Design, Synthesis,and Biological Activity of 18β-Glycyrrhetinic Acid Derivatives and Their Metal Complexes

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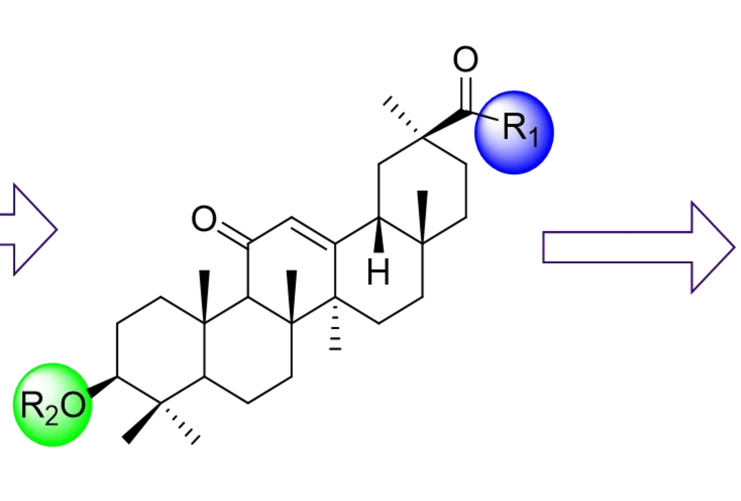
Introduction

The increasing morbidity and mortality caused by infections with pathogenic bacteria (fungus or bacteria) have highlighted an urgent requirement for developing novel anti-bacterial agents to protect the health and integrity of human life. 18*β*-glycyrrhetinic acid has a wide range of pharmacological effects including anti-bacterial, anti-inflammatory and anti-tumor. However, its relatively low biological activity and high toxicity limit its potential for anti-bacterial and other pharmaceutical applications. To improve the anti-bacterial activity of 18*β*-glycyrrhetinic acid, we designed and synthesized a series of glycyrrhizic acid derivatives.

Results

Licorice



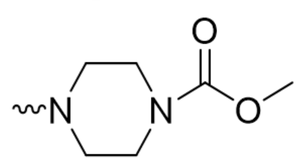
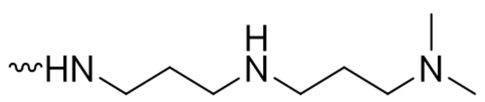
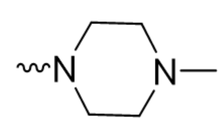
	R_1	R_2	Yield
1		H	50%
3		H	41%
20		BOC-Gly	72%

Fig.1 Structures and yields of compounds **1**,**3** and **20**

Table 1.In Vitro antibacterial and antifungual activity of selected derivatives

Compounds	MIC_{80} (μg/mL)					
	Fungal			Bacteria		
	C.albicans	*C.neoformans*	*A.fumigatus*	*S.aureus*	*E.coli*	*P.aeruginosa*
1	4	2	nd	nd	nd	nd
3	4	2	nd	nd	nd	nd
20	16	>256	32	128	256	4
Fluconazole	2	2	2	nt	nt	nt
Amphotericin B	2	64	16	nt	nt	nt
Streptomycin	nt	nt	nt	2	2	2

nd:Not determined; nt:Not tested.

Conclusion

In the present work, we synthesized a series of 18*β*-glycyrrhetinic acid derivatives and studied their inhibitory effects on three pathogenic fungi and three pathogenic bacteria. The results showed that most of the derivatives had a good inhibitory effects on fungi and bacteria. Among them, the inhibitory activity of compounds **1** (MIC:2 μg/mL)and **3** (MIC:2 μg/mL) against *Candida albicans* and the inhibitory activity of compound **20** (MIC:4 μg/mL) against *Pseudomonas aeruginosa* were comparable to those of the positive drugs. We will elucidate the mechanism and further identify biological targets for drug design.

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