SYNTHESIS AND ADMET EVALUATION OF CHLOROPYRIDINE-BASEDHYDRAZONE DERIVATIVES

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Nitrogen-containing heterocycles are widely used in medicinal chemistry due to their presence in numerous biologically active compounds and approved drugs [1]. Among these, pyridine derivatives have attracted attention because of their favourable physicochemical properties and compatibility with a variety of pharmacological targets. Hydrazide and hydrazone functionalities are also well known for their biological relevance and are frequently explored as key structural motifs in the design of potential drug candidates [2,3].

In this study, a series of chloropyridine-based hydrazone derivatives were synthesized starting from 2-amino-5-chloropyridine. The reaction of the aminopyridine with acrylic acid in toluene under reflux conditions led to the formation of the corresponding β-alanine derivative. Its subsequent treatment with hydrazine monohydrate afforded the desired hydrazide, which further reacted with various aromatic and heteroaromatic aldehydes in methanol to yield a set of novel hydrazone derivatives. The synthesized compounds, bearing different aromatic substituents such as unsubstituted phenyl, halogenated phenyl, methoxyphenyl, and heteroaromatic moieties, were obtained in good yields and were characterized by standard spectroscopic methods.

To compare the drug-likeness and predict pharmacokinetic behaviour of the synthesized hydrazones, their *in silico* ADMET analysis was performed. The molecular weights of the evaluated compounds were in the range of 300 – 395 Da, and calculated LogP values ranged from 2.78 to 4.20, indicating moderate lipophilicity across the series. Topological polar surface area values remained below 100 $Å^2$ for all the derivatives. The differences in predicted blood-brain barrier permeability were observed depending on the aromatic substituent, with hydrazones bearing unsubstituted or less polar aromatic groups showing a higher likelihood of BBB penetration, while compounds containing more polar or heteroaromatic substituents were classified as non-BBB permeant. Human intestinal absorption and Caco-2 permeability predictions were comparable among the compounds, suggesting similar intestinal transport characteristics despite structural variation.

Overall, the synthesized chloropyridine-based hydrazone derivatives display suitable *in silico* drug-likeness and pharmacokinetic profiles. These results support their further evaluation in future biological studies.

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