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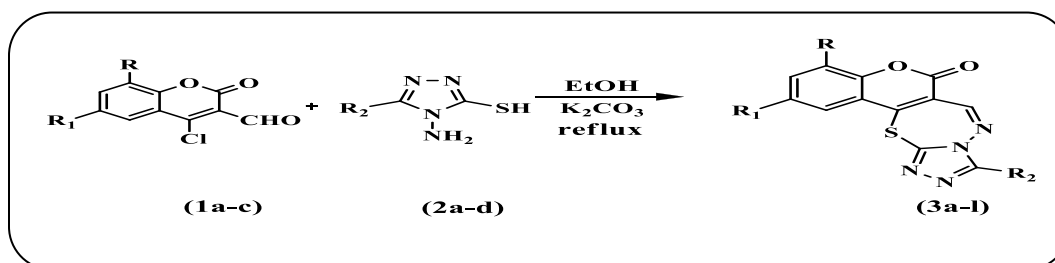
### A NOVEL ONE POT FACILE SYNTHESIS OF 1,2,4- TRIAZOLO- 1,3,4- THIADIAZEPINO FUSED COUMARINS AND THEIR ANTIMICROBIAL AND ANTITUBERCULOSIS ACTIVITY STUDIES

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**Abstract:** A novel series of [1,2,4]triazolo[3',4':2,3][1,3,4]thiadiazepino[7,6-b]coumarins (**3a-l**) was synthesized by the reaction of appropriate 4-chloro 3-formyl coumarins (**1a-c**) with various 4-amino-5-substituted-3-mercapto-1,2,4-triazoles (**2a-d**) in ethanol in the presence of a catalytic amount of  $K_2CO_3$  under refluxing conditions. The structure of the synthesized compounds were established by elemental analysis and spectral data like IR,  $^1H$ -NMR,  $^{13}C$ -APT and mass analysis. The synthesized compounds were screened for their antimicrobial and antituberculosis activity. Among all the synthesized compounds, the compounds **3a**, **3e**, **3j** and **3k** were found to be more active against tested pathogens.



**Keywords:** 3- mercapto-1,2,4- triazole , 1,3,4-thiadiazepines, Coumarins, antituberculosis and antifungal activity



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## INTRODUCTION

1,2,4-Triazoles, a five member heterocyclic compounds with three nitrogen atom in the ring are best known class of triazoles and these compounds have drawn a special attention due to their promising biological activities such as antimicrobial [1], anti-inflammatory[2], antiviral [3], analgesic [4] and anticancer[5]. In addition to these important biological applications, 4-amino-1,2,4-triazole-3-thiols are also of greater utility in the preparation of organic compounds by heterocyclization. The amino and mercapto groups are ready-made nucleophilic centers for the synthesis of condensed heterocyclic rings such as triazolothiadiazoles, triazolothiadiazines, triazolotetrazines and triazolothiadiazepines.[6-7]

From the literature survey, it is revealed that 1, 3, 4-thiadiazepines are better therapeutic agents due to the presence of the -N=C-S group. Various groups of researcher have reported their outstanding biological activities such as, antiviral[8], antimicrobial [9], antitumor [10], antidepressant [11], anticonvulsant [12], anti HIV [13], antiinflammatory [14] and antifungal [15]. These compounds are not only known for their potent biological activity but they are also known for their excellent charge generating property [16].

During past few decades, considerable reports are documented in literature for the efficiency of triazolo thiadiazepines as good therapeutic agents. They are found to possess good to excellent in vitro antibacterial [17], antifungal [18] and antitubercular activity [19]. Based on these compounds many potential drugs have been documented, particularly in cancer and virus research.[20-21]

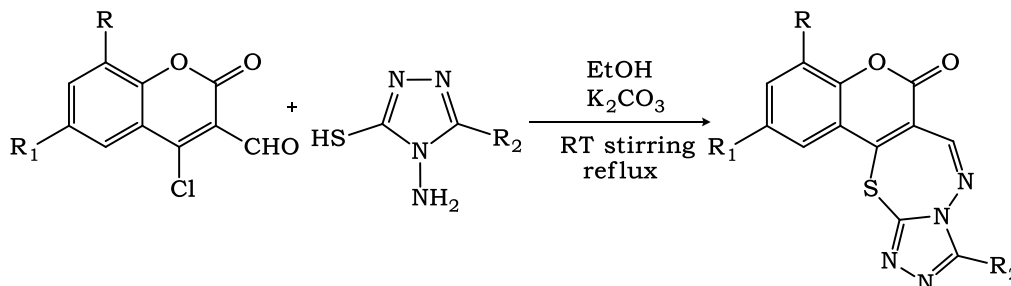
During our literature survey on the further fusion of triazolo thiadiazepines with other heterocycle we noticed that researcher have reported various furano fused triazolo thiadiazepines[22] benzopyrano fused triazolo thiadiazepines[23], quinolino fused triazolo thiadiazepines[24], hydrazono triazolo thiadiazepines [25], pyrazolo fused triazolo thiadiazepines [26]. All these heterocyclic fused compounds are also reported to have excellent biological activities. The survey also revealed that so far no chemists have made efforts to synthesize triazolo thiadiazepino fused coumarins and therefore in the present work it was thought worthwhile to synthesize triazolo thiadiazepino fused coumarins via simple condensation reaction and therefore herein we report synthesis of various [1,2,4]triazolo-[3',4':2,3][1,3,4]-thiadiazepino[7,6-b]coumarins.

## 2. RESULTS AND DISCUSSION:

### 2.1. CHEMISTRY:

In the present work, various[1,2,4]triazolo-[3',4':2,3][1,3,4]-thiadiazepino[7,6-b]coumarins (**3a-l**) have been synthesized by reacting various 4-chloro-3-formyl coumarins (**1a-c**) with

appropriate 4-amino 5-substituted-3-mercapto -1,2,4-triazoles (**2a-d**) in ethanol in the presence of catalytical amount of  $K_2CO_3$  under reflux condition (**Scheme.1**). 4-Chloro-3-formyl coumarins (**1a-c**) and 4-amino-5-substituted-3-mercapto-1,2,4-triazole (**2a-d**) were prepared by reported methods [27-31].



Scheme.1

Comp No.	R	R <sub>1</sub>	R <sub>2</sub>	Comp No.	R	R <sub>1</sub>	R <sub>2</sub>
<b>3a</b>	H	H	CH <sub>3</sub>	<b>3g</b>	H	H	4-Pyridyl
<b>3b</b>	H	CH <sub>3</sub>	CH <sub>3</sub>	<b>3h</b>	H	CH <sub>3</sub>	4-Pyridyl
<b>3c</b>	H	Cl	CH <sub>3</sub>	<b>3i</b>	H	Cl	4-Pyridyl
<b>3d</b>	H	H	Phenyl	<b>3j</b>	H	H	2-Thiophenyl
<b>3e</b>	H	CH <sub>3</sub>	Phenyl	<b>3k</b>	H	CH <sub>3</sub>	2-Thiophenyl
<b>3f</b>	H	Cl	Phenyl	<b>3l</b>	H	Cl	2-Thiophenyl

## 2.2 BIOLOGICAL RESULTS:

### 2.2.1 ANTIMICROBIAL ACTIVITY:

The newly synthesized target compounds (**3a-l**) were evaluated for their *in vitro* antibacterial activity against two Gram positive bacteria *Staphylococcus aureus* (MTCC 96) and *Bacillus subtilis* (MTCC 441) and two Gram negative bacteria *Escherichia coli* (MTCC 443) and *Salmonella typhi* (MTCC 98). They were also evaluated for their *in vitro* antifungal activity against *Candida albicans* (MTCC 227) and *Aspergillus niger* (MTCC 282) as fungal strains. Broth dilution method was used for the determination of the antibacterial and antifungal activity as recommended by NCCLS [32]. Ampicillin, Chloramphenicol and Norfloxacin were used as standard antibacterial drugs, whereas Griseofulvin and Nystatin were used as standard antifungal drugs. The synthesized compounds (**3a-l**) were screened for their antibacterial and antifungal activity at the concentration of 1000, 500 and 250  $\mu\text{g}/\text{mL}$  for the primary screening. The synthesized

compounds showing activity against microbes in the primary screening were further screened in a second set of dilution at concentrations of 200, 100, 62.5, 50 and 25  $\mu\text{g}/\text{mL}$ . The suspension of 10  $\mu\text{L}$  from each well were further incubated and growth was noted at 37°C after 24 hour for bacteria and 48 hour for fungi. The lowest concentration which showed no visible growth (turbidity) after spot subculture was considered as the minimum inhibitory concentration (MIC) for each compound.

The investigation of the data summarized in (Table-1) reveals that many compounds were found to be active against Gram-positive bacteria while some of the compounds were found to be active against Gram-negative bacterial and fungal species as compared to that of the standard antimicrobial drugs.

### 2.2.2. ANTIMICROBIAL EVALUTION:

The compounds (3a-l) were screened for their *in vitro* antibacterial and antifungal evaluation against various bacterial and fungal pathogens by broth dilution method. Ampicillin, Chloramphenicol, Norfloxacin, Griseofulvin and Nystatin were used as standard drugs. The values of MIC are summarized in Table-1.

Table-1: *In vitro* Antimicrobial activity of compounds (3a-l)

Compound	Minimum Inhibitory Concentration (MIC, $\mu\text{g}/\text{mL}^{-1}$ )					
	Gram +ve bacteria		Gram -ve bacteria		Fungi	
	<i>B.s.</i>	<i>S.a.</i>	<i>E.c.</i>	<i>S.t.</i>	<i>A.n.</i>	<i>C.a.</i>
	MTCC441	MTCC98	MTCC443	MTCC98	MTCC282	MTCC227
3a	250	200	62.5	100	500	>1000
3b	200	100	125	200	1000	500
3c	500	200	100	125	1000	500
3d	500	250	100	250	500	500
3e	100	100	62.5	200	>1000	1000
3f	500	500	125	250	>1000	250
3g	125	125	250	250	1000	500
3h	250	250	500	250	>1000	>1000
3i	500	500	250	500	>1000	>1000
3j	100	100	62.5	200	500	500
3k	100	62.5	200	100	500	1000
3l	200	500	250	250	1000	1000
Ampicillin	250	250	100	100	-	-
Chloramphenicol	50	50	50	50	-	-
Norfloxacin	100	10	10	10	-	-
Griseofulvin	-	-	-	-	100	500
Nystatin	-	-	-	-	100	100

Review of the antimicrobial activities of synthesized compounds (**3a-l**) in (**Table-1**) indicated that compounds **3e**, **3j** and **3k** (MIC=100,  $\mu\text{g}/\text{mL}$ ) exhibited excellent activity toward Gram-positive bacteria *Bacillus subtilis* as compared to Ampicillin (MIC=250,  $\mu\text{g}/\text{mL}$ ) and showed equipotent activity to Norfloxacin (MIC=100,  $\mu\text{g}/\text{mL}$ ). Against Gram-positive bacteria *Bacillus subtilis*, compound **3g** (MIC=125,  $\mu\text{g}/\text{mL}$ ) showed activity higher than that of Ampicillin (MIC=250,  $\mu\text{g}/\text{mL}$ ). Compounds **3b** and **3l** (MIC=200,  $\mu\text{g}/\text{mL}$ ) displayed better activity than Ampicillin (MIC=250,  $\mu\text{g}/\text{mL}$ ) toward Gram-positive bacteria *Bacillus subtilis*. Compounds **3a** and **3h** (MIC=250,  $\mu\text{g}/\text{mL}$ ) showed results equivalent to that of Ampicillin (MIC=250,  $\mu\text{g}/\text{mL}$ ) toward Gram-positive bacteria *Bacillus subtilis*. Compounds **3b**, **3e** and **3j** (MIC=100,  $\mu\text{g}/\text{mL}$ ) were found to be more effective against Gram-positive bacteria *Staphylococcus aureus* than Ampicillin (MIC=250,  $\mu\text{g}/\text{mL}$ ). Against Gram-positive bacteria *Staphylococcus aureus*, compounds **3g** (MIC=125,  $\mu\text{g}/\text{mL}$ ) showed activity higher than that of Ampicillin (MIC=250,  $\mu\text{g}/\text{mL}$ ). Compounds **3a** and **3c** (MIC=200,  $\mu\text{g}/\text{mL}$ ) showed good activity against Gram-positive bacteria *Staphylococcus aureus* as compared to Ampicillin (MIC=250,  $\mu\text{g}/\text{mL}$ ). Against Gram-positive bacteria *Staphylococcus aureus*, compounds **3d** and **3h** (MIC=250,  $\mu\text{g}/\text{mL}$ ) showed equipotent activity to that of Ampicillin (MIC=250,  $\mu\text{g}/\text{mL}$ ).

Moreover, Against Gram-negative bacteria *Escherichia coli*, compounds **3c** and **3d** (MIC=100,  $\mu\text{g}/\text{mL}$ ) showed activity comparable to Ampicillin (MIC=100,  $\mu\text{g}/\text{mL}$ ). Against Gram-negative bacteria *Salmonella typhi*, compounds **3a**, **3e** and **3j** (MIC=62.5,  $\mu\text{g}/\text{mL}$ ) showed excellent activity as compared to Ampicillin (MIC=100,  $\mu\text{g}/\text{mL}$ ). Whereas compounds **3a** and **3k** (MIC=100,  $\mu\text{g}/\text{mL}$ ) showed equipotent to Ampicillin (MIC=100,  $\mu\text{g}/\text{mL}$ ) toward Gram-negative bacteria *Salmonella typhi*.

Furthermore, against *Candida albicans* fungal pathogen, however compound **3f** (MIC=250,  $\mu\text{g}/\text{mL}$ ) showed better inhibition action as compare to the standard drug Griseofulvin (MIC=500,  $\mu\text{g}/\text{mL}$ ). Whereas compounds **3b**, **3c**, **3d**, **3g** and **3j** (MIC=500,  $\mu\text{g}/\text{mL}$ ) showed activity comparable to Griseofulvin (MIC=500,  $\mu\text{g}/\text{mL}$ ) against fungal pathogen *Candida albicans*.

### 2.2.3. ANTI TUBERCULOSIS ACTIVITY:

The in vitro antitubercular activity of all the synthesized compounds were determined by using Lowenstein-jensen medium (Conventional method against Mycobacterium tuberculosis H37Rv strain as described by Rattan [33]). The results of the activity data are presented in Table 2. in the form of % inhibition, relative to that of standard drugs isoniazide and rifampicin. Upon study of the activity data it was observed that compound **3d** and **3h** showed good activity in comparison with isoniazide.

Comp No.	% inhibition	Comp No.	% inhibition
3a	59	3g	45
3b	72	3h	90
3c	89	3i	54
3d	91	3j	36
3e	55	3k	54
3f	32	3l	85
ISONIAZIDE= 0.20 µg/ml 99% inhibition			

Table.2 Antitubercular activity data of compounds (3a-l)

### 3. EXPERIMENTAL:

All the melting points are uncorrected. All reactions were performed with commercially available reagents and they were used without further purification. Organic solvents were purified by standard methods and stored over molecular sieves. All the IR spectra (KBr disc) were recorded on Shimadzu FT-IR 8400-S spectrometer. <sup>1</sup>H-NMR and <sup>13</sup>C APT spectra were recorded on Bruker Advance 400 spectrometer operating at 400 MHz for <sup>1</sup>H-NMR and 100 MHz for <sup>13</sup>C-APT. The chemical shift (δ) is reported in ppm using chloroform-d as a solvent and calibrated standard solvent signal. Mass spectra were recorded on Shimadzu QP 2010 spectrometer. Elemental analysis was carried out on Perkin- Elmer 2400 C-H-N-S-O Analyzer Series-II. Column chromatography was performed with silica gel 60–120 mesh (Merck, Mumbai, India.). All the compounds were routinely checked for completion of the reaction on silica gel 60 F254 TLC plates and their spots were visualized by exposure to a UV lamp, iodine vapour or KMnO<sub>4</sub> reagents.

#### 3.1 General method for the synthesis of [1,2,4]triazolo[3',4':2,3][1,3,4]thiadiazepino[7,6-b]coumarins(3a-l):

A solution of appropriate 4-amino-5-substituted-3-mercapto-1,2,4-triazoles (0.025mol) (**2a-d**) in ethanol (5 ml) was taken in 100ml round bottom flask. To this catalytical amount of K<sub>2</sub>CO<sub>3</sub> (0.03 mol) was added and stirred for 30 minutes at room temperature. The after an appropriate 4-chloro-3-formyl coumarin (**1a-c**) (0.025mol) in ethanol (15 mL) was added dropwise followed by addition of 2-3 drops of acetic acid to above well stirred solution during 10 minutes at room temperature. The reaction mixture was then refluxed for 10 minute and further stirred at room

temperature for two hours. The solid obtained was filtered out and washed with hexane and dried. The compounds were obtained as yellowish colored solid, which were recrystallized from chloroform-hexane.

The structure of all the synthesized compounds (**3a-l**) were confirmed by their analytical and spectral data like IR, <sup>1</sup>H-NMR, <sup>13</sup>C-APT, elemental analysis and representative mass spectral data given below.

**3-Methyl-[1,2,4]triazolo[3',4':2,3][1,3,4]thiadiazepino[7,6-b]coumarins(3a):** Yellow solid, Yield= 85% ;M.P; 198-201 Anal. Calcd. For C<sub>13</sub>H<sub>8</sub>N<sub>4</sub>O<sub>2</sub>S: C, 54.92; H, 2.84; N, 19.71, %. Found: C, 54.90; H, 2.80; N, 19.69 %. IR (KBr, ν<sub>max</sub>, cm<sup>-1</sup>); 756(C-S-C Stretching), 1714 (C=O stretching of δ-lactone of coumarin), 1586 (aromatic C=C stretching), 1476 (aromatic C=N stretching), 2852(aliphatic C-H Stretching), 3043 (aromatic C-H stretching). <sup>1</sup>H NMR (400MHz, CDCl<sub>3</sub>, δ): 2.47 (3H, s, CH<sub>3</sub>), 7.20-8.39 (5H, m, aromatic protons). <sup>13</sup>C APT (100MHz, CDCl<sub>3</sub>, δ): 20.88 (CH<sub>3</sub>), 112.80 (C), 113.76(C), 115.83(C), 117.54 (C), 125.24(CH), 128.77(CH), 130.48(CH), 134.98(CH), 136.63(C), 138.50(CH), 155.90(C), 160.43(CO of coumarin). The mass spectrum of compound showed M<sup>+</sup> peak at 284 (18%) (m/z%) along with some other fragments peaks at 257(23%), 77(12%), 57(11%), 44(100%) etc. The appearance of molecular ion peak at 284 mass unit supports the structure of compound **3a**.

**3,9-Dimethyl-[1,2,4]triazolo[3',4':2,3][1,3,4]thiadiazepino[7,6-b]coumarins (3b):** yellow solid; yield = 75% ; mp 193-196°C; Anal. Calcd. For C<sub>14</sub>H<sub>10</sub>N<sub>4</sub>O<sub>2</sub>S: C, 56.34; H, 3.36; N, 18.78%. Found: C, 56.37; H, 3.38; N, 18.75%. IR (KBr, ν<sub>max</sub>, cm<sup>-1</sup>); 750(C-S-C Stretching), 1714 (C=O stretching of δ-lactone of coumarin), 1586 (aromatic C=C stretching), 1476 (aromatic C=N stretching), 2852(aliphatic C-H Stretching), 3043 (aromatic C-H stretching). <sup>1</sup>H NMR (400MHz, CDCl<sub>3</sub>, δ): 2.64 (6H, s, 2×CH<sub>3</sub>), 7.33-8.42 (4H, m, Ar-H). <sup>13</sup>C APT (100MHz, CDCl<sub>3</sub>, δ): 20.85 (CH<sub>3</sub>), 23.14 (CH<sub>3</sub>), 115.14(C), 117.85(CH), 119.40(C), 123.15(C), 124.55(CH), 128.05(C), 129.45 (CH), 131.51 (CH), 135.95(C), 138.43(C), 152.80(C), 162.61(CO of coumarin).

**3-Methyl-9-Chloro-[1,2,4]triazolo[3',4':2,3][1,3,4]thiadiazepino[7,6-b]coumarins (3c):** pale yellow solid; yield = 79% ; mp 200-202°C; Anal. Calcd. For C<sub>13</sub>H<sub>7</sub>N<sub>4</sub>O<sub>2</sub>SCl: C, 48.99; H, 2.21; N, 11.12%. Found: C, 48.96; H, 2.18; N, 11.08%. IR (KBr, ν<sub>max</sub>, cm<sup>-1</sup>); 752(C-S-C Stretching), 1719 (C=O stretching of δ-lactone of coumarin), 1584 (aromatic C=C stretching), 1473 (aromatic C=N stretching), 2854(aliphatic C-H Stretching), 3041 (aromatic C-H stretching). <sup>1</sup>H NMR (400MHz, CDCl<sub>3</sub>, δ): 2.35 (3H, s, CH<sub>3</sub>), 7.33-8.38 (4H, m, Ar-H). <sup>13</sup>C APT (100MHz, CDCl<sub>3</sub>, δ): 20.95 (CH<sub>3</sub>), 115.34(C), 117.35(CH), 119.50(C), 123.25(C), 125.55(CH), 128.69(C), 129.99(CH), 131.25(C), 134.95(C), 138.43(CH), 157.80(C), 161.81(CO of coumarin).

**3-Phenyl -[1,2,4]triazolo-[3',4':2,3][1,3,4]-thiadiazepino[7,6-b]coumarins (3d):** pale yellow solid; yield = 79% ; mp 212-214°C; Anal. Calcd. For C<sub>18</sub>H<sub>10</sub>N<sub>4</sub>O<sub>2</sub>S: C, 62.42; H, 2.91; N, 16.18 %.

Found: C,62.40; H, 2.89; N, 16.13%. IR (KBr,  $\nu_{\max}$ ,  $\text{cm}^{-1}$ ); 756(C-S-C Stretching), 1715 (C=O stretching of  $\delta$ -lactone of coumarin), 1585 (aromatic C=C stretching), 1476 (aromatic C=N stretching), 3045 (aromatic C-H stretching).  $^1\text{H}$  NMR (400MHz,  $\text{CDCl}_3$ ,  $\delta$ ):7.21-8.95 (10H,m, Ar-H).  $^{13}\text{C}$  APT (100MHz,  $\text{CDCl}_3$ ,  $\delta$ ): 114.55(C), 115.60(C), 115.65(C), 117.12(CH) 124.05(CH), 125.36(CH), 125.99(CH), 128.95(CH), 129.55(C), 130.01(CH), 133.70(CH), 141.94(C), 143.56(C), 150.88(C), 156.66(C), 161.56(CO of coumarin).

**3-Phenyl-9-methyl-[1,2,4]triazolo-[3',4':2,3][1,3,4]-thiadiazepino[7,6-b]coumarins (3e):** pale yellow solid; yield = 75% ; mp 230-232°C; Anal. Calcd. For  $\text{C}_{19}\text{H}_{12}\text{N}_4\text{O}_2\text{S}$ : C,63.32; H, 3.36; N, 15.55 %. Found: C,62.32; H, 3.35; N, 15.50%. IR (KBr,  $\nu_{\max}$ ,  $\text{cm}^{-1}$ ); 751(C-S-C Stretching), 1719 (C=O stretching of  $\delta$ - lactone of coumarin), 1581 (aromatic C=C stretching), 1475 (aromatic C=N stretching), 2956 (aliphatic C-H stretching) ,3041 (aromatic C-H stretching).  $^1\text{H}$  NMR (400MHz,  $\text{CDCl}_3$ ,  $\delta$ ):2.34(3H, s,  $\text{CH}_3$ ) 7.30-8.52 (9H, m, Ar-H).  $^{13}\text{C}$  APT (100MHz,  $\text{CDCl}_3$ ,  $\delta$ ): 20.68( $\text{CH}_3$ ), 112.80(C), 113.70(C), 115.63(C), 117.52(CH), 118.46(C), 125.04(CH), 128.70(CH), 130.43(CH), 135.03(C), 136.33(CH), 138.90(C), 143.43(CH), 145.73(CH), 153.48(C), 155.04(C),163.98(CO of coumarin).

**3-Phenyl 9-Chloro-[1,2,4]triazolo-[3',4':2,3][1,3,4]-thiadiazepino[7,6-b]coumarins (3f):** pale yellow solid; yield = 80% ; mp 215-217°C; Anal. Calcd. For  $\text{C}_{18}\text{H}_9\text{N}_4\text{O}_2\text{SCl}$ : C, 56.77; H, 2.38; N, 14.71 %. Found: C,56.72 ; H, 2.35; N,14.68 %. IR (KBr,  $\nu_{\max}$ ,  $\text{cm}^{-1}$ ); 754(C-S-C Stretching), 1719 (C=O stretching of  $\delta$ -lactone of coumarin), 1582 (aromatic C=C stretching), 1476 (aromatic C=N stretching), 3043 (aromatic C-H stretching).  $^1\text{H}$  NMR (400MHz,  $\text{CDCl}_3$ ,  $\delta$ ): 7.32-8.59 (9H,m, Ar-H).  $^{13}\text{C}$  APT (100MHz,  $\text{CDCl}_3$ ,  $\delta$ ): 111.57(C), 113.80(C), 114.70(C), 115.63(C) , 117.52 (CH), 118.90(C), 125.04(CH), 128.70(CH), 130.43(CH),135.03(CH), 136.33 (C),138.98(CH), 143.43(CH), 153.04(C), 156.98(C),162.48(CO of coumarin).

**3-Pyridyl-[1,2,4]triazolo-[3',4':2,3][1,3,4]-thiadiazepino[7,6-b]coumarins (3g):** pale yellow solid; yield = 82% ; mp 252-254°C; Anal. Calcd. For  $\text{C}_{17}\text{H}_9\text{N}_5\text{O}_2\text{S}$ : C,58.78; H, 2.61; N,20.16 %. Found: C,58.72; H, 2.63; N, 20.10 %. IR (KBr,  $\nu_{\max}$ ,  $\text{cm}^{-1}$ ); 751(C-S-C Stretching), 1719 (C=O stretching of  $\delta$ - lactone of coumarin), 1581 (aromatic C=C stretching), 1475 (aromatic C=N stretching), 3041 (aromatic C-H stretching).  $^1\text{H}$  NMR (400MHz,  $\text{CDCl}_3$ ,  $\delta$ ): 7.22-8.88 (9H, m, Ar-H).  $^{13}\text{C}$ -APT(100MHz,  $\text{CDCl}_3$ ,  $\delta$ ): 110.21(C), 113.02(C), 115.65(C), 117.76(CH), 118.29(C), 120.23(C), 125.86(CH), 125.97(C), 128.96(CH),131.81(CH), 135.28(CH),138.39(CH), 142.98(CH), 152.98(C),163.81(CO of coumarin).

**3-Pyridyl-9-methyl-[1,2,4]triazolo-[3',4':2,3][1,3,4]-thiadiazepino[7,6-b]coumarins (3h):** pale yellow solid; yield = 86% ; mp 268-270°C; Anal. Calcd. For  $\text{C}_{18}\text{H}_{11}\text{N}_5\text{O}_2\text{S}$ : C, 59.82; H,8.07; N,19.38 %. Found: C, 59.75; H, 8.10; N,19.36 %. IR (KBr,  $\nu_{\max}$ ,  $\text{cm}^{-1}$ ); 756(C-S-C Stretching), 1712 (C=O



stretching of  $\delta$ - lactone of coumarin), 1585 (aromatic C=C stretching), 1475 (aromatic C=N stretching), 2854 (Aliphatic C-H stretching), 3045 (aromatic C-H stretching).  $^1\text{H}$  NMR (400MHz,  $\text{CDCl}_3$ ,  $\delta$ ): 2.58(3H, s,  $\text{CH}_3$ ), 7.23-8.89 (8H, m, Ar-H).  $^{13}\text{C}$ -APT (100MHz,  $\text{CDCl}_3$ ,  $\delta$ ): 20.43( $\text{CH}_3$ ), 111.31(C), 112.73(C), 113.80(C), 115.57(C), 117.58(CH), 118.37(C), 125.16(C), 126.13(CH), 131.72(CH), 136.03(C), 139.89(CH), 142.37(CH), 145.13(CH), 152.43(C), 163.79(CO of coumarin).

**3-Pyridyl-9-Chloro-[1,2,4]triazolo-[3',4':2,3][1,3,4]-thiadiazepino[7,6-b]coumarins (3i):** pale yellow solid; yield = 79% ; mp 236-237°C; Anal. Calcd. For  $\text{C}_{17}\text{H}_8\text{N}_5\text{O}_2\text{SCl}$ : C, 53.48; H, 2.11; N, 18.34 %. Found: C, 53.45; H, 2.08; N, 18.30 %. IR (KBr,  $\nu_{\text{max}}$ ,  $\text{cm}^{-1}$ ); 754 (C-S-C Stretching), 1715 (C=O stretching of  $\delta$ - lactone of coumarin), 1580 (aromatic C=C stretching), 1472 (aromatic C=N stretching), 3045 (aromatic C-H stretching).  $^1\text{H}$  NMR (400MHz,  $\text{CDCl}_3$ ,  $\delta$ ): 7.21-8.58 (8H, m, Ar-H).  $^{13}\text{C}$ -APT (100MHz,  $\text{CDCl}_3$ ,  $\delta$ ): 111.22(C), 112.82(C), 115.65(C), 117.77(CH), 118.29(C), 120.23(C), 125.66(CH), 125.77(C), 129.16(CH), 131.81(CH), 136.18(C), 140.36(CH), 143.82(CH), 153.28(C), 163.41(CO of coumarin).

**3-Thiophenyl-[1,2,4]triazolo-[3',4':2,3][1,3,4]-thiadiazepino[7,6-b]coumarins (3j):** pale yellow solid; yield = 84% ; mp 211-214°C; Anal. Calcd. For  $\text{C}_{16}\text{H}_8\text{N}_4\text{O}_2\text{S}_2$ : C, 54.53; H, 2.29; N, 15.90 %. Found: C, 54.50; H, 2.25; N, 15.86 %. IR (KBr,  $\nu_{\text{max}}$ ,  $\text{cm}^{-1}$ ); 754 (C-S-C Stretching), 1712 (C=O stretching of  $\delta$ - lactone of coumarin), 1584 (aromatic C=C stretching), 1475 (aromatic C=N stretching), 3045 (aromatic C-H stretching).  $^1\text{H}$  NMR (400MHz,  $\text{CDCl}_3$ ,  $\delta$ ): 7.06-8.34 (8H, m, Ar-H).  $^{13}\text{C}$ -APT (100MHz,  $\text{CDCl}_3$ ,  $\delta$ ): 101.43(CH), 109.89(CH), 112.72(C), 113.80(C), 115.54(C), 117.50(CH), 118.37(C), 125.06(CH), 126.03(C), 129.11(CH), 131.73(CH), 136.52(C), 139.08(CH), 153.49(C), 163.99(CO of coumarin).

**3-Thiophenyl-9-methyl-[1,2,4]triazolo-[3',4':2,3][1,3,4]-thiadiazepino[7,6-b]coumarins (3k):** yellow solid; yield = 75% ; mp 225-227°C; Anal. Calcd. For  $\text{C}_{17}\text{H}_{10}\text{N}_4\text{O}_2\text{S}_2$ : C, 55.72; H, 2.75; N, 15.29 %. Found: C, 55.70; H, 2.74; N, 15.27 %. IR (KBr,  $\nu_{\text{max}}$ ,  $\text{cm}^{-1}$ ); 754 (C-S-C Stretching), 1715 (C=O stretching of  $\delta$ - lactone of coumarin), 1580 (aromatic C=C stretching), 1472 (aromatic C=N stretching), 2854 (aliphatic C-H stretching) 3045 (aromatic C-H stretching).  $^1\text{H}$  NMR (400MHz,  $\text{CDCl}_3$ ,  $\delta$ ): 2.34(3H, s,  $\text{CH}_3$ ), 7.06-8.33 (7H, m, Ar-H).  $^{13}\text{C}$ -APT (100MHz,  $\text{CDCl}_3$ ,  $\delta$ ): 23.32( $\text{CH}_3$ ), 101.32(CH), 109.92(C), 112.74(C), 115.28(C), 115.57(C), 118.39(C), 119.23(CH), 124.89(CH), 129.10(CH), 131.72(CH), 132.05(C), 137.58(CH), 138.42(CH), 142.38(C), 153.48(C), 163.31(CO of coumarin).

**3-Thiophenyl-9-Chloro-[1,2,4]triazolo-[3',4':2,3][1,3,4]-thiadiazepino[7,6-b]coumarins (3l):** yellow solid; yield = 90% ; mp 226-229°C; Anal. Calcd. For  $\text{C}_{16}\text{H}_7\text{N}_4\text{O}_2\text{S}_2\text{Cl}$ : C, 49.68; H, 1.82; N, 14.40 %. Found: C, 49.65; H, 1.84; N, 14.36 %. IR (KBr,  $\nu_{\text{max}}$ ,  $\text{cm}^{-1}$ ); 756 (C-S-C Stretching), 1718 (C=O stretching of  $\delta$ - lactone of coumarin), 1585 (aromatic C=C stretching), 1475 (aromatic C=N stretching), 3041 (aromatic C-H stretching).  $^1\text{H}$  NMR (400MHz,  $\text{CDCl}_3$ ,  $\delta$ ): 7.08-8.36 (7H, m, Ar-

H).  $^{13}\text{C}$ -APT (100MHz,  $\text{CDCl}_3$ ,  $\delta$ ):101.43(CH), 109.89(CH), 112.72(C), 113.80(C), 115.54(C), 117.50(CH), 118.37(C), 125.06(CH), 126.03(C), 129.11(CH), 131.73(CH), 136.52(C), 139.08(CH), 143.37(C), 155.52(C), 163.49(CO of coumarin).

#### 4. CONCLUSION:

Present study described successful hybridization strategy of three bioactive moieties, coumarin, triazole and thiazepines in a single scaffold. The target compounds were synthesized in good yield by adopting simple condensation reaction. Majority of the compounds were found to be active against Gram positive and gram negative bacteria. Antimicrobial screening results revealed that compounds **3a**, **3e**, **3j** and **3k** were found to be the most proficient members of the series and antitubercular activity data revealed that compound **3d** and **3h** showed good activity in comparison with isoniazide.

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