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1 **Using a natural salivary substitute to improve the**
2 **swallowability of semi-solid foods: an *in vitro* and *in vivo***
3 **study**

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18 **Declarations of interest:** None.
19

20 **Keywords:** Swallowing, Salivary substitute, Flaxseed extracts, Soft robotic, Sensory
21 evaluation.

22 **Abstract**

23 Flaxseed extracts are solutions and suspensions of polysaccharides with extensional and
24 shear rheological properties close to those of saliva, making them promising candidates as natural
25 salivary substitutes (NSS) to manage xerostomia. Both *in vitro* and *in vivo* approaches were
26 considered to investigate the lubricating performance of such NSSs during swallowing of Greek
27 yogurt and apple puree. The choice of these two semi-solid foods made it possible to compare
28 colloidal systems with contrasting properties of composition, structure and rheology. The oral
29 phase of swallowing was simulated *in vitro* with an innovative soft robotic model while sensory
30 evaluations were performed with a healthy cohort ($n=16$) to assess the potential of the NSSs for
31 reducing the amounts of post swallowing food residues into the mouth. Flaxseed extract with 0.40
32 % dry matter showed promising performance, with low amounts of oral residues reported both *in*
33 *vitro* and *in vivo*, and with a bolus that was not prone to undesired fragmentation. The original
34 approach presented in this research offers perspectives to prescreen other salivary substitutes or
35 food textures, in order to help addressing the needs of growing populations affected by swallowing
36 disorders, and in particular those caused by xerostomia. The development of natural saliva
37 substitutes should make it possible to recover a state of oral lubrication which ensures oral comfort,
38 safe swallowing, and which limits the problems of malnutrition resulting from dysphagia.
39

40 Introduction

41 It is expected that by 2050, 21.5 % of the population will be over 60 years old and that age-
42 related diseases will therefore be more prevalent (Lorieau et al., 2018; Schwartz et al., 2018).
43 Swallowing disorders, also known as dysphagia, concern more than 40 % of people over 65 years
44 old (Rofes et al., 2011). Dysphagia affects quality of life by increasing the risk of choking or
45 aspiration in the lungs, and may lead to the avoidance of some food and drink categories, causing
46 dehydration and malnutrition. Three leading causes can generate it: (i) the perturbation of muscle
47 coordination (like with neurological impairments), (ii) the weakness and rapid fatigue of muscles
48 (such as in the case of sarcopenia), and (iii) the decrease in salivary flow rate related to a dry mouth
49 sensation (xerostomia) (Cassolato & Turnbull, 2003; Clavé & Shaker, 2015).

50 Salivary substitutes (SS) are effective treatments for xerostomia and work by coating oral
51 surfaces and imitating saliva lubrication (Hu et al., 2021). Studies have appraised SS concerning
52 oral comfort, wettability, rheology, and lubricity (Bugarin-Castillo et al., 2024; Hu et al., 2021;
53 Pailler-Mattei et al., 2015; See et al., 2019; Shahdad et al., 2005; Spirk et al., 2019; Vinke et al.,
54 2020). These characterizations are essential to imitate saliva lubrication, thickness, and
55 moisturizing properties. The assessment of SS is generally achieved *in vivo* using questionnaires
56 (Hahnel et al., 2009). Besides, instrumental approaches have been proposed to evaluate lubricity
57 and wettability using *ex vivo* tissues to approach human conditions (Vinke et al., 2018).

58 However, the performance of salivary substitutes is not frequently evaluated during food oral
59 processing (FOP) (Piaton et al., 2021). It is well established that a deficiency in saliva during FOP
60 can affect bolus formation and lead to a measurable increase in post-swallowing oral residues
61 (Wirth et al., 2016). Post-swallowing oral residues are described as the amount of food in the oral
62 cavity after the main swallow and the willingness to clean it with multiple swallows (Hadde &
63 Chen, 2021). The accumulation of residues promotes oral discomfort, decreases food palatability,
64 and can cause post-swallow aspiration (Lavoisier et al., 2021). In addition, in the cases of
65 neurological impairments or sarcopenia, poor handling of oral residues might increase the risk of
66 choking (Gallegos et al., 2021). Furthermore, bolus formation is an essential and complex step in
67 the preparation of the oral phase of swallowing. It includes mixing and hydrating food particles
68 with saliva to increase cohesion until a compact bolus is able to flow through the pharynx (Avila-
69 Sierra et al., 2024; Fujiso et al., 2018; Gallegos et al., 2021; Nishinari et al., 2024). During bolus
70 formation, saliva also impacts the perception of food texture and taste. In particular, the bolus
71 extensional properties have been shown in both *in vitro* (Marconati & Ramaioli, 2020) and *in vivo*
72 conditions (Hadde et al., 2019) to foster bolus compactness. Given that the extensional properties
73 of food bolus are the direct consequence of those of saliva, xerostomia could, in some cases, impair
74 the compactness of the bolus.

75 The use of *in vitro* swallowing simulators constitutes a promising approach to study the
76 influence of physiological disturbances on the food bolus flow during swallowing. In particular,
77 they enable to screen different novel food products and assess their oral residence time, *in vitro*
78 oral pressures and post-swallow residues without risks for patient safety. The different physical
79 measurement modalities that are embedded in these devices, along with the control of experimental
80 conditions that they allow, create an ideal environment for gaining a deeper understanding of the

81 mechanisms that govern the flow of food bolus. One example is the soft actuator developed by
82 Marconati et al., (2020) known as the soft-robotic tongue (SRT). The *in vitro* set up is inspired by
83 tongue movements during swallowing, including bolus retention and propulsion through the
84 oropharynx. However, the model does not replicate saliva lubrication, which is critical for
85 enhancing the realism of the SRT. Several issues arise when using real human saliva to lubricate
86 swallowing simulators (technical, ethical, regulatory and microbiological). Moreover, one of the
87 major characteristics of saliva is its strong intra- and inter-individual variability. As a consequence,
88 it would be beneficial to explore the use of synthetic saliva substitutes, as long as their properties
89 can realistically mimic the complex rheological and mucoadhesive properties of natural saliva.

90 Lately, several natural extracts, including flaxseed extracts, have been proposed as potential
91 salivary substitutes (Bugarin-Castillo et al., 2024; Pabois et al., 2023; Wagner, 2015). Moreover,
92 recent formulations show shear and extensional rheological properties similar to human saliva
93 (Bugarin-Castillo et al., 2024).

94 The present study aims at testing these natural salivary substitutes in the swallowing simulator,
95 and investigating how (i) walls and tongue lubrication and (ii) food properties may influence the
96 formation of oral residues during swallowing. Two different semi-solid foods (apple puree and
97 Greek yogurt) were considered. The measurements carried out on the *in vitro* swallowing simulator
98 were also compared to sensory evaluations carried out by a trained panel. Coupling *in vitro* and *in*
99 *vivo* approaches thus allows a better understanding of the mechanisms controlling the formation
100 of oral residues during swallowing, so as to be able to identify strategies to reduce them.

101 **2. Materials & Methods**

102 *2.1. Natural Salivary Substitute (NSS)*

103 Natural Salivary Substitutes (NSS) based on flaxseed extracts were prepared and used to
104 simulate human saliva lubrication. Brown flaxseed (Markal, Saint-Marcel-lès-Valence, France)
105 containing 20 % proteins was used to formulate these NSS. The NSS preparation, rheological &
106 tribological characterization and sensory properties are described in detail by Bugarin-Castillo et
107 al., (2024). Two different formulas for NSS were considered, based on their similarity to human
108 saliva in terms of sensory perceptions (like mouth hydration, tongue-palate slipperiness and
109 adhesion) and rheology (including extensional relaxation times and shear viscosity). The solutions
110 were prepared at concentrations of 0.40 % and 1.0 % dry matter, labeled as F_{0.40} and F_{1.0},
111 respectively.

112 *2.2. Characterization of Semi-Solid Foods*

113 Apple puree (Andros, Biars-sur-Cère, France) and Greek yogurt (Yaourt à la grecque,
114 Cora, Croissy-Beaubourg, France) were used for both *in vitro* and *in vivo* tests due to their thick
115 consistencies generally associated with ease of swallowing (Penman & Thomson, 1998). Both
116 products were commercially available and ready for tasting without modification in the laboratory,
117 facilitating the organization of sensory evaluations. Moreover, both of them are generally
118 appreciated and widely consumed. Additionally, apple puree and yogurt have been previously used
119 in research involving a pediatric swallowing soft-actuator (Lavoisier et al., 2022).

120 Greek yogurt (labeled as G_Y hereafter) contained 8.80 % of fats and 2.80 % of proteins,
121 while apple puree (A_P hereafter) contained 1.20 % of fibers, 0.10 % of fats and 0.30 % of proteins.

123 Both products were purchased at a local store (Cora, Croissy-Beaubourg, France) and kept at 4 °C
124 for storage.

125 The rheological behavior of the semi-solid foods was characterized using a Physica MCR-
126 702 rheometer (Anton Paar GmbH, Graz, Austria). For apple puree, shear viscosity was measured
127 with a Couette geometry between 1 and 500 s⁻¹ (d = 18 mm; gap = 5 mm) at 20 °C. For Greek
128 yogurt, shear viscosity was determined with a sand-blasted plate-plate geometry PP50S (d = 50
129 mm; gap = 1 mm) ranging between 1 to 500 s⁻¹ at 20 °C. An amplitude sweep was performed for
130 both products at a constant angular frequency of 10 rad/s, varying the strain from 0.01 to 1000%
131 at 20 °C. In addition, the yield stress was obtained as the stress at the crossing point of G' and G''
132 based on the method of Espinosa-Muñoz et al., (2013). The measurements were performed in
133 triplicates.

134 The lubricity of apple puree and Greek yogurt were studied by tribology with a biomimetic
135 setup. Srivastava et al., (2021) described the tribometer geometry and design details. To test the
136 semi-solid foods, 1 g of each was placed on a tongue mimicking sample (TMS). The TMS was
137 made out of Ecoflex-030 (Smooth-On, Macungie, USA) and 5 % Span80 (sorbitan mono-oleate
138 from Sigma-Aldrich, St. Louis, USA). The roughness of the TMS was inspired by the human
139 tongue topography using sandpaper P40 (Saint-Gobain Norton, Paris, France), as suggested by
140 Srivastava et al., (2021). An aluminum plate (rectangular, 45 mm × 25 mm) plays the role of the
141 palate and applies an initial normal force of 5 N on the TMS (around 5 kPa). Friction measurements
142 were then conducted during five cycles of back and forth shear motions operated with an
143 amplitude of 10 mm and a constant velocity of 10 mm·s⁻¹. More information about the
144 methodology is provided in Bugarin-Castillo et al., (2024).

145 A laser diffraction analyzer was used to measure the particle size distribution of apple puree
146 and Greek yogurt (Mastersizer 3000, Malvern Panalytical, London, UK). The samples were diluted
147 1:10 (w/w) with purified water. To better compare with literature, particle size at the 90th percentile
148 $d(0.9)$ was calculated from three replicates.

149

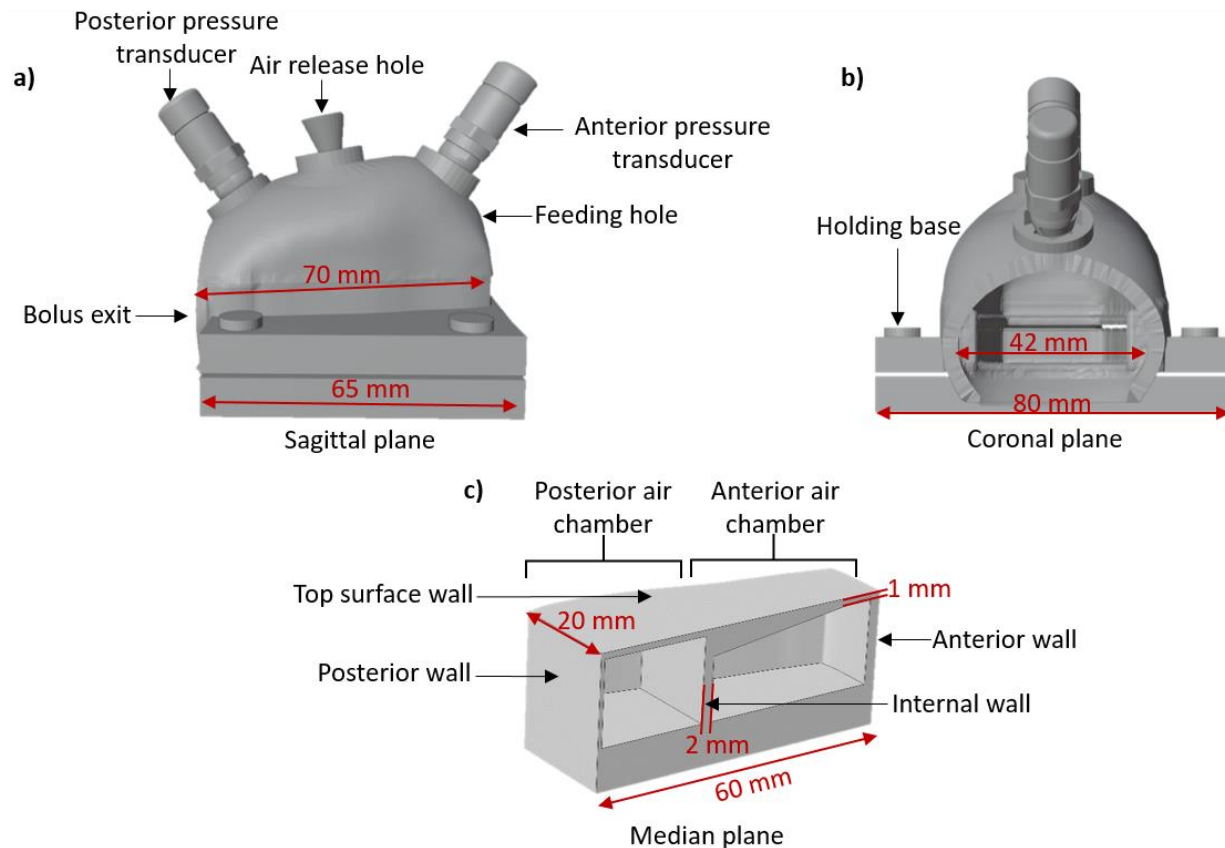
150 2.3. *In Vitro* Soft-Robotic Tongue (SRT)

151 The *in vitro* setup utilized in this study was proposed by Marconati et al., (2020). This *in*
152 *vitro* soft-robotic tongue has been adapted to simulate pediatric swallowing (Avila-Sierra et al.,
153 2023; Lavoisier et al., 2022). The 3D model is based on CT scans of the oral airway of a healthy
154 adult (Xi & Longest, 2007). A comprehensive description of the actuation patterns was reported
155 by Lavoisier et al., (2022). The adult size SRT presented in this study was derived from the original
156 model (Marconati et al., 2020), with minor modifications described in the following sections.

157

158 2.3.1. 3D Oral Cavity

159 The oral cavity was 3D printed using a hard material (VeroClear® resin from Sculpteo,
160 Villejuif, France) chosen for its transparency, allowing image analysis. A schematic representation
161 of the oral cavity design is shown in Figure 1.a&b. A hole (4 mm diameter) located 6 mm from
162 the tongue tip makes it possible to inject the semi-solid foods and the NSS in the cavity, using a
163 syringe. In addition, two holes with 1/8'' metallic nuts glued on the top were used to position
164 pressure transducers. Hence, palatal pressure of the food products during the swallowing sequence
165 were recorded. The central hole was closed with a rubber stopper during *in vitro* swallowing.
166 Conversely, when feeding the oral cavity, the central hole was open to avoid any undesired
167 pressure increase and the incorporation of air bubbles.



168
 169 *Figure 1. Diagram and dimensions of the 3D oral cavity and of the soft-robotic in vitro tongue (SRT). a)*
 170 *Sagittal plane of the 3D oral cavity, b) Coronal plane of the 3D oral cavity, c) 3D view of the soft-robotic*
 171 *tongue proposed by Marconati et al., (2020) and used in this study.*

172 **2.3.2. Soft-Robotic Tongue (SRT)**

173 The soft-robotic tongue by Marconati et al., (2020) was used in this study. Marconati et al.,
 174 (2020) designed a geometry possessing two air chambers that can inflate and deflate independently
 175 (see Figure 1.c). The tongue is obtained by molding a solution of Ecoflex-030 (Smooth-On,
 176 Macungie, USA) mixed with 5 % Span80 (sorbitan mono-oleate from Sigma-Aldrich, St. Louis,
 177 USA).

178 An important modification was introduced in this study, which involved patterning the top
 179 surface of the SRT. The roughness imitates the topography of the human tongue, which is mostly
 180 driven by the presence of the filiform papillae. To achieve this, sandpaper P40 (Saint-Gobain
 181 Norton, Paris, France) was used to cover the mould in which the silicon was poured, following the
 182 technique used by Srivastava et al., (2021).

183
 184 **2.3.3. Wettability and Papillae Dimensions of the SRT**

185 Mechanical properties of the SRT were similar to those from the SRT developed and
 186 characterized in the previous study (Marconati et al., 2020). Due to the addition of roughness on
 187 the top surface wall, its wettability and topography were evaluated.

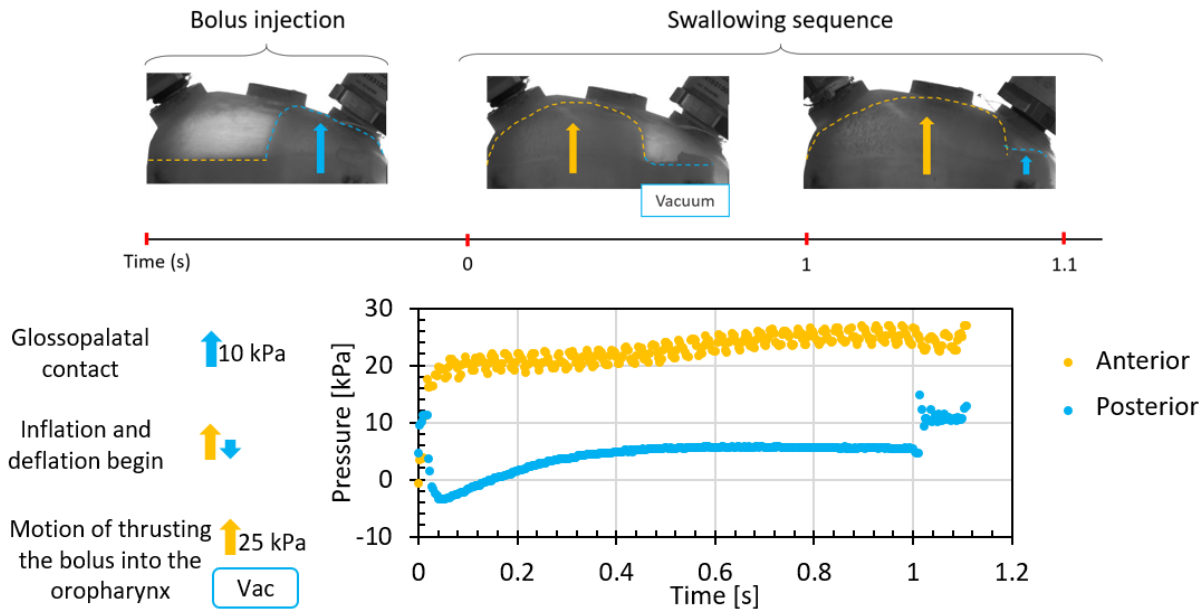
188 The contact angle of water and NSS were measured by depositing a 20 μ L droplet on a
 189 portion of the SRT surface; images of the drop were captured for 15 seconds after 1 minute of
 190 deposition. A camera (Vision Research, Wayne, USA) with a 50 mm lens (Opto Engineering,
 191 Mantova, Italy) was used to record (50 fps) the shape evolution of the droplet, which was processed

192 with ImageJ® and the contact angle plugin (Avila Sierra et al., 2023). All measurements were
193 repeated in triplicate.

194 The topography of the SRT was characterized by optical microscopy using an Olympus
195 BX51 (Olympus, Tokyo, Japan) and a 10x objective. The samples were sliced on a thin layer to
196 measure the height and diameter of the *in vitro* papillae. All measurements were repeated five
197 times. Results are detailed in Appendix B and Appendix A.

198 2.3.4. Swallowing Sequence

199 The design of the *in vitro* tongue allows the independent displacement of the posterior and
200 anterior chambers by applying different pressures, determined based on *in vivo* data. The *in vitro*
201 swallowing sequence established by Marconati et al., (2020) was used in this study. The schematic
202 representation of the timeline of this sequence is provided in Figure 2. The bolus is injected in the
203 oral cavity through the feeding hole located in its front, while a pressure of 10 kPa is imposed in
204 the posterior chamber in order to allow bolus holding (consistently with *in vivo* glossopalatal
205 pressures) (Fujiwara et al., 2014). The swallowing sequence then starts (t = 0 s) with two
206 simultaneous actions: the inflation of the anterior chamber (25 kPa) and the deflation of the
207 posterior chamber with an imposed vacuum of -5 kPa. The pressure in the anterior chamber (25
208 kPa) was set based on tongue-palate maximal pressure values available in the literature (around 60
209 kPa), attenuated by a factor of 40% as the foods considered here have a low viscosity and do not
210 require intense mechanical efforts to flow (Fei et al., 2013; J.-S. Park et al., 2016). At t = 0.6 s, the
211 maximum pressure in the anterior chamber is reached, consistently with *in vivo* timings of the oral
212 phase of swallowing for liquids (Dodds et al., 1990; Zhang et al., 2012). After t = 1.1 s, pressure
213 was no longer applied to either chamber, causing both chambers to return to their resting positions.
214
215



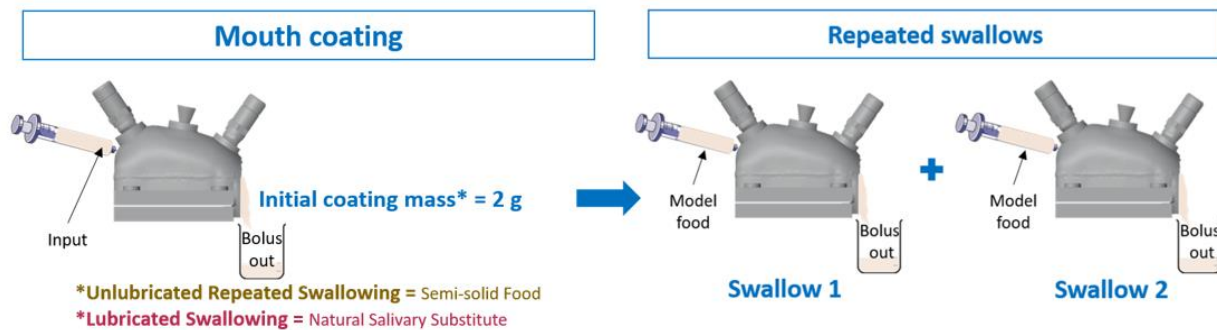
216 Figure 2. Schematic timeline of the swallowing sequence. Bolus injection represents bolus holding and
217 swallowing sequence illustrates the *in vitro* swallowing displacement inspired by the oral phase of
218 swallowing of liquids. Pressure evolution with time, corresponding to the pressures in each chamber.
219

222 2.3.5. *In Vitro Swallowing Protocol*

223 Two *in vitro* conditions were assessed for evaluating the lubricating performance of the
224 NSS: (i) “Lubricated Swallowing” (referred to as “LS”) and (ii) “Unlubricated Repeated
225 Swallowing” (referred to as “URS”). Figure 3 illustrates the steps involved in each of these two *in*
226 *vitro* protocols.

227 The *in vitro* device used in this study is not suitable for performing swallowing in
228 completely dry conditions, due to excessive amounts of residues observed in the first dry swallow.
229 To avoid the positive bias that would result from comparing a dry swallow with a swallow in
230 presence of oral lubrication, it was decided to focus on the repeated feeding and swallowing of a
231 product in absence of salivation: a condition that is representative of the repeated consumption by
232 a xerostomic person. The protocol used for simulating this condition was referred to as
233 “Unlubricated Repeated Swallowing” (“URS”).

234 The “Lubricated Swallowing” (“LS”) protocol comprised an initial feeding of NSS (2 g)
235 to coat the *in vitro* oral cavity. The URS protocol involved an initial coating of semi-solid food (2
236 g). The two conditions thus started with the same initial mouth coating mass (2 ± 0.3 g), to avoid
237 the bias that would result from a different initial degree of filling of the *in vitro* oral cavity.
238 Following the coating step, two consecutive semi-solid food swallows were completed (5 g each)
239 in each sequence. The masses of the semi-solid food injected in the system and of bolus expelled
240 from the system after *in vitro* swallowing were carefully weighted using a precision scale of 1 mg
241 (Sartorius PRACTUM513-1S, Göttingen, Germany).



242
243 *Figure 3. In vitro protocol for “Unlubricated Repeated Swallowing” (URS) and “Lubricated Swallowing”*
244 *(LS) conditions. Firstly, the mouth coating step consisted in coating the swallowing simulator either with*
245 *Natural Salivary Substitute (NSS) or with semi-solid food (apple puree or Greek yogurt). Then, two*
246 *repeated swallows (called #1 and #2) with semi-solid food (5 g) were completed.*

247 2.3.6. *Measured Variables*

248 2.3.6.1. *Post-Swallowing In Vitro Residue (g)*

249 Human saliva has the ability of reducing the residues in the throat (Wirth et al., 2016).
250 Based on this, the performance of the salivary substitutes was evaluated by quantifying the amount
251 of semi-solid food residues after two successive *in vitro* swallows. The quantity of residue could
252 be quantified by measuring the difference between the masses injected into the instrument and
253 those expelled after the swallowing sequence. To quantify semi-solid food residues, it was
254 necessary to adapt the method according to the lubrication condition. Hence, two distinct
255 approaches were followed for LS and URS protocols.

256 For URS, the mass of semi-solid food residues induced by a swallowing sequence simply
257 resulted in the difference between injected and expelled masses.

258 For LS condition, the method had to be adapted because residues collected after each
259 swallow consist of a mixture of semi-solid food and NSS. The NSS concentration in the samples

260 collected at the exit of the device was quantified using a refractometer (ATAGO®, Tokyo, Japan).
261 The refractometer was calibrated to confirm a linear relation between the obtained Brix degrees
262 and the dilution rate of semi-solid foods with flaxseed extracts. The calibration curves are reported
263 in Appendix C at concentrations between 0 to 0.86 w/w. The Brix degree measured on samples
264 expelled after swallows #1 and #2 were then converted into the mass of semi-solid food ejected
265 during each swallow. The mass differences between semi-solid food injected and bolus expelled
266 could thus be used to characterize the residual mass of semi-solid food in the oral cavity at the end
267 of each swallow.

268

269 2.3.6.2. *In Vitro Bolus Transit Time (s)*

270 The *in vitro* bolus transit time was defined as the time required for the front of the bolus to
271 exit the oral cavity (bolus FO, for “Front Out”). Two cameras were recording the bolus transit and
272 were positioned at different views. A high-speed camera (Vision Research, Wayne, USA) recorded
273 the sagittal plane, and a Basler acA2000-165uc (Basler AG, Ahrensburg, Germany) recorded the
274 side view, both of them at 100 fps. To obtain the bolus transit time, the image analysis consisted
275 in identifying manually the frame where the sequence started (frame “0”) and the frame where the
276 front of the bolus exits the SRT (frame “bolus FO”). The difference in frames and the acquisition
277 rate of the tests allowed to quantify the time required for the front of the bolus to exit the oral
278 cavity (bolus FO).

279

280 2.3.6.3. *Palatal Pressure (kPa)*

281 The anterior and posterior palatal pressures were measured by two pressure sensors
282 operating from 0 to 0.2 MPa (model PX2AG2XX002BAAAX, from Honeywell, Charlotte, USA)
283 located in the 3D oral cavity (see Figure 1). The pressures were acquired at a sampling rate of 294
284 data points per second by using an Arduino Uno board (Arduino AG, Chiasso, Switzerland) and a
285 control algorithm through Arduino IDE v1.8.16 (Arduino AG, Chiasso, Switzerland). These
286 results are expressed as a relative pressure (in kPa) and as a function of time during the course of
287 each swallowing sequence. The maximum palatal pressure recorded for each swallowing sequence
288 was used to compare different *in vitro* conditions (LS and URS).

289

290 2.4 *Sensory Evaluation*

291 2.4.1 *Panel*

292 The present sensory study followed the ethical standards defined by the Declaration of
293 Helsinki. A panel of 16 healthy volunteers (9 women and 7 men, 23-60 years old) was recruited
294 based on motivation, availability and food allergies. The study comprised four sessions (including
295 two for training and two for evaluation) of 40 min each. The study aimed to evaluate the impact
296 of different oral lubrication conditions on the amount of oral residues perceived after swallowing
297 A_p or G_Y . At the end of the sensory study, the panelists were compensated for their participation.
298 Panelists were instructed to refrain from eating, drinking or smoking for at least an hour prior to
299 the sessions. The study took place in a sensory laboratory featuring 16 individual tasting booths,
300 each equipped with a sink. The booths were air-conditioned (20°C) and illuminated with red
301 lighting to reduce visual biases. For the evaluation sessions, panelists were presented with different
302 combinations of oral coating conditions and of semi-solid foods, which were arranged in a
303 balanced order across participants using a Latin square and divided into three replicate blocks.

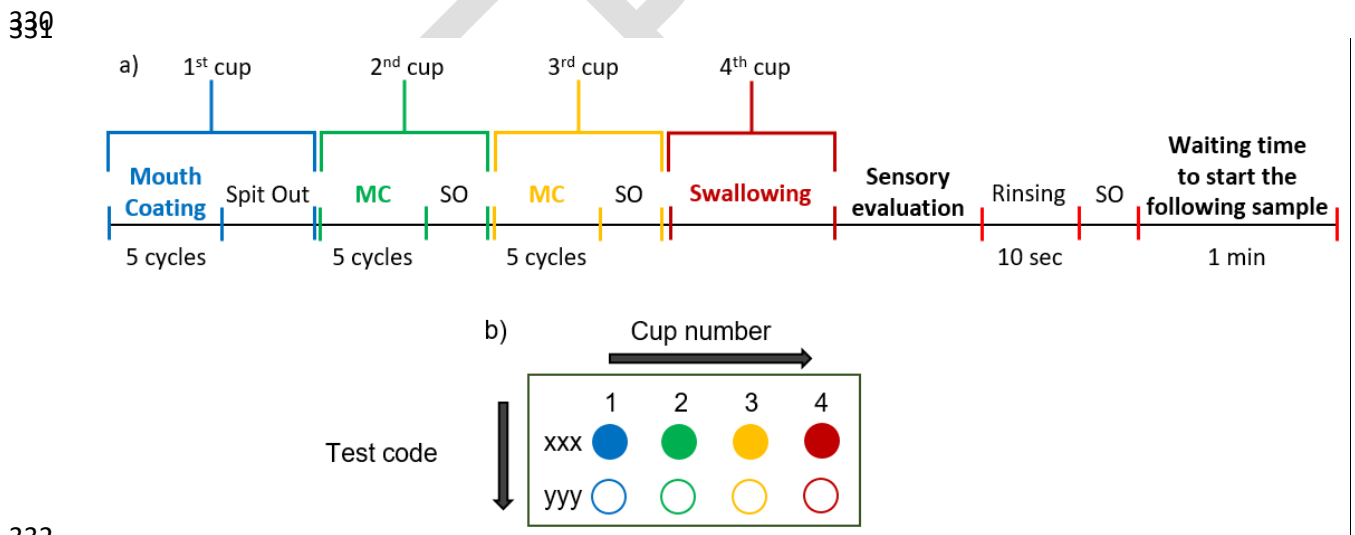
304 The panel was provided with a tablet and trained to use a data acquisition interface called Fizz
305 software (version 2.7; Biosystemes, Couternon, France). For each test, the panelists were asked to

306 rate the intensity of the attribute by moving a slider on a scale from 0 to 10, where 0 indicated "no
 307 residues" and 10 indicated "a lot of residues". During training sessions, contrasting samples were
 308 presented to the panel, allowing them to become familiar with the ends of the notation scale: a full
 309 spoon of water to indicate "no residues" and a full spoon of mashed potatoes to indicate "a lot of
 310 residues".

311
 312 **2.4.2 Mouth Coating Protocol**

313 To evaluate the mouth coating conditions, up to six distinct conditions were tested *in vivo*. The
 314 first condition, referred to as "S" for saliva, involved taking a reference measurement without
 315 altering the natural salivary coating in the volunteers' mouths. To achieve this, volunteers were
 316 asked to rinse their mouths with water, wait for a minute to reach natural oral lubrication, and then
 317 swallow the semi-solid food. The other conditions consisted of drastically altering the natural
 318 lubrication, by performing a series of mouth rinses (Nayak & Carpenter, 2008) with five different
 319 products: water (referred to as "W", Evian Danone, Évian-les-Bains, France), the two types of
 320 NSS formulas ("F_{0.4}" and "F_{1.0}") and the two types of foods ("A_P" and "G_Y").

321 The products were served in 30 mL graduated plastic cups with a lid. The tray carrying the
 322 cups was organized into rows and columns, with each row corresponding to a specific test
 323 composed of four cups (Figure 4.a&b). The test code was labeled at the beginning of each row and
 324 on each cup lid, ensuring easy identification. On each row, the first three cups were identical and
 325 intended for the mouth coating step, while the fourth cup contained the food sample for which
 326 post-swallowing oral residues were investigated. The volunteers were instructed to pour the entire
 327 content of the first cup into their mouth and swirl it around for five seconds, making sure it came
 328 into contact with all the oral mucous membranes, before spitting it out. They were then asked to
 329 repeat this step with the next two cups (Bugarin-Castillo et al., 2024).



332 **Figure 4. Sensory protocol.** a) Description of a testing sequence and rinsing protocol after each evaluation.
 333 The testing sequence includes three mouth rinsing steps and swallowing one full spoon of food.
 334 Abbreviations: (MC) Mouth Coating, (SO) Spit Out. b) Schematic representation of the organization of the
 335 trays on which the samples were presented to the panelists. Each line corresponds to a test, with cups #1
 336 to #3 dedicated to mouth rinsing, followed by cup #4 for sensory evaluation of oral residues.

338 After that, the panelists were asked to pour into their mouth the entire content of the fourth
339 cup, which contained either apple puree or Greek yogurt. They were then asked to evaluate the
340 amount of food residues in their mouth immediately after swallowing. The process was the same
341 for all rows on the tray. To prepare for the next test on the following row, the trained panelists
342 were instructed to rinse their mouths with water for 10 seconds and wait a minute to sufficiently
343 attenuate residual perceptions and recover their natural state of oral lubrication as much as possible
344 (Figure 4.a). For more clarity, all the mouth coating combinations are illustrated in Appendix D.
345

346 2.4.3 Post-Swallowing In Vivo Residue

347 The objective of the sensory study was to investigate and quantify the perception of food
348 residues remaining in the mouth after swallowing, under various conditions of oral lubrication.
349 The lubrication conditions investigated were designed to be as similar as possible to those used in
350 *in vitro* swallowing experiments.

351 To reproduce specific lubrication conditions, the panelists were instructed to rinse their mouths
352 with different samples (details provided in 2.4.2). The volunteers tasted various semi-solid foods
353 and evaluated a single attribute - the amount of post-swallowing oral residues. This attribute was
354 defined based on oral sensations of food remaining in the oral cavity after the first swallow, as
355 well as sensations of requiring multiple swallows to clear the mouth after the first main swallow
356 (Hadde & Chen, 2021).
357

358 2.5 Statistical Analysis

359 The data were analyzed using XLSTAT (v.2023.1.1 Addinsoft, Paris, France) for each variable
360 in the *in vitro* and physico-chemical measurements and for each testing condition in the sensory
361 evaluation. To determine if there were significant differences for each factor, analyses of variance
362 (ANOVA) ($\alpha=0.05$) were applied. The study used the Newman-Keuls multiple comparison test to
363 compare the means of different conditions. If significant differences were found, the variables used
364 in the analysis are useful in explaining the variability of the dependent variable. However, if no
365 significant differences were found, it may indicate that the variables used do not provide significant
366 information to the model or that some covariates that help explain the variability are missing. The
367 performances of the panel (repetition, discrimination and homogeneity) were evaluated by
368 investigating three different independent variables (condition, panelist identity, and replicate) and
369 one order of interaction (panelist*condition).
370

371 3. Results and Discussion

372 The results of this study are divided in three sections: (i) the characterization of the semi-
373 solid foods such as rheology, tribology, and particle size, (ii) the influence of different Natural
374 Salivary Substitutes (NSS) on swallowing apple puree, and (iii) the influence of the properties of
375 apple puree and Greek yogurt on the swallowing performance of a NSS. The second and third parts
376 contain both *in vitro* and *in vivo* approaches.
377

378 3.1. Rheology, Tribology, and Particle Size of Semi-Solid Foods

379 Apple puree (A_P) and Greek yogurt (G_Y) were used as semi-solid foods to assess the
380 performance of various oral lubrication conditions under *in vitro* and *in vivo* configurations. These
381 commercial products have a thick consistency and can be easily swallowed without chewing.

382 Following the classification tests proposed by the International Dysphagia Diet Standardization
383 (IDDSI), A_P is classified as Level 4, while no IDDSI Level applies to G_Y due to its stickiness.
384 These products show different compositions and matrices that can affect their sensory perceptions
385 (Mossaz et al., 2010). Fruit purees have soft and deformable insoluble particles (cell walls of the
386 fruit), which are dispersed into an aqueous solution of sugars, organic acids, and pectic substances
387 called serum (Cepedaand & Gómez, 2002; Espinosa-Muñoz et al., 2013). Yogurt is achieved by
388 acidification of milk with lactic acid bacteria (inducing the coagulation of the protein network),
389 also containing fat and additional stabilizers (Gilbert & Turgeon, 2021).

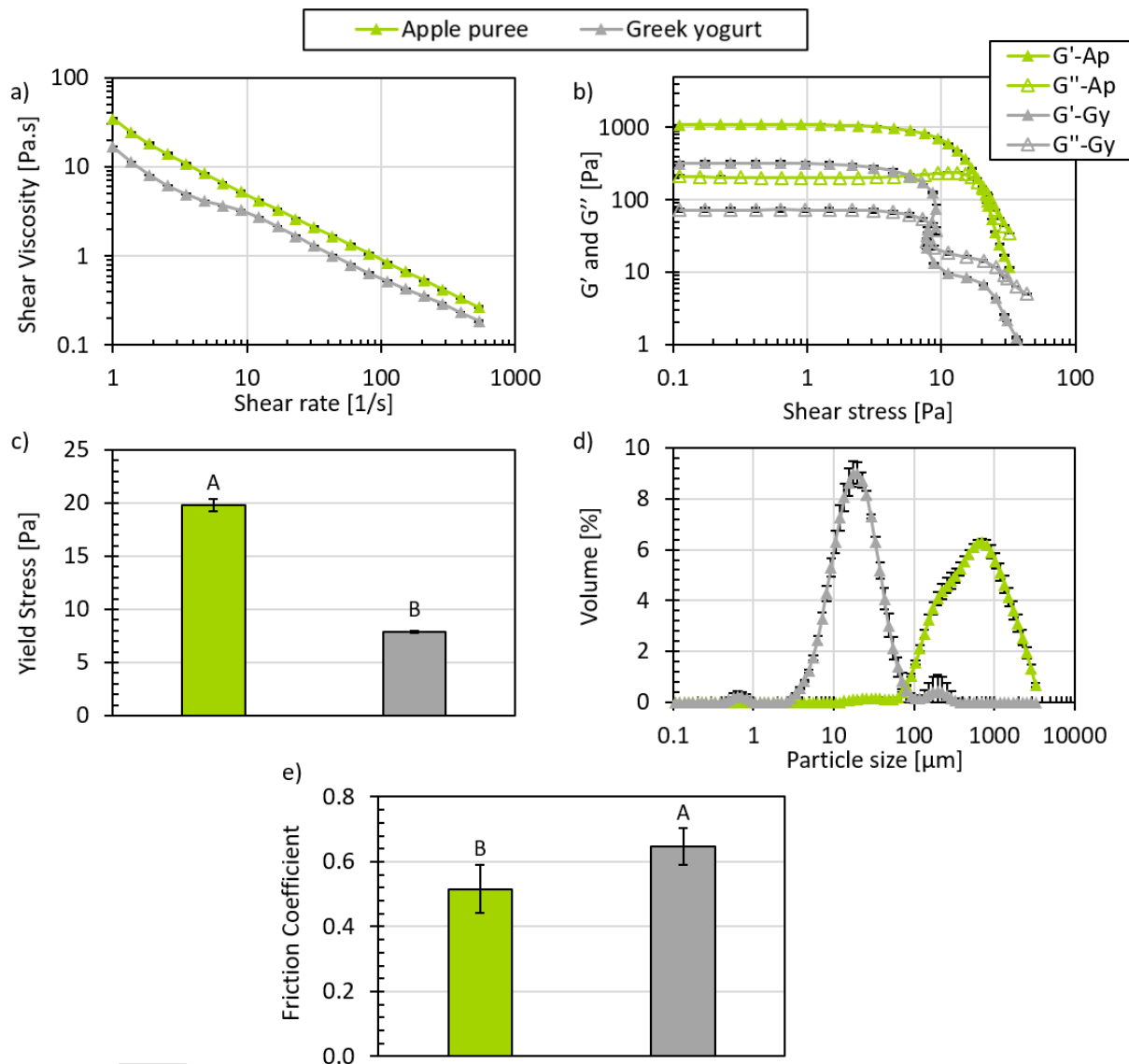
390 Figure 5.a illustrates the average flow curves of apple puree and Greek yogurt. The two
391 food products exhibit shear-thinning behavior, with apple puree approximately twice more viscous
392 than Greek yogurt.

393 The two semi-solid foods demonstrated higher values in storage modulus (G') than in loss
394 modulus (G'') when low shear stress is applied (Figure 5.b). Apple puree shows higher values of
395 G' and G'' than Greek yogurt (approximately four times higher). Moreover, in Figure 5.c, the yield
396 stress (shear stress at the crossover point between storage and loss moduli) was found to be higher
397 for A_P (19.8 ± 0.6 Pa) than for G_Y (7.9 ± 0.1 Pa). This minimal stress required to initiate flow of
398 the products may be related to their structural network (Sun & Gunasekaran, 2009). Comparable
399 orders of magnitude were found in the literature when studying apple puree, establishing that the
400 viscoelastic properties of this food product strongly depend on the insoluble solid content
401 (Espinosa-Muñoz et al., 2013; Leverrier et al., 2016). Greek yogurt's yield stress has been found
402 to fluctuate between 6 and 25 Pa (Costa et al., 2019; Fangary et al., 1999; Mookoolall et al., 2016).

403 In addition, the particle size of the products was also assessed and it is illustrated in Figure
404 5.d. The mean and standard deviation values of $d(0.9)$ were of 1693.3 ± 77.7 μm for A_P and of
405 44.5 ± 7.7 μm in G_Y . For apple puree, the peak was centered at 555.3 μm , resembling an almost
406 monomodal size distribution. In contrast, Greek yogurt showed three peaks: one around 0.5 μm ,
407 the second centered at 18.6 μm and the third between 150 μm and 190 μm . The small peak could
408 be the representation of fat globules, which are usually between 0.2 μm and 1.4 μm (Truong et
409 al., 2014). Moreover, the central peak might be the cluster aggregates of fat droplets interacting
410 with the protein network (mainly whey protein/casein micelle complexes) (Moussier et al., 2019).
411 These clusters can range from 1 to 40 μm (Mellema et al., 2002). Lastly, the third peak showed
412 high variability, probably due to the reorganization between the cluster aggregates such as
413 sedimentation or syneresis, usually fluctuating from 40 μm to macroscale (Mellema et al., 2002;
414 Moussier, 2019).

415
416 Friction coefficients were 0.52 ± 0.1 for A_P and 0.65 ± 0.1 for G_Y . These tribological tests
417 were carried out at constant normal force and shearing velocity. In these conditions, the lubrication
418 regime may then be influenced by various factors related to the rheology and to the structure of
419 food, which plays a role of lubricant at the interface between the tribopairs. The average
420 dimensions of the asperities of the artificial tongue used on the tribometer (around 200 μm in
421 height and 400 μm in diameter – see Appendix B) are above particle size distribution quantified
422 in G_Y , whereas they fall in the range of particle size distribution measured in A_P . For this reason,
423 the shape and rigidity of the particles in A_P are more likely to influence the contact surfaces and
424 the friction phenomena. In addition, some components of the two food products (such as

425 polysaccharides in A_P or fat in G_Y) are likely to affect wettability and spreading on the surfaces of
 426 the tribopairs, with consequences on friction. Liu et al., (2016) stated that the lubrication properties
 427 of foodstuffs containing fat reduce friction due to “fat film patches” formation. This fat film may
 428 lead to hydrophobic interactions between the TMS and the Greek yogurt.
 429



430
 431 *Figure 5. Rheology, tribology and particle size of apple puree and Greek yogurt. a) Shear viscosity of apple*
 432 *puree and Greek yogurt, b) Storage (G') and Loss (G'') Modulus, c) Yield stress, obtained from the overlap*
 433 *between G' and G'' , d) Particle size distribution, e) Friction coefficient. The capital letters above the*
 434 *histogram bars correspond to the groups resulting from multiple comparison tests, indicating statistically*
 435 *significant differences ($p < 0.05$).*

436 3.2 Influence of different Natural Salivary Substitutes on swallowing Apple Puree

437 3.2.1 In vitro Swallowing Assessment

438 To further explore the mechanisms governing the formation of food residues in the oral
 439 cavity after swallowing, an *in vitro* simulator of swallowing was employed. The physiological
 440 relevance of such simulators requires appropriate consideration of oral lubrication. Previous works

441 investigating *in vitro* swallowing of Newtonian (Glycerol) and non-Newtonian (THICKEN UP®
442 CLEAR, Nestle) fluids have shown that using water to lubricate the oral cavity of the SRT
443 simulator was equivalent to not lubricating at all (Marconati, 2019). Due to water's Newtonian
444 properties, attempts at lubrication failed to produce a regular and homogeneous film. To achieve
445 a mouth-coating effect in the SRT and to prevent any leakage from the cavity, a viscoelastic fluid
446 is preferable. With their interesting extensional and shear rheological properties, the flaxseed
447 extract solutions studied in our previous article (Bugarin-Castillo et al., 2024) are interesting
448 candidates for overcoming these aforementioned limitations.

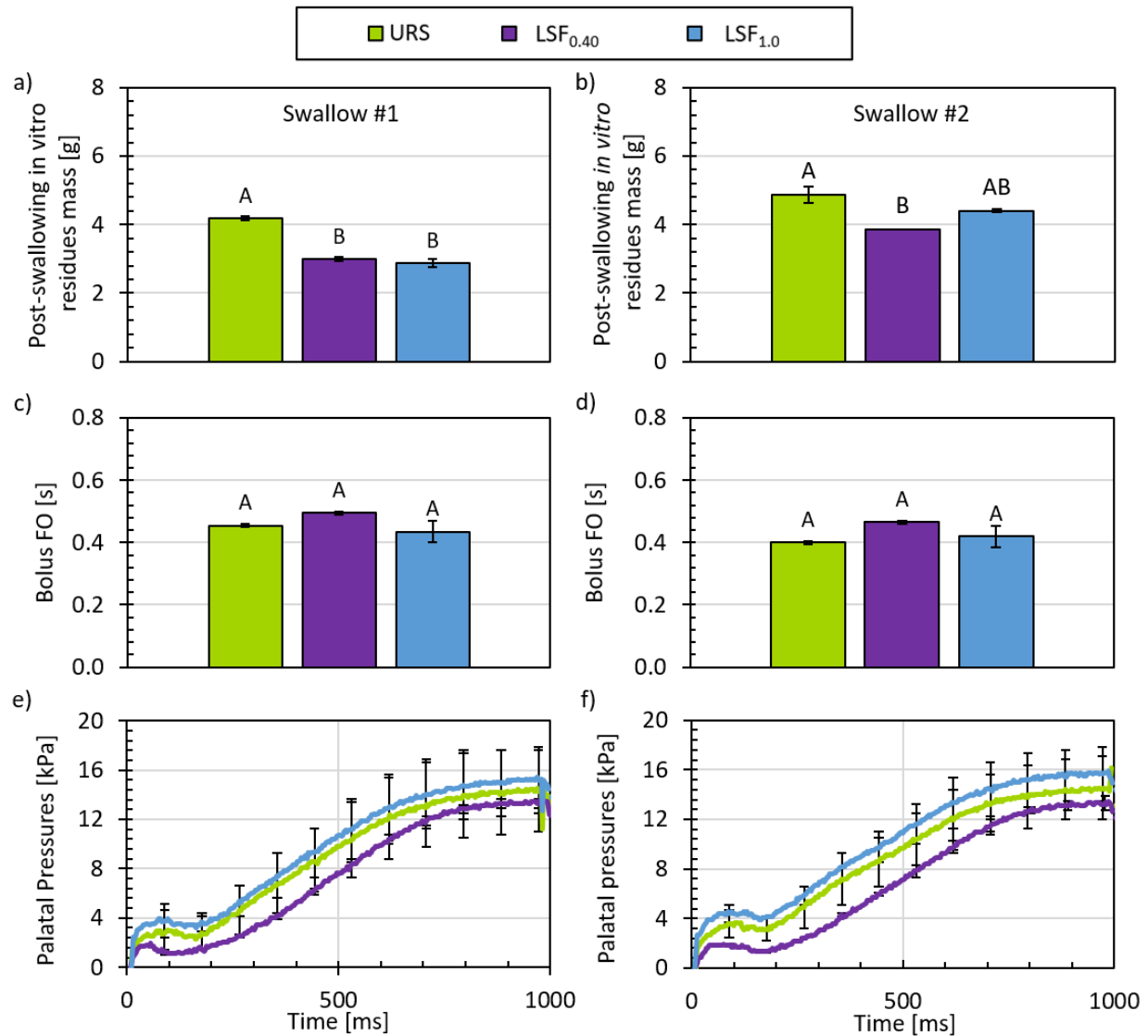
449 Therefore, two concentrations of the NSS were evaluated *in vitro* to determine their ability
450 to reduce post-swallowing *in vitro* residues. To avoid any bias, the objective was to use the same
451 mass of initial coating (2 g) in both the “Lubricated Swallowing” and “Unlubricated Repeated
452 Swallowing” conditions.

453 As illustrated in Figure 6.a&b, the masses of *in vitro* residues remaining after swallows #1
454 and #2 were determined. The statistical analysis of post-swallowing *in vitro* residues showed *P*-
455 values < 0.01 for the variables “condition” (LS and URS) and “swallow” (swallow #1 and #2), and
456 *F*-values of 94.95 and 220.31, respectively. After the first swallow (see Figure 6.a), the URS
457 condition led to a higher mass of *in vitro* residues (4.2 ± 0.1 g) compared to both LS conditions
458 (3.0 ± 0.1 g and 2.9 ± 0.1 g for $F_{0.40}$ and $F_{1.0}$, respectively). The effect of lubrication with NSS is
459 also observed in the residues after swallow #2 (Figure 6.b), with a higher level also observed in
460 URS, when compared to LS with $F_{0.4}$ and $F_{1.0}$. This observation confirms that the different
461 conditions of oral lubrication resulting from swallow #1 have an influence on the residues obtained
462 after swallow #2. Whatever the lubrication condition, the quantity of residues after swallow #2
463 was significantly greater than the corresponding one measured after swallow #1.

464 Moreover, Figure 6.c&d display the bolus FO of the different conditions during swallows
465 #1 and #2. The statistical results from bolus FO revealed no significant difference between URS
466 and LS when comparing both swallows. It has been studied in an *in vitro* model that bolus flow
467 velocity might be mitigated by bolus viscosity, yield stress, and firmness of the products
468 (increasing transit times) (Patel et al., 2020). The similar results obtained in bolus transit times
469 under the three conditions are thus consistent with the close rheological behaviors of the expelled
470 boli provided in Appendix E.

471 Figure 6.e&f display the palatal pressures recorded from the anterior sensor of the SRT
472 during swallows #1 and #2. No significant differences could be observed between the URS and
473 LS($F_{1.0}$) conditions. However, a slightly lower pressure is remarked in the LS($F_{0.4}$) condition in
474 both swallows. Corresponding *in vivo* pressures were estimated in the literature (Moritaka et al.,
475 2018; Nicosia et al., 2000; Steele et al., 2010) using flat pressure sensors, during swallowing of
476 foods with wide ranges of rheological properties: nectar-thick apple juice (0.497 Pa·s at 50 s⁻¹),
477 semi-solid barium, and carrot puree (0.2 Pa·s at 50 s⁻¹). For healthy volunteers, *in vivo* palatal
478 pressures from the anterior flat sensor ranged from 11.2 to 20 kPa with a duration of ~1 s. These
479 orders of magnitude are consistent with the data obtained *in vitro* employing the SRT (Figure
480 6.e&f).

481
482



483
 484 *Figure 6. In vitro swallowing using the Soft-Robotic Tongue under different mouth coatings when testing*
 485 *apple puree as semi-solid food. Average and standard deviation values of post-swallowing in vitro residues*
 486 *after swallow #1 (a) and #2 (b). Average and standard deviation values of Bolus FO time from swallow #1*
 487 *(c) and #2 (d). Average curves of palatal pressures from swallow #1 (e) and #2 (f). The capital letters above*
 488 *the histogram bars correspond to the groups resulting from multiple comparison tests, indicating*
 489 *statistically significant differences ($p < 0.05$). Abbreviations are: (URS) unlubricated repeated swallowing,*
 490 *(LSF_{0.40}) lubricated swallowing using NSS at 0.40 % dry matter, and (LSF_{1.0}) lubricated swallowing using*
 491 *NSS at 1.0 % dry matter.*

492
 493 **3.2.3 In vivo Assessment**

494 The influence of the NSS in the formation of post-swallowing residues was also assessed
 495 *in vivo*. The ANOVA results from the sensory profile showed $F = 4.615$ and $P\text{-value} < 0.01$ for the
 496 conditions tested, $F = 4.381$ and $P\text{-value} < 0.01$ for the panelists and $F = 2.197$ and $P\text{-value} < 0.01$
 497 for the interaction panelist*condition. In this study, all repetitions were not significantly different,

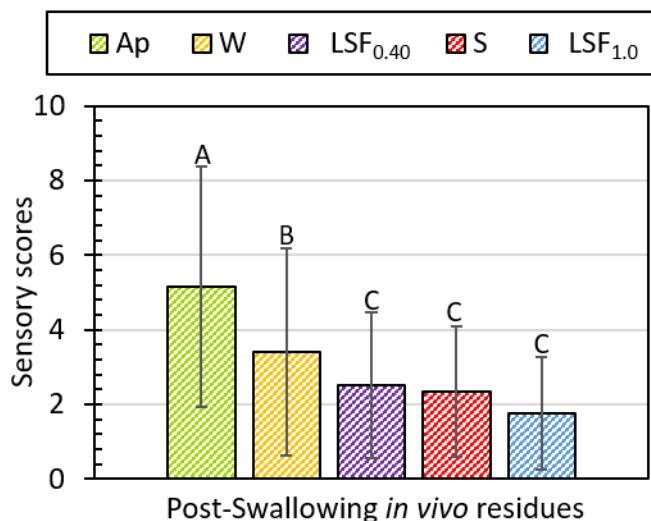
498 participants differentiated all conditions and were consistent in their evaluation
499 (panelist*condition). Overall, the results showed confidence in the panel performance.

500 The results of this evaluation are presented in Figure 7. It is observed that no significant
501 difference in perceived residues were reported between condition *S* (close to natural saliva coating
502 state) and conditions $F_{0.4}$ and $F_{1.0}$ (oral coating with the two NSS candidates). Contrastingly,
503 lubrication with water (*W*) and with A_P led to significantly higher levels of residues (greater for A_P
504 than for *W*).

505 The strong perception of post-swallowing residues when the pre-coating step was with
506 apple puree may be related to the accumulation of particles on the mouth surfaces. Previous studies
507 have put in evidence a relationship between the increase in post-swallowing residue perception
508 and the increase of particle size in apple puree and mashed potatoes (Espinosa-Muñoz et al., 2012;
509 H. W. Park & Yoon, 2018).

510 Moreover, the results obtained after coating the mouth with water can be related to a study
511 conducted by Nayak & Carpenter, (2008), where rinsing the mouth with water reduced the mobile
512 phase of the salivary film. Additionally, Bugarin-Castillo et al., (2024) showed that rinsing the
513 mouth with water results in a reduction of perceptions such as slipperiness and adhesion between
514 the tongue and the palate, when compared to a natural oral lubrication state. This might facilitate
515 food adhesion during swallowing, and affect the perception of post-swallowing residues.

516 In addition, Bugarin-Castillo et al., (2024) showed comparable oral perceptions (mouth
517 hydration, tongue-palate adhesion and slipperiness) between the natural coating state and the
518 coating with the two NSS, which could be related to the significant similarities in post-swallowing
519 *in vivo* residues. However, shear viscosity values and thickness perceptions of $F_{0.4}$ were closer to
520 human saliva than $F_{1.0}$. Therefore, $F_{0.4}$ was chosen for the subsequent sections of the study to avoid
521 biases in the perception of mouth coating thickness.



522
523 *Figure 7. Sensory scores of post-swallowing in vivo residues when testing apple puree as semi-solid food.*
524 *Evaluation of five mouth coatings conditions (panel means). The capital letters above the histogram bars*
525 *correspond to the groups resulting from multiple comparison tests, indicating statistically significant*
526 *differences ($p < 0.05$). Sensory scores on a scale from 0 to 10, where 0 meant "no residues" and 10 meant*
527 *"a lot of residues". Abbreviations are: (Ap) apple puree, (W) water, (LSF_{0.40}) natural salivary substitute at*
528 *0.40 % dry matter, (S) saliva, and (LSF_{1.0}) natural salivary substitute at 1.0 % dry matter.*

529 *3.3 Influence of the properties of apple puree and Greek yogurt on swallowing performance of a*
530 *Natural Salivary Substitute*

3.3.1 In vitro Swallowing Assessment

To further understand the mechanisms of food residue formation during swallowing with *in vitro* and *in vivo* approaches, attention was focused on lubrication by NSS F_{0.4}, seeking to better understand how its performance (in terms of quantity of oral residues) evolves depending on the type of food studied. Greek yogurt was thus also considered, making it possible to account for high changes in composition, structure and rheology when compared to apple puree. The differences between *in vitro* swallowing of Greek yogurt and apple puree were evaluated by ANOVA both for post-swallowing *in vitro* residues and for bolus FO (see Table 1). The variables considered were the type of food product (G_Y or A_P), the lubrication condition (URS or LS), the swallowing number (#1 or #2), and the interaction between lubrication condition and product type. It is observed in Table 1 that there are significant differences between products, lubrication conditions, and swallowing number when comparing post-swallowing *in vitro* residues. Moreover, significant differences are observed for product type and swallowing number in bolus FO.

Table 1. ANOVA results (food product+condition+swallow+panelists* food product). P-values are in bold ($\alpha < 0.05$). Abbreviations: Post-Swallowing (P-S)

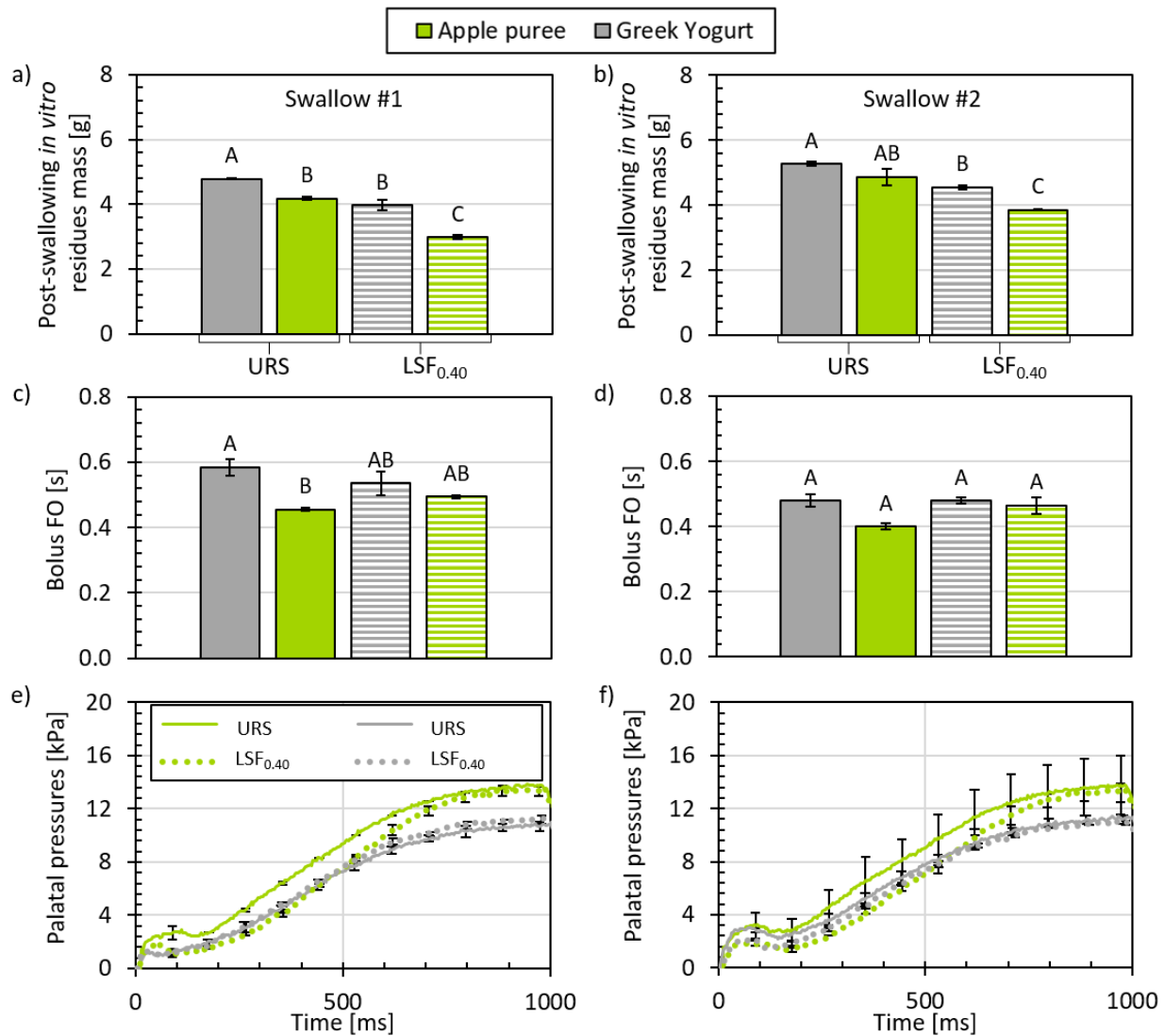
ANOVA	Product		Condition		Swallow		Condition*Product	
	F	Pvalue	F	Pvalue	F	Pvalue	F	Pvalue
P-S <i>in vitro</i> residues	68.803	<0.01	134.503	<0.01	66.27	<0.01	4.196	0.06
Bolus FO	20.948	<0.01	0.902	NS	17.906	<0.01	7.167	0.02

Figure 8.a&b display the averages and standard deviations of post-swallowing *in vitro* residues obtained for Greek yogurt (G_Y) and apple puree (A_P), under lubricated swallowing (LSF_{0.4}) and unlubricated repeated swallowing (URS) conditions. In the URS condition, higher amounts of food residues were reported for G_Y than for A_P. Significant differences were also observed in the LSF_{0.4} condition between the two products, with slightly higher amounts of residues of G_Y than of A_P. Swallow #2 follows similar trends as swallow #1, but with higher amounts of residues, depicting accumulation. Literature suggests that thicker liquids leave higher levels of residues in the pharynx (Marconati, Engmann, et al., 2019). However, in the present study, higher amounts of residues were found for G_Y, which had the lowest yield stress and viscosity.

Figure 8.c&d display the averages and standard deviations of bolus FO in the same conditions. Longer times were reported for G_Y than for A_P to transit through the cavity in swallow #1 (both in URS and LS conditions). Patel et al., (2020) studied yogurt using an *in vitro* model and suggested that yogurt showed a greater dependency over G' (negative slope), creating a weaker structure and affecting the boli flow. Additionally, the product adhesion to the SRT might impact bolus transit time and post-swallowing *in vitro* residues. Lavoisier et al., (2022) evaluated the adhesion force of apple puree and yogurt, both diluted with artificial saliva (with the incorporation of mini tablets) on a Pediatric Soft Robotic Tongue (PSRT). Despite the absence of significant differences, a trend was observed where yogurt (1.11 mN) showed higher adhesion force than apple puree (0.72 mN). Interestingly, during swallow #2 the bolus transit time was similar for all conditions, additionally, the bolus FO tended to decrease between swallow #1 and swallow #2.

Figure 8.e&f show the variations of pressure recorded from the anterior sensor during swallow #1 and #2, respectively. No difference in pressure was observed between LSF_{0.4} or URS for G_Y (solid and dashed grey lines), while some could be reported for A_P (solid and dashed green

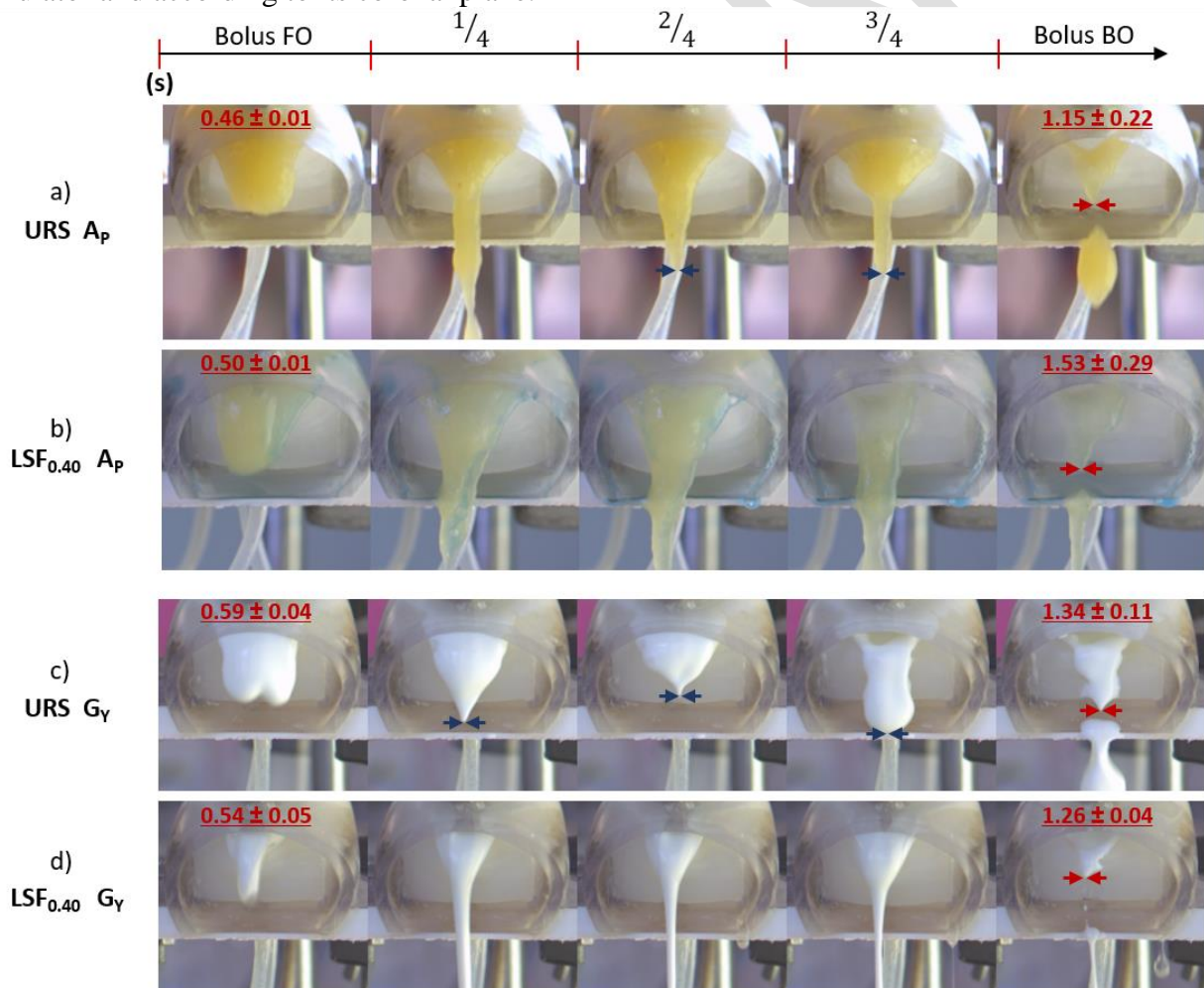
571 lines). The palatal pressures from A_p showed higher pressures for URS during 700 ms when
 572 compared to lubricated conditions $LSF_{0.4}$. Moreover, differences are observed depending on the
 573 type of semi-solid food. Food products with higher viscosities were shown to require higher
 574 swallowing pressures to be propelled from the oral cavity to the pharynx (Marconati, Engmann, et
 575 al., 2019). The results in Figure 8.e&f are consistent with these trends, higher values of palatal
 576 pressures being observed for A_p (13.2 ± 0.7 kPa) than for G_Y (10.3 ± 0.3 kPa) (higher values of
 577 shear viscosity and yield stress in apple puree). Overall, post-swallowing *in vitro* residues were
 578 impacted by oral lubrication, the type of food product and the number of swallows.



579
 580 *Figure 8. In vitro swallowing using the Soft-Robotic Tongue under different mouth coatings when testing*
 581 *apple puree and Greek yogurt as semi-solid foods. Average and standard deviation values of post-*
 582 *swallowing in vitro residues after swallow #1 (a) and #2 (b). Average and standard deviation values of*
 583 *Bolus FO time from swallow #1 (c) and #2 (d). Average curves of palatal pressures from swallow #1 (e)*
 584 *and #2 (f). Dotted lines and dashed bars represent LS condition and solid lines and bars represent URS*
 585 *condition. The capital letters above the histogram bars correspond to the groups resulting from multiple*
 586 *comparison tests, indicating statistically significant differences ($p < 0.05$). Abbreviations are: (URS)*
 587 *unlubricated repeated swallowing, ($LSF_{0.40}$) lubricated swallowing using NSS at 0.40 % dry matter, (Bolus*
 588 *FO) bolus front out.*

589 The shape of the boli expelled from the *in vitro* simulator at the end of a swallowing
 590 sequence was also observed. The impact of the product composition, and of the coating conditions
 591 could thus be studied. Cohesiveness is a term that has been employed in sensory and food
 592 instrumentation approaches, referring to all the forces which participate in maintaining the food
 593 bolus compact, in the form of a single mass without fragmentation. Lately, cohesiveness might be
 594 defined as the food product ability to maintain its structure during stretching (Gallegos et al., 2021).
 595 Conversely, the absence of cohesiveness can in fact lead to fragmentation of the food bolus, which
 596 at the time of swallowing increases the risk of aspiration.

597 Figure 9 aims at providing a qualitative illustration of the evolution of the shape of the boli
 598 expelled from the swallowing simulator during swallow #1 of A_P and G_Y under $LSF_{0.40}$ and URS
 599 conditions. Images from swallow #2 could not be analyzed due to food accumulation which could
 600 introduce bias in comparing conditions. Figure 9 displays representative cases of four distinct
 601 experimental conditions: swallowing of A_P and G_Y combined with URS and $LSF_{0.4}$ coating
 602 conditions “Unlubricated Repeated Swallowing” and “Lubricated Swallowing”. For each test, a
 603 sequence of images was taken under similar shooting conditions, all of them at the back of the
 604 simulator and according to its coronal plane.



605
 606 *Figure 9. Coronal view of the posterior part of the Soft-Robotic Tongue, where the bolus is expelled out of*
 607 *the oral cavity. Images were taken from bolus Front Out (bolus FO) until bolus Back Out (bolus BO).*

608 *Respective times are indicated in red (average and standard deviations in seconds, calculated over all the*
609 *repetitions). Blue arrows indicate bolus fragmentation and red arrows indicate bolus BO.*

610 To appreciate visually the cohesiveness of the food boli, the images provided for each test
611 were taken at a constant frequency (100 fps). The time corresponding to each first image refers to
612 the bolus FO, where the front of the bolus exits the SRT. Additionally, the time corresponding to
613 the last image describes the moment the bolus stops flowing out the *in vitro* cavity breaking in two
614 parts; one flowing down and the other one sticking to the SRT, labeled as bolus BO (bolus Back
615 Out) and represented in red arrows (see Figure 9). Intermediate frames corresponding to $1/4$, $2/4$ and
616 $3/4$ of the duration between FO and BO were displayed.

617 The two first rows of images in Figure 9.a&b represent URS and LS conditions when
618 swallowing apple puree. Under URS (Figure 9.a), the bolus separates in two parts during $t = 2/4$
619 and $t = 3/4$ (dark blue arrows), one part getting suspended to the device and climbing up due to
620 the elasticity, while the second part flows down. In comparison, under LS (Figure 9.b) the bolus
621 continues elongating, preventing fragmentation. This shows that using $F_{0.40}$ provides cohesiveness
622 to the food bolus, preventing bolus fragmentation. The properties of elastic rheology of the NSS
623 may thus have been transmitted to the food bolus during *in vitro* tongue-palate compressions
624 (Bugarin-Castillo et al., 2024). Similar trends were observed in Figure 9.c&d for swallowing
625 experiments with Greek yogurt, with bolus fragmentation in URS compared to continuous flow in
626 the LS. Overall, when coating or not with NSS ($F_{0.40}$), the difference in bolus cohesiveness is
627 visible.

628 It has been stated in the literature that a bolus is perceived safe for swallowing when the
629 cohesive forces between the food and saliva are strong enough to prevent the detachment of
630 particles from the food bolus, preventing fragmentation (Gallegos et al., 2021). In this study, the
631 observations of the shape of the bolus resulting from high-speed camera images indicate that in
632 the presence of $F_{0.40}$, bolus cohesiveness was improved. Such analysis should be extended to the
633 study of other NSS candidates, as well as to the effect of the conditions of mixing between the
634 food and the salivary substitute. To better identify and understand the mechanism by which
635 salivary substitutes promote this cohesiveness of the bolus, two options could be considered,
636 consisting of (i) changing the characteristics of the bolus introduced into the simulator (pre-
637 prepared mixtures with controlled food/saliva ratios), or (ii) varying the amount of salivary
638 substitutes initially coating the internal walls of the simulator. In this way, it would be possible to
639 distinguish the respective contributions (i) of the bulk rheology of the bolus (food diluted with
640 saliva) and (ii) of the film of salivary substitute which envelops the bolus during its flow, on the
641 ability of the bolus to keep a cohesive form.

642

643 3.3.3 *In Vivo* Performance

644 To reflect actual food consumption conditions, the influence of oral coating conditions was
645 as well evaluated *in vivo* using Greek yogurt as food to swallow. The ANOVA results from the
646 panel performance showed $F = 7.683$ and $P\text{-value} < 0.01$ for the conditions tested, $F = 3.666$ and
647 $P\text{-value} < 0.01$ for the panelists and $F = 2.845$ and $P\text{-value} < 0.01$ for the interaction
648 panelist*condition. These results showed confidence in the panel performance.

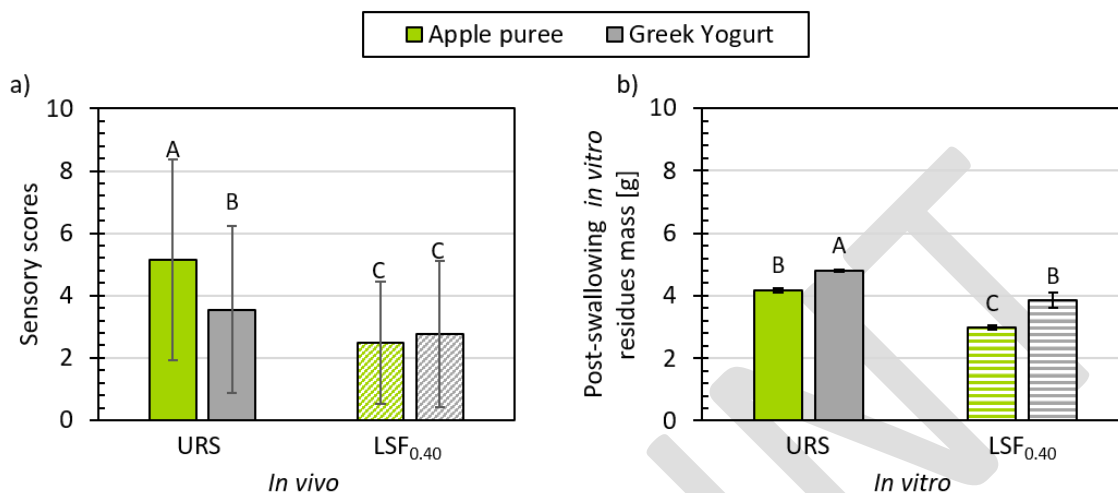
649 Figure 10 illustrates a comparison between (a) *in vivo* and (b) *in vitro* assessments of post-
650 swallowing oral residues of food, for the four combinations of the two foods (apple puree (A_P) and
651 Greek yogurt (G_Y)) with the two lubrication conditions (Unlubricated Repeated Swallowing (URS)
652 and Lubricated Swallowing (LS)). *In vivo* sensations of post-swallowing residues and *in vitro*
653 assessments of the amount of residues were both lower under LS than URS lubrication conditions.
654 However, a difference is observed when the scores of G_Y and A_P are compared *in vitro* and *in vivo*.
655 During *in vitro* measurements, A_P showed lower amounts of oral residues than G_Y in URS and LS.
656 During *in vivo* measurements, the inverted trend was observed in URS, whereas no difference
657 could be reported in LS. The differences between *in vivo* and *in vitro* results may be due to the
658 quantification method. Throughout *in vitro*, post-swallowing residues were determined by
659 objective quantifications of masses. *In vivo*, the perception of post-swallowing residues might be
660 influenced by various factors. For instance, a possible reason for the higher scores obtained *in vivo*
661 from A_P than for G_Y under URS condition could be due to the positive correlation between oral
662 residues and particle size (Aguayo-Mendoza et al., 2021; Espinosa-Muñoz et al., 2012; Marconati,
663 Lopez, et al., 2019). Participants accumulated apple puree particles from the three pre-coating steps
664 performed, potentially enhancing their ability to detect particles in the mouth (graininess) and
665 increasing their perception to post-swallowing residues. An additional cause for the lower scores
666 of G_Y under *in vivo* URS might be due to its sourness, which is characteristic of fermented dairy
667 products (Desai et al., 2013). Acid stimulation of saliva is due to its buffer capacity, where saliva
668 increases its volume to reduce acidity in the mouth (Lugaz et al., 2005). The perception of sourness
669 has been related to the type and concentration of acid used, as sourness is not only related to pH,
670 but also to titratable acidity (Muñoz-González et al., 2018). Literature shows that A_P and G_Y pH
671 values are within similar ranges ($A_P=3.4-4.8$ and $G_Y=4.4-4.9$). Nevertheless, the percentage of
672 lactic acid in G_Y (3.3-5.7%) is higher than that of malic acid in A_P (0.4-0.82%) (Brisset, 2012;
673 Desai et al., 2013; Lan et al., 2022; Picouet et al., 2009; Viquez-Barrantes et al., 2023). The
674 repeated steps of mouth rinsing performed by the participants for G_Y in URS conditions might
675 have led to an increase in saliva flow stimulation (when compared to A_P case). One could thus
676 have expected lower perceptions of residues due to dilution effects of saliva.

677 In addition, under $LSF_{0.40}$ participants perceived lower levels of post-swallowing residues
678 as compared to those under URS. Also they perceived similar results for both apple puree and
679 Greek yogurt. Under $LSF_{0.40}$, participants pre-rinsed their mouths three times with NSS and had
680 only one exposure to the food product at the time of swallowing, suggesting that less saliva was
681 produced due to acidic stimulation. Despite the lower dilution effect that saliva could have created,
682 the condition $LSF_{0.40}$ still exhibited lower post-swallowing residues than URS. This suggests that
683 saliva's ability to reduce post-swallowing food residues depends not only on its quantity but also
684 on its physical-chemical properties. It has been stated that stimulated saliva has lower viscosity,
685 viscoelasticity, and mucin content and leads to higher friction than unstimulated saliva (Sarkar et
686 al., 2019). Thus, these results might be influenced by the higher elasticity resemblance of the NSS
687 to unstimulated saliva observed in our previous study (Bugarin-Castillo et al., 2024).

688 These findings suggest further work on testing the NSS in an environment where saliva
689 stimulation will not interfere in the perception of post-swallowing residues. This work emphasizes

690 the importance of *in vitro* devices able to simulate unhealthy conditions to encourage new ways of
691 developing personalized food for specific swallowing disorders.

692



693
694 *Figure 10. Comparison in vivo and in vitro of post-swallowing residues when testing apple puree and Greek*
695 *yogurt. a) “In vivo” sensory scores of perception of residues in mouth on a scale from 0 to 10, where 0*
696 *meant “no residues” and 10 meant “a lot of residues”, b) “In vitro” results from Soft-Robotic Tongue. The*
697 *capital letters above the histogram bars correspond to the groups resulting from multiple comparison tests,*
698 *indicating statistically significant differences (p < 0.05). Abbreviations are: (URS) unlubricated repeated*
699 *swallowing and (LSF_{0.40}) lubricated swallowing using NSS at 0.40 % dry matter.*

700 4. Conclusion and Next Steps

701 In this study, *in vitro* and *in vivo* approaches were employed to investigate the performance
702 of natural salivary substitutes obtained from flaxseed extracts, to help swallowing food. The *in*
703 *vitro* method employed a soft actuator, able to reproduce human tongue surface properties,
704 displacements and pressures. For *in vivo* evaluations, healthy volunteers followed a new protocol
705 to imitate lubricated and unlubricated conditions. From this study, oral food residues were
706 influenced by lubrication and food matrix composition—shear viscosity and yield stress were
707 related to higher palatal pressures *in vitro*. Apple puree and Greek yogurt were considered. For
708 both of them, *in vitro* and *in vivo* results show that oral coating with flaxseed extracts at 0.40 %
709 dry matter makes it possible to reduce the amount of post-swallowing oral residues; suggesting an
710 increase in bolus moisture and a more compact bolus. Such promising reduction of oral residues
711 suggests that this salivary substitute should be tested clinically to confirm whether it can help
712 promoting food oral processing for xerostomic patients. Apple puree and Greek yogurt were found
713 to be noticeably different in terms of composition, rheology, tribology, or even of structure. In
714 future work, the emphasis may be placed on model semi-solid foods produced or adapted in the
715 laboratory. A reduced number of controlled targeted properties could thus be selected and varied.
716 Such an approach could help understanding the role of these properties on the interactions between
717 semi-solid foods and salivary substitutes during swallowing.

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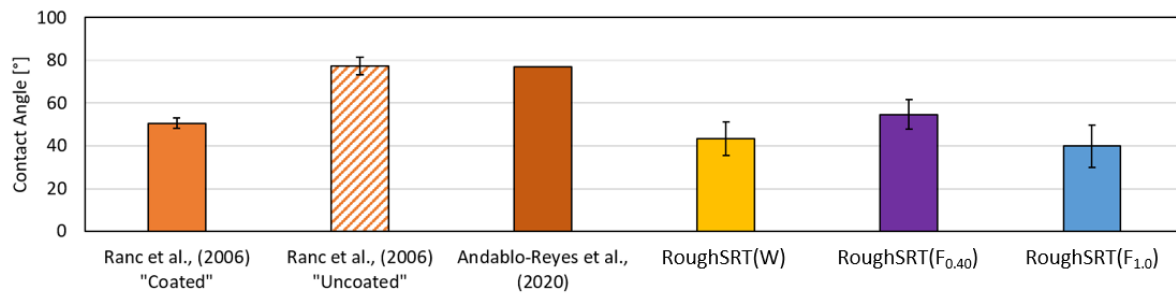
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971 **Appendix / Supplementary Data**

972

973 *Appendix A - Wettability of the Soft-Robotic Tongue*

974 The contact angle of water, $F_{0.40}$, and $F_{1.0}$ were tested on the roughness of the *in vitro* tongue
975 (RoughSRT). The values are compared with *ex vivo* data trials using pig tongues. The results of
976 two studies are illustrated. Ranc et al., (2006) evaluated the contact angle of cleaned tongues. Half
977 of the samples were assessed dried “uncoated”, and the other half were plunged into fresh human
978 saliva for 45 min, called “coated”. They observed that the contact angle of water reduced when the
979 tongue was “coated”. In addition, Andablo-Reyes et al., (2020) evaluated the static water contact
980 angle on fresh pig tongues. Similar values from *ex vivo* are reached when adding roughness to the
981 SRT and by evaluating water and NSS.



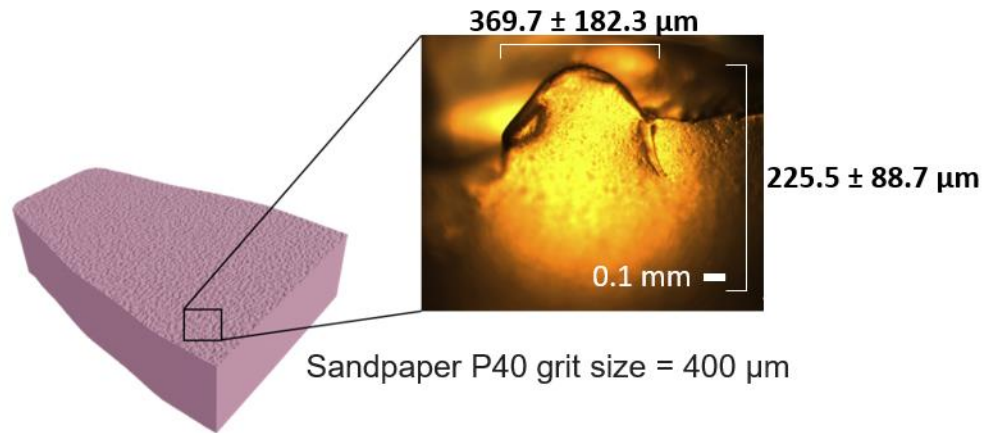
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Figure A.1. Contact angle of the Soft-Robotic Tongue compared with *in vivo* data.

984 *Appendix B - In Vitro Papillae Dimensions of the Soft-Robotic Tongue*

985 The *in vitro* dimensions of the asperities on the surface of the SRT were tested using optical
986 microscopy. It was obtained $369.7 \pm 182.3 \mu\text{m}$ of diameter and $225.5 \pm 88.7 \mu\text{m}$ of height. An
987 example of the view of the SRT surface is represented. Values are comparable with *in vivo* filiform
988 data from the literature; diameter = $355 \mu\text{m}$ and height = $195 \mu\text{m}$ (Andablo-Reyes et al., 2020).



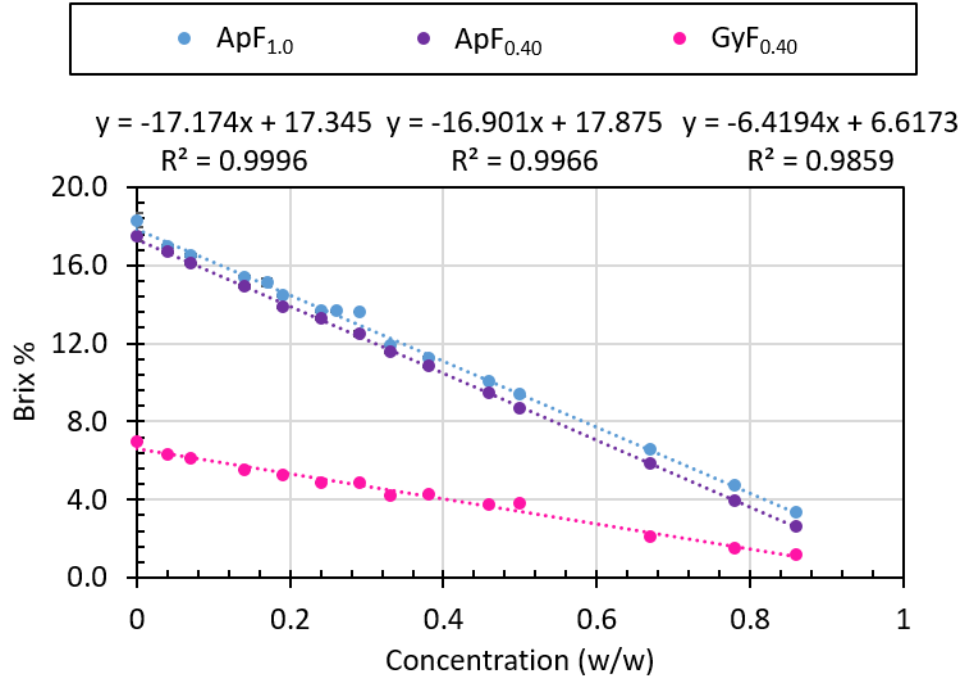
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Figure B.1. *In vitro* papillae dimensions of the Soft-robotic Tongue.

PREPRINT

991 *Appendix C - Degree Brix Calibration Curves*

992 The refractometer was calibrated to ensure a linear relationship between Brix percentage
993 and the mixing ratio of different combinations of flaxseed extracts and semi-solid foods. The
994 calibration curves are in a range of concentrations between 0 to 0.86 w/w. Data shows good
995 agreement with $R^2 = 0.9996$ for Ap(F_{1.0}), $R^2 = 0.9966$ for Ap(F_{0.4}) and $R^2 = 0.9859$ for Gy(F_{0.4}).



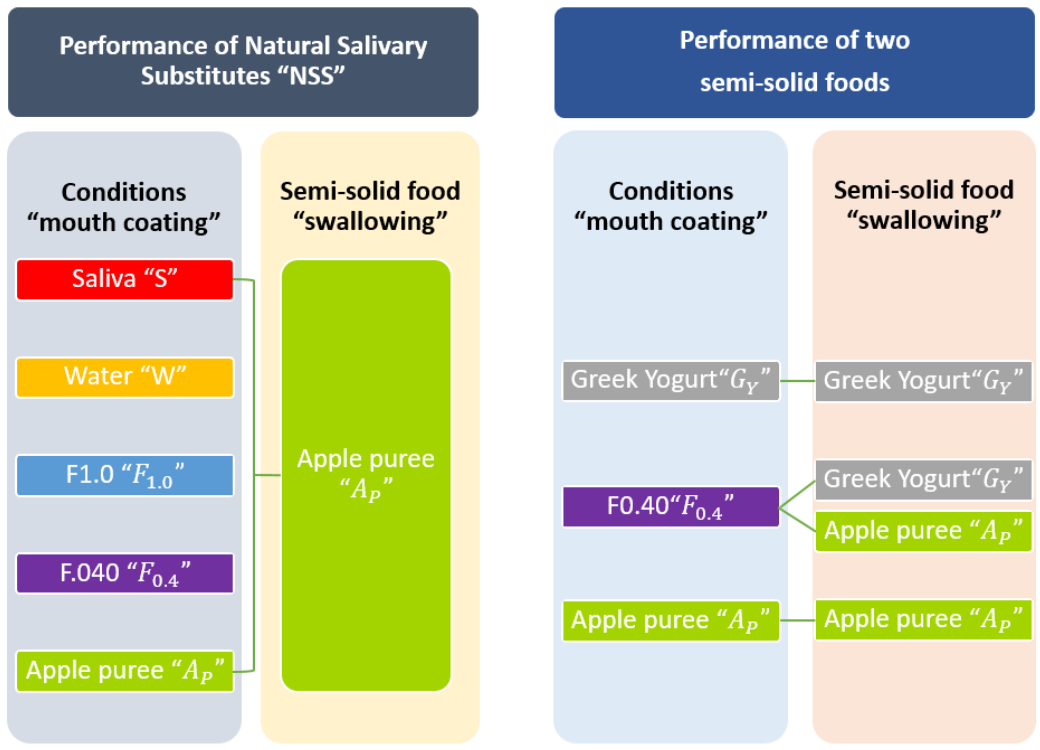
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997 *Figure C.1. Brix calibration curves of apple puree and Greek yogurt using natural salivary substitutes at 0.40 % and 1.0 % dry*
998 *matter.*

PREVIEW

999 *Appendix D - Mouth Coating Combinations*

1000 The study analyzed six different mouth coating conditions and two types of food to be
 1001 swallowed. In total, nine different combinations were investigated. To evaluate the performance
 1002 of natural salivary substitutes formulated from flaxseed extracts, only apple puree was used as
 1003 semi-solid food to swallow. This decision was based on the presence of particles in apple puree
 1004 which makes easier the evaluation of residues perception. Then, the performance of a particular
 1005 NSS ($F_{0.4}$) was focused on with swallowing experiments using two semi-solid foods (apple puree
 1006 and Greek yogurt). Three different mouth coating conditions were tested. The "LS" condition was
 1007 assessed when using $F_{0.40}$ as a mouth coating, while the "URS" condition was evaluated by using
 1008 Greek yogurt or apple puree.



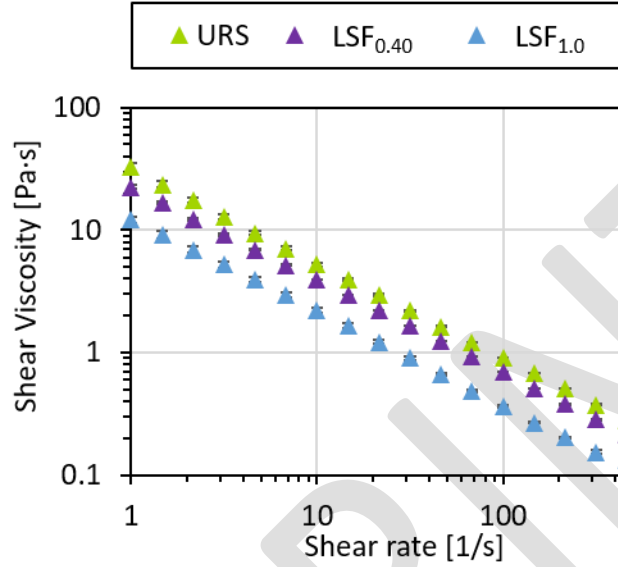
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Figure D.1. Mouth coating combinations.

1011 *Appendix E - Mouth Coating Combinations - Bolus Viscosity Swallow #1 with Apple Puree*

1012 The bolus viscosity after *in vitro* swallowing was characterized and it is presented in Figure
1013 E.1. These results correspond to section 3.2, where the influence of natural salivary substitutes was
1014 compared when swallowing apple puree.
1015



1016

1017 *Figure E.1. Bolus viscosity from swallow #1 with apple puree. Abbreviations are: (URS) unlubricated repeated swallowing,*
1018 *(LSF_{0.40}) lubricated swallowing using NSS at 0.40 % dry matter, and (LSF_{1.0}) lubricated swallowing using NSS at 1.0 % dry matter.*