Natural Product Scaffolds for the Synthesis of new Chemical Entities for Medicinal Chemistry

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In recent years, new chemical entities derived from natural products have gained importance in the search for therapeutic drugs.[1] In this context, we have investigated different carbon skeletons like Cucurbitanes, Cinnamates and Abietanes as a starting point or inspiration of our synthetic work.

Our research group is interested in the preparation of synthetic and semisynthetic analogues of bioactive compounds from natural sources with the aim of improving their biological activity and pharmacokinetical and pharmacological properties (ADME).

We designed analogues bearing modifications at different positions by substitution, elimination or by bioisosteric replacements, as well as by molecular simplification of the natural scaffold. To accomplish these changes we have worked with radical organic synthesis, difluoromethyl group insertion and nitrogen insertion by activation of C-H bond.

Depending on their structural features the different compound groups have different biological targets. In the case of cucurbitanes show cytotoxic and deterrent activities,[2-4] cinnamates have antioxidant and antimicrobial activities and abietanes show antimicrobial and trypanocidal activities.[5]

In this presentation, the latest results on the semisynthesis of cucurbitacin, cinnamate and abietane derivatives will be discussed, especially modifications of cucurbitacin B and dihydrocucurbitacin B, synthesis of difluomethyl cinnamates and dehydroabietic acid derivatives. Further results on the evaluation of the biological activities of the natural and semisynthetic compounds will also be presented.

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