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Review Article

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TRIAZOLO-THIADIAZINE AND THEIR DERIVATIVES AS A POTENTIAL BIOLOGICAL ACTIVITY: A REVIEW

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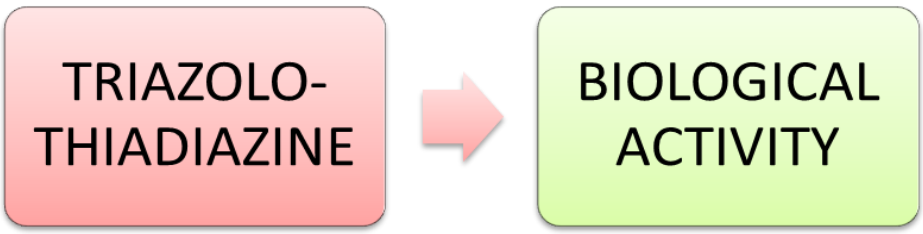
ABSTRACT

Triazolothiadiazine-based scaffolds possess versatile medicinal uses such as antibacterial activity, antifungal activity, antiviral activity, anti-inflammatory activity.



KEYWORDS: Triazolo-Thiadiazine, Anti-viral activity, Anti-fungal activity.

INTRODUCTION

The 1,2,4-triazole substituted with amino and mercapto groups have been reported to possess a variety of biological activities such as antibacterial[1], antifungal[2], antitubercular[3], anticancer[4], diuretic[5], and hypoglycemic.[6] The amino and mercapto groups are readymade nucleophilic centers for synthesis of fused heterocyclic systems.[7] Further, the triazole fused with thiadiazine have promising biological activities such as anti-HIV[8], CNS stimulant[9], antifungal[10], anti-inflammatory[11] and anti *Candidal* activity.[12]

BIOLOGICAL ACTIVITY

Triazolothiadiazine-based scaffolds possess versatile potent biological activity such as antibacterial activity, antifungal activity, antiviral activity and anti-inflammatory activity. **Figure A.**

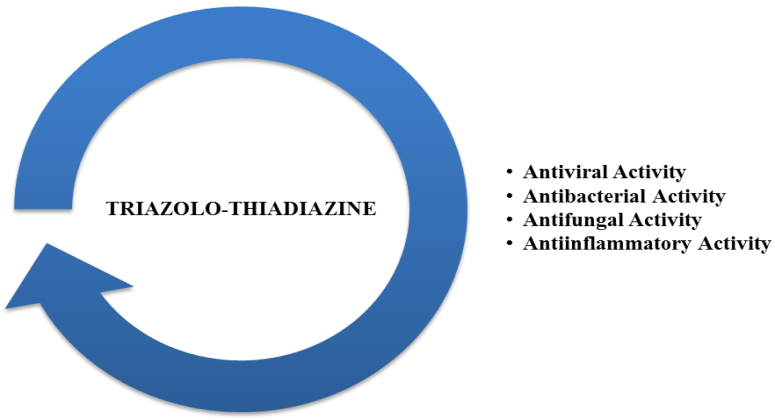
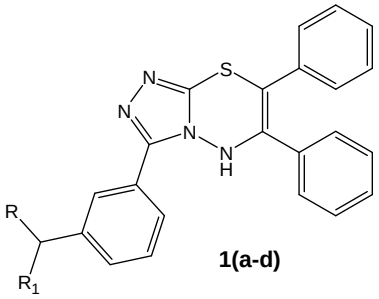


Figure A.

Figure 1: According to Vinod Kumar *et al*.[13] the novel triazolo-thiadiazine derivatives **1** were synthesised and evaluation for their anti viral activity using two animal viruses, *Japanese encephalitis virus* (JEV) strain P20778 and *herpes simplex virus-1* (HSV-1) strain 753166.

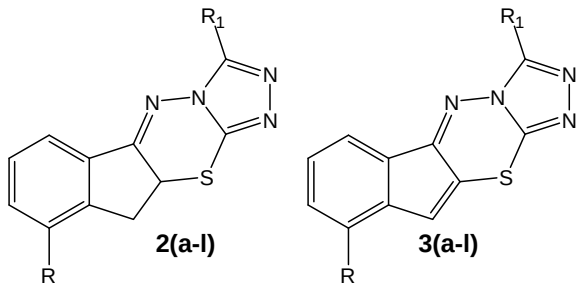


R = a) phthalimido
b) phthalimidomethyl
c) 2-phenyl-3-methyl-quinazolin-(3*H*)-4-one
d) nicotinamido

R_1 = H or phenyl

Figure 1.

Figure 2: Dihydroindeno and indeno[1,2-*e*][1,2,4]triazolo[3,4-*b*][1,3,4]thiadizines **2(a-l)** and **3(a-l)** were synthesised, and their effects on the *in vitro* growth of microorganisms that cause microbial infection were assessed by Om *et al*.[14] *Staphylococcus aureus*, *Bacillus subtilis*, *Escherichia coli*, and *Pseudomonas aeruginosa* were the four strains tested *in vitro* for antibacterial activity. *Aspergillus niger*, *Aspergillus flavus*, and *Penicillium species* were tested for antifungal activity. Some of these compounds out of all the ones that were tested for activity had antibacterial and antifungal activity that was noticeably higher than that of conventional antibiotics.



a) R=H, R_1=H
b) R=H, R_1=Me
c) R=H, R_1=Et
d) R=H, R_1=pr
e) R=H, R_1=i-pr
f) R=H, R_1=Ph
g) R=Me, R_1=H
h) R=Me, R_1=Me
i) R=Me, R_1=Et
j) R=Me, R_1=Pr
k) R=Me, R_1=i-Pr
l) R=Me, R_1=Ph

Figure 2.

Figure 3: New triazolothiadiazines were synthesised, tested *in vitro* against different *Candida species*, and contrasted with ketoconazole, according to Mehlika *et al*.[15] The triazolothiadiazine ring **4** compound with a cyclohexyl moiety and a 4-chlorophenyl substituent was discovered to be the most effective derivative against *Candida albicans* (ATCC 90028). It is evident that two functional components, namely the cycloaliphatic group and the 4-chlorophenyl substituent on the triazolothiadiazine ring, positively correlate with anticandidal activity. Using the MTT assay, the compounds were also examined for their cytotoxic effects.

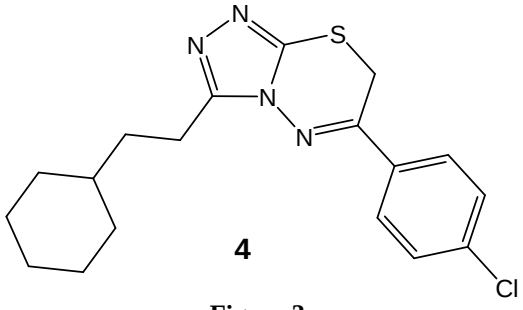
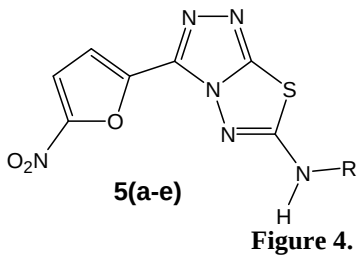


Figure 3.

Figure 4: Several new fused 1,2,4-triazole series **5(a-e)** has been synthesised and tested for the *in vitro* antibacterial activity. Intriguing antibacterial activity was demonstrated by the majority of the investigated compounds against *Staphylococcus aureus*. The *in vitro* cytotoxic activity of the most potent antibacterial agents, **5(c-e)**, against human cancer cell lines was also tested. When compared to the norm, it was discovered that compounds **5c** and **5e** were more cytotoxic to the Hep-G2 cell line.[16]



R = a) C_2H_5
b) n-C_4H_9
c) C_6H_5
d) 4-F-C_6H_4
e) 4-CH_3CH_2-C_6H_4

Figure 4.

Figure 5: A number of fused 1,2,4-triazoles with six membered heterocycles **6**, **7**, and **8** were synthesised, according to El Shehry *et al*.[17] The newly synthesised compounds were tested for their molluscicidal and anti-inflammatory properties. In a dose-dependent manner,

the compounds **6** and **8** demonstrated strong anti-inflammatory effects.

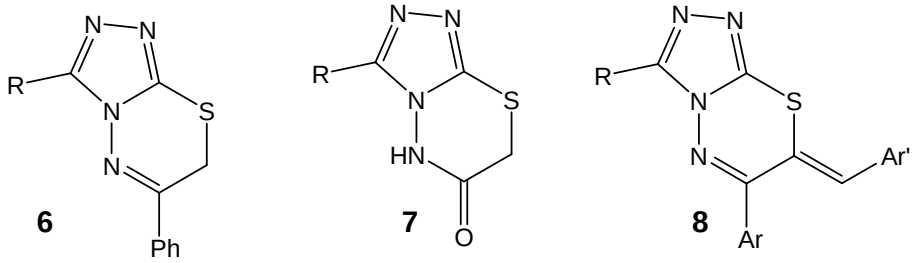


Figure 5.

Figure 6: The synthesis of nitrophenylfurfurylidene-1,2,4-triazolo[3,4-*b*][1,3,4]thiadiazines and testing of their antibacterial and antiviral activities were reported by Holla *et al.*[18] The 4-nitrophenyl and methyl groups in compound **9**, one of the investigated compounds, demonstrated excellent antibacterial activity against all the bacteria examined. Compared to Furacin, compound **9** has higher levels of antibacterial activity against *E. coli*, *S. aureus*, and *P. aeruginosa*. The remaining compounds antibacterial properties, however, were on par with those of furacin. Consequently, it is worthwhile to research these compounds for various biological functions.

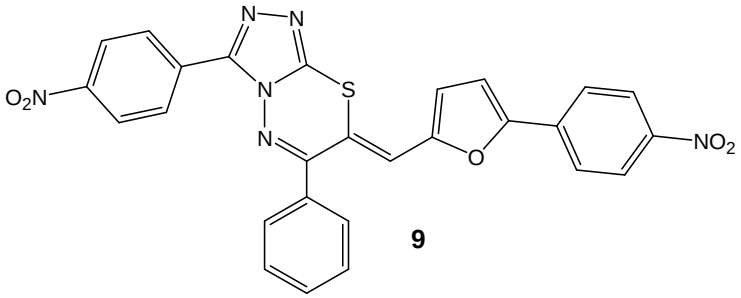


Figure 6.

Figure 7: A new series of 2-phenyl-3-(6-aryl-7H-[1,2,4]triazolo[3,4-b][1,3,4] thiadiazin-3-yl)-4H-4-chromenone **10(a-j)** has been synthesized by the reaction of 3(4-amino-5-sulfanyl-4H-1,2,4-triazol-3-yl)-2-phenyl-4H-4-chromenone **7** with a variety of phenacyl bromides in ethanol under reflux.Nagaraj *et al.*[19] All newly synthesized compounds were screened for their in vitro antibacterial activities against S. aureus, B. cereus and P. aeruginosa. Compounds **10d**, and **10h** were highly active against Bacillus cereus, compound **10a** was highly active whereas compounds **10b** and **10d** were moderately active against Staphylococcus aureus, compounds **10f** and **10h** was moderately active against Pseudomonas aureginosa.

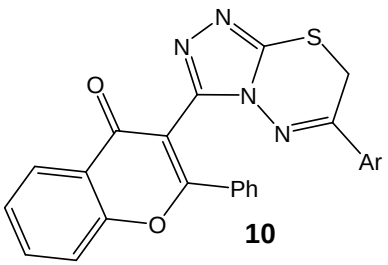


Figure 7.

CONCLUSION

This review outlined the triazolo-thiadiazine and their derivatives served as a resource for both basic and applied research on the subject.

CONFLICTS OF INTEREST

There are no conflicts to declare.

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