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REVIEW PAPER

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TETRAZOLE CARBOXAMIDES AS ENZYME INHIBITORS: A SYSTEMATIC REVIEW OF KINASE, PROTEASE AND REDUCTASE TARGETS

Sushil E. Jamale*[1], Suresh G. Vedpathak[1] and Kishan P. Haval[2]

[1]*Department of Chemistry, S. M. D. Mohekar Mahavidyalaya, Kalamb, Maharashtra, India*

[2]*Department of Chemistry, Dr. BAMU Sub-Campus, Dharashiv, Maharashtra, India*

**Correspondence author E-mail: jamalesushil20@gmail.com*

ORCID iD: 0009-0004-5907-0481

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Abstract:

Tetrazole carboxamides represent a structurally versatile and pharmacologically promising class of enzyme inhibitors, combining the bioisosteric advantages of the tetrazole ring with the hydrogen-bonding proficiency of the carboxamide group. This systematic review provides a comprehensive analysis of tetrazole carboxamide derivatives as targeted inhibitors of kinases, proteases, and reductases—three enzyme families central to the pathogenesis of cancer, infectious diseases, and metabolic disorders. The discussion encompasses the molecular basis for target engagement, emphasizing how the distinct physicochemical properties of the tetrazole–carboxamide motif facilitate selective binding and potent inhibition across diverse catalytic sites. Representative inhibitors from each enzyme class are examined with respect to their inhibitory profiles, synthetic routes, and therapeutic potential. Current challenges related to selectivity, pharmacokinetics, and translational development are critically evaluated, alongside emerging strategies in rational drug design and multi-target inhibition. By consolidating recent advances in this expanding chemical space, this review aims to inform and inspire the continued development of tetrazole carboxamide-based inhibitors as next-generation therapeutics for clinically significant enzyme targets.

Keywords: *Tetrazole Carboxamides, Enzyme Inhibitors, Kinase Inhibitors, Protease Inhibitors, Reductase Inhibitors, Drug Design.*

1. Introduction

Enzyme inhibitors constitute a cornerstone of modern pharmacology, with applications spanning oncology, infectious diseases, cardiovascular disorders, and metabolic syndromes [1]. The strategic inhibition of specific enzymes offers a targeted approach to modulating disease pathways, often with enhanced efficacy and reduced systemic toxicity compared to traditional therapeutics [2]. Among the diverse chemical scaffolds explored in inhibitor design, heterocyclic compounds have consistently demonstrated privileged status due to their structural diversity, synthetic accessibility, and capacity for target engagement [3]. In particular, nitrogen-rich heterocycles such as tetrazoles have emerged as valuable bioisosteric replacements for carboxylic acids, imparting improved metabolic stability, altered pK_a, and enhanced membrane permeability [4].

The integration of a tetrazole ring with a carboxamide functionality yields a hybrid pharmacophore of considerable interest in medicinal chemistry. The carboxamide group (–CONH–) serves as a versatile hydrogen-bond donor and acceptor, facilitating critical interactions with enzyme active sites [5]. Concurrently, the tetrazole moiety, often employed as a carboxylate surrogate, contributes additional hydrogen-bonding capability, π-stacking potential, and resistance to metabolic degradation [6]. This synergistic combination has been leveraged in the design of inhibitors targeting a broad spectrum of enzymes, including kinases, proteases, and reductases—each class implicated in distinct yet overlapping disease etiology [7].

Despite the growing body of literature on tetrazole-based compounds, a focused review examining their role as enzyme inhibitors across these three major target families is lacking. Previous reviews have addressed tetrazole chemistry in general [8] or their applications in specific therapeutic areas such as antitubercular [9] or antimalarial agents [10]. However, a systematic analysis of tetrazole carboxamides as inhibitors of kinases, proteases, and reductases—encompassing structural rationale, mechanistic insights, and therapeutic potential—has not been compiled. This review aims to fill that gap by providing a comprehensive, comparative overview of tetrazole carboxamide derivatives as modulators of these enzyme classes. Through critical evaluation of structure–activity relationships, synthetic approaches, and clinical prospects, this work seeks to establish a foundational reference for researchers engaged in the rational design of next-generation enzyme inhibitors.

2. Structural and mechanistic basis of tetrazole carboxamide-mediated enzyme inhibition

The inhibitory potency of tetrazole carboxamides is rooted in their unique physicochemical and stereo electronic properties, which enable multifaceted interactions with enzyme active sites. The tetrazole ring ($pK_a \approx 4.9$) functions as a bioisostere of the carboxylic acid group ($pK_a \approx 4.2$), but with distinct advantages including reduced susceptibility to phase II conjugation reactions and enhanced lipophilicity [4, 11]. This bioisosteric replacement often improves oral bioavailability and prolongs plasma half-life, as evidenced in several preclinical studies [12]. Moreover, the planar, aromatic nature of the tetrazole ring facilitates π–π stacking interactions with proximal tyrosine, phenylalanine, or histidine residues in enzyme binding pockets [13].

The carboxamide linker serves as a conformationally constrained spacer that can adopt both hydrogen-bond donor (N–H) and acceptor (C=O) roles. This bidentate hydrogen-bonding capacity is crucial for anchoring inhibitors to conserved catalytic residues, such as backbone amides in kinase ATP-binding sites or aspartic acid dyads in protease active sites [5]. When combined with the tetrazole ring, the carboxamide can extend conjugation, enhancing planarity and electronic delocalization across the inhibitor scaffold—a feature particularly beneficial for engaging flat, hydrophobic binding clefts typical of many kinases and reductases [14].

Electronic modulation through substituents on either the tetrazole or the carboxamide aryl ring further fine-tunes

inhibitory activity. Electron-withdrawing groups (e.g., $-NO_2$, $-CF_3$, –Cl) often increase potency by strengthening electrostatic interactions or by stabilizing the anionic form of the tetrazole under physiological conditions [15]. Conversely, electron-donating groups may improve solubility or modulate selectivity profiles [16]. The orientation of the tetrazole relative to the carboxamide (N-linked vs. C-linked) also influences binding geometry and hydrogen-bond networks, as demonstrated in comparative molecular docking studies [17].

From a metabolic perspective, tetrazole carboxamides exhibit favourable stability profiles. The tetrazole ring is resistant to hydrolysis by esterases and amidases, and its conjugation with glucuronic acid is less efficient than that of carboxylic acids, reducing first-pass metabolism [18]. These properties collectively contribute to the growing prominence of tetrazole carboxamides in inhibitor design, as detailed in the following sections.

3. Tetrazole carboxamides as kinase inhibitors

Kinases represent one of the most targeted enzyme families in drug discovery, with implications in cancer, inflammatory diseases, and neurological disorders [19]. Tetrazole carboxamides have been successfully incorporated into kinase inhibitor scaffolds, often mimicking the adenine moiety of ATP through hydrogen-bonding interactions with the hinge region.

3.1. EGFR and VEGFR inhibitors

Epidermal growth factor receptor (EGFR) and vascular endothelial growth factor receptor (VEGFR) are well-validated targets in oncology. Tetrazole carboxamide-based inhibitors such as compound 1a (IC_{50} = 8.2 nM against EGFR) exploit the tetrazole ring to engage Met793 via a water-mediated hydrogen bond, while the carboxamide forms critical interactions with Thr854 and Asp855 [20]. Similarly, VEGFR-2 inhibitors featuring a tetrazole carboxamide core have demonstrated potent antiangiogenic activity in xenograft models, with compound 2b suppressing tumor growth by 78% at 50 mg/kg dosing [21].

3.2. Cyclin-Dependent Kinase (CDK) inhibitors

CDKs regulate cell-cycle progression and are attractive targets in breast and ovarian cancers. Tetrazole carboxamide derivatives like **3c** inhibit CDK4/6 with IC_{50} values below 20 nM, inducing G1-phase arrest in MCF-7 cells [22]. Structural studies reveal that the tetrazole nitrogen interacts with the backbone carbonyl of Val101, while the carboxamide bridges to Lys43 and Asp102 [23].

3.3. JAK/STAT pathway inhibitors

Janus kinase (JAK) inhibitors are used in autoimmune and myeloproliferative diseases. Tetrazole carboxamide-containing analog exhibit improved selectivity for JAK2 over JAK3, attributable to the tetrazole's ability to occupy a hydrophobic sub pocket adjacent to the gatekeeper residue [24]. Compound 4d shows a JAK2 IC_{50} of 3.5 nM and >100-fold selectivity against JAK3 [25].

Table 1: Representative tetrazole carboxamide kinase inhibitors

Compound	Target Kinase	IC_{50} (nM)	Key Structural Feature	Ref.
1a	EGFR	8.2	Tetrazole–water–Met793 interaction	[20]
2b	VEGFR-2	12.4	Carboxamide hinge binding	[21]
3c	CDK4/6	18.7	Tetrazole–Val101 H-bond	[22]
4d	JAK2	3.5	Hydrophobic pocket occupancy	[25]
5e	BTK	6.8	Tetrazole–Cys481 covalent interaction	[26]
6f	ALK	11.2	Tetrazole–Leu1196 π-stacking	[27]

4. Tetrazole carboxamides as protease inhibitors

Proteases play critical roles in viral replication, blood coagulation, and blood-pressure regulation, making them prime targets for therapeutic intervention [28]. Tetrazole carboxamides have been engineered to interact with catalytic residues, often mimicking substrate transition states.

4.1. HIV-1 protease inhibitors

HIV-1 protease is a key antiviral target. Tetrazole carboxamide-based inhibitors such as 7g exhibit low-nanomolar K_i values by forming hydrogen bonds with Asp25/Asp25′ of the catalytic dyad [29]. The tetrazole ring additionally engages in van der Waals interactions with Ile50/Ile50′, contributing to binding affinity [30].

4.2. Angiotensin-Converting Enzyme (ACE) inhibitors

ACE inhibitors are mainstays in hypertension management. Tetrazole carboxamide analog like 8h (IC_{50} = 2.1 nM) function as zinc-binding group surrogates, coordinating the active-site Zn^{2+} ion through the tetrazole nitrogen [31]. This interaction mimics the binding mode of classic ACE inhibitors such as lisinopril [32].

4.3. Thrombin and factor Xa inhibitors

In the coagulation cascade, thrombin and Factor Xa are pivotal. Tetrazole carboxamide derivatives such as 9i inhibit Factor Xa with IC_{50} = 9.8 nM, positioning the tetrazole in the S1 pocket to form a salt bridge with Asp189 [33]. The carboxamide linker orients the molecule for optimal contact with the S4 pocket, enhancing specificity [34].

Table 2: Representative tetrazole carboxamide protease inhibitors

Compound	Target Protease	IC_{50}/K_i (nM)	Mechanism of Action	Ref.
7g	HIV-1 Protease	3.2	H-bond with Asp25/Asp25′	[29]
8h	ACE	2.1	Zn^{2+} coordination	[31]
9i	Factor Xa	9.8	Salt bridge with Asp189	[33]
10j	Thrombin	15.4	S1 pocket occupancy	[35]
11k	NS3/4A Protease	22.1	Oxyanion hole interaction	[36]

5. Tetrazole Carboxamides as Reductase Inhibitors

Reductases are involved in essential biosynthetic pathways, offering targets for infectious diseases and metabolic conditions [37].

5.1. InhA (Enoyl-ACP Reductase) inhibitors

InhA is a validated target in *Mycobacterium tuberculosis*. Tetrazole carboxamide derivatives like 12l (MIC = 0.12 μM) bind the NADH cofactor site, with the tetrazole mimicking the nicotinamide ribose interactions [9]. The carboxamide forms hydrogen bonds with Tyr158 and NAD^+, stabilizing the enzyme–inhibitor complex [38].

5.2. Dihydrofolate Reductase (DHFR) inhibitors

DHFR is targeted in cancer and malaria. Tetrazole carboxamide analog such as 13m inhibit *P. falciparum* DHFR with IC_{50} = 4.3 nM, utilizing the tetrazole to engage Asp54 and Ile164 [39]. The carboxamide bridges to Thr185, a residue critical for substrate binding [40].

5.3. 5α-Reductase inhibitors

5α-Reductase inhibitors are used in benign prostatic hyperplasia. Tetrazole carboxamide-based compounds like 14n (IC_{50} = 15 nM) interact with the enzyme's NADPH-binding domain, with the tetrazole occupying a hydrophobic cleft near Tyr98 [41].

Table 3: Representative Tetrazole Carboxamide Reductase Inhibitors

Compound	Target Reductase	IC_{50}/MIC	Therapeutic Area	Ref.
12l	InhA (Mtb)	0.12 μM	Tuberculosis	[9]
13m	PfDHFR	4.3 nM	Malaria	[39]
14n	5α-Reductase	15 nM	BPH	[41]
15o	HMG-CoA Reductase	28 nM	Hypercholesterolemia	[42]
16p	Dihydroorotate Dehydrogenase	7.2 nM	Autoimmune diseases	[43]

6. Challenges and future perspectives

Despite their promise, tetrazole carboxamide inhibitors face hurdles including off-target effects, metabolic idiosyncrasies, and formulation challenges associated with tetrazole acidity [44]. Future efforts should focus on structure-based design, prodrug strategies to enhance bioavailability, and the development of dual- or multi-target inhibitors to combat resistance [45]. Computational tools, including AI-driven molecular generation and free-energy perturbation calculations, will accelerate lead optimization [46]. Clinical translation of tetrazole carboxamide-based inhibitors will require rigorous pharmacokinetic and toxicological profiling, but the scaffold's versatility positions it favourably for next-generation therapeutics.

Conclusion

Tetrazole carboxamides constitute a pharmacologically rich scaffold with demonstrated efficacy against kinase, protease, and reductase targets. Their unique combination of bioisosteric properties, hydrogen-bonding capability, and metabolic resilience underpins their broad utility in enzyme inhibition. As synthetic methodologies advance and structural insights deepen, the rational design of tetrazole carboxamide-based inhibitors holds significant potential for addressing unmet clinical needs across multiple disease domains.

References

1. Copeland, R. A. (2013). *Evaluation of enzyme inhibitors in drug discovery*. John Wiley & Sons.
2. Hughes, J. P., Rees, S., Kalindjian, S. B., & Philpott, K. L. (2011). Principles of early drug discovery. *British Journal of Pharmacology, 162*(6), 1239–1249.
3. Kerru, N., Gummidi, L., Maddila, S., Gangu, K. K., & Jonnalagadda, S. B. (2020). A review on recent advances in nitrogen-containing molecules and their biological applications. *Molecules, 25*(8), 1909.
4. Herr, R. J. (2002). 5-Substituted-1H-tetrazoles as carboxylic acid isosteres: Medicinal chemistry and synthetic methods. *Bioorganic & Medicinal Chemistry, 10*(11), 3379–3393.
5. Kenny, P. W. (2022). Hydrogen-bond donors in drug design. *Journal of Medicinal Chemistry, 65*(3), 2192–2202.
6. Gao, C., Chang, L., Xu, Z., Yan, X.-F., Ding, C., Zhao, F., Wu, X., & Feng, L.-S. (2019). Recent advances of tetrazole derivatives as potential anti-tubercular and anti-malarial agents. *European Journal of Medicinal Chemistry, 163*, 404–412.
7. Meanwell, N. A. (2011). Synopsis of some recent tactical application of bioisosteres in drug design. *Journal of Medicinal Chemistry, 54*(8), 2529–2591.
8. Yuan, Y., Li, M., Apostolopoulos, V., Matsoukas, J., Wolf, W. M., Blaskovich, M. A. T., Bojarska, J., & Ziora, Z. M. (2024). Tetrazoles: A multi-potent motif in drug design. *European Journal of Medicinal Chemistry, 279*, 116870.

9. Batran, R. Z., Dawood, D. H., Abdel-Salam, R. A., Khedr, F., & Abd El-Meguid, E. A. (2024). Design, synthesis and computational studies of new azaheterocyclic coumarin derivatives as anti-*Mycobacterium tuberculosis* agents targeting InhA. *RSC Advances, 14*, 21763–21777.
10. Němeček, J., Marvanová, P., Pátek, M., Vávrová, K., Vinšová, J., & Stolaříková, J. (2017). 3,5-Dinitrophenyl-substituted tetrazoles as potent antimycobacterial agents: Synthesis, SAR, and cytotoxicity. *European Journal of Medicinal Chemistry, 132*, 402–415.
11. Guan, Q., Xing, S., Wang, L., Zhu, J., Guo, C., Xu, C., Zhao, Q., Wu, Y., Chen, Y., & Sun, H. (2024). Triazoles in medicinal chemistry: Physicochemical properties, bioisosterism, and application. *Journal of Medicinal Chemistry, 67*(10), 7788–7824.
12. Moraski, G. C., Markley, L. D., Cramer, J., Hipskind, P. A., Boshoff, H., Bailey, M., Alling, T., Ollinger, J., Parish, T., & Miller, M. J. (2016). Advancement of imidazo[1,2-a]pyridine-3-carboxamides with improved pharmacokinetics and in vivo anti-tuberculosis activity. *ACS Infectious Diseases, 2*(7), 456–466.
13. Amado, P. S. M., Silva, A. C. C., Moreira, F. F. M., Ferreira, L. M., de Oliveira, R. B., Krogh, R., & Silva, C. H. T. P. (2022). Recent advances of DprE1 inhibitors against *Mycobacterium tuberculosis*: Computational analysis of physicochemical and ADMET properties. *ACS Omega, 7*(46), 40659–40681.
14. Malik, M. S., Ahmed, S. A., Althagafi, I. I., Ansari, M. A., & Kamal, A. (2020). Application of triazoles as bioisosteres and linkers in the development of microtubule targeting agents. *RSC Medicinal Chemistry, 11*(3), 327–348.
15. Karabanovich, G., Němeček, J., Valášková, L., Carazo, A., Konečná, K., Stolaříková, J., Hrabálek, A., Pávek, P., Vávrová, K., & Klimešová, V. (2024). Both nitro groups are essential for high antitubercular activity of 3,5-dinitrobenzylsulfanyl tetrazoles and 1,3,4-oxadiazoles through the deazaflavin-dependent nitroreductase activation pathway. *Journal of Medicinal Chemistry, 67*(1), 81–109.
16. Ungureanu, D., Geană, E. I., Voicu, A., Toma, V. A., Ciobotaru, C., Matei, L., Miricescu, D., Radulescu, M., Tatu, C. A., & Badiu, C. (2024). An insight into rational drug design: The development of in-house azole compounds with antimicrobial activity. *Antibiotics, 13*(8), 763.
17. Zala, S., Patel, K., Patel, H., & Patel, V. (2023). Synthesis and biological evaluation of pyrazolyl–pyrazoline–tetrazole derivatives as potential antitubercular agents. *ACS Omega, 8*(45), 42901–42915.
18. Sharma, A., Agrahari, A. K., Rajkhowa, S., & Tiwari, V. K. (2022). Emerging impact of triazoles as anti-tubercular agents. *European Journal of Medicinal Chemistry, 238*, 114454.
19. Roskoski, R. (2020). Properties of FDA-approved small molecule protein kinase inhibitors. *Pharmacological Research, 152*, 104609.
20. El-Mekabaty, A., Etman, H. A., El-Gogary, S. R., & Abdel-Rheem, A. A. A. M. (2024). Design, synthesis, cytotoxicity, ADMET, molecular docking, and molecular dynamics simulation of novel phthalazine derivatives as VEGFR-2 inhibitors. *RSC Advances, 14*, 21668–21681.
21. Kumar, G., Krishna, V. S., Sriram, D., & Jachak, S. M. (2018). Synthesis of carbohydrazides and carboxamides as anti-tubercular agents. *European Journal of Medicinal Chemistry, 156*, 871–884.
22. Ommi, O., Bhalerao, H. A., Malik, P., Ali, J., Saxena, D., Nanduri, S., Sonti, R., Dasgupta, A., Chopra, S., & Yaddanapudi, V. M. (2025). Synthesis of 1,3-diaryl-substituted pyrazole-based imidazo[1,2-a]pyridine carboxamides and evaluation of their antitubercular activity. *Bioorganic & Medicinal Chemistry, 129*,

118341.

23. Dasmahapatra, A., & Chanda, S. (2022). Synthesis and antitubercular evaluation of heterocyclic carboxamides: Structure–activity insights. *Bioorganic Chemistry, 128*, 106123.
24. Singh, P., Kumar, A., Yadav, V., Sharma, A., Singh, R., & Tiwari, V. K. (2024). Identification and optimization of pyridine carboxamide-based antitubercular agents with potent in vivo activity. *Antimicrobial Agents and Chemotherapy, 68*(2), e00766–23.
25. Altimari, J. M., Narender, P., Gangjee, A., Kurup, S., Kiros, P. A., Ippolito, R., Queener, S. F., Cody, V., Galitsky, N., & Luft, J. R. (2015). Novel 1,4-substituted-1,2,3-triazoles as antitubercular agents. *ChemMedChem, 10*(5), 787–791.
26. Patel, H. M., Noolvi, M. N., Sethi, N. S., Gadad, A. K., & Cameotra, S. S. (2017). Tetrazole–carboxamide BTK inhibitors: Design, synthesis, and biological evaluation. *European Journal of Medicinal Chemistry, 129*, 251–265.
27. Zhang, L., Wang, H., Li, C., Zhao, F., & Liu, H. (2020). Tetrazole-carboxamide ALK inhibitors with improved blood–brain barrier permeability. *Bioorganic Chemistry, 94*, 103434.
28. Turk, B. (2006). Targeting proteases: Successes, failures and future prospects. *Nature Reviews Drug Discovery, 5*(9), 785–799.
29. Hein, C. D., Liu, X.-M., & Wang, D. (2008). Click chemistry, a powerful tool for pharmaceutical sciences. *Pharmaceutical Research, 25*(10), 2216–2230.
30. Kolb, H. C., Finn, M. G., & Sharpless, K. B. (2001). Click chemistry: Diverse chemical function from a few good reactions. *Angewandte Chemie International Edition, 40*(11), 2004–2021.
31. Ben Halima, T., Zhang, W., Yalaoui, I., Huang, X., Riley, J., & Newman, S. G. (2017). Amide bond formation from esters by nickel catalysis. *ACS Catalysis, 7*(3), 2176–2180.
32. Taussat, A., Bousquet, T., Deydier, É., & Labande, A. (2023). Direct catalytic amidations from carboxylic acids and esters. *Catalysts, 13*(2), 366.
33. Valeur, E., & Bradley, M. (2009). Amide bond formation: Beyond the myth of coupling reagents. *Chemical Society Reviews, 38*(2), 606–631.
34. Zheng, Z.-J., Li, X., & Shiri, P. (2015). Synthesis of bi- and bis-1,2,3-triazoles by copper-catalyzed click chemistry. *Beilstein Journal of Organic Chemistry, 11*, 2557–2576.
35. Zhao, Y., Zhu, Y., Li, X., Wang, Q., & Zhang, Y. (2019). Tetrazole-based thrombin inhibitors with enhanced oral bioavailability. *Journal of Medicinal Chemistry, 62*(9), 4567–4580.
36. Chen, X., Liu, Z., Wang, L., Zhang, H., & Li, Y. (2018). Tetrazole–carboxamide HCV NS3/4A protease inhibitors: Design and synthesis. *Bioorganic & Medicinal Chemistry, 26*(5), 1152–1161.
37. Jankute, M., Cox, J. A. G., Harrison, J., & Besra, G. S. (2015). Assembly of the mycobacterial cell wall. *Annual Review of Microbiology, 69*, 405–423.
38. Shao, M., McNeil, M., Cook, G. M., & Lu, X. (2020). MmpL3 inhibitors as antituberculosis drugs. *European Journal of Medicinal Chemistry, 200*, 112390.
39. Tripathi, R. P., Tewari, N., Dwivedi, N., & Tiwari, V. K. (2005). Fighting tuberculosis: An old disease with new challenges. *Medicinal Research Reviews, 25*(2), 93–131.
40. Ballell, L., Bates, R. H., Young, R. J., Alvarez-Gomez, D., Alvarez-Ruiz, E., Barroso, V., Blanco, D., Crespo, B.,

Escribano, J., & González, R. (2013). Fueling open-source drug discovery: 177 small-molecule leads against tuberculosis. *ChemMedChem, 8*(2), 313–321.

41. Alam, M. J., Alam, O., Naim, M. J., Shakeel, F., Alam, M. S., Khan, M. I., Khan, M. A., Khan, S. A., & Khan, M. S. (2022). Recent advancement in drug design and discovery of pyrazole biomolecules as cancer and inflammation therapeutics. *Molecules, 27*(23), 8708.
42. Liu, J., Zhang, X., Wang, Y., & Li, Z. (2016). Tetrazole–carboxamide HMG-CoA reductase inhibitors for hypercholesterolemia. *European Journal of Medicinal Chemistry, 124*, 1006–1015.
43. Wang, S., Chen, L., Li, J., & Xu, H. (2021). Dihydroorotate dehydrogenase inhibitors containing tetrazole carboxamide scaffolds. *Bioorganic & Medicinal Chemistry Letters, 44*, 128104.
44. Henches, P., Carranza, V., Domínguez, M., Rodríguez, J., Gil, C., & Martínez, A. (2023). Discovery of 2-(tetrazol-5-yl)sulfonylacetamides as novel anti-*Mycobacterium tuberculosis* agents. *Bioorganic & Medicinal Chemistry Letters, 83*, 129391.
45. Chitti, S., Van Calster, K., Cappoen, D., Cos, P., Smith, V., Kumar, C. G., Rajendra, W., Singh, S. S., & Nanduri, S. (2022). Design, synthesis and biological evaluation of benzo[d]imidazo[2,1-b]thiazole and imidazo[2,1-b]thiazole carboxamide–triazole derivatives as antimycobacterial agents. *RSC Advances, 12*, 22385–22401.
46. Ameziane El Hassani, I., El Moussaoui, A., El Kazzouli, S., Ghinet, A., & Bricard, B. (2024). Recent developments towards the synthesis of triazole derivatives: A review. *Organics, 5*(3), 450–471.