists for their synthesis in sophisticated ways. Several methods for their synthesis have been reported in the literature. The use of green green catalyst in synthesis has gained considerable interest due to their environmental benefits. In this context, *Citrullus colosynthis* L. (Sherni) Fruits Juice as catalyst is highly efficient for the synthesis of 1-(5-(2-substitutedphenyl)thiazol-2-yl)thiourea (3), yielding good results. Similar derivatives were also synthesized using the same procedure.

**Table: 1.1 Synthesis of Different 1-(5-(2-Substituted phenyl)thiazol-2-yl)-3-(4-substituted phenyl) thiourea**

Entry	Thiocyanate	Product	Yield in %	M.P. in $^\circ\text{C}$
1	$\text{NH}_4\text{N}=\text{C}=\text{S}$	(3a) 	80	152-154
2	$\text{NH}_4\text{N}=\text{C}=\text{S}$	(3b) 	85	120-123
3		(3c) 	80	162-165
4		(3d) 	70	150

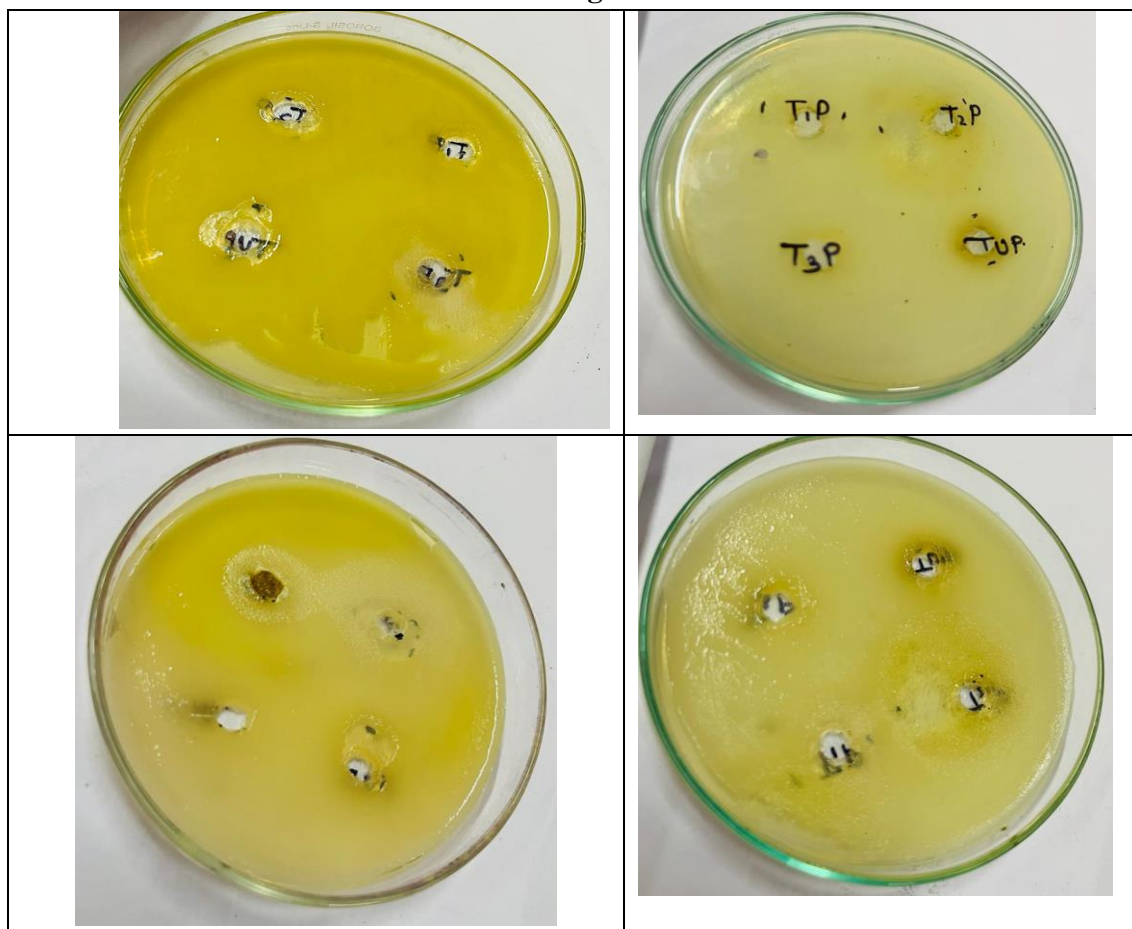
5		(3e) 	80	140
6		(3f) 	80	155
7		(3g) 	85	138
8		(3h) 	85	182
9		(3i) 	75	130
10		(3j) 	75	160

### Antimicrobial Study:

The synthesized some 1-(5-(2-Substituted phenyl)thiazol-2-yl)-3-(4-substituted phenyl)thiourea compounds mentioned above were tested in vitro for their

bactericidal activity against four species of Gram-positive bacteria and Gram-negative bacteria including *Staphylococcus aureus*, *Escherichia coli*, *Salmonella Typhi*, and *Pseudomonas aeruginosa*, using the agar well diffusion assay method.

Table 1.2: Showing the Zone of Inhibition

**Conclusion:**

This study presents a new alternative approach for synthesizing the title compound, eliminating the use of hazardous catalysts and solvents. The research introduces an eco-friendly easily available and low cost catalyst and successfully synthesizes the compound. All the synthesized compounds show moderate to high antimicrobial activity.

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