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In Silico Design and Discovery of Novel 2-pyrazoline Methanone Derivatives as Antioxidant Agents for Cosmetic Applications: A Bioinformatics Analysis and Molecular Docking Study

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INTRODUCTION & AIM

The cosmetic industry is actively looking for innovative compounds to combat oxidative stress and prevent premature aging, with a specific focus on the role of antioxidants [1,2]. There is a trend towards using natural and synthetic antioxidants in cosmetic formulations due to increasing consumer awareness and demand for effective anti-aging products [2].

2-pyrazoline derivatives have emerged as a versatile and promising class of compounds with a wide range of biological activities, including potential antioxidant properties. This family of compounds has been extensively studied for various potential applications, such as antidepressant, antimalarial, and anticancer properties [3]. Their versatility suggests potential for application in cosmetic science, particularly as antioxidant agents.

The development of new cosmetic ingredients traditionally involves time-consuming and costly experimental processes. However, the advent of *in silico* design and molecular docking studies has revolutionized the field of drug discovery and cosmetic science [4].

The present study aims to leverage these advanced computational techniques to design and discover novel 2-pyrazoline methanone derivatives as potential antioxidant agents for cosmetic applications. By employing a comprehensive bioinformatics analysis and molecular docking approach, we seek to identify compounds with optimal binding affinities to Human erythrocyte catalase, a key enzyme in the antioxidant defense system.

METHOD

2D Structure creation and 3D Optimization

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***In Silico* ADME and Toxicity Predictions**

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Ligands and Enzymes Preparation

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Molecular Docking Simulations

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Post-Docking Analysis

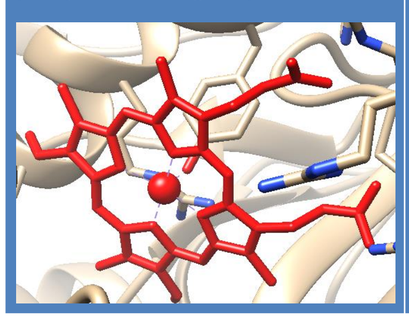
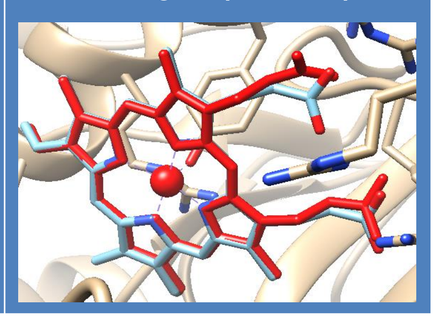
RESULTS & DISCUSSION

Table 1: Analysis of theoretical oral bioavailability of the designed compounds based on Lipinski's rule of five, GI absorption, predicted LD_{50} and Toxicity Class

Compound ID	Lipinski's rule of five[b]							
	Mol.Wt[a]	HbA	HbD	MLogP	GI	Inference	LD_{50}	Toxicity class
P25	420.89	4	0	3.89	High	Pass	1000mg/kg	IV
P27	450.91	5	0	3.55	High	Pass	1000mg/kg	IV
P28	455.33	4	0	4.36	High	Pass	1000mg/kg	IV
P29	395.28	2	0	5.1	High	Pass	1000mg/kg	IV
P30	485.36	5	0	4.02	High	Pass	1000mg/kg	IV
P31	431.44	6	0	2.5	High	Pass	1000mg/kg	IV
P33	461.47	7	0	2.2	High	Pass	1000mg/kg	IV
P34	404.43	5	0	3.79	High	Pass	1880mg/kg	IV
P37	370.4	4	0	3.61	High	Pass	1660mg/kg	IV

[a] Molecular weight in g/mol, [b] [5] (Mwt≤500, MLogP≤4.15, N or O≤10, NH and OH≤5) and LD_{50}= Lethal dose 50

Table 2: Displays the crystal structure of enzyme complexes with the re-docked ligand superimposed on the crystal structure for validation purposes

Crystal structure complex (Enzyme and Ligand)	Crystal structure complex with Re-docked ligand (Validation)
	

The cyan-blue colored molecule represents the re-docked ligand, while the red colored molecule indicates the co-crystallized ligand

Table 3: Binding affinity of the designed 2-pyrzoline methanone compounds against the target enzyme

Compound code	Human erythrocyte catalase (1DGB) kcal/mol
HEM	-14.1
P25	-10.4
P27	-10.5
P28	-10.4
P29	-10.3
P30	-10.6
P31	-9.9
P33	-10.2
P34	-10.4
P37	-8.7

HEM= co-crystalized ligand

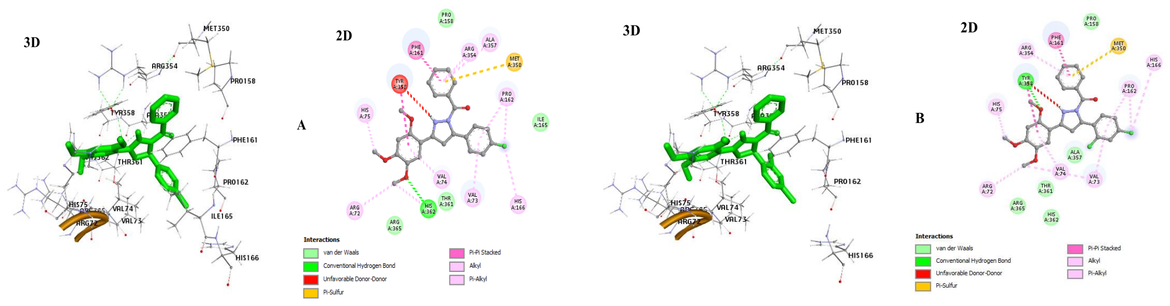


Figure 1: 3D and 2D Binding Pose Interaction of P27 (A) and P30 (B) at the Binding Site of Human Erythrocyte Catalase

CONCLUSION

This study presents a comprehensive *in silico* design and discovery of novel 2-pyrazoline methanone derivatives as potential antioxidant agents for cosmetic applications. Through a rigorous bioinformatics analysis and molecular docking study, we have identified promising compounds that exhibit strong binding affinities to Human erythrocyte catalase, a key enzyme in the antioxidant defense system.

FUTURE WORK / REFERENCES

Future research should focus on *in vitro* and in vivo studies to assess the actual performance of these derivatives in biological systems.

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