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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 **1. Introduction**

2 Saliva is a complex and essential physiological fluid involved in different functions during
3 food oral processing (FOP); lubrication, mastication, clearance, taste, and swallowing
4 (Humphrey and Williamson, 2001). The functionalities of saliva depend to a large extent on its
5 interactions with the surfaces of the mouth, contributing to the formation of complex layers such
6 as the mucosal pellicle. This salivary film mainly comprises saliva proteins such as mucins
7 (MUC5B and MUC7), serves as a protective layer of the oral mucosa and ensures moisture
8 retention (Hannig et al., 2017). The high water-retaining capacity and viscoelasticity explain the
9 oral lubrication provided by mucins (Agorastos et al., 2023; Assy et al., 2022; Laguna et al.,
10 2021).

11 Quantitative and qualitative changes in saliva composition may be related to a subjective
12 feeling of dryness in the mouth, also known as xerostomia (Piaton et al., 2021). When suffering
13 from xerostomia, patients may experience mucosa dryness, lack of salivation, and decreased
14 salivary film thickness, causing difficulties when speaking and eating (Bongaerts et al., 2007; Hu
15 et al., 2021; Humphrey and Williamson, 2001). Its prevalence is 20% in the general population,
16 with an increased prevalence in women (up to 30%) and in the elderly (up to 50%) (Piaton et al.,
17 2021). Additionally, xerostomia may be caused by drug side effects, exposure to radiotherapy,
18 and chronic diseases like Sjögren's disease. The therapies related to improving the quality of life
19 of these patients mostly rely on salivary stimulants and salivary substitutes (Hu et al., 2021).
20 Salivary stimulants work until the extent of the patient salivary glands preservation; depending
21 on the severity, salivary stimulants may not provide oral relief. Conversely, salivary substitutes
22 are indicated for all patients to mitigate oral dryness discomfort by providing saliva texture
23 resemblance; if the latter is not achieved, patients could experience unfamiliar and unpleasant
24 sensations (Hahnel et al., 2009; Hu et al., 2021).

25 The development of salivary substitutes is essential in the medical domain but also in the
26 field of food oral processing research (FOP), in which the oral phase of swallowing is studied.
27 Throughout the oral phase, saliva moisturizes the food and forms a food bolus ready for
28 swallowing. Hence, the bolus requires a certain level of cohesiveness to guarantee safe
29 swallowing (Prinz and Lucas, 1997; Steele et al., 2015). For this reason, when investigating *in*
30 *vitro* bolus formation and swallowing phenomena, being able to lean on a fluid approaching
31 human saliva's rheological characteristics (non-Newtonian and elastic) is required (Gittings et al.,
32 2015; Stokes and Davies, 2007; Turcanu et al., 2015; Wagner, 2015; Zussman et al., 2007). The
33 simulated salivary fluid established by InfoGest (Brodkorb et al., 2019; Minekus et al., 2014)
34 provides a standardized protocol to imitate human saliva's ion strength, pH buffering, and
35 amylase activity. This Newtonian fluid was found to be relevant when investigating the
36 enzymatic hydrolysis of starchy food (Bugarin-Castillo et al., 2023; Freitas et al., 2018;
37 Lavoisier et al., 2022). However, the lack of the rheological relevance of artificial saliva models
38 may induce limitations when investigating *in vitro* the mechanisms of bolus formation,
39 lubrication, or swallowing (Marconati et al., 2018).

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

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

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

74 **2. Materials & Methods**

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

79

80 *2.1. Preliminary evaluation of different sources of natural salivary substitutes*

81

82 *2.1.1 Materials*

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

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

91
92 *2.1.2 Formulations*

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

97
98 *Table 1. Summary of protocols used during the preliminary evaluation of Natural Salivary Substitute*
99 *(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.

100
101 *2.1.3 Shear Rheology*

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

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

111
112 *2.1.4 Extensional Properties*

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

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

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

126 (1)

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

127

128 *2.2 Investigating the rheological, tribological, and sensory properties of flaxseed extracts*

129 The flaxseed formulation (Flax0.20%) was improved to reach an extensional rheology closer
130 to human saliva. An extract was obtained by stirring at 250 rpm a solution of 10% w/w flaxseed
131 and mineral water (Vittel, Nestlé) at 72 ± 1 °C for 1 hour. The extract was then strained till
132 removing all seeds. This new formulation having 1.50 % of solids was then diluted to produce
133 0.40 % and 1.0 % DM extracts. The solutions were characterized on the same production day to
134 avoid rheological changes over time.

135

136 *2.2.1 Rheological characterization and analysis of flaxseed extracts*

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

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

147 (2)

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

148

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

151 (3)

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

152

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

154

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

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

$$\eta_{extensional} = \frac{2\sigma/D_{min}}{\dot{\epsilon}_{el}} \quad (4)$$

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:

$$Tr(\dot{\epsilon}) = \frac{\eta_{extensional}(\dot{\epsilon})}{\eta_{shear}(\dot{\epsilon})} \quad (5)$$

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.

196 2.2.3 Sensory Evaluation

197 2.2.3.1 Conditions of sensory tests

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

212 The study was carried out using 16 sensory booths and individual sinks. During the sessions,
213 the booths were air-conditioned (20 °C) and had red lighting to minimize visual biases. The
214 sensory study aimed to compare four distinct conditions of mouth rinsing, which were proposed
215 following a balanced order across panelists, using a Latin square and divided into three replicate
216 blocks. The four conditions included two formulations based on flaxseed extracts (two dilutions :
217 0.40 % and 1.0 %), which were compared with two others aiming at mimicking natural and
218 altered oral lubrication. The first was the natural lubricating state of the volunteers' oral cavity, a
219 condition called "saliva". The second condition, referred to as "water", consisted of drastically
220 reducing the natural lubrication by saliva by performing a series of mouth rinses with still
221 mineral water (Nayak and Carpenter, 2008a).

222

223 2.2.3.2 Attribute selection

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

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

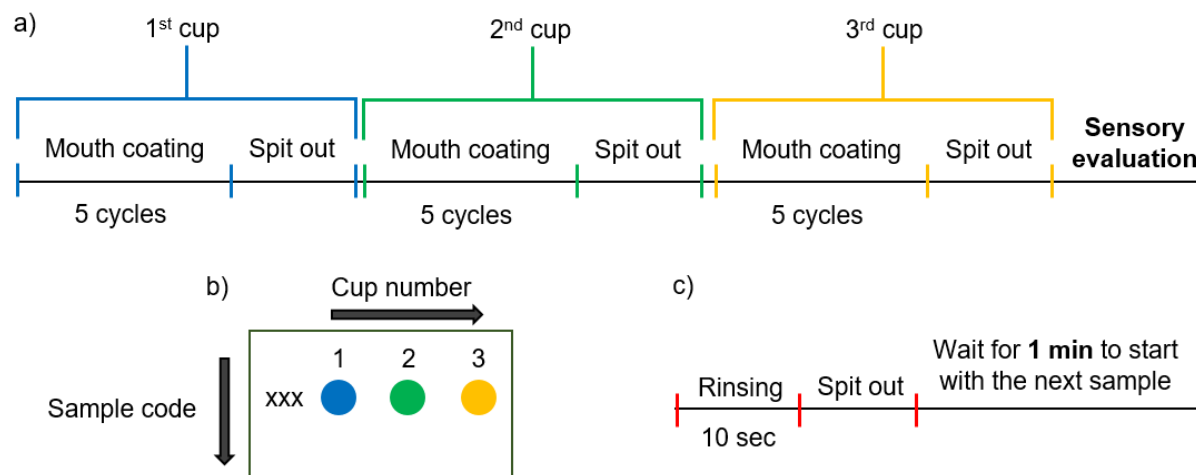
235 Two attributes were evaluated without requiring any particular action, based on the
236 definitions for which a consensus was reached with the panelists during the training phase. Thus,
237 *Mouth Hydration* referred to the amount of saliva or lubricant perceived in the mouth, having a
238 scale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

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

249 *Table 2. Attributes and scales used during the sensory evaluation of flaxseed extracts at 0.40 % and 1 %*
 250 *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

251
 252 *2.2.3.3 Mouth rinsing protocol*
 253 Four distinct mouth rinsing conditions were evaluated. The first method consisted in rinsing
 254 the mouth with a sip of still mineral water (Evian Danone, Évian-les-Bains, France) and then
 255 waiting for 1 min in order to restore a natural oral lubrication. This condition, referred to as
 256 "saliva", aims at characterizing the reference perception of the volunteers in the absence of the
 257 use of salivary substitutes.
 258 The three other conditions then consisted in following the same protocol with three different
 259 fluids: flaxseed extracts at two concentrations levels (0.40 % and 1.0 %) and still mineral water,
 260 all served in 30 mL graduated plastic cups with a lid at 20 °C. The plate containing the samples
 261 was organized in different rows and columns of cups, each row corresponding to a specific test
 262 including three different cups. The volunteers were asked to pour the full content of the first cup
 263 into their mouths, then to make movements to circulate the fluid five times in contact with all the
 264 oral mucosa, before spitting it out. The same operation was then repeated with the two remaining
 265 cups (three cups with the same formulation per evaluation). The volunteers were asked to
 266 evaluate the 5 attributes just after spitting out the content of the 3rd cup (Figure 1.a&b). Before
 267 moving on to the next test, volunteers were asked to rinse their mouths with water for 10 seconds
 268 and then wait a minute in order to sufficiently attenuate residual perceptions and recover as much
 269 as possible their natural state of oral lubrication (Figure 1c).



270
 271 *Figure 1. Sensory protocol. a) Mouth rinsing steps. b) Representation of sensory plate, c) Rinsing*
 272 *protocol after each sample.*

273 2.2.4 Statistical analysis of the sensory data

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

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

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

288

289 3. Results and Discussion

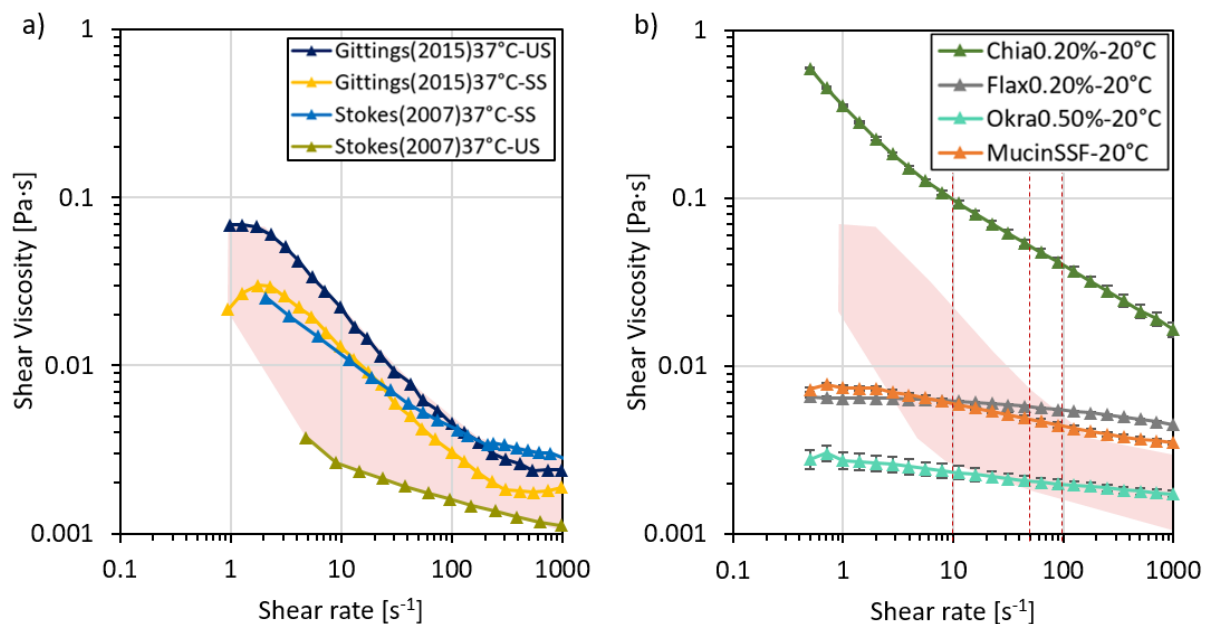
290

291 3.1. Assessment of potential natural salivary substitutes: shear and extensional rheology

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

302 properties that are relevant bounds for the properties of the natural salivary substitutes (Figure
 303 2a). Figure 2a illustrates two literature studies evaluating the shear viscosity of unstimulated
 304 (whole saliva produced at rest) and stimulated (saliva produced after inducing mechanical or acid
 305 stimulation) human saliva at body temperature (37 °C). Food texture and in mouth food
 306 residence times affect heat transfer during bolus formation (Taylor and Linfoth, 1996). Thus, in
 307 mouth bolus temperature is generally intermediate between the serving temperature and body
 308 temperature. If a salivary substitute is sprayed (or applied in other ways) by a xerostomic person
 309 just before the consumption of food at room temperature, the temperature of the salivary
 310 substitute will also certainly be intermediate between serving and body temperature. As a
 311 consequence, in case of consumption by xerostomic people, the natural salivary substitute is
 312 expected to have in mouth a shear viscosity lower or at most equal to the viscosity of human
 313 saliva for healthy patients (at 37°C). This makes the salivary substitute effective in both in vivo
 314 and in vitro studies at room temperature.

315 Figure 2a shows the range of variability of human saliva shear viscosity as characterized by
 316 Gittings et al., (2015) and Stokes and Davies, (2007), highlighted in the red area. The variability
 317 is high at low shear rates ($<100 \text{ s}^{-1}$) and interestingly the variability reduces when higher shear
 318 rates are applied (i.e., $>100 \text{ s}^{-1}$), as highlighted by the red area in the figures. Overall, these
 319 results show that human saliva has shear thinning behavior with a more or less pronounced
 320 constant viscosity plateau at higher shear rates.
 321



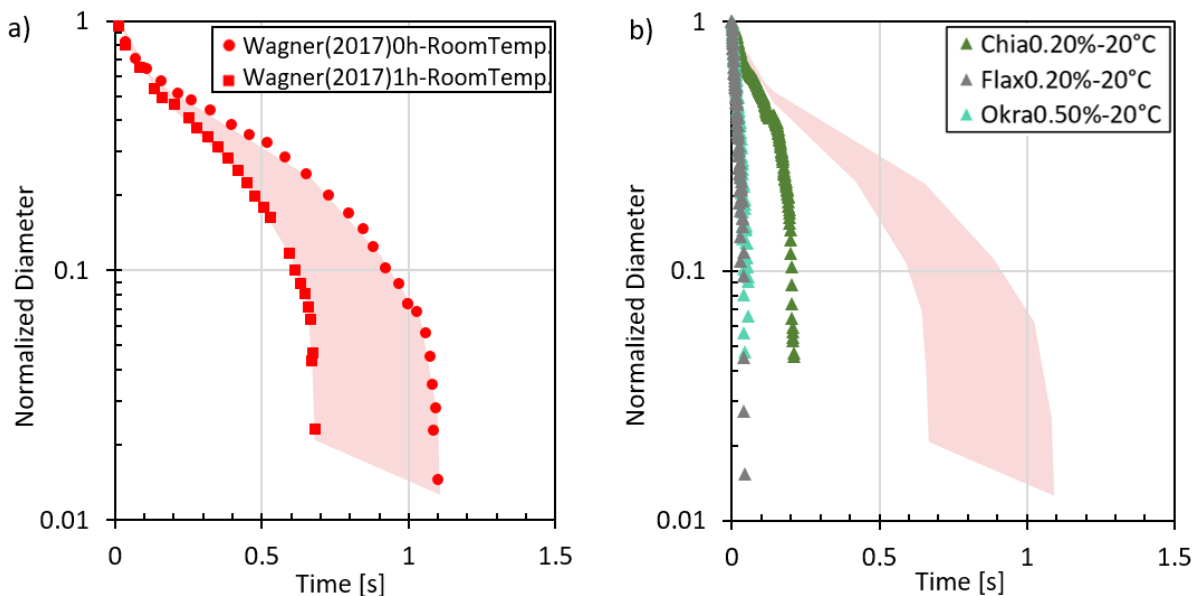
322
 323 *Figure 2. Rheological properties of the initial natural salivary substitute formulations. a) Human saliva*
 324 *flow curves from literature data used to establish the natural variability range (Gittings et al., 2015;*
 325 *Stokes and Davies, 2007). US: unstimulated saliva; SS: stimulated saliva b) Shear viscosities of*
 326 *formulations against the range of human saliva in vivo data (red area); important shear rates for*
 327 *comparison (10, 50 and 100 s^{-1}) are highlighted with vertical dashed lines.*

328 Figure 2b compares the flow curves obtained in steady shear for the four formulations. The
329 red highlighted surface indicates the range of shear viscosities reported for human saliva in the
330 literature, taken from Figure 2a. The initial formulations were first compared to human saliva at
331 10 s^{-1} , 50 s^{-1} , and 100 s^{-1} (vertical dashed lines). These shear rates are believed to relate to the
332 food oral processing stage (Steele et al., 2015). In addition, positive correlations have been found
333 between sensory attributes such as oral cohesiveness and post-swallowing residue, and shear
334 rates at 10 s^{-1} and 100 s^{-1} in a wide range of viscosity products ($0.221 - 2.359 \text{ Pa}\cdot\text{s}$) ($0.103 - 0.64$
335 $\text{Pa}\cdot\text{s}$), respectively. These two attributes link saliva's ability to form a safe bolus for swallowing.
336 The initial formulations were also compared with MucinSSF due to its important resemblance in
337 ion strength, pH buffering, and chemical composition with human saliva.

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

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

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



358
 359 *Figure 3. Extensional properties of potential natural salivary substitutes. a) Normalized diameter from*
 360 *literature data of human saliva, used to establish the variability range (Wagner and McKinley, 2017). b)*
 361 *Normalized diameter of formulations against the range of human saliva in vivo data extracted from*
 362 *Figure 3a (red area)*

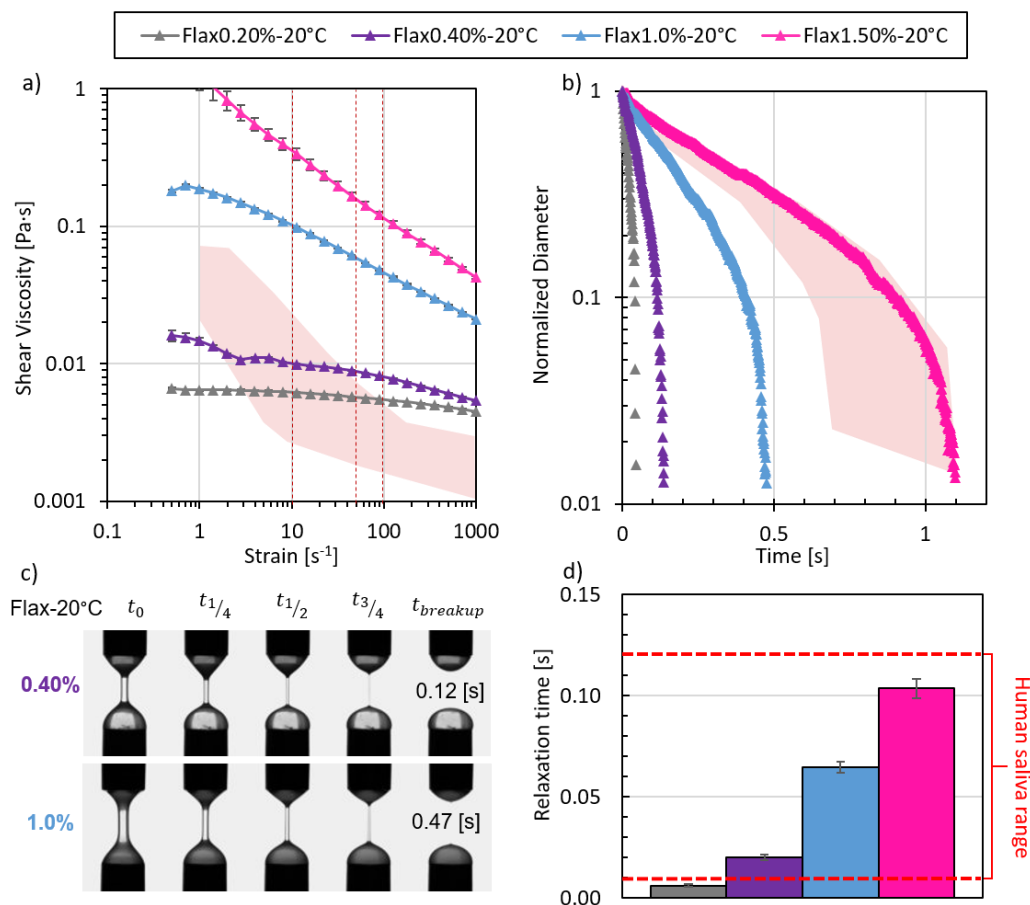
363 A key rheological property measured is the extensional relaxation time, obtained by fitting an
 364 elastic model to the filament thinning dynamics (Eq. 1). Relaxation times obtained from the
 365 literature data were also displayed in A.4.

366 Interestingly, no filament could be formed and no measurement could be obtained for
 367 MucinSSF, due to the instability of the initial meniscus between the plates. The surface tension
 368 of the sample may have been too low, preventing the analysis with CaBER. Conversely, in the
 369 work of Ahmad et al. (2018) MucinSSF (at the same concentration used in this work) showed a
 370 break-up time of 0.122 seconds. Although we can speculate that there may have been a
 371 difference in surface tensions, we have no robust explanation for this discrepancy. Chia, Flax,
 372 and Okra formulations presented filament thinning very rapidly over time and short break-up
 373 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
 374 s. Overall, the three formulations did not show break-up times close to human saliva (Figure 3b).
 375 Albeit chia displayed longer break-up times, the shear viscosity of this formulation was out of
 376 the variability range of human saliva. The flax and okra formulations presented lower
 377 extensional properties. Nevertheless, shear viscosity values of Flax0.20% were within the limits
 378 of human saliva at 10, 50, and 100 s^{-1} and Okra0.5% was too low at 10 s^{-1} . Thus Flax0.20%
 379 might be a better candidate than Okra at 0.5%, to imitate the shear viscosity of saliva at 37°C .
 380 Given the shear behavior discussed previously, Flaxseed was considered as the most interesting
 381 extract and further studies were carried out to improve the extensional properties.

382

383 *3.2 Formulation of flaxseed extracts towards matching saliva rheological properties*

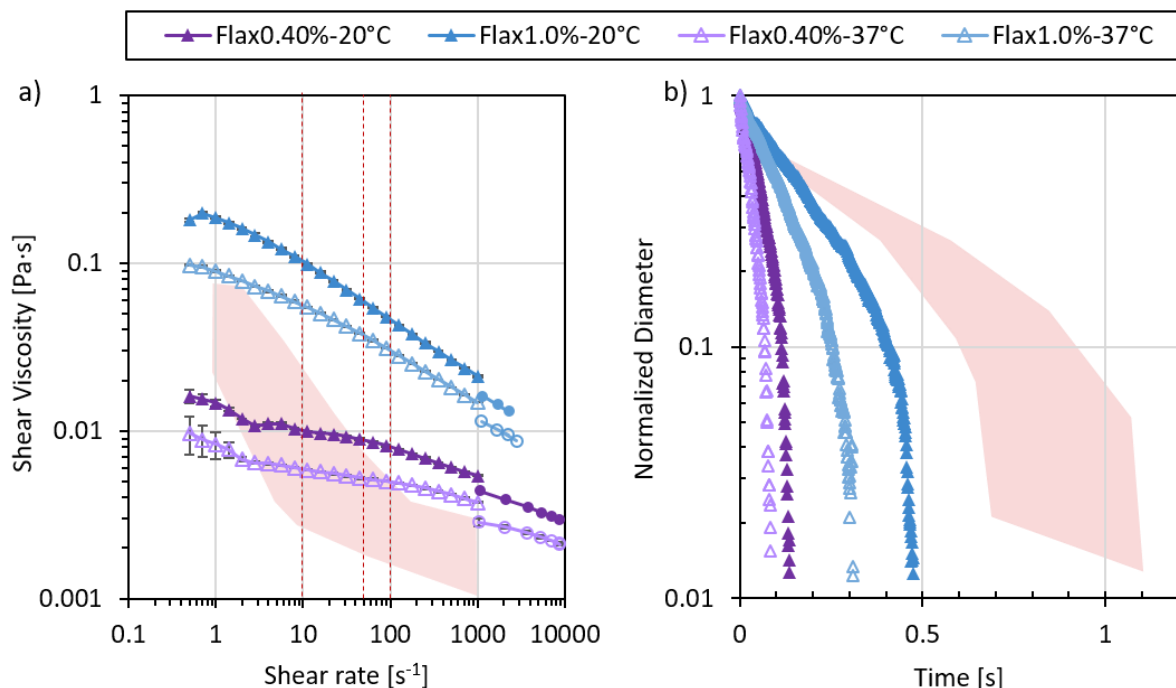
384 Flaxseed extract at different concentrations were considered to match close enough the
 385 saliva rheological properties (Section 2.2). Steady shear and extensional rheological
 386 measurements were evaluated at 20 °C (Figure 4) and also at 37 °C (Figure 5). Shear viscosities
 387 of Flax1.0% are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



389
 390 *Figure 4. Comparison of rheological properties of flaxseed extracts at different concentrations evaluated*
 391 *at 20 °C. a) Flow curves of flaxseed extracts compared to in vivo data (red area) and the three dash lines*
 392 *representing 10, 50 and 100 s^{-1} . b) Normalized diameter of flaxseed extracts compared to in vivo data*
 393 *(red area). c) Filament evolution of Flax0.40% and Flax1.0%. (please note that $t_{1/4}$ indicates one fourth*
 394 *of the interval between $t_{breakup}$ and t_0 , etc.) d) Relaxation times of flaxseed extracts compared to human*
 395 *saliva data; range found in A.4 (Turcanu et al., 2015; Wagner, 2015; Zussman et al., 2007).*

396 Figure 4a shows the evolution of the shear viscosity with the shear rate of the different
 397 flaxseed extracts, measured at 20 °C. The concentration of 0.40 % has viscosity values within the
 398 range of human saliva at shear rates of 10 and 50 s^{-1} , while it exceeds slightly saliva at 100 s^{-1} . At
 399 37 °C, the viscosity of Flax0.40% falls within the range of human saliva from 10 to 100 s^{-1}
 400 (Figure 5a). The 1.0 % flaxseed concentration shows shear viscosities higher to those of human
 401 saliva. When increasing the temperature (37 °C), the viscosity of Flax1.0% lowers, and similar
 402 values to human saliva are observed for ~ 1 to 2 s^{-1} . All in all, Flax1.0% shows shear viscosity
 403 higher than human saliva at 10, 50, or 100 s^{-1} , but comparable values in relaxation times are

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



407
 408 *Figure 5. Shear viscosity and normalized diameter of flaxseed extracts at 0.40 % and 1.0 %. a) Shear*
 409 *viscosity was analyzed at two different temperatures 20 °C (full) and 37 °C (empty) and with two methods*
 410 *Physica MCR-702 rheometer (triangle) and microVISCTM (circle). b) Normalized diameter was analyzed*
 411 *at two different temperatures 20 °C (full) and 37 °C (empty). Saliva variability is represented in the red*
 412 *area.*

413 Figure 4b summarizes the filament thinning dynamics at 20°C of different flaxseed extract
 414 concentrations, confirming their relevance to imitate human saliva elasticity. The two dilutions
 415 (0.40 % and 1.0 %) were formulated to approach as much as possible shear and elastic rheology
 416 of human saliva. It is observed that the filament diameters of the literature data decrease
 417 exponentially with time, which is a typical feature of elastic fluids (Anna and McKinley, 2001).
 418 The elasticity of human saliva decreases within one hour; break-up time from 1.1 to 0.7 s and
 419 relaxation time from 0.12 to 0.9 s (Figure A.11). Flaxseed at 1.0 % analyzed at 20 °C shows a
 420 break-up time of ~0.5 s compared to 0.3 s when investigated at 37 °C (Figure 5b). For flaxseed at
 421 0.40 % studied at 20 and 37 °C, the change in break-up time is not significant. Temperature is an
 422 important variable when developing salivary substitutes. As observed, flaxseed extract shear and
 423 extensional rheological properties changed with temperature. This could influence the sensory
 424 perceptions depending on the oral temperature and residence time of the salivary substitute in the
 425 mouth.

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

429 is placed (t_0), followed by a uniaxial displacement which assists the filament break-up
430 ($t_{breakup}$). The initial t_0 on the filament 1.0 %, shows viscous drainage due to the higher
431 concentration of polymer molecules that might enhance the total time the liquid bridge remains
432 connected, which is not seen at t_0 for 0.40 % (Anna and McKinley, 2001). Afterward, the
433 thinning behavior of 1.0 % is similar to 0.40 % as the filament changes over time (from $t_{1/4} =$
434 $1/4(t_{breakup} - t_0)$ to $t_{breakup}$).

435 The relaxation times of the flaxseed extracts are presented in Figure 4d and compared with
436 data from the literature demonstrated in the red pointed line (Figure A.11) (Turcanu et al., 2015;
437 Wagner, 2015; Zussman et al., 2007). Wagner (2015) analyzed the unstimulated saliva “whole
438 saliva produced at rest” (US) of two donors; sample aging decreased the relaxation time (0.12,
439 0.09, and 0.07 s). Moreover, when Turcanu et al. (2015) measured mechanically stimulated
440 saliva (MSS), and citric acid stimulated saliva (CASS), they obtained higher values of relaxation
441 times when it was promoted with citric acid (0.722 s) than mechanically (0.01 s). Similar results
442 were obtained by Stokes & Davies (2007) when they analyzed CASS by fitting G' and G'' into a
443 multi-mode Maxwell model getting a relaxation time of 0.94 s. In contrast, Zussman et al. (2007)
444 obtained relaxation times of CASS at 0.018 s from the submandibular/sublingual glands of
445 healthy volunteers.

446 The relaxation time of Flax0.20% (0.006 s) is lower in comparison to stimulated saliva,
447 whereas Flax1.50% (0.10 s) is close to unstimulated saliva after 0 hrs collection. Nevertheless,
448 Flax1.50% shear viscosity was too high compared to literature data of human saliva. The
449 relaxation time of Flax1.0% (0.06 s) is comparable with the unstimulated saliva measurements of
450 1h and 2h after collection. Conversely, Flax0.40% had similar relaxation time (0.02 s) to
451 mechanically stimulated saliva. Further work should be pursued to develop new salivary
452 substitutes considering the additional relaxation times in the literature (0.722 to 0.94 s). All the
453 comparable results were evaluated by uniaxial elongational flow, except the work from Stokes &
454 Davies (2007) where they employed shearing flow. Due to the closer values in *in vivo* shear
455 viscosities from Flax0.40% and the comparable values in relaxation times from Flax1.0% to *in*
456 *vivo* data, these two formulations were selected to continue the study.

457 3.3 Apparent extensional viscosity and Trouton ratio of flaxseed extracts at 0.40 % and 1.0 %

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

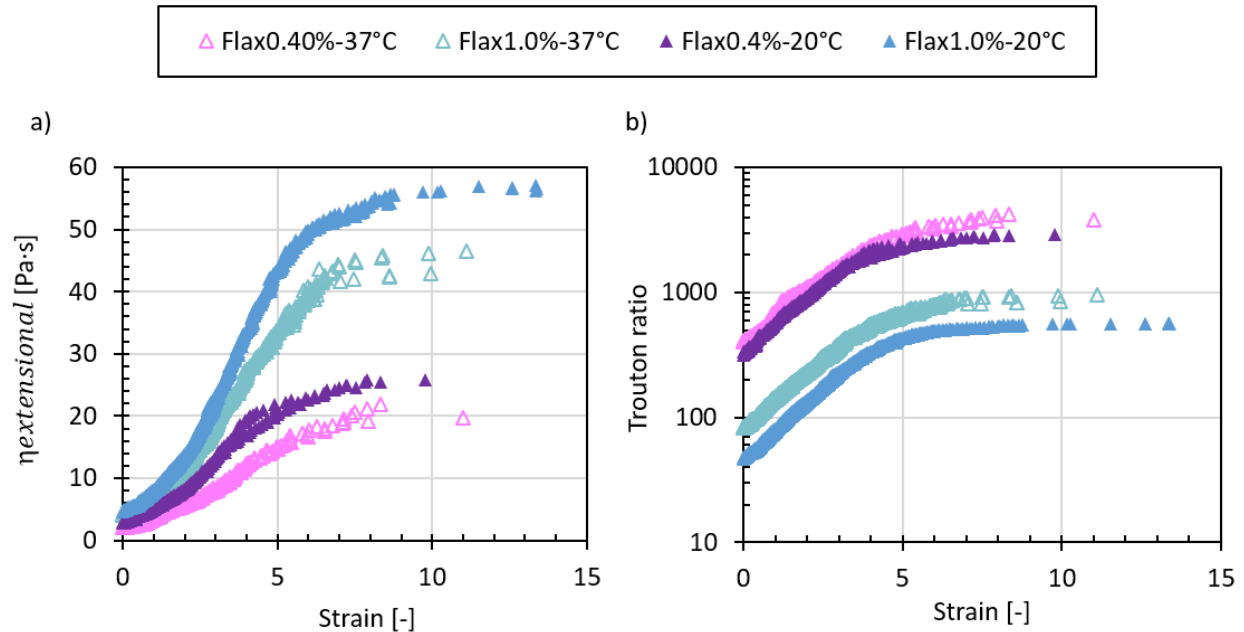
467 The experimental data showed exponential midpoint filament diameter decay in time for both
468 concentration of flaxseed extracts. The fitting into the elastic model described in Eq.1 displayed
469 coefficient of determination of 0.970 ± 0.012 for 0.40 % and 0.949 ± 0.005 for 1.0%. The surface

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

473 Figure 6a illustrates the increase in $\eta_{\text{extensional}}$ with increasing strain for both concentrations.
474 This behavior is typical for viscoelastic fluids and is established as extension-thickening (Sochi,
475 2010). Figure 6a also shows the higher $\eta_{\text{extensional}}$ results of Flax1.0% compared to Flax0.40%
476 which is due to the concentration effect of the sample and has been observed in other studies
477 (Marconati and Ramaioli, 2020). Additionally, the temperature effect demonstrates that for both
478 concentrations $\eta_{\text{extensional}}$ decreases when increasing the temperature. As both extracts have
479 different thinning dynamics the maximum $\eta_{\text{extensional}}$ and Tr are at different strains. For
480 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,
481 whereas the maximum $\eta_{\text{extensional}}$ at 37 °C is 19.8 ± 1.4 Pa·s and 44.7 ± 1.8 Pa·s, respectively.
482 These results demonstrate that flaxseed extracts have higher $\eta_{\text{extensional}}$ than human saliva (0.6
483 Pa·s) and than salivary substitutes in the market (BioXtra[®] 12.9 ± 4.8 Pa·s and Boots[®] 5.2 ± 0.6
484 Pa·s) based on Pabois et al., (2023).

485 The Trouton ratio (Tr) measures the relative importance of extensional and shear viscosity.
486 For elastic liquids, (Tr) is expected to be greater than or equal to 3; when $\text{Tr} = 3$ is generally for
487 Newtonian fluids (Marconati and Ramaioli, 2020; Sochi, 2010). The Trouton ratio in Figure 6b
488 was computed using a constant shear viscosity at a shear rate equal to the extensional rate. Figure
489 6b shows the higher elasticity of Flax0.40% compared to Flax1.0% at 20 and 37 °C. This
490 difference is due to the higher shear viscosity of Flax1.0%. These findings could be related to the
491 work of Vieira et al. (2021), where they described a solution of 1.5% w/w of flaxseed as a
492 flexible and random coil polymer chain—considering as well that Gallegos et al. (2021)
493 explained that linear stretched coil polymer solutions present large values of Trouton ratio.

494 In addition, the (Tr) of flaxseed extracts were higher to the data obtained from salivary
495 substitutes in the market based on the study of Pabois et al., (2023). The comparison is illustrated
496 in Figure A.10 where Flax0.40% shows 4017.6 ± 180.1 and Flax1.0% 2576.8 ± 257.2 at 20 °C,
497 and 4869.3 ± 242.9 and 2058.1 ± 249.1 at 37 °C, respectively in comparison to Boots[®] $289 \pm$
498 35 , Oralieve[®] 8 ± 1 and BioXtra[®] 20 ± 9 . Overall, studying extensional rheology of potential
499 salivary substitutes is important due to its likely significant impact on texture perception in the
500 mouth during food oral processing (Haward et al., 2011).



501

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

504 *3.4. Sensory and Tribological study of flaxseed extracts at 0.40 % and 1.0 % concentration, of*
 505 *water and human saliva*

506

507 *3.4.1 Panel performance*

508 The results of the ANOVA tests on the sensory profile results are reported in Table A.5. The
 509 panel could discriminate the products, as the product factor was significant for all attributes
 510 (5/5). The homogeneity of the panel is assessed by looking at the panelist*product interaction,
 511 which was close to being significant for all the attributes, also the F values are negligible in
 512 regards to F product. However, such interactions are common when sensory attributes are
 513 difficult to control, even when panelists have undergone extensive training (Cosson et al., 2021).
 514 Moreover, the weighting information provided by the F score reveals that for each attribute, the
 515 effect of the panelist*product interaction is systematically lower than the product effect. These
 516 results therefore bring confidence in the panel performance for all the products tested.

517

518 *3.4.2 Comparison of the sensory characteristics of flaxseed extracts at 0.40 % and 1.0 %*
 519 *concentration, of water, and saliva*

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

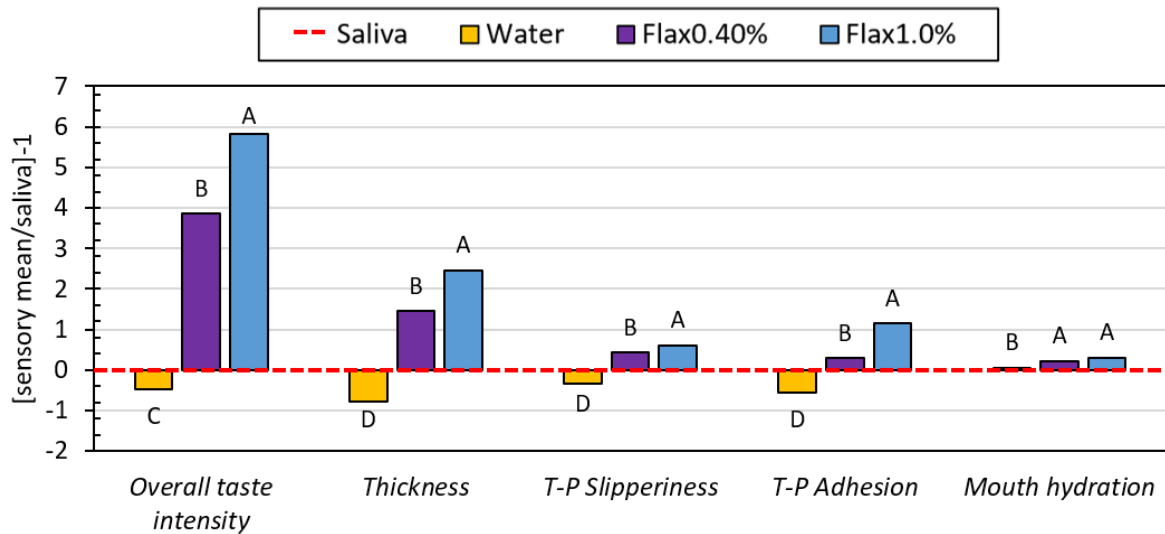
527 normalized using the expression: $\frac{\text{Product sensory mean}}{\text{Saliva sensory mean}} - 1$ are reported in Figure 7. Saliva therefore
528 corresponds to the normalized score equal to zero.

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

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

543 Surprisingly, when rinsing with water, *Mouth Hydration* was statistically similar to saliva.
544 This result undermined the hypothesis of reducing the perception of saliva's natural lubrication
545 when performing a series of water mouth rinses. Nevertheless, 37.5 % of the participants
546 evaluated *Mouth Hydration* using water, with scores less than 5 (5/10). In contrast, flaxseed
547 extracts offered an increase in hydration perception (8.2 ± 0.4 and 7.7 ± 0.4) (Figure A.12). Figure
548 7 demonstrates that regardless of the flaxseed concentration (0.40 % and 1.0 %), these solutions
549 led to higher perceived *Mouth Hydration* than that induced by water or saliva. In addition, when
550 rinsing with water, participants perceived a reduction in *T-P Slipperiness* and *T-P Adhesion*
551 compared to their natural oral lubrication state. This is in striking contrast to the higher *T-P*
552 *Slipperiness* and *T-P Adhesion* perceived for flaxseed extracts.

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

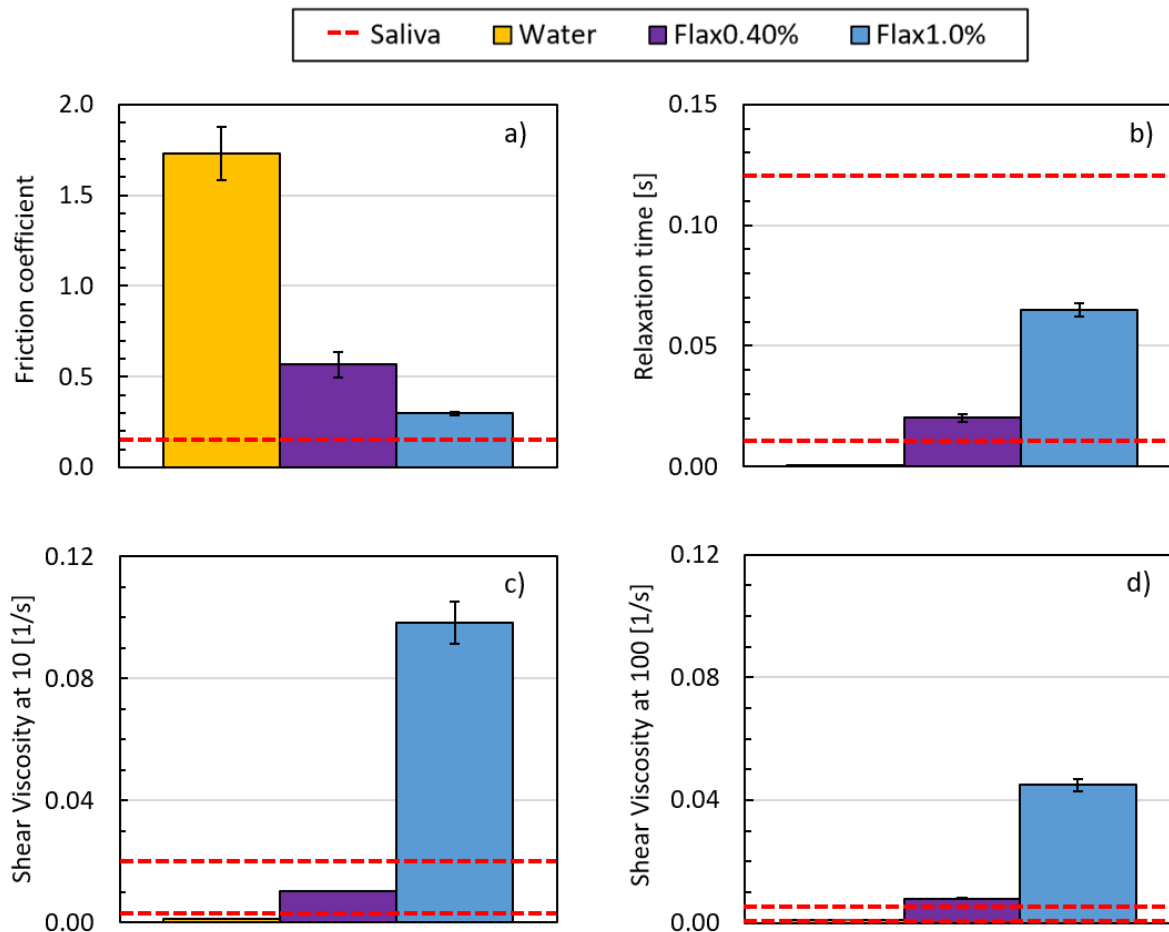


566
 567 *Figure 7. Means from the sensory scores normalized by the saliva scores for Saliva, Water and two*
 568 *concentrations of flax seed extracts. Five attributes were considered: Overall Taste Intensity, Thickness,*
 569 *Tongue-Palate (T-P) Slipperiness, Tongue-Palate Adhesion and Mouth Hydration. Letters indicate the*
 570 *statistically significant differences, based on the ANOVA test.*

571 *3.4.3 Tribological results*

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

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



593

594 *Figure 8. Friction coefficient, relaxation time, shear viscosities at 10 s⁻¹ and shear viscosities at*
 595 *100 s⁻¹ compared with human saliva literature data represented with a red pointed line.*

596 3.4.4 Correlation between instrumental measurements and sensory perceptions

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

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

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

615 *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

616
 617 Figure 9 displays the four products well distributed along axes F1 and F2 (89.59 %) and
 618 the variables on three out of the four quadrants of the correlation circle. “Shear Viscosities at 10
 619 s⁻¹” were strongly correlated to “Relaxation Time” (r=0.872) and negatively correlated to
 620 “Friction Coefficient” (r=-0.577). The relation between “Shear Viscosity at 10 s⁻¹” and
 621 “Relaxation Time” is probably driven by the higher relaxation time and shear viscosity at 10 s⁻¹
 622 of saliva compared to Flax0.40%. In the literature, “Viscosities at 10 s⁻¹” have been related to
 623 oral cohesiveness, this may indicate saliva’s ability to form and maintain an intact bolus (Ross et
 624 al., 2019). Additionally, the negative strong correlation between “Friction Coefficient” and
 625 “Shear Viscosities at 10 s⁻¹” is consistent with the mixed lubrication regime. Also, the negative
 626 correlation between “Friction Coefficient” and “Relaxation Time” suggests that salivary
 627 substitutes with higher elasticity would be more lubricious, reducing the friction coefficient.
 628 Similar results were obtained when evaluating polysaccharide–protein gel particle dispersions,
 629 observing negative correlations between slipperiness and friction coefficients (Chojnicka-Paszun
 630 et al., 2014).

631 *Table 4. Spearman correlation coefficients between sensory attributes and instrumental data.*
 632 *Abbreviations: Tongue-Palate slipperiness (TPS) and Tongue-Palate adhesion (TPA)*

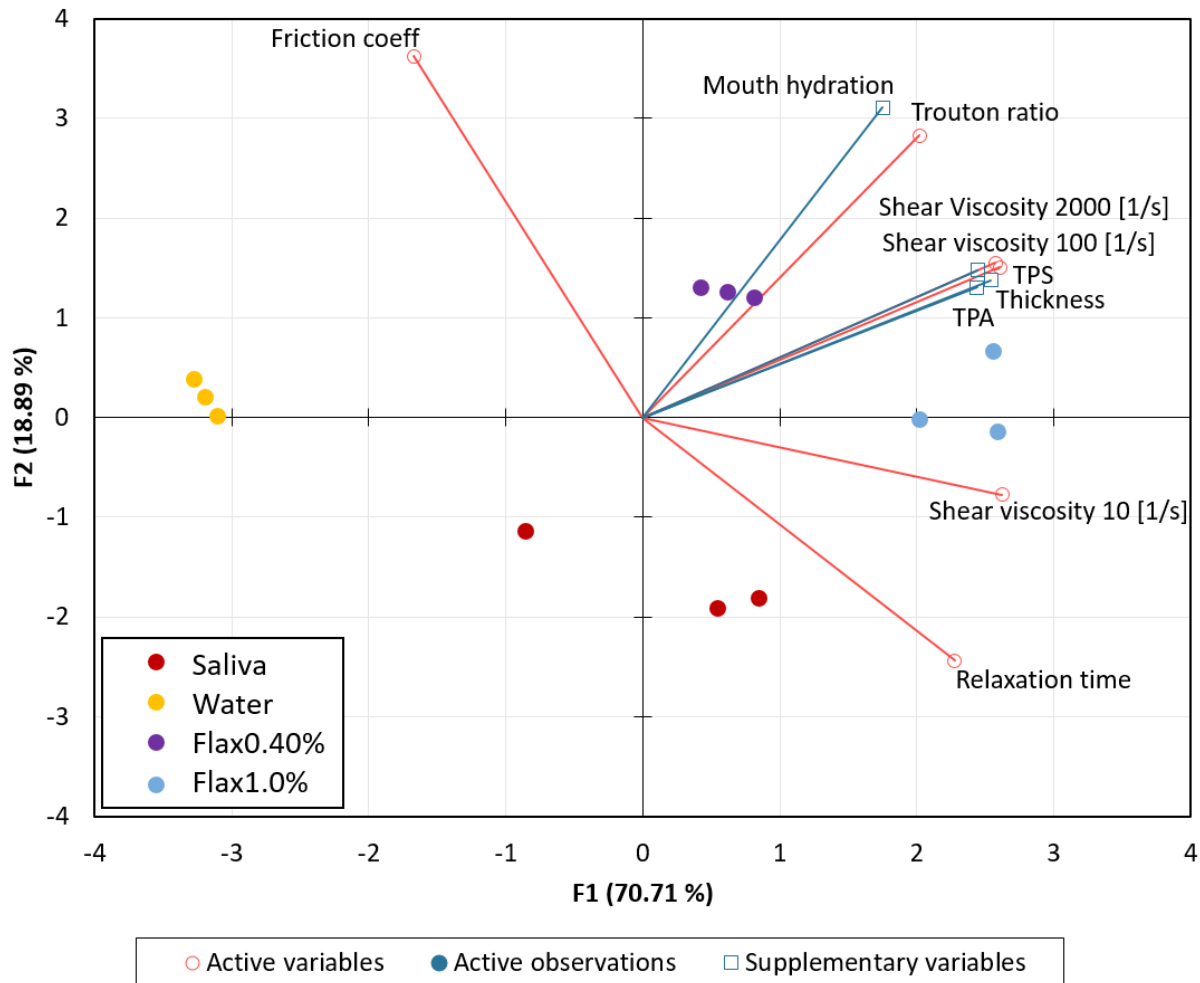
Variables	Shear viscosity 10 s ⁻¹	Shear viscosity 100 s ⁻¹	Shear viscosity 2000 s ⁻¹	Relax. time	Friction coeff.	Trouton ratio	Mouth hydration	Thickness	TPS	TPA
Shear viscosity 10 s ⁻¹	1	0.894	0.848	0.872	-0.577	0.514	0.599	0.775	0.852	0.803
Shear viscosity 100 s ⁻¹	0.894	1	0.978	0.638	-0.345	0.771	0.810	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 $\alpha=0.05$

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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-Munyo 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.



657
 658 *Figure 9. Correlation between instrumental and sensory data represented in a PCA. Active variables are*
 659 *the physical properties measured instrumentally (red axes), while supplementary variables are sensory*
 660 *mean scores (blue axes). The four products evaluated are represented as active observations (full*
 661 *circles); saliva, water, flaxseed extracts at 1.0 % and 0.40 % DM.*

662 **4. Conclusion and perspectives**

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

671 The complex rheological behaviour of human saliva is not easy to mimic, due to its low
 672 shear viscosity and high relaxation time and apparent extensional viscosity. Additionally, the
 673 variability of *in vivo* data is wide. However, flaxseed extracts at concentrations of 0.40% and
 674 1.0% have been found to have similar shear and extensional properties to human saliva. A

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

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

683 **Appendix A. Additional Data**

684 *Appendix A.1. Shear viscosity and normalized diameter of flaxseed extracts at different* 685 *temperatures*

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

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

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

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

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

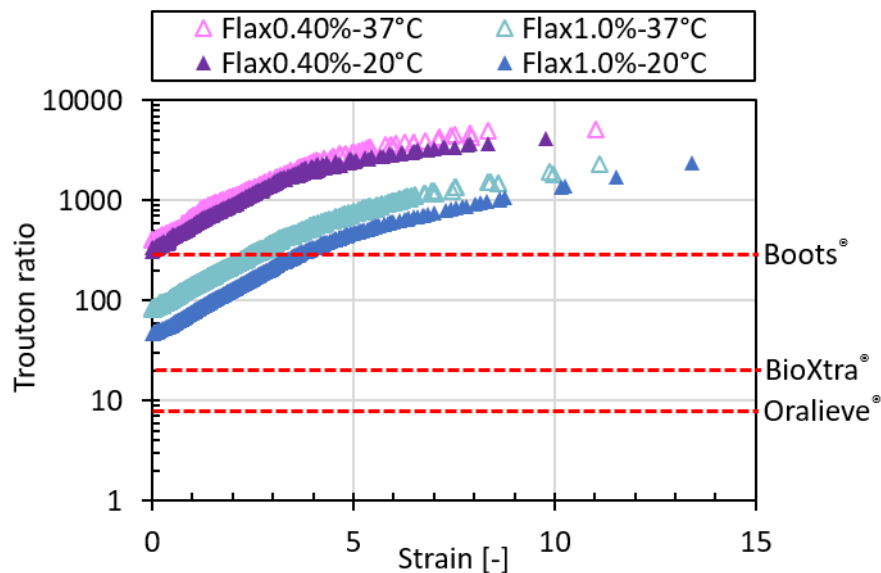
$$\dot{\gamma}_{non-Newtonian} = \frac{\dot{\gamma}}{3} \left(2 + \frac{\partial \ln \dot{\gamma}}{\partial \ln \tau} \right)$$

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

705

706 Appendix A.2. Trouton ratio using variable shear viscosity of flaxseed extracts at 0.40 % and 1.0
707 % at 20 and 37 °C

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



712
713 Figure A.10. Trouton ratio using variable shear viscosity of flaxseed extracts at 0.40 % and 1.0 % at 20
714 and 37 °C. Data from salivary substitutes in the market are represented in dashed lines. Results from
715 Boots, BioXtra and Oralieve were extracted from (Pabois et al., 2023)

716 Appendix A.3. Panelist training

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

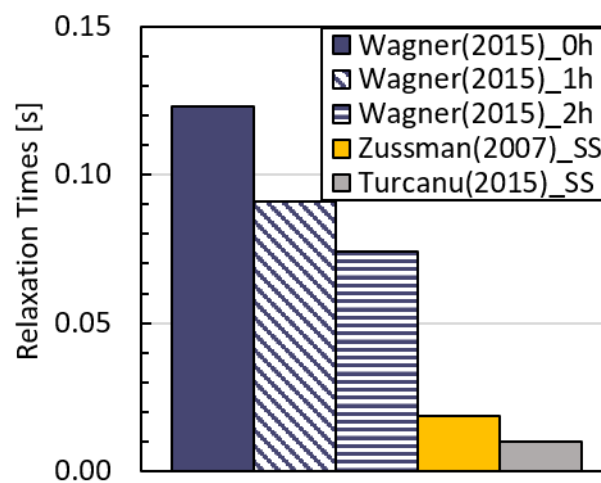
726 To display TPS and TPA, the panel was (i) given a tactile experience followed by (ii) tongue
727 movement training, and (iii) a food reference was provided. In the case of TPS, a piece of
728 sandpaper (10 x 5 cm, P80) was provided to illustrate: rough and slippery. The index finger was
729 moved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

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

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

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

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



752
753 *Figure A.11. Values established to define variability for human saliva relaxation times.*

754 *Appendix A.5 Panel performance*

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

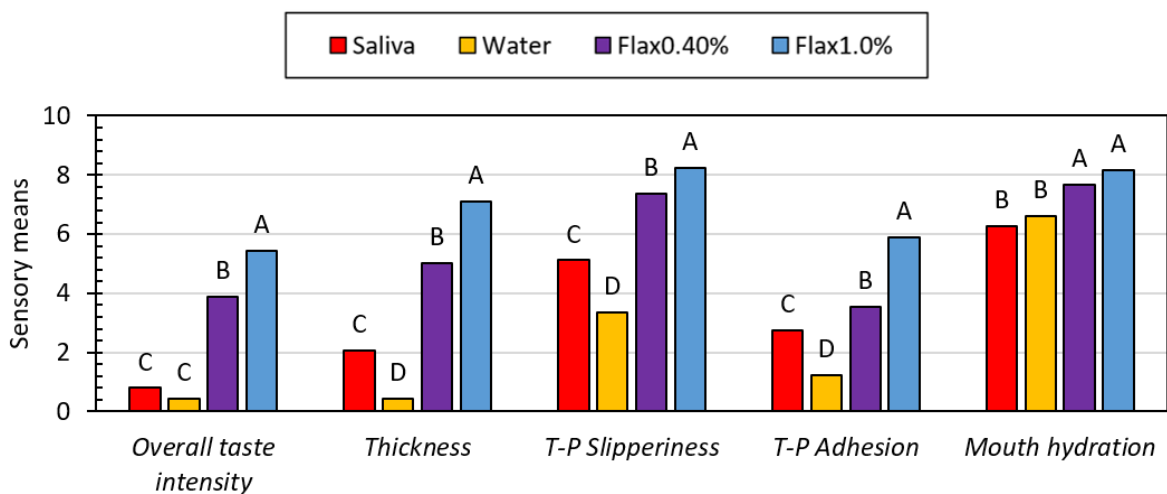
757 Table A.5. ANOVA results (product+panelist+panelists*product). P-values are in bold ($\alpha < 0.05$).
 758 Abbreviations: Tongue-Palate Slipperiness (TPS) and Tongue-Palate Adhesion (TPA)

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

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761 Appendix A.6. Averages of sensory ratings

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



765

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

767 Appendix A.7. Data employed for PCA

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

772 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

773

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776

777 **References**

778 Agorastos, G., van Halsema, E., Bast, A., Klosse, P., 2023. On the importance of saliva in mouthfeel

779 sensations. *Int. J. Gastron. Food Sci.* 31, 100667. <https://doi.org/10.1016/j.ijgfs.2023.100667>

780 Ahmad, M., Ritzoulis, C., Chen, J., 2018. Shear and extensional rheological characterisation of mucin

781 solutions. *Colloids Surf. B Biointerfaces* 171, 614–621.

782 <https://doi.org/10.1016/j.colsurfb.2018.07.075>

783 Anna, S.L., McKinley, G.H., 2001. Elasto-capillary thinning and breakup of model elastic liquids. *J. Rheol.*

784 45, 115–138. <https://doi.org/10.1122/1.1332389>

785 Assy, Z., Jager, D.H.J., Brand, H.S., Bikker, F.J., 2022. Salivary film thickness and MUC5B levels at various

786 intra-oral surfaces. *Clin. Oral Investig.* 27, 859–869. [https://doi.org/10.1007/s00784-022-04626-](https://doi.org/10.1007/s00784-022-04626-3)

787 3

788 Bongaerts, J.H.H., Rossetti, D., Stokes, J.R., 2007. The Lubricating Properties of Human Whole Saliva.

789 *Tribol. Lett.* 27, 277–287. <https://doi.org/10.1007/s11249-007-9232-y>

790 Brodkorb, A., Egger, L., Alminger, M., Alvito, P., Assunção, R., Ballance, S., Bohn, T., Bourlieu-Lacanal, C.,

791 Boutrou, R., Carrière, F., Clemente, A., Corredig, M., Dupont, D., Dufour, C., Edwards, C.,

792 Golding, M., Karakaya, S., Kirkhus, B., Le Feunteun, S., Lesmes, U., Macierzanka, A., Mackie, A.R.,

793 Martins, C., Marze, S., McClements, D.J., Ménard, O., Minekus, M., Portmann, R., Santos, C.N.,

794 Souchon, I., Singh, R.P., Vegarud, G.E., Wickham, M.S.J., Weitschies, W., Recio, I., 2019.

795 INFOGEST static in vitro simulation of gastrointestinal food digestion. *Nat. Protoc.* 14, 991–1014.

796 <https://doi.org/10.1038/s41596-018-0119-1>

797 Brüksch, L., Stringer, F.J., Kuster, S., Windhab, E.J., Fischer, P., 2019. Chia seed mucilage – a vegan
798 thickener: isolation, tailoring viscoelasticity and rehydration. *Food Funct.* 10, 4854–4860.
799 <https://doi.org/10.1039/C8FO00173A>

800 Bugarin-Castillo, Y., Rando, P., Clabaux, M., Moulin, G., Ramaioli, M., 2023. 3D printing to modulate the
801 texture of starch-based food. *J. Food Eng.* 350, 111499.
802 <https://doi.org/10.1016/j.jfoodeng.2023.111499>

803 Chojnicka-Paszun, A., Doussinault, S., de Jongh, H.H.J., 2014. Sensorial analysis of polysaccharide–gelled
804 protein particle dispersions in relation to lubrication and viscosity properties. *Food Res. Int.* 56,
805 199–210. <https://doi.org/10.1016/j.foodres.2013.12.035>

806 Cosson, A., Blumenthal, D., Descamps, N., Souchon, I., Saint-Eve, A., 2021. Using a mixture design and
807 fraction-based formulation to better understand perceptions of plant-protein-based solutions.
808 *Food Res. Int.* 141, 110151. <https://doi.org/10.1016/j.foodres.2021.110151>

809 Freitas, D., Le Feunteun, S., Panouillé, M., Souchon, I., 2018. The important role of salivary α -amylase in
810 the gastric digestion of wheat bread starch. *Food Funct.* 9, 200–208.
811 <https://doi.org/10.1039/C7FO01484H>

812 Gallegos, C., Turcanu, M., Assegehegn, G., Brito-de la Fuente, E., 2021a. Rheological Issues on
813 Oropharyngeal Dysphagia. *Dysphagia*. <https://doi.org/10.1007/s00455-021-10337-w>

814 Gallegos, C., Turcanu, M., Assegehegn, G., Brito-de la Fuente, E., 2021b. Rheological Issues on
815 Oropharyngeal Dysphagia. *Dysphagia*. <https://doi.org/10.1007/s00455-021-10337-w>

816 Gittings, S., Turnbull, N., Henry, B., Roberts, C.J., Gershkovich, P., 2015. Characterisation of human saliva
817 as a platform for oral dissolution medium development. *Eur. J. Pharm. Biopharm.* 91, 16–24.
818 <https://doi.org/10.1016/j.ejpb.2015.01.007>

819 Glumac, M., Bosc, V., Menut, P., Ramaioli, M., Restagno, F., Mariot, S., Mathieu, V., 2023. Signal analysis
820 to study the impact of tongue roughness on oral friction mechanisms with a custom-built
821 tribometer. *Biotribology* 35–36, 100257. <https://doi.org/10.1016/j.biotri.2023.100257>

822 Hahnel, S., Behr, M., Handel, G., Bürgers, R., 2009. Saliva substitutes for the treatment of radiation-
823 induced xerostomia—a review. *Support. Care Cancer* 17, 1331–1343.
824 <https://doi.org/10.1007/s00520-009-0671-x>

825 Hannig, C., Hannig, M., Kensche, A., Carpenter, G., 2017. The mucosal pellicle – An underestimated
826 factor in oral physiology. *Arch. Oral Biol.* 80, 144–152.
827 <https://doi.org/10.1016/j.archoralbio.2017.04.001>

828 Haward, S.J., Odell, J.A., Berry, M., Hall, T., 2011. Extensional rheology of human saliva. *Rheol. Acta* 50,
829 869–879. <https://doi.org/10.1007/s00397-010-0494-1>

830 He, Q., Hort, J., Wolf, B., 2016. Predicting sensory perceptions of thickened solutions based on
831 rheological analysis. *Food Hydrocoll.* 61, 221–232.
832 <https://doi.org/10.1016/j.foodhyd.2016.05.010>

833 Hu, J., Andablo-Reyes, E., Mighell, A., Pavitt, S., Sarkar, A., 2021. Dry mouth diagnosis and saliva
834 substitutes—A review from a textural perspective. *J. Texture Stud.* 52, 141–156.
835 <https://doi.org/10.1111/jtxs.12575>

836 Humphrey, S.P., Williamson, R.T., 2001. A review of saliva: Normal composition, flow, and function. *J.*
837 *Prosthet. Dent.* 85, 162–169. <https://doi.org/10.1067/mpr.2001.113778>

838 Johnston, J.H., 1927. The Surface Tension of Protein Solutions. Part III. *Biochem. J.* 21, 1314–1328.

839 Laguna, L., Fizman, S., Tarrega, A., 2021. Saliva matters: Reviewing the role of saliva in the rheology and
840 tribology of liquid and semisolid foods. Relation to in-mouth perception. *Food Hydrocoll.* 116,
841 106660. <https://doi.org/10.1016/j.foodhyd.2021.106660>

842 Lavoisier, A., Boudrag, S., Ramaioli, M., 2022. Effect of α -amylase and pH on the rheological properties
843 of thickened liquids containing starch in in vitro conditions relevant to oral processing and
844 swallowing. *J. Texture Stud.* 53, 550–557. <https://doi.org/10.1111/jtxs.12693>

845 Mackie, A., Rigby, N., 2015. InfoGest Consensus Method, in: Verhoeckx, K., Cotter, P., López-Expósito, I.,
846 Kleiveland, C., Lea, T., Mackie, A., Requena, T., Swiatecka, D., Wichers, H. (Eds.), *The Impact of*
847 *Food Bioactives on Health: In Vitro and Ex Vivo Models*. Springer International Publishing, Cham,
848 pp. 13–22. https://doi.org/10.1007/978-3-319-16104-4_2

849 Marconati, M., Pani, S., Engmann, J., Burbidge, A., Ramaioli, M., 2020. A soft robotic tongue to develop
850 solutions to manage swallowing disorders. *ArXiv200301194 Phys. Q-Bio*.

851 Marconati, M., Ramaioli, M., 2020. The role of extensional rheology in the oral phase of swallowing: an
852 in vitro study. *Food Funct.* <https://doi.org/10.1039/c9fo02327e>

853 Marconati, M., Raut, S., Burbidge, A., Engmann, J., Ramaioli, M., 2018. An in vitro experiment to
854 simulate how easy tablets are to swallow. *Int. J. Pharm.* 535, 27–37.
855 <https://doi.org/10.1016/j.ijpharm.2017.10.028>

856 McKinley, G.H., 2005. VISCO-ELASTO-CAPILLARY THINNING AND BREAK-UP OF COMPLEX FLUIDS. *Annu.*
857 *Rheol. Rev.* 1–49.

858 Minekus, M., Alming, M., Alvito, P., Ballance, S., Bohn, T., Bourlieu, C., Carrière, F., Boutrou, R.,
859 Corredig, M., Dupont, D., Dufour, C., Egger, L., Golding, M., Karakaya, S., Kirkhus, B., Feunteun,
860 S.L., Lesmes, U., Macierzanka, A., Mackie, A., Marze, S., McClements, D.J., Ménard, O., Recio, I.,
861 Santos, C.N., Singh, R.P., Vegarud, G.E., Wickham, M.S.J., Weitschies, W., Brodkorb, A., 2014. A
862 standardised static in vitro digestion method suitable for food – an international consensus.
863 *Food Funct.* 5, 1113–1124. <https://doi.org/10.1039/C3FO60702J>

864 Nayak, A., Carpenter, G.H., 2008a. A physiological model of tea-induced astringency. *Physiol. Behav.* 95,
865 290–294. <https://doi.org/10.1016/j.physbeh.2008.05.023>

866 Nayak, A., Carpenter, G.H., 2008b. A physiological model of tea-induced astringency. *Physiol. Behav.* 95,
867 290–294. <https://doi.org/10.1016/j.physbeh.2008.05.023>

868 Pabois, O., Avila-Sierra, A., Ramaioli, M., Mu, M., Message, Y., You, K.-M., Liamas, E., Kew, B., Durga, K.,
869 Doherty, L., Sarkar, A., 2023. Benchmarking of a microgel-reinforced hydrogel-based aqueous
870 lubricant against commercial saliva substitutes. *Sci. Rep.* 13, 19833.
871 <https://doi.org/10.1038/s41598-023-46108-w>

872 Pang, Z., Bourouis, I., Liu, X., 2022. Function of saliva in creaminess perception during food oral
873 processing: In perspective of lubrication. *J. Agric. Food Res.* 10, 100377.
874 <https://doi.org/10.1016/j.jafr.2022.100377>

875 Piaton, S., Duconseille, A., Roger-Leroi, V., Hennequin, M., 2021. Could the use of saliva substitutes
876 improve food oral processing in individuals with xerostomia? A systematic review. *J. Texture*
877 *Stud.* 52, 278–293. <https://doi.org/10.1111/jtxs.12591>

878 Pico-Munyo, R., Laguna, L., Tarrega, A., 2023. Thirstiness, body hydration and thickened water: A study
879 about their relationship. *Food Qual. Prefer.* 111, 104988.
880 <https://doi.org/10.1016/j.foodqual.2023.104988>

881 Prinz, J.F., Lucas, P.W., 1997. An optimization model for mastication and swallowing in mammals. *Proc.*
882 *R. Soc. Lond. B Biol. Sci.* 264, 1715–1721. <https://doi.org/10.1098/rspb.1997.0238>

883 Ross, A.I.V., Tyler, P., Borgognone, M.G., Eriksen, B.M., 2019. Relationships between shear rheology and
884 sensory attributes of hydrocolloid-thickened fluids designed to compensate for impairments in
885 oral manipulation and swallowing. *J. Food Eng.* 263, 123–131.
886 <https://doi.org/10.1016/j.jfoodeng.2019.05.040>

887 Sarkar, A., 2019. Lubrication of soft oral surfaces. *Interface Sci.* 15.

888 Sochi, T., 2010. Non-Newtonian flow in porous media. *Polymer* 51, 5007–5023.
889 <https://doi.org/10.1016/j.polymer.2010.07.047>

890 Srivastava, R., Bosc, V., Restagno, F., Tournier, C., Menut, P., Souchon, I., Mathieu, V., 2021. A new
891 biomimetic set-up to understand the role of the kinematic, mechanical, and surface
892 characteristics of the tongue in food oral tribological studies. *Food Hydrocoll.* 115, 106602.
893 <https://doi.org/10.1016/j.foodhyd.2021.106602>

894 Steele, C.M., Alsanei, W.A., Ayanikalath, S., Barbon, C.E.A., Chen, J., Cichero, J.A.Y., Coutts, K., Dantas,
895 R.O., Duivestein, J., Giosa, L., Hanson, B., Lam, P., Lecko, C., Leigh, C., Nagy, A., Namasivayam,
896 A.M., Nascimento, W.V., Odendaal, I., Smith, C.H., Wang, H., 2015. The Influence of Food
897 Texture and Liquid Consistency Modification on Swallowing Physiology and Function: A
898 Systematic Review. *Dysphagia* 30, 2–26. <https://doi.org/10.1007/s00455-014-9578-x>

899 Stokes, J.R., Davies, G.A., 2007. Viscoelasticity of human whole saliva collected after acid and mechanical
900 stimulation. *Biorheology* 44, 141–160.

901 Taylor, A.J., Linforth, R.S.T., 1996. Flavour release in the mouth. *Trends Food Sci. Technol.* 7, 444–448.
902 [https://doi.org/10.1016/S0924-2244\(96\)10046-7](https://doi.org/10.1016/S0924-2244(96)10046-7)

903 Timilsena, Y.P., Adhikari, R., Kasapis, S., Adhikari, B., 2015. Rheological and microstructural properties of
904 the chia seed polysaccharide. *Int. J. Biol. Macromol.* 81, 991–999.
905 <https://doi.org/10.1016/j.ijbiomac.2015.09.040>

906 Turcanu, M., Tascon, L.F., Balan, C., Gallegos, C., 2015. Capillary breakup extensional properties of whole
907 human saliva, in: 2015 9th International Symposium on Advanced Topics in Electrical
908 Engineering (ATEE). Presented at the 2015 9th International Symposium on Advanced Topics in
909 Electrical Engineering (ATEE), IEEE, Bucharest, Romania, pp. 269–274.
910 <https://doi.org/10.1109/ATEE.2015.7133778>

911 Vieira, J.M., Andrade, C.C.P., Santos, T.P., Okuro, P.K., Garcia, S.T., Rodrigues, M.I., Vicente, A.A., Cunha,
912 R.L., 2021. Flaxseed gum-biopolymers interactions driving rheological behaviour of

913 oropharyngeal dysphagia-oriented products. *Food Hydrocoll.* 111, 106257.
914 <https://doi.org/10.1016/j.foodhyd.2020.106257>

915 Vieira, J.M., Mantovani, R.A., Raposo, M.F.J., Coimbra, M.A., Vicente, A.A., Cunha, R.L., 2019. Effect of
916 extraction temperature on rheological behavior and antioxidant capacity of flaxseed gum.
917 *Carbohydr. Polym.* 213, 217–227. <https://doi.org/10.1016/j.carbpol.2019.02.078>

918 Vieira, J.M., Oliveira, F.D., Jr., Salvaro, D.B., Maffezzoli, G.P., de Mello, J.D.B., Vicente, A.A., Cunha, R.L.,
919 2020. Rheology and soft tribology of thickened dispersions aiming the development of
920 oropharyngeal dysphagia-oriented products. *Curr. Res. Food Sci.* 3, 19–29.
921 <https://doi.org/10.1016/j.crfs.2020.02.001>

922 Wagner, C., 2015. An experimental and theoretical investigation of the rheological properties and
923 degradation of mucin solutions (or why saliva becomes watery when removed from your
924 mouth) (Ph.D Thesis). Massachusetts Institute of Technology.

925 Wagner, C.E., McKinley, G.H., 2017. Age-dependent capillary thinning dynamics of physically-associated
926 salivary mucin networks. *J. Rheol.* 61, 1309–1326. <https://doi.org/10.1122/1.4997598>

927 Yuan, B., Ritzoulis, C., Chen, J., 2018a. Extensional and shear rheology of okra hydrocolloid–saliva
928 mixtures. *Food Res. Int.* 106, 204–212. <https://doi.org/10.1016/j.foodres.2017.12.051>

929 Yuan, B., Ritzoulis, C., Chen, J., 2018b. Extensional and shear rheology of a food hydrocolloid. *Food*
930 *Hydrocoll.* 74, 296–306. <https://doi.org/10.1016/j.foodhyd.2017.08.019>

931 Zussman, E., Yarin, A.L., Nagler, R.M., 2007. Age- and Flow-dependency of Salivary Viscoelasticity. *J.*
932 *Dent. Res.* 86, 281–285. <https://doi.org/10.1177/154405910708600316>

933