

Anti-bacterial and Anti-inflammatory Activity of Series of (5-{{[(1H-1,2,3-triazol-5-yl)sulfanyl] methyl}-4H-1,2,4-Triazole-3-Thiols and (4-((1-phenyl-1H-1,2,3-Triazol-4-yl)methoxy) phenyl) diazenyl) benzo[d]Thiazoles

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ABSTRACT

Herein, we report the Anti-bacterial and Anti-inflammatory activity of Series of (5-{{[(1H-1,2,3-triazol-5-yl)sulfanyl] methyl}-4H-1,2,4-Triazole-3-Thiols **1a-j** and (4-((1-phenyl-1H-1,2,3-Triazol-4-yl)methoxy)phenyl) diazenyl) benzo[d]Thiazoles **2a-m** shown in **Table-I** to **VIII**. The antibacterial activity of the compounds prepared was evaluated by the filter paper disc technique of Vincent and Vincent. The bacteria used in the present study were *Escherichia coli*, (Gram-negative) and *Bacillus subtilis* (Gram-positive). The compounds were dissolved in acetone and tried at two different concentrations (250 and 500 µg/disc). The anti-inflammatory activity was evaluated by Carrageenan-induced rat paw edema method. All the experiments were carried out using male, Wistar rats (200-250g). Test compound and Diclofenac sodium were suspended in 0.1% W/V carboxy methylene cellulose sodium (CMC) and administered intraperitoneally to animals. Carrageenan was diluted separately in normal saline and injected. Compounds **1e**, **1f** and **1j** showed promising antibacterial activity. The most active compound of the series was **1e**. Compounds **2g**, **2j** and **2m** exhibited high inhibition, whereas **2b**, **2c**, **2e** and **2h** were moderately active. The most active compound of the series was **2g**. Compounds **1c**, **1e**, **1f** and **1j** showed significant anti-inflammatory activity. Compounds **2c**, **2e**, **2g**, **2j** and **2m** showed very good anti-inflammatory activity.

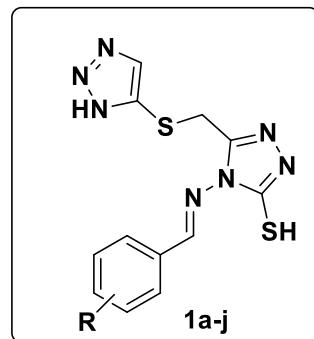
Introduction

The rise of antimicrobial resistance has become one of the most pressing global public health issues, with its prevalence increasing at a concerning rate.¹⁻² The growing incidence and spread of resistant to antibiotics bacterial strains are gradually undermining the effectiveness of nowadays antimicrobial treatments for common bacterial infections.³⁻⁷

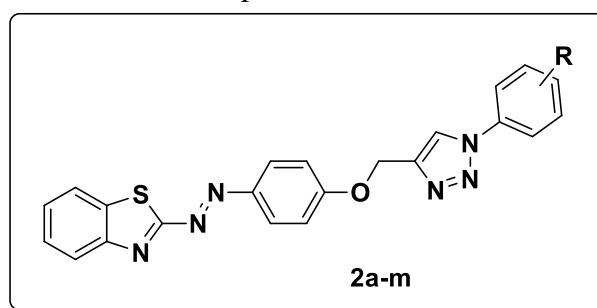
Escherichia coli, a prominent Gram-negative bacillus, acts as an important etiological agent associated to a variety of infections, including urinary tract infections and bacteraemia.⁶⁻⁸ The occurrence of multi-drug resistance in *E. coli* poses a concerning issue in both human and veterinary medicine around the world as a whole. This computational process permits the identification of high-potential analogues, or 'hits,' which can be synthesized and investigated experimentally to evaluate their biological activity and therapeutic potential.¹⁰⁻¹⁴

The antimicrobial properties of triazole derivatives have been extensively studied and have shown considerable efficacy against many pathogenic microbes, including both Gram-positive and Gram-negative bacteria, as well as fungi.¹⁵⁻¹⁶

Manasa *et.al.*,¹⁷ (E)-5-{{(1*H*-1,2,3-triazol-5-yl)sulfanyl}methyl}-4-(benzylideneamino)-4*H*-1,2,4-triazole-3-thiols were synthesized. We have taken samples from Manasa and screened for their anti -bacterial and anti-inflammatory evaluation of compounds **1a-j** shown below.



Manasa *et.al.*,¹⁸ (E)-2-((1-phenyl-1*H*-1,2,3-triazol-4-yl)methoxy)phenyl)-1-(benzo[d]thiazol-2-yl)diazenes were synthesized. We have screened for their anti -bacterial and anti-inflammatory evaluation of compounds **2a-m** shown below.



Results and Discussion

Antibacterial activity

The antibacterial activity of the compounds prepared was evaluated by the filter paper disc technique of Vincent and Vincent¹⁹. The bacteria used in the present study were *Escherichia coli*, (Gram-negative) and *Bacillus subtilis* (Gram-positive). The compounds were dissolved in acetone and tried at two different concentrations (250 and 500 µg/disc). The Whatman filter paper discs (6 mm diameter) with different compounds were placed aseptically

on seeded nutrient agar plates with different bacteria and incubated for 72 hours at $37\pm1^{\circ}\text{C}$. At the end of the incubation period, the diameter of the growth inhibition zones was measured. At least 10 paper discs were observed and repeated twice.

Anti-inflammatory activity

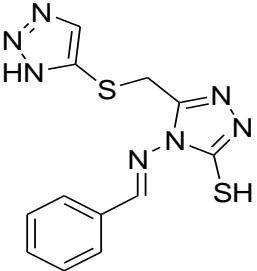
The anti-inflammatory activity was evaluated by Carrageenan-induced rat paw edema method.^{20,21} All the experiments were carried out using male, Wistar rats (200-250g). Test compound and Diclofenac sodium were suspended in 0.1% W/V carboxy methylene cellulose sodium (CMC) and administered intraperitoneally to animals. Carrageenan was diluted separately in normal saline and injected.

Wistar Strain albino rats weighed between 200-250 g, fasted 24 hours before the test were divided into five groups of six animals each. The volume of right hind paw was measured using a plethysmometer. This constituted the initial reading. Compounds were tested in dose 100mg/kg body weight. Diclofenac sodium (10mg/kg) was used as standard. The compounds were administered as suspension in sodium CMC (0.1% W/V) intraperitoneally 1 hour before the injection of Carrageenan. Control group of animals received a suspension of sodium CMC only. 0.1 ml of 1.0% W/V Carrageenan suspension in normal saline was injected into the plantar region of right hind paw. The inflammation produced after injection of the phlogistic agent was measured at hourly for 4 hours.

Percentage of inhibition of edema was calculated by using the formula given below.

$$\% \text{ inhibition of edema} = \frac{\text{Mean edema of control groups} - \text{Mean edema of treated groups}}{\text{Mean edema of control groups}} \times 100$$

Table I -Names and Structures of (*E*)-4-(R-Benzylideneamino)-5-{{[1*H*-1,2,3-triazol-5-yl)sulfanyl]methyl}-4*H*-1,2,4-triazole-3-thiols **1a-j**

Entry	IUPAC Name	Structure
1a	(<i>E</i>)-4-Benzylideneamino)-5-{{[1 <i>H</i> -1,2,3-triazol-5-yl)sulfanyl]methyl}-4 <i>H</i> -1,2,4-triazole-3-thiols	

1b	(<i>E</i>)-5-(((1 <i>H</i> -1,2,3-triazol-5-yl)thio)methyl)-4-((4-methylbenzylidene)amino)-4 <i>H</i> -1,2,4-triazole-3-thiol	
1c	(<i>E</i>)-5-(((1 <i>H</i> -1,2,3-triazol-5-yl)thio)methyl)-4-((4-methoxybenzylidene)amino)-4 <i>H</i> -1,2,4-triazole-3-thiol	
1d	(<i>E</i>)-5-(((1 <i>H</i> -1,2,3-triazol-5-yl)thio)methyl)-4-((2-chlorobenzylidene)amino)-4 <i>H</i> -1,2,4-triazole-3-thiol	
1e	(<i>E</i>)-5-(((1 <i>H</i> -1,2,3-triazol-5-yl)thio)methyl)-4-((4-chlorobenzylidene)amino)-4 <i>H</i> -1,2,4-triazole-3-thiol	
1f	(<i>E</i>)-5-(((1 <i>H</i> -1,2,3-triazol-5-yl)thio)methyl)-4-((4-fluorobenzylidene)amino)-4 <i>H</i> -1,2,4-triazole-3-thiol	
1g	(<i>E</i>)-5-(((1 <i>H</i> -1,2,3-triazol-5-yl)thio)methyl)-4-((2-nitrobenzylidene)amino)-4 <i>H</i> -1,2,4-triazole-3-thiol	

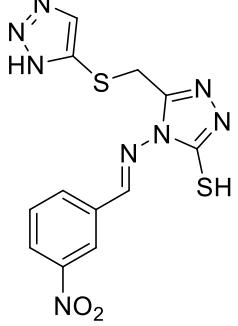
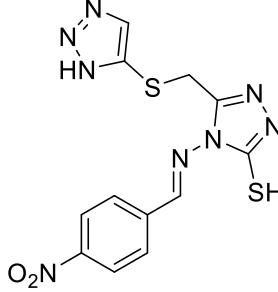
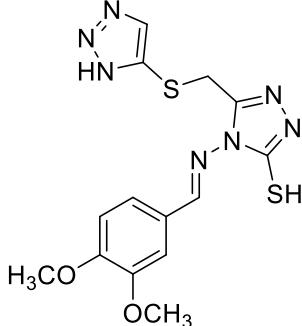
1h	((E)-5-(((1H-1,2,3-triazol-5-yl)thio)methyl)-4-((3-nitrobenzylidene)amino)-4H-1,2,4-triazole-3-thiol	
1i	((E)-5-(((1H-1,2,3-triazol-5-yl)thio)methyl)-4-((4-nitrobenzylidene)amino)-4H-1,2,4-triazole-3-thiol	
1j	((E)-5-(((1H-1,2,3-triazol-5-yl)thio)methyl)-4-((3,4-dimethoxybenzylidene)amino)-4H-1,2,4-triazole-3-thiol	

Table II – Anti-bacterial screening results of (E)-4-(R-Benzylideneamino)-5-[(1H-1,2,3-triazol-5-yl)sulfanyl]methyl]-4H-1,2,4-triazole-3-thiols 1a–j

Entry	Ar	Inhibition zone (in mm)			
		<i>E. coli</i> at		<i>B. subtilis</i> at	
		250 μg/disc	500 μg/disc	250 μg/disc	500 μg/disc
1a	C ₆ H ₅	7.5	15.5	5.0	8.0
1b	2-CH ₃ C ₆ H ₄	8.0	14.0	5.5	9.0
1c	4-CH ₃ OC ₆ H ₄	7.0	12.5	4.5	8.5

1d	2-ClC ₆ H ₄	8.5	18.0	5.5	11.0
1e	4-ClC ₆ H ₄	10.0	20.0	6.0	13.0
1f	4-FC ₆ H ₄	9.0	18.5	6.0	12.0
1g	2-NO ₂ C ₆ H ₄	8.0	9.5	4.0	6.0
1h	3-NO ₂ C ₆ H ₄	5.5	8.5	4.5	9.0
1i	4-NO ₂ C ₆ H ₄	7.0	11.0	5.5	9.5
1j	3,4-(CH ₃ O) ₂ C ₆ H ₃	9.0	18.0	5.5	10.0
Gentamycin		12.0	22.0	8.0	15.0

From the antibacterial activity results obtained (Table II), it was evident that all the compounds **1** were active against both Gram-negative and Gram-positive bacteria at the concentration of 250 µg/disc. The compounds showed varying degree of antibacterial activity against these organisms. The activity of the compound depends upon the nature and position of the substituent at the aryl moiety. Compounds having chloro, fluoro and dimethoxy substituents are more anti-bacterial than the other substituents. On the other hand, compounds having nitro group diminishes the activity of the compounds. Compounds **1e**, **1f** and **1j** showed promising antibacterial activity. The most active compound of the series was **1e**.

Table III – Anti-inflammatory activity data of (E)-4-(R-Benzylideneamino)-5-[(1H-1,2,3-triazol-5-yl)sulfanyl]methyl]-4H-1,2,4-triazole-3-thiols 1a–j (Carrageenan-induced paw edema test in rats)

Entry ^a	Ar	Rat paw edema in mL ^b			
		(Treatment in hours)			
		1h	2h	3h	4h
1a	C ₆ H ₅	2.31±0.310	2.01±0.346**	1.29±0.280***	0.89±0.265***

1b	4-CH ₃ C ₆ H ₄	2.12±0.325	1.70±0.368***	1.06±0.264***	0.70±0.281***
1c	4-CH ₃ OC ₆ H ₄	2.19±0.261	1.85±0.359***	1.23±0.368***	0.59±0.268***
1d	2-ClC ₆ H ₄	2.09±0.320	1.82±0.345***	1.11±0.275***	0.68±0.282***
1e	4-ClC ₆ H ₄	2.06±0.342	1.61±0.364***	1.01±0.267***	0.54±0.263***
1f	4-FC ₆ H ₄	2.21±0.367	1.81±0.348***	1.05±0.332***	0.62±0.258***
1g	2-NO ₂ C ₆ H ₄	2.31±0.332	2.06±0.371*	1.60±0.274***	0.85±0.269***
1h	3-NO ₂ C ₆ H ₄	2.30±0.325	1.74±0.339***	1.26±0.281***	0.74±0.308***
1i	4-NO ₂ C ₆ H ₄	2.15±0.317	1.73±0.394***	1.18±0.269***	0.72±0.267***
1j	3,4-(CH ₃ O) ₂ C ₆ H ₃	2.13±0.343	1.80±0.379**	1.62±0.272**	0.63±0.273***
control		2.74±0.242	2.87±0.254***	3.12±0.289***	3.15±0.291***
Diclofenac sodium		1.84±0.251***	1.32±0.251***	0.91±0.257***	0.52±0.309***

^aDose level: test compounds (100mg/kg b.wt), Diclofenac sodium (10mg/kg b.wt)

^bValues are expressed as mean± SD (number of animals N= 6 rats)

Statistically significant compared to respective control values, ***P<0.001, **P<0.01, *P<0.05 (Dunnet's test)

Table IV – Anti-inflammatory activity data of (E)-4-(R-Benzylideneamino)-5-{[(1*H*-1,2,3-triazol-5-yl)sulfanyl]methyl}-4*H*-1,2,4-triazole-3-thiols 1a–j (Carrageenan-induced paw edema test in rats)

Entry ^a	Ar	% inhibition of paw volume			
		(Treatment in hours)			
		1h	2h	3h	4h
1a	C ₆ H ₅	15.69	29.96**	58.65***	71.74***

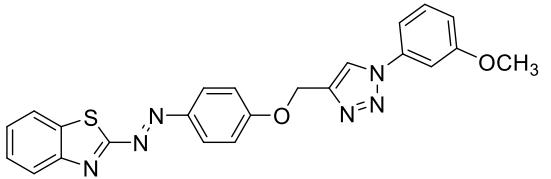
1b	4-CH ₃ C ₆ H ₄	22.62	40.76***	66.02***	77.77***
1c	4-CH ₃ OC ₆ H ₄	20.05	35.54***	60.57***	81.26***
1d	2-ClC ₆ H ₄	23.72	36.58***	64.42***	78.41***
1e	4-ClC ₆ H ₄	24.81	43.90***	67.62***	82.85***
1f	4-FC ₆ H ₄	19.36	36.93***	66.34***	80.31***
1g	2-NO ₂ C ₆ H ₄	15.69	28.22*	48.71***	73.01***
1h	3-NO ₂ C ₆ H ₄	16.03	39.37***	59.61***	76.50***
1i	4-NO ₂ C ₆ H ₄	21.53	39.72***	62.27***	77.14***
1j	3,4-(CH ₃ O) ₂ C ₆ H ₃	22.26	37.28**	48.07**	80.00***
control		NA	NA	NA	NA
Diclofenac sodium		32.84***	54.01***	70.83***	83.49***

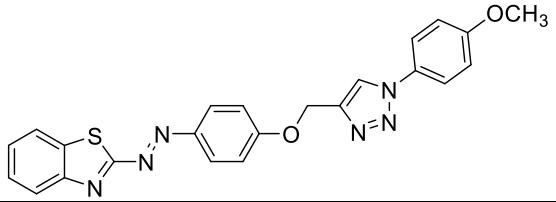
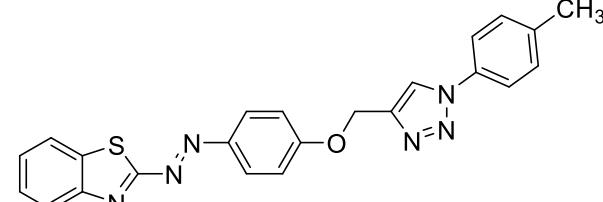
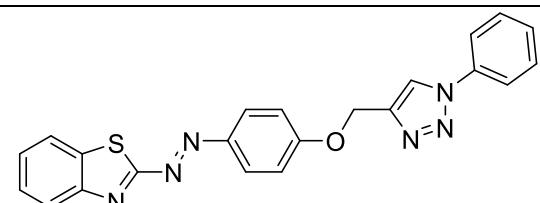
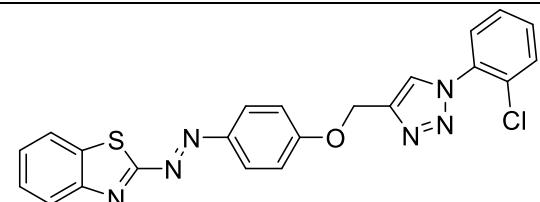
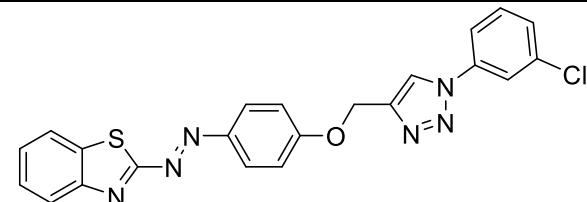
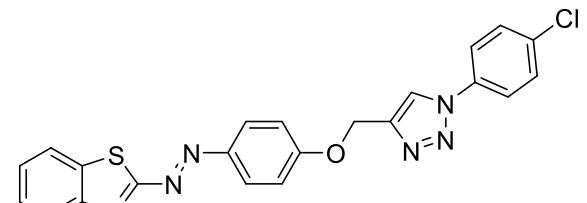
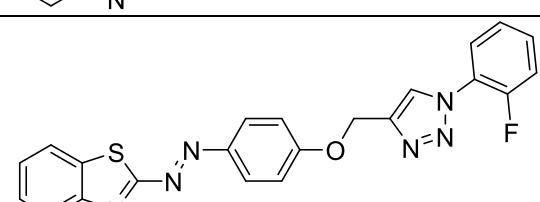
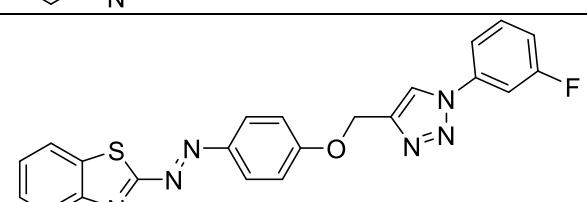
^aDose level: test compounds (100mg/kg b.wt), Diclofenac sodium (10mg/kg b.wt)

Statistically significant compared to respective control values, ***P<0.001, **P<0.01, *P<0.05 (Dunnet's test)

The anti-inflammatory activity screening data (**Table III** and **IV**) indicate that all the compounds **1** exhibited interesting activity, however with a degree of variation. Compounds **1c**, **1e**, **1f** and **1j** showed significant anti-inflammatory activity. Other compounds displayed moderate anti-inflammatory activity.

Table V -Names and Structures of (E)-2-((4-((1-phenyl-1*H*-1,2,3-triazol-4-yl)methoxy)phenyl)diazaryl)benzo[*d*]thiazole 2a-m

Entry	IUPAC Name	Structure
2a	(<i>E</i>)-2-((4-((1-(3-methoxyphenyl)-1 <i>H</i> -1,2,3-triazol-4-yl)methoxy)phenyl)diazaryl)benzo[<i>d</i>]thiazole	

2b	(<i>E</i>)-2-((4-((1-(4-methoxyphenyl)-1 <i>H</i> -1,2,3-triazol-4-yl)methoxy)phenyl)diazenyl)benzo[<i>d</i>]thiazole	
2c	(<i>E</i>)-2-((4-((1-(p-tolyl)-1 <i>H</i> -1,2,3-triazol-4-yl)methoxy)phenyl)diazenyl)benzo[<i>d</i>]thiazole	
2d	(<i>E</i>)-2-((4-((1-phenyl-1 <i>H</i> -1,2,3-triazol-4-yl)methoxy)phenyl)diazenyl)benzo[<i>d</i>]thiazole	
2e	(<i>E</i>)-2-((4-((1-(2-chlorophenyl)-1 <i>H</i> -1,2,3-triazol-4-yl)methoxy)phenyl)diazenyl)benzo[<i>d</i>]thiazole	
2f	(<i>E</i>)-2-((4-((1-(3-chlorophenyl)-1 <i>H</i> -1,2,3-triazol-4-yl)methoxy)phenyl)diazenyl)benzo[<i>d</i>]thiazole	
2g	(<i>E</i>)-2-((4-((1-(4-chlorophenyl)-1 <i>H</i> -1,2,3-triazol-4-yl)methoxy)phenyl)diazenyl)benzo[<i>d</i>]thiazole	
2h	(<i>E</i>)-2-((4-((1-(2-fluorophenyl)-1 <i>H</i> -1,2,3-triazol-4-yl)methoxy)phenyl)diazenyl)benzo[<i>d</i>]thiazole	
2i	((<i>E</i>)-2-((4-((1-(3-fluorophenyl)-1 <i>H</i> -1,2,3-triazol-4-yl)methoxy)phenyl)diazenyl)benzo[<i>d</i>]thiazole	

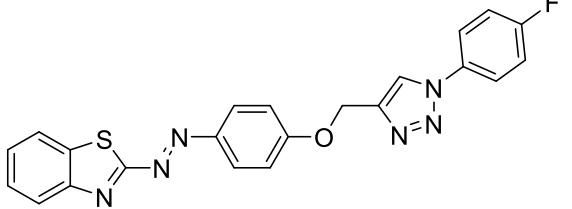
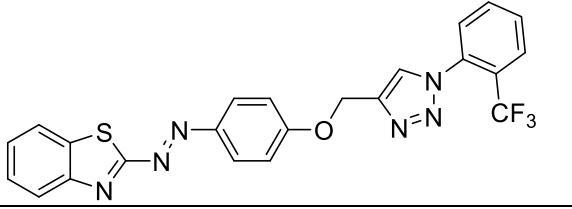
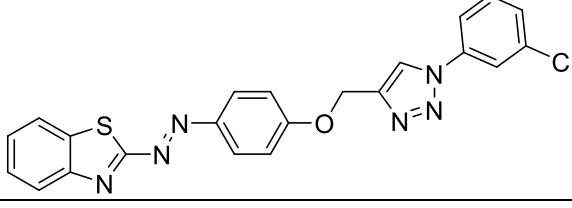
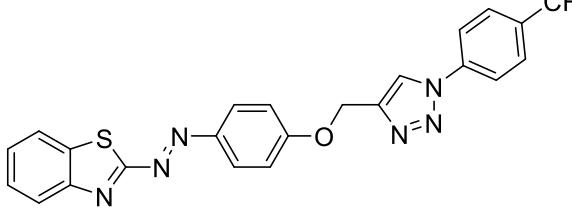
2j	(<i>E</i>)-2-((4-((1-(4-fluorophenyl)-1 <i>H</i> -1,2,3-triazol-4-yl)methoxy)phenyl)diazenyl)benzo[<i>d</i>]thiazole	
2k	(<i>E</i>)-2-((4-((1-(trifluoromethyl)phenyl)-1 <i>H</i> -1,2,3-triazol-4-yl)methoxy)phenyl)diazenyl)benzo[<i>d</i>]thiazole	
2l	(<i>E</i>)-2-((4-((1-(3-(trifluoromethyl)phenyl)-1 <i>H</i> -1,2,3-triazol-4-yl)methoxy)phenyl)diazenyl)benzo[<i>d</i>]thiazole	
2m	(<i>E</i>)-2-((4-((1-(4-(trifluoromethyl)phenyl)-1 <i>H</i> -1,2,3-triazol-4-yl)methoxy)phenyl)diazenyl)benzo[<i>d</i>]thiazole	

Table VI – Anti-bacterial activity results of (*E*)-2-((4-((1-phenyl-1*H*-1,2,3-triazol-4-yl)methoxy)phenyl)diazenyl)benzo[*d*]thiazole 2a-m

Entry	Ar	Inhibition zone (in mm)			
		<i>E. coli</i> at		<i>B. subtilis</i> at	
		250 μg/disc	500 μg/disc	250 μg/disc	500 μg/disc
2a	3-CH ₃ OC ₆ H ₄	7.0	14.5	5.5	9.0
2b	4-CH ₃ OC ₆ H ₄	7.5	16.0	6.0	10.5
2c	4-CH ₃ C ₆ H ₄	8.0	17.5	6.5	11.5
2d	C ₆ H ₅	7.0	13.5	5.5	8.5
2e	2-ClC ₆ H ₄	7.5	16.5	6.5	10.5

2f	3-ClC ₆ H ₄	7.0	15.0	5.5	9.5
2g	4-ClC ₆ H ₄	10.5	20.0	7.0	13.0
2h	2-FC ₆ H ₄	7.5	16.5	6.0	10.0
2i	3-FC ₆ H ₄	7.0	14.5	5.5	9.0
2j	4-FC ₆ H ₄	10.0	19.5	6.5	12.0
2k	2-CF ₃ C ₆ H ₄	7.0	16.0	6.5	11.0
2l	3-CF ₃ C ₆ H ₄	6.5	15.0	5.5	9.0
2m	4-CF ₃ C ₆ H ₄	9.5	19.0	6.5	12.5
Gentamycin		12.0	22.0	8.0	15.0

The activity data recorded in **Table V**, indicate that all the compounds **15** were active against both the bacteria at the concentration of 250 µg/disc. Compounds **15g**, **15j** and **15m** exhibited high inhibition, whereas **15b**, **15c**, **15e** and **15h** were moderately active. Rest of the compounds showed weak activity. The most active compound of the series was **15g**.

**Table VII – Anti-inflammatory activity data of ((E)-2-((4-((1-phenyl-1*H*-1,2,3-triazol-4-yl)methoxy)phenyl)diazenyl)benzo[*d*]thiazole 2a-m
(Carrageenan-induced paw edema test in rats)**

Entry ^a	Ar	Rat paw edema in mL ^b			
		(Treatment in hours)			
		1h	2h	3h	4h
2a	3-CH ₃ OC ₆ H ₄	2.09±0.313	2.03±0.346**	1.06±0.280***	0.73±0.265***
2b	4-CH ₃ OC ₆ H ₄	2.13±0.325	1.64±0.363***	1.21±0.264***	0.69±0.281***
2c	4-CH ₃ C ₆ H ₄	2.06±0.343	1.62±0.365***	1.01±0.267***	0.54±0.264***
2d	C ₆ H ₅	2.20±0.320	1.78±0.315***	1.10±0.282***	0.68±0.271***
2e	2-ClC ₆ H ₄	2.17±0.263	1.85±0.356**	1.23±0.368***	0.59±0.267***
2f	3-ClC ₆ H ₄	2.12±0.320	1.82±0.345***	1.24±0.275***	0.68±0.283***
2g	4-ClC ₆ H ₄	2.01±0.342	1.58±0.364***	1.02±0.267***	0.52±0.262***
2h	2-FC ₆ H ₄	2.19±0.367	1.81±0.348***	1.05±0.332***	0.62±0.255***
2i	3-FC ₆ H ₄	2.34±0.335	2.08±0.371*	1.62±0.274**	0.82±0.269***
2j	4-FC ₆ H ₄	2.08±0.341	1.54±0.366***	1.04±0.267***	0.55±0.263***

2k	2-CF ₃ C ₆ H ₄	2.21±0.367	1.73±0.348***	1.07±0.332***	0.63±0.258***
2l	3-CF ₃ C ₆ H ₄	2.28±0.332	2.06±0.371*	1.54±0.274***	0.84±0.269***
2m	4-CF ₃ C ₆ H ₄	2.07±0.345	1.60±0.364***	1.03±0.267**	0.57±0.292***
Control		2.74±0.242	2.87±0.254***	3.12±0.289***	3.15±0.291***
Diclofenac sodium		1.84±0.251***	1.32±0.251***	0.91±0.257***	0.52±0.309***

^aDose level: test compounds (100mg/kg b.wt), Diclofenac sodium (10mg/kg b.wt)

^bValues are expressed as mean± SD (number of animals N= 6 rats)

Statistically significant compared to respective control values, ***P<0.001, **P<0.01, *P<0.05 (Dunnet's test)

**Table VIII – Anti-inflammatory activity data of ((E)-2-((4-((1-phenyl-1*H*-1,2,3-triazol-4-yl)methoxy)phenyl)diazenyl)benzo[*d*]thiazole 2a-m
(Carageenan-induced paw edema test in rats)**

Compd ^a	Ar	% inhibition of paw volume			
		(Treatment in hours)			
		1h	2h	3h	4h
2a	3-CH ₃ OC ₆ H ₄	23.72	29.26**	66.02***	76.82***
2b	4-CH ₃ OC ₆ H ₄	22.26	42.85***	61.21***	78.09***
2c	4-CH ₃ C ₆ H ₄	24.81	43.55***	67.62***	82.85***
2d	C ₆ H ₅	19.70	37.97***	64.74***	78.41***
2e	2-ClC ₆ H ₄	20.80	35.54**	60.57***	81.26***
2f	3-ClC ₆ H ₄	22.62	36.58***	60.25***	78.41***
2g	4-ClC ₆ H ₄	26.64	44.94***	67.30***	83.49***
2h	2-FC ₆ H ₄	20.07	36.93***	66.34***	80.31***
2i	3-FC ₆ H ₄	14.59	27.52*	48.07**	73.96***
2j	4-FC ₆ H ₄	24.08	46.34***	66.66***	82.54***
2k	2-CF ₃ C ₆ H ₄	19.34	39.72***	65.70***	80.00***
2l	3-CF ₃ C ₆ H ₄	16.78	28.22*	50.64**	73.33***
2m	4-CF ₃ C ₆ H ₄	24.45	44.25***	66.98***	81.90***

Control	NA	NA	NA	NA
Diclofenac sodium	32.84***	54.01***	70.83***	83.49***

^aDose level: test compounds (100mg/kg b.wt), Diclofenac sodium (10mg/kg b.wt)

Statistically significant compared to respective control values, ***P<0.001, **P<0.01, *P<0.05 (Dunnet's test)

The anti-inflammatory activity data of compounds **2** are presented in **Table VII** and **Table VIII**. The compounds bearing halo substituents increased the anti-inflammatory activity. Compounds **2c**, **2e**, **2g**, **2j** and **2m** showed very good anti-inflammatory activity. The remaining compounds exhibited moderate anti-inflammatory activity.

Conclusion

Compounds **1e**, **1f** and **1j** showed promising antibacterial activity. The most active compound of the series was **1e**. Compounds **2g**, **2j** and **2m** exhibited high inhibition, whereas **2b**, **2c**, **2e** and **2h** were moderately active. Rest of the compounds showed weak activity. The most active compound of the series was **2g**. Compounds **1c**, **1e**, **1f** and **1j** showed significant anti-inflammatory activity. Other compounds displayed moderate anti-inflammatory activity. Compounds **2c**, **2e**, **2g**, **2j** and **2m** showed very good anti-inflammatory activity. The remaining compounds exhibited moderate anti-inflammatory activity.

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