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The therapeutic efficacy of 1,2,3-triazoles in cancer

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Abstract

The financial and human toll of cancer's global impact cannot be quantified. Unfortunately, the side effects of cancer treatments are often severe. Drug resistance is another issue doctors must address when treating cancer. Other factors that contribute to an increased risk of cancer include alcohol consumption, poor nutrition, water and air pollution, and tobacco use.

Derivatives of 1,2,3 triazole and their groups have gained a lot of importance due to their diverse biological activities and their ability to treat cancer. This is evident in the toxic effect of transition metal compounds and heterocyclic compounds in the formation of stable communities, which increases their effect on diverse groups of cancer cells through the direct pharmacological effect on the target cells. This is due to the unique structure of the triazole ring, which allows hydrogen bonds and stacking of π–π in coordination with the metal center.

The acyclic part contains nitrogen 1-2-3-triazoles, five groups that perform various therapeutic functions. There are many drugs approved for the treatment of a wide range of cancers that contain 1-2-3-triazoles, in addition to pharmaceutical compounds that are in the clinical research stage. Therefore, the importance of the compound is increasing in the field of cancer research.

Keywords: Cancer; 1,2,3 Triazole; Global impact; Side effects; Treatments

1. Introduction

Cancer is one of the main causes of death. It is likely that the number of people with cancer will reach 29.5 million in 2040. This highlights the need to develop more appropriate and effective cancer drugs that overcome the obstacles resulting from side effects.(1)

This makes it a duty for researchers to produce effective drugs against cancer. Heterocyclic compounds, triazoles, have clearly shown promise in the future due to their distinctive biological properties and ease of synthesis. Among them, 1-2-3-triazoles have received great attention if the development of cancer drugs becomes possible. (2)

In addition to being a drug carrier, the 1-2-3 triazole structure has the ability to react and add an alkane-aide ring, carrying both drugs One of the mechanistic properties of the compound is that it inhibits the growth of cancer cells. Many hybrid compounds containing 1-2-3-triazole have been produced and synthesized due to their anticancer properties in vitro and in vivo. Inorganic compounds contain biologically active heteroatoms, such as nitrogen, sulfur oxygen, and others, which are toxic to target cells. (3)

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The nitrogen ring is a heterocyclic molecule containing five parts called azoles. It represents a promising future. This is due to the presence of two heterogeneous nitrogen atoms, which play a significant role in changing the structure and biological reactions.This review includes the role of the compound in combating various types of cancer. (4)

2. Chemistry: synthesis and properties of the 1,2,3-triazoles

1-2-3-Triazole is prepared by the reaction of azide with alkynes. The preparation is facilitated by techniques called RuAAC or CuAAC by using Click Chemistry The chemical and physical properties of the compound are characterized by high stability against hydrolysis or oxidation thanks to the double bonds present in the ring. The hydrogen atoms are the reason for the polarity of triazole and its solubility in water. The electronic nature allows it to be easily bound to proteins or enzymes through hydrogen bonds. (5)

Image (1) shows three different forms of the 1,2,3-triazole compound. The 1,2,3-triazole types (tautomers) differ in the location of the hydrogen atom bonded to the nitrogen atoms in the five-membered ring.

- In this form (1), the hydrogen atom is bonded to nitrogen atom number 1H-1,2,3-Triazole
- In this form (2), the hydrogen atom is bonded to nitrogen atom number 2 (N2),
- which changes the electron distribution in the ring and affects the chemical properties of the compound.4H-1,2,3-TriazoleIn this form, the hydrogen atom is bonded to carbon atom number 4 (C4)
- rather than to any of the nitrogen atoms. This form is less common
- and may be less stable than the other forms. (6)

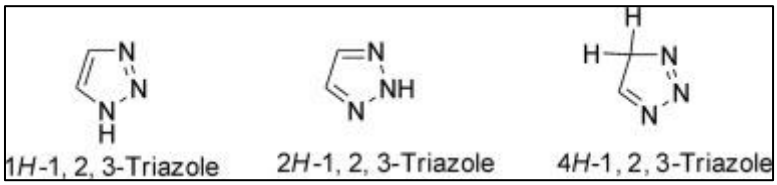

Figure 1 The formulas in which 1-2-3-triazoles exit

2.1.1. triazoles anti-cancer

study shows that 4-1-(3,4-dichlorophenyl)-1H-1,2,3-triazol-4-yl)-methoxy, a new derivative of 1,2,3-triazole, was produced. The compound 2-hydroxybenzaldehyde was produced by CuAAC, which stands for copper(I)-catalyzed azide-alkyne cycloaddition. Fourier transform infrared spectroscopy (FTIR), 1H NMR, 13C NMR, and UV-vis spectroscopy were performed to study the structure of the compound. The molecule was adapted to a monoclinic crystal system with space group P21/c, according to X-ray crystallography experiments. (7). The study showed that hydrogen bonds and van der Waals interactions are the main interactions that developed in the crystal packing. The unit cell volume of the crystal space was determined to be 152.10 Å3, and the proportion of free space in it was 9.80%.Through energy analysis, it was found that dispersion energy dominated the stability of the complex (8)The study on the binding activity of the complex to DNA/bovine serum albumin (BSA) showed that interference was mediated in the binding activity of the complex to CT DNA and that BSA binding activity was mediatedThe 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) assay was also used to study the anticancer activity of the compound using human cell lines such as MDA-MB-231, LNCaP, Caco-2, and HEK-293. On Caco-2 cancer cells, the compound showed greater cytotoxicity than cisplatin and etoposide, with an IC50 value of

After 48 hours, a value of 16.63 ± 0.27 μM was observed. Annexin V recommends the use of apoptosis to increase cell death. The study showed that reactive oxygen species (ROS) may lead to programmed cell death through the production of ROS. (9)

Chemotherapy is a primary method of combating breast cancer, but multidrug resistance and severe side effects epresent major obstacles to successful treatment, highlighting the need to develop new drugs. Hence, we find the role of 1-2-3-triazoles, which can be synthesized by (Click Chemistry) and can function efficiently as a linking group between different drug molecules and as an active drug component in its own right due to the formation of hydrogen bonds, their moderate dipole moment, and their water solubility. This demonstrates the effectiveness of triazoles against various forms of breast cancer and their ability to selectively target multiple biological pathways. (10)

For lung cancer, which is the most common type and causes about a quarter of cancer deaths worldwide, 1-2-3-triazole compounds have shown promising therapeutic potential due to their ability to bind to enzymes and receptors and target important biological pathways, paving the way for the development of anti-lung cancer drugs. (11)

Research indicated biological activity through the effect of anticancer molecules. Novel compounds were selected to screen cancer cell lines in the laboratory. Initially, approximately 60 cell lines were selected at a concentration of 10-5, using a single dose of the primary anticancer assay. (12) These cells represented different types of cancer, represented by human cancer cell lines. Each cell line was injected and pre-incubated on a microtiter plate for 24 to 48 hours as part of the screening protocol. After adding test chemicals at a single concentration, the culture was incubated for an additional 48 hours. Sulforhodamine B (SRB), a protein-binding dye, was used to determine endpoints. The percentage growth of treated cells compared to untreated control cells was used to determine the results for each test agent. (13) The growth rate (GP) was used to infer the results of each compound. The growth range shows the minimum and maximum growth rates observed in various cancer cell lines for the evaluated lines. (14) The 1-2-3-triazole compounds showed low to minimal activity. However, some chemicals were found to have a selective effect on a number of cancer cell lines.Most of the drugs studied have shown inhibition of leukemia and breast cancer cell lines, in addition to kidney cancer cells. (15)

The study demonstrated that 1-2-3-triazole derivatives have effective potential to inhibit acute myeloid leukemia cells. 1-2-benzisoxazole demonstrated strong antiproliferative activity in the MTT assay against MV4-11 cells, with an IC50 of 2 μM.As a compound developer using click chemistry, its antiproliferative potential against cancer cells was tested. (16)

The compound was successful and demonstrated inhibitory activity against MCF-7 (breast cancer) cells with an IC50 value of 46 μM.

However, the biotulin compound, which demonstrated a 30% inhibitory effect on MCF-7 cells and a 90% inhibitory effect on HCT-116 cells after 48 hours of incubation, was found to be more toxic to the cells. (17)

For 1,2,3-triazole compounds, derived from sugars, since carbohydrates can alter drug behavior, these compounds appear to be useful complementary therapies for cancer drugs. They are important in terms of drug kinetics, cellular uptake, target specificity, and bioavailability (18). Studies have shown that carbohydrate-based 1,2,3-triazole drugs exhibit better properties, including greater stability and high-water solubility, which reduces the problems of poor water solubility and reduced chemical stability (19).

Triazole compounds conjugated with carbohydrates protect against rapid clearance from the reticuloendothelial system (RES), increasing systemic exposure and enhancing therapeutic efficacy. Carbohydrates enhance receptor-mediated phagocytosis, enabling anticancer drugs to enter cells and bypass biological barriers that prevent them from entering tumor tissue

Click-triggered hybrid derivatives of ipodophyllotoxin and galactose from 1,2,3-triazoles were used to produce. Compared to cisplatin (16) (IC50 = 9.24 μM, MTT assay) and etoposide (17) (IC50 = 11.92 μM, MTT assay), these compounds demonstrated a potent antiproliferative effect against A549 cells (IC50 = 4.07 μM, MTT assay), a double effect.

The 1,2,3-triazole ring is an important pharmacophore system in nitrogen-containing heterocyclic compounds. These five-membered heterocyclic forms with three heteroatoms are feasible for synthesis using click chemistry and copper- or ruthenium-catalyzed azide-alkyne cycloaddition. (18). New hybrid and conjugated compounds containing 1,2,3-triazoles have been produced, becoming important substrates for various biological behaviors after 1,2,3-triazole compounds were shown to have a "linking" property (19). Their anticancer, antidiabetic, antiviral, antibacterial, antituberculosis, antileishmanial, neuroprotective, and antimalarial properties have been demonstrated.

1,2,3-Triazole metal complexes also exhibit anticancer activity (20). Copper (II) complexes containing triazole ligands, with IC values in the low micromolar range, demonstrated a marked effect against breast and colon cancer cells. Ruthenium-triazole complexes were found to have low toxicity to normal tissues and were capable of targeting malignant cells. (20)

Several triazole-based compounds with antiproliferative properties have been developed to demonstrate their efficacy both in vitro and in vivo. Taking into account their molecular structure, their designed mechanisms of action, and the types of cancer cells targeted, these compounds exhibit significant differences. (21)

3. Conclusion

Triazole metal complexes are inorganic biomolecules with a promising future in cancer therapy.

Since Anticancer compounds derived from triazoles have been widely developed. They vary greatly in their composition and mode of action. Their synthesis methods, efficacy, and targetability have proven promising in the future for the development of broad-spectrum drugs to safely combat all types of cancer.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

References

[1] Manoj Kalita , Devaraja M , Indranil Saha , Amit Chakrabarti.Global burden of cancer pattern in 2020 & prediction to 2040 among older adults.Indian J Med Res,2024 23;160(5):397–406. doi: 10.25259/ijmr_1729_23.

[2] Rasha Saad Jwad, Dania Emad Ibrahim Ali, Ibrahim Abdulkareem Sabri, and Ahmed Abed Temur.Review on significant monosaccharides-based 1,2,3- triazoles; synthesis and their anticancer activity.Journal of University of Kerbala ,2024 Vol. 21, Issue 1.

[3] Dheer D, Singh V, Shankar R. Medicinal attributes of 1,2,3-triazoles: Current developments. Bioorganic Chemistry. 2017;71:30-54. DOI: 10.1016/j.bioorg.2017.01.010

[4] Dhuha K. Slman, Hind A. Satar, Zahraa A. Ketan, Asmaa A. Jawad.Heterocyclic Compounds: A Study of its Biological Activity.Al-Nahrain Journal of Science ANJS,2024, Vol.27 (5), December, pp. 19–24.http://doi.org/10.22401/ANJS.27.5.03.

[5] Flavia Ferrara,Tamás Beke-Somfai,Nina Kann.Recent Developments in the Ruthenium-Catalyzed Azide Alkyne Cycloaddition (RuAAC) Reaction.European Journal of Organic Chemistry2024 27(25) DOI: 10.1002/ejoc.202400113.

[6] Josué Varela-Palma,Jaime González,Gustavo Lopez-Téllez,M. V. Basavanag Unnamatla

[7] Marco A. García-Eleno,Erick Cuevas-Yañez.Synthesis of 1,2,3-Triazoles from Alkyne-Azide Cycloaddition Catalyzed by a Bio-Reduced Alkynylcopper (I) Complex. Chem. Proc. 2021, 3(1), 54; https://doi.org/10.3390/ecsoc-24-08384.

[8] Noor Tariq , Ahmed Ahmed *, Waled Abdo Ahmed and Amamer M. Redwan.Synthesis and Characterization of New 1,2,4-Triazole Derivative Form Methylbenzoate with Sulfur as Bridge Links.Journal of University of Anbar for Pure Science,2024,(18), (02):123 – 129.DOI:10.37652/juaps.2024.147525.1212

[9] Tolga GöktürkTalip ZenginTuncer HökelekShow all 5 authorsRamazan GupSynthesis, Crystal Structure, Hirshfeld Surface Analysis, DNA/BSA Interaction and Molecular Docking Studies of 2-(6-(4-chlorophenyl)-1,2,4-triazin-3-yl)quinoline. 2023Journal of Molecular Structure 1292(6):136128 DOI: 10.1016/j.molstruc.2023.136128

[10] Stefan Jakovljevic , Petar Canovic , Marko Spasic , Marija Zivkovic , Milan Zaric , Radica Zivkovic Zaric , Andjela Franich , Snezana Rajkovic , Zeljko Todorovic, Nenad Relic , Milos Zivic , Nikola Mirkovic.DNA/BSA Binding Affinity and Cytotoxicity of Dinuclear Palladium(II) Complexes with Amino Acids as LigandsMolecules. 2025 Mar 30;30(7):1534. doi: 10.3390/molecules30071534 .

[11] Juntao Song , Shuai Zhang , Bo Zhang , Junwei Ma.The anti-breast cancer therapeutic potential of 1,2,3-triazole-containing hybrids.Arch Pharm (Weinheim),2024 Mar;357(3):e2300641.doi: 10.1002/ardp.202300641.

[12] Ting Liang , Xiangyang Sun , Wenhong Li , Guihua Hou , Feng Gao .1,2,3-Triazole-Containing Compounds as Anti–Lung Cancer Agents: Current Developments, Mechanisms of Action, and Structure–Activity Relationship. Front Pharmacol, 2021 ,11;12:661173.doi: 10.3389/fphar.2021.661173.

[13] Julia Krushkal , Simarjeet Negi , Laura M Yee , Jason R Evans , Tanja Grkovic , Alida Palmisano , Jianwen Fang , Hari Sankaran , Lisa M McShane , Yingdong Zhao , Barry R O'Keefe. Molecular genomic features associated with in vitro response of the NCI-60 cancer cell line panel to natural productsMol Oncol,2020 , 24;15(2):381–406. doi: 10.1002/1878-0261.12849.

[14] Ada Hang-Heng Wong , Haoran Li , Yanwei Jia , Pui-In Mak , Rui Paulo da Silva Martins , Yan Liu , Chi Man Vong , Hang Cheong Wong , Pak Kin Wong , Haitao Wang , Heng Sun , Chu-Xia Deng .Drug screening of cancer cell lines and human primary tumors using droplet microfluidics.Sci Rep 2017 , 22;7:9109. doi: 10.1038/s41598-017-08831-z

[15] Kaitlyn E Johnson , Grant Howard , William Mo , Michael K Strasser , Ernesto A B F Lima , Sui Huang , Amy Brock.Cancer cell population growth kinetics at low densities deviate from the exponential growth model and suggest an Allee effect .PLoS Biol. 2019 Aug 5;17(8):e3000399. doi: 10.1371/journal.pbio.3000399

[16] Khurshed Bozorov , Jiangyu Zhao , Haji A Aisa.1,2,3-Triazole-containing hybrids as leads in medicinal chemistry: A recent overview.Bioorg Med Chem,2019 Jul 4;27(16):3511–3531. doi: 10.1016/j.bmc.2019.07.005.

[17] Mallikarjuna swamy a M M,Kuruvalli Gouthami,Subhasish Maity,Damodara Reddy Vaddi,Lakshmi Basavegowda.Synthesis, characterization, antioxidant, in silico-based virtual screening and anti-cancer potential of substituted 2-(4-acetyl-5- methyl-1h-1,2,3-triazol-1-yl)-n-phenylacetamide derivatives.

[18] Organic Communications2024, 17(4):218-240. DOI: http://doi.org/10.25135/acg.oc.177.2412.3374

[19] Brigitta Kis , Ioana Zinuca Pavel , Stefana Avram , Elena Alina Moaca , Martina Herrero San Juan ,Anja Schwiebs , Heinfried H Radeke , Delia Muntean , Zorita Diaconeasa , Daliana Minda , Camelia Oprean , Florina Bojin , Cristina Adriana Dehelean , Codruta Soica , Corina Danciu .Antimicrobial activity, in vitro anticancer effect (MCF-7 breast cancer cell line), antiangiogenic and immunomodulatory potentials of Populus nigra L. buds extract.BMC Complement Med Ther,2022 16;22:74. doi: 10.1186/s12906-022-03526-z

[20] Mira Jil Vaishnani,Sabera Bijani.Mohamed Rahamathulla,Lalji Baldaniya,Vicky Jain,Kamal Y. Thajudeen,Mohammed Muqtader Ahmed,Syeda Af,Ismail Pasha.

[21] Biological importance and synthesis of 1,2,3-triazole derivatives: a review. Green Chemistry Letters and Reviews,2024, 17(1) DOI: 10.1080/17518253.2024.2307989

[22] Hong-Yan Guo , Zheng-Ai Chen , Qing-Kun Shen , Zhe-Shan Quan .Application of triazoles in the structural modification of natural products.J Enzyme Inhib Med Chem, 2021 ,24;36(1):1115–1144. doi: 10.1080/14756366.2021.1890066.

[23] 20-Fatih çelik,Yasemin Ünver,Burak Barut,Arzu Ozel,Kemal Sancak.Synthesis, Characterization and Biological Activities of New Symmetric Bis-1,2,3-Triazoles With Click Chemistry Medicinal Chemistry,2017, 13(3)DOI: 10.2174/1573406413666171120165226.

[24] 21-GIULIANO BERNAL , GISELA AQUEA , SEBASTIÁN RAMÍREZ-RIVERA .Metal-based molecules in the treatment of cancer: From bench to bedside.Oncol Res 2025 ,19;33(4):759–779. doi: 10.32604/or.2024.057019