



Synthesis, Characterization and Evaluation of Antimicrobial Properties of Novel Oxazine and Thiazine Compounds Derived from Chalcones

SHREEKANT. M. PRAJAPATI^{1*}, SANJAY. S. SHAH² and ARUN. R. MALAVIYA³

^{1*,3}Department of Chemistry, Hemchandracharya North University, Patan, Matarvadi Part, Gujarat 384265, India.

²Department of Chemistry, Shri U. P. Arts, Smt. M. G. Panchal Science & V. L. Shah Commerce College, Pilvai, Gujarat, India

*Corresponding author E-mail: shreekant12041991@gmail.com

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ABSTRACT

In this ongoing research, our objective is to synthesize oxazines and thiazines by employing chalcones, providing an uncomplicated approach for generating diverse heterocyclic derivatives. These substances show a wide spectrum of biological impact, i.e. analgesic, anti-phlogistic, and anti-convulsant properties. To characterize these newly synthesized compounds, we conducted comprehensive analyses employing techniques such as infrared spectroscopy (IR), proton nuclear magnetic resonance (¹H NMR), carbon-13 nuclear magnetic resonance (¹³C NMR) and mass spectrometry. Additionally, we evaluated the antimicrobial potential of these compounds.

Keywords: Chalcone, Antimicrobial, Oxazine, Thiazine.

INTRODUCTION

Oxazines and Thiazines, two classes of organic compounds, exhibit a diverse array of biological activities, making them subjects of significant interest in the field of chemical and pharmaceutical research. In this comprehensive report, the researcher provides an intricate account of the synthesis of a series of chalcones denoted as 1C1 to 1C4. These chalcones were meticulously crafted through Claisen-Schmidt condensation reactions, wherein a variety of substituted benzaldehydes were skillfully combined with acetophenone in the

presence of an alkali catalyst, a well-established methodology as outlined in previous scientific investigations¹⁻². Following the synthesis process, the chalcones underwent a rigorous purification regimen and a thorough characterization that encompassed both physical and spectral analyses. This multifaceted characterization was crucial in confirming the structural integrity and purity of the chalcones. The next pivotal step in this research involved the transformation of the synthesized chalcones into novel Oxazines³⁻⁵ and Thiazines⁶⁻⁸, denoted as 1C1OX to 1C4OX and 1C1TH to 1C4TH, respectively. These transformations were achieved



through distinct reactions with urea and thiourea, resulting in the formation of compounds with significant pharmacological potential. To elucidate the structures of these newly synthesized compounds, the research team relied on a robust array of analytical techniques, including IR spectroscopy, ¹H NMR spectroscopy, ¹³C NMR spectroscopy, and mass spectrometry. These methods provided invaluable insights into the molecular compositions and arrangements of the Oxazines and Thiazines. Furthermore, the study encompassed antimicrobial screening assays⁹⁻¹⁰ to evaluate the potential bioactivity of these compounds. The screening assays were conducted with the use of DMSO as the solvent, and the results were meticulously recorded. This phase of the research aimed to assess the compounds' efficacy against various microbial strains, shedding light on their potential as antimicrobial agents. Subsequently, the resulting product underwent a process of recrystallization in ethanol, a crucial step in enhancing the purity and crystalline structure of the synthesized compounds, thereby ensuring their suitability for further studies and potential applications. This research represents a significant contribution to the field, offering a comprehensive exploration of the synthesis, characterization, and potential bioactivity of these newly developed Oxazines and Thiazines.

MATERIAL AND METHODS

In our experimental procedures, we employed analytical-grade chemicals exclusively. The determination of uncorrected melting points was conducted using the open capillary technique, and the assessment of purity was executed via thin-layer chromatography (TLC). For spectroscopic analysis, Fourier-transform infrared (FTIR) spectra and proton nuclear magnetic resonance (¹H NMR) spectra were acquired utilizing a Varian 400MHz spectrometer, with CDCl₃ serving as the solvent and tetramethylsilane (TMS) as the reference standard. Elemental analysis was carried out using a Thermofinigan Flash EA instrument (Italy), and the sulfur and halogen content was calculated using the carious method. To evaluate antibacterial and antifungal activity, our research team conducted Broth Dilution method tests against a diverse spectrum of both *Gram-positive* and *Gram-negative* bacteria, as well as fungi, as detailed in Table 1.

Synthesis of 1-(3-fluoro-4-hydroxyphenyl) ethanone (A)

In carbon di sulphide, a mixture of 2 fluoro phenol (0.1mole) and Acetyl chloride (0.1mole) reflux for 30 min in presence of aluminium chloride and it was allowed to stay for around 30 min until the hydrochloride gas solution stopped. The carbon di sulphide was then distilled out. Thereafter, the whole Product was steam distilled. The nonvolatile product was 3 fluoro 4 hydroxy Acetophenone.

Synthesis of 1-[4-(benzyloxy)-3-fluorophenyl] ethanone(BFE)(1)

In a 100 mL flask, we combined 1-(3-fluoro-4-hydroxyphenyl)ethanone (0.1 mol), (bromo methyl) benzene (0.1 mol), and Di pottasium carbonate (0.1 mol) with acetone as the solvent. The reaction mixture was vigorously agitated for 7 h under reflux conditions at a degree varying from 50°C to 60°C. After the reaction mixture had cooled to room temperature, 100 mL of cold water was added to quench it. The resulting 1-[4-(benzyloxy)-3-fluorophenyl]ethanone was then filtered and thoroughly rinsed.

Synthesis of 1-(4-(benzyloxy)-3-florophenyl)-4-phenyl)-3-(sub.phenyl) prop-2-en-1-one(1C1to 1C4) General Procedure

A solution was prepared by dissolving 1-[4-(benzyloxy)-3-fluorophenyl]ethanone (0.01 mol) and replaced aromatic aldehydes (0.01 mol) in 30 milliliters of C₂H₅OH. In this solution, a 10% caustic soda solution was steadily added. TLC was used to track the reaction's development after the mixture was agitated for 4 hours. Subsequently, the mixture was added into 400 milliliters of icy water were mixed consistently and then counterbalanced using a 1:9 hydrochloric acid and water solution. The reaction mixture was left to stay as it is for a night in a freezer. The resulting expedite was filtered, cleaned, and subjected to recrystallization via ethanol.

Synthesis of Oxazines and Thiazines Via Chalcones

A mixture containing 0.01 mol of 1-(4-(benzyloxy)-3-fluorophenyl)-4-phenyl)-3-(sub. phenyl) prop-2-en-1-one, 1.0 g of potassium hydroxide (KOH), and 0.01 mol of either Urea or Thiourea was prepared and dissolved in 30 mL of ethanol. This mixture was refluxed in a water bath at a temperature range of 70-80°C for 3 h, with continuous monitoring using thin-layer

chromatography (TLC). Afterward, the solid product that formed was left undisturbed overnight and then purified through recrystallization using ethanol.

Notably, The interaction between chalcone and urea led to the production of Oxazine, while the reaction with thiourea produced Thiazine.

Table 1: Result of Antimicrobial activity of oxazine and thiazine derivatives

No	Coding No	Concentration on minimal inhibition $\mu\text{g/mL}$		
		<i>Escherichia coli</i> MTCC 443	<i>Staphylococcus aureus</i> MTCC 96	<i>Candida albicans</i> MTCC 227
1	1C1OX	125	100	500
2	1C2OX	250	125	1000
3	1C3OX	250	100	>1000
4	1C4OX	125	250	500
5	1C1TH	100	50	500
6	1C2TH	62.5	100	1000
7	1C3TH	100	62.5	>1000
8	1C4TH	50	62.5	>1000
Standard drug	CHLORAMPHENICOL	50	50	
	CIPROFLOXACIN	25	50	
	GRESEOFULVIN			500

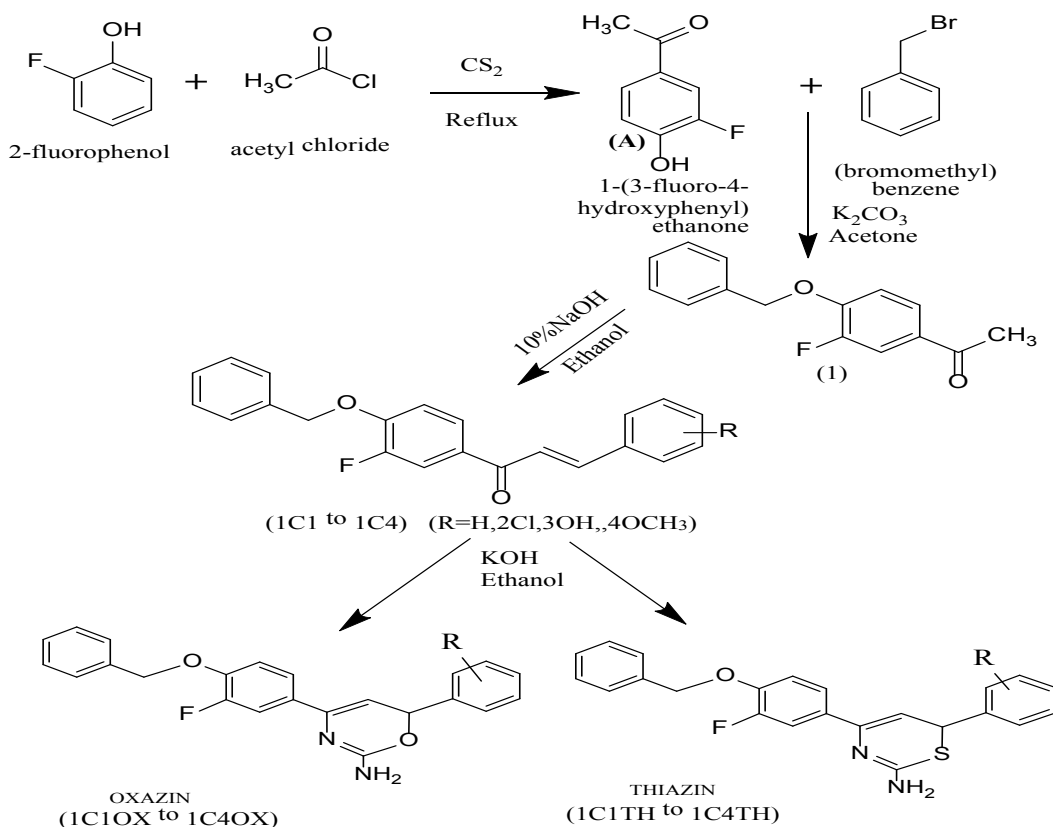


Fig. 1. Reaction Scheme

RESULTS AND DISCUSSION

m/z 244.27,

Characterization of BFE and chalcone derivatives

1-[4-(benzyloxy)-3-fluorophenyl]ethanone (BFE) (1)

Product-66.20%, m.p.-103^o-105^oC, LC-MS:

FT-IR(KBr cm^{-1}): 2930 (C-H Str.Vib) 3047 (Aromatic C-H) 1511, 1455 (C=C strVib), 1081 C-O-C str. vib, 1620 (-C=O str.vib), 611 (C-Fstr.vib)

¹HNMR (400MHz, CDCl₃): 5.314(s, 2H, O-CH₂-), 2.539(s, 3H, COCH₃), 7.0-7.7 (m, 8H, Aromatic)

¹³CNMR (400MHz, CDCl₃): 26.50 (1C, -COCH₃), 71.30(1C, O-CH₂), 110-175 (12C Aeromatic), 196.07 (1C, -CO-) Theoretical for C₁₅H₁₃FO₂: C-73.36, H-5.36 Obtained: C-73.33, H-5.34

1-[4-(benzyloxy)-3-fluorophenyl]-4-phenylbut-2-en-1-one (1C1)

Product-61.33%, m.p.-111^o-113^oC, LC-MS: m/z332.37

FT-IR(KBr cm⁻¹): 3060(Aromatic C-H), 1593, 1494(C=C strVib), 1043(C-O-C str.vib), 1654 (-C=O str.vib), 982(CH=CH bending), 761(C-F str.vib)

¹HNMR: (400MHz, CDCl₃): 5.217(s, 2H, O-CH₂-), 7.55-8.0 (m, 2H, CH=CH) 7.0-7.8 (m, 13H, Aromatic).

¹³CNMR: 71.11(1C, O-CH₂), 110 175(18C, Aeromatic), 187.758 (1C, -CO-), 100-150 (2C, CH=CH) Theoretical for C₂₂H₁₇FO₂: C-79.50, H-5.16 Obtained: C-79.48, H-5.15.

(1-(4-(benzyloxy)-3-fluorophenyl)-3-(2-chlorophenyl)prop-2-en-1-one (1C2)

Product-60.37%, m. p.- 141^o-143^oC, LC-MS: m/z366.82.

FT-IR(KBr cm⁻¹): 3028 (Aromatic C-H), 1567, 1517 (C=C strVib), 1655 (-C=O str.vib), 972 (CH=CH bending), 624 (C-F multi sub. Benzene), 1039 (C-O-C str.vib), 787(C-Cl str.vib).

¹HNMR (400MHz, CDCl₃): 5.214 (s, 2H, O-CH₂-), 7.55-8.0 (m, 2H, CH=CH), 7.0-7.8 (m, 12H, Aromatic).

¹³CNMR: 71.09 (1C, O-CH₂), 110-175 (18C, Aeromatic), 163.52 (1C, -CO-), 100-150 (2C, CH=CH). Theoretical for C₂₂H₁₆ClFO₂: C-72.04, H-4.40 Obtained C-72.02, H-4.42

1-[4-(benzyloxy)-3-fluorophenyl]-4-(3-hydroxyphenyl) but-2-en-1-one (1C3)

Product-58.22%, m. p.-160^o-162^oC, LC-MS: m/z348.37

FT-IR(KBr cm⁻¹): 3056 (Aromatic C-H), 1509, 1455 (C=C strVib), 1061 (C-O-C str. vib), 1667 (-C=O str. vib), 985 (CH=CH bending), 636 (C-F str. vib), 3554(C-OH str.vib).

¹HNMR (400MHz, CDCl₃): 5.219 (s, 2H, O-CH₂-), 7.55-8.0 (m, 2H, CH=CH), 7.0-7.8 (m, 12H, Aromatic), 4.0-7.0 (s, 1H, Ar-OH)

¹³CNMR: 71.10 (1C, O-CH₂), 110-175 (18C, Aeromatic), 187.758 (1C, -CO-), 100-150 (2C, CH=CH). Theoretical for C₂₂H₁₇FO₃: C-75.85, H-4.92 Obtained C-75.83, H-4.93

1-[4-(benzyloxy)-3-fluorophenyl]-4-(4-methoxyphenyl)but-2-en-1-one (1C4)

Product-66.89%, m. p.-118^o-120^oC, LC-MS: m/z362. 40

FT-IR (KBr cm⁻¹): 3063 (Aromatic C-H), 1573, 1431 (C=C strVib), 1021 (C-O-C str. vib), 3576 (O-H str. vib), 1652(-C=O str. vib), 978 (CH=CH bending), 728(C-F str. vib)

¹HNMR (400MHz, CDCl₃): 5.242 (s, 2H, O-CH₂-), 7.55-8.0 (m, 2H, CH=CH) 7.0-7.8 (m, 12H, Aromatic), 3.859 (s, 3H, Ar-OCH₃).

¹³CNMR: 71.06(1C, O-CH₂), 110-175 (18C, Aeromatic), 187.720(1C, -CO-), 100-150 (2C, CH=CH), 55.35 (1C, O-CH₃) Theoretical for C₂₂H₁₉FO₃: C-76.23, H-5.28. Obtained-C-76.22, H-5.30

Characterisation of Synthesized Oxazines

Synthesis of 4-(4-(benzyloxy)-3-fluorophenyl)-6-phenyl-6H-1,3-oxazin-2-amine (1-C-1 OX)

Product- 55.33%, m. p.- 256^o-258^oC, LC-MS: m/z374 FT-IR(KBr cm⁻¹): C-O-C (symmetric) 1230, C-O-C (asymmetric) 1036, NH₂(amine) (N-H stretching) 3435, N-H (bending) 1596, C-N stretching 1337

¹HNMR (400MHz, CDCl₃): 2.544 (s, 2H, -NH₂), 5.219 (s, 2H, -O-CH₂), 7.0-7.8 (m, 15H, Aromatic).

¹³CNMR: 71.104(1C, -OCH₂), 157.601 (1C, C-NH₂), 100-160 (18C, Aeromatic), 115-125 (1C, -C=N), 115-140 (2C, C=C). Theoretical for C₂₃H₁₉FNO₂: C-76.65, H-5.31, N-3.89 Obtained; C-76.62, H-5.28, N-3.88.

4-(4-(benzyloxy)-3-fluorophenyl)-6-(2-chlorophenyl)-6H-1,3-oxazin-2-amine (1-C-2 OX)

Product-61.11%, m. p.-2330-2355°C, LC-MS: m/z 409.58 FT-IR (KBr cm⁻¹): C-O-C (symmetric) 1227, C-O-C (asymmetric) 1041, NH₂ (amine) (N-Hstarching) 3435, N-H (bending) 1528, C-N stretching 1337.

¹H NMR (400MHz, CDCl₃): 2.543 (s, 2H, NH₂), 5.127-5.220 (s, 2H, -OCH₂), 7.07.7 (m, 14H, Aromatic).

¹³C NMR (400MHz, CDCl₃): 71.073 (1C, -OCH₂), 100-160 (18C, Aeromatic), 115-125 (1C, C=N) 157. 456 (1C, C-NH₂), 115-140 (2C, C=C). Theoretical for C₂₃H₁₈ClFNO₂: C-69.96, H-4.59, N-3.55. Obtained: C-69.93, H-4.56, N-3.58

Synthesis of 3-(2-amino-4-(4-(benzyloxy)-3-fluorophenyl)-6H-1,3-oxazin-6-yl)phenol (1-C-3 OX)

Product-56.71%, m. p.- 211^o-213^oC, LC-MS: m/z389.03

FT-IR (KBr cm⁻¹): C-O-C (symmetric) 1230, C-O-C (asymmetric) 1052, NH₂ (amine) (N-H starching) 3435, N-H (bending) 1528, C-N stretching 1337.

¹H NMR (400MHz, CDCl₃): 2.543 (s, 2H, -NH₂), 5.235 (s, 2H, -O-CH₂), 7.0-8.0 (m, 15H Aromatic), 4.0-7.0 (s, 1H, Ar-OH)

¹³C NMR (400MHz, CDCl₃): 70.737 (1C, -OCH₂), 100-160 (18C, Aeromatic), 115-125 (1C, -C=N), 157.787 (1C, C-NH₂), 115-140 (2C, C=C). Theoretical for C₂₃H₁₉FN₂O₃: C-64.87, H-4.50, N-6.58 Obtained: C-64.88, H-4.52, N-6.55

4-(4-(benzyloxy)-3-fluorophenyl)-6-(4-methoxyphenyl)-6H-1,3-oxazin-2-amine (1-C-4 OX)

Product- 66.33%, m. p.-2660-2680C, LC-MS: m/z405.1

FT-IR (KBr cm⁻¹): C-O-C (symmetric) 1230, C-O-C (asymmetric) 1072, NH₂ (amine) (N-H starching) 3436, N-H (bending) 1596, C-N stretching 1336.

¹H NMR (400MHz, CDCl₃): 2.544 (s, 2H, -NH₂), 5.220 (s, 2H, -O-CH₂), 7.0-7.8 (m, 14H Aromatic), 3.864 (s, 3H, O-CH₃)

¹³C NMR (400MHz, CDCl₃): 70.102 (1C, -OCH₂), 100-160 (18C, Aeromatic), 115-125 (1C, -C=N), 157.913 (1C, C-NH₂), 55.334 (1C, O-CH₃), 115-140 (2C, C=C) Theoretical for C₂₄H₂₁FN₂O₃: C-71.27, H-5.23, N-6.93. Obtained: C-71.24, H-5.21, N-6.91

Characterisation of Synthesized Thiazines**4-(4-(benzyloxy)-3-fluorophenyl)-6-phenyl-6H-1,3-thiazin-2-amine (1-C-1 TH)**

Product-63%, m. p.-211^o-213^oC, LC-MS: m/z390.2

FT-IR (KBr cm⁻¹): C-O-C (symmetric) 1275, C-O-C (asymmetric) 1018, NH₂ (amine) (N-H starching) 3435, N-H (bending) 1561, C-N stretching 1327.

¹H NMR (400MHz, CDCl₃): 2.547 (s, 2H, -NH₂), 5.220 (s, 2H, -O-CH₂), 7.0-7.9 (m, 15H Aromatic)

¹³C NMR (400MHz, CDCl₃): 70.834 (1C, -OCH₂), 100-160 (18C, Aeromatic), 115-125 (1C, -C=N) 157.838 (1C, C-NH₂) 115-140 (2C, C=C). Theoretical for: C₂₃H₁₉FN₂OS: C-70.75, H-4.86, N-7.17, S-8.21 Obtained: C-70.73, H-4.84, N-7.15, S-8.21

4-(4-(benzyloxy)-3-fluorophenyl)-6-(2-chlorophenyl)-6H-1, 3-thiazin-2-amine (1-C-2 TH)

Product-61.90%, m.p.-244^o-246^oC, LC-MS: m/z425.2.

FT-IR (KBr cm⁻¹): C-O-C (symmetric) 1248, C-O-C (asymmetric) 1025, NH₂ (amine) (N-H starching) 3434, N-H (bending) 1607, C-N stretching 1330.

¹H NMR (400MHz, CDCl₃): 2.543 (s, 2H, -NH₂), 5.220 (s, 2H, -O-CH₂), 7.0-7.7 (m, 14H Aromatic).

¹³C NMR (400MHz, CDCl₃): 71.073 (1C, -OCH₂), 100-160 (18C, Aeromatic), 115-125 (1C, -C=N), 115-140 (2C, C=C), 157.190 (1C, C-NH₂). Theoretical for: C₂₃H₁₈FN₂OS: C-65.01, H-4.27, N-6.59, S-7.55 Obtained: C-65.00, H-4.25, N-6.56, S-7.53

3-(2-amino-4-(4-(benzyloxy)-3-fluorophenyl)-6H-1,3-thiazin-6-yl)phenol (1-C-3 TH)

Product-55.33, m. p-267^o-269^oC, LC-MS: m/z406.3.

FT-IR (KBr cm^{-1}): C-O-C (symmetric) 1276, C-O-C (asymmetric) 1079, NH_2 (amine) (N-H stretching) 3435, N-H (bending) 1667, C-N stretching 1276.

^1H NMR (400MHz, CDCl_3): 2.544 (s, 2H, $-\text{NH}_2$), 5.220 (s, 2H, $-\text{O}-\text{CH}_2$), 7.0-7.7 (m, 14H Aromatic), 4.0-7.0 (s, 1H, Ar-OH).

^{13}C NMR (400MHz, CDCl_3): 71.401 (1C, $-\text{OCH}_2$), 100-160 (18C, Aromatic), 115-125 (1C, $-\text{C}=\text{N}$), 115-140 (2C, $\text{C}=\text{C}$), 157.168 (1C, $\text{C}-\text{NH}_2$) Theoretical for : $\text{C}_{23}\text{H}_{19}\text{FN}_2\text{OS}$: C-67.96, H-4.71, N-6.89, S-7.89 Obtained: C-67.98, H-4.73, N-6.90, S-7.91.

4-(4-(benzyloxy)-3-fluorophenyl)-6-(4-methoxyphenyl)-6H-1,3-thiazin-2-amine (1C-4 TH)

Product-68.66%, m.p.- 281 $^\circ$ -283 $^\circ\text{C}$, LC-MS: m/z421.4.

FT-IR(KBr cm^{-1}): C-O-C (symmetric) 1247, C-O-C (asymmetric) 1037, NH_2 (amine) (N-H stretching) 3435, N-H (bending) 1583, C-N stretching 1269.

^1H NMR (400MHz, CDCl_3): 2.544 (s, 2H, $-\text{NH}_2$), 5.221 (s, 2H, $-\text{O}-\text{CH}_2$), 7.0-7.8 (m, 14H Aromatic), 3.865 (s, 3H, $\text{O}-\text{CH}_3$).

^{13}C NMR (400MHz, CDCl_3): 71.064 (1C, $-\text{OCH}_2$), 100-160 (18C, Aromatic), 115-125 (1C, $-\text{C}=\text{N}$), 157.890 (1C, $\text{C}-\text{NH}_2$) 55.304 (1C, $\text{O}-\text{CH}_3$), 115-140 (2C, $\text{C}=\text{C}$) Theoretical for $\text{C}_{24}\text{H}_{21}\text{FN}_2\text{O}_2\text{S}$: C-68.55, H-5.03, N-4.52, S-7.63. Obtained: C-68.56, H-5.04, N-4.54, S-7.64.

Antimicrobial activity

We conducted *in vitro* antimicrobial assessments of the synthesized compounds, namely 1C1OX, 1C2OX, 1C3OX, 1C4OX, 1C1TH, 1C2TH, 1C3TH, and 1C4TH, against bacterial strains *S. aureus* and *E. coli*, in addition to the fungal strain *C. albicans*. Using the Broth Dilution Method, these compounds' antibacterial activity was assessed. Chloramphenicol and Ciprofloxacin served as standard drugs for bacterial strains, while Griseofulvin was used as a reference for fungi.

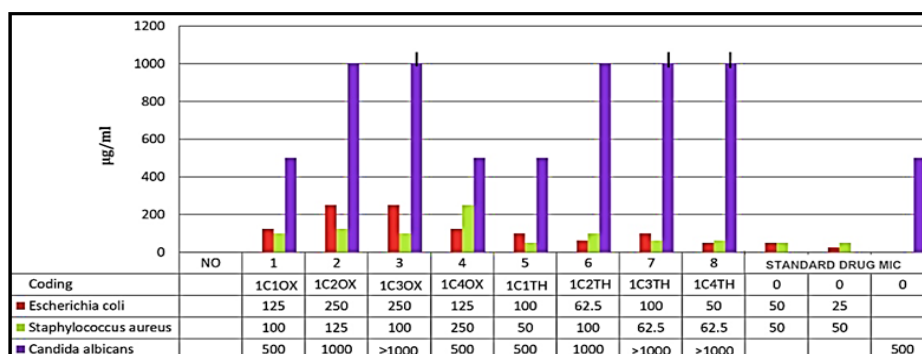


Fig. 2. Histogram of antimicrobial activity of derivatives

CONCLUSION

In this article, we have outlined our preliminary endeavors aimed at uncovering novel and potentially active oxazine and thiazine compounds derived from chalcones. Notably, Compound 1C1TH exhibited the most significant inhibitory effect on the growth of *Gram-positive S. aureus*, with a Minimum Inhibitory Concentration (MIC) value as low as 50 $\mu\text{g}/\text{mL}$. were compound 1C3TH and 1C4TH shows moderate MIC value 62.5 $\mu\text{g}/\text{mL}$. The *Gram-negative E. coli* bacterial growth is inhibited by compound 1C1TH at A minimum inhibitory concentration (MIC) of 50 $\mu\text{g}/\text{mL}$. were compound 1C3TH, 1C4TH

shows moderate MIC value 62.5 $\mu\text{g}/\text{mL}$. Oxazines and Thiazines exhibited potent antifungal activity. Among all the synthesized oxazine and thiazine compounds, specifically 1C1OX, 1C1TH, and 1C4OX, these three compounds demonstrated notable antifungal efficacy. They exhibited strong activity against *C. albicans* fungi at a concentration of 500 $\mu\text{g}/\text{mL}$, comparable to Griseofulvin¹¹. Newly discovered Oxazines and Thiazines are chemically active components that readily undergo different types of substitutions on their heterocyclic rings, enabling them to display various biological effects. These novel chemical compounds offer medicinal chemists an opportunity to create and advance

Oxazine and Thiazine derivatives as potential lead compounds in drug invention.

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Conflict of Interest

There are no competing interests are found.

REFERENCES

- Nowakowska Z.; A review of anti-infective and antiinflammatory chalcones. *Eur J. Med Chem.*, **2007**, *42*(2), 125-137.
- Go M L.; Wu X.; Liu X L. Chalcones: An Update on Cytotoxic and Chemoprotective Properties. *Current Medicinal Chemistry.*, **2005**, *12*(4), 483-499.
- Sawant RL.; Bhatia MS., Applications of Topliss modified approach in the design and synthesis of GABA-nergic anticonvulsants. *Res J Pharm Tech.*, **2008**, *1*, 273-275.
- Mathew BP.; Kumar A.; Sharma S.; Shukla.; Nath M., An eco-friendly synthesis and antimicrobial activities of dihydro-2H-benzo- and naphtho-1,3-oxazine derivatives. *Eur J Med Chem.*, **2010**, *45*, 1502-1507.
- Ouberai M.; Asche C.; Carrez D.; Croisy A.; Dumy P.; Demeunynck M., 3, 4-Dihydro-1H-[1,3] oxazino[4,5-c]acridines as a new family of cytotoxic drugs. *Bioorg Med Chem, Lett.*, **2006**, *16*, 4641-4643.
- Koketsu M.; Tanaka K, Takenaka Y.; Kwong C D.; Ishihara H., Synthesis of 1, 3-Thiazin derivatives and their Evaluation as Potential Antimycobacterial Agents. *Eur J Pharm Sci.*, **2002**, *15*, 307-310.
- Bozsing D.; Sohar P.; Gigler G.; Kovacs G., Synthesis and Pharmacological Study of New 3,4-Dihydro 2H, 6H-pyrimido (2,1-b) (1, 3) thiazines. *Eur J Med Chem.*, **1996**, *31*, 663-668.
- Koketsu M.; Tanaka K.; Takenaka Y.; Kwong C D.; Ishihara H., Synthesis of 1,3-Thiazine derivatives and their Evaluation as Potential Antimycobacterial Agents. *Eur J Pharma Sci.*, **2002**, *15*, 307-310.
- Jyothi MV.; Venkatesh P., Preparation and Biological Evaluation of Novel Pyrimidines from Novel Chalcones. *Orient. J. Chem.*, **2012**, *28*(3), 1437-1442.
- H W Seely.; Van Demark P J.; Microbes in action. A laboratory manual of Microbiology, D.B Taraporewala sons, Bombay., **1975**, *55*.
- S.M. Prajapati "Synthesis and *In vitro* Antibacterial and Antifungal Evaluation of Quinoline Analogue Azetidin and Thiazolidin Derivatives", *International Letters of Chemistry, Physics and Astronomy.*, **2014**, *39*, 195-210.