Study on antimicrobial activity of α-pyrone-derivatives toward Gram-(+) and Gram-(–) pathogenic bacteria

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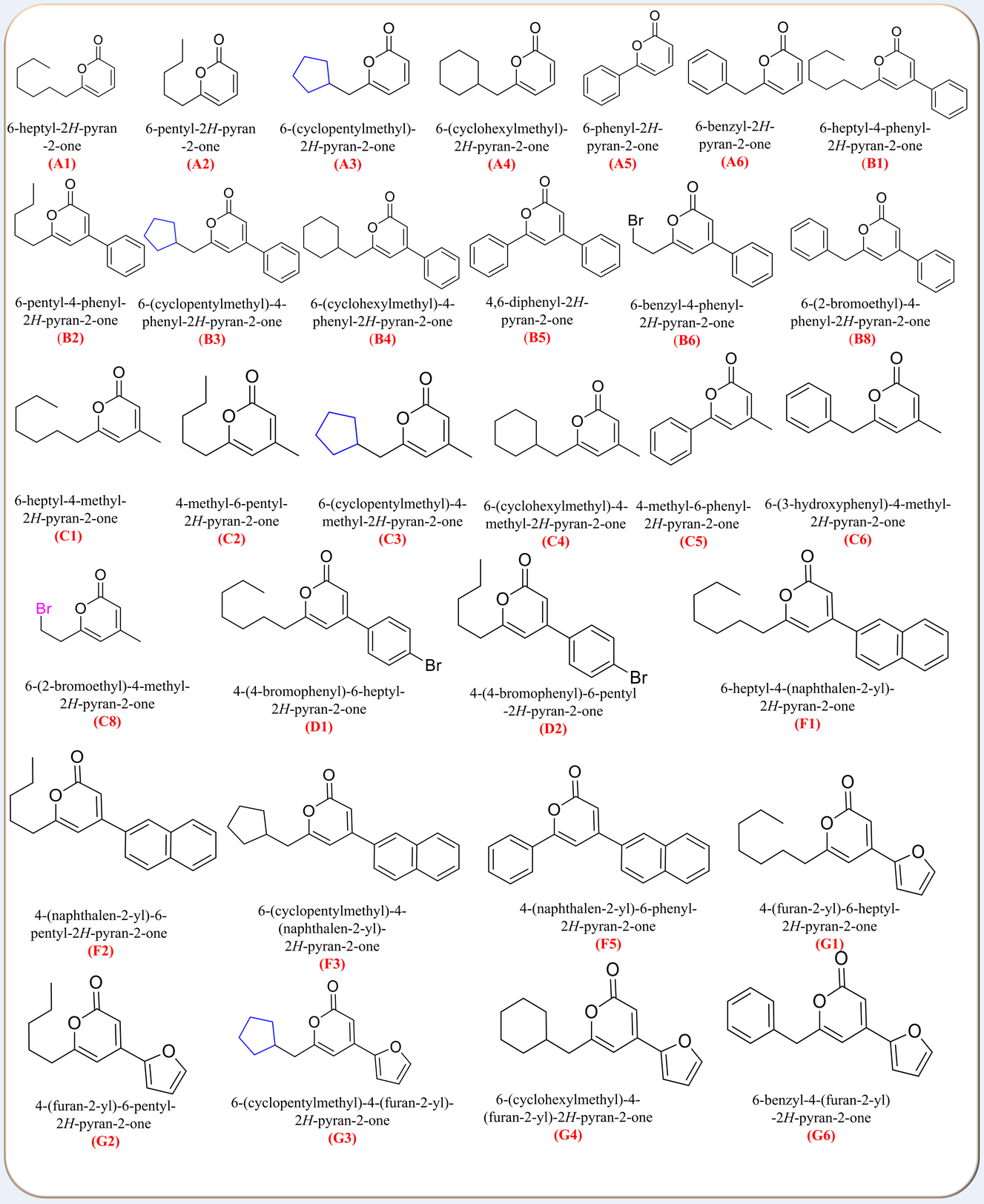
Introduction

6-Pentyl-2*H*-pyran-2-one **(A2)** is a natural product isolated from marine-derived fungus, *Trichoderma* sp., which showed a broad spectrum of bioactivities, including anti-bacterial activity and anti-settlement of barnacle cyprids. Thus, we are interested in the investigation in the chemistry and biology of α-pyrone (2-pyrone) [1]. Aromatic heterocycles represent about two-third of total organic compounds that define the history, present and future of modern drugs [2]. This class of compounds comprises a broad range of biologically active entities; and over the years, these molecules have drawn considerable attention. In past, these metabolites showed promising biological activities such as, neurotoxic, cytotoxic, phytotoxic, antifungal properties and so on which revealed their pharmaceutical values. Interestingly, α-pyrone contains six membered lactone which naturally exist as a part of coumarin ring system and coumarin molecules are well known for their lipophilic properties and this also influence bioactivities in many ways. Due to its planner molecular structure and lipophilic character, such types of molecules can penetrate in the cell wall which results inhibiting action towards microbial growth. Literature survey reveals that a simple change in the substitution pattern on the 2-pyrone ring system often leads to diverse biological activities, therefore we design and synthesized versatile scaffold of pyrones (series A to G) to study their biological activities in different bioassay systems such as, antimicrobial, antibiofilm formation, anti-inflammatory and antibiofouling activities. In this poster, we are reporting antibacterial activity of α-pyrone derivatives toward Gram-(+) and Gram-(–) pathogenic bacteria.

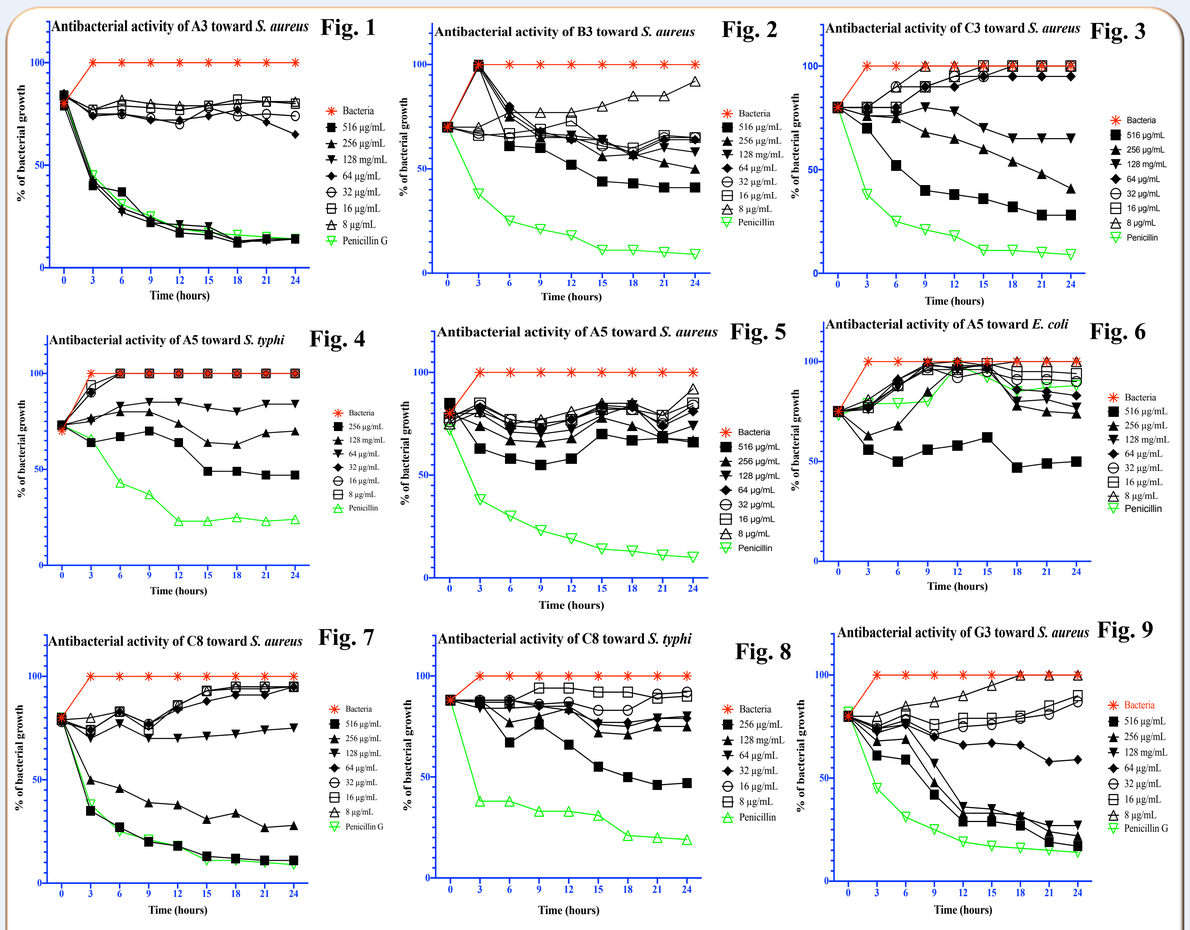
Synthesis of α-pyrone and bioassay

α-pyrone derivatives were synthesized by gold coupling reaction at ambient temperature [3]. Herein, 32 α-pyrone-derivatives were tested toward four bacterial pathogen including, two Gram-(+) bacteria *Staphylococcus aureus*, *Salmonella typhi* and two Gram-(–) *Escherichia coli* and Enterotoxigenic *E. coli*, respectively. These α-pyrone-derivatives were serially diluted to desired concentrations and transferred to 96 well plate containing bacteria (MCF 0.5). The activity of pyrones toward bacteria were recorded every three hour by ELISA reader at OD_{600}.

Structures of the α-pyrone-derivatives



Antibacterial assay results



Chemical Name	Inhibition % toward *S. aureus*	Inhibition % toward *S. typhi*	Inhibition % toward *E. coli*	EC_{50}
6-(cyclopentylmethyl)-2*H*-pyran-2-one (**A3**)	86%	29%	–	128 & 256 µg/mL
6-phenyl-2*H*-pyran-2-one (**A5**)	34%	53%	50%	512, 512 & 256 µg/mL
6-(cyclohexylmethyl)-4-phenyl-2*H*-pyran-2-one (**B3**)	50%	–	–	256 µg/mL
6-(cyclopentylmethyl)-4-methyl-2*H*-pyran-2-one (**C3**)	59%	–	–	256 µg/mL
6-(2-bromoethyl)-4-methyl-2*H*-pyran-2-one (**C8**)	72 %	53%	–	256 µg/mL
6-(cyclopentylmethyl)-4-(furan-2-yl)-2*H*-pyran-2-one (**G3**)	73%	–	NT	128 µg/mL
6-(cyclohexylmethyl)-4-(furan-2-yl)-2*H*-pyran-2-one (**G4**)	50%	–	–	256 µg/mL

Table 1: Antimicrobial activity of α-pyrone-derivatives are shown here. Whereas, bacterial growth inhibition represent in percentage (%); (–) represent no inhibition activity and (NT) represent not tested.

Conclusion and Future study

In present work, we successfully synthesized α-pyrone-derivatives and profiled their antibacterial activity toward Gram-(+) and Gram-(–) pathogenic bacteria. Among the tested derivatives, compound **A3**, **B3**, **C3**, **C8**, **G3** and **G4** exhibited inhibitory activity toward Gram-(+) *S. aureus* at 128–256 µg/mL and **A5** and **C8** possesses bacterial growth inhibition against *S. typhi* at 512–256 µg/mL and **A5** also showing half of the bacterial inhibition towards *E.coli* and Enterotoxigenic *E. coli*, respectively [Table 1]. Structure activity relationship (SAR) of active compound **A3**, **B3**, **C3** & **G3** revealed that, presence of cyclopentane ring showed better bacterial growth inhibition toward *S. aureus* [Fig. 1, 2, 3 & 9]. In future, we will continue screening of these synthetic α-pyrone analogues (series A to G) in antbiofilm formation, antifouling and anti-inflammatory bioassay systems. At the completion of these screenings, we are expecting to discover potent agents towards targeted bioassay systems.

References

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