CHAPTER 2

REVIEW OF LITERATURE

Epidemiology of Caries

Epidemiology of oral health in Thai children and adolescents revealed that dental caries continues to be a disease with a high frequency of occurrence. Results from the most recent national oral health survey indicate that half of the 12-year-olds were not caries free and most of carious or filled surfaces were occlusal surfaces (6). This attributes to the morphology of the occlusal surfaces, with deep pits and fissures that are susceptible to decay. The development of pit and fissure caries continues to occur from childhood when the permanent teeth first erupt throughout adolescence and early adulthood (7). Analysis of caries incidence by tooth type clearly demonstrates that first and second permanent molars are the most caries-prone teeth in the mouth. For children and young adults, the occlusal caries rate is relatively high on the occlusal surfaces and low in the proximal areas, which makes this age group the most suited for sealant application. In older age groups, the benefit from sealant application may be less due to the relatively lower caries incidence of new occlusal lesions and higher rates of proximal caries (20). Although the use of fluoride has been shown to be highly effective in prevention of caries on smooth surfaces, the surfaces with pits and fissures receive minimal caries protection from either systemic or topical fluorides. These findings reaffirm the need for specific protection on the pit and fissure areas of those teeth.

The susceptibility of the occlusal surfaces to caries is related to the anatomy of deep pits and fissures which can easily trap food and microorganisms. Thoroughly clean of these areas is difficult. Moreover, the base of a pit or fissure is found to be relatively close to the dentinoenamel junction, leading to rapid caries progression due to thin enamel.

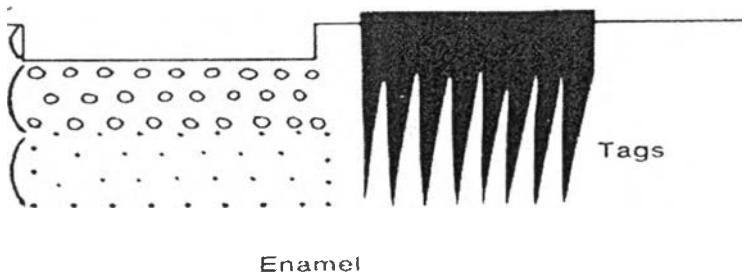
Prevention of Pit and Fissure Caries

'Occlusal sealants' or known as ' *pit and fissure sealants*' is defined as the application and mechanical bonding of a resin material to an acid-etched enamel surface, thereby sealing existing pits and fissures from the oral environment. The retention to the tooth is gained by conditioning enamel surface with an appropriate acid. This mechanism prevents bacteria from colonizing in the pits and fissures, and the sealant acts as a physical barrier between the caries susceptible pits and fissures and the rest of the oral environment (21, 22).

The development of pit and fissure sealants was based on the discovery that etching enamel with phosphoric acid increased the retention of resin restorative materials. An initial study evaluating the effects of acid-etching on enamel were performed by Buonocore in 1955 (23). The first sealant material that involved the acid-etch technique was introduced in the mid-1960s (11, 24).

The retention of pit and fissure sealant materials to the tooth is the result of the acid modifying the enamel surfaces of the teeth. Pretreatment of tooth enamel with phosphoric acid creates microporosities on the surface where resin sealant can penetrate. Infiltration of the etched enamel results in formation of resin tags, which provide the mechanical means for sealant retention (Figure 2.1). Typically, resin tags penetrate etched enamel to a depth of 25 to 50 μm (7).

Figure 2.1 Diagram showing the retention of pit and fissure sealant material to the tooth surface. The resin sealant penetrates into porosities created by acid exposure, forming retentive resin tags (from Pinkham JR: Pediatric Dentistry: Infancy Through Adolescence, 3rd ed. Philadelphia, W.B. Saunders Company, 1999.)



Types of Pit and Fissure Sealants

The most used pit and fissure sealant is a reaction product of bisphenol A and glycidyl methacrylate, an acronym of Bis-GMA. The vast majority of restorative resin materials are based on the Bis-GMA formulation. Restorative resin materials differ from sealants in that they include filler particles such as quartz, glass, and porcelain to improve their strength, whereas the majority of sealants either are unfilled or have relatively few filler particles added (7, 25).

Although sealants are based on similar basic components, a wide variety of materials are available. They often are classified by various properties, such as method of polymerization, composition, fluoride releasing property, color, etc. A major difference between sealants in the market is the method of polymerization. Two methods of polymerization have been employed. Autopolymerization (chemically initiated, or 'chemical cured') systems involve mixing two liquids, a base resin and catalyst resin. The material sets by an exothermic reaction, usually within 1 to 2 minutes. Photoactivated (light-initiated, or 'light cured') polymerization is currently the most popular means for curing sealant. In this system, polymerization is initiated by exposure to visible light of 470 nm wavelength. The benefits of the visible light cured sealant

include the following: the material sets in 10 to 20 seconds; elimination of the mixing step, therefore reducing air bubbles that may occur with chemical cured sealants.

Sealant materials with additional ingredients, e.g. filler particles, color or fluoride, are commercially available. The addition of filler particles to the sealants appears to have little effects on clinical results (25). Filled and unfilled sealants penetrate the fissures equally well (26) and have similar retention rates (27, 28).

Pit and fissure sealants are available as clear, opaque or tinted. No product has demonstrated a superior retention rate. However, the tinted and opaque sealants have the advantage of more accurate evaluation by the dentist at recall visits (25). Rock et al., found significant differences in the accuracy to determine retention rate when three dentists identified a clear and an opaque fissure sealant (29).

The well-known property of fluoride in caries prevention has brought about the attempt to include fluoride in sealant. Both fluoride-releasing and non fluoride-releasing sealants are available. All materials currently available appear to provide comparable clinical results (25). There is not enough evidence to clearly demonstrate the advantage of one type of sealant over others. Therefore, selection of a specific sealant product depends on clinician's preference.

Indications for Pit and Fissure Sealants

Sealant application is indicated for both children and adults who are at moderate or high risk of dental caries, and have existing anatomically susceptible pits and fissures. Teeth with the highest priority for sealant placement are usually the first and second permanent molars (30, 31). Primary molars and premolars generally are not as susceptible to caries as permanent molars because of their shallow occlusal structure.

Sealant Effectiveness

Because sealants are effective as long as they remain firmly adhered to the tooth, an assessment of their clinical success involves: (1) a determination of the

occlusal caries reduction associated with their use; and (2) an evaluation of their clinical retention (32).

Clinical studies to evaluate the caries- inhibitory potential of sealants usually compare sealant-treated teeth to untreated contralateral teeth in the same mouth. Thus, the treated and control teeth are exposed to the same intraoral environment, the only difference being the intervention of the sealant. Nevertheless, after the American Dental Association granted acceptance to a marketed sealant, it would be unethical to conduct the no treatment study design (33).

Since sealants contain no active ingredients, their preventive function is achieved by their adhering to the enamel surface, physically occluding the pits and fissures from the rest of the oral environment. As long as the sealants adhere firmly to the teeth, they are considered caries preventive. Thus, in this context, the longevity of sealant coverage, i.e. clinical retention, is the determinant of sealant success.

Numerous clinical trials, ranging in length from 6 months to 20 years, have been carried out to assess retention rates, caries incidence, and the effectiveness of sealants in preventing pit and fissure caries. In the majority of clinical studies, a single application of sealant is reported, followed by periodic evaluations to determine the retention rate and caries incidence. Based on the literature reviewed, Weintraub reported that the median complete retention, following one application of sealant, declines from 92 percent after one year to 66 percent after seven years (20).

In a meta-analysis to analyze the effectiveness of fissure sealants in preventing dental caries, Llodra and colleagues reviewed published studies during 1975 to 1990 and found that the overall effectiveness of autopolymerized resin was 71%. Additionally, the effectiveness in caries prevention of sealants decreased with time (34).

Table 2.1 presents the long-term retention rates of pit and fissure sealants. It is clearly seen that the resin sealants do stay on the majority of teeth for a considerable length of time. Resin material is progressively lost from the tooth surface as time goes by. Following one application of sealant, percent effectiveness and complete

retention decline over time (8, 35). The first six months was the most critical period where the highest sealant loss is observed (36), followed by a further progressive loss of about 5 to 10% per year (8, 36). Therefore, reapplication of a sealant is recommended to maintain its preventive effect over time (37).

Table 2.1 Long-term retention of pit and fissure sealants

First author	Year	Teeth	Age (Years)	Observation period (Years)	Complete retention (%)
Mertz-Fairhurst (38)	1984	First permanent molars	<8	1	95
				7	66
Simonsen(39, 40)	1987	First permanent molars	5-15	5	82
	1991			10	57
				15	28
Wendt(41, 42)	1988	First and second permanent molars	6-9	8	80
				10	-
	2001			20	65
Romcke(43)	1990	First permanent molars	3-16	8	59
				10	41

Several factors influencing sealant retention include type of sealant, the position of teeth in the mouth, the clinical skill of the operator and the age of the child being treated (33). Better sealant retention was reported for the more anterior teeth and the more skilled or clinically experienced operators produce better sealant retention. Moreover, the younger the child, the more difficult to maintain a dry field because of uncooperative behavior, resulting in poor retention. The most common reasons for sealant failure are inadequate isolation and subsequent contamination (31). Sealant success is positively associated with eruption status of teeth because in the more fully erupted teeth, the operator has greater ability to maintain a dry field (30). It should be emphasized that sealant success depends on meticulous operator technique (25).

The highest rate of sealant loss occurred during the first 6 months (44, 45) through the first year following sealant application (33, 36). The initial loss of sealant was attributed to factors at the time of application, e.g. errors in technique or material failure whereas gradual additional loss is considered to result from occlusal wear, shearing forces, and marginal failure (8).

The application of dental sealants is minimally invasive and can be done by auxiliary personnel. Sealants have been shown to be highly effective in preventing pits and fissure caries. The reduction in occlusal caries from this preventive method has been impressive since the results are usually achieved with a single treatment.

The efficacy of sealant is based on the retention of the sealant. With complete retention, sealed surfaces are virtually impervious to decay whereas some studies have shown that "partial loss" of sealant leaves a tooth equally susceptible to caries as a unsealed control tooth (8, 35, 46). Although sealants are very effective in preventing pit and fissure caries when completely retained on the tooth surface (47), deficient sealants were at higher risk of developing carious lesions compared with fully sealed surfaces (8, 48, 49).

Cost-Effectiveness of Sealants

Pit and fissure areas are generally recognized as highly susceptible to caries and least likely to benefit from systemic or topical fluoride. Placement of sealant to prevent caries in pits and fissures are therefore considered cost effective (35, 50). It is also recognized that the cost-effectiveness is dependent upon a number of factors that are related to its use, e.g. the caries prevalence in the population; the different tooth types (premolar, molar); and the retention of sealants (51). The caries rate in premolars are generally lower than in molars. In populations with an average caries rate it has been calculated that 25-40 sealants must be placed in premolars to save one surface from becoming carious, while the corresponding rate is 5-10 for molars (8). If the retention rate is low, the need for resealing and restorative treatment of carious fissures after sealant loss increases, which reduces the cost-effectiveness of sealant.

The total expense incurred with sealant placement must be compared with the cost of restoration of the teeth should sealants not be placed and caries eventually develop (7). Appropriate placement of a sealant to an at-risk surface would provide significant initial savings with some additional maintenance expenses secondary to sealant loss and caries development over time. When comparing the cost of a preventive program including sealants with the expense of restoration placement, one must also consider the intangible value of maintaining caries-free tooth surfaces and promoting a low incidence of dental caries in the child and adolescent population.

Although the cost of sealant procedure and the chair time spent are much less than restorative treatment, the unit cost of this technique is still high due to cost of imported product. If the sealant is produced locally in Thailand, consequently the cost will be reduced.

Risk Associated with the Use of Sealants

The risk associated with the use of pit and fissure sealants is minimal. Sealants are safe when properly placed using standard materials and procedures (9, 31). In addition, sealant placement is a non-invasive technique, which avoids unnecessary loss of tooth structure.

In considering the possible systemic and local effects of the use of sealants. No systemic toxicity from the clinical use of sealants has been reported. To date, there is only one case of an adverse reaction to a pit and fissure sealant in the literature (52). The report was of a six-year-old girl who developed an allergic reaction to the application of pit and fissure sealants on her first permanent molars.

Concerns have been expressed that the placement of sealants in excessive thickness could cause occlusal disharmonies. However, there is no evidence to indicate that this has been a significant problem.

Recently, there were safety concerns regarding leaching of Bisphenol-A (BPA) and Bisphenol-A dimethacrylate (BPA-DMA) from composites and sealants, and a possible estrogenic effect (53, 54). It is known that incomplete conversion of BPA during

the setting reaction may allow this unreacted monomer to be released into the oral environment. BPA and BPA-DMA possess estrogen-like effects on cultures of breast cancer tumor cells, and this was the basis for safety concerns regarding sealants and composite resins. It appeared that based on the presently available evidence, there was no potential concern about the estrogenicity of dental sealants (55-60) except from publications from one group of researchers (53, 54). No reports of adverse health effects have been attributed to the leached components of dental sealants.

Local-Made Sealants

The first local-made pit and fissure sealant was developed by the National Metal and Material Technology Center (MTEC). Several studies have demonstrated the mechanical and physical properties of this material to be similar to imported standard materials including the hardness, diametral tensile strength, depth of cure, water sorption and solubility, and thickness of unpolymerized layer (14-17). In addition, biological and toxicity tests in vitro show favorable results (18). At present, the materials are available in the market under a trade name of 'Dent Guard', a commercial kit consists of an etching gel, and one bottle of each clear and opaque sealant.

The first clinical study of Dent Guard was published in 2001, comparing the retention rates of the clear type material to the standard sealant of similar appearance. After one-year follow-up, the new sealant had the complete retention rate of 47.4% compared to 65.3% for the control material, Delton (Dentsply, U.S.A.) (19).

The Faculty of Dentistry, Chulalongkorn University aims to develop dental materials for domestic use. The development of a light-activated pit and fissure sealant was the very first product of this " CU Dental Products" project. During 2000-2002, the research group has developed a light-initiated sealant with optimal physical properties and safe for use in the clinical setting. The material was tested for its physical and mechanical properties according to the ISO standards. In addition, biological property was evaluated regarding toxicity to cell culture and biocompatibility test in Vista rats. The findings reveal that the experimental material is comparable to those of imported materials in terms of physical, mechanical and biological properties. Thus, a

randomized clinical trial is needed in order to support the effectiveness of this recently developed local material.

Half-Mouth Design

Many of the first sealant trials used a randomized, half mouth design where children with pairs of eligible, sound, first permanent molars were selected so that one member of the pair could be sealed and the other molar left unsealed (47).

The split mouth or half mouth study design for clinical trials is frequently used in dental research (61). It is defined as divisions of the mouth that constitute the experimental units which are randomly assigned to treatment modalities. The design allows restorative materials, local caries preventive agents or techniques, such as fissure sealants, to be tested and compared. The method is unsuitable for testing agents that affect the whole mouth, such as fluoride rinses or gel applications, because the effect cannot be limited to the test sites involved. In other words, validity issues such as carry-over effects should always be carefully evaluated. Since the sites are subjected to almost identical oral environments, the method is able to control for potentially confounding factors, particularly those affected by physiological characteristics of the subject, dietary, oral hygiene habits, and preventive regimens. Possible bias due to better oral hygiene on the left side of the mouth in right-handed people may be eliminated by random allocation of test and control sides. The split mouth study design is potentially very efficient.

The principal advantages of using split-mouth design for clinical investigation are the elimination of subject factor from the experimental error, and it is an economical usage of patients (62, 63). However, the essential characteristic of this design is that statistical comparisons are made on a within-patient basis, not on a between-patient basis.

Equivalence Trial

The gold standard in clinical research is the randomized placebo controlled double blind clinical trial. This design is favored for confirmatory trials carried

out as part of the phase III development of new medicines. Because of the vast number and range of medicines already available, however, new medicines are increasingly being developed for indications in which a placebo control group would be unethical. In such situations one obvious solution is to use as an active comparator an existing drug already licensed and regularly used for the indications in question. When an active comparator is used, sometimes the new treatment is expected to be better than the standard. The objective is thus to demonstrate this fact unequivocally. Sometimes the new treatment is simply expected to match the efficacy of the standard treatment, but with advantages in safety, convenience, or cost. Under these circumstances the objective of such trial is to show equivalent efficacy- the so-called "equivalence trial". The aim of an equivalence trial is to show the therapeutic equivalence of two treatments, usually a new drug under development and an existing drug for the same disease used as a standard active comparator (64).