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Antibacterial activity against glucansucrase of Streptococcus mutans, in silico molecular docking analysis, ADMET analysis of isothiocyanates and glucosinolates compounds from Brassica oleracea l. var. italica

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Abstract:

INTRODUCTION: Medicinal plants have been essential to the development of primary healthcare and are a rich source of novel bioactive chemicals for medication discovery. The bioactive components of Brassica oleracea var. Italica and their roles in supporting health are diverse. The aim of the study is used to confirm the mode of binding for antibacterial activity, elucidating quantum chemical properties, and ADME-drug-likeness of isothiocyanates and glucosinolates isolated from Brassica oleracea. L. Var. Italica.

METHODS: Docking studies were performed against 3AIC employing a flexible ligand docking approach using Autodock vina. SwissADME prediction and toxicology predictions were done using ADMET. The optimized structure and electrostatic potential of the isolated compounds were predicted by DFT analysis using B3LYP/31G basis levels.

RESULTS AND DISCUSSION:

Docking results revealed that Indole-3 acetic acid and Glucobrassicin showed better docking scores compared to other compounds. The SwissADME prediction results showed that Indole-3 acetic acid and Glucobrassicin having higher affinity value with Indole-3 acetic acid satisfying Lipinski's rule of five with zero violations. Toxicological prediction results suggested that compounds are non-hepatotoxic, non-carcinogenic, non-irritant, immunogenic, and non-cytotoxic. The DFT analysis suggesting better bioactivity and chemical reactivity with considerable intra-molecular charge transfer between electron-donor to electron-acceptor groups.

CONCLUSION: Indole-3 acetic acid and Glucobrassicin compound may serve as a lead molecule and further work is recommended for functional group inclusion, modification, and SAR study to develop novel antibacterial agents with therapeutic activity against *S. mutans.*

KEYWORDS: Lux S binding domain, de novo DFT, flavonoids, phenolic and docking studies

INTRODUCTION:

Broccoli seedlings are a superior source of phytochemicals that promote health, such as nitrogen-sulfur derivatives like glucosinolates and isothiocyanates, polyphenols like derivatives of chlorogenic and sinapic acids and flavonoids, minerals like selenium, potassium, and manganese, and vitamins like A, C, K, and B6 (Baenas, Moreno, and García-Viguera 2012)(Aparna et al. 2021). The usage of pesticides and herbicides is eliminated, food waste is decreased, and the amount of phytochemicals that are beneficial to health is increased by ten times when compared to commercial adult plants when using sprouts and microgreens as a novel way for functional meals.(Le, Chiu, and Hsieh 2020)(Janani et al. 2020). Due to their high nutritional value and bioactive content, vegetable crops are an essential part of the human diet and may help to increase food security and nutritional quality (Montaner et al. 2022) (Johnson et al. 2022). Since broccoli (Brassica oleracea L. var. Italica) contains significant amounts of health-promoting compounds like vitamins, glucosinolates, phenolic compounds, and dietary essential minerals, it offers benefits to health beyond just basic nutrition. As a result, consumption of broccoli has been rising over time.(Ares, Nozal, and Bernal 2013)(Nasim and Professor and Head, Departm...). A vast class of secondary plant metabolites known as glucosinolates has physiologically active substances and nutritional benefits (Prieto, López, and Simal-Gandara 2019). The most significant GLSs in broccoli are glucoraphanin, which makes up more than half of the total, glucoiberin, glucoerucin, glucobrassicin, and neoglucobrassicin. (Orlando et al. 2022).

According to their metabolic development and production of quorum sensing (QS)-controlled virulence factors, bacterial species of the Streptococcus genera are classified as either commensal bacteria or prospective pathogens.(Bernabè et al. 2022)(Kamath et al. 2020)(Siddique et al. 2020). According to their metabolic evolution and production of virulence factors controlled by quorum sensing (QS), bacteria of the Streptococcus genera are classified as either commensal bacteria or potential pathogens (Krzyściak et al. 2014)(Kamath et al. 2022) .Quorum sensing is a form of communication used by bacteria to organise a population's response.(Shanker and Federle 2017). The two-component signal transduction system used by quorum sensing in S. mutans produces a signal that suppresses the formation of bacteriocin and genetic competence. (Lemos et al. 2019)(Nasim et al. 2022)

Computational pharmacology is a fast-growing research field focusing on the development of techniques for employing software and databases to generate and analyze molecular, biological and medical data from diverse sources.(Bitew et al. 2021). Although access to physical samples is restricted, the design and development of pharmacological molecules need earlier evaluation of pharmacokinetic characteristics, absorption, distribution, metabolism, and excretion (ADME).(Daina, Michielin, and Zoete 2017). Compared to experimental methodologies, computer-aided methods in the search for novel drug-like compounds conserve time, human, and material resources.(Plewczynski et al. 2011).

In the present study, a computational de novo design approach was used to confirm the mode of binding for antibacterial activity, elucidating quantum chemical properties and ADMET-drug-likeness of phenolic and flavonoids isolated from Brassica oleracea. L. Var. Italica.

MATERIALS AND METHODS:

MOLECULAR STRUCTURES:

The 2D structures (.mol) of each chemical were generated and scrutinised using ChemDraw 16.0. All of the compounds are converted into 3D structures using Chem3D 16.0. The RCSB Protein Data Library is used to find the protein target 3AIC. Canonical Simple Molecular Input Line Entry System (SMILE) of the secondary metabolites were retrieved using the zinc database.

MOLECULAR DOCKING STUDIES OF ISOLATED COMPOUNDS:

For molecular docking, AutoDockTools, a free graphic user interface (GUI) for the AutoDockVina programme, was utilised. 23 Brassica oleracea l. var. italica secondary metabolites such as isothiocyanates and glucosinolates were docked using autodock vina against streptococcus mutans glucansucrase (3AIC). The post-docking analysis made use of PyMOL and AutoDock Tools. Using PyMOL, the interactions between the target receptor and the ligands were examined by selecting the conformations with the most (least) favourable free binding energies.

Physicochemical property, drug likeness, and pharmacokinetic predictions:

Brassica oleracea l var italica's secondary metabolites were anticipated to have physical characteristics that are relevant to medicine**.**(Dufour, Stahl, and Baysse 2015). The physicochemical characteristics (molar refractivity, topological polar surface area, number of hydrogen bond donors/acceptors, lipophilicity (logPO/w), pharmacokinetics characteristics (gastrointestinal (GI) absorption, blood-brain barrier (BBB) permeation, P-gp substrate, cytochrome-P enzyme inhibition, skin permeation (log Kp), and drug likeness (Lipinski's rule of five) that are crucial parameters for prediction of the absorption and distribution of drugs within the body (Daina, Michielin, and Zoete 2017).

ADMET AND TOXICITY PROPERTIES OF THE COMPOUNDS:

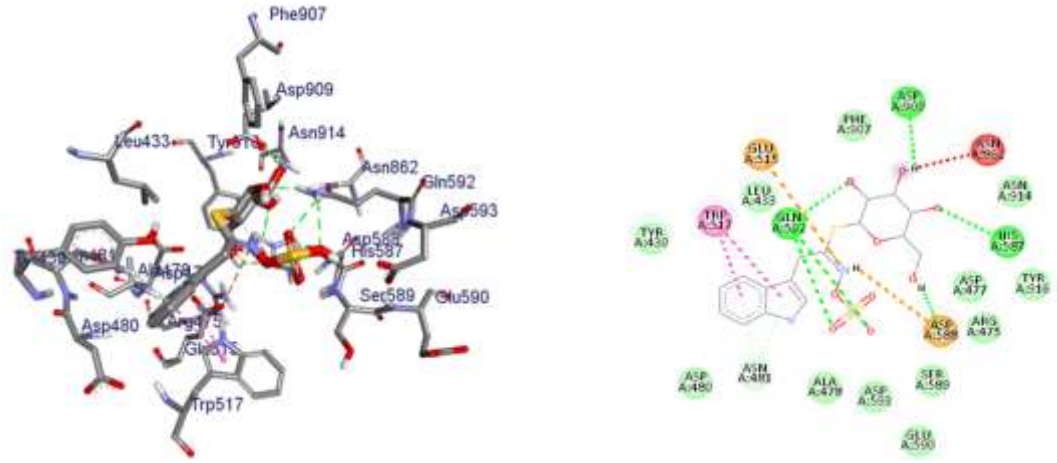
Predictions of the physicochemical properties (logS, logD, and logP) were made using the ADMETlab web server; Human intestinal absorption (HIA), 20% bioavailability (F20%), 30% bioavailability (F30%), CaCO3 permeability (CaCO2), and P-gp inhibitor/substrate (Pgp); Blood Brain Barrier (BBB), Volume Distribution (VD), Plasma Protein Binding (PPB), Excretion: Half Life (T1/2), and Clearance (CI). A total of 19 parameters were predicted to study the toxicity profile of the sixteen flavonoids and the two controls. The toxicological endpoints (Hepatotoxicity, Carcinogenicity, Immunotoxicity, Mutagenicity) and the level of toxicity (LD50, mg/Kg) of the studied flavonoids were determined using ProTox-II server (Banerjee et al. 2018). The median lethal dose (LD50) values were found to be in the range from 159–3919 mg/Kg. The compound possessing molecular weight greater than 500 and LogP value greater than 5 has poor absorption or permeation.

QUANTUM COMPUTATIONAL STUDIES:

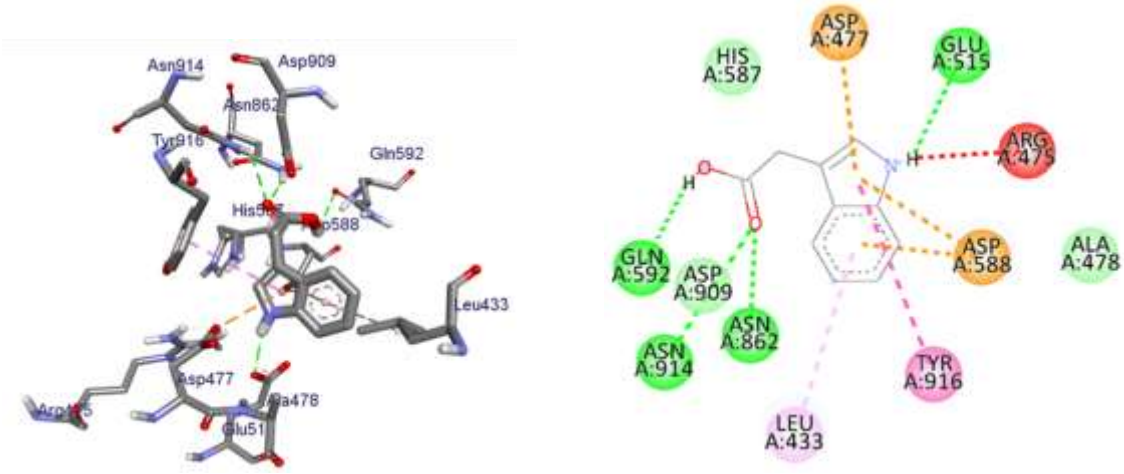
Knowing the coordinates of a reaction and its transition state is crucial for the creation of mechanism-based inhibitors, which often mimic the transition state(Anza et al. 2021). Density functional theory (DFT) is emerging as a viable tool to analyze biomolecular systems, performed using Gaussian 09 and visualized through gauss view 5.0. B3LYP/6-31G used to predict the electrostatic potential properties of isolated compounds (Eswaramoorthy et al. 2021). The molecular DFT analysis was done for the

compounds satisfying lipinski rule of five, having molecular weight less than 500 (g/mol), non-toxic to immunogenicity, carcinogenicity. Mutagenicity. (Figure 1)

RESULTS AND DISCUSSION:



A) Glucobrassicin



B) Indole 3 acetic acid

FIGURE 1: The 2D and 3D binding interactions of compounds Glucobrassicin(a) and Indole 3 acetic acid (b) against glucansucrase (3AIC) of streptococcus mutans. Hydrogen bond between compounds and amino acids are shown as green dashed lines, hydrophobic interactions are shown as pink lines

MOLECULAR DOCKING AGAINST 3 AIC Glucansucrase:

Molecular docking analysis of isolated compounds showed better docking score within the active site of S mutans.Among 15 Compounds in glucosinolates and 17 compounds in isothiocyanates, 13 compounds of glucosinolates and 2 compounds in isothiocyanates (−8.4, −8.3, -7.9 and −6.9 kcal/mol, respectively) showed equal to better docking affinity than the control drug chloroquine (−6.6 kcal/mol) and

erythromycin (-6.2 Kcal/mol), whereas 2 compounds in glucosinolates showed smaller docking affinity (−6, -6.1 kcal/mol) and 15 compounds of isothiocyantes showed smaller docking affinity value (-4, -4.3, -4.4kcal/mol) compared to control drug when tested against 3aic protein of Streptococcus mutans. Among the 15 Compounds in glucosinolates 5 compounds followed Lipinski's rule of five and among 17 compounds in isothiocyanates all compounds followed Lipinski's rule.

In-Silico PHARMACOKINETICS (Drug-likeness) analysis and toxicity analysis:

Research on the absorption, distribution, metabolism, excretion, and toxicity (ADMET) of isolated compounds was forecasted using Swiss ADMET**.** (Anza et al. 2021).

Kp values of all compounds ranged from −4.75 to –10.61 cm/s suggesting low skin permeability and glucosinolates compounds (1, 8) and all isothiocyantes compounds satisfying the lipinski's rule of 5 with zero violations, The CYP's interaction result showed that all glucosinolates compound and isothiocyantes compound (16-28, 31)) are inhibitors of CYP1A2, and CYP2D6, CYP3A4 except isothiocyantes compound (29,30, 32) are not inhibitors of CYP1A2 and the molecular weight of the compounds should be lesser than 500g/mol. Among 15 Compounds in glucosinolates, all compounds had molecular weight less than 500g/mol and among 17 compounds in isothiocyanates, all compounds had lesser molecular weight. The lipophilicity values (ilogP)must be lesser than 5, all the molecules of glucosinolates and isothiocyantes had kp value in between −2.37 to 2.75. Acute toxicity values (LD 50) and the toxicological endpoints (Hepatotoxicity, Carcinogenicity, Immunotoxicity, Mutagenicity) was evaluated among the 15 compounds of glucosinolates and 17 compounds of isothiocyantes, in that all compounds of glucosinolates except (15) which has carcinogenicity and all compounds except (20, 27, 32) had no carcinogenicity, mutagenicity and cytotoxicity. (Table 1-4)

Table 1: ADME Predictions of Compounds, Computed by Swiss ADME and PreADMET

s. no	**Molecule**	**log Kp cm/s**	**GI Absorption**	**BBB Permeability**	**Inhibitor Interaction (SwissADME/PreADMET)**					
					P-gp Substrate	**CYP1A2 Inhibitor**	**CYP2C19 Inhibitor**	**CYP2C9 Inhibitor**	**CYP2D6 Inhibitor**	**CYP3A4 Inhibitor**
1	Sinigrin	-9.48	Low	No	Yes	No	No	No	No	No

2	Glucoraphanin	-10.43	Low	No	Yes	No	No	No	No	No
3	Progoitrin	-10.01	Low	No	Yes	No	No	No	No	No
4	Glucochlearin	-8.88	Low	No	yes	No	No	No	No	No
5	Glucoiberviri n	-9.4	Low	No	Yes	No	No	No	No	No
6	Glucoiberin	-10.61	Low	No	Yes	No	No	No	No	No
7	Glucoraphenin	-10.38	Low	No	Yes	No	No	No	No	No
8	Glucoerucin	-9.23	Low	No	Yes	No	No	No	No	No
9	Glucoraphanin	-10.43	Low	No	Yes	No	No	No	No	No
10	Glucoalyssin	-10.27	Low	No	Yes	No	No	No	No	No
11	Glucohirsutin	-9.37	Low	No	Yes	No	No	No	No	No
12	Glucosinalbin	-9.3	Low	No	No	No	No	No	No	No

13	Gluconasturtiin	-8.83	Low	No	Yes	No	No	No	No	No
14	Glucobrassicin	-9.1	Low	No	No	No	No	No	No	No
15	Neoglucobrassicin	-9.03	Low	No	Yes	No	No	No	No	No
16	Butyronitrile	-6.35	High	Yes	No	No	No	No	No	No
17	Allyl isothiocyanate	-5.19	High	Yes	No	No	No	No	No	No
18	2-Methyl-2-nitropropane	-6.1	High	Yes	No	No	No	No	No	No
19	4-(Methylthio)-butanenitrile	-7.02	High	No	No	No	No	No	No	No
20	Butyl isothiocyanate	-4.93	High	Yes	No	No	No	No	No	No
21	Isobutyl isothiocyanate	-5	High	Yes	No	No	No	No	No	No
22	Iberin	-6.55	High	No	No	No	No	No	No	No
23	4-Isothiocyanato-1-butene	-5.24	High	Yes	No	No	No	No	No	No

24	3-Methylbutyl isothiocyanate	-4.75	High	Yes	No	No	No	No	No	No
25	Isoamyl methyl sulfoxide	-5.59	High	Yes	No	No	No	No	No	No
26	Erucin	-5.18	High	Yes	No	No	No	No	No	No
27	Sulforaphene	-6.32	High	No	No	No	No	No	No	No
28	Sulforaphane	-6.38	High	No	No	No	No	No	No	No
29	Indole-3-carbinol	-6.45	High	Yes	No	Yes	No	No	No	No
30	Indole-3-carboxylic acid	-5.87	High	Yes	No	Yes	No	No	No	No
31	Indole-3-acetic acid	-6.37	High	Yes	No	No	No	No	No	No
32	1-Methoxyindole-3-carbaldehyde	-6.04	High	Yes	No	Yes	No	No	No	No

Table 2: Drug-Likeness Predictions of Compounds, Computed by SwissADME

s no	Molecule	Mol.Wt. (g/mol)	NHD	NHA	NRB	TPSA (A°2)	LogP (cLogP)	Lipinski's Rule of Five Violation
1	Sinigrin	397.46	4	10	7	202.62	-2.37	0
2	Glucoraphanin	436.5	4	11	10	215.84	-2.35	1
3	Progoitrin	389.4	6	11	8	220.02	-1.71	2
4	Glucochlearin	375.42	9	20	19	199.79	-0.79	0
5	Glucoibervirin	407.48	5	10	9	238.59	-0.77	0
6	Glucoiberin	423.48	5	11	9	236.07	-1.83	1
7	Glucoraphenin	435.49	5	11	9	236.07	-1.45	1
8	Glucoerucin	420.5	4	10	10	227.92	-0.5	0
9	Glucoraphanin	436.5	4	11	10	238.9	-1.61	1
10	Glucoalyssin	451.53	5	11	11	236.07	-1.09	1
11	Glucohirsutin	493.61	5	11	14	236.07	0.1	1
12	Glucosinalbin	425.43	6	11	7	220.02	-0.94	2
13	Gluconasturtiin	423.46	5	10	8	199.79	-0.23	0
14	Glucobrassicin	448.47	6	10	7	215.58	-0.45	2
15	Neoglucobrassicin	478.49	5	11	8	213.95	-0.08	1

16	Butyronitrile	69.11	0	1	1	23.79	0.88	0
17	Allyl isothiocyanate	99.15	0	1	2	44.45	1.99	0
18	2-Methyl-2-nitropropane	103.12	0	2	1	45.82	0.45	0
19	4-(Methylthio)-butanenitrile	130.21	1	2	3	75.11	0.48	0
20	Butyl isothiocyanate	115.2	0	1	3	44.45	2.47	0
21	Isobutyl isothiocyanate	115.2	0	1	2	44.45	2.38	0
22	Iberin	163.26	0	2	4	80.73	1.58	0
23	4-Isothiocyanato-1-butene	159.27	0	1	4	69.75	2.72	0
24	3-Methylbutyl isothiocyanate	129.22	0	1	3	44.45	2.75	0
25	Isoamyl methyl sulfoxide	190.35	0	1	6	36.28	2.8	0
26	Erucin	161.29	0	1	5	69.75	2.8	0
27	Sulforaphene	175.27	0	2	4	80.73	1.92	0
28	Sulforaphane	177.29	0	2	5	80.73	1.93	0
29	Indole-3-carbinol	147.17	2	1	1	36.02	1.45	0

30	Indole-3-carboxylic acid	161.16	2	2	1	53.09	1.56	0
31	Indole-3-acetic acid	175.18	2	2	2	53.09	1.51	0
32	1-Methoxyindole-3-carbaldehyde	175.18	0	2	2	31.23	1.66	0

Table 3: Prediction of Toxicity of Compounds, Computed by Pro-Tox II and OSIRIS Property Explorer

S. no	**Molecules**	**Organ Toxicity**						
		Hepatotoxicity	**Carcinogenicity**	**Immunogenicity**	**Mutagenicity**	**Cytotoxicity**	**LD50(Mg/Kg)**	**Acute toxicity class**
1	Sinigrin	No	No	No	No	No	15	2
2	Glucoraphanin	No	No	No	No	No	16	2
3	Progoitrin	No	No	No	No	No	16	2
4	Glucochlearin	No	No	No	No	No	16	2
5	Glucoiberviriin	No	No	No	No	No	16	2
6	Glucoiberin	No	No	No	No	No	16	2

7	Glucoraphenin	No	No	No	No	No	n.a	n.a
8	Glucoerucin	No	No	No	No	No	16	2
9	Glucoraphanin	No	No	No	No	No	16	2
10	Glucoalyssin	No	No	No	No	No	n.a	n.a
11	Glucohirsutin	No	No	No	No	No	n.a	n.a
12	Glucosinalbin	No	No	No	No	No	n.a	n.a
13	Gluconasturtiin	No	No	No	No	No	n.a	n.a
14	Glucobrassicin	No	No	No	No	No	n.a	n.a
15	Neoglucobrassicin	No	Yes	No	No	No	n.a	n.a
16	Butyronitrile	No	No	No	No	No	24	2
17	Allyl isothiocyanate	No	No	No	Yes	No	112	3
18	2-Methyl-2-nitropropane	No	No	No	No	No	455	4

19	4-(Methylthio)-butanenitrile	No	No	No	No	No	1750	4
20	Butyl isothiocyanate	Yes	No	Yes	No	No	1190	4
21	Isobutyl isothiocyanate	No	No	No	No	No	112	3
22	Iberin	No	No	No	No	No	4550	5
23	4-Isothiocyanato-1-butene	No	No	No	No	No	112	3
24	3-Methylbutyl isothiocyanate	No	No	No	No	No	150	3
25	Isoamyl methyl sulfoxide	No	No	No	No	No	1990	4
26	Erucin	No	No	No	No	No	1000	4
27	Sulforaphene	No	No	No	No	Yes	112	3
28	Sulforaphane	No	No	No	No	No	1000	4
29	Indole-3-carbinol	No	No	No	No	No	1000	4

30	Indole-3-carboxylic acid	Yes	No	No	No	No	2190	5
31	Indole-3-acetic acid	Yes	No	No	No	No	1200	4
32	1-Methoxyindole-3-carbaldehyde	Yes	No	Yes	No	No	1190	4

Table 4: Molecular Docking Scores and Residual Amino Acid Interactions of Compounds Against Lux S Binding Domain

S.NO	MOLECULE	AFFINITY (kcal/mol)	H-bond	Residual Hydrophobic/Pi-Cation/Pi-Anion/Pi-Alkyl Interactions
1	Sinigrin	-7.1	ASN-481, GLN-592	TYR-610, LEU-382, LEU-433, TRP-517, GLU-515, ALA-478, ASP-477, ARG-475, HIS-587, ASP-588, TYR-916, ASN-914, ASP-909, ASN-862, PHE-907, SER-589, ASP-593
2	Glucoraphanin	-7.1	ASP-477, TRP-517, ASP-909, HIS-587	TYR-430, ASP-480, ASN-481, ALA-478, LEU-433, GLU-515, TYR-916, ASN-862, ASN-914, PHE-907, LEU-434, GLN-592, SER-589, ASP-588

3	Progoitrin	-6.8	ASP-477	ARG-475, LEU-433, GLU-515, ALA-478, ASN-481, TRP-517, TYR-610, GLN-592, ASP-588, ASP-593, ASN-862, ASN-914, TYR-916, HIS-587
4	Glucochlearin	-6	ASN-481, TRP-517, ASP-909, ASP-477	GLN-960, HIS-587, TYR-916, ASN-914, PHE-907, ASN-862, LEU-433, LEU-382, ASN-481, ASP-588, TRP-517, ASP-593, TYR-610
5	Glucoibervirin	-6.2	ASP-477, ASP-909, TRP-517, ASN-481	ASN-914, TYR-916, HIS-587, ARG-475, GLU-515, ALA-478, LEU-433, TYR-61, SER-589, ASP-593, ASP-480, ASP-588, PHE-907
6	Glucoiberin	-6.6	TRP-517, ASP-909, ASP-477, GLN-592	ASP-480, ASP-588, LEU-434, ASN-862, ASN-914, HIS-587, TYR-916, GLN-960, GLU-515, LEU-382, TYR-610
7	Glucoraphenin	-6.9	GLN-592, ASP-593, ASP-909, HIS-587	TYR-916, GLN-960, ASP-477, LEU-433, ASN-481, TRP-517, ASP-480, TYR-430, TYR-610, SER-589, VAL-591, GLU-590, PHE-907, ASN-914, ASN-862, LEU-434
8	Glucoerucin	-6.1	ASP-909, GLN-592	SER-589, ASP-477, TYR-916, HIS-587, ASN-862, PHE-907, LEU-382, LEU-433, TRP-517, ASN-481,TYR-610, ASP-588
9	Glucoraphanin	-6.9	ASP-909, GLN-592, ASP-477, ASN-481	GLN-960, TYR-916, ASN-914, LEU-434, TYR-430, GLY-429, ASP-480, LEU-433, ASP-588, GLU-515, TRP-517, ALA-478

10	Glucoalyssin	-6.4	TRP-517, ASN-862, GLU-515, GLN-592	SER-589, TYR-610, ASP-588, LEU-382, PHE-907, ASP-588, HIS-587, ASP-909, TYR-916, ASN-481, ALA-478, ARG-475, ASP-577, LEU-433, LEU-434
11	Glucohirsutin	-6.9	GLN-960, ASP-593, GLN-592	VAL-957, ASP-477, TYR-916, ASN-914, LEU-434, ASP-909, ASN-862, ALA-478, LEU-433, ASN-481, ASP-480, TRP-517, TYR-430, TYR-610, SER-589, VAL-591, ASP-588, HIS-587, PHE-907
12	Glucosinalbin	-7.9	GLU-515, ASP-909, GLN-592, ASN-481	TYR-916, LEU-433, PHE-907, LEU-434, LEU-382, TRP-517, ALA-478, TYR-430, VAL-591, ASP-593, GLU-590, SER-589, ASP-588, TYR-610
13	Gluconasturtiin	-7.5	ASN-481, GLU-515	HIS-587, ASN-862, PHE-907, LEU-382, TRP-517, ALA-478, ASP-480, LEU-433, TYR-430, ASP-593, SER-589, TYR-610, GLN-592, ASP-588, LEU-434, TYR-916, ASP-909
14	Glucobrassicin	-8.4	GLN-592, HIS-587, ASP-909	TYR-430, TRP-517, LEU-433, GLU-515, PHE-907, ASN-914, ASP-477, TYR-916, ARG-475, SER-589, GLU-590, ASP-593, ALA-478, ASN-481, ASP-480,
15	Neoglucobrassicin	-8.3	ASP-593, GLN-592	GLU-590, ALA-516, VAL-479, ASP-480, TRP-517, ASN-481, TYR-43O, ASP-588, ASN-862, HIS-587, ASN-914, TYR-916, AS909, LEU-433, GLN-960, ASP-477, SER-589, ALA-478, TYR-610, GLU-515

16	Butyronitrile	-3.5	GLN-960	HIS-587, ASP-477, ASP-588, ARG-475, TYR-916, ASP-909
17	Allyl isothiocyanate	-3.4	ASP-909	HIS-587, PHE-907, TYR-916, ARG-475, ASP-477, ASP-588, ASN-862, ASN-914, GLN-592
18	2-Methyl-2-nitropropane	-4.1		GLN-592, PHE-907, ASN-862, ASP-588, HIS-587, TYR-916, ASP-909, LEU-434
19	4-(Methylthio)-butanenitrile	-4	ASP-909, GLN-592	PHE-907, ASN-914, ASP-588, HIS-587, ASP-477, TYR-916, LEU-433
20	Butyl isothiocyanate	-3.7	ASP-477, GLU-515	TYR-916, HIS-587, ALA-478, ASP-588, ASN-914, ASN-862, ASP-909
21	Isobutyl isothiocyanate	-3.9	ASP-909	GLN-960, HIS-587, GLN-592, ASN-914, ASP-588, ARG-475, TYR-916, PHE-907, ASP-477
22	Iberin	-4.1	GLU-515, GLN-592, ASP-477	PHE-907, TYR-916, HIS-587, ALA-478, LEU-433, GLN-960, ASP-909, ASP-588, ASN-862
23	4-Isothiocyanato-1-butene	-4.2	ASP-477	ASP-588, ASN-862, ASN-914, GLN-592, PHE-907, HIS-587, TYR-916, ASP-909, GLN-960, ARG-475, GLU-515, LEU-433, ASN-481, ALA-478
24	3-Methylbutyl isothiocyanate	-4.3	GLU-515, ASP-477	GLN-592, ASP-909, ASN-862, TYR-916, ASN-914, ASP-588, GLU-515, HIS-587, ALA-478, ASP-477

25	Isoamyl methyl sulfoxide	-4.9	HIS-587	ASN-862, PHE-907, ASP-588, GLN-592, LEU-382, LEU-434, ALA-478, GLN-960, ASP-477, LEU-433, TYR-916, ASP-909, ASN-914, ASN-862, PHE-907, ASP-588, GLN-592, LEU-382, LEU-434

CONCLUSION:

In the present work, a computational de novo approach was used to confirm mode of binding for antibacterial activity, elucidating quantum chemical properties and the ADMET-drug-likeness of a isothiocyanntes and glucosinolates compounds isolated from brassica oleracea. L. var. Italica. Compared with other compounds Glucobrassicin in glucosinolates and indole 3 acetic acid in isothiocyanates had higher affinity value and binding score. Toxicological prediction results suggested that Glucobrassicin and indole 3 acetic acid are non-hepatotoxic, non-carcinogenic, non-irritant, immunogenic, and non-cytotoxic. Based on the results of the present investigation, Glucobrassicin and indole 3 acetic acid compound may serve as a lead molecule and further work is recommended for functional group inclusion, modification, and SAR study to develop novel antibacterial agents with therapeutic activity against *S. mutans.*

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