FABRICATION AND CHARACTERIZATION OF ECO-FRIENDLY DENTURE ADHESIVE FILLED WITH STARCHES FOR DENTAL APPLICATION

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by

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LIST OF SYMBOLS

%	Percentage
°C	Degree Celsius
µL	Microliter
µm	Micrometer
cm	Centimeter
cm^{-1}	Per centimeter
cm^2	Square centimeter
g	Gram
g.s	Gram-second
g/mL	Gram per milliliter
g/mol	Gram per mol
kDa	Kilo Dalton
kN	Kilo Newton
kPa	Kilo Pascal
kV	Kilo Volt
M	Molar
mg	Milligram
mg/mL	Milligram per milliliter
mL	Milliliter
mm	Millimeter
mm/min	Millimeter per minute
mm/s	Millimeter per second
mm^2	Square millimeter

mol/L	Mol per liter
MPa	Mega Pascal
mV	Milli Volt
N	Newton
nm	Nanometer
rpm	Rotation per minute
v/v	Volume per volume
w/v	Weight per volume
wt. %	Weight percentage

LIST OF ABBREVIATIONS

A/A	Antibiotic/antimycotic
AB	Alamar Blue
ASTM	American Society for Testing and Materials
ATP	Adenosine triphosphate
B. cereus	*Bacillus cereus*
C. albicans	*Candida albicans*
C. glabrata	*Candida glabrata*
C. parasilosis	*Candida parasilosis*
C. tropicalis	*Candida tropicalis*
C=O	Carbonyl groups
CAD/CAM	Computer-aided design and computer-aided manufacturing
CDA	Commercial denture adhesive
$-CH_2-$	Methylene
Cl_2	Chlorine gas
CMC	Carboxymetylcellulose
CO_2	Carbon dioxide
COOH	Carboxyl group
DIS	Denture-induced stomatitis
DMEM	Dulbecco's Modified Eagle Medium
DMSO	Dimethyl sulfoxide
DPBS	Dulbecco's Phosphate Buffered Saline
DPSC	Dental pulp stem cell
E. coli	*Escherichia coli*

EFDA	Eco-friendly denture adhesives
FBS	Foetal bovine serum
FDA	Food and Drug Administration
FTIR	Fourier transform infrared
GMP	Good manufacturing practice
GRAS	Generally recognised as safe
H_2O	Water
H_2O_2	Hydrogen peroxide
HCl	Hydrochloric acid
HGF	Human gingival fibroblast
IR	Infrared
ISO	International Organization for Standardization
K. pnemoniae	*Klebsiella pnemoniae*
KBr	Potassium bromide
LPS	Lipopolysaccharides
MIC	Minimum inhibitory concentration
MRSA	Methicillin-resistant *Staphylococcus aureus*
MTT	3-(4,5-dimethyl-2-thiazolyl)-2,5-diphenyl-2H-tetrazolium bromide
NaOCl	Sodium hypochlorite
NaOH	Caustic soda/sodium hydroxide
-O-	Ether oxygen
OH	Hydroxyl group
P. aeruginosa	*Pseudomonas aeruginosa*
P. syringe	*Pseudomonas syringe*
P. vulgaris	*Proteus vulgaris*

PDL	Periodontal ligament
PDLF	Periodontal ligament fibroblast
PEG	Polyethylene glycol
PEO	Polyethylene oxide
PMO	Peppermint oil
PSA	Particle size analyser
PVA	Polyvinyl acetate
PVM/MA	Poly (methyl vinyl ether-maleic anhydride)
S. aureus	*Staphylococcus aureus*
S. mitis	*Streptococcus mitis*
S. typhimurium	*Salmonella typhimurium*
SEM	Scanning electron microscopy
TBS	Tensile bond strength
Ti	Titanium
TPA	Texture profile analysis
TTO	Tea tree oil
UTM	Universal Testing Machine
UV-vis	Ultraviolet-Visible
VCO	Virgin coconut oil

LIST OF APPENDICES

FABRIKASI DAN PENCIRIAN PELEKAT GIGI PALSU MESRA ALAM TERISI KANJI UNTUK APLIKASI PERGIGIAN

ABSTRAK

Kanji digunakan secara meluas dalam pelbagai aplikasi industri kerana mempunyai ciri pelekatan yang baik dan banyak ciri-ciri cemerlang yang lain. Walau bagaimanapun, masih terdapat kekurangan dalam kanji semula jadi dari segi kekuatan mekanikal tetapi kekurangan ini boleh diatasi dengan teknik-teknik pengubahsuaian. Oleh kerana penggunaan kanji dalam aplikasi pergigian yang terhad dan pelekat gigi palsu yang sedia ada telah dilaporkan mempunyai beberapa batasan dan kelemahan sebagai contoh, kurang kekuatan ikatan untuk memegang gigi palsu, kanji dikaji untuk melihat potensinya sebagai pelekat gigi palsu. Oleh itu, penyelidikan ini memberi tumpuan kepada pembangunan pelekat gigi palsu dengan formula baru yang dipanggil pelekat gigi palsu mesra alam (EFDAs) dengan mengkaji kesan penambahan pelbagai jenis kanji semulajadi dan yang diubahsuai sebagai pengisi dalam sifat pelekat gigi palsu untuk aplikasi pergigian. Sifat-sifat seperti kekuatan ikatan tegangan (TBS), kekuatan ricih, pelekatan, kekerasan, pH dan kelarutan fabrikasi EFDA berbanding dengan pelekat gigi palsu komersil terpilih (CDA) telah dikaji. Jenis kanji yang dikaji adalah jagung, kentang, sagu, ubi kayu dan gandum. EFDA disediakan dengan 5, 10 dan 15 peratus pengisian kanji. Kanji diubahsuai melalui teknik pengoksidaan dengan menggunakan natrium hipoklorit (NaOCl) dan hidrogen peroksida (H_2O_2). Ujian pencirian serbuk kanji seperti analysis saiz zarah (PSA), spektroskopi FTIR dan spektrometri UV-vis telah dilakukan. Ujian mekanikal dan fizikal seperti TBS, kekuatan ricih, pelekatan, kekerasan, ujian pH dan kelarutan telah dilakukan pada EFDA yang dihasilkan.

Tambahan pula, ujian antimikrob dengan menggunakan kaedah penyerapan agar dalam lubang dan kaedah cairan *broth* serta ujian ketoksikan dengan menggunakan ujian AB dan MTT untuk analisis biologi telah dijalankan. Analisis mekanikal menunjukkan bahawa EFDA yang dihasilkan mempunyai kekuatan ikatan tegangan (TBS), kekuatan ricih, pelekatan dan kekerasan yang lebih tinggi berbanding dengan CDA dengan peratusan peningkatan masing-masing sehingga 121.8%, 162.3%, 368.2% dan 343.5%. Ciri-ciri optimum dikaitkan dengan pengisian kanji gandum pada 5% dan diikuti oleh kanji jagung, sagu, kentang dan ubi kayu. Ciri-ciri juga berkurang apabila pengisian kanji meningkat kepada 10% dan 15%. EFDA yang dimasukkan dengan minyak daun pudina and minyak pokok teh telah menghalang pertumbuhan mikroorganisma *C. albicans*, *S. aureus* dan *E. coli* dan sampel EFDA juga tidak toksik kepada fibroblas ligamen periodontal (PDLFs) sehingga hari keempat. EFDA mempunyai potensi yang cemerlang untuk digunakan sebagai pelekat gigi semulajadi kerana sifat-sifat yang memberangsangkan terutamanya EFDA yang diisi kanji gandum yang diubahsuai dengan NaOCl pada pengisian 5% kerana ia menunjukan sifat mekanikal terbaik serta mempunyai kesan tidak toksik yang penting dalam persekitaran biologi.

FABRICATION AND CHARACTERIZATION OF ECO-FRIENDLY DENTURE ADHESIVE FILLED WITH STARCHES FOR DENTAL APPLICATION

ABSTRACT

Starch is widely used in various industrial applications due to its good adhesiveness and many other excellent properties. However, there are still some drawbacks of native starch in terms of mechanical strength, but the limitations can be overcome by modification techniques. Since there is limited involvement of starch in dental application and the current available denture adhesives are reported to have several limitations and shortcomings for example, lack of bonding strength to hold the denture, the starches are explored for its potential in denture adhesive. Hence, this research focuses on the development of new formulation of denture adhesives which is called as eco-friendly denture adhesives (EFDAs) by studying the effects of the addition of different types of native and modified starches as fillers in denture adhesive properties for dental applications. The properties such as tensile bonding strength (TBS), shear strength, adhesiveness, hardness, pH and solubility of fabricated EFDAs in comparison with a selected commercial denture adhesive (CDA) were investigated. The investigated starches were corn, potato, sago, tapioca and wheat. The EFDAs were prepared with 5, 10 and 15% of starch filler loading. The starches were modified via oxidation technique by using sodium hypochlorite (NaOCl) and hydrogen peroxide (H_2O_2). The characterization tests of starch powders such as particle size analysis (PSA), Fourier Transform Infrared (FTIR) spectroscopy and UltraViolet-visible (UV-vis) spectrometry were performed. The mechanical and physical tests such as TBS, shear strength, adhesiveness, hardness, pH test and solubility were conducted on the fabricated EFDAs. Furthermore, antimicrobial test

by using agar well diffusion and broth dilution methods and cytotoxicity test by using an Alamar Blue (AB) and 3-(4,5-dimethyl-2-thiazolyl)-2,5-diphenyl-2H-tetrazolium bromide (MTT) assays for biological analysis were conducted. Mechanical analysis indicated that produced EFDAs have higher TBS, shear strength, adhesiveness and hardness as compared to the CDA with the increase percentage up to 121.8%, 162.3%, 368.2% and 343.5%, respectively. The optimum properties were associated with wheat starch filler loading at 5% and followed by corn, sago, potato, and tapioca starches. The properties also decreased as the starch filler loading increased to 10% and 15%. The EFDAs incorporated with peppermint oil and tea tree oil were inhibiting the growth of *C. albicans*, *S. aureus* and *E. coli* microorganisms and the EFDA samples were also non-toxic to the periodontal ligament fibroblasts (PDLFs) up to day four. EFDA has good potential to be used as a natural based denture adhesive due to the promising properties especially EFDA with wheat starch modified by NaOCl at 5% filler loading because it shows the highest mechanical properties as well as non-toxic effect which are important in biological environment.

CHAPTER 1

INTRODUCTION

1.1 Research background

Dentures are chosen over the dental implant as the option for treatment of edentulism due to affordability of the people. However, to elude the unwanted movement, slide and slip of denture because of its poor adhesion, denture adhesive are usually employed (Fallahi et al., 2018). Denture adhesives are known as the commercially available dental materials and known as the useful accessory for improving the stability, retention and function of the denture (da Rosa et al., 2015). Denture adhesive are regularly used to attach the denture base to the surface of gum tissues or oral mucosa. The maxillary denture base is also known as the top teeth denture base can attach to the upper oral mucosa while the mandibular denture base is also known as bottom teeth denture base can attach to the lower oral mucosa. Proper attachment and adhesion of denture to oral mucosa can improve the patients' sense of security, satisfaction and comfort to do the routine activities especially in the public (da Rosa et al., 2015; Kumar et al., 2015).

Nowadays, commercial denture adhesives are available in various types and forms with assorted of components and formulations. The components of denture adhesive are normally divided into adhesive, antimicrobial and other additive agents such as plasticizing, flavouring and colouring agents. The synthetic polymer, poly (methyl vinyl ether-maleic anhydride) or PVM/MA is a well-known adhesive agent in most available denture adhesives. Although PVM/MA has a promising adhesive

property and suitable for denture adhesive, it takes longer time to activate its adhesiveness due to its low solubility. Consequently, calcium or zinc salt are added in the denture adhesive component to enhance the effectiveness (Grasso, 2004). Synthetic polymers are widely used in the denture adhesive formulation, not only as adhesive agent but also as antimicrobial agents such as sodium borate, hexachlorophene and hydroxybenzoate. Synthetic polymers are accepted in many industrial applications because of their better mechanical and physical properties as well as better chemical and thermal stability (Simionescu & Ivanov, 2015). For the response to current and ongoing awareness of globalization issues, it is essential to reduce the use of synthetic polymers in industrial application especially in health care products as they can be harmful and hazardous to environmental and health. According to Qiao et al. (2014), natural occurring polymer such as starch may take the role of these synthetic polymers. In this research, starch has been chosen to be incorporated in the formulation of new denture adhesive.

Starch is known as renewable bio-resource with several advantages such as abundant, low production cost, edible, biodegradable, biocompatible and non-toxic. Thus, due to these lists of advantageous properties, starch is used extensively in assorted applications (Moubarik et al., 2010). Unfortunately, minimum reports are found on the usage of starch in dental application and this is also the reason why starch has been chosen as one of the main material in the new denture adhesive as to explore its potential in denture adhesive.

Therefore, in this research, the new materials formulation of denture adhesive has been developed and studied. This new denture adhesive is known as eco-friendly denture adhesive (EFDA) as it is mostly made from natural materials and all

materials are environmental and economically friendly. Polyethylene oxide (PEO) is the only synthetic polymer and acts as adhesive agent. PEO, carboxymethylcellulose (CMC) which acts as thickener or viscosity modifier and starches are selected as the main materials for this new denture adhesive. Besides that, several natural polymers are included as antimicrobial agents as well as glycerol and peppermint oil are also added in the formulation as plasticizing and flavouring agents, respectively. The EFDAs are studied for their mechanical, physical and biological properties.

1.2 Problem statement

There are several reports regarding the limitation and disadvantages of the available denture's adhesives. Welch et al. (2010) have reported that the commercial denture adhesive consisting PVM/MA as the main ingredient exhibited lack of bonding strength to hold the denture base which led to short time of denture adhesive's service even its properties were promising. Besides that, there are zinc-containing denture adhesives available in the market. The excessive used of zinc-containing denture adhesive can cause the neurological disease such as hyperzincermia which is the numbness of the feet's and hands' fingers (Singh et al., 2015). Other than that, there are denture adhesives containing parabens in their formulation which act as the antimicrobial agent. Parabens are known as the chemical that are hazardous to human health. It is also known as cancer related chemical as reported by Khanna et al. (2014), parabens were detected in the mammary gland of the patient with breast cancer.

According to Adusumilli et al. (2008), most of the available denture adhesives in the market contained mineral oil or petrolatum in their formulation. This kind of denture adhesive can cause discomfort among the denture user as they can experience and taste the oiliness once they apply it in the mouth. This oily denture adhesive also gives problem to the users as they experience difficulty in cleaning their oily and slippery denture after use with denture adhesive. The other problem related to the available and commercial denture adhesives is they demonstrated the microbial contamination even when they are incorporated with antimicrobial agent. Sampaio-Maia et al. (2012) reported that the tested available denture adhesives for antimicrobial activity did not inhibit the microorganism growth and unfortunately, the denture adhesives themselves have been contaminated by the microorganism. Furthermore, as reported by de Gomes et al. (2011), the available denture adhesives exhibited cytotoxic effect to the oral related cells. Therefore, the denture adhesive should not bring harm to the human health, should not be toxic to the oral tissues and should not promote oral microorganism growth for it to be accepted as the problems-free and ideal denture adhesive.

For that reasons, the new formulation denture adhesives have been developed with inclusion of natural polymers to decrease the accumulation of synthetic polymers in the environment. This EFDA is also free from PVM/MA, zinc, parabens, mineral oil and petrolatum to overcome the limitations and problems of the previous, commercial and available denture adhesives. One of the natural polymers, starch is included in the formulation of the new denture adhesive due to its adhesiveness besides having many good properties. Nevertheless, Naz and Sulaiman (2014) have mentioned that the native starch had limited strength and poor water resistance to be

used as adhesive material. These drawbacks of native starch can be solved by modification techniques (Ferdosian et al., 2017). Thus, the modification techniques which can improve the starch properties including mechanical strength will be explored in this research works. In this research, the native starches will be modified via oxidation technique as it is the most commonly used method for starch modification by using oxidizing agents such as sodium hypochlorite (NaOCl) and hydrogen peroxide (H_2O_2).

1.3 Research objectives

The main objective of this research is to develop the eco-friendly denture adhesive incorporated with the economically- and environmental-friendly materials and with aim to be the ideal denture adhesive by fulfilling all the required characteristics. In order to accomplish the main objective, the specific objectives of this research are as follows:

i) To investigate the effect of different filler loading of new denture adhesive using both native and modified starches.
ii) To compare the mechanical and physical properties of EFDAs produced using native and modified starches at different filler loading with commercial denture adhesive.
iii) To assess the different types of antimicrobial agents to be incorporated in the EFDA and to evaluate the antimicrobial activity of EFDA incorporated with antimicrobial agent towards the microorganisms' growth.
iv) To evaluate the biocompatibility and cytotoxic effect of the eco-friendly denture adhesive on the oral-related cell.

1.4 Research scope

This research project was to prepare the eco-friendly denture adhesive with the inclusion of starch as filler. This inclusion was due to the excellent properties of starch including its good adhesiveness. The particle sizes for all types of native starches were standardized into the same class of particle size by sieving process to eliminate the preference effect of different particle size. The native starches were also be evaluated for their amylose content as the amylose content affected the mechanical properties of starch-filled product. The starches were prepared with two conditions; native starch and modified starch prior to the fabrication of EFDA. Modified starches were prepared by using oxidation method with two different oxidizing agents. Both native and modified starches were characterized for their structure by Fourier Transform Infrared (FTIR) spectroscopy to confirm the modification process. All the fabricated EFDA regardless the types of starches and filler loading were characterized by mechanical tests such as tensile bond strength (TBS), shear stress, adhesiveness and hardness and by physical tests to determine the pH, solubility and shelf-life. The fabricated EFDAs were also assessed for their antimicrobial activity by using agar well diffusion method and broth dilution method. For biological properties, the EFDAs were evaluated for their biocompatibility and cytotoxicity properties by conducting *in vitro* study.

1.5 Thesis outline

This thesis is organized into five chapters; introduction, literature review, materials and methodology, results and discussion, and conclusions and future recommendations.

Chapter 1 introduces about the research background, problems statements, objectives of research, the scope of research and the organization of thesis.

Chapter 2 introduces on the edentulism and the strategies for its treatments. This chapter presents the literature review about denture adhesive including history, mechanism of action, ideal characteristics, types, and compositions of denture adhesive. Besides that, the literature review about the starch including the available modification techniques are also presented in this Chapter. Furthermore, this chapter involves the clinical manifestations related to denture usage and the last part of this chapter presents the oral-related cells for biological assessment.

Chapter 3 covers the details of all the materials used and detail description on the methods for fabrication of EFDAs as well as the methods for characterization including antimicrobial and *in vitro* tests.

Chapter 4 describes the obtained results and discussion which is divided into four parts. The first part discusses about the characterization of both native and modified starch powders. The second part discusses on the mechanical and physical properties of all fabricated EFDAs incorporated with different types of starches and different starch filler loadings. The third part discusses on the antimicrobial assessment of antimicrobial agents and antimicrobial activity of EFDAs incorporated with antimicrobial agents. In the last part, it discusses about the cytotoxic effect of EFDAs at different concentration on the periodontal ligament fibroblasts (PDLFs).

Chapter 5 presents the summary of the research study and several suggestions and recommendations for improvements in future studies.

CHAPTER 2

LITERATURE REVIEW

2.1 Prevalence of edentulism

Edentulism is defined as an irreversible state or condition for losing natural teeth, either one, partial or total loss (Sussex, 2008). It is also known as a significant public health issue and remains as a major problem around the world, especially among older people (Pengpid & Peltzer, 2018). Even though edentulism is not fatal, it can directly lead to negative impacts and a reduced quality of life such as affecting daily routine activities including speaking, swallowing, chewing and socializing (Gerritsen et al., 2010). Since teeth have a crucial role in facial appearance, edentulism can also jeopardize social life by decreasing self-esteem and reducing psychosocial well-being (Naik & Pai, 2011). Edentulous people tend to avoid and not likely to participate or involved in social activities as they are embarrassed to speak, eat or smile in front of the crowd and this will lead to isolation and depression (Rodrigues et al., 2012).

According to Kassebaum et al. (2017), in 2015, there were about 3.5 billion people with untreated oral conditions around the globe, and 276 million from that value were edentulous people. In the United States alone, about 26% of total the population in the United States are people with ages between 65 to 74 years old, and approximately 23 million of these people are entirely edentulous. At the same time, around 12 million are edentulous at least one tooth (Dye et al., 2015). On the other hand, in China, older people with ages between 65 to 74 years old are 11 times

susceptible to edentulous and the people with ages more than 75 are 24 times susceptible to edentulous as compared to the adults with 45 to 54 years old (Ren et al., 2017). The prevalence of edentulism in several countries for people with 50 years and older is displayed in Table 2.1. On the other hand, Table 2.2 shows the prevalence of edentulism among the older people in the several Southeast Asian countries.

Table 2.1: Prevalence of edentulism in people with 50 years and older from different countries (Peltzer et al., 2014).

Country	Sample size	Prevalence of edentulism
China	13,367	9.0%
Russia	3,938	18.0%
Ghana	4,724	3.0%
India	7,150	16.3%
Mexico	2,315	21.7%
South Africa	3,840	8.5%

Table 2.2: Prevalence of edentulism among the older people in Southeast Asian countries (Pengpid & Peltzer, 2018).

Country	Prevalence of edentulism
Laos	4.2%
Malaysia	22.2%
Myanmar	2.4%
Philippines	14.6%
Vietnam	5.6%
Indonesia	17.6%

Furthermore, there are many factors associated with edentulism, including caries and periodontal diseases (Sudiono, 2008), as well as sociodemographic factors such as increasing age, no or low education, low economic status, female gender, and rural area (Hewlett et al., 2015; Olofsson et at., 2017). According to Kailembo et al. (2016), smoking behaviour is also one of the strong predictors of edentulism. Besides that, having chronic diseases have also related to the edentulism such as diabetes

(Islas-Granillo et al., 2011), arthritis (de Pablo et al., 2008), asthma (Peltzer et al., 2014), depression (Saman et al., 2014), obesity (Nascimento et al., 2016), hypertension (Peres et al., 2012), and strokes (Del Brutto et al., 2017). Replacement of the missing teeth becomes the essential needs for the edentulous people to restore oral functions and aesthetics (Al-Quran et al, 2011). Fortunately, there are two strategies or options to tackle this edentulism problem and they are dental implant and dentures usage.

2.2 Dental implant

The dental implant is a common treatment for edentulism, and it is defined as an artificial root that is inserted into the jawbone through minor surgery. This implantation is to support a single tooth replacement, fixed partial, complete denture or maxillofacial prosthesis (Kohli et al., 2015). Figure 2.1 illustrates the dental implants for single tooth replacement, multi-tooth replacement and complete denture. According to Gupta et al. (2010), the dental implants were placed in the patients about 100,000 to 300,000 per year which was almost similar to the numbers of artificial hip and knee joints that have been placed in patients per year.

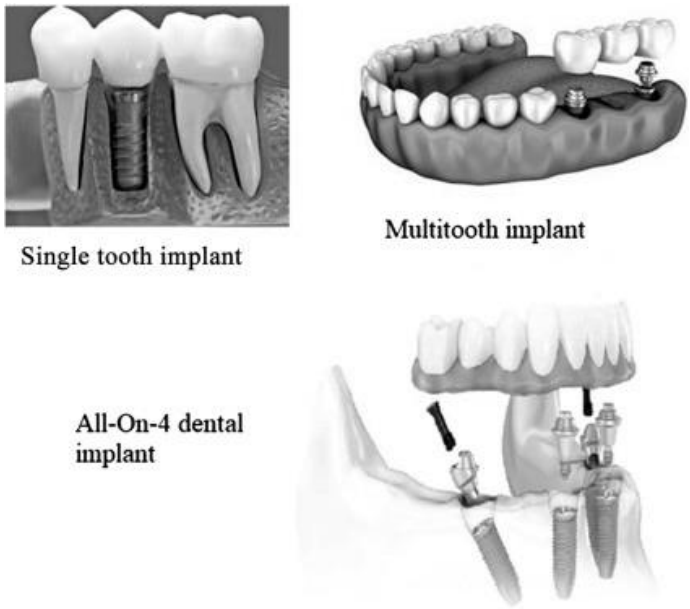

Figure 2.1: Dental implants for several edentulous conditions (Das & Bhattacharjee, 2019).

2.2.1 History of dental implant

The history of a dental implant can be traced back to ancient times and early civilizations where they replaced the missing teeth by using the carved stones, seashells, bones and golds (Gaviria et al., 2014). On the other hand, the modern dental implant began during World War II when Dr Norman Goldberg thought about dental restoration by using metals and later, with the help of Dr Aaron Gershkoff, they produced the first successful dental implant. Besides that, in 1957, a Swedish orthopaedic surgeon named Per-Ingvar Brånemark studied bone healing and regeneration and found that bone could grow and adhere to the titanium (Ti) without being rejected. Later in 1965, he placed the first titanium dental implant into the patient and fortunately, the dental implant serves for more than 40 years. This success led him to start a company for the development and marketing of dental implant. In 1982, the United States Food and Drug Administration (FDA) approved

the use of a titanium dental implant. The later technologies for dental implant were the fabrication of dental implant by using computer-aided design and computer-aided manufacturing (CAD/CAM) method, as well as the usage of ceramics, started in 1992 as material for dental implant (Gaviria et al., 2014). Recent findings showed that several surface modification techniques have been used in titanium dental implants to reduce corrosion such as electro-polishing, anodic oxidation and coating (Nicholson, 2020).

2.2.2 Advantages and disadvantages of dental implant

Dental implant treatments are acceptable as a prosthetic treatment for edentulous patients due to several advantages. Firstly, the dental implant gives better aesthetics as it provides the patient with a natural tooth-like appearance. Secondly, a dental implant offers better strength, support, stability and retention to the edentulous patients. All these terms are the main mechanical aspect for the success of dental prosthesis. The implanted dental has better strength and retention as it is rooted in the jawbone. The better support feature helps in maintaining the implant in position to horizontal forces, and the better stability feature avoids the harmful effects of vertical forces during chewing. Besides that, a dental implant also serves its function for a long duration as it does not need changes for every five to eight years. Besides, the dental implant has shown a significant improvement in edentulous patient's quality of life (Gbadebo et al., 2014; Ulku et al., 2017).

Despite the positive impacts of the dental implant, it also has several drawbacks. The main disadvantage of dental implant is extremely high cost due to the cost involves typically the expensive equipment such as CT scan and specialized radiographic procedures as well as the safe and biocompatible material price

(Přikrylová et al., 2019). According to Přikrylová et al. (2019), a dental implant procedure is also consisting of complex treatment as it requires a lot of visits to install and complete the implantation, and it also requires surgery. This procedure and process will consume the patient's time for several months. The other drawbacks of a dental implant are material corrosion and biofilm formation. Titanium material can corrode under oral conditions and can produce metallic debris. The corrosion of metallic dental implant and the metallic debris can affect the mechanical stability of prosthesis and induce the inflammatory response (Barbieri et al., 2017; Delgado-Ruiz & Romanos, 2018). Besides that, the neglected oral hygiene of dental implant can cause bacterial infection. The high concentration of micro bacteria at the dental implant and the surrounding tissues causes the formation of biofilm. The biofilm leads to conditions and diseases such as tooth decay, gingivitis, periodontitis, and peri-implantitis (Manson & Eley, 2000).

2.3 Dentures

Another option for the replacement of missing tooth beside the dental implant is dentures. Dentures are removable and custom-made teeth that commonly crafted from acrylic, nylon or metal. They are sometimes called removable false teeth, and they look like the set of teeth that mounted on the acrylic base, which made into the similar colour of gums (Jayaraman et al., 2016). Dentures are divided into partial dentures and complete or full dentures depending on how many tooth are loss, as shown in Figure 2.2. Kattadiyil et al. (2017) have mentioned that denture usage was still one of the most popular and traditional prosthodontics treatments for replacement of missing teeth of a patient with anatomic and financial limitations.

These are because firstly, the dental implant is only suitable for patient with high jawbone in order to support the dental implant. Secondly, the cost of manufacturing of denture is cheap and affordable to middle- and low-income society. Thirdly, the fabrication of denture is not time-consuming, and the patient can get the denture as fast as within a week. Finally, the dentures do not involve complex treatment as they do not need for any surgery (Lee & Saponaro, 2019). However, the denture requires denture adhesive to help hold and adhere the denture to the oral mucosa due to the limitation of adhesion strength between those two structures. Overall, from both strategies mentioned, the expenses for the denture, including denture adhesive, are much lower than the cost of an expensive dental implant. Thus, the denture is an affordable solution for the underprivileged people to treat edentulous.

Figure 2.2: Illustration of a full denture and partial denture (Meenakshi et al., 2017).

2.4 Introduction of denture adhesive

A comfortable and durable denture plays a significant role not only towards functionality but also psychosocial of a patient. It has been every patient's right and desire to have a functional and long-lasting denture. An exemplary technique during

fabrication of the denture as well as useful patient management and patient awareness on possible additional management options are among the key elements in maximizing patient's satisfaction and to have a complete and successful denture treatment (Kumar et al., 2015; Musani et al., 2010; Shekar et al., 2016). Although excellent care and precaution during the fabrication were taken, the need for using denture retention enhancement material such as denture adhesives is still necessary. Furthermore, even though decades of researches have been done in the relation of the use of denture adhesives in enhancing denture retention and stability, dental professionals are slow in accepting the use additional intervention such as denture adhesives as they viewed it as a poor reflection of their expertise (Chowdhry et al., 2010). Kumar et al. (2015) asserted that achieving patient's satisfaction and expectation in denture application can be difficult even for most accomplished practitioners and therefore, it is necessary to prescribe denture adhesives in such cases.

Kumar and Thombare (2011) mentioned that denture retention could be influenced by several factors which include physical, physiological, psychological, mechanical and surgical. Besides that, Duqum et al. (2012) and Von Fraunhofer (2012) stated that cohesion, adhesion, atmospheric pressure, surface tension and viscosity between the prosthesis and oral tissue could also be factors that are influencing denture retention as shown by schematic diagram in Figure 2.3. Cohesion is defined as the physical attraction between similar molecules which mainly as the result of chemical bonding that is formed between the same individual molecules. It is also called as the internal strength of the denture adhesive. While adhesion is any physical attraction between different molecular species which come in direct contact

to the applied surface or substrate. In other words, adhesion is the attraction forces between molecules of denture adhesive and molecules of oral mucosa and denture base which cause the hold of denture base for certain times (Von Fraunhofer, 2012). Darvell and Clark (2000) have defined atmospheric pressure was the pressure that resist the dislodging forces that applied to dentures if the dentures had the seal around their borders.

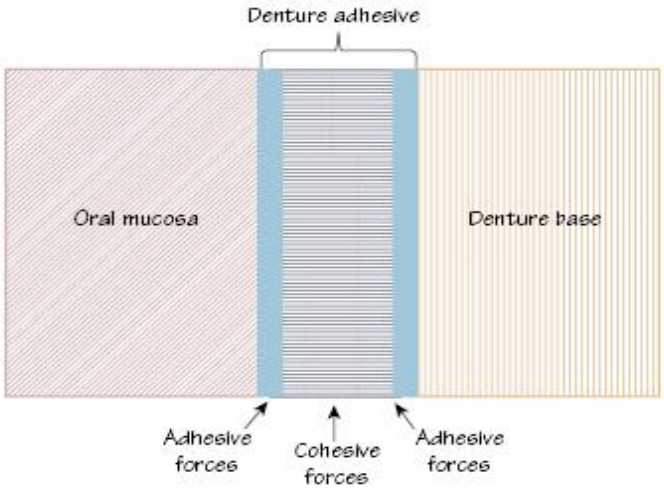

Figure 2.3: Schematic diagram of adhesive force and cohesive force in denture adhesive between oral tissue and prosthesis (Von Fraunhofer, 2013).

Also, the incidence of insufficient retention may increase with time as an effect from residual bone resorption where patients may experience loosening of denture over time (Kreisler et al., 2003). Apart from that, biological and physiological changes such as alteration in production of saliva due to effect of the medication and older age weakened bite force, as well as reduced neuromuscular control, is also the factor that jeopardizing the functionality of a denture (Felton, 2009). Thus, new techniques to enhance retention and fitting of an ageing denture, which includes the use of denture adhesive, are indispensable (Mascolo et al., 2015).

According to the Glossary of Prosthodontic Terms, the definition of denture retention is “the resistance of a denture to dislodgement” (The Academy of Prosthodontics, 2005). On the other hand, the United States Food and Drug Administration (FDA) stated that the placement of denture adhesives such as pastes, powders or adhesive pads in/on dentures to help them stay in place. In other words, as stated by Kumar and Thombare (2011), denture adhesives are non-toxic, soluble materials that are commercially available and could enhance the denture retention, stability and function when applied to the tissue surface of the dentures.

2.4.1 History of denture adhesive

The usage of denture adhesives is said to have started around the late 18th century, but only first mentioned in literature in the early 19th century. The earliest patent issued for denture adhesive in the year 1913 and other patents are reported later in the 1920s and 1930s. In the old days, denture adhesives were plant-based, where different vegetable gums were mixed to produce a substance that could absorb the humidity of saliva which later forming an adhesive layer that adheres the dentures to the oral mucosa. Vegetable gums such as acacia, tragacanth, and karaya were usually used to make denture adhesives (Katiyar & Nigam, 2013; Ke et al., 2011; Kumar et al., 2015; Tella et al., 2013; Yadav & Yadav, 2016). However, the adhesive properties of these plant-based mixtures were not very satisfactory as they are highly soluble in water and have the tendency to be washed out, especially in hot liquids. This later could cause the denture adhesive to be useful for only short time (Ke et al., 2011; Tella et al., 2013). Due to this limitation, the investigation to improve the composition of denture adhesive was carried out, and efforts in improving the

composition and functionality of denture adhesive have been one of the objectives in prosthodontics researches.

2.4.2 Mechanism of action of denture adhesive

The mechanism of action for most of the denture adhesives has been explained by Shay (1991). From his study, the denture adhesives swelled from 50 to 150% by volume with the presence of water from saliva. They filled the spaces by eliminating the voids between the denture base and the basal seat, as illustrated by the schematic diagram in Figure 2.4. The materials also provide the retention and stability of denture by increasing the adhesive, cohesive and viscosity properties of the medium lying between the denture and the gum's tissues (Shay, 1991). According to the principle of interfacial surface tension, the increase of the viscosity of the liquid between two disks or plates will increase the force that required to pull them apart (Rangarajan & Padmanabhan, 2017). Interfacial surface tension is defined as the resistance to separate the liquid between two surfaces as it is the result of strong cohesive forces among the liquid's molecules (Darvell & Clark, 2000). Figure 2.5 displays the schematic diagram of a sample between two plates has been pulled in the opposite direction. As the viscosity of the denture adhesive is increased by saliva, the force to separate the prosthesis from oral mucosa is also increased (Chowdhry et al., 2010; Kumar et al., 2015; Musani et al., 2010; Yadav & Yadav, 2016).

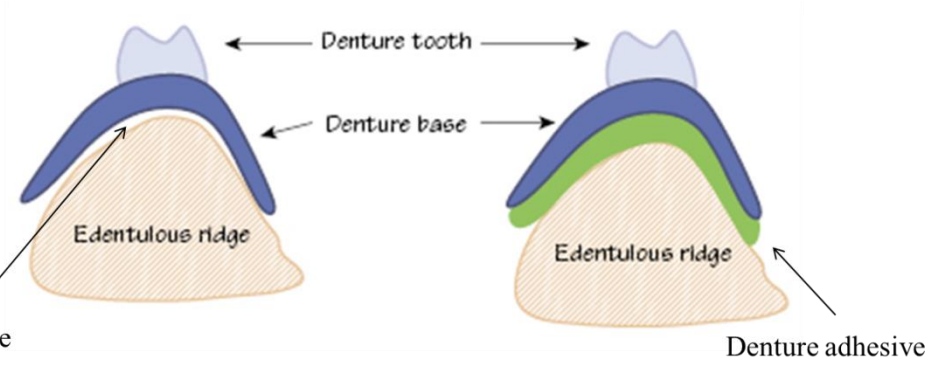

Figure 2.4: Schematic diagram of the swelled denture adhesive fills the void space between the denture base and edentulous ridge (Von Fraunhofer, 2013).

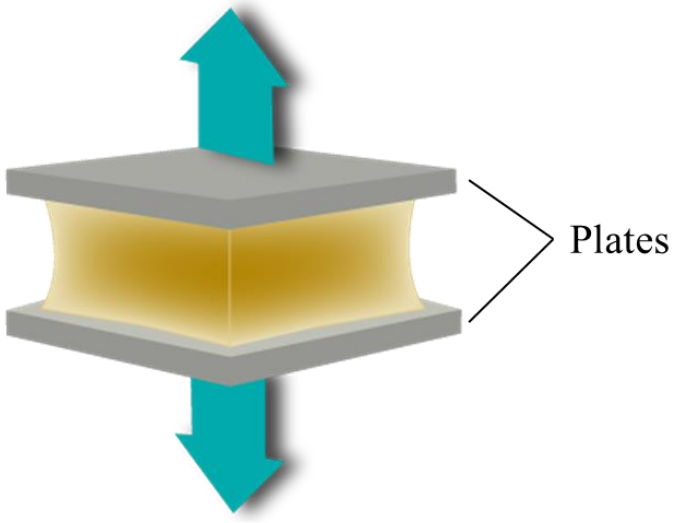

Figure 2.5: Schematic diagram of the attached sample between two plates (Panda et al., 2019).

Together with the physical forces, the modern denture adhesives also provide strong chemical effect via carboxyl groups that rich in the materials such as methylcellulose, hydroxyl methyl-cellulose, sodium carboxyl-methyl-cellulose or poly-methyl vinyl ether-maleic anhydride. Usually, free carboxyl groups are formed by the hydration of these materials from the adsorption of water and saliva and result in the formation of an anionic layer, as shown in Figure 2.6. This layer is attracted to the cationic protein that presents in the mucus membrane. Hence, electrovalent or ionic bonds are formed and lead to stickiness and thus holding the denture in place

(Katiyar & Nigam, 2013; Kumar et al., 2015; Musani et al., 2010; Yadav & Yadav, 2016).

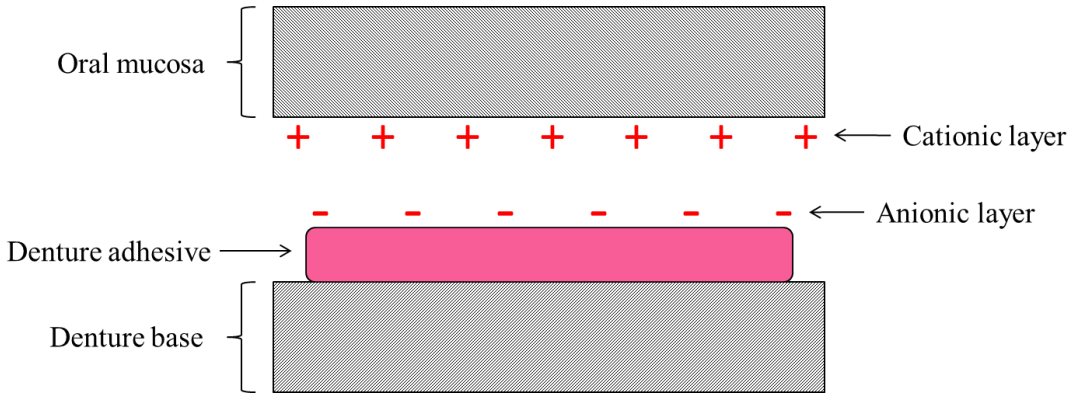

Figure 2.6: Formation of the anionic layer from the hydration of free carboxyl group by water and saliva (Katiyar & Nigam, 2013).

2.4.3 Ideal characteristics of denture adhesive

The denture adhesive should fulfil several criteria to be known as an ideal denture adhesive. These features also become the guidelines and criteria for producing or formulating the new denture adhesive. According to Duqum et al. (2012) and Zhao et al. (2004), an ideal denture adhesive (i) should be biocompatible to the oral mucosa, nontoxic and non-irritant to the systemic or oral health of the users regardless of the using time, (ii) should be odourless and tasteless or have acceptable aroma and taste, (iii) should not promote microorganism growth such as bacteria and fungus, (iv) should be easy to apply and remove from the denture base, (v) should retain its adhesiveness for 12-16 hours before another new application, (vi) should provide comfort, improve retention and stability to the denture as well as ensure the user's ability to function with security and effectiveness especially during a routine activity such as speaking and chewing. Besides that, it should have a neutral or slightly basic pH as it will not cause tooth demineralization or disturb the normal oral flora.

Finally, the ideal denture adhesive should not cause damage to either denture materials or other dental restorative materials, should not change or degrade the surface of the denture base and should not modify the occlusion of the dentures (Duqum et al., 2012, Zhao et al., 2004).

2.4.4 Types of denture adhesives

There are several types of denture adhesives. They can be categorized into an insoluble group; pads and wafers and soluble group; powders, creams, pastes and liquids (Ilakkiya, 2016; Ke et al., 2011; Tella et al., 2013). There are several types of denture adhesive that available and commercialized in the market today and listed in Table 2.3. Pads and wafers usually consist of adhesive-impregnated fabric carrier which can be trimmed and cut to fit the contours of the prosthesis. It also may need to be made wet before placing it on the denture to increase its holding power. Effortless application and removal are one of the advantages of using denture adhesive in pads or wafers form.

Table 2.3: Various types and manufacturers of the commercial denture adhesive.

Brand's name	Type	Manufacturer
Effergrip Denture Adhesive Cream	Cream	Prestige Consumer Healthcare, Virginia, Unite States
Reline-It Denture Reliner	Liquid and Powder	Majestic Drug Co. Inc., New York, United States
Super Poligrip Denture Adhesive Powder	Powder	GlaxoSmithKline, Ireland
Super Poligrip Zinc Free Denture Adhesive Cream	Cream	GlaxoSmithKline, Ireland
Fixodent Denture Adhesive Cream	Cream	Procter & Gamble, Ohio, United States
Fixodent Extra Hold Denture Adhesive Powder	Powder	Procter & Gamble, Ohio, United States
Secure Denture Adhesive Comfort Strips	Pad	Bioforce USA, New York, United States
Secure Denture Adhesive Cream	Cream	Bioforce USA, New York, United States
Y-Kelin Denture Adhesive Cream	Cream	Wuhe Greenland Biotech Co., Ltd., Anhui, China
Y-Kelin Denture Adhesive Cushions	Pad	Wuhe Greenland Biotech Co., Ltd., Anhui, China
Sea-Bond Denture Adhesive Seals	Pad	Combe Incorporated, New York, United States
Sea-Bond Denture Adhesive Cream	Cream	Combe Incorporated, New York, United States
Polident Denture Adhesive	Paste	GlaxoSmithKline, Ireland

On the other hand, for powder adhesives, the base of the denture must be dried before sprinkling a thin and even coat of the adhesive on the tissue surface of the denture as shown in Figure 2.7 (A). Any excess powder should be shaken off

before fitting the denture firmly in place. While, for cream type adhesive, it can be applied in two methods – the strip method and the dot method. The strip method requires a thin strip of adhesive to be placed on denture surface usually in the molar, premolar ridges and in the maxillary ridges as illustrated in Figure 2.7 (B). In cases of a mandibular ridge, the adhesive is also placed in the incisor area. Meanwhile, in the maxillary denture, one strip is placed anterior-posteriorly along the hard palate and one strip each along the ridges. Unlike the powder type, the tissue surface of the denture base can be wet with a little water to increase its efficiency. For the spot method, several spots approximately the size of the tube's diameter are placed throughout the tissue surface of the denture as displayed in Figure 2.7 (C). Controlled and even application of adhesives and reduced oozing are among the reasons why the latter method is preferable (Tella et al., 2013).

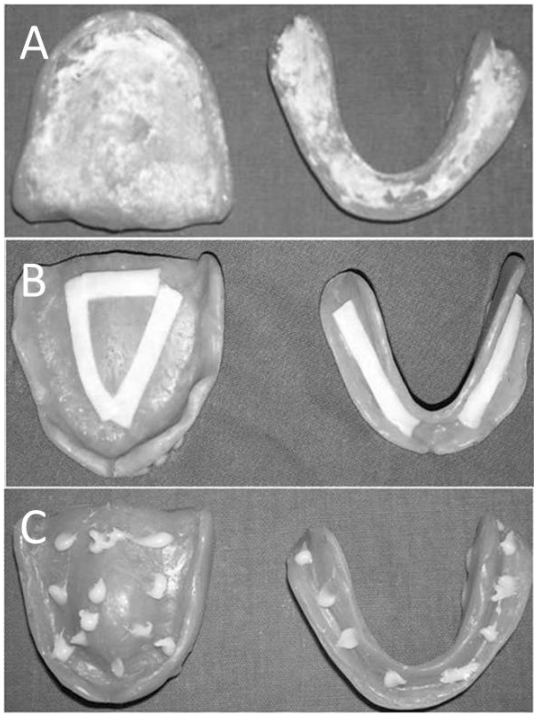

Figure 2.7: Application of different types and methods of denture adhesive on maxillary denture (left) and mandibular denture (right); powder denture adhesive (A), strip method of cream denture adhesive (B) and dot method of cream denture adhesive (C) (Kalra et al., 2012).

2.4.5 Compositions of denture adhesives

The composition of denture adhesive can be classified into 3 groups; adhesive, antimicrobial and other agents. For the adhesive agents and antimicrobial agents, they can be divided into natural and synthetic polymers. The other agents can be further divided into plasticizing agent, flavouring agent, wetting agent and colouring agent. The examples of polymer and material which are included in compositions of denture adhesives are shown in Table 2.4 (Ilakkiya, 2016; Katiyar & Nigam, 2013; Ke et al., 2011; Kumar et al., 2015; Mañes et al, 2011; Yadav & Yadav, 2016).

Table 2.4: Compositions of denture adhesive in different classes.

Adhesive agents	Antimicrobial agents	Other agents
Natural polymers: • Karaya gum • Pectine • Gelatine • Tragacanth • Acacia • Chitosan • Carboxymethylcellulose • Hydroxylmethylcellulose Synthetic polymers: • Poly (methyl vinyl ether-maleic anhydride) (PVM/MA) • Acrylamides • Acetic • Polyvinyl acetate (PVA) • Polyethylene oxide (PEO)	Natural polymers: • Citric acid • Aloe vera • Peppermint oil • Tea tree oil • Virgin coconut oil Synthetic polymers: • Sodium tetraborate • Ethanol • Hexachlorophene • Sodium borate • Methyl salicylate • Propylhydroxy benzoate	Plasticizing agents: • Glycerol • Sorbitol Flavouring agents: • Peppermint oil • Wintergreen oil • Salvia oil • Olive oil • Chamomile oil • Menthol oil Colouring agent: • Red dye