STUDIES ON THE PHARMACOLOGY AND TOXICOLOGY OF MATERIALS APPLIED TO DENTINE

A thesis submitted for the degree of Doctor of Dental Science in the University of Adelaide

by

Wyatt Roderic Hume B.Sc.Dent. (Hons)., B.D.S., Ph.D.

Department of Dentistry

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ABSTRACT

The studies described in the thesis were concerned with the release, diffusion through dentine, local pharmacology and local toxicology of active components of materials which are applied to teeth with therapeutic intent.

Zinc oxide-eugenol (ZOE) mixtures are known to be therapeutic when applied to intact dentine, but toxic when applied to soft tissue. Eugenol, the probable active component of ZOE, was shown to be a vasodilator in two in vitro models, with characteristics which indicated that the oil reversibly depressed smooth muscle contractility, with slow onset and recovery. This phenomenon was unusual. The oil also depressed cell respiration in homogenates of human dental pulp and in mouse fibroblasts, with a threshhold at 10^{-4} mol/L and a maximum at 10^{-3} mol/L, concentrations which corresponded closely to those causing vasodilatation. Cells survived indefinitely in the presence of 10^{-4} mol/L or less, but died with higher concentrations, the time of exposure necessary for death decreasing as concentration increased. The release of eugenol from ZOE into and through dentine in vitro was examined; such release was markedly less than release into water, and was sustained at a low level for many weeks. The concentration gradient across dentine between cavity and pulp was determined in vitro; it was shown that concentrations above 10^{-4} mol/L were unlikely to develop in the odontoblastic or sub-odontoblastic layer if dentine was intact, but that much higher levels were likely to develop in wet tissue adjacent

to ZOE. On the basis of these various data a resolution of the paradox of the therapeutic and toxic effects of ZOE was proposed.

The method of study of ZOE release was combined with test methods for cytotoxicity in vitro to give a new model system for the prediction of pulpal toxicity of restorative materials where the potential toxins might be unknown. The system was the first in vitro test in which ZOE was shown to be non-toxic; previous systems had the major shortcoming that ZOE, which is bland when applied to dentine in vivo, killed all cells. The new model system was used to demonstrate the effects of dentine etching on the potential for toxicity of resin materials, and the protective effect of lining materials. A similar experimental system was used to examine the movement of hydrogen ions (H^+) and hydroxyl ions from various acids and alkalis through human dentine in vitro; unexpectedly, the diffusion of H^+ from strong inorganic acids occurred very slowly or not at all, with observation periods up to 16 days. It was suggested that this poor penetration was because of the very effective buffering of H^+ by dentine. Finally, it was shown that the toxicity of glass ionomer cement in vitro was markedly reduced by intervening dentine; proposed mechanisms for the reduction were limited water availability at the dentine-cement interface and thus limited dissolution of components, buffering of acid components, or other chemical interactions with dentine.