Institution: University of Bristol

Unit of Assessment: 4 – Psychology, Psychiatry and Neuroscience

Title of case study: Developing new toothpastes to improve well-being for people who suffer with sensitive teeth

1. Summary of the impact

Research conducted by Professor Matthews at the University of Bristol, has led to the alleviation of pain for people who suffer from sensitive teeth through the development of improved desensitising toothpaste products sold globally by leading toothpaste manufacturers. In 2000 and 2007, Matthews' group provided the first direct evidence that fluid flow in dentinal tubules results in activation of the sensory nerves in teeth and that this fluid flow is responsible for the pain associated with sensitive teeth. This evidence underpinned the development of a new generation of desensitising toothpastes, which act by blocking the dentinal tubules and preventing the movement of fluid, providing pain relief from thermal sensitivity.

2. Underpinning research

Background

Professor Matthews has worked at the School of Physiology and Pharmacology, University of Bristol since 1966; he retired in 2004 and continues his research as a Senior Research Fellow and Emeritus Professor. His published work represents a substantial and unique contribution to understanding the causes of sensation derived from teeth and jaws, especially causes of dental sensitivity. His research has focused on understanding the sensory nature of dentine – the porous, but hard, middle layer between the inner pulp and the outer enamel of teeth. He has made significant contributions toward understanding how stimuli applied to dental hard tissues result in sensation.

Matthews has collaborated with colleagues in Bangkok, where orthodontic treatment of adults commonly involves tooth extraction. This practice is rare in most Western countries as treatment is usually carried out in childhood, yet it provides a very valuable resource for this research.

Investigating the causes of dental sensitivity

Dentine's porosity derives from microscopic tubes – dentinal tubules – which open to the inner pulp as well as to the outer coating of a tooth's enamel. Though early research showed that dentine did not appear to contain nerve fibres, it was nonetheless known to be sensitive to external stimuli. Research in the 1960s from Stockholm introduced the hypothesis that intradental nerves are stimulated by the flow of fluids through dentinal tubules.

Mathews' work over many years established the experimental techniques required to test this hypothesis. He developed novel techniques for recording from intrapulpal sensory nerves in experimental animals. In 2000 and 2007, he used these techniques to characterise the properties of sensory receptors associated with pain in teeth using a cat model [1, 2].

Matthews and his colleagues at Bristol also developed techniques for the measurement of fluid flow through dentine *in vivo,* and are the only research group to date that have been able to obtain a continuous record of fluid flow from dentine in living teeth. In order to demonstrate a correlation between the discharge of nerves supplying dentine and flow in the dentinal tubules, Matthews developed a system for recording fluid flow rates, which was several orders of magnitude more sensitive than any used previously. By combining his techniques for recording from intrapulpal sensory nerves and measuring flow rates through the dentinal tubules, Matthews was able to provide the first direct experimental evidence that the firing of intrapulpal sensory nerves was

caused by fluid flow in dentinal tubules [1, 2]. also In 2007, Matthews and his colleagues were able to establish the direction and magnitude of the flow produced by stimuli that evoked pain in humans [3].

Evidence that potassium salts in desensitising toothpastes are ineffective

Desensitising toothpastes, such as Sensodyne, claimed to reduce dentine sensitivity by using high concentrations of potassium salts that were thought to reduce the sensitivity of the nerve endings in dentine. Matthews and his colleagues studied this potential mechanism of desensitisation and showed experimentally that topical applications of potassium salts to exposed dentine neither reduced the response of nerves in teeth in experimental animals [4] nor the pain experienced by human subjects [5]. As a result of these studies, and several clinical trials conducted by others that have shown no more than a placebo effect of these toothpastes, new toothpastes have been developed that aim to block the dentinal tubules.

3. References to the research

[1] Andrew, D. and Matthews, B. (2000) 'Displacement of the contents of dentinal tubules and sensory transduction in intradental nerves in the cat', *Journal of Physiology,* 529 (3): 791-802. DOI: 10.1111/j.1469-7793.2000.00791.x

[2] Vongsavan, N. and Matthews, B. (2007) 'The relationship between the discharge of intradental nerves and the rate of fluid flow through dentine in the cat', *Archives of Oral Biol*ogy, 52(7): 640-7. DOI: 10.1016/j.archoralbio.2006.12.019

[3] Charoenlarp, P., Wanachantararak, S., Vongsavan, N. and Matthews, B. (2007) 'Pain and the rate of dentinal flow produced by hydrostatic pressure stimulation of exposed dentine in man', *Archives of Oral Biology,*52(7): 625-31. DOI: 10.1016/j.archoralbio.2006.12.014

[4] Wanachantararak, S., Vongsavan, N., and Matthews, B. (2011) 'Electrophysiological observations on the effects of potassium ions on the response of intradental nerves to dentinal tubular flow in the cat', *Archives of Oral Biology,* 56: 294-305. DOI: 10.1016/j.archoralbio.2010.10.005

[5] Ajcharanukul, O., Kraivaphan, P., Wanachantararak, S., Vongsavan, N., and Matthews, B. (2007) 'Effects of potassium ions on dentine sensitivity in man', *Archives of Oral Biology* 52: 632-639. DOI: 10.1016/j.archoralbio.2006.12.015

4. Details of the impact

Matthew's research has had significant impact with respect to:

1) the well being of people who suffer from sensitive dentine (Health Impact)

2) the worldwide sales by GSK and Colgate of newer desensitizing toothpastes (Economic Impact)

New generation of desensitising toothpastes underpinned by Bristol research

Matthews' revelation of the mechanism behind dentine sensitivity has led to a new generation of desensitising dentifrices that contain compounds to form plugs that block the dentinal tubules, stopping movement of fluid through the tubules and preventing activation of the pulpal nerves. In 2009, results of a breakthrough technology that incorporated arginine and calcium carbonate into a daily-use toothpaste were published in a special issue of *The Journal of Clinical Dentistry.* This new generation of toothpastes worked by plugging and sealing dentin tubules [a, cites Matthews and Vongsavan (1994) *Arch Oral Biol* 39 (Suppl):87S-95S].

Improved well being for people who suffer from sensitive teeth

Hypersensitive, exposed dentine at the neck of a tooth is a very common cause of pain. Studies have estimated that "*dentine hypersensitivity affects up to 57% of dental patients of different*

lifestyles and cultures, and appears to peak between the ages of 20 and 40 years" [b] . Colgate Sensitive Pro-Relief (also marketed as elmex Sensitive Professional) contains 8.0% arginine, calcium carbonate and 1450 ppm fluoride and has been shown through numerous clinical trials to provide significant reductions in dentine hypersensitivity both immediately after application and over long-term use, with one study showing a 266% improvement over baseline values after four weeks [c, cites 5].

Industry benefits from global sales of new desensitising toothpastes

In 2011, Colgate's share of the global toothpaste market was 44.7% [d]. It's line of sensitive toothpastes were credited for an improved market share in North America, continued leadership in oral care in Latin America and expansion into European, South Pacific, Greater Asia and African markets [d]. Colgate incorporates Matthews' research indirectly in its public information regarding the mode of action of Sensitive Pro-Relief [e].

Matthews acted as a scientific consultant to GlaxoSmithKline (GSK) on mechanisms and treatment of dentine hypersensitivity in 2003, prior to them buying Sensodyne, and again in 2009, when they sought scientific justification for the inclusion of potassium chloride or nitrate in toothpastes as a desensitising agent. Matthews shared his experimental evidence that the potassium ions [4-5] included in Sensodyne toothpastes, did not reduce sensitivity. In 2010, GSK launched Sensodyne Rapid Relief with the active ingredient strontium acetate, which provides a physical plug for the dentinal tubules. In 2013, GSK overtook Colgate in the sensitivity segment [f] and won product of the year for its latest desensitising product, Sensodyne Repair & Protect [g].

5. Sources to corroborate the impact

[a] Petrou, I *et al.* (2009) 'A breakthrough therapy for dentin hypersensitivity: how dental products containing 8%arginine and calcium carbonate work to deliver effective relief of sensitive teeth', *The Journal of Clinical Dentistry,* 20 (Special Issue): 23-31. <http://www.chem.ucla.edu/dept/Faculty/gimzewski/publications/213_2009_JClinDent.pdf> This publication links Matthews' identification of the mechanism underlying dentine sensitivity with the mode of action of new generation desensitising toothpastes.

[b] Li, Y. *et al.* (2011) 'Comparison of clinical efficacy of three toothpastes in reducing dentin hypersensitivity', *The Journal of Clinical Dentistry*, 22 (Special Issue): 113-120. <http://www.colgateprofessional.gr/LeadershipGR/ProfessionalEducation/Articles/Resources/pdf/Journal_of_Clinical_Dentistry_Pro-Argin_Special_Issue_2011.pdf> [cites 5].

[c] Docimo, R. *et al.* (2011) 'Comparative evaluation of the efficacy of three commercially available toothpastes on dentin hypersensitivity reduction: an eight-week clinical study', *The Journal of Clinical Dentistry,*22 (Special Issue): 121-127. <http://www.gaba-dent.de/data/docs/download/8148/de_DE-1996/J-Clin-Dent-2011-Pro-Argin-vs-strontium.pdf#page=21-> [cites 5].

[d] Colgate-Palmolive (April 28, 2011) *Colgate announces 1st quarter results – diluted earnings per share in line with expectations* (press release). URL: http://investor.colgate.com/releasedetailpop.cfm?ReleaseID=572739 [accessed online 17th Sept 2013]. Evidence that Colgate's line of desensitising toothpastes has led to business expansion and financial gains for the company.

[e] Colgate (2013) *How does Pro-Argin Technology Work?* (website) URL: http://www.colgatesensitiveprorelief.com.au/articles/how-does-pro-argin-work?callingPage=/how-does-it-work&title=How%20does%20it%20Work:%20Article [accessed online 17th Sept 2013].

[f] Pinto, V.S. (April 18, 2013) 'GSK overtakes Colgate in sensitivity segment: Nielsen', *Business Standard* (online news). URL: http://www.business-standard.com/article/companies/gsk-overtakes-colgate-in-sensitivity-segment-nielsen-113041800016_1.html [accessed online 17th Sept 2013].

[g] Talking Retail (January 25, 2013) '2013 Product of the Year winners announced' (online news). URL: http://www.talkingretail.com/news/industry-news/2013-product-of-the-year-

winners-announced [accessed online 17th Sept 2013].