Preparation of self-assembled 6,7-dehydroroyleanone nanoparticles

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6,7-dehydroroyleanone (**Figure 1**) is an abietane diterpene that can be isolated from *Plectranthus madagascariensis* Pers. Benth. var. *madagascariensis* essential oil, and has already shown significant cytotoxic activity against different tumoral cells [1].

In this work, the reactivity of the lead molecule was explored through its functionalization by the introduction of a proper linker on the C-12 hydroxyl group (12-OH) attached to a self-assembling inducer: squalene. Squalene is a natural precursor of many steroids and has shown the ability, when linked to biologically active compounds, to achieve a spontaneous formation of nanoassemblies in water [2].

As such, the introduction of a squalene-type chain using a labile linker, including a squalene conjugate with a labile disulfide bond (**Figure 2**) was performed through a Sterglich reaction.
The previously prepared monoester – obtained through the condensation and esterification of a dicarboxylic acid (ditiobutiric acid) with a squalene-type chain (1,1',2-tris-norsqualene alcohol) - was then used to be coupled with the abietane compound. 1D-NMR spectra was performed in order to confirm the structure of the obtained compound, and its results were then compared to the NMR spectra of the lead compound as well as the monoester.
Afterwards, the nanoparticles were prepared through the solvent displacement method: an organic solution was prepared by dissolving the compound in organic solvent to then be subjected to nanoprecipitation in water. After the addition of Milli-Q water, the organic solvent was removed in vacuo, thus assuring the presence of the compound in the aqueous phase.

In terms of physical characterization, the diameter (particle size) and polydispersity index (PI) of the diterpene conjugated nanoparticles were assessed by dynamic light scattering and its general toxicity assessed by the *Sacharomyces cerevisae* model.

Figures

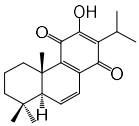

Figure 1: 6,7-dehydroroyleanone

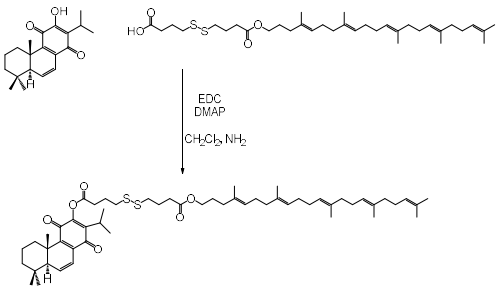

Figure 2: Conjugation of 6,7-dehydroroyleanone with squalene-type chain using a labile linker

References

[1] Catarina Garcia *et al.*, Future Medicinal Chemistry (2017), under review.

[2] Stella Borreli *et al.*, European Journal of Medicinal Chemistry, 85 (2014), 179-190