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Screening Methods for Organic Acids: Based on Skin Protein Receptors and Molecular Docking Techniques

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1. Introduction

Organic acids are core functional components in cosmetics, possessing effects such as regulating pH, treating acne, and controlling oil [1,2]. However, in current cosmetic formulations, the selection and optimization of organic acids rely on experience and repeated trials, which are costly, time - consuming, and difficult to fully explore their potential.

In recent years, molecular docking technology has achieved remarkable success in the field of drug design [3]. By simulating the fine interactions between molecules through computers, it can accurately predict the binding modes and affinities between small molecules and macromolecular targets. Although the application of this technology in the cosmetics field is still in the initial exploration stage, especially the practice in the optimization of organic acids is still relatively rare, with the rapid development of artificial intelligence and machine learning technologies, there is great potential in using these cutting - edge technologies to optimize cosmetic formulations [4].

In this study, based on the molecular docking technology of computational chemistry theory, accurately and effectively identifies organic acids with high affinity for skin protein receptors, and then constructs a more targeted combination of organic acids.

2. Materials and Methods

2.1 Molecular Docking Software and Databases

The software and databases involved in this article include ChemDraw, OpenBabel, AutoDockTools, PyMol, Origin, etc.; biological activity databases of organic small molecules such as Pubchem, target prediction/detection database PDB, protein database Uniprot, efficacy target collection databases such as NCBI and GeneCards, etc.

2.2 Molecular Docking Method

Download the three-dimensional structure of organic acids in SDF format from the PubChem database, and convert it to mol2 format using the OpenBabel software. Meanwhile, obtain the structure files of three receptor proteins, namely 5 α -reductase, tyrosinase, and desmocollinase, from the UniProt database, and then perform molecular docking using AutoDockTools. If the binding energy between the receptor and the ligand is negative, it indicates that the docking can occur spontaneously. If the binding energy is positive, it means

that the docking is unsuccessful. Finally, use the Origin software to draw a heatmap, and use the PyMol software to visualize the docking results.

2.3 Docking Contents

Information of small molecule organic acid ligands (Table 1): Lactic acid, azelaic acid, salicylic acid, glycolic acid, tartaric acid, malic acid, gluconolactone and lactobionic acid;

Macromolecular skin protein receptors (Table 2): 5 α -reductase, tyrosinase and desmocollinase.

Table 1. Information of macromolecular skin protein receptors

skin protein receptors	UniProt ID	Entry name	Resolution of the structure (Å)
5 α -reductase	P18405	S5A1_HUMAN	2.70
tyrosinase	P14679	TYRO_HUMAN	2.54
desmocollinase	Q08188	TGM3_HUMAN	2.10

Table 2. Information of small molecule organic acid ligands

Ligant	CAS	Pubchem CID
Lactic Acid	50-21-5	612
Azelaic Acid	123-99-9	2266
Salicylic Acid	69-72-7	338
Hydroxyacetic Acid	79-14-1	757
Tartaric Acid	133-37-9	875
Malic Acid	6915-15-7	525
Gluconolactone	90-80-2	7027
Lactobionic Acid	96-82-2	7314

3. Results

3.1 Docking Results of Organic Acids and Skin Protein Receptors

The docking results of organic acids and skin protein receptors are presented in Table 3. The binding energies of various organic acids to different skin targets, ordered from the smallest to the largest, are as follows: For 5 α - reductase, the binding energies are arranged as follows: salicylic acid was found to have a binding energy of -4.02 kCal/mol, lactic acid -3.24 kCal/mol, azelaic acid -3.21 kCal/mol, gluconolactone -3.15 kCal/mol, glycolic acid -2.94 kCal/mol, tartaric acid -2.86 kCal/mol, malic acid -2.22 kCal/mol, and lactobionic acid 1.33 kCal/mol. For tyrosinase, it was observed that lactic acid had a binding energy of -4.3 kCal/mol, azelaic acid -3.29 kCal/mol, salicylic acid -3.08 kCal/mol, tartaric acid -2.87 kCal/mol, malic acid -2.66 kCal/mol, gluconolactone -2.55 kCal/mol, glycolic acid -2.29 kCal/mol, and lactobionic acid 1.64 kCal/mol. For desmocollinase, azelaic acid was determined to have a binding energy of -5.08 kCal/mol, desmocollinase -4.67 kCal/mol, lactic acid -4.47 kCal/mol, gluconolactone -4.19 kCal/mol, glycolic acid -3.05 kCal/mol, malic acid -2.94 kCal/mol, tartaric acid -2.41 kCal/mol, and lactobionic acid 43.15 kCal/mol.

The heatmap of the docking results of organic acids and skin protein receptors is shown in Figure 1. It is noted that the darker the color in the heatmap, the better the molecular docking result.

Table 3. Binding energies of docking between organic acids and skin protein receptors

Docking score		Binding energy, kCal/mol						
Ligant								
Skin protein receptors	Lactic Acid	Azelaic Acid	Salicylic Acid	Hydroxy acetic Acid	Tartaric Acid	Malic Acid	Gluconol actone	Lactobionic Acid
5α-reductase	-3.24	-3.21	-4.02	-2.94	-2.86	-2.22	-3.15	1.33
Tyrosinase	-4.3	-3.29	-3.08	-2.29	-2.87	-2.66	-2.55	1.64
Desmocollinase	-4.47	-5.08	-4.67	-3.05	-2.41	-2.94	-4.19	43.15

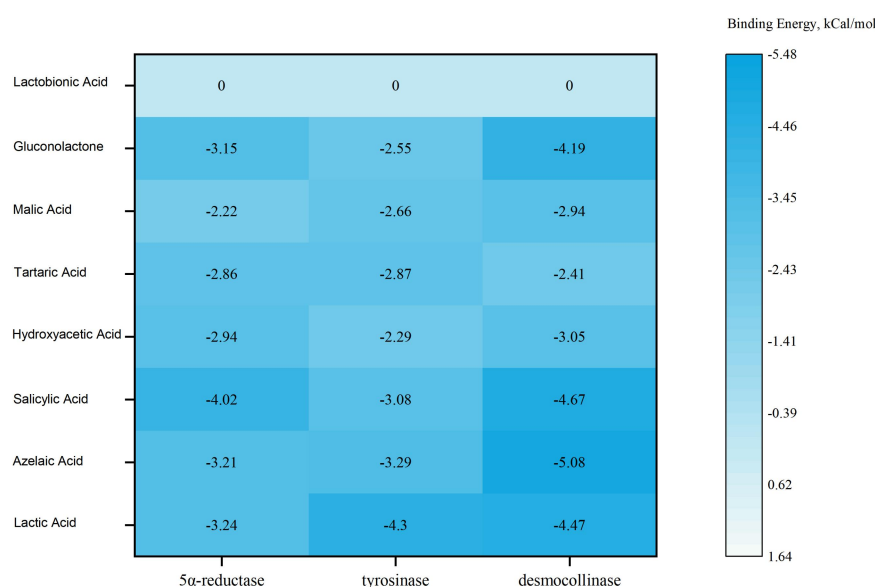


Figure 1 Heatmap of the binding energies of docking between organic acids and skin protein receptors. *A binding energy ≥ 0 kCal/mol indicates that there is no binding between molecules, and the docking score is set to 0 for the heatmap plotting.

3.2 Visualization Examples of Molecular Docking Results of Organic Acids

The molecular docking results of organic acids, visualized using PyMOL software, are presented in Figure 2. In Figure 2A, it is indicated by the visualized molecular docking results between salicylic acid and 5 α -reductase that salicylic acid is precisely bound to the active site of 5 α -reductase. The benzene ring structure of salicylic acid is found to form hydrophobic interactions with the hydrophobic amino acid residues within the active site of 5 α -reductase, allowing stable embedding into the hydrophobic pocket of the active site. Meanwhile, hydrogen bonds are formed between the hydroxyl group of salicylic acid and the polar amino acid residue (GLN-20) near the active site, with bond lengths of 2.8 Å and 3.1 Å, respectively, by which the binding stability between the two is enhanced. In Figure 2B, the visualized molecular docking results between lactic acid and tyrosinase demonstrate that lactic acid is bound to the active site region of tyrosinase in a specific spatial conformation. The carboxyl

group of the lactic acid molecule is observed to interact with the polar amino acid residues (ASP-30, ARG-6) within the active site of tyrosinase through hydrogen bonds, with bond lengths of 1.8 Å and 1.9 Å, as well as 1.9 Å and 2.2 Å, respectively. Strong directionality and stability for the binding between the two are provided by this polar interaction. In Figure 2C, the visualized molecular docking results between azelaic acid and desmocollinase show that azelaic acid is bound to the active site region of desmocollinase in a specific spatial conformation. The carboxyl group of the azelaic acid molecule is found to interact with the polar amino acid residues (THR-294, VAL-292, ILE-161) within the active site of desmocollinase through hydrogen bonds, with bond lengths of 1.9 Å, 2.3 Å, and 2.5 Å, respectively. Strong directionality and stability for the binding between the two are conferred by this polar interaction.

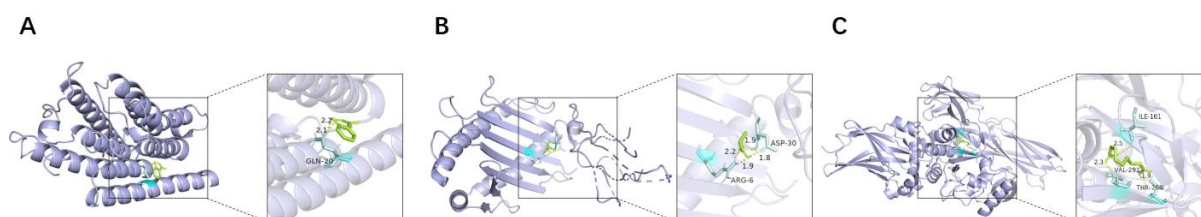


Figure 2 The visualized diagrams of molecular docking for salicylic acid - 5 α -reductase (A), lactic acid - tyrosinase (B), and azelaic acid - desmocollinase (C), which have been processed by PyMOL. *Amino acid abbreviation, GLN: Glutamine; ASP: Aspartic acid; ARG: Arginine; THR: Threonine; VAL: Valine; ILE: Isoleucine.

4. Discussion

In this study, the molecular docking technology based on the theory of computational chemistry was applied to the field of organic acid screening. This technology provides a powerful and forward-looking tool for the screening of functional ingredients in cosmetics, showing great potential in the field of cosmetic raw material screening. It can not only improve the efficiency and accuracy of organic acid screening, help to construct more targeted combinations of organic acids, but also drive the research and development of cosmetics into a new era of precision and high efficiency.

5. Conclusion

In this study, based on the molecular docking technology of computational chemistry theory, accurately and effectively identifies organic acids with high affinity for skin protein receptors, and then constructs a more targeted combination of organic acids.

References

1. Tang, S C, Yang J H. Dual effects of alpha-hydroxy acids on the skin[J]. *Molecules*, 2018, 23(4): 863.
2. Panchal P, Miller A J, Giri J. Organic acids: versatile stress-response roles in plants[J]. *Journal of Experimental Botany*, 2021, 72(11): 4038-4052.
3. Wu G, Robertson D H, Iii C L B, et al. Detailed analysis of grid-based molecular docking: A case study of CDOCKER-A CHARMM-based MD docking algorithm[J]. *Journal of Computational Chemistry*, 2010, 24(13): 1549-1562.

4.Kokcu Y, Kecel-Gunduz S, Budama-Kilinc Y, et al. Structural analysis, molecular dynamics and docking calculations of skin-protective tripeptides and design, characterization and cytotoxicity studies of their PLGA nanoparticles[J]. Journal of Molecular Structure, 2020, 1200: 127046.