

Polysaccharide food matrices for controlling the release, retention and perception of flavours

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1 Polysaccharide food matrices for controlling the release, retention and
2 perception of flavours

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11

12 Abstract

13 Polysaccharides have many roles across both the food and pharmaceuticals
14 industries. They are commonly used to enhance viscosity, stabilise emulsions
15 and to add bulk to food products. In the pharmaceuticals industry, they are also
16 utilised for their mucoadhesive nature. Mucoadhesive polysaccharides can
17 facilitate retention of active ingredients at mucosal sites for a prolonged time
18 and formulations can be designed to control their release and bioavailability.
19 This study investigates how polysaccharides, with differing physicochemical
20 properties (e.g. functional groups and molecular weight), affect the release
21 and perception of flavour compounds from films. Polysaccharide films were
22 prepared using either high or low viscosity carboxymethyl cellulose, pullulan
23 or hydroxypropyl methylcellulose. Glucose, vanillin or a combination of both
24 was also added to the films to assess the effect of flavour release and
25 perception over time. The films were assessed for glucose release *in vitro*,
26 swelling and disintegration times, and mucoadhesive ability. Results show
27 that flavour release and perception depend on the polysaccharide matrix
28 properties; this includes how quickly the films dissolves, the rate of release of

29 tastant compounds, and the mucoadhesive strength of the polysaccharide. A
30 higher viscosity and slower disintegration time resulted in slower release of
31 glucose *in vitro* and flavour perception *in vivo*.

32

33 Key words: polysaccharides, flavour, controlled, release, mucoadhesion

34

35 1. Introduction

36 Flavour perception requires the release of taste and aroma compounds from
37 the food matrix and the subsequent transport of those compounds to the
38 respective receptors. This process is dependent on many factors including the
39 properties of the compound, the components of the food matrix constituents,
40 food structure, how it is manipulated in the mouth and the physiological
41 conditions of the mouth, nose and throat during consumption of the food.
42 Furthermore, the onset and duration of flavour delivery is dependent on
43 factors such as partitioning, mass transport and diffusion. These factors play
44 varying roles and combined, result in a characteristic flavour profile for a food.

45

46 Typically, the polysaccharides, proteins and fats present in liquid food
47 systems determine the structure. The influence of these large molecules on
48 smaller molecules, such as aroma and tastant compounds, has been
49 investigated with various studies concluding that viscosity changes
50 (Hollowood, Linforth, & Taylor, 2002; Izutsu, Taneya, Kikuchi, & Sone, 1981;
51 Kokini, Bistany, Poole, & Stier, 1982; Secouard, Malhiac, Grisel, & Decroix,
52 2003; Stevenson & Mahmut, 2011) and physical entrapment of compounds
53 (Keršiene, Adams, Dubra, Kimpe, & Leskauskaite, 2008; Kora, Souchon,

54 Latrille, Martin, & Marin, 2004; Kuo & Lee, 2014) together explain perceptual
55 differences (S. L. Cook, Bull, Methven, Parker, & Khutoryanskiy, 2017). These
56 studies tend to focus on the matrix structure and the release characteristics
57 when contemplating changes in perception.

58

59 Chemical interactions between the flavour compounds and the food matrix is
60 also important (Heilig, Heimpel, Sonne, Schieberle, & Hinrichs, 2016;
61 Rodríguez-Bencomo et al., 2011; Scherf, Pflaum, Koehler, & Hofmann, 2015).
62 Factors such as charge of the flavour compound and other food constituents
63 will influence interactions between the two. For example, sodium is positively
64 charged and will therefore interact with negatively charged polysaccharides,
65 such as carboxymethyl cellulose, affecting the ions availability to elicit a salt
66 taste (Scherf et al., 2015). Retention of flavour compounds in the matrix will
67 obviously decrease their perception, as they will not reach the respective
68 receptors to be perceived and risk being swallowed in the food bolus before
69 triggering perception. However, if the matrix also adheres to the oral mucosa
70 then fewer tastant molecules may be swallowed allowing for release of the
71 flavour over time.

72

73 Many studies have investigated the impact on aroma release when reducing
74 fat in foods (Arancibia, Jublot, Costell, & Bayarri, 2011; Bayarri, Taylor, &
75 Hort, 2006). They have found, in general that aroma retention in the matrix of
76 a high fat food will increase as the P (partition coefficient of a molecule
77 between a lipophilic and an aqueous phase, usually octanol and water,
78 respectively) of the aroma compound increases. This means it will favour

79 being in the fatty matrix over partitioning into the aqueous saliva. Hydrophilic
80 compounds (log P equal to or less than zero) on the other hand tend to be
81 less dependent on changing fat levels (Arancibia, Castro, Jublot, Costell, &
82 Bayarri, 2015; Arancibia et al., 2011). In low fat systems, the release of
83 hydrophobic aromas will be faster leading to an unbalanced flavour profile.

84

85 More recently, interactions between food components and the oral and nasal
86 mucosa have been investigated. Specifically, interactions between flavour
87 molecules and the oral mucosa may explain persistence of aromas in certain
88 foods (Esteban-Fernández, Rocha-Alcubilla, Muñoz-González, Moreno-
89 Arribas, & Pozo-Bayón, 2016; Sánchez-López, Ziere, Martins, Zimmermann,
90 & Yeretizian, 2016). Furthermore, interactions between food matrices and the
91 oral mucosa have been of interest with regard to negative sensory
92 characteristics of dairy products (Bull et al., 2015; Hilal Y et al., 2015; Withers,
93 Cook, Methven, Godney, & Khutoryanskiy, 2013) and the impact of fat
94 reduction on perception of foods (De Hoog, Prinz, Huntjens, Dresselhuis, &
95 Van Aken, 2006; Dresselhuis, van Aken, de Hoog, & Martien, 2008).

96

97 Many polysaccharides are mucoadhesive, meaning they adhere to mucosal
98 surfaces in the body via intermolecular forces (hydrogen bonding, electrostatic
99 attraction, hydrophobic interactions and covalent bonds) and physical
100 penetration and entanglement of polymer chains (Andrews, Lavery, & Jones,
101 2009; Huang, Leobandung, Foss, & Peppas, 2000; Jabbari, Wisniewski, &
102 Peppas, 1993). Though this phenomenon has been of interest and well
103 utilised in the pharmaceuticals field for decades, the importance in the food

104 industry is beginning to gain interest (Bull et al., 2015; S. L. Cook, Bull, et al.,
105 2017; S. L. Cook, Woods, Methven, Parker, & Khutoryanskiy, 2018; Gibbins &
106 Carpenter, 2013; Hilal Y et al., 2015; Malone, Appelqvist, & Norton, 2003;
107 Withers et al., 2013).

108

109 Mucoadhesive polymers can retain and control the release of active
110 pharmaceutical ingredients (APIs) at mucosal surfaces including those in the
111 oral cavity (Andrews et al., 2009). The mechanisms of mucoadhesion have
112 been described in the literature numerous times (Peppas & Huang, 2004;
113 Shaikh, Singh, Garland, Woolfson, & Donnelly, 2011; Smart, 2005, 2014). The
114 physicochemical interactions depend on the polymeric substance (e.g ionic
115 groups, chain length), the state of hydration of the polymer, the mucosal
116 secretions (e.g. pH, thickness, mucin concentration) and the epithelial
117 structure and morphology (e.g. roughness and presence of micro cracks). The
118 fact that mucoadhesive polymers can retain small molecules at mucosal
119 surfaces and control their release will be important for the food industry to
120 consider as these frequently used polysaccharides may also retain tastant
121 and aroma molecules in a similar way (S. L. Cook, Woods, et al., 2018).

122

123 Many polysaccharides used in the food industry that are also mucoadhesive
124 include, but are not limited to; carboxymethyl cellulose (Yehia, El-Gazayerly,
125 & Basalious, 2008, 2009), sodium alginate (Juliano, Gavini, Cossu, Bonferoni,
126 & Giunchedi, 2004; Richardson, Dettmar, Hampson, & Melia, 2004) and
127 pectin (Kaur & Kaur, 2012; Thirawong, Nunthanid, Puttipipatkachorn, &
128 Sriamornsak, 2007). Buccal films are a formulation type made by dissolving a

129 polymer in a solvent, adding the API and evaporating the solvent to leave a
130 thin film of polymer matrix containing the API (Gherman, Zavastin, Ochiuz,
131 Biliuta, & Coseri, 2016; Kaur & Kaur, 2012; Satishbabu & Srinivasan, 2008;
132 Semalty, Semalty, Kumar, & Juyal, 2008). Buccal films can be designed to
133 release API over differing periods of time.

134

135 The only study investigating the effect of mucoadhesive polysaccharides on
136 flavour retention and perception was within an aqueous system. Also from our
137 group, our findings suggest that sodium ions are retained in the mouth for
138 longer when mucoadhesive polysaccharide is used as a thickener compared
139 to non-mucoadhesive matrices (S. L. Cook, Woods, et al., 2018). This current
140 study is concerned with the effect of mucoadhesive polysaccharides on
141 flavour perception from a solid food system (films). Various food grade
142 polysaccharides that differ in their chemical and physical properties were used
143 to assess the effect on release, retention and perception of flavours from
144 polysaccharide films.

145

146 Polysaccharides were cast into films containing glucose and/or vanillin.
147 These were based on films usually made for pharmaceutical applications. The
148 mucoadhesive properties, swelling ratio, dissolution rate, film thickness, water
149 activity and temporal sensory perception were assessed. Whilst this study
150 takes those factors into consideration, a further interaction between the food
151 matrix and the oral anatomy, mucoadhesion, is investigated. The aim for this
152 study was to assess the differences in flavour release from different
153 polysaccharide matrices in a solid state. It was hypothesised that films made

154 with more viscous, slower dissolving polysaccharides will reduce the intensity
155 but prolong the perception of flavours over time. Furthermore, the
156 mucoadhesive properties of the matrices were assessed and related to
157 flavour delivery. This study, therefore, provides a foundation of understanding
158 of the mechanisms by which mucoadhesive ingredients can alter the
159 perception of flavour over time, which may help in the development of
160 reformulated products.

161

162 2. Methods

163 2.1. *Materials*

164 Four different polysaccharides were chosen for this study due to their differing
165 chemical properties (Table 1). Pullulan (PUL) (Hayashibara nagase europa
166 group, Düsseldorf, Germany) was chosen as a non-ionic, low viscosity and
167 fast dissolving film former. Hydroxypropyl methyl cellulose (HPMC) (product
168 code METHOCEL K4M, Dow The Chemical Company, Staines, UK) was
169 chosen as a high viscosity, non-ionic film former. Two carboxymethyl cellulose
170 products were used, one low molecular weight (LCMC) (product code
171 AKUCCELL AF 0305, AkzoNoble, Amsterdam, The Netherlands) and one high
172 molecular weight (HCMC) (product code WALOCEL 4500, Dow The Chemical
173 Company, Staines, UK). Carboxymethyl cellulose was chosen as it is well
174 known for its mucoadhesive properties due to its ionic nature and high
175 viscosity.

176

177

178

179 Table 1. Polysaccharide characteristics

Sample	Molecular weight (Da)	Sodium content (% w/v)	Degree of substitution	Viscosity of 2% (w/v) solution at 25°C (mPa.s)
PUL	250, 000	<0	N/A	11
LCMC	140, 000	15.4 *	0.8	450
HPMC	300, 000	<0	1.8 methoxyl 0.13 hydroxypropyl	4500
HCMC	950, 000	8.7	0.8	5200

180 All data provided by the respective manufacturer except those indicated by *.

181 * Sodium content determined by flame photometry

182

183 2.2. Samples

184 Films were prepared by dissolving polysaccharides in deionised water (2%
 185 w/v) with glucose, vanillin (Sigma- Aldrich, St. Louis, Missouri, United States)
 186 or glucose and vanillin (Table 2). The solution (30g) was weighed into circular
 187 petri dishes (90 mm) and placed in an oven at 65°C for 20 hours. Once the
 188 films were dry they were removed from the petri dish and cut into squares
 189 (approx. 1cm²). Glucose containing films weighed 100 mg and the aroma only
 190 films 30 mg. This was to ensure that each sample contained the same amount
 191 of polysaccharide. The water activity (a_w) of the films was measured after the
 192 drying process using a HygroLab C1 Bench-Top Water Activity Monitor.

193

194

195 Table 2. Final concentrations of ingredients in each type of film

Film type	Polysaccharide (%)	Glucose (%w/v)	Vanillin (%)
Sweet	30	70	-
Vanilla	99.1	-	0.9
Sweet and Vanilla	29.5	69.4	0.9

196

197 *2.3. Artificial saliva*

198 Artificial saliva (AS) was used for all *in vitro* experiments to emulate conditions
 199 in the mouth. This was adapted from Madsen *et al.* (2013) and consisted of
 200 0.21 g/L NaHCO₃, 0.43 g/L NaCl, 0.75 g/L KCl, 0.22 g/L CaCl₂·2H₂O, 0.91 g/L
 201 NaH₂PO₄·2H₂O dispersed in deionized water. For the mucoadhesion
 202 experiment 2.5 g/L pig gastric mucin (PGM) type II (Sigma- Aldrich, St. Louis,
 203 Missouri, United States) was also added. The pH of the AS was adjusted to
 204 6.8 and kept at 37 °C during experiments and at 4 °C when not in use.

205

206 *2.4. Swelling and disintegration*

207 Swelling studies were carried out in an incubator set to 37 °C. Each film was
 208 placed on to netting and fully submerged in a petri dish with 40 mL of AS. At
 209 set time periods the sample was removed from the AS, excess water was
 210 carefully absorbed with tissue paper and the film on the netting was weighed.
 211 This process was repeated until the weight had returned to that of the netting
 212 alone. Each type of film was tested 6 times with duplicate batch repeats. Film
 213 thickness was measured before these experiments with a micrometer. The

214 maximum swelling ratio was determined by dividing the weight of the film at
215 set time points with the original weight of the film.

216

217 *2.5. Dissolution*

218 Each film containing glucose was placed onto netting and carefully
219 submerged into an individual beaker with 200 mL AS. The solution was stirred
220 by a magnetic stirrer bar at a constant rate throughout the experiment. At set
221 time points 1 mL aliquots of the AS medium were removed and put into
222 labelled Eppendorfs for analysis. The glucose in the samples was quantified
223 spectrophotometrically using an Amplex Red, glucose oxidase kit following
224 the advised protocol (Fisher Scientific, Loughborough, UK). Each sample was
225 tested 6 times with duplicate batch repeats. The time taken to release 50 and
226 100 % of the glucose was calculated from the results.

227

228 *2.6. In vitro mucoadhesion*

229 Adhesion experiments were carried out using a texture analyser (TA) with a
230 10mm cylindrical probe (on a TA-XT plus, Stable Micro Systems, UK). Porcine
231 tongues were collected from a local butcher (P D Jennings, Hurst, UK) less
232 than 24 hours after slaughter. They were stored on ice whilst the majority of
233 muscle and connective tissue was removed leaving a thin section of the
234 surface mucosa. These sections were stored at -20°C until required when
235 they were thawed in the fridge for 3 hours before use.

236

237 Each area of the tongue was cut into 1 cm² sections and secured on the
238 bottom platform of the TA. The film sample to be tested was stuck to the

239 probe with double-sided sticky tape. Before each experiment, the tongue
240 tissue section was conditioned with 100µL of AS and incubated at 37°C. The
241 contact time between the probe and the tissue was 60 seconds before pulling
242 apart with a removal speed of 1mm/s.

243

244 *2.7. In vivo retention*

245 The study was given a favourable opinion for conduct by the University of
246 Reading, School of Chemistry, Food and Pharmacy (study number 27/15).
247 Five volunteers (3 males and 2 females, age range 23-30) were asked to
248 place a film sample on their tongue and keep it between the tongue and roof
249 of their mouth for the duration of the experiment. They were instructed to treat
250 the film like a hard candy with some manipulation by the tongue. The
251 experiment was timed and volunteers were asked to note the time (s) when
252 the film began to adhere, when the adherence ceased and when the film
253 dissolved. They were also asked where in the mouth the film adhered to.
254 Adherence was noted as an inability to move the film with their tongue.

255

256 *2.8. Sensory perception*

257 Time intensity; profiling involves trained sensory panellists continuously
258 recording the intensity of one or two attributes over a specified time. This
259 enables perception to be captured during consumption and can be
260 summarised as parameters such as onset, persistence and duration. Over a
261 period of three weeks, 8 trained panellists from the University of Reading
262 Sensory Science Centre panel scored each of the film samples in duplicate.
263 There were 12 samples in total. For each polysaccharide, films were made

264 with either glucose alone, vanillin alone or glucose with vanillin. Each week
265 was used for one set of polysaccharide films. For example, in week 1 the
266 glucose only films were scored, in a balanced order, for sweetness over time.

267

268 Training took place before each scoring week to familiarise the panel to the
269 samples and the time intensity protocol. Each film was presented to the panel
270 and a discussion of the different flavour release behaviours for each of them
271 took place. During these sessions, the panel were given 3 standards for both
272 glucose and vanillin. Glucose standards were 8%, 4% and 2%, and aroma
273 samples were 0.02%, 0.01%, and 0.005%. The panellists decided where
274 these standards scored on the line scale with their strongest standard
275 representing 100 on a standard 100-point scale. These standards were given
276 to the panellists at the start of each scoring sessions to re-familiarise them
277 with the standard intensities.

278

279 Panellists were trained on single and dual attribute time intensity scoring
280 using Compusense@hand software (Ontario, Canada) and feedback was
281 given to those who were not showing good reproducibility. The time intensity
282 test lasted for 5 minutes, which was the agreed amount of time that the
283 panellists could concentrate for without fatigue or boredom. The attributes
284 scored were sweet for glucose only films, vanilla for aroma only films and both
285 sweet and vanilla for the combined films. Panellists were also trained on how
286 to manipulate the sample in the mouth. They were asked to gently rub the film
287 between the tongue and roof of the mouth to facilitate flavour release.

288 Panellists were instructed to treat each sample the same way to avoid biasing
289 release.

290

291 Each week the panellists were given a training session on the first day
292 followed by two days of scoring the samples. Four samples were served
293 monadically, in a petri dish, in a balanced order with individual blinding codes
294 each day with the duplicate being served on a consecutive scoring day.
295 Panellists were provided with isolated sensory booths, computers with
296 Compusense Software and warm water for palate cleansing. There was a 2-
297 minute delay between samples to allow for palate cleansing. Time intensity
298 curves were produced for each panellist and each sample in duplicate.

299

300 *2.9. Statistical analysis*

301 One way or two way repeated measures ANOVA (rmANOVA) was used for
302 the appropriate test. Bonferroni or Tukey's HSD corrections were used on
303 pairwise analysis to account for multiple comparisons, at a significance level
304 of $p \leq 0.05$.

305

306 3. Results & Discussion

307 *3.1. Film characteristics*

308 A range of standard methods were used to characterise the polymeric films
309 (Morales & McConville, 2011; Nair et al., 2013). Each film was measured for
310 thickness, water activity (a_w), glucose release, and swelling / disintegration
311 times (Table 3).

312

313 The thickness of the films varied between the different polysaccharides and
314 between the films with and without glucose. The order of film thickness was
315 HPMC>HCMC>LCMC>PUL. This is not surprising as HPMC and HPMC were
316 higher viscosity grades than LCMC and PUL and therefore will occupy more
317 space, retain more water and form thicker films. Glucose films were thicker
318 than those without glucose, which was expected, as the glucose was in
319 addition to the polysaccharides. The thickness of a film will impact the
320 dissolution rate as a thicker film will have a smaller surface area to volume
321 ratio and this can slow water uptake from the surrounding medium. This will
322 impact mucoadhesion as hydration of the dosage form is integral for polymer -
323 mucin interactions to occur.

324

325 PUL and LCMC films fully dissolved after a similar time; however, LCMC films
326 swelled more before beginning to disintegrate (Table 3 & Figure S1). This is
327 because LCMC is more viscous than PUL (table 1) and possesses ionic
328 groups, which interact strongly with water molecules due to the higher osmotic
329 pressure induced by the high entropy of the counter-ions. LCMC and HPMC
330 films swelled considerably more than the non-ionic, PUL and HPMC films with
331 relation to their disintegration time. The carboxymethyl cellulose films
332 absorbed more water, forming a swollen gel-like layer, before beginning to
333 degrade. HPMC samples took the longest time to dissolve and swelled the
334 most due to their high viscosity. All films without glucose had higher swelling
335 ratios than their glucose containing counterparts and took longer to dissolve.
336 This is because the small, highly hydrophilic glucose molecules contained
337 within the film matrix will quickly dissolve into the surrounding medium,

338 leaving pores for the water molecules to enter, effectively increasing the
339 surface area of the film.

340

341 The glucose release from the films followed a similar pattern to the dissolution
342 rates. PUL and LCMC released glucose fully after 7.0 and 7.8 min
343 respectively, followed by HPMC (186 min) and then HCMC (300 min). HPMC
344 quickly released 50% of the total glucose in the film over a mean of 14
345 minutes. This fast initial release is most likely due to crystallisation of the
346 glucose molecules on the outside of the film. This was visually observed, as
347 these films were cloudy with a fine powder covering them. Furthermore, the
348 HPMC samples took a long time to fully dissolve, most likely due to the high
349 viscosity network it forms which will slow permeation of water molecules. The
350 HCMC released the glucose at a constant rate. The HCMC films swelled
351 considerably so the swollen, surface of the film contained loosely associated
352 polymer chains, which would then allow the glucose molecules to diffuse out
353 and dissolve in the surrounding medium. The increased surface area caused
354 by the high swelling degree of the HCMC films may facilitate glucose release,
355 however, the thick gel layer covering the outer surface of the film may also
356 decrease diffusion by physical entrapment. Additionally, the thick gel layer
357 may prevent matrix disintegration and affect subsequent water uptake when
358 unperturbed (Rodriguez, Bruneau, Barra, Alfonso, & Doelker, 2000). HPMC
359 did not swell substantially but took a long time to dissolve, therefore the
360 glucose molecules would essentially be trapped in the film matrix until is
361 started to erode.

362

363 Table 3. Characteristics of films

Polymer	Glucose content (%)	a_w (mean)	Thickness (mm)	Dissolution time (min)		Max swelling ratio	50% glucose release (min)	100% glucose release (min)		
PUL	-	0.451 ^a	0.071 ^a	5	^a	5.8 ^a	-	-		
LCMC	-	0.486 ^b	0.094 ^{a,b}	4	^a	11.6 ^a	-	-		
HPMC	-	0.478 ^b	0.148 ^b	147	^b	11.6 ^a	-	-		
HCMC	-	0.474 ^b	0.104 ^{a,b}	357	^c	34.9 ^b	-	-		
PUL	70	0.502 ^b	0.281 ^a	5	^a	1.8 ^a	3.2 ^a	7.0 ^a		
LCMC	70	0.491 ^b	0.369 ^{a,b}	5	^a	3.4 ^b	3.3 ^a	7.8 ^a		
HPMC	70	0.460 ^a	0.429 ^b	153	^b	4.4 ^b	14.4 ^b	186.1 ^b		
HCMC	70	0.496 ^b	0.360 ^{a,b}	210	^c	16.0 ^c	150.0 ^c	300.0 ^c		

364 Films are separated into those without glucose and those with glucose. Each
365 value is the mean of 6 replications for the measured parameters (2 batch
366 repeats). Mean values within a column and film group not sharing the same
367 letter were significantly different from each other at $p \leq 0.05$ using Tukey's
368 HSD correction.

369

370 It was expected that changes in flavour perception over time would be
371 influenced by the parameters measured (Table 3). For example, it was
372 hypothesised that PUL films would result in a high intensity flavour that
373 decreased in intensity quickly as they dissolved faster and released glucose
374 quickly. Conversely, it was expected that as the HCMC would slow the

375 release of glucose and aroma and therefore reduce the initial intensity of
376 flavour but prolong the sensation over time. The results gained from this study
377 are in concordance with the authors expectations.

378

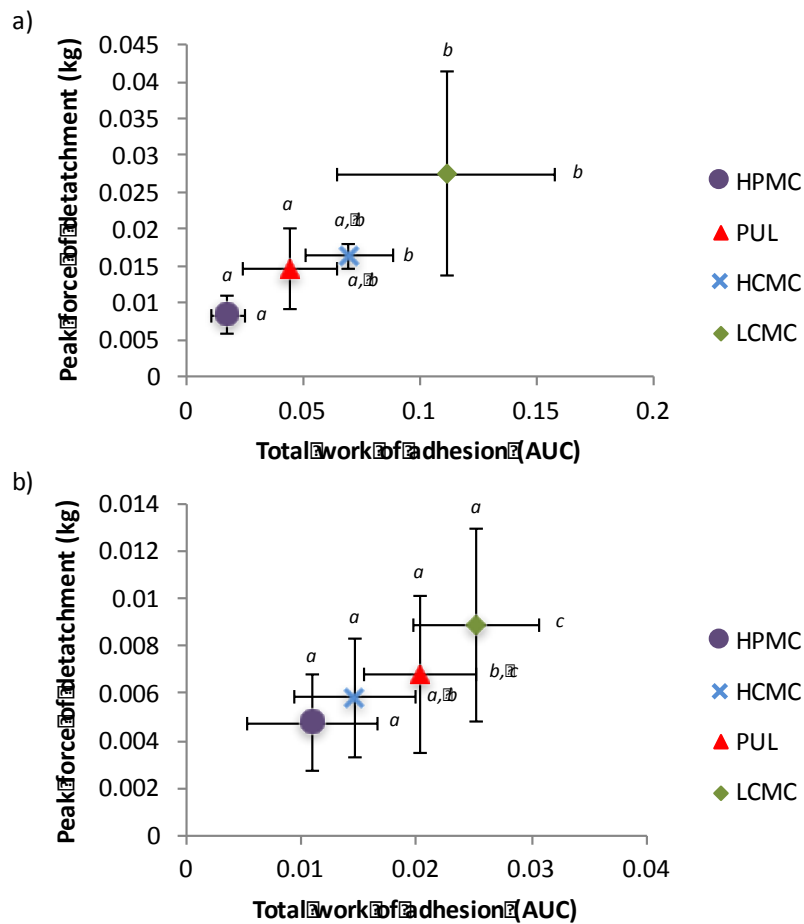
379 *3.2. Mucoadhesion in vitro*

380 Two values were obtained from the TA experiments; the maximum force
381 required to separate the probe from the tongue (peak force of detachment)
382 and the area under the curve (total work of adhesion). The mean values for
383 peak force of attachment and total work of adhesion decreased in order of
384 LCMC, HCMC, PUL and HPMC for films without glucose and LCMC, PUL,
385 HCMC and HPMC for films with. In films both with and without glucose the
386 LCMC film was significantly more mucoadhesive than the HPMC film (Figure
387 1a & b). The films without glucose required a significantly higher force to
388 separate the film from the tissue suggesting a stronger adhesive joint (Figure
389 1a). This is not surprising as the glucose content was high and therefore the
390 relative amount of polymer in contact with the tissue was smaller. The HPMC
391 films with glucose exerted the lowest total work of adhesion and peak force of
392 detachment (Figure 1). This is probably due to the non-ionic nature of HPMC
393 along with the large molecule size and slow swelling (Table 3 & Figure S1).

394

395 Mucoadhesion of solid polymeric substances is dependent on the hydration of
396 the formulation, which will create a polymeric mesh enabling the interactions
397 between polymer and mucin chains. The mucin used in the artificial saliva
398 were PGM purchased from Sigma-Aldrich, which is dehydrated and potentially
399 denatured due to production processes (Kocevar-Nared, Kristl, & Smid-

400 Korbar, 1997). Therefore, the interactions that may occur with salivary mucin
 401 may not be represented by this commercial mucin. Furthermore, an adhesive
 402 joint is formed due to the viscous gel formed between the film and the moist
 403 mucosal surface. However, over-hydration of the film will lead to a slippery
 404 mucilage being formed and will result in an adhesive joint failure. The swelling
 405 ability of a polymeric substance is important for establishing a mucoadhesive
 406 bond as this enables polymer chains to be available to interact with the
 407 mucosa.



408
 409 Figure 1. Total work of adhesion against the peak force of detachment for
 410 films a) without glucose and b) with glucose. Results determined by texture
 411 analysis. Data points are means of 6 measurements and error bars are SD.
 412 Superscript letters represent statistically different groupings ($p < 0.05$). Letters

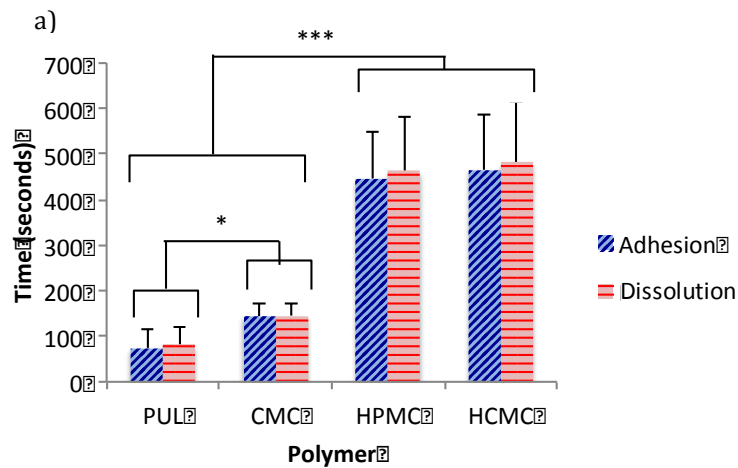
413 on top of the data point refer to the y axis and those to the right hand side
414 refer to the x axis.

415

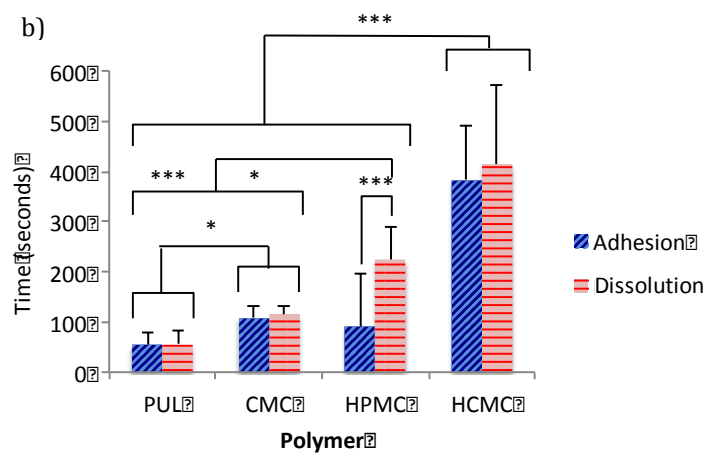
416 3.3. *Mucoadhesion in vivo*

417 *In vivo* mucoadhesion experiments were carried out with 5 panellists that were
418 asked to record the following: where the film stuck, for how long and when it
419 dissolved. All films, except for HPMC with glucose, were reported to adhere
420 for the duration of the time that the film was in the mouth (Figure 2a & b).
421 Adherence was mainly to the roof of the mouth but also the tongue. The time
422 that the films took to dissolve reflected the *in vitro* dissolution (Table 3) as
423 PUL and LCMC took the least amount of time to dissolve followed by HPMC
424 then HCMC. For films without glucose, HPMC and HCMC films did not differ
425 in time for dissolution *in vivo* (Figure 2a) despite the difference in the *in vitro*
426 test. This is probably due to the participants manipulating the film with their
427 tongue during these experiments, thereby exerting mechanical stress on the
428 film. Therefore, as the HCMC swells and takes up water to produce a gel-like
429 layer, the tongue pressure will remove it and therefore speed up the time of
430 erosion.

431



432



433

434 Figure 2. *In vivo* mucoadhesion of a) polymer films without glucose and b)
 435 polymer films with glucose. Each bar represents the mean of 10 separate data
 436 points, error bars represent standard deviation. N= 5 in duplicate. * = $p < 0.05$,
 437 *** = $p < 0.001$.

438

439 The HPMC films with glucose were reported to adhere for a significantly
 440 shorter time than it took to dissolve and 3 out of 5 of the panellists reported
 441 that the film did not adhere at all (Figure 2b). This reflects the *in vitro* tensile
 442 experiments where HPMC was concluded to be significantly less adhesive
 443 than the other films. Contrary to these *in vitro* tensile experiments, HPMC
 444 films without glucose were mucoadhesive in the *in vivo* experiments, with all

445 panellists reporting adherence after an initial delay. There are two
446 explanations to this. Firstly, AS was used in the *in vitro* experiments, which
447 contained Sigma-Aldrich PGM as opposed to human salivary mucin. This may
448 affect interactions between the polysaccharide matrix and the saliva due to
449 differences in denaturation states and response to pH. For example, mucin
450 chains must be flexible and uncoiled enough to allow interpenetration with
451 polymer chains. Secondly, the hydration of the oral cavity *in vivo* may be
452 different to that which was on the porcine tongue in the *in vitro* experiments.
453 This may have led to a stronger adhesion *in vivo*, as the film did not become
454 overhydrated.

455

456 The PUL film dissolving and adherence time was significantly quicker for
457 LCMC films in these experiments. The PUL films dissolved on average at 81
458 seconds compared to 145 seconds for the LCMC films during these
459 experiments. This is in contrast to the results obtained from the *in vitro*
460 dissolution tests (table 3) where they were not significantly different. This
461 difference was expected to have an impact on flavour release from LCMC
462 films compared to PUL. Film thickness is the most likely explanation for the
463 differences observed, LCMC films were thicker than PUL and therefore, when
464 in contact with the moist mucosal surface, will take longer to take up water. To
465 properly assess the impact of polysaccharide type on dissolution times, the
466 thickness of the films would need to be matched.

467

468 *3.4. Perception of tastant and aroma from films over time changes depending*
469 *on polysaccharide used*

470 Panellists produced time intensity curves for each sample and repeat. They
471 continuously scored either sweetness or vanilla, or both attributes at the same
472 time, over the course of 5 minutes using an unstructured line scale. Various
473 parameters were extrapolated from the curves including the area under the
474 curve (AUC), time to maximum intensity (T_{max}), maximum intensity (I_{max}),
475 duration of perception, and incline and decline angles (Figure S2). One-way
476 rmANOVA was used for each parameter

477

478 3.4.1. *Glucose only films*

479 Time intensity curves were averaged across all panellists and both replicates
480 (Figure 3). The mean sweetness AUC and I_{max} values for the films decreased
481 in order of PUL >LCMC >HPMC >HCMC with the reverse order for T_{max}
482 (Table 4) where PUL was significantly higher than HCMC and higher for all
483 other films for I_{max} . This suggests a fast onset of intensity for PUL and LCMC,
484 which is supported by their larger incline angles compared to HPMC and
485 HCMC. Furthermore, PUL and LCMC decline angles were also larger than the
486 other two film types suggesting a quicker rate of decline. These results were
487 expected as *in vitro* results (Table 3) show that PUL and LCMC films were
488 faster dissolving and release glucose quicker than HPMC and HCMC films
489 (table 3). Although the total duration of perception was not significantly
490 different between the films, there was a trend that HPMC and HCMC films
491 prolonged the flavour perception compared to PUL and LCMC (see “duration”
492 in table 4).

493

494 Regarding mucoadhesion, the HPMC films containing glucose were found to
495 have poor adhesive abilities (Figures 1 & 2). In the perception experiments
496 panellists were asked not to swallow these films and, therefore, the perception
497 may have been artificially prolonged due to consciously keeping the film in the
498 mouth. During normal consumption in a real food system the material would
499 be chewed into a bolus and, without mucoadhesive ability, it may well be
500 swallowed with the food bolus thereby negating any further release. On the
501 other hand, HCMC films showed strong adhesion (Figures 1 & 2) and
502 therefore would be more likely to adhere to the oral cavity for longer,
503 prolonging the release.

504

505 *3.4.2. Vanillin only films*

506 For films containing the polysaccharide and vanillin the mean scores for I_{max}
507 decreased in order of PUL>LCMC>HPMC>HCMC (Table 4, Figure 3b).
508 Where PUL was significantly higher than HCMC. T_{max} and AUC were not
509 dependent on polysaccharide type. The duration of perception was longest in
510 the HPMC samples followed by HCMC. This suggests that although the total
511 intensity of perception was the same for each film, the aroma was delivered at
512 a slightly lower intensity for longer in the HPMC and HCMC samples. This is
513 supported by the decline angles being larger for PUL and LCMC samples
514 suggesting the intensity decreased more quickly in these films.

515

516 To date, the only studies investigating aroma release and perception in food
517 thickened with polysaccharides are in liquid and semi-solid foods. These
518 studies have found confounding results with regard to interactions between

519 aroma molecules and the food matrix. Arancibia et al. (2011) found that
520 thickener type affected total aroma release from dairy desserts with CMC
521 thickened samples reducing the cumulative release of hydrophobic aroma
522 (linalool) compared to starch. Furthermore, a follow up study by Arancibia,
523 Castro, Jublot, Costell, & Bayarri (2015) found that thickener type affected
524 both hydrophilic aroma (cis-3-hexen-1-ol) and hydrophobic (linalool) aroma.
525 The CMC thickened dairy desserts reduced the release of both aromas,
526 though it had more of an impact on the hydrophilic compound. Cook, Linforth,
527 et al., (2003) on the other hand found that in-nose measurements of
528 hydrophobic aroma release were not dependent on thickener type or on an
529 increase in viscosity. These studies exemplify the complex behaviour of
530 aroma release and its dependence on the food matrix.

531

532 In this current study, vanillin, a slightly hydrophobic molecule with a log P of
533 1.2, was used as the aroma. Perception results show that films made with
534 slow dissolving polysaccharides (HPMC and HPMC) reduced the I_{max} but
535 prolonged the duration of perception. Perception results for the aroma only
536 films were not as distinguishable as the films containing glucose. This may be
537 because the panel found scoring the aroma only films particularly difficult as
538 they contained no tastant along with the aroma, which does not normally
539 occur in food products.

540

541 3.4.3. *Glucose & vanillin films*

542 Dual attribute time intensity was used to simultaneously and continuously
543 monitor sweetness and vanilla attributes over 5 minutes. Results for the

544 sweetness attribute were similar for the dual attribute and single attribute tests
545 (Table 4, Figure 3c and d). The AUC and I_{max} were highest for PUL and
546 lowest for HPMC. HPMC and HPMC took longer to reach T_{max} compared to
547 PUL and LCMC.

548

549 The AUC for the vanilla attribute did not significantly differ with the different
550 polysaccharides (Table 4). HPMC and HPMC had reduced I_{max} and increased
551 T_{max} results compared to PUL and LCMC. The total duration of perception
552 was striking in these films with the HPMC averaging 53 seconds longer than
553 PUL. HPMC also increased the duration significantly compared to PUL and
554 LCMC. Although not statistically significant, LCMC followed the trend of
555 prolonging the perception compared to PUL. The incline angles for HPMC and
556 HPMC were, again, smaller than PUL and CMC suggesting a slower rate of
557 onset.

558

559 These results suggest that PUL films give a quick burst of flavour that
560 declines quickly. LCMC films are almost as quick to release as PUL but take
561 somewhat longer to reach I_{max} . HPMC has a slower onset to reach I_{max} and
562 the perception continues for longer than LCMC and PUL. Finally, HPMC films
563 have the slowest onset with a steady release over time. This is particularly
564 evident for the vanilla attribute, which prolongs the perception for longer than
565 the faster dissolving films.

566

567 Although from this perception data HPMC films appear to give a sustained,
568 medium level intensity of flavour, this formulation was not particularly

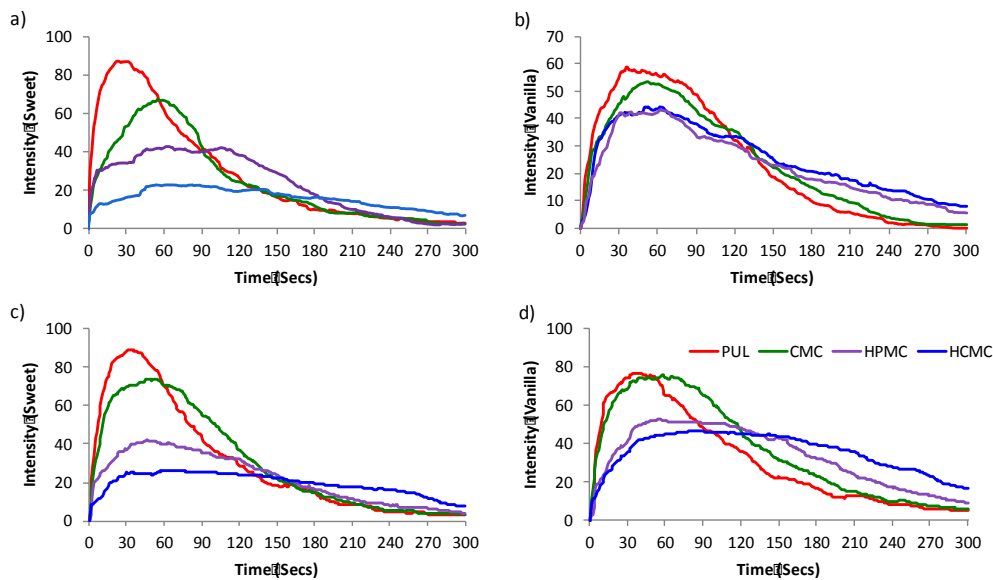
569 mucoadhesive and, therefore, it would most likely be swallowed along with the
 570 bolus in a real food system. Participants were instructed not to chew or
 571 swallow the film and many suggested that this would have been possible if
 572 they were eating normally. However, the other formulations were firmly
 573 adhered to the roof or tongue tissue and would not be easily swallowed.

574

575 Table 4. Parameters from time intensity results.

Film type	Attribute	Polymer	AUC	I _{max}	T _{max} (secs)	Duration (secs)	Incline angle (°)	Decline angle (°)
Glucose Sweet		PUL	8410 ^b	91 ^d	22 ^a	200 ^a	73 ^b	30 ^b
		LCMC	7468 ^{a,b}	75 ^c	48 ^b	201 ^a	58 ^b	27 ^b
		HPMC	7126 ^b	54 ^b	61 ^b	231 ^a	38 ^a	20 ^a
		HCMC	4834 ^a	31 ^a	88 ^b	249 ^a	34 ^a	11 ^a
Aroma Vanilla		PUL	7291 ^a	68 ^b	41 ^a	196 ^a	57 ^a	25 ^{b,c}
		LCMC	7154 ^a	59 ^{a,b}	40 ^a	195 ^a	50 ^a	28 ^c
		HPMC	7622 ^a	53 ^{a,b}	50 ^a	264 ^b	47 ^a	14 ^a
		HCMC	6176 ^a	51 ^a	38 ^a	230 ^{a,b}	54 ^a	19 ^{a,b}
Aroma and Glucose Vanilla	Sweet	PUL	9154 ^{b,c}	92 ^d	25 ^a	221 ^a	73 ^c	28 ^{b,c}
		LCMC	9295 ^c	82 ^c	32 ^a	224 ^a	64 ^b	27 ^c
		HPMC	6661 ^{a,b}	50 ^b	64 ^b	245 ^a	41 ^a	17 ^{a,b}
		HCMC	5864 ^a	36 ^b	64 ^b	266 ^a	34 ^a	12 ^a
	PUL	9499 ^a	87 ^b	29 ^a	239 ^a	67 ^b	21 ^a	
	LCMC	10957 ^a	82 ^b	35 ^a	254 ^{a,b}	67 ^b	23 ^a	
	HPMC	10081 ^a	56 ^a	54 ^{a,b}	276 ^b	46 ^a	14 ^a	
	HCMC	10770 ^a	54 ^a	73 ^b	292 ^b	43 ^a	16 ^a	

576 8 panellists scored each sample in duplicate therefore each result is the mean
577 of 16 separate results. Statistical analysis was done for each attribute
578 separately comparing the different polysaccharides. Different letters represent
579 significantly different groupings for each set of data.



580

581 Figure 3. A panel of 8 trained panellists scored different polysaccharide films
582 in duplicate for either sweetness or vanilla perception over time. Time intensity
583 curves for a) glucose only films, b) vanillin only films were produced from
584 single attribute time intensity tests. Dual attribute time intensity tests produced
585 the curves for glucose and vanillin films in c) and d).

586

587 3.5. Comparing perception results to *in vivo* dissolution

588 During the *in vivo* experiments where participants were asked to record the
589 adhesion and dissolution of the films, PUL was reported to dissolve after an
590 average of 57 seconds. When comparing these timings to the perception data
591 it is clear that perception of flavour is continuing after the film has completely
592 dissolved (Table 4 & Figure 3). There are two explanations for this. Firstly, the
593 glucose and aroma molecules may still be present at the respective receptors,

594 thereby initiating a response. Secondly, as the intensity of sweetness was
595 very high, an adaptation type response could occur where the sweet signal is
596 switched on for a longer time even after the stimulus has gone.

597

598 The physiological differences between participants were not collected for the
599 in vivo mucoadhesion nor the sensory perception experiments. Factors such
600 as salivary flow and constituents varies between individuals (Fenoli-
601 Palomares et al., 2004) and will therefore impact the mucoadhesive strength
602 and rate of film dissolution. Despite not adding these covariates in analysis,
603 there were still significant results gained from the experiments.

604

605 *3.6. Comparisons between different film types*

606 Time intensity results were compared between 5 panellists who were
607 consistent for both experiments. The AUC for the vanilla attribute differed
608 between films with and without glucose (Figure 4). Significant increases in the
609 total perception intensity (AUC) of vanilla were observed for LCMC, HPMC
610 and HCMC films containing vanillin plus glucose compared to those without
611 glucose.

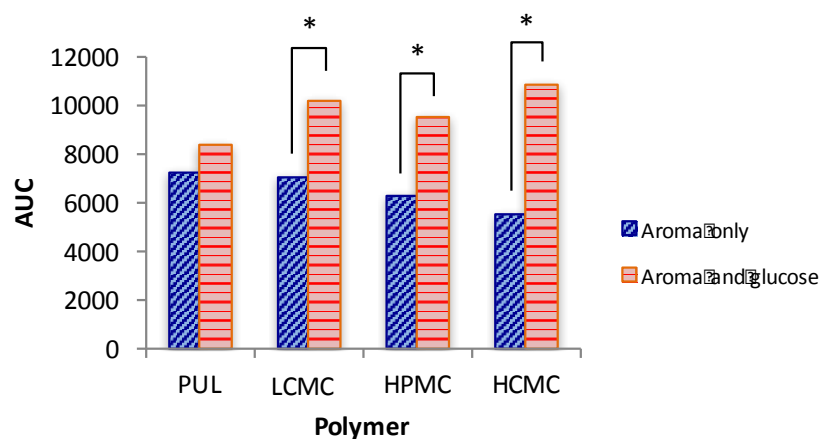
612

613 During single attribute time intensity, the attribute is scored horizontally but
614 during dual attribute, one must be scored vertically. The vanilla attribute was
615 scored vertically in the dual attribute tests, which may have affected the
616 results. Duizer, Bloom, & Findlay, (1995) investigated this issue and found
617 that scoring an attribute vertically lead to approximately 13% increase in

618 scores. However, as the increase is more substantial it is unlikely this is the
619 only factor.

620

621 A more likely explanation is that the presence of glucose in the films
622 enhanced the aroma through cross modality (D. J. Cook et al., 2003; Niimi,
623 Eddy, Overington, Heenan, et al., 2014; Niimi, Eddy, Overington, Silcock, et
624 al., 2014). T_{max} was also significantly ($p < 0.05$) increased for vanillin in the
625 HCMC films going from 26 to 89 seconds (Figure S3). This suggests that
626 when glucose was present the perception of aroma had a slower onset, which
627 lasted for longer and was sustained.



628

629 Figure 4. Comparisons of the area under the curve for the vanilla attribute of
630 films with and without glucose. * denotes significant differences $p = < 0.05$
631 using Bonferroni correction.

632

633 4. Conclusions

634 This study has shown that polysaccharides affect the retention, release and
635 perception of flavour compounds, dependant on the physicochemical
636 properties of the polysaccharide matrix. The viscosity and swelling ability of

637 the polysaccharide influences the release of flavour molecules from the
638 matrix. This in turn has an impact on the flavour perception. Fast dissolving
639 polysaccharides resulted in a quick burst of flavour at high intensity that
640 tapered more quickly whereas slow dissolving films gave a slower onset and a
641 more consistent release over time. The mucoadhesive ability of the films will
642 influence how long the matrix stays in the mouth whilst releasing the flavour
643 compounds before being swallowed. Furthermore, in line with previous
644 literature, this study shows that aroma intensity is dependent on the
645 perception of a congruent tastant, giving more evidence for cross modal
646 interactions.

647

648 The mucoadhesive nature of some of the polysaccharides tested will have an
649 effect on flavour delivery over time as those that adhere to the oral cavity will
650 continue to release flavour whilst those that are not mucoadhesive will be
651 swallowed. This study investigated flavour release from very simple food
652 matrices, polysaccharide films; of course in a real food there will be many
653 other food components that could affect flavour release. However, this study
654 provides some fundamental understanding of how different polysaccharide
655 matrices affect flavour release. Results from this study can be used to inform
656 the food industry of the impact that the addition of these polysaccharides can
657 have on temporal flavour perception. Possible applications include topical
658 coatings, confectionary, low fat and low sugar foods. However, there is a need
659 for further research into this area to understand the full impact on the
660 organoleptic properties of foods.

661

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