EFFECT OF PRODUCT FORMULATION ON TRICLOSAN EFFECTIVENESS

Michael L. Barnett, D.D.S.

An assessment prepared for the Colgate-Palmolive Company

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Although the antimicrobial triclosan is incorporated in a variety of product types, the development of triclosan-containing oral care products with significant antiplaque and antigingivitis effectiveness has been especially challenging. Dentifrice formulations, in particular, are extremely complex and must be exquisitely optimized in order to assure, for example, that the triclosan is not bound to other components, such as surfactants, and that the triclosan will be substantive in the mouth following product use and thereby continue to exert an effect\textsuperscript{1-4}. This being the case, there have been only a few effective antiplaque/antigingivitis triclosan-containing products marketed worldwide, and these tend to be based on proprietary, patented formulations.

Oral care products companies have taken two approaches to developing effective triclosan-containing dentifrices. The first, used by Colgate-Palmolive Co. for its Total\textsuperscript{®} products, is to incorporate ingredients (i.e., a copolymer such as Gantrez\textsuperscript{®}) that will enhance the delivery and retention of triclosan to oral surfaces. This formulation has been granted a US patent\textsuperscript{5} and is supported by numerous long-term plaque/gingivitis clinical trials\textsuperscript{6,7}. In addition, this formulation was approved by the FDA for marketing in the U.S. via the New Drug Application (NDA) process\textsuperscript{8} and was granted the American Dental Association’s Seal of Acceptance.

The second approach, used by Unilever, is to incorporate a second antimicrobial agent, zinc citrate, to increase overall product effectiveness. The Unilever products, too, are based on patented formulations\textsuperscript{9} and supported by clinical trial data\textsuperscript{10-16}. However, these are combination products containing two antimicrobial agents, triclosan and zinc citrate, and are not marketed in the U.S.

A third approach was taken by Procter and Gamble in the development of triclosan/pyrophosphate dentifrice formulations. However, these products lack sufficient antigingivitis effectiveness\textsuperscript{17,18} and are not marketed in the U.S.

The experience with formulating triclosan into effective antiplaque/antigingivitis products suggests that while the individual Colgate and Unilever dentifrices might be generally accepted as effective, difficulties in achieving optimized formulations and the very different approaches taken by the two companies to achieve product effectiveness preclude classifying the ingredient triclosan by itself as generally effective at this time. The activity of this agent is clearly dependent upon the way in which it is formulated and the Colgate triclosan dentifrice, whose NDA is based on the overall formulation rather than the active ingredient \textit{per se}, is the only effective triclosan-containing antigingivitis dentifrice marketed today in the U.S. Unlike an OTC monograph ingredient review, the NDA does not require a final formulation test (“performance test”) for comparing new formulations to the clinically tested standard, nor should it. It is unlikely that any clinical test short of the 6-month clinical trials required for evaluation of antiplaque and antigingivitis effectiveness would be able to accurately evaluate any new triclosan-containing products. However, the requirement of such extensive studies prior to marketing, while the standard for an NDA and the initial OTC ingredient review, is clearly inconsistent with the intent of an OTC monograph. Until such time as evidence is presented to demonstrate that triclosan can be \textit{readily} formulated in
effective antiplaque/antigingivitis products as a single active ingredient and a clinically relevant, validated final formulation test procedure specific for triclosan is established, it is my opinion that it would not be appropriate to consider triclosan for inclusion in the OTC monograph being developed for such products as there would otherwise be no reasonable assurance that any newly and differently formulated products would be clinically effective.

References

CURRICULUM VITAE

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ADDRESS: 9 Bennington Road
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EDUCATION:
1960-63 Columbia College, New York City
1963-67 School of Dental and Oral Surgery, Columbia University, NYC - D.D.S.
1967-68 Postdoctoral Fellowship, Department of Oral Biology, School of Dentistry,
University of Washington, Seattle, WA
1970-73 Postdoctoral Fellowship, Harvard School of Dental Medicine, Boston, MA -
Certificate in Periodontology and Oral Medicine

MILITARY SERVICE:
1968-70 Captain, U.S. Army Dental Corps, Chief of Oral Medicine, Fort Lewis, WA

APPOINTMENTS:
1964-65 NIH Summer Research Fellow, Department of Physiology, College of
Physicians & Surgeons, Columbia University, NY
1967-68 Postdoctoral Fellow, Department of Oral Biology, University of Washington
School of Dentistry, Seattle, WA
1968-70 General Dentistry Residency Faculty Member (Oral Medicine), Fort Lewis
Dental Activities, Tacoma, WA
1970-73 Research Fellow in Periodontology and Oral Medicine, Harvard School of
Dental Medicine, Boston, MA
1973-74 Assistant Professor, Department of Periodontics, New Jersey Dental
School, UMDNJ, Jersey City, NJ
1974-77 Visiting Lecturer in Periodontology, Harvard School of Dental Medicine,
Boston, MA
1974-75 Assistant Professor, Department of Periodontics, School of Dentistry,
State University of New York, Buffalo, NY
1975-79 Associate Professor, Department of Periodontics, School of Dentistry,
State University of New York, Buffalo, NY
1975-79 Associate Consulting Dentist, Department of Dentistry, E. J. Meyer
Memorial Hospital, Buffalo, NY
1979-82 Associate Professor and Coordinator of Postgraduate Education,
Department of Periodontics, School of Dentistry, University of Louisville,
Louisville, KY
1982-87 Chairman, Department of Dentistry and Director, General Practice
Residency, Morristown Memorial Hospital, Morristown, NJ
1982-87 Associate Clinical Professor of Dentistry, Division of Periodontics,
School of Dental and Oral Surgery, Columbia University, New York, NY
1983-87 Director, Dental Program for the Developmentally Disabled, Department of
Dentistry, Morristown Memorial Hospital, Morristown, NJ
1987-99  Consulting Staff, Department of Dentistry, Morristown Memorial Hospital, Morristown, NJ
1987-90  Associate Director, Dental Affairs, Warner-Lambert Company, Morris Plains, NJ
1992-04  Visiting Professor, Department of Periodontics, New Jersey Dental School-UMDNJ, Newark, NJ
2000-01  Senior Director, Dental Affairs/Oral Technology Development, Pfizer Consumer Healthcare, Morris Plains, NJ
2002-    Independent Consultant to the Oral Care Products Industry, Morristown, NJ
2004-    Clinical Professor of Oral Biology and Interim Associate Dean for Research, New Jersey Dental School-UMDNJ, Newark, NJ

MEMBERSHIPS:
American Dental Association
American Academy of Periodontology
American Association for Dental Research
American Association for the Advancement of Science
New Jersey Dental Association, Tri-County Dental Association

HONORS:
1960-67  New York State Regents Scholarship
1967    Block Drug Award
1970    U.S. Army Commendation Medal
1986    Fellow, American College of Dentists
1998    Fellow, American Association for the Advancement of Science
2002    Jack Hein Public Service Award, American Association for Dental Research

LICENSES: New Jersey

BOARDS:
Northeast Regional Board
National Board of Dentistry

SERVICE TO PROFESSIONAL ORGANIZATIONS:
American Association for the Advancement of Science
1992-95  Member, Section on Dentistry Electorate Nominating Committee
         (Chair 1994-95)
1996-99  Council Representative, Section on Dentistry
American Association for Dental Research
1980-81  President, Louisville Section
1981-82  Periodontal Research Group Program Committee
1989-92  Member, Exhibits Committee
1989-90  Secretary-Treasurer, NJ Section
Colgate-Palmolive Company  
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1990-91 Vice-President, NJ Section  
1991-92 President, NJ Section  
1992-96 Councilor, NJ Section  
1992-00 Member, National Affairs Committee  
1992- Member, AADR Cohorts  
1996-00 Councilor, Institutional Member Section  
1996-00 Ad hoc Industry Affairs Advisory Committee (Chair, 1996-98)  
1997-99 Member-at-Large, Board of Directors  
2000-04 Councilor, New Jersey Section

American College of Dentists  
1989-91 Member, Executive Board, NJ Section  
1989-91 Secretary-Treasurer, NJ Section

American Dental Association  
1991-01 Member (non-voting), Selection Committee, Dr. Norton M. Ross Award for Excellence in Clinical Research  
1999-04 Member, Board of Directors, ADA Health Foundation  
1999-01 Member, US Delegation to ISO/TC106 Meetings

Columbia University School of Dental and Oral Surgery  
1992-94 Executive Member, John W. Hein Research Fellowship Committee  
1996- Dean's Advisory Council and Campaign Committee

Forsyth Dental Center  
1990-91 Executive Member, John W. Hein Research Fellowship Committee  
1992-98 Member, Board of Overseers

Friends of the National Institute of Dental Research  
1998-2001 Member-at-Large, Executive Committee, Board of Directors (Secretary 1999-00)

Harvard School of Dental Medicine  
1980-83 Associate Chairman, The Alumni-Faculty Campaign

National Institute of Dental Research  
1994 Ad hoc Reviewer, Small Business Innovation Research Grants

New Jersey Commission on Science and Technology  
1999 Ad hoc Reviewer, R&D Excellence Program

University of Medicine and Dentistry of New Jersey  
2002- Member, Dean's Advisory Board, New Jersey Dental School  
2004- Member, Strategic Planning Subcommittee on Strategic Connections to New Jersey's Pharmaceutical Industry

EDITORIAL ACTIVITIES:  
1965-67 Assistant Editor, Journal of Oral Pharmacology and Pharmacotherapeutics  
1977-81 Ad hoc Reviewer, Archives of Oral Biology, Journal of Dental Research  
1991-95 Ad hoc reviewer: Journal of Periodontology; Archives of Oral Biology  
2002- Manuscript reviewer, Journal of the American Dental Association

PRIVATE PRACTICE EXPERIENCE:  
I have been a participant in the intramural faculty practice plan at each of the schools or hospitals at which I have been between 1973 and 1987.

COMMITTEE ASSIGNMENTS:
Harvard School of Dental Medicine
  Dean's Faculty Committee
  Undergraduate Admissions Committee

New Jersey Dental School (1973-74)
  Executive Faculty Committee
  Curriculum Committee
  Chairman, Subcommittee on Curricular Evaluation
  Search Committee for Chairman of Periodontics

School of Dentistry, State University of New York at Buffalo
  Curriculum Committee
  Facilities Planning Committee
  Student Research and Honors Committee
  Research Library Committee

School of Dentistry, University of Louisville
  Postgraduate Academic Advisory Committee (Chairman, 1980-81)
  Search Committee for Chairman of Physiology
  Board of Governors, Faculty Practice Plan

Morristown Memorial Hospital
  Medical-Dental Staff Executive Committee
  Medical Education Committee
  Long Range Planning Committee
  Medical Isotope and Radiation Safety Committee
  Developmental Disabilities Advisory Committee
  Diabetes Education Advisory Committee
  Outpatient Services Committee
  Grants Committee
  Research Advisory Committee
  Institutional Review Board
  Cancer Committee

**GRANTS AND CONTRACTS:**

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<th>Year</th>
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<td>1974-79</td>
<td>&quot;Role of Mast Cells in Gingival and Periodontal Lesions&quot;, National Institute of Dental Research, DE-04162</td>
<td>$22,500</td>
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<td>1979-80</td>
<td>&quot;Characterization of Surface Antigens of S. Mutans&quot;, National Institute of Dental Research, DE-05017</td>
<td>$29,568 (Co-Investigator)</td>
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<td>1974-76</td>
<td>&quot;Studies on the Ultrastructure of Human Gingival Epithelium&quot;, BRSG/NSF and Special Funds, SUNY at Buffalo</td>
<td>$3,000</td>
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<td>1980-81</td>
<td>&quot;Ultrastructural and Clinical Studies of Periodontal Diseases&quot;. BRSG Funds, University of Louisville School of Dentistry</td>
<td>$5,000</td>
</tr>
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<td>1983-87</td>
<td>&quot;Dental Program for the Developmentally Disabled&quot;, Division of Mental Retardation, New Jersey Department of Human Services, Contract No. EP094PC</td>
<td>$100,264 per year</td>
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<td>1984-87</td>
<td>&quot;Residency Training in the General Practice of Dentistry&quot;, Division of Associated and Dental Health Professions, Department of Health and Human Services, D30 DHl2079</td>
<td>$150,409</td>
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PUBLICATIONS:


GUEST EDITORIALS:

ABSTRACTS:


