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YST029 - PYRRO-3: IN SILICO STUDY OF A MULTI-TARGET INHIBITOR

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ABSTRACT

Hypertension, diabetes, and bacterial infections are major global health problems, and patients with more than one of these conditions often require multiple medications. This increases cost, inconvenience, and the potential of side effects. A promising solution is a single compound hitting multiple diseases. This project conducted a virtual screening of pyrrolidine-based compounds to assess their potential as multi-target inhibitors for three key targets: angiotensin-converting enzyme (ACE) to reduce blood pressure, α-amylase to control blood sugar, and bacterial enzymes to combat infections. Pyrrolidine is well-known in medicinal chemistry for its wide range of biological activities. However, its possible role as a multi-target inhibitor is underexplored, especially through computational studies. Using molecular docking, several promising candidates were identified with strong predicted binding to all three targets. This study employs computational screening that provides a faster, more cost-effective, and greener path for the early stage of drug discovery. The findings provide valuable leads for the pharmaceutical industry, supporting the development of broad-spectrum therapeutics to improve treatment for patients with multiple health problems.

Keywords – docking, pyrrolidine, ACE, antidiabetic, antibacterial

INTRODUCTION

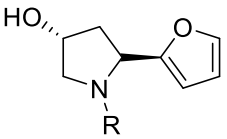
Pyrrolidine-based compounds are one of the important scaffolds in contemporary drug development due to their conformational adaptability and the potential to engage in hydrogen bonding. This versatile nitrogen heterocycle is known for its inhibition properties for the treatment of diabetes, hypertension, cancer, and bacterial infections (Seema et al., 2025). Patients who suffer from more than one of these conditions often require multiple medications, which can be costly, inconvenient, and may cause side effects from drug interactions. Thus, it is important to develop a single compound that can target multiple diseases. However, incorporating a computational approach with experimental design for the development of pyrrolidine-based compounds as drug candidates for the multi-target inhibitor is scarce. Furthermore, pyrrolidine rings are present in at least 37 FDA-approved drugs from different therapeutic classes, indicating their central role in medicinal chemistry (Li Petri et al., 2021).

OBJECTIVE

This project aims to perform virtual screening of a designed library of pyrrolidine derivatives against three different targets (ACE, α-amylase, and *E. coli*) through a molecular docking study using Autodock Vina (Troot & Olson, 2010).

DESCRIPTION OF THE PROJECT

This project investigates the potential of pyrrolidine-based compounds for multi-target inhibition of α-amylase, ACE, and bacterial enzymes (*E. Coli*). The core structure of the studied compound is given in Figure 1, and the binding energy from the docking study is tabulated in Table 1.



R = H, CH_3, $CH_2CH_2CH_3$, C_6H_5, CH_2CH_2OH

Figure 1: The core structure of the target pyrrolidine derivatives

Table 1: Binding energy of pyrrolidine derivatives against ACE (PDB ID: 1O86), α-amylase (PDB ID: 2QV4), and *E. Coli* (PDB ID: 1W3R).

Derivatives	Binding energy (kcal)		
	ACE	α-amylase	Antibacterial
H	-5.2	-5.6	-3.6
CH_3	-5.4	-5.4	-3.5
$CH_2CH_2CH_3$	-5.7	-5.7	-3.7
C_6H_5	-7.0	-6.8	-4.2
CH_2CH_2OH	-5.6	-5.8	-3.7
Standard	-5.3 (captopril)	-5.5 (miglitol)	-5.1 (norfloxacin)

NOVELTY

This project explores the multi-target potential of the design compounds, whereas other studies focus on a single target. The virtual screening approach employed in this work promotes early leads for pharmaceutical development and a green approach to drug discovery, thereby reducing cost, time, and use of harmful chemicals. If it could be commercialized in the later stage, it would reduce patient burden and risk of side effects.

CONCLUSION

The designed pyrrolidine derivatives exhibit a strong binding energy against ACE and α-amylase compared to their standard drugs, captopril and miglitol, respectively. Derivatives

with a phenyl group emerge as a promising multi-target inhibitor due to the highest binding energy among others.

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