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Research Article

Molecular docking studies of abelmoschus esculentus for anti diabetics and anti inflammatory

M.S. Kumaran[1], P. Sivaselvi[2], P. Brindha[2], T. Vimala[2]

[1]Gensilico Bio Solution, West Tambaram, Chennai-45, [2]Department of Bioinformatics, Sri Krishna Arts and Science College, Coimbatore, India

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ABSTRACT

Okra (Abelmoschus esculentus (L) Moench) or bhendi also known as ladies' finger is an important vegetable crop in India, and African regions. Abelmoscus esculentus having the medicinal property of anti-inflammatory, anti-diabetics, anti-oxidant activities. In these studies, we are going to analysis the anti-diabetics and anti-inflammatory property of Abelmoscus esculentus by using molecular docking studies. Diabetics is a major cause of death and the number of new cases, as well as the number of individuals living with Diabetics, is expanding continuously. Now a days It is one of the most common diseases in the worldwide. Foot ulceration remains a major health problem for diabetic patients and has a major impact on the cost of diabetes treatment. One major complication of diabetes is foot ulceration, which occurs in as many as 15–25% of type 1 and type 2 diabetic patients over their lifetimes. The phytochemicals of Abelmoscus esculentus are analysed and optimized with the Arguslab to investigate the interactions between the target compounds and the amino acid residues of the Mafa and Mmp9. All the compound has shown binding pose between from – 3.25 to -7.95 and -7.95 into -11.40 out of ten compounds. [E,E] Farenesal with Mafa protein and gossypol with Mmp9 protein show best ligand energy -10.55 and -8.88 Kcal/mol with 1 and 1 hydrogen bond of distance is 3.0 and 2.3 respectively .

Key words: Molecular docking, Argus lab, Mafa, Mmp9, Abelmoscus esculentus

INTRODUCTION

Okra *(Abelmoschus esculentus* (L) Moench) or bhendi also known as ladies' finger is an important vegetable crop being native of tropical Africa. Okra Abelmoschus esculentus (L) moench is a tall annual dicotyledonous plant related to cotton and thought to be of African origin [1]. It is the flowering plant in the mallow family. Even though, the plant is cultivated in tropical and warm temperate region around the world. *Abelmoschus esculentus* (AE) is also one the potential natural plant that been used to manage diabetes[2]. In Asia, okra is typically prepared as traditional medicine as a dietary meal in the treatment of gastric irritations [3]. The plant has a wide range of medicinal value and has been used to control various diseases and disorders. The fiber in okra helps to stabilize blood sugar by regulating the rate at which sugar is absorbed from the intestinal tract. It is a good vegetable for those feeling weak, exhausted, and suffering from depression and it is also used in ulcers, lung inflammation, sore throat as well as irritable bowel. Okra is good for asthma patients and it also normalizes blood sugar and cholesterol levels. *A. esculentus* peel and seed possess blood glucose normalization and lipid profiles lowering action in diabetic condition [4][5].

Diabetes is a metabolic disorder that occurs when the pancreas does not produce enough insulin or when the body cannot effectively use the insulin it produces. It is classified in to two basic forms Type I and Type II diabetes [6] . As a result of this sugar accumulates in the blood leading to various complications such as cataract, retinopathy, nephropathy and neuropathy. High intake of plant foods may help to treat diabetes and the advantages can be linked to the presence of specific compounds in plants [7]. Classic signs and symptoms of diabetes include polyuria, polydipsia, polyphagia, weight loss, headache, palpitations, and blurred vision. The main risk factors for diabetes are age, family history, obesity, physical

***Corresponding Author Address: M.S. Kumaran, Gensilico Bio Solution, West Tambaram, Chennai-45, Tamil Nadu, India; Email:** gensilico@gmail.com*

inactivity and sedentary living, insulin resistance, stress etc. Complications of Diabetes mellitus may develop after many years (10-20). The major long-term complications include damage to blood vessels. Nearly 45% of all diabetics have peripheral vascular disease. Type 2 diabetes is one of the major life threatening diseases worldwide these cases are progressing at an incremental rate every year and number of research works are going on to control the disease by targeting its enzymes or proteins.[8] Type 2 diabetes mellitus (T2DM) is a genetically heterogeneous, polygenic disease with a complex inheritance pattern and is caused by genetic predisposition and environmental factors [9].With comparison with Cancer and HIV infection, Diabetes has emerged as a major healthcare problem in India. With comparison with Cancer and HIV infection, Diabetes has emerged as a major healthcare problem in India. According to Diabetes Atlas published by the International Diabetes Federation (IDF), there were an estimated 40 million persons with diabetes in India in 2007 and this number is predicted to rise to almost 70 million people by 2025. The countries with the largest number of diabetic people will be India, China and USA by 2030[10]. Islet β-cells loose their ability to synthesize insulin under diabetic conditions, which is at least partially due to the decreased activity of insulin transcription factors such as MafA[11]. MafA, a recently isolated pancreatic β-cell-specific transcription factor, is a potent activator of insulin gene transcription.[12]. It is known that the insulin gene is specifically expressed in pancreatic β-cells and that insulin plays a crucial role in maintaining blood glucose levels. It was previously shown that an unidentified β-cell-specific nuclear factor binds to a conserved cis-regulatory element called RIPE3b in the insulin gene promoter region and is likely to function as an important transactivator for the insulin gene[13][14].

Foot ulceration remains a major health problem for diabetic patients and has a major impact on the cost of diabetes treatment[15]. Antimicrobial resistance mediated by extended-spectrum b-lactamases (ESBLs) production by bacteria is considered to be a major threat for foot amputation[16]. One major complication of diabetes is foot ulceration, which occurs in as many as 15–25% of type 1 and type 2 diabetic patients over their lifetimes. Studies show that between 2 and 6% of diabetic patients will develop a foot ulcer every year. The feet of patients with diabetes are at risk for ulceration due to a wide range of pathological conditions, the major three being peripheral neuropathy, foot deformity, and trauma, which may be exacerbated by comorbid peripheral vascular disease. If left untreated, foot ulcers lead to infection and deep-tissue necrosis[17][18]. Diabetics (7–10%) develop chronic foot ulcers, a severe and expensive complication with life and/or limb threatening conditions. Chronic DFU are one of the most common indications for hospitalization in diabetics, and almost 50% of all non-traumatic amputations are performed on diabetic patients. Chronic DFU do not follow the well-described sequence of wound healing[19][20].

One other potentially important finding in diabetes is a disturbance in the expression and activation of matrix metalloproteinases (MMPs), a group of enzymes responsible for extracellular matrix (ECM) degradation. MMPs can be divided into four subgroups based on substrate specificity – interstitial collagenases, stromelysins, type IV collagenases and membrane type-MMPs (MT-MMPs). They are secreted in latent forms which are cleaved to become biologically active. Their activities are also tightly regulated by their inhibitors, the tissue inhibitors of metalloproteinases (TIMPs), which bind to the active MMP enzyme with high affinity. Four TIMPs (TIMP 1-4) have been identified; each has the ability to bind and inhibit MMP activities to a varying extent. MMPs are produced by many cell types involved in wound healing including fibroblasts, keratinocytes and inflammatory cells. Their expression is modulated in response to signals from cytokines, growth factors, cell– matrix interactions and altered cell-cell contacts[22].

MATERIALS AND METHODS

The Structure of the Protein MAFa and MMMP9 with the PDB ID (4EOT and 2OW2) was retrieved from the Protein Data Bank. It is a repository for the 3-D structural data of large biological molecules, such as proteins and nucleicacids.

Active site prediction: After obtaining the PDB ID (4EOT and 2OW2), the possible binding sites of MAFA and MMP9 were searched using Computed Atlas of Surface Topography of Proteins (CASTp). These include pockets located on protein surfaces and voids buried in the interior of proteins. CASTp includes a graphical user interface, flexible interactive visualization, as well as on-the-fly calculation for user uploaded structures

Docking: Docking the inhibitors against the active site of the MAFA and MMP9 Docking is a computational technique that samples conformations of small molecules in protein binding sites; scoring functions are used to assess which of these conformations best complements the protein binding site. The inhibitor and target

protein was geometrically optimized and docked using docking engine Argus Dock

RESULTS AND DISCUSSION

Molecular modelling (docking) study was carried out for compound like from homogalacturonan, folacin, rutin, quertin, gossypol, cyanidin 4 glucoside, [E,E] Farenesal, glysine, i amyl butanate, ash from Abelmoscus esculentus (1A-13) fig 1(A,B,C,D ,E,F,G,H,,I, and J) for Diabetics and Foot ulcer.

The target protein and inhibitors were geometrically optimized. Given the three-dimensional structure of a target receptor molecule usually a protein; chemical compounds having potential affinity toward site are designed rationally, with the aid of computational methods. Detailed bioinformatics analysis offers a convenient methodology for efficient insilico preliminary analysis of possible function of new drug. Figure 3 shows the structure Mafa and Mmp9.

All the Ten inhibitors were docked against active site of the target proteins using Argus lab which gives an insight into the binding modes for the various inhibitors. Out of 10 inhibitors analyzed i.e. homogalacturonan, folacin, rutin, quertin, gossypol, cyanidin 4 glucoside, [E,E] Farenesal , glysine, i amyl butanate, ash.has showed higher binding energy of -10.55 Kcal/mol and -8.88 Kcal/mol against the target proteins. The binding energy of all the inhibitors was shown in Table 1. Figure 4 represents the docked complex of the inhibitors to that of the target protein

The Table 2 describes the molecular properties of Mafa and Mmp9 protein in [E,E] Farenesal and gossypol (Table 2). [E,E] Farenesal and gossypol is a small sized molecule with a molecular weight of 220.35046 g/mol and 518.5544 g/mol Respectively. It has two hydrogen bond donors and four hydrogen bond acceptors with two rotatable bond. The chrysophanic acid and Colchicine compound has the LogP value of 4.9 and 6.9. Thereby it satisfies all the criteria of Lipinski's rule of five (Christopher et al., 1997).

Homogalacturonan

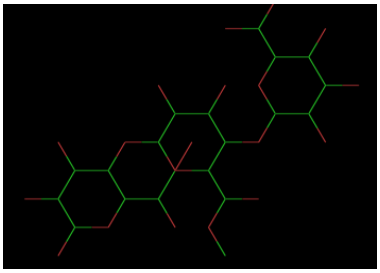


fig.1A

Folacin

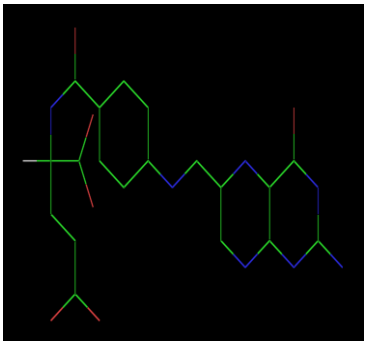


fig.1B

Rutin

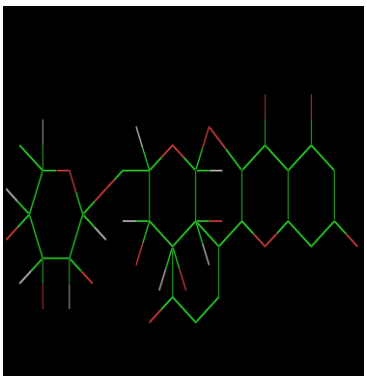


fig.1C

Quertin

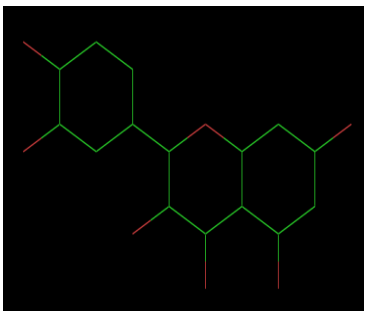


fig.1D

Gossypol

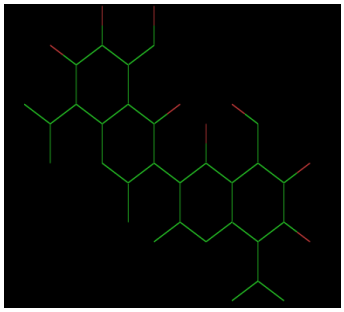


fig.1E

Cyanidin 4 glucoside

fig.1F

[E,E] Farenesa

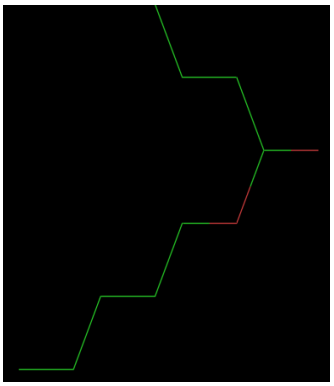


fig.1G

Glysine

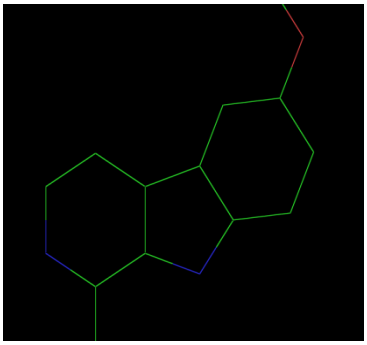


fig.1H

I amyl butanate

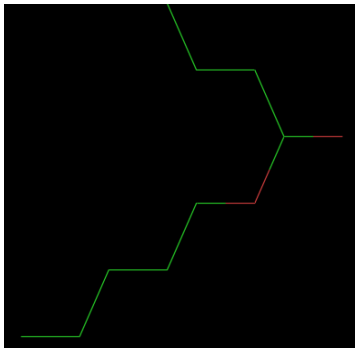


fig.1I

Ash

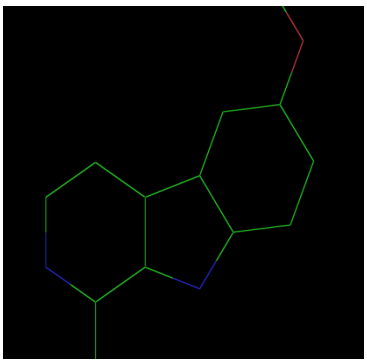
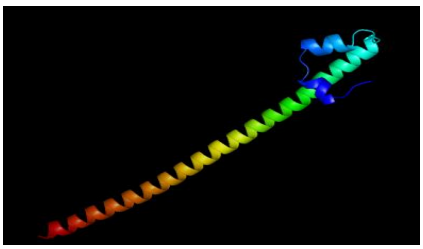


fig.1J

Fig -1A, 1B, 1C, 1D, 1E,1F, 1G ,1H,1I and 1J: It Shows compound from Abelmoscus esculentus plant homogalacturonan, folacin , rutin, quertin, gossypol, cyanidin 4 glucoside, [E,E] Farenesal , glysine, i amyl butanate, ash.



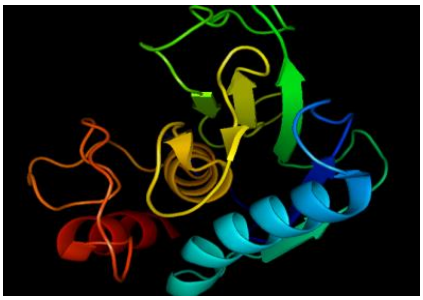


Fig. 3: Shows the structure Mafa and Mmp9 visualised using pyMol

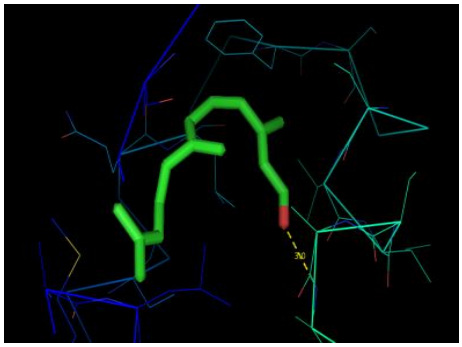
Table 1A: It shows the Docking results of ABELMOSCUS ESCULENTUS derived compounds against Mafa protein

S.no	Compound Name	Binding energy value(kcal/mol)	No.of Hydrogen bond
1	homogalacturonan	-5.74	6
2	folacin	-8.39	5
3	rutin	-6.35357	1
4	quertin	-7.40644	1
5	cyanidin 4 glucoside	-7.14	1
6	gossypol	-9.27	Nill
7	gossypol	-10.55	1
8	glysine	-6.65	7
9	i amyl butanate	-7.62	1
10	ash	-7.81	Nill

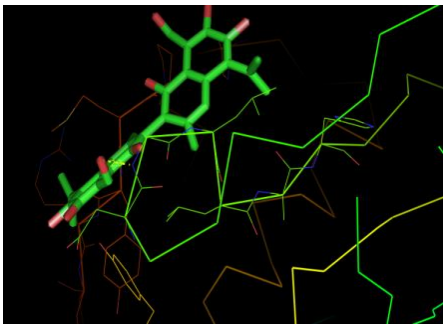
Table 1B: It shows the Docking results of ABELMOSCUS ESCULENTUS derived compounds against MMP9 protein

S.no	Compound Name	Binding energy value(kcal/mol)	No.of Hydrogen bond
1	homogalacturonan	-8.16	7
2	folacin	-9.04431	9
3	rutin	-7.36	2
4	quertin	-7.32951	1
5	cyanidin 4 glucoside	-7.33	3
6	gossypol	-8.88	1
7	gossypol	-12.81	Nill
8	glysine	-6.74	5
9	iamyl butanate	-8.99	2
1o	ash	-7.72	2

Docking complex of MAFA and MMP9 protein



Mafa protein with [E,E] Farenesal



Mmp9 protein with gossypol

Table 2A: Molecular property of (E, E)-farnesal

S.no	PROPERTY	VALUE
1	Molecular formula	C15H24O
2	Formula weight	220.35046 [g/mol]
3	A logp	4.9
4	No. of hydrogen acceptors	1
5	No. of hydrogen donors	0

Table 2B: Molecular property of gossypol

S.no	PROPERTY	VALUE
1	Molecular formula	C30H30O8
2	Formula weight	518.5544 [g/mol]
3	A logp	6.9
4	No. of hydrogen acceptors	8
5	No. of hydrogen donors	6

CONCLUSIONS

The present study indicates that analysis the property Abelmoschus esculentus herbal plant can be used in the treatment of Diabetes and Foot ulcer which shows a strong binding affinity towards MAFA and MMP9 protein. This brings a strong focus towards these plant that, when administered during the treatment of Diabetes and Foot ulcer may block MAFA and MMP9 Abelmoschus esculentus showed the highest affinity towards MAFA and MMP9 compared to other compounds. This creates a strong hypothesis that the effects of complex formation by MAFA and MMP9. Abelmoschus esculentus contribute towards combating against Diabetes and Foot ulcer. Hence, Abelmoschus esculentus may become a prospective target for inhibition of Diabetes and Foot ulcer and may unlock a strong initiative in

developing novel ligand which is specified towards it. Hence the compound specified in this work can undergo certain specification to improve its drug properties and could act as a best drug for Diabetes and Foot ulcer. The mechanism of action of Abelmoschus esculentus inhibit the activity of MAFA and MMP9 That is involved Diabetes and Foot ulcer hence Abelmoschus esculentus having both property of anti-Diabetes and anti-inflammatory.

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