

# PHARMACOLOGICAL PROFILE OF THIADIAZOLE DERIVATIVE: A REVIEW

1 Shubha Shrivastava\* and 2 Dharmendra Ahuja

1 Department of Pharmaceutical Science, Jayoti Vidyapeeth Women's University, Jaipur.

Corresponding Author: Shubha Shrivastava,

2 Department of Pharmaceutical Science, Jayoti Vidyapeeth Women's University, Jaipur.

Email Id: shrivastava.shubha4@gmail.com

## Abstract

It has long been a fascinating area of research to examine the chemistry of heterocyclic molecules. An essential group of substances for the creation of novel drugs is heterocyclic nucleus 1,3,4-thiadiazole. In recent decades, the synthesis of novel thiadiazole derivatives as well as research into their chemical and biological behavior have become more crucial. A focus of ongoing research in medicinal chemistry is the hunt for antiepileptic substances with higher selectivity and lower toxicity. The pharmacological effects of various classes of thiadiazole compounds, including those with antimicrobial, anticonvulsant, antifungal, anti-diabetic, anti-inflammatory, antioxidant, and other activities, have been the focus of intense research in recent years. A significant global issue is the rise of drug resistance to current treatments. The versatile moiety thiadiazole has a wide range of biological effects. The thiadiazole moiety functions as a "two-electron donor system" and a "hydrogen binding domain." Additionally, it serves as a restricted pharmacophore.

**Key word:** Thiadiazole, pharmacological activity, heterocyclic compounds.

## Introduction

Cholera, syphilis, anthrax, leprosy, and plague are examples of bacterial illnesses that can be fatal. In contrast, fungi infections like Tinea, Candida, and athlete's foot are related to bacterial infections that are potentially fatal.

Consequently, the prevalence of global public health issues is rising due to harmful bacteria and their antibiotic resistance. Several bacterial species that may survive after being exposed to one or more antibiotics may be the cause of antibiotic resistance. In some situations, pathogens can develop resistance to numerous antibiotics to become multidrug resistant (MDR) species.

Multi-drug-resistant (MDR) infections are to blame for the deaths of millions of patients worldwide every year due to the degree of their fatal effect and their enormous impact on morbidity and mortality. Because of all these issues, it is vital that powerful antibiotics with distinct properties be developed. Thiadiazole is a five-membered heterocyclic ring structure that contains two nitrogen atoms and one sulphur atom. It can be found in nature in four isomeric forms: 1,2,3, 1,2,5, 1,2,4, and 1,3,4-thiadiazole.

Structure of 1,2,3, 1,2,4, 1,2,5, and 1,3,4-thiadiazole.

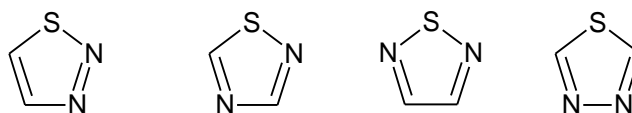


Figure (1) (2) (3) (4)

Tijen onkol et al [1] were prepared new series of 2-[[1(2H)-phthalazinone-2-yl] methyl/ethyl]-5-arylamino-1,3,4-thiadiazole derivatives obtain by the cyclization of [1(2H)-phthalazinone-2-yl] -acetyl/propanoyl thiosemicarbazide under the acidic condition. Using the broth microdilution method, the antimicrobial activities of the title compounds were examined against two Gram positive bacteria (*S. aureus*, *B. subtilis*), two Gram negative bacteria (*P. aeruginosa*, *E. coli*), and two yeast-like fungi (*C. albicans* and *C. parapsilosis*). In general, the compounds were found to be potent against

*B. subtilis* and the fungi. All synthesized compounds shown no activity against *S. aureus*, *P. aeruginosa* and *E. coli* but some synthesized compounds were found the activity against *B. subtilis* and the fungi. Phenyl derivative showed potent antibacterial activity against *B. Subtilis* than other derivatives. b, g, i, k & l derivatives also showed moderate antibacterial activity against *B. Subtilis*. c, e & i compounds showed antifungal activity against *C. Albicans* and g & l exhibit the antifungal activity against *C. parapsilosis*

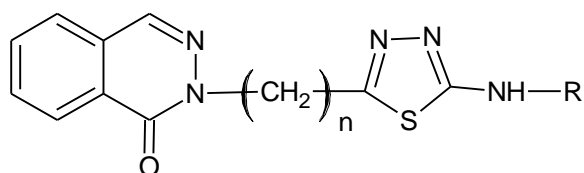


Figure-5

Where	n	R
a	1	Phenyl
b	1	Benzyl
c	1	Phenethyl
d	1	4-chlorophenyl
e	1	4-methoxyphenyl
f	1	4-methylphenyl
g	2	Phenyl
h	2	Benzyl
i	2	Phenethyl
j	2	4-chlorophenyl
k	2	4-methoxyphenyl
l	2	4-methylphenyl

Alok Pandey et al [2] were synthesized some new 1,3,4-thiadiazole derivative of Schiff bases with different aromatic aldehyde. The antimicrobial screening of synthesized compounds against gram positive (*S. Aureus*) and gram negative (*E. coli*) bacterial strain by

cup plate diffusion method. The compounds A,D,E, and J showed good antibacterial activity against gram positive bacteria and the compounds B,D,E, and J showed good antibacterial activity against gram negative bacteria.

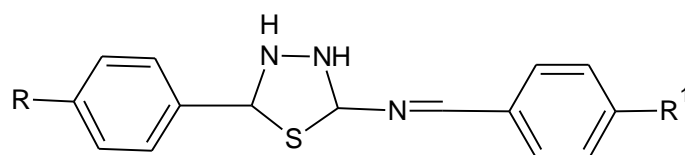


Figure-6

Where	R	R <sup>1</sup>
A	OCH <sub>3</sub>	OH
B	OH	OH
C	Cl	OH
D	NO <sub>2</sub>	OH
E	N(CH <sub>3</sub> ) <sub>2</sub>	OH
F	OCH <sub>3</sub>	NO <sub>2</sub>
G	OH	NO <sub>2</sub>
H	Cl	NO <sub>2</sub>
I	NO <sub>2</sub>	NO <sub>2</sub>
J	N(CH <sub>3</sub> ) <sub>2</sub>	NO <sub>2</sub>

Lincy Joseph et al [3] produced new series of 5-aryl N-phenyl-1, 3, 4-thiadiazole 2-amino derivatives by the oxidative cyclization of substituted phenyl thiosemicarbazone with FeCl<sub>3</sub> as a catalyst. Antibacterial, anti-inflammatory, anti-diabetic, anti-oxidant, anxiolytic, and locomotor properties were investigated in these compounds. Antibacterial activity was determined using the disc diffusion method, in vitro anti-inflammatory activity was determined using the protein denaturation method, in vitro anti-diabetic activity was determined using the amylase inhibitory activity method, in vitro anti-oxidant activity was determined using the H<sub>2</sub>O<sub>2</sub> scavenging method, in vivo

anxiolytic activity was determined using the hole board apparatus, and in vivo locomotor activity was determined using the actophotometer. N-phenyl 5-(2, 3, 4-trimethoxyphenyl)-1, 3, 4-thiadiazole-2-amine exhibited the greatest antibacterial and anti-inflammatory activity. N 5-diphenyl-1,3,4-thiadiazole-2-amine exhibited the highest antioxidant and anxiolytic efficacy. N-phenyl 5-(2, 4-dimethoxyphenyl)-1, 3, 4 -thiadiazole-2-amine exhibited the greatest anti-diabetic action, while N-phenyl 5-(3-bromophenyl)-1, 3, 4 -thiadiazole-2-amine exhibited the most anxiolytic activity.

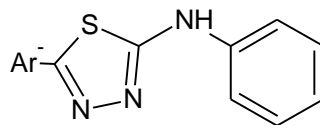


Figure-7

Molecular formulas of 5-aryl N-phenyl-1, 3, 4- thiadiazole 2-amino derivatives

S no.	Molecular formula
1	C <sub>14</sub> H <sub>11</sub> N <sub>3</sub> S
2	C <sub>14</sub> H <sub>10</sub> N <sub>3</sub> SCl
3	C <sub>14</sub> H <sub>11</sub> N <sub>3</sub> SBr
4	C <sub>14</sub> H <sub>10</sub> N <sub>3</sub> SCl
5	C <sub>16</sub> H <sub>15</sub> N <sub>3</sub> SO <sub>2</sub>
6	C <sub>17</sub> H <sub>17</sub> N <sub>3</sub> SO <sub>3</sub>
7	C <sub>16</sub> H <sub>15</sub> N <sub>3</sub> SO <sub>2</sub>
8	C <sub>16</sub> H <sub>16</sub> N <sub>3</sub> S
9	C <sub>15</sub> H <sub>13</sub> N <sub>3</sub> S
10	C <sub>14</sub> H <sub>10</sub> N <sub>3</sub> SBr

Mallesappa N Noolvi et al [4] synthesized a series of 1,3,4-thiadiazole derivatives of 2-(4-formyl-2-methoxyphenoxy) acetic acid Using thiosemicarbazide and the carboxylic acid group of 2-(2-methoxy-4-(3-oxo-3-substituted phenylprop-1-enyl) phenoxy) acetic acid. The antibacterial and antifungal activity of each of the synthesized 1,3,4-thiadiazole derivatives were examined by Using the cup-plate agar diffusion method. Eight different bacterial strain and one fungus strain were used for antimicrobial activity. *S. aureus*, *Salmonella enterica*, *Vibrio cholera*, *Bacillus subtilis*, *Proteus mirabili*, *Escherichia coli* V517, *Mycobacterium smegmatics*, *Pseudomonas aeruginosa* in nutrient agar medium, and one fungal culture *Candida*

*albicans* in sabouraud's dextrose agar medium were used.

The 1,3,4-thiadiazole 4-NO<sub>2</sub> derivative showed antibacterial activity against all the strain. 3-NO<sub>2</sub> derivative showed maximum inhibition against *Salmonella enterica*, & *Vibrio cholera*, 3-OH compound showed activity against *S. Aureus*, 2,4-dihydroxy derivative exhibit maximum activity against *Escherichia coli* V517 and 4-NH<sub>2</sub> showed activity against *Pseudomonas aeruginosa*. Rest of all the 1,3,4-thiadiazole derivative showed moderate to good activity. Whereas 4-NO<sub>2</sub> derivative exhibit inhibition against fungal strain and other all showed moderate to good activity.

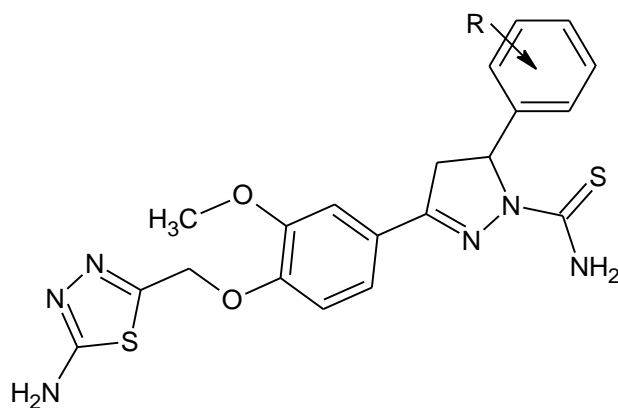


Figure – 8

Where =R

H	2-OCH <sub>3</sub>	2,4 dichloro	3-NH <sub>2</sub>	3-NO <sub>2</sub>
4-OCH <sub>3</sub>	4-P	4-NO <sub>2</sub>	4-Br	4- CH <sub>3</sub>
3-OH	2-OH	4-Cl	2-NH <sub>2</sub>	2,4-Dihydroxy
4-NH <sub>2</sub>	2-Cl	4-OH	4- CH <sub>3</sub>	

S.G.Shingade, and S.S. Shirodkar [5] were prepared some derivatives of isatin base 1,3,4-thiadiazole. The agar well diffusion method was used to test all of the produced compounds for in vitro antibacterial activity. The results showed that all of the compounds had better antibacterial and antifungal action against the selected strains. Compounds with an electron-withdrawing

substituent in the isatin's fifth position i.e.compounds A,B,D,F,I & J showed good antibacterial activity as well as antifungal activity . due to presence of electron withdrawing substituent at the fifth position of isatin, compound D exhibit antitubercular activity, compound I showed better activity due to the presence of electron withdrawing group at position 5<sup>th</sup> and 7<sup>th</sup> .

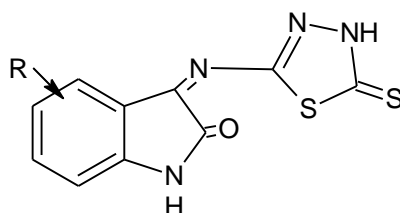


Figure -9

Where	R
A	5-Cl
B	5-Br
C	6-Cl
D	5-F
E	3-H
F	5-CH <sub>3</sub>
G	7-CH <sub>3</sub>
H	4,5-dichloro
I	5,7- dichloro
J	5-NO <sub>2</sub>

Zi-Ning Cui et al [6] were synthesized new series under microwave irradiation, Lawesson's reagent was effectively used to create a variety of 2,5-disubstituted 1,3,4-thiadiazoles in good yields.Their in vitro and in vivo fungicidal activities showed that the title

compounds had a lot of activity against Phytophthora infestans and five other fungi. Transmission electron micrographs (TEM) and scanning electron micrographs (SEM) were used to demonstrate the action of the title compounds against P. infestans. The antifungal

activities of compounds 10, 18, 19, and 25 were superior to those of both pyrimorph and hymexazol C. fulvum, and it was noteworthy that compounds 18 and 20, whose efficacy rates were found to be significantly more effective than the fungicide pyrimorph, showed a

significant inhibition effect (exceeding 80% efficacy rate) against *P. infestans*. All of the evaluated substances, nonetheless, were discovered to be secure for plants.

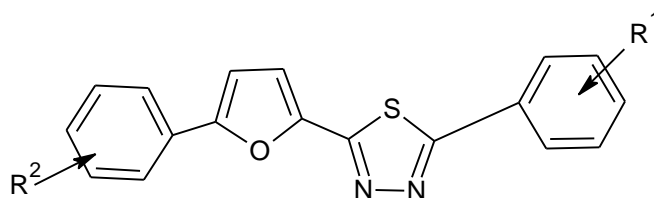


Figure - 10

Where	R <sup>1</sup>	R <sup>2</sup>
1	4-OCH <sub>3</sub>	4-NO <sub>2</sub>
2	4-Br	2-Cl
3	4-Cl	4-OCH <sub>3</sub>
4	2-OCH <sub>3</sub>	4-Cl
5	3-Cl	4-Cl
6	4-OCH <sub>3</sub>	4-Br
7	4-Cl	2-Cl
8	2-Cl	2-Cl
9	4-OEt	2-Cl
10	H	2-Cl
11	4-Cl	2,4-di-F
12	2-Cl	2,4-di-F
13	4-CH <sub>3</sub>	2,4-di-F
14	4-OCH <sub>3</sub>	2,4-di-F
15	3-CH <sub>3</sub>	4-F
16	2-Cl	3-F
17	4-CH <sub>3</sub>	4-F
18	H	4-F
19	4-Cl	H
20	2-Cl	H
21	3-CH <sub>3</sub>	4-OCH <sub>3</sub>

22	4-Cl	4-CH <sub>3</sub>
23	4-OCH <sub>3</sub>	2-F
24	3-CH <sub>3</sub>	2-F
25	H	2-F
26	4-CH <sub>3</sub>	4-Cl
27	4-OCH <sub>3</sub>	2,6-di-F
28	4-Cl	2,6-di-F
29	2-Cl	2-NO <sub>2</sub>
30	4-CH <sub>3</sub>	2-NO <sub>2</sub>
31	4-OCH <sub>3</sub>	3-NO <sub>2</sub>
32	H	2,6-di-F

P. K. Upadhyay and P.Mishra [7] a sequence of 5-(4-substituted phenyl)-1,3,4-thiadiazole-2-amines were produced by the 4 substituted benzoyl thiosemicarbazides were dehydrocyclized with strong sulfuric acid. These substances were tested for their ability to inhibit the growth of *Aspergillus niger* and *Candida albicans* while also having antibacterial effects against *Staphylococcus aureus*, *Bacillus subtilis*,

*Escherichia coli*, and *Pseudomonas aeruginosa*. According to the data, compounds (a), (b), and (c) have strong antibacterial activity, whereas compounds (f) and (g) have significant antifungal activity. c, f, and g are substances having moderate to good anticancer activity. As a result, synthetic substances may be found to have strong antibacterial action and modest antifungal activity.

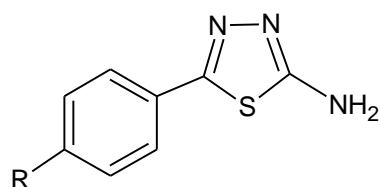


Figure - 11

Where	R
a	F
b	Cl
c	Br
d	I
e	CH <sub>3</sub>
f	OH
g	OCH <sub>3</sub>
h	OC <sub>2</sub> H <sub>5</sub>

Mazin Nadhim Mousa [8] were created Six compounds that include 1,3,4-thiadiazole and Schiff base. Four microorganisms were used to test the antibacterial activity: two gram positive *S. aureus* and *B. cereus*, two gram negative *E. coli*, and *P. aeruginosa* bacteria. The disc diffusion method was employed. When compared

to a conventional medicine, the synthesized molecule demonstrated a noticeable antibacterial activity. The examined germs were most effectively combated by compound **f**, while compound **b** displayed the least effective antibacterial action. The antibacterial activity of compounds **a** and **c** was greater than that of

compounds **b** and lower than that of compounds **d**, **e**, and **f**. The impact on gram-negative bacteria (*E. Coli*)

was greater than that on gram-positive bacteria, with *P. Aeruginosa* seeing the least impact.

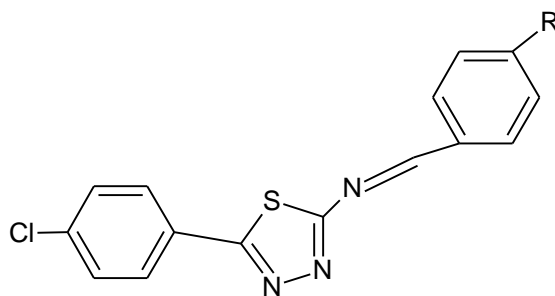


Figure - 12

Where	R
a	H
b	CH <sub>3</sub>
c	OH
d	NO <sub>2</sub>
e	Cl
f	Br

Hanif Shirinzadeh et al [9] were synthesized the new series of 1,3,4-thiazole derivatives. Standard strains were tested for antibacterial and antifungal activities. Antimicrobial activity was tested using the following strains: Gram-positive bacteria include *S. aureus* ATCC 25923, MRSA ATCC 43300, and *Bacillus subtilis* ATCC 6633. Gram-negative bacteria include *E. coli* ATCC 25922, yeast include *Candida albicans* ATCC

10231 and *Candida krusei* ATCC 6258. Chloro phenyl indole 1,3,4 thiazole derivative exhibit excellent activity against *S. Aureus* bacteria. NH<sub>2</sub> containing 1,3,4 thiazole derivative showed excellent activity against MRSA. Other derivatives exhibit good antibacterial activities. All the derivatives showed excellent antifungal activities against *C. krusei* and moderate activities against *C. Albicans*.

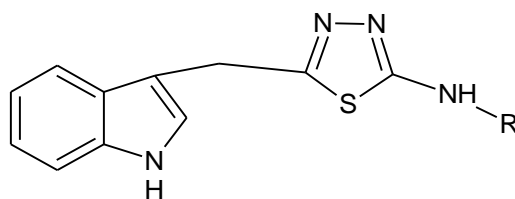
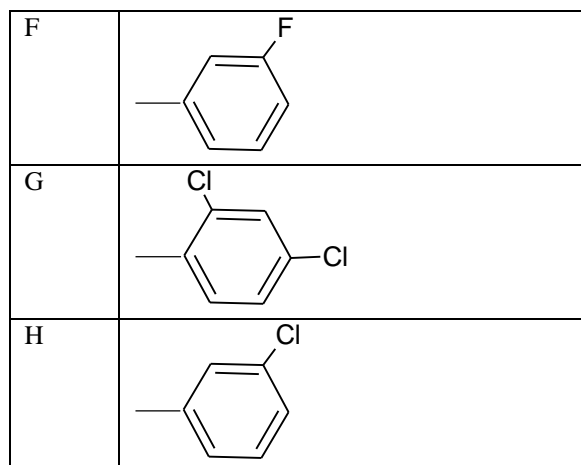


Figure- 13

Where	R
A	CH <sub>3</sub> -CH <sub>2</sub> -
B	CH <sub>3</sub> -CH <sub>2</sub> - CH <sub>2</sub> -
C	H
D	
E	



Ajit Kumar Pandey et al [10] were prepared different novel series of Schiff bases of 2,5 disubstitue 1,3,4-thiadiazole. The analgesic efficacy of 1, 3, and 4-thiadiazole derivatives was assessed in adult male Swiss albino rats (250 g) using the acetic acid-induced writhing reflex method. Swiss albino male adult rats (250 g) were utilized to assess 1, 3, and 4 thiadiazole

compounds' anti-inflammatory efficacy paw edema model produced by carrageenan. The synthesis of a novel class of substances with analgesic and anti-inflammatory effects. Compound f in particular was found to have a low incidence of stomach ulcers and a superior analgesic and anti-inflammatory profile.

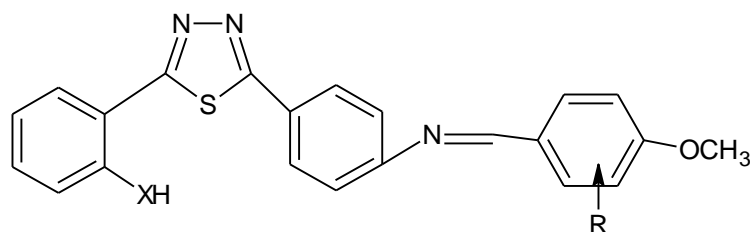


Figure- 14

Where	X	R
a	2-OH	2-NH <sub>2</sub>
b	2-OH	4-NH <sub>2</sub>
c	2-OH	3-NH <sub>2</sub>
d	2-SH	3-NH <sub>2</sub>
e	2-OH	4-NH <sub>2</sub>
f	2-SH	4-NH <sub>2</sub>

Harigopal S Sawarkar et al [11] A unique series of [(5-[4-(acetylamino) phenoxy] methyl-1,3,4-thiadiazol-2-yl) sulfanyl] Under the circumstances of a Schotten-Baumann reaction, sodium salts of N-4-[(5-sulfanyl-1,3,4-thiadiazole-2-yl)methoxy]phenyl acetamide were condensed with variously substituted carboxamides to produce N substituted 2-acetamide and 2/3-propanamide. By using the serial dilution method, all recently synthesized compounds were tested for antibacterial activity against the pathogenic bacteria Staphylococcus aureus (gram positive) and Escherichia

coli (gram negative), as well as for antifungal activity against Aspergillus flavus and Candida albicans. Significant antibacterial activity comparable to that of the conventional medication was present in the majority of the compounds. Among the substances studied, a few showed antibacterial action against bacteria that was as effective as conventional medicine. Due to the presence of electron-withdrawing groups like -NO<sub>2</sub> and -Cl, the compounds' greater activity was explained. Additionally, the compound's phenyl group demonstrated acceptable antibacterial activity.



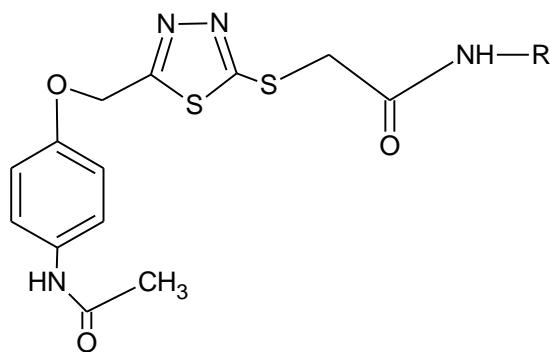


Figure- (15a)

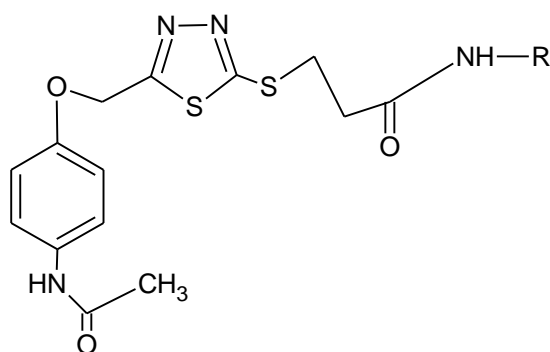


Figure-(15b)

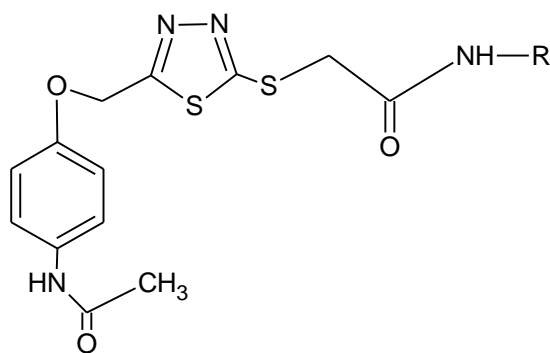


Figure -(15c)

Where R	1	2	3
a	C <sub>6</sub> H <sub>5</sub>	C <sub>6</sub> H <sub>5</sub>	C <sub>6</sub> H <sub>5</sub>
b	2-CH <sub>3</sub> -C <sub>6</sub> H <sub>4</sub>	2-CH <sub>3</sub> -C <sub>6</sub> H <sub>4</sub>	2-CH <sub>3</sub> -C <sub>6</sub> H <sub>4</sub>
c	C <sub>10</sub> H <sub>7</sub>	C <sub>10</sub> H <sub>7</sub>	C <sub>10</sub> H <sub>7</sub>
d	2-Cl-C <sub>6</sub> H <sub>4</sub>	2-Cl-C <sub>6</sub> H <sub>4</sub>	2-Cl-C <sub>6</sub> H <sub>4</sub>
e	4-NO <sub>2</sub> -C <sub>6</sub> H <sub>4</sub>	4-NO <sub>2</sub> -C <sub>6</sub> H <sub>4</sub>	4-NO <sub>2</sub> -C <sub>6</sub> H <sub>4</sub>

Sagar Sahu et al [12] were synthesized some new compounds of heterocyclic containing 1,3,4-thiadiazole derivative. By cyclizing a group of diverse

benzaldehydes with thiosemicarbazide in the presence of various reagents such FeCl<sub>3</sub>, HCHO, and losing a molecule of water, a series of 1,3,4-Thiadiazole

derivatives were created. These derivatives were discovered to have strong antibacterial action. New

series of synthesized compounds were exhibit the antifungal activity rather than antibacterial activity.

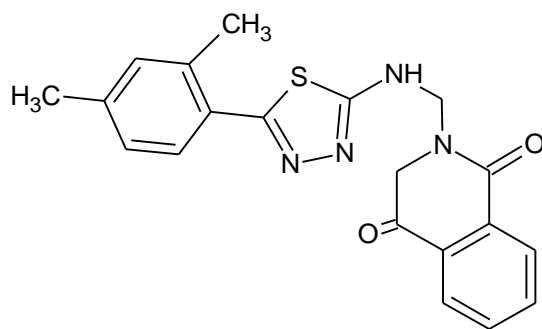


Figure – (16A)

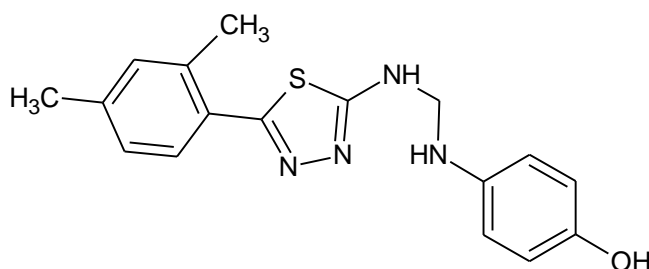


Figure –(16B)

Meihang Chen et al [13] by using the ingredients D-glucose and 5-amino-1,3,4-thiadiazole-2-thiol and following a convergent synthesis method, a number of novel 1,3,4-thiadiazole derivatives of glucosides were produced in good yields. According to the bioactivities' findings, some of the target compounds have effective antifungal properties. The target compounds had moderate to poor antibacterial activity against *Xanthomonas oryzae* pv. *oryzae* (Xoo) and

*Xanthomonas campestris* pv. *citri* (Xcc), in particular, compounds I showed greater bioactivities against *Phytophthora infestans* (*P. infestans*). The poison plate method is used to assess the in vitro antifungal properties of the target compounds against *G. zeae*, *Botryosphaeria dothidea* (*B. dothidea*), *Phomopsis* sp., *P. infestans*, and *Thanatephorus cucumeris* (*T. cucumeris*).

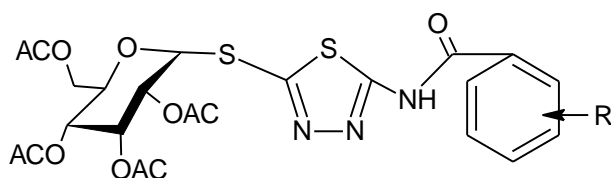


Figure -17

Where	R
A	2-CH <sub>3</sub>
B	3-CH <sub>3</sub>
C	4-CH <sub>3</sub>
D	2-OCH <sub>3</sub>
E	3-OCH <sub>3</sub>
F	4-OCH <sub>3</sub>

G	2-F
H	3-F
I	4-F
J	2- Cl
K	3- Cl
L	4- Cl
M	2-Br
N	3- Br
O	4 -Br
P	2-NO <sub>2</sub>
Q	4 NO <sub>2</sub>

Aadesh Kumar et al [14] were prepared novel series of 1,3,4-thiadiazole derivatives. all the novel compounds were synthesized with the help of different benzaldehydes were mixed with phosphorous oxychloride and thiosemicarbazide in same quantity. The novel synthetic compounds' antimicrobial effects

were investigated using the agar diffusion method and common strains of Gram-positive and -negative bacteria. compounds 1,2,3 and 4 exhibit good antibacterial activity against gram positive and gram negative bacteria.

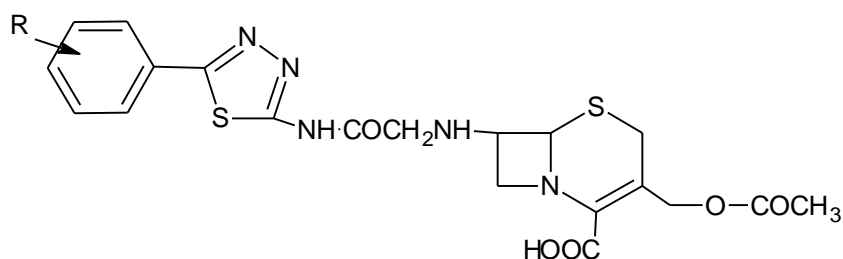


Figure - 18

Where	R
1	H
2	o-CH <sub>3</sub>
3	p- CH <sub>3</sub>
4	o-Cl
5	p-Cl
6	o-Br
7	p-Br
8	m-NO <sub>2</sub>
9	p- NO <sub>2</sub>
10	2,4-Cl
11	OH
12	OCH <sub>3</sub>

Ahmad E. Mohamed et al [15] were chitosan has been used to create the synthetic 1,3,4-thiadiazole compounds, which have been used to create two novel polymers known as Cs-EATT and Cs-BATT. The activity of two synthesized chitosan derivatives designated as Cs-EATT and Cs-BATT to control the growth of pathogenic Gram-positive bacteria (*Staphylococcus aureus* ATCC6538 and *Bacillus*

*subtilis* ATCC6633), Gramnegative bacteria (*Escherichia coli* ATCC8739 and *Pseudomonas aeruginosa* ATCC9022), and *Candida albicans* ATCC10231 (unicellular fungi) was assessed by the agar well diffusion technique. Data analysis revealed that Cs-EATT had stronger activity against all types of bacteria than Cs-BATT. *C. albicans* was not among the organisms tested.

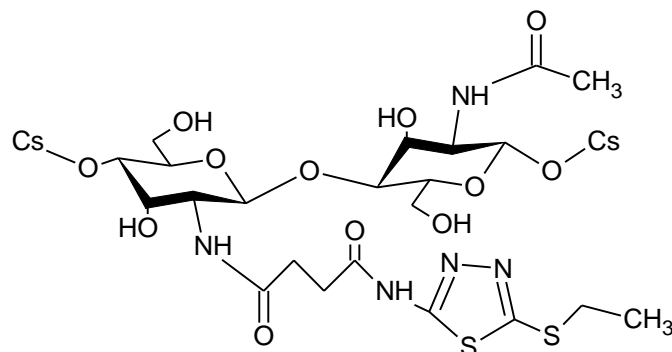


Figure -(19 a)

Cs-EATT = chitosan [5-(ethyl)-1,3,4-thiadiazole-2-amine  
Where Cs =  $\text{CH}_2\text{Cl}_2/(\text{C}_2\text{H}_5)_3\text{N}$

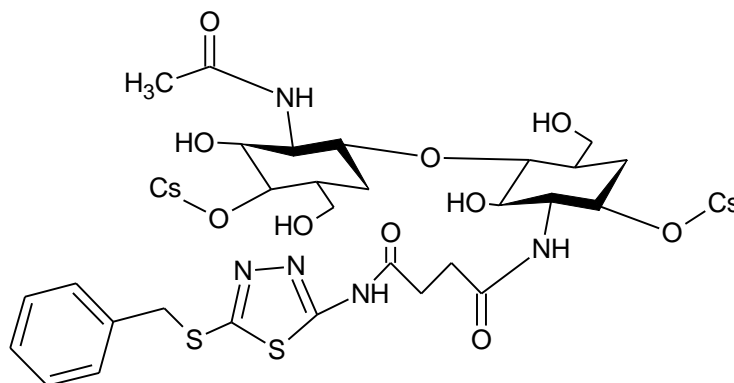


Figure-(19 b)

Cs-BATT= chitosan [5-(benzylthio)-1,3,4-thiadiazole-2-amine  
Where Cs =  $\text{CH}_2\text{Cl}_2/(\text{C}_2\text{H}_5)_3\text{N}$

Asrat Ergena et al [16] were made seven 1, 3, and 4-thiadiazole 5- and 2-thioate derivatives by utilizing acetone as a solvent and  $\text{K}_2\text{CO}_3$  as a base in a substitution procedure. On Swiss albino mice, the diuretic action of the substances was assessed by measuring urine volume, urinary pH, and urinary  $\text{Na}^+$ ,  $\text{K}^+$ , and  $\text{Cl}^-$ . The result revealed an increase in the excretion of water and electrolytes through the urine.

When compared to the negative control and the 5-amino-substituted derivatives, the 5-methyl-substituted derivatives of 1, 3, and 4-thiadiazoles significantly increased the excretion of both water and electrolytes. The 2-thioate group of 5-methyl-1, 3, 4-thiadiazole's para-nitro-substituted benzene ring displayed the maximum diuretic activity, whilst the propanethioate group in the second position and the amine group in the fifth position displayed the lowest diuretic activity. The results of this investigation revealed that all of the substances have diuretic activity, particularly 5-methyl derivatives of 1, 3, and 4-thiadiazoles showed notable diuretic activity.

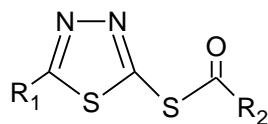


Figure- 20

Where	R <sub>1</sub>	R <sub>2</sub>
1	CH <sub>3</sub>	
2	CH <sub>3</sub>	
3	NH <sub>2</sub>	
4	CH <sub>3</sub>	
5	CH <sub>3</sub>	
6	NH <sub>2</sub>	CH <sub>3</sub> -CH <sub>2</sub>
7	NH <sub>2</sub>	

Hakan S. Sayiner et al [17] were prepared a new series 1,3,4-thiadiazole by using Phenylthiosemicarbazide and methoxy cinnamic acid in the presence of phosphorus oxychloride. The 1,3,4-thiadiazole molecules were synthesized, and tests on several Gram-positive and Gram-negative bacterial strains were done to determine their antibacterial activity. The Gram-negative bacteria are made up of Salmonella kentucky, Enterobacter aerogenes, Klebsiella pneumoniae, Escherichia coli, Proteus, and Pseudomonas aeruginosa. The Gram-positive microorganisms under investigation

include Listeria monocytogenes, Staphylococcus aureus, Enterococcus durans, Serratia marcescens, Staphylococcus epidermidis, alpha Streptococcus haemolyticus, Staphylococcus hominis, and Enterococcus faecium. Staphylococcus epidermidis and alpha-Streptococcus haemolyticus were both inhibited by molecules 1, 3, and 4. The docking investigation employing the Kinase ThiM from Klebsiella pneumoniae confirmed the experimental findings. The Staphylococcus epidermidis protein was inhibited by every substance that was studied.

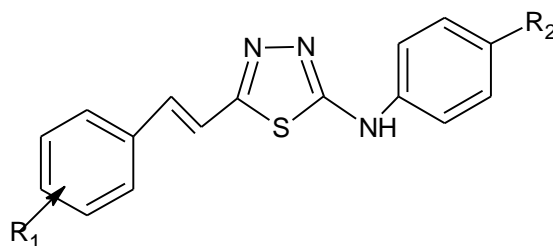


Figure – 21

Where	R <sub>1</sub>	R <sub>2</sub>
1	5-OCH <sub>3</sub>	NO <sub>2</sub>
2	6-OCH <sub>3</sub>	NO <sub>2</sub>
3	5-OCH <sub>3</sub>	CH <sub>3</sub>
4	6-OCH <sub>3</sub>	CH <sub>3</sub>

Monica G. Kamel et al [18] were by using N-(4-nitrophenyl)acetohydrazonoyl bromide and 1-[3,5-dimethyl-1-(4-nitrophenyl)-1H-pyrazol-4-yl]ethan-1-one as starting materials, a number of 1,3,4-thiadiazole derivatives were developed and created. 1-[3,5-dimethyl-1-(4-nitrophenyl)-1H-pyrazol-4-yl]ethan-1-one can be converted into 2-[1-[5-methyl-1-(4-nitrophenyl)-1H-pyrazol-4-yl]ethylidene]hydrazine derivatives by treating it with methyl hydrazine carbodithioate or hydrazine carbthioamide. In order to create the desired 1,3,4-thiadiazolyl derivatives, 2-[1-[5-methyl-1-(4-nitrophenyl)-1H-pyrazol-4-yl] ethylidene] hydrazine derivatives were combined with derivatives of hydrazonoyl chloride. In the presence of

triethylamine, N-(4-nitrophenyl)acetohydrazonoyl bromide was reacted with 2-[(methylthio)carbonyl]hydrazones to produce the appropriate 1,3,4-thiadiazole derivatives. The newly created compounds were examined for their potential as antibacterial agents. Gram-positive bacteria (*B. mycoides*) were found to have the most antibacterial action, whilst yeast (*C. albicans*) and gram-negative bacteria (*E. coli*) were shown to be the least sensitive to the chemical compounds. Compound 14 demonstrated more antibacterial activity than the positive control, suggesting that this substance may one day be employed to stop the spread of microorganisms.

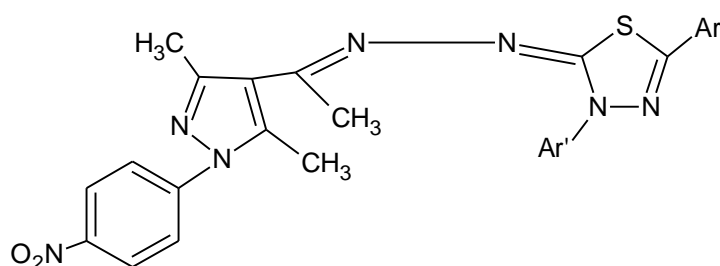


Figure (-22 A)

Where	Ar	Ar'
A	C <sub>6</sub> H <sub>5</sub>	C <sub>6</sub> H <sub>5</sub>
B	C <sub>6</sub> H <sub>5</sub> -CH=CH	C <sub>6</sub> H <sub>5</sub>
C	2-furyl	4-NO <sub>2</sub> C <sub>6</sub> H <sub>4</sub>
D	2-thienyl	4-NO <sub>2</sub> C <sub>6</sub> H <sub>4</sub>

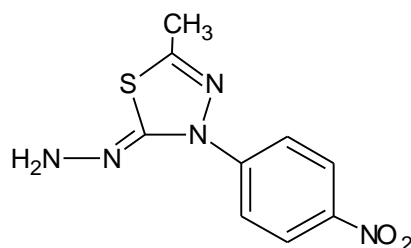


Figure- (22B)

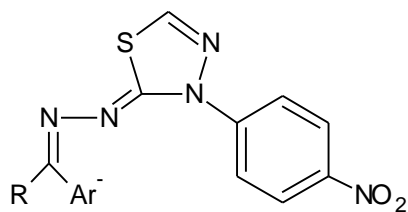


Figure- (22C)

Where	R	Ar
A	CH <sub>3</sub>	EtOCO
B	H	2-Thienyl
C	CH <sub>3</sub>	2-Thienyl
D	H	2-Furyl
E	CH <sub>3</sub>	2-Furyl
F	CH <sub>3</sub>	C <sub>6</sub> H <sub>5</sub>
G	CH <sub>3</sub>	2-Pyridinyl
H	H	3-indolyl

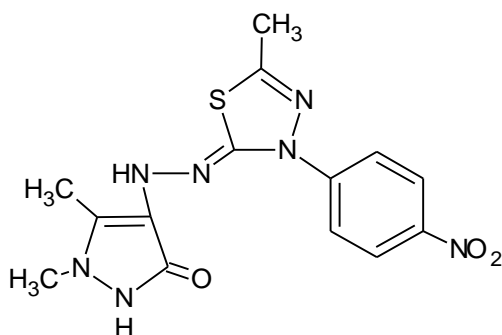


Figure- (22D)

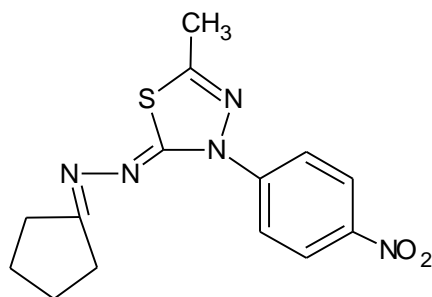


Figure- (22E)

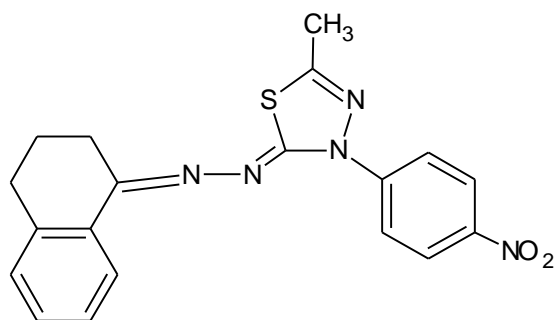


Figure- (22F)

Roaa Salman Baiwn et.al.[19] a number of brand-new 1,3,4 thiadiazole derivatives with imine groups were created. Novel thiadiazole derivatives (e1-6) were examined for their ability to fight against gram-positive strains of bacteria including *Staphylococcus aureus* and *Enterococcus faecalis* as well as gram-negative strains

like *Escherichia coli* and *Klebsiella pneumoniae*. Against the majority of studied bacterial species, all thiadiazole compounds exhibit antibacterial activity. The antibacterial activity of the compounds containing electron-donating groups in the para position appeared to be higher.

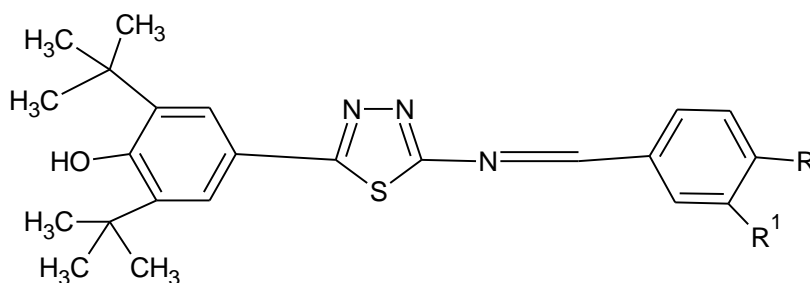


Figure- 23

Where	R	R <sup>1</sup>
1	H	H
2	H	OCH <sub>3</sub>
3	Cl	H
4	OH	H
5	NO <sub>2</sub>	H
6	OCH <sub>3</sub>	H

### Conclusion

Significant antibacterial activity was found in thiadiazole's heterocyclic derivatives. To develop better agents, additional research is required for a number of compounds that exhibit promise. These could serve as leading compounds in the future. After examining their IR and H-NMR studies, the structures of newly synthesized thiadiazole derivatives were determined. Following the antimicrobial screening, it was determined whether every derivative that had been generated had effective activity against the pathogens tested.

### Reference:

1. Tijeno Nkol, Denizs. Dog Ruer, Leylaurun, Selcenadak, Semihao Zkan, & M. Fethi S, Ahin Synthesis and antimicrobial activity of new 1,2,4-triazole and 1,3,4-thiadiazole derivatives *Journal of Enzyme Inhibition and Medicinal Chemistry*, April 2008; 23(2): 277–284
2. Alok Pandey, R. Rajavel, Sandeep Chandraker, And Deepak Dash Synthesis of Schiff Bases of 2-amino-5-aryl-1,3,4-thiadiazole and Its Analgesic, AntiInflammatory and Anti-Bacterial Activity Synthesis of Schiff Bases of 2-amino-5-aryl-1,3,4-thiadiazole and



- Its Analgesic, Anti-Inflammatory and Anti-Bacterial Activity ISSN: 0973-4945; CODEN ECJHAOE-Journal of Chemistry 2012, 9(4), 2524-2531
- Lincy Joseph, Mathew George and Prabha Mathews synthesis and characterization of novel 1, 3, 4-thiadiazole derivatives and screening for certain biological activities IJPCBS 2015, 5(4), 928-937 ISSN: 2249-9504
  - Malleshappa N. Noolvi a,\*, Harun M. Patel b, Sarita Kamboj c, Swaranjit Singh Cameotra Synthesis and antimicrobial evaluation of novel 1,3,4-thiadiazole derivatives of 2-(4-formyl-2-methoxyphenoxy) acetic acid Arabian Journal of Chemistry (2016) 9, S1283–S1289
  - S.G. Shingade, S.S. Shirodkar Synthesis and antimicrobial screening of thiadiazole derivatives Journal of Advanced chemical Science 2(3) (2016) 309-312
  - Zi-Ning Cui, Ya-Sheng Li, De-Kun Hu, Hao Tian, Jia-Zhen Jiang, Yuan Wang & Xiao-Jing Yan Synthesis and fungicidal activity of novel 2,5-disubstituted-1,3,4-thiadiazole derivatives containing 5-phenyl-2-furan Scientific Reports | 6:20204 | DOI: 10.1038/srep20204 Published: 29 January 2016
  - P. K. Upadhyay and P. Mishra synthesis, antimicrobial and anticancer activities of 5-(4-substituted-phenyl)-1,3,4 thiadiazole-2-amines Vol. 10 | No. 1 | 254 -262 | January - March | 2017 ISSN: 0974-1496 | e-ISSN: 0976-0083 | CODEN: RJCABP
  - Mazin Nadhim Mousa synthesis, characterization and evaluation of antibacterial activity of 1,3,4- thiadiazole derivatives containing Schiff bases IJPCBS 2017, 7(1), 71-76 ISSN: 2249-9504
  - Hanif Shirinzadeh, Sibel Süzen, Nurten Altanlar, Andrew D. Westwell Antimicrobial Activities of New Indole Derivatives Containing 1,2,4-Triazole, 1,3,4-Thiadiazole and Carbothioamide Turk J Pharm Sci 2018;15(3):291-297 DOI: 10.4274/tjps.55707
  - Ajit Kumar Pandey, Pranita P Kashyap, Chanchal Deep Kaur, Hemant A Sawarkar, Hemant J Dhongade and Mukesh Kumar Singh New 1,3,4-thiadiazole Derivatives Endowed with Analgesic and Anti-inflammatory Activities Chiang Mai J. Sci. 2018; 45(2) : 917-926
  - Harigopal S Sawarkar, Mahavir Singh, Birendra Shrivastav, R. L. Bakal synthesis and antimicrobial activities of novel 1,3,4-thiadiazole bearing carboxamides derivatives journal of critical reviews ISSN- 2394-5125 VOL 7, ISSUE 02, 2020
  - Sagar Sahu, Tanesh Sahu, Gunjan Kalyani, Bina Gidwani Synthesis and Evaluation of Antimicrobial Activity of 1, 3, 4-Thiadiazole Analogues for Potential Scaffold journal of pharmacopuncture 2021,.
  - Meihang Chen, Xun Zhang, Daowang Lu, Hairong Luo, Zengyan Zhou, Xufeng Qin, Wenneng Wu and Guoping Zhang ,Synthesis and Bioactivities of Novel 1,3,4-Thiadiazole Derivatives of Glucosides, Frontiers in Chemistry March 2021 | Volume 9 | Article 645876 doi: 10.3389/fchem.2021.645876
  - Aadesh Kumar, N.A Farooqui, Nidhi Dhama and Vikrant Verma novel thiadiazole derivatives: synthesis, characterization and its antibacterial activity, RASĀYAN J. Chem., Special Issue, 2021 ISSN: 0974-1496
  - Ahmad E. Mohamed, Walid E. Elgammal, Aya M. Dawaba, Ahmed G. Ibrahim, Amr Fouda and Saber M. Hassan A novel 1,3,4-thiadiazole modified chitosan synthesis, characterization, antimicrobial activity, and release study from film dressings Applied Biological Chemistry (2022) 65:54 <https://doi.org/10.1186/s13765-022-00725-7>
  - Asrat Ergena, Yerra Rajeshwar, and Gebremedhin Solomon Synthesis and Diuretic Activity of Substituted 1,3,4-Thiadiazoles Hindawi Scientifica Volume 2022, Article ID 3011531, 9 pages <https://doi.org/10.1155/2022/3011531>
  - Hakan S. Sayiner, Mehmet . Yilmazer, Aisha. T. Abdelsalam, Mohamed A. Ganim, Cengiz Baloglu, Yasemin Celik Altunoglu, Mahmut Gur, Murat Saracoglu, Mohamed S. Attia, Safwat A. Mahmoud, Ekram H. Mohamed, Rabah Boukherroub, Nora Hamad Al-Shaalan, Sarah Alharthi, Fatma Kandemirli and Mohammed A. Amin Synthesis and characterization of new 1,3,4-thiadiazole derivatives: study of their antibacterial activity and CT-DNA binding rsc.li/rsc-advances, October 2022. DOI: 10.1039/d2ra02435g
  - Monica G. Kamel Farid M. Sroor Abdelmageed M. Othman Hamdi M. Hassaneen Tayseer A. Abdallah Fatma M. Saleh Mohamed A. Mohamed Teleb Synthesis and biological evaluation of new 1,3,4-thiadiazole derivatives as potent antimicrobial agents. Monatshefte für Chemie - Chemical Monthly (2022) 153:929–937 <https://doi.org/10.1007/s00706-022-02967-z>
  - Roaa Salman Baiwn, Hiba Najeh Alsaad, Ali Khamas Mohammed Synthesis, Characterization, and Evaluation of the Antibacterial Activity of Novel 5-aryl-2-amino 1,3,4 Thiadiazole Derivatives Egypt. J. Chem. Vol. 65, No. 3 pp. 111 - 116 (2022)