TMKARPIŃSKI
PUBLISHER

ISSN 2300-7257

Volume 1
Number 1
April-June 2013

Archives of Biomedical Sciences

http://www.journals.tmkarpinski.com/index.php/abms
e-mail: abms@interia.eu

Archives of Biomedical Sciences

Cover: http://openwalls.com/image?id=20115,
Licence Creative Commons Attribution 3.0 Unported (CC BY 3.0)

Publisher and Editor's office:
Tomasz M. Karpiński, ul. Szkółkarska 88B, 62-002 Suchy Las, Poland, e-mail: ambs@interia.eu

Archives of Biomedical Sciences is abstracting and/or indexing in:
- Google Scholar
- Open Archives
- Public Knowledge Project
- WorldCat

Aims and Scope

The aim of the Archives of Biomedical Sciences (ABMS) is to provide the platform for exchange of scientific progress in the field of Medicine and Medical Biology, and to do so at the highest possible level. The ABMS also aims to facilitate the application of new scientific knowledge to the daily practice of the concerned disciplines and addresses both researchers and academics. The ABMS publishes original contributions, case reports and review articles in the fields of biology, medicine and earth sciences.
Its scope encompasses:
1. in field of biology: botany, ecology, zoology, microbiology, molecular biology, cellular biology, genetics, taxonomy and allied,
2. in field of medicine: all medical aspects of human biology,
3. in field of earth sciences: geology, mineralogy, petrography, paleontology, geography, geophysics, soil sciences and allied.

Editorial Policy

The Archives of Biomedical Sciences (ABMS) is a peer-reviewed, open-access, article-based, international, scientific Journal, that publishes full-length articles on biological, medical and earth sciences. Journal accepts original research articles, case reports and review articles.
All manuscripts received by the Editor are considered as confidential documents. A notification of receiving the manuscript is sent by e-mail to the corresponding author.
All manuscripts are subjected to pre-screening by the Editor in Chief and can be rejected at this stage or returned for corrections before evaluation (if they do not meet the criteria given in the Instruction to Authors, including language quality or are out of the scope of ABMS). After passing the pre-screening stage the manuscripts are sent to at least two qualified outside referee, but the editors themselves may also act as reviewers. Reviewers are from behind of scientific unit in which is affiliated author of the publication. Papers that do not conform to the general aims and scope of the journal will, however, be returned immediately without review. Archives of Biomedical Sciences uses double blinded review process. The names of the reviewers will not be disclosed to the author submitting a paper, and the names of authors will not be disclosed to the reviewers.
The review process lasts approximately 4-8 weeks.
ITEMS EVALUATED
Referees, in confidence, evaluate the manuscript according to the following aspects: Present-day interest, Originality, Adequacy of methodology, Theoretical background, Essential level, Results and interpretation, Importance in its field, Conclusions, Language correctness.
All the above items can be evaluated as Excellent, Good, Fair or Poor. The manuscript can be evaluated as:
- acceptable in its present form
- acceptable after minor revision (no further review required)
- reconsidered after major revision
- not acceptable for publication.

When the review process is finished, a decision e-mail will be sent to the corresponding author, including the comments of the referee(s). Any corrections suggested by the reviewers, should be made within the period of time indicated in the e-mail. If the paper is accepted after major revisions, it will be submitted again for peer review to the same evaluator(s). After a second review of the corrected manuscript, a final decision e-mail concerning publication is sent to the authors. A proof is provided to the corresponding author before the article is published. The checked proof should be returned to the Editorial Office by e-mail within 7 working days.

The Journal is issued at least twice a year in electronic version. Each article is published online in PDF format at www.journals.tmkarpinski.com/index.php/abms as soon as it is ready for publication. Public access to articles in the Archives of Biomedical Sciences is free of charge.

Instructions for authors

1. GENERAL

The Archives of Biomedical Sciences (ABMS) is a peer-reviewed, Open-Access, article-based, international, scientific Journal, that publishes full-length articles on biological, medical and earth sciences. Journal accepts original research articles, case reports and review articles. The ABMS is issued at least twice a year in electronic version. Public access to all articles is free of charge.

2. ETHICAL GUIDELINES

2.1. Authorship and Acknowledgements

Authors submitting a paper do so on the understanding that the manuscript have been read and approved by all authors and that all authors agree to the submission of the manuscript to the Journal.

2.2. Ethical Approvals

All experimental studies using human or animal subjects should include an explicit statement in the Material and Methods section identifying the review and ethics committee approval for each study.

2.3. “Ghostwriting” and “guest authorship” prevention

The editors of ABMS quarterly lead the policy of “ghostwriting” and “guest authorship” prevention.

“Ghostwriting” is the case of contributing a publication without revealing one’s participation as one of the authors or without reference to their role in the acknowledgments in the publication. “Guest authorship” (honorary authorship) is the case of insignificant contribution of the author or its complete absence and nevertheless being the author or co-author of the publication. The editors reserve the right to reveal all aspects of scientific dishonesty, i.e. failure to comply with actions eliminating the occurrence of the aforementioned practices.

The editors require that Authors should reveal individual co-authors’ contribution to the publication. Potential contributions include:

Conception and design
Development of methodology
Acquisition of data
Analysis and interpretation of data
Writing, review and/or revision of the manuscript
Administrative, technical, or material support
Study supervision
Other

However, the author submitting the manuscript will chiefly be held responsible. (The ghostwriting and guest authorship prevention procedure in ABMS was written according to the guidelines of the Ministry of Science and Higher Education).

2.4. Plagiarism

Plagiarism is when an author attempts to pass off someone else's work as his or her own. Duplicate publication, sometimes called self-plagiarism, occurs when an author reuses substantial parts of his or her own published work without providing the appropriate references. By submitting your manuscript to us you accept that your manuscript may be screened for plagiarism against previously published works.

Manuscripts that are found to have been plagiarized will incur plagiarism sanctions:

- immediate rejection of the submitted manuscript or published article
- no return of article-processing charge (if any)
- prohibition against all of the authors for any new submissions.

2.5. Conflict of Interest and Sources of Funding

Authors are requested to provide a statement concerning any commercial associations or patent licenses that might result in a conflict of interest with the work presented in the submitted paper.

2.6. Permissions

Materials copied from other sources must be accompanied by a written statement from both the author and publisher giving permission to Archives of Biomedical Sciences for reproduction. It is the author’s responsibility to ensure that such permissions are obtained.

2.7. Copyright Assignment

Authors submitting a paper do so on the understanding that the work and its essential substance have not been published before and is not being considered for publication elsewhere. The articles published in this journal are open-access articles distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

3. MANUSCRIPT SUBMISSION PROCEDURE

3.1. Cover Letter

Each manuscript should be accompanied by a Cover Letter. The cover letter should contain all important details such as: your full name (submitted by), full title of article and short title, full list of authors with affiliations, e-mail of the corresponding author, contact address, telephone/fax numbers of the corresponding author. In the cover letter Authors should propose 3-5 reviewers giving names, affiliations and e-mails.

All authors of the manuscript are responsible for its content; they must have agreed to its publication and have given the corresponding author the authority to act on their behalf in all matters pertaining to publication. The corresponding author is responsible for informing the coauthors of the manuscript status throughout the submission, review, and production process.

3.2. Manuscript Files Accepted

The final version of the manuscript, figures and tables should be submitted by site
http://www.journals.tmkarpinski.com/index.php/abms

Main text and tables must be in Microsoft Word (.doc) format (not write-protected).

Photographs must be in JPG or TIFF format, preferred resolution >300 dpi.

Drawings and graphs must be in JPG or EPS format, preferred resolution >300 dpi.

The manuscript must be accompanied by: a written Licence Form, and in case of experimental studies a statement that the protocol of study and informed consent were in compliance with the Helsinki Convention and were approved by local Ethics Committee. Upon acceptance of the manuscript, the author(s) will be asked to send Licence Form to the publisher.

3.3. Double-Blinded Review

All submitted manuscripts will be reviewed by two experts in the field, who are from behind of scientific unit in which is affiliated author of the publication. Papers that do not conform to the general aims and scope of the journal will, however, be returned immediately without review. ABMS uses double blinded review process. The names of the reviewers will not be disclosed to the author submitting a paper, and the names of authors will not be disclosed to the reviewers.

3.4. E-mail Confirmation of Submission

In course of 5 working days after submission you will receive an e-mail to confirm receipt of your manuscript. If you do not receive the confirmation e-mail, please check your e-mail address carefully in the system. The error may be caused by some sort of spam filtering on your e-mail server.

3.5. Manuscript Status

The Journal will inform you by e-mail once a decision has been made.

3.6. Submission of Revised Manuscripts

To submit a revised manuscript, send it by e-mail:
abms@interia.eu

4. MANUSCRIPT TYPES ACCEPTED

Archives of Biomedical Sciences publishes original research articles, case reports and reviews.

Original Research Articles must describe significant and original experimental observations and provide sufficient detail so that the observations can be critically evaluated and, if necessary, repeated.

Instructions for authors cont.

Case Reports must describe an individual phenomenon, uncommon case or a new or improved method.
Reviews are selected for their broad general interest; should take a broad view of the field.

5. MANUSCRIPT FORMAT AND STRUCTURE

5.1. Language
The language of publications is English. Authors whose native language is not English are strongly advised to have their manuscripts checked by a professional translator or a native speaker prior to submission.

5.2. Structure
All articles should include Title Page, Abstract, and References and in addition sections on Source of Funding and Conflict of Interests. Figures, Figure Legends and Tables should be included where appropriate.
Title Page: The title must contain no more than 100 characters including spaces. The title page should include a running title of no more than 40 characters; 5-10 key words, complete names of institutions for each author, and the name, address, telephone number, fax number and e-mail address for the corresponding author.
Conflict of Interest and Source of Funding: Authors are requested to provide a statement concerning any commercial associations or patent licenses that might result in a conflict of interest with the work presented in the submitted paper. Author's conflict of interest (or the absence of conflicts of interest) and the sources of funding for the research will be published under a heading "Conflict of Interest and Source of Funding Statement".
Abstract: is limited to 250 words in length and should not contain abbreviations or references.
Acknowledgements: Under acknowledgements please specify contributors to the article other than the authors accredited.

5.3. Original Research Articles
Main Text should be organized with Introduction, Materials and Methods, Results, Discussion (or Results and Discussion). The background and hypotheses underlying the study, as well as its main conclusions, should be clearly explained.

5.4. Case Report Articles
These should be divided into the following sections: Title page, Abstract, Introduction, Case presentation, Discussion, Conclusions.

5.5. Review Articles
Reviews should take a broad view of the field rather than merely summarizing the authors´ own previous work. The use of state-of-the-art evidence-based systematic approaches is expected. Main text should be organized with Introduction, Review, Conclusions.

5.6. References
Citations in the text should be marked by Arab numbers in square brackets.
a) The arrangement of the references should be in consecutive order (as they are cited in the text).
b) The first six authors should be presented; if are more than six, please use a phrase: et al.
c) The order of the items in each reference should be as in examples:
Nowak MA, Kowalski A. Natural antibiotics. J Biol Earth Sci. 1992; 4(1): E1-E6.
Nowak Z. 2003. Moss flora of Poznań. 4th edition: pp. 1014. Warszawa, Scientific Publishing.
Kowalski T. 1980. Skin infections. In: Microbiology. Ed. Nowak D. pp. 269-278. Warszawa, PublishMe.

5.7. Tables and Figures
Tables: should be with no vertical rulings, with a single bold ruling beneath the column titles. Units of measurements must be included in the column title. Max. format A4.
Figures: All figures should be planned to fit within either 1 column width (8.2 cm) or 2 column widths (17.0 cm). Lettering on figures should be in a clear typeface; the same typeface should be used for all figures.
Units should have a single space between the number and the unit, and follow SI nomenclature or the nomenclature common to a particular field (defined in the legend). Do not use pixel-oriented programmes.
Permissions: If all or parts of previously published illustrations are used, permission must be obtained from the copyright holder concerned. It is the author's responsibility to obtain these in writing and provide copies to the Publishers.

6. AFTER ACCEPTANCE
Upon acceptance of a paper for publication, the manuscript will be forwarded to the production of the journal.

6.1. Proof Corrections
The corresponding author will receive an email with the proof PDF file. Corrected proof must be scanned and returned to the Editor within 7 working days. Excessive changes made by the author in the proof, excluding typesetting errors, will be charged separately. Please note that the corresponding author is responsible for all statements made in his work, including changes made by the copy editor. Manuscripts submitted under multiple authorship are published on the assumption that the final version of the manuscript has been seen and approved by all authors.

6.2. Article-processing charge
Publication in ABMS is free of charge.

6.3. Online publication
Online publication will normally be within 2 weeks of receipt of corrected proof by the TMKarpinski Publisher. Authors should note that online articles are complete and final and thus no changes can be made after online publication.

Contents

TMKARPIŃSKI
PUBLISHER

Archives
of Biomedical
Sciences
ISSN: 2300-7257

REVIEW

Human defensins

Tomasz M. Karpiński[1]*, Anna K. Szkaradkiewicz[2]

ABSTRACT

Defensins are small (3–5 kDa), cationic peptides produced by many types of cells. Defensins have a characteristic β-sheet-rich fold and 3 disulphide bonds. Human defensins form two genetically distinct subfamilies: alpha and beta. α-defensins are mainly packaged in azurophil granules of neutrophils (HNP-1 to HNP-4) or secreted by intestinal Paneth cells (HD5 and HD6). β-defensins (HBD-1 to HBD-6) are produced by various mucosa and epithelial cells. Defensins play an important role in innate immunity against bacteria, fungi, protozoa, and viruses.

Key Words: Defensins; Antimicrobial activity; Innate immunity; Bacteria; Viruses.

INTRODUCTION

Defensins are small antimicrobial peptides, which have the structure of β-sheet, usually containing six cysteine residues joined by three disulfide bonds. Currently, there are about 360 known defensins [http://defensins.bii.a-star.edu.sg], occurring in vertebrates, invertebrates and plants. Defensins are produced by various cells of many tissues. Mature defensins contain six cysteine residues (Cys1-6) forming three intramolecular disulphide bonds. Depending on the bonds arrangement they are classified into alpha, beta and theta subfamilies. Human defensin genes are located in a single cluster on chromosome 8p23 [1, 2]. In humans, occur α-defensins (HNP-1 to HNP-4, HD-5 and HD-6) and β-defensins (HBD-1 to HBD-4). There is also a θ-defensins pseudogene, whose mRNA precursor has premature "stop" codon in the signal sequence, which prevents its translation [3].

REVIEW

Defensins α

Alpha-defensins are the first discovered group of defensins, which in 1980 Lehrer, isolated from rabbits macrophages. Until now were described about 80 defensins α. The first human defensin was isolated from neutrophils in 1985 [4]. In humans have been characterized six α-defensins, four of which occur mainly in azurophilic granules of granulocytes (HNP-1, HNP-2, HNP-3 and HNP-4) and the other two in the Paneth cells of small intestine crypts and in the epithelial cells of female reproductive tract (HD-5 and HD-6). α-defensins (HNP-1 to 4) have been described also in the walls of coronary vessels [5], in immature monocyte-derived dendritic cells [6] and in specific subpopulations of lymphocytes and monocytes [7].

Defensins α have a length of 29-35 amino acids comprise a 3 disulfide bonds in the positions C1-C6, C2- C4 and C3-C5. Defensins have a conformation

Correspondence: tkarpin@interia.pl
[1]Poznań University of Medical Sciences, Department of Medical Microbiology, Wieniawskiego 3, 61-712 Poznań, Poland
[2]Poznań University of Medical Sciences, Department of Conservative Dentistry and Periodontology, Poznań, Poland

Received: May 08, 2013; **Accepted:** June 04, 2013; **Published:** June 06, 2013

http://www.journals.tmkarpinski.com/index.php/abms **E-mail:** abms@interia.eu

that contains a three-lane structure of β-sheet and the loop connecting these bands. Human defensins create dimeric forms [8, 9]. Enteric α-defensins play an important role in regulation of bacterial colonization of the gut. They also activate pro- and anti-inflammatory response of the adaptive immune system cells in lamina propria. The main inducers of α-defensins secretion by Paneth cells are the products of degradation of Gram-positive and Gram-negative bacteria, including: muramyl dipeptide, bacterial lipopolysaccharide, flagellin, lipid A, and unmethylayed CpG sequences in bacterial DNA [10]. Alpha-defensins secreted by neutrophils can be detected in biological fluids [11-14]. Neutrophils can enter the mouth by traversing gingival crevices, therefore crevicular fluid contains high concentrations of HNP1–3 [15].

Alpha defensins demonstrate antimicrobial, antiviral, and immunomodulatory properties. The antimicrobial activity of defensins begins after approximately 3-4 hours, and the mechanism of action is multistage. It depends on binding of the defensin with membrane of attacked cell and then its internalization, endocytosis and run of metabolic processes leading to apoptosis [16]. It has been shown that the strongest bactericidal activity against S*taphylococcus aureus* has a HNP-2 defensin, and against *Escherichia coli* and *Enterobacter aerogenes* has HNP-4. Defensin HD-5 exhibits a high activity against Gram-negative bacteria [17]. α-defensins also inactivate several potent bacterial exotoxins that include *Bacillus anthracis* lethal factor, *Corynebacterium diphteriae* diphtheria toxin and *Pseudomonas aeruginosa* exotoxin A [18-20]. Increased concentrations of HD5 have been observed in *Neisseria gonorrhoeae* and *Chlamydia trachomatis* urethral infections [21]. Defensins HNP1–3 inactivate a variety of viruses, including HIV-1 [22-24], influenza virus [25] and papilloma-viruses [26]. HNP1 have a potent direct inhibitory effect on herpes simplex viruses 1 and 2, and little effect on cytomegalovirus [27].

The concentration of defensins in neutrophils, in airway epithelial cells and airway secretion appreciably change in acute inflammatory processes and cystic fibrosis [28]. HNP1–3 have been reported to increase the production of proinflammatory cytokines (TNF and IL-1), while decreasing the production of IL-10 by monocytes [29]. Reduction of α-defensins in Paneth cells has a causal relationship with Leśniowski-Crohn's disease [30, 31]. α-defensins were found to be expressed in a variety of human tumours. HNP1–3 peptides are proposed as a tumour biomarker [32]. Elevated levels of HNP1–3 were detected in plasma and tumour tissue of patients with colorectal cancer [33, 34]. HNP1–3 were also detected in other tumour types, e.g. lung cancers [35], renal cell carcinomas [36], bladder carcinomas [37] and tongue squamous cell carcinomas [38].

Defensins β

The first β-defensin was isolated from cow tongue in 1991 and was called the TAP (tracheal antimicrobial peptide) [39]. β-defensins have been identified in cattle, sheep, goats, pigs, birds and humans. These peptides have a length of 36-42 amino acids and their disulfide bonds are arranged in the positions C1-C5, C2-C4, C3-C6. β-defensins demonstrate antibacterial properties against gram-negative and gram-positive bacteria and antifungal properties against *Candida* species. In the amino acid sequences of β-defensins are six cysteine residues whose position is conserved [40]. The core of β-defensins is composed of the three β-sheet forming antiparallel β-sheet. β-sheet is flanked by α-helical segment of variable length. α-helix orientation relative to β-sheet is stabilized by disulfide bridges [41]. To date, six human β-defensins (hBD1 to 6) have been identified and characterized [42].

The first human β-defensin was discovered in 1995 (HBD-1). Defensin HBD-1 (human beta-defensin) is produced by epithelial cells (among others trachea, bronchi, parotid gland, mouth, small intestine, pancreas, kidney, vagina, uterus, fallopian tubes) and also by neutrophils and leukocytes. Defensin HBD-1 acts against Gram-negative bacteria [43, 44]. It has been proven that the highest concentration of HBD1 found to be in urine of pregnant women, a smaller amount at women without pregnancy, and the lowest concentration at men [45]. Defensin HBD-2 is produced in the epithelial cells of the skin, lung, intestines and genitourinary tract, HBD-3 in the nasal epithelial cells, tonsils, bronchi, pancreas and in saliva and vaginal fluid, and HBD-4 in the testes, stomach, uterus, lungs and kidneys [46, 47].

Defensins such as HBD-2 and HBD-3 are produced in high concentrations in the sites of infection or skin injury and in inflammatory reactions, act antibacterial, chemotactic and

participate in the remedial action [48-50]. HBD-2 and HBD-3 exhibit their antiviral activity against HIV by interacting with the virion particle and through modulation of the CXCR4 co-receptor [51]. HBD3 has been found to disrupt bacterial cell wall biosynthesis by binding lipid-II-rich regions of the cell wall [52]. Defensin HBD-4 has antimicrobial activity against various bacteria and yeasts and stimulates monocytes [53]. Defensin HBD-1 is down-regulated, especially in urologic cancers, therefore is a candidate tumour suppressor [54, 55]. HBD2 but not HBD1 inhibits the entry of respiratory syncytial virus and disrupts its envelope [56]. On the contrary, HBD3, but not HBD1 and HBD2, exhibit anti-viral activity against vaccinia virus [57, 58].

HBD-1-3 play a key role during pregnancy in the protective mechanisms of the maternal and fetal tissues. HBD1-3 are expressed by placental and chorion trophoblasts, amnion epithelium, and decidua from term pregnancies [59]. The recent studies have shown that selective stimulation of amniochorionic membranes with Candida albicans results in tissue-specific secretion of HBD-1 and HBD-2 [60], but the stimulation of human fetal membranes with *Escherichia coli* or *Streptococcus agalactiae* results in a secretion of HBD-1, HBD-2, and HBD-3 [61, 62].

CONCLUSIONS

Defensins are small peptides very important in innate immunity. In humans defensins are found in many cells and tissues. They kill microorganisms or inhibit their growth, act bactericidal on Gram-negative and Gram-positive bacteria, neutralize toxins, and act antiviral. They are also important in inflammatory and neoplastic processes.

TRANSPARENCY DECLARATION

The authors declare no conflicts of interest.

REFERENCES

1. Liu L, Zhao C, Heng HHQ, Ganz T. The human β-defensin-1 and α-defensins are encoded by adjacent genes: two peptide families with differing disulfide topology share a common ancestry. Genomics. 1997; 43: 316-320.
2. Liu L, Wang L, Jia HP, Zhao C, Heng HHQ, Schutte BC, et al. Structure and mapping of the human β-defensin HBD-2 gene and its expression at sites of inflammation. Gene. 1998; 222: 237-244.
3. Nguyen TX, Cole AM, Lehrer RI. Evolution of primate theta-defensins: a serpentine path to a sweet tooth. Peptides. 2003; 24: 1647-1654.
4. Ganz T, Selsted M, Szklarek D, Harwig SS, Daher K, Bainton DF, Lehrer RI. Defensins. Natural peptide antibiotics of human neutrophils. J Clin Invest. 1985; 76: 1427-1435.
5. Barnathan ES, Raghunath PN, Tomaszewski JE, Ganz T, Cines DB. Immunohistochemical localization of defensin in human coronary vessels. Am J Pathol. 1997; 150: 1009-1020.
6. Rodríguez-García M, Oliva H, Climent N, García F, Gatell JM, Gallart T. Human immature monocyte-derived dendritic cells produce and secrete alpha-defensins 1–3. J Leukoc Biol. 2007; 82: 1143-1146.
7. Agerberth B, Charo J,Werr J, Olsson B, Idali F, Lindbom L, et al. The human antimicrobial and chemotactic peptides LL-37 and alpha-defensins are expressed by specific lymphocyte and monocyte populations. Blood. 2000; 96: 3086-3093.
8. Hill CP, Yee J, Selsted ME, Eisenberg D. Crystal structure of defensin HNP-3, an amphiphilic dimer: mechanisms of membrane permeabilization. Science. 1991; 251: 1481-1485.
9. Pardi A, Zhang XL, Selsted ME, Skalicky JJ, Yip PF. NMR studies of defensin antimicrobial peptides. 2. Three-dimensional structures of rabbit NP-2 and human HNP-1. Biochem. 1992; 31: 11357-11364.
10. Lisitsyn NA, Bukurova YA, Nikitina IG, Krasnov GS, Sykulev Y, Beresten SF. Enteric alpha defensins in norm and pathology. Ann Clin Microbiol Antimicrob. 2012; 11: 1.
11. Panyutich AV, Voitenok NN, Lehrer RI, Ganz T. An enzyme immunoassay for human defensins. J Immunol Methods. 1991; 141: 149-155.
12. Panyutich AV, Panyutich EA, Krapivin VA, Baturevich EA, Ganz T. Plasma defensin concentrations are elevated in patients with septicemia or bacterial meningitis. J Lab Clin Med. 1993; 122: 202-207.
13. Panyutich AV, Szold O, Poon PH, Tseng Y, Ganz T. Identification of defensin binding to C1 complement. FEBS Lett. 1994; 356: 169-173.
14. Hofman J, Szkaradkiewicz AK, Karpiński TM. Estimate the prevalence of defensins (HNP 1-3) in

the saliva and serum of adults with chronic periodontitis [in Polish]. Czas Stomatol. 2008; 61(12): 881-885.
15. Lundy FT, Orr DF, Shaw C, Lamey PJ, Linden GJ. Detection of individual human neutrophil alpha-defensins (human neutrophil peptides 1, 2 and 3) in unfractionated gingival crevicular fluid – a MALDI-MS approach. Mol Immunol. 2005; 42: 575-579.
16. Niedźwiedzka-Rystwej P, Deptuła W. Defensins: An important innate element of the immune system in mammals [in Polish]. Postepy Hig Med Dosw. 2008; 62: 524-529.
17. Ericksen B, Wu Z, Lu W, Lehrer RI. Antibacterial activity and specificity of the six human {alpha}-defensins. Antimicrob Agents Chemother. 2005; 49: 269-275.
18. Selsted ME, Ouellette AJ. Mammalian defensins in the antimicrobial immune response. Nat Immunol. 2005; 6: 551-557.
19. Lehrer RI. Multispecific myeloid defensins. Curr Opin Hematol. 2007; 14: 16-21.
20. Kim C, Gajendran N, Mittrücker HW, Weiwad M, Song YH, Hurwitz R, et al. Human alpha-defensins neutralize anthrax lethal toxin and protect against its fatal consequences. Proc Natl Acad Sci USA. 2005; 102: 4830-4835.
21. Porter E, Yang H, Yavagal S, Preza GC, Murillo O, Lima H, et al. Distinct defensin profiles in *Neisseria gonorrhoeae* and *Chlamydia trachomatis* urethritis reveal novel epithelial cell-neutrophil interactions. Infect Immun. 2005; 73(8): 4823-4833.
22. Klotman ME, Chang TL. Defensins in innate antiviral immunity. Nat Rev Immunol. 2006; 6: 447-456.
23. Gallo SA, Wang W, Rawat SS, Jung G, Waring AJ, Cole AM, et al. Theta-defensins prevent HIV-1 Env-mediated fusion by binding gp41 and blocking 6-helix bundle formation. J Biol Chem. 2006; 281: 18787-18792.
24. Furci L, Sironi F, Tolazzi M, Vassena L, Lusso P. Alpha-defensins block the early steps of HIV-1 infection: interference with the binding of gp120 to CD4. Blood. 2007; 109: 2928-2935.
25. Salvatore M, Garcia-Sastre A, Ruchala P, Lehrer RI, Chang T, Klotman ME. Alpha-defensin inhibits influenza virus replication by cell-mediated mechanism(s). J Infect Dis. 2007; 196: 835-843.
26. Buck CB, Day PM, Thompson CD, Lubkowski J, Lu W, Lowy DR, et al. Human alpha-defensins block papillomavirus infection. Proc Natl Acad Sci USA. 2006; 31(103): 1516-1521.
27. Daher KA, Selsted ME, Lehrer RI. Direct inactivation of viruses by human granulocyte defensins. J Virol. 1986; 60: 1068-1074.
28. Ganz T. Antimicrobial polypeptides in host defense of the respiratory tract. J Clin Invest. 2002; 109: 693-697.
29. Chaly YV, Paleolog EM, Kolesnikova TS, Tikhonov II, Petratchenko EV, Voitenok NN. Neutrophil α-defensin human neutrophil peptide modulates cytokine production in human monocytes and adhesion molecule expression in endothelial cells. Eur Cytokine Netw. 2000; 11: 257-260.
30. Wehkamp J, Salzman NH, Porter E, Nuding S, Weichenthal M, Petras RE, et al. Reduced Paneth cell a-defensins in ileal Crohn's disease. Proc Natl Acad Sci USA. 2005; 102: 18129-18134.
31. Wehkamp J, Schmid M, Fellermann K, Stange EF. Defensins deficiency, intestinal microbes, and clinical phenotypes of Crohn's disease. J Leukoc Biol. 2005; 77: 460-465.
32. Droin N, Hendra J-B, Ducoroy P, Solary E. Human defensins as cancer biomarkers and antitumour molecules. J Proteomics. 2009; 72: 918-927.
33. Melle C, Ernst G, Schimmel B, Bleul A, Thieme H, Kaufmann R, et al. Discovery and identification of alpha-defensins as low abundant, tumor-derived serum markers in colorectal cancer. Gastroenterol. 2005; 129: 66-73.
34. Albrethsen J, Møller CH, Olsen J, Raskov H, Gammeltoft S. Human neutrophil peptides 1, 2 and 3 are biochemical markers for metastatic colorectal cancer. Eur J Cancer. 2006; 42: 3057-3064.
35. Bateman A, Singh A, Jothy S, Fraser R, Esch F, Solomon S. The levels and biologic action of the human neutrophil granule peptide HP-1 in lung tumors. Peptides. 1992; 13: 133-139.
36. Muller CA, Markovic-Lipkovski J, Klatt T, Gamper J, Schwarz G, Beck H, et al. Human alpha-defensins HNPs-1, -2, and -3 in renal cell carcinoma: influences on tumor cell proliferation. Am J Pathol. 2002; 160: 1311-1324.
37. Holterman DA, Diaz JI, Blackmore PF, Davis JW, Schellhammer PF, Corica A, et al. Overexpression of alpha-defensin is associated with bladder cancer invasiveness. Urol Oncol. 2006; 24: 97-108.
38. Lundy FT, Orr DF, Gallagher JR, Maxwell P, Shaw C, Napier SS, et al. Identification and overexpression of human neutrophil alpha-defensins (human neutrophil peptides 1, 2 and 3) in squamous cell carcinomas of the human tongue. Oral Oncol. 2004; 40: 139-144.
39. Diamond G, Zasloff M, Eck H, Brasseur M, Maloy WL, Bevins CL. Tracheal antimicrobial peptide, a cysteine-rich peptide from mammalian tracheal mucosa: peptide isolation and cloning of a cDNA. Proc Natl Acad Sci USA. 1991; 88: 3952-3956.
40. Żyłowska M, Wyszyńska A, Jagusztyn-Krynicka EK. Defensins - the peptides with antimicrobial activity [in Polish]. Post Mikrobiol. 2011; 50(3): 223-234.
41. Xie C, Prahl A, Ericksen B, Wu Z, Zeng P, Li X, et al. Reconstruction of the conserved beta-bulge in

mammalian defensins using D-amino acids. J Biol Chem. 2005; 280: 32921-32929.
42. Pazgier M, Hoover DM, Yang D, Lu W, Lubkowski J. Human beta-defensins. Cell Mol Life Sci. 2006; 63: 1294-131.
43. Bensch KW, Raida M, Magert HJ, Schulz-Knappe P, Forssmann WG. hBD-1: a novel beta-defensin from human plasma. FEBS Lett. 1995; 368: 331-335.
44. Tollin M, Bergman P, Svenberg T, Jornvall H, Gudmundsson GH, Agerberth B. Antimicrobial peptides in the first line defence of human colon mucosa. Peptides. 2003; 24: 523-530.
45. Valore EV, Park CH, Quayle AJ, Wiles KR, McCray PB Jr, Ganz T. Human b-defensin-1: an antimicrobial peptide of urogenital tissues. J Clin Invest. 1998; 101: 1633-1642.
46. Guani-Guerra E, Santos-Mendoza T, Lugo-Reyes SO, Teran LM. Antimicrobial peptides: general overview and clinical implications in human health and disease. Clin Immunol. 2010; 135: 1-11.
47. Schwaab M, Gurr A, Hansen S, Minovi AM, Thomas JP, Sudhoff H, Dazert S. Human beta-defensins in different states of diseases of the tonsilla palatina. Eur Arch Otorhinolaryngol. 2010; 267: 821-830.
48. Liu AY, Destoumieux D, Wong AV, Park CH, Valore EV, Liu L, Ganz T. Human b-defensin-2 production in keratinocytes is regulated by interleukin-1, bacteria, and the state of differentiation. J Invest Dermatol. 2002; 118: 275-281.
49. Ong PY, Ohtake T, Brandt C, Strickland I, Boguniewicz M, Ganz T, et al. Endogenous antimicrobial peptides and skin infections in atopic dermatitis. N Engl J Med. 2002; 347: 1151-1160.
50. Sorensen OE, Cowland JB, Theilgaard-Monch K, Liu L, Ganz T, Borregaard N. Wound healing and expression of antimicrobial peptides/polypeptides in human keratinocytes, a consequence of common growth factors. J Immunol. 2003; 170: 5583-5589.
51. Quiñones-Mateu ME, Lederman MM, Feng Z, Chakraborty B, Weber J, Rangel HR, et al. Human epithelial beta-defensins 2 and 3 inhibit HIV-1 replication. AIDS. 2003; 17: F39-F48.
52. Sass V, Schneider T, Wilmes M, Korner C, Tossi A, Novikova N, et al. Human beta-defensin 3 inhibits cell wall biosynthesis in staphylococci. Infect Immun. 2010; 78: 2793-2800.
53. Garcia JR, Krause A, Schultz S, Rodriguez-Jimenez FJ, Klüver E, Adermann K, et al. Human β-defensin 4: a novel inducible peptide with a specific salt-sensitive spectrum of antimicrobial activity. FASEB J. 2001; 15: 1819-1821.
54. Sun CQ, Arnold R, Fernandez-Golarz C, Parrish AB, Almekinder T, He J, et al. Human beta-defensin-1, a potential chromosome 8p tumor suppressor: control of transcription and induction of apoptosis in renal cell carcinoma. Cancer Res. 2006; 66: 8542-8549.
55. Gambichler T, Skrygan M, Huyn J, Bechara FG, Sand M, Altmeyer P, et al. Pattern of mRNA expression of beta-defensins in basal cell carcinoma. BMC Cancer. 2006; 6: 163.
56. Kota S, Sabbah A, Chang TH, Harnack R, Xiang Y, Meng X, Bose S. Role of human beta-defensin-2 during tumor necrosis factor-alpha/NF-kappaB-mediated innate anti-viral response against human respiratory syncytial virus. J Biol Chem. 2008; 283: 22417-22429.
57. Howell MD, Jones JF, Kisich KO, Streib JE, Gallo RL, Leung DY. Selective killing of vaccinia virus by LL-37: implications for eczema vaccinatum. J Immunol. 2004; 172: 1763-1767.
58. Howell MD, Streib JE, Leung DY. Antiviral activity of human beta-defensin 3 against vaccinia virus. J Allergy Clin Immunol. 2007; 119: 1022-1025.
59. King AE, Paltoo A, Kelly RW, Sallenave JM, Bocking AD, Challis JR. Expression of natural antimicrobials by human placenta and fetal membranes. Placenta. 2007: 28: 161-169.
60. Zaga-Clavellina V, Ruiz M, Flores-Espinosa P, Vega-Sanchez R, Flores-Pliego A, Estrada-Gutierrez G, et al. Tissue-specific human beta-defensins (HBD)-1, HBD-2 and HBD-3 secretion profile from human amniochorionic membranes stimulated with *Candida albicans* in a two-compartment tissue culture system. Reprod Biol Endocrinol. 2012; 10: 70. doi: 10.1186/1477-7827-10-70.
61. Garcia-Lopez G, Flores-Espinosa P, Zaga-Clavellina V. Tissue-specific human beta-defensins (HBD)1, HBD2, and HBD3 secretion from human extra-placental membranes stimulated with *Escherichia coli*. Reprod Biol Endocrinol. 2010; 8: 146. doi: 10.1186/1477-7827-8-146.
62. Zaga-Clavellina V, Garcia-Lopez G, Flores-Espinosa P. Evidence of in vitro differential secretion of human beta-defensins-1, -2, and -3 after selective exposure to *Streptococcus agalactiae* in human fetal membranes. J Matern Fetal Neonatal Med. 2012; 25(4): 358-363.

TMKARPIŃSKI
PUBLISHER

Archives
of Biomedical
Sciences
ISSN: 2300-7257

CASE REPORT

Treatment of the large periapical lesion - a case report

Anna K. Szkaradkiewicz

ABSTRACT

The case report describes the patient with large periapical lesion around the tooth root 23. Endodontic treatment was performed. On the first visit the root canal was developed mechanically and chemically, its lumen was filled with calcium hydroxide preparation. After two weeks root canal was tightly filled with gutta-percha points with Endomethasone N paste using lateral condensation method. After a week, the patient did not report any discomfort, so the tooth was filled with composite material. On the X-ray picture just after the final filling of the root canal can be observed reconstruction of periapical tissues. In the future, the tooth 23 can be used as a pillar to the prosthetic reconstruction.

Key Words: Periapical lesion; Inflammation; Endodontics; Teeth; Gutta-percha.

INTRODUCTION

The most common causes of periapical tissues diseases are irreversible inflammations, necrosis of the pulp and stimuli that arise during endodontic treatment of these diseases. Infections of the dental pulp involve a mixed, predominantly Gram-negative, anaerobic bacterial flora [1].

Chronic inflammations of periapical tissues are slow and in most cases asymptomatic, they are only detected during X-ray examination. Treatment of chronic inflammations of periapical tissues finishes with a success when follows the change withdrawal. Lost tissues undergo regeneration. The repair process is considered as complete when the periodontal ligament reconstruction occurs [2].

Correspondence: aniaszk@op.pl
Poznań University of Medical Sciences, Department of Conservative Dentistry and Periodontology, Bukowska 70, 60-812 Poznań, Poland

CASE REPORT

An 45-year-old patient came forward for treatment of tooth 23, which was open. In the interview, he did not specify general diseases. On the X-ray picture was found the periapical lesion around the tooth root 23, pocket depth was 10 mm (Fig. 1). On the basis of X-ray image with the tool inserted into the root canal the working length was established. Endodontic treatment was performed with the use of rubber dam in accordance with the applicable rules. The root canal was developed mechanically and chemically, its lumen was filled with calcium hydroxide preparation Calcipast + I (Cerkamed). Loss in the crown was closed with glass-ionomer cement GC Fuji IX.

On the next visit (after two weeks) root canal was tightly filled with gutta-percha points with Endomethasone N paste (Septodont) using lateral condensation method. After a week, the patient did not report any discomfort, so the tooth was

Received: June 13, 2013; **Accepted:** June 28, 2013; **Published:** July 03, 2013

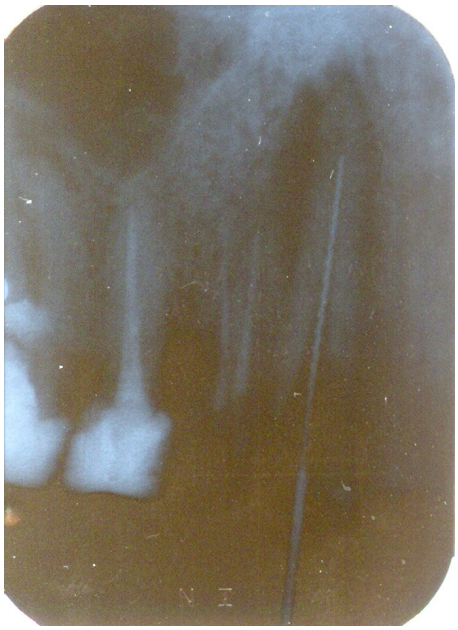

Fig. 1. Large periapical lesion around the tooth root 23.

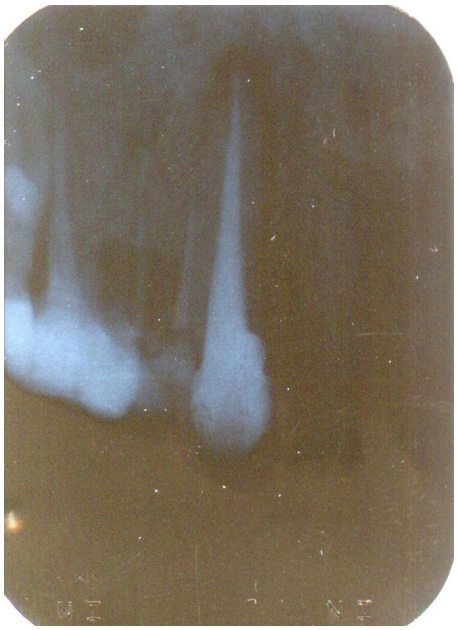

Fig. 2. Tooth 23 after treatment.

filled with the Charisma (Kulzer) composite material. On the X-ray picture just after the final filling of the root canal can be observed reconstruction of periapical tissues (Fig. 2). The course of bone regeneration is properly. Thanks to conservative treatment was able to maintain the full length of the root, and the tooth is full blown. In the future, the tooth 23 can be used as a pillar to the prosthetic reconstruction.

DISCUSSION

The causes of apical parodontium inflammatory processes are infections in the root canal system of the tooth, and dentin, as well as the passage of infection from other surrounding periodontal tissues. Among the most frequently isolated microorganisms are bacteria *Actinomyces israelli*, *Propionibacterium propionicum*, *Enterococcus faecalis* and also yeast *Candida albicans* [3].

In the treatment of periapical lesions are used different preparations and antiseptics [4]. One of the newest is the Pro Root MTA-Mineral trioxide Aggregate. This material is intended for reparation of any losses of dentin, cement and bone [5]. In turn, the calcium hydroxide introduced into the biological treatment in 1920 is widely used to the present day, especially in infected root canals. The hydroxyl ion is responsible for the high pH, and antimicrobial activity. Calcium hydroxide also has the ability to change the properties of bacterial lipopolysaccharides, whereby the bacteria lose their toxic properties. A calcium hydroxide-based paste was used as an antibacterial dressing in this case.

The exact mechanism of action of calcium hydroxide is still speculative. It is suggested that the action of calcium hydroxide beyond the apex may be fourfold:

1. anti-inflammatory activity;
2. neutralisation of acid products;
3. activation of the alkaline phosphatase; and
4. antibacterial action [6-8].

The basic condition for success is correct, antiseptic treatment of the root canal, but still is searched for new and effective methods for speeding up the healing of periapical tissues. Repair of periapical tissues is a complex regenerative process involving bone, periodontal ligament and cement [2, 9].

CONCLUSION

In this case report, root canal treatment proved successful in promoting the healing of a large periapical lesion. This confirms that even large periapical lesions can respond favourably to non-surgical treatment.

TRANSPARENCY DECLARATION

The author declares no conflicts of interest.

REFERENCES

1. Marsh PD, Martin MV. 2009. Oral microbiology. 5th ed. Churchill Livingstone.
2. Bołtacz-Rzepkowska E, Żęcin A. The treatment of large periapical lesions [in Polish]. Czas Stomat. 2005; 58(3): 158-166.
3. Szkaradkiewicz AK, Karpiński TM. Microbiology of chronic periodontitis. J Biol Earth Sci. 2013; 3(1): M14-M20.
4. Torabinejad M, Abu-Tahun I. Management of teeth with necrotic pulps and open apices. Endod Topics. 2010; 23(1): 105-130.
5. Gomes-Filho JE, Watanabe S, Cintra LT, et al. Effect of MTA – based sealer on the healing of periapical lesions. J Appl Oral Sci. 2013; 21(3): S1678-775720 13000300235.
6. Barańska-Gachowska M. 2004. Endodoncja wieku rozwojowego i dojrzałego [Endodontics of developmental and mature age]. 1st ed. Czelej, Lublin.
7. Hargreaves KM, Cohen S. 2011. Cohen's Pathways of the pulp. 10th ed. Mosby Elsevier.
8. Barekatain B, Hasheminia SM, Shadmehr E, Attary Z. The effect of calcium hydroxide placement on pH and calcium concentration in periapical environment: an in vitro study. Ind J Dent Res. 2012; 23(2): 226-229.
9. Saatchi M. Healing of large periapical lesion: A non-surgical endodontic treatment aproach. Aust Endod J. 2007; 33: 136-140.