Review Article

A SHORT REVIEW ON ANTIMICROBIAL ACTIVITIES OF INDOL COANTAINING SUBSTITUTED PYRIDAZINE AND PHTHALAZINE DERIVATIVES

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ABSTRACT

Various of indolylpyridazinone and phthalazine derivatives are biological active and are well known as antimicrobial agents, antiphlogistics, antipyretics, inflammation inhibitor, blood platelet aggregation inhibitors, cardiovascular and antihypertensive agents, intermediates for drugs and agrochemicals. Some indolylpyridazinone and phthalazine derivatives are study in this review and showed antibacterial activity against different pathogenic microbes both bacterial and fungal strains.

Keywords: Pyridazinones, indole, pyridazinoindoles, phthalazinones, antibacterial and antifungal activity

INTRODUCTION:

The pyridazino[4,5-b]indole scaffold, due to its bio-isosterism with β-carboline as well as γ-carboline, has found considerable pharmaceutical interest as the core structure of a wide variety of bio-active compounds. During the past few years, we have investigated the synthesis and biological activity of various new representatives of this “aza-carboline” ring system, mainly focusing on potential antitumor agents. The title ring system now became interesting also in the context of an ongoing program in search of new and selective inhibitors of copper-containing amine oxidases [1]. Based on preliminary structure-activity information, the need arose to prepare a focused compound library of indole-fused pyridazinones and pyridazinediones bearing various alkyl substituents at the indole nitrogen. Despite their simplicity, surprisingly few representatives of this general structure have been known so far [1].

The aryl-pyridazinones have demonstrated a range of pharmacological activities, most of which are related to the cardiovascular system and especially to their properties as ionotropic or platelet aggregation inhibitors. Among these compounds, Imazodan, CI- 930, Indolindan, Bemoradan, Pimobendan and Zardaverine are a few examples of pyridazinones that are active as cardiotonic agents [2-5]. Various aryl-pyridazinones have been reported to possess antimicrobial, analgesic, anti-inflammatory, antifeedant, herbicidal, antihypertensive, antiplatelet, anticancer and other anticipated pharmacological properties [6-15]. various of indolylpyridazinone derivatives are...
well known as antimicrobial agents, intermediates for drugs and agrochemicals, antipyretics, inflammation inhibitor, blood platelet aggregation inhibitors, cardiovascular and antihypertensive agents [16,17].

The diverse biological activities of various functional derivatives of substituted phthalazinones are well known. Some of the phthalazinone derivatives have found application in clinical medicine due to their pronounced antipyretic, analgesic and tuberculostatic activity while others have shown interesting vasodialator and antihypertensive properties. Phthalazinones bearing a substitution at C-4 represent key intermediates in the synthesis of various compounds with highly interesting pharmacological properties, such as the blood platelet aggregation inhibitor MV-54454 [1-(3-chloroanilino)-4-phenylphthalazine] which has been found to be a selective phosphodiesterase VA inhibitor or the thromboxane A2 synthetase inhibitor and bronchodilator, 2-[2-(1-imidazolyl)ethyl]-4-[3-pyridyl]-phthalazine-1[2H]-one. The phthalazinone nucleus has been proved to be a versatile system in medicinal chemistry. Moreover, a number of established drug molecules like Hydralazine, Budralazine, Azelastine, Ponalrestat or Zopolrestat are accessible starting from the corresponding phthalazinones. The development of new and efficient methodologies for the synthesis of such potentially bioactive phthalazine derivatives is important. Despite the useful nature of phthalazinone, there are very few synthetic approaches in the literature for the formation of 4-phenyl and 4-substituted alkyl-1-(2H)-phthalazinones and its derivatives [18-21]. Therefore, functionalization of the nucleus continues to be of synthetic interest. In general, most of the structural modifications of the parent system which have been carried out in order to optimize the biological activity of phthalazine-derived drugs can be seen as a variation of the substitution pattern at position 1, 2 and 4, i.e. the substitution pattern of the 1,2-diazine part of the bicyclic system. Considerably less efforts has been devoted in the modification of the benzene part of the phthalazine skeleton. These results motivated us to develop new and efficient synthetic strategies to allow the preparation of pyridazinones bearing different functional groups at different position of the heterocyclic ring.

**ANTIMICROBIAL ACTIVITIES:**

The antimicrobial activity of 2-[(4-substituted phthalazine-1-yl)alkyl]-1H-isoindole-1,3(2H)-diones 1a-d and 2-{2-[4-(1,3-dioxo-1,3-dihydro-2H-isoindole-2-yl-alkyl)-1-oxophthalazine-2(1H)-yl]alkoxy}-1H-isoindole-1,3(2H)-diones 2a-d were tested in vitro against a variety of Gram+ve bacteria Baccillus stablius; the Gram–ve bacteria Proteus mirabilis, Klebsiella pneumoniae, Salmonella typhi and fungi-Candida albicans (MTCC 227) and Aspergillus fumigatus (MTCC 2550). Flucanazole and Etraconazole were used as standard for antibacterial and antifungal activity respectively. Compound 1a and 1d possess good activity against P. mirabilis, K. pneumoniae, but show only moderate activity against B. stablius and S. typhi. Other compounds (1b and 1c) and (2a-d) were exhibited low antibacterial activity against all organisms. Almost all compounds were showed good activity against both fungal strains as
CRITICAL REVIEW IN PHARMACEUTICAL SCIENCES

compared to standard Etraconazol. Compound 1d showed lowest antifungal activity. These compounds were exhibited relatively better antifungal activity, but weak activity against Gram+ve bacteria than those of Gram-ve bacteria [22].

The antibacterial activity of some 6-anthracenepyridazinones containing indolyl moieties compounds (3a-d), (4a,4b), (5a-d), (6a-d), 7, (8a-d) against representative Gram positive bacteria S. aureus and S. epidermis and negative bacteria E. coli and P. vulgaris. Compounds 6b, 8d possess high activity against both types of bacteria, while compound 6c displays low activity. Compounds 6b possess high activity, compounds 3a-d, 4a, 5a, 5d, 8c, 8d possess moderate
activity and compounds 6c and 7 possess less activity against Gram positive strains. As far as Gram negative microorganisms are concerned, compound 8d showed high activity, while compounds 3a, 3b, 3d, 4a, 5a, 5d, 6b, 7 and 8c all displayed moderate activity and 3c and 6c possess less activity against such microorganisms [23].
Additionally, the antimicrobial activity of selected compounds against Gram positive and negative bacteria is reported.

CONCLUSION:

In conclusion, a variety of new indole-fused pyridazinones and pyridazinediones bearing small to medium-sized alkyl residues at the indole nitrogen were made accessible by short and convenient synthetic pathways. The pyridazine ring plays an essential role in several biological processes. Accordingly a massive research effort has been expended to synthesis of the novel
congeners bearing these biologically active structural moieties within a molecular framework likely to constitute potent antimicrobial agents, further screenings for biological activity are in progress.

REFERENCES

22. Salvi VK, Bhambi D, Jat JL, Talesara GL. Synthesis and antimicrobial activity of some 2-[1-(4-oxo-3,4-dihydrophthalazine-1-yl)alkyl]-1H-isoindole-1,3(2H)-dione and their imidoxy derivatives. Arkivoc 2006 (xiv) 133-140.