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On the rheological and sensory properties of a novel natural salivary substitute.

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Abstract

The prevalence of xerostomia, the sensation of dry mouth, is estimated at 20% in the general population and up to 50% in older adults. Saliva plays different roles during bolus formation: lubrication, mixing, coating, hydration, dissolution, and comminution of food particles. This study proposes and tests artificial saliva formulations mimicking human saliva rheological and sensory perceptions. Shear and extensional rheology were assessed to select the type of formulation closest to saliva rheological characteristics. After evaluating three alternative sources, an extract simulating saliva rheology was produced from flax seeds. Friction coefficient and rheological properties, such as flow curves, relaxation times, and Trouton ratios, were compared favorably with human saliva. The sensory evaluation demonstrated that flaxseed extracts induce perceived mouth hydration, slipperiness, and adhesion exceeding that of human saliva. The flaxseed extract proposed in this can i) be used to study *in vitro* food oral processing and ii) pave the way to novel natural salivary substitutes to alleviate the symptoms of xerostomia.

Keywords: Xerostomia, Saliva, Salivary Substitute, Flaxseed, Perception, Shear Rheology, Extensional Rheology.

1. Introduction

Saliva is a complex and essential physiological fluid involved in different functions during food oral processing (FOP); lubrication, mastication, clearance, taste, and swallowing (Humphrey and Williamson, 2001). The functionalities of saliva depend to a large extent on its interactions with the surfaces of the mouth, contributing to the formation of complex layers such as the mucosal pellicle. This salivary film mainly comprises saliva proteins such as mucins (MUC5B and MUC7), serves as a protective layer of the oral mucosa and ensures moisture retention (Hannig et al., 2017). The high water-retaining capacity and viscoelasticity explain the oral lubrication provided by mucins (Agorastos et al., 2023; Assy et al., 2022; Laguna et al., 2021).

Quantitative and qualitative changes in saliva composition may be related to a subjective feeling of dryness in the mouth, also known as xerostomia (Piaton et al., 2021). When suffering from xerostomia, patients may experience mucosa dryness, lack of salivation, and decreased salivary film thickness, causing difficulties when speaking and eating (Bongaerts et al., 2007; Hu et al., 2021; Humphrey and Williamson, 2001). Its prevalence is 20% in the general population, with an increased prevalence in women (up to 30%) and in the elderly (up to 50%) (Piaton et al., 2021). Additionally, xerostomia may be caused by drug side effects, exposure to radiotherapy, and chronic diseases like Sjögren's disease. The therapies related to improving the quality of life of these patients mostly rely on salivary stimulants and salivary substitutes (Hu et al., 2021). Salivary stimulants work until the extent of the patient salivary glands preservation; depending on the severity, salivary stimulants may not provide oral relief. Conversely, salivary substitutes are indicated for all patients to mitigate oral dryness discomfort by providing saliva texture resemblance; if the latter is not achieved, patients could experience unfamiliar and unpleasant sensations (Hahnel et al., 2009; Hu et al., 2021).

The development of salivary substitutes is essential in the medical domain but also in the field of food oral processing research (FOP), in which the oral phase of swallowing is studied. Throughout the oral phase, saliva moisturizes the food and forms a food bolus ready for swallowing. Hence, the bolus requires a certain level of cohesiveness to guarantee safe swallowing (Prinz and Lucas, 1997; Steele et al., 2015). For this reason, when investigating *in vitro* bolus formation and swallowing phenomena, being able to lean on a fluid approaching human saliva's rheological characteristics (non-Newtonian and elastic) is required (Gittings et al., 2015; Stokes and Davies, 2007; Turcanu et al., 2015; Wagner, 2015; Zussman et al., 2007). The simulated salivary fluid established by InfoGest (Brodkorb et al., 2019; Minekus et al., 2014) provides a standardized protocol to imitate human saliva's ion strength, pH buffering, and amylase activity. This Newtonian fluid was found to be relevant when investigating the enzymatic hydrolysis of starchy food (Bugarin-Castillo et al., 2023; Freitas et al., 2018; Lavoisier et al., 2022). However, the lack of the rheological relevance of artificial saliva models may induce limitations when investigating *in vitro* the mechanisms of bolus formation, lubrication, or swallowing (Marconati et al., 2018).

Piaton et al. (2021) reviewed different saliva substitutes, concluding that they do not yet make it possible to improve food oral processing for xerostomic patients. Indeed, it turns out that some salivary substitutes have additional flavoring (mint, lemon, etc.) that can affect the sensory perception of food and alter the oral comfort of individuals. In addition, some have animal-based

ingredients (mucins) that can go against individuals' cultures, beliefs, or diets; others lack rheological relevance (Newtonian fluids such as carboxymethyl cellulose, glycerol, and glycerin-based). However, the increased study on biopolymers has led to the opportunity of investigating potential non-Newtonian and elastic materials coming from natural sources. Despite the natural production of water-soluble polysaccharides (mucilage), there are few which are food-graded, and few have convenient shear and elongational viscosity to formulate salivary substitutes (Brütsch et al., 2019; Vieira et al., 2020; Wagner, 2015; Yuan et al., 2018a). One example is the mucilage from Okra (*Abelmoschus esculentus* L.), known for its value in food preparations, pharmaceutical formulations, and biomaterials (Yuan et al., 2018a). The biopolymer has been compared with Carboxymethyl cellulose (CMC), showing particular extensional viscosities, achieving relaxation times equal to 1 s, making it a great candidate to mimic human saliva (Yuan et al., 2018b). Chia (*Salvia hispanica* L.) on the other side, is known for its outstanding nutritional profile: source of ω -3 and ω -6 fatty acids, soluble and insoluble fibers, antioxidants, vitamins, and minerals (Brütsch et al., 2019). Timilsena et al., (2015) stated that chia mucilage shows a pseudoplastic behavior even at concentrations as low as 0.02% (w/v). This drives using chia seeds to attain low viscosity values with shear thinning behavior, such as human saliva. Finally, flaxseed (*Linum usitatissimum* L.) mucilage can be used in the food industry owing to its sustainable, biodegradable, and functional properties (Vieira et al., 2019). It has demonstrated significant relaxation times ($\lambda=500$ ms), possessing viscoelastic properties comparable to human saliva (Wagner, 2015).

In this context, the objective of this study is to benefit from the original rheological properties of seed mucilages (flax, okra, and chia) to address the complexity of human saliva when exposed to shear and extensional forces. Shear viscosities and relaxation times on human saliva were extracted from literature data to compare potential formulations. After evaluating three alternative sources, flaxseed extracts were chosen for evaluating Trouton ratio, tribology, and sensory perceptions. A sensory evaluation relevant to food oral processing was then assessed. Correlations between sensory perceptions and instrumental data were also accomplished. The results of this study can be valuable for the development of *in vitro* devices investigating food oral processing and for the research on natural salivary substitutes for xerostomic patients.

2. Materials & Methods

This study was divided into two parts; the first part presents the development and the rheological characterization of different natural salivary substitute formulations. The second part focuses on flaxseed extracts, presenting a detailed characterization of rheology, tribology, and sensory analysis.

2.1. Preliminary evaluation of different sources of natural salivary substitutes

2.1.1 Materials

The following raw materials were used to formulate three categories of natural salivary substitutes. Brown flaxseed (Markal, Saint-Marcel-lès-Valence, France) and Chia seeds (Markal, Saint-Marcel-lès-Valence, France) were bought in a local store (Naturalia, Clichy, France), containing respectively 20% and 16.7% of proteins. Okra pods were purchased at a local store

(Auchan, Croix, France), taking care of picking the freshest seed pods. Additionally, this study aimed to test and compare a formulation that was previously investigated by Ahmad et al. (2018) as it shows both shear-thinning and extensional viscosity. Thus, mucins from porcine stomach type II were from Sigma-Aldrich and stored at 4 °C (Sigma-Aldrich, St. Louis, USA).

2.1.2 Formulations

Four formulations were developed to compare their rheological profile to human saliva. A summary of the formulation protocols is shown in Table 1. The dry matter of all extracts was determined by oven drying at 105 °C (EM10 NG, Chopin Tech, Villeneuve-la-Garenne, France). Dry matter was weighed and expressed as percentage of solids.

Table 1. Summary of protocols used during the preliminary evaluation of Natural Salivary Substitute (NSS)

Formulation name	Protocol
Chia0.20%	The mucilage extraction procedure proposed by Brüttsch et al. (2019) was respected. The seeds were hydrated for 2h in a ratio of 1:20 at 25 °C. Later, centrifugation was carried out for gel extraction.
Flax0.20%	The conditions proposed by Wagner (2015) were considered using 3g of flaxseed and 75 mL of water. The mix was heated at 70 °C for 30 min. No dilution was made once the supernatant was separated from the seeds.
Okra0.50%	The cooking time and quantities outlined by Yuan et al. (2018) were followed. 100 g of okra were cooked for 90 min at 55 °C. The liquid remaining after cooking was used for characterization.
MucinSSF	A Simulated Salivary Fluid containing mucins was prepared following the protocol of Ahmad et al., (2018), by combining the SSF proposed by the InfoGest consortium (Brodkorb et al., 2019; Minekus et al., 2014) at pH 6.8 and with 4 g dL ⁻¹ of mucins.

2.1.3 Shear Rheology

To ensure a fair comparison between methods, all experiments were conducted at a temperature of 20 °C. This also ensures that the salivary substitute developed will be effective for *in vivo* and *in vitro* experiments at room temperature. It is important to keep this in mind when comparing the temperature of *in vivo* literature data.

The rheological behavior of the formulations was characterized on the same day of production using a Physica MCR-702 rheometer (Anton Paar GmbH, Graz, Austria). Shear viscosity was measured with a double gap-cylinder measuring system (DG26.7-SN17105) in a range of shear rates between 0.5 and 1000 s⁻¹ at 20 °C. All measurements were repeated in triplicate.

2.1.4 Extensional Properties

The extensional properties were measured by capillary break-up extensional rheometry using a HAAKE CaBER 1 (Thermo Electron, Karlsruhe Germany) at 20 °C. The filament thinning is measured with a laser beam of 1 mm diameter and resolution of 20 µm. High-speed videos of the

experiments were also taken at 1000 frames per second to record the shape evolution of the capillary thread using a PhantomV1612 high-speed camera (Vision Research, Wayne, USA).

The sample was placed in 3 mm gap between two circular plates (6 mm in diameter), followed by an axial displacement (10 mm) imposed at 50 ms. All measurements were repeated five times. The extensional relaxation time (λ), was calculated with the Capillary Breakage Extensional Rheometry (CaBER) Analysis software (Haake RheoWin Software, v5.0.12) by fitting the diameter evolution with the elastic (exponential) model. For Newtonian fluids, the viscocapillary regime leads to a linear decay with time of the midpoint diameter. On the contrary, for elastic fluids, the elasto-capillary regime leads to an exponential midpoint filament diameter (D_{mid}) decay in time (McKinley, 2005) (Eq.1).

(1)

$$D_{mid}(t) \sim e^{-\frac{t}{3\lambda}}$$

2.2 Investigating the rheological, tribological, and sensory properties of flaxseed extracts

The flaxseed formulation (Flax0.20%) was improved to reach an extensional rheology closer to human saliva. An extract was obtained by stirring at 250 rpm a solution of 10% w/w flaxseed and mineral water (Vittel, Nestlé) at 72 ± 1 °C for 1 hour. The extract was then strained till removing all seeds. This new formulation having 1.50 % of solids was then diluted to produce 0.40 % and 1.0 % DM extracts. The solutions were characterized on the same production day to avoid rheological changes over time.

2.2.1 Rheological characterization and analysis of flaxseed extracts

The steady shear was evaluated following the approach described in section 2.1.3 with a supplementary evaluation at 37 °C and verifying the absence of major thixotropic character. Additionally, shear viscosities at higher shear rates and different temperatures were obtained by employing a microVISCTM (Rheosense, San Ramon, USA) equipped with a A05 chip (50 μ m flow channel) and placed in a temperature controller unit HVROC-T. Results and further description on the method are shown in Figure 5 and Section A.1. Likewise, the extensional properties were measured following the methodology described in section 2.1.4, with an additional evaluation at 37 °C.

For flaxseed extracts, further analysis on extensional rheology was performed. Following the method proposed by McKinley (2005), the strain (ε) in a cylindrical element can be expressed as:

(2)

$$\varepsilon = -2 \ln \frac{D_{mid}}{D_0}$$

where D_0 is the initial diameter before the thinning starts. The strain rate ($\dot{\varepsilon}$) can be expressed as:

(3)

$$\dot{\varepsilon} = \frac{-2}{D_{mid}} \frac{dD_{mid}}{dt}$$

For ideal elastic liquids $\dot{\varepsilon}$ is constant and equal to:

$$\dot{\epsilon}_{el} = 2/(3\lambda) \quad (4)$$

This expression was used to define the apparent extensional viscosity ($\eta_{extensional}$) as:

$$\eta_{extensional} = \frac{2\sigma/D_{min}}{\dot{\epsilon}_{el}}$$

where σ is the liquid surface tension that was measured using a Krüss tensiometer (Krüss ST10, KRÜSS GmbH, Hamburg, Germany). A Wilhelmy plate was used with an immersion depth of 2 mm, at 20 °C. The detection speed was 0.5 mm/min and all measurements were repeated three times.

The Trouton ratio (Tr) is defined as the ratio of extensional and shear viscosity:

$$Tr(\dot{\epsilon}) = \frac{\eta_{extensional}(\dot{\epsilon})}{\eta_{shear}(\dot{\epsilon})}$$

In the literature, the Trouton ratio is often computed using a constant, reference shear viscosity, usually the zero-shear viscosity. In this study, the zero-shear viscosity could not be measured for all samples. Therefore, a definition considering a constant shear viscosity computed at a shear rate equal to the extensional rate is preferred and shown in Figure 6b. In addition, a second approach similar as the one of Pabois et al., (2023) was considered, where the Trouton ratio is obtained varying the shear viscosity; these results are displayed in Figure A.10.

2.2.2 Tribological characterization

The lubricity of the flaxseed extracts was studied by tribology with a new biomimetic setup. The tribometer geometry and design details are described in Glumac et al., (2023); Srivastava et al., (2021). In its superior part, the set-up includes an aluminum plate (rectangular, 45 mm × 25 mm), playing the role of the hard palate. A vertical translational stage was used to lower the palate plate until reaching a target value of normal load equal to 5 N against the tongue mimicking sample (TMS), equivalent to ~4.5 kPa. The TMS was a parallelepiped (80 mm × 45 mm × 10 mm) made of Ecoflex-030 (Smooth-On, Macungie, USA) and 5 % Span80 (sorbitan mono-oleate from Sigma-Aldrich, St. Louis, USA). The two components of Ecoflex-030 were mixed in equal amounts by weight; the surfactant was then added and mixed. Before pouring into the mould cast, the mixture was degasified to avoid any air bubbles. The topography of the tongue roughness was accounted for by covering the lid of the mould cast in which the TMS was cured with sandpaper P40 (Saint-Gobain Norton, Paris, France) following the strategy of Srivastava et al., (2021). 1 mL of the sample was placed in droplets on the TMS's surface and spread using a plastic spatula. Once the palate was lowered until reaching the target level of normal load, five cycles of back and forward at 10 mm·s⁻¹ were performed. The results presented are the mean values obtained during the 0.3 s before the displacement of the TMS stops moving. After each trial, the TMS was cleaned with water and dried; all samples were repeated five times. One limitation of this method was the lack of a temperature control system. Therefore, all the experiments were performed at room temperature (20 °C), ensuring a fair comparison between all the methods.

2.2.3 Sensory Evaluation

2.2.3.1 Conditions of sensory tests

A panel of 16 healthy individuals (9 women and 7 men, 23-60 years in age) was recruited based on their desire and availability to participate in a sensory analysis. The study was composed of six sessions (including two for training and four for evaluation) of around 30-40 min each. The study aimed to perform a sensory profile to describe the intensity of different sensory attributes after three mouth rinsing (0.40 % and 1.0 % flaxseed extracts and still mineral water) protocols are detailed in the following subsection. Panelists had no prior experience with the sensory characterization of salivary substitutes. The present sensory study followed the ethical standards defined by the Declaration of Helsinki. Informed consent was provided to the participants before participating to the study. The participants included in the study declared not to have a severe or chronic illness, and not to have food allergies. Consistently, participants were asked not to smoke (for those of them possibly concerned), eat or drink (apart from water) in the hour preceding the session. The overall aim of the study was explained to the panel so that they all gave their free and informed consent to participate. At the end of the study, a remuneration for their participation was offered.

The study was carried out using 16 sensory booths and individual sinks. During the sessions, the booths were air-conditioned (20 °C) and had red lighting to minimize visual biases. The sensory study aimed to compare four distinct conditions of mouth rinsing, which were proposed following a balanced order across panelists, using a Latin square and divided into three replicate blocks. The four conditions included two formulations based on flaxseed extracts (two dilutions : 0.40 % and 1.0 %), which were compared with two others aiming at mimicking natural and altered oral lubrication. The first was the natural lubricating state of the volunteers' oral cavity, a condition called "saliva". The second condition, referred to as "water", consisted of drastically reducing the natural lubrication by saliva by performing a series of mouth rinses with still mineral water (Nayak and Carpenter, 2008a).

2.2.3.2 Attribute selection

Generation and selection steps were performed to identify a list of five attributes. These attributes include: *Overall Taste Intensity*, *Mouth Hydration*, *Thickness*, *Tongue-Palate (T-P) Slipperiness*, and *Tongue-Palate (T-P) Adhesion*. The panelists were provided with proper training to define, evaluate, and quantify all these attributes. During each test, the panelists had to judge the intensity of the attributes on a scale from 0 to 10 that ranges from low to high. They were provided with a tablet that had a data acquisition interface programmed using the Fizz software (v.2.7; Biosystemes, Couternon, France). The training sessions were conducted to help the panelists get familiarized with the hardware and interface.

Overall Taste Intensity was systematically evaluated initially, so that the panelists would not focus on taste while evaluating texture attributes. The order of the other four attributes was varied across participants to avoid a tiredness bias.

Two attributes were evaluated without requiring any particular action, based on the definitions for which a consensus was reached with the panelists during the training phase. Thus, *Mouth Hydration* referred to the amount of saliva or lubricant perceived in the mouth, having a scale ranging from 0 for "dry" (dry mouth) to 10 for "hydrated" (highly lubricated mouth). Next, *Thickness* refers to the consistency of saliva or lubricating fluid, with a scale ranging from 0 for "thin" (low viscosity) to 10 for "thick" (high viscosity).

Panelists were asked to perform specific tongue movements for other attributes. *T-P Slipperiness* refers to the sensations associated with friction during shearing movements between the tongue and the palate. The scale ranged from 0 for "rough" (feeling of dry friction characterized by the perception of the roughness of the tongue) to 10 for "slippery" (sliding facilitated by a lubricating layer). *T-P Adhesiveness* refers to the adhesion of the tongue to the palate during a detachment movement. The scale ran from 0 for "non-sticky" to 10 for "sticky". Attributes and scale definitions are presented in Table 2, and additional information on the panelist training protocol is provided in A.3.

Table 2. Attributes and scales used during the sensory evaluation of flaxseed extracts at 0.40 % and 1 % DM, water and saliva

Attributes	Axis limit legend (0 → 10)
Taste intensity	Low → High
Mouth hydration	Dry → Hydrated
Thickness	Thin → Thick
Tongue-Palate slipperiness	Rough → Slippery
Tongue-palate adhesiveness	Non-sticky → Sticky

2.2.3.3 Mouth rinsing protocol

Four distinct mouth rinsing conditions were evaluated. The first method consisted in rinsing the mouth with a sip of still mineral water (Evian Danone, Évian-les-Bains, France) and then waiting for 1 min in order to restore a natural oral lubrication. This condition, referred to as "saliva", aims at characterizing the reference perception of the volunteers in the absence of the use of salivary substitutes.

The three other conditions then consisted in following the same protocol with three different fluids: flaxseed extracts at two concentrations levels (0.40 % and 1.0 %) and still mineral water, all served in 30 mL graduated plastic cups with a lid at 20 °C. The plate containing the samples was organized in different rows and columns of cups, each row corresponding to a specific test including three different cups. The volunteers were asked to pour the full content of the first cup into their mouths, then to make movements to circulate the fluid five times in contact with all the oral mucosa, before spitting it out. The same operation was then repeated with the two remaining cups (three cups with the same formulation per evaluation). The volunteers were asked to evaluate the 5 attributes just after spitting out the content of the 3rd cup (Figure 1.a&b). Before moving on to the next test, volunteers were asked to rinse their mouths with water for 10 seconds and then wait a minute in order to sufficiently attenuate residual perceptions and recover as much as possible their natural state of oral lubrication (Figure 1c).

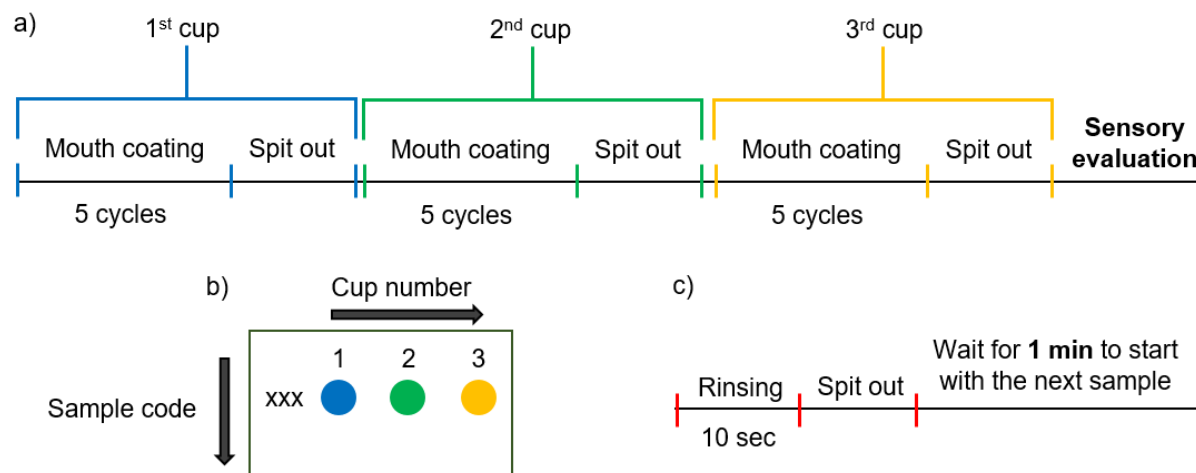


Figure 1. Sensory protocol. a) Mouth rinsing steps. b) Representation of sensory plate, c) Rinsing protocol after each sample.

2.2.4 Statistical analysis of the sensory data

Fizz Acquisition software (v.2.7; Biosystemes, Couternon, France) was used to acquire the data automatically. Data were then analyzed using XLSTAT (v.2023.1.1 Addinsoft, Paris, France).

Panel performance was evaluated by applying analyses of variance (ANOVA) ($\alpha=0.05$) to each attribute, including product, and panelist as main effects, and it was considered one order of interaction (product*panelist). Panel performance was also assessed based on the participants' ability to differentiate the attributes among the products and score repeatability.

The data was analyzed using a Principal Component Analysis (PCA) to emphasize variations and show patterns between sensory and instrumental data. Spearman correlation with a significant value of $\alpha=0.05$ was used to plot the PCA. The instrumental variables ("Shear viscosities at 10 s^{-1} ", "Shear viscosities at 100 s^{-1} ", "Friction Coefficient", "Relaxation Time", and "Trouton Ratio") were considered as active variables, and the sensory attributes (*Mouth Hydration*, *Thickness*, *T-P Slipperiness* and *T-P Adhesion*) were considered as supplementary variables.

3. Results and Discussion

3.1. Assessment of potential natural salivary substitutes: shear and extensional rheology

This study aimed to develop a natural salivary substitute that accurately mimics the characteristics of human saliva in mouth (that is naturally at body temperature), when the salivary substitute is used at room temperature (defined as $20 \text{ }^{\circ}\text{C}$). This is the temperature at which in vitro tribology and other in vitro FOP tests (e.g. swallowability testing) are performed and one use of the natural salivary substitute is as a substitute for saliva in in vitro tests. Thus, the rheological properties of the initial formulations of salivary substitutes were compared with human saliva in terms of viscosity curves as a function of shear rate and filament thinning curves (normalized filament diameter as a function of time). The human saliva properties were obtained from previously published works (Gittings et al., 2015; Stokes and Davies, 2007; Wagner and McKinley, 2017). The literature data helped establishing the range of variability of the saliva

properties that are relevant bounds for the properties of the natural salivary substitutes (Figure 2a). Figure 2a illustrates two literature studies evaluating the shear viscosity of unstimulated (whole saliva produced at rest) and stimulated (saliva produced after inducing mechanical or acid stimulation) human saliva at body temperature (37 °C). Food texture and in mouth food residence times affect heat transfer during bolus formation (Taylor and Linfoth, 1996). Thus, in mouth bolus temperature is generally intermediate between the serving temperature and body temperature. If a salivary substitute is sprayed (or applied in other ways) by a xerostomic person just before the consumption of food at room temperature, the temperature of the salivary substitute will also certainly be intermediate between serving and body temperature. As a consequence, in case of consumption by xerostomic people, the natural salivary substitute is expected to have in mouth a shear viscosity lower or at most equal to the viscosity of human saliva for healthy patients (at 37°C). This makes the salivary substitute effective in both in vivo and in vitro studies at room temperature.

Figure 2a shows the range of variability of human saliva shear viscosity as characterized by Gittings et al., (2015) and Stokes and Davies, (2007), highlighted in the red area. The variability is high at low shear rates ($<100 \text{ s}^{-1}$) and interestingly the variability reduces when higher shear rates are applied (i.e., $>100 \text{ s}^{-1}$), as highlighted by the red area in the figures. Overall, these results show that human saliva has shear thinning behavior with a more or less pronounced constant viscosity plateau at higher shear rates.

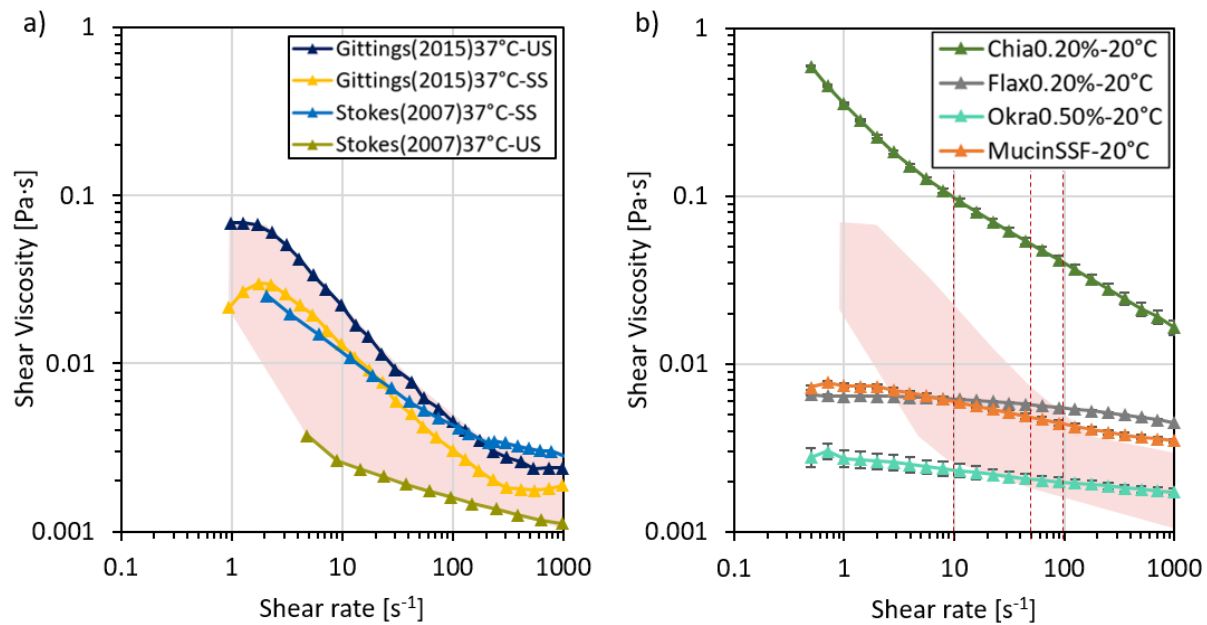


Figure 2. Rheological properties of the initial natural salivary substitute formulations. a) Human saliva flow curves from literature data used to establish the natural variability range (Gittings et al., 2015; Stokes and Davies, 2007). US: unstimulated saliva; SS: stimulated saliva b) Shear viscosities of formulations against the range of human saliva in vivo data (red area); important shear rates for comparison (10, 50 and 100 s^{-1}) are highlighted with vertical dashed lines.

Figure 2b compares the flow curves obtained in steady shear for the four formulations. The red highlighted surface indicates the range of shear viscosities reported for human saliva in the literature, taken from Figure 2a. The initial formulations were first compared to human saliva at 10 s^{-1} , 50 s^{-1} , and 100 s^{-1} (vertical dashed lines). These shear rates are believed to relate to the food oral processing stage (Steele et al., 2015). In addition, positive correlations have been found between sensory attributes such as oral cohesiveness and post-swallowing residue, and shear rates at 10 s^{-1} and 100 s^{-1} in a wide range of viscosity products ($0.221 - 2.359\text{ Pa}\cdot\text{s}$) ($0.103 - 0.64\text{ Pa}\cdot\text{s}$), respectively. These two attributes link saliva's ability to form a safe bolus for swallowing. The initial formulations were also compared with MucinSSF due to its important resemblance in ion strength, pH buffering, and chemical composition with human saliva.

Overall, the three formulations showed very modest shear-thinning behavior (except 0.20% Chia). At low and high shear rates, the Chia formulation had shear viscosity values one order of magnitude higher than in vivo data and two orders of magnitude higher than MucinSSF at low shear rates. On the other side, Okra presented the lowest shear viscosity values. Okra shear viscosity was outside the range at 10 s^{-1} and was within the viscosity limits at 50 s^{-1} and 100 s^{-1} . Flax, was slightly more viscous than okra and presented similar values to MucinSSF.

To the best of our knowledge, only data from *Wagner and McKinley, (2017)* are available in the literature in terms of filament thinning of unstimulated saliva at room temperature (temperature not reported). Please note that human unstimulated saliva measurements at 37°C could not be considered (see Figure 3a). *Wagner and McKinley, (2017)* studied the evolution of saliva with time, from 0 hours after extracting the samples to 1, 3, 5, and 10 hours. The samples were evaluated at room temperature by capillary break-up extensional rheometry (CaBER) and results are presented in terms of the time evolution of the filament diameter normalized by initial diameter before the thinning starts. The thinning stops with filament breakage and the break-up time is recorded.

The two data sets reflecting the variation over the first hour after collection are illustrated in Figure 3a where a red area shows the expected short time decay. Similarly to the approach followed for shear properties, the range highlighted in the red area was used to establish the target range for the natural salivary substitute extensional properties.

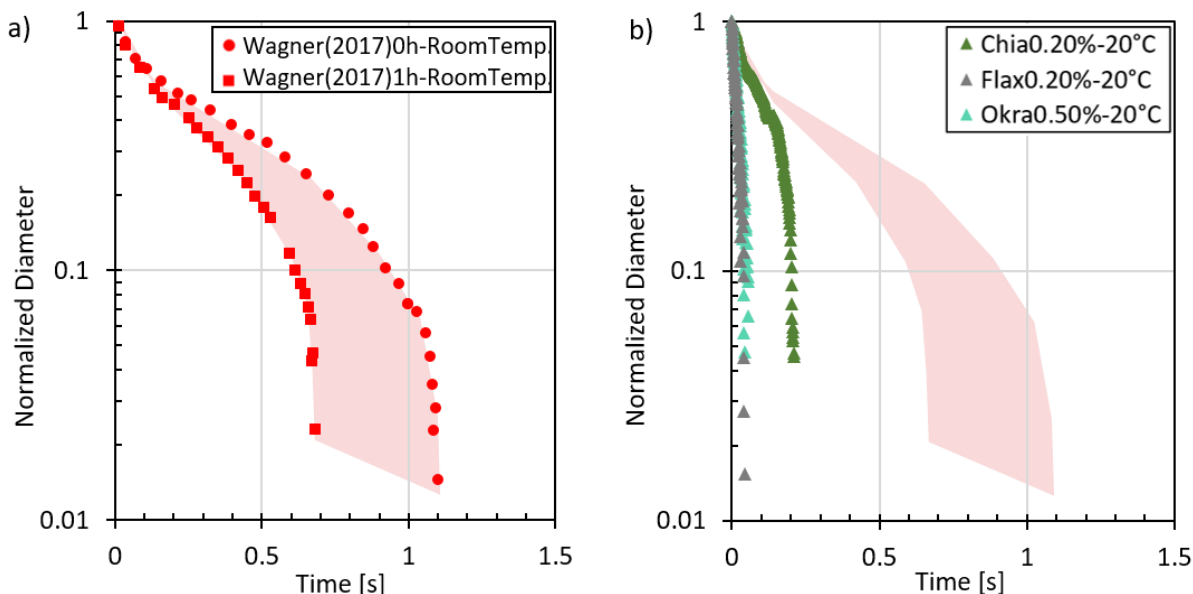


Figure 3. Extensional properties of potential natural salivary substitutes. a) Normalized diameter from literature data of human saliva, used to establish the variability range (Wagner and McKinley, 2017). b) Normalized diameter of formulations against the range of human saliva in vivo data extracted from Figure 3a (red area)

A key rheological property measured is the extensional relaxation time, obtained by fitting an elastic model to the filament thinning dynamics (Eq. 1). Relaxation times obtained from the literature data were also displayed in A.4.

Interestingly, no filament could be formed and no measurement could be obtained for MucinSSF, due to the instability of the initial meniscus between the plates. The surface tension of the sample may have been too low, preventing the analysis with CaBER. Conversely, in the work of Ahmad et al. (2018) MucinSSF (at the same concentration used in this work) showed a break-up time of 0.122 seconds. Although we can speculate that there may have been a difference in surface tensions, we have no robust explanation for this discrepancy. Chia, Flax, and Okra formulations presented filament thinning very rapidly over time and short break-up times. Flax formulation broke up at 0.04 ± 0.01 s, Okra at 0.06 ± 0.01 s, and Chia at 0.19 ± 0.03 s. Overall, the three formulations did not show break-up times close to human saliva (Figure 3b). Albeit chia displayed longer break-up times, the shear viscosity of this formulation was out of the variability range of human saliva. The flax and okra formulations presented lower extensional properties. Nevertheless, shear viscosity values of Flax0.20% were within the limits of human saliva at 10, 50, and 100 s^{-1} and Okra0.5% was too low at 10 s^{-1} . Thus Flax0.20% might be a better candidate than Okra at 0.5%, to imitate the shear viscosity of saliva at 37°C . Given the shear behavior discussed previously, Flaxseed was considered as the most interesting extract and further studies were carried out to improve the extensional properties.

3.2 Formulation of flaxseed extracts towards matching saliva rheological properties

Flaxseed extract at different concentrations were considered to match close enough the saliva rheological properties (Section 2.2). Steady shear and extensional rheological measurements were evaluated at 20 °C (Figure 4) and also at 37 °C (Figure 5). Shear viscosities of Flax1.0% are indeed higher than saliva, but this formulation was considered due to its higher elasticity than Flax0.40% (higher relaxation times and within the range of human saliva).

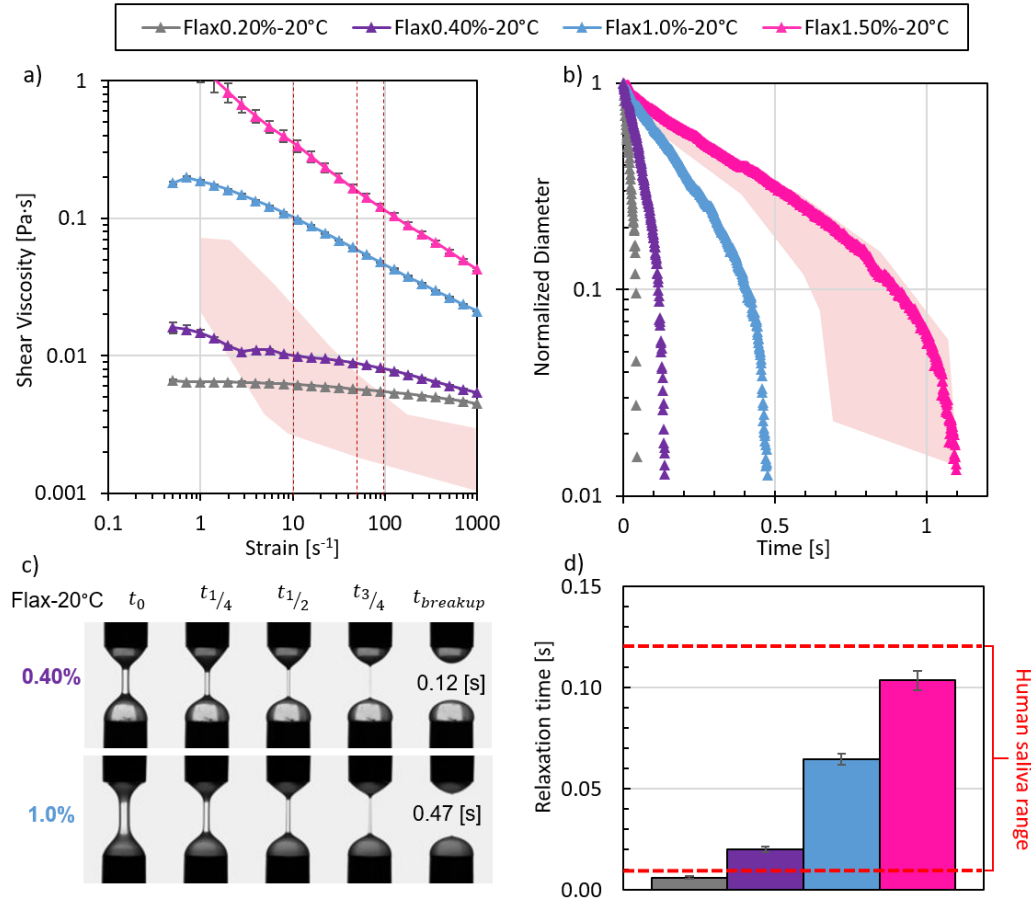


Figure 4. Comparison of rheological properties of flaxseed extracts at different concentrations evaluated at 20 °C. a) Flow curves of flaxseed extracts compared to in vivo data (red area) and the three dash lines representing 10, 50 and 100 s⁻¹. b) Normalized diameter of flaxseed extracts compared to in vivo data (red area). c) Filament evolution of Flax0.40% and Flax1.0%. (please note that $t_{1/4}$ indicates one fourth of the interval between $t_{breakup}$ and t_0 , etc.) d) Relaxation times of flaxseed extracts compared to human saliva data; range found in A.4 (Turcanu et al., 2015; Wagner, 2015; Zussman et al., 2007).

Figure 4a shows the evolution of the shear viscosity with the shear rate of the different flaxseed extracts, measured at 20 °C. The concentration of 0.40 % has viscosity values within the range of human saliva at shear rates of 10 and 50 s⁻¹, while it exceeds slightly saliva at 100 s⁻¹. At 37 °C, the viscosity of Flax0.40% falls within the range of human saliva from 10 to 100 s⁻¹ (Figure 5a). The 1.0 % flaxseed concentration shows shear viscosities higher to those of human saliva. When increasing the temperature (37 °C), the viscosity of Flax1.0% lowers, and similar values to human saliva are observed for ~1 to 2 s⁻¹. All in all, Flax1.0% shows shear viscosity higher than human saliva at 10, 50, or 100 s⁻¹, but comparable values in relaxation times are

observed (Figure 4d). Given that most commercial salivary substitutes are thicker than saliva, it was decided to study this solution too. The objective is to show the compromise that shear and extensional properties can provide to a potential formulation for salivary substitutes.

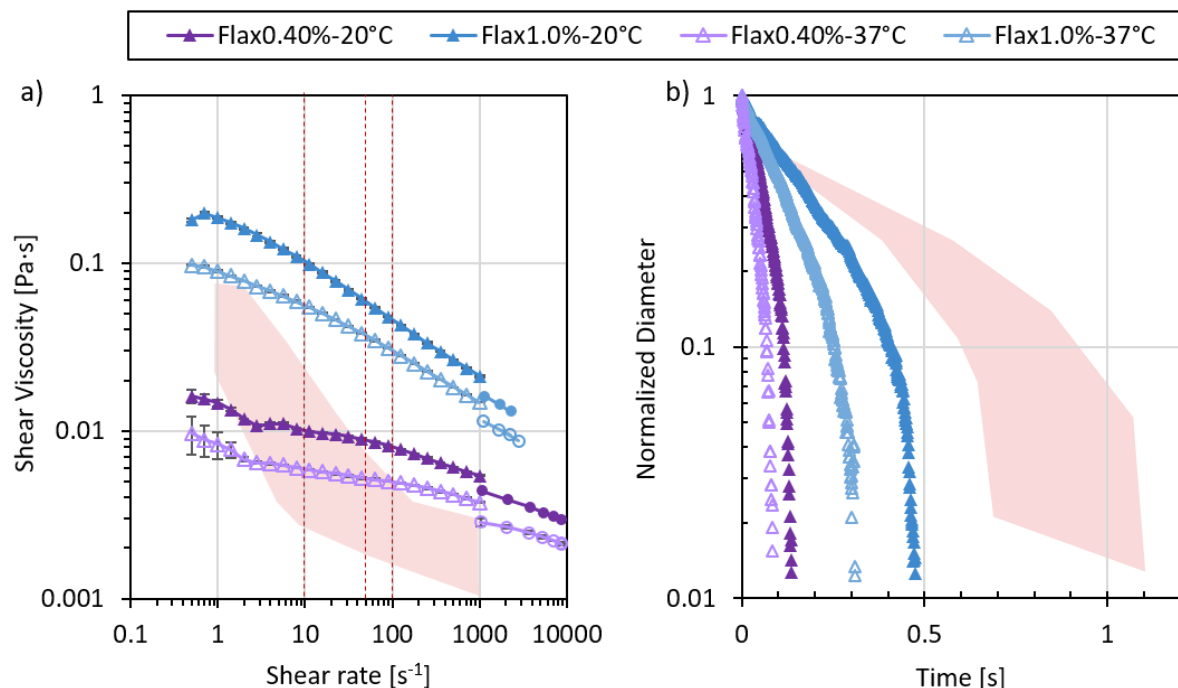


Figure 5. Shear viscosity and normalized diameter of flaxseed extracts at 0.40 % and 1.0 %. a) Shear viscosity was analyzed at two different temperatures 20 °C (full) and 37 °C (empty) and with two methods Physica MCR-702 rheometer (triangle) and microVISCTM (circle). b) Normalized diameter was analyzed at two different temperatures 20 °C (full) and 37 °C (empty). Saliva variability is represented in the red area.

Figure 4b summarizes the filament thinning dynamics at 20°C of different flaxseed extract concentrations, confirming their relevance to imitate human saliva elasticity. The two dilutions (0.40 % and 1.0 %) were formulated to approach as much as possible shear and elastic rheology of human saliva. It is observed that the filament diameters of the literature data decrease exponentially with time, which is a typical feature of elastic fluids (Anna and McKinley, 2001). The elasticity of human saliva decreases within one hour; break-up time from 1.1 to 0.7 s and relaxation time from 0.12 to 0.9 s (Figure A.11). Flaxseed at 1.0 % analyzed at 20 °C shows a break-up time of ~0.5 s compared to 0.3 s when investigated at 37 °C (Figure 5b). For flaxseed at 0.40 % studied at 20 and 37 °C, the change in break-up time is not significant. Temperature is an important variable when developing salivary substitutes. As observed, flaxseed extract shear and extensional rheological properties changed with temperature. This could influence the sensory perceptions depending on the oral temperature and residence time of the salivary substitute in the mouth.

Liquid filaments were prepared on the CaBER following the same procedure that is used to quantify the filament thinning dynamics. The images acquired are displayed in Figure 4c. The filament thinning dynamics starts with the steady state of the two circular plates where the liquid

is placed (t_0), followed by a uniaxial displacement which assists the filament break-up ($t_{breakup}$). The initial t_0 on the filament 1.0 %, shows viscous drainage due to the higher concentration of polymer molecules that might enhance the total time the liquid bridge remains connected, which is not seen at t_0 for 0.40 % (Anna and McKinley, 2001). Afterward, the thinning behavior of 1.0 % is similar to 0.40 % as the filament changes over time (from $t_{1/4} = 1/4(t_{breakup} - t_0)$ to $t_{breakup}$).

The relaxation times of the flaxseed extracts are presented in Figure 4d and compared with data from the literature demonstrated in the red pointed line (Figure A.11) (Turcanu et al., 2015; Wagner, 2015; Zussman et al., 2007). Wagner (2015) analyzed the unstimulated saliva “whole saliva produced at rest” (US) of two donors; sample aging decreased the relaxation time (0.12, 0.09, and 0.07 s). Moreover, when Turcanu et al. (2015) measured mechanically stimulated saliva (MSS), and citric acid stimulated saliva (CASS), they obtained higher values of relaxation times when it was promoted with citric acid (0.722 s) than mechanically (0.01 s). Similar results were obtained by Stokes & Davies (2007) when they analyzed CASS by fitting G' and G'' into a multi-mode Maxwell model getting a relaxation time of 0.94 s. In contrast, Zussman et al. (2007) obtained relaxation times of CASS at 0.018 s from the submandibular/sublingual glands of healthy volunteers.

The relaxation time of Flax0.20% (0.006 s) is lower in comparison to stimulated saliva, whereas Flax1.50% (0.10 s) is close to unstimulated saliva after 0 hrs collection. Nevertheless, Flax1.50% shear viscosity was too high compared to literature data of human saliva. The relaxation time of Flax1.0% (0.06 s) is comparable with the unstimulated saliva measurements of 1h and 2h after collection. Conversely, Flax0.40% had similar relaxation time (0.02 s) to mechanically stimulated saliva. Further work should be pursued to develop new salivary substitutes considering the additional relaxation times in the literature (0.722 to 0.94 s). All the comparable results were evaluated by uniaxial elongational flow, except the work from Stokes & Davies (2007) where they employed shearing flow. Due to the closer values in *in vivo* shear viscosities from Flax0.40% and the comparable values in relaxation times from Flax1.0% to *in vivo* data, these two formulations were selected to continue the study.

3.3 Apparent extensional viscosity and Trouton ratio of flaxseed extracts at 0.40 % and 1.0 %

Haward et al., (2011) demonstrated the highly elastic nature of saliva by evaluating its apparent extensional viscosity (0.6 Pa·s at $\sim 1200 \text{ s}^{-1}$) and Trouton ratio (~ 120 at $\sim 400 \text{ s}^{-1}$). Albeit, the definition of shear viscosity used to acquire the Trouton ratio is lacking, this study is the single presenting apparent extensional viscosity and Trouton ratio of human saliva in the literature. These authors stated that saliva elasticity is linked to some of its important functionalities in FOP: lubrication, surface adhesion within the oral cavity, and the ability to form a bolus. For these reasons, the apparent extensional viscosity ($\eta_{\text{extensional}}$) and the Trouton ratio (Tr) were also computed in this study to evaluate the ability of flaxseed extracts to elongate through the pharynx and form an elastic bolus.

The experimental data showed exponential midpoint filament diameter decay in time for both concentration of flaxseed extracts. The fitting into the elastic model described in Eq.1 displayed coefficient of determination of 0.970 ± 0.012 for 0.40 % and 0.949 ± 0.005 for 1.0%. The surface

tension of the liquids were 53.0 ± 1.2 mN/m for the concentration 0.40 % and 49.5 ± 1.8 mN/m for the 1.0 % concentration. Figure 6a illustrates the extensional viscosity (Eq. 5) as a function of strain (Eq. 2) of flaxseed extracts (0.40 % and 1.0 %.) at 20 and 37 °C.

Figure 6a illustrates the increase in $\eta_{\text{extensional}}$ with increasing strain for both concentrations. This behavior is typical for viscoelastic fluids and is established as extension-thickening (Sochi, 2010). Figure 6a also shows the higher $\eta_{\text{extensional}}$ results of Flax1.0% compared to Flax0.40% which is due to the concentration effect of the sample and has been observed in other studies (Marconati and Ramaioli, 2020). Additionally, the temperature effect demonstrates that for both concentrations $\eta_{\text{extensional}}$ decreases when increasing the temperature. As both extracts have different thinning dynamics the maximum $\eta_{\text{extensional}}$ and Tr are at different strains. For Flax0.40% the maximum $\eta_{\text{extensional}}$ is 26.8 ± 1.3 Pa·s and 56.6 ± 0.5 Pa·s for Flax1.0% at 20 °C, whereas the maximum $\eta_{\text{extensional}}$ at 37 °C is 19.8 ± 1.4 Pa·s and 44.7 ± 1.8 Pa·s, respectively. These results demonstrate that flaxseed extracts have higher $\eta_{\text{extensional}}$ than human saliva (0.6 Pa·s) and than salivary substitutes in the market (BioXtra[®] 12.9 ± 4.8 Pa·s and Boots[®] 5.2 ± 0.6 Pa·s) based on Paboïs et al., (2023).

The Trouton ratio (Tr) measures the relative importance of extensional and shear viscosity. For elastic liquids, (Tr) is expected to be greater than or equal to 3; when $\text{Tr} = 3$ is generally for Newtonian fluids (Marconati and Ramaioli, 2020; Sochi, 2010). The Trouton ratio in Figure 6b was computed using a constant shear viscosity at a shear rate equal to the extensional rate. Figure 6b shows the higher elasticity of Flax0.40% compared to Flax1.0% at 20 and 37 °C. This difference is due to the higher shear viscosity of Flax1.0%. These findings could be related to the work of Vieira et al. (2021), where they described a solution of 1.5% w/w of flaxseed as a flexible and random coil polymer chain—considering as well that Gallegos et al. (2021) explained that linear stretched coil polymer solutions present large values of Trouton ratio.

In addition, the (Tr) of flaxseed extracts were higher to the data obtained from salivary substitutes in the market based on the study of Paboïs et al., (2023). The comparison is illustrated in Figure A.10 where Flax0.40% shows 4017.6 ± 180.1 and Flax1.0% 2576.8 ± 257.2 at 20 °C, and 4869.3 ± 242.9 and 2058.1 ± 249.1 at 37 °C, respectively in comparison to Boots[®] 289 ± 35 , Oralieve[®] 8 ± 1 and BioXtra[®] 20 ± 9 . Overall, studying extensional rheology of potential salivary substitutes is important due to its likely significant impact on texture perception in the mouth during food oral processing (Haward et al., 2011).

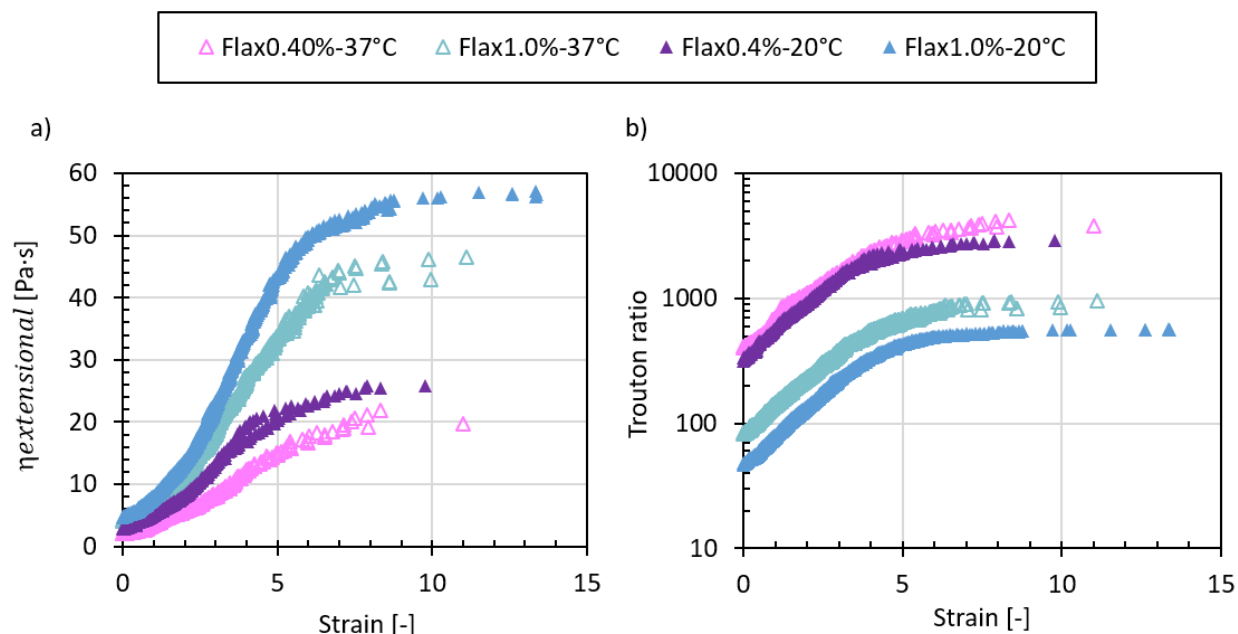


Figure 6. Apparent extensional viscosity and Trouton ratio of flaxseed extracts at 0.40 % and 1 %. Trouton ratio was computed using a constant zero-shear viscosity.

3.4. Sensory and Tribological study of flaxseed extracts at 0.40 % and 1.0 % concentration, of water and human saliva

3.4.1 Panel performance

The results of the ANOVA tests on the sensory profile results are reported in Table A.5. The panel could discriminate the products, as the product factor was significant for all attributes (5/5). The homogeneity of the panel is assessed by looking at the panelist*product interaction, which was close to being significant for all the attributes, also the F values are negligible in regards to F product. However, such interactions are common when sensory attributes are difficult to control, even when panelists have undergone extensive training (Cosson et al., 2021). Moreover, the weighting information provided by the F score reveals that for each attribute, the effect of the panelist*product interaction is systematically lower than the product effect. These results therefore bring confidence in the panel performance for all the products tested.

3.4.2 Comparison of the sensory characteristics of flaxseed extracts at 0.40 % and 1.0 % concentration, of water, and saliva

It is important to remember that the samples were served at 20 °C and the residence time of the products in mouth was low. Participants were asked to swirl the samples and to spit them out, before moving to another product at 20 °C. This process was repeated 3 times and participants were asked to evaluate the oral perceptions as fast as possible. Figure A.12 shows the mean sensory score for each product and their significance obtained from ANOVA. A comparison with saliva, considered as the baseline panelist lubrication state was obtained from the mean scores and is shown in Figure 7 where a red dashed line represents the saliva baseline. Mean scores

normalized using the expression: $\frac{\text{Product sensory mean}}{\text{Saliva sensory mean}} - 1$ are reported in Figure 7. Saliva therefore corresponds to the normalized score equal to zero.

Higher absolute scores in *Overall Taste Intensity* are observed for flaxseed extracts at 1.0 % and 0.40 % (5.4 ± 0.6 and 3.9 ± 0.5) compared to water (0.8 ± 0.3) (Figure A.12). Water, *Overall Taste Intensity* is statistically similar to human saliva. Taste results concerning this attribute confirm that the flaxseed extracts are not neutral in taste and aroma. This was taken into account in panelist evaluation, limiting a halo-dumping effect. In addition, the taste perception was higher at higher concentrations. However, from a qualitative point of view, the panelists did not express rejection for these lubricants.

In contrast, significant differences between all the products were noted for *Thickness*, *Tongue-Palate (T-P) Slipperiness*, and *T-P Adhesion*. Furthermore, similar trends were followed when compared to *Overall Taste Intensity* and *Mouth Hydration*. For *Thickness*, *T-P Slipperiness*, and *T-P Adhesion*, the scores increased from water < saliva < Flax 0.40% < Flax 1.0% (Figure A.12). *Overall Taste Intensity* and *Thickness* were the attributes with the highest differences compared to the natural oral lubrication “saliva”. Conversely, *Mouth Hydration*, *T-P Slipperiness* and *T-P Adhesion* are closer to “saliva”.

Surprisingly, when rinsing with water, *Mouth Hydration* was statistically similar to saliva. This result undermined the hypothesis of reducing the perception of saliva's natural lubrication when performing a series of water mouth rinses. Nevertheless, 37.5 % of the participants evaluated *Mouth Hydration* using water, with scores less than 5 (5/10). In contrast, flaxseed extracts offered an increase in hydration perception (8.2 ± 0.4 and 7.7 ± 0.4) (Figure A.12). Figure 7 demonstrates that regardless of the flaxseed concentration (0.40 % and 1.0 %), these solutions led to higher perceived *Mouth Hydration* than that induced by water or saliva. In addition, when rinsing with water, participants perceived a reduction in *T-P Slipperiness* and *T-P Adhesion* compared to their natural oral lubrication state. This is in striking contrast to the higher *T-P Slipperiness* and *T-P Adhesion* perceived for flaxseed extracts.

This may be explained by the results from Nayak and Carpenter, (2008). These authors remarked that the action of washing the mouth out with water appears to remove the mobile salivary film (saliva in a mobile phase) but leaves mucosal pellicle intact (saliva adhered to oral epithelial cells). Thus, our results indicate that the attribute *Mouth Hydration* might be related to the saliva adhered to the oral epithelial cells, due to the significant similarity between the natural lubrication state of participants and after rinsing with water. Conversely, the attributes *T-P Slipperiness* and *T-P Adhesion* are probably linked to the oral salivary film since rinsing with water promoted a significant decrease compared to the saliva mean scores. However, flaxseed extracts may potentially affect both the mobile salivary film and the mucosal pellicle as demonstrated higher values compared to water in *Mouth Hydration*, *T-P Slipperiness* and *T-P Adhesion*; further tests should be performed to confirm this hypothesis. Additionally, further work is required to potentially decrease flavoring and aroma of the flaxseed extracts to acquire closer overall taste perceptions to saliva.

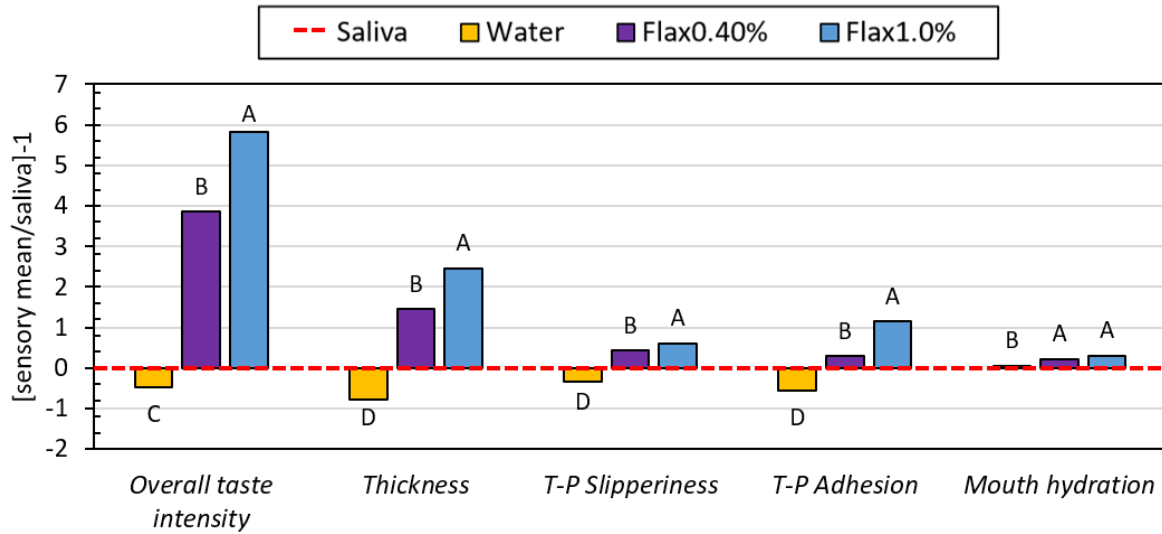


Figure 7. Means from the sensory scores normalized by the saliva scores for Saliva, Water and two concentrations of flax seed extracts. Five attributes were considered: Overall Taste Intensity, Thickness, Tongue-Palate (T-P) Slipperiness, Tongue-Palate Adhesion and Mouth Hydration. Letters indicate the statistically significant differences, based on the ANOVA test.

3.4.3 Tribological results

The interactions between saliva and tongue surfaces are essential in oral tribology (Sarkar, 2019). The Stribeck curve helps to explain the lubrication behavior of materials in three different regimes. At low speed, in the "boundary" regime, the friction is influenced by the contact between the asperities of the two surfaces. The second regime, at intermediate speed, is called the "mixed" regime, which is influenced by the friction of both the fluid and the surface asperities. The third regime, the "hydrodynamic" regime, dominates at high speeds, where friction is influenced by the bulk rheology of the fluid. Thus, the lubrication behavior of the flaxseed dilutions and water were analyzed by using a tribological set-up that tried to imitate tongue papillae dimensions, but also the contact angle, and elastic modulus of the human tongue (Glumac et al., 2023; Marconati et al., 2020).

The mean and standard deviation of the friction coefficient are shown in Figure 8a. When comparing the two flaxseed extracts, the friction coefficient was significantly higher for 0.40 % than for 1.0 %. Friction level displayed was tenfold higher for water than unstimulated saliva (red dashed line). Given the constant experimental normal force and shearing velocity conditions, in the absence of particles or heterogeneities in the lubricating phase, it is expected that the viscosity entirely governs the lubrication regime. When looking in particular at the cases of water and the two flaxseed solutions for which the flow curves are entirely distinct, it can be noted that the friction coefficient decreases when the viscosity increases (Figure 8a&c). Such a trend is characteristic of the mixed regime of lubrication, where some regions experience boundary lubrication with direct contact between asperities, while others have a sufficient fluid film to separate surfaces and provide full lubrication.

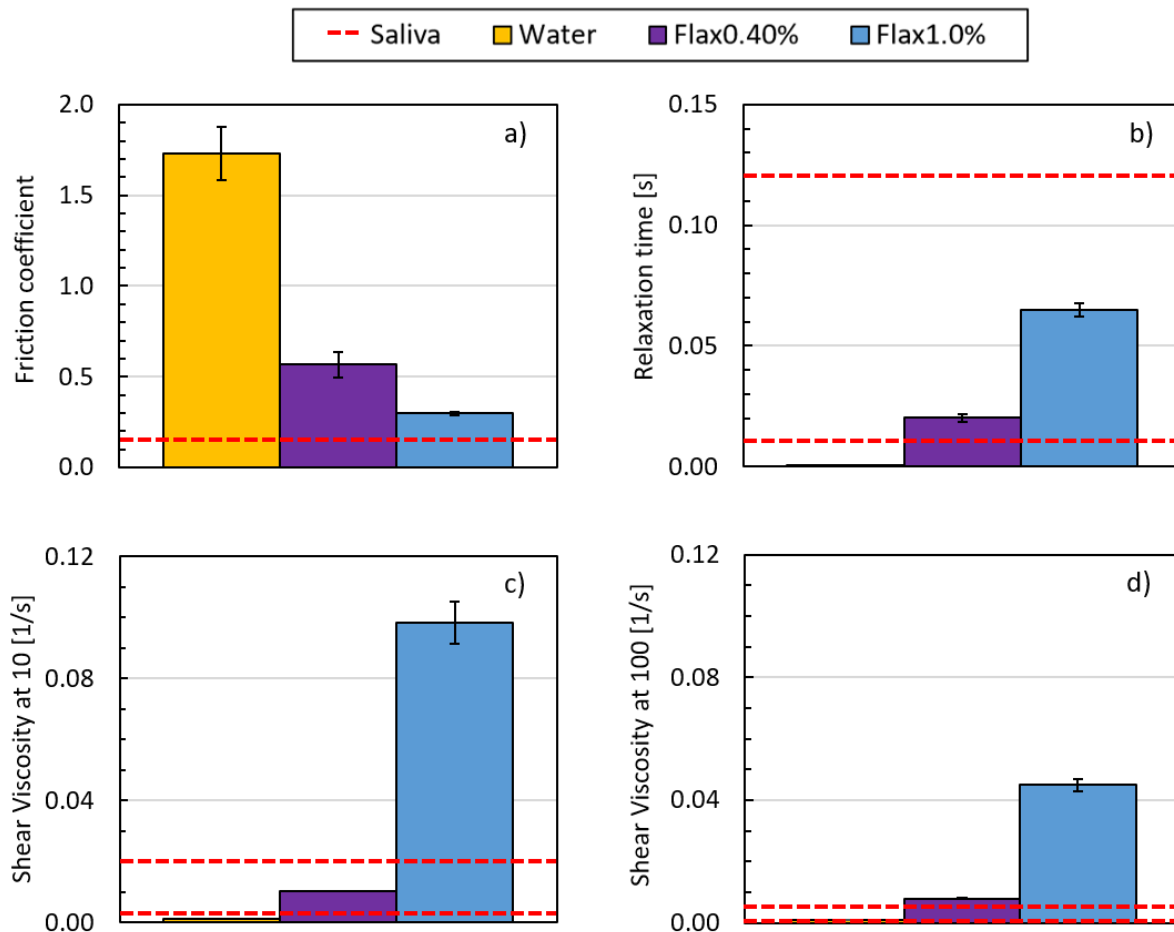


Figure 8. Friction coefficient, relaxation time, shear viscosities at 10 s^{-1} and shear viscosities at 100 s^{-1} compared with human saliva literature data represented with a red pointed line.

3.4.4 Correlation between instrumental measurements and sensory perceptions

A PCA was performed to capture the essential factors differentiating the products in terms of the properties obtained from instrumental measurements and evaluate the links between instrumental data, sensory perceptions, and products (Figure 9). The mean data used to obtain the PCA are reported in Table A.6. Nevertheless, the PCA represents the three repetitions for each instrumental and sensory evaluation to illustrate variability. For this section shear viscosities at low (10 s^{-1}), middle (100 s^{-1}) and high (2000 s^{-1}) shear rates were considered.

Table 3 reports the correlation between variables and factors in the PCA (Figure 9). The F1 axis has 70.71% of the data, clustering shear viscosities, extensional and sensory variables on the right side of the biplot. Conversely, the friction coefficient shows a negative correlation with axis F1, locating itself on the left side of the biplot. Additionally, F2 represents 18.89% and correlates negatively (bottom) with relaxation time ($r=-0.457$) and positively (top) with friction coefficient ($r=0.678$), Trouton ratio ($r=0.530$) and *Mouth Hydration* ($r=0.581$). Moreover, the contribution mean percentage of the observations to each factor were 11.4 % and 20 % for Flax1.0% and water respectively to F1. For F2, Flax0.40% showed 11.6 % and saliva 20.2 %. This suggests that positioning Flax1.0% on the right side of the biplot indicates its higher

lubricity, shear, extensional, and sensory properties as opposed to water. In contrast, the position on the positive axis of F2 for Flax0.40% implies higher Trouton ratio, *Mouth hydration* and lower lubricity and relaxation times than human saliva.

Table 3. Correlation between variables and factors

Variables	Factors	
	F1	F2
Shear viscosity 10 [s ⁻¹]	0.950	-0.145
Shear viscosity 100 [s ⁻¹]	0.944	0.282
Shear viscosity 2000 [s ⁻¹]	0.933	0.290
Relaxation time	0.824	-0.457
Friction coefficient	-0.605	0.678
Trouton ratio	0.732	0.530
Mouth hydration	0.634	0.581
Thickness	0.885	0.276
TPS	0.920	0.258
TPA	0.883	0.244

Figure 9 displays the four products well distributed along axes F1 and F2 (89.59 %) and the variables on three out of the four quadrants of the correlation circle. “Shear Viscosities at 10 s⁻¹” were strongly correlated to “Relaxation Time” (r=0.872) and negatively correlated to “Friction Coefficient” (r=-0.577). The relation between “Shear Viscosity at 10 s⁻¹” and “Relaxation Time” is probably driven by the higher relaxation time and shear viscosity at 10 s⁻¹ of saliva compared to Flax0.40%. In the literature, “Viscosities at 10 s⁻¹” have been related to oral cohesiveness, this may indicate saliva’s ability to form and maintain an intact bolus (Ross et al., 2019). Additionally, the negative strong correlation between “Friction Coefficient” and “Shear Viscosities at 10 s⁻¹” is consistent with the mixed lubrication regime. Also, the negative correlation between “Friction Coefficient” and “Relaxation Time” suggests that salivary substitutes with higher elasticity would be more lubricious, reducing the friction coefficient. Similar results were obtained when evaluating polysaccharide–protein gel particle dispersions, observing negative correlations between slipperiness and friction coefficients (Chojnicka-Paszun et al., 2014).

Table 4. Spearman correlation coefficients between sensory attributes and instrumental data.

Abbreviations: Tongue-Palate slipperiness (TPS) and Tongue-Palate adhesion (TPA)

Variables	Shear viscosity 10 s ⁻¹	Shear viscosity 100 s ⁻¹	Shear viscosity 2000 s ⁻¹	Relax. time	Friction coeff.	Trouton ratio	Mouth hydration	Thickness	TPS	TPA
Shear viscosity 10 s ⁻¹	1	0.894	0.848	0.872	-0.577	0.514	0.599	0.775	0.852	0.803
Shear viscosity 100 s ⁻¹	0.894	1	0.978	0.638	-0.345	0.771	0.810	0.923	0.958	0.937
Shear viscosity 2000 s ⁻¹	0.848	0.978	1	0.587	-0.389	0.788	0.820	0.972	0.972	0.950

Relaxation time	0.872	0.638	0.587	1	-0.704	0.364	0.239	0.521	0.620	0.528
Friction coefficient	-0.577	-0.345	-0.389	-0.704	1	-0.199	0.091	-0.420	-	-
Trouton ratio	0.514	0.771	0.788	0.364	-0.199	1	0.617	0.766	0.752	0.716
Mouth hydration	0.599	0.810	0.820	0.239	0.091	0.617	1	0.776	0.825	0.769
Thickness	0.775	0.923	0.972	0.521	-0.420	0.766	0.776	1	0.944	0.937
TPS	0.852	0.958	0.972	0.620	-0.371	0.752	0.825	0.944	1	0.902
TPA	0.803	0.937	0.950	0.528	-0.420	0.716	0.769	0.937	0.902	1

Values in bold are different from 0 with a significance level $\alpha=0.05$

Mouth Hydration was found to be strongly correlated with different variables: *Thickness* ($r=0.776$), *T-P Slipperiness* ($r=0.825$), *T-P Adhesion* ($r=0.769$), “Shear Viscosity at 2000 s^{-1} ” ($r=0.820$) and “Trouton ratio” ($r=0.617$) (Table 4). It suggests that higher perception of mouth hydration is related to higher perception of slipperiness and adhesion between the tongue and the palate. This may be related to the mouthfeel perception of the coating created on the surface of the mouth (Sarkar, 2019). In addition, Mouth Hydration appears to have strong correlations with shear and extensional properties of the fluids; implying the importance of both properties in the development of salivary substitutes. The correlation between Mouth Hydration, “Shear Viscosity at 2000 s^{-1} ” and “Trouton ratio” may be related to the findings of Pico-Munoz et al. (2023). They discovered that viscous liquids can contribute to a quenched thirst sensation, which could be associated to a hydration sensation. However, it has been previously stated (in section 3.4.2) that flaxseed extracts may potentially affect both the mobile salivary film and the mucosal pellicle. Nayak & Carpenter (2008) suggest that the mobile phase of saliva, which can be washed away by water, modulates the feeling of astringency, which is a rough, dry, puckering feeling in the oral mucosa (Nayak and Carpenter, 2008b; Pang et al., 2022). Hence, flaxseed extracts may provide lubricant perceptions and enhance mouth hydration. Nevertheless, to our knowledge, no published study investigated the relation between mouth hydration perception and shear viscosity at low, middle and high shear rates. Interestingly, this result confirms the suggestion made by He et al., (2016), who stated that the oral flow is highly complex and better predictions could be made including variables like shear viscosity at high and low shear rates and considering shear and extensional flow properties.

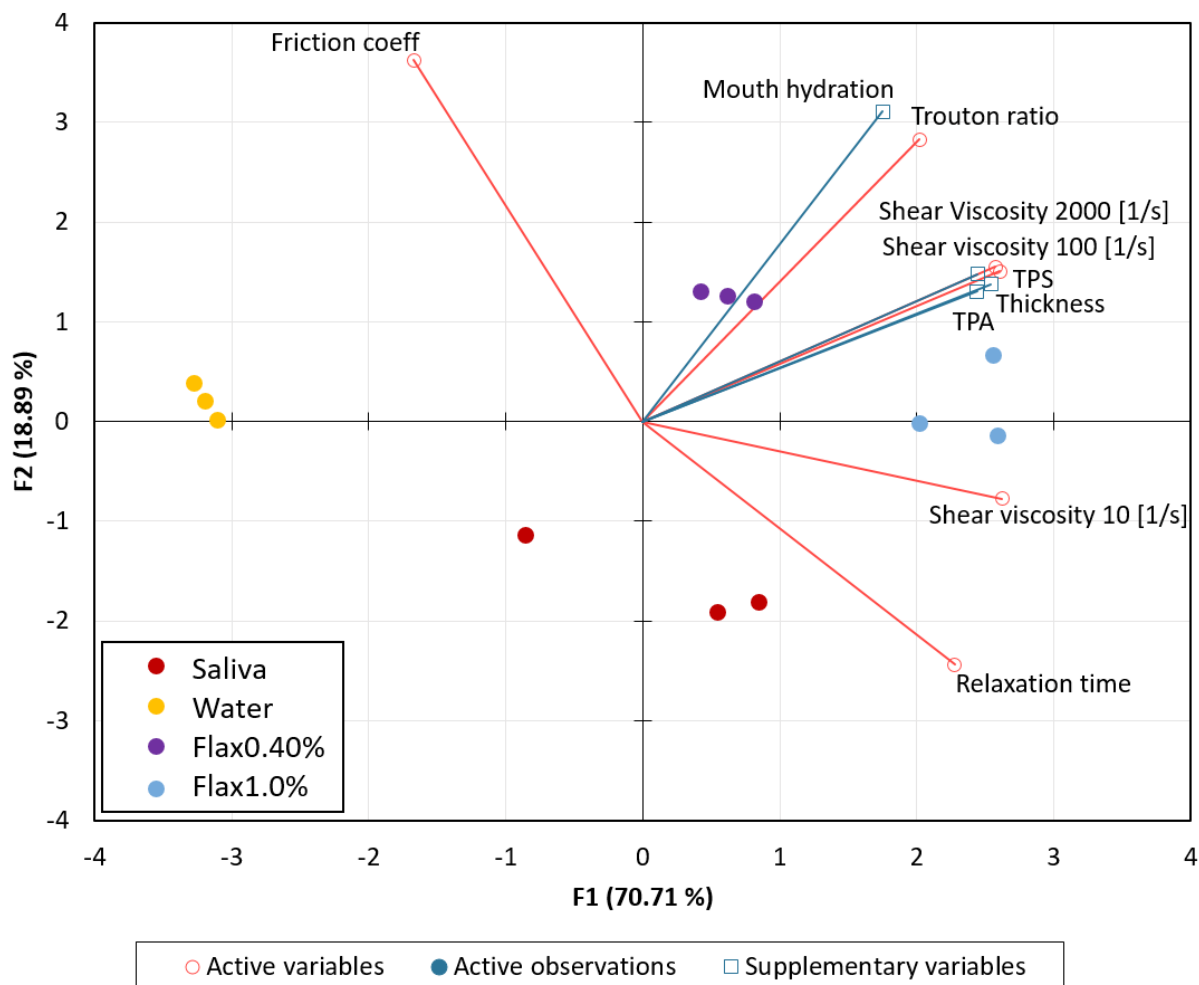


Figure 9. Correlation between instrumental and sensory data represented in a PCA. Active variables are the physical properties measured instrumentally (red axes), while supplementary variables are sensory mean scores (blue axes). The four products evaluated are represented as active observations (full circles); saliva, water, flaxseed extracts at 1.0 % and 0.40 % DM.

4. Conclusion and perspectives

In this study, three mucilages were extracted from Okra, Chia, and Flaxseed to produce a salivary substitute reflecting human saliva's shear and extensional properties. Literature data were utilized for the comparison of the different mucilages. Moreover, flaxseed extracts at 1.0 % and 0.40 % DM were chosen due to their similarity to saliva in terms of relaxation time and/or shear viscosities at 10 s^{-1} , 50 s^{-1} , and 100 s^{-1} . In addition, the Trouton ratio, apparent extensional viscosity, and friction coefficient were evaluated. A sensory evaluation assessed salivary substitutes in terms of *Mouth Hydration*, *Tongue-Palate (T-P) Slipperiness*, *T-P Adhesion*, *Thickness* and *Overall Taste Intensity*.

The complex rheological behaviour of human saliva is not easy to mimic, due to its low shear viscosity and high relaxation time and apparent extensional viscosity. Additionally, the variability of *in vivo* data is wide. However, flaxseed extracts at concentrations of 0.40% and 1.0% have been found to have similar shear and extensional properties to human saliva. A

sensory study also revealed that flaxseed extracts are close to human saliva in terms of *mouth hydration*, *T-P slipperiness*, and *T-P adhesion*. When comparing instrumental and sensory variables, flaxseed extracts demonstrated higher lubricity and sensory properties than water, as well as a higher Trouton ratio and mouth hydration than human saliva.

This study proves that flaxseed extracts is a promising salivary substitute, when sensory evaluation are performed by healthy individuals. Leveraging on this first *in vivo* proof of concept and on the physical characterization and mechanistic understanding supporting it, a clinical study should be organized with xerostomic patients.

Appendix A. Additional Data

Appendix A.1. Shear viscosity and normalized diameter of flaxseed extracts at different temperatures

Figure 5a shows the shear viscosity of flaxseed extracts at 0.40 % and 1.0 % DM analyzed at two different temperatures (20 and 37 °C) using a Physica MCR-702 rheometer and a microVISCTM. The microVISCTM calculates viscosity by pressure drop using four pressure sensors. Thus, the calculated shear stress on the wall of the rectangular flow channel is as follows:

$$\tau = -\frac{\partial P}{\partial x} \frac{wh}{2(w+h)}$$

Where P is the difference in pressure along the different positions of the sensors (x), w is considered the width of the channel and h the height. Based on a controlled volume flow rate (Q) and assuming the fluid evaluated is Newtonian, the shear rate ($\dot{\gamma}$) is obtained as:

$$\dot{\gamma} = \frac{6Q}{w^3}$$

The apparent dynamic viscosity is attained using these two equations as the ratio between shear stress and shear rate ($\eta = \frac{\tau}{\dot{\gamma}}$). This is relevant when the fluid is Newtonian. When non-Newtonian liquids are evaluated such as flaxseed extracts, the viscosity varies along the cross-section, changing the velocity profile to non-parabolic. Hence, a correction to the shear rate has to be applied by employing the Weissenberg-Rabinowitsch-Mooney (WRM) expression for a rectangular channel:

$$\dot{\gamma}_{non-Newtonian} = \frac{\dot{\gamma}}{3} \left(2 + \frac{\partial \ln \dot{\gamma}}{\partial \ln \tau} \right)$$

The results at higher shear rates obtained with microVISCTM show a small decline in shear viscosity compared to the results from Physica MCR-702 rheometer (Figure 5a). At higher shear rates ($> 1000 \text{ s}^{-1}$), flaxseed extracts exhibit similar shear-thinning trends compared to lower shear rates. Overall, the shear and extensional rheology of both dilutions decrease when reaching human body temperature.

Appendix A.2. Trouton ratio using variable shear viscosity of flaxseed extracts at 0.40 % and 1.0 % at 20 and 37 °C

The Trouton ratio considered as variable shear viscosity computed at a shear rate equal to the extensional rate is illustrated in Figure A.10. This method is comparable to the one used by Pabois et al., (2023). Flaxseed extracts at 0.40 % and 1.0 % reveal higher values of Trouton ratio compared to salivary substitutes in the market.

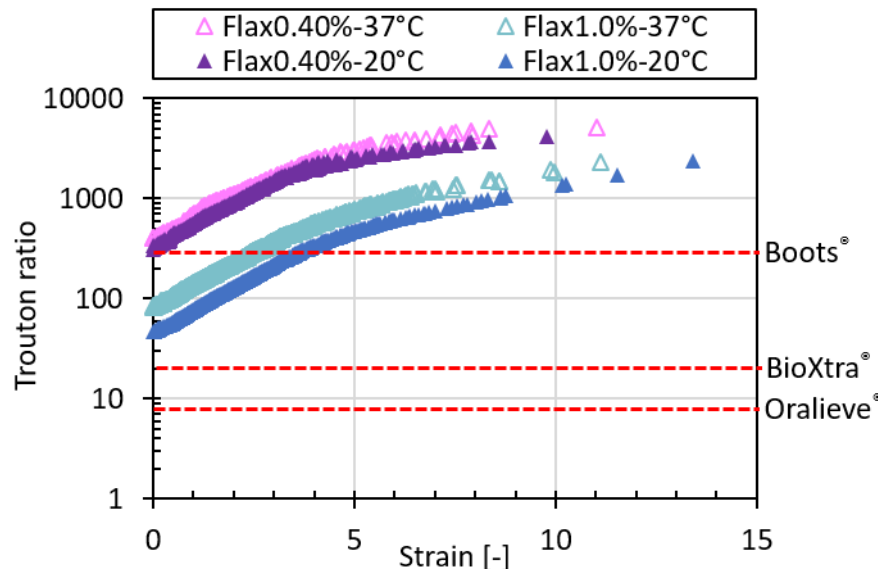


Figure A.10. Trouton ratio using variable shear viscosity of flaxseed extracts at 0.40 % and 1.0 % at 20 and 37 °C. Data from salivary substitutes in the market are represented in dashed lines. Results from Boots, BioXtra and Oralieve were extracted from (Pabois et al., 2023)

Appendix A.3. Panelist training

Two training sessions were provided, each of them lasted 45 min. To train the panel for “taste intensity”, 15 mL of water (low) and a full spoon of honey (intense) were used as references to illustrate both extremes on the scale. For “thickness”, 15 mL of water (thin) and a full spoon of Clinutren® Thicken UP® (Nestlé, Vevey, Switzerland) at Level 3 on the international dysphagia diet standardization initiative (IDDSI) (thick) were used as standards. Mouth hydration, Tongue-Palate Slipperiness (TPS), and Tongue-Palate Adhesiveness (TPA) were explained using different sensory experiences and food references. Throughout “mouth hydration,” participants were requested to breathe with their mouth open for over 10 seconds (lack of saliva) and to chew a piece of bubble gum for 10 seconds (excess of saliva).

To display TPS and TPA, the panel was (i) given a tactile experience followed by (ii) tongue movement training, and (iii) a food reference was provided. In the case of TPS, a piece of sandpaper (10 x 5 cm, P80) was provided to illustrate: rough and slippery. The index finger was moved back and forward on the sandpaper for roughness. For slipperiness, a drop of lubricant (BioXtra) was positioned on the sandpaper, and the middle finger was used to slide back and forward. This example facilitated the mouthfeel perception of both definitions. TPS tongue movement consisted of positioning the tongue against the hard palate and doing movements back and forward, such as the tactile example. Once the movement was mastered, 15 mL of green tea

and a full spoon of oat porridge were used to showcase “roughness” and “slipperiness,” respectively.

Finally, TPA was illustrated with a Post-it. Participants had to attach and detach the finger from the adhesive gum (sticky) and non-adhesive part (non-sticky). The tongue movement for TPA was described as placing the anterior section of the tongue against the palate and separating it several times (up and down). To clarify, 15 mL of water and a full spoon of oats porridge were offered to explain “non-sticky” and “sticky” accordingly.

Appendix A.4. Relaxation times from literature review on human saliva.

Figure A.11 displays the variability of saliva relaxation times obtained in different studies. Wagner, (2015) assessed the evolution of saliva with time; Figure A.11 illustrates the relaxation times of whole saliva at 0, 1, and 2 hours. Zussman et al., (2007) evaluated the relaxation times of saliva from different glands, at rest and under stimulation. Figure A.11 shows the relaxation time of citric acid stimulation coming from the submandibular/sublingual glands. They obtained saliva values at rest between 0.001 to 0.003 s and 0.018 to 0.003 s for citric acid stimulation. In addition, Turcanu et al. (2015) measured mechanically stimulated saliva and citric acid saliva. Figure A.11 demonstrates the relaxation time during mechanical stimulation (0.01 s). All tests were evaluated at room temperature and by capillary break-up extensional rheometry (CaBER) with healthy volunteers.

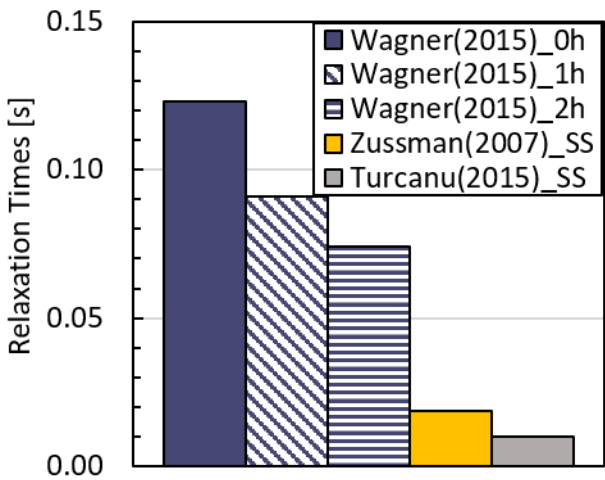


Figure A.11. Values established to define variability for human saliva relaxation times.

Appendix A.5 Panel performance

The ANOVA results from the panel performance is detailed in **Erreur ! Source du renvoi introuvable..**

Table A.5. ANOVA results (product+panelist+panelists*product). P-values are in bold ($\alpha<0.05$).
Abbreviations: Tongue-Palate Slipperiness (TPS) and Tongue-Palate Adhesion (TPA)

Sensory attribute	Product		Panelist		Panelist * Product	
	F	Pvalue	F	Pvalue	F	Pvalue
Overall taste intensity	37.93	<0.01	3.63	<0.01	3.65	<0.01
Mouth hydration	5.21	<0.01	2.13	0.03	2.81	<0.01
Thickness	115.61	<0.01	2.15	0.02	1.57	0.03
TPS	49.54	<0.01	8.33	<0.01	1.75	<0.01
TPA	24.38	<0.01	2.74	<0.01	2.35	<0.01

Appendix A.6. Averages of sensory ratings

Sensory scores obtained through the four mouth coating conditions for the five attributes: Overall Taste Intensity, Thickness, Tongue-Palate (T-P) Slipperiness, T-P Adhesion and Mouth Hydration. Letters indicate the significance differences, based on ANOVA statistical test.

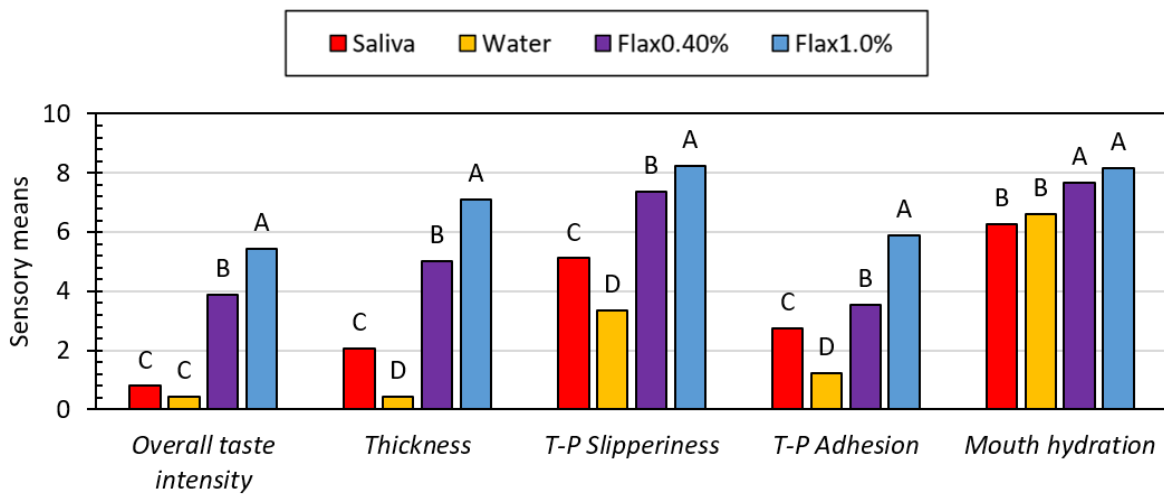


Figure A.12. Averages of sensory ratings (panelists * replicates)

Appendix A.7. Data employed for PCA

Instrumental data extracted from flow curves, Trouton ratio, filament thinning, and tribology tests were used to plot Figure 9. As well as sensory data such as mouth hydration, thickness, tongue-palate slipperiness, and tongue-palate adhesion. All averages and standard deviations employed to plot the PCA are listed in **Erreur ! Source du renvoi introuvable.**

Table A.6. Summary of instrumental and sensory data employed for PCA

Sample	Mouth hydration [0-10]	Thickness [0-10]	TPS [0-10]	TPA [0-10]	Shear viscosity 10s ⁻¹ [Pa.s]	Shear viscosity 100 s ⁻¹ [Pa.s]	Shear viscosity 2000 s ⁻¹ [Pa.s]	Relax. time [s]	Friction coeff. [-]	Trouton ratio
Saliva	6.3±0.6	2.1±0.1	5.1±0.1	2.7±0.1	0.013±0.010	0.003±0.002	0.0016±0.0	0.07±0.06	0.13±0.01	120±0.0

Water	6.6±0.4	0.4±0.2	3.4±0.3	1.2±0.1	0.001±0.000	0.001±0.000	0.0010±0.0	0.00±0.00	1.70±0.08	0.0±0.0
Flax0.40%	7.7±0.4	5.0±0.5	7.4±0.4	3.5±0.7	0.010±0.000	0.008±0.000	0.0039±0.0	0.02±0.00	0.58±0.02	3015.5±142.6
Flax1%	8.2±0.4	7.1±0.5	8.2±0.3	5.9±0.2	0.098±0.007	0.045±0.002	0.0131±0.0	0.06±0.00	0.29±0.01	561.4±5.2

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