IJPSR (2024), Volume 15, Issue 3 **(Research Article)**

INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES AND RESEARCH

Received on 12 July 2023; received in revised form, 16 December 2023; accepted, 30 December 2023; published 01 March 2024

SYNTHESIS, CHARACTERIZATION AND ANTICANCER STUDIES OF NOVEL SULPHONAMIDES

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Keywords:

Campholenic aldehyde, DCM, Characterization, HELA and MCF7 cell line

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ABSTRACT: Currently, the arise of drug resistance and undesirable off-target effects of anti-cancer agents are major challenges for cancer treatment, which energizes medicinal chemists to develop more anti-cancer agents with high efficiency and low toxicity continuously. sulphonamide derivatives are a class of promising compounds with diverse biological activities including anti-cancer, and parts of them have been marketed for cancer therapy. In this review, we summed up the synthesis of sulphonamide derivates and their anticancer activities. Today Cancer remains to be one of the deadliest diseases in the world. Due to the potential anticancer activity of the campholinicaldehyde and sulfonamide moieties, five novel hybrid compounds containing both structures have been designed and synthesized in 3 steps. The synthesized compounds were characterized on the basis of IR, ^{1}H NMR, ^{13}C NMR spectral data, and elemental analysis and also, they were screened for *in-vitro* anticancer activity on human breast cancer cell line MCF-7 and HELA by the MTT assay method. Among them,4-fluoro-N-(4-(4-oxo-2-((2,2,3-trimethylcyclopent-3-en-1-yl) methyl) thiazolidine-yl)phenyl) benzene sulfonamide (Fig. 5b) showed the most potent anticancer activity against MCF-7 cell line. We hope this review could provide a clear insight for medicinal chemists in the rational design of more potent and bio-target specific anti-cancer agent.

INTRODUCTION: Sulfonamides (sulfa drugs) were the first drugs largely employed and systematically used as preventive and chemotherapeutic agents against various diseases. More recently, sulfonamides are used as an anticancer agent, as the antiviral HIV protease inhibitor amprenavir, and in Alzheimer's disease.

QUICK RESPONSE CODE

DOI: 10.13040/IJPSR.0975-8232.15(3).710-25

This article can be accessed online on www.ijpsr.com

DOI link: https://doi.org/10.13040/IJPSR.0975-8232.15(3).710-25

The lipophileicity of the N group has the largest effect on protein binding, and generally, the more lipids soluble a sulfonamide is the more of it will be protein bound.

Moreover, sulfonamides are also inactive if the p-amino group is acylated, benzene is substituted, sulfonamide group is not attached directly to the benzene ring. Primary sulfonamides exhibit more pharmacological properties than secondary sulfonameds. However, recent investigation shown that secondary sulphonamides have great potential over cancer properties. It was also reported that sulphonamides had a number of interesting functionalities than the primary sulphonamides.

Secondary sulphonamides represent particularly improved structural modifies in several classes of drugs **Fig. 1** [1-9]. In this study, new designs of sulfa drugs containing campholinicaldehyde and thiazolidinone moieties were utilized to obtain N-(4-(4-oxo-2-((2,2,3-trimethylcyclo pent-3-en-1-yl)methyl)thiazolidin-3-yl) phenyl) benzene sulfonamide, 4-fluoro-N-(4-(4-oxo-2-((2, 2, 3-trimethylcyclopent-3-en-1yl) methyl) thiazolidineyl) phenyl) benzene sulfonamide, 4-chloro-N-(4-(4-oxo-2-((2,2,3-trimethyl cyclopent-3-en-1-yl) methylthiazolidin-3yl)p henyl) benzenesulfonamide, 4-methyl-N-(4-(4-oxo-2-((2, 2, 3-trimethylcyclopent-3-en-1-yl) methyl) thiazolidin-3-yl) phenyl) benzene sulfonamide, 4-methoxy-benzene sulfonamide, 4-methoxy – N - (4 - (4 – oxo – 2 - ((2, 2, 3 - trime thylcyclopent-3-en-1-yl) methylthiazolidin- 3-yl) phenyl) benzene sulfonamide. Campholelenic aldehyde can be obtained by multistep synthesis from monoterpene α-pinene isolate d from turpentine oil. Hybrids with 4-thiazol idinone scaffolds as potent anticancer agents 1-5. Selvakumar, Dinesh kumar *et al.* reported that an equimolar concentration of benzene sulfonyl chloride (1mmol), 4-aminobenzoicacid (1 mmol), fly-ash: H3PO4 (0.02 mg) catalyst and 10 ml of ethanol were taken in 50ml conical flask and mixed thoroughly. This mixture was subjected to ultrasound irradiation for 20-25 min in an ultrasonic ate bath at room temperature. During the reaction 0.1 mg of potassium carbonate was added to neutralize the format ion of hydrochloride. The completion of the reaction was monitored by thin-layer chromatography. The resulting product was washed with n-hexane and separate the catalyst by filtration and dried to obtain the solids. Further, the crude was purified by column chromatogram using dichloromethane and ethyl acetate (3:1) as eluants **Fig. 3** [11-16].

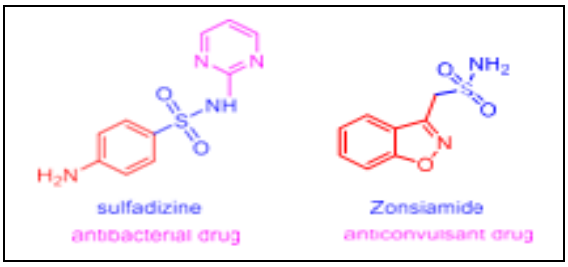

FIG. 1: SULPHONAMIDE CONTAINING DRUGS

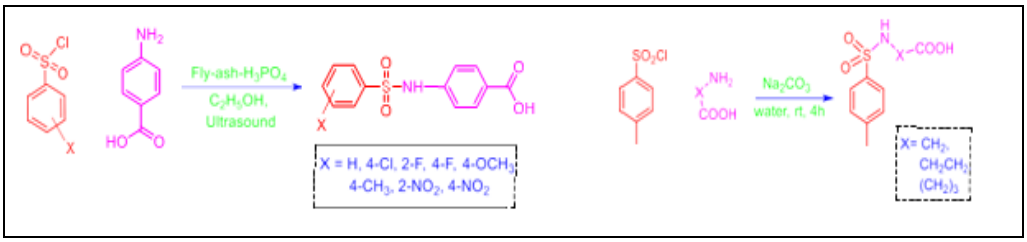

FIG. 2: SYNTHETIC METHODS OF SULPHONAMIDE

MATERIALS AND METHODS:

Materials: Campholenic aldehyde, benzene sulphonylch loride, 4-chloro benzene sulphonyl chloride, 4-floro benzene sulfonylchloride,4-methyl benzene sulphonyl chloride and 4-methoxy benzene sulphonyl chloride (from Aldrich Chem.), dichloromethane and triethyl amine (from Merck) were used.

Methods:

Synthesis of 3-(4-nitrophenyl)-2-((2,2,3-tri methylcyclopent-3-en-1-yl)methyl) thiazoli din-4-one (Fig 3): Campholenic aldehyde (10mmol), nitroaniline (10mmol), and thioglycolic acid (20mmol) in DMF (5 ml) in the presence of MK-10 as acid catalyst was stirred for 12.0 h at rt then, 6 h for refluxing at 70–90°C. The reaction w as monitored by TLC and the product was filtered, extracted with ethyl acetate and washed with hexane.

The purified product w as dried under vacuum and recrystallized fro m ethanol at rt to furnish the product. TLC system for 3-(4-amino phenyl)-2-((2,2, 3-trimethylcyclopent-3-en-1-yl) methyl) thiazolidin-4-one: stationary phase: silica gel mobile phase: hexane: ethyl acetate(v/v=6:4) visualizing agent: UV cabinet Rf value: 0.6 cm.

Synthesis is of 3-(4-aminophenyl)-2((2,2,3-trimethycyclopent-3-en-1-yl) methyl) thiaz olidin-4-one (Fig. 4): 2g tin in ethanol and 3M HCl was stirred and heated to 70oC to become clear solution. To this hot solution addition of 3-(4-nitrophenyl)-2-((2,2,3-trimethylcyclopent-3-en-1yl) methyl) thiazolidin-4-one and then this mixture was heated for 1.5 h. TLC system for 3-(4-aminophenyl)-2-((2,2, 3-trimethylcyclopent-3-en-1-yl) methyl) thiazolidin-4-one: stationary phase: silica gel mobile phase: hexane: ethyl acetate(v/v=7:3) visualizing agent: UV cabinet Rf value: 0.4 cm.

Synthes is of N-(4-(4-oxo-2-((2,2,3-trimeth ylcyclopent3-en-1-yl) methyl) thiazolidine- 3yl) phenyl) benzene sulphonamide derivatives (Fig. 5a, 5b, 5c, 5d, 5e): 1:1 mole equivalent of 3-(4-aminoophenyl)- 2-((2,2,3-trimethyl1cyclopent-3-en-1-yl) methyl) thiazolidin-4-one and phenyl sulphonyl chloride is taken in DCM and then added 1.0 mole equivalent of triethyl amine. The reaction mixture was stirred at rt for 6 h, cooled and filtered to obtain the pure product in good yield. TLC system for benzene sulphonamide derivates stationary phase: silica gel mobile phase: hexane: ethyl acetate (v/v=8:2) visualizing agent: UV cabinet Rf value: 0.7 cm.

Optimization Conditions for Sulphonamides: 3-(4-aminophenyl)-2-((2,2,3-trimethyl cyclopent-3-en-1-yl) methyl) thiazolidin-4-one and various phenyl sulphonylchloride were used for the model studies, which is shown below. 1:1 ratio of 3-(4-aminoophenyl)-2-((2,2,3- trimethyl1cyclopent-3-en-1-yl) methyl) thiazolidin-4-one and substituted phenyl sulphoneyl chloride in CH_2Cl_2 (0.3M), this suspenseon was stirred for 5 min, and then, 2 equivalents of Et3N were added to the above reaction mixture. The stirring continued at rt. Some h eat generation was observed and the suspense on became clear, with precipitates appearing later. The reaction was worked up after 6 h to give a 70-80% yield. The reaction to stirovernight, improved the yield to 89%. Next, the effect of different solvents on the reaction was examined. In CH_2Cl_2 and pyridine as a catalyst, after 6h the reaction preceded to 41% conversion to the desired product while after 16 h, 48% of the desired product had formed. The use of a polar solvent like THF in Et3N, gave 55% product after 6 h. From these screening results, CH_2Cl_2 appeared to be the best non-polar solvent and triethylamine as a catalyst for conducting the coupling reaction. Since, the reaction profile in CH_2Cl_2 w as much cleaner than that of THF, CH_2Cl_2 w as chosen as the standard solvent. By increasing the amount of Et3N from 2 to 3 equivalents, the yield of the Et3N from 2 to 3 equivalents, the yield of the Et3N from 2 to 3 equivalents, the yield of the reaction was significantly improved to 98% in 6 h.

TABLE 1:

S. no.	Solvent	Temperature	Yield %
1	Pyridine/MDC	RT	<50
2	TEA/THF	RT	55
3	TEA/MDC	RT	70-80

Experimental Details:

Synthesis of 3 - (4 - nitrophenyl) – 2 - ((2, 2, 3-trimethylcyclopent-3-en-1-yl) methyl) thia zolidin-4-one (Fig. 3): Campholenic aldehyde (10mmol), nitroaniline (10mmol) and thioglycolic acid (20mmol) in DMF (5mL) in the presence of MK-10 as acid catalyst were stirred for 12 h at rt and then, 6 h for refluxing at 70–90°C and got viscous oil, yield is about 70.8%. Soluble in DCM and ethanol. The spectral data obtained as shown below. ^{1}H NMR δ: 7.24 (d, 2H, J=8.3Hz), 6.84 (d, 2H, J=8.1Hz), 5.19-14.71 (m, 1H), 4.42-4.06 (t, 1H, J=4.0 Hz, 8.0 Hz), 3.83 (s, 2H), 1.70 (s, 3H), 1.51-1.48 (m, 2H), 1.25 (d, 2H, J=8.1 Hz), 1.24-1.20 (t, 1H, J=4.0 Hz, 8.0 Hz), 1.00 (m, 6H). ^{13}C NMR δ: 164.40, 146.85, 146.00, 138.22, 138.80, 120.36, 118.50, 57.75, 44.60, 35.50, 28.86, 20.68, 17.45. Mass (m/z): 347.44 (M+H+). IR (neat): cm^{-1} 2850, 2790, 1678, 1500, 963.

Synthesis of 3-(4-amino phenyl)-2-((2,2,3-trimethylcyclopent-3-en-1-yl) methyl) thia zolidin-4-one (Fig. 4): 2g tin in ethanol and 3M HCl and this mixture was stirred, heated to 70^{o}C to become clear solution. To this hot solution, addition of 3- (4-nitrophenyl) – 2 - ((2, 2, 3-trimethylcyclopent 3-en-1-yl) methyl) thiazolidin-4-one, mixture was heated for 1.5 h and got brown

coloured melting point 383.57°C, yield is about 85.6%. Soluble in DCM and ethanol. The spectral data obtained as shown below. ^{1}H NMR δ: 16.47 (d, 2H, J=8.3 Hz), 6.0 (d, 2H, J=8.1 Hz), 5.32-5.25 (m, 1H), 4.51-4.49(t, 1H, J=4.0 Hz, 8.0 Hz), 4.40 (s, 2H,), 3.87 (s, 2H, J=8.1 Hz), 5.32-5.25 (m, 1H), 4.51-4.49 (t, 1H, J=4.0 Hz, 8.0 Hz), 4.40 (s, 2H,), 3.87 (s, 2H), 1.73 (s, 3H), 1.67-1.66 (m, 2H), 1.56-1.53 (t, 1H, J=4.0 Hz, 8.0 Hz), 1.52 (d, 2H, J=8.1 Hz), 0.79 (m, 6H). ^{13}C NMR δ: 164.35, 146.76, 143.86, 138.21, 130.84, 123.01, 120.27, 59.86, 45.82, 43.71, 32.69, 24.43, 20.68, 17.40. Mass (m/z): 317.33 ($M+H^+$). IR (neat): cm^{-1} 3658, 2950, 1509, 963.

Synthesis of N-(4-(4-oxo-2-((2,2,3-trimethy lcyclopent-3-en-1-yl)methyl) thiazolidin-3-yl)phenyl) benzene sulfonamide (Fig. 5a): The reaction involves 1:1mole equivalent of 3-(4-aminophenyl)-2-((2,2,3-trimethylcyclo pent-3-en-1-yl)methyl) thiazolidin-4-one and benzene sulphonylchloride in DCM and the n, added 1.0 mole equivalent of triethylamine, stirred at rt, maintain it for 24 h and got light yellow-green ppt, yield is about 72.5%. and melting point 447.01°C. soluble in DCM, ethyl acetate and ethanol. The spectral data obtained as shown below.

^{1}H NMR δ: 9.93 (s, 1H), 8.07 (d, 2H, J=8.0Hz), 7.52 (d, 2H, J=8.0 Hz), 7.23 (d, 2H, J=8.0Hz), 6.64 (d, 2H, J=8.0 Hz), 6.38-6.36 (m, 1H), 5.07-5.04 (t, 1H, J=4.0 Hz, 8.0 Hz) 3.84 (s, 2H), 1.73 (s, 3H), 1.68-1.63 (t, 1H, J=4.0 Hz, 8.0 Hz), 1.63-1.61 (m, 2H), 1.58-1.55 (m, 2 H), 1.55-1.53 (m, 1H), 1.05 (m, 6H). ^{13}C NMR δ: 164.35, 146.76, 143.86, 141.40, 138.21, 131.57, 130.84, 129.70, 128.55, 125.99, 124.83, 124.80, 120.27, 59.86, 45.82, 43.71, 32.65, 24.43, 17.40. Mass (m/z): 393.40 (M+H+). IR (neat): cm-1 3310, 3220, 1660, 1597, 1284, 837.

Synthesis of 4-fluoro-N-(4-(4-oxo-2-((2,2,3-trimethylcyclopent-3-en-1-yl) methyl) thia zolidine-yl)phenyl) benzene sulfonamide (Fig. 5b): The reaction involves 1:1 mole1equivalent of 3-(4-aminophenyl)-2-((2,2,3-trimethylcyclo pent-3-en-1-yl) methyl) thiazolidin-4-one and 4-floro benzene sulphonyl chloride in DCM and then, added 1.0 mole equivalent of triethylamine, the mixture was stirred at rt, maintained it for 24 h and got pinkish-blue ppt, melting point 452.25°C yield is about 68.3%. Solub le in DCM, ethyl acetate and ethanol. The spectral data obtained as shown below.

^{1}H NMR δ: 110.17 (s, 1H), 8.09 (d, 2H, J=8.0Hz), 7.24 (d, 2H, J=8.0 Hz),7.14 (d, 2H, J=8.0Hz), 7.10 (d, 2H, J=8.0 Hz), 5.89-5.86 (t, 1H, J=4.0 Hz, 8.0Hz), 4.28-4.27 (t, 1H, J=8 Hz), 4.26 (s, 2H), 3.93 (s, 3H), 1.88-1.85 (m, 2H),1.42-1.41 (m, 2H), 0.80 (m, 6H). ^{13}C NMR δ: 166.11, 1149.16, 134.88, 133.33,133.17, 132.67, 132.47, 132.27, 129.71, 129.03, 123.80, 115.20, 58.65, 45.31, 43.69, 36.30, 29.73, 20.24, 17.49. Mass (m/z): 492.11($M+H^+$). IR (neat): cm^{-1} 3296, 3115, 1657, 1450, 837.

Synthesis of 4-methyl-N-(4-(4-oxo-2-((2,2, 3-trimethylcyclopent-3-en-1-yl) methyl) thi azolidine-3-yl)phenyl)benzenesulfonamide (Fig. 5d): The reaction involves 1:1 mole equivalent of 3-(4-aminophenyl)-2-((2,2,3-trimethylcyclo pent-3-en-1-yl)methyl) thiazolidin-4-one and 4-methyl benzene sulphonylchloride in DCM and then, added 1.0 mole equivalents of triethylamine, stirred at rt, maintained for 24 h and got pinkish-blue solid, melting point 449.89°C, yield is about 65.9%. soluble in DCM ethyl acetate and ethanol. The spectral data obtained as shown below.

^{1}H NMR δ: 9.371(s, 1H), 8.09 (d, 2H, J=8.0Hz), 7.24 (d, 2H, J=8.0 Hz), 7.14 (d, 2H, J=8.0 Hz), 7.10 (d, 2H, J=8.0 Hz), 5.89-5.86 (t,1H, J=4.0 Hz, 8.0 Hz), 4.28-4.26 (t, 1H, J=4.0 Hz, 8.0 Hz), 4.25 (s, 2H), 3.93 (s, 3H), 1.89-1.85 (m, 2H), 1.42-1.41 (m, 4H), 0.97 (s,3H), 0.80 (m, 6H). ^{13}C NMR δ: 166.11, 149.16, 134.88, 133.33,133.17, 132.67, 132.47, 132.27, 129.71, 129.03, 123.79, 115.20, 58.65, 45.31, 43.69, 36.30, 29.73, 23.74, 20.24, 17.40. Mass (m/z): 471.27 ($M+H^+$). IR (neat): cm^{-1} 3320, 3122, 1649, 1449, 963.

Synthesis of 4-methoxy-N-(4-(4-oxo-2-((2, 2,3-trimethylcyclopent-3-en-1-yl) methylth iazolidin-3-yl) phenyl) benzene sulfonamide (Fig. 5e): The reaction involves 1:1 mole equivalent of 3-(4-aminophenyl)-2-((2,2,3-trimethyl cyclo pent-3-en-1-yl) methyl) thiazolidin-4-one and 4-methoxy benzene sulphonylchloride in DC M and then, added 1.0 mole equivalent of tri ethyl amine, stirred at rt, maintained it for 24 h and got pink-white solid, yield is about 61.5%. and melting point 430.58°C. soluble in DCM, ethyl

acetate and ethanol. The spect ral data obtained as shown below.

^{1}H NMR δ: 9.37 (s, 1H), 8.09 (d, 2H, J=8.0Hz), 7.24 (d, 2H, J=8.0 Hz), 7.15 (d, 2H, J=8.0 Hz), 7.12 (d, 2H, J=4.0 Hz), 5.89-5.86 (t,1H, J=8.0 Hz, 4.0 Hz), 4.28- 4.25 (t, 1H J=8.0 Hz, 4.0 Hz), 4.25 (s, 2H), 3.93 (s, 3H), 3.70 (s,3H), 1.88-1.85 (m, 2H), 1.45-1.44 (m,1H), 1.42 (d, 2H, J=4) Hz), 0.97 (m, 6H).

^{13}C NMR δ: 157.40, 149.18, 134.88, 133.33, 133.17, 132. 67, 132.47, 125.92, 123.80, 41.45-1.44 (m, 2H), 1.44-1.41 (m, 1H), 0.80 (m, 6H).

^{13}C NMR δ: 166.11, 149.18, 134.88, 133.33, 133.17, 132.47, 132.27, 129.71, 129.03, 123.80, 115.20, 58.65, 45.31, 43.69, 36.30, 29.73, 20.24, 17.49.

Mass (m/z): 475.15 ($M+H^{+}$). IR (neat): cm^{-1} 3335, 3292, 1656, 1514, 1284, 837.

Synthesis of 4-chloro-N-(4-(4-oxo-2-((2,2,3-tri methyl cyclopent-3-en-1-yl) methyl) thiazolidin-3-yl) phenyl) benzene sulfonamide (Fig. 5c): The reaction involves 1:1 mole equivalent of 3-(4-aminophenyl)-2-((2,2,3-trimethyl cyclo pent-3-en-1-yl)methyl) thiazolidin-4-one and 4-chloro benzene sulphonylchloride in DCM and then, added 1.0 mole equivalent of triethy l amine, stirred at rt, maintained the mixture for 24 h and got light pink-white solid, melting point 450.96°C. Yield is about 72.3%. solub le in DCM, ethyl acetate and ethanol. The spectral data obtained as shown below. ^{1}H NMR δ: 110.83 (s, 1H), 18.09 (d, 2H, J=8.0 Hz), 7.24 (d, 2H, J=8.0 Hz), 7.14 (d, 2H, J=8.0 Hz), 17.10 (d, 2H, J=8.0 Hz), 5.90 - 5.8 86 (t, 1H, J=8Hz), 4.29-4.26 (t, 1H, J=8Hz), 4.25 (s, 2H), 3.92 (s, 3H), 1.88-1.85 (m, 2H), 123.79, 115.20, 58.65, 54.46, 45.31, 43.69, 36.30, 29.73, 23.74, 20.24, 17.49. Mass (m/z): 471.27 (M/H+). IR: cm-1 3447, 3168, 1659, 1449, 963.

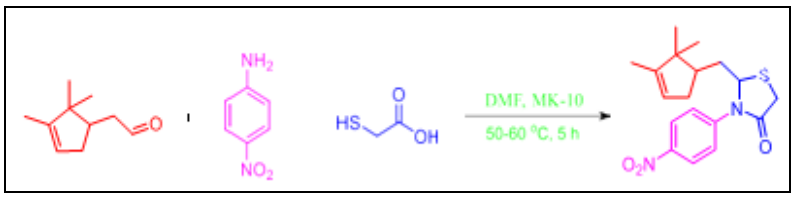

FIG. 3: SYNTHESIS OF THAZOLIDINONE DERIVATIVE

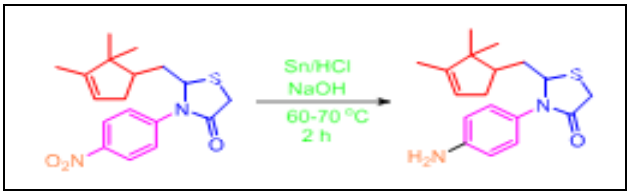

FIG. 4: SYNTHESIS OF AMINE DERIVATIVE

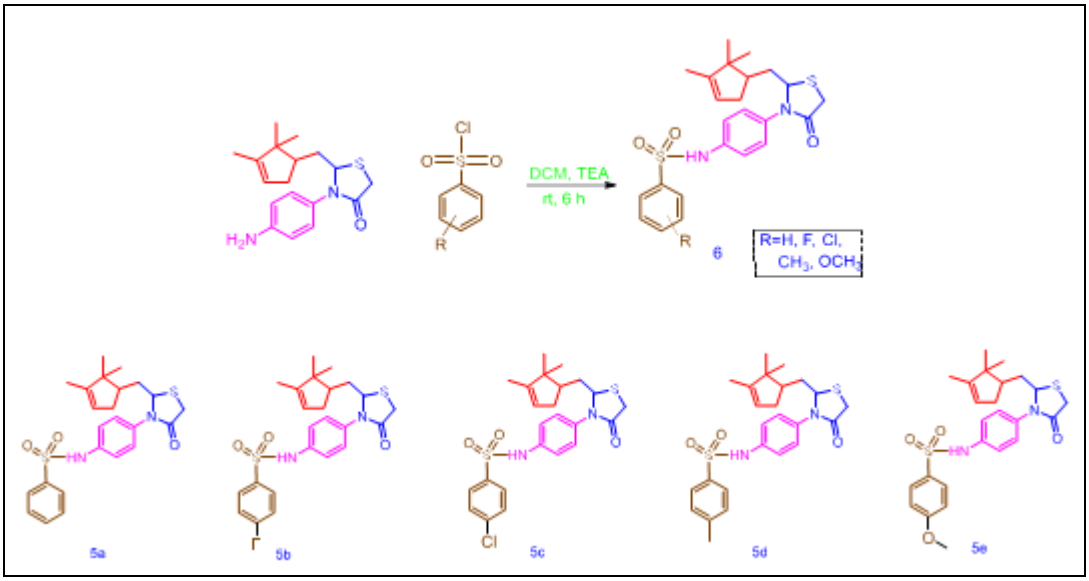

FIG. 5: SYNTHESIS OF SULPHONAMIDE DERIVATIVES

RESULTS AND DISCUSSION: Sulphonamide group can act as a directing group in promoting C–H activation. Simple and straightforward synthetic procedures were adopted for the synthesis of our target sulfonamide 4-thiazolidinone derivatives. synthesis of 1,3-thiazolidin-4-ones involves three main components: an amine, a carbonyl compound and a mercaptoacetic acid, the synthetic process either prepared in a one-pot three-component condensation or in a two-step process **Fig. 3**. The reaction pathway involves the in-situ formation of intermediate 5-triazolyli mines by condensation of the amine with the appropriate aldehydes. The produced imines undergo attack by generated sulphurnucleophile when refluxed with mercapto acetic acid followed by the intramolecular cyclizati on to yield the substituted 1,3-thiazolidin-4- ones **Fig 3**.

All of the synthesized compounds were characterized by spectroscopic techniques (^{1}H-NMR, ^{13}C NMR and mass spectra). The proton spectra clearly represent the structure having different hetero-atoms, through which the value of the proton appeared at different ranges. The spectral data of the synthesized compound **Fig. 3** was in agreement with their proposed structures. The IR data clearly showed a strong C=O stretching band around 1730 cm^{-1} and 1259 cm^{-1}, which were characteristic for 4-thiazolidinones, in addition to the aromatic C-H absorption band around 3030 cm^{-1}. The ^{1}H NMR data indicated the presence of characteristic peaks for 4-thiazolidinone protons of the triplet peak of CH around 4.51-4.49 ppm and a singlet peak at around 4.40 ppm of CH2 for 4-thiazolidinone. characteristic peaks for aromatic protons app ear in their expected range of 6–7 ppm. The absence of any peaks in the range of δ 5–6 ppm indicated the presence of δ 5–6 ppm indicated the presence of unsaturated structure. ^{13}C NM R of synthesized compounds showed characteristic peaks for carbon 3’ and carbon 5’ of the thiazolidinone ring at their expected. Chemical shift δ 164.35 and 146.76 ppm, respectively. The ^{13}C value was also shown by the carbonyl carbon of the thiazolidinonering at 123.0 1 ppm, showing the thiazole carbon directly attached with two nitrogen atoms. Next, the carbon appeared at 143.86 ppm of the thiazolidinone ring, attached to CH proton of campholenic and emerged in both the nitrogen and sulfur of the thiazolidinone ring. Then, carbon appeared at 146.76 ppm in between the thiazolidinone and aniline rings, with 138.21 ppm carbon of the aniline attached to –NH2 as shown in **Fig 4**. FT-IR; the characteristics band at 2850-2980 cm^{-1} of (C-H), 1678-1710 cm^{-1} of (C=O), 1565-1603 cm^{-1} of (C-N).

The synthesis of N-(4-(4-oxo-2-((2,2,3-trime thyl1cyclopent-3-en-1-yl) methyl) thiazoldine-3-yl) phenyl) benzene sulfonamide derivative s involves 1:1mole equivalent of 3-(4-amino phenyl)-2-((2,2,3-trimethylcyclopent-3-en-1-yl) methyl) thiazolidin-4-one and substituted phenyl sulphonyl chloride were taken in DC M and then, added 1.0 mole equivalent of tri ethyl amine **Fig. 5A-5E**. The condensation of with benzene sulphonylchloride involved nucleophilic substitution. The synthesized compounds were characterized by FT-IR; the characteristics band at 3528-3660 cm^{-1} of (N– H) and 1650-1689 cm^{-1} of (C=O) and 1413-1294 cm^{-1} of S=O stretching and 1266-133 3 cm^{-1} of (C-N).

Spectral Data of Synthesised Compounds (Fig. 3-5):

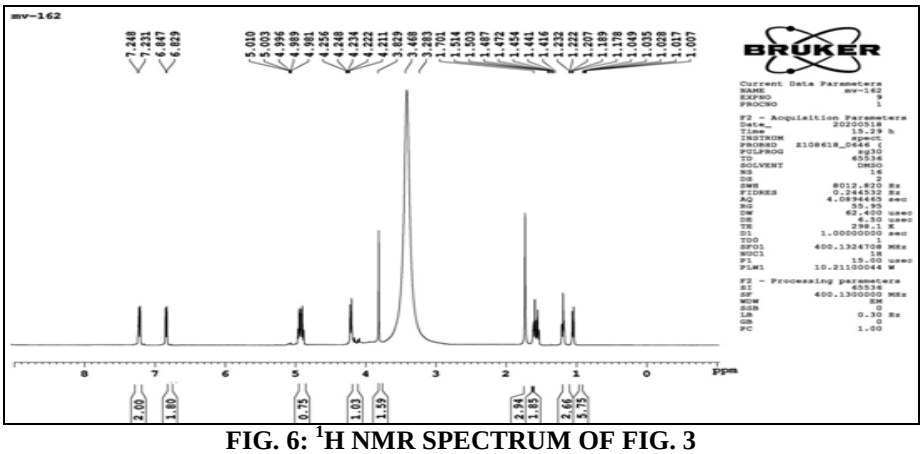

FIG. 6: ^{1}H NMR SPECTRUM OF FIG. 3

Its ^{1}H NMR spectrum showed downfield singlet signals at 9-11 ppm NH protons. Next, the carbon appeared at 45.31 ppm of the aromatic ring, attached to S=O of sulphonamide. ^{1}H NMR which displayed compounds showed singlet OCH3 group in the region of δ 3.70 and ^{13}C NMR showed signal for Carbon of -OCH3 group at signal at 58.65 ppm.

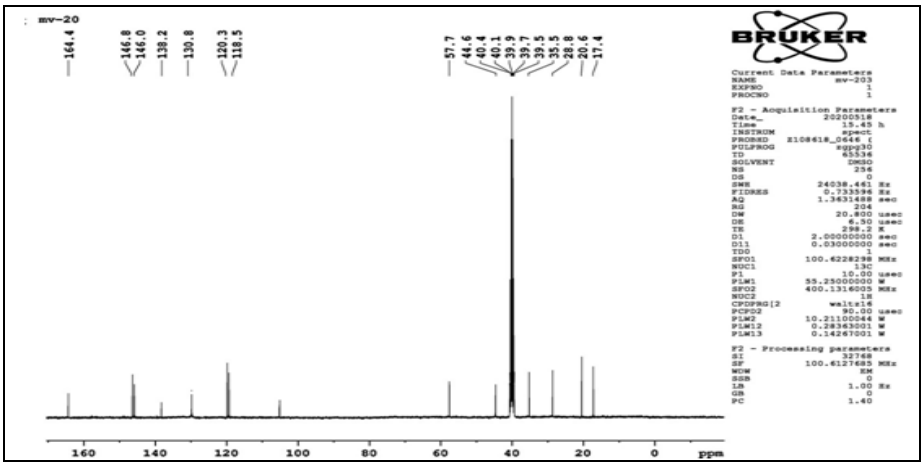

FIG. 7: 13C NMR SPECTRUM OF FIG. 3

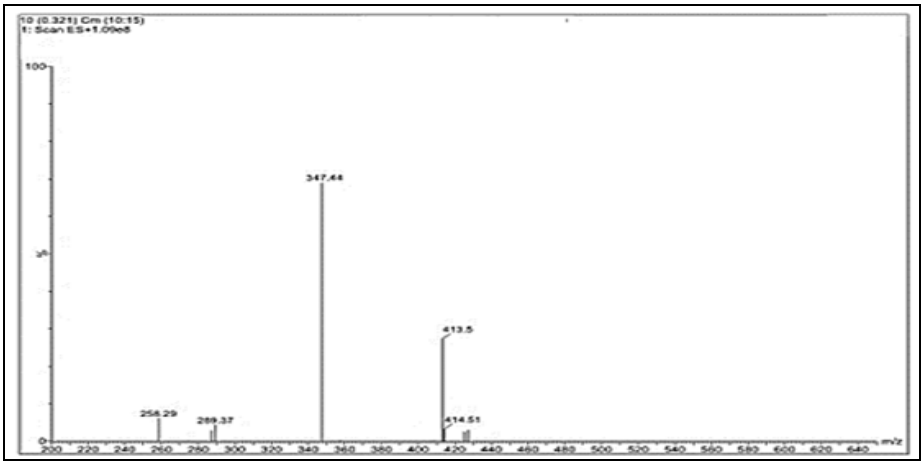

FIG. 8: MASS SPECTRUM OF FIG. 3

Mass (m/z): The molecular weight of the compound is 347.44 ($M+H^{+}$).

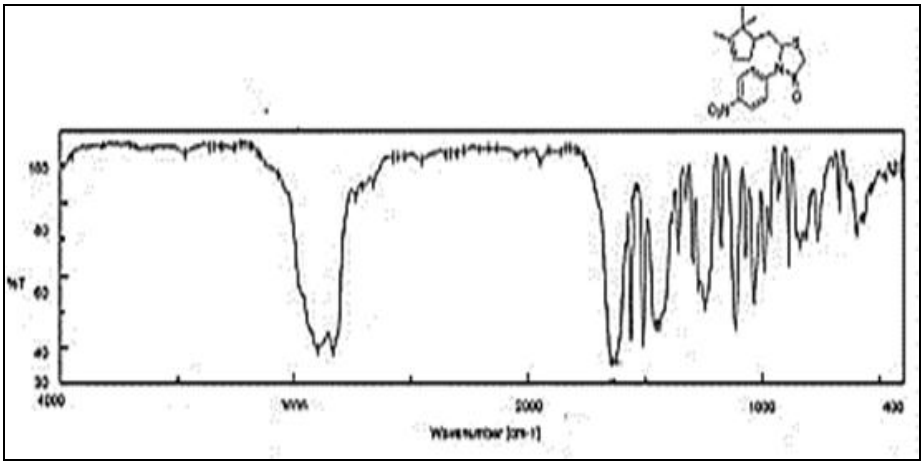

FIG. 9: IR SPECTRUM OF FIG. 3

IR (cm^{-1}): The characteristics band at 2850-2980 cm^{-1} of (C-H), 1678-1710 cm^{-1} of (C=O), 1565-1603 cm-1 of (C-N).

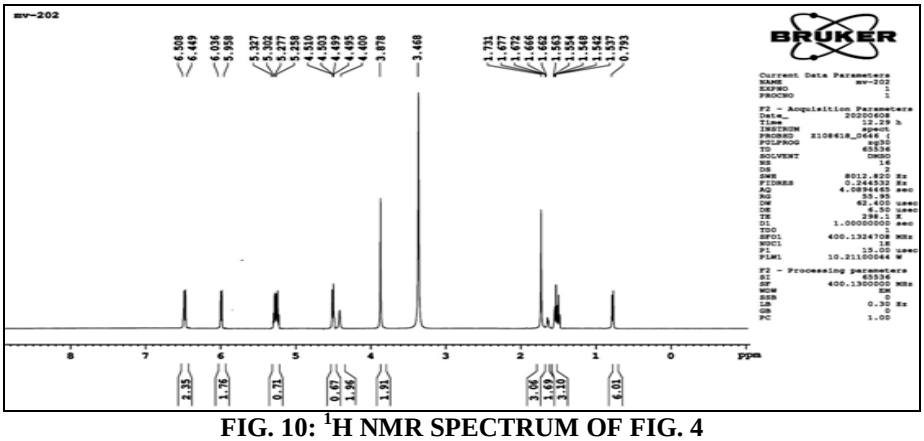

FIG. 10: ^{1}H NMR SPECTRUM OF FIG. 4

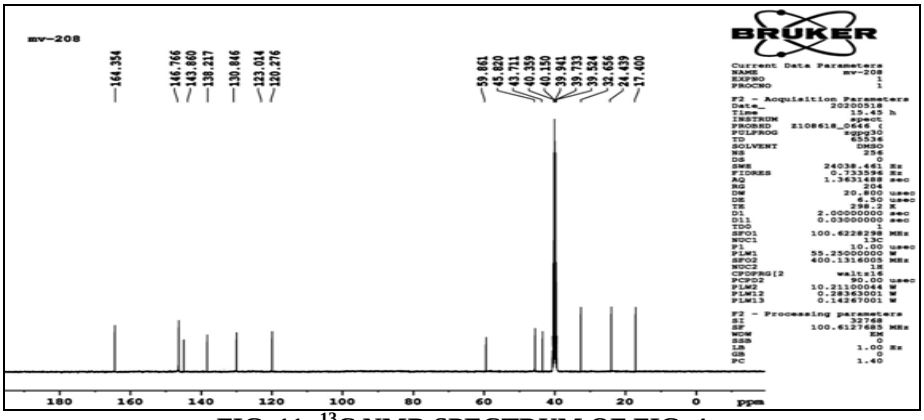

FIG. 11: ^{13}C NMR SPECTRUM OF FIG. 4

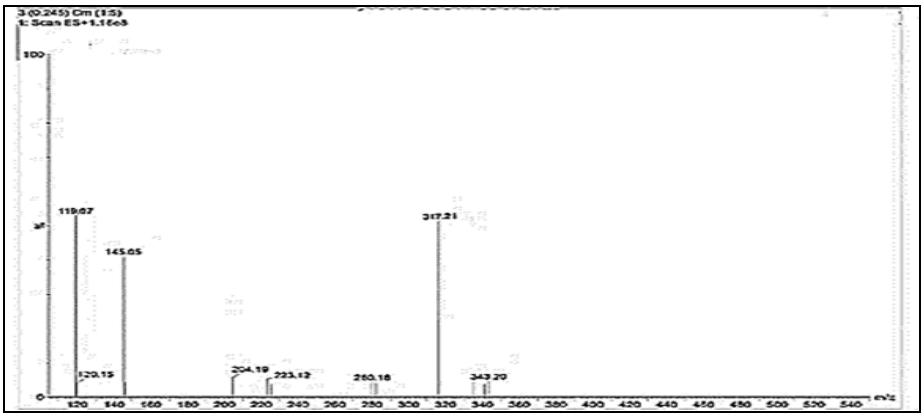

FIG. 12: MASS SPECTROMETRY OF FIG. 4

Mass (m/z): The molecular weight of the compound is 317.21 ($M^{+}H^{+}$)

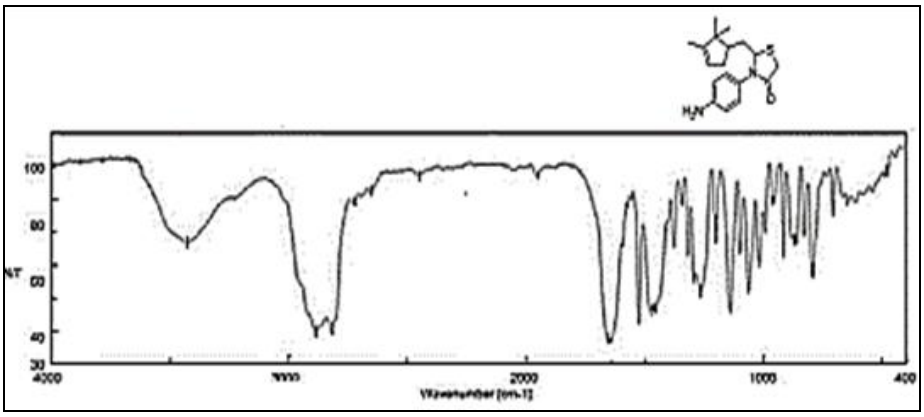

FIG. 13: IR SPECTRUM OF FIG. 4

IR (cm^{-1}): The characteristics band at 3528-3676 cm^{-1} of (N–H).

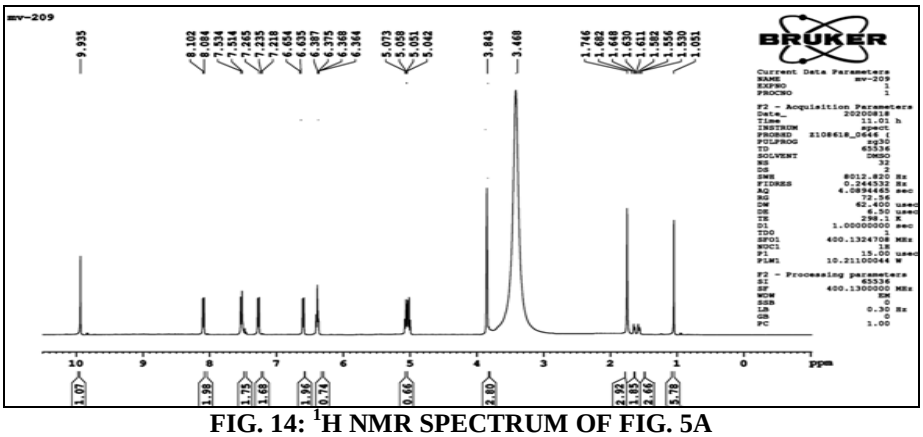

FIG. 14: ^{1}H NMR SPECTRUM OF FIG. 5A

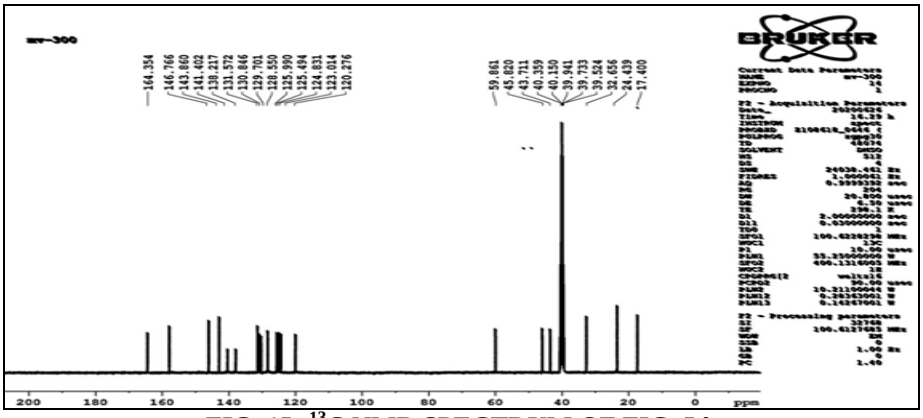

FIG. 15: ^{13}C NMR SPECTRUM OF FIG. 5A

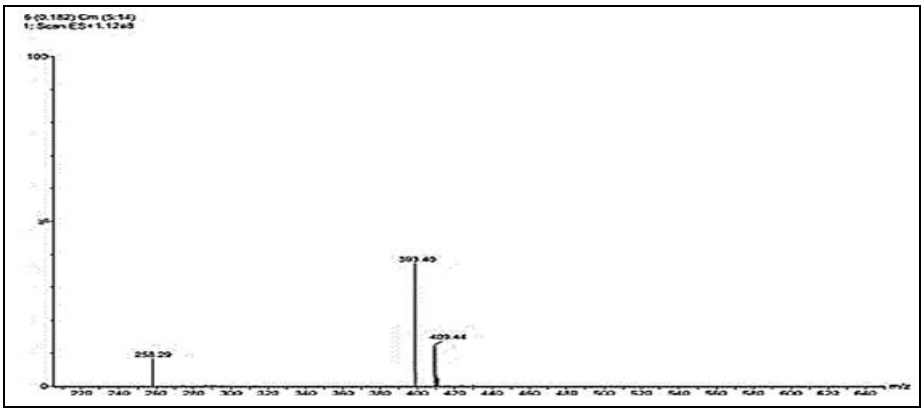

FIG.16: MASS SPECTRUM OF FIG. 5A

Mass (m/z): The molecular weight of the compound is 393.40 (M+H^{+}).

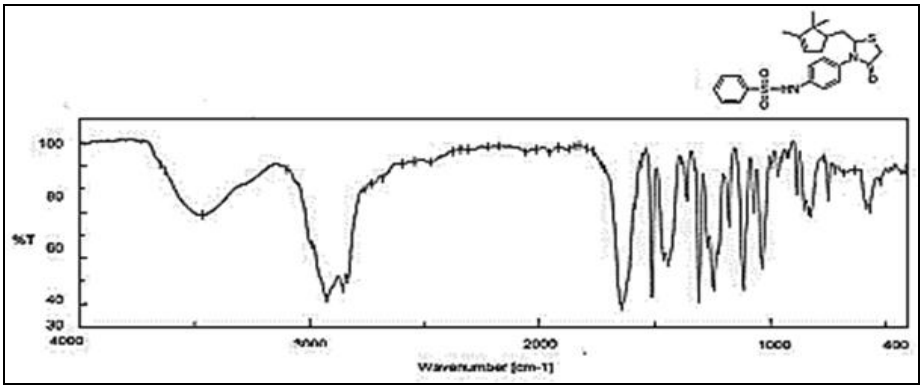

FIG. 17: IR SPECTRUM OF FIG. 5A

IR (cm^{-1}): The characteristics band at 3528-3476 cm^{-1} of (N–H) and 1650-1689 cm^{-1} of (C=O) and 1495-1504 cm^{-1} of S=O stretching and 1266 - 1333 cm^{-1} of (C-N).

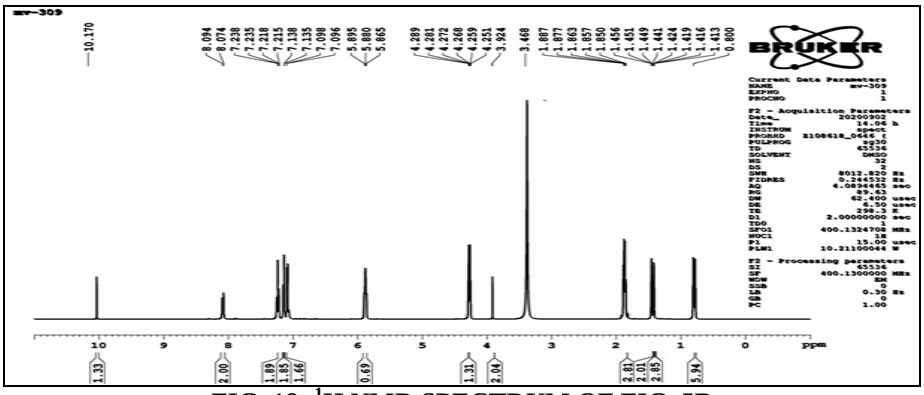

FIG. 18: ^{1}H NMR SPECTRUM OF FIG. 5B

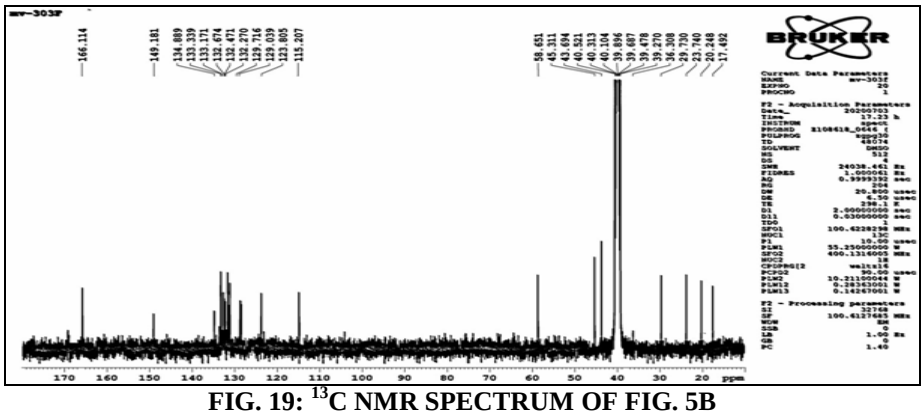

FIG. 19: ^{13}C NMR SPECTRUM OF FIG. 5B

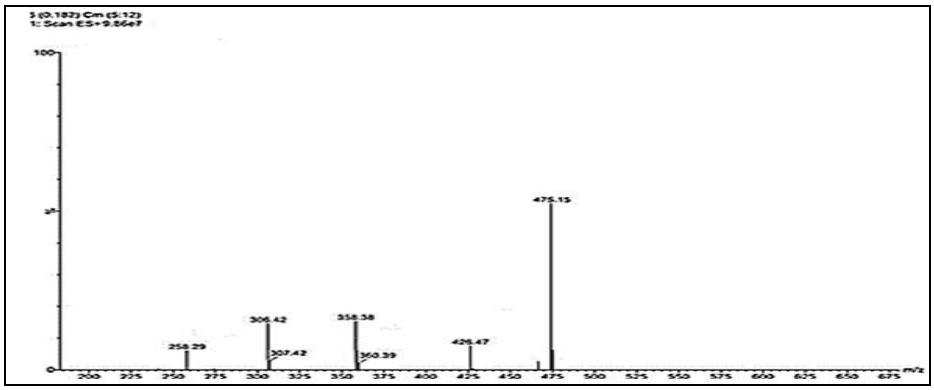

FIG. 20: MASS SPECTRUM OF FIG 5B

Mass (m/z): The molecular weight of the compound is 475.15 ($M+H^{+}$).

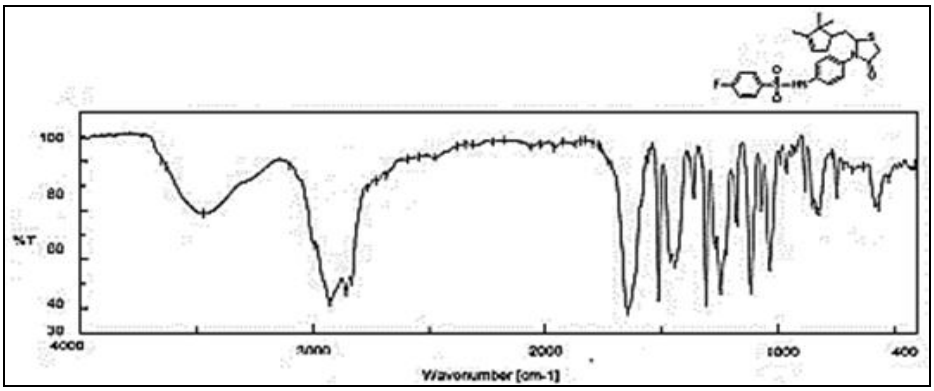

FIG. 21: IR SPECTRUM OF FIG 5B

IR (cm^{-1}): The characteristics band at 3568-3446 cm^{-1} of (N–H) and 2986-2748 cm^{-1} of (C-H), 1650-1689 cm^{-1} of (C=O) and 1495-1504 cm^{-1} of S=O stretching and 1266 - 1333 cm^{-1} of (C-N).

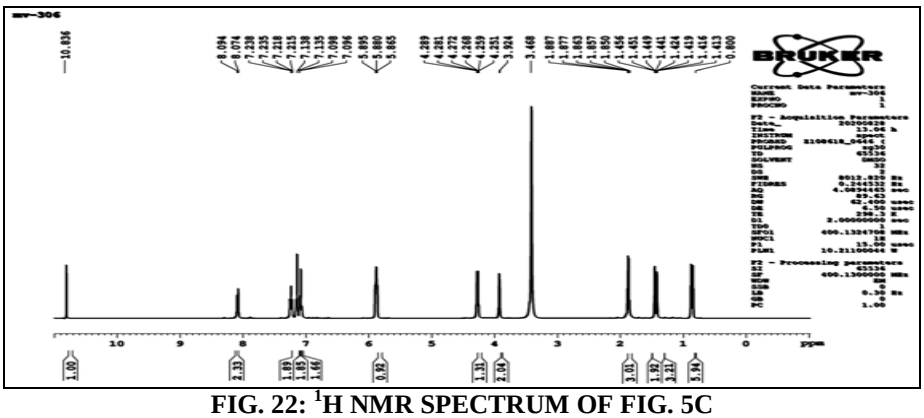

FIG. 22: ^{1}H NMR SPECTRUM OF FIG. 5C

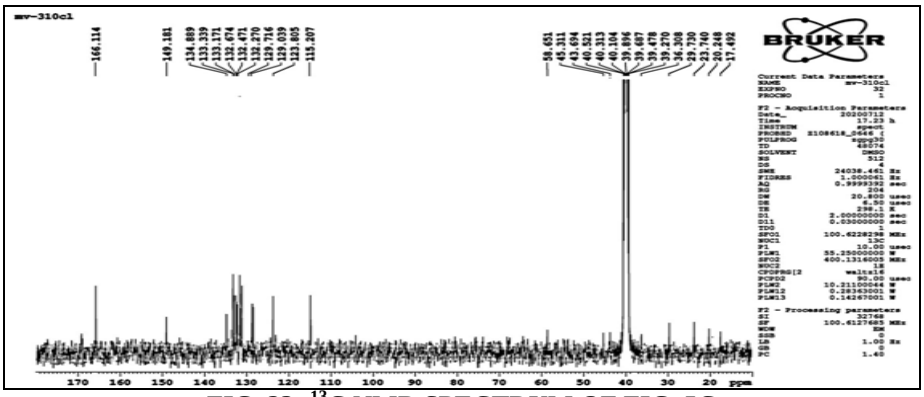

FIG. 23: ^{13}C NMR SPECTRUM OF FIG. 5C

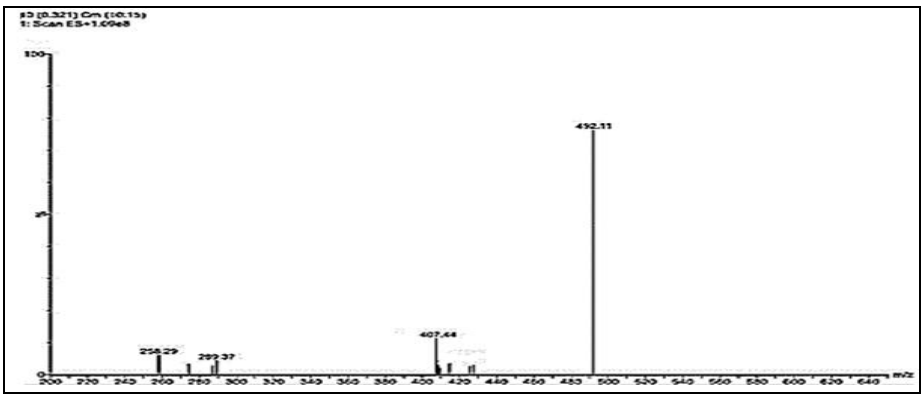

FIG. 24: MASS SPECTRUM OF FIG. 5C

Mass (m/z): The molecular weight of the compound is 492.11 ($M+H^{+}$).

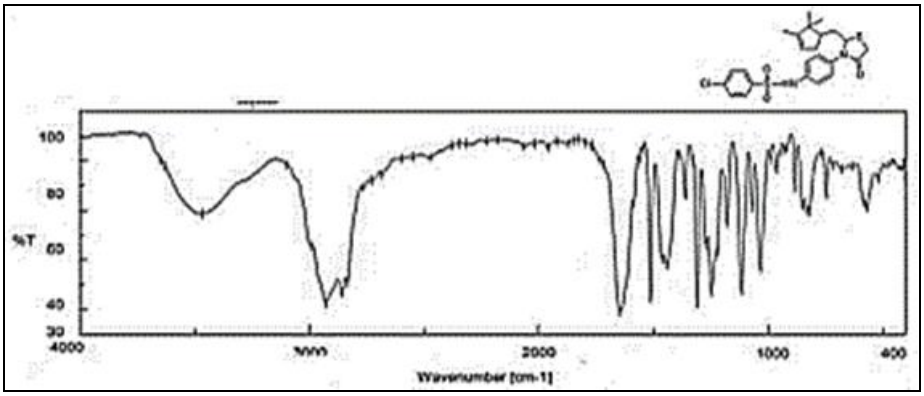

FIG. 25: IR SPECTRUM OF FIG. 5C

IR (cm^{-1}): The characteristics band at 3568-3446 cm^{-1} of (N–H) and 2986-2748 cm^{-1} of (C-H), 1650-1689 cm^{-1} of (C=O) and 1495-1504 cm^{-1} of S=O stretching and 1266-1333 cm^{-1} of (C-N).

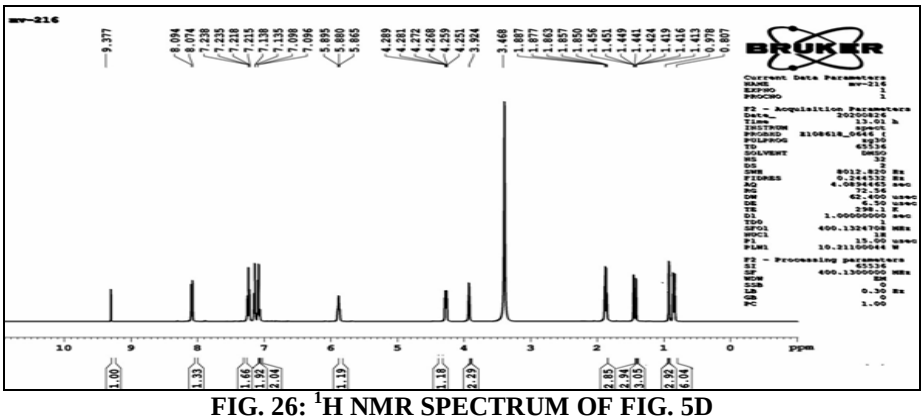

FIG. 26: ^{1}H NMR SPECTRUM OF FIG. 5D

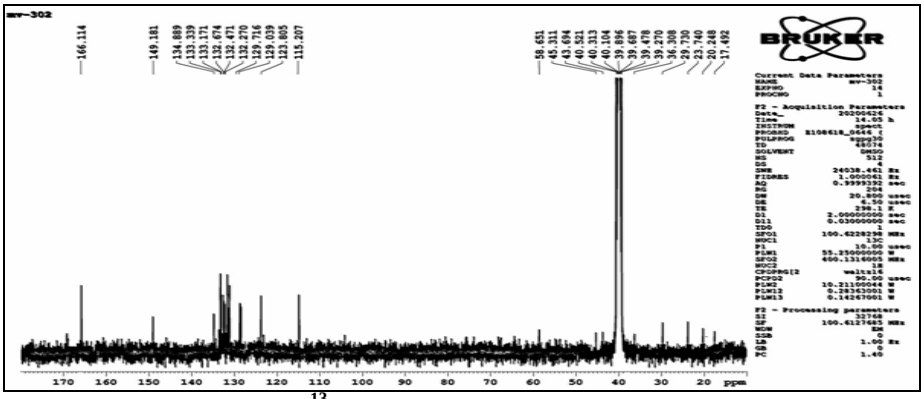

FIG. 27: ^{13}C NMR SPECTRUM OF FIG. 5D

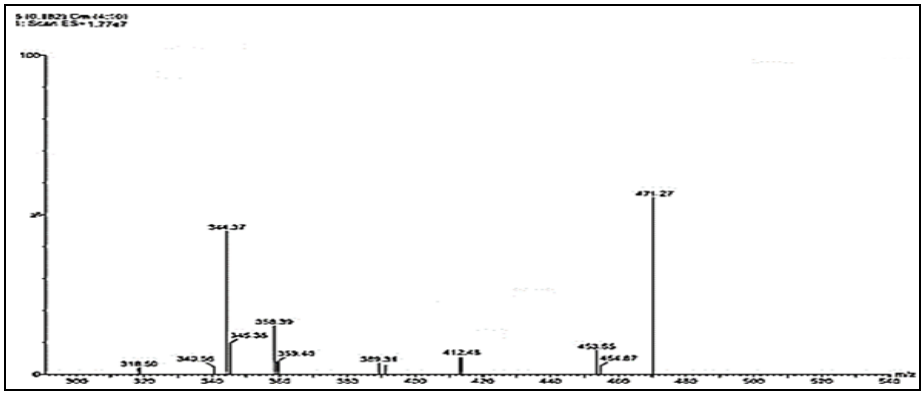

FIG. 28: MASS SPECTRUM OF FIG. 5D

Mass (m/z): The molecular weight of the compound is 471.27 (M+H^{+}).

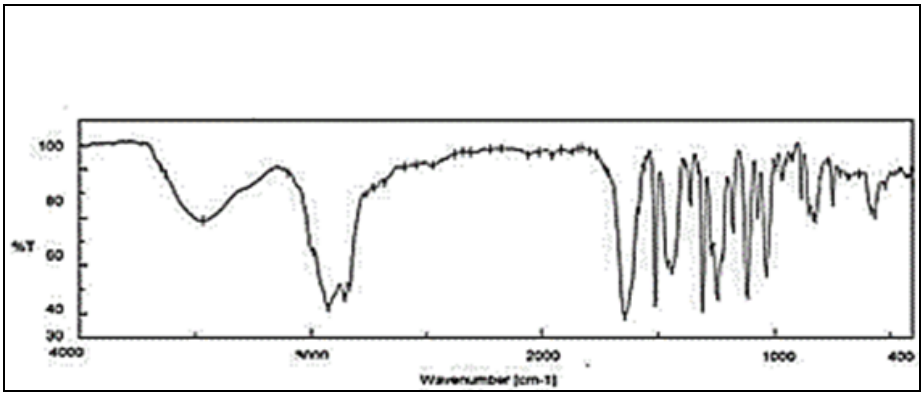

FIG. 29: IR SPECTRUM OF FIG. 5D

IR (cm^{-1}): The characteristics band at 3568-3446 cm^{-1} of (N–H) and 2993-2848 cm^{-1} of (C-H) 1650-1689 cm^{-1} of (C=O) and 1495-1504 cm^{-1} of S=O stretching and 1266-1333 cm^{-1} of (C-N).

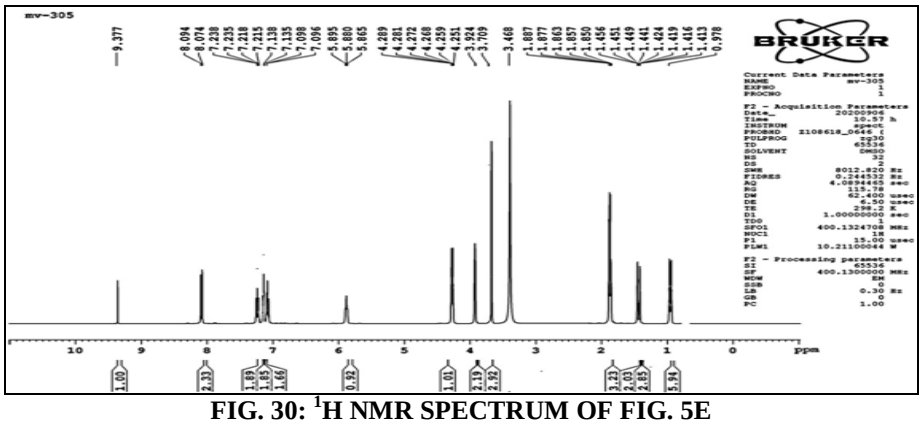

FIG. 30: ^{1}H NMR SPECTRUM OF FIG. 5E

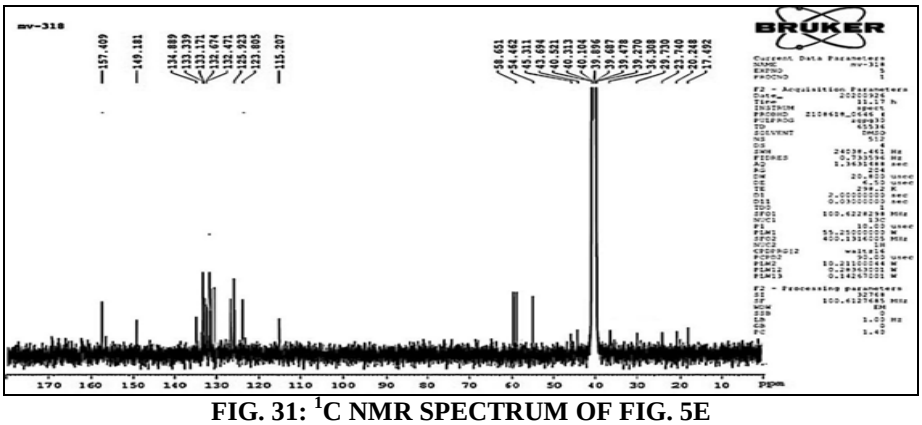

FIG. 31: ^{1}C NMR SPECTRUM OF FIG. 5E

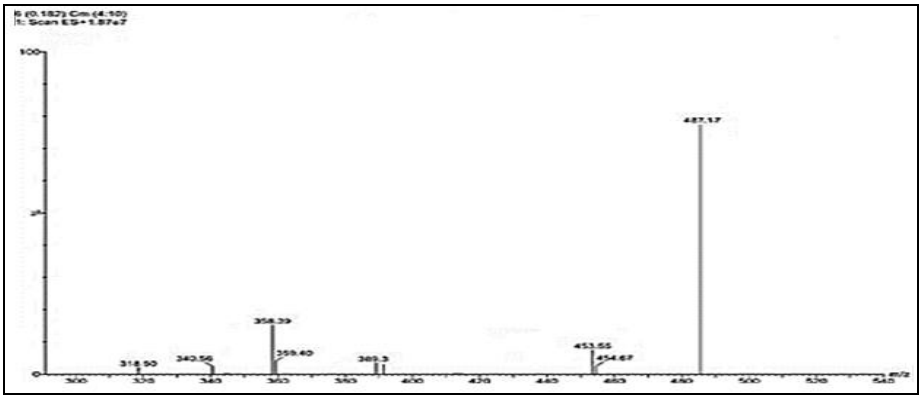

FIG. 32: MASS SPECTRUM OF FIG. 5E

Mass (m/z): The molecular weight of the compound is 487.17 ($M+H^{+}$).

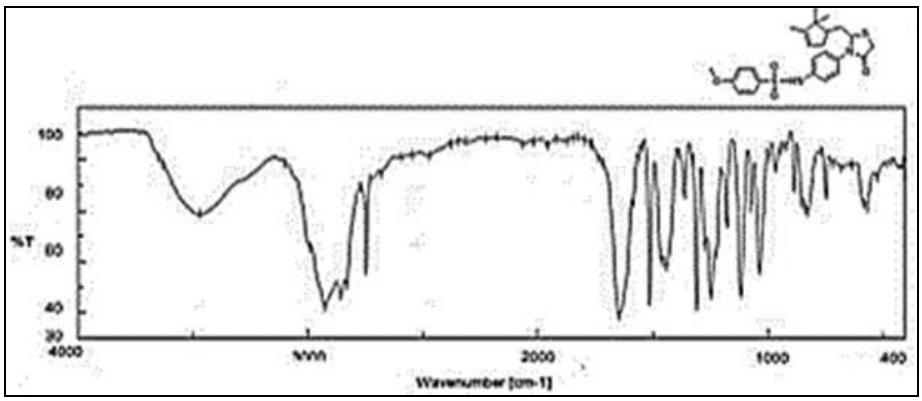

FIG. 33: IR SPECTRUM OF FIG. 5E

IR (cm^{-1}): The characteristics band at 3568-3446 cm^{-1} of (N–H) and 2993-2848 cm^{-1} of (C-H), 1650-1689 cm^{-1} of (C=O) and 1495-1504 cm^{-1} of S=O stretching and 1266-1333 cm^{-1} of (C-N).

Anticancer Activity: MTT Ass Ay Method Results:

MTT Assay Method (as per the Standard Protocol): It was performed by monitoring the reduction of yellow dye to a blue product. After culture ng the cells in the monolayer cell culture plates, cells were harvested and then seeded with RPMI1640 medium into a 96-well plate and incubated overnight.

Then, cells were treated with different concentrations of sulphonamide agents in four replicates each and incubated for 72 h. DMSO control wells received concentrations equal to those in the drug-treated cells. 100 µL of 0.5 mg/mL of MTT reagent in the fresh medium was added after the removal of the old medium.

Then, cells were incubated in the CO2 incubator at 37°C for 1 h. supernatants were removed from the wells, and then 100 µL DMSO was added to the reduced MTT dye. The final absorbency measurements were determined using a plate read at 440 nm and the values[12-15].

TABLE 2: DETAILS OF TEST COMPOUNDS

S. no.	Sample name/code	Cell line	Concentration
1	Blank		Only Media without cells
2	Untreated	MCF7 and HELA	No treatment
3	Fig. 5b	MCF7 and HELA	5(25, 50, 100, 200, 400µg/mL)

TABLE 3: CONCERTATION OF CELL LINE DETAILS

S. no.	Sample name/code	Cell line	Concentration
1	Fig. 5b	HELA	5 (25, 50, 100, 200, 400µg/mL)
2	Fig. 5b	MCF7	5 (25, 50, 100, 200, 400µg/mL)

TABLE 4: MTT ASSAY CONCERTATION VALUES OF HELA CELL LINE (FIG: 5b)

	Concentration Unit: µG							
	Blank	**Untreated**	**CPT (5.5uM)**	**25**	**50**	**100**	**200**	**400**
Reading 1	0.017	0.657	0.257	0.403	0.248	0.187	0.116	0.078
Reading 2	0.018	0.665	0.288	0.387	0.236	0.195	0.118	0.061
Mean	0.0175	0.661	0.2725	0.395	0.242	0.191	0.117	0.0695
Mean OD-Mean B	NA	0.6435	0.255	0.3775	0.2245	0.1735	0.0995	0.052
Standard Deviation		0.005656854	0.02192031	0.011314	0.008485	0.005657	0.001414	0.012021
Standard Error		0.004000604	0.015502341	0.008001	0.006001	0.004001	0.001	0.008501
Viability %	NA	100	39.62703963	58.66356	34.88733	26.96193	15.46232	8.080808
IC50= 29.51								

TABLE 5: DETAILS OF IC50 VALUES (FIG 5B)

S. no.	Sample name/code	Cell line	IC50(µG/ml)
1	Fig. 5b	HELA	29.51
2	Fig. 5b	MCF7	22.59

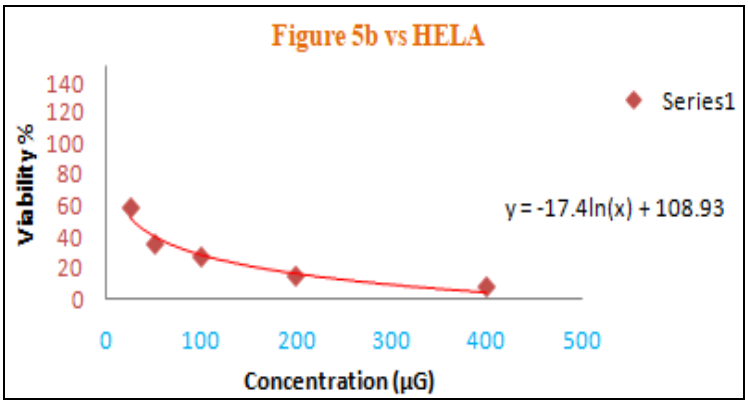

FIG. 34: GRAPH OF HELA CELL LINE OF FIG. 5B)

TABLE 6: MTT ASSAY CONCERTATION VALUES OF MCF7 CELL LINE (FIG. 5B)

Concentration Unit: µG								
	Blank	**Untreated**	**CPT (4.8uM)**	**25**	**50**	**100**	**200**	**400**
Reading 1	0.013	0.677	0.222	0.588	0.452	0.228	0.177	0.127
Reading 2	0.015	0.681	0.229	0.551	0.464	0.223	0.183	0.132
Mean	0.014	0.679	0.2255	0.5695	0.458	0.2255	0.18	0.1295
Mean OD-Mean B	NA	0.665	0.2115	0.5555	0.444	0.2115	0.166	0.1155
Standard Deviation		0.002828427	0.004949747	0.026163	0.008485	0.003536	0.004243	0.003536
Standard Error		0.002000302	0.003500529	0.018503	0.006001	0.0025	0.003	0.0025
Viability %	NA	100	31.80451128	83.53383	66.76692	31.80451	24.96241	17.36842
IC50= 29.51								

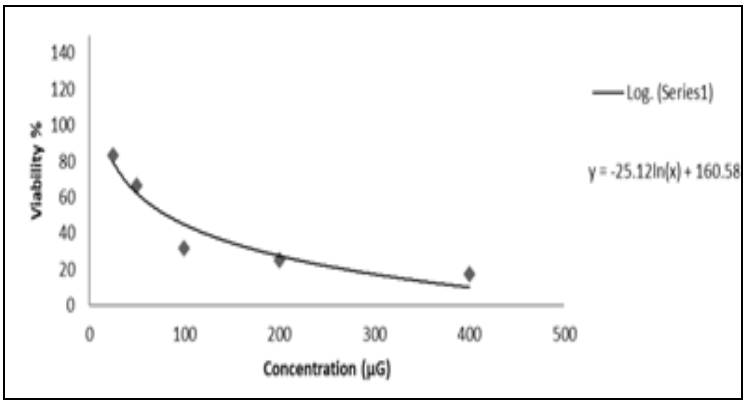

FIG. 35: GRAPH OF MCF7 CELL LINE

CONCLUSION: We described in this communication, the synthesis of 4-thaizolidinone derivatives by multicomponent reaction involving an easy work up procedure and the products were characterized by spectral techniques. Besides, anticancer activity studies are also reported

ACKNOWLEDGEMENT: Author is thankful to GITAM (deemed to be) University for providing a lab for experimental work.

CONFLICTS OF INTEREST: Nil

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How to cite this article:
Madhavi B and Sharma GVR: Synthesis, characterization and anticancer studies of novel sulphonamides. Int J Pharm Sci & Res 2024; 15(3): 710-25. doi: 10.13040/IJPSR.0975-8232.15(3).710-25.