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Research paper

Synthesis and antimicrobial activity of styryl/pyrrolyl/pyrazolyl sulfonylmethyl-1,3,4-oxadiazolyl amines and styryl/pyrrolyl/pyrazolyl sulfonylmethyl-1,3,4-thiadiazolyl amines

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ABSTRACT

A new class of mono and bis heterocycles - styryl sulfonylmethyl-1,3,4-oxadiazolyl/1,3,4-thiadiazolyl amines, pyrrolyl sulfonylmethyl-1,3,4-oxadiazolyl/1,3,4-thiadiazolyl amines and pyrazolyl sulfonylmethyl-1,3,4-oxadiazolyl/1,3,4-thiadiazolyl amines were prepared from the synthetic intermediate *Z*-styrylsulfonylacetic acid adopting simple and well versed synthetic methodologies and studied their antimicrobial activity. Amongst all the tested compounds styryl thiadiazole **5c** exhibited promising antimicrobial activity against *Pseudomonas aeruginosa* and *Penicillium chrysogenum*.

1. Introduction

Nitrogen containing heteroarenes have great utility in synthetic medicinal and material chemistry. One such class of compounds are oxadiazoles, thiadiazoles, pyrroles and pyrazoles. 1,3,4-Oxadiazoles are associated with potent pharmacological activities due to the presence of toxophoric −N=C−O linkage and display antimicrobial [1], antimycobacterial [2], antiviral [3] and anticancer [4] activities. Further, they are very good bioisosteres of amides and esters, which can contribute substantially in increasing pharmacological activity by participating in hydrogen bonding interactions with the receptors. Thiadiazole derivatives are known to possess anticancer [5], antibacterial [6], antifungal [7], anti-inflammatory [8] and analgesic [9] activities. On the other hand, pyrroles have been widely used as building blocks in total synthesis of many natural products and exhibit biological activities such as powerful antibacterial, antiviral, anti-inflammatory, antitumor, and antioxidant activities [10]. Pyrrole containing drugs Netropsin and Distamycin are naturally anticancer antibiotics [11] (Fig. 1). Among the various synthetic methods, the notable classical ones are Knorr [12] and Hantzsch [13] including multicomponent and metal-catalyzed routes [14]. Literature survey indicates that pyrazole derivatives are well known for their antibacterial [15], antifungal [16], antimicrobial [17], anticancer [18], analgesic and anti-inflammatory [19,20] activities. Pyrazole moiety makes the core structure of various drugs such as Difenamizole [21], Celecoxib [22], Tepoxalin [23] etc (Fig. 1). The 1,3-dipolar cycloaddition methodology is widely used for the syntheses of pyrazoles using diverse synthons such as nitrilimines and alkynes [24] hydrazones and nitroolefins [25] and azomethine imines and alkynes [26]. In recent years there is still a great demand for designing new compounds and broad spectrum antimicrobial agents remains a challenge for medicinal chemistry researchers. Motivated by the aforesaid findings and in continuation of our studies towards the development of a variety of biologically potent heterocycles [27], herein we plan to synthesize a new class of mono and bis heterocycles – styryl/pyrrolyl/pyrazolyl sulfonylmethyl-1,3,4-oxadiazolyl amines and styryl/pyrrolyl/pyrazolyl sulfonylmethyl-1,3,4-thiadiazolyl amines and to study their antimicrobial activity.

2. Chemistry

A new class of mono and bis heterocycles- 5-*Z*-styrylsulfonylmethyl-1,3,4-oxadiazolyl/thiadiazolyl amines, pyrrolyl sulfonylmethyl-1,3,4-oxadiazolyl/thiadiazolyl amines and pyrazolyl sulfonylmethyl-1,3,4-oxadiazolyl/thiadiazolyl amines from

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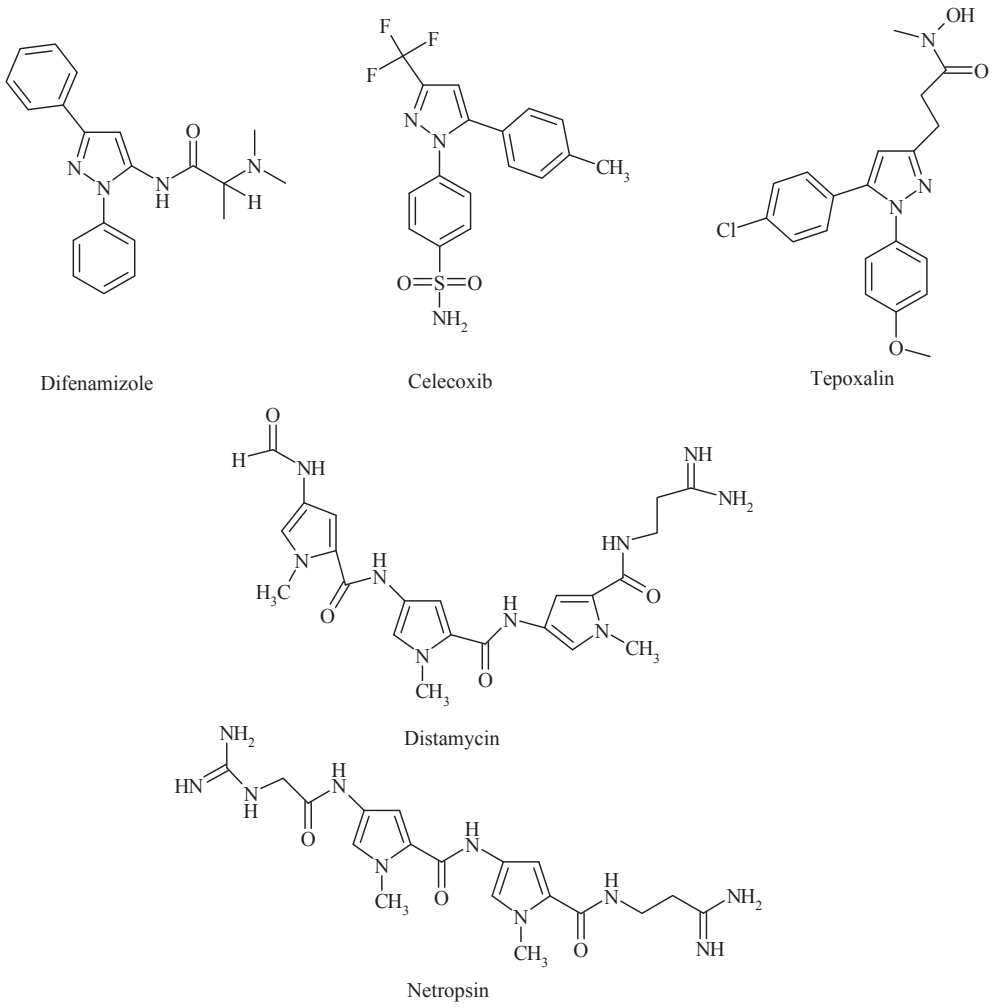

Fig. 1. Drugs containing pyrrole and pyrazole moieties.

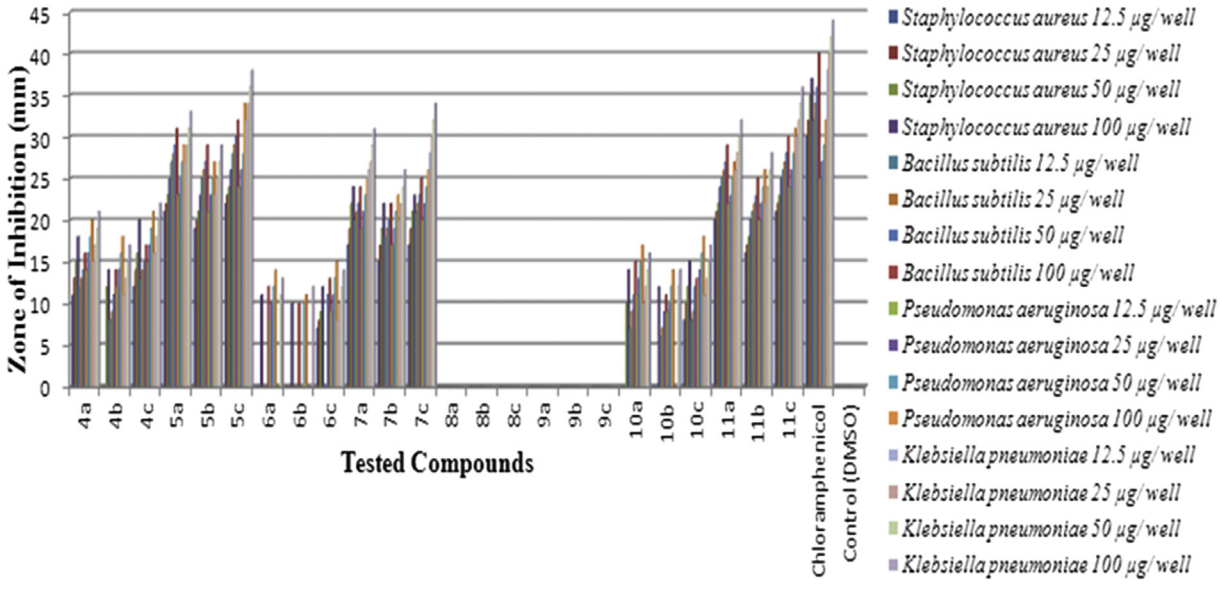

Fig. 2. The *in vitro* antibacterial activity of compounds **4**–**11**.