Effects of temperature-responsive hydrogel on viscosity of denture adhesives

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The cream type of denture adhesives after use cannot be easily removed from oral mucosa and have the potential risk to change the oral flora. The effects of the temperature-responsive hydrogel Pluronic F-127 (PF) on the complex viscosity of denture adhesives were evaluated. Carboxymethylcellulose (CMC) mass fractions (1, 2, 3 and 4%) were added to 20 and 25% PF hydrogels. Complex viscosity was measured over a temperature cycle (40→10→40°C) and fixed temperature points (23 and 37°C). Adhesive strength tests were performed with 2 resin plates at 23 and 37°C. One commercial cream-type denture adhesive, New Poligrip® (NP), was evaluated as a control. Complex viscosity values for PF20% groups at 23°C were lower than those for NP at 37°C. Adhesive strength of PF20% with CMC2%, was higher at 23°C when compared to NP at 37°C, which suggests that PF20%CMC2% is an effective adhesive and is easily removed after mouth rinsing.

Keywords: Denture adhesives, Viscosity, Adhesive strength, Pluronic F-127

INTRODUCTION

Denture adhesives are formulated with synthetic polymers that provide a highly viscous layer between the tissue surface of the denture and denture-bearing mucosa by absorbing saliva. Denture adhesives enhance the retention, stability and masticatory performance of dentures\(^1\)-\(^4\). In contrast, the removal of adhesives from oral mucosa after use is difficult\(^5\)-\(^6\), and the materials can exhibit cytotoxicity\(^7\)-\(^9\). Although current research indicates that the materials do not promote the growth of C. albicans\(^10\)-\(^12\), the long-term effects of adhesives on oral health are uncertain as no longitudinal studies have been conducted. Denture adhesives in the form of creams are not easily removed from the oral mucosa and possess the potential to change oral flora, thus necessitating the complete removal of the adhesive from the mucosa after use. As such there is a need to develop new methods for enhancing the removal of this type of adhesive, and the ideal material would be easily removed from the oral mucosa after mouth rinsing\(^13\).

Sato et al. evaluated gel-type denture adhesives comprising carboxymethyl cellulose (CMC) and distilled water as basic components\(^5\). The authors found that repeated mouth rinsing (five times) was insufficient to remove commercially available cream-type adhesives, as compared with the proposed experimental gel adhesives that only required rinsing the mouth twice for complete removal. To achieve optimal removal, it is best if the gel does not contain any oil-based ointment and by hydrating the gel with water beforehand. However, adhesive forces and unilateral bite force with gel-type adhesives is lower than that of cream-type adhesives. Patient surveys also showed lower denture retention with the use of gel-type adhesives when compared with cream-type adhesives\(^5\).

The long-term complex viscosity of cream-type adhesive makes it increasingly difficult to remove from the oral mucosa\(^5\). Therefore, it would be ideal for removal if the complex viscosity decreased with mouth rinsing. To obtain desirable properties, temperature-responsive hydrogels can be applied to cream-type denture adhesive ointment base instead of oil-based white petrolatum and liquid paraffin. The temperature-responsive polymer exhibits a continuous and marked change in properties with temperature. Pluronic F-127 was used in this study as a temperature-responsive polymer, which is a block copolymer made of poly (oxy ethylene) and poly (oxy propylene). The PF hydrogel displayed reversible sol-gel transition with changing temperature; sol at low temperature, gel at body temperature. PF has been used as a suitable vehicle to prepare controlled-release drug delivery systems for humans owing to its low toxicity in the 20–25% concentration range\(^14\)-\(^16\). For dental applications, PF127-based dental gel can be applied to treat patients with sensitive gums and teeth\(^17\).

The aim of this study was to investigate the use of temperature-responsive hydrogel as an ointment base instead of petrolatum to produce easily removable cream-type denture adhesives. Our null hypothesis is that complex viscosity of denture adhesives would not be affected when PF127 is added. Carboxymethyl cellulose was used as the emulsifying and thickening ingredient\(^18\), and PF hydrogel was used as the ointment base in order to examine the influence of composition on complex viscosity and adhesive strength.

MATERIALS AND METHODS

Sample preparation

A commercial cream-type denture adhesive (New Poligrip®, GSK, Tokyo, Japan) and experimental denture adhesives were evaluated in this study. Components of the commercial cream-type adhesive are shown in Table 1; and composition of the experimental denture
The major chemical components of commercial denture adhesive are shown in Table 1. The composition includes Sodium/Calcium, Methoxypolyethylene maleic anhydride copolymer, Sodium carboxymethyl cellulose, Light liquid Paraffin, and Petrolatum.

Table 1: Major chemical components of commercial denture adhesive

<table>
<thead>
<tr>
<th>Commercial Product</th>
<th>Code</th>
<th>Batch No.</th>
<th>Manufacturer</th>
<th>Composition*</th>
</tr>
</thead>
<tbody>
<tr>
<td>New Poligrip®</td>
<td>NP</td>
<td>H2908K</td>
<td>GC, Tokyo, Japan / GlaxoSmithKline K.K., Tokyo, Japan</td>
<td>Sodium/Calcium, Methoxypolyethylene maleic anhydride copolymer, Sodium carboxymethyl cellulose, Light liquid Paraffin, Petrolatum</td>
</tr>
</tbody>
</table>

* Information as provided by manufacturers.

The composition of experimental denture adhesives is shown in Table 2. PF (Pluronic F-127, AnaSpec, CA, USA) and CMC (Carboxymethyl cellulose, Wako Pure Chemical Industries, Osaka, Japan) were dispersed in distilled water at 4°C, and were stored at 4°C for 48 h. Various aqueous formulations containing 20 and 25% PF, and 1, 2, 3 and 4% CMC were evaluated. PF and CMC solutions were mixed by hand and stored at 4°C for 24 h, and five samples (n=5) were prepared for each experimental condition.

Table 2: Composition of experimental denture adhesives

<table>
<thead>
<tr>
<th>Ingredient</th>
<th>Formulations (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pluronic F-127</td>
<td>20  20  20  20  25  25  25  25</td>
</tr>
<tr>
<td>Carboxy methyl cellulose</td>
<td>1    2    3    4    1    2    3    4</td>
</tr>
</tbody>
</table>

Complex viscosity measurement
Complex viscosity (η*) was measured using a rheometer (MCR302, Anton Paar, VA, USA) in oscillatory mode with parallel plates. The oscillatory tests were performed under controlled strain mode. The deformation and the measured time-delayed shear stress response were used to calculate the storage modulus G’ and the loss modulus G”. The storage modulus G’ measures the deformation energy stored in the system. It is a representation of the solid characteristic (the elastic part) of the sample. The loss modulus G” is a measurement on the lost deformation energy and therefore characterizes the liquid properties (the viscous part) of the sample (tanδ=G”/G’).

\[ G^*(\text{complex modulus}) = G’/\cos\delta = G’/G’ \sin\delta. \]

\[ \eta^* = G^*/\omega. \]

More details on the specific conditions can be found in Table 3 and in Fig 1. For each measurement, five samples were used for each composition. For condition 1 the test parameters are as follows: frequency (ω): 1 Hz; strain: 1%; gap: 0.6 mm; parallel plate: diameter 25 mm; temperature range: 40°C (hold for 3 min) → 10°C (hold for 3 min) → 40°C; temperature change rate: 2°C/min. For condition 1, Ti was defined as the temperature of the complex viscosity inflection point, at which complex viscosity values showed the largest change. Similarly, for conditions 2, the measurement of the samples was with the same frequency (ω=1 Hz), strain (1%) and gap (0.6 mm) as to condition 1, but with a different plate diameter (20 mm) and under 23°C and 37°C.

Adhesive strength measurement
The adhesion strength test was performed with a pair of acrylic resin sample (Fig. 2). A pressure sensitive shaft with a circular base (diameter: 20±1 mm) made of heat-polymerized denture base acrylic resin was...
fixed at the position of the load detector of the tester. A sample holder made of poly (methyl methacrylate) with an indentation sized 22±1 mm in diameter and a depth of 0.5±0.1 mm was fixed onto the sample stand of the tester. These parameters settings are all in accordance to ISO specification 10873. The hole in the holder was filled with denture adhesive and a load of 9.8±0.2 N was applied to the sample using a pressure sensitive shaft at a cross-head speed of 5 mm/min for 30 s (Fig. 2). The sample was then pulled in the reverse direction at a cross-head speed of 5 mm/min. The maximum force per unit area was set as the adhesive strength. Adhesive strength measurements were performed at 23 and 37°C, respectively, and five specimens were assessed for each condition.

**Statistical analyses**

Under the first condition, where complex viscosity values included heating and cooling at 37 and 23°C, respectively, the values were subjected to t-test. Two-way analysis of variance (ANOVA) test was performed to evaluate the differences between PF and CMC concentrations with respect to Ti. Comparison of complex viscosity under condition 2 and adhesive strength values between 23 and 37°C with each sample were assessed by t-test. To compare adhesive strength values, one-way analysis of variance (ANOVA) test was performed to evaluate the differences between experimental samples and NP at 37°C. Under condition 2 and adhesive strength measurement, experimental samples at 23°C and NP at 37°C were compared by one-way analysis (ANOVA) combined with Tukey-HSD test. The level of significance level was set at 5% (p<0.05). All statistical analyses were performed using SPSS Statistics 16.0.

**RESULTS**

**Complex viscosity measurement (condition 1)**

The influence of temperature changes on complex viscosity values is shown in Figs. 3 and 4. The complex viscosity of all PF groups decreased with ambient temperature. PF20% groups showed higher temperatures at which complex viscosity changed rapidly when compared with PF25% groups. Table 4 showed no significant differences between heating up and cooling down at 37°C (p>0.05), while significant differences were observed among the PF20%CMC2%, PF25%CMC1% and PF25%CMC2% groups at 23°C (p<0.05). The results for Ti are summarized in Table 5. Significant differences were observed between Ti and PF (p<0.05), and there were no significant differences between Ti and CMC (p=0.711).

**Complex viscosity measurement (condition 2)**

Changes in NP complex viscosity (Fig. 5) were inversely proportional to temperature changes. One-way ANOVA results showed significant differences between samples at 23°C and NP at 37°C (p<0.05) for complex viscosity values. Complex viscosity values for the PF20% group at 23°C were lower than those for NP at 37°C.
Table 4 Representative data for Conditon 1

<table>
<thead>
<tr>
<th></th>
<th>PF20%CMC1%</th>
<th>PF20%CMC2%</th>
<th>PF20%CMC3%</th>
<th>PF20%CMC4%</th>
<th>PF25%CMC1%</th>
<th>PF25%CMC2%</th>
<th>PF25%CMC3%</th>
<th>PF25%CMC4%</th>
</tr>
</thead>
<tbody>
<tr>
<td>37°C Heating</td>
<td>1,750.67 (544.96)</td>
<td>1,341.60 (609.61)</td>
<td>970.27 (578.41)</td>
<td>730.53 (689.50)</td>
<td>2,713.33 (100.64)</td>
<td>2,434.00 (256.46)</td>
<td>2,742.00 (565.36)</td>
<td>2,652.00 (849.50)</td>
</tr>
<tr>
<td>(SD)</td>
<td>1,728.00 (180.21)</td>
<td>1,361.60 (440.53)</td>
<td>1,536.00 (407.51)</td>
<td>1,337.40 (660.20)</td>
<td>1,850.00 (107.07)</td>
<td>1,793.33 (771.57)</td>
<td>2,248.00 (428.96)</td>
<td>2,395.33 (846.91)</td>
</tr>
<tr>
<td>23°C Heating</td>
<td>722.67 (645.71)</td>
<td>542.20 (125.51)</td>
<td>686.07 (275.95)</td>
<td>697.87 (346.50)</td>
<td>1,850.00 (88.97)</td>
<td>1,793.33 (226.29)</td>
<td>2,248.00 (400.00)</td>
<td>2,395.33 (599.07)</td>
</tr>
<tr>
<td>(SD)</td>
<td>676.67 (128.60)</td>
<td>805.40 (122.17)</td>
<td>884.26 (253.63)</td>
<td>824.33 (400.68)</td>
<td>2,143.33 (82.32)</td>
<td>2,424.00 (485.10)</td>
<td>2,890.67 (799.83)</td>
<td></td>
</tr>
</tbody>
</table>

* Indicates significant difference (p<0.05)

Table 5 Effects of PF and CMC on Ti

<table>
<thead>
<tr>
<th></th>
<th>PF20%CMC1%</th>
<th>PF20%CMC2%</th>
<th>PF20%CMC3%</th>
<th>PF20%CMC4%</th>
<th>PF25%CMC1%</th>
<th>PF25%CMC2%</th>
<th>PF25%CMC3%</th>
<th>PF25%CMC4%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ti (ºC) Heating</td>
<td>25.65 (2.79)</td>
<td>24.95 (1.38)</td>
<td>28.18 (6.54)</td>
<td>26.32 (9.91)</td>
<td>20.72 (0.34)</td>
<td>19.18 (0.88)</td>
<td>17.63 (0.94)</td>
<td>16.15 (1.09)</td>
</tr>
<tr>
<td>(SD)</td>
<td>21.48 (0.92)</td>
<td>24.93 (2.73)</td>
<td>21.57 (5.68)</td>
<td>19.87 (9.10)</td>
<td>27.90 (0.45)</td>
<td>29.41 (0.92)</td>
<td>30.93 (1.28)</td>
<td>32.54 (1.01)</td>
</tr>
</tbody>
</table>

Significant differences were observed between Ti and PF (p<0.05)

Adhesive strength measurement
One-way ANOVA results showed significant differences between samples at 37°C and NP at 37°C with regard to adhesive strength (p<0.05). All experimental denture adhesives samples demonstrated higher adhesive strength values when compared with NP (6.6 kPa) at 37°C (Fig. 6). There were significant differences between experimental samples at 23°C and NP at 37°C (p<0.05). However, PF20%CMC1% at 23°C and NP at 37°C (p=0.998) showed no significant differences.

DISCUSSION
Since the results of our experiments showed adding PF127 would affect complex viscosity of denture adhesives, the null hypothesis was rejected. The ideal denture adhesive should possess a low initial complex viscosity, which allows for easy manipulation, followed by high complex viscosity to maximize retention in the oral cavity, and it should remain effective for as long as possible. The concern with high complex...
viscosity is that the adhesive is difficult to clean due to residual adherent mass on the mucosa after use. Desirable materials should have comparatively lower complex viscosity to facilitate cleaning by mouth rinsing. In previous studies, it was shown that denture adhesives are not easily removed from the mucosa of the oral tissue, as non-active ingredients, such as petrolatum, mineral oil and polyethylene oxide, which act as binding materials to facilitate placement, are present in the denture adhesives. These substances can then be stranded in the oral tissues and denture fitting surface, thus making effective removal more difficult.

From the preliminary experimental results of NP (Fig. 7), we found that when the temperature is near the oral cavity temperature (37°C), the complex viscosity of NP with 25% water is higher than NP without water. Obviously, in actual application, it is difficult to clean the denture adhesive from the mucosa.

Oscillatory measurement under condition 1 involves complex viscosity to temperature test, which is used to determine the curing of reactive systems or to analyze the behavior of the sample at different temperatures. If the strain exerted on the samples is within a linear complex viscosity range, the structure is not destroyed during measurement. The larger the diameter of the plate, the greater the shear stress. As such, it is easy to destroy the structure of gel-type samples. The results shown in Table 4 confirmed significant differences between the PF20%CMC2%, PF25%CMC1% and PF25%CMC2% at 23°C, and suggest that hysteresis occurred during heating process in condition 1. We performed oscillatory measurement in condition 2 in order to avoid destroying the structure of the sample. Significant differences were observed between Ti and PF, but were not seen in CMC (Table 5). Cooling led to a reduction in Ti with increasing PF concentration. In other words, PF showed different effects with changes in temperature, while CMC had no effect on temperature changes. The preliminary experimental results presented in Fig. 8 also suggest that PF had a much larger influence on temperature variations (The test conditions of preliminary experiments were the same as the condition 1).

On complex viscosity evaluation in condition 2, NP showed the opposite trend with decreasing ambient temperature (Fig. 5); complex viscosity of NP was higher at 23°C than at 37°C, which suggests that this change enhances the ability of NP complex viscosity when rinsed with water around 20°C. This confirms our assumption that removal of commercial grade denture adhesives from the oral mucosa is difficult as a result of increasing complex viscosity. Therefore, complex viscosity values can reflect on the degree-of-difficulty of denture adhesive removal from the oral cavity. Results from this study also confirm the findings of Sato’s study. Complex viscosity values from the PF20% group at 23°C are lower than NP at 37°C (Fig. 5). The complex viscosity values of the PF20% group are lower than those products currently available on the market at lower temperatures. Complex viscosity values of the PF25% groups at 23°C are higher than NP at 37°C. Therefore, when compared to NP, PF25% groups are difficult to remove. Nevertheless, PF20% groups at 23°C showed lower values than NP at 37°C, which demonstrates that the PF20% groups possess better properties than the PF25% groups, as they are easier to remove. However, there are no significant differences between 23 and 37°C for PF20%CMC3% and PF20%CMC4% ($p>0.05$), which confirm that these two hydrogel samples show little temperature variation. In addition, PF20%CMC1% and PF20%CMC2%, which are temperature-responsive hydrogel samples, can be easily removed from mucosa as temperature decreases during mouth rinsing.

With regard to adhesive strength, our results indicate that the PF20% and PF25% groups at 37°C possessed sufficient adhesive strength to be used as
components in denture adhesives for clinical application (Fig. 6). Based on the complex viscosity characteristics of PF20%CMC1% and PF20%CMC2%, these formulations can be used as effective temperature-responsive hydrogels. Within both samples, the adhesive strength of PF20%CMC2% is much higher at 23°C than NP at 37°C (p<0.05). This suggests that although the temperature changed from 37 to 23°C, the sample also has a high level of adhesive strength, while there were no significant differences between PF20%CMC1% at 23°C and NP at 37°C (p>0.05). Consequently, temperature-responsive hydrogels have the best performance at PF20% with CMC2% compositions, showing both improved removal efficiency and good retention.

The long-term effects of this denture adhesive in terms of composition and optimal time duration have yet to be determined and are currently under investigation. These materials can be applied directly in patients as water-based solutions. Nevertheless, this study also has limitations. CMC additives have a higher initial strength, but this begins to decline gradually from optimal adhesive strength after immersion in water for 1–10 min\(^2\). This means it has high solubility, dissolving quickly and losing its effectiveness within a relatively short period. Therefore, the durability of adhesive strength is a crucial issue. Further studies could aim to add long-acting salts, such as polyvinylether methyl cellulose (PVM-MA), to these formulations.

CONCLUSION

Denture adhesives with PF added instead of petrolatum as an ointment base showed equivalent adhesive strength as a commercial cream-type product. The complex viscosity of experimental denture adhesives rapidly decreased when temperature in the oral cavity decreased by rinsing the mouth with water. The optimal formulation was found to be PF20% with CMC2%, which is an effective adhesive and is easily removed from the oral mucosa.

REFERENCES