香港浸會大學 HONG KONG BAPTIST UNIVERSITY
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SEMI-SYNTHESIS AND ANTI-INFLAMMATORY ACTIVITIES EVALUATION OF TAXAMAIRINS

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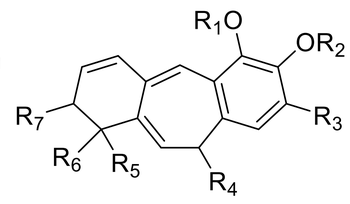
INTRODUCTION

The taxamairins are tricyclic diterpenes containing ketones isolating from Taxus species with potential pharmaceutical value. However, the low yield of taxamarins isolating from natural plants strongly limits their further development (yield < 0.05%).[1] Therefore, organic synthesis method is considered to be an accessible way to prepare taxamairins. Recently, the reported synthesis methods commonly have disadvantages of long synthetic routes, low yield and not feasible in large scale,[2] which strongly limits the application in industrial. The objection of this work is to provide a practical method for semi-synthesis for taxamairins and analysis the anti-inflammatory activities in vivo and vitro.

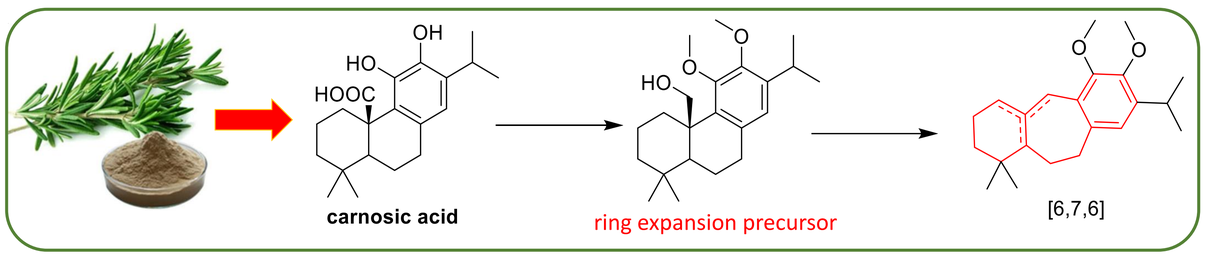
Red List of Threatened Species

Poor isolation yield

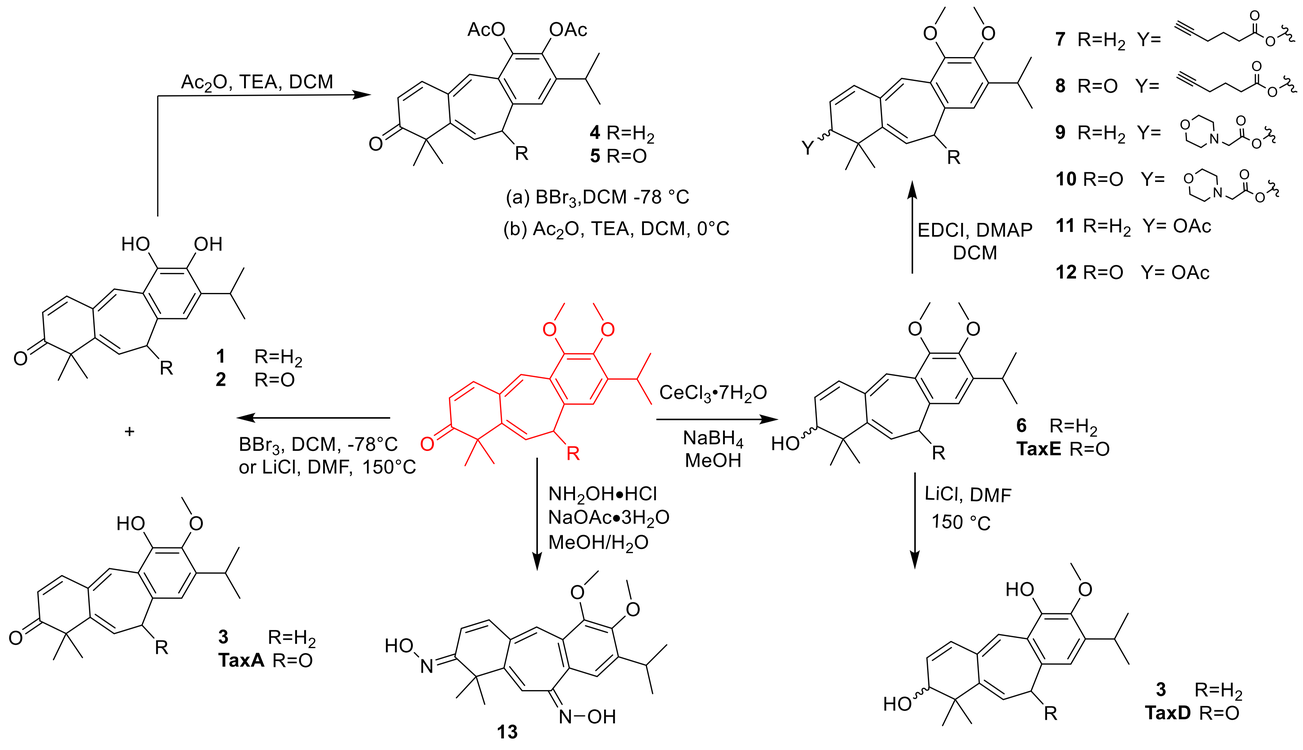


taxamairins

SEMI-SYNTHESIS OF TAXA AND TAXB



SYNTHESIS OF TAXAMAIRINS



ANTI-INFLAMMATORY ACTIVITY STUDY IN VIVO

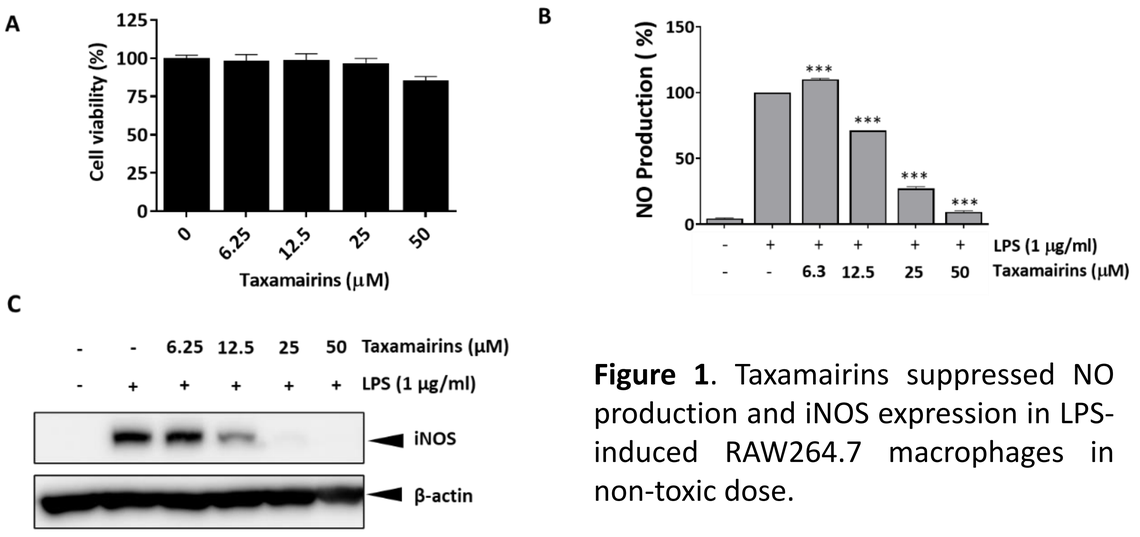


Figure 1. Taxamairins suppressed NO production and iNOS expression in LPS-induced RAW264.7 macrophages in non-toxic dose.

ANTI-INFLAMMATORY ACTIVITY STUDY IN VITRO

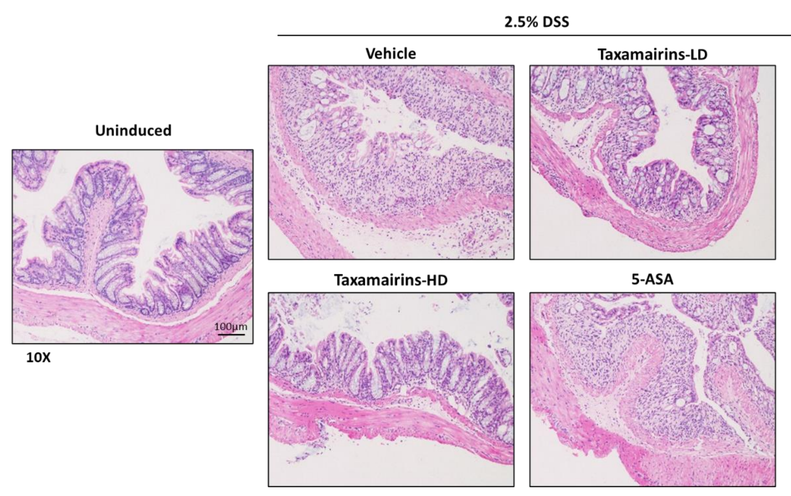


Figure 2. Taxamairins decreased the susceptibility of mice to DSS-induced experimental colitis.
C57BL/6 mice were induced with 2.5% DSS in their drinking water for 7 days. Mice received daily orally administration of vehicle (0.5% CMC), taxamairins-LD (50mg/kg in 0.5% CMC), taxamairins-HD (100mg/kg in 0.5% CMC), or 5-ASA (200mg/kg in 0.5% CMC) alongside DSS induction.

CONCLUSION

- From commercially available compound carnosic acid, TaxA and TaxB was obtained in 7 and 6 steps with total yield of 12% and 21% respectively.
- Based on the practical semi-synthesis method, 18 analogous and intermediates were obtained and the SAR study is in processing.
- Taxamairins exhibited potent anti-inflammatory activities in LPS-induced macrophages and DSS-induced acute colitis mouse models.

REFERENCE

1. Yang, S.-J. *et al*. Diterpenes from Taxus mairei. *Phytochemistry* **1998,** *49* (7), 2037-2043.
2. (a) Wang, X. *et al* The Total Synthesis of Taxamairin B. *Synthetic Communications* **1995**, *25* (21), 3413-3419. (b) Ning, C. *et al*, A Practical Total Synthesis of Taxamairin B. *Synthetic Communications* **1999**, *29* (12), 2115-2122.

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