Abstract: Triazoles act as important pharmacophores in showing biological activity such as antibacterial, antifungal, antitumour/anticancer, anti-inflammatory activities. Literature review suggests that triazoles have been maximally used in carrying research related activities in reference to biological evaluation as compared to other nitrogen containing five membered heterocycles like tetrazoles, pentazoles, pyrazoles, and imidazoles. The first compound of this class was discovered by Janseen Group in 1960s. The microbes act counteractively towards antibiotics which in turn challenge the efficacy of the drugs and thus create room for the progression of more potent avant-garde drugs. Thus, the synthesis of hybrid molecules has been accelerated from last two decades as the hybrids possess more potency, vigour, and adequacy than its constituting pharmacophores. So, this review represents a condensed report of the research carried out in relation to synthetical procedures and assessment of the antibacterial and antifungal activity of triazoles.

Keywords: triazoles, antibacterial, antifungal, antioxidant, anti-inflammatory, anticonvulsant, hybrids

1 Introduction

Heterocyclic organic chemistry is among the most prominent branches of medicinal chemistry. Heterocyclic compounds can be of different types depending upon the heteroatom (atom other than carbon) it contains which can be oxygen, sulphur, nitrogen, and others. As per the statistics, above 85% of biologically effective molecules possess a heterocycle [1]. Scientists on daily basis isolate various heterocyclic compounds and study them for drug discovery. More than 70% of the drugs used today have heterocycle in them, and out of it, more than 60% drugs have nitrogen in their scaffold [2]. The Scopus database reports suggest that the most frequently studied 5-membered heterocycles in medicinal chemistry are triazoles, particularly 1,2,3-triazoles [3]. The annual report of GARDP 2022 suggests that drug resistant microbes are causing death of 1.3 billion people every year. The main reason of this drug resistance is that bacteria form biofilms against the antibiotics [4]. So, the process of development of new more potent drug is an incessant process and one of the most propitious accessions to this target is achievable through the molecular hybridisation approach [5,6].

1.1 Properties of triazoles

Triazoles are the 5-segment heterocycles comprising two C atoms, three N atoms, and two double bonds [7]. The two isomeric forms of this molecule are 1,2,3-triazole and 1,2,4-triazole depending upon the position of nitrogen [8]. 1,2,3-triazole (Figure 1) exist in the form of colourless, hygroscopic crystals with melting point (m.p.) 24°C and boiling point (b.p.) 209°C and 1,2,4-triazole (Figure 2) exist in the form of water-soluble colourless crystals with m.p. 121°C and b.p. 260°C [9]. These compounds show exciting features like good solubility and effective H-bonding and π-stacking [10]. Extensive literature is available which proves that triazoles are favourable scaffolds in the genre of medicinal chemistry in virtue of their therapeutic activity such as anti-inflammatory, antioxidant, antibacterial, antitumour, antifungal, antiviral, antitubercular and antidepressant [11].

2 Most commonly adopted synthetic strategies of action adopted for the formation of 1,2,3-triazoles

Some of the common methodical procedures involving the formation of 1,2,3-triazole nucleus are copper catalysed azide-alkyne cycloaddition (CuAAC), ruthenium catalysed azide-alkyne cycloaddition RuAAC, and Huisgen azide-alkyne 1,3-dipolar cycloaddition.
a) **CuAAC** – Himo et al. contended that the reactants (azide, alkyne) undergo addition in cyclic form catalysed by copper forming a part of “Click Chemistry” [12].

**Proposed catalytic cycle** – Worrell et al. illustrated the mechanistic representation of desired derivative catalysed by Cu. Alkyne collaborates with Cu forming a $\pi$-complex. Azide then comes into play and upon interacting with the $\pi$-complex, forms a $\sigma$-complex. Cu is ejected forming the desired derivative [13].

![Scheme 1: Designing of 1,2,3-triazole nucleus under balmy conditions.](image)

b) **RuAAC** – Boren et al. contended that azide and alkyne undergo addition in cyclic form catalysed by Ruthenium [14].

**Proposed catalytic cycle** – Azide interacts with alkyne in the presence of ruthenium catalyst via 1,3-dipolar mechanism to form $\pi$-complex which then rearranges to form $\sigma$-complex. Latter ejects ruthenium catalyst to generate the desired derivative of triazole.
c) 

**Huisgen azide-alkyne 1,3-dipolar cycloaddition** – Kalyani Keerthi (2020) synthesised triazole moiety from azide and alkyne which undergo Huisgen cycloaddition regioselectively [15].

**Proposed catalytic cycle** – Reactants undergo 2s + 4s cycloaddition which is akin to Diels–Alder reaction. The following representation shows the mechanism of above reaction.

As we all know that time is a preeminent asset in the research, so the methods which involve less consumption of time are worthy of adoption while performing the research. There are two types of approach of synthesis - Green methodical approach of synthesis and Conventional approach of synthesis. Some **Green approaches** of synthesis are as follows:

1. Moorhouse and Moses (2008) initiated a microwave irradiated process of formation of substituted product and azides are derived via one-pot azidation reaction of amines [16].

2. Nasrollahzadeh et al. adopted a clean and green method of synthesis of the molecule under consideration substituted at first as well as fourth position with the use of copper nanoparticles (NPs). The conditions are mild, and Cu NPs act as heterogenous catalyst and is obtained from the leaves of *Otostegia persica* [17].

3. Boominathan et al. adopted a new green method to synthesise 1,2,3-triazole derivatives. A base of TiO2 supported Au NPs is formed which is mixed with ethyl propiolate, phenylacylazide, and water and then heated on a water bath for 20–30 min to get our desired product [18].

4. Singh et al. evolved a green method which takes only 2 min to synthesise 1,2,3-triazole derivatives employing microwave irradiation and 1,8-Diazabicyclo[5.4.0]undec-7-ene (DBU)-water catalyst at room temperature. The catalytic exercise of DBU increases substantially in water [19].

Some synthetic procedures used for the formation of triazoles which take time of less than 3 h to complete are listed as under.

1. Shu et al. proposed that N-tosylhydrazones undergo coupling cyclisation reaction with sodium azide mediated by molecular iodine to form 1,2,3-triazole nucleus [20].

2. Huang et al. proposed that 1-aminopyridinium iodide, methyl ketone, and *p*-toluenesulfonyl hydrazine undergo [2 + 2 + 1] cyclisation mediated by iodine to form 1,2,3-
triazole nucleus held down by the case of azide-free and metal-free plight [21].

3. Quan et al. proposed that nitroolefins and sodium azide undergo 1,3-dipolar cycloaddition reaction mediated by p-TsOH which results in the rapid fabrication of the desired molecule in good yield [22].

4. Yamada et al. proposed that the catalyst exhibited in the picture enables the effective cycloaddition of alkynes and azides to provide excellent yield of product [23].

5. Shao et al. proposed a synthesis which is a Cu catalysed azide alkyne cycloaddition promoted jointly by acid-base with crisp reaction time [24].

6. Liu et al. recommended that the substituted triazole nucleus is formed by cycloaddition of alkyne and azide using Grignard Reagent [25].

7. Kim et al. suggested that this method is applicable to both aliphatic and aromatic substrates and 1,2,3-triazoles are synthesised in aqueous and ambient conditions [26].

8. Khalili et al. proposed the cyclisation of non-terminal alkynes/terminal alkynes and azide using CuAl₂O₄ nanoparticles in less time under aqueous conditions [27].

9. Ferrini et al. proposed a ruthenium catalysed cycloaddition synthesis. Reaction of aryl/alkyl azides along with

---

**Scheme 6:** Formation of 1,2,3-triazole nucleus using Au NPs.

**Scheme 7:** Formation of 1,2,3-triazole using DBU-water catalyst and microwave radiations.

**Scheme 8:** Formation of 1,2,3-triazole using DMSO, iodine, and methane sulfonic acid.

**Scheme 9:** Formation of 1,2,3-triazole using DMSO and iodine.

**Scheme 10:** Formation of 1,2,3-triazole nucleus using DMF and p-toluene sulfonic acid.

**Scheme 11:** Formation of desired nucleus using sodium nitride, sodium ascorbate, water, butanol, and catalyst.

**Scheme 12:** Formation of 1,2,3-triazole using acid and base.
N-Boc-arylamide is regioselective reaction and with N-Boc-alkylamide, formation of mixture of regioisomers takes place [28].

10. Cheng et al. suggested a solitary vessel fabrication of disubstituted 1,2,3-triazoles at first as well as fourth position [29].

11. Vadivelu et al. adopted a method of selective formation of the befitting molecule having −NO₂ substitution at its fourth position. The method executes the synthesis of

Scheme 13: Formation of 1,2,3-triazole using Grignard reagent, Phenyl nitride, THF, and NH₄Cl.

Scheme 14: Formation of 1,2,3-triazole using aqueous caesium carbonate.

Scheme 15: Synthesis of 1,2,3-triazole using Nanoparticles.

Scheme 16: Formation of 1,2,3-triazole employing ruthenium catalyst.

Scheme 17: Formation of 1,2,3-triazole having copper iodide, sodium ascorbate, DBU, and DMSO in the vessel.

Scheme 18: Formation of 1,2,3-triazole using ball milling method.
product in soaring yield, forming non-toxic by-product
and the catalyst is recyclable and non-toxic [30].
2.1 Synthetic strategies of action for designing 1,2,4-triazoles

Some Green approaches of synthesis are as follows:

1. Venigalla et al. designed an innovative and productive method to synthesise 1,2,4-triazole derivatives with magnificent yield in which hydrazine carboxamide reacts with the substituted benzaldehyde in one pot containing ethanol as a solvent. This pot is treated with ultrasonic waves at room temperature. This method does not need any catalyst. The product is formed in less than 6 min [31].

2. Shelke et al. planned a method which involves microwave irradiated formation of 1,2,4-triazole using hydrazines and formamide, which does not require any catalyst [32].

3. Nakka et al. planned an environmentally congenial methodical procedure used in the designing of 3,4,5-trisubstituted-1,2,4-triazoles using PEG (which is recyclable) and ceric ammonium nitrate as a catalyst. This method is a commercially feasible method [33].

4. Jatangi et al. steered an environmentally congenial and beneficial approach used in the formation of substituted nucleus. It is mediated by iodine under mild conditions. This method illustrates great substrate endurance [34].

Some conventional methods which take less than 3 h are listed below: (Tables 1 and 2)

1. Tseng et al. designed a method that enables the formation of 1,3,5-trisubstituted product in good harvest by virtue of 1,3-dipolar cycloaddition [35].

2. Ma et al. proposed a method that enables a regiospecific synthesis of broad range of aryl and cyano substituted

### Table 1: Detailed comparative analysis of all the schemes mentioned above

<table>
<thead>
<tr>
<th>Scheme</th>
<th>Yield (%)</th>
<th>Benefit</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Scheme 1</td>
<td>84–94</td>
<td>Conducive and decent procedure</td>
<td>[12]</td>
</tr>
<tr>
<td>Scheme 2</td>
<td>75–93</td>
<td>Entire utilisation of starting materials procuring of regioselectivity</td>
<td>[14]</td>
</tr>
<tr>
<td>Scheme 3</td>
<td>94–99</td>
<td>Smooth product segregation stereospecific product</td>
<td>[15]</td>
</tr>
<tr>
<td>Scheme 4</td>
<td>80–99</td>
<td>MW radiations substantially augment the rate of reaction</td>
<td>[16]</td>
</tr>
<tr>
<td>Scheme 5</td>
<td>86–93</td>
<td>Budgetary, harmless, and efficacious procedure</td>
<td>[17]</td>
</tr>
<tr>
<td>Scheme 6</td>
<td>86–97</td>
<td>NPs lift up the rate of reaction, regiosomer formation is accomplished</td>
<td>[18]</td>
</tr>
<tr>
<td>Scheme 7</td>
<td>82–94</td>
<td>Magnificent salvageable reaction medium</td>
<td>[19]</td>
</tr>
<tr>
<td>Scheme 8</td>
<td>46–85</td>
<td>Metal-free blueprint, swift procedure</td>
<td>[20]</td>
</tr>
<tr>
<td>Scheme 9</td>
<td>69</td>
<td>Contribution pointing to pragmatic and rational approach to preclude IDO</td>
<td>[21]</td>
</tr>
<tr>
<td>Scheme 10</td>
<td>63–96</td>
<td>Correspondent to infamous 1,3-dipolar cycloaddition</td>
<td>[22]</td>
</tr>
<tr>
<td>Scheme 11</td>
<td>94–99</td>
<td>Efficacious catalyst</td>
<td>[23]</td>
</tr>
<tr>
<td>Scheme 12</td>
<td>90–98</td>
<td>Benign for usage in non-aqueous solvents</td>
<td>[24]</td>
</tr>
<tr>
<td>Scheme 13</td>
<td>58–83</td>
<td>Tepid conditions, regioselective product</td>
<td>[25]</td>
</tr>
<tr>
<td>Scheme 14</td>
<td>89</td>
<td>Viably smooth, reaction advances in aqueous and non-aqueous solvents at room temperature</td>
<td>[26]</td>
</tr>
<tr>
<td>Scheme 15</td>
<td>79–96</td>
<td>Reducing agent is not requisite, segregation of catalyst by plain filtration</td>
<td>[27]</td>
</tr>
<tr>
<td>Scheme 16</td>
<td>79–90</td>
<td>Regiocontrolled product</td>
<td>[28]</td>
</tr>
<tr>
<td>Scheme 17</td>
<td>73–86</td>
<td>Uncomplicated method, effortlessly accessible substrates</td>
<td>[29]</td>
</tr>
<tr>
<td>Scheme 18</td>
<td>77–98</td>
<td>Non-lethal by-products, detainment of −NO₂ group</td>
<td>[30]</td>
</tr>
<tr>
<td>Scheme 19</td>
<td>94–98</td>
<td>Crisp reaction time, green procedure</td>
<td>[31]</td>
</tr>
<tr>
<td>Scheme 20</td>
<td>54–81</td>
<td>Single pot synthesis, nominal side reactions</td>
<td>[32]</td>
</tr>
<tr>
<td>Scheme 21</td>
<td>88–96</td>
<td>Crisp reaction time, ambient conditions</td>
<td>[33]</td>
</tr>
<tr>
<td>Scheme 22</td>
<td>82–92</td>
<td>Reaction assuages the concern of green chemistry</td>
<td>[34]</td>
</tr>
<tr>
<td>Scheme 23</td>
<td>53–91</td>
<td>Method is adapted for distinct aldehydes</td>
<td>[35]</td>
</tr>
<tr>
<td>Scheme 24</td>
<td>40–84</td>
<td>Tepid reaction conditions</td>
<td>[36]</td>
</tr>
<tr>
<td>Scheme 25</td>
<td>90–91</td>
<td>Competent and diverse synthesis</td>
<td>[37]</td>
</tr>
<tr>
<td>Scheme 26</td>
<td>62–88</td>
<td>Secure and ascendible synthesis</td>
<td>[38]</td>
</tr>
<tr>
<td>Scheme 27</td>
<td>81–85</td>
<td>Judicious and productive synthesis</td>
<td>[39]</td>
</tr>
</tbody>
</table>
product using a 3-component Cu enables \([3 + 2]\) annulation reaction [36].

3. Zhao et al. planned a method that gives access to the formation of disubstituted nucleus in good yield under tepid conditions [37].

4. Wong et al. designed a method in which 1,3,4-oxadiazolium hexafluorophosphate salt reacts with cyanamide to form desired product in satisfactory yield [38].

5. Bechara et al. planned the activation of triflic anhydride trailed by cyclodehydration induced by microwave irradiation. It forms the basis of single canister formation of 3,4,5-trisubstituted-1,2,4-triazoles [39].

3 Laboratory tests used to test antimycobacterial activity

Microbial resistance is augmenting per diem which urges the progression of more efficient antimicrobial drugs. The methods generally used for testing the activity are disk diffusion method, agar or broth dilution, cross streak, poisoned food technique, flow cytfluorometric test, time-kill test, ATP bioluminescence assay, and antimicrobial gradient method [48].

Minimum inhibitory concentration (MIC) values are compared with the reference standards. More the MIC

<table>
<thead>
<tr>
<th>S. No.</th>
<th>Name of drug</th>
<th>Structure</th>
<th>Activity</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Tazobactam [40]</td>
<td><img src="image1.png" alt="Structure" /></td>
<td>Antibacterial</td>
</tr>
<tr>
<td>2.</td>
<td>Fluconazole [41]</td>
<td><img src="image2.png" alt="Structure" /></td>
<td>Antifungal</td>
</tr>
<tr>
<td>3.</td>
<td>Ravuconazole [42]</td>
<td><img src="image3.png" alt="Structure" /></td>
<td>Antifungal</td>
</tr>
<tr>
<td>4.</td>
<td>Ceftrizine [43]</td>
<td><img src="image4.png" alt="Structure" /></td>
<td>Antibacterial</td>
</tr>
<tr>
<td>5.</td>
<td>Itraconazole [44]</td>
<td><img src="image5.png" alt="Structure" /></td>
<td>Antifungal</td>
</tr>
<tr>
<td>6.</td>
<td>Posaconazole [45]</td>
<td><img src="image6.png" alt="Structure" /></td>
<td>Antifungal</td>
</tr>
<tr>
<td>7.</td>
<td>Voriconazole [46]</td>
<td><img src="image7.png" alt="Structure" /></td>
<td>Antifungal</td>
</tr>
<tr>
<td>8.</td>
<td>I-A09 (under clinical evaluation) [47]</td>
<td><img src="image8.png" alt="Structure" /></td>
<td>Antitubercular</td>
</tr>
</tbody>
</table>
value, the less effective the drug is and lesser the MIC value, the more effective the drug is.

4 Literature review

This work reviews various pharmacological activities shown by triazoles.

4.1 Antimycobacterial activity

Patel et al. synthesised a parent moiety in which benzothiazole ring was clubbed with 1,2,4-triazole (both separately have antimicrobial properties) and studied their antimicrobial activity using microdilution method. Analogues carrying halogen, nitro, and methyl group as substituents acted as promising antibacterial agents and antifungal activity is shown promisingly by analogues having methyl substituent. Compounds showing promising antibacterial activity showed comparable antitubercular activity too. One compound (Compound 1) having Cl at fourth position shows better antitubercular activity out of all the synthesised compounds [49]. Figure 3 shows the pictorial representation.

Singh and Kumar Singh (2010) synthesised 1, 2, 4- triazole (substituted with aryl and pyridyl groups at fourth and fifth positions, respectively) molecules and studied their bactericidal activity. Desired compounds are formed with 70–85% yield. Significant bactericidal activity is shown by the newly formed compounds (Compounds 2a, 2b, and 2c). TLC was used to check the purity of the formed compounds [50]. Figure 4 shows the pictorial representation.

Patil et al. synthesised compounds shown in Figure 5 and tested the compounds for antibacterial and antifungal activity. Satisfactory yields were obtained. MIC of targeted compounds was compared with reference standards, and it was established that synthesised compounds (Compounds 3a and 3b) exhibited poor antifungal activity but significant antibacterial activity against the strains mentioned above [51].

Zhang et al. synthesised propionates and acetates and studied their antifungal activity using mycelial growth rate method. Benzimidazole and 1,2,4-triazole moieties have been found to hog antifungal and antibacterial activities. Targeted compounds were found to be more operative against B. cinerea than S. sclerotiorum when compared with EC50 Values of Carbendazim. No significant difference in EC50 values of acetates (4a) and propionates (4b) was found when compared, which means both class of compounds (4a and 4b) showed similar fungicidal activity [52]. Figure 6 shows the pictorial representation.
Ouahrouch et al. contended that the targeted compounds were synthesised using Cu-AAC reaction with the assistance of microwave radiations. Kremsner and Kappe noted that various organic synthesis could be performed efficiently by irradiating the substrates with microwaves [53]. Antifungal activity was studied against phytopathogenic fungi *Fusarium oxysporum* (Fo) and *Verticillium dahliae* (VD). Standard antibacterial drugs used for comparison were Ciprofl oxacin and Linezolid and positive control used for comparing antifungal activity was PELT (a fungicide which is a precursor of benzimidazole having 70% of methyl thiophanate). MICs were tested for the targeted compounds, and all showed less antibacterial activity than the standard drugs. All the title compounds (5a–h) except a compound carrying CF$_3$ group showed less antifungal activity and the reason might be attributed to the good lipophilicity of CF$_3$ group which might increase absorption and thus enhanced its activity [54]. Figure 7 and Chart 1 shows the synthesised compounds and their activity.

Shi & Zhou synthesised triazole derivatives of coumarin by clubbing 1,2,4-triazolyl ring with coumarin in order to increase their efficiency against microbes and two-fold serial dilution technique was adopted to gauge antimicrobial activity. Antibacterial and antifungal activity were shown more promisingly by coumarin bis-triazoles as compared to their mono-triazole analogues. With increment in the length of aliphatic chain of substituent, the antimicrobial activity decreased because increase in chain decreases the water solubility of the compounds and water-soluble alkyl triazole hydrochloride precursors of coumarin show stronger antimicrobial efficacy than less water soluble aralkyl triazole precursors which is also supported by literature [55]. Figure 8 and Charts 2–4 show the graphical representations.

Afreen et al. performed synthesis of compounds 10–12 and their anti-TB activity was analysed. Yields of products were found to be in the range of 62–82%. TLC was used to check the purity of compounds and solvent system used for TLC is CH$_3$OH:CHCl$_3$:CH$_3$CO$_2$H = 1:2:7. MIC (µg/mL) was analysed and paralleled with the reference drug and one compound exhibited MIC 12.5 µg/mL and Streptomycin exhibited MIC 6.25 µg/mL [56]. MIC values of compounds 10–12 are shown graphically in Chart 5 and structures in Figure 9.

Seelam et al. synthesised new heterocyclic compounds in which different moiety like pyrazole, 1,2,4-triazole, thiazole, and isoxazole were clubbed together as all...
Chart 1: Paralleling of inhibition rate of compounds 5a–h on eighth day against VD and Foa at 20 µg/mL.

Figure 8: Structure of the synthesised compounds.

Chart 2: Paralleling of MIC of coumarin triazoles, coumarin bis-triazoles, and their corresponding hydrochlorides with reference standard against Gram-positive bacteria.
**Chart 3:** Comparison of MIC of coumarin triazoles, coumarin bis-triazoles, and their corresponding hydrochlorides with reference standard against Gram-negative bacteria.

**Chart 4:** Comparison of MIC of coumarin triazoles, coumarin bis-triazoles, and their corresponding hydrochlorides with reference standard against different fungal strains.
separately possess biological activity. Antimycobacterial and Antitubercular activities of the targeted compounds were studied. The targeted compounds were endowed to possess property against Gram positive bacteria than the negative one. MIC was studied for comparing the activity. Potentiality of electron withdrawing groups cause an accretion in bactericidal property of compounds. All the synthesised compounds showed modest antifungal activity. The tested compounds showed propitious antitubercular activity 

Sivkæ et al. synthesised [1,3]thiazolo[3,2-b][1,2,4] triazol-7-ium salts via regioselective halocyclisation. Bromine was found to be a better stereoselective electrophilic reagent than Iodine and Iodine monobromide as almost 90% E-isomer of product was formed using bromine and mixture of E- and Z- isomers were formed using Iodine and Iodine monobromide. The compounds were synthesised by electrophilic heterocyclisation and their regioselectivity and stereoselectivity were analysed. Use of tellurium tetrahalogenides resulted in the synthesis of blend of geometrical isomers of the salts. Non-selective halogenated products were formed with less non-polar solvents. Use of selenium tetrahalides in place of tellurium counterparts led to formation of products i.e. amorphous selenium and other oily products that posed a challenge in purification and it complied with the literature which states that selenium containing products are unstable. Out of several derivatives, compound 15 shown in Figure 11 showed antimicrobial activity [58].

Marepu et al. synthesised new moiety in which 1,2,3-triazole was merged with pyridine/pyrimidine and studied their antimycobacterial activity. Targeted compounds were synthesised regioselectively using Buchwald’s strategy. Promising antibacterial activity was shown by two of the triazolopyridines when compared with Streptomycin. Triazolopyrimidines did

![Figure 9: Figure showing structure of the above discussed compounds.](image)

![Figure 10: Pictorial representation showing increase in antibacterial activity on the grounds of potentiality of electron withdrawing groups.](image)

![Figure 11: Picture showing the structure of formed compound.](image)

![Chart 5: Comparison of MIC values of different synthesised compounds with reference standards.](image)
not work as desired so they possess future scope of study as further improvement can be done in these molecules to make them more effective antimycobacterial agents [59]. Figure 12 (compounds 16 and 17) shows the pictorial representation.

Santosh et al. contended to orchestrate and design an exclusive streak of 1,2,3-triazole-chalcone scaffolds for studying their antibacterial activity. α, β-unsaturated carbonyl group of moiety was further modified to pyrazole, pyrimidine, isoxazoline, and cyanopyridine as these groups separately have biological activity as per literature. Fluoro-substituted chalcone and nitro-substituted pyrazoles showed good antibacterial activity as both possessed inhibitory activity against Chorismate synthase. Substituted pyrimidine and cyano-substituted pyridine showed good DPPH radical scavenging activity. Title compounds also possessed great binding affinity for DNA [60]. Figure 13 (compounds 18a and b) shows the pictorial representation of activity.

Singh et al. reported that formation of SBTBS was welded by Cu(i) catalysed click silylation reaction (a single step reaction) from SBTBOTS as individually all three, i.e. 1,2,3-triazole, Schiff base and silatrane show antibacterial activity. Yield was found to be greater than 90%. Literature says that trigonal bipyramidal structure of silatrane causes increase in electronegativity and dipole moment which facilitates their chemisorption in cell membrane by H-bonding with equatorial oxygen atom and dipole-dipole interactions and the fact of showing specific chemical properties by silatranes might be attributed to the transannular N–Si dative bond. Literature also supports that 2-hydroxy-1-naphthaldehyde act as versatile fluorophores, so, clubbing it with 1,2,3-triazole bridged silatrane and primary amine presents a coherent fluorophore unit. All the formed compounds were tested for antibacterial activity. The synthesised bridged silatranes were established to be more stable towards hydrolysis as compared to their triethoxysilane analogues. Out of all compounds, the entity having methoxy substituent, compound 19 (Figure 14) was endowed to acquire highest counter-bacterial property, even comparable to its −ve counterpart because latter possess an extra membrane [61].

Paneth et al. orchestrated a streak of innovative Mannich bases containing fluorophenyl moiety and Broth microdilution process was mobilised to study in vitro activity against bacterial −ve and +ve strains. 90% yield was obtained for targeted compounds. The derivatives with single chlorine group on phenylpiperidine showed the maximum activity. Presence of two chlorine atoms on phenylpiperidine substituent increased the activity against Gram −ve bacteria by two-fold but decreased the activity against Gram +ve bacteria. Furanopiperazine derivative exhibited a considerable reduction in activity as paralleled to phenylpiperazine derivatives. The ubiquity of phenyl group at piperazine’s fourth position attached to the synthesised compound 20 (Figure 15) was established to be a necessary state of affairs to display counter-bacterial property. Nearly all the targeted compounds showed less activity than the reference standards used [62].
Nalawade et al. reported that title compounds were synthesised after clubbing thiazole, pyrazole, and 1,2,3-triazole ring together and their counter-microbial property was studied. Literature survey suggests that clubbed thiazole-pyrazole possess antitubercular, antimicrobial and anti-inflammatory activity; the clubbed thiazole-triazole possess antitubercular and antimicrobial activity; the clubbed triazole-pyrazole possess anticancer, antibacterial and antifungal activity which is comparable to antibacterial drug Streptomycin and antifungal drug Fluconazole. Moderate antibacterial activity was shown by the title compounds against Gram +ve bacteria. Promising activity was shown by compounds against fungi under testing which concluded that azole derivatives might have blocked ergosterol biosynthesis by impeding the activity of cytochrome P450 enzyme which is required for formation of ergosterol from lanosterol where ergosterol, being a considerable part and parcel of fungal membrane, helps in maintaining the functions of the fungal cell. To confirm the mechanism, molecular docking analysis was done. The targeted compounds 21a–i shown in Figure 16 exhibited parallel activity with standard drugs under testing [63].

Agisho et al. reported that 3,5-disubstituted-1,2,4-triazoles and 1,3,5-trisubstituted-1,2,4-triazoles were synthesised in which tert-butyl hydroperoxide is used as an oxidant and tetra N-butylammonium iodide as catalyst. Yields obtained were more than 70%. The exact mechanism is unclear yet and provides a demand for future scope of study though a radical pathway had been suggested and radical trapping method was used to confirm the mechanism. The synthesised compounds 22a–d shown in Figure 17 exhibited bactericidal activity more against E. coli than S. aureus [64].

Bangalore et al. says that usnic acid obtained from lichens was clubbed with 1,2,3-triazoles and further modifications were done in the clubbed structure on which antitubercular and antibacterial activity were studied. The desired products were obtained in average yield, i.e. >40%. It was proved that the presence of two fluorine atoms was beneficial for antitubercular property. Presence of more or less fluorine atoms decreased the activity. Structure activity relationship studies implied that potency of the molecules augmented due to the ubiquity of fluorine atoms as compared to chlorine atoms. Though p-halogen is favourable, but the deciding factor is the m-halogen. Antitubercular activity had not been shown by the compounds having methoxy substituent whereas the same compound showed good antibacterial activity. Cyclic sulphonamide moiety was proved to be a complementing feature to usnic acid enamine. Tricyclic systems with structural modification might be effective in showing the activity. Compounds with difluorophenylacetyl and biphenylacetyl substituents can be further used for future drug development [65]. The synthesised compound 23 is shown in Figure 18.

Maddila et al. synthesised an array of unique pyrano [2,3-d]-pyrimidine via cycloaddition of alkynyl pyranomycinimidinone with differently substituted aryl azides. Titled compounds got tested for bactericidal and fungicidal properties. Zol of titled compounds was studied and paralleled
with the reference standards. Presence of \( \text{e}^{-} \) withdrawing groups, i.e. fluoro and nitro, on benzene moiety affixed to 1,2,3-triazole of pyranomyrimidine ring (compounds 24 and 24a, shown in Figure 19) caused increase in antibacterial and antifungal activities. The ubiquity of \( \text{e}^{-} \) donating groups on benzene moiety affixed to 1,2,3-triazole of pyranomyrimidine ring caused decrease in antibacterial activity [66].

Pradeep Kumar et al. synthesised unique 1,2,3-triazole based imidazole derivatives. The titled compounds were synthesised using CuAAC reaction and compounds were obtained with satisfactory yields. The compounds containing amino and amido substitution were proved to be good anti-TB agents and cytotoxicity studies proved that the titled compounds showed low toxicity. But these hybrid compounds 25 and 25a (Figure 20) could be further modified by trying different substitutions to get more potent molecules [67].

Negi and Rawat (2022) synthesised 21 novel hybrid compounds \textit{in vitro} having thymol and 1,2,3-triazole and certified against germ causing tuberculosis, i.e. \textit{Mycobacterium tuberculosis} and 13 compounds were found to be effective against \( \text{H}_{37}\text{Rv} \) strain of bacteria at 50 \( \mu \text{g/mL} \) (Figure 21).

The reference standards used are isoniazid, ethambutol, and rifampicin whose MIC99 are 0.2, 0.5, and 0.25 \( \mu \text{g/mL} \) respectively. Further accrual can be done to increase the potency of the synthesised molecules [68].

Basheen (2022) synthesised innovative class of compounds of hydrazones and bis-hydrazones possessing 1,2,3-triazole component. Yields are above 80%. The characterisation was done adopting distinctive spectroscopic approach. The synthesised compounds 28a–c (Figure 22) show balanced activity against bacteria [69].

Reddyrajula et al. synthesised 36 hybrid molecules comprising phenothiazine, 1,2,3-triazole using avenue of molecular hybridisation and tested against H37Rv strain of \textit{Mycobacterium tuberculosis} and out of these synthesised compounds, 19 compounds display symbolic antibacterial activity with MIC 1.6 \( \mu \text{g/mL} \). The reference drugs used are pyrazinamide and isoniazid. The synthesised compounds have good oral bioavailability and are non-toxic. The studies advocated that ubiquity of \( \text{e}^{-} \) attracting moieties like \( -\text{NO}_2, -\text{CN}, -\text{F} \) on phenyl ring affixed to 1,2,3-triazole heightens pharmacological property of synthesised compounds [70]. Figure 23 shows the pictorial representation of the strategy.
4.2 Anti-inflammatory activity

Paprocka et al. contended that a plethora of novel 1,2,4-triazole compounds along with methacrylic acid got synthesised and out of all the targeted compounds, the compound 29 depicted in Figure 24 showed proportionate anti-inflammatory activity with ibuprofen [71].

Haider et al. synthesised novel series of compounds which were bis-heterocycles possessing 1,2,3-triazole moiety and found that out of all the synthesised compounds, the compound 30 shown in the Figure 25 came out as a compelling anti-inflammatory agent and the logic for this activity is attributed to the presence of one extra π-π bond [72].

Shaﬁ et al. prepared a series of compounds which are bis-heterocycles bearing 1,2,3-triazole moiety and discovered a compound 31 (Figure 26) exhibiting good...
anti-inflammatory activity as Ibuprofen and biochemical cyclooxygenase activity [73].

Almasirad et al. proposed the orchestration of hybrid compounds containing imidazole and 1,2,4-triazole moiety. Their anti-inflammatory profiles were tested. They found out that two compounds 32 and 33 depicted in Figure 27 showed unmatched anti-inflammatory activity [74].

### 4.3 Anti-convulsant activity

Song et al. synthesised the hybrid compounds possessing 1,2,4-triazole and certified for anticonvulsant property using seizure models in mice. The compound 34 in Figure 28 proved to be a roseate anticonvulsant agent showing ED50 values (effective dosage of a medicine that produces 50% of the achievable response) of 23.7 and 18.9 mg/kg [75].

Mahdavi et al. synthesised two novel compounds and tested them for anticonvulsant activity by measuring ED50 values and Diazepam was used as a reference standard. It was found that out of two synthesised compounds 35 and 36 (Figure 29), one of them (compound 36) showed comparable activity with the reference standard [76] (Chart 6).

Wang et al. formed a library of various molecules possessing 1,2,4-triazole and tested for anticonvulsant property adopting MES and scPTZ studies. Also, the neurotoxicity of the targeted compounds was detected by Rotarod test. It was found that a compound 37 (Figure 30) showed outstanding anticonvulsant activity which was comparable to the clinical drugs such as Ethosuximide and Carbamazepine [77].

Dehestani et al. orchestrated a library of phenacyl-1,2,4-triazole hydrazones via hybridisation approach. The above mentioned compounds were checked for the anticonvulsant property adopting MES and PTZ tests. A compound 38 (Figure 31) emerged out to be a strong anticonvulsant agent [78].

---

**Figure 26:** Compound showing excellent anti-inflammatory activity.

**Figure 27:** Compounds showing distinguished anti-inflammatory activity.

**Figure 28:** Compound showing promising anti-convulsant activity.

**Figure 29:** Novel synthesised compounds.

**Figure 30:** A potent anticonvulsant compound.

**Chart 6:** Graphical comparison of the anticonvulsant activity of the synthesised compounds with the reference standard using ED50 values. Smaller the ED50 values, more potent the drug is.
4.4 Anticancer activity

Ma et al. synthesised hybrids containing pyrimidine and 1,2,3-triazole and checked for anticancer property. A compound 39 (Figure 32) was found to act like a futuristic clinical anticancer drug with IC$_{50}$ value ranging from 1.42–6.52 µM [79].

Aouad et al. prepared di- and tri-substituted 1,2,3-triazoles clubbed with piperazine and benzothiazole with and without copper(I) catalyst. The series of compounds formed were endowed to possess activity against cancer cells chosen to test anticancer property. The compound 40 (Figure 33) emerged out to be a star compound in showing anticancer activity [80].

Saftic et al. synthesised a library of novel derivatives and a derivative having smallest substituent at fourth carbon of triazole (Compound 41, Figure 34) was endowed being active out of all synthesised ones against cancer cell lines [81].

Duan et al. performed the formation of array of unique hybrids having 1,2,3-triazole and thiocarbamate and tested against cancerous cells. Two compounds (42 and 43, Figure 35) were established as more active against cancerous cells as compared to other synthesised compounds having IC$_{50}$ value ranging from 0.73–11.61 µM [82].

4.5 Antioxidant activity

Vieira Veloso et al. synthesised 30 glucal based mono- and bis-1,2,3-triazoles. They found out that a compound 44 (Figure 36) had antioxidant properties and it reduced the oxidative stress by acting on red blood corpuscles which in turn helps in the treatment of sickle cell disease [83].

AlNeyadi et al. synthesised various triazole derivatives. These molecules are checked for antioxidant property using DPPH (a common method to test the antioxidant activity) and found a compound 45 (Figure 37), which possessed antioxidant activity with IC$_{50}$ value of 5.84 µg/mL [84].

Shaikh et al. synthesised derivatives possessing 1,2,3-triazole and coumarin and assessed various biological properties. The antioxidant activity was tested
using DPPH radical scavenging activity and a compound 46 (Figure 38) was found, which had good antioxidant activity [85].

Kaushik and Chahal synthesised a library of various hybrids possessing 1,2,3-triazole and coumarin moiety and found that two compounds 47 and 48 (Figure 39) possessed good antioxidant properties and four compounds 49–52 (Figure 40) possessed antimalarial activity [86].
4.6 Antiviral activity

He et al. synthesised two strings of various compounds and tested for antiviral activity counter to influenza A and influenza B virus. It was established that one compound 53 (Figure 41) retained good activity against influenza A virus and three compounds 54–56 (Figure 42) retained valuable activity against influenza B virus [87].

El-Sayed et al. synthesised a unique string of compounds suspended with 1,2,3-triazole, pyridine, and carbohydrate moiety. Their antiviral property was checked against H5N1 strain of influenza virus. It was found that a compound 57 (Figure 43) possessed better antiviral activity out of all the synthesised compounds [88].
Witkowski et al. synthesised ribonucleoside suspended 1,2,4-triazole moieties. Their antiviral activity was checked against different virus. It was found that compounds 58–60 (Figure 44 and Chart 7) showed antiviral activity [89].

De Lourdes et al. synthesised various hybrid compounds of 1,2,3-triazole. Their antiviral activity was paralleled with reference standard Ribavirin. A compound 61 (Figure 45) was endowed to have activity commensurable to the master reference with IC$_{50}$ value of 14 µM for influenza A virus and 3.8 µM for HIV-1 virus [90].

5 Conclusion

Triazoles can be synthesised by various time-saving and energy-saving methods. Nitrogen compounds being versatile elements provide a huge platform to be incorporated with other elements to form various therapeutic agents. The groups which show biological activity are benzothiazole, coumarin, benzimidazole, pyridine, pyrazole, imidazole, pyrimidine, thiazole, chalcone, silatrane, phenothiazine, hydrazine, thymol, benzoxazole, benzothiazole, and glycoside which can be clubbed either together or with 1,2,3-triazole and 1,2,4-triazole with some modifications to form a new moiety which act as more potent remedial agent.

Acknowledgements: School of Basic and Applied Sciences of K. R. Mangalam University, Sohna, Gurugram is acknowledged for guiding us and providing us adequate sources to prepare the review.

Funding information: Authors state no funding involved.

Author contributions: Akshi Goyal – Conceptualization Data curation, Formal analysis, writing of First draft. Meena Bhandari – Supervision, Revision, Editing, Verification.

Conflict of interest: Authors state no conflict of interest.
Data availability statement: The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

References

Akshi Goyal and Meena Bhandari


