

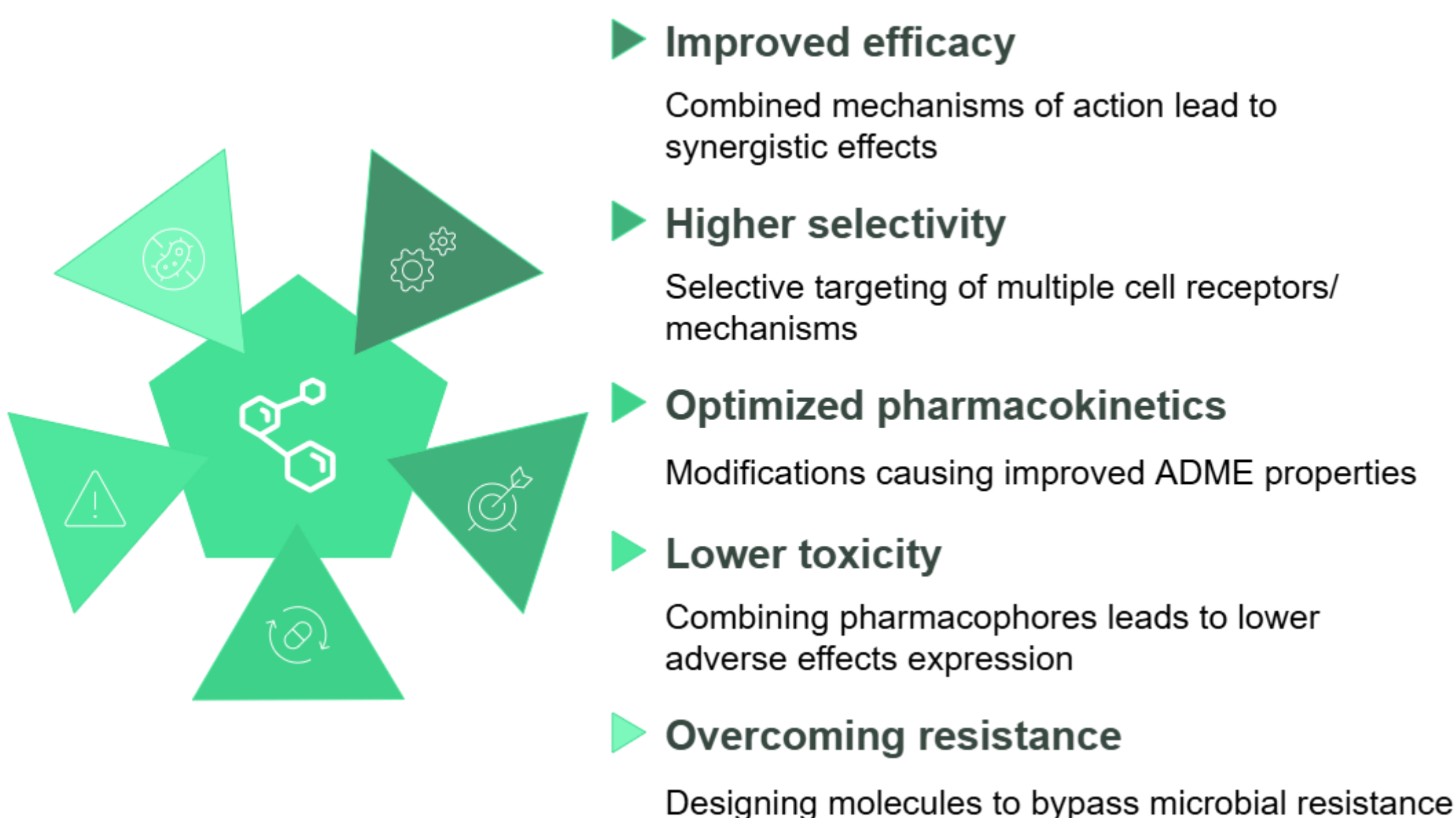
Structure-Based Design and Synthesis of Novel Hybrid Molecules Derived from Anthranilic Acid as Drug Candidates

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INTRODUCTION & AIM

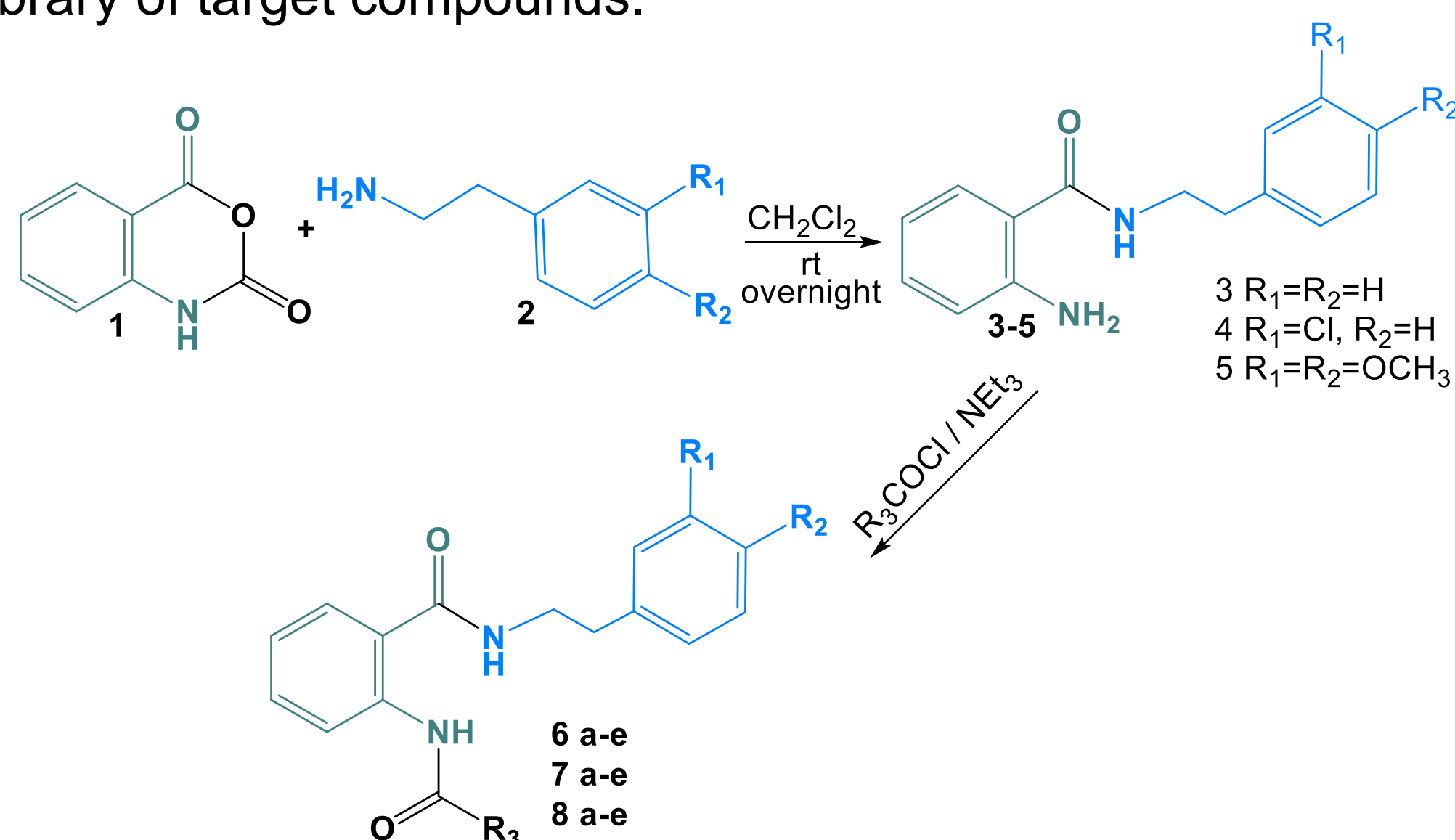
Modern drug discovery increasingly relies on molecular hybridization, a strategy in which two or more pharmacophoric elements are combined into a single scaffold. This approach enables modulation of multiple biological targets simultaneously, potentially yielding compounds with improved selectivity, synergistic efficacy, and reduced side effects, compared to single-target agents. Recent reviews have highlighted that hybrid molecules are especially promising in tackling complex, multifactorial diseases such as inflammation, cancer, metabolic syndrome, and neurodegeneration [1,2].



In this context, our study aims to design and synthesize novel anthranilic acid-based hybrid molecules that not only retain the broad spectrum of biological activities associated with anthranilic analogues, but also exhibit improved pharmacokinetic and pharmacodynamic properties through rational hybrid design and *in silico* filtering.

METHOD

A combination of cheminformatics tools (SwissADME, PASS Online, ProTox 3.0) was used to guide the design of a focused library of target compounds.

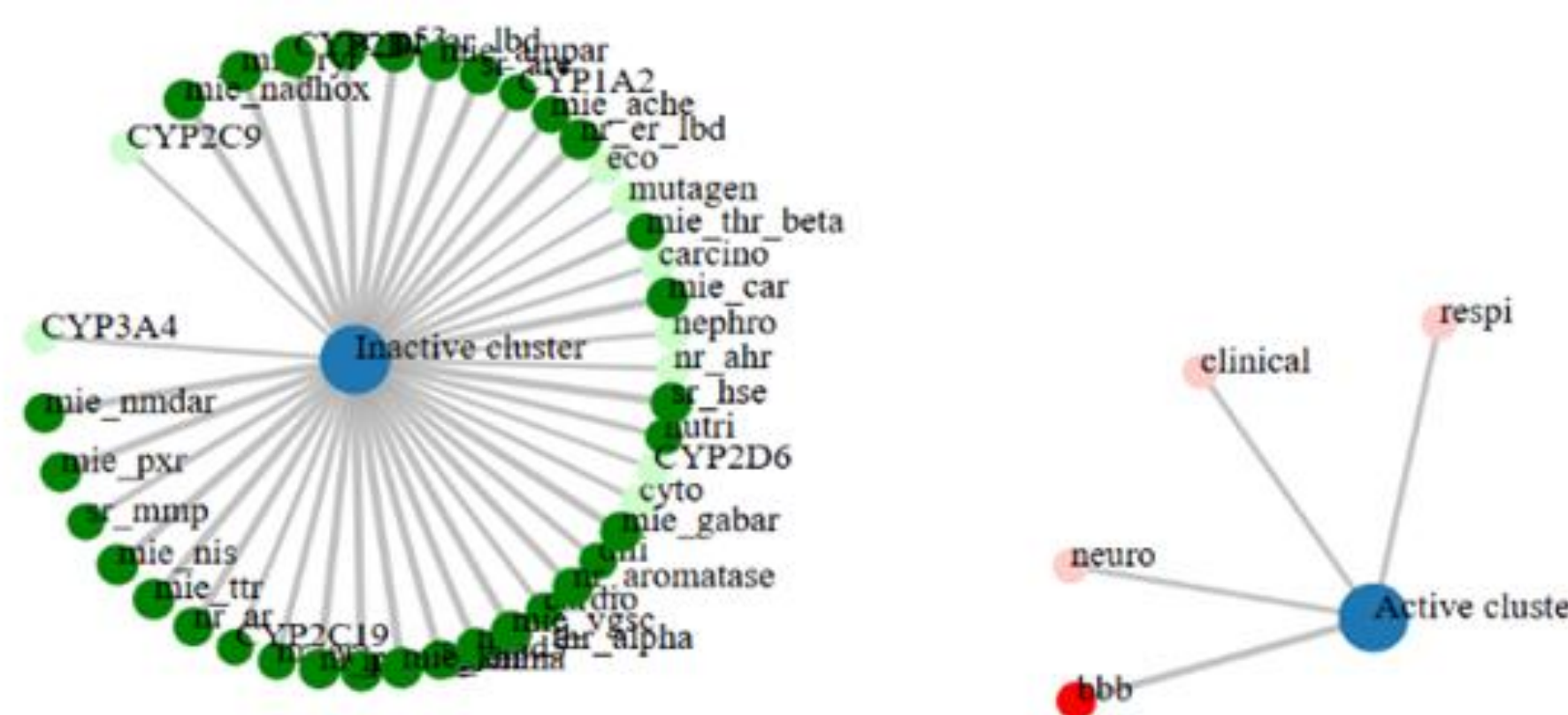


All compounds were obtained following the above synthetic scheme, purified and characterized using standard spectroscopic techniques, including NMR, IR, and HRMS, and melting point temperature determination.

RESULTS & DISCUSSION

The applied *in silico* approaches generated a comprehensive dataset on the physicochemical, pharmacokinetic, and toxicological profiles of the tested structures. After analyzing the key parameters, three phenylethylanthranilamide compounds and their diamide derivatives were identified as the most promising candidates. The hybrid compounds were synthesized in good yields (78–83%), purified, and spectroscopically characterized [3–5].

Preliminary toxicity assessment placed the compounds in toxicity class 4, with calculated LD₅₀ values ranging from 1000 to 2025 mg/kg. The SwissADME tool confirmed overall organ safety, yet predicted 70% probability of respiratory and neurotoxicity. In this study, these findings are interpreted as potentially favorable, since BBB penetration is a desired feature for potential therapeutic applications. Comparable or even higher toxicity levels have been reported for clinically used drugs in this therapeutic area, suggesting that the investigated structures remain within an acceptable safety range for further pharmacological exploration.



Toxicity calculation results for compound **6b**, obtained with SwissADME.

CONCLUSION

The resulting hybrid structures integrate multiple pharmacophores and demonstrate favorable predicted ADME properties and toxicity, suggesting promising drug-likeness. The synthetic procedures were efficient and reproducible, yielding structurally confirmed compounds ready for further biological exploration.

Combining rational design and synthetic precision, this work provides a strong foundation for developing new small molecules for the treatment of smooth muscle dysfunction and inflammation, with planned evaluation in disease-relevant biological models to guide their translation into drug candidates.

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