European Review for Medical and Pharmacological Sciences 2022; 26: 7833-7839

Chemical-physical characteristics of artificial saliva substitutes: rheological evaluation

A. FOGLIO-BONDA[1], P.L. FOGLIO-BONDA[2], M. BOTTINI[3], F. PEZZOTTI[3], M. MIGLIARIO[2]

[1]Department of Pharmaceutical Sciences, [2]Department of Translational Medicine, University of Eastern Piedmont, Novara, Italy
[3]Dental Clinic, AOU Maggiore della Carità, Novara, Italy

Abstract. – OBJECTIVE: We aimed at evaluating some chemical-physical properties of artificial saliva substitutes easily available on the E.U. market, such as viscosity, pH, buffering capacity, superficial tension, density and spinnbarkeit and to compare the results with human natural saliva bibliographic data.

MATERIALS AND METHODS: Based on the easy availability on the market, twelve artificial saliva solutions in liquid formulation were analyzed. Kinematic viscosity (cSt) was determined using a micro-Ubbelohde model capillary viscosimeter (ViscoClock, SCHOOT-GERATE Mainz, Germany). Dynamic viscosity (mPas) was determined, through a simple multiplication between density (g/cm^3) and kinematic viscosity of each solution. pH analyses were carried out at room temperature using a pH-meter (Mettler Toledo®–Five Easy, Columbus, OH, USA). Spinnbarkeit analysis was performed by a self-owned instrument built for the purpose.

RESULTS: The median density value, obtained from the cohort of artificial saliva substitutes, was 1.036 g/cm^3. The median value of the kinematic viscosity value was 8.984 cSt. The median spinnbarkeit value was 3.2 mm and the median pH value was 6.29. In this study we found an almost linear correlation between the kinematic viscosity and spinnbarkeit values of the artificial saliva substitutes evaluated.

CONCLUSIONS: Saliva substitutes should be as faithful as possible to the characteristics of human saliva, in order to completely replace its functions in the oral cavity. Nevertheless, despite several R&D efforts, it is difficult to reproduce all the different features that belongs to natural saliva in one device. Therefore, it would be desirable to create more products reproducing saliva with various rheological characteristics in respect of the main salivary functions such as: chewing, speaking and tissue coating.

Key Words:
Saliva, Artificial salivary substitutes, Viscosity, Spinnbarkeit.

Introduction

In oral cavity human saliva is responsible for many different functions, such as: the maintenance of correct moisture balance, the removal of micro-organisms and the lubrication during speaking, mastication and swallowing[1]. An extensive review has been conducted by Dawes et al[2], who summarized all the known functions of saliva. Buffering ability, for example, is fundamental to protect oral mucosae and teeth from acid insults. Furthermore, the presence in saliva of antibacterial, antifungal and antiviral agents modulates oral microbial flora[1,2]. Human saliva influences oral homeostasis through its physical and chemical characteristics[1,2]. The importance of saliva and its proprieties in the determination and maintenance of oral homeostasis are widely documented in the literature[3-6]. The complexity of the system is easily noticeable, it consists of water (more than 99%), glycoproteins (mucins), antimicrobial substances, proteins and a large variety of electrolytes. The most common proteins present in saliva are α-amylase, maltase, serum albumin, mucins and immunoglobulins. At rest, without any stimulation, saliva is constantly produced. This phenomenon is called unstimulated whole saliva (UWS), that covers, moisturizes and lubricates oral tissues. Exogenous and pharmacological stimulations can increase the Flow Rate (FR). Daily salivary production in a healthy subject is around 1 L nevertheless, regarding salivary FR, there is a large biological variation[7]. In fact, in humans, FR has a value of range between 0.25 and 0.83 mL/min[8-11]. A research paper about FR has been conducted in 2013 about UWS, samples were collected from a selected cohort of healthy young adult[6]. Values of UWS/FR ranged from 0.164 to 1.656 mL/min (percentile 25=0.400 mL/min, per-

Corresponding Author: Pier Luigi Foglio-Bonda, MD; e-mail: andrea.fogliobonda@uniupo.it

centile 50=0.643 mL/min, percentile 75=0.832 mL/min) and they were not normally distributed ($p<0.05$)[6]. Understanding daily production of saliva is important as to know its biophysical properties such as viscosity: where values alteration has been associated with development of oral diseases[5,12]. A review of the literature indicated that there are several viscosity values obtained from the population through different analytical techniques, giving different results but generally do not exceed 10 mPa×s[5]. Although saliva's presence is often taken for granted, a decrease in production or worst, or its absence, can lead to a strong decrease in life quality, increasing cervical caries, mucosal infections, ulcerations, etc. Xerostomia or hyposalivation (FR<0.16 mL/min) may occur in many different situations[6,7,11]. The most common is a drug side effect (chemotherapy, antihypertensives, antidepressants, diuretics, etc.)[13] and in this case, an alternative medication may be suggested. Radiotherapy of the head and neck regions may indeed induce hyposalivation and xerostomia. Immunological diseases, such as HIV, may affect saliva production as well. Those clinical pictures need to be treated; the most common approach is the use of palliative medicines (moisturizing products) together with oral complications preventive measures[13].

Artificial saliva substitutes are meant to have the same biophysical properties of natural saliva, such as lubricative and mucoadhesive function, still on the other hand they cannot act as substituents for the enzymatic-digestive actions. In order to obtain such properties, saliva replacers need to be as close as possible to the composition of human saliva[14]. There are many available approaches used to obtain rheological properties comparable to those of natural saliva. For example, it is possible to add either mucins or polymers, carboxymethyl-cellulose (CMC), hydroxyethyl-cellulose (HEC), hydroxypropylmethyl-cellulose (HPMC) or polyethylenoxide (PEO)[12,15]. Mucin based products seem to show very good rheological properties, which make them useful for protection against desiccation and environmental insults, lubrication and, moreover, they show anti-microbial effects[16]. Previous works on artificial substitutes' properties comparison have already been published, but it is still not possible to find a study conducted on a relatively high number of products and focused on the determination of multiple characteristics. For example, in Preetha et al[14] work, attention was focused on viscosity and surface tension characterization, which was done only on three commercial products, however other properties were not taken into account. Another interesting scientific paper, but not representative of all products that are currently commercially available, has been conducted by Vissink et al[16]. They compared the apparent viscosities of three different types of saliva substitutes with those of human whole saliva. One product was based upon carboxymethylcellulose, one was mucin-containing and the last one, a solution of polyethylenoxide. Hatton et al[12] compared five different *CMC*-based products and one mucin-based saliva substitute and tested their viscosity at different shear rates. Christersson et al[17] and Foglio Bonda et al[1] published studies about saliva substitutes taking into consideration more properties, such as viscosity, pH, surface tension and absorption to surfaces. In the present study, we considered a heterogeneous group of artificial saliva substitutes based on their easy accessibility on the market. Our attention has been directed towards determining a set of chemical-physical properties: kinematic and dynamic viscosity, pH, and density. Moreover, spinnbarkeit has been considered to increase the rheological characterizations.

Materials and Methods

Commercial Product Collection

All of the saliva substitutes were purchased on the net or at the local pharmacies. It was asked to five students of "University of Eastern Piedmont" to spend one month in web-searching activities for artificial saliva products. At the end of this time, the students had provided the list of products and they found indicating if they could purchase them or not. Consequently, the products were directly purchased anonymously.

Density

The density was calculated through a volumetric flask of 10 mL capacity. Said volumetric flask was first weighted with a technical scale, which showed its actual weight (m_0) and was then filled with the artificial saliva solution to be analyzed up to its capacity. This way, a second weighing of the volumetric flask containing the solution (m_1) was carried out. The density value, expressed in g/cm[3], was given by the following formula:

$$\rho = \frac{m_1 - m_0}{10\ mL}$$

Kinematic Viscosity Measurement

Viscosity was determined using a micro-Ubbelohde model capillary viscosimeter (ViscoClock, SCHOOT-GERATE Mainz, Germany). Kinematic viscosity of the artificial saliva substitutes was always evaluated at controlled temperature (20°C). Viscosity was calculated on the time that the liquid meniscus took to flow from the upper photocell (M_1) to the lower photocell (M_2). The flow time detected by the viscosimeter, expressed in seconds, was then multiplied by the capillary constant (k=0.031 mm^2/s), obtaining kinematic viscosity expressed in CentiStokes (cSt).

Dynamic Viscosity Calculation

Once the density of each individual substance was determined, through a simple multiplication, we calculated the dynamic viscosity (η), expressed in CentiPoise (cP). The equation was given by the following formula:

$$\eta = \rho v$$

where v is the kinematic viscosity, expressed in centiStokes.

PH Determination

pH analyses were carried out at room temperature using a pH-meter (Mettler Toledo®- Five Easy, Columbus, OH, USA). A 12 mL sample was taken from each product and pH was analyzed. These measurements were repeated three times.

Spinnbarkeit Measurement

Spinnbarkeit analyses were performed by a self-owned instrument built for the purpose. Each sample (50 µL) was transferred to a steel base and was brought into contact with a fixed punch, moving the base with a lifter. Consequently, the lifter was lowered until the formed liquid wire broke. The distance was then measured using a caliper placed behind the instrument. Three samples from each product were collected and measurements were repeated ten times for each sample.

Statistical Analysis

The data were statistically analyzed using Microsoft Excel (V 16.57). The variables were descriptively analyzed with mean, maximum, minimum, median and relative standard deviation. The correlation coefficients (R) among the variables were also calculated. To assess the existence of statistically significant differences the Student's *t*-test with the two-tailed method was used (minimum p-value <0.05).

Results

Commercial Product Collection

Of the 18 artificial saliva substitutes found and commercially available, 12 were in liquid form while the others were in gel or tablet formulations. The latter were excluded from the characterizations because it was difficult or impossible to determine their viscosity and spinnbarkeit with the available tools. Three artificial salivas based on carboxymethyl cellulose as a rheological modifier component were obtained: Glandosane®, Saliveze® and Xerotin®. Three are hydroxyethyl-cellulose based: Biotene Oral Rinse®, Bioxtra Spray® and Xeros®. Three are xanthan gum based: Biotene Spray®, GUM® and Oralis®. Saliva Orthana® has been designated as mucin-based saliva substitute and Saliva Natura® is vegetable mucin based. While Xerostom® is a complex mixture of natural oils. For each product, three different samples were purchased and analyzed. A summary of the main characteristics of the commercial product found is summarized in Table I.

Characterizations

Results obtained from analyses showed a standard deviation (RSD), lower than 2.5%, indicating good repeatability of analysis and batches produced; the values are summarized in Table II. In detail, the median density value was 1.036 g/cm^3 (between Biotene® and Oral Rinse®) with a maximum of 1.126 g/cm^3 (Oralis®) and a minimum of 1.007 g/cm^3 (Saliveze®). The median kinematic viscosity value was 8.984 cSt (between Biotene Spray® and Biotene Oral Rinse®), the maximum value was 23.564 cSt (Bioxtra Spray®) and the minimum was 1.601 cSt (Saliva Natura®). The median spinnbarkeit value was 3.2 mm (Glandosane®, GUM® and Saliva Orthana®), with a maximum value of 3.8 mm (Saliva Natura®) and minimum of 2.5 mm (Biotene Spray®). Moreover, the median pH value was 6.29 (Saliva Orthana® and Xerotin®), the maximum 6.81 (Bioxtra Spray®) and the minimum 4.97 (Glandosane®).

Discussion

Viscosity

The viscosity of natural saliva is known to be non-Newtonian across the range of shear rates present in the oral cavity. A shear rate of 4 s^{-1} corresponds to the movement of particles across

Table I. The different artificial saliva substitutes available on the market, included in the study.

Sample	Main components	Instruction for daily use
Biotene® Oral Rinse	Hydroxyethyl-cellulose (HEC), xylitol and sorbitol.	With approximately 15 mL rinse for 30 seconds and then expel.
Biotene® Spray	Xanthan gum, glycerin and xylitol.	Administer as required.
Bioxtra Spray®	Hydroxyethyl-cellulose (HEC), lactoperoxidase, citric acid, xylitol and sorbitol.	Administer 3 or 4 times a day to the mouth cavity.
Xeros®	Hydroxyethyl-cellulose (HEC), sodium phosphate, xylitol and sorbitol.	With approximately 15 mL rinse for 30 seconds and then expel.
Glandosane®	Carboxymethyl-cellulose (CMC) and xylitol.	Administer 1 or 2 times a day to the mouth cavity.
GUM®	Xanthan gum, carrageenan and xylitol.	Administer as required.
Oralis®	Xanthan gum, benzoic acid lactoperoxidase, the dispenser. Rinse for 30-45 seconds and then expel.	Use the amount corresponding to lysozyme, lactoferrin and xylitol.
Saliva Natura®	Yerba Santa extract, citric acid, xylitol and sorbitol.	Administer as required.
Saliva Orthana®	Porcine gastric mucin (PGM) and xylitol.	Administer 3 or 4 times a day to the mouth cavity.
Saliveze®	Carboxymethyl-cellulose (CMC) and potassium phosphate.	Administer 2 or 3 times a day to the mouth cavity.
Xerostom®	Xylitol, PEG-40 Hydrogenated Castor Oil, Betaine, Glycerin, Olea Europaea	Administer 1 or 2 times a day to the mouth cavity.
Xerotin®	Carboxymethyl-cellulose (CMC), potassium phosphate and sorbitol.	Spray the product several times a day

the tongue whilst 60 s^{-1} and 160 s^{-1} correspond to swallowing and speech, respectively[18]. This feature is peculiar and contributes to increase the oral cavity protection of the human saliva. Based on the aforementioned, the first approach in saliva substitute development could be to mimic this rheological behavior. Nevertheless, this imitation could be extremely complex to transfer in an in-

Table II. Summary of samples characterization at 20°C.

Sample	Kinematic viscosity (cSt)	Dynamic viscosity (mPas)	pH	Density (g/cm³)	Spinnbarkeit (mm)
Natural Saliva	1.40 ± 0.39[5]	2.330[22]; 2.520[23]; 2.800-15.500[14]; < 6 × < 7[24]	6.95[6]	1.002-1.012[20,21]	1.90-4.90[19]
Biotene® Oral Rinse	10.224	10.544	6.60	1.031	2.9
Biotene® Spray	7.749	8.064	6.11	1.041	2.5
Bioxtra Spray®	23.564	25.923	6.81	1.100	3.6
Xeros®	4.071	4.116	6.20	1.011	3.6
Glandosane®	3.746	3.784	4.97	1.010	3.2
GUM®	18.638	19.594	6.25	1.051	3.2
Oralis®	14.318	16.115	6.71	1.126	3.0
Saliva Natura®	1.601	1.682	5.40	1.051	3.8
Saliva Orthana®	3.114	3.178	6.29	1.021	3.2
Saliveze®	14.801	14.908	6.38	1.007	3.0
Xerostom®	2.730	2.879	6.70	1.054	2.8
Xerotin®	21.567	21.727	6.29	1.007	3.7

dustrial product without the certainty to obtain a clinically satisfactory result. It's necessary to consider that the specific rheological behavior of human saliva occur as a liquid that constantly flows during all day on the mucosa. An artificial saliva substitute will be applied only sometimes during the day, meaning that probably a different rheological behavior could be required compared to that human saliva. During the analysis of our saliva viscosity data, it's necessary to consider all the problems related to our analytical methods where saliva viscosity has been determined in a lot of different ways[13]. In our study the capillary rheometer was used; in this analysis it is not possible to set the shear rate and so is not possible to discriminate a non-Newtonian behavior from a Newtonian one. For this reason, the capillary rheometer analysis was coupled with saliva spinnbarkeit analysis which is more related to the elasticity properties of a liquid[19].

From the data collected in Table II, it is evident that only seven artificial salivary substitutes, represented by Saliva Orthana®, Biotene Spray®, Biotene Oral Rinse®, Xeros®, Glandosane®, Saliveze® and Xerostom®, present a dynamic viscosity comparable to the viscosity of human saliva, in accordance with the study conducted by Preetha et al[14] that is 2.800 and 15.500 mPas. These behaviors can be related to the different substances dissolved in the artificial saliva substitutions. In particular Xeros® is mainly co-composed by HEC while Saliva Natura® contain vegetable mucin from Yerba Santa extract. Xanthan gum is found, not only in Biotene Spray®, but also in the solution of GUM® and Oralis®. If we compare these substances, which contain xanthan gum we can observe a considerable variation in viscosity. Oralis® has a viscosity about 2.4 times higher than the solution represented by Biotene Spray® (7.749 cSt). Instead, HEC, besides being the main component of Xeros®, is the main agent present in Biotene Oral Rinse® and Bioxtra Spray® solutions. In spite of the presence of HEC, these three salivary substitutes present a distinct kinematic viscosity, respectively of 4.071 cSt, 10.224 cSt and 23.564 cSt. These data indicate how in the solutions of artificial saliva, characterized by the presence of the same main agents, are dissolved substances able to change also considerably the value of viscosity.

Spinnbarkeit

Human saliva spinnbarkeit has been reported to be in the range between 1.9 and 4.9 mm by use of an automatic device for measuring the saliva spinnbarkeit (Neva Meter)[19]. In contrast with Neva Meter®, it is necessary to bear in mind the operator error during the measure with our equipment. Spinnbarkeit detection, using Neva Meter, occurs automatically due to the break of the electric flow by the sample wire breakage. Moreover, Neva Meter equipment is electrically actuated having a more reliable and constant speed than our equipment. The Spinnbarkeit values of the artificial substitutes fall into the range reported by Ghoara et al[19]. The obtained results seem to be similar among them, in contrast with the differences obtained in viscosity determination. Probably spinnbarkeit analysis could not detect differences between industrial products; moreover, taking into consideration that among the rheological modifiers, those used in these products are small in number (only four) a narrow range of spinnbarkeit values could be expected. Observing the data shown in Table II, a correlation emerged for some products, between viscosity and spinnbarkeit; in particular, increasing the viscosity, there is an increase in the spinnbarkeit of the analyzed solutions. This situation is graphically represented in Figure 1. Indeed, for a kinematic viscosity generally higher than 14 cSt, a spinnbarkeit value higher or equal to 3.0 mm is associated. While, for a viscosity lower than 10 cSt, a spinnbarkeit value lower than 2.9 mm is found. However, this correlation is not always verifiable. An example is given by the data of Xeros®, which has a low kinematic viscosity (4.071 cSt) and a slightly high spinnbarkeit (3.6 mm). The latter behavior is also characteristic by Saliva Natura®, which has a low kinematic viscosity (1.601 cSt), which determines the minimum viscosity value found in this study, and a high spinnbarkeit value (3.8 mm).

pH

Human saliva pH bibliographic data are summarized in Table II. It is known that values change depending on subjects age, collection methods, cohort selection[7]. Especially, human saliva has a pH that varies between 5.75 and 7.05. According to the study by Foglio Bonda et al[6], the average pH value in young and healthy subjects is 6.95. The latter value is approximately comparable to the pH values of artificial saliva substitutes except for two products, represented by Glandosane® and Saliva Natura®, whose pH values were 4.97 and 5.40, respectively. The latter acid pH could be related to the presence of citric acid, dissolved in the solution.

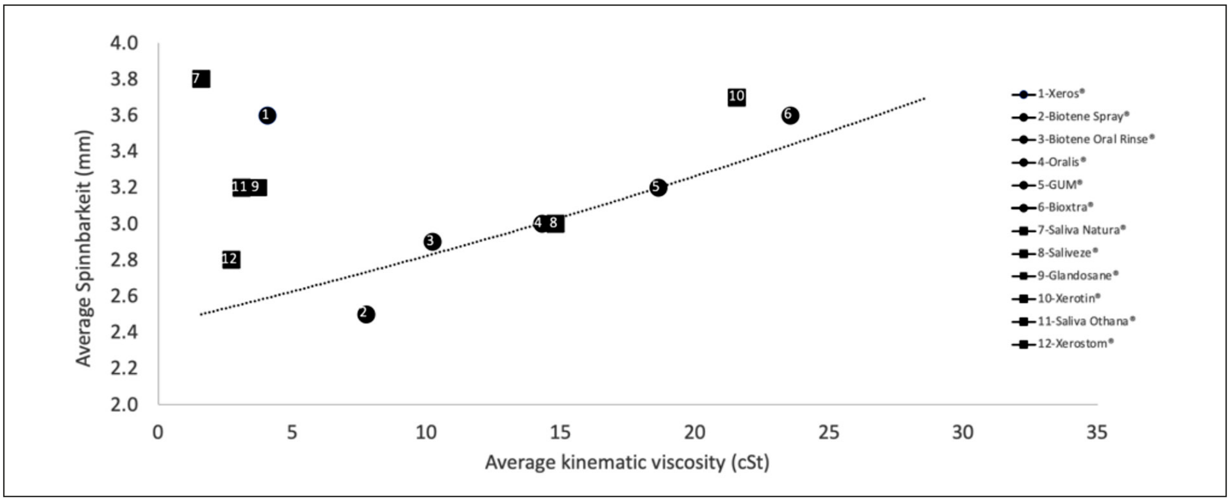

Figure 1. The graph shows an almost linear correlation between the kinematic viscosity and spinnbarkeit values of the artificial saliva substitutes, evaluated in this study.

Density

Human saliva, since it consists of water for 99%, has a density value that range from 1.002 to 1.012 g/cm^3,[3,20,21]. Indeed, the density values found in this study are almost comparable to those of human saliva. Among all the samples analyzed, two artificial salivary substitutes, Oralis® and Bioxtra Spray®, show a slight increase in density of 1.126 g/cm^3 and 1.100 g/cm^3, respectively. Probably, this could be accounted to the presence of more substances. However, it is evident that between all the products and human saliva there is not a sensible change in density values, because they all consist mainly of water.

Conclusions

In this study, different chemical-physical characterizations we conducted over different saliva substitutes, easily available on market, gave useful information about the artificial saliva market offer. The technical specifications (data sheets and leaflets) of artificial saliva don't show the rheological characteristics. It is our main concern to continue improving our analysis techniques (such as viscosity) to get more detailed results. Moreover, it may be useful to compare data from clinical studies with physico-chemical characterizations, understanding what aspects in which saliva substitutes need to be improved. Saliva substitutes should be as faithful as possible to the characteristics of human saliva, in order to completely replace its functions in the oral cavity. Nevertheless, despite several R&D efforts, it is difficult to reproduce all the different features that belong to natural saliva in one device. Therefore, it would be desirable to create more products reproducing saliva with various rheological characteristics in respect of the main salivary functions such as chewing, speaking and tissue coating.

Conflict of Interest

The Authors declare that they have no conflict of interests.

Funding

This research is original and has a financial support from the University of Eastern Piedmont, Novara, Italy.

References

1) Foglio Bonda PL, Farinone M, Pattarino F, Foglio Bonda A. Artificial saliva substitutes evaluation: the role of some chemical-physical proprerties. GJRA 2018; 7: 67-70.
2) Dawes C, Pedersen AML, Villa A, Ekström J, Proctor GB, Vissink A, Aframian D, McGowan R, Aliko A, Narayana N, Sia YW, Joshi RK, Jensen SB, Kerr AR, Wolff A. The functions of human saliva: A review sponsored by the World Workshop on Oral Medicine VI. Arch Oral Biol 2015; 60: 863-874.
3) Epstein JB, Scully C. The role of saliva in oral health and the causes and effects of xerostomia. J Can Dent Assoc 1992; 58: 217-221.

4) Dodds MW, Johnson DA, Yeh CK. Health benefits of saliva: a review. J Dent 2005; 33: 223-233.
5) Foglio Bonda A, Pattarino F, Foglio Bonda PL. Kinematic viscosity of unstimulated whole saliva in healthy young adults. Eur Rev Med Pharmacol Sci 2014; 18: 2988-2994.
6) Foglio Bonda PL, Migliario M, Rocchetti V, Pattarino F, Foglio Bonda A. Daily and annualy variation of unstimulated whole saliva flow rate and pH and their relation with body profile in healthy young adults. Eur Rev Med Pharmacol Sci 2013; 17: 2538-2545.
7) Del Vigna P, Trinidade Grégio AM, Naval Machado MA, Soares de Lima AA, Reis Azevedo L. Saliva Composition and Functions: A Comprehensive Review. J Contemp Dent Pract 2008; 9: 72-80.
8) Mandel ID. The role of saliva in maintaining oral homeostasis. J Am Dent Assoc 1989; 119: 298-304.
9) Fenoll-Palomares C, Muñoz Montagud JV, Sanchiz V, Herreros B, Hernández V, Mínguez M, Benages A. Unstimolated salivary flow rate, pH and buffer capacity of saliva in healthy volunteers. Rev Esp Enferm Dig 2004; 96: 773-783.
10) Kariyawasam AP, Dawes C. A circannual rhythm in unstimulated salivary flow rate when the ambient temperature varies by only about 2 degrees C. Arch Oral Biol 2005; 50: 919-922.
11) Bergdahl M. Salivary flow and oral complaints in adult dental patient. Community Dent Oral Epidemiol 2000; 28: 59-66.
12) Hatton MN, Levine MJ, Margarone JE, Aguirre A. Lubrication and Viscosity Features of Human Saliva and Commercially Available Saliva Substitutes. J Oral Maxillofac Surg 1987; 45: 496-499.
13) Guggenheimer J, Moore PA. Xerostomia Etiology, recognition and treatment. J Am Dent Assoc 2003; 134: 61-69.
14) Preetha A, Banerjee R. Comparison of Saliva Substitutes. Trends Biomater Artif Organs 2005; 18: 178-186.
15) Hu J, Andablo-Reyes E, Mighell A, Pavitt S, Sarkar A. Dry mouth diagnosis and saliva substitutes – A review from a textural perspective. J Texture Stud 2021; 52: 141-156.
16) Vissink A, Waterman HA, s-Gravenmade EJ, Panders AK, Vermey A. Rheological properties of saliva substitutes containing mucin, carboxymethylcellulose or polyethylenoxide. J Oral Pathol 1984; 13: 22-28.
17) Christersson CE, Lindh L, Arnebrant T. Film-forming properties and viscosities of saliva substitutes and human whole saliva. Eur J Oral Sci 2000; 108: 418-425.
18) Gittings S, Turnbull N, Henry B, Roberts CJ, Gershkovich P. Characterisation of human saliva as a platform for oral dissolution medium development. Eu J Pharm Biopharm 2015; 91: 16-24.
19) Gohara K, Ansai T, Koseki T, Ishikawa M, Kakinoki Y, Shibuya K, Nishihara T, Takehara T. A new automatic device for measuring the spinnbarkeit of saliva: the Neva Teter. J Dent 2004; 32: 335-338.
20) Amerongen AV, Veerman ECI. Saliva-the defender of the oral cavity. Oral Dis 2002; 8: 12-22.
21) Schneyer LH, Young JA, Schneyer CA. Salivary secretion of electrolytes. Physiol Rev 1972; 52: 720-777.
22) Sajewicz E. Effect of saliva viscosity on tribological behavior of tooth enamel. Tribol Int 2009; 42: 327-332.
23) Park MS, Chung JW, Kim YK, Chung SC, Kho HS. Viscosity and wettability of animal mucin solutions and human saliva. Oral Dis 2007; 13: 181-186.
24) Rantonen PJ, Meurman JH. Viscosity of whole saliva. Acta Odontol Scand 1998; 56: 210-214.