Chemical Modifications on Filifolinol. New Derivatives Potentially Suitable for Oral Administration

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INTRODUCTION

The Complement system is a phylogenetically conserved element which emerged about 600-700 million years ago, preceding antibody development, and evolved as a sophisticated, distinct and important part of the innate immune system, reflecting its relevance in protection against non-self. Several diseases involve improper activation of the Complement system (Alzheimer's disease; rheumatoid arthritis; multiple sclerosis, etc.). Hyperacute rejection of transplants, isquemia re-perfusion and others pathologies also take place with an unregulated response of this system. Unfortunately, only few drugs are available to treat disorders based on Complement system, and none of them can be administrated orally.[1]

Synthesis is one of the most relevant methodologies to opitmize the pharmacological profile of an active molecule. In this context, we have been able to produce new derivatives of filifolinol (**1**), a natural product structurally reminiscent of the well established Complement inhibitor K-76 (**2**, isolated form *Stachybotrys complementii*) and its acid derivative (**3**). We have synthesized (Figure 1) filifolinol derivatives modified on C3' and C7 with improved bioactivity (**4**-**6**).[2]

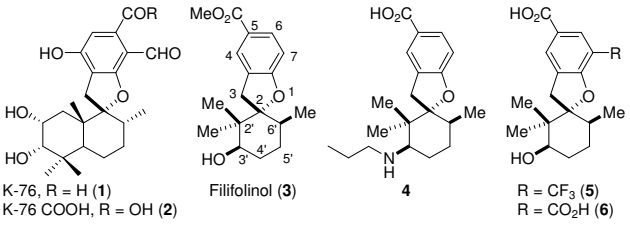
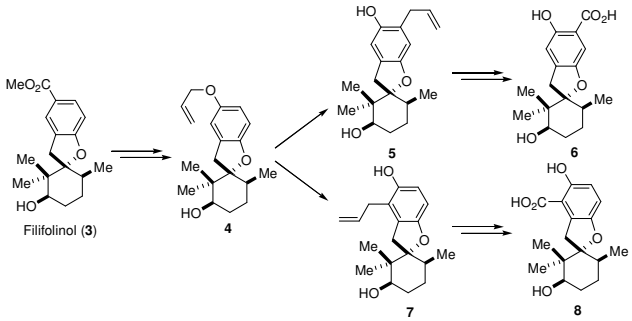


Figure 1. Complement inhibitors form natural and semisynthetic sources.

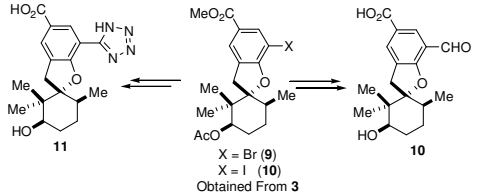
RESULTS AND DISCUSSION

Now, we would like to disclose our findings about new filifolinol derivatives modified on C4, C6 and C7.



Scheme 1. Modifications on positions C4 and C6.

Scheme 2 exhibits the modifications carried on C7.



Scheme 2. Modifications on positions C7.

CONCLUSION

The synthesis of new derivatives of Filifolinol, displaying interesting complement inhibitory activity was achieved.

ACKNOWLEDGEMENTS

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REFERENCES

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