European Journal of Research in Dentistry 2020; 4(2): 89–93
DOI: 10.35333/ERD.2020.272

REVIEW / DERLEME

Lipids and Their Importance in Dentistry

Lipidler ve Diş Hekimliğindeki Önemi

Özge ÇİBUK, Ayşen YARAT

Abstract

Lipids in the structure of cell membranes in the oral environment determine the elasticity, fluidity and permeability of the cell membrane and participate in intercellular transport and signal transduction pathways between the salivary glands and other tissues. Lipids are also important main components of saliva. The properties and number of lipid component in cells and tissues vary according to various physiological and pathological conditions. Identification of lipids, which play a major role in disease states, is used to evaluate the diagnosis and treatment response of diseases. This also applies to various oral diseases. For example, in the presence of chronic periodontititis, caries and calculus, the amount of lipids in saliva increases. Oral surface lipids of pathogenic bacteria such as *Porhynomonas gingivalis*, one of the main bacteria causing periodontitis, also cause negative effects.
Keywords: Lipids, saliva, oral health

Öz

Ağız ortamındaki hücre zarlarının yapısında bulunan lipidler, hücre zarının elastikiyetini, akışkanlığını ve geçirgenliğini belirler ve tükürük bezleri ile diğer dokular arasında hücreler arası taşıma ve sinyal iletim yollarına katılırlar. Lipidler ayrıca tükürüğün önemli ana bileşenleridir. Hücrelerdeki ve dokulardaki lipid bileşeninin özellikleri ve sayısı çeşitli fizyolojik ve patolojik koşullara göre değişiklik gösterir. Hastalık durumlarında önemli bir rol oynayan lipidlerin tanımlanması, hastalıkların tanı ve tedavi yanıtını değerlendirmek için kullanılır. Bu aynı zamanda çeşitli ağız hastalıkları için de geçerlidir. Örneğin kronik periodontititis, çürük ve diş taşı varlığında tükürükteki lipit miktarı artar. Periodontitise neden olan ana bakterilerden biri olan *Porhynomonas gingivalis* gibi patojenik bakterilerin oral yüzey lipidleri de olumsuz etkilere neden olur.
Anahtar Kelimeler: Lipidler, tükürük, ağız sağlığı

Özge Çibuk (✉)
Marmara University, Faculty of Dentistry, Başıbüyük Sağlık Yerleşkesi, Başıbüyük Yolu 9/3 34854, Başıbüyük / Maltepe / İstanbul, Turkey
e-mail: ozgecibuk@hotmail.com
Marmara University, Faculty of Dentistry, Dentist

Ayşen Yarat
Marmara University, Faculty of Dentistry, Department of Basic Medical Sciences, Biochemistry, Istanbul, Turkey.

Submitted / Gönderilme: 07.09.2020 **Accepted/Kabul:** 08.10.2020

Lipids and Saliva

Lipids are apolar compounds that are insoluble in water but soluble in organic solvents

[Alturfan, 2019]. Saliva contains fatty acids, triglycerides, glycerophospholipids, sphingolipids and sterol lipids [Slomiany et al., 1983]. The physical condition of lipids in saliva is not fully known. Since they are water-insoluble apolar compounds, they should be complexed with the help of a carrier in order to exist in saliva. Saliva lipids are mostly released from the large salivary glands in the mouth, but cholesterol and some fatty acids can pass directly from serum to saliva [Murty et al., 1985]. The cholesterol concentration in the saliva of healthy adults reflects cholesterol levels in serum. Limited information is still available on the relationship between salivary lipids and systemic diseases. As a result of the studies, lipids are important in cases such as Cystic Fibrous, Sjögren's Syndrome, caries, early childhood caries, calculus periodontitis, preventive dentistry applications, sphingolipid and serine dipeptide lipids of *Porhynomonas Gingivalis,* calcium-phosphate-lipid system, use of lipids in systemic toxicity of local anesthetics.

Lipids and Cystic Fibrous

Submandibular saliva from patients with cystic fibrous, a genetically transmitted disease that affects all the glands of the body, contains 66% more lipids than a healthy individual [Matczuk et al., 2017]. These patients' saliva contains 54% more fatty acids, 35% more triglycerides and 42% more

cholesterol than a healthy individual [Slomiany et al., 1985]. In addition, the amount of phospholipids present in the saliva of these patients is 2 times higher than those of the healthy [Fernandis and Wenk., 2007].

Lipids and Sjögren's Syndrome

Another disease is genetically transmitted Sjögren's Syndrome, in which the salivary glands are directly affected. Patients with Sjogren's Syndrome have a 2-fold higher level of salivary lipid originated from parotis gland than those in the healthy [Quehenberger et al., 2010]. Parotid-derived saliva has been found to contain 4 times more glycolipids and 20 times more phospholipids than healthy people [Bligh and Dyer., 1959].

Lipids and Pellicle

All surfaces in the oral cavity are covered with organic material called pellicle [Schweigel et al., 2016]. It is a homogeneous, membranous, cell-free film layer formed after tooth eruption. Inside the pellicle there are lipids, proteins and glycolipids that pass through saliva or gingival fluid. This pellicle is selectively permeable to ions, it also plays a role in the process of caries and erosion. In addition, lipids present in the pellicle protect the tooth demineralization [Hannig and Hannig., 2014]. This protection function takes place when the lipids in the pellicle stop the diffusion of acids produced by acid-producing bacteria. In this way, the size of the demineralization of the tooth covered with a pellicle is under control [Slomiany et al., 1990].

Lipids and Tooth Enamel and Dentine

Tooth enamel and dentine naturally contain lipids. There is no difference between the sclerotic dentine located near the pulp chamber and the level of cholesterol and / or triglycerides contained in a normal dentine. The saliva of the people with caries secreted from the parotid and submandibular salivary glands contains more lipids than those without caries. The main reason for this change in lipid concentration is the fraction of neutral lipids and phospholipids. In addition, the saliva of people without caries contains much less free fatty acids, triglycerides, cholesterol esters, phospholipids, free cholesterol and monoglycerides [Slomiany et al., 1982].

Lipids and Dental Calculus

The main ingredient of the calculus in the mouth is minerals. The calculus is formed by the hardening of the microbial dental plaque. The organic content of the dry matter is 54.9% protein and 10.2% lipid. Teeth lipids contain high amounts of free fatty acids and less triglycerides, glycolipids and phospholipids. People with more calculus have a 50% higher lipid rate in their saliva than those with less calculus [Cajka and Fiehn., 2014].

Lipids and Early Childhood Caries

Early childhood caries one or more caries occurring in the primary teeth of children under 6 years of age are defined as missing and filled tooth surface due to caries. It is also known that lipids increase glucoseyltransferase enzyme activity, which enhances the cariogenic potential of oral microorganisms [Zaura and Twetman., 2019]. Attractive hydrophobic forces change between the lipophilic molecules on the cell surface of bacteria as a result of the increase in lipid level in saliva. This change facilitates the attachment of harmful bacteria in saliva to the pellicle layer of the tooth. The total lipid and triglyceride levels in the saliva of children with early childhood caries are higher compared to children without caries, but there is no specific difference in saliva cholesterol levels [Shama et al., 2019]. The increase in the ratio of total lipids and triglycerides may be due to the fact that children with early childhood caries consume more sugary, fatty nutrients [Evans et al., 2013, Kasbek and Verrips., 1994]. These children had a lower saliva flow rate compared to healthy children. This is also effective in caries formation. It has also been shown that the number of bacteria in the saliva of children with early childhood caries is higher [Kaewkamnerdpong and Krisdapong., 2018]. The excess number of bacteria in saliva serves as a lipid source for saliva. Periodontitis is an inflammatory disease that affects the periodontium, the supporting tissues around the tooth. When serum lipid levels of periodontitis patients were examined, it was observed that they were higher than healthy people.

Lipids and Periodontitis

The presence of periodontitis increases the level of triglyceride and total cholesterol in serum. When the periodontitis patients' triglyceride and cholesterol levels were compared with those of healthy people, the difference

was not significant. However, contrary to this situation in some studies, triglyceride and cholesterol levels were significantly higher [Thomas et al., 2017]. Age is a factor that increases the effect of chronic diseases. Considering this factor, the difference in serum triglyceride, cholesterol and LDL (Low density lipoprotein) levels of older periodontitis patients increased compared to the healthy ones. The increase in the severity of periodontal disease causes an increase in triglyceride levels. However, contrary to this situation, no relation was observed between periodontal disease degree and cholesterol level. Also, there is no difference in VLDL (Very low density lipoprotein) and HDL (High density lipoprotein) levels between groups. Today, periodontitis is accepted as a complication of Diabetes Mellitus. It is said that there is a bilateral relationship between two chronic diseases. Periodontitis and Diabetes Mellitus are diseases that lead to the production of various means of inflammation. Today, there are studies showing that Type 2 Diabetes Mellitus is related to the increase in the prevalence and severity of periodontal disease [Mealey and Oates., 2006]. When lipid profile analysis of a healthy chronic periodontitis patient and chronic periodontitis patient with Type 2 Diabetes Mellitus were compared, TC (Total cholesterol), VLDL-C (Very low density lipoprotein cholesterol) and TGL (Triglyceride) levels significantly increased, while HDL-C (High density lipoprotein cholesterol) and LDL-C (Low density lipoprotein cholesterol) levels did not show a significant change. As a result of these findings, it is understood that chronic periodontitis has systemic symptoms. In addition, it shows that the evaluation of the lipid profile may be a possible marker for chronic periodontitis.

Lipids and Preventive Dentistry

Dentistry applications are divided into two as preventive dentistry and treatment applications. Preventive dentistry for children is a life-long process that begins 6 months after the first tooth lasts [Curzon., 2015] It is assumed that the lipophilic components modulate the process of bioadhesion to the oral hard tissues, as well as to the composition and substructure of the initial oral biofilm or pellicle [Kensche et al., 2013]. Thus, lipids can be characterized as components with hydrophobic properties that prevent bacterial colonization on the outer surface and ultimately reduce caries sensitivity [Azizi et al., 2003]. In case of exposure to a lipid-enriched topical acid, the teeth can be more resistant to demineralization and therefore abrasive mineral loss is reduced. In addition, anti-inflammatory effects have been observed on oral soft tissues. However, only limited information is available for these beneficial effects. Neither the saliva and the pellicle lipid composition nor the interactions of lipids with the initial oral biofilm and the pellicle layer have been adequately studied. However, edible oils can be considered as a light supplement for the prevention of caries, erosion and periodontal diseases. The calcium-phosphate-lipid system has been successful in various treatment strategies due to its effective encapsulation ability and antimicrobial properties [Satterlee and Huang., 2016].

Due to the fact that lipids are easily designed, synthesized and characterized, they have wide application areas [Zhi et al., 2018, Williams and Grant., 2019]. Many factors on the surface of the nanoparticle used in the calcium-phosphate-lipid system can affect blood retention time and organ-specific accumulation [Alexis et al., 2008, Nuti et al., 2018]. Pulp viability of the young immature tooth is important for root development and the formation of a repertoire dentine because it is easily affected by external factors. Irreversible pulpitis in an immature permanent tooth disrupts root development, causing further loss of function and reduced tooth retention time. It has been proven that the calcium-phosphate-lipid system, a commonly used vector, suppresses the expression of inflammatory cytokines and promotes osteoodontogenic differentiation of dental pulp stem cells by demonstrating itself as a biocompatible anti-inflammatory material [Zhu et al., 2019]. The calcium-phosphate-lipid system has a broad application prospect due to its bioactivity and flexible physical property, and therefore represents a promising pulpal regeneration material to improve the response of dental pulp precursor cells [Reich et al., 2013].

Sphingolipid and Serine Dipeptide Lipids of *Porhynomonas Gingivalis*

Porhynomonas gingivalis is not the only important agent in peridontitis but as the keystone in the task group. The periodontal pathogen *Porphyromonas Gingivalis*, which acts as a keystone, produces phosphorylated dihydroceramide lipids (sphingolipids) such as phosphoethanolamine dihydroceramide (PEDHC) and phosphoglyceride dihydroceramide (PGDHC) lipids [Olsen and Nichols., 2018]. Bacterial serine dipeptide lipids are known to support inflammatory processes and are detected in human tissues associated with periodontal disease or atherosclerosis.

Bacterial sphingolipids and serine dipeptide lipids are classified as virulence factors because they have important biological properties that affect inflammation and host responses. The serine dipeptide lipids of *Porhynomonas Gingivalis* cause alveolar bone loss in chronic periodontitis by promoting the differentiation of osteoblast functions and the activities of osteoclasts [Tsuda et al., 2005]. Lipid components are used by the periodontal pathogen *Porhynomonas Gingivalis* for entry into host epithelial cells [Tsuda et al., 2008]. *Porhynomonas Gingivalis* produces virulence factor with capsule rich in polysaccharide. The liposaccharide of *Porhynomonas Gingivalis* is thought to be important in bone destruction in periodontitis. Sphingolipids and serine dipeptide lipids of *Porphynomonas Gingivalis* are particularly associated with the basic pathological features of periodontitis. It also produces many cellular effects, including promoting osteoclastogenesis and inhibition of osteoblast function [Olsen and Nichols., 2018].

Lipids and Local Anesthetics

Dentists use local anesthetics to routinely relieve pain in their daily treatments. During treatment, systemic toxicity may develop in overdose of local anesthetics. The lipid solution is used for the treatment of systemic toxicity [Oksuz et al., 2018]. The lipid solution is an emulsion of soybean oil, egg phospholipids and glycerin; It is available in 10%, 20% and 30% concentrations. Overdose exposure, anatomy and other patient-specific factors can cause systemic toxicity. Tongue and lip numbness, metallic taste in the mouth, tinnitus, dizziness and convulsions, including cardiovascular stimulation effects, respiratory depression and loss of consciousness, hypertension, post-bradycardia arrhythmia, cardiac collapse, cardiac arrest are present signs of systemic toxicity [Jensen-Gadegaard et al., 2011]. If one or more signs of systemic toxicity are present, local anesthesia injection should be stopped immediately. Then the patient's airway should be checked and 100% oxygen administration should be started. IV (Intravenous) lines should be placed and benzodiazepines should be used if seizures develop. During cardiac arrest, the clinician should begin CPR (Cardiopulmonary Resuscitation). An IV (intravenous) bolus of the 1.5 mg / kg lipid solution should then be administered. If cardiac arrest continues after 1 minute of CPR, 15 ml / kg / h lipid solution infusion should be initiated. Bolus lipid infusion can be repeated up to 3 times and should be given every 5 minutes. CPR should be continued until the maximum dose of lipid solution of 12 mL / kg is applied. The 20% concentration of the lipid solution should be available at the dentists' clinic, despite the development of systemic toxicity [Basaranoglu et al., 2010].

Conclusion

Lipids are one of the main components of saliva. In the case of illness and health, the amount, composition and properties of lipids can vary. In terms of dentistry, lipids are important in cases such as caries, early childhood caries, calculus, Sjögren's Syndrome, cystic fibrous, chronic periodontitis, and their amounts in saliva vary. Identification of lipids, which have a major role in oral diseases as well as in various diseases, may be important for evaluating the diagnosis and treatment response of diseases.

References

1. Alexis F, Pridgen E, Molnar LK, and Farokhzad OC. Factors Affecting the Clearance and Biodistribution of Polymeric Nanoparticles. Mol Pharm. 2008; 5,505–515.
2. Alturfan EI. Lipidlerin yapısı. Bölüm 11. Biyokimyada Temel ve Özel Konular, Editörler, Prof. Dr. Ayşen Yarat, Prof.Dr. Tuğba Tunalı Akbay, Prof. Dr. Ebru Işık Alturfan, pp: 139-155, 2019
3. Azizi F, Rahmani M, Ghanbarian A, Emami H, Salehi P, Mirmiran P, et al. Serum lipid levels in an Iranian adults population: Tehran Lipid and Glucose Study. Eur J Epidemiol. 2003;18(4):311–9
4. Basaranoglu G, Teker MG, Saidoglu L, Muhammedoglu N, Ozdemir H. The Knowledge of the Physicians who Use Local Anaesthetics About Their Toxicity and Intralipid Therapy. Turk J Anaesthesiol Reanim 2010;38:262-7
5. Bligh EG and Dyer WJ., A rapid method of total lipid extraction and purification., Can J Biochem 1959; 37(8): 911–917.
6. Cajka T and Fiehn O., Comprehensive analysis of lipids in biological systems by liquid chromatography-mass spectrometry., Trends Anal Chem 2014; 61:192– 206.
7. Curzon ME. Preventive dentistry: Early childhood caries in infants. Br Dent J 2015 Apr 24;218(8):438-9. doi: 10.1038/sj.bdj.2015.300.
8. Evans E, Hoyes C, Carole A, Palmer O, Steven A, Cohen D. Dietary Intake and Severe Early Childhood Caries in Low-Income, Young Children. J Acad Nutr Diet 2013; 113(8): 1057-610.
9. Fernandis AZ and Wenk MR., Membrane lipids as signaling molecules., Curr Opin Lipidol 2007; 18(2):121–128.
10. Hannig M, Hannig C. The pellicle and erosion. Monogr Oral Sci 2014;25:206-14.doi:10.1159/000360376
11. Jensen-Gadegaard P, Skjønnemand M, Damgaard-Jensen J, Gottschau B. Limited knowledge of lipid rescue therapy

in local anaesthetic systemic toxicity. Dan Med Bull 2011;58:A4226.

12. Kaewkamnerdpong I, Krisdapong S. The Associations of School Oral Health-Related Environments with Oral Health Behaviours and Dental Caries in Children. Caries Res 2018;52(1-2):166-175 doi: 10.1159/000485747. Epub 2018 Jan 23
13. Kalsbek H, Verrips GH. Consumption of Sweet Snacks and Caries Experience of Primary School Children. Caries Res. 1994; 28:477-83.
14. Kensche A, Reich M, Hannig C. Lipids in Preventive Dentistry. Clin Oral Invest. 2013; 17:669-685
15. Matczuk J, Piotrowska M, Maciejczyk M, Kurek K. Salivary Lipids: A Review. Adv Clin Exp Med 2017; 1021-1029
16. Mealey BL, Oates TW; American Academy of Periodontology. Diabetes Mellitus and Periodontal Diseases. J Periodontol. 2006; 77:1289 -303
17. Murty VL, Slomiany BL, Laszewicz W, Slomiany A, Petropoulou K, Mandel ID. Lipids of developing dental plaque in caries-resistant and caries-susceptible adult people. Arch Oral Biol 1985; 30(2):171-175.
18. Nuti S, Fernández-Lodeiro J, Del Secco B, Rampazzo E, Rodríguez-González B, Capelo JL, et al. Engineered Nanostructured Materials for ofloxac in delivery. Front Chem. 2018; 6:554.
19. Oksuz G, Urfalioglu A, Sekmen T, Akkececi N, Alpay N, Bilal B. Dentists Knowledge of Lipid Treatment of Local Anaesthetic Systemic Toxicity. Niger J Clin Pract 2018; 21-3: 327-331.
20. Olsen I, Nichols FC. Are Sphingolipids and Serine Dipeptide Lipids Underestimated Virulence Factors of Porhynomonas Gingivalis. Infect Immun. 2018; 86:1-10.
21. Quehenberger O, Armando AM, Brown AH et al., Lipidomics reveals a remarkable diversity of lipids in human plasma., J Lipid Res 2010; 51(11):3299– 3305.
22. Reich M, Kümmerer K, Al-Ahmad A, Hannig C. Fatty acid profile of the initial oral biofilm (pellicle): an in-situ study. Lipids 2013; 48: 929 – 937.
23. Satterlee AB, and Huang L. Current and Future theranostic Applications of the Lipid-Calcium-Phosphate Nanoparticle Platform. Theranostics. 2016; 6, 918–929. doi: 10.7150/thno.14689
24. Schweigel H, Wicht M, Schwendicke F. Salivary and pellicle proteome: A datamining analysis. Sci Rep. 2016 14;6: 38882. doi: 10.1038/srep38882.
25. Shama A, Sindhuja M, Subramaniam P. Association of Salivary Lipids and Early Childhood caries in an Indian Subpopulation. J Clin Pediatr Dent. 2019; 43: 393-397.
26. Slomiany BL, Murty VLN, Aono M, Slomiany A, Mandel ID. Lipid Composition of Human Parotid and Submandibular Saliva from Caries-Resistant and Caries-Susceptible Adults. Arch Oral Biol 1982; 27: 803-8
27. Slomiany BL, Murty VLN, Mandel ID, Sengupta S, Slomiany A. Effect of Lipids on the Lactic Acid Retardation Capacity of Tooth Enamel and Cementum Pellicles Formed in Vitro from Saliva of Caries-Resistant and Caries Susceptible Human Adults. Arch Oral Biol 1990; 35: 175-80
28. Slomiany BL, Murty VL, Slomiany A. Salivary lipids in health and disease. Prog Lipid Res 1985; 24: 311-24.
29. Slomiany BL, Witas H, Murty VL, Slomiany A,Mandel ID. Association of lipids with proteins and glycoproteins in human saliva. J Dent Res 1983;62:24-27.
30. Thomas B, Rajendra B, Prasad, Shetty S, Vishakh R. Comparative Evaulation of the
31. Lipid Profile in the Serum of Patients with Type 2 Diabetes Mellitus and Healthy Individuals
32. with Periodontitis. Contemp Clin Dent. 2017; 8:96-101.
33. Tsuda K, Amano A, Umebayashi K, Inaba H, Nakagawa I, Nakanishi Y, Yashimori T. Molecular Dissection of Internalization of Porhynomonas Gingivalis Cells Using Fluorescent Beads Coated with Bacterial Membrane Vesicle. Cell Struct Funct. 2005; 30:81-91.
34. Tsuda K, Furuta N, Inaba H, Kawai S, Hanada K, Yashimori T, Amano A. Functional Analysis of Alpha5betal Integrin and Lipid Rafts in Invasion of Epithelial Cells by Porhynomonas Gingivalis Using Fluorescent Beads Coated with Bacterial Membrane Vesicles. Cell Struct Funct. 2008; 33:123-132.
35. Williams DE, and Grant KB. Metal-Assisted Hydrolysis Reactions Involving Lipids: a Review. Front Chem. 2019; 7:14.
36. Zaura E, Twetman S. Critical Appraisal of Oral Pre – and Probiotics for Caries Prevention and Care. Caries Res 2019;53(5):514-526. doi: 10.1159/000499037
37. Zhi D, Bai Y, Yang J, Cui S, Zhao Y, Chen H, et al. A Review Oncationic Lipids with Different Linkers for Gene Delivery. Adv Colloid Interface Sci 2018; 253, 117–140.
38. Zhu N, Chatzistavrou X, Ge L, Qin M, Papagerakis P, and Wang Y. Biological Properties of Modified Bioactive Glass on Dental Pulp Cells. J Dent. 2019; 83: 18–26.