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DESIGN, SYNTHESIS AND ANTIMICROBIAL EVALUATION OF SCHIFF BASE 4-THIAZOLIDINONES FOR PHARMACEUTICALS

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ABSTRACT

Illness has been a part of man's history since the dawn of time, and the hunt for cures is possibly as old. Kidneys & liver are major organs valued for medication removal from body. This study was based on to synthesize novel Schiff bases by combining 4-aminosalicylic acid with diverse 2-chloro, 2-hydroxy, and 2-thio-3-formylquinolines. In thioglycolic acid and anhydrous Zinc chloride, all Schiff bases will be transformed into thiazolidinones. Using a conventional approach, all such compounds are tested for their antibacterial potential against diverse strains. Antibacterial and antifungal properties were tested on all produced substances. In tests, substances showed high potency to moderate antibacterial activity against S. pyogenus (Gm-ve) and E. coli bacteria. These compounds were found microbes sensitive but not fungus. It suggests to test their antibacterial potential in vivo using animals then human beings. A significant data in preclinical and clinical trials will prove their use in clinical settings.

KEYWORDS: Synthesis, antimicrobial, Schiff base 4-thiazolidinones, E. coli

INTRODUCTION

Illness has been a part of man's history since the dawn of time, and the hunt for cures is possibly as old. Man's sincere endeavour to control and cure illnesses that led to development of new medications or suitable versions of current drugs.[1] Previously, medications were derived from different sources but having lack of action and final cure, as well as increased toxicity, the creation of new drugs that are more potent and less poisonous is critical. This has promoted synthetic derivatives for illness treatment, management, and diagnostics.[2] Today, ≥60% of medications used in practise are synthesised derivatives and scope of medicinal chemistry is expanding daily.[3] Pharmaceutical chemistry is a specialised science that relies on other disciplines for the discovery of new pharmaceuticals i.e., inorganic, organic, pharmacology etc.[4] Among the numerous heterocycles containing these atoms, thiazolidinones have been demonstrated to have anti-bacterial, anti-fungal, anti-viral, diuretic, anti-tuberculostatic, anti-HIV, anti-histaminic, anti-cancer, anticonvulsant, anti-inflammatory, and analgesic properties.[5]

Quinoline derivatives have long been known to have anti-malarial action. Quinoline compounds have a wide range of clinically relevant activities, including analgesic, anti-inflammatory, anti-malarial, anti-neoplastic, anti-leishmanial, immuno-modulator, anti-convulsant, anti-fungal, anti-bacterial, neurotropic, vasorelaxant, and anti-viral properties.[6] Quinoline derivatives have been claimed to be useful in the manufacture of various dyes and pigments.[7][8]

This research was based on the synthesis and evaluation (antibacterial and antifungal) of the possibility of obtaining novel antimicrobial drugs by connecting 4-thiazolidinone of amino salicylic acid with substituted 2-chloro, 2-hydroxy, and 2-thio-3-formylquinolines.

MATERIALS AND METHODS

Synthesis of 2-chloroquinoline-3-carboladehyde

Procedure: In a three-necked flask with a drying tube, N, N-dimethyl formamide (0.125 mol, 9.13g, 9.65ml) was cooled to 0ºC, then phosphorus oxychloride (0.35mol, 53.55g, 32.2ml) was added dropwise while stirring. Acetanilide (0.05mol, 6.75g) was added to this solution after 5 minutes, and the mixture was then heated under reflux for 16 hours at 85-90ºC. After cooling, the reaction mixture was put into ice water and agitated for 30 min at 0-10ºC. when the yellow precipitate of 2-Chloroquinoline-3-carbaldehyde separated. It was extracted from ethyl acetate, filtered, washed with cold water, dried, and recrystallized to produce light yellow glossy needle-shaped crystals with a melting point of 149ºC and an 82% yield.[10]

Synthesis of 2-thiones- 3-formylquinoline

A solution of 2-chloro-3-formyl quinoline (0.001mol, 0.191grm), dry N, N-dimethyl formamide (5ml), and sodium sulphide (0.015mol, 0.114g fused flakes) were added to a clean, dry round bottom flask. The reaction mixture was then stirred for 1–2 hours at room temperature while being monitored by TLC. After the reaction was complete, the mixture was poured into ice The product had been thoroughly cleaned with water, dried, and was now pure enough to be used again. 0C, M.P.287–288; yield, 84%.

General method for synthesis of 4-[(2-Chloroquinolin-3-yl) methyleneamino]- 2-hydroxybenzoic acid (M-1)

In dry round-bottom flask, a mixture of P-Aminosalicylic acid (0.001 mol, 0.153 gm), 2-chloro-3-formylquinoline (0.001mol, 0.191gm) and glacial acetic acid (1-2drops) in alcohol (20-30 ml) was taken and refluxed 18-20hrs until a distinct spot-on TLC was obtained. The reaction mixture was cooled and solid thus obtained was filtered, washed with water, dried and recrystalized from aqueous N, N - Dimethyl formamide to give brown solid powder 4-[(2-Chloroquinolin-3-yl) methyleneamino]-2-hydroxybenzoicacid.[11]

Synthesis of 2-hydroxy-4-{(2-hydroxyquinolin-3-yl) methylidene] amino} Benzoic acid (M-5)

In dry round-bottom flask, a mixture of P-Aminosalicylic acid (0.001 mol, 0.153 gm),2-hydroxy-3-formylquinoline (0.001 mol, 0.173 gm), and glacial acetic acid (1-2drops) in alcohol (20-30 ml) was taken and refluxed for 20-24 until a distinct spot-on TLC was obtained. The reaction mixture was cooled and solid thus obtained was filtered, washed with water, dried and recrystalized from aqueous N,N- dimethylformamide to give 2-hydroxy-4-{(2-hydroxyquinolin-3-yl) methylidene] amino} benzoic acid.[12]

Similarly,2-hydroxy-4-{(2-hydroxyquinolin-6-mehylquinoline-3-yl) methylidene] amino} benzoic acid (M-6),2-hydroxy-4-{(2-hydroxyquinolin-8-mehylquinoline-3- yl)methylidene]amino}benzoicacid (M-7),2-hydroxy-4-{(2-hydroxyquinolin-7- mehylquino line-3-yl) methylidene] amino}benzoic acid (M-8) were prepared by adopting the procedure given above whose physical data are given in below Table.

Synthesis of 2-hydroxy-4-{[(2-sulfanylquinolin-3-yl) methylidene] amino} benzoic acid (M-9

In dry round-bottom flask, a mixture of P-Aminosalicylic acid (0.001 mol, 0.153 gm,) 2-Thione-3-formylquinoline (0.001 mol, 0.189 gm), and glacial acetic acid (1-2drops) in alcohol (20-30 ml) was taken and refluxed for 22hrs until a distinct spot-on TLC was obtained. The reaction mixture was cooled and solid thus obtained was filtered, washed with water, dried and recrystallized from aqueous N,N-dimethyl formamide to give 2-hydroxy-4-{[(2-sulfanylquinolin-3-yl) methylidene] amino} benzoic acid, physical data are given in below Table.[13]

Synthesis of 4-Thiazolidinones from 4-[(2-Chloroquinolin-3-yl)methyleneamino]- 2-hydroxybenzoicacid(MS-1)

Add 4-[(2-Chloroquinolin-3-yl) methylene amino] mixture. Thioglycolic acid was added to dry 1,4-dioxane (20–30 ml) containing -2-hydroxy benzoic acid (0.0lmol, 3.26gm), followed by a pinch of anhydrous Zncl2. The reaction mixture was refluxed for 19–20 hours in order to get a clear spot-on TLC. After cooling, the reaction mixture was placed into ice water. To create 4-[2-(2-chloroquinolin-3-yl)-4-oxo-1,3-thiazolidin-3-yl)-2-hydroxybenzoicaicd, the solid mass was filtered, washed with sodium bicarbonate (10% w/v in water), dried, and recrystallized from aqueous N, N-dimethylformaide.[14]

Physical information about 2-hydroxybenzoic acid (MS-4) is provided in Table 2.

Synthesis of 4-Thiazolidinones from 2-hydroxy-4-{(2-hydroxyquinolin-3-yl) methylidene] amino} benzoic acid (MS-5)

To a mixture of 2-hydroxy-4-[2-(2-hydroxyquinolin-3-yl) benzoic acid (0.01 mol, 3.08gm) in dry 1,4-dioxane (20-30ml), thioglycolic acid(0.01mol,0.92gm,0.693ml) was added followed by pinch of anhydrous Zncl2. The reaction mixture was refluxed for 21-23hrs until a distinct spot-on TLC was obtained. Reaction mixture were cooled and then poured on to ice cold water. The solid mass obtained was filtered, washed with sodium bicarbonate (10% w/v in water) solution, dried and recrystalized from aqueous N, N-dimethylformamide to give2-hydroxy-4-[2-(2-hydroxyquinolin-3-yl)-4- oxo-1,3-thiazolidin-3-yl] benzoic acid.

Synthesis of 4-Thiazolidinones from 2-hydroxy-4-{[(2-sulfanylquinolin-3-yl) methylidene] amino} benzoic acid (MS-9)

To a mixture of 2-hydroxy-4-[4-oxo-2-(2-sulfanylquinolin-3-yl)] benzoic acid (0.01 mol, 3.08gm) in dry 1,4-dioxane (20-30 ml), thioglycolic acid (0.01mol,0.92gm,0.693ml) was added followed by pinch of anhydrous $ZnCl_2$. The reaction mixture was refluxed for 25hrs until a distinct spot-on TLC was obtained. Reaction mixture were cooled and then poured in to ice cold water. The solid mass obtained was filtered, washed with sodium bicarbonate (10% w/v in water) solution, dried and recrystallized from aqueous N, N-dimethylformaide to give 2-hydroxy-4-[4- oxo-2-(2-sulfanylquinolin-3-yl)-1,3-thiazolidin-3-yl]benzoic acid. Physical data are given in Table-2.

Melting Point estimation

The open capillary tube method was used to determine the melting points of the organic compounds. As a pure crystal has a distinct and sharp melting point, an organic compound's melting point is a valuable indicator of purity. When a chemical is subjected to purification by recrystallization, the purity should not be taken for granted; rather, it must be verified by monitoring any changes in the melting point.

Preparation of Chromatoplate
We took several cleaned and dried glass plates. A uniform silica Gel-G to water slurry was created in the proportion of 1:2. The TLC applicator chamber was then filled with the slurry, and the thickness was adjusted to 0.5 mm. To apply a consistent layer of slurry to the glass plates, the applicator was pushed smoothly over the plates. The plates were first allowed to dry at room temperature before being stored for activation or 1 hour at 110 0C.[15]

Preparation of Solvent System and chamber saturation
The solvent was developed by mixing chloroform and ethanol as shown further-
Chloroform: Ethanol (9.5: 0.5)

Application of sample
In a tiny drilled capillary tube, the parent chemicals and their derivatives were identified 2 cm from the plate's base end. The plates were spot-spotted, allowed to air dry, and then moved to a chromatographic chamber with a solvent system for development.

Development of Chromatogram
When the solvent front had risen to 10 to 12 cm, plates were developed using the ascending procedure, and they were removed, dried, and stored at room temperature.

Detection of Rf value
The spots are detected by using iodine vapours/UV chamber.
The R_f values is calculated as.

$$R_f = \frac{\text{Distance traveled by solute}}{\text{Distance traveled by solvent}}$$

Every single time, it was discovered that the sample had travelled a different distance than the parent molecule that had been discovered alongside it. This supported the idea that the new compounds were wholly distinct from the parent compound. Additionally, since the entire sample only revealed one location, the compounds were assumed to be pure. Compounds' Rf values were listed in Table 2.

Every single time, it was discovered that the sample had travelled a different distance than the parent molecule that had been discovered alongside it. This supported the idea that the new compounds were wholly distinct from the parent compound. Additionally, since the entire sample only revealed one location, the compounds were assumed to be pure.

Infrared spectroscopy
Infrared spectroscopy of synthesized compounds was performed using IR Spectrophotometer. Infrared spectroscopy deals in the identification of functional groups present in the compound. Shimadzu FTIR-8400S spectrophotometer was used with KBr pellet technique.[16]

NMR Profile
Synthesized compounds were sent for NMR analysis. NMR spectroscopy deals with the identification of number and types of protons in any sample.
We may learn about the various chemical and magnetic environments that correspond to protons in molecules thanks to the proton NMR spectrum. On an Advance 300 MHz spectrometer, the samples are examined.[17]

Mass spectroscopy
Synthesized compounds were characterized using mass spectroscopy. Mass spectroscopy deals with the identification of molecular weight of compounds. Determination of mass is the most trusted method of identification of the compounds.[18]

Evaluation of the Anti-bacterial activity
All synthetic compounds were tested using MIC for in-vitro antibacterial role against 4 different strains of microbes, including S. aureus (MTCC96), P. aeruginosa (MTCC1688), S. pyogenes (MTCC442), and E. coli (MTCC 443) (Broth dilution method). The test bacteria were grown and the medication suspension was diluted using Mueller Hinton broth as a nutrition medium. Here, DMSO was employed as a diluent or vehicle to dilute the necessary number of medications before testing them on common bacterial strains. This method hinges on the lowest possible medication concentration that prevents microbial growth in a serial antibacterial dilution in a fluid medium that would otherwise be ideal for its rapid growth. This technique allows for the detection of the least inhibitory concentration, which is the lowest concentration at which an antibacterial agent prevents the growth of the test organism. By comparing the turbidity of and, the inoculum size for test strain was adjusted up to 108 Cfu per milliliter.[9]

Evaluation
Each synthetic medication was diluted to a stock solution concentration of 2000 g/ml.

Primary examination
1000g/ml, 500g/ml, and 250g/ml concentrations of the synthesised medicines were used in the initial screening. The main screening's active manufactured medication was then subjected to a second round of dilution testing against every type of bacterium.

Secondary examination

The principal screening-identified active medicines were similarly diluted to obtain concentrations i.e., 200g/ml, 10g/ml, 50g/ml, 25g/ml, 12.5g/ml & 6.25g/ml.

The greatest dilution that exhibits an inhibitory zone with at least 99% is taken as the MIC. The size of the inoculum has a significant impact on the outcome. The test mixture must have 108 organisms per milliliter. Using distilled water, the ampicillin was produced to have a concentration range of 1000 g/ml to 6.250 g/ml.[19]

Table 1: Preparation of Muller-Hinton Broth.

Component	Qty
Beef extract	30.0%
Casein	1.75%
Starch	0.15%
Agar	1.7%
Distilled water	50ml

These components were mixed in water and pH adjusted to neutral at 25^0C and the medium was sterilized by autoclave at 15lb for 15 min.

Preparation of micro-organisms

The *S. aureus, S. pyogenes, P. aeruginosa & E. coli* are transferred from the culture to 5ml of normal saline (0.09%) solution.[20]

Determination of minimal inhibitory concentration

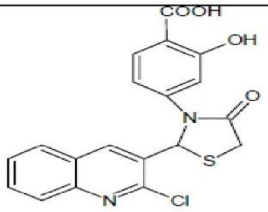
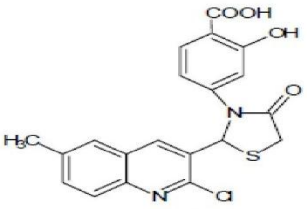
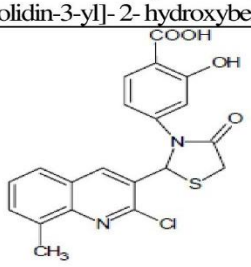
1 ml of various serially diluted test samples were added to the sterile test tubes with 1 ml of sterile medium. These tubes received 0.1 ml of the appropriate microbe suspension in normal saline, which was added, and were then incubated at 37 2 0C for 24 hours. After the culture's agar medium had been cultured for 24 hours at 37°C, a loop full of sample was streaked over it in a zigzag pattern. The lowest sample concentration that prevented microbial growth in the petridish was then found, and this is referred to as the MIC. This process was carried out to validate the MIC.[21]

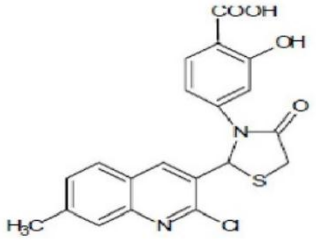
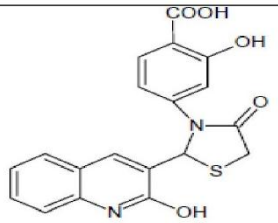
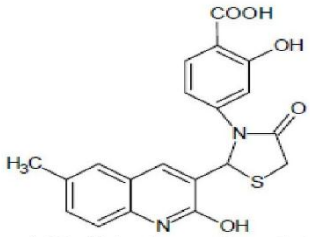
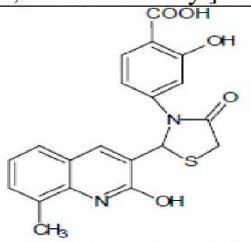
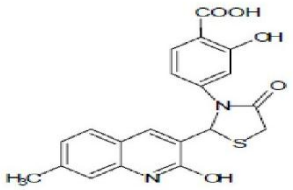
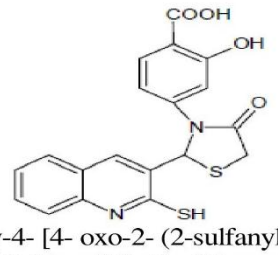
RESULTS AND DISCUSSION

List of synthesised compounds

Table 1 depicts the list of synthesized compounds as below.

Table 2. Synthesised compounds

S. No.	Compound code	Name of compound and chemical name
1.	MS-1	 4- [2- (2-chloroquinolin-3-yl)-4-oxo-1, 3-thiazolidin-3-yl]- 2-hydroxybenzoic acid
2.	MS-2	 4- [2- (2- chloro-6-methylquinolin-3-yl)- 4-oxo- 1, 3-thiazolidin-3-yl]- 2- hydroxybenzoic acid
3.	MS-3	 4- [2- (2-chloro-8-methylquinolin-3-yl)-4- oxo-1, 3-thiazolidin-3-yl]- 2-hydroxybenzoic acid

4.	MS-4	 4- [2 -(2-chloro-7-methylquinolin-3-yl)- 4- oxo-1, 3-thiazolidin-3-yl]- 2-hydroxybenzoic acid
5.	MS-5	 2-hydroxy-4- [2- (2-hydroxyquinolin-3-yl)-4-oxo-1, 3-thiazolidin-3-yl] benzoic acid
6.	MS-6	 2-hydroxy-4-[2- (2-hydroxy-6-methylquinolin-3-yl)-4- oxo-1,3-thiazolidin-3-yl] benzoic acid
7.	MS-7	 2-hydroxy-4-[2- (2-hydroxy-8-methylquinolin-3-yl)-4- oxo-1,3- thiazolidin-3-yl] benzoic acid
8.	MS-8	 2-hydroxy-4- [2- (2-hydroxy-7-methylquinolin-3-yl)-4-oxo-1, 3-thiazolidin-3-yl] benzoic acid
9.	MS-9	 2-hydroxy-4- [4- oxo-2- (2-sulfanylquinolin-3-yl)-1, 3-thiazolidin-3-yl] benzoic acid

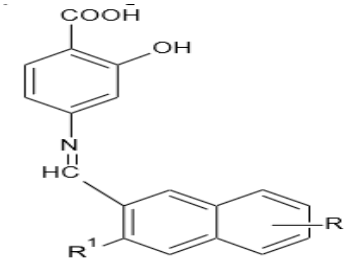


Fig 1: Structure of 2-Hydroxy-4- [(quinolin-3yl- methylidene) amino] benzoic acid.

Table 3: Characteristic analytical data of 2-Hydroxy-4- [(quinolin-3yl- methylidene) amino] benzoic acid derivatives.

Comp. Code	m.p. (˚C)	% Yield	Mol. Formula	Mol. Wt.	Rf Value *	Calculated (%)		
						C	H	N
M-1	288	84	$C_{17}H_{11}N_2O_3Cl$	326.69	0.80	62.49	3.39	8.57
M-2	242	84	$C_{18}H_{13}ClN_2O_3$	340.72	0.64	63.44	3.85	8.22
M-3	230	80	$C_{18}H_{13}N_2O_3Cl$	340.72	0.95	63.44	3.85	8.22
M-4	246	78	$C_{18}H_{13}N_2O_3Cl$	340.72	0.76	63.44	3.85	8.22
M-5	256	81	$C_{17}H_{12}N_2O_4$	308.22	0.74	66.23	3.92	9.09
M-6	268	75	$C_{18}H_{14}N_2O_4$	322.24	0.68	67.07	4.38	8.69
M-7	280	79	$C_{18}H_{14}N_2O_4$	322.24	0.71	67.07	4.38	8.69
M-8	270	66	$C_{18}H_{14}N_2O_4$	322.24	0.57	67.07	4.38	8.69
M-9	290	71	$C_{17}H_{12}N_2O_3S$	326.32	0.83	62.95	3.73	8.64

Solvent- Chloroform: alcohol (9: 1)

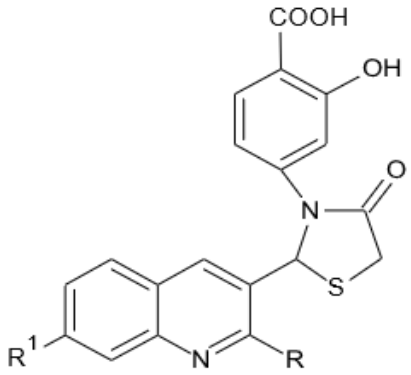


Fig. 2: Structure of 2-Hydroxy-4-[4-oxo-2 (quinolin- 3yl)1, 3-thiazolidin-3yl)benzoic acid.

Table 4: Characteristic analytical data of 2-Hydroxy-4-[4-oxo-2 (quinolin- 3yl)1, 3-thiazolidin-3yl)benzoic acid derivatives.

Comp. Code	MP (˚C)	% Yield	Mol. Formula	M. Wt.	Rf Value *	Calculated (%)		
						C	H	N
MS-1	274	80	$C_{19}H_{13}N_2O_4S$	400.83	0.85	56.93	3.27	8.84
MS-2	294	80	$C_{20}H_{15}N_2O_4S$	414.86	0.78	57.90	3.64	6.75
MS-3	298	78	$C_{20}H_{15}N_2O_4S$	414.86	0.80	57.90	3.64	6.75
MS-4	287	88	$C_{20}H_{15}N_2O_4S$	414.86	0.82	57.90	3.64	6.75
MS-5	276	80	$C_{19}H_{14}N_2O_5S$	382.38	0.68	59.68	3.69	7.33
MS-6	268	66	$C_{20}H_{16}N_2O_5S$	396.41	0.76	60.60	4.07	7.07
MS-7	305	73	$C_{20}H_{16}N_2O_5S$	396.41	0.79	60.60	4.07	7.07
MS-8	299	76	$C_{20}H_{16}N_2O_5S$	396.41	0.68	60.60	4.07	7.07
MS-9	314	88	$C_{19}H_{14}N_2O_4S_2$	398.45	0.73	57.27	3.54	7.03

Solvent- chloroform: alcohol (9:1)

IR Spectroscopy

The FTIR data was shown of best 7 synthesized compound out of 9.

$_1$H-NMR spectroscopy

The characteristic $_1$HNMR spectral data of newly synthesized compounds of 2-hydroxy-4-[4-oxo-2(quinolin-3yl)-1,3-thiazolidin-3yl] benzoic acid derivatives were reported in Table-3. The NMR profile is given in form of spectra.

Mass spectroscopy

It gives the confirmation about the skeleton of the compounds.

Infrared spectrum of the compound (MS-2): (KBr Pellet method, Fig-I-1) showed absorption bonds at (in cm-1): 1714 (C=O), 1495 (C=C), 626 (C-Cl).

1H-NMR spectrum of the compound (MS-2): (in DMSO-d6: Fig-N-1) has been found to exhibit characteristic proton signals at (in, ppm): 7.99 (s, 1H, -OH), 1.25 (s,2H,-CH2),3.30(s,1H,-CH),2.15(s,3H,-CH3),6.75-7.15(m,4H,Ar-H).

Mass spectrum of the compound (MS-2): (Fig M-1) The Mass spectrum of the compounds has recorded. Its molecular ion peak at m/z 414 (M+).

Similarly, P-Amino salicylic acid has been condensed as many as nine different substituted 2-Chloro, 2-hydroxy and 2-thione-3-formyl quinolines and the single product uniquely obtained on each such reaction could be characterized as their respective2-Hydroxy-4-[4-oxo-2(quinolin-3yl)-1,3-thiazolidin-3yl]benzoicacid derivatives.

Table 5: FTIR, NMR & Mass spectral data of derivatives.

Compound code	C=O Cm^{-1}	C = C Cm^{-1}	C = Cl Cm^{-1}	C - S Cm^{-1}	^{1}H NMR Spectral Values (δ values)	Mass spectral values (M^+m/z values)
MS-1	1490	1716	-	-	7.98(s, 1H-OH), 1.25 (S, 2H, CH_2), 3.29(s, 1H, CH)	
MS-2	1495	1731	-	626	7.99(s, 1H-OH), 1.25 (S, 2H, CH_2), 3.30(s, 1H, CH),2.15(S,3H, CH_3),6.75-7.15(m,4H, Ar-H)	M/z 414(M^+), 414(M+1).
MS-3	1487	1716	-	764		
MS-4	1504	-	-	713	7.95(s, 1H-OH), 1.25 (S, 2H, CH_2), 3.71(s, 1H, CH),2.54(S,3H, CH_3),6.25-7.35(m,4H, Ar-H)	
MS-5	1497	-	-	755	7.88(s, 1H-OH), 1.25 (S, 2H, CH_2), 3.3(s, 1H, CH)	
MS-6	1435	1715	-	601		
MS-7	1506	-	-	772	7.94(s, 1H-OH), 1.24 (S, 2H, CH_2), 3.43(s, 1H, CH),2.57(S,3H, CH3),6.44- 6.95(m,4H, Ar-H)	
MS-8	1489	-	-	-		
MS-9	1489	-	611	-		

FTIR and NMR profiles were detemined of best 7 among 9 developed derivatives as below.

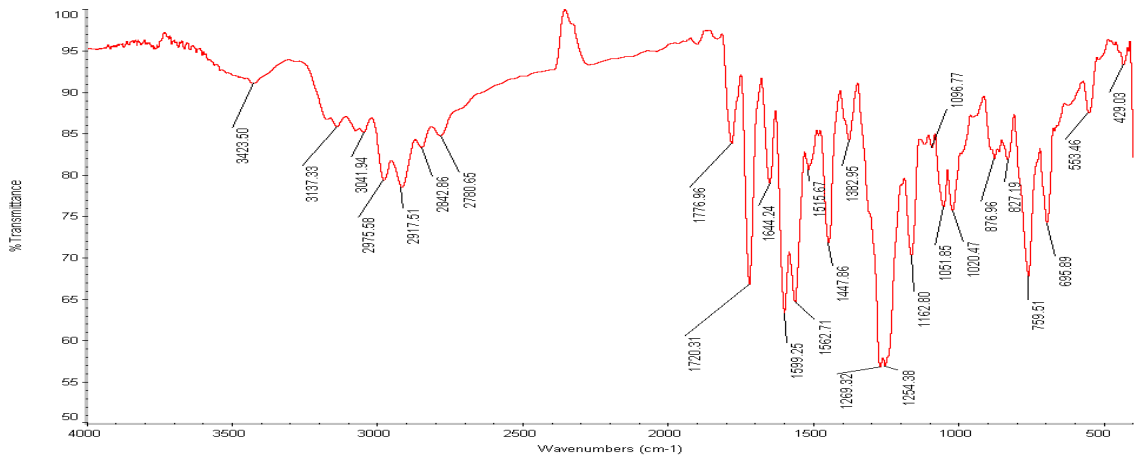


Fig. 3: a. IR data of MS-1.

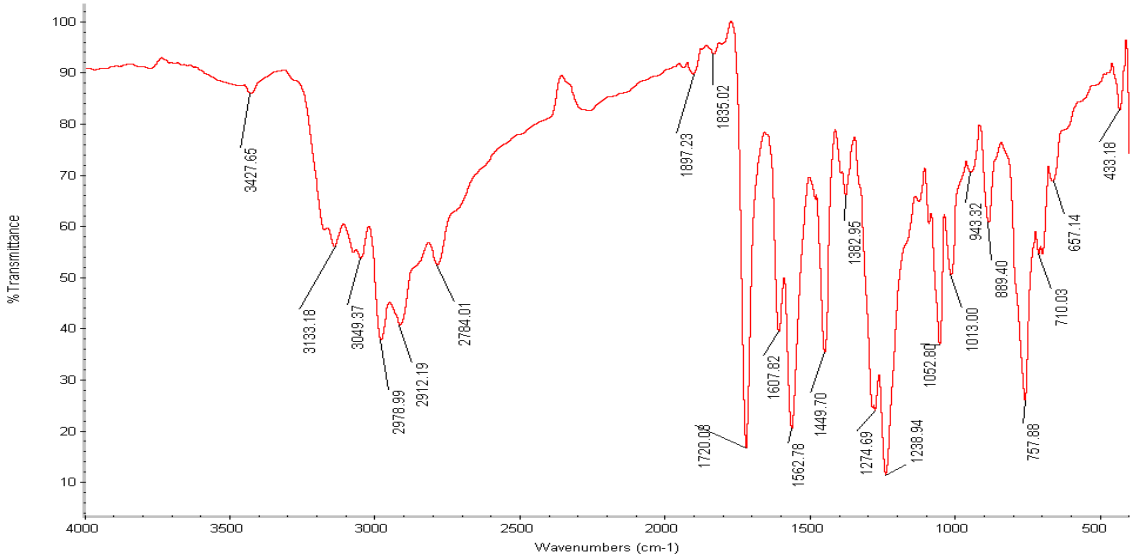


Fig. 3: b. IR data of MS-2.

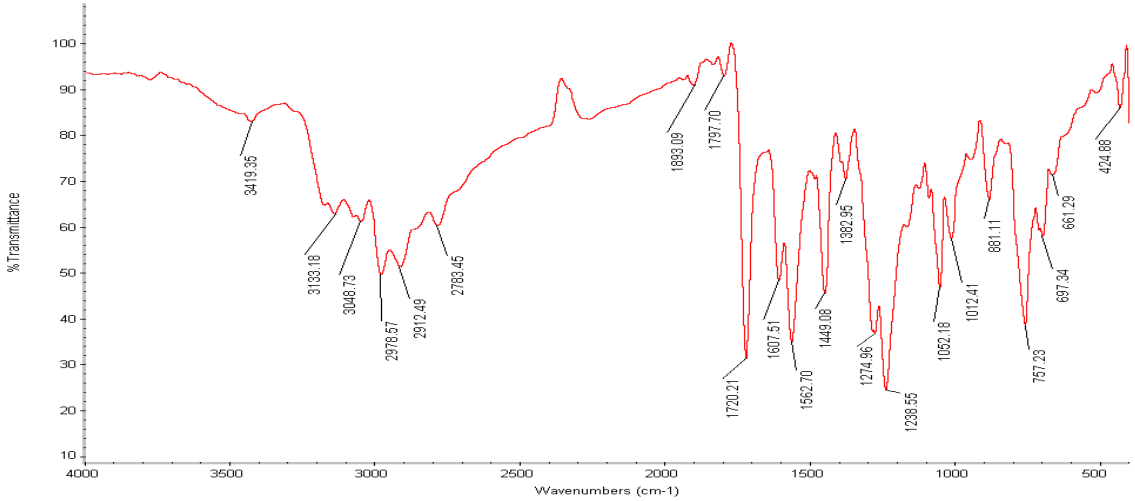


Fig. 3: c. IR data of MS-3.

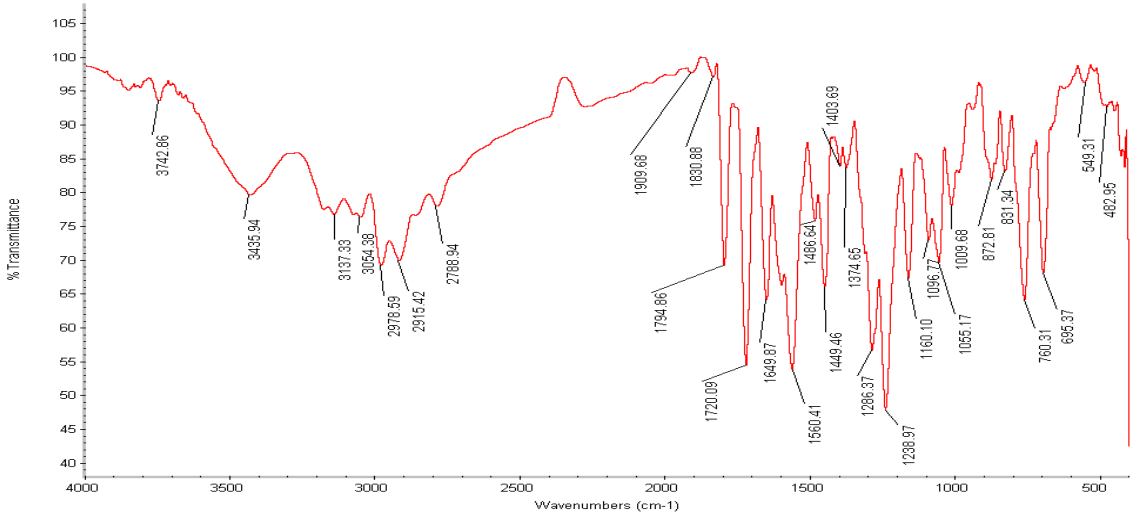


Fig. 3: d. IR data of MS-4.

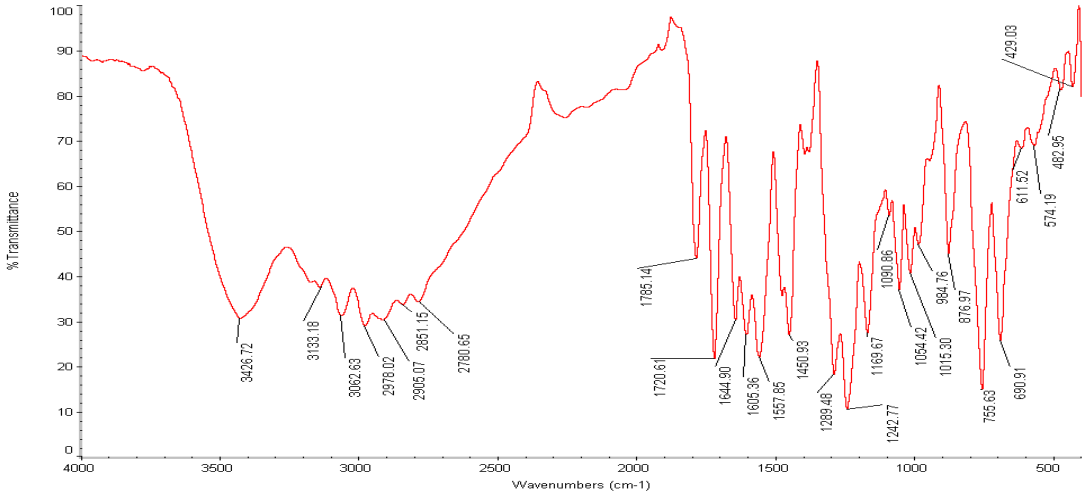


Fig. 3: e. IR data of MS-5.

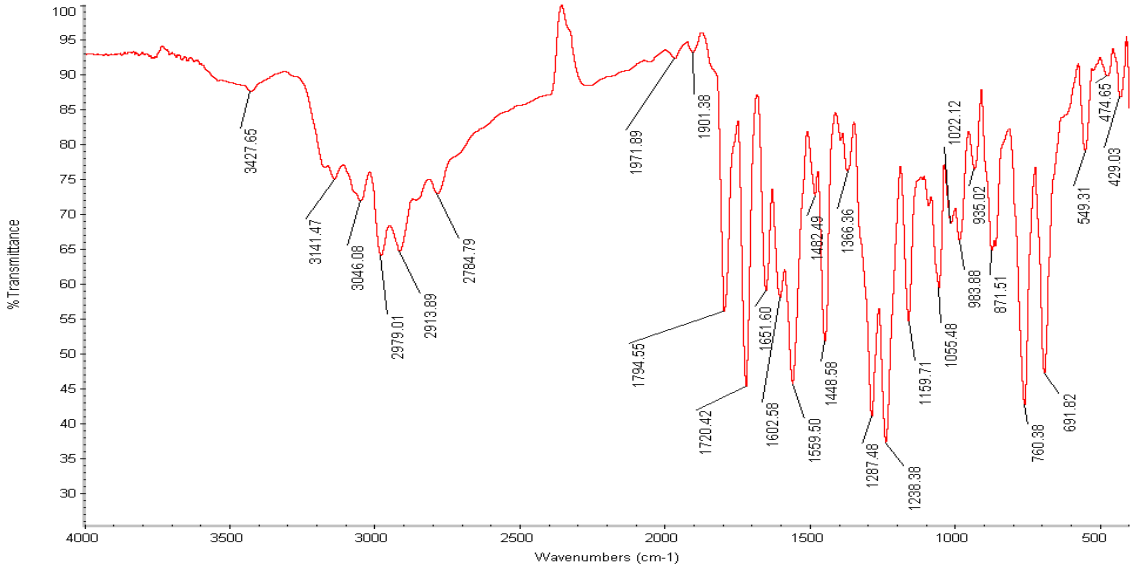


Fig. 3: f. IR data of MS-6.

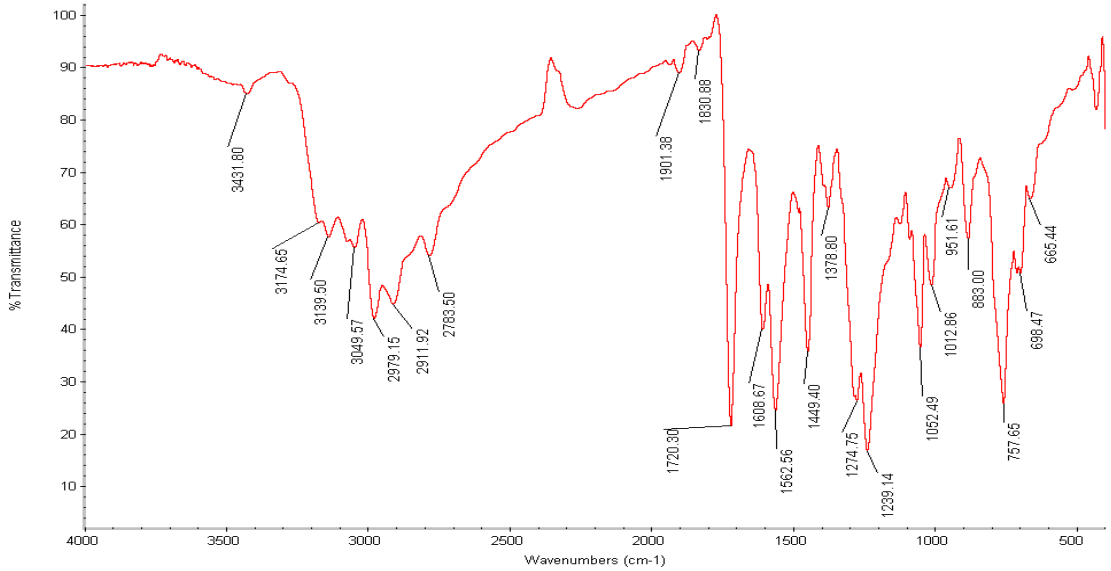


Fig. 3: g. IR data of MS-7.

Followings are NMR illustrations

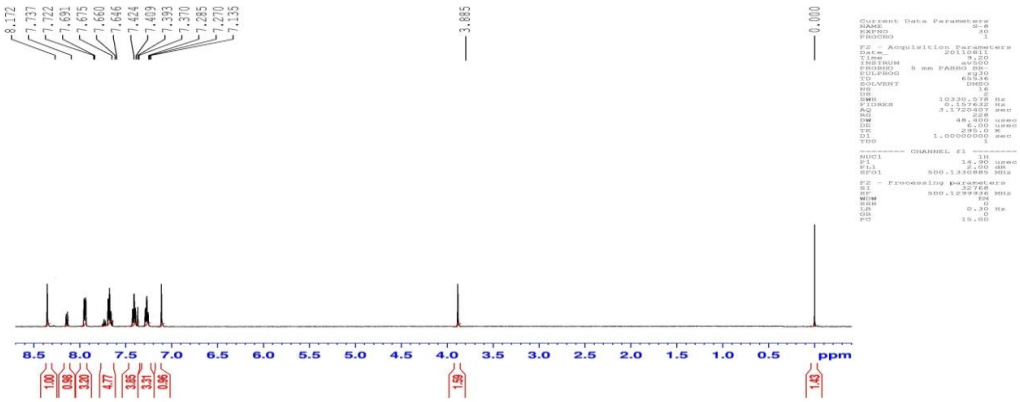


Fig. 4: ^{1}H-NMR data of MS-1.

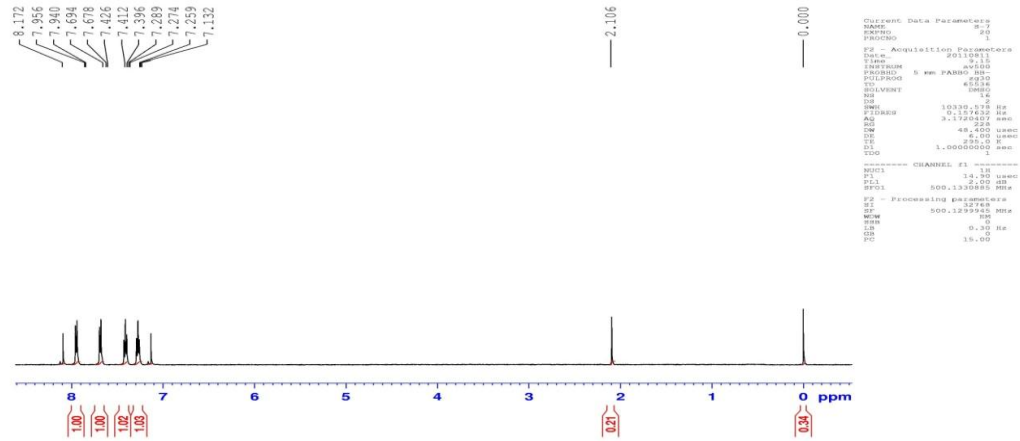


Fig. 4: a. ^{1}H-NMR data of MS-2.

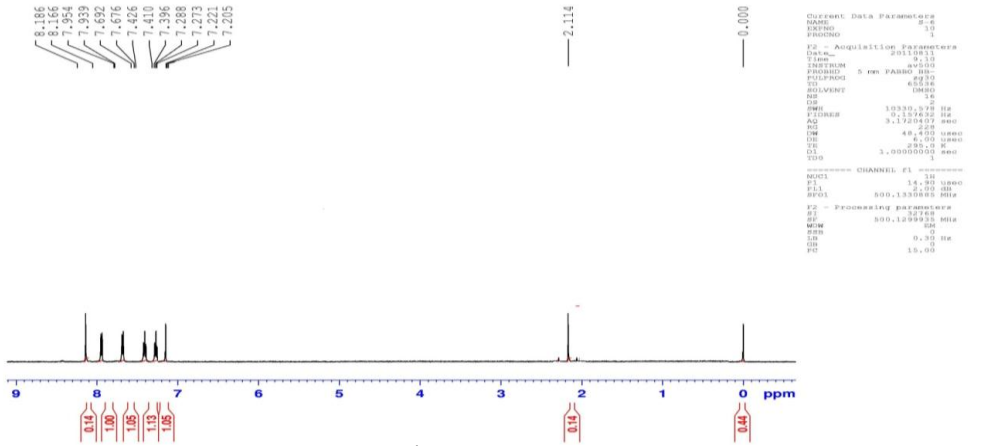


Fig. 4: b. ^{1}H-NMR data of MS-3.

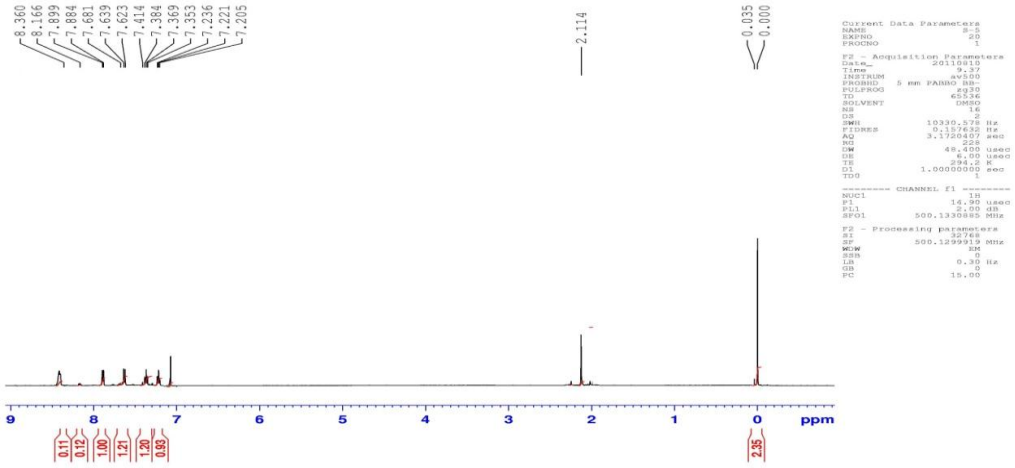


Fig. 4: c. ^{1}H-NMR data of MS-4.

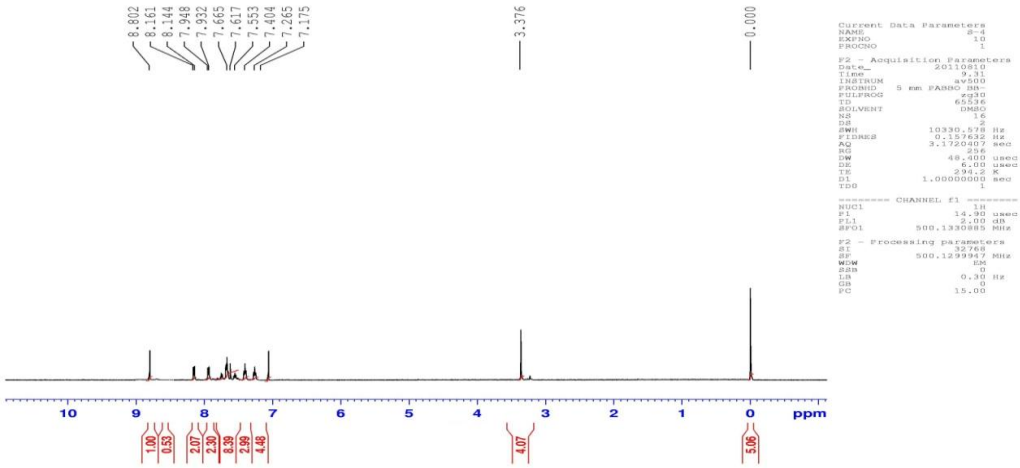


Fig. 4: d. ^{1}H-NMR data of MS-5.

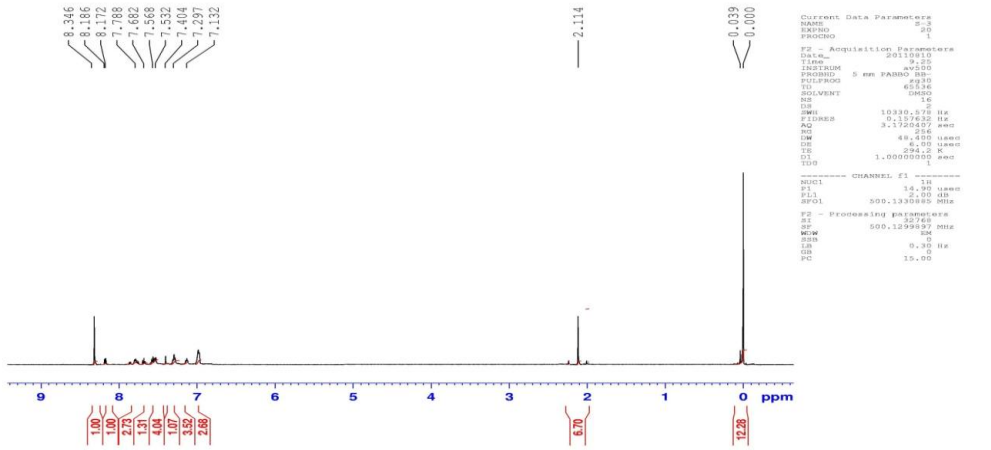


Fig. 4: e. ^{1}H-NMR data of MS-6

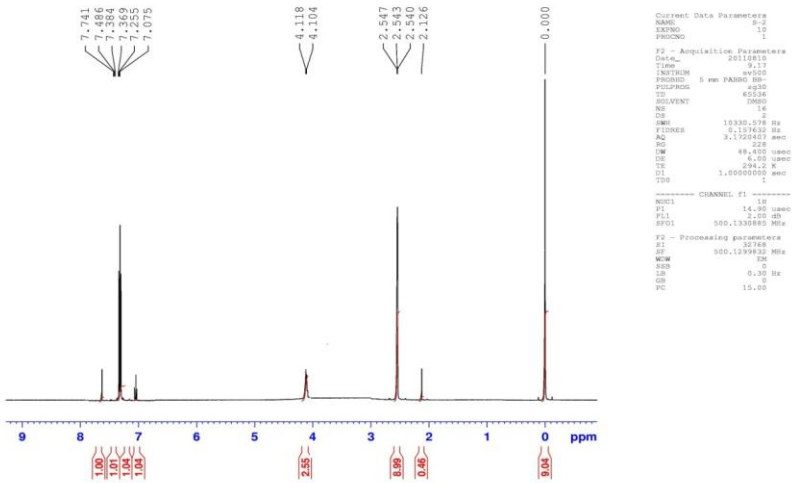


Fig. 4: f. ^{1}H-NMR data of MS-7.

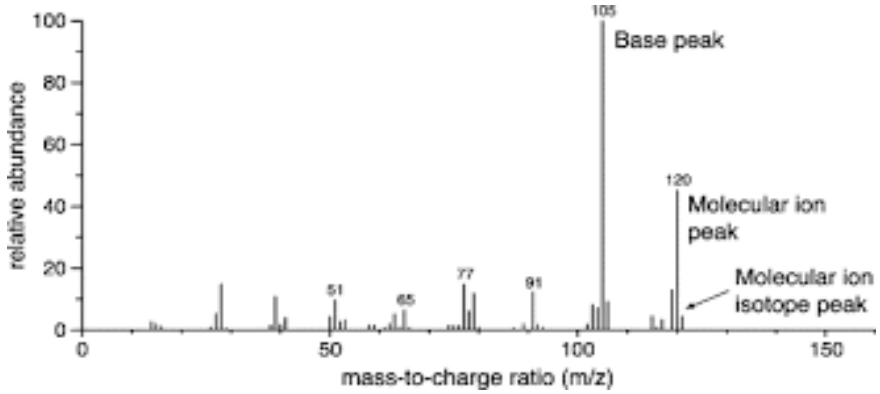


Fig 5: Mass Spectrum of 4-[2-(2-chloro-6-methylquinolin-3-yl)-4-oxo-1, 3-thiazolidin-3-yl]-2-hydroxybenzoic acid.

The results are summarized in Table 4.5a.

Table 6 Results of anti-bacterial by mic method

Sl. No	Compound Code	*Escherichia coli* [MTCC442]	*Pseudomonas aeruginosa* [MTCC441]	*Staphylococcus aureus* [MTCC96]	*Staphylococcus pyogenus* [MTCC443]
1	Ampicillin (Std)	100	100	250	100
2	MS -1	125	200	250	250
3	MS -2	100	100	250	250
4	MS-3	250	250	250	250
5	MS-4	250	200	250	250
6	MS -5	100	100	250	250
7	MS -6	125	125	100	125
8	MS -7	200	200	100	100
9	MS -8	100	125	200	100
10	MS -9	62.5	100	250	25

Out of the test substances, MS-9 shown highly effective activity against S. pyogenus and E. coli at MICs of 12.5 and 25 g/ml, respectively. Equipotent activity was demonstrated by MS-2, MS-5, and MS-8 against E. coli, MS-2, MS-5, and MS-9 against P. aeruginosa, MS-1-5 and MS-9 against S. aureus, while MS-7 and MS-8 demonstrated Equipotent activity against S. pyogenus. Comparing the remaining produced compounds to the reference standard ampicillin at 100 g/ml, they all were weak to moderate active against 9 strains of the tested organisms.

More potent activity was preferred by the compound that contained an electron withdrawing group and an unsubstituted phenyl ring.

Using the broth dilution method against 4 pathogenic microorganisms, including Escherichia coli, Pseudomonas aeruginosa (Gm-ve), Staphylococcus aureus, and Staphylococcus pyogenus (Gm+ve) at different concentrations, the antibacterial activity of the synthesised compounds MS1-9 was assessed in vitro. ranging from 6.125 g/ml to 1000 g/ml. Out of the test substances, MS-9 shown highly effective activity against S. pyogenus and E. coli at MICs of 12.5 and 25 g/ml, respectively. Equipotent activity was demonstrated by MS-2, MS-5, and MS-8 against E. coli, MS-2, MS-5, and MS-9 against P. aeruginosa, MS-1-5 and MS-9 against S. aureus, while MS-7 and MS-8 demonstrated Equipotent activity against S. pyogenus. Comparing the remaining produced compounds to the reference standard ampicillin at 100 g/ml, they all showed weak to moderate activity against all strains of the tested organisms. More potent activity was preferred by the compound that contained an electron withdrawing group and an unsubstituted phenyl ring.

When compared to other evaluated compounds, MS-9 among the produced compounds demonstrated excellent antibacterial activity against both Gm+ve and Gm ve infections. The 2-sulfonyl group is present in this molecule. This demonstrates a connection between the compound's structure and antibacterial action. To clearly understand the relationship between anti-bacterial activity and compound structure, more study is needed.

CONCLUSION

All 9 new compounds of 2-Hydroxy-4-[4-oxo-2(quinolin-3yl)-1, 3-thiazolidin- 3yl] benzoic acid derivatives synthesised were. A small number of produced substances were characterised using analytical and spectral data. Antibacterial and antifungal properties were tested on all produced substances. In tests, substances showed high potency to moderate antibacterial activity against S. pyogenus (Gm-ve) and E. coli bacteria. These compounds were found microbes sensitive but not fungus.

It suggests to test their antibacterial potential in vivo using animals then human beings. A significant data in preclinical and clinical trials will prove their use in clinical settings.

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