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REVIEW ARTICLE

Recent Advances in Synthesis and Anticancer Potential of Triazole-containing Scaffolds

Devidas S. Bhagat[1,*], Gurvinder S. Bumbrah[2], Pooja A Chawla[3,*], Wasudeo B. Gurnule[4] and Sampada K. Shejul[5]

[1]Department of Forensic Chemistry and Toxicology, Government Institute of Forensic Science, Aurangabad 431 004, (MS), India; [2]Department of Chemistry, Biochemistry and Forensic Science, Amity School of Applied Sciences, Amity University, 122413, Haryana, India; [3]Department of Pharmaceutical Chemistry and Analysis, ISF College of Pharmacy, Moga 142001, Punjab, India; [4]Department of Chemistry, Kamla Nehru Mahavidyalaya, Nagpur-440024, (MS) India; [5]Department of Life Science, Vivekanand Arts, Sardar Dalipsingh Commerce and Science College, Aurangabad 431 001, (MS), India

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Abstract: Cancer is the most lethal disease that may be found anywhere globally. Approximately 10% of individuals die due to cancer of various types, with 19.3 million new cancer cases and 10 million deaths reported in 2020. More than 100 medications are commercially available for the treatment of cancer, but only a few candidates have high specificity, resulting in several side effects. The scientific community has spent the past decades focusing on drug discovery. Natural resources are used to isolate pharmaceutically active candidates, which are then synthesized in laboratories. More than 60% of all prescribed drugs are made from natural ingredients. Unique five-membered heteroaromatic center motifs with sulfur, oxygen and nitrogen atoms are found in heterocyclic compounds, such as indazole, thiazole, triazole, triazole, and oxazole, and are used as a core scaffold in many medicinally important therapies. Triazole possesses a wide range of pharmacological activities, including anticancer, antibacterial, antifungal, antibiotic, antiviral, analgesic, anti-inflammatory, anti-HIV, antidiabetic, and antiprotozoal activities. Novel triazole motifs with a variety of biological characteristics have been successfully synthesized using versatile synthetic methods. We intend here to facilitate the rational design and development of innovative triazole-based anti-cancer medicines with increased selectivity for various cancer cell lines by providing insight into various ligand-receptor interactions.

Keywords: 1, 2, 3-triazole, 1, 2, 4-triazole, anticancer activity, drug discovery, synthesis, pharmacological activities.

1. INTRODUCTION

Several research groups have been working on the design of biologically active motifs in which five-member nitrogen-containing heterocycles possess great significance in medicinal chemistry and new drug design. The triazoles are the prominent heterocyclic motifs containing five-membered ring that exists in two isomeric forms, including 1,2,3-triazole (**1**) [1] and 1,2,4-triazole (**2**) [2]. Triazoles have been associated with several biological activities, including anticancer activity (**3**) and anti-HIV activity (**4**) [1-2]. Medicinally important triazole-containing scaffolds are in great demand for the development of new therapeutics [3].

Nowadays, many triazole-containing candidates are clinically approved and used in routine practice [4]. Itraconazole (**5**) is clinically used as an antifungal agent. These candidates effectively inhibit the proliferation of human umbilical vein endothelial cells *in vitro* [5]. Voriconazole (**6**) is a diastereoselective antifungal drug obtained by the condensation reaction of the substituted pyridine derivatives and triazole [6]; not only this, but triazole is also a building block of the ribavirin (**7**) (antiviral drugs), with proven anti RNA viral activity. Mubritinib (**8**), a clinically tested anticancer drug possesses a triazole motif in its structure, and it is used for the treatment of acute myeloid leukemia, breast cancer, urinary bladder cancer, and prostate cancer [7]. Tazobactam (**9**) shows antibiotic properties, made of penicillin and triazole motifs. It acts as the β-lactamase inhibitor with a broad spectrum of antibacterial activity against both gram-positive and gram-negative bacterial species [8].

Triazoles are significant pharmacophores due to their dipole forming attractiveness, rigidity, hydrogen bond forming tendency, and efficient solubility [9-11]. Triazoles exhibit a wide range of biological activity, *i.e.*, antioxidant [12], antimalarial [13], antiviral [14], anticonvulsant [15], cannabinoid CB1 receptor antagonists [16], anti-urease [17], antibacterial [18], and antifungal [19]. Fluconazole (**10**) possesses antifungal activity against *Candida albicans* [20]. Isavuconazole (**11**) exhibits broad spectrum antifungal activity [21]. Substituted triazole exhibits potential anticancer activity (**12**) [22]. Triazole is a privileged scaffold in various fields of chemistry, including supramolecular chemistry [23], acting as photo stabilizer [24], liquid crystal [25], corrosion inhibitor [26], polymer [27], agrochemical [28], photo stabilizer [29], and ligand [30].

1,2,4-triazole derivatives also possess a wide range of biological activities, including anticonvulsant, anxiolytic (estazolam **13**), a broad spectrum of antifungal potential (posaconazole **14**) [31], antimigraine (rizatriptan **15**) [32], anticancer (anastrozole **16**) [33], antiplatelet (trapidil **17**) [34], and anticonvulsant (**18** lorecelezole) [35].

2. SYNTHETIC STRATEGIES

1,2,3-triazole moiety has been focused in intense research work due to its wide range of pharmaceutical potential. In the last three decades, many researchers have worked on the development of

*Address correspondence to these authors at the Department of Forensic Chemistry and Toxicology, Government Institute of Forensic Science, Aurangabad 431 004, (MS), India; E-mail: dsbhagat999@gmail.com; Department of Pharmaceutical Chemistry and Analysis, ISF College of Pharmacy, Moga 142001, Punjab, India; E-mail: pvchawla@gmail.com

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