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

Yurixy BUGARIN-CASTILLO^a, Pascale BOU FADEL^a, Anne SAINT-EVE^a, Marco RAMAIOLI^a, Vincent MATHIEU^{a,b,*}

^a Université Paris-Saclay, INRAE, AgroParisTech, UMR SayFood, 91120, Palaiseau, France

^b INRAE, Institut Agro, STLO, 35042 Rennes, France

*Corresponding Author

Vincent Mathieu

Email: vincent.mathieu@inrae.fr

Paris-Saclay Food and Bio-product Engineering Research Unit (SayFood UMR 782)

University Paris Saclay, INRAE, AgroParisTech

22, place de l'Agronomie

91120 Palaiseau, France

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Abstract

Flaxseed extracts have extensional and shear rheological properties close to those of saliva, making them promising candidates as natural salivary substitutes (NSS) to manage xerostomia. The performance of such NSSs was evaluated by comparing their *in vitro* and *in vivo* behaviors during swallowing of two semi-solid foods with different composition, structure and rheology. The oral phase of swallowing was simulated *in vitro* with an innovative soft robotic model while sensory evaluations were performed with a healthy cohort ($n=16$) to assess the potential of the NSSs for reducing the amounts of oral residues. Flaxseed extract with 0.40 % dry matter showed promising performance, with low amounts of oral residues reported both *in vitro* and *in vivo*, and with a bolus that was not prone to undesired fragmentation. The novel methodology presented in this study could be used in the future to prescreen other salivary substitutes or food textures adapted for xerostomia.

Industrial relevance: This work opens up perspectives for meeting the expectations and needs of growing populations affected by swallowing disorders, and in particular by xerostomia. The development of natural saliva substitutes should make it possible to recover a state of oral lubrication which ensures oral comfort, safe swallowing, and which limits the problems of malnutrition resulting from dysphagia.

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

1 **1. Introduction**

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

11 Salivary substitutes (SS) are effective treatments for xerostomia and work by coating oral
12 surfaces and imitating saliva lubrication (Hu et al., 2021). Studies have appraised SS concerning
13 oral comfort, wettability, rheology, and lubricity (Bugarin-Castillo et al., 2024; Hu et al., 2021;
14 Pailler-Mattei et al., 2015; See et al., 2019; Shahdad et al., 2005; Spirk et al., 2019; Vinke et al.,
15 2020). These characterizations are essential to imitate saliva lubrication, thickness, and
16 moisturizing properties. The assessment of SS is generally achieved *in vivo* using questionnaires
17 (Hahnel et al., 2009). Besides, instrumental approaches have been proposed to evaluate lubricity
18 and wettability using *ex vivo* tissues to approach human conditions (Vinke et al., 2018).

19 However, the performance of salivary substitutes is not frequently evaluated during food oral
20 processing (FOP) (Piaton et al., 2021). It is well established that a deficiency in saliva during
21 FOP can affect bolus formation and lead to a measurable increase in post-swallowing oral
22 residues (Wirth et al., 2016). Post-swallowing oral residues are described as the amount of food
23 in the oral cavity after the main swallow and the willingness to clean it with multiple swallows
24 (Hadde & Chen, 2021). The accumulation of residues promotes oral discomfort, decreases food
25 palatability, and can cause post-swallow aspiration (Lavoisier et al., 2021). In addition, in the
26 cases of neurological impairments or sarcopenia, poor handling of oral residues might increase
27 the risk of choking (Gallegos et al., 2021). Furthermore, bolus formation is an essential and
28 complex step in the preparation of the oral phase of swallowing. It includes mixing and hydrating
29 food particles with saliva to increase cohesion until a compact bolus is able to flow through the
30 pharynx (Avila-Sierra et al., 2024; Fujiso et al., 2018; Gallegos et al., 2021; Nishinari et al.,
31 2024). During bolus formation, saliva also impacts the perception of food texture and taste. In
32 particular, the bolus extensional properties have been shown in both *in vitro* (Marconati &
33 Ramaioli, 2020) and *in vivo* conditions (Hadde et al., 2019) to foster bolus compactness. Given
34 that the extensional properties of food bolus are the direct consequence of those of saliva,
35 xerostomia could, in some cases, impair the compactness of the bolus.

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

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

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

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

64 **2. Materials & Methods**

65 *2.1. Natural Salivary Substitute (NSS)*

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

76 *2.2. Characterization of Semi-Solid Foods*

77 Apple puree (Andros, Biars-sur-Cère, France) and Greek yogurt (Yaourt à la grecque,
78 Cora, Croissy-Beaubourg, France) were used for both *in vitro* and *in vivo* tests due to their thick
79 consistencies generally associated with ease of swallowing (Penman & Thomson, 1998).
80 Additionally, apple puree and yogurt have been previously used in research involving a pediatric
81 swallowing soft-actuator (Lavoisier et al., 2022).

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

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

86 The rheological behavior of the semi-solid foods was characterized using a Physica
87 MCR-702 rheometer (Anton Paar GmbH, Graz, Austria). For apple puree, shear viscosity was
88 measured with a Couette geometry between 1 and 500 s⁻¹ (d = 18 mm; gap = 5 mm) at 20 °C.
89 For Greek yogurt, shear viscosity was determined with a sand-blasted plate-plate geometry
90 PP50S (d = 50 mm; gap = 1 mm) ranging between 1 to 500 s⁻¹ at 20 °C. An amplitude sweep was
91 performed for both products at a constant angular frequency of 10 rad/s, varying the strain from
92 0.01 to 1000% at 20 °C. In addition, the yield stress was obtained as the stress at the crossing
93 point of G' and G'' based on the method of Espinosa-Muñoz et al., (2013). The measurements
94 were performed in triplicates.

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

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

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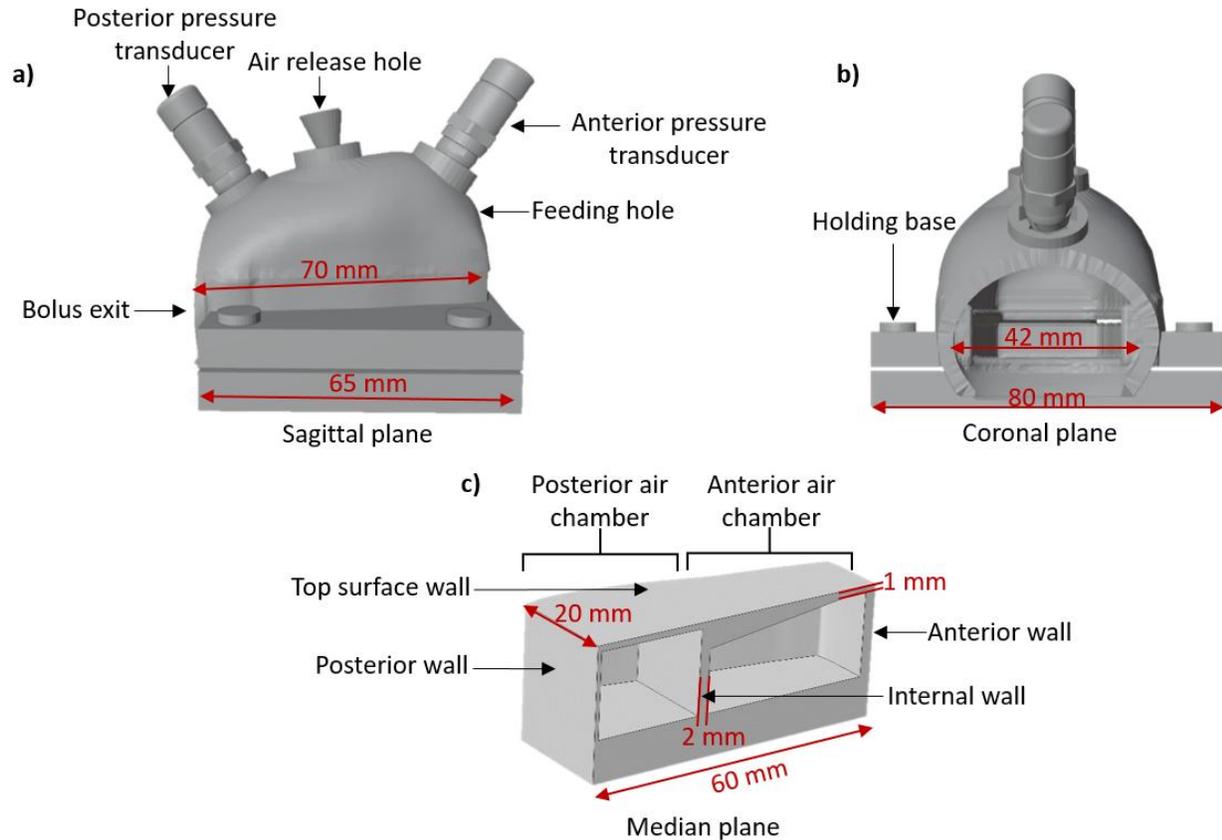
111 2.3. *In Vitro* Soft-Robotic Tongue (SRT)

112 The *in vitro* setup utilized in this study was proposed by Marconati et al., (2020). This *in*
113 *vitro* soft-robotic tongue has been adapted to simulate pediatric swallowing (Avila-Sierra et al.,
114 2023; Lavoisier et al., 2022). The 3D model is based on CT scans of the oral airway of a healthy
115 adult (Xi & Longest, 2007). A comprehensive description of the actuation patterns was reported
116 by Lavoisier et al., (2022). The adult size SRT presented in this study was derived from the
117 original model (Marconati et al., 2020), with minor modifications described in the following
118 sections.

119

120 2.3.1. 3D Oral Cavity

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



130
 131 *Figure 1. Diagram and dimensions of the 3D oral cavity and of the soft-robotic in vitro tongue (SRT). a)*
 132 *Sagittal plane of the 3D oral cavity, b) Coronal plane of the 3D oral cavity, c) 3D view of the soft-robotic*
 133 *tongue proposed by Marconati et al., (2020) and used in this study.*

134 **2.3.2. Soft-Robotic Tongue (SRT)**

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

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

145

146 **2.3.3. Wettability and Papillae Dimensions of the SRT**

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

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

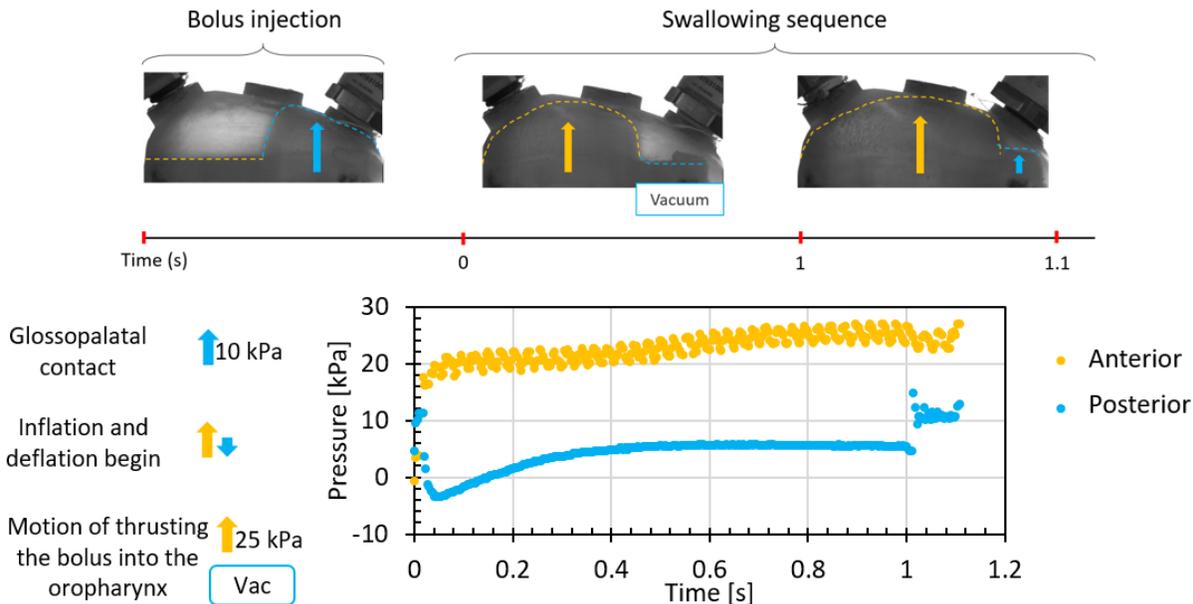
154 processed with ImageJ® and the contact angle plugin (Avila Sierra et al., 2023). All
155 measurements were repeated in triplicate.

156 The topography of the SRT was characterized by optical microscopy using an Olympus
157 BX51 (Olympus, Tokyo, Japan) and a 10x objective. The samples were sliced on a thin layer to
158 measure the height and diameter of the *in vitro* papillae. All measurements were repeated five
159 times. Results are detailed in Figure A 1 and Figure A 2.

160
161 **2.3.4. Swallowing Sequence**

162 The design of the *in vitro* tongue allows the independent displacement of the posterior
163 and anterior chambers by applying different pressures, determined based on *in vivo* data. The *in*
164 *vitro* swallowing sequence established by Marconati et al., (2020) was used in this study. The
165 schematic representation of the timeline of this sequence is provided in Figure 2. The bolus is
166 injected in the oral cavity through the feeding hole located in its front, while a pressure of 10 kPa
167 is imposed in the posterior chamber in order to allow bolus holding (consistently with *in vivo*
168 glossopalatal pressures) (Fujiwara et al., 2014). The swallowing sequence then starts ($t = 0$ s)
169 with two simultaneous actions: the inflation of the anterior chamber (25 kPa) and the deflation of
170 the posterior chamber with an imposed vacuum of -5 kPa. The pressure in the anterior chamber
171 (25 kPa) was set based on tongue-palate maximal pressure values available in the literature
172 (around 60 kPa), attenuated by a factor of 40% as the foods considered here have a low viscosity
173 and do not require intense mechanical efforts to flow (Fei et al., 2013; J.-S. Park et al., 2016). At
174 $t = 0.6$ s, the maximum pressure in the anterior chamber is reached, consistently with *in vivo*
175 timings of the oral phase of swallowing for liquids (Dodds et al., 1990; Zhang et al., 2012).
176 After $t = 1.1$ s, pressure was no longer applied to either chamber, causing both chambers to
177 return to their resting positions.

178



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

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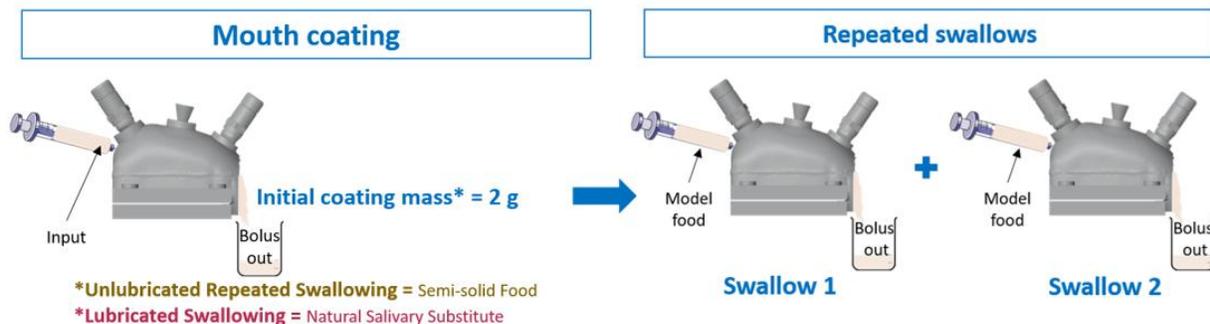
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2.3.5. In Vitro Swallowing Protocol

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

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

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



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

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2.3.6. Measured Variables

2.3.6.1. Post-Swallowing In Vitro Residue (g)

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

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

221 For LS condition, the method had to be adapted because residues collected after each
222 swallow consist of a mixture of semi-solid food and NSS. The NSS concentration in the samples
223 collected at the exit of the device was quantified using a refractometer (ATAGO®, Tokyo,
224 Japan). The refractometer was calibrated to confirm a linear relation between the obtained Brix
225 degrees and the dilution rate of semi-solid foods with flaxseed extracts. The calibration curves
226 are reported in Figure A 3 at concentrations between 0 to 0.86 w/w. The Brix degree measured on
227 samples expelled after swallows #1 and #2 were then converted into the mass of semi-solid food
228 ejected during each swallow. The mass differences between semi-solid food injected and bolus
229 expelled could thus be used to characterize the residual mass of semi-solid food in the oral cavity
230 at the end of each swallow.

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232 2.3.6.2. *In Vitro Bolus Transit Time (s)*

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

242

243 2.3.6.3. *Palatal Pressure (kPa)*

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

252

253 2.4 *Sensory Evaluation*

254 2.4.1 *Panel*

255 The present sensory study followed the ethical standards defined by the Declaration of
256 Helsinki. A panel of 16 healthy volunteers (9 women and 7 men, 23-60 years old) was recruited
257 based on motivation, availability and food allergies. The study comprised four sessions
258 (including two for training and two for evaluation) of 40 min each. The study aimed to evaluate
259 the impact of different oral lubrication conditions on the amount of oral residues perceived after
260 swallowing A_P or G_Y . At the end of the sensory study, the panelists were compensated for their
261 participation. Panelists were instructed to refrain from eating, drinking or smoking for at least an
262 hour prior to the sessions. The study took place in a sensory laboratory featuring 16 individual
263 tasting booths, each equipped with a sink. The booths were air-conditioned (20°C) and
264 illuminated with red lighting to reduce visual biases. For the evaluation sessions, panelists were
265 presented with different combinations of oral coating conditions and of semi-solid foods, which

266 were arranged in a balanced order across participants using a Latin square and divided into three
267 replicate blocks.

268 The panel was provided with a tablet and trained to use a data acquisition interface called
269 Fizz software (version 2.7; Biosystemes, Couternon, France). For each test, the panelists were
270 asked to rate the intensity of the attribute by moving a slider on a scale from 0 to 10, where 0
271 indicated "no residues" and 10 indicated "a lot of residues". During training sessions, contrasting
272 samples were presented to the panel, allowing them to become familiar with the ends of the
273 notation scale: a full spoon of water to indicate "no residues" and a full spoon of mashed
274 potatoes to indicate "a lot of residues".

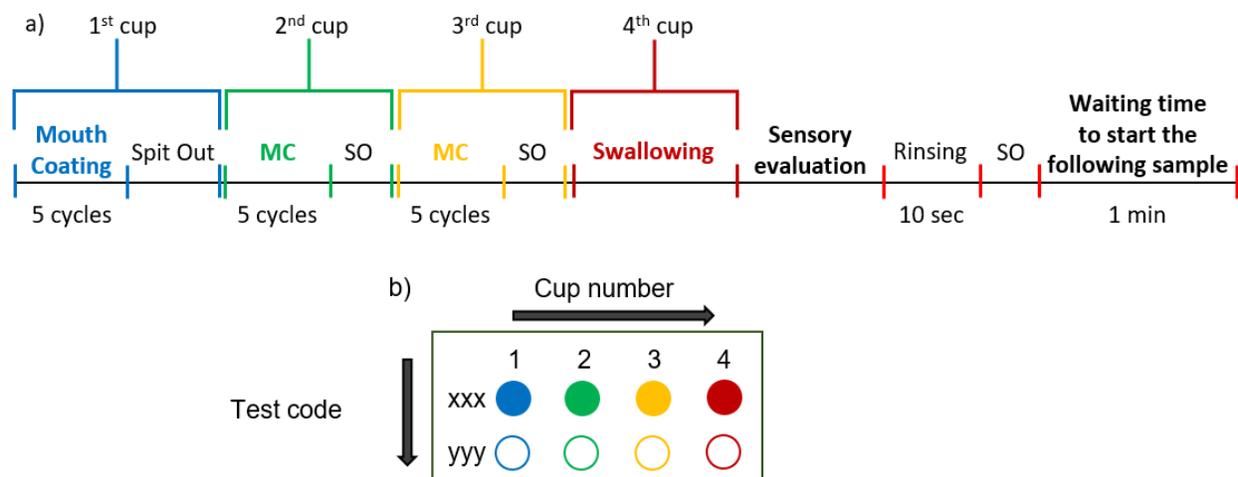
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276 2.4.2 Mouth Coating Protocol

277 To evaluate the mouth coating conditions, up to six distinct conditions were tested *in vivo*.
278 The first condition, referred to as "S" for saliva, involved taking a reference measurement
279 without altering the natural salivary coating in the volunteers' mouths. To achieve this,
280 volunteers were asked to rinse their mouths with water, wait for a minute to reach natural oral
281 lubrication, and then swallow the semi-solid food. The other conditions consisted of drastically
282 altering the natural lubrication, by performing a series of mouth rinses (Nayak & Carpenter,
283 2008) with five different products: water (referred to as "W", Evian Danone, Évian-les-Bains,
284 France), the two types of NSS formulas (" $F_{0.4}$ " and " $F_{1.0}$ ") and the two types of foods (" A_P " and
285 " G_Y ").

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

295



297
 298 *Figure 4. Sensory protocol. a) Description of a testing sequence and rinsing protocol after each*
 299 *evaluation. The testing sequence includes three mouth rinsing steps and swallowing one full spoon of*
 300 *food. Abbreviations: (MC) Mouth Coating, (SO) Spit Out. b) Schematic representation of the organization*
 301 *of the trays on which the samples were presented to the panelists. Each line corresponds to a test, with*
 302 *cups #1 to #3 dedicated to mouth rinsing, followed by cup #4 for sensory evaluation of oral residues.*

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

311 2.4.3 Post-Swallowing In Vivo Residue

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

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

322 2.5 Statistical Analysis

323 The data were analyzed using XLSTAT (v.2023.1.1 Addinsoft, Paris, France) for each
 324 variable in the *in vitro* and physico-chemical measurements and for each testing condition in the
 325 sensory evaluation. To determine if there were significant differences for each factor, analyses of
 326 variance (ANOVA) ($\alpha=0.05$) were applied. The study used the Newman-Keuls multiple
 327 comparison test to compare the means of different conditions. If significant differences were
 328
 329

330 found, the variables used in the analysis are useful in explaining the variability of the dependent
331 variable. However, if no significant differences were found, it may indicate that the variables
332 used do not provide significant information to the model or that some covariates that help
333 explain the variability are missing. The performances of the panel (repetition, discrimination and
334 homogeneity) were evaluated by investigating three different independent variables (condition,
335 panelist identity, and replicate) and one order of interaction (panelist*condition).

336

337 **3. Results and Discussion**

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

343

344 *3.1. Rheology, Tribology, and Particle Size of Semi-Solid Foods*

345 Apple puree (A_P) and Greek yogurt (G_Y) were used as semi-solid foods to assess the
346 performance of various oral lubrication conditions under *in vitro* and *in vivo* configurations.
347 These commercial products have a thick consistency and can be easily swallowed without
348 chewing. Following the classification tests proposed by the International Dysphagia Diet
349 Standardization (IDDSI), A_P is classified as Level 4, while no IDDSI Level applies to G_Y due to
350 its stickiness. These products show different compositions and matrices that can affect their
351 sensory perceptions (Mossaz et al., 2010). Fruit purees have soft and deformable insoluble
352 particles (cell walls of the fruit), which are dispersed into an aqueous solution of sugars, organic
353 acids, and pectic substances called serum (Cepedaand & Gómez, 2002; Espinosa-Muñoz et al.,
354 2013). Yogurt is achieved by acidification of milk with lactic acid bacteria (inducing the
355 coagulation of the protein network), also containing fat and additional stabilizers (Gilbert &
356 Turgeon, 2021).

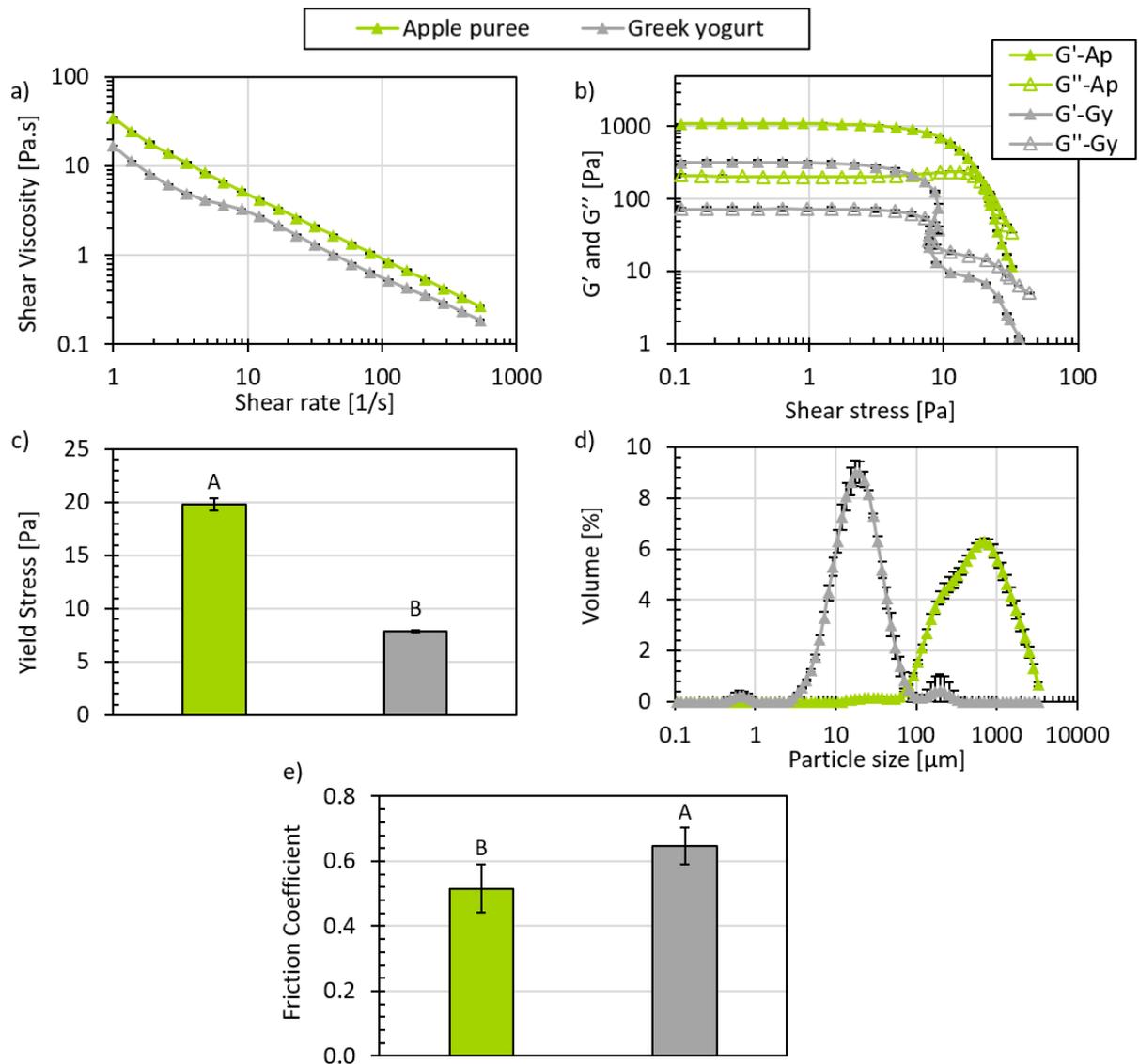
357 Figure 5.a illustrates the average flow curves of apple puree and Greek yogurt. The two
358 food products exhibit shear-thinning behavior, with apple puree approximately twice more
359 viscous than Greek yogurt.

360 The two semi-solid foods demonstrated higher values in storage modulus (G') than in
361 loss modulus (G'') when low shear stress is applied (Figure 5.b). Apple puree shows higher
362 values of G' and G'' than Greek yogurt (approximately four times higher). Moreover, in Figure
363 5.c, the yield stress (shear stress at the crossover point between storage and loss moduli) was
364 found to be higher for A_P (19.8 ± 0.6 Pa) than for G_Y (7.9 ± 0.1 Pa). This minimal stress required
365 to initiate flow of the products may be related to their structural network (Sun & Gunasekaran,
366 2009). Comparable orders of magnitude were found in the literature when studying apple puree,
367 establishing that the viscoelastic properties of this food product strongly depend on the insoluble
368 solid content (Espinosa-Muñoz et al., 2013; Leverrier et al., 2016). Greek yogurt's yield stress
369 has been found to fluctuate between 6 and 25 Pa (Costa et al., 2019; Fangary et al., 1999;
370 Mookoonlall et al., 2016).

371 In addition, the particle size of the products was also assessed and it is illustrated in
372 Figure 5.d. The mean and standard deviation values of $d(0.9)$ were of $1693.3 \pm 77.7 \mu\text{m}$ for A_P
373 and of $44.5 \pm 7.7 \mu\text{m}$ in G_Y . For apple puree, the peak was centered at $555.3 \mu\text{m}$, resembling an
374 almost monomodal size distribution. In contrast, Greek yogurt showed three peaks: one around
375 $0.5 \mu\text{m}$, the second centered at $18.6 \mu\text{m}$ and the third between $150 \mu\text{m}$ and $190 \mu\text{m}$. The small
376 peak could be the representation of fat globules, which are usually between $0.2 \mu\text{m}$ and $1.4 \mu\text{m}$
377 (Truong et al., 2014). Moreover, the central peak might be the cluster aggregates of fat droplets
378 interacting with the protein network (mainly whey protein/casein micelle complexes) (Moussier
379 et al., 2019). These clusters can range from 1 to $40 \mu\text{m}$ (Mellema et al., 2002). Lastly, the third
380 peak showed high variability, probably due to the reorganization between the cluster aggregates
381 such as sedimentation or syneresis, usually fluctuating from $40 \mu\text{m}$ to macroscale (Mellema et
382 al., 2002; Moussier, 2019).

383
384 Friction coefficients were 0.52 ± 0.1 for A_P and 0.65 ± 0.1 for G_Y . These tribological tests
385 were carried out at constant normal force and shearing velocity. In these conditions, the
386 lubrication regime may then be influenced by various factors related to the rheology and to the
387 structure of food, which plays a role of lubricant at the interface between the tribopairs. The
388 average dimensions of the asperities of the artificial tongue used on the tribometer (around 200
389 μm in height and $400 \mu\text{m}$ in diameter – see Figure A 2) are above particle size distribution
390 quantified in G_Y , whereas they fall in the range of particle size distribution measured in A_P . For
391 this reason, the shape and rigidity of the particles in A_P are more likely to influence the contact
392 surfaces and the friction phenomena. In addition, some components of the two food products
393 (such as polysaccharides in A_P or fat in G_Y) are likely to affect wettability and spreading on the
394 surfaces of the tribopairs, with consequences on friction. Liu et al., (2016) stated that the
395 lubrication properties of foodstuffs containing fat reduce friction due to “fat film patches”
396 formation. This fat film may lead to hydrophobic interactions between the TMS and the Greek
397 yogurt.

398



399
 400 *Figure 5. Rheology, tribology and particle size of apple puree and Greek yogurt. a) Shear viscosity of*
 401 *apple puree and Greek yogurt, b) Storage (G') and Loss (G'') Modulus, c) Yield stress, obtained from the*
 402 *overlap between G' and G'' , d) Particle size distribution, e) Friction coefficient. Letters indicate*
 403 *significant differences ($p < 0.05$).*

404 3.2 Influence of different Natural Salivary Substitutes on swallowing Apple Puree

405 3.2.1 In vitro Swallowing Assessment

406 To further explore the mechanisms governing the formation of food residues in the oral
 407 cavity after swallowing, an *in vitro* simulator of swallowing was employed. The physiological
 408 relevance of such simulators requires appropriate consideration of oral lubrication. Previous
 409 works investigating *in vitro* swallowing of Newtonian (Glycerol) and non-Newtonian
 410 (THICKEN UP® CLEAR, Nestle) fluids have shown that using water to lubricate the oral cavity
 411 of the SRT simulator was equivalent to not lubricating at all (Marconati, 2019). Due to water's
 412 Newtonian properties, attempts at lubrication failed to produce a regular and homogeneous film.
 413 To achieve a mouth-coating effect in the SRT and to prevent any leakage from the cavity, a
 414 viscoelastic fluid is preferable. With their interesting extensional and shear rheological

415 properties, the flaxseed extract solutions studied in our previous article (Bugarin-Castillo et al.,
416 2024) are interesting candidates for overcoming these aforementioned limitations.

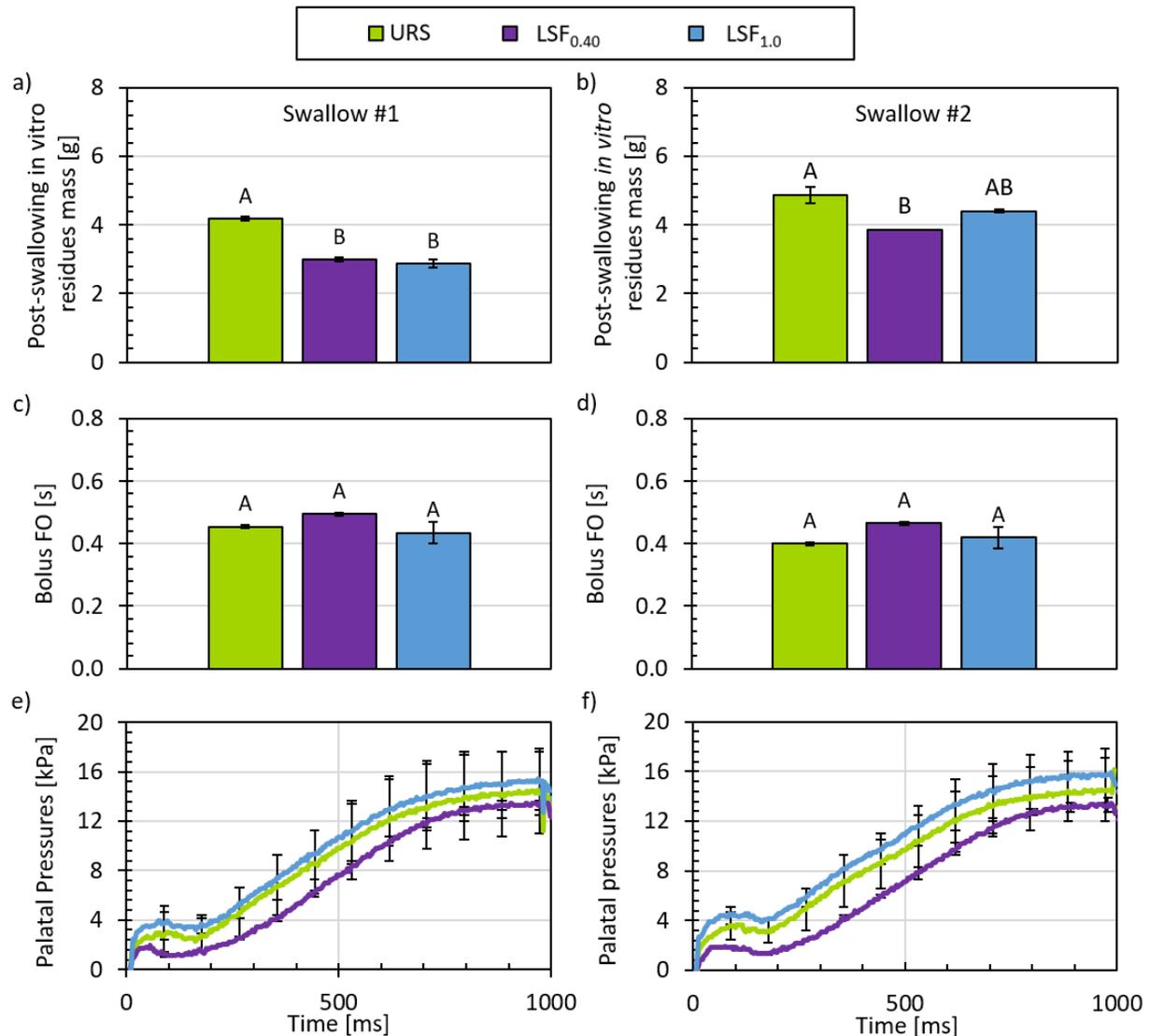
417 Therefore, two concentrations of the NSS were evaluated *in vitro* to determine their
418 ability to reduce post-swallowing *in vitro* residues. To avoid any bias, the objective was to use
419 the same mass of initial coating (2 g) in both the “Lubricated Swallowing” and “Unlubricated
420 Repeated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

421 As illustrated in Figure 6.a&b, the masses of *in vitro* residues remaining after swallows #1
422 and #2 were determined. The statistical analysis of post-swallowing *in vitro* residues showed *P*-
423 values < 0.01 for the variables “condition” (LS and URS) and “swallow” (swallow #1 and #2),
424 and *F*-values of 94.95 and 220.31, respectively. After the first swallow (see Figure 6.a), the URS
425 condition led to a higher mass of *in vitro* residues (4.2 ± 0.1 g) compared to both LS conditions
426 (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
427 also observed in the residues after swallow #2 (Figure 6.b), with a higher level also observed in
428 URS, when compared to LS with $F_{0.4}$ and $F_{1.0}$. This observation confirms that the different
429 conditions of oral lubrication resulting from swallow #1 have an influence on the residues
430 obtained after swallow #2. Whatever the lubrication condition, the quantity of residues after
431 swallow #2 was significantly greater than the corresponding one measured after swallow #1.

432 Moreover, Figure 6.c&d display the bolus FO of the different conditions during swallows
433 #1 and #2. The statistical results from bolus FO revealed no significant difference between URS
434 and LS when comparing both swallows. It has been studied in an *in vitro* model that bolus flow
435 velocity might be mitigated by bolus viscosity, yield stress, and firmness of the products
436 (increasing transit times) (Patel et al., 2020). The similar results obtained in bolus transit times
437 under the three conditions are thus consistent with the close rheological behaviors of the expelled
438 boli provided in Figure A 5.

439 Figure 6.e&f display the palatal pressures recorded from the anterior sensor of the SRT
440 during swallows #1 and #2. No significant differences could be observed between the URS and
441 LS($F_{1.0}$) conditions. However, a slightly lower pressure is remarked in the LS($F_{0.4}$) condition in
442 both swallows. Corresponding *in vivo* pressures were estimated in the literature (Moritaka et al.,
443 2018; Nicosia et al., 2000; Steele et al., 2010) using flat pressure sensors, during swallowing of
444 foods with wide ranges of rheological properties: nectar-thick apple juice (0.497 Pa·s at 50 s⁻¹),
445 semi-solid barium, and carrot puree (0.2 Pa·s at 50 s⁻¹). For healthy volunteers, *in vivo* palatal
446 pressures from the anterior flat sensor ranged from 11.2 to 20 kPa with a duration of ~1 s. These
447 orders of magnitude are consistent with the data obtained *in vitro* employing the SRT (Figure
448 6.e&f).

449
450



451
 452 *Figure 6. In vitro swallowing using the Soft-Robotic Tongue under different mouth coatings when testing*
 453 *apple puree as semi-solid food. Average and standard deviation values of post-swallowing in vitro*
 454 *residues after swallow #1 (a) and #2 (b). Average and standard deviation values of Bolus FO time from*
 455 *swallow #1 (c) and #2 (d). Average curves of palatal pressures from swallow #1 (e) and #2 (f). Letters*
 456 *indicate significant differences ($p < 0.05$). Abbreviations are: (URS) unlubricated repeated swallowing,*
 457 *(LSF_{0.40}) lubricated swallowing using NSS at 0.40 % dry matter, and (LSF_{1.0}) lubricated swallowing using*
 458 *NSS at 1.0 % dry matter.*

459
 460 **3.2.3 In vivo Assessment**

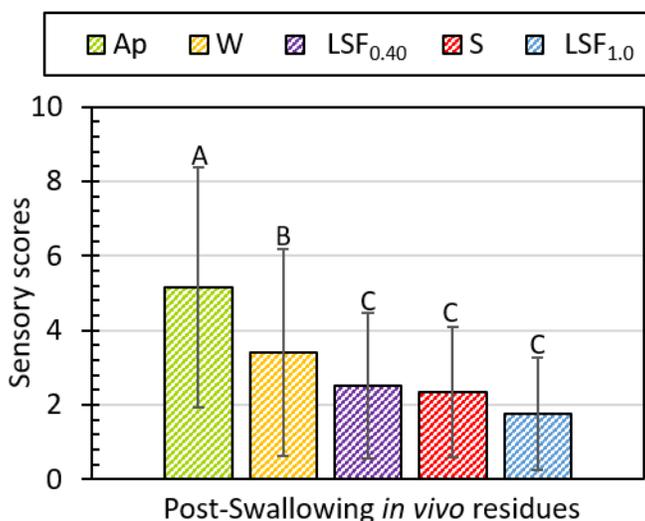
461 The influence of the NSS in the formation of post-swallowing residues was also assessed
 462 *in vivo*. The ANOVA results from the sensory profile showed $F = 4.615$ and $P\text{-value} < 0.01$ for
 463 the conditions tested, $F = 4.381$ and $P\text{-value} < 0.01$ for the panelists and $F = 2.197$ and $P\text{-value} <$
 464 0.01 for the interaction panelist*condition. In this study, all repetitions were not significantly
 465 different, participants differentiated all conditions and were consistent in their evaluation
 466 (panelist*condition). Overall, the results showed confidence in the panel performance.

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

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

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

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



490
491 *Figure 7. Sensory scores of post-swallowing in vivo residues when testing apple puree as semi-solid food.*
492 *Evaluation of five mouth coatings conditions (panel means). Letters indicate significant differences ($p <$*
493 *0.05) between conditions. Sensory scores on a scale from 0 to 10, where 0 meant "no residues" and 10*
494 *meant "a lot of residues". Abbreviations are: (A_P) apple puree, (*W*) water, ($LSF_{0.40}$) natural salivary*
495 *substitute at 0.40 % dry matter, (*S*) saliva, and ($LSF_{1.0}$) natural salivary substitute at 1.0 % dry matter.*

496 3.3 Influence of the properties of apple puree and Greek yogurt on swallowing performance of a 497 Natural Salivary Substitute

498 3.3.1 *In vitro* Swallowing Assessment

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

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

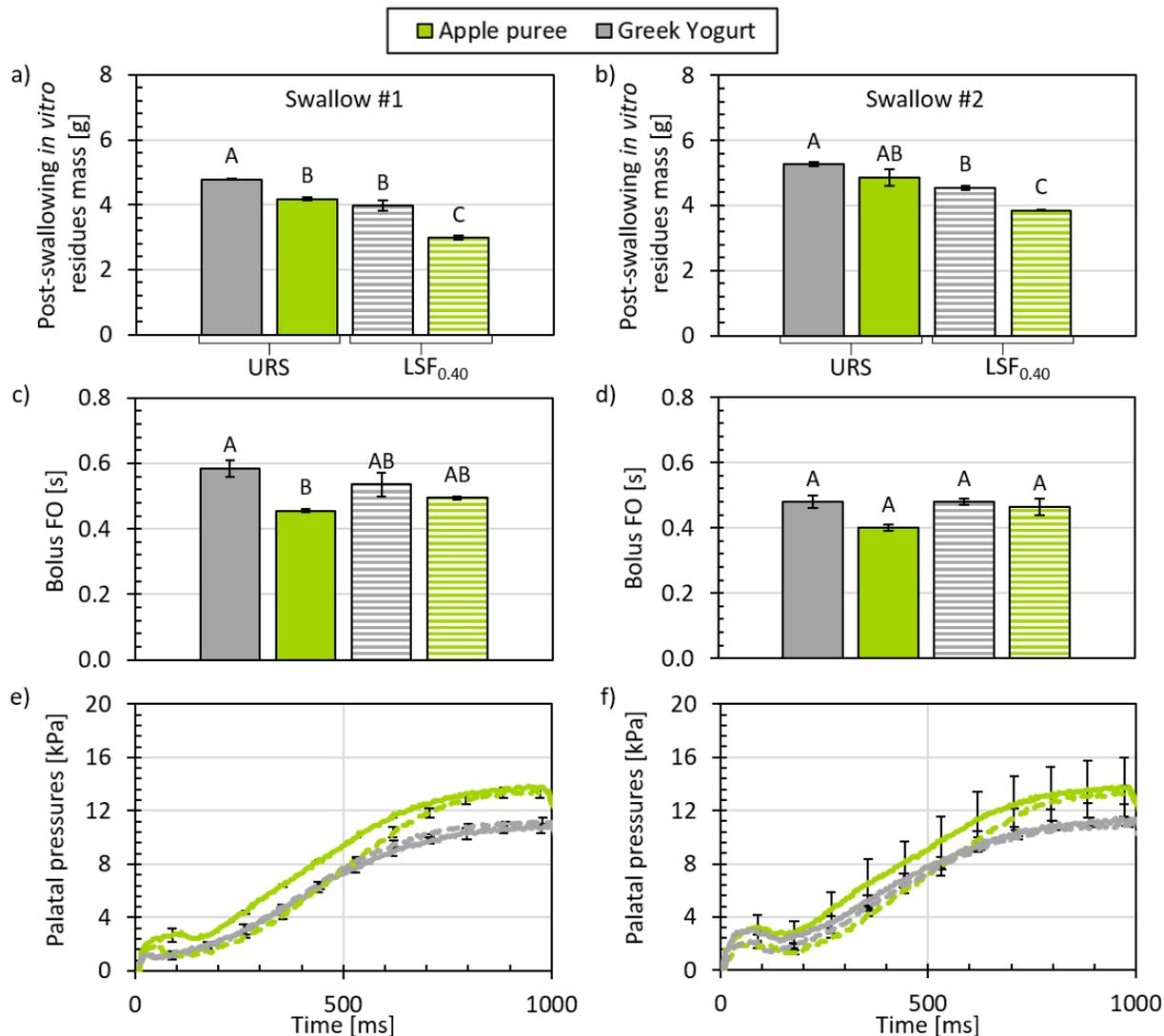
ANOVA	Product		Condition		Swallow		Condition*Product	
	F	Pvalue	F	Pvalue	F	Pvalue	F	Pvalue
P-S <i>in vitro</i> residues	68.803	<0.01	134.503	<0.01	66.27	<0.01	4.196	0.06
Bolus FO	20.948	<0.01	0.902	NS	17.906	<0.01	7.167	0.02

514
 515 Figure 8.a&b display the averages and standard deviations of post-swallowing *in vitro*
 516 residues obtained for Greek yogurt (G_Y) and apple puree (A_P), under lubricated swallowing
 517 ($LSF_{0.4}$) and unlubricated repeated swallowing (URS) conditions. In the URS condition, higher
 518 amounts of food residues were reported for G_Y than for A_P . Significant differences were also
 519 observed in the $LSF_{0.4}$ condition between the two products, with slightly higher amounts of
 520 residues of G_Y than of A_P . Swallow #2 follows similar trends as swallow #1, but with higher
 521 amounts of residues, depicting accumulation. Literature suggests that thicker liquids leave higher
 522 levels of residues in the pharynx (Marconati, Engmann, et al., 2019). However, in the present
 523 study, higher amounts of residues were found for G_Y , which had the lowest yield stress and
 524 viscosity.

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

537 Figure 8.e&f show the variations of pressure recorded from the anterior sensor during
 538 swallow #1 and #2, respectively. No difference in pressure was observed between $LSF_{0.4}$ or URS

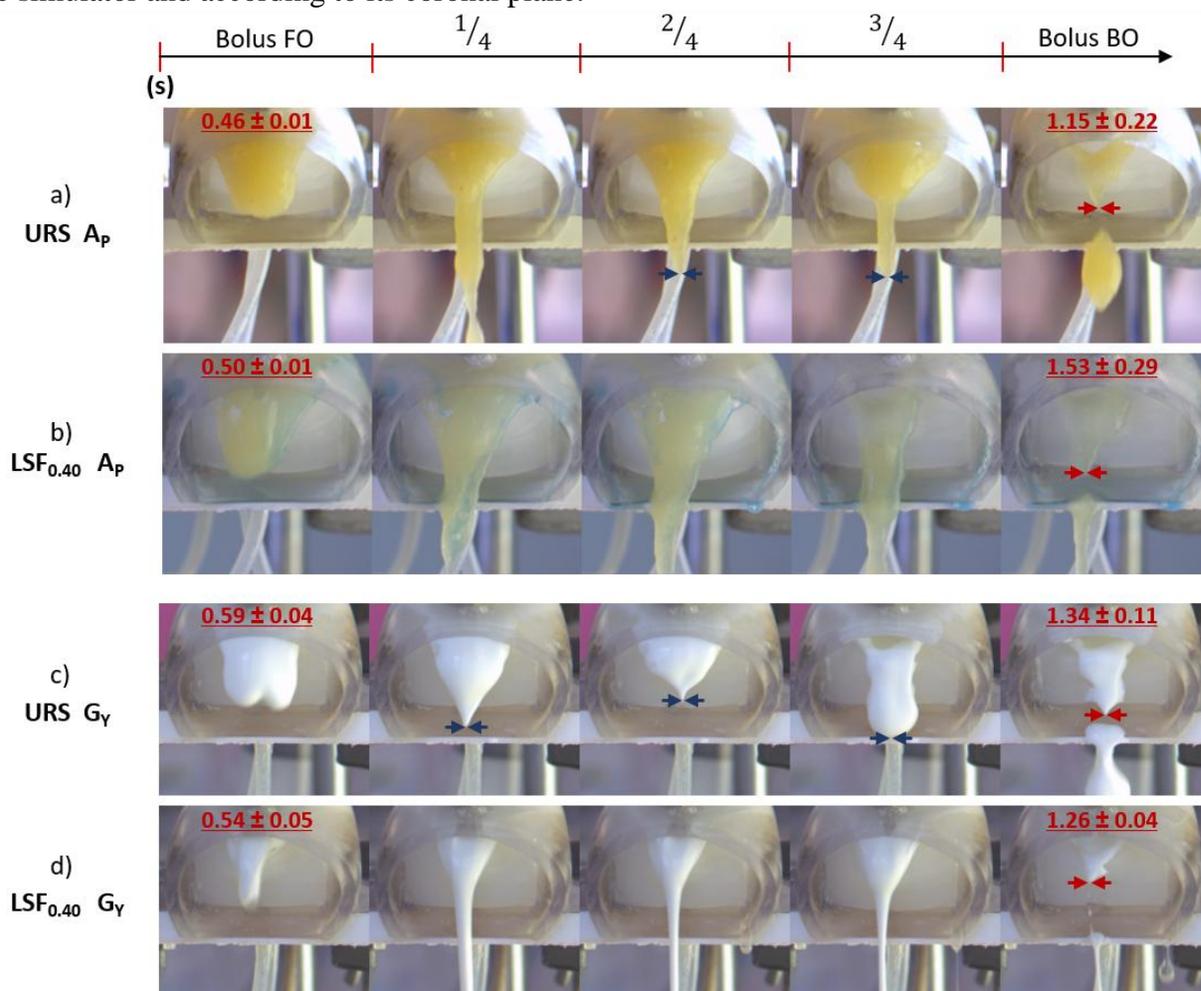
539 for G_Y (solid and dashed grey lines), while some could be reported for A_p (solid and dashed
 540 green lines). The palatal pressures from A_p showed higher pressures for URS during 700 ms
 541 when compared to lubricated conditions $LSF_{0.4}$. Moreover, differences are observed depending
 542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



548
 549 *Figure 8. In vitro swallowing using the Soft-Robotic Tongue under different mouth coatings when testing*
 550 *apple puree and Greek yogurt as semi-solid foods. Average and standard deviation values of post-*
 551 *swallowing in vitro residues after swallow #1 (a) and #2 (b). Average and standard deviation values of*
 552 *Bolus FO time from swallow #1 (c) and #2 (d). Average curves of palatal pressures from swallow #1 (e)*
 553 *and #2 (f). Dashed lines and bars represent $LSF_{0.40}$ condition and solid lines and bars represent URS*
 554 *condition. Letters indicate significant differences ($p < 0.05$). Abbreviations are: (URS) unlubricated*
 555 *repeated swallowing, ($LSF_{0.40}$) lubricated swallowing using NSS at 0.40 % dry matter, (Bolus FO) bolus*
 556 *front out.*

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

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



573
 574 Figure 9. Coronal view of the posterior part of the Soft-Robotic Tongue, where the bolus is expelled out
 575 of the oral cavity. Images were taken from bolus Front Out (bolus FO) until bolus Back Out (bolus BO).

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

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

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

596 It has been stated in the literature that a bolus is perceived safe for swallowing when the
597 cohesive forces between the food and saliva are strong enough to prevent the detachment of
598 particles from the food bolus, preventing fragmentation (Gallegos et al., 2021). In this study, the
599 coating of a swallowing simulator shows that the NSS might form a pellicle that envelops the
600 bolus, providing cohesiveness to two semi-solid foods and preventing them from breakage.

601 3.3.3 *In Vivo* Performance

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

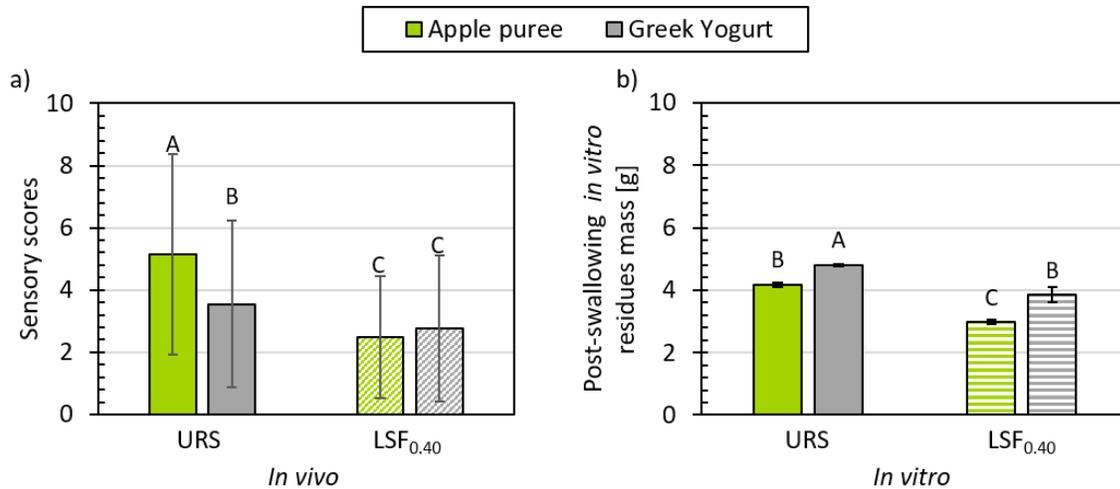
607 Figure 10 illustrates a comparison between (a) *in vivo* and (b) *in vitro* assessments of
608 post-swallowing oral residues of food, for the four combinations of the two foods (apple puree
609 (A_P) and Greek yogurt (G_Y)) with the two lubrication conditions (Unlubricated Repeated
610 Swallowing (URS) and Lubricated Swallowing (LS)). *In vivo* sensations of post-swallowing
611 residues and *in vitro* assessments of the amount of residues were both lower under LS than URS
612 lubrication conditions. However, a difference is observed when the scores of G_Y and A_P are
613 compared *in vitro* and *in vivo*. During *in vitro* measurements, A_P showed lower amounts of oral
614 residues than G_Y in URS and LS. During *in vivo* measurements, the inverted trend was observed
615 in URS, whereas no difference could be reported in LS. The differences between *in vivo* and *in*
616 *vitro* results may be due to the quantification method. Throughout *in vitro*, post-swallowing
617 residues were determined by objective quantifications of masses. *In vivo*, the perception of post-
618 swallowing residues might be influenced by various factors. For instance, a possible reason for

619 the higher scores obtained *in vivo* from A_P than for G_Y under URS condition could be due to the
620 positive correlation between oral residues and particle size (Aguayo-Mendoza et al., 2021;
621 Espinosa-Muñoz et al., 2012; Marconati, Lopez, et al., 2019). Participants accumulated apple
622 puree particles from the three pre-coating steps performed, potentially enhancing their ability to
623 detect particles in the mouth (graininess) and increasing their perception to post-swallowing
624 residues. An additional cause for the lower scores of G_Y under *in vivo* URS might be due to its
625 sourness, which is characteristic of fermented dairy products (Desai et al., 2013). Acid
626 stimulation of saliva is due to its buffer capacity, where saliva increases its volume to reduce
627 acidity in the mouth (Lugaz et al., 2005). The perception of sourness has been related to the type
628 and concentration of acid used, as sourness is not only related to pH, but also to titratable acidity
629 (Muñoz-González et al., 2018). Literature shows that A_P and G_Y pH values are within similar
630 ranges (A_P=3.4-4.8 and G_Y=4.4-4.9). Nevertheless, the percentage of lactic acid in G_Y (3.3-
631 5.7%) is higher than that of malic acid in A_P (0.4-0.82%) (Brisset, 2012; Desai et al., 2013; Lan
632 et al., 2022; Picouet et al., 2009; Viquez-Barrantes et al., 2023). The repeated steps of mouth
633 rinsing performed by the participants for G_Y in URS conditions might have led to an increase in
634 saliva flow stimulation (when compared to A_P case). One could thus have expected lower
635 perceptions of residues due to dilution effects of saliva.

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

648 These findings suggest further work on testing the NSS in an environment where saliva
649 stimulation will not interfere in the perception of post-swallowing residues. This work
650 emphasizes the importance of *in vitro* devices able to simulate unhealthy conditions to encourage
651 new ways of developing personalized food for specific swallowing disorders.

652



653

654 *Figure 10. Comparison in vivo and in vitro of post-swallowing residues when testing apple puree and*
 655 *Greek yogurt. a) “In vivo” sensory scores of perception of residues in mouth on a scale from 0 to 10,*
 656 *where 0 meant “no residues” and 10 meant “a lot of residues”, b) “In vitro” results from Soft-Robotic*
 657 *Tongue. Letters indicate significant differences ($p < 0.05$) between conditions. Abbreviations are: (URS)*
 658 *unlubricated repeated swallowing and (LSF_{0.40}) lubricated swallowing using NSS at 0.40 % dry matter.*

659 **4. Conclusion and Next Steps**

660 In this study, *in vitro* and *in vivo* approaches were employed to investigate the
 661 performance of natural salivary substitutes obtained from flaxseed extracts, to help swallowing
 662 food. The *in vitro* method employed a soft actuator, able to reproduce human tongue surface
 663 properties, displacements and pressures. For *in vivo* evaluations, healthy volunteers followed a
 664 new protocol to imitate lubricated and unlubricated conditions. From this study, oral food
 665 residues were influenced by lubrication and food matrix composition—shear viscosity and yield
 666 stress were related to higher palatal pressures *in vitro*. Apple puree and Greek yogurt were
 667 considered. For both of them, *in vitro* and *in vivo* results show that oral coating with flaxseed
 668 extracts at 0.40 % dry matter makes it possible to reduce the amount of post-swallowing oral
 669 residues; suggesting an increase in bolus moisture and a more compact bolus. Such promising
 670 reduction of oral residues suggests that this salivary substitute should be tested clinically to
 671 confirm whether it can help promoting food oral processing for xerostomic patients.

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675

676 **Credit author statement**

677 **Y. Bugarin-Castillo:** Conceptualization, Methodology, Validation, Formal analysis,
 678 Investigation, Writing – original draft, Writing – review & editing, Visualization. **P. Bou Fadel:**
 679 Methodology, Investigation. **A. Saint-Eve:** Conceptualization, Methodology, Formal analysis,
 680 Writing – review & editing. **M. Ramaioli:** Conceptualization, Methodology, Validation, Formal
 681 analysis, Writing – review & editing, Supervision, Project administration, Funding acquisition.
 682 **V. Mathieu:** Conceptualization, Methodology, Validation, Formal analysis, Writing – review &
 683 editing, Supervision.

684 **References**

- 685 Aguayo-Mendoza, M. G., Chatonidi, G., Piqueras-Fizman, B., & Stieger, M. (2021). Linking oral
686 processing behavior to bolus properties and dynamic sensory perception of processed cheeses
687 with bell pepper pieces. *Food Quality and Preference*, *88*, 104084.
688 <https://doi.org/10.1016/j.foodqual.2020.104084>
- 689 Andablo-Reyes, E., Bryant, M., Neville, A., Hyde, P., Sarkar, R., Francis, M., & Sarkar, A. (2020). 3D
690 Biomimetic Tongue-Emulating Surfaces for Tribological Applications. *ACS Applied Materials &*
691 *Interfaces*, *12*(44), 49371–49385. <https://doi.org/10.1021/acsami.0c12925>
- 692 Avila Sierra, A., Bugarin, Y., Voisin, J., Mathieu, V., & Ramaioli, M. (2023). *Toward a More Realistic 3D*
693 *Biomimetic Soft Robotic Tongue to Investigate Oral Processing of Semi-solid Foods* (pp. 131–
694 140). https://doi.org/10.1007/978-3-031-39504-8_9
- 695 Avila-Sierra, A., Decerle, N., Ramaioli, M., & Peyron, M.-A. (2024). Effect of salivary fluid characteristics
696 on the physical features of in vitro bread bolus: From the absence of saliva to artificially
697 simulated hypersalivation. *Food Research International*, *175*, 113753.
698 <https://doi.org/10.1016/j.foodres.2023.113753>
- 699 Avila-Sierra, A., Lavoisier, A., Timpe, C., Kuehl, P., Wagner, L., Tournier, C., & Ramaioli, M. (2023).
700 Paediatric solid oral dosage forms for combination products: Improving in vitro swallowability of
701 minitablets using binary mixtures with pellets. *European Journal of Pharmaceutical Sciences*,
702 *187*, 106471. <https://doi.org/10.1016/j.ejps.2023.106471>
- 703 Brisset, L. C. E. M. (2012). *Texture de la purée de pomme: Influence de la structure sur les propriétés*
704 *rhéologiques et la perception sensorielle - effet du traitement mécanique*. [Phdthesis,
705 AgroParisTech]. <https://pastel.hal.science/pastel-00749695>
- 706 Bugarin-Castillo, Y., Bou Fadel, P., Mohamed Ismail, S., Huang, N., Saint- Eve, A., Mathieu, V., & Ramaioli,
707 M. (2024). *On the rheological and sensory properties of a novel natural salivary substitute*.
708 <https://hal.science/hal-04534534>

709 Cassolato, S. F., & Turnbull, R. S. (2003). Xerostomia: Clinical Aspects and Treatment. *Gerodontology*,
710 20(2), 64–77. <https://doi.org/10.1111/j.1741-2358.2003.00064.x>

711 Cepedaand, E., & Gómez, R. (2002). Rheological Characteristics of Pimento Purée: Theoretical
712 Interpretation. *Journal of Food Science*, 67(7), 2734–2738. [https://doi.org/10.1111/j.1365-
713 2621.2002.tb08806.x](https://doi.org/10.1111/j.1365-2621.2002.tb08806.x)

714 Clavé, P., & Shaker, R. (2015). Dysphagia: Current reality and scope of the problem. *Nature Reviews*
715 *Gastroenterology & Hepatology*, 12(5), 259–270. <https://doi.org/10.1038/nrgastro.2015.49>

716 Costa, M. F., Pimentel, T. C., Guimaraes, J. T., Balthazar, C. F., Rocha, R. S., Cavalcanti, R. N., Esmerino, E.
717 A., Freitas, M. Q., Raices, R. S. L., Silva, M. C., & Cruz, A. G. (2019). Impact of prebiotics on the
718 rheological characteristics and volatile compounds of Greek yogurt. *LWT*, 105, 371–376.
719 <https://doi.org/10.1016/j.lwt.2019.02.007>

720 Desai, N. T., Shepard, L., & Drake, M. A. (2013). Sensory properties and drivers of liking for Greek
721 yogurts. *Journal of Dairy Science*, 96(12), 7454–7466. <https://doi.org/10.3168/jds.2013-6973>

722 Dodds, W. J., Stewart, E. T., & Logemann, J. A. (1990). Physiology and radiology of the normal oral and
723 pharyngeal phases of swallowing. *American Journal of Roentgenology*, 154(5), 953–963.
724 <https://doi.org/10.2214/ajr.154.5.2108569>

725 Espinosa-Muñoz, L., Renard, C. M. G. C., Symoneaux, R., Biau, N., & Cuvelier, G. (2013). Structural
726 parameters that determine the rheological properties of apple puree. *Journal of Food*
727 *Engineering*, 119(3), 619–626. <https://doi.org/10.1016/j.jfoodeng.2013.06.014>

728 Espinosa-Muñoz, L., Symoneaux, R., Renard, C. M. G. C., Biau, N., & Cuvelier, G. (2012). The significance
729 of structural properties for the development of innovative apple puree textures. *LWT - Food*
730 *Science and Technology*, 49(2), 221–228. <https://doi.org/10.1016/j.lwt.2012.06.020>

731 Fangary, Y. S., Barigou, M., & Seville, J. P. K. (1999). Simulation of Yoghurt Flow and Prediction of Its End-
732 of-Process Properties Using Rheological Measurements. *Food and Bioproducts Processing*, 77(1),
733 33–39. <https://doi.org/10.1205/096030899532231>

734 Fei, T., Polacco, R. C., Hori, S. E., Molfenter, S. M., Peladeau-Pigeon, M., Tsang, C., & Steele, C. M. (2013).
735 Age-related Differences in Tongue-Palate Pressures for Strength and Swallowing Tasks.
736 *Dysphagia*, 28(4), 575–581. <https://doi.org/10.1007/s00455-013-9469-6>

737 Fujiso, Y., Perrin, N., van der Giessen, J., Vrana, N. E., Neveu, F., & Woisard, V. (2018). Swall-E: A robotic
738 in-vitro simulation of human swallowing. *PLOS ONE*, 13(12), e0208193.
739 <https://doi.org/10.1371/journal.pone.0208193>

740 Fujiwara, S., Ono, T., Minagi, Y., Fujiu-Kurachi, M., Hori, K., Maeda, Y., Boroumand, S., Nitschke, I.,
741 Ursula, V., & Bohlender, J. (2014). Effect of Supraglottic and Super-supraglottic swallows on
742 Tongue Pressure Production against Hard Palate. *Dysphagia*, 29(6), 655–662.
743 <https://doi.org/10.1007/s00455-014-9556-3>

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

746 Gilbert, A., & Turgeon, S. L. (2021). Studying stirred yogurt microstructure and its correlation to physical
747 properties: A review. *Food Hydrocolloids*, 121, 106970.
748 <https://doi.org/10.1016/j.foodhyd.2021.106970>

749 Hadde, E. K., & Chen, J. (2021). Texture and texture assessment of thickened fluids and texture-modified
750 food for dysphagia management. *Journal of Texture Studies*, 52(1), 4–15.
751 <https://doi.org/10.1111/jtxs.12567>

752 Hadde, E. K., Cichero, J. A. Y., Zhao, S., Chen, W., & Chen, J. (2019). The Importance of Extensional
753 Rheology in Bolus Control during Swallowing. *Scientific Reports*, 9(1), Article 1.
754 <https://doi.org/10.1038/s41598-019-52269-4>

755 Hahnel, S., Behr, M., Handel, G., & Bürgers, R. (2009). Saliva substitutes for the treatment of radiation-
756 induced xerostomia—A review. *Supportive Care in Cancer*, *17*(11), 1331–1343.
757 <https://doi.org/10.1007/s00520-009-0671-x>

758 Hu, J., Andablo-Reyes, E., Mighell, A., Pavitt, S., & Sarkar, A. (2021). Dry mouth diagnosis and saliva
759 substitutes—A review from a textural perspective. *Journal of Texture Studies*, *52*(2), 141–156.
760 <https://doi.org/10.1111/jtxs.12575>

761 Lan, W., Jaillais, B., Chen, S., Renard, C. M. G. C., Leca, A., & Bureau, S. (2022). Fruit variability impacts
762 puree quality: Assessment on individually processed apples using the visible and near infrared
763 spectroscopy. *Food Chemistry*, *390*, 133088. <https://doi.org/10.1016/j.foodchem.2022.133088>

764 Lavoisier, A., Avila-Sierra, A., Timpe, C., Kuehl, P., Wagner, L., Tournier, C., & Ramaioli, M. (2022). A novel
765 soft robotic pediatric in vitro swallowing device to gain insights into the swallowability of mini-
766 tablets. *International Journal of Pharmaceutics*, *629*, 122369.
767 <https://doi.org/10.1016/j.ijpharm.2022.122369>

768 Lavoisier, A., Shreeram, S., Jedwab, M., & Ramaioli, M. (2021). Effect of the rheological properties of the
769 liquid carrier on the in vitro swallowing of solid oral dosage forms. *Journal of Texture Studies*,
770 *52*(5–6), 623–637. <https://doi.org/10.1111/jtxs.12618>

771 Leverrier, C., Almeida, G., Espinosa-Mu Noz, L., & Cuvelier, G. (2016). Influence of Particle Size and
772 Concentration on Rheological Behaviour of Reconstituted Apple Purees. *Food Biophysics*, *11*(3),
773 235–247. <https://doi.org/10.1007/s11483-016-9434-7>

774 Liu, K., Tian, Y., Stieger, M., van der Linden, E., & van de Velde, F. (2016). Evidence for ball-bearing
775 mechanism of microparticulated whey protein as fat replacer in liquid and semi-solid multi-
776 component model foods. *Food Hydrocolloids*, *52*, 403–414.
777 <https://doi.org/10.1016/j.foodhyd.2015.07.016>

778 Lorieau, L., Septier, C., Laguerre, A., Le Roux, L., Hazart, E., Ligneul, A., Famelart, M.-H., Dupont, D.,
779 Flourey, J., Feron, G., & Labouré, H. (2018). Bolus quality and food comfortability of model
780 cheeses for the elderly as influenced by their texture. *Food Research International*, *111*, 31–38.
781 <https://doi.org/10.1016/j.foodres.2018.05.013>

782 Lugaz, O., Pillias, A.-M., Boireau-Ducept, N., & Faurion, A. (2005). Time–Intensity Evaluation of Acid Taste
783 in Subjects with Saliva High Flow and Low Flow Rates for Acids of Various Chemical Properties.
784 *Chemical Senses*, *30*(1), 89–103. <https://doi.org/10.1093/chemse/bji004>

785 Marconati, M. (2019). *In vitro models for the formulation of easy-to-swallow products* [Ph.D Thesis].
786 University of Surrey.

787 Marconati, M., Engmann, J., Burbidge, A. S., Mathieu, V., Souchon, I., & Ramaioli, M. (2019). A review of
788 the approaches to predict the ease of swallowing and post-swallow residues. *Trends in Food*
789 *Science & Technology*, *86*, 281–297. <https://doi.org/10.1016/j.tifs.2019.02.045>

790 Marconati, M., Lopez, F., Tuleu, C., Orlu, M., & Ramaioli, M. (2019). In vitro and sensory tests to design
791 easy-to-swallow multi-particulate formulations. *European Journal of Pharmaceutical Sciences*,
792 *132*, 157–162. <https://doi.org/10.1016/j.ejps.2019.02.026>

793 Marconati, M., Pani, S., Engmann, J., Burbidge, A., & Ramaioli, M. (2020). A soft robotic tongue to
794 develop solutions to manage swallowing disorders. *arXiv:2003.01194 [Physics, q-Bio]*.
795 <http://arxiv.org/abs/2003.01194>

796 Marconati, M., & Ramaioli, M. (2020). The role of extensional rheology in the oral phase of swallowing:
797 An in vitro study. *Food & Function*, *5*, Article arXiv:2001.07810.
798 <https://doi.org/10.1039/c9fo02327e>

799 Mellema, M., Walstra, P., Van Opheusden, J. H. J., & Van Vliet, T. (2002). Effects of structural
800 rearrangements on the rheology of rennet-induced casein particle gels. *Advances in Colloid and*
801 *Interface Science*, *98*(1), 25–50. [https://doi.org/10.1016/S0001-8686\(01\)00089-6](https://doi.org/10.1016/S0001-8686(01)00089-6)

802 Mookoonlall, A., Nöbel, S., & Hinrichs, J. (2016). Post-processing of fermented milk to stirred products:
803 Reviewing the effects on gel structure. *Trends in Food Science & Technology*, *54*, 26–36.
804 <https://doi.org/10.1016/j.tifs.2016.05.012>

805 Moritaka, H., Mineki, M., Kobayashi, M., Ono, T., & Hori, K. (2018). Effect of carrot puree in vegetable
806 juice on linguapalatal swallowing pressure. *Journal of Texture Studies*, *49*(2), 240–246.
807 <https://doi.org/10.1111/jtxs.12315>

808 Mossaz, S., Jay, P., Magnin, A., Panouillé, M., Saint-Eve, A., Déléris, I., Juteau, A., & Souchon, I. (2010).
809 Measuring and predicting the spreading of dairy products in the mouth: Sensory, instrumental
810 and modelling approaches. *Food Hydrocolloids*, *24*(8), 681–688.
811 <https://doi.org/10.1016/j.foodhyd.2010.03.006>

812 Moussier, M. (2019). *Structuration de la matière grasse dans une matrice protéique laitière en fonction*
813 *de la composition et du procédé: Influence sur les propriétés du produit* [Phdthesis, Université
814 Paris Saclay (COMUE)]. <https://theses.hal.science/tel-02294430>

815 Moussier, M., Guénard-Lampron, V., Lachin, K., Moulin, G., Turgeon, S. L., Michon, C., Huc-Mathis, D., &
816 Bosc, V. (2019). What do stirred yogurt microgels look like? Comparison of laser diffraction, 2D
817 dynamic image analysis and 3D reconstruction. *Food Structure*, *20*, 100107.
818 <https://doi.org/10.1016/j.foostr.2019.100107>

819 Muñoz-González, C., Feron, G., & Canon, F. (2018). Main effects of human saliva on flavour perception
820 and the potential contribution to food consumption. *Proceedings of the Nutrition Society*, *77*(4),
821 423–431. <https://doi.org/10.1017/S0029665118000113>

822 Nayak, A., & Carpenter, G. H. (2008). A physiological model of tea-induced astringency. *Physiology &*
823 *Behavior*, *95*(3), 290–294. <https://doi.org/10.1016/j.physbeh.2008.05.023>

824 Nicosia, M. A., Hind, J. A., Roecker, E. B., Carnes, M., Doyle, J., Dengel, G. A., & Robbins, J. (2000). Age
825 Effects on the Temporal Evolution of Isometric and Swallowing Pressure. *The Journals of*

826 *Gerontology Series A: Biological Sciences and Medical Sciences*, 55(11), M634–M640.
827 <https://doi.org/10.1093/gerona/55.11.M634>

828 Nishinari, K., Peyron, M.-A., Yang, N., Gao, Z., Zhang, K., Fang, Y., Zhao, M., Yao, X., Hu, B., Han, L.,
829 Mleko, S., Tomczyńska-Mleko, M., Nagano, T., Nitta, Y., Zhang, Y., Singh, N., Suk Meng, A. G.,
830 Pongsawatmanit, R., Gamonpilas, C., ... Su, L. (2024). The role of texture in the palatability and
831 food oral processing. *Food Hydrocolloids*, 147, 109095.
832 <https://doi.org/10.1016/j.foodhyd.2023.109095>

833 Pabois, O., Avila-Sierra, A., Ramaioli, M., Mu, M., Message, Y., You, K.-M., Lamas, E., Kew, B., Durga, K.,
834 Doherty, L., & Sarkar, A. (2023). Benchmarking of a microgel-reinforced hydrogel-based aqueous
835 lubricant against commercial saliva substitutes. *Scientific Reports*, 13(1), Article 1.
836 <https://doi.org/10.1038/s41598-023-46108-w>

837 Pailler-Mattei, C., Vargiolu, R., Tupin, S., & Zahouani, H. (2015). Ex vivo approach to studying bio-
838 adhesive and tribological properties of artificial salivas for oral dryness (xerostomia). *Wear*, 332–
839 333, 710–714. <https://doi.org/10.1016/j.wear.2015.02.020>

840 Park, H. W., & Yoon, W. B. (2018). Effect of drying and grinding characteristics of colored potato
841 (*Solanum tuberosum* L.) on tribology of mashed colored potato paste. *CyTA - Journal of Food*,
842 16(1), 135–145. <https://doi.org/10.1080/19476337.2017.1348394>

843 Park, J.-S., Oh, D.-H., & Chang, M. (2016). Comparison of maximal tongue strength and tongue strength
844 used during swallowing in relation to age in healthy adults. *Journal of Physical Therapy Science*,
845 28(2), 442–445. <https://doi.org/10.1589/jpts.28.442>

846 Patel, S., McAuley, W. J., Cook, M. T., Sun, Y., Hamdy, S., & Liu, F. (2020). The Swallowing Characteristics
847 of Thickeners, Jellies and Yoghurt Observed Using an In Vitro Model. *Dysphagia*, 35(4), 685–695.
848 <https://doi.org/10.1007/s00455-019-10074-1>

849 Penman, J. P., & Thomson, M. (1998). A review of the textured diets developed for the management of
850 dysphagia. *Journal of Human Nutrition and Dietetics*, 11(1), 51–60.
851 <https://doi.org/10.1046/j.1365-277X.1998.00079.x>

852 Piaton, S., Duconseille, A., Roger-Leroi, V., & Hennequin, M. (2021). Could the use of saliva substitutes
853 improve food oral processing in individuals with xerostomia? A systematic review. *Journal of*
854 *Texture Studies*, 52(3), 278–293. <https://doi.org/10.1111/jtxs.12591>

855 Picouet, P. A., Landl, A., Abadias, M., Castellari, M., & Viñas, I. (2009). Minimal processing of a Granny
856 Smith apple purée by microwave heating. *Innovative Food Science & Emerging Technologies*,
857 10(4), 545–550. <https://doi.org/10.1016/j.ifset.2009.05.007>

858 Ranc, H., Elkhyat, A., Servais, C., Mac-Mary, S., Launay, B., & Humbert, Ph. (2006). Friction coefficient
859 and wettability of oral mucosal tissue: Changes induced by a salivary layer. *Colloids and Surfaces*
860 *A: Physicochemical and Engineering Aspects*, 276(1–3), 155–161.
861 <https://doi.org/10.1016/j.colsurfa.2005.10.033>

862 Rofes, L., Arreola, V., Almirall, J., Cabré, M., Campins, L., García-Peris, P., Speyer, R., & Clavé, P. (2011).
863 Diagnosis and management of oropharyngeal Dysphagia and its nutritional and respiratory
864 complications in the elderly. *Gastroenterology Research and Practice*, 2011, 818979.
865 <https://doi.org/10.1155/2011/818979>

866 Sarkar, A., Xu, F., & Lee, S. (2019). Human saliva and model saliva at bulk to adsorbed phases –
867 similarities and differences. *Advances in Colloid and Interface Science*, 273, 102034.
868 <https://doi.org/10.1016/j.cis.2019.102034>

869 Schwartz, C., Vandenberghe-Descamps, M., Sulmont-Rossé, C., Tournier, C., & Feron, G. (2018).
870 Behavioral and physiological determinants of food choice and consumption at sensitive periods
871 of the life span, a focus on infants and elderly. *Innovative Food Science & Emerging*
872 *Technologies*, 46, 91–106. <https://doi.org/10.1016/j.ifset.2017.09.008>

873 See, L., Mohammadi, M., Han, P. P., Mulligan, R., & Enciso, R. (2019). Efficacy of saliva substitutes and
874 stimulants in the treatment of dry mouth. *Special Care in Dentistry*, 39(3), 287–297.
875 <https://doi.org/10.1111/scd.12370>

876 Shahdad, S. a., Taylor, C., Barclay, S. c., Steen, I. n., & Preshaw, P. m. (2005). A double-blind, crossover
877 study of Biotène Oralbalance and BioXtra systems as salivary substitutes in patients with post-
878 radiotherapy xerostomia. *European Journal of Cancer Care*, 14(4), 319–326.
879 <https://doi.org/10.1111/j.1365-2354.2005.00587.x>

880 Spirk, C., Hartl, S., Pritz, E., Gugatschka, M., Kolb-Lenz, D., Leitinger, G., & Roblegg, E. (2019).
881 Comprehensive investigation of saliva replacement liquids for the treatment of xerostomia.
882 *International Journal of Pharmaceutics*, 571, 118759.
883 <https://doi.org/10.1016/j.ijpharm.2019.118759>

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

888 Steele, C. M., Bailey, G. L., & Molfenter, S. M. (2010). Tongue Pressure Modulation During Swallowing:
889 Water Versus Nectar-Thick Liquids. *Journal of Speech, Language, and Hearing Research*, 53(2),
890 273–283. [https://doi.org/10.1044/1092-4388\(2009/09-0076\)](https://doi.org/10.1044/1092-4388(2009/09-0076))

891 Sun, A., & Gunasekaran, S. (2009). Yield Stress in Foods: Measurements and Applications. *International*
892 *Journal of Food Properties*, 12(1), 70–101. <https://doi.org/10.1080/10942910802308502>

893 Truong, T., Bansal, N., Sharma, R., Palmer, M., & Bhandari, B. (2014). Effects of emulsion droplet sizes on
894 the crystallisation of milk fat. *Food Chemistry*, 145, 725–735.
895 <https://doi.org/10.1016/j.foodchem.2013.08.072>

896 Vinke, J., Kaper, H. J., Vissink, A., & Sharma, P. K. (2018). An ex vivo salivary lubrication system to mimic
897 xerostomic conditions and to predict the lubricating properties of xerostomia relieving agents.
898 *Scientific Reports*, 8(1), 9087. <https://doi.org/10.1038/s41598-018-27380-7>

899 Vinke, J., Kaper, H. J., Vissink, A., & Sharma, P. K. (2020). Dry mouth: Saliva substitutes which adsorb and
900 modify existing salivary condition films improve oral lubrication. *Clinical Oral Investigations*,
901 24(11), 4019–4030. <https://doi.org/10.1007/s00784-020-03272-x>

902 Viquez-Barrantes, D., Lau-Lee, N., Cubero-Castillo, E., & Cordero-García, M. (2023). Comparing consumer
903 acceptance, sensory profile, and chemical properties in artisanal and industrial Greek-style
904 yogurts processing: A path to enhancing food safety. *NFS Journal*, 33, 100156.
905 <https://doi.org/10.1016/j.nfs.2023.100156>

906 Wagner, C. (2015). *An experimental and theoretical investigation of the rheological properties and*
907 *degradation of mucin solutions (or why saliva becomes watery when removed from your mouth)*
908 [Ph.D Thesis]. Massachusetts Institute of Technology.

909 Wirth, R., Dziewas, R., Beck, A. M., Clave, P., Heppner, H. J., Langmore, S., Leischker, A., Martino, R.,
910 Pluschinski, P., Rösler, A., Shaker, R., Warnecke, T., Sieber, C. C., Volkert, D., & Hamdy, S. (2016).
911 Oropharyngeal dysphagia in older persons – from pathophysiology to adequate
912 intervention: A review and summary of an international expert meeting. *Clinical Interventions in*
913 *Aging*, 189. <https://doi.org/10.2147/CIA.S97481>

914 Xi, J., & Longest, P. W. (2007). Transport and Deposition of Micro-Aerosols in Realistic and Simplified
915 Models of the Oral Airway. *Annals of Biomedical Engineering*, 35(4), 560–581.
916 <https://doi.org/10.1007/s10439-006-9245-y>

917 Zhang, S., Olthoff, A., & Frahm, J. (2012). Real-time magnetic resonance imaging of normal swallowing.
918 *Journal of Magnetic Resonance Imaging*, 35(6), 1372–1379. <https://doi.org/10.1002/jmri.23591>

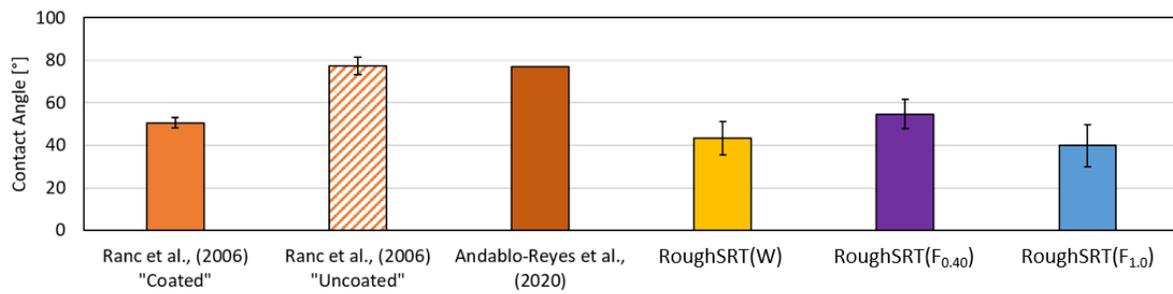
919

920 **Appendix / Supplementary Data**

921

922 *Appendix A.1. Wettability of the Soft-Robotic Tongue*

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



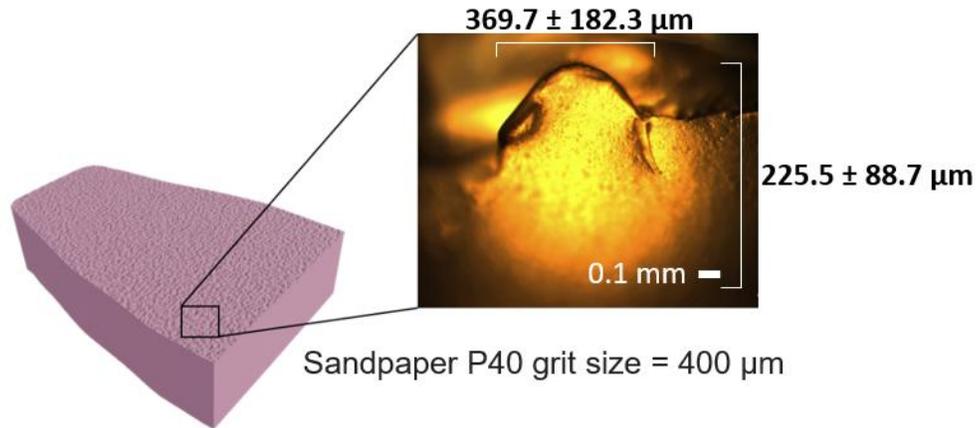
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932

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

933 *Appendix A.2. In Vitro Papillae Dimensions of the Soft-Robotic Tongue*

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

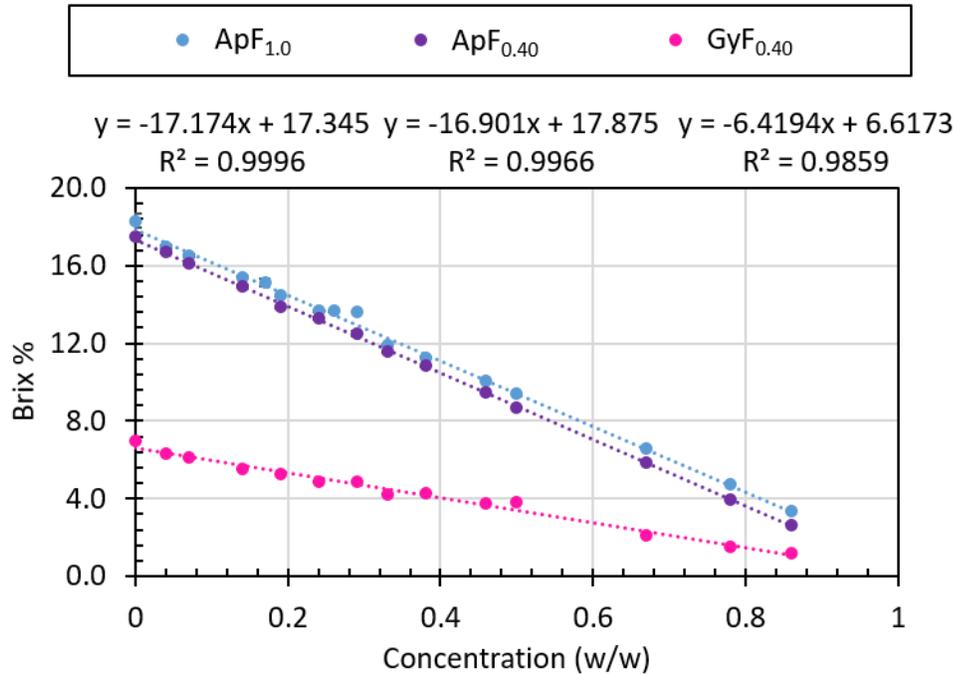


939
940

Figure A 2. In vitro papillae dimensions of the Soft-robotic Tongue.

941 *Appendix A.3. Degree Brix Calibration Curves*

942 The refractometer was calibrated to ensure a linear relationship between Brix percentage
943 and the mixing ratio of different combinations of flaxseed extracts and semi-solid foods. The
944 calibration curves are in a range of concentrations between 0 to 0.86 w/w. Data shows good
945 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}).

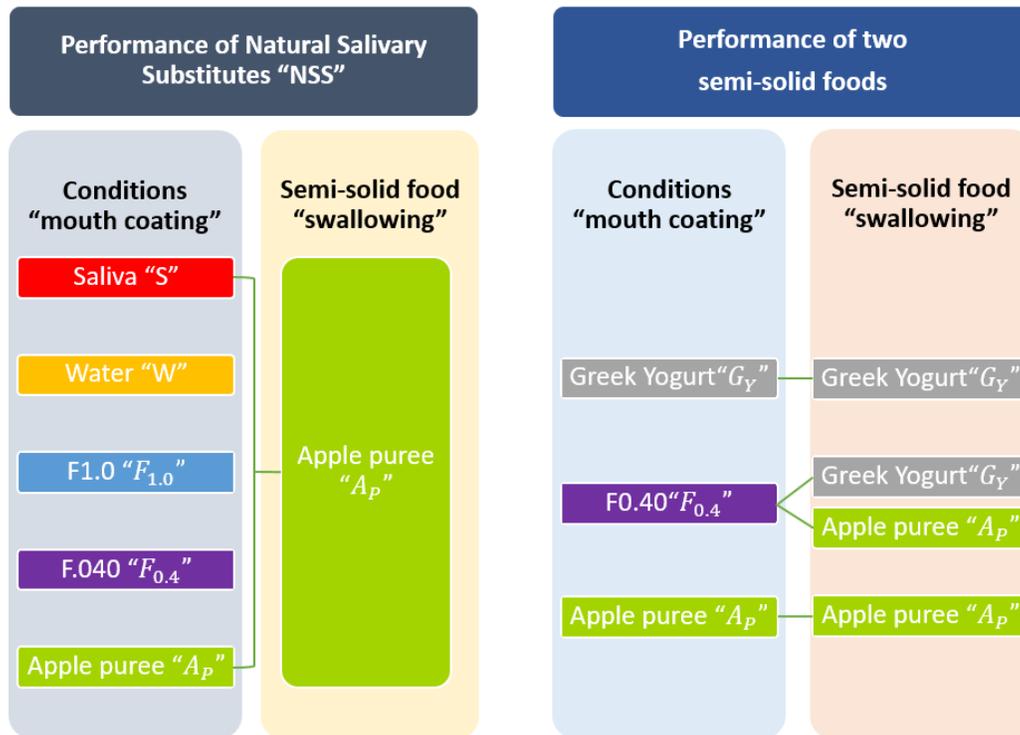


946

947 *Figure A 3. Brix calibration curves of apple puree and Greek yogurt using natural salivary substitutes at*
948 *0.40 % and 1.0 % dry matter.*

949 *Appendix A.4. Mouth Coating Combinations*

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



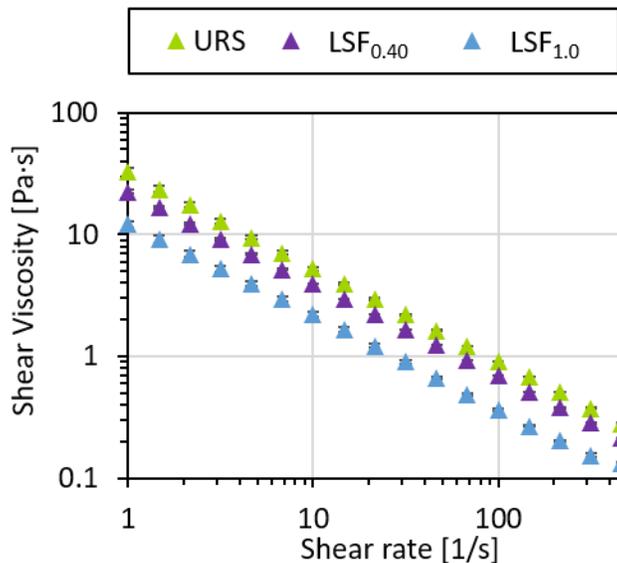
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960

Figure A 4. Mouth coating combinations.

961 *Appendix A.5. Bolus Viscosity Swallow #1 with Apple Puree*

962 The bolus viscosity after *in vitro* swallowing was characterized and it is presented in
963 Figure A 5. These results correspond to section 3.2, where the influence of natural salivary
964 substitutes was compared when swallowing apple puree.
965



966
967 *Figure A 5. Bolus viscosity from swallow #1 with apple puree. Abbreviations are: (URS) unlubricated*
968 *repeated swallowing, (LSF_{0.40}) lubricated swallowing using NSS at 0.40 % dry matter, and (LSF_{1.0})*
969 *lubricated swallowing using NSS at 1.0 % dry matter.*