SYNTHESIS AND ANTIMICROBIAL PROPERTIES 2-(1-ALLYL-1*H*-TETRAZOL-5-YLSULFANYL)-ACETAMIDES

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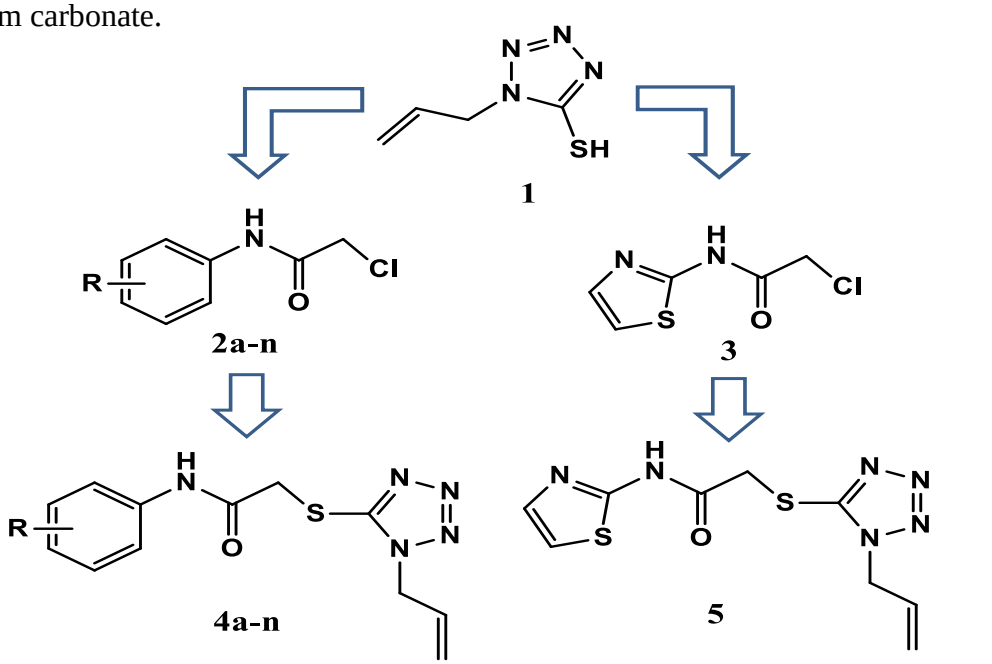
The wide variety of pathogens biological forms, the standing emergence of new multiresistant pathogenic strains make it difficult to treat and prevent infectious diseases. At least 30 new infections haverisen insidiously and scattered to threaten the health of billions of humans across the planet especiallyin low-income countries. Infortunately, there are nosuccessful pharmaceuticals or vaccines for many of these new infections. So, in order to meet above mentioned challenges, there is an urgent need for the development of novel antimicrobial drugs

Nitrogen-containing organic molecules have acquired special attention in the field of organic, bioorganic and medicinal chemistry. They contributed to the development of numerous organic synthesis protocols and found abundant applications in the chemical sciences. Tetrazoles are an important class of nitrogen-comprising heterocycles. The heterocyclic tetrazole moiety has admirable biological, pharmaceutical and clinical applications.

The desired compounds (**4a-n** and **5**) were prepared by reacting 1-allyl-1*H*-tetrazole-5-thiol **1** with appropriate 2-chloro-N-aryl-acetamides **2a-n** and 2-chloro-*N*-thiazol-2-yl-acetamide **3**. This nucleophilic substitution reaction was carried out in the presence of potassium carbonate.



R=4-C_2H_5 (a); 4-C_3H_7 (b); 2,5-$(CH_3)_2$ (c); 3,4-$(CH_3)_2$ (d); 2,4,6-$(CH_3)_3$ (e); 4-Cl (f); 2-CH_3, 5-Cl (g); 3-Cl, 4-CH_3 (h); 2-OCH_3 (i); 3,4- $(OCH_3)_2$ (j); 4-OC_2H_5 (k); (CH_3)N (l); 3-$COCH_3$ (m); 4-$COCH_3$ (n);

The antimicrobial study was performed by CO-ADD (The Community for Antimicrobial Drug Discovery), funded by the Wellcome Trust (UK) and The University of Queensland Australia. Evaluation of all synthesized compounds for their antimicrobial activity against five pathogenic bacteria, *methicillin-resistant Staphylococcus aureus* (ATCC 43300) as Gram-positive bacteria, *Escherichia coli* (ATCC 25922), *Klebsiella pneumonia* (ATCC 700603), *Acinetobacter baumannii* (ATCC 19606) and *Pseudomonas aeruginosa.*

All compounds have weak or moderate antibacterial activity against against *Staphylococcus aureus* and do not possess activity against tested Gram-negative bacteria. The derivatives **4a-e** and **5** have moderate antifungal activity against *C. neoformans* with growth inhibition 29.1–78.1% while the derivatives **4f-h**, have high antifungal activity against this fungi with growth inhibition ranged from 85.5 to 101.5%.

The minimal inhibitory concentrations (MIC μg/ml) measurements were performed for compounds with significant microbial growth inhibition 4f-h using Amphotericin as a reference drugs. As shown in Table 4 compound 4f has antifungal activity comparable to that of Amphotericin. All tested compounds were not toxic against human embryonic kidney cells and erythrocytes.

In summary, we presented an efficient synthetic approach to a number of 2-(1-allyl-1*H*-tetrazol-5-ylsulfanyl)-acetamides. The antimicrobial findings exhibited that the compounds possessed weak or moderate antibacterial activity and high antifungal potential.