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Research Article

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MMP9 and MAFA Protein Molecular Docking with Novel Derivatives of Isoflavone from *Cicer Arietinum L.* as Anti-Diabetic and Anti-Inflammatory Agents

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Abstract

Objectives: *Chickpea, also known as Cicer Arietinum L. is a widely cultivated and consumed legume that is rich in carbohydrates, lipids, and high-quality proteins. It contains a diverse array of micronutrients, macronutrients, vitamins, and carotenoid compounds, which contribute to its nutritional value. Additionally, chickpea has medicinal properties due to the presence of various bioactive compounds, including genistein, Biochanin-A, and formononetin, which possess antidiabetic and anti-inflammatory properties. Chickpeas are a possible contender for addressing health conditions such as cardiovascular disease, type 2 diabetes, digestive disorders, and cancer due to these qualities. In this study, we looked into the consequences of genistein, Biochanin-A, and formononetin on the activity of the MMP9 and MafA proteins. Our findings provide insights into the potential therapeutic applications of chickpea compounds and their role in regulating protein activity in various biological processes.*

Methodology: *This study employed molecular docking analysis using the CB-Dock program to investigate the interactions between three anti-diabetic and anti-inflammatory chemicals found in chickpeas - Biochanin-A, Genistein, and Formononetin - and two target proteins - MMP-9 and MaFA.*

Results: *Analysis of compounds' remarkable decrease in binding energy to MMP9 target receptors, especially for Formononetin (-11 kcal/mol), Biochanin-A (-10.1 kcal/mol), Genistein (-10 kcal/mol) and Mafa for Formononetin (-8.8 kcal/mol), Biochanin-A (-8.1 kcal/mol), Genistein (-8.2 kcal/mol).*

Conclusion: *Potential chemical molecules found in this study may be used as a starting point by the pharmaceutical sector to create molecules for anti-diabetic drugs.*

Key words: Chickpea, CB-Dock, MMP9, MAFA, Genistein, Biochanin-A, Formononetin.

1. Introduction

High blood glucose levels brought on by a lack of insulin secretion, action, or both characterize diabetes, a chronic metabolic condition. The prevalence of diabetes has been expanding worldwide, affecting 537 million people between the ages of 20 and 79 [1]. Additionally, it is anticipated that this number will increase to 643 million by 2030 and 783 million by 2045. Diabetes affects three out of four persons who reside in low- and middle-income countries., making it a serious public health risk. Furthermore, almost half of the adults living with diabetes remain undiagnosed. With 6.7 million deaths caused by it each year, diabetes is the greatest cause of death in the world. It also imposes a significant financial burden, causing at least USD 966 billion in health expenditure, which accounts for 9% of total spending on adults [2]. Over 1.2 million children and adolescents have type 1 diabetes, and about 1 in 6 live births are affected by the condition when a woman is pregnant. Additionally, type 2 diabetes is more likely to occur in 541 million adults. Hormones such as insulin, glucagon, and somatostatin play a critical role in glucose metabolism and diabetes. As such, there is a pressing need for continued research aimed at improving

the understanding of diabetes and developing new treatments to mitigate its effects. An increasing percentage of deaths occur due to diabetes and its consequences. The age-specific death rate due to diabetes increased by 3 percent between the years 2000 and 2019 [3]. According to estimates, renal problems and diabetes-related kidney disease would claim the lives of 2 million individuals worldwide in 2019. The edible seed of chickpea is known as the pulse of the legume family. It is a valuable and abundant resource of lipids, carbohydrates, and proteins and also contains micro and macronutrients [4]. In more than 50 countries across the globe, the chickpea ranks as the world's third-most-valuable pulse crop [5]. Chickpea is a crop that is primarily grown in Asia. Famously, India is the most prolific chickpea producer in the world. Chickpea is used considerably by people and has good effects on blood sugar both as a food and as a medicine. Recent studies show that isoflavones extracted from chickpea have good effects on blood sugar [6]. However, these studies only looked at the active parts. Also, there hasn't been enough research on the compounds' hypoglycemic effects. based on traditional Chinese medicine's multiple target effect theory and the extraction and isolation of isoflavonoids from chickpeas. Isoflavones are the 2nd bioactive phytochemistry component in the chickpea. Chickpea's major isoflavonoids are Biochanin-A, formononetin, and genistein. In type 2 diabetic rats, genistein from chickpeas significantly increased glucose tolerance and total cholesterol, reduced serum levels of insulin, triglycerides, liver glycogen, low-density lipoprotein cholesterol, and muscle glycogen [7]. Genistein can not only be employed in the treatment of type 2 diabetes but it can also be used to help people with type 1 diabetes and make more insulin [8]. When formononetin and hanfangichin B were given together, helped rats with diabetes caused by streptozotocin, and formononetin lowered blood sugar by causing insulin to be released [9]. Chickpea also has a large amount of the isoflavone biochanin Isoflavone amount in chickpea vary depending on the type and variety of chickpea, harvest year, and the geographic area of cultivation. The total content of the isoflavone in the chickpea ranges from 0.016 percent to 0.06 percent [10]. Chickpea has significantly contributed to the significant advancements in the management of weight issues, in actions for addressing obesity and overweight are crucial to controlling type II diabetes. Mafa, also known as v-maf avian musculoaponeurotic fibrosarcoma oncogene homolog A, is a crucial transcription factor required for the proper formation and functioning of pancreatic beta cells. It belongs to the Mafa family of transcription factors, which are distinguished by a basic leucine zipper DNA-binding domain that is conserved. Recent studies have identified Type 2 diabetes treatment using Mafa as a possible therapeutic target, where Mafa expression and function are impaired in diabetic β-cells [11]. Multiple studies have indicated that inhibition of Mafa activity could be a potential treatment for diabetes [12]. MMPs (Metalloproteinases) are a group of enzymes that are responsible for the degradation of extracellular matrix (ECM). There are four subgroups of MMPs based on the specificity of the substrate which is divided into IV collagenases, strome lysins, interstitial collagenases, and membrane-type- MMPs (MTMMPs). Their secretion form is latent which is cleaved thus resulting in biological activation. TIMPs, the tissue inhibitors bind with high affinity to the active MMP enzyme. MMPs are involved in the healing of the wound thaludes keratinocytes, fibroblasts, and also inflammatory cells. The expression of matrix metalloproteinases (MMPs) has been modified in reaction to signals originating from growth factors, cytokines, changes in cell-cell interactions, and interactions between cells and the extracellular matrix [13]. A metabolic disorder of diabetes that takes place because the pancreas cannot produce enough insulin or when the body cannot utilise the insulin that is produced. It is categorized into two types i.e. Type I and II diabetes [14]. Diabetes signs and symptoms are polydipsia, polyuria, polyphagia and weight loss. Other symptoms that are analyzed at diagnosis are relevant to a history of itchiness, recurrent vaginal infections, blurred vision, peripheral neuropathy, and fatigue [15]. Various studies have revealed the potential of natural compounds and synthetic molecules in inhibiting MMP9 activity and reducing diabetes-associated complications. For example, curcumin, a natural polyphenol derived from turmeric, has been shown to suppress MMP9 expression and inhibit the inflammatory response in diabetic animal models [16]. Similarly, a synthetic MMP9 inhibitor, SB-3CT, in high-fat diet-induced diabetic rats has been found to improve glucose tolerance and insulin sensitivity [17].

The link between diabetes and chickpea seeds lies in the isoflavones present in the chickpea, specifically genistein, formononetin, and Biochanin-A. These isoflavones have been found to have positive effects on blood sugar levels, making them useful in the management of type 1 and type 2 diabetes. Genistein has been shown to increase glucose tolerance and reduce insulin levels in type 2 diabetic rats, while formononetin has been found to lower blood sugar levels by causing insulin release in rats with diabetes caused by streptozotocin. Additionally, chickpea has significantly contributed to the effective management of weight issues, which is crucial in controlling type 2 diabetes. MMPs, a group of enzymes responsible for the degradation of extracellular matrix, have been found to be involved in diabetes-associated complications. Natural compounds and synthetic molecules such as curcumin and SB-3CT have been shown to inhibit MMP9 activity and improve glucose tolerance and insulin sensitivity in diabetic animal models. Therefore, the consumption of chickpea seeds and the use of natural and synthetic compounds can potentially aid in the management of diabetes and its associated complications.

2. Materials and Methods

The Structure of receptor proteins were downloaded from the Protein Data Bank (PDB) [18]. The Pubchem database was used to get the ligand's structural information [19].

2.1 Docking

The chemical bonding among ligands and receptor complexes comes into being by docking and their relative reliabilities and stabilities have been analyzed by the online tool CB-Dock (Cavity-detection guided Blind Docking) [20]. In this study, blind docking has been applied among receptors and ligands by CB-

Dock. The protein data bank has given the structure of receptors. Inhibitors have been docked against the sites that are active in the structure of receptor proteins and then their binding affinities were evaluated. This computational method includes the sample-related conformations of tiny molecules precisely in the binding sites; the conformations are complementary for the binding protein sites as being accessed by scoring functions. Inhibitors and target protein had been geometrically optimized as well as been docked by CB-Dock.

2.2 Prediction of ADMET Properties

The tool MedChem Designer v5 and internet resources like Swiss ADME (http://www.swissadme.ch/index.php) are applied to explore the absorption, distribution, metabolism, and excretion (ADMET) properties of the studied molecules from chickpea. BOILED-Egg plot of chickpea compounds are constructed by Swiss ADME [21]. Bioavailability radar graphs are also constructed to predict the bioavailability of selected compounds [22].

3. Results

3.1 Structure and Molecular Characteristics

The Structures of receptor proteins Mafa (4EOT) and Mmp9 (2OW2) shown in (Figure-1 A, B) were obtained from the Protein Data Bank (PDB). The PDB ID of both proteins was also retrieved from the PDB. It serves as a database of large biological compounds' three-dimensional structures like proteins and nucleic acids. The PubChem database was used to retrieve the structures of the ligand compounds Biochanin-A, Genistein, and Formononetin found in chickpea in Figure-2, A, B, and C. The molecular weight, molecular formula, boiling point, melting point, and physical description of chickpea Compounds are given in table 1.

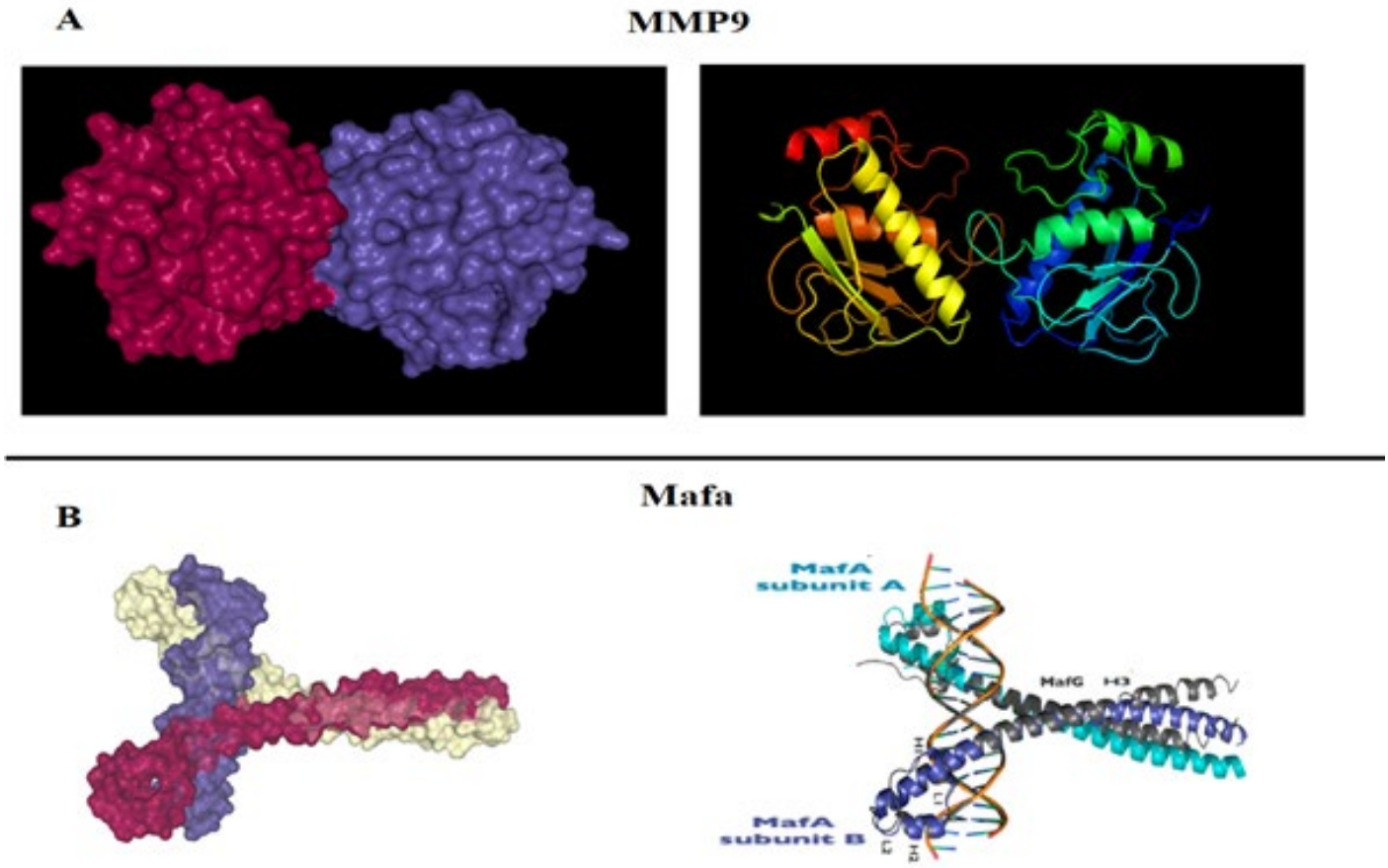


Figure 1: (A) Human matrix metalloproteinase 9 (MMP-9) (B) Mafa transcription factor

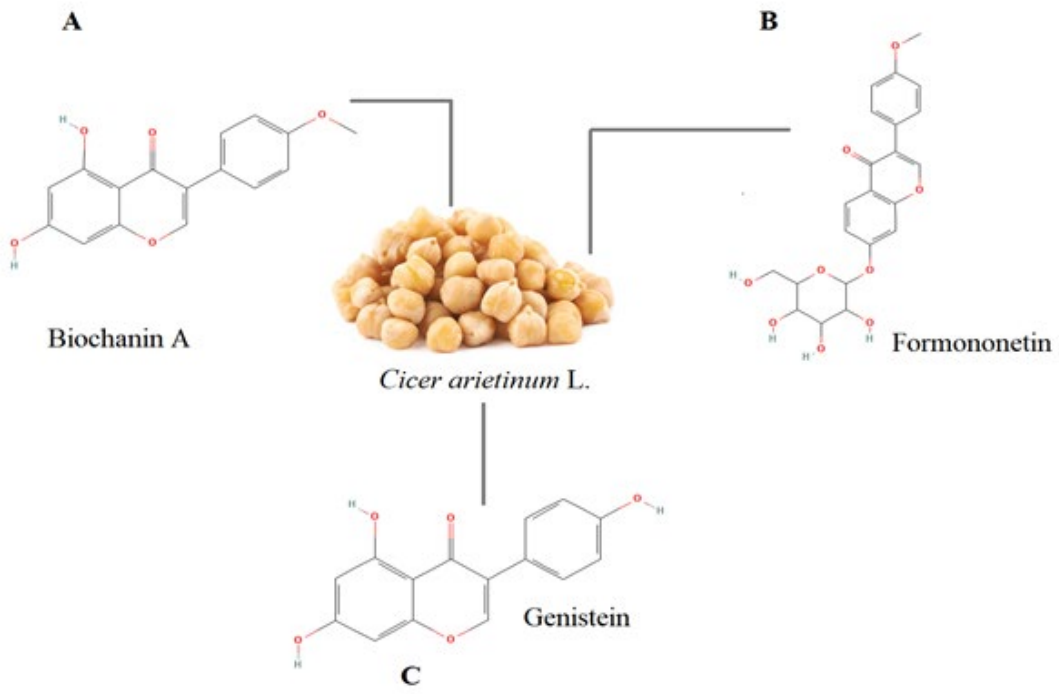


Figure 2: Chickpea's major isoflavonoids (A) Biochanin-A, (B) Formononetin, and (C) Genistein

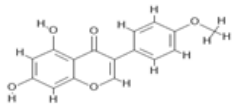
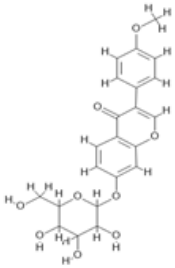
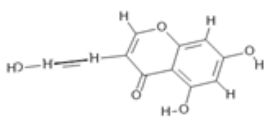
NO.	Compounds Name	Molecular Formula	Molecular Weight	Melting Point	Boiling point	Physical Description
1	Biochanin-A Pubchem CID-5280373 	C16H12O5	284.26g/mol	210-213 °C	518.57 °C (Boiling point) @ 760.00 mm Hg (est)	Solid
2	Formononetin Pubchem CID-3733033 	C22H22O9	430.4g/mol	218 - 219 °C	697.80 °C @ 760.00 mm Hg (est)	Solid
3	Genistein Pubchem CID-5280961 	C15H10O5	270.24g/mol	297-298 °C (slight decomposition) 301.5 °C (decomposition)	555.5±50.0 °C at 760 mmHg (est)	solid

Table 1: Molecular characteristics of different compounds of chickpea

3.2 Docking Results

In this study, Mmp9 and Mafa were used as the receptor and the compounds Genistein, Biochanin-A, and Formononetin from chickpea were used as ligands. Blind docking has been applied among receptors and ligands by CB-Dock. Inhibitors have been docked against the sites that are active in the structure of Mmp9 and Mafa, then their binding affinities were evaluated. Figure 3 depicts the interaction of Mmp9 with low binding affinities of Biochanin-A, Genistein, and Formononetin. Mafa's interactions with low binding affinities of Biochanin-A, Genistein, and Formononetin predict the efficacy of the interaction between the ligand and receptor as well as the conformation and orientation of the ligand inside the receptor's binding site. As anticipated, the docking methodology used to forecast the binding modes in Figure 4 proved to be quite effective. Tables 2 and 4 list the Mmp9 and Mafa cavities that produce the best outcomes. The binding affinity score, expressed as the predicted free binding energy is a measure of how well the ligand binds to the receptor. The Docking analysis results of Genistein, Biochanin-A, and Formononetin with MMP9 and Mafa revealed low binding affinities and the RMSD values were ≤ 2.0 Å given in table 3 and table 5. Among all isolates, Formononetin exhibited the highest docking score (−11 kcal/mol), with MMP9 and (−8.8 kcal/mol) with Mafa. The binding of Formononetin to MMP9 and Mafa was greater than those of Genistein and Biochanin-A (−10 and −10.1 kcal/mol with MMP9) AND (−8.2 and −8.1 kcal/mol with Mafa), respectively.

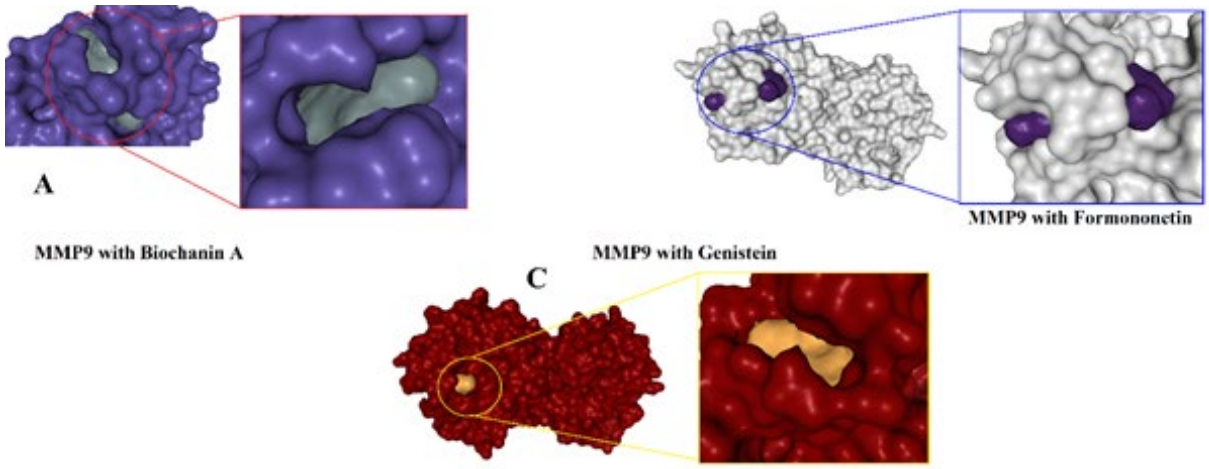


Figure 3: (A) Ligand 1 (Biochanin-A) interaction with receptor Mmp9 (B) Ligand 2 (Formononetin) interaction with receptor Mmp9 (C) Ligand 3 (Genistein) interaction with receptor Mmp9

Compounds	volume	center_x	center_y	center_z	size_x	size_y	size_z	score
Biochanin-A	813	67.344	23.007	56.227	21	21	21	-10.1
Formononetin	686	23.667	2.695	51.289	26	26	26	-11.0
Genistein	813	67.344	23.007	56.227	21	21	21	-10.0

Table 2: Binding Cavities of MMP9 with Compounds of Chickpea

Compounds	Affinity (kcal/mol)	dist from rmsd l.b.	best mode rmsd u.b.
Biochanin-A	-10.1 kcal/mol	0.000	0.000
Formononetin	-11.0 kcal/mol	0.000	0.000
Genistein	-10.0 kcal/mol	0.000	0.000

Table 3: The Docking results of *Cicer Arietinum* derived compounds against MMP9 protein

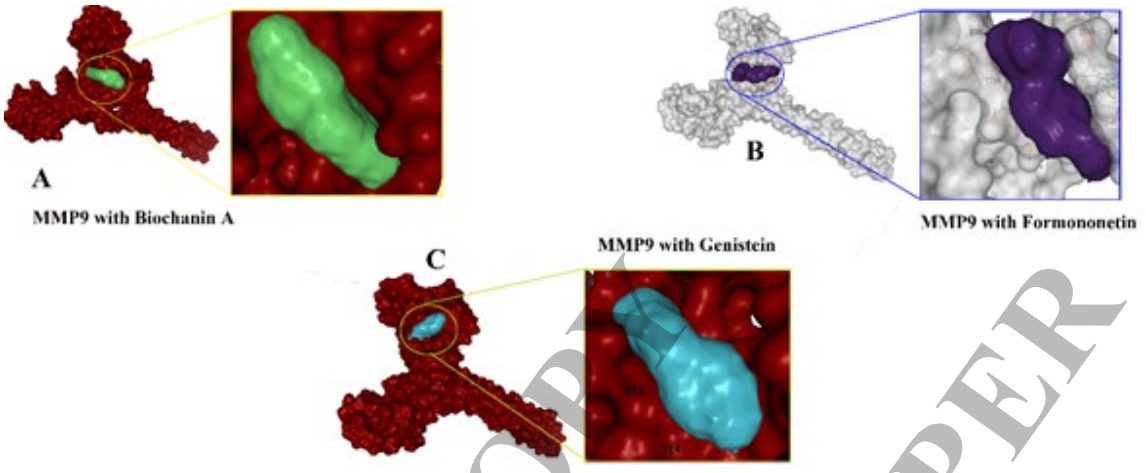


Figure 4: (A) Ligand 1 (Biochanin-A) interaction with receptor Mafa (B) Ligand 2 (Formononetin) interaction with receptor Mafa (C) Ligand 3 (Genistein) interaction with receptor Mafa

Ligands	volume	center_x	center_y	center_z	size_x	size_y	size_z	score
Biochanin-A	1711	-55.621	5.778	0.583	21	32	21	-8.1
Formononetin	1711	-55.621	5.778	0.583	21	32	21	-8.8
Genistein	143	-40.345	35.274	-3.582	21	21	21	-8.2

Table 4: Binding cavities of Mafa with Compounds of Chickpea

Compounds	Affinity (kcal/mol)	dist from rmsd l.b.	best mode rmsd u.b.
Biochanin-A	-8.1 kcal/mol	0.000	0.000
Formononetin	-8.8 kcal/mol	0.000	0.000
Genistein	-8.2 kcal/mol	0.000	0.000

Table 5: The Docking results of *Cicer Arietinum* derived compounds against Mafa protein

3.3 ADMET Properties of Compounds

The absorption, distribution, metabolism, excretion, and toxicity of a chemical in and through the human body are covered by its ADMET characteristics. These characteristics make up a drug's pharmacokinetic profile and are crucial for assessing its pharmacodynamic actions. Utilizing ADME features, the ligand molecule's drug-like activity is described. The intended properties of a specific molecule can be improved by concentrating lead optimization efforts using ADME prediction. The expected ADMET properties (Structure Name, Lipophilicity (MlogP, S+logP, S+logD), Rule of 5, MWt. (Molecular weight), T_PSA (Topological Polar Surface Area), Serum hydroxybutyrate dehydrogenase level (HBDH) of the tested compound was evaluated with medchem designer and other ADMET properties (Num. H-bond acceptors (HBA), Num. H-bond donors (HBD) Lipinski violation, Drug likeness, Gastrointestinal absorption (GIA), Bioavailability score, Synthetic accessibility) given in (Table 6). The chosen characteristics are known to affect bioavailability, cell permeability, and metabolism. Almost all of the tested compounds' expected features meet Lipinski's criterion of five to be deemed as having drug-like potential.

Attributes	Biochanin-A	Formononetin	Genistein
Structure Name	5280373	3733033	5280961
MlogP	1.546	-0.463	1.296
S+logP	2.805	1.009	2.449
S+logD	2.658	1.009	2.914
RuleOf5	0.000	0.000	0.000
M Wt.	284.270	430.414	270.243

T_PSA	79.900	138.820	90.900
HBDH	2	4	3
HBA	5	9	5
HBD	2	4	3
Lipinski	0	0	0
Drug likeness	Yes	Yes	Yes
GIA	High	High	High
Bio. score	0.55	0.55	0.55
Syn. accessibility	2.89	5.12	2.87

Table 6: ADMET Properties of Chickpea Compounds

3.4 BOILED-Egg Predictive Model Plot

BOILED-Egg (Brain or Intestinal Estimated permeation predictive model) models of Genistein, Biochanin-A, and Formononetin are constructed for accurate prediction by calculating the polarity (WLOGP) and lipophilicity (tPSA). The white zone represents the physicochemical space with the highest likelihood of being absorbed by the gastrointestinal system, whereas the yellow region (yolk) indicates the physicochemical space with the highest likelihood of molecules penetrating the brain. This model revealed that the compounds Biochanin-A, Genistein, and Formononetin are present in the gastrointestinal absorption region (Figure 5).

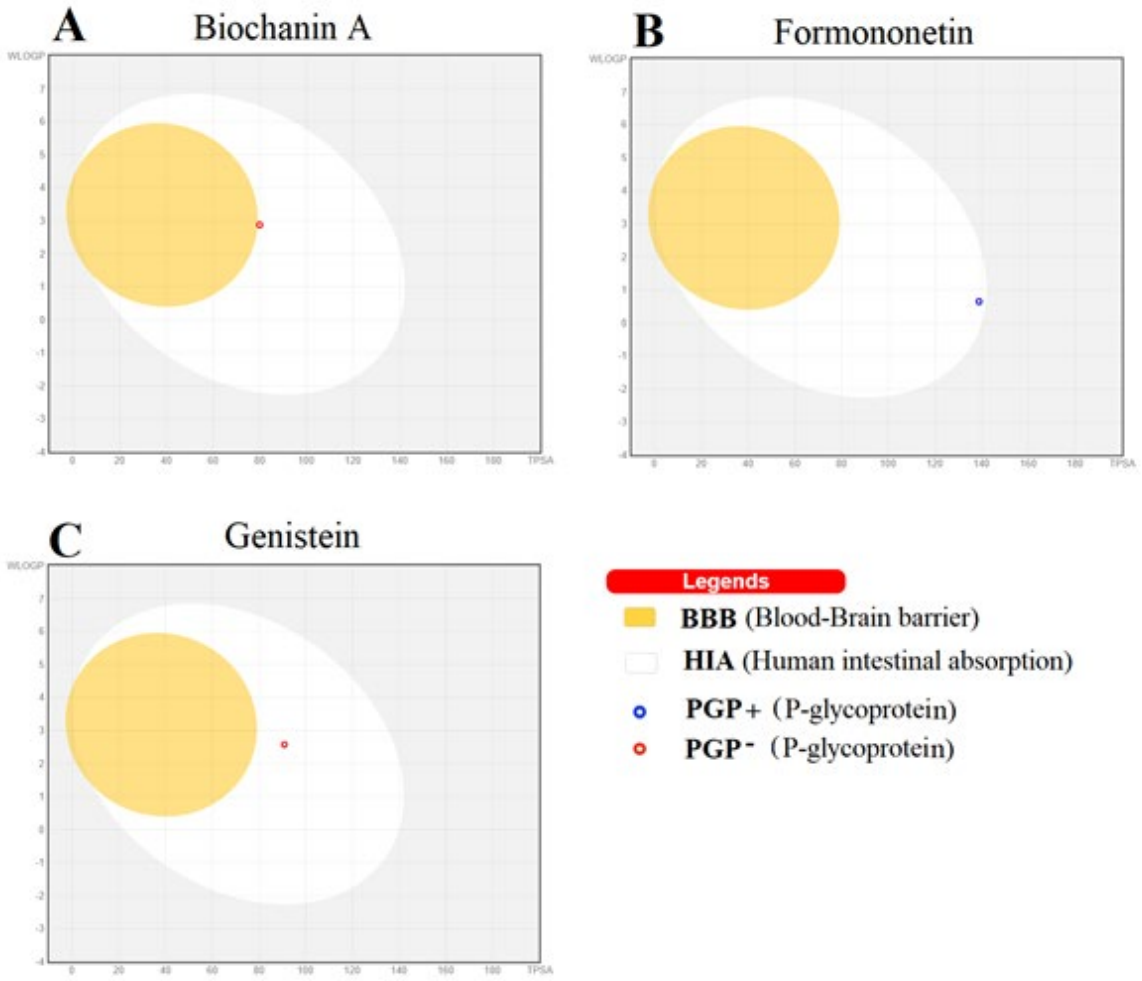


Figure 5: BOILED-Egg predictive model of chickpea compounds (A) Biochanin-A, (B) Formononetin and (C) Genistein.

3.5 The Bio-availability Radar

The Bioavailability Radar graphs revealed the drug-likeness. The ideal range for each property is represented by the pink area LIOP ((lipophilicity: between 0.7 and +5.0 for XLOGP3), size (MW ranging from 150 to 500 g/mol), POLAR (polarity: between 20 and 130 TPSA 2), INSOLU (solubility: log S not exceeding 6), INSATU (saturation: not less than 0.25 percent of carbons in the sp3 hybridization), and FLEX (flexibility: 9 maximum rotatable bonds maximum). In this radar, the compound Formononetin is predicted that all the parameters are present in the pink area within the optimal range. The compounds Biochanin-A and Genistein predicted properties (lipophilicity, solubility, size, polarity, flexibility) are found in the pink area within the optimal range while parameter saturation is placed outside the pink region shown in (figure 6).

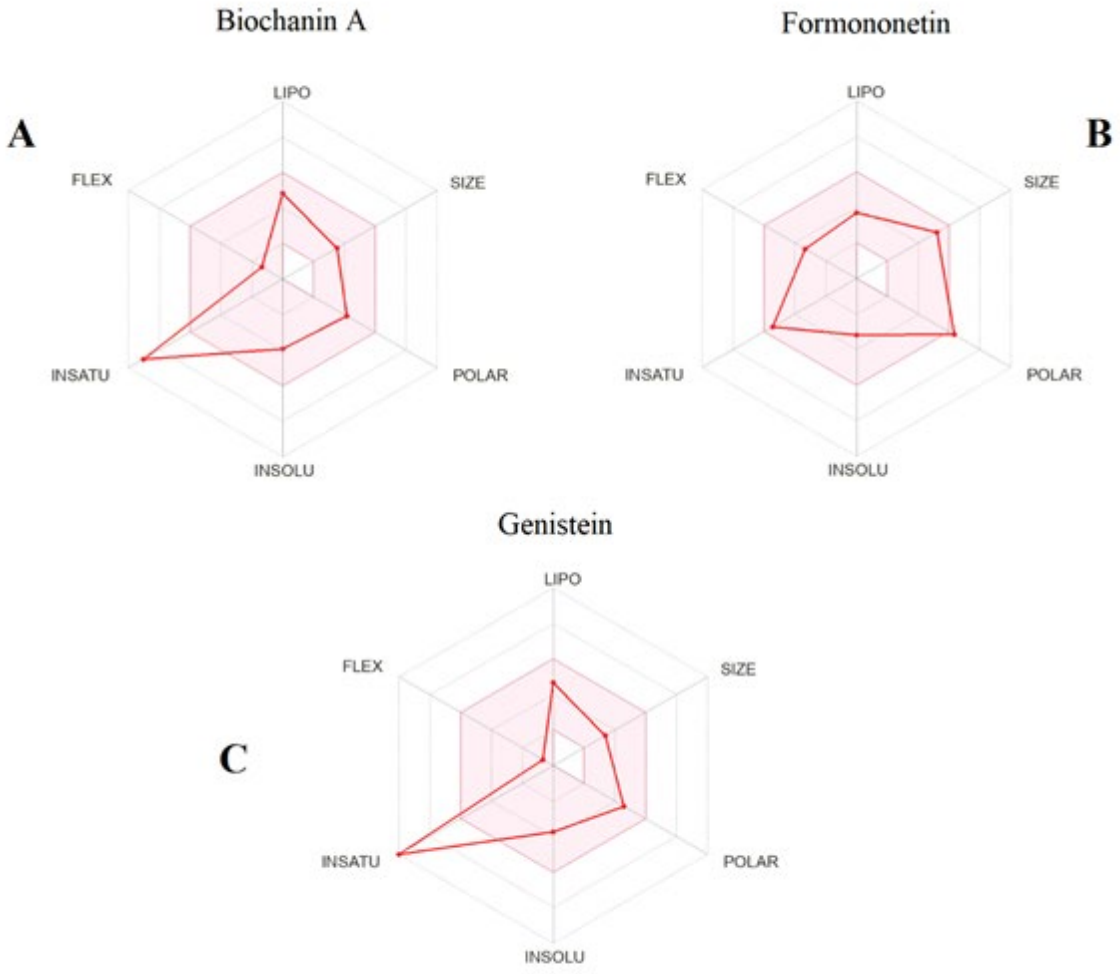


Figure 6: Bioavailability Radar of chickpea compounds (A) Biochanin-A, (B) Formononetin and (C) Genistein.

4. Discussion

Docking is a process that allows the screening of compound databases and evaluating the strongest binders that are based on different roles. It finds methods in which two molecules as enzymes and drugs are interacted together. Molecules might bind to receptor with modified functions. CB-Dock is a blind docking tool that is designed to predict the binding mode of ligands to proteins that do not know the binding site in advance [20]. Blind docking tools are useful in situations where the binding site of the protein is unknown or uncertain, like when it comes to membrane proteins or large protein complexes. CB-Dock is based on a combination of machine learning and a genetic algorithm, which enables it to efficiently explore the conformational space of the ligand and predict the most probable binding modes. The machine learning component of CB-Dock is trained on a dataset of already known protein-ligand complexes, which enables it to become familiar with the characteristics necessary for protein-ligand interactions. Hydrogen bonding, **Van der Waals Interactions** and electrostatic interactions are some of these characteristics. Once trained, the machine learning component can predict the binding affinity of a given ligand to a protein, which is used to guide the genetic algorithm in the search for the optimal binding mode [23]. CB-Dock has been shown to perform well in blind docking experiments, achieving high success rates and accuracy in

predicting the binding modes of a wide range of ligands to various proteins. For example, in a study by Liu et al., CB-Dock was able to accurately predict the binding modes of 12 out of 15 ligands to the protein Bcl-xL, with an average root-mean-square deviation (RMSD) of 2.6 Å [20]. In addition to its accuracy, CB-Dock is also computationally efficient, with a typical docking run taking only a few minutes on a standard computer. This makes it a valuable tool for high-throughput screening of large chemical libraries, as well as for the prediction of binding modes in drug discovery [24]. Overall, CB-Dock is a powerful blind docking tool that combines machine learning and genetic algorithms to efficiently explore the conformational space of ligands and predict their binding modes to proteins. Its high accuracy and computational efficiency make it a valuable tool for drug discovery and other applications in structural biology. MMP9, also known as matrix metalloproteinase-9, is a zinc-dependent enzyme involved in extracellular matrix remodeling and important role in a number of pathological and physiological processes, including inflammation, angiogenesis, and tissue repair. Recent studies have identified a potential link between MMP9 and type 2 diabetes, where MMP9 levels were shown to be substantially higher in diabetic patients than in people without diabetes [25]. Thus, targeting MMP9 could be a potential therapeutic strategy for the treatment of type 2 diabetes. Furthermore, molecular docking studies have been used to predict the binding affinity and interaction of various compounds with MMP9. One study published in the Journal of Biological Chemistry showed that knockdown of Mafa in cultured beta cells led to decreased insulin secretion and reduced glucose-stimulated insulin secretion, suggesting that Mafa inhibition could be used to reduce insulin secretion in cases of hyperinsulinemia or type 2 diabetes where excessive insulin production is a problem [26]. Another study published in the journal Diabetes showed that Mafa inhibition in mice led to increased insulin sensitivity, improved glucose tolerance and, suggesting that Mafa inhibition could be used to treat insulin resistance in type 2 diabetes [11]. However, it's important to note that these studies were conducted in vitro or in animal models and Further investigation is required to determine the effectiveness and safety of Mafa inhibition as a diabetes treatment in humans. Additionally, the potential side effects of inhibiting Mafa activity are not yet fully understood, and it's possible that other important cellular processes could be affected by Mafa inhibition (Gao T. et al., 2010). BOILED-Egg model of Genistein, Biochanin-A, and Formononetin predicted that these molecules have high gastrointestinal absorption but not in brain permeation. Bioavailability Radar enables a quick assessment of a molecule's drug-likeness. The optimal limit for each property is indicated by the pink area [21]. In previous studies, Compounds 6 and 11 are the most orally bioavailable since most of their expected properties are located within the pink region, whereas 8 and 12 are regarded to be not orally bioavailable because the majority of their predicted properties are located outside the pink zone [22]. In our study, the pink area shows the anticipated properties of formononetin and in Biochanin-A, and Genistein all the predicted properties are within the pink region except INSATU (saturation) property. The main metric that provides us with an indication of the strength and affinity of the interaction between the ligand and the receptor is binding energy. The interaction is weaker the higher the binding energy increases; therefore, we want to find the ligand that has the lowest binding energy, the test compounds with the highest affinity. For instance, a recent study investigated the binding affinity of several small molecule inhibitors to the SARS-CoV-2 main protease using docking simulations. The results showed that the inhibitor N3 had the strongest binding affinity, with a predicted free energy of binding of -6.1 kcal/mol. This was in agreement with experimental results, which showed that N3 inhibited the SARS-CoV-2 main protease with an IC50 of 0.67 μM [27]. Another study investigated the binding affinity of several compounds to the human angiotensin-converting enzyme 2 (ACE2) receptor, which is the target of the SARS-CoV-2 spike protein. In this study, the binding affinity of several small molecule inhibitors to the MDM2-p53 interaction was investigated using docking simulations. The results showed that the inhibitor RG7388 had the strongest binding affinity, with a predicted free energy of binding of -9.3 kcal/mol. This was in agreement with experimental results, which showed that RG7388 inhibited the MDM2-p53 interaction of 11 nM for the IC50 [28]. Other research When compared to the standard (7.0 kcal/mol), quercetin demonstrated the highest binding affinity with a molecular target (8.5 kcal/mol). According to these findings, quercetin glycosides may be a potential ligand for the treatment of hypertension, myocardial infarction and heart failure [29]. In our study the results showed that Genistein, Biochanin-A, and Formononetin have a high binding affinity towards MMP9, with a docking score of - Formononetin (-11 kcal/mol), Biochanin-A (-10.1 kcal/mol), Genistein (-10 kcal/mol). Genistein, Biochanin-A, and Formononetin also showed a high binding affinity towards Mafa for Formononetin (-8.8 kcal/mol), Biochanin-A (-8.1 kcal/mol), Genistein (-8.2 kcal/mol). Thus, Chickpea's major isoflavonoids Biochanin-A, Formononetin and Genistein possibly potential candidates for the generation of innovative MMP9 and Mafa inhibitors for the treatment of diabetes.

5. Conclusion

In conclusion, the identification of MMP9 and Mafa as prospective therapeutic targets for type 2 diabetes treatment represents a tremendous development in diabetes research. MMP9 and Mafa modulation have been demonstrated to play an important role in the pathophysiology of type 2 diabetes, making them an appealing target for the development of innovative treatment approaches. Furthermore, the use of natural drugs and synthetic chemicals to decrease MMP9 and Mafa function has yielded promising results, implying that the discovery of novel inhibitors targeting these proteins could be a viable technique for the treatment of type 2 diabetes. Molecular docking studies have provided valuable insights into the potential of compounds to interact with MMP9 and Mafa and could aid in the development of novel inhibitors with improved specificity and potency.

One interesting finding from the current analysis is that Chickpea, a commonly consumed legume, shows great potential as a natural

compound for diabetes treatment. The molecular docking studies demonstrated that Chickpea has a high binding affinity towards both MMP9 and Mafa, with affinity values ranging from -10.1 to -11 kcal/mol and -8.1 to -8.8 kcal/mol, respectively. The high affinity of Chickpea towards these proteins establishes an elaborative hypothesis about the effects of complex formation by MMP9 and Mafa. This new information on Chickpea's properties could lead to the development of novel dietary interventions for the prevention and treatment of type 2 diabetes. Overall, the identification of MMP9 and Mafa as potential therapeutic targets, the use of natural compounds and synthetic molecules to inhibit their activity, and molecular docking studies have provided significant advances in the understanding and treatment of type 2 diabetes. The potential of Chickpea as a natural compound for diabetes treatment adds to the growing body of evidence supporting the use of dietary interventions for the management of type 2 diabetes [30-38].

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