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Antibacterial activity against glucansucrase of Streptococcus mutans, in silico molecular docking analysis, ADMET and DFT analysis of flavonoids and phenolic compounds from Brassica oleracea l. var. Italica

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Introduction: Increased attention has been given to natural plants owing to several presumed health-promoting biological activities. Brassica oleracea var. Italica and their bioactive compounds exhibit health-promoting roles as well as antimicrobial, antioxidant, and anti-inflammatory properties. 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 phenolic and flavonoids 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 Kaempferol and isochlorogenic acid showed better docking scores compared to other compounds. The SwissADME prediction results showed that kaempferol and isochlorogenic acid compounds satisfy Lipinski's rule of five with zero violations having higher affinity value. 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: Kaempferol and isochlorogenic 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.*

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

INTRODUCTION:

Sprouts and microgreens, of vegetables and herbs, have received increasing attention owing to their valuable health-promoting properties (Butkutė, Taujenis and Norkevičienė, 2018) (Aparna et al. 2021). Bioactive compounds, minerals, and nutrients are found in sprouted seeds and microgreens (Le, Chiu and Hsieh, 2020)(Thanh et al.2020). Cruciferous vegetables in the family *Brassicaceae* have health-promoting phytochemicals which play an important role in the human diet and nutritional value (Hu *et al.*, 2019). phytochemicals with anti-cancer, anti-degenerative and antioxidant properties have led scientific efforts towards the search for improvement in their phytochemical content (Moreira-Rodríguez *et al.*, 2017)(Janani et al. 2020). Phenolic compounds are secondary metabolites that are the main components responsible for the antioxidant behaviour of vegetables(Cartea *et al.*, 2010) (Nasim et al. 2022). The main phenolic compounds include Hydroxycinnamic acids and flavonoid glycosides are found in broccoli(Torres-Contreras *et al.*, 2017)(Vallejo, Tomas-Barberan and Garcia-Viguera, 2003; Villarreal-García *et al.*, 2016). Sprouts and microgreens contain higher levels of functional components such as phenolics, flavonoids, pigments, vitamins, and minerals compared with mature counterparts of the same type (Mir, Shah and Mir, 2017)(Gan *et al.*, 2017). Gram-positive bacteria are more sensitive to broccoli sprout extract than Gram-negative bacteria(da Silva *et al.*, 2016)(Silva *et al.*, 2013). Antimicrobial peptides in broccoli floret extract have antimicrobial activity against pathogenic bacteria, yeast, and phytopathogenic fungi(Pacheco-Cano *et al.*, 2018). The high-sulforaphane broccoli sprouts powder has a considerable effect on *H. pylori* eradication in type 2 diabetic patients with positive *H. pylori (Bahadoran et al., 2014)*(Johnson et al. 2022). Phenolics, flavonoids, and glucosinolates, which are plant-derived bioactive compounds can inhibit the growth and activity of various microorganisms(Takó *et al.*, 2020). Dental caries is a diet-dependent oral biofilm disease, mutans streptococci (MS), lactobacilli resulting in the formation of microbiome dysbiosis(Zhan, 2018) (Nasim and Professor and Head, Departm...). *S. mutans* possesses high-affinity surface adhesins that enable colonization even in the absence of sucrose, quorum sensing in s mutans acts by a two-component signal transduction system in which com CDE and comRS acts as a signal which inhibits both genetic competence and bacteriocin production (Lemos *et al.*, 2019). Collagen binding proteins help in facilitating colonization and persistence of S. mutans in root canals and their role in the pathogenesis of endodontic infections(Lima *et al.*, 2020) (Kamath et al. 2020)(Siddique et al. 2020). The antibacterial agents commonly used, exert their action through inhibition of cell wall, alteration of the membrane, inhibition of nucleic acid synthesis, and protein synthesis(Vijayashree Priyadarshini, 2019)(Kamath et al. 2022). 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:

Utilizing ChemDraw 16.0, the 2D structures (.mol) of each chemical were created and examined. Using Chem3D 16.0, all the chemicals are transformed into 3D structures. The protein target 3AIC is obtained from the RCSB Protein Data Bank. Using the zinc database Canonical Simplified Molecular input line entry system (SMILE) of the secondary metabolites were obtained.

MOLECULAR DOCKING STUDIES OF ISOLATED COMPOUNDS:

AutoDockTools were used for molecular docking, which is a free graphic user interface (GUI) for the AutoDockVina program.23 Autodock vina was used to dock the secondary metabolites of Brassica oleracea l. var italica against glucansucrase (3AIC) of streptococcus mutans. AutoDock Tools and PyMOL were used for the post-docking analysis. PyMOL was used to analyze the interactions between the target receptor and ligands by choosing the conformations that had the most favorable (least favorable) free binding energy.

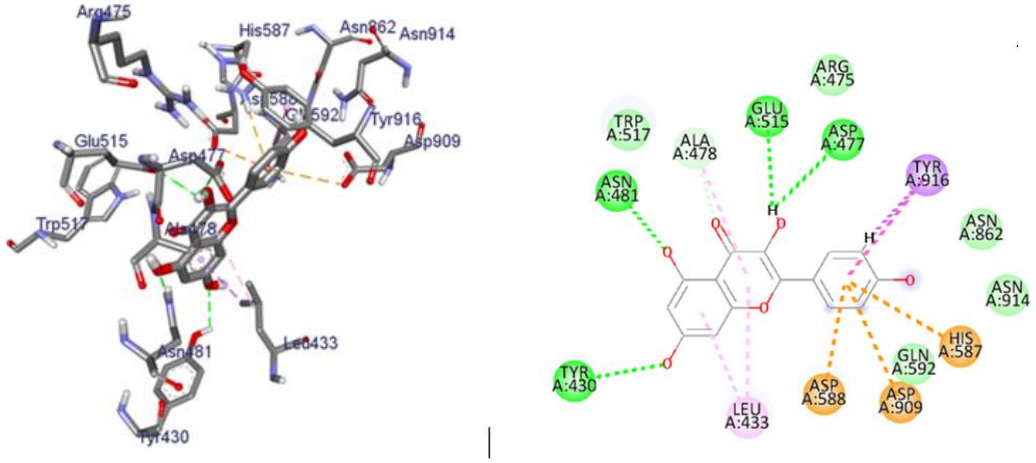
ADMET AND TOXICITY PROPERTIES OF THE COMPOUNDS:

The canonical simplified Molecular input line entry system (SMILE) of the secondary metabolites were subjected to SwissADME, to calculate in silico pharmacokinetics, such as the quantity of hydrogen donors and acceptors, rotatable bonds, total polar surface area of a chemical and their molecular weight. The organ toxicity, toxicological end points of the ligands, the mutagenicity, carcinogenicity, immunogenicity, hepatotoxicity and level of toxicity (LD 50 Mg/Kg) determined using Pro Tox II. Drug likeness property of the secondary metabolites to being an orally active drug is determined using Lipinski rule of five. The compound possessing molecular weight greater than 500 and LogP value greater than 5 has poor absorption or permeation.

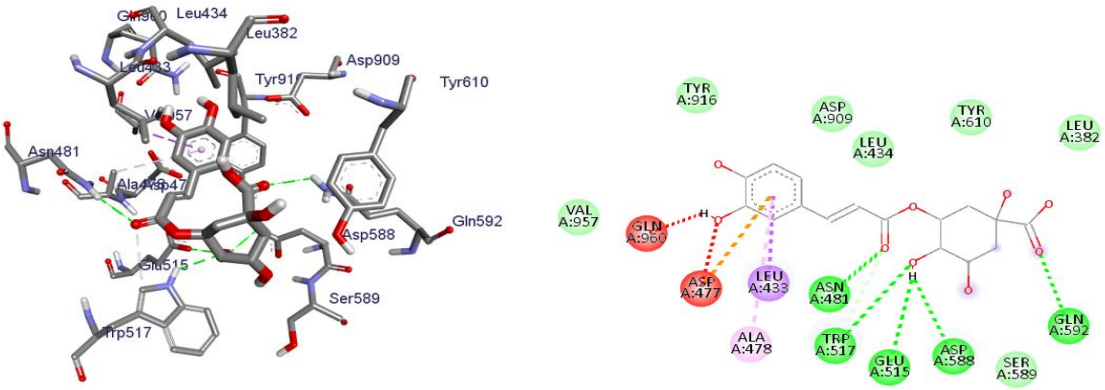
QUANTUM COMPUTATIONAL STUDIES:

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) KAEMPFEROL



b) ISOCHLOROGENIC ACID

FIGURE 1: The 2D and 3D binding interactions of compounds Kaempferol (a) and isochlorogenic 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 8 Compounds in flavonoids and 27 compounds in phenolic, 7 compounds of flavonoids (−8.2, −8.9, and −7.9 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 1 compound showed smaller docking affinity (−1.9 kcal/mol) and 9 compounds of phenolic showed better docking affinity value (−8.2, −7.7, −7.4kcal/mol) compared to control drug when tested against 3aic protein of Streptococcus mutans. Among the 27 phenolic compounds 15 compounds followed Lipinski's rule of five and among 8 flavonoids compounds 4 compounds followed Lipinski's rule. (Figure 2)

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

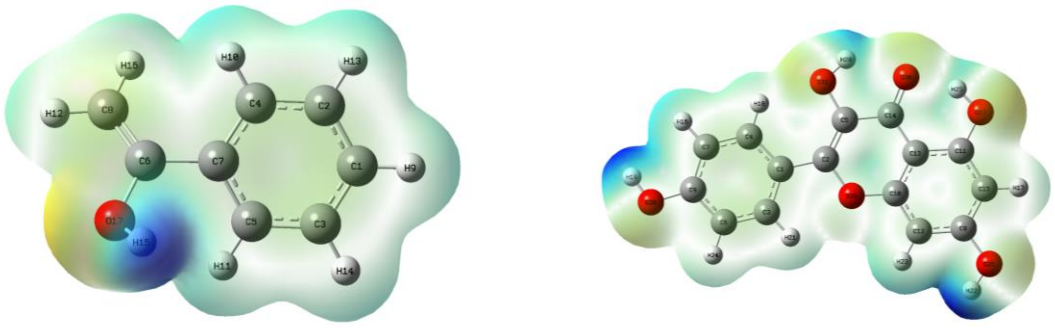
Swiss ADMET was used to forecast the results of research on the absorption, distribution, metabolism, excretion, and toxicity (ADMET) of isolated substances ((Anza et al. 2021).

Kp values of all compounds ranged from −1.90 to −4.96 cm/s suggesting low skin permeability and phenolic compounds (1−12,15,19,20) and flavonoid compounds (28−31) satisfying the lipinski's rule of 5 with zero violations, The CYP's interaction result showed that phenolic compound 9 inhibitors of CYP1A2 and flavonoid compound (28−32) are inhibitors of CYP1A2, and CYP2D6, for CYP3A4 phenolic compound (4−6) and flavonoid compound (28−32) are potent inhibitor and the molecular weight of the compounds should be lesser than 500g/mol. Among 27 compounds of phenolic, 21 compounds had molecular

weight less than 500g/mol and among 8 compounds of flavonoids, 6 compounds had lesser molecular weight. The lipophilicity values (ilogP)must be lesser than 5, all the molecules of flavonoids and phenolic had kp value in between −5.72 and −11. Acute toxicity values (LD 50) and the toxicological endpoints (Hepatotoxicity, Carcinogenicity, Immunotoxicity, Mutagenicity) was evaluated among the 27 compounds of phenolic and 8 compounds of flavonoids, in that 22 phenolic compounds and 4 flavonoids compounds had no carcinogenicity, mutagenicity and cytotoxicity.

DFT ANALYSIS:

An effective approach for analyzing the relationship between the geometry and the electrical characteristics of chemical compounds is the DFT (density functional theory) analysis. (Eswaramoorthy *et al.*, 2021). Red/Yellow regions indicate negative electrostatic potentials and the blue region shows positive, and the green color designates potential neutral region. The results revealed compounds benzoic acid 8.3 (kcal/mol) and isochlorogenic acid 8.2 (kcal/mol) had higher affinity value more than other compounds. (Table 1-4)



A) BENZOIC ACID B) KAEMPFEROL

FIGURE 2: Molecular electrostatic potential surface of compounds

Table 1: ADME Predictions of Compounds Computed by SwissADME 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	benzoic	-5.72	High	Yes	No	No	No	No	No	No

	acid									
2	Salicylic acid	-5.54	High	Yes	No	No	No	No	No	No
3	p-hydroxybenzoic acid	-6.02	High	Yes	No	No	No	No	No	No
4	Protocatechuic acid	-6.42	High	No	No	No	No	No	No	Yes
5	Gentisic acid	-6	High	No	No	No	No	No	No	Yes
6	Gallic acid	-6.84	High	No	No	No	No	No	No	Yes
7	Vanillic acid	-6.31	High	No	No	No	No	No	No	No
8	p-Coumaric acid	-6.26	High	Yes	No	No	No	No	No	No
9	Esculetin	-6.52	High	No	No	Yes	No	No	No	No
10	Caffeic acid	-6.58	High	No	No	No	No	No	No	No

11	Ferulic acid	-6.41	High	Yes	No	No	No	No	No	No
12	Sinapic acid	-6.63	High	No	No	No	No	No	No	No
13	Gallic acid hexoside	-9.52	Low	No	No	No	No	No	No	No
14	Gallic acid 4-O-glucoside	-9.52	Low	No	No	No	No	No	No	No
15	sinapoyl malate	-7.73	High	No	No	No	No	No	No	No
16	Isochlorogenic acid	-8.76	Low	No	No	No	No	No	No	No
17	chlorogenic acid	-8.76	Low	No	No	No	No	No	No	No
18	caffeoyl-quinic acid	-8.76	Low	No	No	No	No	No	No	No
19	1-O-sinap	-8.9	Low	No	No	No	No	No	No	No

	oyl-b-D-glucose									
20	5-O-Sinapoylquinic acid	-8.82	Low	No	Yes	No	No	No	No	No
21	Digalloylhexoxide	-9.83	Low	No	No	No	No	No	No	No
22	1,2-Diferuloylgentiobiose	-10.67	Low	No	Yes	No	No	No	No	No
23	2-Feruloyl-1-sinapoylgentiobiose	-10.87	Low	No	Yes	No	No	No	No	No
24	1,2-Disinapoylgentiobiose	-11.07	Low	No	Yes	No	No	No	No	No
25	1-Sinapoyl-2,2′-diferuloylgentiobio	-10.33	Low	No	Yes	No	No	No	No	No

	se									
26	2-Feruloyl-1,2'-disinapoylgentiobiose	-10.54	Low	No	Yes	No	No	No	No	No
27	1,2,2'-Trisinapoylgentiobiose	-10.74	Low	No	Yes	No	No	No	No	No
28	Apigenin	-5.8	High	No	No	Yes	No	No	Yes	Yes
29	Kaempferol	-6.7	High	No	No	Yes	No	No	Yes	Yes
30	Luteolin	-6.25	High	No	No	Yes	No	No	Yes	Yes
31	Quercetin	-7.05	High	No	No	Yes	No	No	Yes	Yes
32	Myricetin	-7.4	Low	No	No	Yes	No	No	No	Yes
33	Astragalin	-8.52	Low	No	No	No	No	No	No	No
34	Rutin	-10.26	Low	No	Yes	No	No	No	No	No

35	Robinin	-11.73	Low	No	Yes	No	No	No	No	No

Table 2: 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	benzoic acid	-5.4	ASP-588, ASP-909, GLN-592	LEU-434,TYR-916, ASP-477, HIS-587, ASN-914, ASN-862, PHE-907
2	Salicylic acid	-5.7	ASN-862	ASP-588, ASP-909, LEU-434, PHE-907, GLN-592, SN-914, HIS-587, TYR-916, ASP-477
3	p-hydroxybenzoic acid	-5.9	GLN-960, ASP-477	TYR-916, HIS-587, ASN-862, ALA-478, LEU-433, LEU-434, PHE-907, SDP-909, ASP-588
4	Protocatechuic acid	-6.2	ASN-862, ASP-909, ASP-588	TYR-916, ARG-475, GLU-515, ASP-477, HIS-587, ASN-914, LEU-908, GLN-592, PHE-907
5	Gentisic acid	-6	GLN-592, ASN-914, HIS-587, ASP-477	ARG-475, TYR-916, GLN-960, LEU-433, ASP-909, LEU-434, PHE-907
6	Gallic acid	-6.5	ASP-477, GLU-515, GLN-592	ASN-914, HIS-587, TYR-916, ASP-588, PHE-907, GLN-592, LEU-908

7	Vanillic acid	-6.2	GLN-960, GLN-592, ASP-477	LEU-433, LEU-382, LEU-434, ASN-862, PHE-907, HIS-587, ASP-909, ASN-914, ASP-588, TYR-916, ALA-478, LEU-382
8	p-Coumaric acid	-5.9	ASN-481, GLU-515, ASP-909	ALA-478, LEU-433, ASP-588, HIS-587, TYR-916, ASN-862, GLN-592
9	Esculetin	-7	GLN-592, ASN-862, ASP-909	LEU-433, GLU-515, ALA-478, ASP-477, HIS-587, ASN-914, LEU-908, PHE-907,ASP-588, TYR-916
10	Caffeic acid	-6.4	ASN-481, GLN-592, ASP-909, ASN-862	TRP-517, ASP-477, TYR-916, ASP-588, PHE-907
11	Ferulic acid	-5.7	ASP-477, GLN-960	VAL-957, TYR-916, GLU-515, ASP-588, TRP-517, TYR-610, GLN-592, PHE-907, LEU-434, LEU-433, ALA-478, ASP-959
12	Sinapic acid	-6	GLN-960, GLN-592	HIS-587, TRP-517, ASP-588, LEU-433, ALA-478, ASP-959, ASP-477, VAL-957, TYR-916, ASN-862, ASN-914, ASP-909
13	Gallic acid hexoside	-7.5	ASN-914, HIS-587, ASP-909, ASP-477, GLU-515	GLN-592, PHE-907, ASP-588, LEU-434, LEU-382, ARG-475, ASP-480, ASN-481, TRP-517, ALA-478, TYR-430, LEU-433, TYR-916, LEU-908, ASN-862

14	Gallic acid 4-O-glucoside	-7.4	GLU-515, TYR-430, ASP-480, TRP-517, GLN-960	ARG-475, ASN-481, VAL-479, ALA-478, LEU-433, ASP-959, LEU-434, PHE-907, LEU-382, SER-589, GLN-592
15	sinapoyl malate	-7.2	ASN-481, GLU-515, GLN-592, ASN-914, ASP-477	TYR-430, TRP-517, LEU-433, LEU-382, PHE-907, TYR-610, ASP-588, ASP-909, TYR-610, ASN-862, HIS-587, ARG-475, GLN-960
16	Isochlorogenic acid	-8.2	GLN-592, TYR-430, GLN-960, ASP-909, ASN-481	ASP-477, ARG-475, ASP-588, ASN-862, ASN-914, LEU-433, ALA-478, TRP-517, GLU-515, PHE-907, TYR-916, LEU-434
17	chlorogenic acid	-7.9	ASN-481, TRP-517, GLU-515, ASP-588, GLN-592	ALA-478, LEU-433, VAL-957, TYR-916, ASP-909, LEU-434, TYR-610, LEU-382, SER-589

18	caffeoyl-quinic acid	-7.7	ASP-593, ASP-909, GLN-914, GLN-592	TYR-610, GLU-590, SER-589, GLU-515, ASN-481, TRP-517, PHE-907, TYR-916, LEU-908, ASN-914, HIS-587, ASP-588
19	1-O-sinapoyl-b-D-glucose	-7.7	TYR-430, ASN-481, GLN-592, GLU-515	LEU-908, ASN-914, ALA-478, HIS-587, TYR-916, GLN-960, ASP-477, ARG-475, ASP-588, PHE-907, ASP-909, TYR-610, TRP-517, LEU-433
20	5-O-Sinapoylquinic acid	-7.9	ASP-481, ASP-477, ASP-588, GLN-592, ASP-909	TRP-517, LEU-434, ALA-478, GLU-515, GLN-960, ARG-475, TYR-916, HIS-587, ASN-914, PHE-907, TYT-610, LEU-433, TYR-430
21	Digalloyl hexoxide	-7.5	ASN-481, TRP-517, ASP-477, GLN-960, ASP-909, GLN-592	TYR-430, LEU-382, TYR-610, LEU-433, ASP-588, HIS-587, ASP-593, ASN-914, TYR-916, LEU-434, ALA-478, GLU-515
22	1,2-Diferuloylgentiobiose	-3.6	GLN-960, ASN-481, TYR-430, ASP-477	LEU-382, TYR-610, LEU-433, ASP-593, ASP-909, SER-589, PHE-907, ASN-862, GLN-592, TYR-916, ASN-914, ARG-475, HIS-587, GLY-429, ASP-480, TRP-517, ALA-478

23	Apigenin	-7.9	ASN-862, ASP-9O9	VAL-479,GLU-515, LEU-433, GLN-592, ASN-914, HIS-587, ASP-588, TYR-916, LEU-382, TYR-430, ALA-478, ASN-481, TRP-517
24	Kaempferol	-8.3	ASN-481, TYR-430, GLU-515, ASP-477	TRP-517, ALA-478, ARG-475, ASN-862, ASN-914, TYR-916, HIS-587, GLN-592, ASP-909, ASP-588, LEU-433
25	Luteolin	-8.2	TYR-430, GLN-592	ASN-481, ASP-480, TRP-517, GLU-515, ALA-478, LEU 433, PHE 907, ASP-588, ASP-909, TYR-916, HIS-587, ASN-914
26	Quercetin	-8.9	GLU-515, TYR-430	TRP-517, ARG-475, ASP-477, TYR-916, ASP-588, HIS-587, ASP-909, ASN-914,, PHE-907, ALA-478, LEU-433
27	Myricetin	-8.2	GLN-592, ASN-481	ASN-862, ASN-914, HIS-587, GLN-960, VAL-957, ASP-588, TRP-517, TYR-916, LEU-433, TYR-430
28	Astragalin	-8.2	GLN-592, ASP-477, ASP-593	ASP-480, ASN-481, VAL-479, ALA-478, LEU-434, PHE-907, ASP-909, TYR-916, HIS-587, GLU-515, ASP-588, TYR-610, TRP-517
29	Rutin	-7.2	ASP-477, ASP-588, GLN-592, ASN-481	PHE-907, LEU-382, LEU-908, ASP-480, TYR-430, ASN-914, ASP-909, TYR-916, HIS-587, LEU-433, ALA-478, LEU-434, GLN-960, ARG-475, SER-589, ASP-593, TYR-610, TRP-517

30	Robinin	-1.9	GLN-592, GLU-515, TYR-430	TYR-962, GLN-960, TYR-916, ASP-909, HIS-587, ASN-914, ASN-862, PHE-907, LEU-908, LEU-382, TYR-610, TYR-430, GLY-429, ASP-480, LEU-433, ASN-481, ASP-477, ALA-478, LEU-434

Table 3: Drug-Likeness Predictions of Compounds, Computed by SwissADME

s no	Molecule	Mol.Wt. (g/mol)	NRB	NHA	NHD	TPSA (A°2)	LogP (cLogP)	Lipinski's Rule of Five Violation
1	benzoic acid	122.12	1	2	1	37.3	1.44	0
2	Salicylic acid	138.12	1	3	2	57.53	1.24	0
3	p-hydroxybenzoic acid	138.12	1	3	2	57.53	1.05	0
4	Protocatechuic acid	154.12	1	4	3	77.76	0.65	0
5	Gentisic acid	154.12	1	4	3	77.76	0.74	0
6	Gallic acid	170.12	1	5	4	97.99	0.21	0
7	Vanillic acid	168.15	2	4	2	66.76	1.08	0

8	p-Coumaric acid	164.16	2	3	2	57.53	1.26	0
9	Esculetin	178.14	0	4	2	70.67	1.12	0
10	Caffeic acid	180.16	2	4	3	77.76	0.93	0
11	Ferulic acid	194.18	3	4	2	66.76	1.36	0
12	Sinapic acid	224.21	4	5	2	75.99	1.31	0
13	Gallic acid hexoside	332.26	4	10	7	177.14	-1.62	1
14	Gallic acid 4-O-glucoside	332.26	4	10	7	177.14	-1.62	1
15	sinapoyl malate	340.28	9	9	3	139.59	0.88	0
16	Isochlorogenic acid	354.31	5	9	6	164.75	-0.38	1
17	chlorogenic acid	354.31	5	9	6	164.75	-0.38	1
18	caffeoyl-quinic acid	354.31	5	9	6	164.75	-0.4	1
19	1-O-sinapoyl-b-D-glucose	386.35	7	10	5	155.14	-0.34	0
20	5-O-Sinapoylquinic acid	398.36	7	10	5	162.98	0	0

21	Digalloyl hexoxide	484.36	7	14	9	243.9	-0.89	2
22	1,2-Diferuloylgentiobiose	694.63	14	17	8	260.59	-0.46	3
23	2-Feruloyl-1-sinapoylgentiobiose	724.66	15	18	8	269.82	-0.59	3
24	1,2-Disinapoylgentiobiose	754.69	16	19	8	279.05	-0.43	3
25	1-Sinapoyl-2,2′-diferuloylgentiobiose	900.83	20	21	8	305.35	1	3
26	2-Feruloyl-1,2’-disinapoylgentiobiose	930.85	21	22	8	314.58	0.65	3
27	1,2,2′-Trisinapoylgentiobiose	960.88	22	23	8	323.81	1.3	3
28	Apigenin	270.24	1	5	3	2.11	1.89	0
29	Kaempferol	286.24	1	6	4	1.58	1.7	0
30	Luteolin	286.24	1	6	4	1.73	1.86	0
31	Quercetin	302.24	1	7	5	1.23	1.63	0
32	Myricetin	318.24	1	8	6	0.79	1.08	1

33	Astragalin	448.38	4	11	7	-0.25	0.53	2
34	Rutin	610.52	6	16	10	-1.12	2.43	3
35	Robinin	740.66	8	19	11	-1.82	2.99	3

Table 4: Prediction of Toxicity of Compounds (1–4), 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	benzoic acid	Yes	No	No	No	No	290	3
2	Salicylic acid	Yes	No	No	No	No	1034	4
3	p-hydroxybenzoic acid	No	No	No	No	No	2200	5
4	Protocatechuic acid	No	Yes	No	No	No	2000	4
5	Gentisic acid	No	No	No	No	No	4500	5
6	Gallic acid	No	Yes	No	No	No	2000	4
7	Vanillic acid	No	No	No	No	No	2000	4
8	p-Coumaric acid	No	Yes	No	No	No	2850	5

9	Esculetin	No	Yes	No	No	No	945	4
10	Caffeic acid	No	Yes	No	No	No	2980	5
11	Ferulic acid	No	No	Yes	No	No	1772	4
12	Sinapic acid	No	No	Yes	No	No	1772	4
13	Gallic acid hexoside	No	No	No	No	No	3750	5
14	Gallic acid 4-O-glucoside	No	No	No	No	No	3750	5
15	sinapoyl malate	No	No	Yes	No	No	3800	5
16	Isochlorogenic acid	No	No	Yes	No	No	5000	5
17	chlorogenic acid	No	No	Yes	No	No	5000	5
18	caffeoyl-quinic acid	No	No	Yes	No	No	5000	5
19	1-O-sinapoyl-b-D-glucose	No	No	Yes	No	No	n.a	n.a
20	5-O-Sinapoylquinic acid	No	No	Yes	No	No	5000	5
21	Digalloyl hexoxide	No	No	No	No	No	2260	5
22	1,2-Diferuloylgentiobiose	No	No	Yes	No	No	5000	5

23	2-Feruloyl-1-sinapoylgentiobiose	No	No	Yes	No	No	n.a	n.a
24	1,2-Disinapoylgentiobiose	No	No	Yes	No	No	5000	5
25	1-Sinapoyl-2,2′-diferuloylgentiobiose	No	No	Yes	No	No	5000	5
26	2-Feruloyl-1,2'-disinapoylgentiobiose	No	No	Yes	No	No	5000	5
27	1,2,2′-Trisinapoylgentiobiose	No	No	Yes	No	No	5000	5
28	Apigenin	No	No	No	No	yes	2500	5
29	Kaempferol	No	No	No	No	No	3919	5
30	Luteolin	No	Yes	No	Yes	No	3919	5
31	Quercetin	No	Yes	No	Yes	No	159	3
32	Myricetin	No	Yes	No	Yes	No	159	3
33	Astragalin	No	No	No	No	No	n.a	n.a
34	Rutin	No	No	Yes	No	No	5000	5
35	Robinin	No	No	Yes	No	No	5000	5

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 flavonoids and phenolic compounds isolated from brassica oleracea. L. var. Italica. Compared with other compounds Kaempferol in flavonoids and isochlorogenic acid in phenolic had higher affinity value and binding score. Toxicological prediction results suggested that all kaempferol and isochlorogenic acid are non-hepatotoxic, non-carcinogenic, non-irritant, immunogenic, and non-cytotoxic. The DFT results revealed that compound Kaempferol and Benzoic acid has better bioactivity and chemical reactivity with considerable intramolecular charge transfer between electron-donor and electron-acceptor groups. Based on the results of the present investigation, Kaempferol and isochlorogenic 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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