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Original Article

Inhibitory Effects of Administration of Curcumin Against on *Streptococcus Mutans*: *In vitro* and *In vivo* Studies

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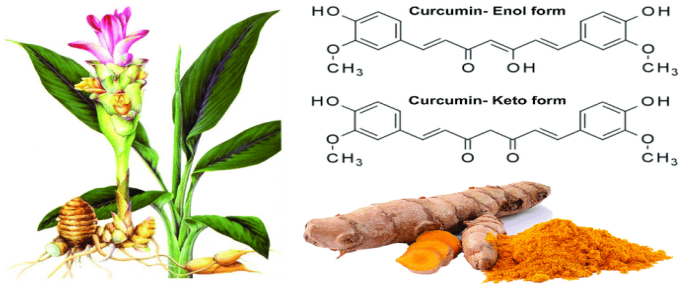
ABSTRACT

Streptococcus mutans is a harmful bacterium that destroys teeth and increases the development of caries. The use of a safe antibacterial compound can decrease the population of *S. mutans* and increase teeth healthiness. Curcumin is an antibacterial compound that may decrease *S. mutans*. The present study was conducted to evaluate the antibacterial effects of the administration of curcumin against *S. mutans*. Minimum inhibitory concentration (MIC) and minimum bactericidal concentration (MBC) values of tested extracts were determined by a micro-dilution method using a 96-well microliter plate. Biofilm formation was also investigated. In order to investigate dental caries development a study was conducted on rats. The results showed antibacterial activity of curcumin against *S. mutans* in terms of MIC and MBC compared to the control group (P<0.05). The results also revealed that biofilm formation was significantly lower in higher doses of curcumin. The administration of curcumin also decreased dental caries development in rats. In sum, curcumin can be considered as an appropriate compound for antibacterial activity against *S. mutans*. We suggest using curcumin for tooth care.

GRAPHICAL ABSTRACT



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Introduction

Oral diseases are significant challenges for healthiness all over the world. Carbohydrate oral diseases fermentation of foods by oral bacteria reduces the pH of plaque and demineralizes enamel that results from the formation of dental caries [1-3]. Dental caries and periodontal diseases are the most common challenges for oral healthiness, following oral and pharyngeal cancers and oral tissue lesions [4]. Oral healthiness is an integral status for general well-being related to the quality of life and increases beyond the functions of the craniofacial complex [5]. The association between and the activities of microbial species present in the oral cavity has been reported [4]. Bacteria species inhabit the oral cavity, and some cause oral diseases [5]. The increase in dental caries increases acidogenic and aciduric Gram-positive bacteria, such as *Streptococcus mutans* and *S. sobrinus*, lactobacilli, and actinomycetes that metabolize sucrose to organic acids (mainly lactic acid) that dissolve the calcium phosphate in teeth and cause decalcification and eventual decay [6]. *Streptococcus mutans* is the principal cariogenic bacterium in humans [7, 8]. It was reported that *S. mutans* bacteria are colonized in environments rich in sucrose and glucan-mediated on tooth surfaces [9]. The sticky polymer produced by sucrose named glucan produced of S. mutans is a starting factor for dental caries formation due to trapping oral bacteria, food debris, and salivary components [10]. Researchers seek a safe antibacterial compound with anti-cariogenic properties that have minimum side effects. Chemotherapeutic structures prepared from natural products have significant importance for producing novel drugs [11]. Some studies have reported using medicinal plants as a source of chemotherapeutic agents to inhibit oral diseases [12, 13]. Curcumin is a natural component of the rhizome *Curcuma longa*, also known as turmeric, and it is used for medicinal purposes, mainly to treat inflammatory conditions [14]. Curcumin shows antibacterial activity by disordering the 1,2-dipalmitoyl-sn-glycero-3-phosphocholine (DPPC) membranes in the bacteria [15]. Studies have reported the antibacterial activity of curcumin against Gram-positive (*S. aureus* and *Enterococcus faecalis)* and Gram-negative (*Escherichia coli* and *Pseudomonas aeruginosa)* [14].

Since curcumin is an antibacterial compound, but it has not been used against *S. mutans*, biofilm formation, and dental caries development. The present study was conducted to evaluate the antibacterial effects of administration of curcumin against *S. mutans*, biofilm formation, and dental caries development.

Materials and Methods

Materials

Curcumin (EC No. 2072805) was prepared from Sigma-Aldrich Chemical Company (St. Louis, MO). *Streptococcus mutans* (PTCC 1683) was prepared from the Iranian Biological Resources Center (Tehran, Iran). Approval for this study was obtained from International Center for Intelligent Research (ICIR-2020-184163).

The investigation antibacterial activity by minimum inhibitory concentration (MIC) and minimum bactericidal concentration (MBC)

Antibacterial activity of curcumin MIC and MBC against *S. mutans* was investigated by microdilution procedure as reported by previous studies [16]. The MIC was considered the lowest concentration that prevents visible bacterial growth and MBC as the highest dilution that produced no bacterial growth on solid medium. All the experiments were replicated in triplicate.

Biofilm formation assay

Biofilm formation for *S. mutans* was conducted as reported by others [17] by using 10^5-10^6 CFU mL^{-1} *S. mutans,* 150 µL of BHI with 5% (w/v) sucrose at different times.

Dental caries Development

The effects of curcumin on oral colonization and cariogenic potential of *S. mutans* were investigated in 16 rats and two experimental groups (8 rats per group), as grouped as control and curcumin. The animals were fed with erythromycin water (100 µg mL-1) and a regular diet for 7 days to minimize the microbial load. The bacteria were colonized by oral swab, and animals received a 5% sucrose diet in all the

trials. To colonize, the rats were inoculated with 1.4 × 10^{10} CFU of a streptomycin-resistant strain of *S. mutans* (MT8148R), in molars surfaces once for 7 days. The rats were received curcumin twice/a day (20 mg/kg body weight daily) by topical administration for 28 days. The samples were collected 4 weeks next and scored based on previous studies [16].

Data Analysis

The data were analyzed by SPSS software (version of 23). The data for *In vitro* sections were analyzed by ANOVA test. The data for In vivo section were analyzed by T-test. Since data were normal, Pearson correlation was also used.

Results and Discussion

Antibacterial Activity

The results showed that using curcumin in the concentration of 128 µg/mL could inhibit the growth of *S. mutans*, while in the concentration of 256 µg/mL could kill *S. mutans*. The results for killing *S. mutans* are presented in Figure 1.

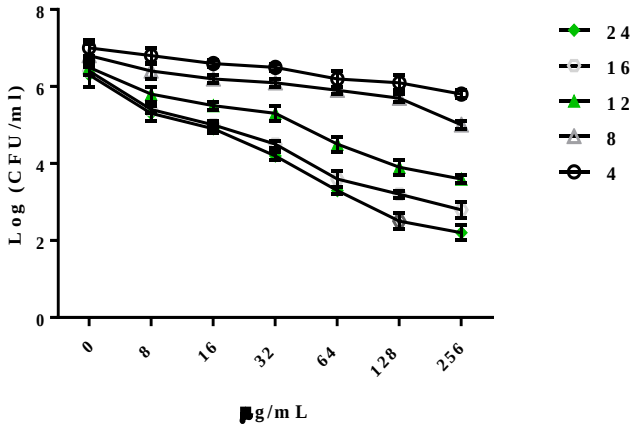

Figure 1: Kinetic of killing curve during 24 h incubation. Higher time and concentrations resulted in killing more bacteria

Biofilm Formation

The results for biofilm production are depicted in Figure 2. The results revealed that the increase in concentration and time decreased biofilm formation. The results approve that curcumin decreases biofilm formation in higher concentrations, but it needs more time. The results showed a positive correlation (r^2=0.985, *P*=0.001) between biofilm formation and antibacterial activity. The decrease in bacterial count results in a decrease in biofilm formation.

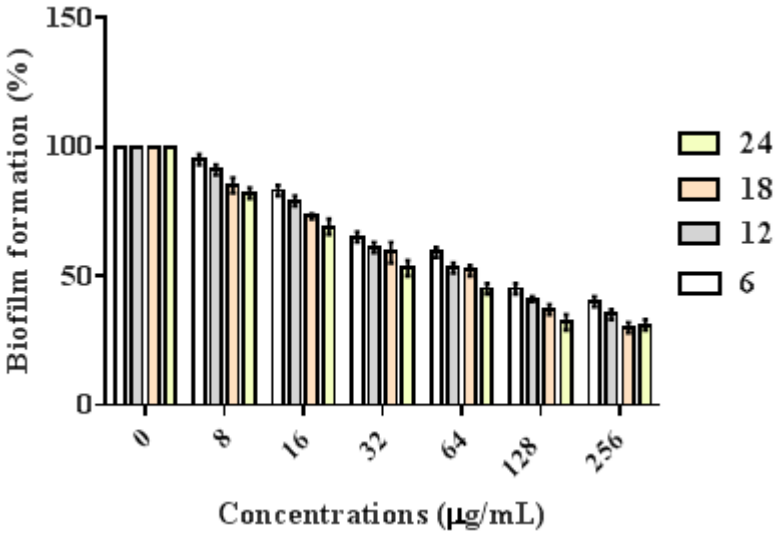

Figure 2: The results for biofilm production. Higher time and concentrations resulted in decreased biofilm formation

Dental caries development

The results for dental caries development are illustrated in Figure 3. The results demonstrated that administration of curcumin reduced caries scores in smooth surface caries (Figure 3-A) and sulcal surface caries (Figure 3-B) compared to the control group (P<0.05).

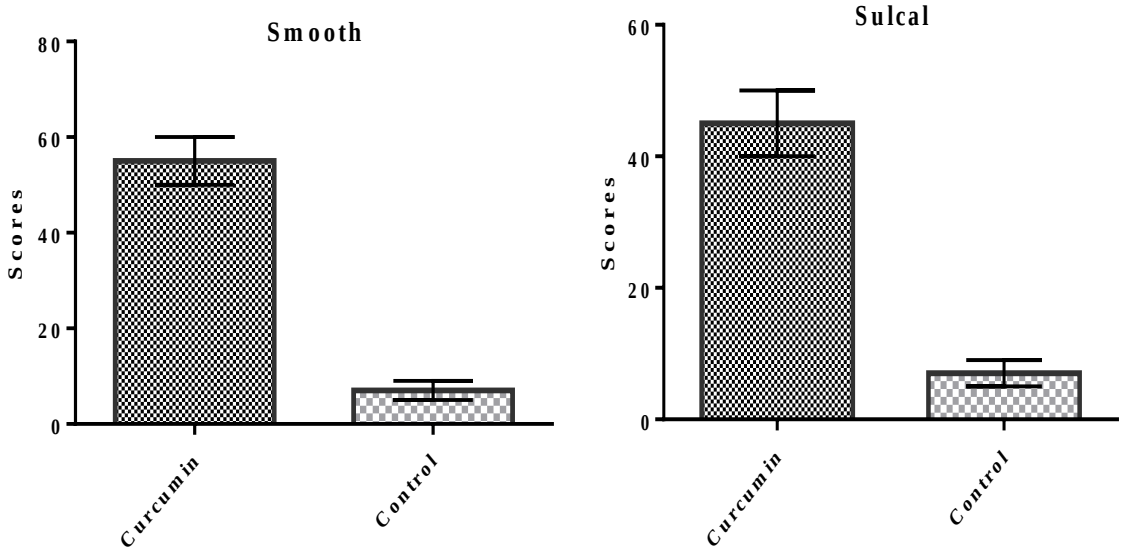

Figure 3: The effects of curcumin on dental caries in rats. The administration of curcumin reduced dental caries development in smooth and sulcal

This study was conducted to evaluate the effects of administration of curcumin against *S. mutans*, biofilm formation, and dental caries development. The results showed that administration of curcumin showed antibacterial activity and decreased biofilm formation and dental caries development. The results revealed that administration of curcumin in more time and higher concentrations decreased a significant number of bacteria. It means that curcumin needs more time for killing *S. mutans*. Studies have reported the antibacterial activity of curcumin against Gram-positive (*S. aureus* and *E. faecalis)* and Gram-negative (*E. coli* and *P. aeruginosa)* [14]. Curcumin shows antibacterial activity by disordering DPPC membranes in the bacteria [15]. Another study showed that curcumin changes bacteria membrane by thinning and disrupting the membrane [18]. Therefore, curcumin shows antibacterial activity by influencing on bacteria membrane. It needs more time for killing and inhibiting bacteria. Seemingly, curcumin slowly penetrates in bacteria membrane and destroys bacteria. Parallel with this claim, and it was reported that natural compounds slowly change the permeability of the cell membrane and penetrate bacteria [19,20]. It shows the highest effect in the highest concentration. It could be argued that curcumin may be degraded while affecting the bacteria and thus higher concentration of curcumin provides enough curcumin for affecting the bacteria. It was observed a positive correlation between antibacterial activity and biofilm formation. Seemingly, curcumin shows antibacterial activity and decreases *S. mutans*, resulting in decreased biofilm formation. It is well known that glucans mediate biofilm formation. It was reported that anti-biofilm agents decrease biofilm formation by damaging physical integrity and stability and reducing the availability of binding sites for *S. mutans* [21]. Curcumin may decrease biofilm formation, reducing the availability of binding sites for *S. mutans*, because it showed antibacterial activity.

Curcumin administration reduced caries scores in smooth surface caries and sulcal surface caries. The results approve the topical administration of curcumin reduces caries development. The efficiency of curcumin on caries scores might be attributed to its effects on the pathogenicity of *S. mutans*. The *S. mutans* damages teeth by enzyme

GTF activity. Studies have reported that *S. mutans* have adverse effects on teeth by increasing GTF activity and bacterial glycolytic [22]. In sum, the results approve that the administration of curcumin decreases *S. mutans* population resulting in caries scores.

Conclusions

In conclusion, curcumin showed antibacterial activity and anti-biofilm formation. It also decreased reduced caries scores. All the findings approve of curcumin as a safe agent that could be used as a compound in toothpaste structure. Curcumin can be considered an appropriate compound for antibacterial activity against *S. mutans*. We suggest using curcumin for tooth care.

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Authors' contributions

All authors made substantial contributions to conception and design, acquisition of data, or analysis and interpretation of data; took part in drafting the article or revising it critically for important intellectual content; gave final approval of the version to be published; and agree to be accountable for all aspects of the work.

Conflict of Interest

The authors declared no conflicts of interest in the present study.

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References

[1]. Clarkson B.H., *Dent. Clin. North. Am.*, 1999, **43**:569 [Google Scholar], [Publisher]
[2]. Baneriee A., Watson T.F., Kidd E.A.M., *Dent. Update*., 2000, **27**:272 [Crossref], [Google Scholar], [Publisher]
[3]. Ramya R., Srinivasan R., *Clinical Operative Dentistry: Principles and Practice*.1st ed. EMM ESS Medical Publishers. 2007 [Publisher]
[4]. Petersen P.E., *Community Dent. Oral Epidemiol.*, 2003, **31**:3 [Crossref], [Google Scholar], [Publisher]
[5]. Jenkinsonand H.F., Lamont R.J., *Trends Microbiol.*, 2005, **13**:589 [Crossref], [Google Scholar], [Publisher]
[6]. Palombo E.A., *Evid. Based Complementary Altern. Med.*, 2011, 680354 [Crossref], [Google Scholar], [Publisher]
[7]. Loesche W.J., *Microbial. Rev.*, 1986, **50**:353 [Crossref], [Google Scholar], [Publisher]
[8]. Tanzer J.M., Livingston J., Thompson A.M., *J. Dent. Educ.*, 2001, **65**:1028 [Crossref], [Google Scholar], [Publisher]
[9]. Mandava K., Rajeswari Batchu U., Kakulavaram S., Repally S., Chennuri I., Bedarakota S., Sunkara N., *BMC Complement. Altern. Med.*, 2019, **19**:197 [Crossref], [Google Scholar], [Publisher]
[10]. Nosrati M., Behbahani M., Mohabatkar H., Shakeran Z., *J. Herbmed Pharmacol.*, 2018, **7**:176 [Crossref], [Google Scholar], [Publisher]
[11]. Jeon J.G., Rosalen P.L., Falsetta M.L., Koo H., *Caries. Res.,* 2011, **45**:243 [Crossref], [Google Scholar], [Publisher]
[12]. Ferrazzano G.F., Amato I., Ingenito A., Zarrelli A., Pinto G., Pollio A., *Molecules,* 2011, **16**:1486 [Crossref], [Google Scholar], [Publisher]
[13]. Hasan S., Danishuddin M., Khan A.U., *BMC Microbiol.,* 2015, **15**:1 [Crossref], [Google Scholar], [Publisher]
[14]. Tyagi P., Singh M., Kumari H., Kumari A., Mukhopadhyay K., *PLoS One*, 2015, **10**:e0121313 [Crossref], [Google Scholar], [Publisher]
[15]. Barry J., Fritz M., Brender J.F., Smith P.E.S., Lee D.K., Ramamoorthy A., *J. Am. Chem. Soc*., 2009, **131**:4490 [Crossref], [Google Scholar], [Publisher]

[16]. Askari F., Davoodi M., Ghelichli M., Asadi I., Jazideh F., *Eurasian Chem. Commun.*, 2020, **2**:1164 [Crossref], [Google Scholar], [Publisher]
[17]. Loo C.Y., Corliss D.A., Ganeshkumar N., *J. Bacteriol.,* 2000, **182**:1374 [Crossref], [Google Scholar], [Publisher]
[18]. Anand P., Nair H.B., Sung B., Kannumakkara A.B., Yadav V.R., Tekmal R.R., Aggarwal B.B., 2010, **79**:330 [Crossref], [Google Scholar], [Publisher]
[19]. Burt S., *Int. J. Food Microbiol.,* 2004, **94**:223 [Crossref], [Google Scholar], [Publisher]
[20]. Moshfeghi M., Beglou A., Mortazavi H., Bahrololumi N., *J. Clin. Exp. Dent.,* 2016, **8**:e550 [Crossref], [Google Scholar], [Publisher]
[21]. Xu X., Zhou X.D., Wu C.D., *Antimicrob. Agents Chemother,* 2011, **55**:1229 [Crossref], [Google Scholar], [Publisher]
[22]. Hasan S., Danishuddin M., Khan A.U., *BMC Microbiol.,* 2015, **15**:1 [Crossref] [Google Scholar], [Publisher]

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