Synthesis, Molecular Docking and Anticancer Activity of Novel (E)-5-((1-phenyl-1H-1,2,3-triazol-4-YL)Methylene)-2-thioxothiazolidin-4-one Analogues

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ABSTRACT: *A novel series of (E)-5-((1-Phenyl-1H-1,2,3-triazol-4-yl)methylene)-2-thioxothiazolidin-4-one analogues were designed for anticancer activity and synthesized by the reaction of 1-Aryl-1H-1,2,3-triazole-4-carbaldehydes with 2-thioxothiazolidin-4-one. The synthesized compounds were analyzed by IR, ^{1}HNMR, ^{13}CNMR, and mass spectrometry. The compounds were screened for in vitro anticancer activity using four cancer cell lines viz. Lung (A549), Colon (HT-29), Breast (MCF-7), and Melanoma (A375), resulted from most of the compounds showed moderate to better activity against all cell lines, among them the compounds 6g and 6j were the most potent in all investigated cancer cell lines (lung, colon, breast, and melanoma. The compounds were studied in molecular docking studies, which resulted in a significant dock score shown with all the compounds. The compounds 6i and 6b have shown the highest dock scores.*

KEYWORDS: *Anticancer activity; 2-Tioxhothiazolidin-4-one; 1,2,3-triazole; Molecular docking studies.*

INTRODUCTION

Cancer is a global health issue affecting a major proportion of the human population. Cancer is the second leading cause of death globally and is responsible for an estimated 9.6 million deaths in 2018. Globally, about 1 in 6 deaths is due to cancer. For this purpose, chemotherapy is the most commonly used treatment worldwide but it has several serious side effects and problems [1]. Despite the availability of a variety of anticancer agents, such as cisplatin [2], but no currently available agents can entirely eradicate cancer cells without also having toxic effects on patients' noncancerous, healthy tissues. Thus, further exploration of new chemotherapeutic agents with high efficacy and low adverse effects is critically important for medicinal chemists. These limitations are compelling we search for novel anticancer agents with diverse chemical structures and herein it is reported the synthesis and anticancer evolution of 1,2,3-triazolylthiazolidinones derivatives. Meanwhile, various heterocyclic derivatives have been active against different cancer cells. In this class 2-thioxothiazolidin-4-one and 1,2,3-Triazole derivatives also inhibit the growth of various cancer cell developments. The 2-thioxothiazolidin-4-one prototype

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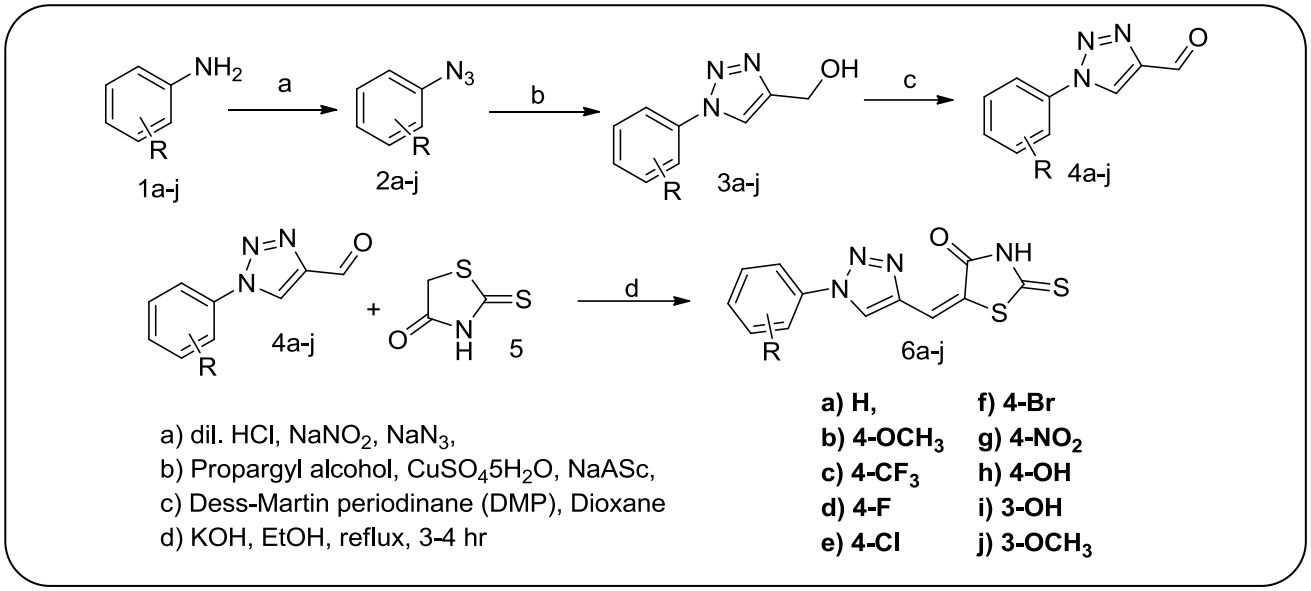

Scheme 1: Synthesis of 1,2,3-triazolyl-thioxothiazolidin-4-one analogues

is one of the privileged structure fragments in modern medicinal organic chemistry considering its broad biological spectrum and affinity for various bio-targets. The 2-thioxothiazolidin-4-one derivatives possess various biological activities including antimicrobial [3], anti-diabetic [4], anti-inflammatory [5], antiviral [6], and antitubercular [7]. Recently, much attention has been paid to the antitumor activity of 2-thioxothiazolidin-4-one derivatives as novel potential anticancer agents [8]. In addition, 1,2,3-Triazole and its derivatives enhanced considerable attention for the past few decades due to their chemotherapeutical value such as antimicrobial [9], antioxidant [10], anticonvulsant [11], anticancer [12], anti-HIV [13], and anti-tubercular [14] activities. Based on the biological significance, it has been envisaged the integration of 2-thioxothiazolidin-4-one and 1,2,3-triazole pharmacophores units with C-C double band linkage in one molecular platform to generate a new 1,2,3-triazolylthiazolidones analog framework with anticancer activity (Scheme-1).

RESULTS AND DISCUSSION

The synthesis of novel series of (E)-5-((1-Phenyl-1H-1,2,3-triazol-4-yl)methylene)-2-thioxothiazolidin-4-one derivatives have been carried out according to the steps shown in Scheme 1. The 1-substitutedphenyl-1H-1,2,3-triazole-4-carbaldehydes were synthesized starting from various aniline derivatives by using azide formation, click reaction followed by oxidation alcohols to aldehydes [15]. The targeted compounds were synthesized by Knoevenagel condensation by reacting 1-substitutedphenyl-1H-1,2,3-triazole-4-carbaldehydes with 2-thioxothiazolidin-4-one (Table 1). The derivatives are synthesized by using a simple base such as potassium hydroxide under mild reaction conditions with a short period of reaction time in good yields. The structures of compounds were established using different spectroscopic techniques, including IR, ^{1}H-NMR, ^{13}CNMR, and mass spectroscopy. The target 2-thioxothiazolidin-4-one compounds gave satisfactory analytical and spectroscopic data, which were in full accordance with their depicted structures. The IR spectrum of 2-thioxothiazolidin-4-one derivatives revealed the presence of thiocarbonyl stretching vibration band around 1642cm^{-1} and the free N-H frequency appeared around 3400 cm^{-1}. In the ^{1}H-NMR spectrum characteristically a single methylidene proton was observed in the range of δ 7.60 ppm as a singlet, and NH proton was observed in the range of δ 13.70 ppm as a broad signal. Both observations were diagnostic and consistent with previously reported data in the literature, more characteristic singlet triazole ring proton was observed in the range of δ 9.20 ppm and the absence of aldehyde proton resonance of confirmed the structure of desired (E)-5-((1-Phenyl-1H-1,2,3-triazol-4-yl)methylene)-2-thioxothiazolidin-4-one analogs. The ^{13}C-NMR spectral analyses were consistent with the

Table-1: Physical data of 1,2,3-triazolyl-thioxothiazolidin-4-one analogues.

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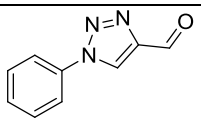
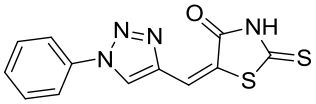
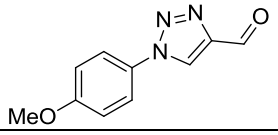
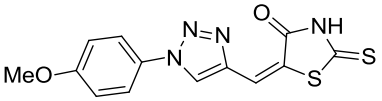
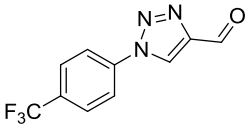
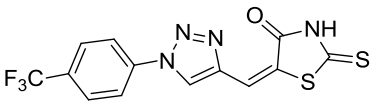
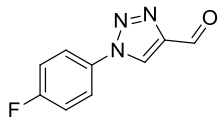
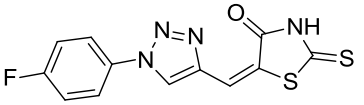
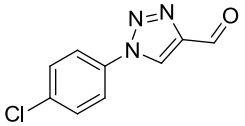
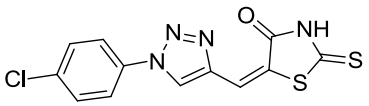
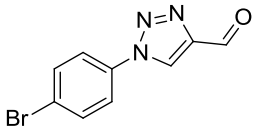
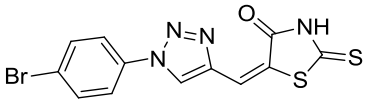
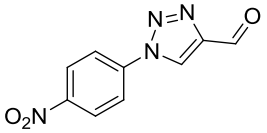
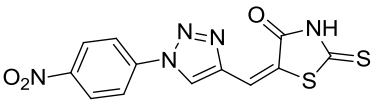
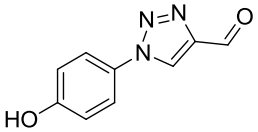
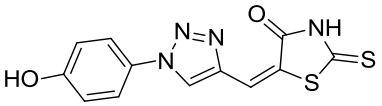
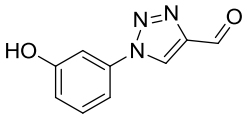
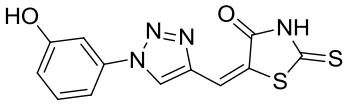
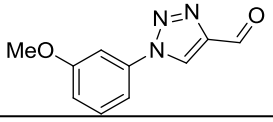
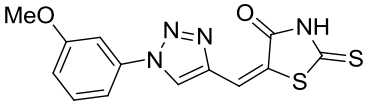
a			182-184	3	82
b			175-178	3	84
c			177-180	3	80
d			191-194	3.5	78
e			169-172	3.5	80
f			195-198	3	78
g			155-158	4	80
h			202-205	3	79
i			192-195	4	76
j			144-147	3	82

assigned structures. No large differences were found in ^{13}C chemical shift for methylene carbon of 5-benzylidene carbon range of 134-136 ppm in all title compounds. In addition, in ^{13}C NMR spectra exhibited signals at around δ169 ppm is due to the (C=O) keto carbonyl, and resonance at around δ 198 ppm is due to the (C=S) thiocarbonyl carbon of 2-thioxothiazolidin-4-one ring. In the mass spectroscopy, all the synthesized compounds gave their mass value as m/z at [M+H] peak.

Anticancer activity

The anticancer activity of synthesized compounds was evaluated against four human cancer cell lines including lung (A549), breast (MCF-7), melanoma (A375), and colon

Table 2: In vitro cytotoxicity activity of 1,2,3-triazolyl-thioxothiazolidin-4-one analogues (6a-j).

Compound	A549	MCF-7	A375	HT-29
6a	1.75	10.5	0.66	4.01
6b	0.31	4.01	1.45	0.33
6c	4.55	0.40	2.01	2.18
6d	1.28	1.76	0.36	1.22
6e	1.88	15.2	2.56	6.70
6f	6.01	2.44	5.70	5.01
6g	0.14	1.14	2.88	1.89
6h	3.01	2.88	1.09	0.17
6i	0.79	1.60	0.44	12.5
6j	0.10	0.32	0.19	1.53
Combretastatin-A4	0.11	0.18	0.21	0.93

(HT-29), that had shown in Table 1. Interesting results were observed shown Table 2, the highest activity in lung cancer cells is displayed by compounds 6j (3-methoxy), 6g (4-nitro) and 6b (4-methoxy) (IC_{50} = 0.10, 0.14, 0.31 μM) respectively. The next molecule in this series is compound 6i (3-hydroxy) also exhibited relatively high activity (IC_{50} = 0.79 μM) compared to all the remaining compounds which were proved inactive in lung cancer cells. The next high activity in breast cancer cell lines was demonstrated by compounds **6j** (3-methoxy) and 6c (4-trifluoromethyl) (IC_{50} = 0.32 and 0.40 μM). In this series, compounds **6g** (4-nitro) and **6b** (4-methoxy) (IC_{50} = 1.14 μM) also showed good activity compared to remaining all compounds. The utmost activity in melanoma cancer cell lines was shown by compounds **6j** (3-methoxy), 6d (4-methoxy) and **6i** (3-hydroxy) (IC_{50} = 0.19, 0.36 and 0.44 μM). Similarly, the highest activity in colon cancer cells was again displayed by compound **6g** (4-nitro) and **6b** (4-methoxy) (IC_{50} = 0.17 and 0.33 μM) and the compounds **6d** (4-fluoro) and **6j** (3-methoxy) (IC_{50} = 1.22 and1.53 μM) exhibited good activities. These results clearly indicated that 3_{rd} and 4_{th} substitution on phenyl ring with electronegativity atom were shown better activities than the other substitution due to the substituted compounds are may easily form bonding with respective protein supported by docking studies results and the compounds are very closely associated with Combretastatin-A4, among them the compounds **6g** (4-nitro) and **6j** (3-methoxy) were shown most potent anticancer activities against investigated all cell lines (lung, colon, breast, and melanoma) shown in Table 2.

Molecular docking studies

In order to better understand, it has been observed that the structures-activity relationships and molecular docking study of the compounds **6a-j** with a therapeutical target of cancer showed that have shown significant dock score with all the compounds. From the results of docking, compounds 6i (3-hydroxy) and **6b** (4-methoxy) have shown the highest docking scores. Compound 6i (3-hydroxy) has shown an H-bond with active site amino acid with -5.879 dock score (Fig. 1). The docking results revealed that amino acids Asp112 located in the binding pocket of protein played an important role. The C=S group of sulfur acts as H-bond acceptor atom and NH of the thioxothiazolidin-4-one forms an H-bond with LYS53. The compound 6i (3-hydroxy) triazole nitrogen atom also forms an H-bond with MET109 shown in Figure-1. In a similar way, compound **6b** (4-methoxy) has shown H bonds with the docking score of - 5.724. The sulfur atom act as an H-bond acceptor atom and the amine of the thioxothiazolidin-4-one forms an H-bond with LYS53. The triazole nitrogen atom also forms an H-bond with MET109. Based on the characterization of protein-ligand interactions, it is evidenced that 1,2,3-triazolylthiazolidinedione analogs played a key role in forming H-bond interactions. The docking score of all the compounds 6a-j was also depicted in Table 3.

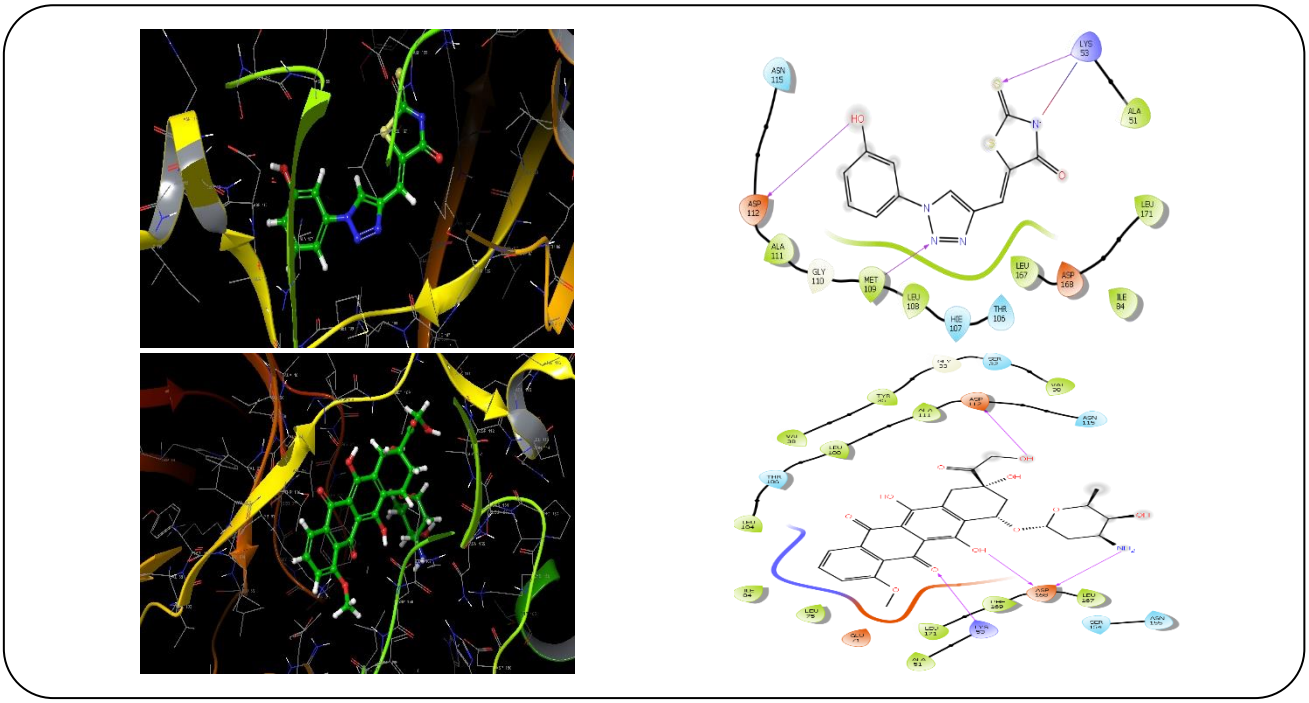


Fig. 1: Molecular docking poses of compound 6i and Doxorubcin.

EXPERIMENTAL SECTION

Melting points were determined in open capillary tubes and are uncorrected. The purity of the compounds was checked by TLC using percolated silica gel plate 60_{254}(Merck). IR (KBr) spectra were recorded on a Shimadzu FT-IR-8400s spectrophotometer. ^{1}HNMR and ^{13}CNMR spectra were recorded on Bruker Avance II 400 MHz spectrometer using tetramethylsilane as an internal standard. Mass spectra were recorded on a GCMS-QP 1000 EX mass spectrometer. The anticancer activity of synthesized compounds was evaluated by using MTT assay method.

General synthetic procedure for 1,2,3-triazolyl-thioxothiazolidin-4-one analogs

A methanolic solution of 1-substitutedphenyl-1*H*-1,2,3-triazole-4-carbaldehydes (1 mmol), 2-thioxothiazolidin-4-one (1 mmol), and potassium hydroxide (2 mmol) were stirred at room temperature for 3 h. Progress of the reaction was monitored by TLC, after completion of the reaction. The reaction mixture was poured into ice-cold water, slowly the solid separates out, it filtered, washed with water, dried, and purified by using column chromatography using n-hexane:ethyl acetate (9:1) to afford pure (*E*)-5-((1-Phenyl-1*H*-1,2,3-triazol-4-yl)methylene)-2-thioxothiazolidin-4-one derivatives.

Spectral data

(E)-5-((1-phenyl-1H-1,2,3-triazol-4-yl)methylene)-2-thioxothiazolidin-4-one (6a)

IR(KBr): 3414, 1642 and 1591 cm^{-1}; ^{1}H NMR spectrum, δ, ppm: 7.55-7.64 (m, 4H, Ar-H), 7.91-7.93 (m, 2H, Ar-H), 9.21 (s, 1H, triazole ring proton), 13.72 (bs, 1H, NH); ^{13}C NMR spectrum, δC, ppm: 118.0, 120.5, 126.1, 126.9, 129.3, 129.9, 136.0, 142.0, 169.1, 198.4; *MS* 288 $(M+H)^{+}$.

(E)-5-((1-(4-methoxyphenyl)-1H-1,2,3-triazol-4-yl)methylene)-2-thioxothiazolidin-4-one (6b)

IR(KBr): 3420, 1644 and 1593 cm^{-1}; ^{1}H NMR spectrum, δ, ppm: 3.84 (s, 3H, OMe), 7.16-7.18 (d, 2H, Ar-H), 7.60 (s, 1H, Ar-H), 7.81-7.84 (d, 2H, Ar-H), 9.10 (s, 1H, triazole ring proton), 13.72 (bs, 1H, NH); ^{13}C NMR spectrum, δC, ppm: 55.62, 114.9, 118.1, 122.2, 126.1, 126.8, 129.3, 141.8, 159.7, 169.2, 198.5; *MS* 318 $(M+H)^{+}$.

(E)-2-thioxo-5-((1-(4-(trifluoromethyl)phenyl)-1H-1,2,3-triazol-4-yl)methylene) thiazolidin-4-one (6c)

IR(KBr): 3418, 1642 and 1595 cm^{-1}; ^{1}H NMR spectrum, δ, ppm: 7.62 (s, 1H, Ar-H), 7.87-7.95 (m, 2H, Ar-H), 8.28-8.32 (m, 2H, Ar-H), 9.37 (s, 1H, triazole ring proton), 13.76 (bs, 1H, NH); ^{13}C NMR spectrum, δC, ppm:

Table 3: Molecular docking scores for the compounds 6a-j.

S.No	Comp.	DockScore (5XYY)
1	6a	-5.020
2	6b	-5.724
3	6c	-5.133
4	6d	-4.992
5	6e	-5.136
6	6f	-5.212
7	6g	-4.927
8	6h	-4.911
9	6i	-5.879
10	6j	-5.564
11	Doxorubcin	-6.097

117.4, 117.7, 122.1, 124.6, 125.8, 126.5, 127.4, 131.4, 136.5, 142.2, 169.1, 198.3; *MS* 356 $(M+H)^+$.

(E)-5-((1-(4-fluorophenyl)-1H-1,2,3-triazol-4-yl)methylene)-2-thioxothiazolidin-4-one (6d)

IR(KBr): 3428, 1645 and 1596 cm^{-1}; ^1H NMR spectrum, δ, ppm: 7.47-7.53 (m, 3H, Ar-H), 7.95-8.00 (m, 2H, Ar-H), 9.13 (s, 1H, triazole ring proton), 13.74 (bs, 1H, NH); ^{13}C NMR spectrum, δC, ppm: 115.8, 117.8, 122.0, 126.5, 130.2, 133.4, 142.2, 161.0, 169.4, 198.2; *MS* 306 $(M+H)^+$.

(E)-5-((1-(4-chlorophenyl)-1H-1,2,3-triazol-4-yl)methylene)-2-thioxothiazolidin-4-one (6e)

I R(KBr): 3414, 1646 and 1592 cm^{-1}; ^1H NMR spectrum, δ, ppm: 6.95-6.98 (d, 2H, Ar-H), 7.61 (s, 1H, Ar-H), 7.68-7.70 (d, 2H, Ar-H), 9.04 (s, 1H, triazole ring proton), 13.71 (bs, 1H, NH); ^{13}C NMR spectrum, δC, ppm: 117.9, 122.2, 126.2, 129.9, 133.6, 134.8, 142.1, 169.1, 198.3; *MS* 322 $(M+H)^+$.

(E)-5-((1-(4-bromophenyl)-1H-1,2,3-triazol-4-yl)methylene)-2-thioxothiazolidin-4-one (6f)

IR(KBr): 3424, 1645 and 1594 cm^{-1}; ^1H NMR spectrum, δ, ppm: 7.12 (s, 1H, HC=C), 7.81-7.84 (d, 2H, Ar-H), 7.90-7.93 (d, 2H, Ar-H), 8.95 (s, 1H, triazole ring proton; ^{13}C NMR spectrum, δC, ppm: 117.7, 122.1, 123.5, 126.7, 128.9, 132.7, 133.5, 142.1, 169.2, 198.3; *MS* 366 $(M+H)^+$.

(E)-5-((1-(4-nitrophenyl)-1H-1,2,3-triazol-4-yl)methylene)-2- thioxothiazolidin-4-one (6g)

IR(KBr): 3416, 1646 and 1592 cm^{-1}; ^1H NMR spectrum, δ, ppm: 7.63 (s, 1H, Ar-H), 8.24-8.26 (d, 2H, Ar-H), 8.48-8.51 (d, 2H, Ar-H), 9.39 (s, 1H, triazole ring proton), 13.76 (bs, 1H, NH); ^{13}C NMR spectrum, δC, ppm: 118.1, 122.2, 124.5, 126.5, 127.3, 139.2, 143.1, 148.8, 169.3, 198.4; *MS* 332 $(M+H)^+$.

(E)-5-((1-(4-hydroxyphenyl)-1H-1,2,3-triazol-4-yl)methylene) -2-thioxothiazolidin-4-one (6h)

IR(KBr): 3420, 1644 and 1594 cm^{-1}; ^1H NMR spectrum, δ, ppm: 6.95-6.97 (d, 2H, Ar-H), 7.60 (s, 1H, Ar-H), 7.68-7.70 (d, 2H, Ar-H), 9.04 (s, 1H, triazole ring proton), 10.5 (s, 1H, OH), 13.72(bs, 1H, NH); ^{13}C NMR spectrum, δC, ppm: 117.9, 122.2, 126.2, 129.9, 133.6, 134.8, 142.1, 169.1, 198.3; *MS* 305 $(M+H)^+$.

(E)-5-((1-(3-hydroxyphenyl)-1H-1,2,3-triazol-4-yl)methylene) -2-thioxothiazolidin-4-one (6i)

IR(KBr): 3422, 1645 and 1596 cm^{-1}; ^1H NMR spectrum, δ, ppm: 6.91-6.94 (d, 1H, Ar-H), 7.58 (s, 1H, Ar-H), 7.30-7.32 (m, 2H, Ar-H), 7.39-7.44 (t, 1H, Ar-H), 9.15 (s, 1H, triazole ring proton), 10.13 (s, 1H, OH), 13.73 (bs, 1H, NH); ^{13}C NMR spectrum, δC, ppm: 116.8, 117.9, 118.4, 122.0, 125.4, 126.2, 126.7, 129.9, 133.4, 142.1, 169.1, 198.3; *MS* 305 $(M+H)^+$.

(E)-5-((1-(3-methoxyphenyl)-1H-1,2,3-triazol-4-yl)methylene)-2-thioxothiazolidin-4-one (6j)

IR(KBr): 3409, 1645 and 1598 cm^{-1}; ^1H NMR spectrum, δ, ppm: 7.12 (s, 1H, HC=C), 7.81-7.84 (d, 2H, Ar-H), 7.90-7.93 (d, 2H, Ar-H), 8.95 (s, 1H, triazole ring proton; ^{13}C NMR spectrum, δC, ppm: 55.6, 115.4, 116.0, 117.8, 122.2, 126.2, 126.5, 129.0, 132.5, 142.0, 159.5, 169.3, 198.3; *MS* 319 $(M+H)^+$.

CONCLUSIONS

In conclusion, we have successfully synthesized the 1,2,3-triazolyl-thioxothiazolidinone derivatives by an easy and simple chemical method by using potassium hydroxide, and different analytical data fully agreement the synthesized derivatives. The anticancer evaluation result suggested that the compounds **6g** (4-nitro) and **6j** (3-methoxy) were the most potent in all investigated cancer cell lines (lung, colon, Breast and melanoma).

From the results of molecular docking observed that the compounds **6i** (3-hydroxy) and **6b** (4-methoxy) have shown the highest docking scores.

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REFERENCES

[1] Sak K., Chemotherapy and Dietary Phytochemical Agents, *Chemother Res Pract.*, **282570**: 1-11 (2012).

[2] Aldossary S.A., Review on Pharmacology of Cisplatin: Clinical Use, Toxicity and Mechanism of Resistance of Cisplatin, *Biomed Pharmacol J.*, **12(1)**: 7-15 (2019).

[3] Bhatt H.B., Sharma S., Synthesis and Antimicrobial Activity of Pyrazole Nucleus Containing 2-thioxothiazolidin-4-one Derivative, *Arab. J. Chem.*, **10(2)**: S1590-S1596 (2017).

[4] Murugan R., Anbazhagan S., Sriman Narayanan S., Synthesis and in Vivo Antidiabetic Activity of Novel Dispiropyrrolidines Through [3+2] Cycloaddition Reactions with Thiazolidinedione And Rhodanine Derivatives, *Eur. J. Med. Chem.*, **44(8)**:3272-3279 (2009).

[5] Koppireddi S., Komsani J.R., Avula S., Pombala S., Vasamsetti S., Kotamraju S., Yadla R., Novel 2-(2,4-dioxo-1,3-thiazolidin-5-yl)acetamides as Antioxidant and/or Anti-Inflammatory Compounds, *Eur. J. Med. Chem.*, **66**: 305-313 (2013).

[6] Mousavi S.M., Zarei M., Hashemi S.A.R, Babapoor A., Amani A.M., A conceptual Review of Rhodanine: Current Applications of Antiviral Drugs, Anticancer and Antimicrobial Activities, *Artif. Cells Nanomed. Biotechnol.*, **47**:1132-1148 (2019).

[7] Mallikarjuna B.P., Sastry B.S., Suresh Kumar G.V., Rajendraprasad Y., Chandrashekar S.M., Sathisha K., Synthesis of New 4-Isopropylthiazole Hydrazide Analogs and Some Derived Clubbed Triazole, Oxadiazole Ring Systems--A Novel Class of Potential Antibacterial, Antifungal and Antitubercular Agents, *Eur. J. Med. Chem.*, **44(11)**:4739-46 (2009).

[8] Sherihan El-Sayed, Kamel Metwally, Abdalla A. El-Shanawani, Lobna M. Abdel-Aziz, Harris Pratsinis. Dimitris Kletsas, Synthesis and Anticancer Activity of Novel Quinazolinone-Based Rhodanines, *Chem. Cent. J.*, **11**:102 (2017).

[9] Ashok D., Arram G., Vijaya Lakshmi B., Ravi S., Ramesh B., Microwave-Assisted Synthesis and Antimicrobial Activity of Novel 1-[1/2-(1-Benzyl-1H-[1,2,3]triazol-4-ylmethoxy)-naphthalen-2/1- yl]-3-(1-phenyl-3-aryl-1H-pyrazol-4-yl)-Propenones, *Org. Commun.*, **8(2)**: 24 (2014).

[10] Ashok D., Ravi S., Ganesh A., Vijaya Lakshmi B., Adam Sh., Murthy S.D.S., Microwave-Assisted Synthesis and Biological Evaluation of Carbazole-Based Chalcones, Aurones and Flavones, *Med. Chem. Res.*, **25(5)**: 909-922 (2016).

[11] Song M.X., Deng X.Q., Steroids Interfere with Human Carbonic Anhydrase Activity by Using Alternative Binding Mechanisms, *J. Enz. Inhibition Med. Chem.*, **33**:1453-1459 (2018).

[12] Kumar A., Sathish Kumar B., Sreenivas E., Subbaiah T., Synthesis, Biological Evaluation, and Molecular Docking Studies of Novel 1,2,3-Triazole Tagged 5-[(1H-Indol-3-yl)methylene]pyrimidine-2,4,6(1H,3H,5H) trione, *Russ. J. Gen. Chem.*, **88(3)**: 587-595 (2018).

[13] Lazrek H.B., Taourirte M., Oulih T., Barascut J.L., Imbach J.L., Pannecouque C., Witrouw M., De Clercq E., Synthesis and anti-HIV Activity of New Modified 1, 2, 3-triazole Acyclonucleosides, *Nucleos Nucleot Nucl.*, **20(12)**: 1949-1960 (2001).

. [14] Shaikh M.H., Ubhedar D.D., Nawale L., Sarkar S., Kalam Khan F.A., Sangshettic J.N., Shingate B.B., 1, 2, 3-Triazole Derivatives as Antitubercular Agents: Synthesis, Biological Evaluation and Molecular Docking Study, *Med. Chem. Comm.*, **6**: 1104-1116 (2015).

[15] Linga Goud G., Ramesh S., Ashok D., Prabhakar Reddy V., Green Synthesis and Antibacterial Evaluation of Some New 1-aryl-3-(1-aryl-1H-[1,2,3]triazol-4-yl)-Propenones, *Russ. J. Gen. Chem.*, **86**: 1419-1423 (2016).