Understanding the Adhesion Mechanism of Conventional Denture Adhesives

A thesis submitted by

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Abstract

Denture adhesives are widely used to avoid the detachment and sliding of dentures. However, their adhesion properties can be affected by variation in mouth condition and underlying conditions such as level of salivation. The objective of this study is to understand the mechanisms governing the properties of a commercially available denture adhesive and identifying the reasons for the observed variation in its adhesion strength. *In vitro* models mimicking the denture gingival interface are designed to evaluate the performance of the adhesive. Changes in adhesion strength in response to three major factors related to the oral conditions including level of salivation, pH, and temperature are measured. The results of lap-shear, tensile test and internal interactions suggested a cohesion failure, where the lowest adhesion strength was due to hyposalivation. Fourier transform infrared spectroscopy (FTIR) and rheological analysis confirmed various involved mechanisms in governing the adhesion characteristics of the paste. We observed that the incorporation of tripropylene glycol methyl ether (TPME) to enhance hydrogen bonding could significantly improve adhesion in hyposalivation scenario.

Keywords: Denture adhesives, Adhesion-tissue interaction, Lap shear, Tensile strength, Intrinsic characteristics

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1. Introduction

Dentures are commonly used especially by the elderly population. Around the world approximately 600 million people are aged 60 years and over, and this number will double by 2025 and by the year 2050 it is projected to be 2 billion and 80% of this population are living in developing countries (Aging and Health, WHO). In the coming decades, dental practitioners will face the challenge of providing dental care for a growing number of elderly who fail to retain their natural teeth. Just considering North America, 37 million of the population are in need of dentures. This number is projected to increase over the next 30 years. Therefore, by adding the existing patients who need to replace the worn dentures, the number of new dentures is expected to be over 61 million (Douglass, Shih, & Ostry, 2002; Mojon, Thomason, & Walls, 2004). The use of denture adhesives in complete dentures can be justified when it is not possible to obtain sufficient retention and stability and when implants or surgical ridge augmentation procedures are not an option because of the patients' economic situation, systemic conditions, or age. To avoid the unwanted movement and sliding of dentures in the mouth, adhesives which are shear thinning pastes are widely employed. Proper adhesion of dentures to gum (or gingival tissue) can improve patients' comfort and quality of life. In addition, the use of denture adhesives can result in a reduction of denture mediolateral movement and dislodgment as well as greater bite force (Papadiochou, Emmanouil, & Papadiochos, 2015; Rendell, Gay, Grasso, Baker, & Winston, 2000). The majority of in vivo studies indicates the significant increase of stability and retention of denture after use of denture adhesive (Papadiochou et al., 2015; Polyzois, Partalis, Lagouvardos, & Polyzois, 2014). Denture adhesive can help to reduce the mastication time and increase in mastication bite which leads to patient's comfort,

specially for elderly patients with less ability to chew (Fujimori, Hirano, & Hayakawa, 2002; Rendell et al., 2000). Patients with either ill-fitted denture or new fabricated dentures are showing the increase effectiveness in regards to incisal bite force, masticatory function and patient satisfaction after applying the denture adhesive (Chew, Boone, Swartz, & Phillips, 1985; Fujimori et al., 2002).

A denture adhesive should be ideally biocompatible, non-irritating, and comfortable to the oral mucosa. It should be easy-to-apply and to-remove, and maintain adhesion strength for 12–16 h. The adhesive should also maintain its properties in various conditions such as variation in the level of pH, temperature induced by different foods, and level of salivation (Kalra, Nadiger, & Shah, 2012; Sato, Kaiba, & Hayakawa, 2008). A denture adhesive interfaces with the denture surface from one side and the underlying oral mucosa from the other side. The adhesion strength of denture adhesives is maximized after their application; however, the strength diminishes over time (Yamaga, Sato, & Minakuchi, 2013). Immediately, after adhesive application and exposure to saliva, the material water content increases, which results in the enhancement in paste viscosity and adhesion. Continuous introduction of saliva into the paste reduces the adhesion properties of the paste. Thus, it is expected that the level of salivation affects the adhesion properties of the paste. This is in line with clinical observations showing the significant impact of saliva level on the performance of denture adhesives in different patients (Turner, Jahangiri, & Ship, 2008), (Shimazu, Karibe, & Ogata, 2014) and (Hong, Tsuka, Dilinuer, Wang, & Sasaki, 2011).

In this study, we characterize the adhesion properties of super poligrip$^\circledR$ manufactured by GlaxoSmithKline, which is widely used by consumers around the world.

To apply the adhesive, a thin layer of adhesive is applied to the interior surface of denture, which is then placed on top of gum. The adhesive is in the form of a shear thinning paste, which is highly porous. The tested adhesive was comprised of carboxy methyl cellulose (CMC) and poly (methyl vinyl ether/ maleic acid) (PMVEMA) as of hydrophilic components and mineral oil and petrolatum as hydrophobic compounds. The hydrophilic compounds absorb and maintain water to enhance the adhesion strength and the hydrophobic compounds prevent rapid swelling and dissolution of the paste (Kano, Kurogi, Shimizu, Nishimura, & Murata, 2012), (Han et al., 2014) and (Kore, Kattadiyil, Hall, & Bahjri, 2013).

To measure the adhesion properties, *in vitro* models mimicking the denture oral mucosa interface are developed and used for measuring lap shear strength and tensile adhesion strength of the paste in various conditions including different pH values, levels of salivation, and temperature. We also perform Fourier transform infrared spectroscopy (FTIR), modulated temperature differential scanning calorimetry (MTDSC), thermogravimetric analysis (TGA), and rheological analysis to identify the mechanisms resulting in the observed properties. The results are then used to enhance the adhesion of the paste by increasing the internal interactions between different components of the paste by adding tripropylene glycol methyl ether (TPME).

2. Motivation

Denture adhesives have been widely used by denture wearers since 1935. Denture adhesives improve retention, stability and function of ill-fitting and well-fitting dentures (Özcan, Kulak, Arikan, & Silahtar, 2004). In the beginning, dentists had been reluctant to prescribe denture adhesives due to the suggestion of undesirable effects on soft tissue hyperplasia and alveolar resorption. However, since that time, there has been significant literature and studies conducted to support the usage of denture adhesives. Recently, they are widely acceptable as adjuncts to dental treatment. In particular, elderly patients have difficulty accepting the new contours, occlusion and fit of new or relined dentures both mentally and physically (Joseph E Grasso, 2004) . Therefore, by using denture adhesives, the elderly could use dentures with more self-confidence in social interactions.

By 1939, there were 30 dental adhesives manufactures with sales of $2.5 million per year. The sales increased from $2.5 million in 1939 to $148 million in 1989 and over $200 million in 1994 (Kenneth Shay, 1997). Even though there were changes regarding the dollar value and market competition over time, it reflected the increase in denture adhesive sales (Kenneth Shay, 1997). Global Denture Adhesive Research reported the increase growth of denture adhesive market in 2016. North America is one of the leading markets in denture adhesives. It is expected to growth up to 6% in the future. The increasing aging population is one of the main causes for the growth in the denture adhesives demands. Also, increasing awareness of oral hygiene and healthcare may further affect the market size ("Global Denture Adhesive Market Research Report - Forecast to 2021". 2017).

Dry mouth, or xerostomia, is a common symptom of the geriatric population. The number of patients with dry mouth has increased over time. Dry mouth may compromise oral health and function and eventually lead to poor denture retention and reduce quality of life. Dry mouth may happen because of age, some medications, uncontrolled diabetes, Sjögren syndrome and radiotherapy of the head and neck during cancer treatment (Joseph E. Grasso, Rendell, & Gay). There is limited data available to show the prevalence of xerostomia in the general population. The range of prevalence of xerostomia is estimated from 0.9% to 64.8%. In patients with Sjögren disease or in patients receiving radiation therapy for head and neck cancer, the prevalence approaches 100% (Mahvash Navazesh & Kumar, 2009).

3. Literature Review

3.1 Denture adhesive

Denture adhesives, also known as adherents or fixatives, have been used by denture wearers for a long time. Denture wearers consider denture adhesive as an adjunct to increase the denture retention, stability and function. Although denture adhesives were formulated and introduced in the late eighteenth century, they were not acknowledged by dental societies until 1935, when the American Dental Association (ADA), Council on Dental Materials, Instruments, and Equipment, defined them as nonmedical. The earliest registered patent for denture adhesives was reported in 1913 and followed by patents in the 1920s and 1930s (Joseph E Grasso, 2004).

The early version of denture adhesives was made of vegetable gums such as Acacia, Tragaeanth, or Karya. The vegetable gums absorbed the water and produced a layer between the gum tissue and the denture surface. However, the vegetable gums were highly soluble and sensitive to hot liquid. Therefore, they functioned for a very short duration in the oral environment (K Shay, 1991).

The formulation and composition of denture adhesives have been modified over time. Currently, they are divided into two major groups; soluble and insoluble. The insoluble group includes pads and synthetic wafers; the soluble group includes creams, pastes and powders (Boone, 1983) (Figure 1). The usage of insoluble or soluble denture adhesives is mostly based on personal preferences. However, the advantage of insoluble denture adhesives is ease of cleaning. The amount of adhesive and the viscous component of insoluble denture adhesives which is embedded into the fabric carrier is much less than

soluble ones. Thus, the patients are able to peel off the pads and wafers and clean the small amount of residue in the mouth very easily. Still, there are some claims that the pads and wafers have less retention in comparison to powders and creams.

Figure (1): Different types of soluble and insoluble denture adhesives. (A) Wafer (B) Powder (C) Cream (Joseph E Grasso, 2004).

3.1.1 Insoluble Denture Adhesive

In general, the main components of the insoluble group are a fabric carrier and a component which becomes viscous when hydrated. Even though the formulation of pads and wafers are different among various manufacturers, they consist of a laminated fabric mesh with a component embedded into the mesh which activates when in the hydrated environment. The laminated fabric mesh can consist of woven or unwoven fiber or mesh made of polyproline scrim or cellulose. The viscous hydrated parts are usually made of sodium alginate or ethylene oxide polymer (Weiler & Bohm, 1985). The pads and wafers are similar in structure. The only difference would be the thickness and in this case the pads are much thicker than wafers. Therefore, most dentists use the pads as both adhesive and reliners. Reliners help to recontour the old denture to fit more properly in the mouth (Joseph E Grasso, 2004).

3.1.2 Soluble Denture Adhesive

Soluble denture adhesives are composed of two main parts: active and nonactive parts. The mechanism of action of the soluble group is based on one of the active ingredients, which swells and becomes viscous in the presence of saliva. This chemical ingredient usually swells over 150% after hydration and fills the gap between the denture surface and the gum tissue (K Shay, 1991). This ingredient is usually made of mix polymer salts with different rates of hydration. In other words, the short-term action polymer salt such as Carboxymethylcellulose (CMC) hydrates very quickly but also loose its effectiveness very quickly. On the other hand, a long-term action polymer salt such as Polyvinylether Methyl Cellulose (PVM-MA) hydrates and activates longer than the short-term action salt and stays longer in the mouth (Gasman, Wong, Clarke, & Ahn, 1994). The action of active ingredients has been improved by adding calcium salts and zinc over time.

The soluble groups are composed of nonactive components as well. The non-active components usually improve the effects of the active parts. There are several non-active components that are usually added into the formulation. Examples of non-active components are petrolatum, mineral oil and polyethylene oxide as binding agents, sodium borate and methyl paraben as preservatives, calcium acetate and silicone dioxide as anti-cluster, peppermint and menthol as flavorings and dye for coloring (Clarke et al., 1996).

The bases of active and non-active ingredients are usually similar in powder and cream. The ratio and proportion of each ingredient might be different. However, the petrolatum and mineral oil exist only in cream and Calcium acetate and silicone dioxide exists in powder (Clarke et al., 1996).

3.2 Denture Retention

The best result of complete denture treatment depends on patient satisfaction. In addition to the comfort of the patient, the stationary or retained dentures would help the patient to accept the treatment. Denture retention is defined as: "The resistance to removal in a direction opposite that of insertion" (Kenneth Shay, 1997). There are a couple of factors involved in denture retention. These factors are interfacial force, adhesion and cohesion.

3.2.1 Interfacial Force

Interfacial force is "the resistance to separation of two parallel surfaces that is imparted by a film of liquid between them" (Berg, 1991). This force is divided into two sub divisions: 1) Interfacial surface tension 2) Viscous tension.

3.2.1.1 Interfacial Surface Tension

The interfacial surface tension forms when a layer of liquid is present between two parallel rigid surfaces. This phenomenon happens when the rigid surface has a low surface tension therefore the liquid at the interface can wet the surface. The oral mucosa is hydrophilic. Therefore, saliva is able to spread over the oral mucosa and creates a thin layer. On the other hand, denture base is made of hydrophobic materials with high surface tension. Thus, the liquid will form beads over the surface. However, there is another phenomenon that interferes with surface tension on denture base, which is called capillary attraction. Capillary attraction happens when the liquid rises to the top of the capillary tube. The same phenomenon happens between the denture base and saliva. When the denture base gets close enough to the oral mucosa, a thin layer of saliva spreads over the denture base per capillary attraction. The surface tension force is mostly effective on Maxillary (upper jaw) dentures rather than Mandibular (lower jaw) dentures. The mandible is close

to the saliva duct which is located under the tongue. Therefore, the mandibular denture borders are mainly saturated with saliva as opposed to maxillary denture borders (Berg, 1991).

3.2.1.2 Interfacial Viscous Tension

Interfacial viscous tension denotes the viscosity of liquid present between two parallel surfaces. This phenomenon is described by Stefan's law. This principle defined the force that is necessary to separate two parallel plates. According to Stefan's law (Eq. 1), the viscous force increases when the viscosity of the liquid increases. Also, by increasing the surface plates, the viscous tension will increase. On the other hand, by increasing the distance between two plates, the viscous tension will decrease (Kenneth Shay, 1997).

$$F = \frac{(3/2)\,\pi k r^4}{h^3}\,V \quad (1)$$

F: Force necessary to pull the plates a part
r: radius of two parallel circular plate
k: viscosity of liquid
h: thickness
V: velocity in a direction perpendicular to radius

Stefan's law can be applied to the mouth as well. By fabricating denture with sufficient accuracy, the gap or distance between the denture base and the oral mucosa is minimized. Thus, the viscous tension will increase. Also, by covering more surface of oral mucosa with the denture base, the viscous tension will be elevated. Moreover, in theory, by increasing the viscosity of the liquid or media in between, the viscous tension will improve as well. It can happen when denture adhesive is used to improve the denture retention.

3.2.2 Adhesion Force

Adhesion or attraction force is an ionic attraction between unlike molecules. The attraction between saliva and the oral mucosa or the denture base is an example of adhesion attraction. Based on this attraction, adhesion force occurs among charged salivary glycoproteins and surface epithelium of the oral mucosa or acrylic resin of the denture base. The denture retention created with adhesion attraction depends on the surface area of the oral mucosa that the denture covers . Therefore, the mandibular denture can get less benefit from the adhesion force. It is also true in patients with smaller jaws or flat alveolar ridges (bone resorption).

Another type of adhesion force happens in the xerostomia patients, who have dry mouth. In this category, the adhesion attraction is between the denture base and the oral mucosa (absent of saliva) or the surrounding oral surfaces such as the lip, the cheek or the tongue. This adhesion is not as strong as it is when saliva is present. Also, the patients feel discomfort by repeatedly sticking the denture to the lip and the cheek and cause dislocation.

3.2.3 Cohesion Force

The cohesion force or attraction is an ionic attraction among the same molecules. In the oral environment, the cohesion force causes the retention force within a layer of saliva or in some cases in denture adhesives. It aids to keep the integrity of that paste. Even though the thick and mucin saliva is more viscous than the water base saliva, the retention will not increase in the patients with mucus saliva (Edgar, 1990). The main reason is that in watery saliva, saliva spreads more easily and forms a thinner layer than in Mucus saliva. Usually, normal saliva is not viscous enough to create great denture retention. Most of the retention comes from the adhesion force or interfacial force (Kano et al., 2012).

3.3 Mucoadhesiveness

3.3.1 Mucosal membrane

Different parts of body cavities are covered with mucosal membranes. These body cavities include the respiratory, gastrointestinal and reproductive tracts. Mucosal membranes are the moist surfaces that shield the cellular epithelium from chemical, mechanical and bacterial invasions. Also, mucosal membranes control the moisture of epithelial cells to keep them lubricated. Mucosal membranes have a significant role as semi-permeable barriers to control the diffusion of water, nutrients, small molecules, gas, ions. Also, they prevent the penetration of most bacteria and pathogens (Khutoryanskiy, 2011).

The external layer of mucosal tissue (epithelial layer) is composed of two types of mucins: membrane bounded and secreted soluble hydrated viscoelastic gel layer macromolecules (mucus). Mucins are composed of multiple subunits of glycoproteins with high molecular weights. The subunits are linked together via peptide bonds and intramolecular cystein-cystein disulfide bridges (Figure 2) (Peppas & Sahlin, 1996).
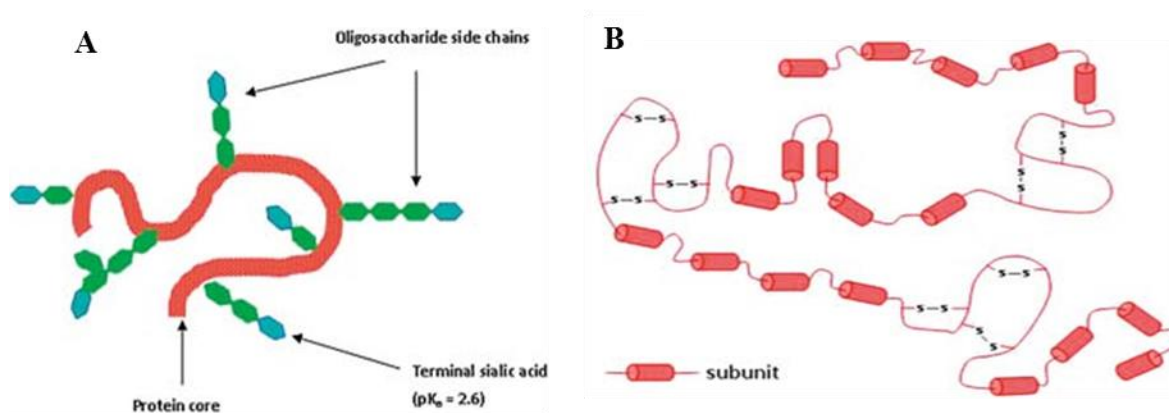
Figure (2): Proposed structure for mucin glycoprotein. (A) subunit with the peptide bond (B) Multiple subunits with intramolecular disulfide bridge (Khutoryanskiy, 2011)

Each subunit is made of proteins as backbones and oligosaccharides as side chains. Over 63% of backbones are covered with the oligosaccharide side chains. Proteins weigh 17% of the total weigh of each subunit and are mainly composed of serine, threonine, and proline amino acids. The oligosaccharide side chains are composed of N-acetylgalactosamine, N-acetylglucosamine, galactose, fucose and N-acetylneuramic acid (sialic acid). Mucins mostly have negative charges due to the presence of the carboxylate group and the sulfates of oligosaccharide side chains. Mucins are completely ionized under physiological conditions. They also change from sol to gel under acidic conditions. (Bansil & Turner, 2006; Yang & Robinson, 1998).

The mucus gel layers are formed consistently through the secretion of mucins from the goblet cells. They have various life cycle periods from 5-7 minutes in the eyes till 4-6 hours in the gastrointestinal tract. The mucus gel layers usually contain 90-98% water. The pH of mucus gel is different based on the location of formation. For instance, the pH of mucus gel is 5.5-5.6 in the lungs and nasal cavity in comparison with 6.2-7.4 in the oral cavity (Lai, Wang, & Hanes, 2009).

3.3.2 Mucoadhesion and Theories of Mucoadhesion

Mucoadhesion is defined as a temporary attachment that various polymers with different charges form with the mucosal membrane. This principle has been vastly used in buccal, oral, nasal, ocular and vaginal drug delivery (Khutoryanskiy, 2011). One of the early applications of this phenomenon was reported in 1947. In order to deliver the penicillin to the oral mucosa, the gum tragacanth was mixed with dental adhesive to make the carrier. (Scrivener. D.D.S & Schantz, 1947). This adhesion is still not totally understood. There have been several studies conducted to determine the true nature of

interaction between "biopolymer-based viscoelastic mucus gels present on mucosal membranes and polymer-based mucoadhesive" drug formulations (Khutoryanskiy, 2011). There are a couple of general theories that may explain this phenomenon:

1) *Electronic Theory:*

    Based on this theory, the mucoadhesion bond will form when the opposite charges exist between the mucoadhesive polymer and the mucosal membrane (mucus). In this case the electrons transfer between molecules and create bonds (Derjaguin, Aleinikova, & Toporov, 1994; Derjaguin, Toporov, Muller, & Aleinikova, 1977).

2) *Adsorption Theory:*

    The hydrogen bonds and Van der Waals forces play major roles in adhering the mucoadhesive polymers with mucus. It is more significant when the polymers have amphiphilic molecules. The hydrophobic effect will strengthen the adhesion (Kinloch, 1980).

3) *Wetting Theory:*

    This theory is based on the surface tension of both mucoadhesive polymers and the mucus layer. In other words, when the surface tension is low, the mucus and mucoadhesive polymers are spread easily over mucosal tissue that leads to strong mucoadhesive bonds. This theory is more related to liquid mucoadhesive polymers (Peppas & Buri, 1985).

4) *Diffusion Theory:*

    Based on the diffusion phenomenon, the mucoadhesive macromolecules penetrate mucus layers and form the interpenetration layers. The gradients

of concentration, size and hydrophobicity of macromolecules effect the formation of this layer. The thickness of this layer influences the adhesion strength. Normally, a thickness of more than 0.2-0.5 µm creates an excellent adhesion (Garti, 2008).

5) *Mechanical Theory*

This theory is more related to the materials that have a rough or porous surface. The mucoadhesion increases in this material since the contact area is increased as well (Garti, 2008).

In reality, mucoadhesion is created by a combination of these theories. Some researchers divide this process into sequential phases. Smart and his colleague explained the adhesion process in 2005 (Figure 3). First, the mucoadhesive polymers wet and swell (Wetting theory). The swelled polymers form the non-covalent and van der waals bonds with mucus (electronic and adsorption theories). Then this complex entangles and penetrates the membrane more strongly (John D. Smart, 2005).
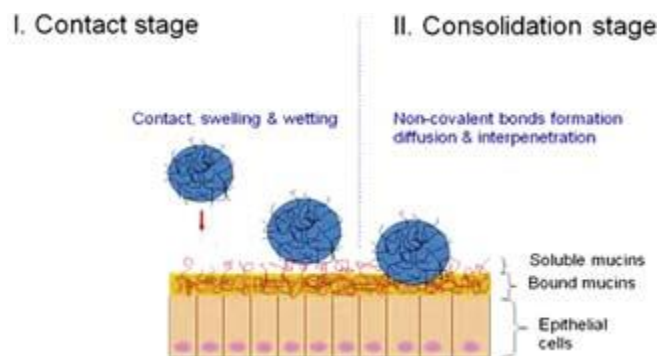
Figure (3): Different stages of mucoadhesion formation. The mucoadhesive polymers wet and swell (Wetting theory). The swelled polymers form the non-covalent and van der waals bonds with mucus (electronic and adsorption theories). Then this complex entangles and penetrates membrane more strongly (Khutoryanskiy, 2011)

3.4 Saliva

Saliva is a clear mucoserous secretion that secretes from major and minor salivary glands. This category is based on the size of the gland and the amount of saliva that is secreted per day. The major salivary glands mainly are located close to the maxillary first molars (Parotid), and the floor of the mouth. The minor glands are found around the cheek, palate, tongue and lower lips (Roth & Calmes, 1981). The minor glands due to their protective nature are more important than major glands. Even though the major glands produce more saliva, their quality and type of protection are different.

The average daily saliva flow varies. The location and anatomy of the salivary gland may influence the flow rate. Edgar reported that major salivary glands, Parotid, submandibular, and sublingual, have different flow capacity during the unstimulated phase. The parotid gland produces 20%, the submandibular gland 65% and the sublingual 8% of daily saliva. Less than 10% of total daily saliva flow is related to minor glands that are spread all over the oral cavity (Edgar, 1990).

Saliva is composed mainly of water (99%) and in lower concentration it is made of different components such as: electrolytes, immunoglobulins, proteins, enzymes, mucins, urea, and ammonia. These components by themselves or combined can act as lubrication, antibacterial, buffering, cleanser, or aggregator and can facilitate demineralization and remineralization. For instance, bicarbonate, phosphate and urea may help to regulate the pH to prevent becoming too acidic or basic after consumption of proteins and immunoglobulins may act as antibacterial and dental plaque removal (Humphrey & Williamson, 2001).

The flow rate is different among the population. The average flow rate for unstimulated saliva is more than 0.1 mL/min. This number will increase up to 0.2 mL/min

if stimulated. On average by considering the unstimulated saliva flow rate would be 0.3mL/min with the average of 16 hours active time, the total unstimulated saliva volume would be 300 mL. On the other hand, stimulated saliva with an average of 0.7 mL/min flow rate may produce 1-1.5L in the active time (Edgar, 1990; Grant, Stern, & Listgarten, 1988). When the flow rate drops below 0.1mL/min, it is called hyposalivation. Approximately, 30% of the population have some degree of hyposalivation (M. Navazesh, Christensen, & Brightman, 1992).

Salivary flow is not consistent and depending on site it may change. Saliva residue on oral mucosa is the least amount. Also based on the different saliva distributions and flow rates of minor and major salivary glands, the hard palate has the least wetness (Hamada, Kawazoe, Sekino, Nagasawa, & Tsuru, 1974). Wolf and Kleinberg studied the mucosal wetness of different regions and the correlation between dryness and salivary flow rate. They concluded that the hard palate followed by the lips had more dryness perception. The average thickness of saliva layer is less than 4-5 µm. On the other hand, the wettest areas were identified as the back of the tongue and the floor of the mouth with the saliva thickness between 14-18 µm (Wolff & Kleinberg, 1998).

The environmental pH value in the mouth is regulated by saliva and temporarily affected by the consumption of food. Normal healthy saliva in the oral cavity has a pH between 6.7 and 7.4. Also, depending on the saliva flow rate the pH of the saliva changes from 5.3 (Slow flow rate) to 7.8 (fast flow rate). The pH of the saliva can temporarily drop to below 5 when sweets, carbonated and fruit drinks, and other dietary acids are consumed. Some drugs, such as beta blocking agents, nitrates, and diuretics, as well as tobacco smoking can also reduce salivary pH. Alkaline-producing foods such as vegetable juices

can increase the saliva pH (D. Aframian, T. Davidowitz, & R. Benoliel, 2006). Table (1)

shows the pH ranges of some common foods and drinks.

Table (1): Examples of pH Food. Most food are alkaline when they are raw. They become acidic when cooked(D. Aframian et al., 2006)

Alkaline pH	10.0	Raw Spinach, Red Cabbage, Raw Cellery, Lemons and Lime, Cauliflower, Cucumber, Carrot
	9.0	Olive Oil, Lettuce, Raw Zucchini, Sweet Potato, Pears, Kiwi
	8.0	Apples, Almonds, Avocado, Mushrooms, Peaches, Strawberry, Cherries, Olives, Pine Apple, Blueberries,
Neutral pH	7.0	Mostly Tap Water Butter, Raw Milk, Unsalted Cream
Acidic pH	6.0	Milk, Yogurt, Fruit Juice, Cooked Spinach, Coconut, Liver, Salmon, Tuna, Oats, Lima Beans, Brown Rice, Eggs, Cocoa
	5.0	Cooked Beans, Chicken, Turkey, Beer, White Rice, Cooked Corn, Rice Cakes, Lentils, Sugar
	4.0	Mostly Bottle Of Water And Sports Drinks, Coffee, White Bread, Sweetened Fruit Juices, Beef, Wheat, Popcorn
	3.0	Lamb, Pork, Wine, Black Tea, Pickles, Goat Cheese, Chocolate, Vinegar, Processed Food, Tobacco Smoke
	2.3	Colas (Off the Chart)

3.5. Paste Component

Denture adhesive contains active and non-active ingredients. The active ingredients which are responsible for adhesive properties include karaya gum, tragacanth, acacia, pectin, gelatin, methyl cellulose, hydroxymethyl cellulose, sodium carboxymethyl cellulose and synthetic polymers (plyethykene oxide, acrylamides, acetic polyvinyl) ((Joseph E Grasso, 2004). The non-active ingredients such as peeling promotion agents, antiseptics, pH control chemicals, pigments and flavor are also available in denture adhesives. Liquid paraffin, and petrolatum provide a creamy condition as ointments and are considered to function as peeling promotion agents, while pH control chemicals such as sodium dihydrogenphosphate control pH within a suitable range and prevent deterioration and changes in the color of denture adhesives (Zhao, Cheng, Chao, Li, & Han, 2004). The Super Poligrip® Zinc Free (Glaxo Smith Kline Inc.) is made of Poly (methylvinylether/ maleic acid) Sodium-calcium mixed partial salt, Carboxymethylcellulose, Petrolatum, Cellulose gum and Mineral oil (Figure 4 E).
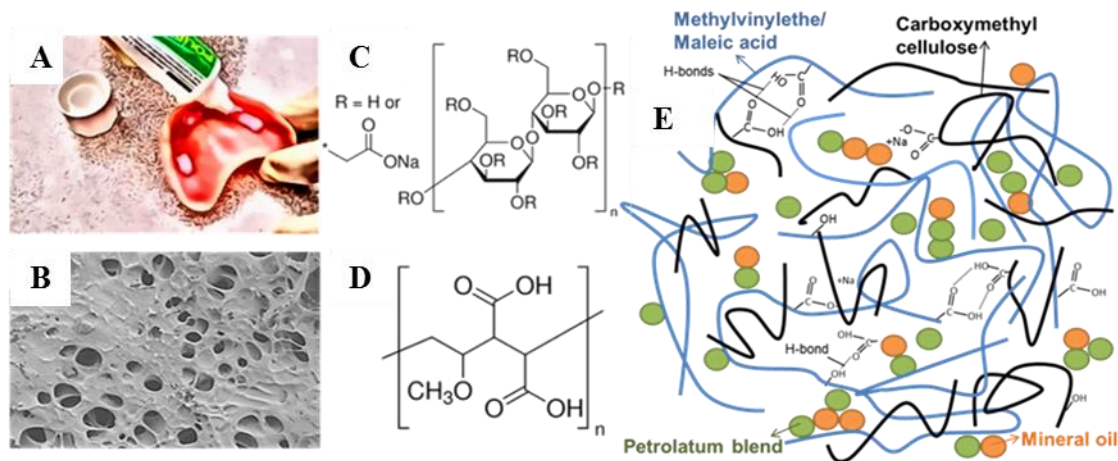
Figure (4). Poligrip® Free denture adhesive, its application and components. (A) Thin layer of the shear-thinning adhesive is applied on the denture and then placed on the gum; (B) SEM image of the freeze-dried paste showing the presence of pores within the material (Scale bar = 100 µm); (C) Chemical structure of CMC; (D) Chemical structure of PMVEMA; (E) Schematic showing various components of the paste and the interactions between them

3.5.1. Carboxymethyl Cellulose (CMC)

Carboxymethyl Cellulose (CMC) is a natural anionic polysaccharide. CMC is a water-soluble heteropolysaccharide with a high molecular weight. It is usually added to provide desirable texture, control moisture and water mobility and improve the stability of products. CMC is used because it has high viscosity and high water content, and it is non-toxic, non-allergenic and biodegradable. Also, due to numerous hydroxyl and carboxylic groups, CMC is able to water bind and absorb moisture (Figure 4 C) (Tongdeesoontorn, Mauer, Wongruong, Sriburi, & Rachtanapun, 2011).

Many studies have been conducted on denture adhesive efficiency. The most popular, successful products consist of a mixture of Carboxymethyl Cellulose sodium salt (Zarb & Bolender, 2004). These denture adhesives first showed low viscosity. With the initial intraoral use, denture adhesives swell and become viscous and sticky in the presence of saliva. As denture adhesives hydrate, free carboxyl groups form ionic adherence between the denture and the oral mucosa (Ellis, Suad, & Lamb, 1980).

3.5.2. Poly (methyl Vinyl Ether-co-Maleic Acid) (PMVEMA)

Poly (methyl Vinyl Ether-co-Maleic Acid) (PMVEMA or Gantrez ®) is a polymer with many applications in different fields. The common applications are as a thickening agent, film former, dispersing agent, emulsion stabilizer, drug delivery adhesive and denture adhesive ((Xi, Bassett, & Vogl, 1983)). PMVEMA is considered as a nanoparticle carrier taking into account its low toxicity and excellent biocompatibility (Yoncheva, Lizarraga, & Irache, 2005)

PMVEMA is an alternating copolymer produced by free radical polymerization. The anhydride group reacts to form a half-ester with alcohol or hydrolyzes to a diacid in water ((K. Chung, C. Wu, & E. Malawer, 1990). Grasto *et al*. showed the maleic anhydride and acrylic acid units on neutral stage help to disperse water. Furthermore, the ethylene and methyl vinyl ether units could transmit the toughness and flexibility to the polymer (Crasto, Own, & Subramanian, 1988).

PMVEMA is a pharmaceutically acceptable copolymer that has bioadhesive properties similar to poly (acrylic acid) and polycarbophil (J. D. Smart, Kellaway, & Worthington, 1984). PMVEMA is used as part of delivery systems designed in the oral cavity for example rinses and toothpastes. In different reports, PMVEMA showed the enhancement of triclosan and sodium fluoride delivery and increase in the effect of anticavity and antiplaque agents in oral cavity (Palomo, et al, 1989 & Nabi N, Muderjee C, Schmid R, Gaffar A, 1989).

4. Engineering In Vitro Models for Assessment of Denture Adhesives' Adhesion

4.1. Mechanical Test

Previous publications have suggested a series of in vitro testing methods to evaluate the performance of denture adhesives in the laboratory using different simplified models. These models are designed to simulate the in vivo fate of a denture adhesive, such as destruction, dilution, and dissolution of the adhesive, by repeated measurements of tensile bond strength for the adhesive over time. However, the lack of a generally accepted in vitro testing model for denture adhesives complicates the comparison of performance based on results from different sources. It is therefore proposed to develop a proper model based on reported methods for the studies proposed.

Floystrand and his colleague proposed a method to test the denture adhesive in 1991. They proposed a balance scale to measure the tensile stress of bond strength of the denture adhesive. They applied pressure with a stream of water to a bucket and increased the stress to 2 N/min. The tensile stress was recorded (Figure 5). In the beginning of the experiment, they pressed the 0.3g denture adhesive between two highly polished acrylate resin plates (3cm diameter) with 2K (≈20 N) weight brass for 15 seconds and measured the bond strength of the adhesive. Then, they merged the resins with the adhesive into 100 mL of isotonic saline and let it sit for 2 minutes. They pressed the resins with 2 Kg of weight again and measured the adhesive bond strength for the second time (Fløystrand, Koppang, Williams, & Ørstavik, 1991). They repeated these steps until no bond strength could be detected.
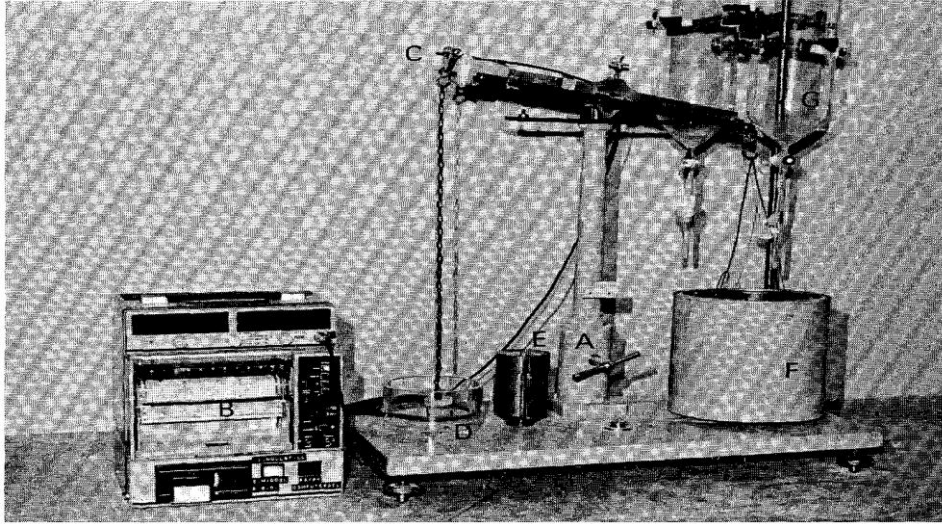
Figure (5): Apparatus to measure the tensile strength of denture adhesive. A: Balance scale; B: Bite force reader; C: Sensory unit; D: Isotonic saline bath with denture adhesive press between two acrylate resin plates; E: Two kilogram weight to press the acrylate resin plates together; F: bucket; G: Water reservoir (Fløystrand et al., 1991)

The problems with Floystrand's method were measuring the bond strength regardless of the effect of surface roughness on the adhesive bonds. Also, normal saline lacks the salts that saliva has. Finally, by repeatedly detaching the resin plates after each measurement, the tensile stress would be negatively affected.

In 1995, Panagiotouni and his associates used a different apparatus to measure the tensile bond. They used a resin plate and a glass slide in this experiment. They applied a thin layer of artificial saliva (0.05 ml) on both surfaces and added 0.3g of denture adhesive over the resin plate and pressed into the glass surface. Adhesion was measured based on the force necessary to separate the adhesive from the glass by increasing the load at the rate of 20 mL/min (Figure 6) (Panagiotouni, Pissiotis, Kapari, & Kaloyannides, 1995).
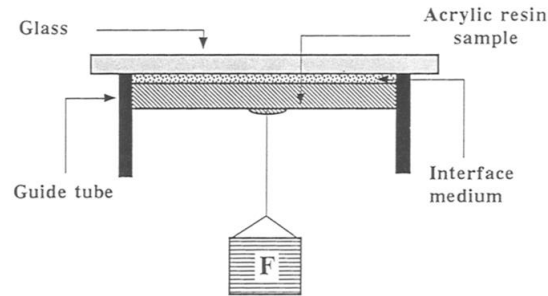
Figure (6): Apparatus used to test adhesion between resin specimen and glass with the film of adhesive material between them (Panagiotouni et al., 1995)

This study, the same as Floystrand's, ignored the effect of surface roughness and saliva. Denture adhesives need moisture to swell. On the other hand, the oral environment usually secrets saliva unstimulated up to 300 ml per day. Therefore, Panagiotouni's method failed to simulate the oral condition.

Between 1995 and 2010, there were other similar adhesive test methods proposed. The test methods mostly overlooked the swelling properties of denture adhesives. In 2010, ISO 10873 proposed the standard tensile test in two different procedures. The sample holders in both procedures were made of poly methyl methacrylate (PMMA). The sample holders had a hole of (22 ±1) mm diameter and a depth of 0.5± 0.1 mm (Figure 7 A). Per ISO 10873, the denture adhesives were applied over the sample holders and soaked in 300 mL distilled water with the temperature of 37 °C for 1 minute. At the end of this period, the extra water was removed from the surface and the sample holder with the denture adhesive was installed in Instron. The sensitive shaft (Figure 7 B) that was covered with PMMA with the dimension of 20 mm was pressed over the denture adhesive with a force load up to (9.8 ±0.2) N with the rate of 5mm/min. After 30 seconds, the sample holder and sensitive shaft pulled in opposite directions with the rate of 5 mm/min. This process was repeated 4 more times to get 5 records of tensile stress. ISO 10873 also proposed a second

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procedure to evaluate the tensile stress. The second procedure was similar to the first one that is described above. The only difference between the two procedures was the sample holder and the denture adhesive were kept in water for 10 minutes before they were installed in instron (Standardization-10873, 2010).
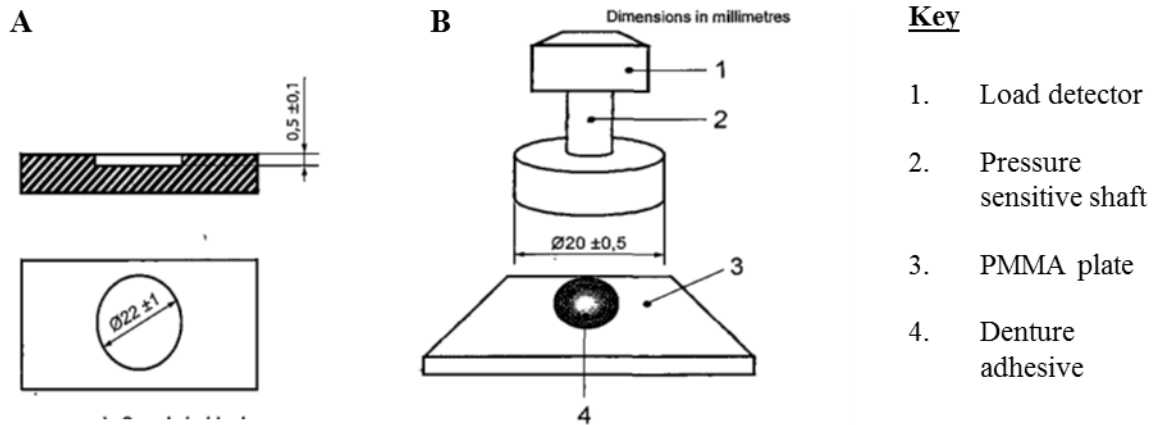
Fig (7): ISO 10873, the standard tensile test (A) Sample holder made of PMMA with the hole. (B) Schematic feature for adhesion test instrument or Instron (Standardization-10873, 2010)

In the working conditions of denture adhesives, two different interfaces are encountered, namely, the interface between the adhesive agent/denture, and the interface between the adhesive agent/gum (oral tissue surfaces). The drastic property differences of these two interfaces would not be well represented by the use of two PMMA plates. Also, the ISO 10873 ignored the effect of saliva components over the denture adhesive.

Another standard test to examine the adhesiveness of the denture adhesive is ASTM F2255, "Standard test methods for strength properties of tissue adhesives in lap shear by tension loading", was defined in 2005 (ASTM-F2255-05, 2005). The purpose of this test is to measure and compare the adhesive strength of the adhesives that are used on soft tissue. In this test, the testing machine is controlling the constant rate of the lap shear test.

The testing machine is made of two plates: one is fixed and the other is movable. The plates are designed so the alignment of movement can be controlled. Figure (8) Shows the fixed and movable parts. They are made of PMMA. Each plate has two sections; the first section is thinner and tissue or another hard plate such as acrylate would be installed, the second section is attached to the first section and is two times thicker than the first section. The second section is usually fixed in the test machine grip. The dimension of the overlap section of these two plates is 10 mm length and 25mm width.
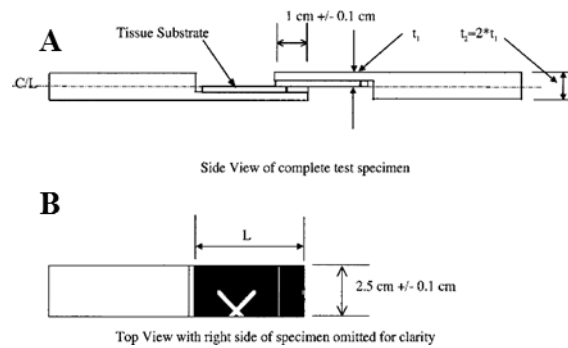
Figure (8): Schematic of the modified standard test method for strength properties of tissue adhesives in lap shear by tension loading (ASTM F2255-05). (A) Side view of complete test specimen. (B) Top view with right side of specimen omitted for clarity (ASTM-F2255-05, 2005).

The soft tissue substrate is usually from frozen or fresh porcine skin graft. The fixed tissue is not usable since the properties of that tissue will interfere with adhesive strength test results. The maximum thickness of the substrate is not more than 5mm since by increasing the thickness the distortion of the substrate will increase and will lead to both shear and tension loads. Moreover, the test should be repeated at least 10 times. The tissue substrate experiments tend to show more variability, therefore, the extra samples are required to get the reasonable mean strength (ASTM-F2255-05, 2005).

We propose to develop new in vitro models for testing the performance of denture adhesives under controlled laboratory conditions. To separately investigate the two different interfaces involved in the application of denture adhesives, we plan to introduce two different substrates in our tests. A polyacrylate part (Dentorium®) will be used as an actual surface of the denture, while a swine skin (porcine skin) will be used to mimic surface properties of the oral tissue. Moreover, saliva was prepared to use instead of distilled water.

4.2 Developing the Adhesive Bond Test Model

We developed models that are extensions of existing standards to better mimic the interface of gingival tissue and dentures. Our models were comprised of two components: one component was formed from denture resin and fabricated with the manufacturer's recommendation; the other component was made from PMMA and supported a piece of porcine skin to mimic the gum tissue. However, in order to optimize the test model without the influence of soft tissue, in the beginning, the experiment was performed on two slides made of PMMA. The slides of PMMA provided the solid surface. Therefore, the results are more consistent with less variety. However, by using porcine skin as a test model, we can assess the effect of surface texture on denture adhesive adhesion, as well. Thus, both the PMMA and Porcine skin models were used to evaluate the effect of saliva on the swelling and adhesion of denture adhesive.

4.2.1 Materials and Test Conditions

All materials were purchased from Sigma-Aldrich and were used as received without more purification. Simulated fresh saliva solution was prepared according to the

formula developed by Fusayama Meyer artificial saliva (AS), (Fusayama, Katayori, & Nomoto, 1963a)(Table 2). The denture Adhesive used was Super Poligrip® Zinc Free (Glaxo Smith Kline Inc.). It was made of Poly (methylvinylether/ maleic acid) Sodium-calcium mixed partial salt, Carboxymethylcellulose, Petrolatum, Cellulose gum and Mineral oil. The commercial denture resin was made of heated polymer methyl methacrylate and monomer ethylene dimethacrylate (Dentorium)®. It was purchased and cured according to standard denture fabrication protocols (O'Rahn A, 2009).

Table 2. Simulated Saliva composition based on Fusayama Meyer Formula (Fusayama, Katayori, & Nomoto, 1963b).

Composition	g/L
KCl	0.4
NaCl	0.4
$CaCl_2.2H_2O$	0.906
$NaH_2PO_4.2H_2O$	0.690
$Na_2S.9H_2O$	0.005
Urea	1

Water content plays a key role in the function of denture adhesives (Hong et al., 2011; Shimazu et al., 2014) . Once applied, saliva penetrates the adhesive and according to the manufacturer's guideline the material will reach its targeted strength within 30 mins. However, the adhesion strength can potentially be affected by the water content of the

paste, which can be changed due to the different levels of saliva production in different patients (Nicolas, Veyrune, & Lassauzay, 2010; Sipahi, Beyzadeoglu, Demirtas, & Ozen, 2007; Turner et al., 2008) . In addition, mouth pH and temperature can also impact the adhesion strength of the paste. These values in the mouth are regulated by saliva and temporarily affected by the consumption of foods and beverages (D. J. Aframian, T. Davidowitz, & R. Benoliel, 2006; Newman & Martin, 2001). For example, the pH of a soda is around 3. The consumption of ice-cold drinks and hot beverages can also affect the denture pH and temperature, and consequently the adhesion strength of the paste. It has been reported that a regular hot beverage can elevate the average oral temperature to 54 °C and a regular cold beverage can drop this temperature to less than 4 °C (Newman & Martin, 2001).

To shed light on the effect of all these parameters, we utilized our *in vitro* models to measure the adhesion strength and other properties of the adhesive paste. In all experiments, the *in vitro* model was exposed to the simulated saliva with a different pH and temperature. The rate of saliva generation varies between different patients. In normal patients, the unstimulated rate of saliva generation is between 0.1 to 1 mL/min. In patients suffering from dry-mouth the rate is less than 0.1 mL/min, while patients with ptyalism the saliva generation rate is more than 1 mL/min (de Almeida, Gregio, Machado, De Lima, & Azevedo, 2008; Humphrey & Williamson, 2001). To mimic these conditions, we changed the hydration time of the paste as will be described in the Experimental Section. Since the total saliva is 200-300 ml per day and denture adhesives are partially in contact with saliva during day, we proposed the 10 minutes soaking in 300 ml saliva to mimic the effect of saliva on denture adhesives. Briefly, in the case of normal salivation, the samples were kept

in an incubator for 30 minutes and then merged into saliva for 10 minutes. To mimic the hyposalivation, the samples were kept in an incubator for 15 min and merged into saliva for 5 minutes. On the other hand, the hypersalivation was mimicked by incubating the samples for 45 min followed by submerging them into saliva for 15 minutes. All tests were carried out with the saliva at a pH of 7 and a temperature of 37 °C. To investigate the effect of pH, saliva with pH of 2, 7, and 10 was used for hydration of the paste. The pH of the saliva was modified by adding the HCl or NaOH (1M) so that the pH of the saliva becomes acidic or basic. The effect of temperature was investigated by exposing the samples to saliva with temperatures of 0, 37, and 60 °C (Table 3).

Table 3. Parameters in three levels including the highest, normal and the lowest values

Factor	Low level	Normal level	High level
X_1: Oral moisture degree	0.1 mL/min	1.5 mL/min	3.5 mL/min
X_2: pH	2	7	10
X_3: Temperature	0 °C	37 °C	60 °C

Table 4. A full factorial design table showing 7 runs and tensile bond strength test and lap shear test

Formulation code	Salivation	pH	Temperature	Y%(Results: mean ± SD(N=10))
F1	0.1 ml/min	7	37 °C	To be determined
F2	1.5 mL/min	7	37 °C	To be determined
F3	3.5 mL/min	7	37 °C	To be determined
F4	1.5 mL/min	2	37 °C	To be determined
F5	1.5 mL/min	10	37 °C	To be determined
F6	1.5 mL/min	7	0 °C	To be determined
F7	1.5 mL/min	7	60 °C	To be determined

4.2.2 Mechanical Test; Tensile Strength and Lap Shear Test

Two mechanical tests, Lap shear and tensile were performed to evaluate the adhesion strength of Super Poligrip® in different conditions. Since no previous experiment had been done to explore the effect of different saliva conditions over denture adhesive bonding, the tensile test and the lap shear test were performed over the solid and even surface of PMMA. Then the experiments were repeated with porcine skin and denture acrylate (Dentorium) ®.

4..2.2.1 Lap Shear Test

In order to test the lap shear, four slides or plates made of PMMA were cut with Laser (VersaLaser, Universal Laser System, Inc.) with dimensions: two 40×22mm pieces and two 30×22mm pieces. The shorter slide was glued over the larger one with the Gel type cyanoacrylate adhesive (super glue). Therefore, two sample holders were prepared (Figure 9).
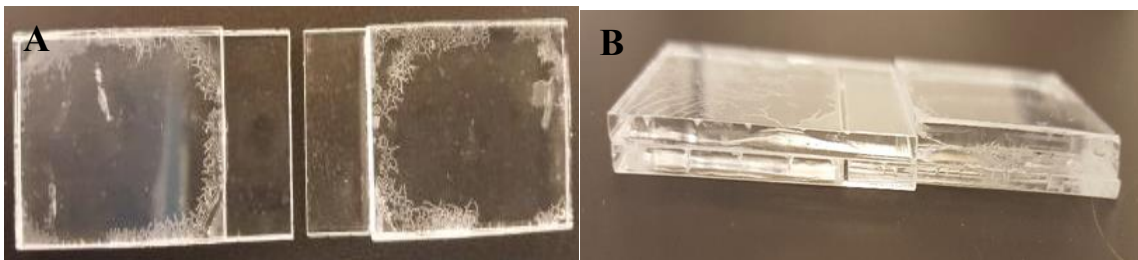

Figure (9): Schematic of the modified standard test method for strength properties of tissue adhesives in lap shear by tension loading. The slides were made of PMMA. (A) Two set slides for lap shear test. (B) Overlap two slides (ASTM F2255-05) (Standard 2005, Cezo, Ferguson et al. 2012)

The same slides made of PMMA were prepared again. The slides made of denture resin (Dentorium)® were prepared as a denture side. The dimensions of these slides were 10mm (L)×22mm (W). They were glued with Gel type cyanoacrylate adhesive (Super Glue) to one of the PMMA slides. Fresh porcine skins with the dimensions of 10mm (L)×20mm (W) were cut and glued to the other set of PMMA slides to mimic the periodontium (Figure 10). The tissue was used within 24h of harvest or was stored in 5-10 °C before the test. After the application of the adhesive, the overlap contact area was 10× 20mm. The tissue was kept damp with wet Kimwipe® and was kept in 37 °C for an hour before measurement.
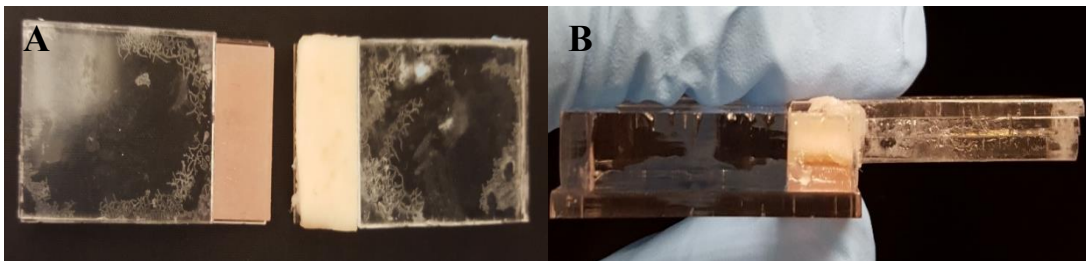
Figure (10): Schematic of the modified standard test method for strength properties of tissue adhesives in lap shear by tension loading. (A) The left slide was made of PMMA and denture acrylate was attached to the first section, the right slide was made of PMMA and porcine skin was glued on the first section (B) The denture adhesive between denture acrylate and porcine skin (ASTM F2255-05) (Standard 2005, Cezo, Ferguson et al. 2012)

Before starting the experiment, all slides were thoroughly washed under tap DI-water and left in the open area to partially dry. This was done to follow the factory recommendation which says patients should wash their dentures and mouth with water before applying the adhesive. After washing the slides, 0.2 g Super Poligrip® was applied over the denture side. After that, the samples were placed in an incubator with 100%

humidity and 37 °C for 30 minutes. After this period, the sample holder with the denture

adhesive was submerged into 200 mL of artificial saliva with different pH, temperature

and duration based on the test conditions for 10 minutes (Table 4). By contrast, to mimic

hyposalivation, the samples were kept in the incubator for 15 minutes and merged into

saliva for 5 minutes. To mimic the hypersalivation, the samples were kept in the incubator

for 45 min followed by submerging them into saliva for 15 minutes. After this period, the

adhesive was pressed gently (2N) onto the skin side and was kept for 30 seconds before it

was loaded into the Instron Mechanical Tester (Norwood, USA). The two slides separated

with the crosshead speed of 5mm/min (Zhao et al., 2004) (Fig).

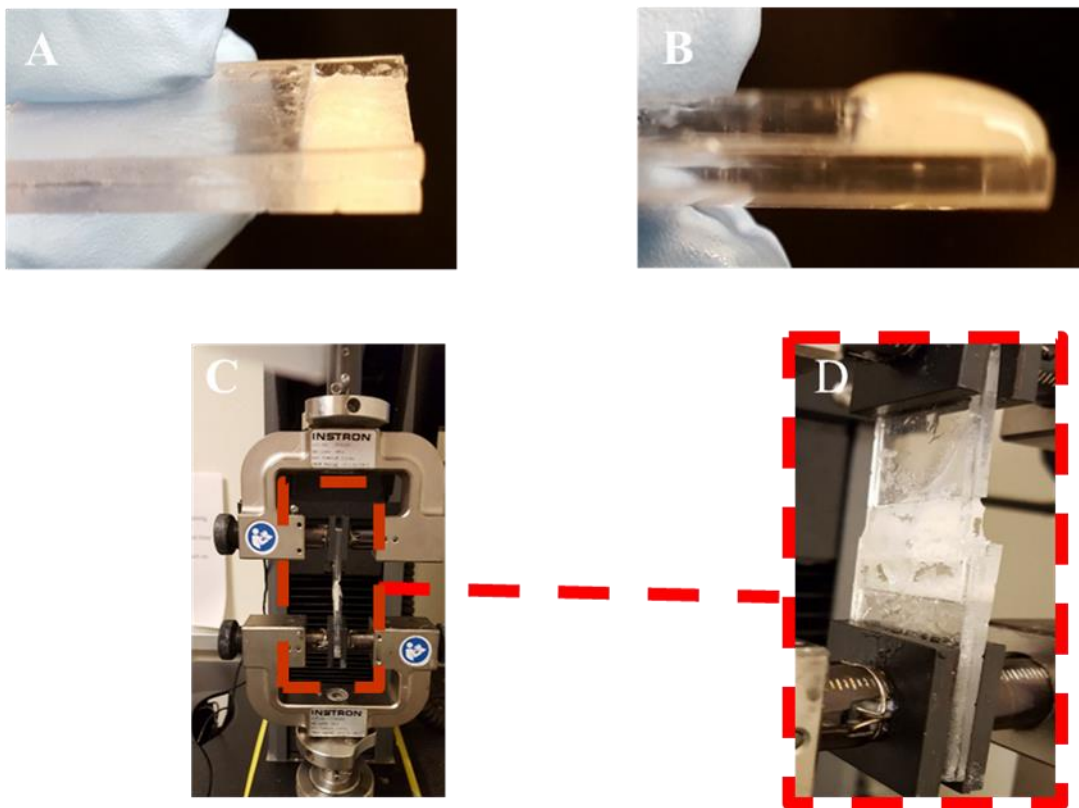Figure (11): Lap shear test to evaluate the adhesive tensile strength base on ASTM F2255-05). (A) Sample holder with the denture adhesive Super Poligrip® before swelling (B) Sample holder with denture adhesive after incubation period and soaking in saliva (C) Pressing sample holder with the denture adhesive into the second sample holder with 2 N force(D) Running the test with 5 mm/min crosshead speed

After full detachment, the area of failure was evaluated. The maximum force before failure was calculated. The shear bond strength (MPa) was the maximum force (N) divided by the bond area (mm^2). The failure mode was categorized as 1) adhesive failure, which is when the adhesive separates completely from one side; 2) cohesive failure, which is when the adhesive debonds inside the adhesive material; or 3) a mixture of both (Figure 12) (Polyzois, Pantopoulos, Papadopoulos, & Hatamleh, 2015). The test was repeated 10 times per variable. The statistical significance was evaluated by one-way ANOVA with the post hoc Tukey test. The test was performed in GraphPad Prism 7.03. The ANOVA test compared three different conditions in each category PMMA or Porcine skin. The statistical significance was valuated by an independent student t-test for two groups of data or analysis of variance (ANOVA) when comparing the PMMA with Porcine skin in each individual condition. Data were calculated as mean ± standard deviation (SD). T test was performed and differences were considered statistically significant when p values were lower than 0.05. P <0.05 (*), P <0.01 (**), P <0.001 (***). P <0.0001 (****).

Figure (12): Representation of failure modes characteristics of adhesive joints submitted to shearing (A) Adhesion failure, detachment material from surface. (B) Cohesive failure, debonds material from inside

4.2.2.2 Tensile Test

In the tensile test, the two sets of sample holders were cylinders made of PDMS with 20mm and 22mm diameters. Both cylinder surfaces were covered with PMMA (Figure 13). Before starting the experiment, both sides were thoroughly washed under tap DI-water and left in the open area to partially dry according to the factory recommendation. After washing the cylinder, 0.2 g Super Poligrip® was applied over the larger cylinder and soaked in 200ml saliva with different conditions. The saliva conditions and soaking duration were the same as the lap shear test (Table 4). After the desired period, the extra saliva was removed from the denture adhesive surface. The sample holders with denture adhesive were mounted in Instron Mechanical Tester (Norwood, USA). The smaller cylinder was pressed to the denture adhesive with 2N force and held for 30 seconds to simulate a gentle occlusal force. At the end of this period, the cylinders were separated with 5mm/min crosshead speed. After full detachment, the area of failure was evaluated and the failure mode was recorded (similar to Figure 12). The maximum force before failure was calculated. The test was repeated 10 times per variable and the mean and the SD were calculated. The tensile test was performed again with different surfaces. The denture acrylate and porcine skin were glued to the PMMA with cyanoacrylate adhesive (Super Glue).
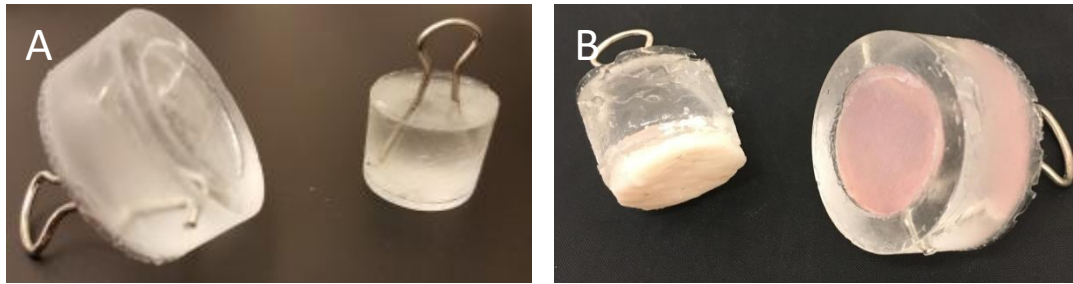
Figure (13): Sample holder for Tensile strength according to ISO 10873. (A) Sample holder is covered with PMMA and (B) porcine skin and denture acrylate.
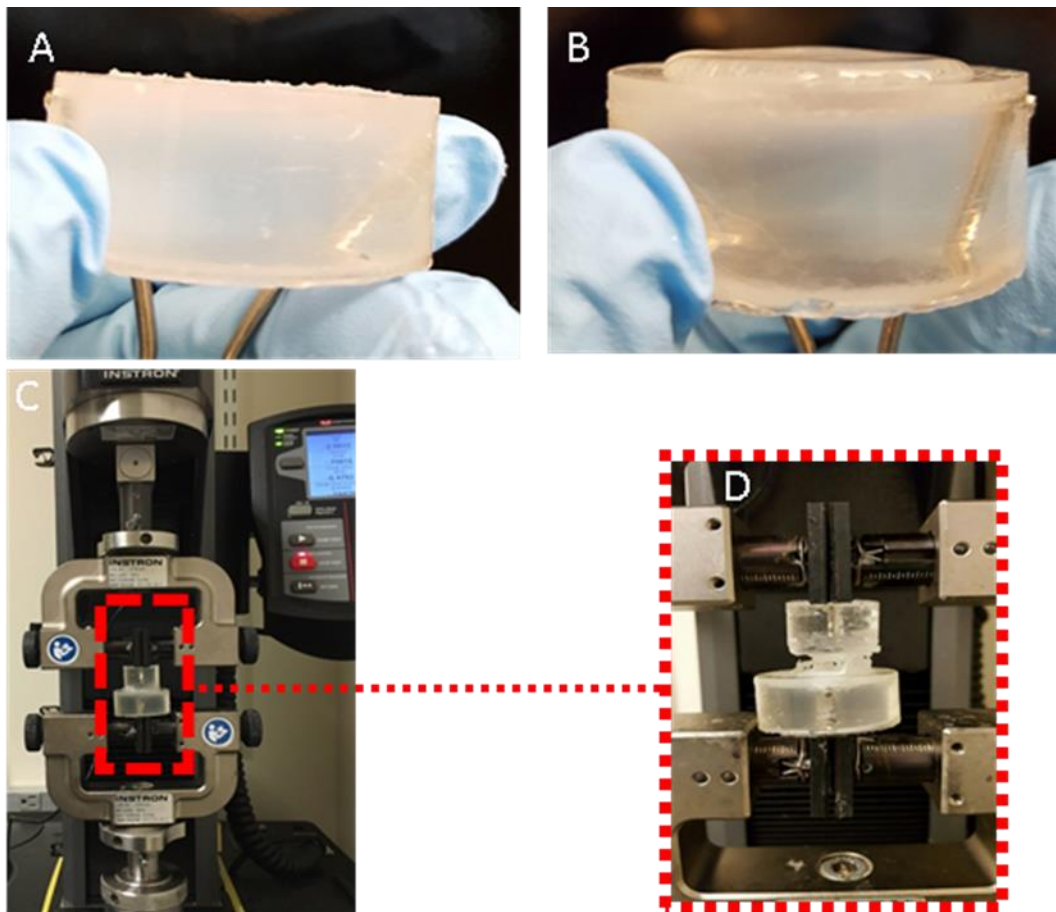
Figure (14): Tensile test to evaluate the adhesive tensile strength base on ISO 10873. (A) Sample holder with the denture adhesive before swelling (B) Sample holder with denture adhesive after incubation period and soaking in saliva (C) Pressing sample holder with denture adhesive into the second sample holder with 2N force (D) Running the test with 5mm/min crosshead speed

5. Effect of Various Conditions on The Adhesion Strength of Denture Adhesives

5.1 Mechanical Test

It is speculated that the environmental conditions affected the paste intrinsic properties and its adhesion strength. The paste is comprised of multiple components including CMC, PMVEMA, mineral oil, and petrolatum. Thus, to find potential solutions for improving the adhesion strength, the effect of environmental condition on adhesion strength should be evaluated through mechanical test.

5.1.1 Lap Shear Test

The graphs bellow showed the adhesive strength of Poligrip over PMMA and Porcine skin in 3 different conditions which were variation in pH, temperature, and level of saliva. The experiment was based on ASTM F2255-05 (ASTM-F2255-05, 2005).

In the temperature group, the three temperatures 0, 37 and 60 ℃ were tested. The adhesive strength became lower in 60 ℃ temperature in comparison with the low (0 ℃) and normal (37 ℃) temperatures both in the PMMA and Porcine skin groups. In the 60 ℃ temperature, the tensile stress was 3660 Pa in the PMMA group and 4772 Pa in the porcine skin group which is significantly different from the normal temperature ($P < 0.01$). On the other hand, the lower temperature (0 ℃) showed adhesiveness no significant difference in porcine skin group in comparison with normal group. The adhesiveness was more prominent in the porcine group rather than the PMMA (Figure 15 &16).
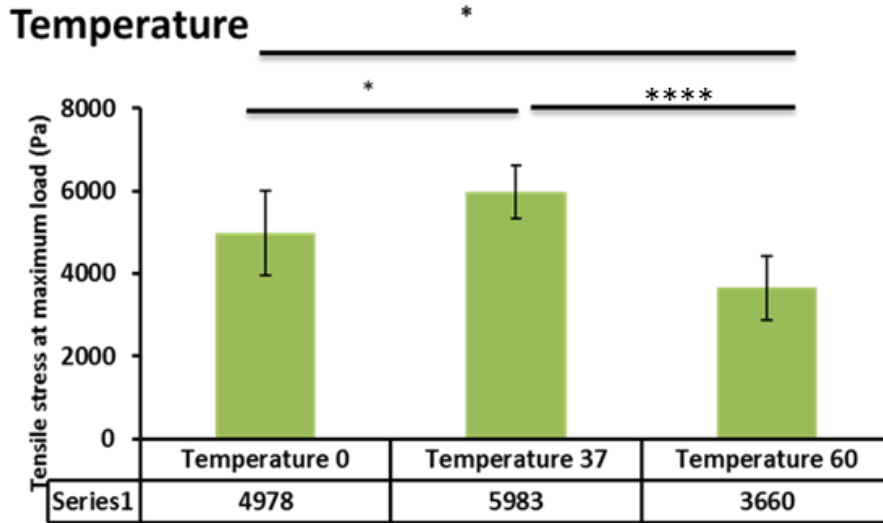
Figure (15): The graph indicated the lap shear test in PMMA covered group. The effect of temperature on adhesiveness showed in higher temperature (60 ℃). It decreased the tensile stress significantly in comparison with other groups.
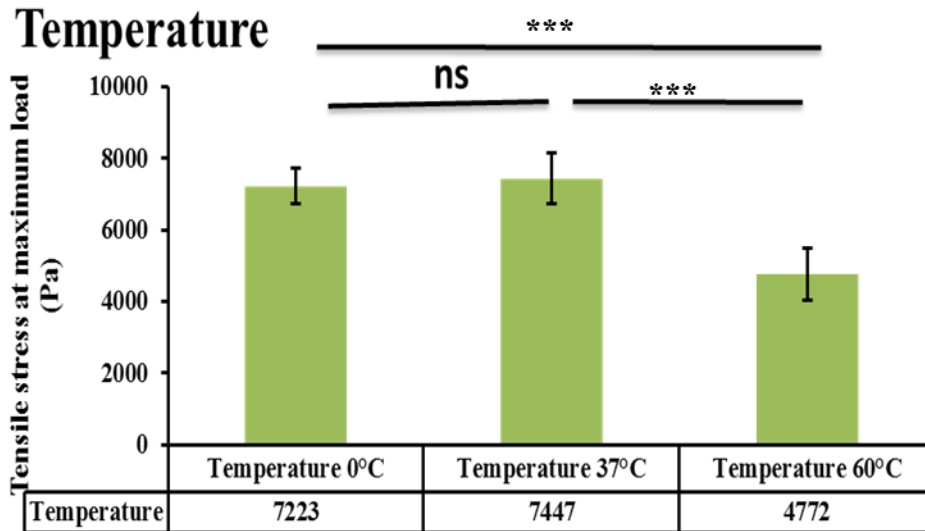
Figure (16): The graph indicated the lap shear test in porcine skin covered group in different temperature. The higher temperature showed decreased of adhesion strength. There was no difference between low and normal temperature

The saliva with the acidic (pH=2), basic (pH=10) and normal pH (pH=7) were used to measure the adhesiveness of the denture adhesive. Apparently, the acidic pH showed significantly higher viscosity compared to the other pH (Figure 17 & 18) in both PMMA and Porcine Skin group. The tensile stress was 8220 Pa in the PMMA and 10034 Pa in the porcine skin group. In contrast, the basic pH showed least adhesion in the pH group both in the PMMA and the porcine skin. The difference was more prominent in Porcine skin than PMMA group
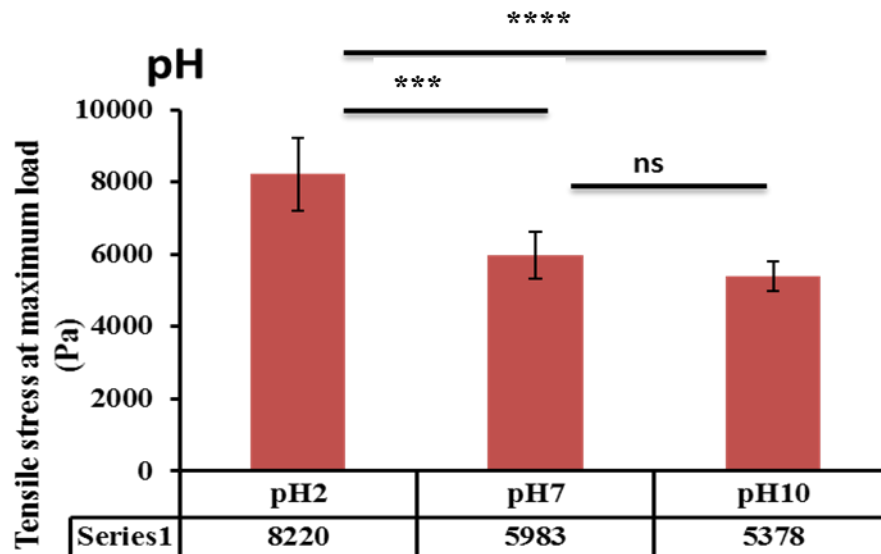
Figure (17): The graph indicated the effect of different pH on adhesiveness in PMMA covered group. The acidic pH showed significantly higher adhesion strength in comparison with the other groups.
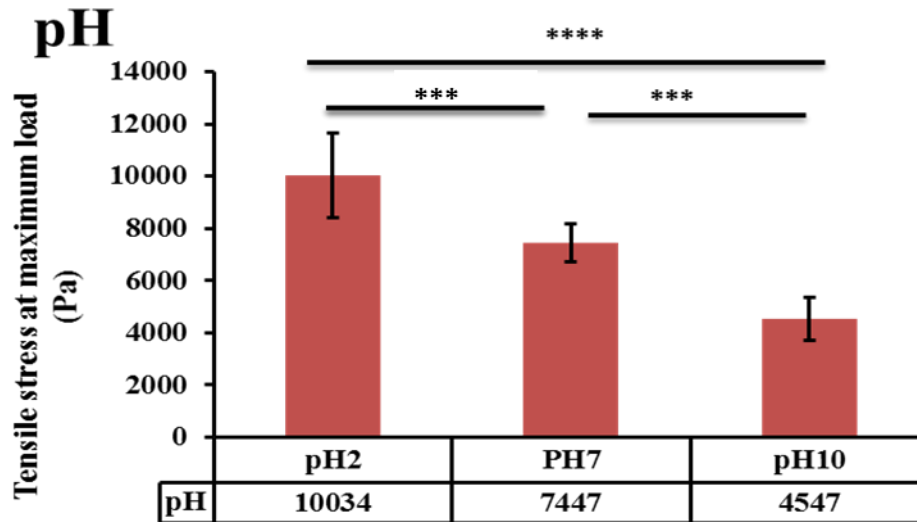
Figure (18): The graph indicated the tensile stress of paste in different pH in porcine skin covered group. The adhesive strength in basic pH was significantly the lowest.

Salivation is a major factor in adhesiveness of denture adhesive since saliva has a main role in the swelling of the paste. This fact was reflected in the data from hyposalivation or low amount of moisture (Figure 19 & 20). Among all groups, the adhesiveness was least in hyposalivation in both the PMMA and the porcine skin. The tensile stress was 2810 Pa in the PMMA and 3439 Pa in the porcine skin which compared with the normal salivation and hypersalivation had significantly less adhesion (P < 0.0001). The interesting result was related to the hypersalivation group. It was expected to have higher tensile strength compared to the normal group. However, the data indicated that the hypersalivation samples both in the PMMA and the porcine skin groups were significantly lower than the normal group. It may be related to solubility of the paste components.
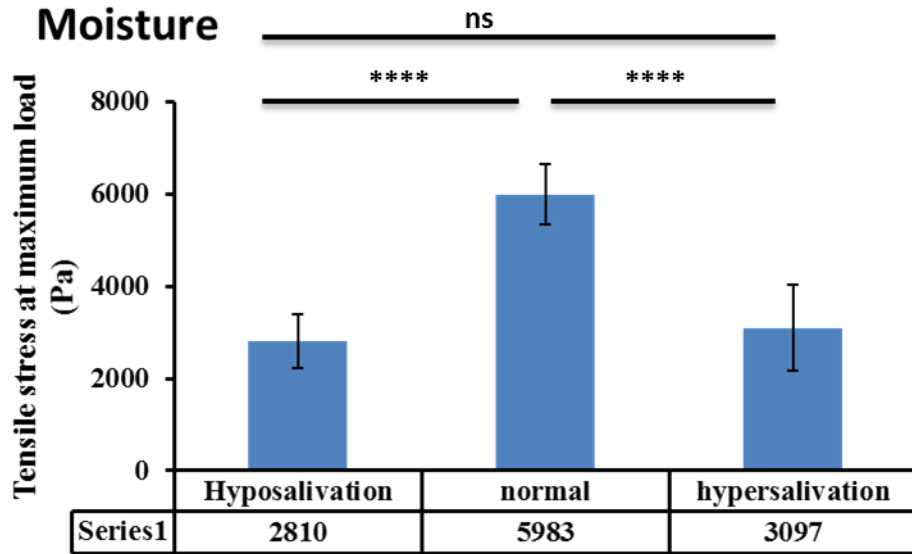
Figure (19): The graph indicated the tensile stress in salivation group in PMMA covered group. The hyposalivation has the most effect on adhesion strength.
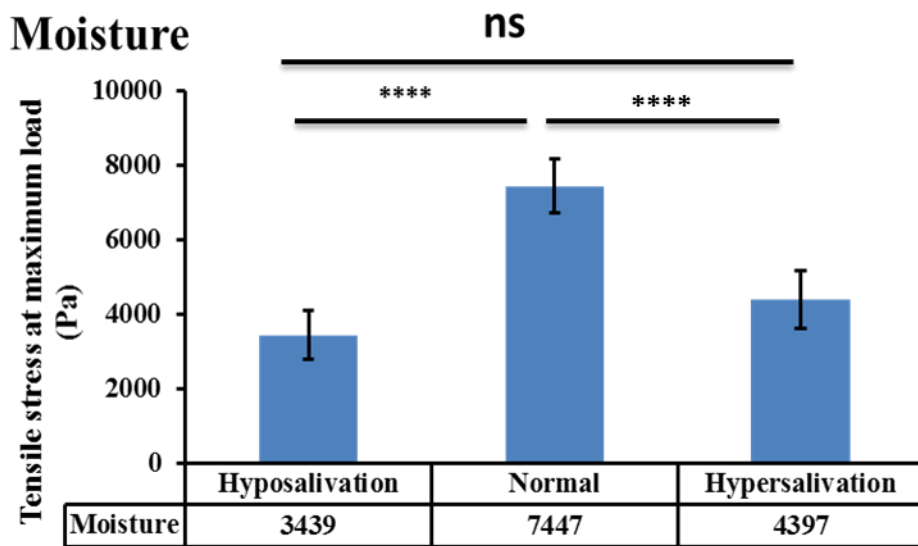
Figure (20): The graph indicated the adhesion strength in different level of salivation in porcine skin covered group. The paste show the lower level of strength in comparison with the other groups

5.1.2. Tensile Strength Test

Tensile strength of Poligrip over PMMA and Porcine skin in 3 different conditions which were variation in pH, temperature, and level of saliva were evaluated.

In the temperature group, the three temperatures 0, 37 and 60 ℃ were tested. The tensile strength became lower in 60 ℃ temperature in comparison with the low (0 ℃) and normal (37 ℃) temperatures both in the PMMA and Porcine skin groups. In the 60 ℃ temperature, the tensile stress was 3177 Pa in the PMMA group and 2674 Pa in the porcine skin group which is significantly different from the normal temperature ($P < 0.01$). However, there is no significant difference between the porcine skin and PMMA groups. On the other hand, the lower temperature (0 ℃) showed higher adhesiveness in comparison with the other groups (Figure 21 & 22). The adhesiveness was more prominent in the porcine group rather than the PMMA.
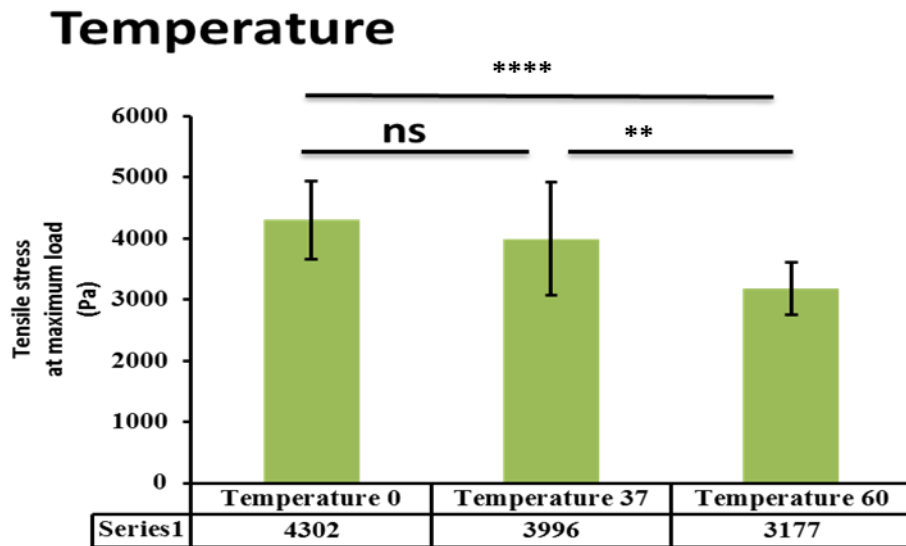
Figure (21): Tensile strength test of PMMA covered group with different temperature. There is no significant difference between low and normal temperature.

Temperature

Temperature	Temperature 0°C	Temperature 37°C	Temperature 60 °C
Temperature	5234	4143	2674
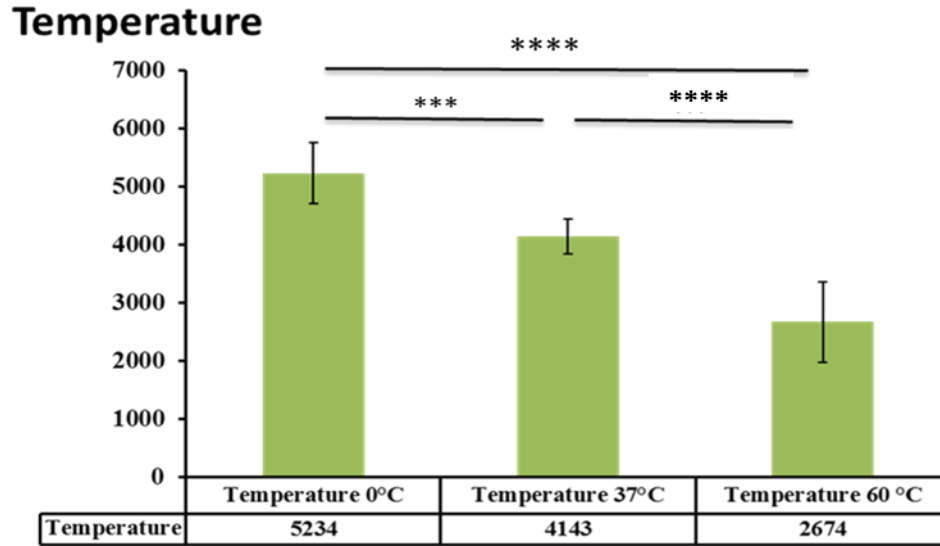
Figure (22): Tensile stress in porcine skin covered group with different temperature. The low temperature showed significantly higher adhesion in comparison with the other groups.

The saliva with the acidic (pH=2), basic (pH=10) and normal pH (pH=7) were used to measure the adhesiveness of the denture adhesive. Apparently, the acidic pH showed significantly higher viscosity compared to the other pH (Figure 23 & 24). The tensile stress was 6096 Pa in the PMMA and 5853 Pa in the porcine skin group. In contrast, the basic pH showed least adhesion in the pH group both in the PMMA and the porcine skin.
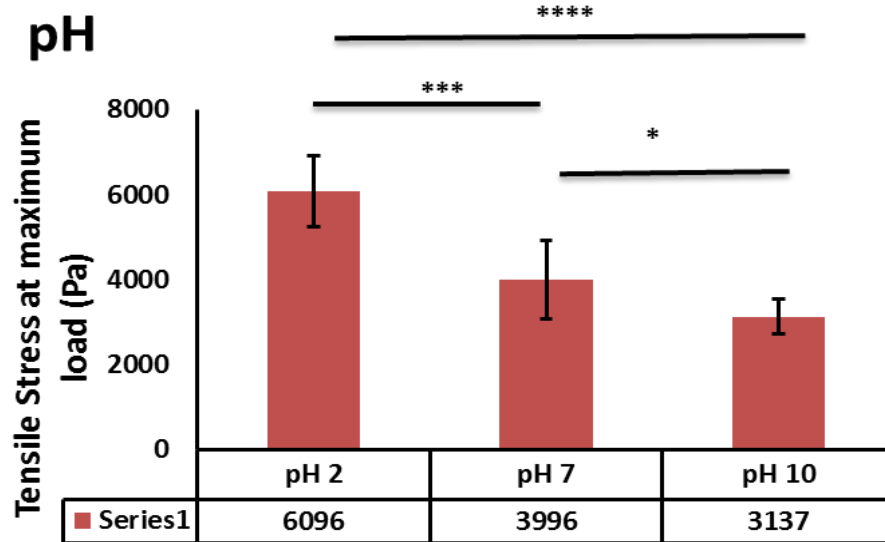
Figure (23): Tensile stress of paste in different pH saliva in PMMA covered group. The pH2 showed the significantly higher strength than the pH10.
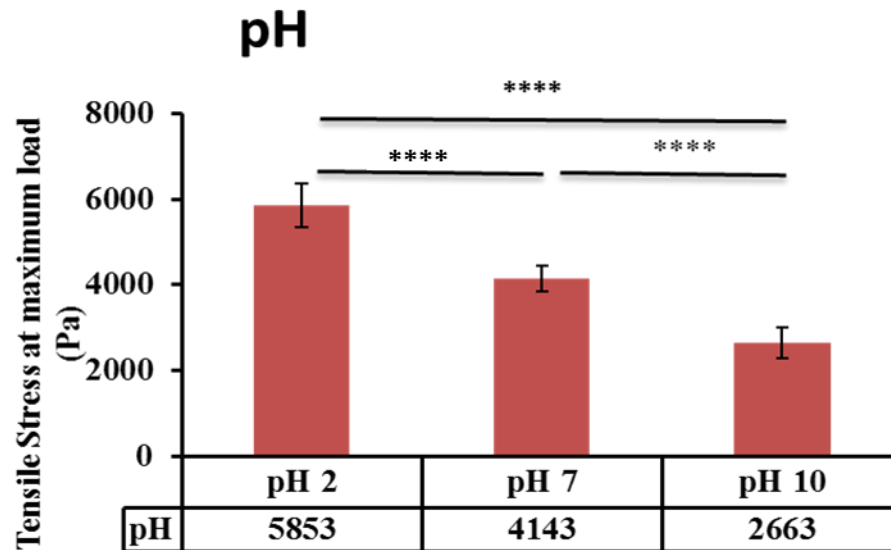
Figure (24): Tensile stress in porcine skin covered group with different pH. pH 10 showed the least viscosity of all pH conditions.

The level of salivation or moisture was the last group of conditions to be tested. Among all groups, the adhesiveness was least in hyposalivation in both the PMMA and the porcine skin. The tensile stress was 2744 Pa in the PMMA and 2282 Pa in the porcine skin which compared with the normal salivation and hypersalivation had significantly less adhesion ($P < 0.0001$). The interesting result was related to the hypersalivation group. It was expected to have higher tensile strength compared to the normal group. However, the data indicated that the hypersalivation samples both in the PMMA and the porcine skin groups were significantly lower than the normal group (Figure 25 & 26). It may be related to solubility of the paste components.
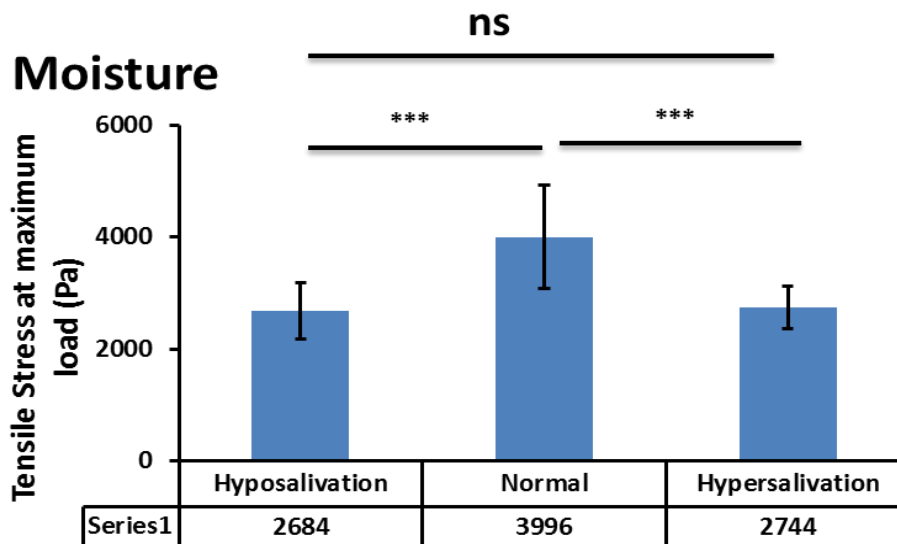
Figure (25): Tensile stress of paste in different salivation level in PMMA covered group. The hyposalivation and hypersalivation showed the significantly effect on adhesion.
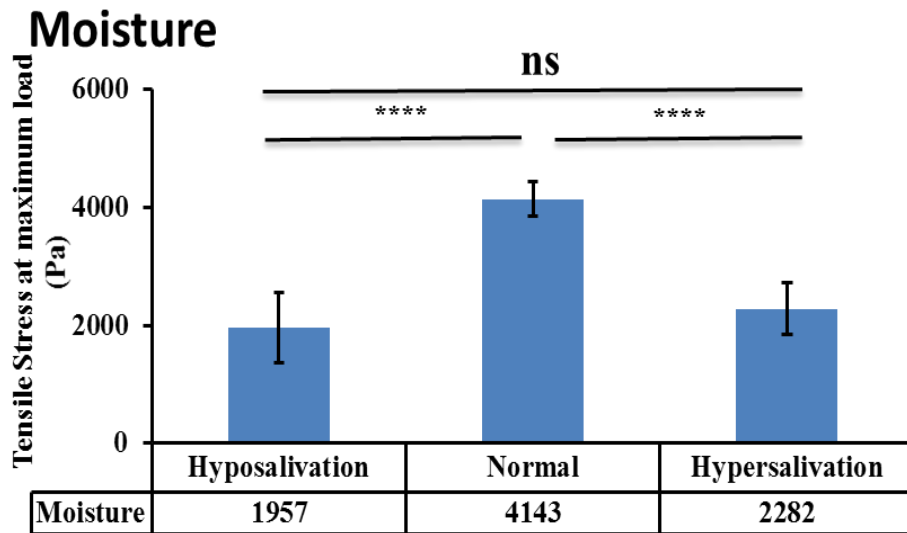
Figure (46): Tensile stress in porcine skin covered group showed that the hyposalivation has lower adhesion in comparison with the other groups.

In general, both the PMMA and the porcine skin groups showed the same pattern in adhesiveness among 7 group conditions. The least adhesiveness was related to the hyposalivation and the strongest tensile strength was related to the acidic condition (Figure 27 & 28). The only condition that showed significant difference between PMMA and porcine skin was 0 ℃ temperature.

	pH2	pH7	pH 10	Hyposalivation	Normal	Hypersalivation	Temperature 0°C	Temperature 37°C	Temperature 60°C
⊠ Porcine Skin	10034	7447	4547	3439	7447	4397	7223	7447	4772
■ PMMA	8220	5983	5378	2810	5983	3097	4978	5983	3660
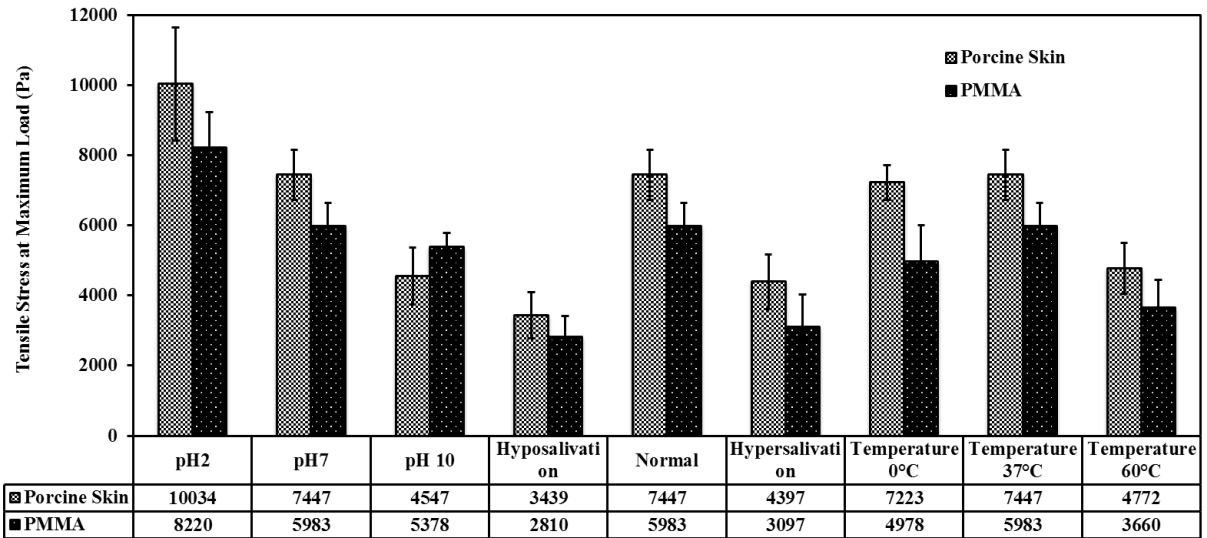
Figure (27): Summary of lap shear test comparison between PMMA and porcine Skin. In all conditions, porcine skin group showed slightly more adhesiveness in comparison with PMMA covered group. However, the pattern among each sub group are the same in both PMMA covered group and porcine skin covered group

	pH2	pH7	pH10	Hyposalivation	Normal	Hypersalivation	Temperature 0°C	Temperature 37°C	Temperature 60°C
⊠ Porcine Skin	5853	4143	2663	1957	4143	2282	5234	4143	2674
▣ PMMA	6096	3996	3137	2684	3996	2744	4302	3996	3177
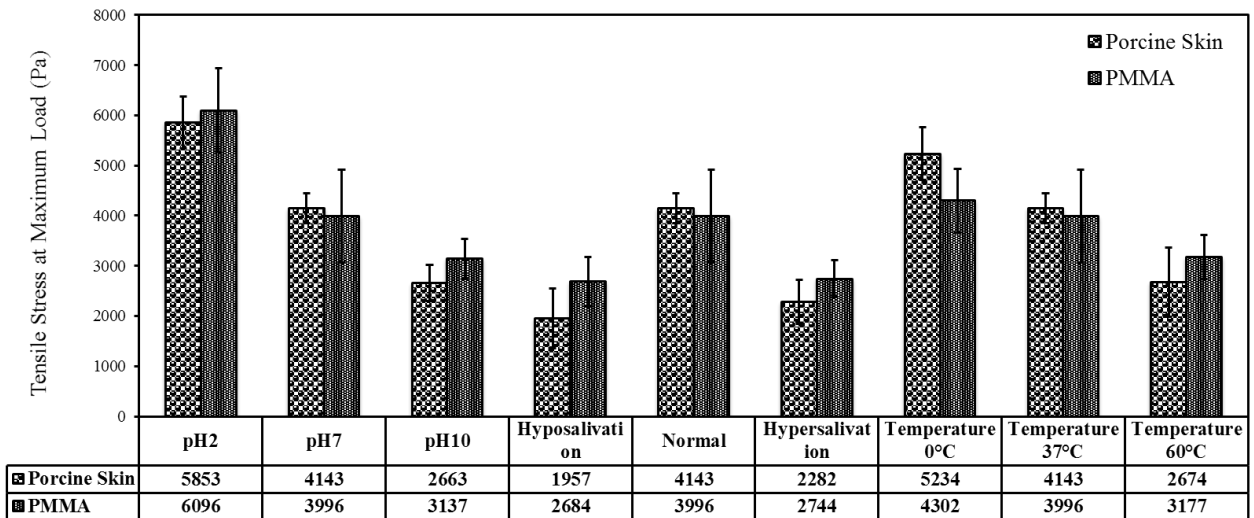
Figure (28): Summary of tensile test comparison between PMMA and porcine Skin. There is no significantly difference between PMMA and porcine skin

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The super Poligrip® mainly consists of CMC and PMVEMA (Poly(methylvinyether/maleic acid) Na/Ca mixed partial salt (Gantrez)) as active ingredients and mineral oil and petrolatum to prevent excessive swelling of the active compounds. The active ingredients of denture adhesives swell and become viscous and sticky in the presence of water or saliva (Han et al., 2014). The increased volume of the swollen hydrophilic ingredients fills the voids between the denture base material and the oral mucosa, creating retentive forces. CMC and PMVEMA are often used as active ingredients in today's denture adhesives, especially in cream type adhesives, which are designed to achieve both short-term and long-term effectiveness. CMC has higher solubility and provides a strong initial hold, but it dissolves quickly and loses its effectiveness within a relatively short period because of its high swelling ratio. PMVEMA is less hydrophilic , allowing it to play a positive role later, and last longer (Barbucci, Magnani, & Consumi, 2000). In a study, it was demonstrated that a different composition of active ingredients influenced the adhesion strength (Han et al., 2014). Samples containing only CMC had a higher initial strength, and achieved their highest adhesive strength after immersion in water for 1–10 min, followed by a reduction in adhesive strength. The initial adhesive strength of the samples containing only PMVEMA was lower, but it increased steadily over time, with very little decrease in adhesive strength over the entire test time. These results are consistent with Kulak's study, who reported that denture adhesive paste based on PMVEMA compounds rated higher than CMC adhesive paste on chewing ability and duration of effectiveness in the mouth (Kulak, Özcan, & Arikan, 2005). The samples containing both CMC and PMVEMA not only had higher initial adhesive strength, but also had a longer duration of effectiveness.

The changing adhesion of CMC over denture resin in different pH environments could be explained with the electrostatic repulsion phenomenon. The Poly (methyl methacrylate) (PMMA) is the resin choice to fabricate the denture base resin. The denture resin has excellent physical properties. The denture resin surface charge is negative. It can gain more negative surface charge through the copolymerization of methacrylic acid to methyl methacrylate (Park, Periathamby, & Loza, 2003). By looking at the surface charge of CMC, the electronegativity increases from acidic toward basic environments. CMC has free acid form (neutral) at acidic pH (pH 3.0). These free acid groups are ionized in pH 9.0 (negatively charged) (Wang & Somasundaran, 2005).Therefore, the adsorption of CMC on denture resin would be changed in different pH environments. By increasing the pH, the adsorption density of CMC would be reduced. This whole process may show the importance of electrostatic interaction role in the adsorption process.

Our tensile and lap shear experiments showed a low adhesion strength in samples prepared under the hyposalivation condition. Since hyposalivation is frequently observed in the elderly population, which is the main age group using dentures, finding solutions for improving the adhesion strength of the paste under the hyposalivation condition is necessary. We speculated that the low adhesion strength under the hyposalivation condition was due to the low hydrogen bonds due to lack of sufficient water or moisture in the paste (Barbucci et al., 2000). Therefore, we next studied more on the molecular level to investigate the main reason for adhesion bond strength in different conditions.

5.2. Understanding Intrinsic Properties of the Paste

After analyzing all these mechanical data, it was obvious that some internal interactions were responsible for different behavior of the paste in different conditions. The paste is comprised of multiple components including CMC, PMVEMA, mineral oil, and petrolatum. Thus, understanding different properties of the components and the paste, as well as the interactions between various components, can provide valuable information resulting in developing strategies for improving the adhesion strength.

There have been several studies conducted regarding the mechanism of adsorption of CMC on solids. The whole process is not still fully understood. Mackenzie, Pugh and Healy suggested that the main interactions between polymers and mineral surfaces were hydrophobic, chemical and electrostatic interactions and hydrogen bonding. However, they did not explain the reason for selectivity of adsorption on minerals (Healy, 1974; Mackenzie, 1986; Pugh, 1989). Steenberg et al and Ralston et al proposed the role of hydrophobic force as a main adsorption between polysaccharide and talc as opposed to Jucker and Rath who proposed the role of hydrogen bonding (Jucker, Harms, Hug, & Zehnder, 1997).

Therefore, we probed swelling and degradation of the paste and its ingredients and measured rheological properties of the paste in the different conditions.

5.2.1 Swelling Ratio Test

Swelling ratio (%)in different pH conditions will indicate the solubility of the denture adhesive in the oral condition. Also, one of the main criteria for any denture adhesive to function properly is swelling. Therefore, swelling rate and degrading the

denture adhesive paste could be an important factor to investigate the mechanism of this paste.

The paste was incubated with saliva with pH 2, 7 and 10 for a duration of 4 hours with 2, 5, 10, 30 minutes and 1-hour intervals. It is expected that the swelling ratio in pH 10 is increased.

The regular poligrip paste was weighted in the beginning of the experiment. The samples were placed in 100μm cell strainers with 11mm saliva with 3 different pH 2,7 and 10. The samples were kept in the incubator for the duration of experiment. Measurment were obtained in certain interval of 2, 5, 10, 30 min and 1 hour for 4 hours duration (4 intervals of 2 minutes, 3 intervals of 5 minutes, 2 intervals of 10 minutes, 1 intervals of 30 minutes and 3 intervals of 1 hours) (Figure 29). The average of swelling ratio percentage and SD were calculated for each group (Eq. 2). Swelling tests confirmed more stability of the paste in pH2 which we can see also in mechanical strength behavior of different pHs.

$$\text{Swelling Ratio \%} = \frac{W_s - W_d}{W_d} \times 100 \qquad W_s \text{ is final weight,} \qquad (2)$$

$$W_d \text{ is initial weight}$$
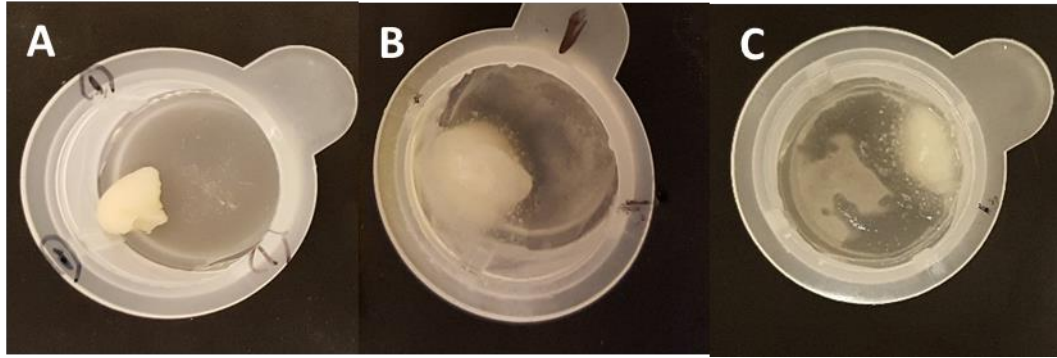
Figure (29) : The swelling and degradation test of paste. The regular Super Poligrip in pH 7 saliva (A) in the beginning (B) after 2 hours (C) after 4 hours. The paste swelling ratio was 200% in 70 mintes. After 2 hours the paste swelling ratio declined graduately.

Figure 30 shows the swelling and the degradation of the paste at different pH values. It could be seen that in an acidic environment, the paste showed the lowest swelling rate. Once the swelling ratio reached 200% of the dry weight, the paste started to dissociate and to degrade. The swelling and the dissolution rates were faster in a basic environment and the dissolution started after 40 min in comparison to 70 min at a neutral pH.
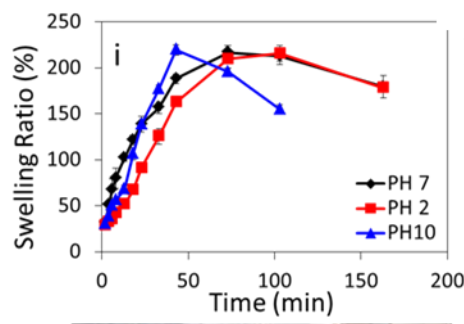
Figure (30): Physical characterization of the paste. Swelling ratio of the Poligrip® Free paste in artificial saliva with pH2, 7 and 10; Swelling tests confirmed more stability of the paste in pH2 which we can see also in mechanical strength behavior of different pHs. The swelling and the dissolution rates were faster in a basic environment and the dissolution started after 40 min in comparison to 70 min at a neutral pH. The same trend was seen for CMC, which is the hydrohilic part of the paste. However, CMC showed a higher swelling ratio in comaprison to the paste.

5.2.2 Modulated Temperature Differential Scanning Calorimetry (MTDSC) and Thermogravimetric Analysis (TGA)

DSC is measuring thermal transition such as melting point (T_m), crystallization (T_c) and glass transition (T_g) in the paste. The results of DSC show what is happening to the paste when it is heated. Thermogravimetric Analysis (TGA) is a process which shows how much the paste will be decomposed by heat. Both of these experiments study the paste on a molecular level and the stability of molecular bonding during temperature changes (K. H. Chung, C. S. Wu, & E. G. Malawer, 1990). Since the samples in the temperature group (0, 37, 60 °C) in both tensile and lap shear tests showed different adhesive bond strengths, the DSC and TGA studies will reveal more mechanisms of adhesion.

MTDSC study was performed on a TA Q1000 over a temperature range from under -80 °C to 150°C. The lyophilized samples were typically between approximately 2.4-3.6mg. The samples were heated from 23°C to 100 °C at a heating rate of 5 °C /min. The nitrogen flow rate was 18 mL/min.

TGA was performed using a TA Q500 in nitrogen atmosphere at a heating rate of 5 °C/min and a temperature range from room temperature to 300 °C. The nitrogen flow rate was 20 mL/min.

TGA curves of the paste and its ingredients are also presented in Figure 31A. The TGA results showed the degradation of all materials is completed in two steps. For the first step, around 20% of material degraded, which was increased to 60% at the next step.

Based on TGA data, illustrated in Figure 31A, all components were stable until 100 °C. Hydrated paste showed 40% weight loss around 90 °C, which might be due to water

evaporation, The DSC diagram of the paste shown in Figure 31B displays transition temperatures and melting points of the paste in different pHs. It seems that at pH 10 the amorphous paste undergoes a faster melting and degradation. At pH 7, two main transitions were observed. However, at pH 2, the paste experienced a smoother transition that could be due to stronger internal interactions and hydrogen bondings. The proposed mechanism for different observations will be discussed in detailed in the following section.
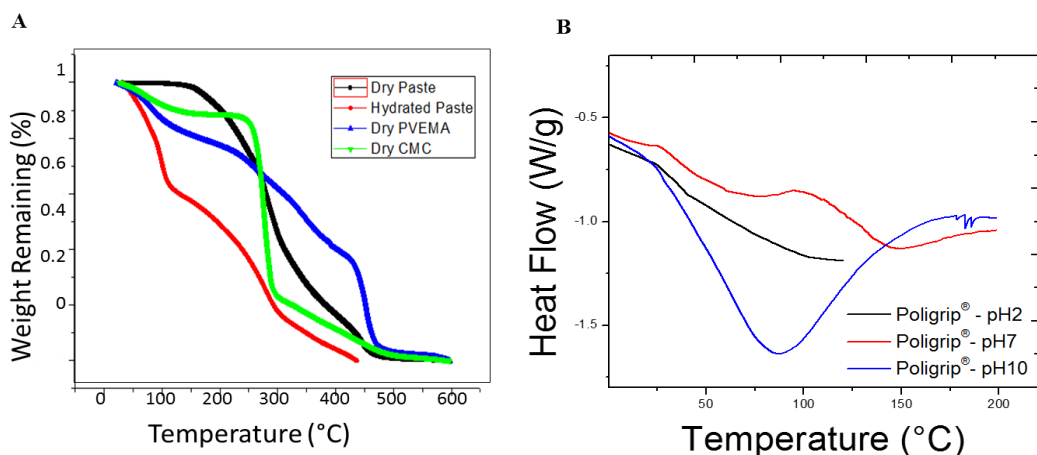
Figure (31): Thermal characterization of paste. (A) Weight loss (TGA) of Dry paste, hydrated paste,. It seems all component are stable till 100 °C. (B) DSC diagrams display transition temperatures and melting points of the paste in different pHs. During the heating process, the paste at pH10 undergo to melting process quicker than the other groups.

5.2.3 Rheology

Rheological properties provide a measure of cohesion properties of soft materials. Rheological measurements were made with a TA Instruments AR-G2 Rheometer. Samples were contained between two horizontal parallel stainless steel plates of 20 mm diameter. Frequency and shear rate sweeps were performed at 0, 37 and 60 °C, sweeping frequencies from 0.001 to 100 Hz at 1% strain and shear rates from 0.001 to 100 s^{-1} with 10

points/decade. Frequency sweeps were performed using a cone-plate rheometer (25 mm diameter, 1 angle, 50 μm truncation gap). Samples were analyzed in different pHs as well as different temperatures based on sample preparation methods for each condition mentioned.

In the case of Poligrip®, our mechanical tests for measuring the adhesion strength of the paste, showed a cohesion failure. Thus, it is expected that the paste viscosity could be used to further verify the failure mechanism of the paste. Thus, the viscosity of the paste was measured at different pHs and temperatures. As illustrated in the figure 32, pH 2 had the highest viscosity, followed by pH 7. The lowest viscosity was recorded at pH 10, which was consistent with the mechanical data. Viscosity of the paste in 0 °C was higher to be measured with the rheometer while at 60 °C the paste viscosity was the lowest.

Fig (32): Rheology of Poligrip, pH2 has the highest viscosity, then pH7 and pH10. It seems this material is working really good in acidic condition, for 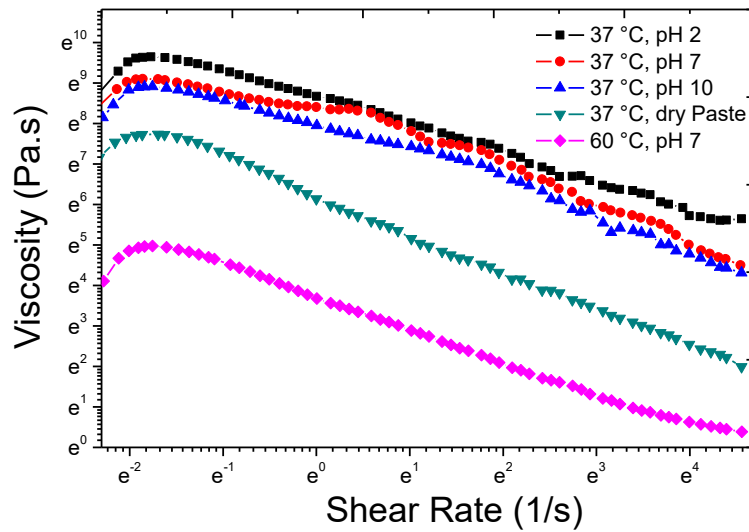the temperature comparison, 0°C could not be examined in Rheometer, but as expected 60°C has the lowest viscosity than 37°C.

5.2.4 Fourier Transform Infrared Spectroscopy (FTIR)

FTIR is used to evaluate the molecular and chemical interaction of compounds. The denture adhesive should be hydrated to show its effects, therefore, the adhesion usually takes place between the hydrogen group and the carbonyl group mainly and to a lesser extend between C-H and C-O-H bondings. The carbonyl vibrations of a carboxylate and a carboxylic acid group occur at very different wavenumbers (1400-1750 cm^{-1}). The shifts in different wavelengthS, reveal the effects of hydration, temperature and pH on denture adhesive.

Attenuated total reflectance Fourier transform infrared (ATR-FTIR) spectra were acquired using a Jasco FTIR-6200 Microscope spectrometer equipped with a Smart Endurance diamond ATR accessory (100 scans, 1 cm^{-1} resolution, wavenumber range 4000-400 cm^{-1}). Spectral manipulations were performed using GRAMS/32 software (Galactic Industries Corp., Salem, NH). External reflection FTIR was recorded on a Specac grazing angle accessory and a mercury cadmium telluride (MCT/A) detector. The samples for each group prepared the same as mechanical tests. Milli Q pore water with different pH values was used as background. The resolution was 1 cm^{-1} and 100 scans where averaged for each sample.

Figure 33 indicated the red shift for C-H bending, alcolic C=O and stretching C=O bonds from 1753 cm^{-1} at 60°C to 1748 cm^{-1} at 37 °C and then to 1733 cm^{-1} at 0°C. The vibrational peaks for carbonyl groups of carboxylate and carboxylic acids appeared at different wavenumbers in the range of 1400-1750 cm^{-1} spectral window in Figure 33 (A, C, E). However, it is difficult to quantify the amount of each component using FTIR (Maeda, 2001; Maeda, Mochiduki, Yamamoto, Nishimura, & Ikeda, 2003; Yuen, Choi,

Phillips, & Ma, 2009). As it is shown in Figure 33 A, at different temperatures, a red shift can be seen for C-H bends, alcoholic C=O and stretching C=O bonds from 1753 cm^{-1} at 60 °C to 1748 cm^{-1} at 37 °C and then to 1733 cm^{-1} at 0°C. The intensity of this peak was reduced by decreasing the temperature. By decreasing the temperature from 60 °C to 37 °C, another growing peak appeared at 1640 cm^{-1}, which got shifted to 1636 cm^{-1} at 0 °C. Also, as the temperature decreased, the stretching O-H bonds showed a shift from 3277 at 60 °C to 3253 at 37 °C and then to 3248cm^{-1} at 0 °C. The non-bonding O-H peak around 3700cm^{-1} almost disappeared at 0 °C, which suggests better bonding formation between polymer chains at lower temperatures. Based on the rheological analysis showing a reduction in paste viscosity by temperature increase, it is postulated that long chains were more cross-linked with stronger internal interactions at 0 °C. The chains however might have been reshaped into a relatively aligned network at 37 °C, but eventually it should have been deformed into a dynamic amorphous scaffold at 60 °C (figure 33 B). For different pH values, O-H stretching bond became sharper at pH 2 in comparison to pH 7 and pH 10; C=O stretching at pH 2 had more intensity with a little shift, and O-H and C=O stretching in the paste was noticeable around 1400-1700 cm^{-1}. C-O stretching and C-O-H stretching, bending and deformation peaks around 1100-1400cm^{-1} were also more remarkable at pH 2. At pH 10, almost all peaks became shallow with some shifts indicating more non-bonding C=O and O-H bonds compared to internal bonds at pH 7 and pH 2. The different water uptake behavior of the paste and CMC in basic condition in compare with acidic and neutral conditions revealed that H-bonding is very important phenomena in this study. Electrostatically charged carboxylic acid groups has key effect on the water uptake and swelling, dissociation and degradation rate of the paste. At low pHs, the hydrophilic parts

of the paste can form hydrogen bonding in protonated -COOH forms, repel entering water molecule inside the structure and slower water uptake. On the contrary at higher pHs, more ionized COO- attracts more water molecules inside the network. It will show faster water uptake as well as faster network dissociation. (Cuba-Chiem, Huynh, Ralston, & Beattie, 2008)

For hypersalivation condition, almost all peaks became broader with less intensity that might have been due to putting samples inside the saliva for longer time and paste dissolution. These observations are in agreement with the mechanical and physical properties of the paste. Less strong internal interactions were observed in the paste at the hyposalivation condition in comparison to the paste receiving sufficient hydration as demonstrated in the FTIR data. In presence of insufficient amount of saliva, the -OH non bonding peak is noticeable around 3600-700 cm^{-1} and another peak existed around 1700-800cm^{-1} which could be associated with the presence of -COOH non bonding groups that may formed as a result of oxidation of -OH groups.
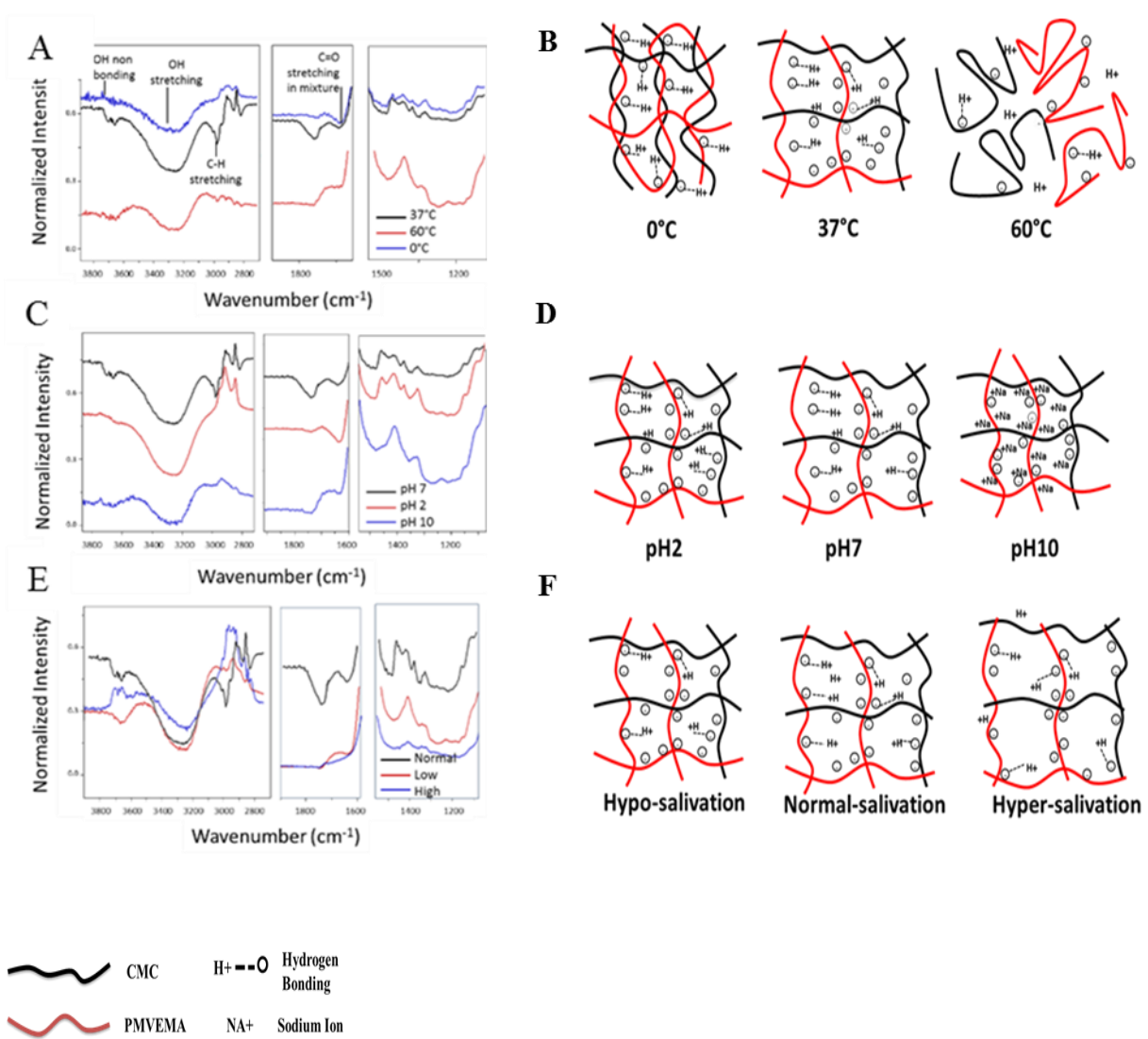
Figure (33): The interactions of various hydrophilic components of the adhesive paste. (A) FTIR spectra showing the interactions between two different hydrophilic components of the paste at various temperatures; (B) Schematic showing polymeric network rearrangements in response to temperature variations; Black chains represent the CMC and red chains represent the PMVEMA. In low temperature, the chains are more cross-linked with stronger internal interactions. On the other hand, in higher temperatures like 60ºC the polymer chains will have higher mobilities and go through a more amorphous-like phase; as they are far from each other, they cannot form very strong internal interactions like hydrogen bond and will dissociate very fast; (C) FTIR spectra showing the interactions between two different hydrophilic components at various pH values; (D) Schematic showing polymeric network structure and internal interactions within two hydrophilic polymer parts; The components have more hydrogen bonding interaction in acidic condition and

fewer hydrogen bond in basic pH. Because of the presence of high negative electrostatic repulsion charges and neutralization with Na+ ions, the network becomes more accessible for water molecules and more dissociation in basic condition; (E) FTIR spectra showing the interactions between two different hydrophilic components of the paste at various moisture contents; (F) Schematic showing potential mechanism of inter- and intra- chain interactions and hydrogen bonds at different moisture contents. In hypersalivation, water molecules are present at higher concentrations within paste structure, which can create high level of swelling, as well as interfer with components' internal interactions and make them very loose inside the paste. Since the quantity of water molecules is really high, the hydrophilic parts of the paste would prefer to dissolve and dissociate inside the aqueous system. In hypo-salivation mode, we have an opposite story of not having enough water molecules so even the hydrogen bond inside the paste will not be sufficient for having a strong adherence and attachments to the surfaces. It seems that normal conditions with normal amount of saliva provide the best environment in this study.

6. Improving the Adhesion of Denture Adhesives

In a study, it was demonstrated that a different composition of active ingredients influenced the adhesion strength (Han et al., 2014). Samples containing only CMC had a higher initial strength, and achieved their highest adhesive strength after immersion in water for 1–10 minutes, followed by a reduction in adhesive strength. The initial adhesive strength of the samples containing only PMVEMA was lower, but it increased steadily over time, with very little decrease in adhesive strength over the entire test time. These results are consistent with Kulak's study, who reported that denture adhesive paste based on PMVEMA compounds rated higher than CMC adhesive paste on chewing ability and duration of effectiveness in the mouth (Kulak et al., 2005). The samples containing both CMC and PMVEMA not only had higher initial adhesive strength, but also had a longer duration of effectiveness.

Tripropylene glycol methyl ether (TPME) is a hydrophilic macromolecule with hydroxyl group and ether and hydroxyl groups, in order, to form hydrogen bonds. TPME is also hygroscopic and could further improve the attraction of water molecules from the oral tissue (McCarron et al., 2004).

The major paste failure was mainly a cohesion failure of the paste. By adding 2.5% TPME, cohesive strength of the paste was improved and after adding 5% TPME the paste was detached from the surface showing an adhesion failure. It confirms our hypothesis of the importance of hydrogen bonds and internal interaction for higher mechanical properties. In Figure 34 (ii & iii), the tensile strength of the paste after adding 2.5 and 5% TPME is demonstrated under all the scenarios discussed before. We observed that the

addition of TPME in general had a positive effect on the adhesion strength of the paste, especially in the hyposalivation condition.

The addition of a compound that can form hydrogen bonds with the paste compounds can also reduce the hydrogen bond formation between the polymer and the substrate, which occurred after adding 2.5% TPME as illustrated in Figure 34C (i, ii & iii) (Rodríguez, Osés, Ziani, & Maté, 2006). Thus, we did not observe any positive effect beyond 2.5% of TPME. Figure 34B shows FTIR of the paste and with two different percentages of TPME. It is done based on hyposalivation method to mimic the situation and compare the peaks in each formula. It is obvious that red shift is happening for C=O peaks and the intensity of peaks is also improved. Also, another bonding peak appeared around $1400cm^{-1}$. For –OH bonds around $3300cm^{-1}$, it is obvious that after adding 2.5% TPME, the polymeric bonding –OH peak intensity improved significantly and non-bonding peaks around $3600cm^{-1}$ were decreased or disappeared. Comparing the failure mechanism of the paste in Figure 34A (ii, iii) shows converting cohesion failure to adhesion after adding more TPME . Due to excessive intra- and intermolecular hydrogen bonding of ether groups and more water uptake after adding TPME, swelling and tensile strength was higher in the paste containing 2.5 % TPME.
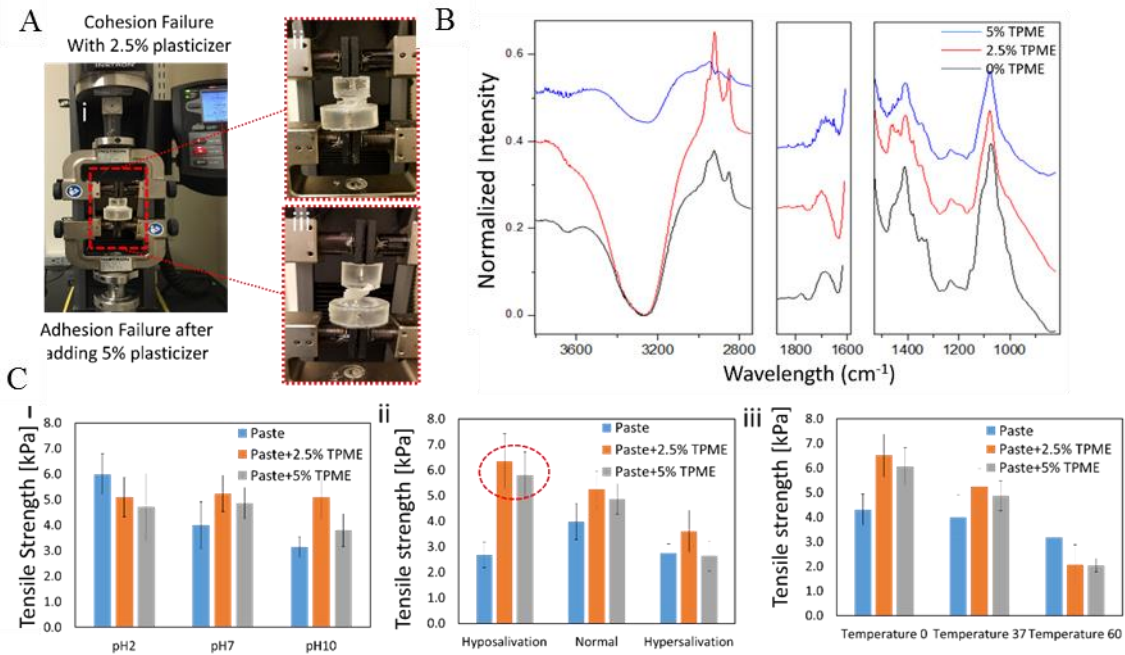
Figure (34): Paste characterization after adding TPME (A) (i) Instron set-up for Tensile strength measurement, (ii) cohesion failure of the paste with applying 2.5% TPME in the paste, (iii) Adhesion failure of the paste after adding 5% TPME; (B) FTIR of the paste before and after adding TPME in hyposalivation scenario; (C) Mechanical properties of the paste (+2.5%, 5% TPME) in different conditions: (i) different pHs, (ii) different hydration states, (iii) different temperatures

7. Conclusion

In this study, the adhesion and cohesion properties of Poligrip® Free manufactured by GSK were investigated with different characterization methods. Evaluating the adhesion properties of the paste, using tensile and lap shear tests in various conditions including different pH values, levels of salivation, and various temperatures revealed that paste had the highest adhesion strength at pH 2, normal salivation condition, and at 0 °C. Different FTIR, DSC and TGA were performed to identify the mechanisms responsible for the observed properties. It was speculated that the mechanism leading to variation in the adhesion strength is based on internal interactions of hydrophilic ingredients of the paste namely CMC and PMVEMA, amount and strength of polymers' inter and intra-chain entanglements and hydrogen bonds. It was observed that acidic conditions resulted in more effective hydrogen bonds between the polymer chains. However, alkaline saliva potentially led to ionic bondings and neutralization of all internal bonds and reduced the adhesion. Saliva content had a significant effect on the adhesion through affecting internal O-H and –COOH bonds or formation of an amorphous extended structure which cannot create strong hydrogen bonds (hypersalivation case). Also, at higher temperatures, based on higher entropy of the chains, no strong and long-lasting internal interactions compared with normal or low temperatures can be observed. Incorporation of 2.5% (w/v) TPME enhanced the formation of hydrogen bonds and can potentially overcome the low adhesion strength of the paste in patients suffering from hyposalivation.

8. Future Plan

Denture stomatitis is one of the most common problems among patients due to poor hygiene and the fact that dentures are a natural breeding ground for microorganisms to grow on. Candida yeast species and other microbes are frequently involved in these stomatitis cases. Antimicrobial medicines are common agents used to prevent the accumulation of these microorganisms, but they have not been used extensively to prevent denture stomatitis. Without an adequate solution, stomatitis continues to be a problem that affects thousands of denture patients.

It is proposed for future plan to use a denture adhesive combined with antimicrobial medicine in an attempt to create a mixture that can reduce stomatitis. Denture adhesives are used to increase the stability of the denture when in a patient's mouth. The effectiveness of each denture adhesive and antimicrobial combination will be measured by its ability to reduce stomatitis while also being non-toxic to patients and able maintain the same mechanical properties as the adhesive alone.

Nystatin, miconazole, and 98% chlorhexidine diacetate are the three antimicrobials to be tested with the adhesive Poligrip at different concentrations. It is hypothesized that one of the antimicrobial adhesive combinations will be superior at reducing and preventing stomatitis. The long term goal of this proposed project is to focus on setting standards for antimicrobial denture adhesives in order to create a new market in the commercial oral care space.

The proposed models to test the antimicrobial are divided into three categories; 1) Test the effectiveness of three types of antimicrobial medications using three

concentrations of antimicrobial. There is expected to be an optimal concentration of antimicrobial. The minimum inhibitory concentration (MIC), will be quantitatively measured through the use of a tetrazolium salt reduction colorimetric assay (XTT assay). Confocal laser scanning microscopy (CLSM) will also be used to qualitatively look at the reduction of *Candida albicans*. 2) Ensure that the antimicrobial medicine is non-toxic to the patients. The cell viability of locations in contact with the antimicrobial/adhesive mixture will be determined by adding the mixture to a fibroblast culture and using an MTT assay to determine toxicity. 3) Test the mechanical properties of the adhesive after the antimicrobial treatment has been applied. *In vitro* tensile bond strengths (TBS) of the antimicrobial/adhesive on denture bases will be directly compared.

In order to use the antimicrobial denture adhesive, it may beneficial if the paste stay intact during the 14 day treatment. Therefore, by incorporating carboxymethyl cellulose into nano-hydroxyapatite/chitosan, it may possible to obtain a novel composite of nano-hydroxyapatite/chitosan/carboxymethyl cellulose (n-HA/CS/CMC) to enhance the paste to stay longer. The surface morphology and properties of the new paste will be investigated by infrared absorption spectra (IR), X-ray diffraction (XRD), scanning electron microscope (SEM), swelling ratio % , degradation test and mechanical testing

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