Information Horizons: AMERICAN Journal of Library and Information Science Innovation
Volume 01, Issue 08, 2023 ISSN (E): XXX-XXX

BIOCHEMICAL ANALYSIS OF ANTIMICROBIAL PEPTIDES IN THE ORAL CAVITY

M.M. Madumarova
Senior Lecturer, Andijan State Medical Institute
G.A. Muminova
PhD, Associate Professor, Andijan State Medical Institute
N.I. Alimov
4th year student of the Faculty of Medicine, Andijan State Medical Institute

Abstract
The paper describes in detail the biochemical analysis of antimicrobial peptides in the oral cavity, which provide the first line of defense of oral tissues from the introduction of pathogenic factors. Several groups of antimicrobial peptides have been found in the oral cavity, which have different origins and are active against bacteria, fungi and viruses, as well as having the properties of immunomodulators and chemoattractants. Antimicrobial peptides play a critical role in maintaining oral health.
Keywords: AMP, mucous membrane, biochemical functions, histatins, salivary glands, adrenomedullin, Hst-5.

Introduction
RELEVANCE OF THE TOPIC
The microflora of the human oral cavity is extremely diverse and is normally represented by several hundred species of microorganisms. In periodontal diseases, as a rule, the quantitative ratio of microbes changes, and their species composition remains constant. This circumstance suggests that the cause of diseases of the tissues of the oral cavity is not the actual bacterial infection, but a violation of the adequate interaction of the macroorganism with the microflora. In this regard, researchers are particularly interested in the study of the protective systems of the oral cavity. Antimicrobial peptides provide the first line of defense for oral tissues against the introduction of pathogens. Several groups of antimicrobial peptides have been found in the oral cavity, which have different origins and are active against bacteria, fungi and viruses, as well as having the properties of immunomodulators and chemoattractants. Antimicrobial peptides play a critical role in maintaining oral health. It has been shown that the violation of their synthesis correlates with the development of periodontitis and multiple dental caries.

THE PURPOSE AND OBJECTIVES OF THE STUDY

The aim of the study was to study the biochemical constants of AMP and their application for the diagnosis and treatment of oral diseases.

The objectives of the study were:

1. Conduct a biochemical analysis of AMP (antimicrobial peptides)
2. Determine their role in diseases of the oral cavity.
3. Creation of diagnostic and therapeutic algorithms for the oral cavity of antimicrobial peptides.

MATERIALS AND METHODS OF INVESTIGATION

Volunteer work was carried out at the Abu Ali ibn Sina College of Public Health and at boarding school No. 13. The work was aimed at determining the functioning of the biochemical properties and characteristics of AMP. In the above-mentioned institutions, 72 students were selected in the age range from 15 to 20 years, among them 35 boys and 37 girls. Within 2 months, large-scale work was carried out to determine the biochemical properties of AMP and identify their special features.

In the course of the study, the medical histories of each student were collected. Every week, routine examinations, interviewing and collecting anamnesis of the subjects were carried out, their regimen and type of diet, living conditions were taken into account. When collecting information, we were helped by questionnaires for students, with the help of which they were able to express the answer in full, which in turn helped us to correctly navigate their results. A bacterial study of smears from the oral mucosa was carried out 3 times a week, where the possibility and level of functioning of the biochemical properties of AMP were determined.

RESULTS

The following types of AMP were found in the oral cavity: histatins, human adrenomedullin, the sources of which are the oral mucosa, salivary glands and neutrophils. In the oral cavity, AMPs not only destroy pathogenic microorganisms, but also participate in maintaining normal microflora. The greatest amount of AMP is produced in the oral mucosa, since the epithelium actively responds to signals from the environment, to infection, integrating innate and acquired immune responses. The β-defensins, adrenomedullin, as well as the antimicrobial protein calprotectin secreted by the mucous membrane complement the protective function of the antimicrobial factors of the salivary glands, lysozyme and immunoglobulins.

Histatins (Hsts) are cationic peptides of saliva, one of the functions of which is to protect against pathogenic fungi. Histatins get their name from the presence of histidine residues and can be called "histidine-rich peptides". Histatins are secreted by the parotid and submandibular glands. The

histatin family includes 12 peptides ranging in length from 7 to 38 amino acids, of which Hst-1 and Hst-3 are separate full-length peptides encoded in various adjacent genes. The rest of the family are smaller in size and are obtained by partial proteolysis from Hst-1 and Hst-3. Under the action of saliva proteinases, Hst-2 is formed from Hst-3 and Hst-1, and the rest of the Hst-4-12 histatins are formed from Hst-3. Hst-5 was found in the highest concentration in saliva. Histatins are active against pathogenic yeast and filamentous fungi, including those resistant to azoles and polyene antimycotics. The antibacterial properties of histatins are much weaker than antifungal ones. The most thoroughly studied Hst-5 has high activity against the yeast fungus C. albicans, which is a representative of the normal microflora of the oral cavity, but can cause damage to the oral mucosa in immunodeficient patients. Hst-5 prevents the transition of C. albicans blastospores to the pseudohyphae stage, which protects tissues from fungal penetration. The level of histatins in patients with recurrent oral candidiasis is increased compared to healthy volunteers, which seems to prevent the development of invasive forms of fungal infection. A decrease in the level of histatin synthesis with age correlates with an increase in the frequency of fungal infections of the oral cavity. One of the reasons for the development of fungal infections of the oral cavity in patients with xerostomia may be precisely the insufficiency of histatins. The special role of histatins in the prevention of oral candidiasis has recently been demonstrated in the works of S. Khan et al., who showed that in HIV-infected patients with a reduced level of Hst-5 in saliva, there is a massive reproduction of C. albicans on the oral mucosa. Based on the foregoing, it can be assumed that histatins support the growth of C. albicans and other fungal microflora of the oral cavity at a certain physiological level. Despite detailed studies, the mechanism of antimicrobial action of histatins is still not fully understood. What is clear is that Hst-5 has several intracellular targets and mechanisms of action. When processing the culture of C. albicans Hst-5, the death of the microorganism occurs as a result of osmotic imbalance due to the loss of potassium ions. In an aqueous solution, histatin-5 forms a messy tangle, but forms a α helix in the lipid bilayer of the membranes. Previously, it was believed that the action of Hst-5 is realized through the formation of pores and impaired permeability of the biological membrane, but subsequent studies have shown that this mechanism does not explain the antifungal activity of this histatin under physiological conditions. However, it can be assumed that at high concentrations in the experiment or when using histatins as drugs, their action will lead to a violation of the barrier function of biological membranes of microorganisms. It has been shown that Hst-5 can enter the C. albicans cell in three different ways: simple or facilitated diffusion using a membrane transporter, as well as endocytosis. One or another mode of transport seems to depend on the concentration of Hst-5. It is possible that the formation of a α helix in the double layer of membrane lipids contributes to the penetration of histatin into the cell. Numerous studies have shown that the action of Hst-5 on C. albicans cells leads to the release of adenosine triphosphate (ATP) macroergue from them. It is

assumed that the death of fungal cells occurs not only due to the loss of ATP, but also due to a special mechanism of cell signaling. The released ATP molecules probably interact with certain receptors on the outer cell membrane, which triggers a cascade of reactions leading to cell death. The main target for Hst-5 in the fungal cell is mitochondria. In the mitochondria of C. albicans cells treated with Hst-5, there is a change in the composition of the enzymes of the respiratory chain and the tricarboxylic acid cycle. One of the mechanisms of action of Hst-5 is thought to be related to oxidative stress, which is caused by impaired mitochondrial function. Due to oxidative stress, the functions of other cellular components are impaired. A disruption of the cell cycle of C. albicans under the influence of Hst-5 has also been shown, which correlates with loss of cell volume. Recently, there has been evidence that a possible mechanism of action of histatins is to compete with pathogens for ions of iron, copper, zinc and other metals. This hypothesis is consistent with previous studies that have shown that Hst-5 complexes with metals can increase oxidative stress. In addition, the binding of iron and copper ions inside the cell can disrupt the work of mitochondria, since the ions of these metals are part of the protein complexes of the respiratory chain. In any case, a change in the number of metal ions can adversely affect the vital activity of C. albicans cells. Histatins are involved in the formation of a protective pellicle on the surface of the teeth, which prevents the development of plaque and prevents demineralization of the enamel. Recent experiments by M. Oudhoff, Hystatins 1 and 2 have been shown to stimulate epithelial cell migration, which appears to promote oral wound healing. Based on the study of the effect of amino acid residue substitution on the properties of Hst-5, two antimicrobial peptides with very high antimicrobial activity were synthesized, but their clinical application was impossible due to hemolytic activity in vivo. Adrenomedullin refers to broad-spectrum regulatory peptides. For the first time, adrenomedullin was isolated by K. Kitamura et al. from the cells of pheochromocytoma, and got its name, as it was found among the peptides of the adrenal medulla. It is now known that adrenomedullin is synthesized by cells of the liver, kidneys, epithelium of the skin, intestines, and oral cavity. Violations of its synthesis were found in diseases of the cardiovascular system, liver, kidneys, preeclampsia of the second half of pregnancy (preeclampsia).

Adrenomedullin consists of 52 amino acid residues. The synthesis of adrenomedullin occurs by partial proteolysis from the larger precursor of preadrenomedullin. At the C-terminus of the peptide backbone there is a residue of amidened tyrosine. Adrenomedullin has homology areas with calcitonin, so it belongs to the calcitonin family. In the cells of the oral cavity, adrenomedullin is expressed constantly, and under the influence of bacterial lipopolysaccharides, IL-1 and TGF-α, its synthesis increases. In the oral cavity, adrenomedullin inhibits the development of gram-positive and gram-negative bacteria, but does not have antifungal and antiviral activity. Its high activity against the causative agent of periodontitis P. gingivalis is shown. In addition to the

antimicrobial effect, adrenomedullin significantly affects hemodynamics, causing the expansion of peripheral blood vessels. In addition, adrenomedullin is involved in endocrine regulation: it inhibits the release of ACTH from the pituitary gland, affects the secretory activity of the adrenal cortex, as well as insulin secretion. The mechanism of antimicrobial action of adrenomedullin is not exactly known, but there is an assumption that it, like most AMPs, violates the barrier function of biological membranes

INFERENCE

Due to the fact that oral AMPs are diverse and act on microorganisms very quickly, the likelihood of developing resistance to them is quite small. This gives hope that AMPs can be used to produce antimicrobials, resistance to which develops very slowly. Therefore, it is proposed to use AMPs with antiviral and antifungal activity in immunocompromised individuals, including AIDS patients, for the prevention and treatment of candidiasis and herpetic gingivostomatitis.

REFERENCES:

1. Inomata M, Into T, Murakami Y. Suppressive effect of the antimicrobial peptide ll-37 on expression of il-6, il-8 and cxcl10 induced by porphyromonas gingivalis cells and extracts in human gingival fibroblasts. European Journal of Oral Sciences. 2010;118(6):574-581. doi:10.1111/j.1600-0722.2010.00775.x.
2. Wu WKK, Wang G, Coffelt SB, Betancourt AM, Lee CW, Fan D, Wu K, Yu J, Sung JJY, Cho CH. Emerging roles of the host defense peptide ll-37 in human cancer and its potential therapeutic applications. International Journal of Cancer. 2010;127(8):1741-1747. doi:10.1002/ijc.25489.
3. Bucki R, Namiot DB, Namiot Z, Savage PB, Janmey PA. Salivary mucins inhibit antibacterial activity of the cathelicidin-derived ll-37 peptide but not the cationic steroid csa-13. J Antimicrob Chemother. 2008;62(2):329-325. doi:10.1093/jac/dkn176.
4. Campese M, Sun X, Bosch JA, Oppenheim FG, Helmerhorst EJ. Concentration and fate of histatins and acidic proline-rich proteins in the oral environment. Arch. Oral Biol. 2009;54(4):345-353. doi:10.1016/j.archoralbio.2008.11.010.
5. Kavanagh K, Dowd S. Histatins: antimicrobial peptides with therapeutic potential. Journal of Pharmacy and Pharmacology. 2004;56(3):285-289. doi:10.1211/0022357022971.
6. Khan SA, Fidel PLJr, Thunayyan AA, Varlotta S, Meiller TF, Jabra- Rizk MA. Impaired Histatin-5 Levels and Salivary Antimicrobial Activity against in HIV Infected Individuals. Journal of AIDS & Clinical Research. 2013;4(2):123-128. doi:10.4172/2155-6113.1000193.

7. Puri S, Edgerton M. How does it kill?: understanding the candidacidal mechanism of salivary histatin 5. Eukaryotic Cell. 2014;13(8):958-964. doi:10.1128/ec.00095-14.
8. Oudhoff MJ, Blaauboer ME, Nazmi K, Scheres N, Bolscher JG, Veerman EC. The role of salivary histatin and the human cathelicidin LL-37 in wound healing and innate immunity. Biological Chemistry. 2010;391(5):541-548. doi:10.1515/bc.2010.057.
9. Kitamura K, Kangawa K, Kawamoto M, Ichiki Y, Nakamura S, Matsuo H, Eto T. Adrenomedullin: a novel hypotensive peptide isolated from human pheochromocytoma. Biochemical and Biophysical Research Communications. 1993;192(2):553-560. doi:10.1016/j.bbrc.2012.08.022.
10. Hart TC, Hart PS, Michalec MD, Zhang Y, Firatli E, Van TE, Stabholz A, Zlotogorski A, Shapira L, Soskolne WA. Haim-munk syndrome and papillon-lefevre syndrome are allelicmutations in cathepsin c. Journal of Medical Genetics. 2000;37(2):88-94. doi:10.1136/jmg.37.2.88.

1. Salomov, S. N. O. G. L., Aliyev, H. M., & Dalimova, M. M. (2022). RECONSTRUCTIVE RHINOPLASTY METHOD WITH EXTERNAL NOSE DEFORMATION AFTER UNILATERAL PRIMARY CHEILOPLASTY. *Central Asian Research Journal for Interdisciplinary Studies (CARJIS)*, *2*(10), 87-90.
2. Shoxabbos, S., & Mahramovich, K. S. M. K. S. (2023). CAUSES OF THE ORIGIN OF CARDIOVASCULAR DISEASES AND THEIR PROTECTION. *IQRO JURNALI*, 1-6.
3. Maxmudovich, A. X., Raximberdiyevich, R. R., & Nozimjon o'g'li, S. S. (2021). Oshqozon Ichak Traktidagi Immunitet Tizimi. *TA'LIM VA RIVOJLANISH TAHLILI ONLAYN ILMIY JURNALI*, *1*(5), 83-92.
4. Maxmudovich, A. X., Raximberdiyevich, R. R., & Nozimjon o'g'li, S. S. (2021). Oshqozon Ichak Traktidagi Immunitet Tizimi. *TA'LIM VA RIVOJLANISH TAHLILI ONLAYN ILMIY JURNALI*, *1*(5), 83-92.
5. Shoxabbos, S., & Mahramovich, K. S. M. K. S. (2023). CAUSES OF THE ORIGIN OF CARDIOVASCULAR DISEASES AND THEIR PROTECTION. *IQRO JURNALI*, 1-6.
6. Salomov, S. N. O. G. L., Aliyev, H. M., & Dalimova, M. M. (2022). RECONSTRUCTIVE RHINOPLASTY METHOD WITH EXTERNAL NOSE DEFORMATION AFTER UNILATERAL PRIMARY CHEILOPLASTY. *Central Asian Research Journal for Interdisciplinary Studies (CARJIS)*, *2*(10), 87-90.
7. Nozimjon o'g'li, S. S., & Makhmudovich, A. H. (2023). NUTRITION RECOMMENDATIONS FOR CARDIAC PATHOLOGIES. *IQRO*, *1*(1), 3-6.
8. Nozimjon o'g'li, S. S. (2022). First Aid Medication and Remedies for Heart Failure. *Academia Open*, *7*, 10-21070.

9. Nozimjon o'g'li, S. S. (2022). Emergency medical care in case of drowning and measures to restore the patient's health. *Academia open*, *7*, 10-21070.
10. Nozimjon o'g'li, S. S. (2022). INFORMATION ABOUT THE STRUCTURE OF THE MEMBRANE OF EPITHELIAL TISSUE AND GLANDS. *British Journal of Global Ecology and Sustainable Development*, *10*, 65-69.
11. Nozimjon O'g'li, S. S. (2022). CAUSES OF THE ORIGIN OF OSTEOCHONDROSIS, SYMPTOMS, DIAGNOSIS AND TREATMENT METHODS. *Conferencea*, 76-77.
12. Nozimjon O'g'li, S. S., & Maksimovna, M. M. (2022). THE ORIGIN OF MIASTHENIA DISEASE AND METHODS USED IN TREATMENT. *Conferencea*, 31-33.
13. Mozimjon o'g'li, S. S., & Makhmudovich, A. H. (2023). Causes of the Origin of Cardiovascular Diseases and their Protection. *AMALIY VA TIBBIYOT FANLARI ILMIY JURNALI*, *2*(2), 185-187.
14. Mavlonovna, R. D., & Akbarovna, M. V. (2021, July). PROVISION OF FAMILY STABILITY AS A PRIORITY OF STATE POLICY. In *Archive of Conferences* (pp. 34-39).
15. Mavlonovna, R. D. (2021, May). PARTICIPATION OF WOMEN IN EDUCATION AND SCIENCE. In *E-Conference Globe* (pp. 158-163).
16. Mavlonovna, R. D. Participation of Uzbek Women in Socio-economical and Spiritual Life of the Country (on the Examples of Bukhara and Navoi Regions). *International Journal on Integrated Education*, *4*(6), 16-21.