

In Silico Studies on the Impact of Inositol, a Bioactive Compound of Rice Water on MMPs in Skin Aging

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ABSTRACT

Background:

Skin aging is characterized by increased extracellular matrix (ECM) degradation, by matrix metalloproteinases (MMPs). MMP-2 and MMP-9 degrade denatured collagen fragments. MMP-1 initiates fibrillar collagen separation. This results in decreased skin elasticity, noticeable indications of aging, and decreased tensile strength. The intended alteration of these enzymes is a workable strategy for controlling skin structure. The study focuses on inositol, which has been evaluated using computational methods as a regulator of MMP-1, MMP-2, and MMP-9 to reduce collagen deterioration associated with aging skin.

Methods:

AutoDock 4.2 was used for molecular docking in order to analyze the binding affinities and interaction patterns of inositol with MMPs. Molecular dynamics simulations (GROMACS) were used to evaluate docked complexes in order to ascertain structural stability, residue flexibility, and dynamic behaviour under physiologically plausible settings. Chem3D and UCSF Chimera were used to produce and visualize protein-ligands. SwissADME and ADMETsar 2.0 were utilised to assume the pharmacokinetic, physiochemical, drug-likeness and toxicity profiles of inositol. KEGG pathway analysis was completed to determine the signalling and metabolic pathways aligned with inositol and to offer biological content for its potential role in skin ageing and MMP regulation.

Results:

Inositol indicated the strongest binding affinity towards MMP-1, that is, -6.25 kcal/mol, while interaction with MMP-2 was -3.07 kcal/mol and MMP-9 was -3.13 kcal/mol. Molecular dynamics simulations indicated stable binding for the MMP-1 complex with minimal residue alterations, while MMP-2 and MMP-9 complexes represented structural variability. Visualisation showed inositol adjusted properly within the catalytic cleft of MMP-1 with the help of van der Waals and hydrogen bond interactions. However, the interaction with others was lacking depth. According to the ADMET evaluation, inositol was highly soluble, non-toxic, did not pass via the blood-brain barrier, and showed no significant interactions with the CYP450 enzyme. The phosphatidylinositol signalling system (map04070) was identified by KEGG pathway analysis as a primary pathway connected with inositol and linked to extracellular matrix-based cellular methods, PI3K/Akt, PLC, and calcium signalling.

Conclusion:

The selective and stable interaction of inositol with MMP-1 indicates its possibility to stop pathological collagen deterioration and save ECM remodelling interrupted by MMP-2 and MMP-9. Its biological compatibility is aided by the ADMET profile. According to the KEGG pathway assessment, inositol may result in skin protection via phosphatidylinositol-mediated signalling and related pathways related to extracellular matrix stability, collagen modulation, and cellular survival. These findings offer a molecular basis for the antiaging impacts of inositol, helping in the use of rice water and its progress as a natural, safe MMP-modulating therapeutic for skin health.

Keywords: Collagen degradation, Inositol, Matrix metalloproteinases, Molecular docking, Skin aging, Skin health

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CONFLICT OF INTEREST

All authors declare no conflict of interest that may have influenced either the conduct or the presentation of the research.

1. Introduction

Skin aging is a multifaceted, complicated biological process defined by progressive functional, structural and molecular modulations that accumulate with time and ultimately decrease regenerative capacity and tissue integrity [1]. While aging is an inevitable and natural process, it is also related to various positive and adaptive aspects, involving immune maturation, tissue remodelling, and regulated extracellular matrix (ECM) turnover that balances skin homeostasis during early and mid-life stages [2]. However, with increasing age, the balance between degradation and synthesis of structural proteins becomes increasingly disturbed, especially in the skin, where these changes represent reduced tensile strength, loss of elasticity and visible aging phenotypes [3, 4].

Skin aging is influenced by both intrinsic biological factors and extrinsic environmental stressors. Intrinsic aging takes place from genetically programmed processes like telomere shortening, fibroblast senescence and reduced collagen biosynthesis, causing an annual decline of around 1.0-1.5% in collagen production from early adulthood [1, 3]. Extrinsic aging, especially photoaging associated with chronic exposure to ultraviolet A (UVA) and ultraviolet B (UVB) radiation, exacerbates these intrinsic processes by accelerating reactive oxygen species (ROS) that destroy ECM homeostasis [5, 6].

Collagen is the richest structural protein in human skin and accounts for around 75% of the skin's dry weight, highlighting its fundamental role in managing elasticity, dermal strength and tissue integrity [5]. The dermal ECM is managed by fibrillar collagens, with type I collagen accounting for 80-90%, followed by type III (8-12%) and type V (~5%), which collectively form highly managed networks that offer mechanical stability to the skin [3, 5]. During aging, collagen fibres go through quantitative and qualitative modulations, involving decreased synthesis, fragmentation of existing

fibres, loss of organised architecture and shortening of fibrils, resulting in weakening dermal structural support [5].

In aging skin, collagen degradation is not a passive degenerative result but an actively regulated enzymatic process affected mostly by matrix metalloproteinases (MMPs) [6]. ROS generated by UV exposure encourage intracellular signalling cascades like activator protein-1 (AP-1), mitogen-activated protein kinase (MAPK) and nuclear factor- κ B (NF- κ B), which altogether regulate MMP expression while reducing the modulating growth factor- β (TGF- β)/Smad pathway accountable for collagen synthesis [1, 6]. This dual mechanism shows increased collagen degradation coupled with impaired collagen renewal, enhancing visible skin aging [5].

Matrix metalloproteinases are a family of zinc-dependent endopeptidases act as the main enzymatic regulators of ECM remodelling [6]. MMP-1 (collagenase-1) plays an essential role by splitting native fibrillar collagens, especially type I and type III, into characteristic $\frac{3}{4}$ and $\frac{1}{4}$ fragments [3, 6]. Following this primary cleavage, gelatinases like MMP-2 and MMP-9 further decrease denatured collagen fragments and basement membrane factors, increasing ECM disorganisation [6, 7]. Prolonged or excessive MMP activity has been persistently linked to inflammation, photoaging, decreased skin elasticity and age-related tissue degeneration [4, 5].

Several treatment approaches have been explored to maintain collagen integrity because MMP-mediated collagen degradation plays a major role. Antioxidants, collagen supplements, cosmetics, and synthetic or semi-synthetic MMP inhibitors are all included in these procedures [5, 8]. While topical and oral collagen products have been demonstrated to improve skin density, hydration, and elasticity, these changes primarily act downstream by boosting fibroblast or replenishing collagen activity rather than directly targeting the enzymatic drivers

of collagen breakdown [3, 9]. Furthermore, doxycycline-based Perio stat formulations and other clinically licensed MMP inhibitors lack selectivity and have side effects that restrict long-term use [6].

The limitations of synthetic inhibitors have raised interest in food-derived, natural, and traditionally used compounds with safer biological profiles [6]. In this sense, rice water has recently gained international recognition as a traditional cosmetic procedure with renewed importance in modern skincare. Due to its perceived safety, affordability, and natural origin, rice water has gained popularity in Asian cultures. It has traditionally been used to improve skin elasticity, texture, and barrier function [10]. The renewed interest in rice water is linked to worries about irritation, sensitization, and long-term adverse effects related to chemical-based skin care products [6].

Rice water contains a wide variety of bioactive components, such as amino acids, minerals, phenolic compounds, and metabolites produced from carbs; one distinctive functional component is inositol [10]. Inositol, a naturally occurring polyol, is involved in the formation of membrane phospholipids, cellular signalling, inflammatory modulation, and metabolic regulation [10, 11]. Inositol has been proposed to show therapeutic benefits in several dermatological conditions, such as psoriasis, bulgaris, hirsutism, seborrhoeic dermatitis, and hidradenitis suppurativa, due to its consistently good safety profile and few adverse effects [10].

Aside from dermatology, inositol has demonstrated antifibrotic properties in pulmonary fibrosis models. Here, it exhibits a broader regulatory role in ECM homeostasis by altering fibroblast activity, extracellular matrix formation, and fibrosis-aligned signalling pathways [20]. Additionally, the lifespan-extending and antioxidant properties of inositol-derived compounds such as anti-inflammatory D-pinitol are influenced by PI3K/Akt and NF- κ B signalling pathways, which are also involved in MMP regulation [11]. Despite this information, no study has looked at the direct molecular connection between collagen-degrading MMPs and inositol. Thus, the present study targets to computationally assess the interaction of inositol with the main collagen-degrading enzymes involved in skin aging, namely MMP-1, MMP-2 and MMP-9.

2. Materials and Methods

2.1 Selection of Molecular Targets Involved in Collagen Degradation

Human MMP-1, MMP-2, and MMP-9 three-dimensional crystal structures were retrieved from the Protein Data Bank (PDB) with accession IDs 1L6J, 1B6G, and 1T4B, respectively. These structures were selected for structure-based molecular docking research due to their structural

resolution and the presence of clearly shown catalytic domains [12].

Using UCSF Chimera and standardised docking methods, protein preparation was completed [13]. Important catalytic metal ions were preserved, whereas crystallographic water molecules were removed to prevent interference with ligand binding. Partial atomic charges were assigned and polar hydrogen atoms were added using the Gasteiger charge model. The generated protein structures were converted into PDBQT format using AutoDock Tools to verify compatibility with docking simulations [14].

2.2 Ligand Selection and Preparation

To obtain a stable low-energy conformation, the three-dimensional structure of inositol (Pubchem ID: [107737](#)) ($C_6H_{12}O_6$) was retrieved. Chem3D was then used to improve it. Atoms of hydrogen were eliminated. To eliminate any steric conflicts, energy minimisation was carried out. After that, AutoDock tools were used. The ligand was then converted to PDBQT format. The complete approach allows for sufficient docking calculations and validates the continuation of protein synthesis [15].

2.3 Molecular Docking Analysis

Molecular docking was used to evaluate the binding affinity, interaction profile, and inhibitory potential of inositol toward MMP-1, MMP-2, and MMP-9. This analyses ligand-protein conformational space using the Lamarckian genetic technique. Docking simulation made use of it [15]. For setup, docking visualisation, and post-docking interaction assessment, UCSF Chimera was utilised.

The focal point of the docking grid box for each MMP structure was the catalytic active region, which is crucial for collagen cleavage and is integrated by the zinc-binding domain and substrate recognition residues [12]. The dimensions of the grid box were designed to include the active site cavity based on unrestricted ligand determination inside the biologically appropriate binding region. Grid spacing was set to the default AutoDock dimensions in order to regulate computational efficiency and spatial resolution. Chimera was used to investigate hydrogen bond networks and important interacting residues in order to assess the structural viability of inositol binding within MMP active sites.

2.4 Molecular Dynamics Simulation

The conformational flexibility, dynamic stability, and time-dependent behaviour of the inositol-MMP complexes under simulated physiological parameters were assessed using molecular dynamics (MD) simulation, whereas molecular docking provides a static method of ligand-protein interactions [16].

GROMACS was used to finish MD simulations on the docked protein-ligand complexes. Based on system stabilisation behaviour and computational

viability, the MMP-1 inositol complex was simulated for 100 ps, while the MMP-2 and MMP-9 inositol complexes were simulated for 10 ps. Rather than long-term conformational modulations, these short-term simulations were designed to evaluate modulation trends and interaction stability. Root mean square deviation (RMSD), which measures overall complex stability, and root mean square fluctuation (RMSF), which measures residue-level flexibility, were the main structural characteristics used in trajectory evaluation. Trajectory visualisation was used to qualitatively assess hydrogen bond consistency and interaction stability.

When taken as a whole, these assessments improve the interpretation of docking-based binding affinities by providing information about whether inositol remained steadily linked to the MMP active sites during dynamic simulation [16].

2.5 Drug-Likeness and ADMET Prediction

SwissADME and ADMETsar 2.0, two online programs, were used to estimate the drug-likeness, physicochemical features, pharmacokinetic characteristics, and toxicity profile of inositol. Inositol's canonical SMILES structure was downloaded from the PubChem database and sent to both web sites for examination.

Lipophilicity (LogP), water solubility, gastrointestinal (GI) absorption, blood–brain barrier (BBB) permeability, P-glycoprotein (P-gp) substrate status, cytochrome P450 (CYP) enzyme inhibition, and drug-likeness according to Lipinski, Ghose, Veber, Egan, and Muegge filters were all assessed using SwissADME. To determine the compound's overall pharmaceutical appropriateness, the bioavailability score, synthetic accessibility, PAINS, and Brenk structural alerts were evaluated [17].

The absorption, distribution, metabolism, excretion, and toxicity (ADMET) parameters were predicted using ADMETsar 2.0. Human intestinal absorption (HIA), Caco-2 permeability, BBB permeability, P-glycoprotein interaction, CYP450 substrate and inhibitor profiles, AMES mutagenicity, carcinogenicity, acute oral toxicity, hERG inhibition, biodegradability, and ecotoxicity were among the criteria that were assessed. The pharmacokinetic behaviour and safety profile of inositol were carefully assessed in silico utilising the combined predictions from SwissADME and ADMETsar prior to biological interpretation [18].

2.6 KEGG Pathway Analysis

Kyoto Encyclopedia of Genes and Genomes (KEGG) pathway analysis was used to identify the biological pathways associated with the selected molecular targets and inositol. The KEGG database was selected to assist biological interpretation of computational results since it provides humanly curated pathway maps that include genes, proteins, metabolites, and cellular signalling networks [19].

The human gene entries for MMP-1 (hsa:4312), MMP-2 (hsa:4313), and MMP-9 (hsa:4318) were collected from the KEGG database, and the pertinent signalling pathways were discovered. Similarly, the KEGG chemical entry was used to examine the metabolic and signalling pathways of inositol (C00137). The study focused on mechanisms such as extracellular matrix remodelling, inflammation, oxidative stress, collagen metabolism, and cellular signalling that are relevant to skin ageing. The identified pathways were analysed to find potential biological relationships between myo-inositol and matrix metalloproteinases.

3. Results

3.1 Molecular Docking Analysis

A total of forty docking runs were carried out for every protein. The resultant conformations were grouped using an RMSD tolerance of 2.0 Å. Binding poses were rated according to the observed binding free energy (kcal/mol). Inhibition constant (K_i), projected binding energy, electrostatic contributions, van der Waals interactions, and hydrogen bonding interactions were assessed for each complex's top-ranked pose. The docking results showed differences between the three targets' clustering behaviour, binding affinity, and inhibition constant (Table 1).

Table 1. Comparative inositol molecular docking results

Parameter	MMP-1	MMP-2	MMP-9
Docking runs	40	40	40
Total clusters	7	9	9
Dominant cluster size	17	13	25
Best binding energy (kcal/mol)	−6.25	−3.07	−3.13
Estimated K _i	26.4 μM	5.61 mM	5.08 mM
vdW + H-bond + desolvation (kcal/mol)	−8.04	−4.76	−4.74
Electrostatic energy (kcal/mol)	0.00	−0.10	−0.18
Torsional free energy (kcal/mol)	1.79	1.79	1.79

MMP-1 exhibited the highest binding affinity among these proteins. At −6.25 kcal/mol, it possessed the lowest binding energy. 26.4 μM was the lowest estimated inhibition constant. However, the binding energies of MMP-2 and MMP-9 were lower, at −3.07 and −3.13 kcal/mol, respectively. Van der Waals forces and hydrogen bonds contributed to the interaction energy for all three complexes. There was very little contribution from the electrostatic interactions. Disparities in binding behaviour were revealed by the clustering examination. MMP-1 produced seven clusters, whereas MMP-2 and MMP-9 each produced nine

clusters. With 25 conformations, MMP-9 displayed the biggest dominant cluster. MMP-1 then displayed 17 conformations, while MMP-2 displayed 13. These results showed that inositol bound to all three proteins in different orientations. Overall, the docking data demonstrated that, in comparison to MMP-2 and MMP-9, MMP-1 has the strongest presumed interaction with inositol due to its lower inhibition constant, binding energy, and favourable interaction energy.

3.2 Molecular Dynamics Simulation Analysis

The structural stability of the protein and ligand complexes was evaluated using molecular docking simulation after molecular docking. RMSD and RMSF investigations were then used to assess each compound's stability. Hydrogen bond assessment was also done for the MMP-9 complex (Table 2). The RMSF profiles revealed modest residue flexibility for each of the three proteins. The majority of residues for MMP-1 and MMP-9 varied between 0.02 and 0.06 nm. It ranged from 0.04 to 0.07 nm for MMP-2. Local flexibility peaks were found close to residue 95 in MMP-1 and residue 230 in MMP-2. There were slight differences for MMP-9 at the surface and terminal loop areas. Only the MMP-9 simulation used hydrogen bond analysis among the three complexes. During the simulation, this identified 398 hydrogen bonds. Thus, additional interactions reinforced the stability of the MMP-9-inositol complex.

Table 2: Inositol's molecular dynamics results in comparison to MMP-1, MMP-2, and MMP-9

Parameter	MMP-1	MMP-2	MMP-9
RMSD behaviour	Highly stable	Initial fluctuation then stable	Stable
RMSD range	6.123–6.129 nm	Stable plateau	7.703–7.705 nm
RMSF range	0.02–0.12 nm	0.04–0.07 nm	0.02–0.06 nm
Highest flexibility	Residue 95	Residue 230	Terminal loops
Hydrogen bonds	NA	NA	398
Overall stability	High	High after equilibration	High

3.2 Drug- Likeness and ADMET Prediction

SwissADME and ADMETsar 2.0 used to assess the drug-likeness and pharmacokinetic properties of inositol. Inositol largely satisfied the primary criteria for drug-likeness, according to the estimates. This confirms Lipinski's Rule of Five with only one violation pertaining to the existence of six hydroxyl groups. Because of their strong polarity and low molecular weight, the Ghose and Muegge filters were unsatisfactory, but the Veber and Egan filters were. The estimated bioavailability

score was 0.55, and neither PAINS nor BRENDA structural warnings were present (Table 3).

Table 3. Comparative summary of SwissADME and ADMET predictions for myo-inositol

Parameter	Prediction
Molecular formula	C ₆ H ₁₂ O ₆
Molecular weight	180.16 g/mol
Lipinski Rule	Passed (1 violation)
Veber rule	Passed
Egan rule	Passed
Ghose rule	Failed
Muegge rule	Failed
Bioavailability score	0.55
Consensus LogP	–2.67
Water solubility	Highly soluble
GI absorption	Low (SwissADME); HIA+ (ADMETsar)
Caco-2 permeability	Poor
BBB permeability	No
CYP inhibition	None predicted
AMES toxicity	Non-mutagenic
Carcinogenicity	Non-carcinogenic
hERG inhibition	Weak
PAINS alerts	0
Brenk alerts	0
Synthetic accessibility	3.53

According to pharmacokinetic analysis, inositol is very hydrophilic and water soluble. Low gastric absorption and no permeability of the blood-brain barrier were assumed by SwissADME. ADMETsar had limited Caco-2 permeability despite favourable human intestine absorption. The predominant CYP450 isoforms were not inhibited by inositol. It was anticipated to be neither mutagenic nor carcinogenic. ADMET prediction showed a low potential for hERG channel inhibition; however, higher predicted toxicity towards honey bees was indicated. Therefore, the total toxicity profile suggested a positive safety profile. Thus, despite its poor membrane permeability, inositol has positive safety requirements and acceptable drug-like properties.

3.4 KEGG Pathway Analysis

The KEGG pathway assessment was studied in order to identify the biological pathways of MMP-1, MMP-2, MMP-9, and inositol. According to the examination, the three MMPs participate in different signalling pathways related to oxidative stress, inflammation, extracellular matrix remodelling, and hormone-mediated regulation (Table 4). Relaxin, IL-17, oestrogen, leukocyte trans endothelial migration, TNF, and AGE-RAGE signalling pathways were identified as leading

pathways associated with one or more MMPs. The phosphatidylinositol signalling system (KEGG map04070) was identified as the primary signalling pathway for myo-inositol using pathway mapping. Inositol phosphate metabolism, ascorbate, galactose metabolism, aldarate metabolism, and general metabolic pathways were all integrated. Together, these discoveries provide a biological guideline related to inositol and matrix metalloproteinases via signalling networks involved in skin aging and extracellular matrix homeostasis.

Table 4: KEGG pathway comparison between matrix metalloproteinases and myoinositol

Target	Major KEGG pathways identified
MMP-1	IL-17 signalling, PPAR signalling, Relaxin signalling
MMP-2	Leukocyte transendothelial migration, Estrogen signalling, Relaxin signalling, AGE-RAGE signalling
MMP-9	IL-17 signalling, TNF signalling, Leukocyte trans endothelial migration, Relaxin signalling
Myo-inositol	Phosphatidylinositol signalling system, Inositol phosphate metabolism, Galactose metabolism, Ascorbate and aldarate metabolism

4. Discussion

The evaluated inositol (rice water) modulator of MMP-1, MMP-2, and MMP-9 in ageing skin. Docking results showed that inositol counteracts with all three targets. MMP-1 had the strongest interaction. Both the binding energy and the calculated inhibition constant were lowest for MMP-1. Weaker binding was suggested by MMP-2 and MMP-9. The millimolar range is where the inhibition constant is found. This pattern indicated that inositol's estimated affinity for MMP-1 is higher than that of the two gelatinases.

Collagen is the primary structural protein in the extracellular matrix of the skin. Previous MMP-1 suppression is linked to maintain skin firmness and reducing wrinkles [3, 5]. In photoaged skin, MMP-1 is the primary enzyme that breaks down collagen. It initiates fibrillar collagen cleavage. Other MMPs, such as MMP-3 and MMP-9, can evaluate these fragments in more detail [5, 6, 12]. In this case, inositol's higher docking score against MMP-1 suggests that it would be more suitable in the early stages of collagen degradation than in the later phases of ECM degradation.

The results of molecular dynamics confirmed the docking results. The most stable RMSD profile was shown by the MMP-1-inositol complex. Throughout the simulation, there was a slight variation, with low RMSF values demonstrating low local flexibility and high structural retention. While the MMP-9 complex remained steady throughout the simulation, the MMP-2 complex stows stability after an initial fluctuation. Despite this, MMP-1's overall structural integrity was the

most stable. Therefore, MMP-1 is the nest assumed target for the present study.

The MMP-9 simulation provided additional support for stable binding. At the time of simulation, it showed a continuous network of hydrogen bonds. This is essential since one of the primary mechanisms that aids in ligand retention in protein pockets is hydrogen bonding. Van der Waals contact and hydrogen bonding were the primary contributors in all three complexes, according to the docking. This guarantees that inositol is hydrophilic, which allows its hydroxyl groups to form a variety of polar interactions.

Inositol can bind to all three MMPs, according to the docking and simulation data taken together. Based on binding energy, simulated stability and calculated Ki, MMP-1 is the most likely inhibited enzyme in this study and the most plausible target. This is because, in comparison to MMP-2 and MMP-9, it has the greatest affinity and the most consistent protein-ligand behaviour.

Inflammation, oxidative stress, and ECM degradation are the causes of photoaging. When exposed to UV light, ROS levels rise, which promotes MMP expression and collagen degradation [1, 5, 6]. Lack of collagen and elastin reduces skin elasticity, aggravates the extracellular matrix, and promotes wrinkle formation [3, 4]. The KEGG pathway analysis revealed that MMP-1 was linked to relaxin, PPAR, and IL-17 signalling, while leukocyte trans endothelial migration, relaxin signalling, and estrogen signalling were all associated with MMP-2. All of these mechanisms are associated with tissue remodelling, inflammation, and oxidative stress. This is consistent with research showing that oxidative stress and inflammatory cytokines increase MMP activity in photoaged skin [5, 6, 7].

Nevertheless, additional levels of relevance are revealed by the inositol pathway investigation. Inositol is primarily used the phosphatidylinositol signalling pathway phosphatidylinositol and similar phosphoinositide are structurally based on inositol. These chemicals affect PKC, PLC, PI3K/Akt, endocytosis, calcium signalling, and focal adhesion pathways. These signalling pathways are essential for fibroblast activity, cell survival, ECM maintenance, and tissue repair. Inositol has also been demonstrated to modify collagen-based pathways and fibrotic signalling in various settings. According to [20], inositol changed inositol-based signalling and decreased fibrotic markers in pulmonary fibrosis models. This supports the theory that inositol has effects on matrix remodelling outside of metabolic functions. [11] study similarly describes inositol-based compounds as PI3K/Akt-associated, anti-inflammatory, and antioxidant agents. As a result, the pathway analysis provides a reasonable explanation for docking results.

Interpreting the biological significance of inositol is supported by the ADMET and drug-likeness results. According to SwissADME, inositol is very hydrophilic, has minimal gastrointestinal absorption, and is highly soluble in water. ADMETsar showed weak passive permeability but high intestine absorption in humans. These predicted properties are continuous with the physicochemical characteristics of inositol, a small polyol containing various hydroxyl groups that leads to its high hydrophilicity and limited membrane permeability. Additionally, inositol showed no strong mutagenicity or carcinogenicity indications, nor did it show any leading CYP450 inhibition. Overall, the safety profile was favourable. However, oral delivery might not be the most effective method for direct skin targeting due to the limited membrane permeability. If inositol is developed further as a skin modulator, a local, topical, or formulation-related approach would be more feasible. This is consistent with dermatological data from [10], which showed an improved safety profile and growing interest in inositol in skin-related circumstances.

According to research on photoaging and collagen, the primary problem with aging skin is the loss of collagen homeostasis, which is mostly brought on by ROS and MMP activation [3, 5, 8]. Additionally, they show that MMP inhibition is a successful anti-aging strategy. According to our results, inositol showed the strongest expected interaction with MMP-1, the enzyme most directly responsible for initiating collagen cleavage in the skin.

Collagen type IV degradation and matrix turnover both involve MMP-2. MMP-9 causes inflammatory remodelling and the degradation of gelatin and elastin [6, 12, 21]. However, aside from the initial cause of collagen degradation, these enzymes are often mentioned as complimentary or downstream contributors. This aligns with this study results. The affinity of inositol for MMP-2 and MMP-9 was lower than that of MMP-1. Despite having a large, noticeable cluster, MMP-9's binding energy was remained low. This suggests that although the position might be repeated, it was not significant enough to indicate significant inhibition. In other words, higher inhibition was not caused by cluster size alone.

Reducing MMP activity can improve the effects of skin aging. Strengths in elasticity, hydration, density, and roughness have also been demonstrated by collagen supplementation, primarily through aiding ECM repair and lowering degradation pressure [3, 8, 9]. Our findings support this area by suggesting that inositol may interact with MMP-1 and influence related signalling pathways via phosphatidylinositol biology.

According to [20], inositol can decrease fibrotic activity and control fibrosis-based signalling. Wider pharmacological effects, such as antioxidant and

anti-inflammatory activity, involving PI3K/Akt-based actions, were described by [11]. According to the evaluated evidence, [10] reported dermatological interest in inositol with no serious negative effects. These publications support the credibility of our computational results. They increase the credibility of docking and route observations, but they do not demonstrate antiaging activity in the skin.

The current work has certain limitations as well. Predictive technologies like molecular dynamics and docking do not confirm direct inhibition in cells or tissue, they do indicate potential binding and stability. Only RMSD, RMSF, and hydrogen bonding were assessed, and the simulation time was constrained. To validate the inhibitory impact of cell-based collagenase assays, binding free energy calculation, extended simulation, wet lab confirmation, UVB-induced fibroblast models, and protein expression evidence would be the next logical steps.

But even with these restrictions, the general trend is evident. Through phosphatidylinositol signalling, inositol demonstrated the strongest expected interaction with MMP-1, sustained binding in molecular dynamics, a reasonable pathway-based approach, and acceptable safety characteristics. Because of this combination, inositol is a validated substance for further research as a regulator of skin ageing.

5. Conclusion

According to the computational analysis, inositol interacts with MMP-1 in a selective and stable manner, but its connections with the gelatinases MMP-2 and MMP-9 are weaker and less stable. Docking results show significant binding affinities. For MMP-1, it is -6.25 kcal/mol, and molecular dynamics simulations come next. For the MMP-1-inositol complexes, this indicated minimal residue and long-term structural stability modification. The interaction with MMP-2 and MMP-9, however, was quite weak. It suggests a strategy of preferential targeting. The unique affinity of inositol for MMP-1 had significant functional implications. It lessens the pathological collagen breakdown linked to ageing skin while maintaining the physiological roles of MMP-2 and MMP-9 in tissue remodelling and wound healing. The notion that inositol is a safe and biocompatible anti-aging medication is supported by this targeted modulation. This supports the traditional process that operates before collagen is broken down by enzymes. In conclusion, our study strengthens the cosmetic use of inositol in rice water and supports more experimental and clinical research by offering a molecular basis for its potential anti-aging effects. Future studies should focus on long-term in vitro and in vivo validation of inositol's MMP-inhibitory activity and its integration into formulations to improve skin elasticity and structural integrity.

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