In silico ADMET profile of newly synthesized A-modified androstane derivatives

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INTRODUCTION

Steroids are a widespread class of natural organic compounds exhibiting important and diverse biological, chemical and pharmaceutical applications. Structural changes in the steroid skeleton can lead to the development of novel synthetic derivatives with anticancer activity [1]. For instance, the introduction of scaffolds possessing heteroatoms into the steroid nucleus represents a useful strategy for the development of new anticancer agents [2].

RESULTS AND DISCUSSION

New 2-cyanoacetohydrazide derivatives, in both 17α-picolyl (**1**) and 17a-homo lactone (**2**) series, were synthesized in reaction of the corresponding androst-4-en-3-ones with cyanoacetohydrazide and ammonium acetate (Scheme 1). New derivatives were characterized by NMR spectroscopy.

Scheme 1. a) $CNCH_2CONHNH_2$, $AcONH_4$, abs. EtOH, reflux, 8h or 13h.

In silico determination of physicochemical and ADMET properties were performed using SwissADME [3] and ProTox-II [4] web tools. Oral bioavailability radar (Fig. 1) provides the first information on whether a compound possesses desirable drug features, based on six physico-chemical properties of the compound: lipophilicity, size, polarity, solubility, flexibility and saturation.

According to this, all parameters for both synthesized compounds **1** and **2** are in the optimal range (pink area).

Figure 1. Oral bioavailability radar.

Further, the BOILED-Egg model (Fig. 2) predicts gastrointestinal absorption of both synthesized compounds (egg white), but not passage through the blood-brain barrier (yolk).

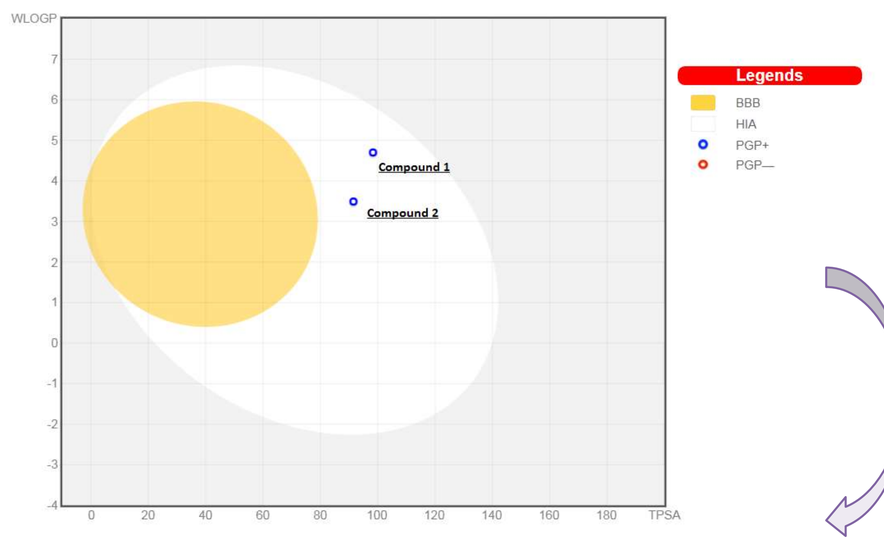

Figure 2. The BOILED-Egg model.

Finally, the predicted toxicity of the synthesized compounds indicates that both androstane derivatives do not have mutagenic and carcinogenic potential, but they possess immunotoxic potential.

CONCLUSION

Based on *in silico* ADMET analysis, it can be concluded that both steroid 2-cyanoacetohydrazide derivatives possess desirable drug properties with a satisfactory safety profile and that they are candidates for further *in vitro* tests.

References:

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[3] http://www.swissadme.ch/

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