ejpmr, 2017,4(8), 464-469

SJIF Impact Factor 4.161

EUROPEAN JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.ejpmr.com

Research Article

ISSN 2394-3211

EJPMR

SYNTHESIS, CHARACTERIZATION AND ANTIMICROBIAL ACTIVITY OF 2-(ARYL)-5-(ARYLIDENE)-4-THIAZOLIDINONE DERIVATIVES.

[1]*Rakesh Kumar and [2]Shailendra Patil

[1]Vaish Institute of Pharmaceutical Education and Research, Rohtak-124001.
[2]SVN Institute of Pharmaceutical Sciences, Swami Vivekanand University, Sagar- 470003.

***Corresponding Author: Rakesh Kumar**

Vaish Institute of Pharmaceutical Education and Research, Rohtak-124001.

Article Received on 14/06/2017 **Article Revised on 04/07/2017** **Article Accepted on 24/07/2017**

ABSTRACT

A series of 2-(aryl)-5-(arylidene)-4-thiazolidinone derivatives (TH1-T15) was synthesized and evaluated for their antimicrobial potential. Antimicrobial Activity was performed by tube dilution and zone of inhibition methods against Gram negative *E. Coli*, Gram positive bacteria: *B. Subtilis, S. aureus*, and fungal strains: A. *niger* and *C. albicans*. Among the synthesized derivatives, compounds 2, 10 and 12 was found to be most active against bacterial strains and 3, 8 and 13 was found to be most active against the fungal strains. All the titled compounds (TH1-T15) were characterized by ^{1}H NMR and IR spectral data.

KEYWORDS: 4-Thiazolidinone, Hydrazone, Thiazole, Antimicrobial activity.

INTRODUCTION

Infectious diseases are responsible for a great number of deaths in the world population. The clinical use of many compounds developed to fight against infectious diseases has been limited by their relatively high risk of toxicity, bacterial resistance and/or pharmacokinetic deficiencies. A major research emphasis to counter this growing problem is the development of antimicrobials structurally unrelated to the existing molecules. The reduction of sensibility to antimicrobial agents in current use has been increasing for a great variety of pathogens and the resistance to multiple drugs is common for several microorganisms, especially for Gram positive bacteria. Infection by methicillin-resistant Staphylococcus aureus (MRSA) and vancomycin-resistant Enterococci (VRE) presents a difficult problem for medicine. Given the evidence for the rapid global spread of resistance the need for discovery or optimization of antimicrobial agents active against these resistant strains is of paramount importance.[1]

Thiazolidinones are of considerable importance as pharmacophoric groups due to their known biological activities that include antimicrobial[2-4], anticancer[5-6], antimycobacterial[7-8], analgesic and anti-inflammatory[9-10], antioxidant activities.[11] These works prompted us to synthesize the novel derivatives of 2-(aryl)-5-(arylidene)-4-thiazolidinone and evaluation their antimicrobial activity.

Experimental

Progress of reaction was checked by thin layer chromatography (TLC) on silica gel coated aluminum sheets (Merck silica gel –G). Melting points were determined in open capillary tubes and are uncorrected. ^{1}H NMR spectra were determined by Bruker Avance II 400 NMR spectrometer in appropriate Dimethyl sulfoxide (DMSO) and are expressed in parts per million (δ, ppm) downfield from tetramethylsilane (internal standard). Infra-red spectra were recorded on Perkin Elmer Spectrum RXI FTIR spectrophotomer in KBr phase. All the synthesized titled derivatives have been evaluated for their antimicrobial potential.

Chemistry

A series of novel 2,5-disubstituted-4-thiazolidinone have been synthesized. The reaction between *p*-Nitro acetophenone, thiourea and iodine yielded the corresponding 4-(4-nitrophenyl)thiazol-2-amine **(2)** which on reaction with required aromatic aldehydes afforded the corresponding hydrazone of 4-(4-nitrophenyl)-thiazol-2-amine **(3)** in appreciable yield. Further the hydrazone were condensed with required amount of thioglycolic acid to yield 2-substituted 4hiazolidinones **(4)**. In the next step 2-disubstituted-4-thiazolidinone was reacted with aromatic aldehydes (0.01 M) and anhydrous sodium acetate in glacial acetic acid yielded title compounds (TH1-TH15) **(5)**.

General procedure of 4-thiazolidinone derivatives

Synthesis of 4-(4-nitrophenyl)thiazol-2-amine

p-Nitro acetophenone, (0.01m), thiourea (0.02m) and iodine (0.01 m) were dissolved in appropriate amount of ethanol and refluxed for 8 hours on a heating mantle. The reaction mixture was then cooled and poured on to the crushed ice and NaOH solution (10%) was added. The

solid thus acquired was filtered, washed with water, and the product was recrystallized from rectified spirit. The purity of the sample was tested by TLC using the solvent system petroleum ether and ethyl acetate 8:2.[12]

Synthesis of hydrazone of 4-(4-nitrophenyl)-thiazol-2-amine

A mixture of (0.025 M) 4-(4-nitrophenyl)thiazol-2-amine was refluxed for about 2 hours with required amount of aldehydes (0.025 M) and methanol in the presence of a catalytic amount of glacial acetic acid. The solid thus acquired was filtered, washed with water, and the product was recrystallized from rectified spirit to give the corresponding hydrazones.

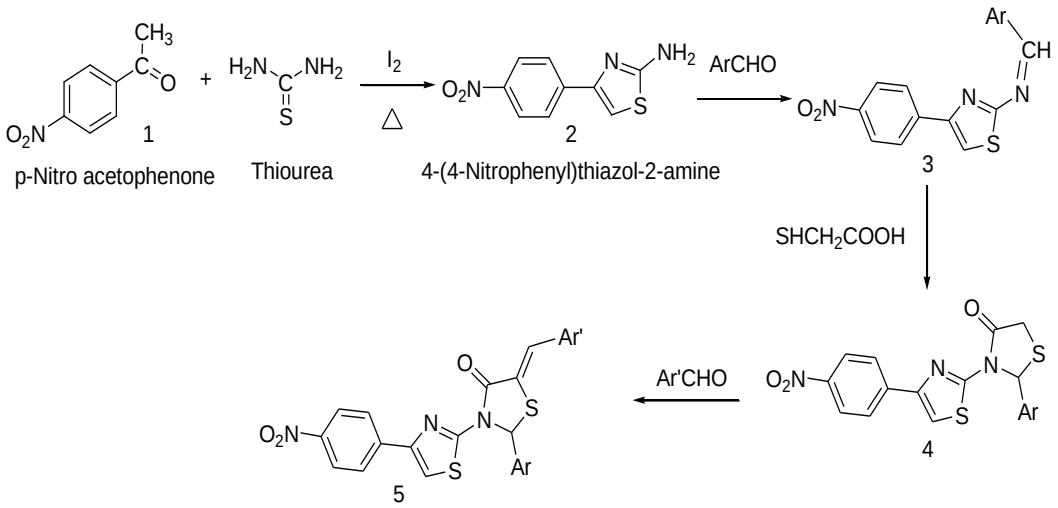
Synthesis of 2-disubstituted-4-thiazolidinone

A mixture of (0.015 M) hydrazone of 4-(4-nitrophenyl)-thiazol-2-amine and required amount of thioglycolic acid (0.015 M) in DMF was refluxed for about 6 h, containing a pinch of anhydrous $ZnCl_2$. The reaction mixture was cooled and poured on to crushed ice. The solid thus acquired was filtered, washed with water and the product was recrystallized from rectified spirit to obtained the titled derivatives.[4]

Synthesis of 2,5-disubstituted-4-thiazolidinone

A mixture of (0.01 M) 2-substituted-4-thiazolidinone required aromatic aldehydes (0.01 M) and anhydrous sodium acetate in glacial acetic acid (20 ml) and refluxed for 5–7 h. After cooling, the solution was poured on crushed ice to precipitate the product. The product was recrystallized from rectified spirit.[4]

Synthetic pathway for preparation of title 4-thiazolidinone derivatives is shown in Scheme 1. Physical and analytical data of synthesized derivatives are presented in Table 1.



Scheme 1

Table 1 Physical data of title compounds (TH1-TH15)

Comp. no.	Ar	Ar'	Molecular Formula	Molecular Weight	Melting Points (°C)	%Yields	R_f
TH1	C_6H_5-	C_6H_5-	$C_{25}H_{17}N_3O_3S_2$	471.55	210-212	72.71	0.64
TH2	C_6H_5	2-$NO_2C_6H_4$	$C_{25}H_{16}N_4O_5S_2$	516.55	198-200	78.21	0.67
TH3	C_6H_5	4-ClC_6H_4	$C_{25}H_{16}ClN_3O_3S_2$	506.00	207-209	75.33	0.62
TH4	C_6H_5	4-OHC_6H_4	$C_{25}H_{17}N_3O_4S_2$	487.55	186-188	81.12	0.76
TH5	C_6H_5	3-BrC_6H_4	$C_{25}H_{16}BrN_3O_3S_2$	550.45	199-201	69.66	0.58
TH6	C_6H_5	4-FC_6H_4	$C_{25}H_{16}FN_3O_3S_2$	489.54	178-180	71.72	0.56
TH7	C_6H_5	3-$OCH_3C_6H_4$	$C_{26}H_{19}N_3O_4S_2$	501.58	227–230	67.22	0.47
TH8	C_6H_5	2-ClC_6H_4	$C_{25}H_{16}ClN_3O_3S_2$	506.00	188–190	84.11	0.62
TH9	C_6H_5	4-$OCH_3C_6H_4$	$C_{26}H_{19}N_3O_4S_2$	501.58	215-217	88.22	0.56
TH10	C_6H_5	3-$NO_2C_6H_4$	$C_{25}H_{16}N_4O_5S_2$	516.55	203-205	79.11	0.60
TH11	2-$NO_2C_6H_4$	C_6H_5-	$C_{25}H_{16}N_4O_5S_2$	516.55	180-182	82.75	0.63
TH12	2-$NO_2C_6H_4$	2-$NO_2C_6H_4$	$C_{25}H_{15}N_5O_7S_2$	561.55	271-272	68.25	0.68
TH13	2-$NO_2C_6H_4$	4-ClC_6H_4	$C_{25}H_{15}ClN_4O_5S_2$	550.99	201-203	75.01	0.58
TH14	2-$NO_2C_6H_4$	4-OHC_6H_4	$C_{25}H_{16}N_4O_6S_2$	532.55	168-170	80.02	0.68
TH15	2-$NO_2C_6H_4$	3-BrC_6H_4	$C_{25}H_{15}BrN_4O_5S_2$	595.44	189-191	79.64	0.56

Chloroform: benzene: glacial acetic acid (3:1:1).

Spectral Data

(Z)-5-benzylidene-3-(4-(4-nitrophenyl)thiazol-2-yl)-2-phenylthiazolidin-4-one (TH1): IR (KBr, cm^{-1}): 3010 (C-H Ar), 1722 (C=O), 1638(C=C Ar), 1603 (C=N), 1561 (NO_2), 1404 (C-N), 693(C-S); ^{1}H NMR (DMSO-*d*6, 400 MHz): 7.41-7.09 (m, 14H, ArH), 7.31 (s, 1H, CH), 6.72(s, 1H, CH, thiazolidinone), 6.69 (s, 1H, CH, thiazole).

(Z)-5-(2-nitrobenzylidene)-3-(4-(4-nitrophenyl)thiazol-2-yl)-2-phenylthiazolidin-4-one (TH2): IR (KBr, cm^{-1}): 3146 (C-H Ar), 1742 (C=O), 1649(C=C Ar), 1622 (C=N), 1519 (NO_2), 1421 (C-N), 670(C-S); ^{1}H NMR (DMSO-*d*6, 400 MHz): 8.99-7.11 (m, 13H, ArH), 7.70 (s, 1H, CH), 6.81 (s, 1H, CH, thiazole), 6.79 (s, 1H, CH, thiazolidinone).

(**Z)-5-(4-chlorobenzylidene)-3-(4-(4-nitrophenyl)thiazol-2-yl)-2-phenylthiazolidin-4-one (TH3):** IR (KBr, cm^{-1}): 3119 (C-H Ar), 1715 (C=O), 1649(C=C Ar), 1622 (C=N), 1519 (NO_2), 1419 (C-N), 736(Cl), 667(C-S); ^{1}H NMR (DMSO-*d*6, 400 MHz): 8.45-7.56 (m, 13H, ArH), 7.59 (s, 1H, CH), 6.72 (s, 1H, CH, thiazole), 6.69 (s, 1H, CH, thiazolidinone).

(Z)-5-(4-hydroxybenzylidene)-3-(4-(4-nitrophenyl)thiazol-2-yl)-2-phenylthiazolidin-4-one (TH4): IR (KBr, cm^{-1}): 3620 (OH), 3075 (C-H Ar), 1626 (C=C Ar), 1607 (C=N), 1521 (NO_2), 1480 (C-N), 676(C-S); ^{1}H NMR (DMSO-*d*6, 400 MHz): 8.80-7.25 (m, 13H, ArH), 7.29 (s, 1H, CH), 6.49 (s, 1H, CH, thiazole), 6.47 (s, 1H, CH, thiazolidinone), 4.45(s,1H, OH).

(Z)-5-(3-bromobenzylidene)-3-(4-(4-nitrophenyl)thiazol-2-yl)-2-phenylthiazolidin-4-one (TH5): IR (KBr, cm^{-1}): 3013 (C-H Ar), 1746 (C=O), 1696(C=C Ar), 1630 (C=N), 1563 (NO_2), 1436 (C-N), 680(C-S), 631(Br); ^{1}H NMR (DMSO-*d*6, 400 MHz): 7.58-7.00 (m, 13H, ArH), 7.21 (s, 1H, CH), 6.33 (s, 1H, CH, thiazole), 5.81 (s, 1H, CH, thiazolidinone).

(Z)-5-(4-fluorobenzylidene)-3-(4-(4-nitrophenyl)thiazol-2-yl)-2-phenylthiazolidin-4-one (TH6): IR (KBr, cm^{-1}): 3025 (C-H Ar), 1658(C=C Ar), 1554 (NO_2), 1490 (C-N), 1169(C-F), 680(C-S); ^{1}H NMR (DMSO-*d*6, 400 MHz): 7.96-7.27 (m, 13H, ArH), 7.27 (s, 1H, CH), 7.22 (s, 1H, CH, thiazole), 6.96 (s, 1H, CH, thiazolidinone).

(Z)-5-(3-methoxybenzylidene)-3-(4-(4-nitrophenyl)thiazol-2-yl)-2-phenylthiazolidin-4-one (TH7): IR (KBr, cm^{-1}): 3107 (C-H Ar), 1634(C=C Ar), 1533 (NO_2), 1486 (C-N), 1296 (C–O–C str), 627(C-S); ^{1}H NMR (DMSO-*d*6, 400 MHz): 7.89-7.11 (m, 13H, ArH), 7.17 (s, 1H, CH), 6.69 (s, 1H, CH, thiazole), 5.58 (s, 1H, CH, thiazolidinone), 3.87 (s, 3H, -OCH_3).

(Z)-5-(2-chlorobenzylidene)-3-(4-(4-nitrophenyl)thiazol-2-yl)-2-phenylthiazolidin-4-one (TH8): IR (KBr, cm^{-1}): 3007 (C-H Ar), 1749 (C=O), 1697(C=C Ar), 1639 (C=N), 1575 (NO_2), 1458 (C-N), 724(Cl), 629(C-S); ^{1}H NMR (DMSO-*d*6, 400 MHz): 7.89-7.13 (m, 13H, ArH), 7.39 (s, 1H, CH), 7.12 (s, 1H, CH, thiazole), 6.84 (s, 1H, CH, thiazolidinone).

(Z)-5-(4-methoxybenzylidene)-3-(4-(4-nitrophenyl)thiazol-2-yl)-2-phenylthiazolidin-4-one (TH9): IR (KBr, cm^{-1}): 3012 (C-H Ar), 1675(C=C Ar), 1626 (C=N), 1558 (NO_2), 1419 (C-N), 1212 (C–O–C str), 672(C-S); ^{1}H NMR (DMSO-*d*6, 400 MHz): 8.71-7.47 (m, 13H, ArH), 7.35 (s, 1H, CH), 7.04 (s, 1H, CH, thiazole), 6.93 (s, 1H, CH, thiazolidinone), 3.82 (s, 3H, -OCH_3).

(Z)-5-(3-nitrobenzylidene)-3-(4-(4-nitrophenyl)thiazol-2-yl)-2-phenylthiazolidin-4-one (TH10): IR (KBr, cm^{-1}): 3010 (C-H Ar), 1723 (C=O), 1629(C=C Ar), 1602 (C=N), 1577 (NO_2), 1470 (C-N), 676(C-S); ^{1}H NMR (DMSO-*d*6, 400 MHz): 8.55-7.19 (m, 13H, ArH), 7.37 (s, 1H, CH), 7.84 (s, 1H, CH, thiazole), 6.77 (s, 1H, CH, thiazolidinone).

(Z)-5-benzylidene-2-(2-nitrophenyl)-3-(4-(4-nitrophenyl)thiazol-2-yl)thiazolidin-4-one (TH11): IR (KBr, cm^{-1}): 3068 (C-H Ar), 1697 (C=O), 1671(C=C Ar), 1620 (C=N), 1543 (NO_2), 1418 (C-N), 693(C-S); ^{1}H NMR (DMSO-*d*6, 400 MHz): 7.94-6.95 (m, 13H, ArH), 7.36 (s, 1H, CH), 6.87 (s, 1H, CH, thiazole), 6.82 (s, 1H, CH, thiazolidinone).

(Z)-5-(2-nitrobenzylidene)-2-(2-nitrophenyl)-3-(4-(4-nitrophenyl)thiazol-2-yl)thiazolidin-4-one (TH12): IR (KBr, cm^{-1}): 3002 (C-H Ar), 1670(C=C Ar), 1588 (C=N), 1566 (NO_2), 1425 (C-N), 685(C-S); ^{1}H NMR (DMSO-*d*6, 400 MHz): 7.84-7.21 (m, 12H, ArH), 7.36 (s, 1H, CH), 6.90 (s, 1H, CH, thiazole), 6.76 (s, 1H, CH, thiazolidinone).

(Z)-5-(4-chlorobenzylidene)-2-(2-nitrophenyl)-3-(4-(4-nitrophenyl)thiazol-2-yl)thiazolidin-4-one (TH13): IR (KBr, cm^{-1}): 3118 (C-H Ar), 1678(C=C Ar), 1588 (C=N), 1525 (NO_2), 1481 (C-N), 721(Cl), 672(C-S); ^{1}H NMR (DMSO-*d*6, 400 MHz): 8.60-7.13 (m, 12H, ArH), 7.40 (s, 1H, CH), 7.10 (s, 1H, CH, thiazole), 6.97 (s, 1H, CH, thiazolidinone).

(Z)-5-(4-hydroxybenzylidene)-2-(2-nitrophenyl)-3-(4-(4-nitrophenyl)thiazol-2-yl)thiazolidin-4-one (TH14): IR (KBr, cm^{-1}): 3627 (OH), 3047 (C-H Ar), 1672 (C=O), 1634 (C=N), 1529 (NO_2), 1422 (C-N), 686(C-S); ^{1}H NMR (DMSO-*d*6, 400 MHz): 8.56-7.01 (m, 12H, ArH), 7.43 (s, 1H, CH), 6.73 (s, 1H, CH, thiazole), 6.63 (s, 1H, CH, thiazolidinone), 4.22 (s, 1H, -OH).

(Z)-5-(3-bromobenzylidene)-2-(2-nitrophenyl)-3-(4-(4-nitrophenyl)thiazol-2-yl)thiazolidin-4-one (TH15): IR (KBr, cm^{-1}): 2957 (C-H Ar), 1701 (C=O), 1667(C=C Ar), 1635 (C=N), 1516 (NO_2), 1423 (C-N), 692(C-S) 637(Br); ^{1}H NMR (DMSO-*d*6, 400 MHz): 7.91-7.01 (m,

12H, ArH), 7.23 (s, 1H, CH), 6.70 (s, 1H, CH, thiazole), 6.60 (s, 1H, CH, thiazolidinone).

Evaluation of antimicrobial activity

Determination of Minimum Inhibitory Concentration

The antimicrobial potential of titled compounds **(2-(aryl)-5-(arylidene)-4-thiazolidinone derivatives)** was performed against Gram-negative bacterium: *E. coli*, Gram-positive bacteria: *B. sublitis*, *S. aureus*, and fungal strains: *A. niger* and *C. albicans* by tube dilution method. Dilutions of test (titled compounds) and standard compounds [ciprofloxacin (antibacterial) and Clotrimazole (antifungal)] was prepared in double strength nutrient broth – I.P. (bacteria) and Sabouraud dextrose broth I.P. (fungi) (Indian Pharmacopoeia 2007). The samples was incubated at 37°C for 24 h (bacteria), at 25°C for 7 d (*A. niger*) and at 37°C for 48 h (*C. albicans*), respectively, and the results will be recorded in terms of Minimum inhibitory concentration (MIC).[13] Results of antimicrobial potential are shown in Table-2.

Table 2. *In Vitro* Antimicrobial Activity of the Title Compounds (T1-T10).

Compound	Minimum inhibitory concentration (µg ml^{-1})				
	Bacterial Strains			Fungal Strains	
	E. coli	***S. aureus***	***B. subtilis***	***C. albicans***	**A. *Niger***
TH1	25	12.5	25	25	12.5
TH2	**1.56**	**3.12**	**3.12**	25	25
TH3	25	12.5	25	**1.56**	**3.12**
TH4	25	25	3.12	6.25	25
TH5	12.5	25	12.5	12.5	25
TH6	12.5	12.5	25	12.5	25
TH7	12.5	25	50	12.5	12.5
TH8	12.5	3.12	6.25	**3.12**	**1.56**
TH9	12.5	25	12.5	50	12.5
TH10	**1.56**	3.12	**1.56**	25	25
TH11	3.12	12.5	25	50	25
TH12	**1.56**	**1.56**	3.12	6.25	25
TH13	12.5	12.5	6.25	**1.56**	**3.12**
TH14	12.5	25	12.5	50	25
TH15	6.25	25	12.5	25	25
Ciprofloxacin (standard drug)	0.01	0.15	0.12	---	--
Clotrimazole (standard drug)	--	--	--	0.10	0.30

Antimicrobial evaluation by Zone of inhibition.

The titled compounds **(2-(aryl)-5-(arylidene)-4-thiazolidinone derivatives)** were also screened for their antimicrobial potential against these strains by zone of inhibition. The experiment performed by disc-diffusion method.[14] A standard inoculum (1-2 x 10^7 c.f.u./ml 0.5 McFarland standards) was introduced on to the surface of sterile agar plates, and a sterile glass spreader was used for even distribution of the inoculum. The disc measuring 6.25 mm in diameter were prepared from Whatman no. 1 filter paper and sterilized by dry heat at 140°C for 1 h. The sterile discs previously soaked with the titled compounds (test compound) solution in DMSO of specific concentration 100 µg/disc were carefully placed on the agar culture plates. The plates were inverted and incubated for 24 h at 37°C. Ciprofloxacin was used as a standard drug for antibacterial activity and clotrimazole was used as a standard drug for antifungal activity. The results of antimicrobial zones of inhibition are presented in table 3.

Table 3 Antimicrobial screening results of the tested compounds.

Comp.	Concentration (µg/ml)	Zone of inhibition (in mm)				
		Gram positive bacteria		Gram negative Bacteria	Fungal strain	
		B.subtilis	***S. aureus***	***E. coli***	***C. albicans***	***A. niger***
TH1	100	19	19	19	19	11
TH 2	100	17	15	15	13	14
TH 3	100	11	17	19	13	14
TH 4	100	15	12	20	15	16
TH 5	100	19	19	22	**20**	15
TH 6	100	19	**29**	22	11	17
TH 7	100	22	15	22	15	12
TH 8	100	22	19	22	19	13
TH 9	100	**25**	15	**29**	17	15
TH 10	100	22	26	19	13	13
TH11	100	19	20	20	15	14
TH12	100	22	15	20	15	**19**
TH13	100	22	19	22	15	15
TH14	100	19	11	22	19	13
TH15	100	13	14	22	16	11
Ciprofloxacin	100	**25**	**30**	**30**	-	-
Clotrimazole	**100**	**-**	**-**	**-**	**20**	**19**

RESULT AND DISCUSSION

All the synthesized derivatives were screened for their antimicrobial potential against Gram negative *E. Coli*, Gram positive bacteria: *B. Subtilis, S. aureus* and fungal strains: A. *niger. and C. albicans.* Ciprofloxacin was taken as standard drug for antibacterial and Clotriamazole was taken as reference drugs antifungal activity. The newly synthesized compounds were characterized by IR and ^{1}H NMR analyses. The results revealed that all synthesized compounds have a significant biological activity against the tested microorganisms.

Among the synthesized derivatives, compounds 2, 10 and 12 was found to be most active against bacterial strains and 3, 8 and 13 was found to be most active against the fungal strains.

All the synthesized derivatives was also evaluated for their antimicrobial activity against Gram negative *E. Coli*, Gram positive bacteria: *B. Subtilis, S. aureus*, and fungal strains: A. *niger. and C. albicans.* by zone of inhibition method. Ciprofloxacin and Clotriamazole were taken as reference drugs for antibacterial and antifungal activity. Among the synthesized derivatives, compounds **5, 6, 9** and **12** showed the excellent zone of inhibition activity as compared to the standard drugs. Results are presented in table 3.

CONCLUSION

In conclusion, we described here a convenient approach to the preparation of 2-(aryl)-5-(arylidene)-4-thiazolidinone derivatives was designed and synthesized. All compounds were synthesized according to Scheme 1. Data obtained were found to be in good agreement with the calculated values of the proposed structure. All the titled compounds evaluated it's *in vitro* antimicrobial against the tested strains. The results of antimicrobial study indicated that the presence of nitro groups in aromatic ring improved antibacterial activity, whereas the presence of chloro group improved antifungal activity of thiazolidinone derivatives.

REFERENCES

1. Deep, A.; Narasimhan, B.; Lim, S. M.; Ramasamy, K.; Mishra, R. K.; Mani, V. 4-Thiazolidinone derivatives: synthesis, antimicrobial, anticancer evaluation and QSAR studies. *RSC Adv.*, 2016; 6: 109485–109494.
2. Desai, N. C.; Dodiya, A. M.; Shihora, P. N. A clubbed quinazolinone and 4-thiazolidinone as potential antimicrobial agents. *Med Chem Res*., 2012; 21(8): 1577–1586.
3. El-Gaby, M. S.; El-Hag, A. G. A.; El-Maghraby, A. A.; Abd El-Rahman, M. T.; Helal, M. H. Synthesis, characterization and *in vitro* antimicrobial activity of novel 2-thioxo-4-thiazolidinones and 4,4'-bis(2-thioxo-4-thiazolidinone-3-yl)diphenylsulfones. *Eur J Med Chem*., 2009; 44(10): 4148-4152.
4. Deep, A.; Jain, S.; Sharma, P. C.; Mittal, S. K.; Phogat, P.; Malhotra, M. Synthesis, characterization and antimicrobial evaluation of 2,5-disubstituted-4-thiazolidinone derivatives. *Arb J Chem.,* 2014; 7: 287–291.
5. Wu, S.; Guo, W.; Teraishi, F.; Pang, J.; Kaluarachchi, K.; Zhang, L.; Davis, J.; Dong, F.; Yan, B.; Fang, B. Anticancer activity of 5-benzylidene-2-phenylimino-1, 3-thiazolidin-4-one (BPT) analogs. *Med. Chem.*, 2006; 2(6): 597-605.
6. Deep, A.; Kumar, P.; Narasimhan, B.; Ramasamy, K.; Mani, V.; Mishra, R. K.; Majeed, A. B. Synthesis, antimicrobial, anticancer evaluation of 2-

(aryl)-4- thiazolidinone derivatives and their QSAR studies. *Curr Top Med Chem*., 2015; 15(11): 990-1002.
7. Srivastava, T.; Gaikwad, A. K.; Haq, W.; Sinha, S.; Katti, S. B. Synthesis and biological evaluation of 4-thiazolidinone derivatives as potential antimycobacterial agents. *ARKIVOC.*, 2005; (ii): 120-130.
8. Patel, R. B.; Desai, P. S.; Desai, K. R.; Chikhalia, K. H. Synthesis of pyrimidine based thiazolidinones and azetidinones: Antimicrobial and antitubercular agents. *Indian J Chem.*, 2006; 45B: 773-778.
9. Deep, A.; Jain, S.; Sharma, P. C. Synthesis and anti-inflammatory activity of some novel biphenyl-4-carboxylic acid 5-(arylidene)-2-(aryl)-4-oxothiazolidin-3-yl amides. *Acta Pol Pharm*., 2010; 67(1): 63-7, 2010.
10. Deep, A.; Jain, S.; Sharma, P. C.; Phogat, P.; Malhotra, M. Synthesis of 2-(aryl)-5-(arylidene)-4-thiazolidinone derivatives with potential analgesic and anti-inflammatory activity. *Med Chem Res.*, 2012; 21: 1652–1659.
11. Ottana, R.; Maccari, R.; Giglio, M.; Del Corso, A.; Cappiello, M.; Mura, U.; Cosconati, S.; Marinelli, L.; Novellino, E.; Sartini, S.; La Motta, C.; Da Settimo, F. Identification of 5-arylidene-4-thiazolidinone derivatives endowed with dual activity as aldose reductase inhibitors and antioxidant agents for the treatment of diabetic complications. *Eur J Med Chem.*, 2011; 46(7): 2797-2806.
12. Kumar, R.; Subban R.; Sundaram.; K.; Venkatachalapthi, S.; Ali Muhammad, S. A. Conventional and microwave assisted synthesis of 2-aminothiazoles and oxazoles and their anti cancer activity. *Indo American J Pharm Res.*, 2015; 5(01): 555-561.
13. Pharmacopoeia, Pharmacopoeia of India, vol. II. Ministry of Health Department, Govt. of India, New Delhi, p. A-88, 1996.
14. Cruickshank, R.; Duguid, J. P.; Marmion, B. P.; Swain, R. H. A. The enterobacteriaceae: Salmonella. In, "Medical Microbiology." Vol. 11, 12th Edition. Churchill Livingstone, Edinburgh, London and New York, 1975; 403-419.