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Original Article

Inhibition of superoxide dismutase using herbal compounds to treat oral diseases caused by *Streptococcus mutans* - An *in silico* study

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ABSTRACT

The aim of this study is to evaluate the efficiency of different herbal compounds in inhibition of superoxide dismutase to treat oral diseases caused by *Streptococcus mutans*. The three-dimensional crystallographic structure of superoxide dismutase was downloaded from RCSB protein data bank, and then, the protein structure was corrected using "What if "server. The three-dimensional chemical structures of compounds cianidanol, punicalagins, quercetin, rutin, and epigallocatechin gallate (EGCG) were obtained from the PubChem compound database. It was prepared using Biovia discovery studio 2016, where the standard delay format of this ligand was converted to PDB file using Pymol version 1.7.4.5 tool to generate atomic coordinate. The active binding sites of target protein were analyzed using the Biovia discovery studio 2016. Docking was carried out by iGemdoc software version 2.1 based on scoring functions. The energy of interaction of herbal components with the adhesion protein is assigned. The binding energy indicates the affinity of the adhesion of protein structure docked with the herbal compounds of which EGCG showed best docking with the superoxide dismutase of which EGCG had a better interaction with target protein based on root-mean-square deviation values compared to standards. EGCG suppresses *S. mutans* at transcriptional level disrupting the initial attachment of *S. mutans* and the formation of mature biofilm. The probable mechanism of EGCG is its interaction with the cell membranes of bacteria causing the disruption of the bacterial cell morphology membrane integrity and permeability. Thus, EGCG has been used in inhibition of superoxide dismutase to treat the oral diseases caused. The docking analysis revealed that EGCG has the maximum binding energy of −90.0926 of all the five herbal compounds.

Keywords: Herbal compounds, molecular docking, *Streptococcus mutans*, superoxide dismutase

Introduction

Herbal extracts are successfully used in dentistry as tooth cleaning and antimicrobial plaque agents. These natural phytochemicals offers an effective alternative to antibiotics and have a promising approach in prevention and therapeutic strategies for dental caries and other oral infections.[1] Oral diseases are mainly due to bacterial infections and have been well-reported that medicinal plants confer considerable antibacterial activity against various microorganisms including bacteria's responsible for dental caries.[2]

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Dental caries are one of the most common and costly diseases in the world, and although rarely life-threatening and it's a major problem for health service providers. To decrease the occurrence of caries, a thorough knowledge on microorganisms is necessary.[3] *Streptococcus mutans* is the name given to a group of seven closely related species collectively referred to as the Mutans Streptococci. The primary habitats for *S. mutans* are mouth, pharynx, and intestine.[4]

Dental caries are mainly due to interaction between three factors carbohydrates, cariogenic bacteria, and host tooth surface.[5] Acidogenic and aciduric Gram-positive bacteria lead to the development of dental caries by metabolizing sucrose to organic acids by dissolving the calcium phosphate in the tooth resulting in decalcification. The global need for alternative source of prevention and treatment in safe, effective, and economical way from an increase in disease incidence, increased resistance to pathogenic bacteria to newer antibiotics chemotherapeutics, opportunistic infections in individuals who are immunocompromised and financial issues in developing nations.[6,7]

Materials and Methodology

The five herbal compounds analyzed in this study are obtained from the pericarp (peel rind) of *Punica granatum* (pomegranate) active compounds are cianidanol is an antioxidant flavonoid, occurring especially in woody plants as both (+)-catechin and (−)-epicatechin (cis) forms. Punicalagin is an ellagitannin, a type of phenolic compound. It is found in forms of alpha and beta in pomegranates (*P. granatum*), in *terminalia catappa* and *Terminalia myriocarpa*. Quercetin is a flavonol with antioxidant property. Rutin is a flavonol glycoside is used in decreasing capillary fragility. Epigallocatechin gallate (EGCG) is a phenolic antioxidant used in inhibition of oxidation of cells and in preventing free damage to cells.

Table: 1 Fitness and energy levels

Compound	Energy	VDW	HBOND	ELEC
Cianidanol	−66.5729	−66.5729	0	0
Punicalagin	385.085	385.085	0	0
Quercetin	−71.4921	−71.4921	0	0
Rutin	−33.2139	−33.2139	0	0
EGCG	−90.0296	−90.0296	0	0

EGCG: Epigallocatechingallate

Table 2: Interaction table

Compounds	E (Pharma)	V-M-LEU-3	V-S-PRO-8	V-M-GLU-53
Quercetin.pdb	0	0	0	−5.49186
Cianidanol.pdb	0	0	0	−4.92613
Rutin.pdb	0	−6.21181	0	−0.59944
Punicalagin.pdb	0	0	−9.9638	0
EGCG.pdb	0	0	0	−6.23799

EGCG: Epigallocatechingallate

Ligand selection

The chemical structure of the cianidanol, punicalagin, quercetin, rutin, EGCG was obtained from the PubChem compound database. The structures are downloaded in MOL standard delay format of this ligand and converted to PDBQT format using PyRx tool to generate atomic coordinates.

Accession of target protein

The three-dimensional crystallographic structure of the target protein superoxide dismutase is obtained from protein data bank.

Target and ligand optimization

The target protein and the five herbal compounds were subjected to docking using discovery studio version 3.0 software. The compound structures are corrected using the clean geometry tool while the protein structure is corrected using what if server.

Analysis of target active binding sites

The ligands active sites and the target protein binding sites were analyzed using discovery studio version 3.0.

Molecular docking analysis

A computational ligand-target docking approach was carried out to analyze structural complexes of superoxide dismutase using IGEM dock software version 2.1.

Table 3: Interaction table

Compounds	V-S-GLU-53	V-S-LEU-78	V-M-ALA-81	V-M-SER-88	V-S-SER-88
Quercetin.pdb	−8.76207	0	0	0	0
Cianidanol.pdb	−6.12716	0	0	0	0
Rutin.pdb	−7.45317	−5.76572	−4.46302	0	0
Punicalagin.pdb	0	0	0	−6.99485	−5.11601
EGCG.pdb	−11.0427	0	0	0	0

EGCG: Epigallocatechingallate

Table 4: Interaction table

Compounds	V-M-PRO-89	V-S-PRO-89	V-S-GLU-90	V-S-ILE-15	V-M-LYS-156
Quercetin.pdb	0	0	0	−6.17462	−4.39157
Cianidanol.pdb	0	0	0	−4.90878	−4.81538
Rutin.pdb	0	0	0	0	0
Punicalagin.pdb	−5.52114	−9.44744	−5.92096	0	0
EGCG.pdb	0	0	0	−5.61161	−5.00711

EGCG: Epigallocatechingallate

Table 5: Interaction table

Compounds	V-S-LYS-156	V-M-PRO-157	V-S-PRO-157	V-M-GLU-198	V-S-GLU-198	V-S-LEU-202
Quercetin.pdb	−11.4789	−4.04626	−5.09345	0	0	0
Cianidanol.pdb	−9.94156	−5.74939	−4.80187	0	0	0
Rutin.pdb	0	0	0	0	0	0
Punicalagin.pdb	0	0	0	0	0	0
EGCG.pdb	−5.72744	−4.8322	−6.25915	−5.52794	−11.7085	−4.55073

EGCG: Epigallocatechingallate

Results

The fitness and energy levels of cianidanol, punicalagin, rutin, quercetin and EGCG are summarized in Tables 1-5 with EGCG showing a maximum binding energy with Superoxide dismutase

Discussion

Factors such as adherence to enamel surfaces, production of acidic metabolites, the capacity to build up glycogen reserves, and the ability to synthesize extracellular polysaccharides (EPS) are present in dental caries.[5] *S. mutans* and *Streptococcus sobrinus* have a central role in the etiology of dental caries.[6] Because these can adhere to the enamel salivary pellicle and to other plaque bacteria.[7] Mutans streptococci and *lactobacilli* have the greater risk of cavities as they are high acid producers.[8] Usually, the appearance of *S. mutans* in the tooth cavities is followed by caries after 6–24 months.[9] The acidogenic *S. mutans* and *S. sobrinus* forms EPS in the presence of sucrose,[10] but also from fructose and glucose. The EPS are long-chained and high molecular mass polymers.[11] The energy rich glycosidic bond between the glucose and fructose moieties supplies the free energy needed for the synthesis of nutrients 2010, 2 292 EPS. Glucose homopolysaccharides and fructose homopolysaccharides are called glucose and fructose, respectively.[12] Glucans are produced by glucosyltransferases while fructans are produced by fructosyltransferases.[13] The production of large quantities of EPSs from sucrose is an important factor of *S. mutans* cariogenicity.[14]

Superoxide dismutases are enzymes that catalyze the dismutation of superoxide into oxygen and hydrogen peroxide. Thus, they are an important antioxidant defence in nearly all cells exposed to oxygen.[15] Superoxide dismutase is a natural product of aerobic metabolism and is often produced in large quantities thus protecting the cell from damage. In dismutation reaction, one superoxide molecule is oxidized and the other is reduced resulting in the formation of molecular oxygen and hydrogen peroxide. The reaction of superoxide catalyzed by superoxide dismutase prevents oxidative stress and enhances cell survival.[16]

Recently, natural products have been evaluated as sources of antioxidant agents with efficacies against a variety of microorganisms. The peel extract of pomegranate shown highest antioxidant activity against the superoxide dismutase in *S. mutans* thereby preventing progression of dental caries. The antioxidant property of EGCG has been proved to show rapid inhibiton of energy metabolism of bacterial cells. The probable mechanism of EGCG is its interaction with the cell membranes of bacteria causing the disruption of the bacterial cell morphology membrane integrity and permeability. The computational docking analysis revealed that all the five herbal compounds binding successfully with the target protein out of which EGCG had the lowest interaction energy proving its potential inhibitory effect against the superoxide dismutase. The concentration of EGCG in range of few mg/ml is sufficient to inhibit the growth or viability of *S. mutans*. Thus, EGCG suppresses *S. mutans* at transcriptional level disrupting the initial attachment of *S. mutans* and thus the formation of mature biofilm. EGCG is an ester of epigallocatechin and gallic acid and is a type of catechin. EGCG has been the subject for number of basic and clinical research studies investigating its potential use as a therapeutic for broad range of disorders.

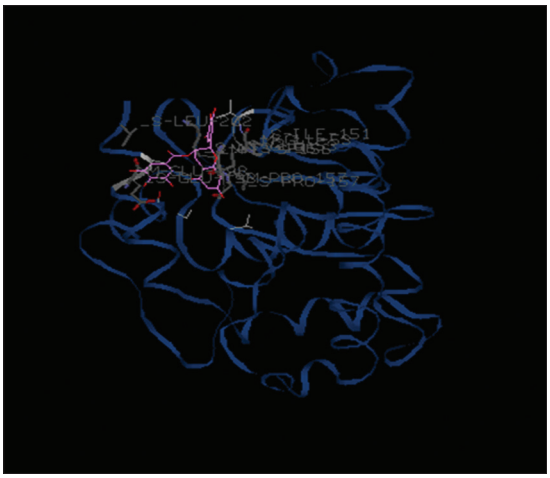

Figure 1: Epigallocatechingallate showing maximum binding energy (−90.0926)

Conclusion

The docking analysis revealed that EGCG has the maximum binding energy of −90.0926 [Figure 1] of all the five herbal compounds. Further studies need to be undertaken to put forward more concrete evidence of antioxidant action of EGCG.

References

1. Borchers AT. Traditional Asian medicine and oral health. J Tradit Med 2004;21:17-26.
2. Singh J, Kumar A, Budhiraja S, Hooda A. Ethnomedicine: Use in dental caries. Braz J Oral Sci 2007;6:21.
3. Marsh PD. Are dental diseases examples of ecological catastrophes? Miacrobiol Sgm 2003;149:279-94.
4. Loesche WJ. Role of *Streptococcus mutans* in human dental decay. Microbiol Mol Biol Rev 1986;50:353-80.
5. Dawes C. Fluorides: Mechanisms of action and recommendations for use. J Can Dent Assoc 1989;55:721-3.
6. Tichy J, Novak J. Extraction, assay, and analysis of antimicrobials from plants with activity against dental pathogens (*Streptococcus* sp.). J Altern Complement Med 1998;4:39-45.
7. Badria FA, Zidan OA. Natural products for dental caries prevention. J Med Food 2014;7:381-4.
8. Trahan L. Xylitol: A review of its action on mutans streptococci and dental plaque--its clinical significance. Int Dent J 1995;45 1 Suppl 1:77-92.
9. Lamont RJ, Demuth DR, Davis CA, Malamud D, Rosan B. Salivary-agglutinin-mediated adherence of *Streptococcus mutans* to early plaque bacteria. Infect Immun 1991;59:3446-50.
10. Tanzer JM, Livingston J, Thompson AM. The microbiology of primary dental caries in humans. J Dent Educ 2001;65:1028-37.
11. Mayooran B, Robin S, John RT. Dental caries is a preventable infectious disease. Aust Dent J 2000;45:235-45.
12. Zero DT. Sugars - The arch criminal? Caries Res 2004;38:277-85.

13. Wiater A, Choma A, Szczodrak J. Insoluble glucans synthesized by cariogenic streptococci: A structural study. J Basic Microbiol 1999;39:265-73.
14. Zisu B, Shah NP. Effects of pH, temperature, supplementation with whey protein concentrate, and adjunct cultures on the production of exopolysaccharides by *Streptococcus thermophilus* 1275. J Dairy Sci 2003;86:3405-15.
15. Monsan P, Bozonnet S, Albenne C, Joucla G, Willemot RM, Remaud-Simeon M. Homopolysaccharides from lactic acid bacteria. Int Dairy J 2001;11:675-85.
16. Toda Y, Moro I, Koga T, Asakawa H, Hamada S. Ultrastructure of extracellular polysaccharides produced by serotype c *Streptococcus mutans*. J Dent Res 1987;66:1364-1369.