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Synthesis and antibacterial activity of novel bisacodyl derivatives

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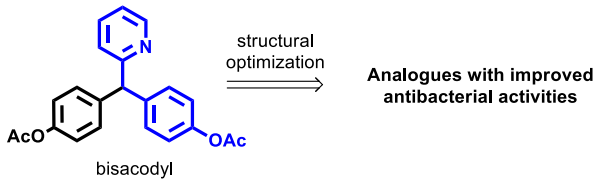
Graphical Abstract



Abstract

The antibacterial activity of a new serie of triarylmethane analogues of bisacodyl, a drug used in therapeutic as laxative, was investigated against Gram-positive and Gram-negative foodborne pathogens. The results showed that synthesized compounds exhibit a higher bacteriostatic activity

Introduction

The global situation of bacterial diseases has become a concern in the last years due to the lack of new drugs and the antibiotic resistance. Since the year 2000, only eight antibacterial molecules have obtained a marketing authorization. Furthermore, despite the discovery over the last twenty years of compounds with an interesting antibiotic activity, few of them belong to new chemical classes or have the required properties to become drugs or to circumvent resistance problems [1-4].

At present, in order to accelerate the development of drugs with relatively low costs and reduced risks, pharmaceutical companies develop new approaches from existing drugs. This methodology known as drug repurposing allows the development of new indications for existing drugs with well-known pharmacokinetic profiles. We have previously described the antimicrobial activity of bisacodyl, drug used in therapeutics as laxative [5].

The aim of this study was to synthesize a new serie of triarylmethane (TAM) analogues of bisacodyl and study the antibacterial activity.

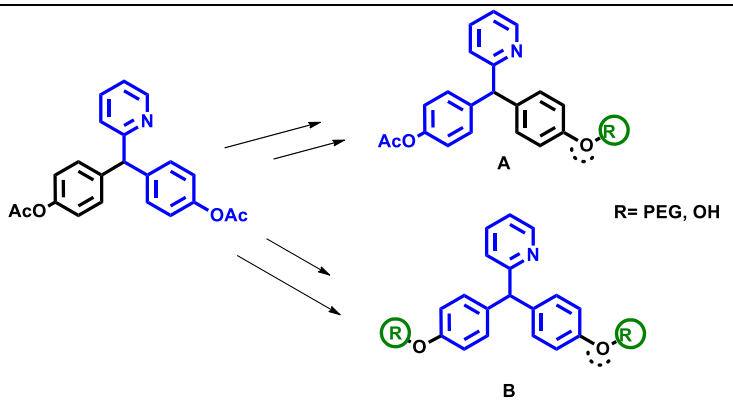


Figure 1: Pharmacomodulation of bisacodyl a) Symmetrical TAM, b) unsymmetrical TAM

Materials and Methods

The analogues of bisacodyl were synthesized from commercially available reagents *via* a Friedel-Crafts reaction followed by an O-alkylation then functionalization with PEG fragments to increase solubility. The bioassay was performed using polystyrene micro-assay plates (96 well) using levofloxacine, a broad-spectrum antibiotic, as a control.

Results and Discussion

The antibacterial activity against Gram-positive and Gram-negative pathogens of the compound 4, 4'-(pyridin-2-ylmethylene) diphenol was evaluated. This compound exhibited antilisterial activity, with minimum inhibitory concentration (MIC) ranging from 6.25 to 12.5 µg/mL against *Salmonella typhimurium*. Additionally, it was active against *Escherichia coli, Listeria monocytogene* and *Staphylococcus aureus* with MIC values between 25-50 µg/mL and 12.5-25 µg/mL. The derivatives bearing PEG groups have also been tested revealing a promising antibacterial activity.

Conclusions

The studied compounds displayed a higher bacteriostatic activity compared to bisacodyl.

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Acknowledgments

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