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In Silico Evaluation of the Potential for the Rational Use of Garlic and Onion Crop Residue Extracts in Cosmetics †

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Abstract: The crop residue after harvesting onion (*Allium cepa*) and garlic (*Allium sativum*) has a great potential in the development of value-added products due to presence of a range of bioactive compounds. A potential of compounds identified in the crop residue extracts to be used in cosmetics was evaluated in silico, including prediction of their interactions with selected skin target proteins (SIRT1, TGF-β and elastase). Molecular docking results obtained using AutoDock Vina revealed that stronger binding affinity was observed between TGF-β protein and small molecules such as rutin and procyanidin A2, compared to the elastase. On the other side, SIRT1 protein showed the best interaction with quercetin and kaempferol. Potential side effects on the skin of individual molecules in extracts of garlic and onion were predicted using regulated databases for skin sensitization tests (Ambit, SkinSensDB, Danish QSAR Database, Skin Doctor CP). These in silico predictions have shown that the most active molecules are not irritating or corrosive to the skin. The obtained results indicate a significant potential for the use of crop residue extracts in the development of skincare products from the sustainable resources while addressing the issues of waste.

Keywords: molecular docking; crop residues; skin sensitization; cosmetics

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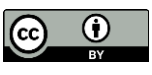

1. Introduction

Global environmental issues related to industrial food processing increases the need to use bio-sustainable and eco-friendly alternatives [1]. The "green" approach emphasizes the importance of renewable products, in particular the value of ingredients derived from natural sources [1]. One of the great ways to improve resource utilization is to recycle biodegradable waste, crop residue or crop by-products and process these natural raw materials for the development of value-added products [2]. Due to the biological nature of products obtained after crop processing, any part of such waste material could be considered potentially useful due to their potential pharmacological activities [1]. Notably, an onion and garlic are known for their use in numerous therapeutic and medicinal purposes [3], that also can have a potential use in cosmetic formulations [1].

Nevertheless, developing cosmetic products can be a time-consuming and expensive process. Hence, in silico experiments offer a cost-effective and efficient way to investigate the therapeutic potential of natural products, before carrying out laboratory experiments [4]. For instance, docking-based virtual screening may be used to evaluate the binding affinities of components of crop residue extracts to the target proteins, thereby eliminating inactive molecules, and this can significantly reduce the number of experiments and speed

up research [4]. Moreover, in silico tools are effective in toxicity prediction, facilitating the exclusion of individual components with potentially harmful effects [4].

Our molecular docking study explores a potential of molecules identified in garlic/onion extracts to interact with selected proteins (SIRT1 (sirtuin 1), TGF-β (transforming growth factor beta) and elastase) known to be involved in skin ageing process. Additionally, potential adverse skin effects of each molecule identified in extracts of garlic and onion were evaluated using databases and web tools for skin sensitization tests.

2. Materials and Methods

2.1. The Extraction Method for Onion (Allium cepa) and Garlic (Allium sativum)

The extraction of garlic and onion was performed using a subcritical water extraction (SWE). The chemical composition of these extracts was then evaluated using high-performance liquid chromatography (HPLC).

2.2. Structure Preparation of Ligands and Proteins

The three-dimensional structures of elastase (PDB ID: 1ELB), SIRT1 (PDB ID: 4I5I), and TGF-β (PDB ID: 1vjy) were downloaded from the RCSB Protein Data Bank. The solvent molecules were removed from all selected protein structures before computational studies and missing hydrogens added using VegaZZ software. The isomeric SMILES strings of compounds found in extracts of garlic and onion (unpublished results) were obtained from the PubChem database (https://pubchem.ncbi.nlm.nih.gov). The SMILES strings of selected compounds were converted into mol2 format using VEGA ZZ 3.2.3. Likewise, fixing atomic potentials and assigning atom charges of ligands was performed in VEGA ZZ 3.2.3 software.

2.3. Computational Studies—Ligands and Proteins Preparation

Virtual screening studies were executed by AutoDock Vina software with VegaZZ software as graphical user interface. The crystalized ligand of each protein structure was used to define the docking site. The dimensions of the grid box size were equally set to 24 Å for all three proteins. The grid centers (x, y, and z) coordinates had the following values: (a) 40, 22, and 38 (elastase), (b) 43, -21, and 20 (SIRT1), and (c) 16, 68, and 6 (TGF-β). The exhaustiveness value was set to 50, while the binding modes value was set to 5. All screened compounds were ranked by binding energy (in kcal/mol) based on the AutoDock Vina scoring function (a more negative value indicates higher binding affinity). The TGF-β docked complexes with the lowest AutoDock Vina docking score were chosen as the initial configuration to display significant interactions with residues in the enzyme binding site. In addition, the 2D diagram of protein–ligand interactions were verified using the Discovery Studio Visualizer program.

3. Results and Discussion

3.1. Molecular Docking

3.1.1. Binding Affinity

In order to predict the potential of bioactive molecules identified in garlic and onion extracts against three selected skin enzymes (elastase, SIRT1 and TGF-β), molecular docking was performed using AutoDock Vina software. Chemical analysis of an onion and garlic extracts revealed that these plants are abundant in polyphenols and the docking scores of representative compounds with the target enzymes are presented in Table 1 and Table 2, where lower values indicate better binding. Generally, selected compounds identified in garlic and onion extracts displayed lower docking scores for elastase and SIRT1. Notably, rutin and procyanidine A2 showed higher binding affinity against TGF-β (−10.8 and −9.5 kcal/mol, respectively) and elastase (−7.9 and −8.3 kcal/mol, respectively), while against SIRT1 exhibited very low binding scores (–4.7 and 16.4 kcal/mol, respectively)

compared to the other compounds. From the perspective of docking scores, these two polyphenols have gained considerable attention in this study since they showed the greatest ability to bind to skin-related proteins, in particular TGF-β enzyme.

Table 1. AutoDock Vina docking scores of potential bioactive compounds from *Allium cepa* extract toward elastase, SIRT1 and TGF-β.

Selected Compounds	Binding Affinity to Skin Target Proteins [1]		
	elastase	SIRT1	TGF-β
procyanidin A2	−8.3	16.4	−9.5
procyanidin B2	−7	3.2	−8.7
caffeic acid	−5.2	−8.2	−7
7-hydroxy-coumarin	−5.6	−8.4	−6.9
quercetin	−6.4	−8.9	−9.2

[1] AutoDock Vina score in kcal/mol.

Table 2. AutoDock Vina docking scores of potential bioactive compounds from *Allium sativum* extract toward elastase, SIRT1 and TGF-β.

Selected Compounds	Binding Affinity to Skin Target Proteins [1]		
	elastase	SIRT1	TGF-β
rutin	−7.9	−4.7	−10.8
kaempferol	−6.4	−8.8	−9.2
epigallocatechin	−6.4	−8.6	−9.2
epicatechin	−6.3	−8.6	−9.2
catechin	−6.3	−8.6	−9.2

[1] AutoDock Vina score in kcal/mol.

3.1.2. 2D Interaction Diagrams

To provide additional insight, we analysed interactions of selected ligands with skin target enzymes. The protein–ligand interactions of the most favourable complexes were presented in 2D diagrams (Figure 1).

Figure 1 illustrates the 2D representations of the most favourable binding pose of rutin (3A), procyanidin A2 (3B), kaempferol (3C) and quercetin (3D) on the TGF-β catalytic domain, since the binding affinity to this protein showed the best results. The most stable conformation of these ligands displayed interactions with several amino acid residues in the enzyme binding pocket, such as Lys232, Asp351 and Glu245, which is supported by interactions that have already been indicated as most important in the crystal structure of the inhibitor [5]. These interactions involve Pi-alkyl and conventional hydrogen bonding and it clearly indicates the possibility of partial inhibition of the enzyme TGF-β by rutin, procyanidin A2, kaempferol and quercetin. Furthermore, it is well known that polyphenols are widely used in cosmetic products and they exhibit valuable bioactivity such as antioxidative, anti-ageing, photoprotective [6]. Therefore, our preliminary in silico calculations provide promising results which may be beneficial in the development of skincare products.

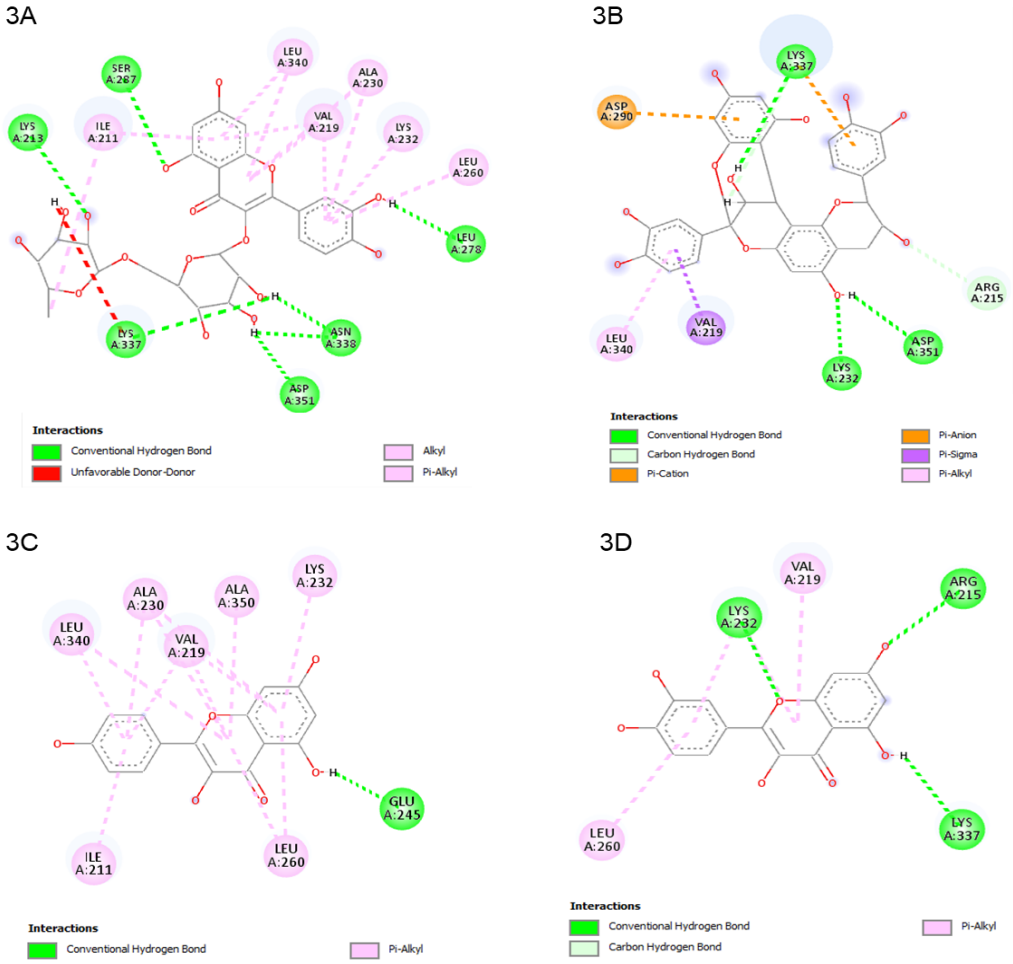

Figure 1. 2D interaction diagrams of the most favorable bioactive compounds ((3A) rutin, (3B) procyanidin A2, (3C) kaempferol and (3D) quercetin) from an onion and garlic extracts toward TGF-β.

3.2. Skin Sensitization Prediction Tools

The toxicity prediction of selected bioactive molecules found in an onion/garlic extract has been investigated using regulated databases through skin sensitization tests (Ambit, SkinSensDB, Danish QSAR Database, Skin Doctor CP) [7–10]. By screening the most active molecules, it was confirmed that rutin and procyanidin A2 are not irritating or corrosive to the skin, while SkinSensDB and Skin Doctor CP test reported quercetin, epicatechin and catechin as non-sensitizer.

4. Conclusions

In summary, in this computational study we examined the binding affinity of different polyphenols identified in garlic and onion extracts to skin target proteins (elastase, SIRT1 and TGF-β). Preliminary results indicated that the most favorable docking scores in AutoDock Vina were achieved between selected molecules present in both extracts and TGF-β protein. Additionally, all molecules have a potential to act as inhibitors of all three proteins to various degree allowing possible use of extracts in preparations with synergistic anti-ageing action. Moreover, the safety of most ot the active molecules has been computationaly investigated using available skin sensitization tests. This type of analysis showed no side effects on the skin, which favors further research in the development of skincare product.

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