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Synthesis, antibacterial and antioxidant activity of N-[(4E)-arylidene-5-oxo-2-phenyl-4, 5-dihydro-1*H*-imidazol-1-yl]-2-(2-methyl-1, 3-thiazol-4-yl) acetamide

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ABSTRACT

A series of N-[(4E)-4-(2-arylidene)-5-oxo-2-phenyl-4, 5-dihydro-1H-imidazol-1-yl]-2-(2-methyl-1, 3-thiazol-4-yl) acetamides have been synthesized by reacting 2-methyl thiazole-4-acetic acid hydrazide with various oxazolones in the presence of pyridine. The structure of these compounds was supported by their IR, ^{1}H-NMR and mass spectral data. All the synthesized compounds were screened for their antibacterial and antioxidant activity by agar-diffusion and DPPH method respectively. Most of the compounds showed significant antioxidant and moderate antibacterial activity.

Key words: Oxazolones, thiazoles, antioxidant, antibacterial.

INTRODUCTION

Thiazole is a heterocyclic organic compound that has a five-member ring molecular structure (C_3H_3NS) containing three carbon atoms, one sulphur atom, and one nitrogen atom. The thiazole ring has been extensively studied and it forms the part of Vit. B_1 (thiamine) which contains both pyrimidine and thiazole ring system. Literature survey reveals that heterocyclic containing nitrogen and sulphur exhibit a wide variety of biological activities. Thiazoles are reported to possess a wide spectrum of biological activities such as antibacterial, anti-inflammatory, antifungal, antitubercular, antitumor, antioxidant, antiparkinsonism, antiviral and analgesic activities [1-6].

Imidazolone is a heterocyclic organic compound that has five membered ring molecular structure ($C_3H_3N_2O$) containing three carbon atoms, two nitrogen atoms placed in the heterocyclic ring at position 1,3 and another heteroatom 'O' placed as 5-one.

Imidazolones are reported to possess a wide spectrum of biological activities such as antibacterial, antimycobacterial, antimitotic, antifungal, antitumor [7-10]

Hence it was thought to synthesize some novel compounds possessing both thiazole and imidazole heterocyclic moiety as target compounds and evaluate their biological potency.

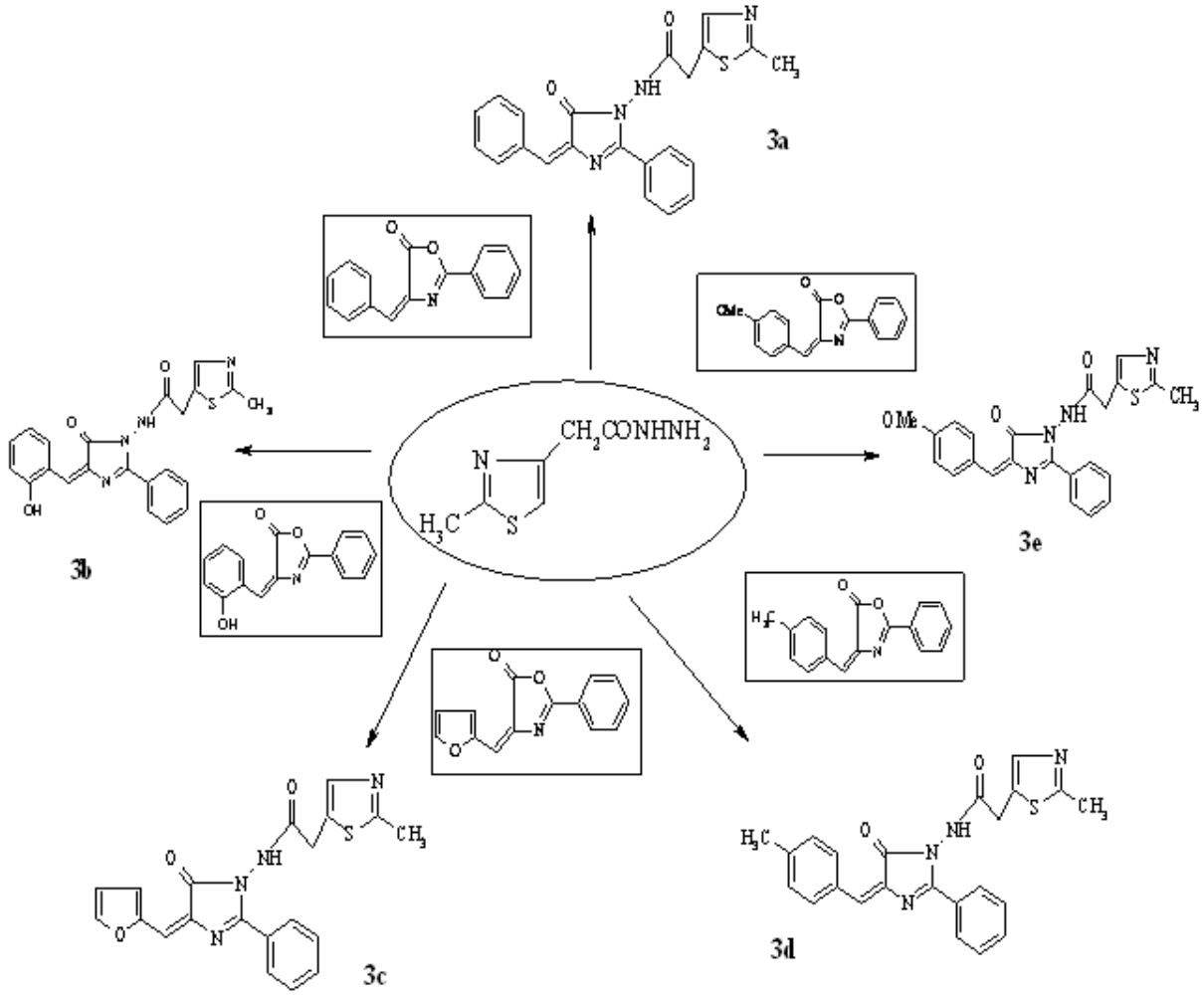

Fig 1: Scheme of synthesis for compounds 3a-e

MATERIALS AND METHODS

Chemistry

Melting points were determined by melting point apparatus and are uncorrected. Silica gel G plates were used for TLC and spots were located by UV or in iodine chamber. The IR spectrum (in KBr pellets) was recorded by using Fourier Transform IR spectrometer (SHIMADZU 8700)

and frequencies are expressed in cm^{-1}. The ^1H NMR spectra was recorded using $CDCl_3$ and DMSO with TMS as an internal standard and values are expressed in ppm (δ values). Mass spectrum was recorded by GC-MS. The scheme of synthesis of target compounds is shown in fig.1. The physical data of all the synthesized compounds is shown

2-Methyl thiazole-4-acetic acid hydrazide (1)
The compound is prepared by following the reported method [11].

(4*E*)-4-Arylidene-2-phenyl-1,3-oxazol-5(4*H*)-one (2a-e).
The condensation products of arylaldehydes with hippuric acid catalysed by anhydrous sodium acetate were prepared in dry acetic anhydride by the method reported [12].

N-[(4E)-4-Arylidene-5-oxo-2-phenyl-4, 5-dihydro-1*H*-imidazol-1-yl]-2-(2-methyl-1, 3-thiazol-4-yl) acetamide (3a-e).
(4*E*)-4-arylidene-2-phenyl-1,3-oxazol-5(4*H*)-one and 2-methyl thiazole-4-acetic acid hydrazide were taken in distilled and dried pyridine and refluxed for 30-36 h, the reaction mixture was cooled to room temperature and added to a beaker containing crushed ice, the solid obtained was filtered, dried and recrystallised from toluene.

All other derivatives of the series have been synthesized following the above procedure (Scheme-1).

Biological Evaluation

Antibacterial Activity [13]

All the newly synthesized compounds were screened for antibacterial activity against *Bacillus subtilis* , *Klebsiella pneumoniae, Staphylococcus aureus* and *Escherichia coli* using Ampicillin as standard and DMSO as control.

Agar Diffusion Method was employed. The sterilized nutrient agar media was cooled to 40ºC and poured into petridishes to obtain 4-6 mm thickness. The media was allowed to solidify at room temperature. 0.1 mL of inoculums (of 10^4 to 10^6 CFU / mL population prepared from standardized culture, adjusted with peptone water) was spread on the agar plate by spread plate technique. Accurately measured (0.1 mL) solution of each sample and standard were added to the cups with a micropipette. All the plates were kept in a refrigerator at 2 to 8ºC for a period of two hours for effective diffusion of test compounds and standards. Later, they were incubated at 37 ºC for 24 hr. The diameter of the zone of inhibition was measured and recorded in table2.

Antioxidant Activity [14]

All the newly synthesized compounds were screened for antioxidant activity using Ascorbic acid as standard and DPPH as control.

Preparation of standard and test solution: 10 mg of ascorbic acid was dissolved in 10 mL of methanol. From this stock solution dilutions were made to obtain concentrations of 10, 20, 30, 40 µg/ mL. 1 mL from each of these solutions was taken in different volumetric flasks to which 1 mL of DPPH solution (700 µg/ mL concentration) was added and volume was made up to 10 mL. The absorbance was recorded for these dilutions at 517 nm after duration of 30 mins.

The test solutions were prepared in similar manner as that of standard Ascorbic acid.

RESULTS AND DISCUSSION

Chemistry

The structure of the synthesized compounds (3a-e) were subjected to physicochemical tests (Table-1) and confirmed based on IR, ^{1}HNMR and Mass spectral data (Table-2).

Table 1: Physicochemical characteristics and spectral data of title compounds (3a-e)

Compound code	Molecular formula	Yield	Melting point
3a	$C_{22}H_{18}N_4O_2S$	24.87	103˚C
3b	$C_{22}H_{18}N_4O_3S$	19.5	162˚C
3c	$C_{20}H_{16}N_4O_3S$	20.92	92˚C
3d	$C_{23}H_{20}N_4O_2S$	25.3	127˚C
3e	$C_{23}H_{20}N_4O_3S$	65.75	118˚C

Table 2: Spectral data of title compounds

Compound code	IR (KBr cm-1), ^{IH} NMR ($CDCl_3$, δ ppm) and MS (m/z (%)	
3a	IR ^{I}H NMR	3365 NH, 2925 Ar-CH, 1710 C=O, 1666 C=N, 1531 NH, 1483 C=C 9.73 (s,1H,NH), 6.95-7.95 [m, 12H, (10H Ar-CH+ 1 thiazole CH+1CH)], 3.81 (s,3H,CH_3), 2.79 (s,2H,CH_2)
3b	IR	3232 OH , 3060 NH, 2923 Ar-CH, 1706 C=O, 1641 C=N, 1527 NH, 1488 C=C
3c	IR	3249 NH, 2925 Ar-CH, 1704 C=O, 1656 C=N, 1514 NH, 1444 C=C
3d	IR	3232 NH, 2923 Ar-CH, 1706 C=O, 1641 C=N, 1527 NH, 1488 C=C
3e	IR MS	3267 NH, 2925 Ar-CH, 1704 C=O, 1652 C=N, 1512 NH, 1446 C=C 431 (M^+ peak), 73 (Base peak), 355, 341, 221 (Other prominent peaks)

Antibacterial and antioxidant activity

N-[(4E)-4-(2-arylidene)-5-oxo-2-phenyl-4,5-dihydro-1H-imidazol-1-yl]-2-(2-methyl-1,3-thiazol-4-yl)acetamide derivatives (3a-3e) exhibited moderate antibacterial and good antioxidant activity. The observations revealed that, 3e exhibited significant antibacterial activity against *B. subtilis* and *E. coli* and antioxidant activity with IC_{50} value at 15 µg/mL. Compounds 3b and 3d exhibited moderate antibacterial activity against *B. subtilis* and *E. coli* and antioxidant activity at 25 µg/mL and 35 µg/mL. However none of the compounds exhibited significant activity against the *S. aureus and K. pneumonia* and greater activity against standard Ascorbic acid (Table 3&4).

Table 3: Antibacterial activity of title compounds (3a-e)

Compound code	*E. coli* (NCIM 2065)	*K. pneumonia* (NCIM 5082)	*S. aureus* (NCIM 2079)	*B. subtilis* (NCIM 2697)
3a	11	4	3	12
3b	16	5	3	18
3c	12	4	6	14
3d	13	4	4	14
3e	20	3	4	21
Control (DMSO)	-	-	-	-
Standard Ampicillin	26	22	25	28

Table 4: Antioxidant activity of title compounds (3a-e)

Compound	Antioxidant activity (IC_{50} in µg / mL)
3a	80
3b	25
3c	45
3d	35
3e	15
Standard Ascorbic acid	10

CONCLUSION

N-[(4E)-4-(2-arylidene)-5-oxo-2-phenyl-4,5-dihydro-*1H*-imidazol-1-yl]-2-(2-methyl-1,3-thiazol-4-yl) acetamide derivatives, 3a-3e was synthesized, characterized and evaluated for their biological activity. Antibacterial and antioxidant studies of these compounds exhibited moderate antibacterial and good antioxidant activity.

REFERENCES

[1] S.D.Srivastava, J.P. Sen , *Indian J Chem*.,**2008**, 47B, 1583-86.
[2] T. Karbasanagouda , A.V. Airody, D.Ramgopal , G.Parameshwarappa ,. *Indian J Chem.* **2008**, 47B, 144-52.
[3] S.R.Pattan, N.S. Dighe, S.A. Nirmal, A. N.Merekar, R.B.Laware, H.V.Shinde *et al. Asian J Research Chem*., **2009**, 196-201.
[4] G.M. Shanta, V.B. Bharati. *Indian J Chem*., **2001**, 40B, 742-47.
[5] S. Nadeem, M.A. Faiz, A. Waquar, M.A. Shamsher. *Intern J Pharm Sci and Drug Research.*, **2009**, 1(3), 136-43.
[6] A. Geronikaki , D.L. Hadjipavlou , C. Chatziopoulos, G. Soloupis. .*Molecules*., **2003**, 8, 472-79.
[7] S.A. Siddiqui, S.R. Bhusare, D.V. Jarikote, R.P. Pawar, Y.B. Vibhute. *Bull Korean Chem Soc*., **2001**, 22, 1033-36.
[8] S .Ewa, K.K. Katarzyna, B .Anna, K .Andrzej. *Farmaco*., 2002, 57, 39–44.
[9] K .Thaker, P .Zalavadiya, H.S. Joshi. *J Sci*., **2005**, 16(2), 139-44.
[10] A.K. Zafer, T.Z. Gülhan, R .Gilbert, G .KIymet. *Arch Pharm Res*., **2004**, *27*, 1081-85.
[11] V.N.Britsun,A.N.Espenko,M.O.Lozinskii, **2008**, *Chem.HeteroCompds.*,44(12),1429-59.
[12] Z.Puterova,H.Sterk,A. Krutosikova, **2004**, *Molecules*, 9, 11-21.
[13] T. Vani, M. Rajani, S. Sarkar, C.J. Shishoo. *Int J Pharmacog.*, **1997**, 35(5), 313. (antioxidant)
[14] V.S. Parmar, J.N. Hirday, A.K. Gupta, A.K. Prasad. *Phytochemistry***1992**, 31 , 2567.