Research Article

Molecular Docking of Surface Adhesin Protein of Streptococcus *mutans* with Epigallacatechin Gallate for the Prevention of Biofilm Formation

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ABSTRACT

Dental plaque biofilms plays an important role in the development of chronic oral infections, causing a severe health burden. Many of these infections cannot be eliminated, as the bacteria in biofilms are resistant to the host's immune defenses and antibiotics. There is a critical need to develop new strategies to control biofilm-based infections. Biofilm formation in Streptococcus mutans is promoted by adhesion of the molecules at adhesion protein binding site. Various chemical compounds investigated in the prevention of biofilm formation but they produced numerous side effects. The current study was designed to identify five different herbal compounds that target adhesion protein, thereby inhibiting S. mutans biofilm formation and with the potential to prevent dental caries. The purpose of this study was to analyze the inhibitory action of adhesion protein by computational docking studies. For this, herbal compounds Epigallocatechin gallate (EGCG), oleonolic acid, ursolic acid, epicatechin, quercetin isolated from cranberry, guava, green tea and oolong tea were used as ligand for molecular interaction. The crystallographic structure of molecular target was obtained from PDB database .Computational docking analysis was performed using iGemdoc option based on scoring functions. The Epigallocatechin gallate showed optimum binding affinity with a molecular target. These results indicated that EGCG could be one of the potential ligands to treat dental caries by inhibiting biofilm formation.

Keywords: Biofilms, Epigallocatechin gallate, oleonolic acid.

INTRODUCTION

Dental caries is a multi-factorial infectious disease characterized by progressive destruction of tooth enamel. It is one of the most prevalent human diseases among all age groups[1].

It is estimated that over 90% of the world's population will experience dental caries atleast once during their life time[2].Dental caries may arise from chronic biofilms containing cariogenic microbes which breakdown fermentable carbohydrates into organic acids that cause demineralization and destruction of tooth tissue.

S. mutans, a member of the oral micro flora, is considered to be the primary causative agent of dental caries (or tooth decay) and is one of the best known biofilm forming bacterium[3].Several studies showed that individuals with dental plaque containing low levels of *S. mutans* are more resistant to exogenous colonization with other cariogenic pathogens and are more resistant to dental caries in the long run[4].

Cariogenic dental biofilms are eradicated mainly through nonspecific mechanical removal (brushing and flossing) or treatment with broad-spectrum antibiotics (chlorhexidine). Apart from the extensive use of fluoride, a number of new anti-cariogenic methods have started to draw attention. Derivatives of natural products, such as cranberry, guava constituent's fractions of green and oolong tea have been shown to have inhibitory effects against *S. mutans* biofilm formation. The study suggested the possible benefits of herbal compounds which inhibit the biofilm formation by *Streptococcus mutans* an oral pathogen.

MATERIALS AND METHODS

The crystallographic structure of molecular target adhesin protein was downloaded from the RCSB protein Data Bank. The chemical structure of Epigallocatechin gallate, oleonolic acid, ursolic acid, epicatechin and quercetin was obtained from PubChem compound database. It was prepared by using Biovia discovery studio 2016 and SDF format of this ligand was converted to PDBQT file using PyMol version 1.7.4.5 tool to generate atomic coordinates. The active sites are the coordinates of the ligand in the original target protein grids, and these active binding sites of target protein were analyzed using the Bravio Discovery Studio version 2016.

A computational ligand-target docking approach was used to analyze structural complexes of the adhesion protein (target) with Epigallocatechin gallate, oleonolic acid, ursolic acid, epicatechin, quercetin (ligand) in order to understand the structural basis of this protein target specificity. Docking was carried out by iGemdoc option based on scoring functions. The energy of interaction of herbal components with the adhesin protein is assigned.

RESULTS AND DISCUSSION

The binding energy indicate that affinity of the Adhesion protein (target enzyme) docked with herbal components. Among the five compounds, EGCG showed, lower negative value which indicates active binding to the target site and also showed the best interaction with

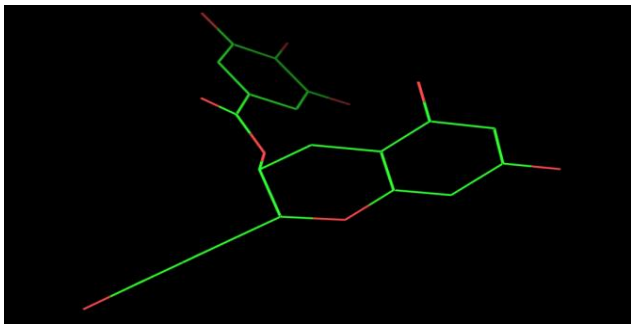
target proteins based on the VDW values as compared to standard and other compounds such as oleonolic acid, ursolic acid, epicathechin, and quercetin.

	A	B	C	D	E
1	Compound	Energy	VDW	HBond	Elec
2	cav3qe5_GLC-EGCG-0.pdb	-59.3457	-59.3457	0	0
3	cav3qe5_GLC-oleonolic acid-1.pdb	-48.4854	-48.4854	0	0
4	cav3qe5_GLC-ursolic acid-1.pdb	-48.0147	-48.0147	0	0
5	cav3qe5_GLC-epicatechin-0.pdb	-56.8983	-56.8983	0	0
6	cav3qe5_GLC-quercetin-0.pdb	-29.1549	-29.1549	0	0

Energy values obtained during docking analysis of Epigallocatechin gallate, oleonolic acid, ursolic acid, epicatechin, quercetin as ligand molecule and adhesin protein as target.

Compound	Energy	V-M LYS 1023	V-S LYS 1023	V-M GLN 1024	V-S GLN 1024	V-S VAL 1112	V-M ASP 1115	V-S ASP 1115	V-S LYS 1259	V-M ALA 1260	V-M GLY 1261	V-M ASP 1317	V-M PHE 1318	V-S PHE 1318
cav3qe5_GLC-EGCG-0.pdb	-59.3	-7.1	-3.7	-4.8	-0.5	-7	-1.7	-1.1	0	0	0	-3.2	-2	-20.6
cav3qe5_GLC-epicatechin-0.pdb	-56.9	-6.8	-6.9	-0.5	0	-2.9	-9.4	-7.3	0	0	0	-1.8	-0.1	-2.9
cav3qe5_GLC-oleonolic acid-1.pdb	-48.5	-0.1	-4.7	-0.6	-4	0	0	-0.1	0	-5.2	-9.2	0	0	0
cav3qe5_GLC-ursolic acid-1.pdb	-48	0.8	-0.2	-8.3	-5.7	0	0	0	-6.5	-0.4	0	-0.3	-5.4	-5.4
cav3qe5_GLC-quercetin-0.pdb	-29.2	0	0	0	0	0	0	-1.1	0	0	0	-5.1	-1.5	-12.2

Pymol molecular graphic structure of Epigallocatechin gallate with target



Adhesions and virulence factors of streptococci have been reviewed extensively. Carcinogenicity capacity of S. mutans is largely dependent on the ability of the bacteria to adhere and produce acid. To establish biofilm, planktonic bacteria attaches to either inert or coated surfaces and this can be mediated by electrostatic contacts or bacterial surface adhesins. Attachment is followed by proliferation of the primary colonizers and their co-aggregation with other planktonic bacteria, production of exopolysaccharide which stabilizes the architecture, leading to the maturation of the biofilm[6].

As the structures of the adhesion protein are considerably specific for *S. mutans*, we expected that a structure-based inhibitor of the *S.mutans* adhesion would possess narrow-spectrum anti-biofilm activity. Our results supported the idea that the compound had modest selectivity toward the cariogenic bacterium *S. mutans.* Another advantage of an adhesion-targeted inhibitor is that it is very likely to possess anti biofilm bioactivity without killing the bacterial cells directly[7].

Within the limitation of this study, is that it may not represent a complete picture of how the small-molecule inhibitor interacts with genetic network responsible for biofilm formation, as we tested only the adhesion protein binding pocket from *S. mutans*. Since oral biofilms are complex, multispecies microbial communities, further research is needed to shed more light on the effect of the compound in real situations.

CONCLUSION

Docking studies of the herbal compounds showed that, this Epigallocatechin gallate ligand is good molecule which docks well with Adhesion protein target. Therefore Epigallocatechin gallate molecule plays an important play role in inhibiting the biofilm formation by Inhibiting Surface Adhesion Protein of Streptococcus Mutans.

REFERENCES

1. Petersen PE, Kwan S. 2009. World Health Organization global oral health strategies for oral health promotion and disease prevention in the twenty-first century. Präv Gesundheitsf 4:100-104
2. Marchisio O, Esposito M, Genovesi A.2010. Salivary pH level and bacterial plaque evaluation in orthodontic patients treated with Recaldent® products. Int J Dent Hyg 580 8:232-236.
3. Tanzer JM, Livingston J, Thompson AM. 2001. The microbiology of primary dentalcaries in humans. J Dent Educ 65:1028-1037
4. Marsh PD.2010. Microbiology of dental plaque biofilms and their role in oral health andcaries. Dent Clin North Am 54:441-454.
5. Xu X, Zhou XD, Wu CD. 2012. Tea catechin epigallocatechin gallate inhibits *Streptococcus mutans* biofilm formation by suppressing *gtf* genes. Arch Oral Biol57:678-683.
6. Hall-Stoodley, L.; Costerton, J.W.; Stoodley, P 2004. Bacterial biofilms: From the natural environment to infectiousdiseases. Nat. Rev. Microbiol. 2, 95–108.
7. Koo H, Xiao J, Klein M, Jeon J. 2010. Exopolysaccharides produced by *streptococcus mutans* glucosyltransferases modulate the establishment of microcolonies within multispecies biofilms. J Bacteriol 192:3024-3032
8. Fukushima K, Okada T, Ochiai K. 1993. Production, characterization, and application of monoclonal antibodies which distinguish three glucosyltransferases from *Streptococcus mutans*. Infect Immun 61:323-328.

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