CODEN [USA]: IAJPBB ISSN : 2349-7750

INDO AMERICAN JOURNAL OF
PHARMACEUTICAL SCIENCES

SJIF Impact Factor: 7.187
https://doi.org/10.5281/zenodo.6798448

Available online at: http://www.iajps.com *Research Article*

SYNTHESIS, CHARACTERIZATION AND ANTICANCER SCREENING OF NEW SULFONAMIDE-THIAZOLE DERIVED ACETAMIDE COMPOUNDS

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Article Received: May 2022 **Accepted:** June2022 **Published:** July 2022

Abstract:

Objective: *The objective of the paper is synthesis and characterization of sulfonamide-thiazole derived acetamide derivatives and evaluated for them for the anticancer potential.*

Material and methods: *The sulfonamide-thiazole derived acetamide derivatives has been prepared by the two step process, in first step, 2-chloro-N-(4-((2,3-dihydro-4H-1,4-oxazin-4-yl)sulfonyl)phenyl) acetamide* ***(Compound 2)*** *was synthesized, and in step 2, N-(4-((2,3-dihydro-4H-1,4-oxazin-4-yl)sulfonyl)phenyl)-2-((4-substitutedthiazol-2-yl)amino)acet-amide* ***(Compound 3)*** *was synthesized by the reaction of synthesized compound 2 with different 4-substituted thiazol-2-amine to from the final compounds* ***(compound 3)****. Total eleven compounds have been synthesized and characterized by physicochemical and IR, NMR and MASS spectral analysis. The final compounds (SA-1 to SA-11) have been evaluated for anticancer activity by SRB assay method.*

Result and Discussion: *The IR spectrum of the compounds (SA-1 to SA-11) has shown the characteristics peak (cm^{-1}) of N-H peak at 3331, N-H peak at 3118, aromatic C-H peak at 3039, C=O peak at 1672, C-H aliphatic peak at 2938, C-Cl peak at 850, C-Br peak at 1018, C-F peak at 1102, N-O peak at 1358 and N=O peak at 1562. The 1HNMR spectra depicted the peak of N-H at 10.25 ppm, Thiazole-H peak at 6.25 ppm, CH2 peak at 4.19. The 13CNMR spectrum denotes the peak in ppm of C=O at 170.5, C=N at 162.3 and CH2 at 45.6. Compound SA-1, mass spectrum has shown peak at m/z = 414.02, which matches the chemical formula $C_{15}H_{15}ClN_4O_4S_2$. The result data of the synthesized compounds by SRB assay stated the IC50 value of compounds SA-1 (7.7), SA-3 (9.5), SA-4 (14.7) and SA-11 (8.1) has shown better activity as compared to the standard drug paclitaxel (31.1)*

Conclusion*: The Cl, Br, NO_2 and F compounds enhance the activity when it attached to 4-position of the thiazole ring as well as presence of sulfonamide bearing thiazole with addition to electronegative atom enhance the anticancer activity of compounds*

Keywords: *Anticancer activity, thiazole, sulfonamide, SRB assay, acetamide*

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Please cite this article in press Surendra Singh et al, ***Synthesis, Characterization And Anticancer Screening Of New Sulfonamide-Thiazole Derived Acetamide Compounds.,*** *Indo Am. J. P. Sci, 2022; 09(7).*

INTRODUCTION:

Cancer remains to be the leading cause of death in humans second only to cardiovascular diseases and more than 70% of all cancer deaths occur in developing and under-developed countries. There is a continuous rise of deaths from various cancers worldwide, with an estimated 12 million deaths in 2030.[1] Despite the advancement in the knowledge of biochemical processes associated with carcinogenesis, the successful treatment of cancer remains a significant challenge because of the general toxicity associated with the clinical use of traditional cancer chemotherapeutic agents. [2] Hence, the design and development of new drugs for cancer therapeutics remains to be an important and challenging task for medicinal chemists worldwide. [3]

Lung cancer is a type of cancer that starts in the lungs. It causes cells to divide in the lungs uncontrollably and form tumors to reduce a person's ability to breathe. Worldwide, about three quarters of lung cancers are attributable to smoking; others are caused by occupational workplace exposure, radon exposure, and air pollution. It is more common in men, and incidence increases with age. [4] Lung cancer is a heterogeneous disease comprising several subtypes with pathologic and clinical relevance. Squamous cell carcinomas start in squamous cells, which are flat cells that line the inside of the airways in the lungs. They are often linked to a history of smoking and tend to be found in the central part of the lungs, near a main airway i.e., bronchus.[5]

The combination of radiotherapy and chemotherapy is an appealing approach that has led to improved treatment results in patients with advanced solid tumors. In particular, the concomitant use of radiotherapy and chemotherapy resulted in a lower recurrence rate and provided good local control for carcinoma and thus higher organ preservation rate. [6]. The heterocycle having the thiazole and sulfonamide moieties having a unique approach towards the treatment of lung cancer. sulfonamides have been found to be associated with comprehensive and broad spectrum of biological activities embracing antibacterial, antifungal, anticarbonic anhydrase, hypoglycemic, diuretic, anti-human immunodeficiency virus (HIV) and anti-thyroid. Additionally, a large number of structurally inventive sulfonamides have recently been reported to display substantial *in-vitro* and *in-vivo* antitumor activity.[7]

The antitumor activity is accomplished by the sulfonamides through dissimilar of mechanisms, such as histone deacetylases (HDACs) inhibition, cell cycle arrest in the G1 phase, NADH oxidase inhibition, carbonic anhydrase (CA) inhibition, matrix metalloproteinase (MMPs) inhibition, cyclin-dependent kinase (CDK) inhibition, methionine aminopeptidases (MetAPs) inhibition, binding to b-Tubulin and disruption of microtubule assembly.[8] In addition, thiazole derivatives demonstrated a broad spectrum of medicinal and biological activities, including antiviral, antimicrobial, anti-inflammatory, antimalarial, anti-HIV and anticancer activities.[9] As an epitome heterocyclic-amines, 2-aminothiazoles and their derivatives are used as key intermediates for the synthesis of plentiful biologically active compounds, such as biocides, fungicides, sulfur drugs.[10]

The sulfonamide group linked with acetamide moiety bearing different aryl, heteroaryl substituents exhibits enormous pharmacological potency, particularly sulfonamide derivatives encompassing short amine fragments reveal promising anticancer activity.[11] The sulfonamide-thiazole derivatives reveled a huge number of biological activities, such as antimicrobial, anticancer and carbonic anhydrase (CA) inhibitors. Dihydrofolate reductase enzyme (DHFR) is a key enzyme in the process of nucleic acid synthesis in both human and bacteria. This enzyme is accountable for catalysis of the reduction of folate or dihydrofolate to tetrahydrofolate using NADPH. This function made of the DHFR is considered as an important target for different antibacterial and cancer agent.[12]

The object of research paper is to synthesize the sulfonamide-thiazole based acetamide derivatives and evaluated for the anticancer activity against NCI-H226 lung cancer cells as continuation of our research interest which deals with the synthesis of new bioactive nitrogen-containing heterocycles.

MATERIALS AND METHOD:

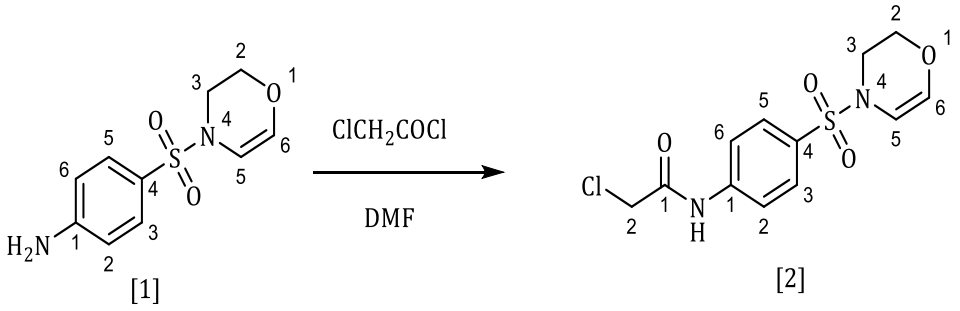
Different substituted 4-((2,3-dihydro-4H-1,4-oxazin-4-yl)sulfonyl)aniline was purchased from Merck, India. The different 4-Substitutedthiazol-2-amine, 2 chloro-acetyl chloride, and Dimethyl formamide was purchased from sigma Aldrich. All the chemicals were purchased from Sigma Aldrich and Merck India. Commercial grade solvents used for the reactions were distilled before use. The melting points of the synthesized compounds were determined in open glass capillaries. IR spectra were recorded on Bruker-alpha FTIR spectrometer. Elemental analysis was performed and found values were within 0.4% of theoretical values. 1HNMR spectra were recorded at 400 MHz, Mass Spectra

were recorded using Mass Spectrometers Jeol FSX-112 (FAB) by ESI.

Chemistry:
Synthetic strategy planning for synthesis

Step 1: Synthesis of 2-chloro-N-(4-((2,3-dihydro-4H-1,4-oxazin-4-yl)sulfonyl)phenyl) acetamide
Step 2: Synthesis of N-(4-((2,3-dihydro-4H-1,4-oxazin-4-yl)sulfonyl)phenyl)-2-((4-substituted thiazol-2-yl)amino)acetamide

(A) Synthesis of 2-chloro-N-(4-((2,3-dihydro-4H-1,4-oxazin-4-yl)sulfonyl)phenyl) acetamide



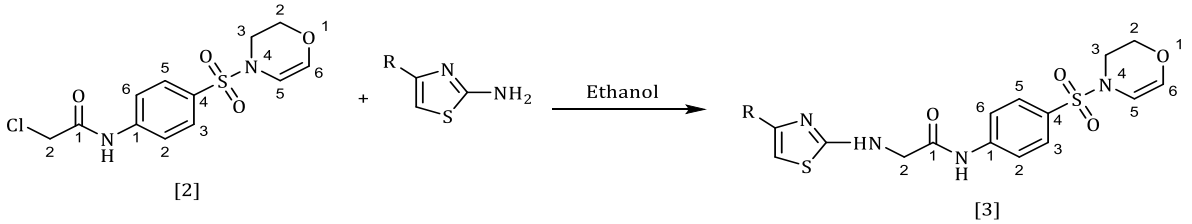
[1] [2]

4-((2,3-dihydro-4*H*-1,4-oxazin-4-yl)sulfonyl)aniline

2-chloro-*N*-(4-((2,3-dihydro-4*H*-1,4-oxazin-4-yl)sulfonyl)phenyl)acetamide

A mixture 4-((2,3-dihydro-4H-1,4-oxazin-4-yl)sulfonyl)aniline **[Compound 1]** (0.1 mol) and 2-chloroacetyl chloride (0.1 mol) was dissolved in dimethyl formamide (DMF; 20 ml) and magnetic stirred at room temperature for 2 hrs. The reaction was monitored by TLC method using n-Hexane: ethyl acetate (2:1) as solvent system. The reaction mixture was poured onto ice cold distilled water.[13] The obtained solid was filtered off and crystallized from ethanol to form 2-chloro-N-(4-((2,3-dihydro-4H-1,4-oxazin-4-yl)sulfonyl)phenyl) acetamide **[Compound 2]**.

(B) Synthesis of N-(4-((2,3-dihydro-4H-1,4-oxazin-4-yl)sulfonyl)phenyl)-2-((4-substituted thiazol-2-yl)amino)acetamide



[2] [3]

2-chloro-*N*-(4-((2,3-dihydro-4*H*-1,4-oxazin-4-yl)sulfonyl)phenyl)acetamide

N-(4-((2,3-dihydro-4*H*-1,4-oxazin-4-yl)sulfonyl)phenyl)-2-((4-substitutedthiazol-2-yl)amino)acetamide

The 2-chloro-N-(4-((2,3-dihydro-4H-1,4-oxazin-4-yl)sulfonyl)phenyl) acetamide (compound 2) and different 4-substituted thiazol-2-amine (0.01 mol) was dissolved in absolute ethanol was refluxed for 4-6 h. The reaction mixtures were concentrated under reduced pressure using rota-evaporator to obtained solid was filtered, washed with n-hexane, dried and recrystallized from ethanol to give the **Compound 3,** N-(4-((2,3-dihydro-4H-1,4-oxazin-4-yl)sulfonyl)phenyl)-2-((4substitutedthiazol-2yl)amino) acetamide.[14]

Pharmacological Evaluation
The *in-vitro* cytotoxic activity was measured for all the newly synthesized compounds on Lung squamous carcinoma cell line (NCI-H226) by applying the Sulfo-Rhodamine-B stain (SRB) assay. [15] Paclitaxel was chosen as a reference and standard anticancer drug due to its potency against NCI-H226. The eleven compound (SA-1 to SA-11) was synthesized and evaluated for the anticancer potential by SRB assay

***Ex-vivo* evaluation of synthesized compounds by SRB assay method:**
Anticancer screening carried out on WI-38 normal lung fibroblast cells and NCI-H226 lung cancer cells**.** The Ex-vivo experiment was performed as the procedure reported by the skehan *et al.*, 1990. Cells were plated in 96-multiwell plate (104 cells/ well) for 24 hrs. before treatment with the compounds to allow attachment of cell to the wall of the plate. Test compounds were dissolved in dimethyl sulfoxide (DMSO) and diluted with saline to the appropriate

volume. Different concentrations of the compounds under test (10, 25, 50 and 100µM) were added to the cell monolayer. Triplicate wells were prepared for each individual dose. [16]

Monolayer cells were incubated with the compounds for 48 hrs. at 37˚C and in atmosphere of 5% CO_2. After 48 hrs., cells were fixed, washed and stained for 30 min. with 0.4% (w/v) SRB dissolved in 1% acetic acid. Unbounded dye was removed by four washes with 1% acetic acid, and attached stain was recovered with Tris-EDTA buffer. Color intensity was measured in an enzyme linked immunosorbent assay (ELISA) reader.[17] The relation between surviving fraction and drug concentration is plotted to get the survival curve of each tumor cell line after the specified time. The concentration required for 50% inhibition of cell viability (IC_{50}) was calculated and compared with the reference drug paclitaxel.

RESULT AND DISCUSSION:

Chemistry:

IR, NMR, mass spectral, and elemental studies were used to characterize the target structures of the synthesized compounds. The 2-chloroacetyl chloride, and dimethyl formamide reacted with the 4-((2,3-dihydro-4H-1,4-oxazin-4-yl)sulfonyl)aniline **(Compound 1)** to form 2-chloro-N-(4-((2,3-dihydro-4H-1,4-oxazin-4-yl)sulfonyl) phenyl) acetamide **[Compound 2]**. The Compound 2 obtained as white crystal product having the melting point 180-190°C. The FT-IR spectrum of compound 2, denotes the characteristics peak of NH at 3296, peak of C-H aromatic at 3120, CH aliphatic at 2950, 1688 C=O at 1688 as well as 1HNMR denotes the characteristics peak of N-H at 8.53 ppm. The 13CNMR spectra shown the peak of C=O at 164.3, CH2 at 66.1, CH2 at 46.2, and 42.8.

The final compound (N-(4-((2,3-dihydro-4H-1,4-oxazin-4-yl)sulfonyl)phenyl)-2-((4-substituted thiazol-2-yl)amino)acetamide) 3, was synthesized by the reaction of compound 2 with different 4-substituted thiazol-2-amine. The physicochemical properties of the synthesized compound (SA-1 to SA-11) was represented in Table 4.4. The compound SA-1 to SA-11 has characterized by the IR, 1HNMR, 13 CNMR and Mass spectral analysis. The IR spectrum of the compounds has shown the characteristics peak (cm^{-1}) of N-H peak at 3331, N-H peak at 3118, aromatic C-H peak at 3039, C=O peak at 1672, C-H aliphatic peak at 2938, C-Cl peak at 850, C-Br peak at 1018, C-F peak at 1102, N-O peak at 1358 and N=O peak at 1562.

The 1HNMR spectra of Synthesized compounds depicted the peak of N-H at 10.25 ppm, Thiazole-H peak at 6.25 ppm, CH2 peak at 4.19. The 13 CNMR spectrum of synthesized compound (SA-1 to SA-11) denotes the peak in ppm of C=O at 170.5, C=N at 162.3 and CH2 at 45.6. COMPOUND 3 (SA-1), mass spectrum has shown peak at m/z = 414.02, which matches the chemical formula $C_{15}H_{15}ClN_4O_4S_2$. All the other synthesized compound has also shown the molecular ion peak similar to their molecular formula and weight. Mass spectrum of all sixteen compound were recorded and it almost similar to the compounds molecular weight. The elemental analysis and melting point of compound were also recorded and analyzed and have in the accepted limit.

SA-1: 2-((4-chlorothiazol-2-yl)amino)-N-(4-((2,3-dihydro-4H-1,4-oxazin-4-yl) sulfonyl) phenyl)acetamide

Chemical Formula: $C_{15}H_{15}ClN_4O_4S_2$; Molecular Weight: 414.88; IR (cm^{-1}): 3331 (N-H); 3118 (N-H); 3039 (Aromatic C-H); 1672 (C=O); 2938 (C-H aliphatic); 850 (C-Cl); 1HNMR (ppm):
δ 10.23 (s, 1H, NH), 5.95 (s, 1H, NH), 6.28 (s, 1H, thiazole), 4.20 (s, 2H, CH2), 3.25 (s, 2H, CH2), 2.80–2.82 (m, 4H, 2CH2), 1.32–1.35 (m, 2H, CH2); 13CNMR (ppm): 170.8 (C=O), 162.5 (C=N), 142.6 (C), 130.2 (C-H), 128.6 (C-H), 118.6 (C-H), 105.3 (C-H), 45.2 (CH2), 42.0 (CH2), 24.6 (CH2), 22.1 (CH2); FAB Mass (m/z): 414.02.

SA-2: 2-((4-bromothiazol-2-yl)amino)-N-(4-((2,3-dihydro-4H-1,4-oxazin-4-yl)sulfonyl) phenyl)acetamide

Chemical Formula: $C_{15}H_{15}BrN_4O_4S_2$; Molecular Weight: 459.33; IR (cm^{-1}): 3329 (N-H); 3112 (N-H); 3042 Aromatic C-H; 1697 (C=O); 2945 (C-H aliphatic); 1018 (C-Br); 1HNMR (ppm):
δ 10.25 (s, 1H, NH), 5.97 (s, 1H, NH), 6.25 (s, 1H, thiazole), 4.25 (s, 2H, CH2), 3.28 (s, 2H, CH2), 2.82–2.84 (m, 4H, 2CH2), 1.30–1.32 (m, 2H, CH2); 13CNMR (ppm): 170.2 (C=O), 162.3 (C=N), 142.5 (C), 130.4 (C-H), 127.9 (C-H), 118.9 (C-H), 105.2 (CH), 45.1 (CH2), 41.9 (CH2), 24.8 (CH2), 22.3 (CH2) ppm; FAB Mass (m/z): 498.97

SA-3: N-(4-((2,3-dihydro-4H-1,4-oxazin-4-yl)sulfonyl)phenyl)-2-((4-nitro-thiazol-2-yl) amino)acetamide

Chemical Formula: $C_{15}H_{15}N_5O_6S_2$; Molecular Weight: 425.43; IR (cm^{-1}): 3328 (N-H); 3110 (N-H); 3041 Aromatic C-H; 1699 (C=O); 2940 (C-H aliphatic); 1358 (N-O); 1562 (N=O); 1HNMR (ppm):
δ 10.22 (s, 1H, NH), 5.94 (s, 1H, NH), 6.35 (s, 1H, thiazole), 4.21 (s, 2H, CH2), 3.28 (s, 2H, CH2), 2.80–2.82 (m, 4H, 2CH2), 1.32–1.35 (m, 2H, CH2); 13CNMR (ppm): 170.5 (C=O), 162.6 (C=N), 142.8

(C), 130.5 (C-H), 128.7 (C-H), 118.2 (CH), 105.6 (C-H), 45.3 (CH2), 41.9 (CH2), 24.8 (CH2), 21.7 (CH2); FAB Mass (m/z): 425.05

SA-4: N-(4-((2,3-dihydro-4H-1,4-oxazin-4-yl)sulfonyl)phenyl)-2-((4-methyl-thiazol-2-yl) amino)acetamide
Chemical Formula: $C_{16}H_{18}N_4O_4S_2$; Molecular Weight: 394.46; IR (cm^{-1}): 3332 (N-H); 3115 (N-H); 3035 (C-H, Aromatic); 1685 (C=O); 2945 (C-H, Aliphatic); 1HNMR (ppm): δ 10.20 (s, 1H, NH), 5.89 (s, 1H, NH), 6.25 (s, 1H, thiazole), 4.18 (s, 2H, CH2), 3.24 (s, 2H, CH2), 2.80–2.82 (m, 4H, 2CH2), 1.32–1.34 (m, 2H, CH2); 13CNMR (ppm): 170.2 (C=O), 162.6 (C=N), 142.8 (C), 132.1 (C-H), 128.5 (C-H), 117.9 (C-H), 105.5 (CH), 45.6 (CH2), 41.9 (CH2), 24.5 (CH2), 21.8 (CH2); FAB Mass (m/z): 394.08

SA-5: N-(4-((2,3-dihydro-4H-1,4-oxazin-4-yl)sulfonyl)phenyl)-2-((4-methoxythiazol-2-yl) amino)acetamide
Chemical Formula: $C_{16}H_{18}N_4O_5S_2$; Molecular weight: 410.46; IR (cm^{-1}): 3339 (N-H); 3105 (N-H); 3032 (Aromatic C-H); 1682 (C=O); 2932 (C-H, Aliphatic); 1HNMR (ppm): δ 10.22 (s, 1H, NH), 5.92 (s, 1H, NH), 6.25 (s, 1H, thiazole), 4.18 (s, 2H, CH2), 3.20 (s, 2H, CH2), 2.78–2.80 (m, 4H, 2CH2), 1.28–1.30 (m, 2H, CH2); 13CNMR (ppm): 170.5 (C=O), 162.8 (C=N), 142.7 (C), 130.5 (C-H), 127.5 (C-H), 118.2 (C-H), 106.5 (C-H), 45.4 (CH2), 42.5 (CH2), 24.8 (CH2), 22.4 (CH2); FAB Mass (m/z): 410.42

SA-6: N-(4-((2,3-dihydro-4H-1,4-oxazin-4-yl)sulfonyl)phenyl)-2-((4-ethylthiazol-2-yl) amino)acetamide
Chemical Formula: $C_{17}H_{20}N_4O_4S_2$; Molecular Weight: 408.49; IR (cm^{-1}): 3325 (N-H); 3114 (N-H); 3045 Aromatic C-H; 1692 (C=O); 2942 (C-H aliphatic); 1HNMR (ppm): δ 10.21 (s, 1H, NH), 5.90 (s, 1H, NH), 6.20 (s, 1H, thiazole-H), 4.22 (s, 2H, CH2), 3.23 (s, 2H, CH2), 2.84–2.86 (m, 4H, 2CH2), 1.30–1.32 (m, 2H, CH2); 13CNMR (ppm): 170.2 (C=O), 162.4 (C=N), 142.8 (C), 130.5 (C-H), 129.2 (CH), 119.6 (CH), 107.3 (CH), 47.1 (CH2), 44.0 (CH2), 25.1 (CH2), 23.3 (CH2); FAB Mass (m/z): 408.45.

SA-7: N-(4-((2,3-dihydro-4H-1,4-oxazin-4-yl)sulfonyl)phenyl)-2-((4-ethoxythiazol-2-yl) amino)acetamide
Chemical Formula: $C_{17}H_{20}N_4O_5S_2$; Molecular Weight: 424.49; IR (cm^{-1}): 3342 (N-H); 3108 (N-H); 3045 Aromatic C-H; 1685 (C=O); 2945 (C-H aliphatic); 1HNMR (ppm): 10.24 (s, 1H, NH), 5.92 (s, 1H, NH), 6.25 (s, 1H, thiazole-H), 4.22 (s, 2H, CH_2), 3.22 (s, 2H, CH_2), 2.82–2.84 (m, 4H, $2CH_2$), 1.30–1.32 (m, 2H, CH_2); 13CNMR (ppm): 169.6 (C=O), 165.8 (C=N), 143.0 (C), 131.4 (CH), 130.1 (C), 129.2 (CH), 119.6 (CH), 107.3 (CH), 47.1 (CH_2), 44.0 (CH_2), 25.1 (CH_2), 23.3 (CH_2); FAB Mass (m/z): 424.42

SA-8: N-(4-((2,3-dihydro-4H-1,4-oxazin-4-yl)sulfonyl)phenyl)-2-((4-propylthiazol-2-yl) amino)acetamide
Chemical Formula: $C_{18}H_{22}N_4O_4S_2$; Molecular weight: 422.52; IR (cm^{-1}): 3329 (N-H); 3112 (N-H); 3045 Aromatic C-H; 1694 (C=O); 2942 (C-H aliphatic); 1HNMR (ppm): 10.25 (s, 1H, NH), 5.92 (s, 1H, NH), 6.35 (s, 1H, thiazole-H), 4.25 (s, 2H, CH2), 3.24 (s, 2H, CH2), 2.82–2.84 (m, 4H, 2CH2), 1.32–1.34 (m, 2H, CH2); 13CNMR (ppm): 170.5 (C=O), 165.8 (C-N), 142.8 (C), 130.5 (C-H), 128.5 (C-H), 118.2 (C-H), 105.2 (C-H), 45.3 (CH2), 41.9 (CH2), 24.8 (CH2), 22.4 (CH2); FAB Mass (m/z): 422.35.

SA-9: N-(4-((2,3-dihydro-4H-1,4-oxazin-4-yl)sulfonyl)phenyl)-2-((4-propoxythiazol-2-yl) amino)acetamide
Chemical Formula: $C_{18}H_{22}N_4O_5S_2$; Molecular weight: 438.52; IR (cm^{-1}): 3326 (N-H); 3105 (N-H); 3045 Aromatic C-H; 1694 (C=O); 2935 (C-H aliphatic); 1HNMR (ppm): 10.25 (s, 1H, NH), 5.98 (s, 1H, NH), 6.25 (s, 1H, thiazole-H), 4.25 (s, 2H, CH2), 3.21 (s, 2H, CH2), 2.78–2.80 (m, 4H, 2CH2), 1.38–1.40 (m, 2H, CH2); 13CNMR (ppm): 170.3 (C=O), 162.2 (C=N), 142.5 (C), 130.2 (C-H), 128.7 (CH), 118.2 (C-H), 105.5 (C-H), 45.5 (CH2), 42.2 (CH2), 24.6 (CH2), 22.5 (CH2); FAB Mass (m/z): 438.10.

SA-10: 2-((4-aminothiazol-2-yl)amino)-N-(4-((2,3-dihydro-4H-1,4-oxazin-4-yl)sulfonyl) phenyl)acetamide
Chemical Formula: $C_{15}H_{17}N_5O_4S_2$; Molecular Weight: 395.45; IR (cm^{-1}): 3325 (N-H); 3105 (N-H); 3046 Aromatic C-H; 1692 (C=O); 2946 (C-H aliphatic); 1HNMR (ppm): 10.25 (s, 1H, NH), 5.98 (s, 1H, NH), 6.25 (s, 1H, thiazole-H), 4.19 (s, 2H, CH2), 3.22 (s, 2H, CH2), 2.80–2.82 (m, 4H, 2CH2), 1.30–1.32 (m, 2H, CH2); 13CNMR (ppm): 170.5 (C=O), 162.3 (C=N), 142.9 (C), 130.5 (C-H), 129.6 (C-H), 119.2 (C-H), 105.1 (C-H), 45.6 (CH2), 42.8 (CH2), 25.8 (CH2), 23.3 (CH2); FAB Mass (m/z): 395.40

SA-11: N-(4-((2,3-dihydro-4H-1,4-oxazin-4-yl)sulfonyl)phenyl)-2-((4-fluorothiazol-2-yl) amino)acetamide
Chemical Formula: $C_{15}H_{15}FN_4O_4S_2$; Molecular weight: 398.43; IR (cm^{-1}): 3325 (N-H); 3107 (N-H); 3038 Aromatic C-H; 1692 (C=O); 2935 (C-H

aliphatic); 1102 (C-F); 1HNMR (ppm): 10.76 (s, 1H, NH), 5.96 (s, 1H, NH), 7.86 (d, 2H, Ph-H), 7.78 (d, 1H, Flu-H), 7.75 (d, 2H, Ph-H), 7.25 (s, 1H, thiazole-H), 4.21 (s, 2H, CH2), 3.65 (s, 2H, CH2), 2.80–2.82 (m, 4H, 2CH2), 1.30–1.32 (m, 2H, CH2); 13CNMR (ppm): 170.6 (C=O), 162.6 (C=N), 142.8 (C), 130.9 (C-H), 128.5 (C-H), 118.2 (C-H), 105.6 (C-H), 45.5 (CH2), 41.6 (CH2), 24.8 (CH2), 22.1 (CH2); FAB Mass (m/z): 398.40

Pharmacological evaluation:

All the synthesized compounds were evaluated for their anticancer activity against Lung cancer cell line (NCI-H226) by SRB assay method. The data of *In-vitro* anticancer activity of the synthesized compounds (SA-1 to SA-11) was represented in Table 1. The graphical representation was shown in Figure 1.

Table 1: *In-vitro* anticancer screening of the synthesized compounds (SA-1 to SA-11) against Lung cancer cell line (NCI-H226) at three different concentrations.

Compounds	Compound concentration (µM)				
	10 (µM)	25 (µM)	50 (µM)	100 (µM)	IC 50 (µM)
	Surviving fraction (mean ± SE)[a]				
Paclitaxel	0.525±0.022	0.435±0.007	0.320± 0.012	0.214 ± 0.016	31.1
SA-1	0.422±0.006	0.225±0.009	0.371± 0.005	0.345 ± 0.011	07.7
SA-2	0.810±0.018	0.548±0.012	0.331± 0.008	0.350 ± 0.015	46.0
SA-3	0.385±0.021	0.251±0.021	0.355± 0.004	0.290 ± 0.009	09.5
SA-4	0.528±0.015	0.328±0.025	0.313± 0.014	0.381 ± 0.007	14.7
SA-5	0.790±0.024	0.545±0.032	0.439± 0.005	0.415 ± 0.006	37.5
SA-6	0.855±0.012	0.608±0.012	0.360± 0.014	0.350 ± 0.009	50.5
SA-7	0.856±0.015	0.615±0.015	0.532± 0.011	0.340 ± 0.015	51.6
SA-8	0.823±0.018	0.588±0.014	0.435± 0.009	0.420 ± 0.018	40.3
SA-9	0.903±0.023	0.612±0.017	0.413± 0.021	0.395 ± 0.021	50.8
SA-10	0.825±0.012	0.668±0.015	0.307± 0.015	0.271 ± 0.017	55.4
SA-11	0.541±0.009	0.375±0.014	0.360± 0.016	0.460 ± 0.015	08.1

[a]**Each value is the mean of three experiments± standard error**

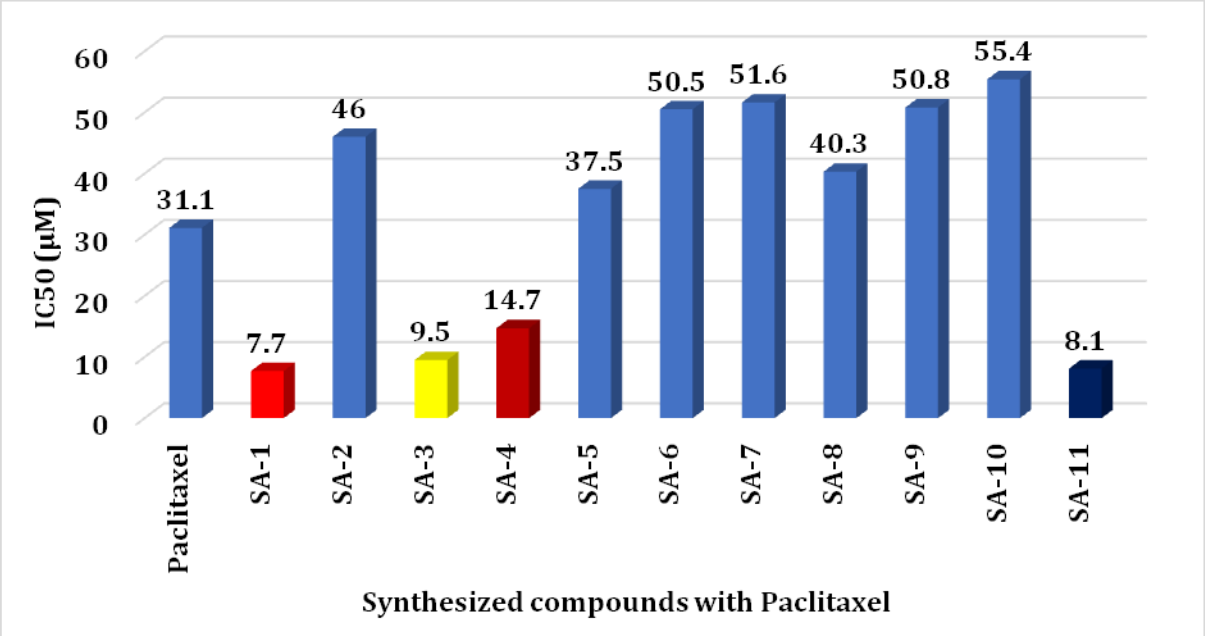


Figure 1: Graphical representation of IC50 value of synthesized compound (SA-1 to SA-11).

The result data of the synthesized compounds by SRB assay stated the IC50 value of compounds SA-1 (7.7), SA-3 (9.5) , SA-4 (14.7) and SA-11 (8.1) has shown better activity as compared to the standard

drug paclitaxel (31.1).

DISCUSSION:

The anticancer activity of synthesized compounds **(SA-1 to SA-11)** was screened against NCI-H226 lung cancer cell line by SRB assay method using paclitaxel as standard drug. The synthesized compound tested with different concentrations of the compounds (10, 25, 50 and 100µM). The anticancer activity data of sulfonamide-thiazole based acetamide compounds indicated that the compounds have significant activity. The result data of the synthesized compounds by SRB assay suggested that Cl, Br, NO_2 and F compounds enhance the activity when it attached to 4-position of the thiazole ring as well as presence of sulfonamide bearing thiazole with addition to electronegative atom enhance the anticancer activity of compounds.

Acknowledgement:

I would like to thank SAIF, Punjab University, Chandigarh for carried out the IR, 1HNMR, and mass spectroscopy for characterization of synthesized compounds.

Conflicts of Interest:

The author declares no conflicts of interest

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