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Bacterial plaque formed on teeth is the main etiologic factor in gingivitis and caries. In a controlled clinical trial, the in vivo plaque inhibiting effect of 11 antibacterial agents was compared with their antibacterial activity against salivary bacteria in vitro. The bis-biguanide salts (chlorhexidine) proved most effective in vivo, while other substances of equal or higher in vitro activity showed no in vivo effect, indicating that other factors are required for plaque inhibition in vivo. [The *SCI*® indicates that this paper has been cited in more than 155 publications.]

Fighting Plaque

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It all began in an airplane over the Atlantic, returning to Europe after having attended the 1st International Conference on Periodontal Research, in Rochester, New York. During the last few months, there had been rumors that H. Löe and coworkers had obtained sensational results concerning the control of the formation of dental plaque—results which might change the possibilities of preventing the two main dental diseases (caries and periodontal disease). Löe, in his final speech at the meeting, had mentioned that this chemical agent was chlorhexidine gluconate—a well-known surface disinfectant that had been on the market for 15 years. He claimed that it was the agent's ability to suppress the oral flora that was important.[1]

I traveled with my friend Gunnar Rölla. He had been working with the acquired pellicle on teeth and, in that connection, had studied various substances and ions and their effect on protein adsorption to hydroxyapatite. When discussing the results reported at the conference, Rölla expressed his doubt about the ability of the antibacterial agent chlorhexidine to play such an important role. He said: "We have known for centuries that dental plaque mainly consists of bacteria, and someone must have tried to affect the flora by means of antimicrobials before! It cannot be that simple! I wonder whether the gluconate with its negative charge may be the important part of the molecule. I have already data showing that gluconate will inhibit protein adsorption to hydroxyapatite in vitro."

My field was clinical trials, and we had recently developed a human test model for studying plaque accumulation on teeth that had shown promise as a quick and relatively good in vivo model for early plaque formation studies. Therefore, we decided to test the hypothesis that gluconate could inhibit plaque formation on teeth in vivo. The protocol for the trial was written on the plane. The next week we carried out the first experiments, and the results showed no effect by gluconate (unpublished). It seemed that antibacterial activity was necessary.

A literature search revealed, as expected, that many experiments had been reported on the use of antibacterial agents in the mouth to prevent plaque formation—most of them with little success.[2,3] However, some Swiss researchers had observed and reported inhibition of plaque and calculus by chlorhexidine but rejected its use in humans due to its bitter taste.[4] It seemed that different antibacterials might work differently, and we decided to screen a number of substances with different chemical compositions and different mechanisms of antibacterial activity for plaque inhibition in our test model.

The results, as they appeared in the article, led to the conclusion that antibacterial activity against oral microorganisms per se would not suffice to inhibit the formation of plaque on teeth in vivo. This challenging discovery prompted a series of experiments in our laboratory to disclose the nature of the antiplaque action of chlorhexidine, resulting in several doctoral theses (including my own).[5]

Chemical inhibition of bacterial plaque on teeth is still an interesting topic, and the conclusions made after the initial rather simple experiments have not been seriously challenged.[6,7] Requirements for ideal plaque inhibitors now comprise properties such as substantivity in the oral cavity, in addition to their antibacterial activity.[8] Several commercial products aiming at improved oral health utilizing these principles are now on the market.

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