

# THE CONCENTRATION OF CHLORHEXIDINE GLUCONATE FROM THE PERIO-CHIP IN GINGIVAL FLUID IN PATIENTS WITH PERIODONTAL DISEASE

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## Abstract

**Purpose:** To determine the concentration of chlorhexidine gluconate (CHX) from the Perio-chip in cervical gingival fluid (FCG) at different time intervals in patients with clinical manifestation of the second stage of periodontal disease.

**Material and method:** A total of 22 patients of both sexes aged 40-65 years of age, who were diagnosed with periodontal disease of the second clinical stage were followed up. The researchers who were part of the research had registered the periodontal pocket depth of 5 mm. Perio-chip was applied to them, where the concentration of chlorhexidine gluconate was measured at certain time intervals (after 1, 24, 48, 96, 168 hours after the application). The determination of chlorhexidine was carried out through two procedures: the extraction of gingival fluid and the quantitative determination of chlorhexidine gluconate in it.

**Extraction of gingival fluid:** For this purpose was used Whatmann filter paper no. 5 with dimensions of 2x6 mm with which the part determined for measurement is inserted into the periodontal pocket 1 mm, where the liquid is drawn through the Whatmann filter paper through the absorption forces against the capillaries through diffusion. The strips taken for determining the concentration of chlorhexidine gluconate in the gingival fluid with the HPLC method, the analyzes at different time intervals for the concentration of chlorhexidine gluconate were carried out at the Institute for Chemical Application and Pharmaceutical Analysis at the Faculty of Pharmacy in Skopje.

**Results:** The highest concentration was reached in the 1st hour after the application of the Perio-chip, while the concentration within 7 days moved from the values of 1148.70-624.37  $\mu\text{g mL}^{-1}$  where it is contained after the application of the medicinal asset.

After 2-4 days certain concentration reaches the value up to 1300  $\mu\text{g mL}^{-1}$ , while after this time interval the concentration gradually decreases but remains at values above 125  $\mu\text{g mL}^{-1}$

**Conclusion:** According to this formulation we can calculate that this formulation has an effective controlled continuous release system of chlorhexidine gluconate.

*Keywords:* Chronic periodontopathy, conventional therapy, gingival fluid, chlorhexidine gluconate - Perio-chip.

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## Introduction

Periodontal disease is defined as "inflammatory disease" to the supporting tissues of the tooth caused by specific microorganisms accompanied by progressive destruction of the periodontal ligament and alveolar bone, where the final effect is the loss of teeth.

Bacterial accumulation on hard oral surfaces is the main cause of the appearance of gingivitis and periodontopathy (1,2), for this reason regular and correct removal of dental plaque from all hard oral surfaces is the main way to prevent periodontal disease (3). Controlling dental plaque through regular oral hygiene, removal of supra and subgingival layers is one of the main ways of maintaining the results achieved towards therapeutic success (4).

Other than the removal of microbial plaques by mechanical ways in clinical practice, local antimicrobial hemotherapy or systemic therapy is also used. Here it should be mentioned the CIST-protocol where in dentistry it is used as a pre-surgical disinfectant where it is later used as an anti-plaque preparation (1) where

its use as an auxiliary or complementary preparation has found application during non-surgical treatment during chronic periodontal disease, known in the USA and Europe (5).

In recent years, recommendations lead to the use of local antimicrobial preparations as a supplement in the conservative treatment of periodontal disease. As the most popular preparations are the use of chlorhexidine gluconate assets or chips (the second generation of local antimicrobial preparations) where applied to the periodontal pocket, it significantly improves clinical parameters against periodontal disease. (6)

Cosyn and Wynn (7) argue that the use of chlorhexidine acetate preparations improves the clinical effects of periodontal disease, while Archana (8) appraises the efficacy of the controlled bioresorption release of chlorhexidine chip (Periocol CG) when used as an adjunctive preparation during the procedure therapeutic is an efficient helper in solving the affected symptoms of periodontal disease.

Taking the data of the contemporary literature and the fact that the use of antiseptics in solution form has a very short effect, the goal of this research is set: to determine the concentration of chlorhexidine gluconate in the cervical gingival fluid at different time intervals through the bioresorption of Perio- chip-it in the periodontal pocket in patients with periodontopathy.

## **Material and method**

In order to achieve the set goal, a total of 22 patients of both sexes aged 40-65 years of age who were clinically and radiologically diagnosed with periodontal disease of the second clinical stage were followed up. The researchers who were part of the research had registered periodontal pocket depth of 5 mm. Perio-chip was applied to them, where the concentration of chlorhexidine gluconate was measured at certain time intervals (after 1, 24, 48, 96, 168 hours after the application).

The determination of chlorhexidine was carried out through two procedures: the extraction of gingival fluid and the quantitative determination of chlorhexidine gluconate in it.

Extraction of gingival fluid. For this purpose was used Whatmann filter paper no. 5 with dimensions of 2x6 mm with which the part determined for measurement is inserted into the periodontal pocket 1 mm, where the liquid is drawn through the Whatmann filter paper through the absorption forces against the capillaries through diffusion.

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## **Results**

Perio-chip represents a controlled release system of chlorhexidine digluconate in periodontal pockets and represents the most productive antiseptic in the prevention of periodontal disease (9, 10).

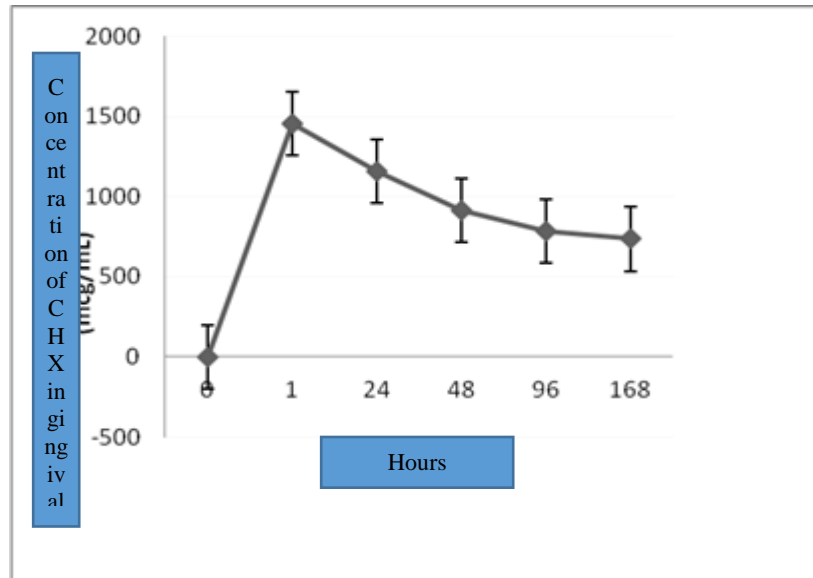
After realizing the optimization and validity of the HPLC method for the determination of CHX in swab from the gingival fluid, the same was applied as a routine analysis in order to determine the concentration of chlorhexidine that reaches the gingival fluid after the application of the Perio-chip in patients with suffering from periodontal disease. The determined concentrations of chlorhexidine in the gingival fluid are shown in table 1. The highest concentration is reached in the 1st hour after the application of the Perio-chip, while the concentration range of 1148.70-624.37  $\mu\text{g mL}^{-1}$  is contained until the 7th day.

### After applying the chip

After 2-4 days, determined concentrations reach the value up to 1300  $\mu\text{g mL}^{-1}$ , while after that time interval the concentration gradually decreases but remains above 125  $\mu\text{g mL}^{-1}$ . This concentration is the minimum inhibitory concentration (MIC) where more than 99% of the subgingival microorganisms that are isolated from the periodontal pocket are destroyed by the therapeutic effect. The results are presented as the average value from the determination of the concentration ( $n=3$ )  $\pm$  standard error and the graphical presentation presented in Graph1.

Patient	Concentration of CHX in gingival fluid ( $\mu\text{g mL}^{-1}$ )				
	1 x	24 x	48 x	96 x (4 days)	168 x (7 days)
1	1438,79	935,73	792,57	633,41	677,67
2	1273,39	895,95	927,31	685,06	1033,08
3	1565,16	1212,43	785,58	687,62	785,17
4	1074,58	1318,58	687,70	687,70	744,30
5	1532,76	1056,79	865,20	949,68	751,75
6	1547,50	1148,70	1006,55	948,54	658,72
7	1556,67	1075,89	932,21	766,25	624,37
8	1501,07	893,81	947,22	817,90	681,84
9	1649,62	1068,76	947,62	876,07	627,92
10	1536,2	1022,63	945,36	852,30	628,31
11	1568,7	1007,22	912,31	807,56	611,69

After the application of chlorhexidine 0.12% solution, designated concentrations were at the detection limit. This is due to the low concentration of chlorhexidine in its solution form (mouthwash solution) which cannot contain biological concentrations of the drug for a long period of time for therapeutic efficacy against periodontal disease.



**Graph 1.** Graphic display of the average value of the designated concentration of CHX in the gingival fluid during the study period in time intervals.

According to the obtained results, we prove that the Perio-chip releases significant clinical concentrations of chlorhexidine in the gingival fluid, which is contained during the 7-day study.

## Discussion

Chlorhexidine is a molecule with a wide spectrum of antibacterial and antiviral action. The presence of two chlorophenyl guanidine groups, located symmetrically, connected by a lipophilic hexamethylene chain, allow the rapid absorption of this molecule through the bacterial wall, causing irreversible damage to the bacterial membrane, cell cytoplasm, as well as enzyme inhibition. (11).

For these specific reasons, it is used as an active therapeutic substance in a variety of formulations for the treatment of skin diseases and finds special application in dentistry.

Antibiotics, antiseptics and some anti-inflammatory medications can be applied locally in the treatment of periodontal disease, which represent an effective adjunct to conventional, mechanical therapy. However, the concentration achieved by these drugs at the site of application as a function of time is an open question for the rationale of their use. Modern trends in the treatment of periodontal disease have enabled the development of new formulations for local application in periodontal pockets. These formulations allow the gradual release of the therapeutic agent into the periodontal pocket, as well as the maintenance of therapeutic drug levels at the site of action that are 10-100 times higher than those that would be achieved if the drug were applied per OS . Perio-chip has an effective system for the controlled release of chlorhexidine digluconate in periodontal pockets and is the most effective antiseptic in preventing the formation of dental plaque.

One hour after inserting the Perio-chip, a concentration of 1649.62 µg mL<sup>-1</sup> was reached. Two to four days later, the determined concentrations reach values up to 1300 µg mL<sup>-1</sup> and after 10 days they gradually decrease, but remain above 125 µg µL<sup>-1</sup>. This concentration is the minimum inhibitory concentration (MIC) for more than 99% of subgingival microorganisms isolated from periodontal pockets. (9).

The results obtained from this study coincide with the results of the study (12), in which the subgingival application of the Perio-chip and its bioresorption and concentration chronologically followed the following dynamics: the initial concentration in the first 2 hours was 2007 µg mL<sup>-1</sup>. After the second day to the fourth

day, the determined concentrations were 1300-1900  $\mu\text{g mL}^{-1}$ , but after the tenth day it decreased to 57  $\mu\text{g mL}^{-1}$ . Similar findings were obtained from the researches of (13-15).

The large variation in CHX concentrations among patients may be due to some biological variation among patients, such as variations in gingival fluid flow, large variability in gingival fluid flow between patients with different degrees of inflammation, as well as reduction of gingival fluid volume reducing periodontal pocket inflammation during treatment (9, 11).

## Conclusion

According to the results obtained, it can be concluded that the Perio-chip releases clinically relevant concentrations of chlorhexidine in the gingival fluid, which are prolonged for 7 or more days. Thanks to their gradual bioresorption, a constant concentration that is present for a long time in the gingival fluid, this formulation can be considered an effective system for the controlled release of chlorhexidine that finds its application as an additional therapy in the treatment of periodontal disease

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