DOA.J



Full Length Research Article

Advancements in Life Sciences – International Quarterly Journal of Biological Sciences

ARTICLE INFO

Open Access

Date Received: 25/11/2023; Date Revised 29/01/2024; Date Published Online 25/02/2024;

Author's Affiliation: Department of Food Science and Nutrition, College of

> Science, Taif University -Saudi Arabia

Identification of Phytochemicals through Virtual Screening for α -Amylase Inhibition: A Promising Approach for Diabetes

Khadija S. Radhi

Corresponding Author: Khadija S. Radhi Email: Ksradhi@tu.edu.sa

How to Cite:

Radhi KS (2024). Identification of Phytochemicals through Virtual Screening for α-Amylase Inhibition: A Promising Approach for Diabetes Management. Adv. Life Sci. 11(1): 220-225

Keywords

Diabetes: α-amylase: Natural compounds; Virtual screening; Drug-likeness

Editorial Note:

You are viewing the latest version of this article having minor corrections related to the use of English language.

Management Abstract

ackground: Type 2 diabetes is caused by a complex combination of genetic predisposition and lifestyle factors, which contributes to its rising global incidence. α-amylase is a critical pharmaceutical target for reducing postprandial hyperglycemia in diabetes and other metabolic diseases. Because of the numerous side effects associated with synthetic anti-diabetic drugs, the use of natural substances for diabetes management has grown in popularity in recent years.

Methods: In this study, potential α -amylase inhibitors were identified using virtual screening approaches, with a focus on bioactive compounds derived from Zingiber officinale. A comprehensive screening of 383 compounds was performed against the α -amylase active site. Following that, 14 compounds were identified as having greater binding energy efficacy than the control compounds.

Results: The compounds LTS0006138, LTS0117761, LTS0176515, LTS0102243, and LTS0018665 exhibited notable interactions with the catalytic residues of α -amylase in this study, particularly by forming hydrogen bonds with multiple residues within the enzyme. Furthermore, an analysis of the molecular properties and descriptors of these five compounds showed promising drug-like properties.

Conclusion: These compounds show promise as potential novel α -amylase inhibitors; nevertheless, further experimental validation is required to optimize their potency as α -amylase inhibitors.



You're reading

Introduction

Diabetes, a chronic metabolic condition, is one of the prominent contributors to premature death globally. According to the International Diabetes Federation (IDF), diabetes affects one out of every ten adults worldwide, implying that over 537 million people are affected by this chronic disease. This amount will more than double to over 643 million by 2030 and 783 million by 2045 [1]. Diabetes-related complications claimed the lives of 6.7 million people worldwide in 2021 alone [2]. Diabetes, specifically type 2 Diabetes (T2D), is characterized by high blood glucose levels, also known as hyperglycemia. The primary underlying factor in this condition is a decrease in pancreatic insulin production, which results in a deficit of insulin secretion and impaired insulin function, or a combination of both [3]. T2D results in weight gain and decreased physical activity due to the body's inability to utilize insulin, with a significant proportion of patients not requiring insulin therapy [4]. This situation puts patients at a higher risk of serious health complications. particularly those related to cardiovascular disease [5]. Chronic diabetes, in the absence of appropriate intervention, can lead to organ failure and frequently results in life-threatening longterm complications [3].

Diabetes is currently managed with insulin and various oral anti-diabetic medications. However, many existing diabetes medications are associated with a wide range of serious side effects, emphasizing the critical need to investigate alternative approaches [6,7]. carbohydrate-hydrolyzing Inhibiting enzymes, particularly α -amylase, to reduce glucose absorption is an effective strategy for preventing postprandial hyperglycemia. α -amylase is a key secretion produced by the salivary glands and pancreas that is required for starch and glycogen digestion. This enzyme catalyzes the first phase of starch hydrolysis, resulting in a mixture of oligosaccharides [8]. Hence, α -amylase is critical in breaking down complex starch molecules simpler sugar constituents. Following into а carbohydrate-rich meal, blood glucose levels rise as starch begins to break down into simpler sugar units. Therefore, α -amylase activity significantly contributes to postprandial glucose elevation. The inhibition of α amylase has the potential to significantly reduce the post-meal surge in blood glucose, making it an effective approach for glycemic control in people with T2D and those on the verge of developing the disease [9].

Ginger, scientifically known as Zingiber officinale, has the ability to address Type 2 Diabetes Mellitus (T2DM) and its associated complications by engaging with the biochemical and cellular pathways that contribute to the development of the disease. Gingerols

and shogaols enhance glucose regulation, increase insulin sensitivity, exhibit anti-inflammatory properties, and demonstrate antioxidant activity. Ginger suppresses the activity of enzymes involved in the breakdown of carbohydrates, decreases inflammation throughout the body, counteracts the harmful effects of oxidative stress, and enhances the composition of lipids in order to enhance the regulation of blood sugar levels and address metabolic imbalances associated with T2DM [10]. This study utilizes a computational approach, specifically structure-based virtual screening, to identify new natural α -amylase inhibitors from the LOTUS database. Upon experimental validations, these inhibitors exhibit potential for utilization as a therapeutic intervention for diabetes.

Methods

Protein preparation

The protein structure used as a prerequisite for molecular docking was retrieved from the Protein Data Bank, with the PDB ID 2QV4 file depicting the threedimensional structure of human pancreatic α -amylase complexed with Acarbose derivative (named as QV4) at a resolution of 1.97 angstroms [11]. This structural model was created by removing heteroatom coordinates, water molecules, and co-crystallized ligand molecules, and the resulting protein structure was saved in .pdb format.

Compound library preparation

The investigation incorporated a widely recognized botanical species, Zingiber officinale. a detailed investigation was conducted within the LOTUS database to identify bioactive compounds originating from this particular species. The compounds that have been found were downloaded in the .sdf format and subsequently subjected to processing in order to facilitate their utilization in subsequent virtual screening.

Virtual screening

PyRx version 0.8 [12], which uses Autodock Vina as the underlying docking engine, was used for molecular docking for virtual screening. The docking grid center was defined as X = 12.384745, Y = 48.136073, and Z = 26.209218. Subsequently, the binding affinities for the most favorable poses were tabulated, and the interaction details were visualized utilizing the Discovery Studio (DS) Visualizer. QV4 (co-crystal ligand) and montbretin A (MbA), a human pancreatic α -amylase inhibitor [11] was used as a positive control for this study.

You're reading Identification of Phytochemicals through Virtual Screening for α -Amylase Inhibition: A Promising Approach for Diabetes Management

Molecular properties and molecular descriptors estimation

The molecular properties and molecular descriptors for the selected five compounds were accessed from the LOTUS database (<u>https://lotus.naturalproducts.net/</u>).

Results

A virtual screening methodology was employed in order to identify a putative natural inhibitor of α -amylase. A total of 383 compounds were obtained from a LOTUS database derived from Zingiber officinale. The secondary structure of α -amylase, specifically the ProMotif, is characterized by the presence of 8 β sheets, 5 $\beta\alpha\beta$ units, 6 β -hairpins, 3 β -bulges, 24 β strands, 23 α -helices, 13 helix-helix interactions, 48 β turns, 7 γ -turns, and 5 disulfide bonds. The catalytic residues responsible for enzymatic activity are located at positions D197-D300-E233, D197-E233, and D197-E233 (Figure 1).



Figure 1: 3D (A) and secondary (B) structure of α -amylase showing α -helices, β -sheets, and domains.

A structure-based virtual screening methodology was adopted to screen the active pockets of α -amylase against the 383 compounds that were retrieved. After conducting virtual screening and conducting a thorough analysis of the screened compounds, which involved evaluating binding energies and visually inspecting their 2D and 3D interactions, it was determined that 14 compounds exhibited greater efficacy in terms of binding energies (Table 2).

Ligand	Binding Affinity (Kcal/mol)
LTS0268251	-7.6
LTS0176515	-7.5
LTS0015210	-7.1
LTS0018665	-7.1
LTS0117761	-6.8
LTS0102243	-6.5
LTS0006138	-6.4
LTS0203280	-6.3
LTS0266647	-6.3
LTS0254603	-6.3
LTS0117764	-6.2
LTS0203906	-6.1
LTS0084287	-6.1
LTS0206935	-6.1
Montbretin A	-6.1
OV4	-57

Table 1: List of the top 14 compounds with binding affinity values higher than the positive controls.

Further investigation was undertaken on the top five prominent compounds that were identified, specifically LTS0006138, LTS0117761, LTS0176515, LTS0102243, and LTS0018665. Figure 2 illustrates the binding conformations of the five compounds under investigation, as well as two positive controls (QV4 and MbA), within the active pocket of α -amylase (Figure 2). The comprehensive analysis of docked complexes demonstrated that these selected compounds exhibited interactions within the identical catalytic pocket of the target protein, comparable to the positive controls.



Figure 2: Binding poses of the control (blue) and top 5 compounds (green) in active pocket of target protein.

The positive control MbA was found to interact with Leu162, Tyr151, Pro54, Thr163, Asn53, Ile51, Trp58, Gln63, His299, Asp300, Asn298, Glu233, Arg195, Asp197, Tyr62, Gly104, Leu165, Trp59, Asp356, and His305 residues of α -amylase; while the co-crystal inhibitor QV4 interacted with Trp58, Leu162, His305, His299, Asp300, Arg195, Asp197, Glu233, Ala198, Tyr62, Gln63, Trp59, Leu165, Glu60, Ala106, Pro54, Ile51, Asn53, Val107, Gly104, and Thr163 residues of α -amylase (Figure 3).



Figure 3: 2D interaction of positive controls with active residues of α -amylase showing several common interacting residues.

LTS0176515 was found to interact with Arg421, Val401, Pro332, Arg398, Ser289, Gly334, Asp290, Arg252, Ser3, Pro4, Thr11, Phe335, Asp402, and Gly403 residues of α -amylase (Figure 4). LTS0018665 interacted with Trp58, Tyr62, Trp59, His299, Asn298, Arg195, Asp300, Glu233, Ala198, and Asp197 residues of α -amylase (Figure 4). LTS0006138 was found to bind with Gly9, Gly403, Arg421, Ser289, Arg398, Pro332, Gly334, Tyr333, Arg252, Asp290, Asp402, Phe335, Thr11, Pro4, Thr6, and Arg10 residues of α -amylase

You're reading Identification of Phytochemicals through Virtual Screening for α-Amylase Inhibition: A Promising Approach for Diabetes Management

(Figure 4). LTS0117761 interacted with Phe335, Pro4, Arg252, Asp290, Gly334, Ser289, Pro332, Gly403, Arg398, Arg421, Thr11, Asp402, Gly9, Arg10, and Thr6 residues of α -amylase (Figure 4). Furthermore, LTS0102243 was found to interact with Ile235, Asp300, Glu233, Arg195, His299, Asp197, Trp59, Tyr62, His305, Trp58, Asn298, Phe256, Asn301, Ala307, and Gly306 residues of α -amylase (Figure 4).



Figure 4: 2D interaction of top 5 hits with active residues of α -amylase showing several common interacting residues.

Compounds	Interacting residues	H-bonded residues
LTS0176515	Arg421, Val401, Pro332, Arg398,	Arg252 and Arg421
	Ser289, Gly334, Asp290, Arg252,	
	Ser3, Pro4, Thr11, Phe335, Asp402,	
	and Gly403	
LTS0018665	Trp58, Tyr62, Trp59, His299,	His299, Arg195,
	Asn298, Arg195, Asp300, Glu233,	Glu233, and Asp197
	Ala198, and Asp197	
LTS0006138	Gly9, Gly403, Arg421, Ser289,	Arg252, Gly334, and
	Arg398, Pro332, Gly334, Tyr333,	Ser289
	Arg252, Asp290, Asp402, Phe335,	
	Thr11, Pro4, Thr6, and Arg10	
LTS0117761	Phe335, Pro4, Arg252, Asp290,	Arg252 and Ser289
	Gly334, Ser289, Pro332, Gly403,	
	Arg398, Arg421, Thr11, Asp402,	
	Gly9, Arg10, and Thr6	
LTS0102243	Ile235, Asp300, Glu233, Arg195,	Glu233 and Arg195
	His299, Asp197, Trp59, Tyr62,	
	His305, Trp58, Asn298, Phe256,	
	Asn301, Ala307, and Gly306	
MbA°	Leu162, Tyr151, Pro54, Thr163,	Asp356, Asp197,
	Asn53, Ile51, Trp58, Gln63, His299,	and Arg195
	Asp300, Asn298, Glu233, Arg195,	
	Asp197, Tyr62, Gly104, Leu165,	
	Trp59, Asp356, and His305	
QV4°	Trp58, Leu162, His305, His299,	His299, Glu63, and
	Asp300, Arg195, Asp197, Glu233,	Thr163
	Ala198, Tyr62, Gln63, Trp59,	
	Leu165, Glu60, Ala106, Pro54,	
	Ile51, Asn53, Val107, Gly104, and	
	Thr163	

*positive control

Table 2: List of interacting residues and H-bonded residues of α -amylase with selected five compounds.

Molecular Properties	LTS0006138	LTS0117761	LTS0176515	LTS0102243	LTS0018665
	1-(3,4-dihydroxy-5- methoxynhenyl)-5-	(1e,4e)-1-(4-hydroxy-3- methoxynhenyl)deca-1 4-dien-	Shogaol	1-(3,4-dimethoxyphenyl)- 5-hydroxydecan-3-one	Butanediol
	hydroxydecan-3-one	3-one		5 hydroxydecan 5 one	
Total atom	48	42	44	50	16
Heavy atom	22	20	20	22	6
Bond count	22	20	20	22	5
Number of carbons	17	17	17	18	4
Minimal number of rings	1	1	1	1	0
Maximal number of rings	1	1	1	1	0

Table 3: Common molecular properties of the selected five compounds.

Molecular Descriptors	LTS0006138	LTS0117761	LTS0176515	LTS0102243	LTS0018665
	1-(3,4-dihydroxy-5-	(1e,4e)-1-(4-hydroxy-3-	Shogaol	1-(3,4-dimethoxyphenyl)-	Butanediol
	methoxyphenyl)-5-	methoxyphenyl)deca-1,4-dien-		5-hydroxydecan-3-one	
	hydroxydecan-3-one	3-one			
NP-likeness score	1.02	1.02	1.02	1.02	1
Alogp	3.21	4.53	4.55	3.72	0.37
Alogp2	10.28	20.51	20.72	13.87	0.14
Apol	51.2666	46.9954	48.329	53.5582	15.3119
Bpol	31.2974	26.9246	29.111	35.3998	10.9321
Eccentric Connectivity	474	430	430	497	31
Index Descriptor					
Fmf Descriptor	0.2727	0.3	0.3	0.2727	0
Fsp3	0.5882	0.3529	0.4706	0.6111	1
Fragment Complexity	1842.05	1384.03	1556.03	2038.04	195.02
Descriptor					
Petitjean Number	0.5	0.5	0.5	0.4667	0.5
LipinskiRule	0	0	0	1	0
(Failures)					
WienerPath	1284	1043	1043	1312	32
Number					
Xlogp	2.793	4.359	4.108	3.091	0.316
Zagreb Index	100	88	88	98	20
TopoPSA	86.99	46.53	46.53	55.76	40.46

 Table 4: Predicted molecular descriptors and NP-likeness scores of the selected five compounds.

You're reading Identification of Phytochemicals through Virtual Screening for α-Amylase Inhibition: A Promising Approach for Diabetes Management

The additional comprehensive data regarding the selected 5 compounds, including their molecular properties (Table 3) and molecular descriptors (Table 4), was obtained from the LOTUS database. Molecular properties including the number of total atoms, heavy atoms, bond count, carbon atoms, minimal number of rings, as well as maximal number of rings were estimated for these compounds.

Drug-like characteristics are evaluated using molecular descriptors during compound design. Size, shape, polarity, and chemical reactivity are all numerical representations of molecule attributes. Various descriptors were calculated for the selected substances, typically comprising the NP (natural product)-likeness score, AlogP, and evaluation for Lipinski's rule violation. These descriptors collectively offered a comprehensive assessment of the compound's drug-like characteristics.

Discussion

Diabetes, a widespread metabolic syndrome, is a formidable and long-lasting global public health challenge. A well-known therapeutic strategy for the prevention and management of diabetes involves lowering postprandial blood glucose levels by inhibiting digestive enzymes such as α -amylase and alpha-glucosidase [13]. The enzyme α -amylase is a critical therapeutic target, and several synthetic drugs, including acarbose, voglibose, and miglitol, have been developed through its inhibition. Natural sources have also yielded numerous amylase inhibitors [14,15].

The goal of this study was to screen chemicals derived from Zingiber officinale for inhibitory effects on α -amylase. Zingiber officinale is widely recognized for its therapeutic properties in the treatment of diabetes, and a plethora of anti-diabetic chemicals have been extracted from this specific species [16]. Following virtual screening and a thorough analysis of the screened compounds, which included an assessment of binding energies as well as a visual inspection of their 2D and 3D interactions, 14 compounds were identified as having greater binding energy efficacy than the positive controls. notably, five key compounds were selected for in-depth interaction analysis: LTS0006138, LTS0117761, LTS0176515, LTS0102243, and LTS0018665.

H-bonds are crucial to the binding stability of ligandprotein complexes [17]. Interestingly, the top 5 compounds (LTS0006138, LTS0117761, LTS0176515, LTS0102243, and LTS0018665) formed H-bonds with several α -amylase residues. LTS0176515 formed Hbonds with Arg252 and Arg421 residues of α -amylase, while His299, Arg195, Glu233, and Asp197 residues H- bonded with LTS0018665. LTS0006138 formed H-bonds with Arg252, Gly334, and Ser289 residues of α -amylase, while LTS0117761 formed H-bonds with Arg252 and Ser289 residues. LTS0102243 also formed H-bonds with the Glu233 and Arg195 residues of α -amylase.

MbA, a glycosylated flavonol that is water soluble, effectively inhibits human pancreatic amylase. the targeted inhibition of the enzyme underscores the importance of this substance in the treatment of diabetes and obesity [18]. The α -amylase residues Leu162, Pro54, Thr163, Asn53, Ile51, Gln63, His299, Asp300, Glu233, Arg195, Asp197, Tyr62, Gly104, Leu165, Trp59, and His305 were found to be important in binding interactions with MbA and the co-crystal inhibitor (QV4). Intriguingly, the compounds LTS0006138, LTS0117761, LTS0176515, LTS0102243, and LTS0018665 showed interactions with these specific α -amylase residues, indicating the need for further exploration of their pharmacological potential.

Drug development is a critical undertaking in the pharmaceutical industry. Computational drug discovery is emerging as an effective strategy for speeding up and streamlining the drug discovery and development process [19-21]. Herbal medicine is a viable option for reducing the negative side effects of synthetic drugs. Diabetes has traditionally been treated using a variety of medicinal plants [22]. Because of their ease of use, low side effects, and low cost, bioactive compounds play a crucial role in modern pharmaceuticals, particularly in rural areas [23]. The hit compounds identified in this study are phytochemical with strong binding affinity for α -amylase, implying potential utility in diabetes management.

 α -amylase is a critical therapeutic target in diabetes management. In this study, natural compounds were virtually screened against α -amylase. Notably, LTS0006138, LTS0117761, LTS0176515, LTS0102243, and LTS0018665 demonstrated strong binding affinity to α -amylase and interactions with the enzyme's active site residues. Furthermore, these compounds demonstrated promising drug-like properties. These compounds show promise as potential novel α -amylase inhibitors; however, additional experimental validation is necessary to optimize their therapeutic potential as α -amylase inhibitors.

Conflict of Interest

The authors declare that there is no conflict of interest.

References

- Kumar A, Gangwar R, Ahmad Zargar A, Kumar R, Sharma A. Prevalence of diabetes in India: A review of IDF Diabetes Atlas 10th edition. Current Diabetes Reviews, (2024); 20(1): e130423215752.
- 2. Magliano DJ, Boyko EJ (2021). IDF DIABETES ATLAS. 10th ed. Brussels.

- 3. Deshpande AD, Harris-Hayes M, Schootman M. Epidemiology of diabetes and diabetes-related complications. Physical Therapy, (2008); 88(11): 1254-1264.
- Galicia-Garcia U, Benito-Vicente A, Jebari S, Larrea-Sebal 4. A, Siddiqi H, et al. Pathophysiology of Type 2 Diabetes Mellitus. International Journal of Molecular Sciences, (2020); 21(17): 6275.
- Martin-Timon I, Sevillano-Collantes C, Segura-Galindo A, 5. Del Canizo-Gomez FJ. Type 2 diabetes and cardiovascular disease: Have all risk factors the same strength? World Journal of Diabetes, (2014); 5(4): 444-470.
- Patel DK, Prasad SK, Kumar R, Hemalatha S. An overview 6. on antidiabetic medicinal plants having insulin mimetic property. Asian Pacific Journal of Tropical Biomedicine, (2012); 2(4): 320-330.
- 7. Saxena A, Vikram NK. Role of selected Indian plants in management of type 2 diabetes: a review. The Journal of Alternative and Complementary Medicine, (2004); 10(2): 369-378
- Peyrot des Gachons C, Breslin PA. Salivary Amylase: 8 Digestion and Metabolic Syndrome. Current Diabetes Reports, (2016); 16(10): 102.
- 9. Kaur N, Kumar V, Nayak SK, Wadhwa P, Kaur P, Sahu SK. Alpha-amylase as molecular target for treatment of diabetes mellitus: A comprehensive review. Chemical Biology & Drug Design, (2021); 98(4): 539-560.
- Akash MS, Rehman K, Tariq M, Chen S. Zingiber officinale 10. and Type 2 Diabetes Mellitus: Evidence from Experimental Studies. Critical Reviews in Eukaryotic Gene Expression, (2015); 25(2): 91-112.
- Maurus R, Begum A, Williams LK, Fredriksen JR, Zhang R, 11. et al. Alternative catalytic anions differentially modulate human alpha-amylase activity and specificity. Biochemistry, (2008); 47(11): 3332-3344.
- 12. Dallakyan S, Olson AJ. Small-molecule library screening by docking with PyRx. Chemical biology: methods and protocols, (2015); 1263: 243-250.
- 13. Kim YM, Jeong YK, Wang MH, Lee WY, Rhee HI. Inhibitory effect of pine extract on alpha-glucosidase activity and postprandial hyperglycemia. Nutrition, (2005); 21(6): 756-761.
- 14. Lankatillake C, Luo S, Flavel M, Lenon GB, Gill H, et al. Screening natural product extracts for potential enzyme inhibitors: protocols, and the standardisation of the usage of blanks in alpha-amylase, alpha-glucosidase and lipase assays. Plant Methods, (2021); 17(1): 3.

- Ogunyemi OM, Gyebi GA, Saheed A, Paul J, Nwaneri-15. Chidozie V, et al. Inhibition mechanism of alpha-amylase, a diabetes target, by a steroidal pregnane and pregnane glycosides derived from Gongronema latifolium Benth. Frontiers in Molecular Biosciences, (2022); 9: 866719.
- Huang FY, Deng T, Meng LX, Ma XL. Dietary ginger as a 16 traditional therapy for blood sugar control in patients with type 2 diabetes mellitus: A systematic review and metaanalysis. Medicine (Baltimore), (2019); 98(13): e15054.
- 17 Chen D, Oezguen N, Urvil P, Ferguson C, Dann SM, Savidge TC. Regulation of protein-ligand binding affinity by hydrogen bond pairing. Science Advances, (2016); 2(3): e1501240.
- 18. Irmisch S, Jancsik S, Man Saint Yuen M, Madilao LL, Bohlmann J. Complete Biosynthesis of the Anti-Diabetic Plant Metabolite Montbretin A. Plant Physiology, (2020); 184(1): 97-109.
- Tarique M, Ahmad S, Malik A, Ahmad I, Saeed M, et al. 19. Correction to: Novel Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV2) and Other Coronaviruses: A Genome-wide Comparative Annotation and Analysis. Molecular and Cellular Biochemistry, (2022); 477(2): 645.
- 20. Jabir NR, Firoz CK, Kamal MA, Damanhouri GA, Alama MN, et al. Assessment of IL-18 Serum Level and Its Promoter Polymorphisms in the Saudi Coronary Artery Disease (CAD) Patients. Journal of Cellular Biochemistry, (2017); 118(7): 1849-1854.
- 21. Alam MZ, Alam Q, Man AG, Shukri HA, Haque A. A surveillance study on the prevalence and antimicrobial resistance pattern among different groups of bacteria isolated from Western province of Saudi Arabia. Biomedical Research (India), (2017); 28(2): 898-906.
- 22 Ghosh Tarafdar R, Nath S, Das Talukdar A, Dutta Choudhury M. Antidiabetic plants used among the ethnic communities of Unakoti district of Tripura, India. Journal of Ethnopharmacology, (2015); 160: 219-226.
- 23 Salehi B, Ata A, N VAK, Sharopov F, Ramirez-Alarcon K, et al. Antidiabetic Potential of Medicinal Plants and Their Active Components. Biomolecules, (2019); 9(10): 551.



nc/4.0/

This work is licensed under a Creative Commons Attribution-NonCommercial 4.0 International License. To read the copy of this license please visit: https://creativecommons.org/licenses/by-