Abstracts of Theses Approved for the MSc at the School of Dental Sciences, Universiti Sains Malaysia, Health Campus, Kubang Kerian, Kelantan, Malaysia

FABRICATION AND CHARACTERIZATION OF EXPERIMENTAL NANOCOMPOSITES FOR DENTAL RESTORATION

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Introduction: Currently, restorative dental composites have become preferred among patients due to their aesthetic characteristic and also their durability. The high costs of composites, as well as the rising demand by patients have lead researchers to produce a local product with equivalent standard as compared to the commercially available dental composites. Recently, monodispersed, spherical silica nanofillers with a size range of 10–20 nm were successfully synthesized via a sol-gel process and have a great potential to be used in fabrication of dental composites. Therefore, this present study was carried out to fabricate and characterize the experimental dental nanocomposite from the synthesized nanosilica fillers.

Methods: Dental composites, namely experimental nanocomposite 1 (ENC1) and experimental nanocomposite 2 (ENC2) with two different filler content, 30 and 35 wt% respectively were fabricated, molded, and polymerized with a light curing unit for 40 s. The properties that were tested including their flexural strength, modulus, compressive strength, micro hardness, degree of conversion, volumetric shrinkage, water sorption, solubility, surface roughness as well as filler distribution. The data obtained were statistically analyzed with one-way ANOVA with the level of significance $P = 0.05$. Various type of commercial composites i.e. FiltekTM Z350 (nanocomposite), Spectrum® TPH®3 (microhybrid), Z100TM (hybrid) and Durafill® VS (microfilled) were chosen to compare their properties with the experimental nanocomposites. The properties of composites were also referred to the ISO and ANSI/ADA No. 27 requirements.

Results: From the results obtained, it can be summarized that the experimental nanocomposites and commercial composites complied with the ISO and ANSI/ADA No. 27 requirements. Similar properties can be found between experimental nanocomposites and Durafill® VS (microfilled composite) regarding their flexural strength, modulus, compressive strength, hardness and also surface roughness. These properties are sufficiently to be applied at the anterior restoration. However the properties of experimental nanocomposites were still inferior compared with the posterior restorative composites (FiltekTM Z350, Spectrum® TPH®3 and Z100TM) particularly in flexural strength, modulus, hardness, shrinkage and water sorption. Comparing both of experimental nanocomposites, ENC2 seems to have better properties compared with ENC1 except for compressive strength. Overall, the main factor that contributes to the properties of dental composites is inorganic fillers including their filler content, size, morphology and distribution. Highly filled composites exhibited excellent properties than the composites with low filler content.

Conclusion: The synthesized nanosilica might be an option to be used for making a dental composite, however concerns also arise regarding their problem of achieving the high filler loading, which limit their application only for making anterior composite.

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ASSOCIATION OF p53 GENE MUTATIONS AND HPV E6 ONCOGENE EXPRESSION IN ORAL SQUAMOUS CELL CARCINOMA

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Introduction: Oral cancer, a subgroup of head and neck cancer is estimated by World Health Organization (WHO) to be the eighth most common cancer worldwide. Genetic alteration is an important event in tumourigenesis in which mutations of the p53 tumour suppressor gene are the most commonly encountered in oral squamous cell carcinoma (OSCC). High-risk human papillomaviruses (HR-HPV) types -16 and -18 are identified in the overwhelming majority of HPV-positive tumour which possesses molecular-genetic alterations indicative of E6 viral oncogene-induced alteration.

Methods: RNA samples were extracted from 65 tissue samples of oral cancer patients, which were confirmed as squamous cell carcinoma (SCCs) by histopathology reports at Universiti Malaya's Oral Cancer Research Coordination Centre (OCRCC); whereas 20 samples from normal individuals in the School of Dental Sciences, Universiti Sains Malaysia were recruited. The RNAs were subsequently reverse-transcript to cDNA and subjected to p53 amplification using three sets of primers 1F/1R, 2F/2R and 3F/4R which amplified exons 2 to 11 of p53 gene. The samples were also amplified using MY09/MY11 and GP5+/GP6+ primers to detect HPV-DNA in the samples. All the amplified products were sequenced for

p53 mutational analysis and HPV typing. Following that, the expression of E6 oncogene was conducted on all samples using Real-Time PCR.

Results: p53 gene mutations were found in 61.5% (40/65) of OSCC subjects and 20% in controls. Among both OSCC subjects and controls, 44/85 (51.8 %) was found to have p53 gene mutation. The analysis showed that the presence of p53 mutation in OSCC was statistically significant (OR = 6.4 (95 % CI 1.92, 21.34); P = 0.003). The prevalence of HPV infection among subjects was 41.2% (35/85) with the commonest type being HPV-18 (67.6%), HPV-16 (26.5%), and HPV-33 (2.9 %). The analysis demonstrated that HPV status was significantly associated with OSCC (OR = 20.8 (95% CI 2.632, 164.969); P = 0.004). HPV E6 mRNAs were found in 20 out of 85 (23.3%) OSCC subjects but none in controls. Therefore, the total prevalence of E6 expression in subjects was 23.3 %. E6 mRNA was significantly associated with mutation of p53 gene in OSCC (OR = 5.603 (95% CI 1.109, 28.312); P = 0.037.

Conclusion: E6 oncogene expression was associated with p53 gene mutations in oral squamous cell carcinoma (OSCC) suggesting that this protein is responsible in disrupting cell cycle regulation and also causes alteration in p53 gene.

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RELIABILITY OF THREE METHODS OF MIXED DENTITION ANALYSIS AND DEVELOPMENT OF NEW REGRESSION EQUATIONS FOR PREDICTING THE SIZE OF UNERUPTED CANINES AND PREMOLARS IN MALAY POPULATION

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Introduction: To firstly determine the reliability of Tanaka-Johnston equations, Moyers tables, and Jaroontham and Godfrey equations, and secondly to develop new regression equations for predicting the mesio-distal width of unerupted canines and pre-molars in Malay population.

Methods: Sample consisted of 200 study models with fully erupted permanent dentition, age ranged 13–21 years, mild crowding, or spacing and no history of orthodontic treatment in Malay subjects having with at least three generations of Malays. Mesio-distal widths of all maxillary and mandibular teeth (except 2nd and 3rd molars) were measured with an electronic digital caliper. A paired t-test, independent t-test, correlation and simple linear regression analyses were performed on the actual and predicted values and new regression equations were developed.

Results: Tanaka- Johnston equations significantly

overestimate the actual mesio-destal widths of tooth (P < 0.001). The Moyers tables at 75th percentile level also overestimate (P < 0.005) the actual widths in the maxillary arch in males and the mandibular arch in females, but the differences were not significant for the mandibular arch in males and maxillary arch in females. The Jaroontham and Godfrey equations tend to overestimate (P < 0.001) the actual widths in maxillary arch in males and mandibular arch in females. However, the differences were not significant for the mandibular arch in males and maxillary arch in females. The correlation coefficients between tooth groups (mandibular incisors and maxillary first molars) with canines and premolars were high; 0.77 in mandible and 0.72 in maxilla. Regression equation for the maxillary arch (males, 0.49 X + 0.64; females, 0.45 X + 0.77) and the mandibular arch (males, 0.50 X + 0.30; females, 0.49 X + 0.13) were derived.

Conclusion: New regression equations are more accurate and applicable in Malay population than Moyers tables, Tanaka-Johnston equations, and Jaroontham and Godfrey equations.

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MICROSATELLITE INSTABILITY AND LOSS OF HETEROZYGOSITY IN ORAL SQUAMOUS CELL CARCINOMA IN A MALAYSIAN POPULATION

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Introduction: Loss of heterozygosity (LOH) and microsatellite instability (MSI) have been documented as important events of oral squamous cell carcinoma (OSCC).

Methods: Five microsatellite markers D3S192, D3S966, D3S647, D3S1228, and D3S659 were selected on chromosome 3p because of high frequency of alterations reported in head and neck squamous cell carcinoma and the involvement of VHL (von Hippel Lindau) at 3p25 – 26 and the FHIT (fragile histidine triad) at 3p14.2 genes proven in many tumor types.

Results: A total of 50 archival tissue samples of OSCC and corresponding normal samples were analyzed for LOH and MSI status. The overall LOH for the markers selected on 3p was 56 out of 189 informative cases (29.6%). The most frequent LOH was identified at the marker D3S966 which is 18/42 (42.8%) of informative cases suggesting the presence of putative of TSGs in this loci. In this study, we found high MSI in D3S966 which is 28.6% of informative cases; this reveals the possibility of mutation of mismatch repair genes in this region. Frequent microsatellite alteration (MA) was observed in D3S966 (71.4%), D3S1228 (56.7%), and D3S192 (41.0%).

Conclusion: There is no significant association between LOH with gender, tumour stage and differentiation grades. However, there is a significant association between tumour stage and differentiation grades with MSI status in OSCC in Malaysian population with *P* values of 0.002 and 0.035. There is also a significant association between MA and differentiation grades with a *P* value of 0.041.

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