In silico toxicity and ADME properties of new drug candidates based on the 2-quinolone scaffold

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The development of new therapeutic compounds is of great importance today due to the growing challenge of drug resistance. However, this process is complex, expensive, and time-consuming. Recently, *in silico* methods have been widely used to predict the toxicity of drug candidates and analyze their properties, such as Absorption, Distribution, Metabolism and Excretion (ADME), in a virtual environment, saving time and resources. This computational approach allows comprehensive evaluation of potential adverse effects and toxicity risks, enabling researchers to prioritize compounds with favorable safety profiles early in the development stage. In this study, we present an assessment of the ADME properties and toxicity of two novel hybrid molecules **A** and **B** incorporating 2-quinolone, 1,2,3-triazole and benzimidazole moieties in one scaffold, both displaying higher potency against *E. coli* compared to ampicillin. In terms of pharmacokinetics, compounds **A** and **B** have high gastrointestinal absorption and demonstrated a non-blood-brain barrier permanent, indicating low risk of neurological side effects. The *in silico* toxicity prediction showed that hybrids A and B are not cytotoxic nor carcinogenic, and don't interact with mitochondrial membrane potential (MMP). Nevertheless, both compounds were predicted to be mildly hepatotoxic and mutagenic with probabilities of 0.50-0.52. Moreover, **A** and **B** were found to be immunotoxic with the probability score of 0.97. Additionally, the tested derivatives **A** and **B** showed LD_{50} with 1000 mg/kg and thus belong to class IV in toxicity. The results obtained provide a foundation for advancing further research and the development of innovative antibiotic drugs with enhanced efficacy and reduced toxicity.

Keywords: toxicity; ADME; drug; quinolone