

1 **TITLE**

2 Development of Sustainable Novel Foods and Beverages Based on Coffee By-products
3 for Chronic Diseases

4

5 **AUTHORS**

6 Nuria Martinez-Saez¹, María Dolores del Castillo²

7 ¹ Basque Culinary Center, Faculty of Gastronomic Sciences, Mondragon University.

8 Paseo Juan Avelino Barriola 101, 20009 San Sebastián, Donostia, Spain.

9 nmartinez@bculinary.com

10 ² Food Bioscience Group, Department of Bioactivity and Food Analysis, Instituto de

11 Investigación en Ciencias de la Alimentación (CIAL) (CSIC-UAM), C/ Nicolás Cabrera,

12 9, Campus de la Universidad Autónoma de Madrid, 28049 Madrid, Spain.

13 mdolores.delcastillo@csic.es

14

15 **Keywords**

16 Antioxidant dietary fiber, chronic metabolic diseases, coffee silverskin, novel beverages,
17 novel foods, obesity, revalorization, spent coffee grounds, sustainability, satiating
18 hormones, type 2 diabetes

19 **Synopsis**

20 Obesity and type 2 diabetes have reached epidemic proportions in the past few years. The
21 market of functional foods has greatly increased for the reduction of risk of chronic
22 diseases. Coffee is one of the most frequently consumed drinks worldwide and large
23 amounts of coffee wastes need to be recycled in order to reduce its environmental impact.
24 Coffee by-products contain appreciable amounts of bioactive nutrients exerting health
25 promoting properties. Therefore, the valorization of coffee wastes represents a great
26 opportunity for the sustainability of the coffee sector and the industry of functional
27 beverages and foods for chronic diseases.

28 **Abstract**

29 At present, the global obesity epidemic is showing no signs of abating, which is fueling
30 an explosion in numbers of type 2 diabetes (T2D) worldwide. In order to control these
31 two associated diseases, lifestyle modification, which encompasses diet, physical activity,
32 and healthy habits, might be useful. The use of bioactive compounds obtained from
33 vegetable sources might be a favorable approach to reduce the risk of metabolic chronic
34 diseases; however, it is still a challenge to face. Coffee silverskin (CS) and spent coffee
35 grounds (SCG) are very abundant coffee wastes worldwide generating global
36 environmental problems. They are natural sources of several bioactive compounds with
37 potential to reduce the risk of chronic non-communicable diseases, such as chlorogenic
38 acid (CGA), caffeine and dietary fiber. The widespread interest in select foods that might
39 promote health has resulted in the use of functional foods to provide specific health
40 benefits beyond basic nutrition. Therefore, these two coffee wastes may become
41 sustainable high value-added ingredients of interest for the management of obesity and
42 T2D. The present chapter presents the feasibility to produce sustainable high sensorial
43 quality beverage and foods, for reducing the risk of chronic metabolic diseases, by means
44 of employing as novel ingredients coffee by-products (CS and SCG) and their derivatives,
45 in combination with other functional ingredients.

46

47 **Introduction**

48 Currently, chronic diseases are the leading global causes of death. It will increase up to
49 52 million of deaths by 2030 (World Health Organization, 2014). Obesity and type 2
50 diabetes (T2D) have reached epidemic proportions and are worldwide health problems.
51 These metabolic chronic diseases are caused, to a large extent, by behavioral risk factors
52 such as changes in dietary macronutrient intake.

53 Obesity is a chronic disease characterized by the expansion of adipose tissue and an
54 inflammatory component. Adipose tissue releases a variety of adipokines, anti- or pro-
55 inflammatory cytokines such leptin, TNF- α and interleukin [IL]-4 (Lee, Lee and Choue,
56 2013). These pro-inflammatory molecules play an important role on the development of
57 metabolic disease such as T2D (Hajer, van Haeften and Visseren, 2008). Diabetes
58 mellitus is a chronic disorder characterized by major derangements in glucose metabolism
59 and abnormalities in fat and protein metabolism (Mentreddy, 2007). T2D is the most
60 common type of diabetes representing 90–95% of all cases. Most patients with T2D, but
61 not all, are overweight or obese, in fact, this excess weight itself causes some degree of
62 insulin resistance. Several epidemiologic studies reveal a parallel increase of obesity and
63 diabetes. Diabesity is a new term, which refers to diabetes occurring in the context of
64 obesity. The increase in the prevalence of T2D is associated to the upsurge in obesity. It
65 is estimated that about 90% of T2D is attributable to excess weight (Verma and Hussain,
66 2017). Previous studies support the protective role of diet, exercise and its combination
67 in individuals genetically susceptible to both pathologies (Temelkova-Kurktschiev and
68 Stefanov, 2012). Table 1 provides information on the role of lifestyle facts on the risk of
69 obesity and T2D.

70 <Table 1 near here>

71

72 Therefore, it is possible to reduce the risk of these metabolic diseases through different
73 strategies being the most sustainable the promotion of a healthy diet. Dietary fiber is
74 positively associated with enhanced weight control and obesity (Slavin, 2008) and
75 reduced risk of T2D (de Munter *et al.*, 2007). Several antioxidant compounds, such as the
76 chlorogenic acid (CGA), which is the main antioxidant of the coffee, have been proposed
77 as anti-obesity and anti-diabetic agents (Meng *et al.*, 2013; Sun, Wu and Chau, 2016).
78 Moreover, a wide range of phytochemicals present in plants and foods, might behave as
79 α -glucosidase and/or lipase inhibitors so they are used as bioactive compounds for
80 glycemic control in T2D (Kim, 2015) and management of obesity (Adisakwattana *et al.*,
81 2012). On the other hand, there are food components that might promote the feeling of
82 fullness by stimulating gut-derived hormones involved in satiety like glucagon-like
83 peptide-1 (GLP-1) and serotonin. Peptides (Geraedts *et al.*, 2010, 2011), carbohydrates
84 (Cani *et al.*, 2005), steviol glycosides (Ripken *et al.*, 2014) and CGA (Olthof *et al.*, 2011)
85 among others, have showed satiating properties.

86 In this sense, coffee by-products could play an important role as natural sustainable
87 sources of functional ingredients. They are natural sources of several bioactive
88 compounds with potential to reduce the risk of chronic non-communicable diseases
89 (Galanakis *et al.*, 2015; María Dolores del Castillo *et al.*, 2016; del Castillo *et al.*, 2017).

90 In this chapter we propose the development of sustainable high sensorial quality beverage
91 and foods, for reducing the risk of chronic metabolic diseases, by means of employing as
92 novel ingredients coffee by-products (CS and SCG) and their derivatives, in combination
93 with other functional ingredients. In addition, the impact of the digestive process of these
94 functional foods containing coffee by-products on the release of satiety hormones is also
95 presented.

96

97 **Coffee silverskin and spent grounds as natural sustainable sources of functional**
98 **ingredients**

99 Due to the great coffee demand, large amounts of by-products are generated in the coffee
100 industry, which might be used as novel products to achieve a global sustainable
101 management. Figure 1 represents coffee silverskin (CS) and spent coffee grounds (SCG)
102 production employing the wet process of the bean and the instant coffee processing.

103 <Figure 1 near here>

104 CS is a thin tegument of the outer layer of the green coffee beans obtained as a by-product
105 of the roasting process, which represents 4% (w/w) of the coffee cherry. CS has a high
106 content in dietary fiber (68-80%) and polysaccharides (60-70%). CS contains protein, fat,
107 and ash, at 16–19%, 2–3%, and 5-7%, respectively (del Castillo *et al.*, 2018). This coffee
108 by-product presents phenolic compounds, mainly CGA, and other phytochemicals that
109 contribute to its high antioxidant capacity. An aqueous CSE from Arabica (*Coffea*
110 *arabica*) and Robusta (*Coffea canephora*) enriched in caffeine and CGA and obtained
111 using an environmentally friendly technology have been patented (del Castillo *et al.*,
112 2013). CSE presents a total dietary fiber content ranging from 29 to 36%, including 4-9%
113 insoluble dietary fiber and 24-26% soluble dietary fiber. CSE is a good source of
114 polyphenols, in particular CGA (1-7%), caffeine (3%) and melanoidins (17-23%) (Mesías
115 *et al.*, 2014).

116 SCG are the most abundant coffee by-product (45%) generated during the treatment of
117 coffee powder with hot water to prepare coffee infusion or steam for the instant coffee
118 preparation (Murthy and Madhava Naidu, 2012). About 2 kg of wet SCG are obtained
119 from each kg of instant coffee produced, with an annual generation of around 6 million
120 tons worldwide. Regarding their chemical composition, polysaccharides are the major
121 macronutrients (75%). Among them, dietary fiber is the most important fraction (43-

122 54%), being the insoluble fiber predominant (47-50%). SCG also contain protein, fat and
123 ashes (14-17%, 2.3% and 1.3-1.6%, respectively). Caffeine ranges from 0.2 to 0.8% and
124 different health-related chemicals bound to dietary fiber and proteins such as CGAs
125 (Bravo *et al.*, 2012; Jiménez-Zamora, Pastoriza and Rufián-Henares, 2015).

126 CS due to its bioactive compounds has been associated to food technology and health
127 properties. This coffee by-product can be used as prebiotic carbohydrate (Borrelli *et al.*,
128 2004) and is involved in the production of short chains of FOS, which have more prebiotic
129 activity and stronger sweetness (Mussatto *et al.*, 2013). Moreover, CS is used to obtain
130 innovative coffee blends rich in bioactive compounds (Ribeiro *et al.*, 2014) and
131 formulations of bread to reduce caloric density and to increase the dietary fiber content
132 (Pourfarzad, Mahdavian-Mehr and Sedaghat, 2013). On the other hand, new evidence on
133 CSE and its effects on reducing the risk of metabolic chronic diseases has been reported
134 (Fernandez-Gomez, Lezama, *et al.*, 2016). Moreover, CSE improves glucose-stimulated
135 insulin secretion, protects against streptozotocin-induced damage in pancreatic INS-1E
136 beta cells (Fernandez-Gomez, Ramos, *et al.*, 2016) and inhibits AGEs formation
137 (Fernandez *et al.*, 2018). Regarding SCG, it has been used as additives and adjuvants
138 for the conversion of isoflavone glycosides into their aglycones with high biological
139 activities in black soymilk (Chen *et al.*, 2013). A distilled beverage with a coffee aroma
140 has been produced from SCG (Sampaio *et al.*, 2013). In addition, dietary fiber can be
141 extracted from SCG employing different processes such as ohmic technology and
142 fermented by colon microbiota producing metabolites that exhibit strong anti-
143 inflammatory potential (Vázquez-Sánchez *et al.*, 2015; Campos-Vega *et al.*, 2016).

144 Therefore, validation of CS and SCG into food ingredients with health promoting
145 properties to reduce the risk of metabolic chronic diseases may contribute to a sustainable
146 nutrition of the population.

147

148 **Novel foods and beverages based on coffee by-products**

149 Sweet drinks, packaged snacks, and biscuits provide significant amounts of energy to the
150 population, which contributes to the risk of obesity and T2D. In order to satisfy
151 consumer's demands, recent research focuses the attention on the design of sustainable
152 healthier beverages and bakery products. These novel foods have been formulated by
153 using CS and SCG as natural sources of health-promoting compounds.

154

155 *Novel beverages*

156 Coffee wastes have been hardly used in the design of functional beverages so far. Two
157 commercial beverages based on coffee husks are attracting the interest of the western
158 consumers: Bai Brands uses coffee husk extract as an ingredient in their beverages which
159 contain antioxidants and caffeine, and KonaRed preserves the majority of the nutrients
160 from the coffee plant and the dominant polyphenols (chlorogenic acid, quinic acid and
161 ferulic acid) in the beverages prepared with coffee husks. However, these drinks have not
162 been associated yet to any particular health benefit beyond those described for their
163 individual bioactive compounds present in the coffee wastes.

164 The use of CS for the preparation of novel beverages has been proposed for the first time
165 in this study (Martinez-Saez *et al.*, 2014). The CSE was obtained by a simple water
166 extraction stage (100 °C for at least 10 min) described in patent WO2013004873 A1,
167 enriched in bioactive compounds. New knowledge on the potential effect of CSE prepared
168 as an antioxidant beverage on body fat accumulation *in vivo* and the responsible bioactive
169 compounds was obtained (Martinez-Saez *et al.*, 2014). The development of novel
170 beverages requires sensorial analyses in order to evaluate the quality attributes of the
171 product and the results concluded that the acceptance level of the beverages made with

172 CSE was satisfactory since 95% of the panel were favorable towards the beverages (figure
173 2). In addition, the beverages presented low sugar content since they were prepared
174 without addition of nutritive sweeteners and glucose amount was not detected. These
175 novel drinks respond to the global obesity concerns and fit perfectly with the requests
176 from the European Union to reformulate drinks and set a target of 10% added sugar
177 reduction.

178 <Figure 2 near here>

179
180 Regarding the *in vivo* biological effects of these new beverages on the body fat reduction,
181 *Caenorhabditis elegans* (*C. elegans*) was employed as the animal model (Martinez-Saez
182 *et al.*, 2014). This worm is considered an excellent candidate for whole organism-based
183 high-throughput screening in drug assessment as a preclinical model (O'Reilly *et al.*,
184 2014) and for initial studies of nutrition interventions prior to confirmation in higher
185 animal species (Gao, King, *et al.*, 2015). The results of the study showed that the main
186 bioactive compounds of the CSE, CGA and caffeine, significantly reduce lipid deposits
187 in *C. elegans*. They were found in physiologically active doses in the beverages prepared
188 with CSE, however unexpectedly a synergic and/or additive effect was not detected.
189 Melanoidins, which are also present in the CSE beverages, are constituted by
190 carbohydrates, including dietary fiber (soluble Maillardized fiber), proteins and
191 polyphenols such as CGA (Silván, Morales and Saura-Calixto, 2010). All of them
192 conform the matrix of the beverage and thereby may be affecting the bioaccessibility and
193 bioavailability of CGA and caffeine, respectively, by adhering them to their complex
194 structure. Moreover, unlike those beverages prepared with ACSE, those containing RCSE
195 achieved higher effects on lipid metabolism and similar to those found in a commercial
196 dietary supplement, made from Robusta decaffeinated green coffee extract. Robusta

197 specie has been shown to possess higher content of bioactive compounds and CGA
198 appears as the main one to affect the lipid metabolism.
199 Recently, it has been demonstrated that CSE and CGA are able to significantly inhibit the
200 activity of pancreatic lipase *in vitro* (M.D. del Castillo *et al.*, 2016), which may be one of
201 the possible mechanisms of action exerted by the CSE beverages to reduce fat
202 accumulation. Moreover, dietary fiber of the beverages from CSE might also have impact
203 on body fat accumulation. Several studies showed effect of dietary fiber from barley and
204 oat (0.5, 1 and 3 %) on the body fat of *C.elegans* wild type N2, primarily mediated via
205 sir-2.1, daf-16, and daf-16/daf-2 and daf-2 gen (Gao, Gao, *et al.*, 2015; Gao, King, *et al.*,
206 2015). In addition, these novel beverages based on CSE have antioxidant properties
207 which may be attributed not only to polyphenols such as CGA but to other compounds
208 like melanoidins. These bioactive compounds present multiple biological activities that
209 may enhance the value of these beverages (Mesías and Delgado-Andrade, 2017).

210

211 *Novel foods*

212

213 Biscuits represent the largest category of snack item among bakery products and
214 compounds from coffee by-products have become excellent ingredients to be
215 incorporated in bakery products in order to enhance their sensorial and nutritional quality
216 and to simultaneously achieve a sustainable effect in the coffee sector. Coffee flour is a
217 new ingredient developed from the coffee pulp presenting high fiber and ash content and
218 low fat level (Ramirez Velez and Jaramillo Lopez, 2015), which has been proposed for
219 its use in different food formulations such as breads, cookies and muffins with better
220 nutritional properties. The high content of dietary fiber in coffee husk appears as an
221 advantage in making “energy bars”, by grinding the whole coffee husk and thereby
222 including all antioxidants and fiber into the product. Then, the coffee husk could be

223 launched as an allergic-friendly ingredient since it's naturally gluten free. (Bondesson,
224 2015). Just one study on the use of chemically pre-treated CS as an ingredient of bread
225 formulations has been reported (Pourfarzad, Mahdavian-Mehr and Sedaghat, 2013). Very
226 recently, research on the use of natural whole SCG and CS as food ingredients for
227 improving technological and nutritional quality of bakery products has been conducted
228 (Garcia-Serna *et al.*, 2014; Martinez-Saez, Tamargo, *et al.*, 2017)

229

230 — *Biscuits based on coffee silverskin*

231 The feasibility and effectiveness of applying 1) CS, 2) CSE, or 3) CSE combined with
232 the solid residue recovered from the extraction process, to non-added sugar biscuits was
233 studied (Garcia-Serna *et al.*, 2014). For the first time a full recovery of CS was achieved
234 through the whole conversion into two products, natural coloring and source of fiber.

235 On one hand, the dietary fiber plays a key role on the technological quality as a texturizing
236 agent and on the nutritional properties enhancing the nutritional value of the biscuits. On
237 the other hand, the coloring has an essential impact on the sensorial properties of the
238 biscuits, which will provide the typical golden color expected of this type of baked
239 products. This double effect of the use of whole CS on sensorial and nutritional quality
240 plays an essential role in achieving high acceptancy by the consumers. Results showed
241 that in sugar-free biscuits the non-enzymatic browning reactions, such as Maillard
242 reaction, phenol oxidation and caramelization, are limited (Garcia-Serna *et al.*, 2014).
243 However, those biscuits containing stevia as non-nutritive sweetener and CSE did not
244 present significant differences in color compared with the sucrose-containing biscuits.
245 The results support the validity of using CSE as a natural coloring (figure 3).

246

247

<Figure 3 near here>

248

249 Furthermore, along with the desired flavor and color related substances, food processing
250 contaminants such as acrylamide and hydroxymethylfurfural (HMF) are formed in the
251 Maillard reaction. Both, acrylamide and HMF, possesses genotoxic and carcinogenic
252 properties (Nguyen *et al.*, 2016). CSE and its main phenolic compound, CGA, have been
253 shown to possess antiglycative properties thereby limiting the Maillard reaction (Mesías
254 *et al.*, 2014). The use of CS as an ingredient of the biscuits partially improves to a great
255 extent this food processing contaminant formation. In addition, the non-nutritive
256 sweetener stevia, plays a key role on the safety quality of the products since results show
257 reduced formation of these food processing contaminants when sugar is replaced with
258 stevia. The combination of both coffee by-product and non-nutritive sugar replacers
259 provide a safer product.

260

261 Likewise, the digestive process plays a decisive role on the release of compounds of
262 interest in health and disease. The results of the research (Garcia-Serna *et al.*, 2014)
263 showed that after *in vitro* simulated oral-gastrointestinal digestion of the biscuits
264 formulations, acrylamide was not bioaccessible to be absorbed. Gastrointestinal
265 conditions and food composition affect the levels of bioavailable acrylamide. Acrylamide
266 possess the potential to react with the nucleophilic groups ($-SH$, $-NH_2$) of amino acid
267 side chains under the digestion conditions and the levels of acrylamide ingested with
268 foods may not directly indicate its absorption rate through gastric, duodenal and colonic
269 routes (Hamzalıoğlu and Gökmen, 2015). Furthermore, these biscuit formulations present
270 low content of bioaccessible glucose, in fact, a serving of four biscuits would provide less
271 than 3 g sucrose. This is in line with the need of formulating food with reduced sugar

272 content as it is suggested by the European Union. Consequently, these innovative foods
273 may be potentially suitable for diabetics or people who want to lose weight.

274

275 — *Biscuits based on spent coffee grounds*

276 The use of SCG from the industrial instant coffee process as food ingredient in the
277 development of a healthy product line of pastry, confectionery and/or bakery products
278 has been recently aimed (*patent WO2014128320 A1*) (del Castillo, Martinez-Saez and
279 Ullate, 2014). The patented application proposes the use of SCG as sustainable natural
280 antioxidant insoluble dietary fiber. Since SCG comes from the food industry, its use as
281 coffee fiber is of grade as well, and its conversion in a co-product may be feasible
282 regarding food safety and traceability. It can be used in the range between 4-8%, which
283 correspond to the nutrition claims “source of fiber” and “high fiber content”, respectively
284 (European Regulation (EC) No 1924/2006). The antioxidant properties of the insoluble
285 coffee fiber present in SCG can be associated with phenolic compounds bound to
286 proteins, polysaccharides and melanoidins (Jiménez-Zamora, Pastoriza and Rufián-
287 Henares, 2015). There is evidence for the existence of a complex named “maillardized
288 insoluble dietary fiber” constituted of dietary fiber, protein, Maillard reaction products
289 and polyphenols, in bakery products (Pérez-Jiménez *et al.*, 2014).

290 The coffee antioxidant insoluble dietary fiber combines beneficial effects of both dietary
291 fibers and antioxidants. Insoluble fiber may play an important role for weight loss during
292 consumption of a high-fat diet (Du *et al.*, 2010) as well as for reducing the risk of T2D
293 (Meyer *et al.*, 2000). The insoluble fiber can result in a reduced appetite and food intake,
294 which may lead to a decreased caloric intake and body mass index (Samra and Anderson,
295 2007). The short chain fatty acids, via fermentation of the insoluble fiber, have been
296 shown to reduce postprandial glucose responses (Ostman, Liljeberg Elmståhl and Björck,

297 2002). On the other hand, the intake of antioxidant dietary fiber has been recommended
298 for health improvement of the gastrointestinal tract. The pathogenesis of various
299 gastrointestinal diseases such as irritable bowel syndrome and inflammatory bowel
300 disease is in part due to oxidative stress. Antioxidant compounds may be beneficial at
301 reducing the risk of these gastrointestinal diseases (Moura *et al.*, 2015).

302 This gluten-free coffee fiber can be used into diverse combinations with other basic and/or
303 novel ingredients such as non-nutritive sweeteners and gluten-free flours, and thereby it
304 may allow their use for people with special nutritional needs such as diabetic people and
305 overweight or obese people. SCG possess a very high amount of insoluble dietary fiber
306 (42%) which is superior to other are natural sources of insoluble fiber such as black beans
307 (16%), lentils (8%) or almonds (12%). This coffee fiber is stable to thermal process such
308 as a baking and to the abiotic gastrointestinal digestion *in vitro* (Martinez-Saez, Tamargo,
309 *et al.*, 2017). On the other hand, it contains low amounts of free CGA and caffeine, none
310 levels of free sugar and small quantity of acrylamide (37 $\mu\text{g}/\text{kg}$) and HMF (61 mg/kg).

311 The acrylamide values are 92–96% lower than the indicative values proposed by
312 European Commission (2013) for roast (200-250 $\mu\text{g}/\text{kg}$) and instant coffee (350-595
313 $\mu\text{g}/\text{kg}$) (European Commission (EC)., 2013). Likewise, HMF levels are also very far from
314 those amounts found in the coffee (100–1900 mg/kg) and instant coffee (400–4100
315 mg/kg) (Capuano and Fogliano, 2011). The coffee fiber is exhausted of these compounds
316 since they were extracted during the preparation of soluble coffee beverage. In addition,
317 the coffee fiber derived from the instant coffee production presented high microbiological
318 safety in this particular case. Therefore, SCG become a cost-friendly source of healthy
319 insoluble dietary fiber that does not require further purification to be used as food
320 ingredient of bakery products to enhance their nutritional and biological quality.

321 Sugar was replaced with non-nutritive sweeteners such as stevia, and FOS were added as
322 soluble dietary fiber and enhancer of the taste of the coffee fiber-containing biscuit (CFB).
323 The sensory and acceptance tests of the novel biscuits show that the coffee fiber and stevia
324 are highly accepted ingredients, and above all when combined with FOS in the
325 formulation. FOS present slightly sweetness and might act masking negative off-flavors
326 from the stevia and the coffee fiber. The novel biscuits containing coffee fiber and non-
327 nutritive sweeteners (figure 2) seem to meet consumer's preferences.

328 CFB presented lower levels of both dietary early Maillard reaction products and advanced
329 glycation end products (AGEs) than the sucrose-containing biscuit (SCB). This indicates
330 that the presence of sucrose during baking increases the amount of compounds that can
331 be limited by the replacement with non-nutritive sweetener. Moreover, it has been
332 reported antiglycative properties of CGA (IC₅₀ = 0.4 mg/ml) and RCSE (0.6 mg/ml)
333 (Mesías *et al.*, 2014). The coffee fiber presents CGA and other phenolic compounds (2
334 mg/g) and one CFB (\approx 10 g) would provide 0.4 mg CGAs. Thereby this coffee fiber might
335 also prevent the formation of these compounds, which are associated with oxidative stress
336 and inflammation, eventually causing higher risk of most chronic diseases such as T2D
337 and obesity (Vlassara and Uribarri, 2014; Sayej *et al.*, 2016). Incorporation of FOS to the
338 biscuits also contributes to the balance of soluble: insoluble dietary fiber and promotes
339 the growth of specific beneficial gut bacteria (Bosscher, Van Loo and Franck, 2006).
340 Recently, relationship between non-digestible carbohydrates, including FOS, and
341 reduction of post-prandial glycemic responses was established by the EFSA (European
342 Food Safety Authority (EFSA)., 2014).

343 Additionally, *in vitro* effects of the bioaccessible food components released during the
344 simulated human digestion of the novel CFB, on α -glucosidase activity and satiety
345 hormones were examined (Martinez-Saez, Hochkogler, *et al.*, 2017). To the best of our

346 knowledge, this is the first report on the potential antidiabetic and satiating effects of
347 foods comprising coffee fiber and non-nutritive sweeteners.

348 The content in glycemic sugars such as glucose and fructose in the biscuit digests was
349 significantly reduced. The CFB can be classified as “no added sugars” declaring that may
350 “contains naturally occurring sugars” (European Regulation (EC) No 1924/2006).
351 Likewise, the content of insoluble and soluble dietary fiber of the novel biscuits provided
352 by the coffee fiber from SCG and FOS respectively, lead to categorize these novel biscuits
353 under the nutrition claim “high fiber” (≥ 6 g of fiber per 100 g or ≥ 3 g of fiber per 100
354 kcal).

355 The present study shows antioxidant character of the CFB digest. The transportation of
356 dietary antioxidants through the gastrointestinal tract has been described as an essential
357 function of dietary fiber. Polyphenols linked to dietary fiber may be released in the colon
358 by the action of the microbiota, producing bioactive metabolites and an antioxidant
359 environment, thereby reducing the risk of gastrointestinal diseases associated with
360 oxidative stress and inflammation (Saura-Calixto, 2011) (figure 4 (i)). CGA, which is
361 present in the coffee fiber, has shown potential to inhibit signaling molecules involved in
362 inflammation processes, thereby acting as an anti-inflammatory antioxidant compound
363 (López-Barrera *et al.*, 2016).

364 <Figure 4 near here>

365

366 Stevia and FOS present in the novel biscuit were effective inhibitors of α -glucosidase
367 activity *in vitro* (figure 4 (ii)). Moreover, previous studies have reported an association of
368 antioxidants, in particular polyphenols, with α -glucosidase inhibition (Xiao *et al.*, 2013).
369 The release of phenolic compounds incorporated in the coffee fiber structure during the
370 digestion process may enhance tolerance to carbohydrates by inhibiting intestinal α -

371 glucosidase. Diterpens such as cafestol and kahweol, which have been described to be
372 present in SCG (Acevedo *et al.*, 2013), might be contributing to this inhibitory effect on
373 α -glucosidase exerted by the novel biscuits. Alpha-glucosidase inhibitors reduce the
374 impact on blood sugar and therefore postprandial hyperglycemia. The control of glucose
375 absorption plays a key role in the management of T2D.

376 The coffee fiber exhibited a potent stimulation of the gut serotonin and GLP-1 hormones
377 *ex vivo* by using Caco-2 and HuTu-80 cells, respectively (figure 4 (iii)). These intestinal
378 hormones can regulate the feeling of fullness via neural paracrine routes with subsequent
379 afferent signaling to brainstem nuclei. GLP-1 also regulates the feeling of fullness via the
380 endocrine pathway through the hepatic portal and cava vein (Steinert, Beglinger and
381 Langhans, 2016). The intestinal secretion of serotonin responds to chemical and
382 mechanical stimuli after food intake (Voigt and Fink, 2015). Thus, the antioxidant coffee
383 fiber is expected to exhibit a greater stimulation of satiety hormones *in vivo* than that
384 described in this study, due to the physical effect of the indigestible material obtained
385 from the digestive process. In addition, the soluble fiber (FOS) incorporated to the novel
386 biscuits may be also positively affect the release of these satiety hormones. It has been
387 described, in a double blind randomized clinical trial, an increase of the satiety feeling
388 when FOS enriched cookies (10 per day) were consumed by obese patients for a month
389 (de Luis *et al.*, 2013). On the other hand, galactomannan, a soluble fiber that is released
390 from the SCG during the digestive process, may enhance satiety by forming a viscous gel
391 in the stomach, and thereby slowing gastric emptying and enhancing fullness. The
392 secretion of GLP-1 hormone also participates in glycemic tolerance via glucose-induced
393 secretion of insulin from pancreatic β -cells and via glucagon release inhibition from
394 pancreatic α -cells (Yabe and Seino, 2011) (figure 4). Therefore, a double antidiabetic and
395 satiating potential effect might be achieved thanks to the secretion of GLP-1.

396

397 **Conclusion**

398 The use of coffee by-products in the development of novel sustainable beverages and
399 foods with enhanced technological, nutritional and sensorial quality is feasible.
400 Technological strategies are achieved for valorization of coffee by-products into novel
401 health promoting food ingredients, avoiding the production of new industrial wastes.
402 Scientific evidences regarding the potential of the sustainable beverages and foods for
403 reducing the risk of obesity and T2D are obtained.

404

405 **Acknowledgements**

406 The SUSCOFFEE (AGL2014-57239-R) project funded this work. N. Martinez-Saez
407 thanks the Autonomous University of Madrid (UAM), Spain, for the FPI-predoc
408 fellowship.

409

410 **References**

411 Acevedo, F. *et al.* (2013) 'Spent coffee grounds as a renewable source of bioactive
412 compounds', *Journal of Biobased Materials and Bioenergy*, 7, pp. 1–9. doi:
413 10.1166/jbmb.2013.1369.

414 Adisakwattana, S. *et al.* (2012) 'Extracts of edible plants inhibit pancreatic lipase,
415 cholesterol esterase and cholesterol micellization, and bind bile acids', *Food Technology
416 and Biotechnology*, 50(1), pp. 11–16.

417 Bondesson, E. (2015) *A nutritional analysis on the by- product coffee husk and its
418 potential utilization in food production*. Swedish University of Agricultural Sciences.
419 Available at: http://stud.epsilon.slu.se/8486/7/bondesson_e_150922.pdf (Accessed: 24
420 April 2017).

421 Borrelli, R. C. *et al.* (2004) 'Characterization of a new potential functional ingredient:
422 coffee silverskin.', *Journal of agricultural and food chemistry*, 52(5), pp. 1338–1343.
423 doi: 10.1021/jf034974x.

424 Bosscher, D., Van Loo, J. and Franck, A. (2006) 'Inulin and oligofructose as prebiotics
425 in the prevention of intestinal infections and diseases.', *Nutrition research reviews*, 19(2),
426 pp. 216–226. doi: 10.1017/S0954422407249686.

427 Bravo, J. *et al.* (2012) 'Evaluation of spent coffee obtained from the most common
428 coffeemakers as a source of hydrophilic bioactive compounds', *Journal of Agricultural
429 and Food Chemistry*, 60, pp. 12565–12573.

430 Campos-Vega, R. *et al.* (2016) 'Proceso de obtención de fibra dietaria antioxidante
431 natural de subproductos mediante calentamiento ohmico y compuesto alto en fibra
432 dietaria antioxidante natural de café usado. MX/a/2016008578.'

433 Cani, P. D. *et al.* (2005) ‘Oligofructose promotes satiety in rats fed a high-fat diet:
434 involvement of glucagon-like peptide-1’, *Obesity Research*, 13(6), pp. 1000–1007. doi:
435 10.1038/oby.2005.117.

436 Capuano, E. and Fogliano, V. (2011) ‘Acrylamide and 5-hydroxymethylfurfural (HMF):
437 A review on metabolism, toxicity, occurrence in food and mitigation strategies’, *LWT -*
438 *Food Science and Technology*. Elsevier Ltd, 44(4), pp. 793–810. doi:
439 10.1016/j.lwt.2010.11.002.

440 del Castillo, M. D. *et al.* (2013) ‘Aplicación de productos de la cascarilla del café en
441 cosmética antienvjecimiento y alimentación funcional. WO 2013004873 A1.’ Spain.
442 Available at:
443 [https://patentscope.wipo.int/search/en/detail.jsf?docId=WO2013004873&recNum=10&](https://patentscope.wipo.int/search/en/detail.jsf?docId=WO2013004873&recNum=10&docAn=ES2012070490&queryString=(IC/A23L-3/00) &maxRec=2660)
444 [docAn=ES2012070490&queryString=\(IC/A23L-3/00\) &maxRec=2660](https://patentscope.wipo.int/search/en/detail.jsf?docId=WO2013004873&recNum=10&docAn=ES2012070490&queryString=(IC/A23L-3/00) &maxRec=2660) (Accessed: 14
445 August 2015).

446 del Castillo, M. D. *et al.* (2016) ‘Coffee silverskin extract for aging and chronic diseases’,
447 in Martirosyan, D. M. (ed.) *Functional Foods for Chronic Diseases*. CreateSpace
448 Independent Publishing Platform, pp. 171–194.

449 del Castillo, M. D. *et al.* (2016) ‘Uso de productos de la cascarilla de café para la
450 prevención y tratamiento de las patologías que conforman el síndrome metabólico y de
451 sus factores de riesgo. PCT/ES2015/070915.’ Spain.

452 del Castillo, M. D. *et al.* (2017) ‘Applications of recovered compounds in food products’,
453 in Galanakis, C. (ed.) *Handbook of Coffee Processing By-Products: Sustainable*
454 *Applications*. Oxford: Elsevier.

455 del Castillo, M. D. *et al.* (2018) ‘Coffee By-Products’, in Farah, A. (ed.) *Coffee:*
456 *Chemistry, Quality and Health Implications*. RSC Publishing Inc., p. In press. Available

457 at: <https://books.google.es/books/about/Coffee.html?id=LMk0jgEACAAJ&pgis=1>
458 (Accessed: 21 January 2016).

459 del Castillo, M. D., Martinez-Saez, N. and Ullate, M. (2014) 'Formulación alimentaria
460 que comprende marros de café y sus aplicaciones. WO2014128320 A1.' Spain.

461 Chen, K. I. *et al.* (2013) 'Enrichment of two isoflavone aglycones in black soymilk by
462 using spent coffee grounds as an immobiliser for β -glucosidase', *Food Chemistry*.
463 Elsevier Ltd, 139, pp. 79–85. doi: 10.1016/j.foodchem.2013.01.093.

464 Du, H. *et al.* (2010) 'Dietary fiber and subsequent changes in body weight and waist
465 circumference in European men and women', *American Journal of Clinical Nutrition*,
466 91(2), pp. 329–336. doi: 10.3945/ajcn.2009.28191.

467 European Commission (EC). (2013) 'Commission Recommendation of 8 November 2013
468 on investigations into the levels of acrylamide in food', *Official Journal of the European*
469 *Union*, p. L 301/15. doi: 10.2903/j.efsa.2012.2938.

470 European Food Safety Authority (EFSA). (2014) 'Scientific opinion on the substantiation
471 of a health claim related to non-digestible carbohydrates and a reduction of post-prandial
472 glycaemic responses pursuant to Article 13 (5) of Regulation (EC) No 1924/2006', *EFSA*
473 *Journal*, 12(1), pp. 1–13. doi: 10.2903/j.efsa.2014.3513.

474 Fernandez-Gomez, B., Ramos, S., *et al.* (2016) 'Coffee silverskin extract improves
475 glucose-stimulated insulin secretion and protects against streptozotocin-induced damage
476 in pancreatic INS-1E beta cells', *Food Research International*, 89, pp. 1015–1022. doi:
477 10.1016/j.foodres.2016.03.006.

478 Fernandez-Gomez, B., Lezama, A., *et al.* (2016) 'Insights on the health benefits of the
479 bioactive compounds of coffee silverskin extract', *Journal of Functional Foods*, 25, pp.

480 197–207. doi: 10.1016/j.jff.2016.06.001.

481 Fernandez, B. *et al.* (2018) ‘Inhibitors of advanced glycation end products from coffee
482 bean roasting by-product’, *European Food Research and Technology*. Springer Berlin
483 Heidelberg. doi: 10.1007/s00217-017-3023-y.

484 Galanakis, C. *et al.* (2015) ‘Patented and commercialized applications’, in Galanakis, C.
485 (ed.) *Food Waste Recovery: Processing Technologies and Industrial Techniques*.
486 Academic Press-Elsevier, pp. 339–362.

487 Gao, C., Gao, Z., *et al.* (2015) ‘Oat consumption reduced intestinal fat deposition and
488 improved health span in *Caenorhabditis elegans* model’, *Nutrition Research*. The
489 Authors., 35(9), pp. 834–843. doi: 10.1016/j.nutres.2015.06.007.

490 Gao, C., King, M. L., *et al.* (2015) ‘Prowashonupana barley dietary fibre reduces body
491 fat and increases insulin sensitivity in *Caenorhabditis elegans* model’, *Journal of*
492 *Functional Foods*. Elsevier Ltd, 18, pp. 564–574. doi: 10.1016/j.jff.2015.08.014.

493 Garcia-Serna, E. *et al.* (2014) ‘Use of coffee silverskin and stevia to improve the
494 formulation of biscuits’, *Polish Journal of Food and Nutrition Sciences*, 64(4), pp. 243–
495 251. doi: 10.2478/pjfns-2013-0024.

496 Geraedts, M. C. P. *et al.* (2010) ‘Release of satiety hormones in response to specific
497 dietary proteins is different between human and murine small intestinal mucosa’, *Annals*
498 *of Nutrition and Metabolism*, 56(4), pp. 308–313. doi: 10.1159/000312664.

499 Geraedts, M. C. P. *et al.* (2011) ‘Direct induction of CCK and GLP-1 release from murine
500 endocrine cells by intact dietary proteins’, *Molecular Nutrition and Food Research*,
501 55(3), pp. 476–484. doi: 10.1002/mnfr.201000142.

502 Hajer, G. R., van Haefen, T. W. and Visseren, F. L. J. (2008) ‘Adipose tissue dysfunction

503 in obesity, diabetes, and vascular diseases', *European Heart Journal*, 29(24), pp. 2959–
504 2971. doi: 10.1093/eurheartj/ehn387.

505 Hamzaloğlu, A. and Gökmen, V. (2015) 'Investigation of the reactions of acrylamide
506 during in vitro multistep enzymatic digestion of thermally processed foods.', *Food &*
507 *function*, 6(1), pp. 109–14. doi: 10.1039/c4fo00884g.

508 Jiménez-Zamora, A., Pastoriza, S. and Rufián-Henares, J. A. (2015) 'Revalorization of
509 coffee by-products. Prebiotic, antimicrobial and antioxidant properties', *LWT - Food*
510 *Science and Technology*, 61(1), pp. 12–18. doi: 10.1016/j.lwt.2014.11.031.

511 Kim, S.-D. (2015) ' α -Glucosidase inhibitor isolated from coffee', *Journal of*
512 *Microbiology and Biotechnology*, 25(2), pp. 174–177. doi: 10.4014/jmb.1411.11057.

513 Lee, H., Lee, I. S. and Choue, R. (2013) 'Obesity, inflammation and diet.', *Pediatric*
514 *gastroenterology, hepatology & nutrition*. Korean Society of Pediatric Gastroenterology,
515 Hepatology and Nutrition, 16(3), pp. 143–52. doi: 10.5223/pghn.2013.16.3.143.

516 López-Barrera, D. M. *et al.* (2016) 'Spent coffee grounds, an innovative source of colonic
517 fermentable compounds, inhibit inflammatory mediators in vitro', *Food Chemistry*,
518 212(May), pp. 282–290. doi: 10.1016/j.foodchem.2016.05.175.

519 de Luis, D. A. *et al.* (2013) 'Double blind randomized clinical trial controlled by placebo
520 with a FOS enriched cookie on satiety and cardiovascular risk factors in obese patients',
521 *Nutrición Hospitalaria*, 28(1), pp. 78–85. doi: 10.3305/nh.2013.28.1.6255.

522 Martínez-Saez, N. *et al.* (2014) 'A novel antioxidant beverage for body weight control
523 based on coffee silverskin', *Food Chemistry*. Elsevier Ltd, 150, pp. 227–234. doi:
524 10.1016/j.foodchem.2013.10.100.

525 Martínez-Saez, N., Hochkogler, C., *et al.* (2017) 'Non-added sugar biscuit containing

526 stevia, coffee fibre and fructooligosaccharides modifies α -glucosidase activity and the
527 release of GLP-1 from HuTu-80 cells and serotonin from Caco-2 cells after in vitro
528 digestion', *Nutrients*, 9, p. 694.

529 Martinez-Saez, N., Tamargo, A., *et al.* (2017) 'Use of spent coffee grounds as food
530 ingredient in bakery products', *Food Chemistry*. Elsevier Ltd, 216, pp. 114–122. doi:
531 10.1016/j.foodchem.2016.07.173.

532 Meng, S. *et al.* (2013) 'Roles of chlorogenic acid on regulating glucose and lipids
533 metabolism: a review.', *Evidence-based complementary and alternative medicine*.
534 Hindawi Publishing Corporation, 2013, pp. 1–11. doi: 10.1155/2013/801457.

535 Mentreddy, S. R. (2007) 'Medicinal plant species with potential antidiabetic properties',
536 *Journal of the Science of Food and Agriculture*, 87, pp. 743–750. doi: 10.1002/jsfa.

537 Mesías, M. *et al.* (2014) 'Antiglycative and carbonyl trapping properties of the water
538 soluble fraction of coffee silverskin', *Food Research International*. Elsevier Ltd, 62, pp.
539 1120–1126. doi: 10.1016/j.foodres.2014.05.058.

540 Mesías, M. and Delgado-Andrade, C. (2017) 'Melanoidins as a potential functional food
541 ingredient', *Current Opinion in Food Science*, 14, pp. 37–42. doi:
542 10.1016/j.cofs.2017.01.007.

543 Meyer, K. A. *et al.* (2000) 'Carbohydrates, dietary fiber, and incident type 2 diabetes in
544 older women', *The American Journal of Clinical Nutrition*, 71, pp. 921–930. Available
545 at: <http://ajcn.nutrition.org/content/71/4/921.full.pdf>.

546 Moura, F. A. *et al.* (2015) 'Antioxidant therapy for treatment of inflammatory bowel
547 disease: Does it work?', *Redox biology*. Elsevier, 6, pp. 617–39. doi:
548 10.1016/j.redox.2015.10.006.

549 de Munter, J. S. L. *et al.* (2007) 'Whole grain, bran, and germ intake and risk of type 2
550 diabetes: A prospective cohort study and systematic review', *PLoS Medicine*. Edited by
551 L. C. Groop. Public Library of Science, 4(8), p. e261. doi:
552 10.1371/journal.pmed.0040261.

553 Murthy, P. S. and Madhava Naidu, M. (2012) 'Sustainable management of coffee
554 industry by-products and value addition - A review', *Resources, Conservation and*
555 *Recycling*. Elsevier B.V., 66, pp. 45–58. doi: 10.1016/j.resconrec.2012.06.005.

556 Mussatto, S. I. *et al.* (2013) 'Maximization of fructooligosaccharides and β -
557 fructofuranosidase production by *Aspergillus japonicus* under solid-state fermentation
558 conditions', *Food and Bioprocess Technology*, 6(8), pp. 2128–2134. doi:
559 10.1007/s11947-012-0873-y.

560 Nguyen, H. T. *et al.* (2016) 'Acrylamide and 5-hydroxymethylfurfural formation during
561 baking of biscuits: Part I: Effects of sugar type', *Food Chemistry*. Elsevier Ltd, 192, pp.
562 575–585. doi: 10.1016/j.foodchem.2015.07.016.

563 O'Reilly, L. P. *et al.* (2014) 'C. elegans in high-throughput drug discovery.', *Advanced*
564 *drug delivery reviews*. NIH Public Access, 0, pp. 247–53. doi:
565 10.1016/j.addr.2013.12.001.

566 Olthof, M. R. *et al.* (2011) 'Acute effects of decaffeinated coffee and the major coffee
567 components chlorogenic acid and trigonelline on incretin hormones', *Nutrition &*
568 *Metabolism*, 8(1), p. 10. doi: 10.1186/1743-7075-8-10.

569 Ostman, E. M., Liljeberg Elmståhl, H. G. M. and Björck, I. M. E. (2002) 'Barley bread
570 containing lactic acid improves glucose tolerance at a subsequent meal in healthy men
571 and women.', *The Journal of nutrition*, 132(6), pp. 1173–5. Available at:
572 <http://www.ncbi.nlm.nih.gov/pubmed/12042429> (Accessed: 5 May 2017).

573 Pérez-Jiménez, J. *et al.* (2014) 'Evidence for the formation of maillardized insoluble
574 dietary fiber in bread: A specific kind of dietary fiber in thermally processed food', *Food*
575 *Research International*, 55, pp. 391–396. doi: 10.1016/j.foodres.2013.11.031.

576 Pourfarzad, A., Mahdavian-Mehr, H. and Sedaghat, N. (2013) 'Coffee silverskin as a
577 source of dietary fiber in bread-making: Optimization of chemical treatment using
578 response surface methodology', *LWT - Food Science and Technology*. Elsevier Ltd,
579 50(2), pp. 599–606. doi: 10.1016/j.lwt.2012.08.001.

580 Ramirez Velez, A. and Jaramillo Lopez, J. C. (2015) 'Process for obtaining honey and/or
581 flour of coffee from the pulp or husk and the mucilage of the coffee bean.
582 US20150017270 A1.' Colombia.

583 Ribeiro, V. S. *et al.* (2014) 'Chemical characterization and antioxidant properties of a
584 new coffee blend with cocoa, coffee silverskin and green coffee minimally processed',
585 *Food Research International*. Elsevier Ltd, 61, pp. 39–47. doi:
586 10.1016/j.foodres.2014.05.003.

587 Ripken, D. *et al.* (2014) 'Steviol glycoside rebaudioside A induces glucagon-like peptide-
588 1 and peptide YY release in a porcine ex vivo intestinal model', *Journal of Agricultural*
589 *and Food Chemistry*, 62(33), pp. 8365–8370. doi: 10.1021/jf501105w.

590 Sampaio, A. *et al.* (2013) 'Production, chemical characterization, and sensory profile of
591 a novel spirit elaborated from spent coffee ground', *LWT - Food Science and Technology*.
592 Elsevier Ltd, 54(2), pp. 557–563. doi: 10.1016/j.lwt.2013.05.042.

593 Samra, R. A. and Anderson, G. H. (2007) 'Insoluble cereal fiber reduces appetite and
594 short-term food intake and glycemic response to food consumed 75 min later by healthy
595 men.', *The American journal of clinical nutrition*, 86(4), pp. 972–9. Available at:
596 <http://www.ncbi.nlm.nih.gov/pubmed/17921373> (Accessed: 5 May 2017).

597 Saura-Calixto, F. (2011) 'Dietary fiber as a carrier of dietary antioxidants: an essential
598 physiological function.', *J. Agric. Food Chem*, 59, pp. 43–49. doi: 10.1021/jf1036596.

599 Sayej, W. N. *et al.* (2016) 'Advanced glycation end products induce obesity and
600 hepatosteatosi s in CD-1 wild-type mice', *BioMed Research International*, 2016, pp. 1–
601 12. doi: 10.1155/2016/7867852.

602 Silván, J. M., Morales, F. J. and Saura-Calixto, F. (2010) 'Conceptual study on
603 maillardized dietary fiber in coffee.', *Journal of Agricultural and Food Chemistry*,
604 58(23), pp. 12244–9. doi: 10.1021/jf102489u.

605 Slavin, J. L. (2008) 'Position of the American Dietetic Association: health implications
606 of dietary fiber.', *Journal of the American Dietetic Association*, 108(10), pp. 1716–1731.
607 doi: 10.1016/j.jada.2008.08.007.

608 Steinert, R. E., Beglinger, C. and Langhans, W. (2016) 'Intestinal GLP-1 and satiation -
609 from man to rodents and back', *International Journal of Obesity*. Nature Publishing
610 Group, 40, pp. 198–205. doi: 10.1038/ijo.2015.172.

611 Sun, N. N., Wu, T. Y. and Chau, C. F. (2016) 'Natural dietary and herbal products in anti-
612 obesity treatment', *Molecules*, 21(10), p. E1351. doi: 10.3390/molecules21101351.

613 Temelkova-Kurktschiev, T. and Stefanov, T. S. (2012) 'Lifestyle and genetics in obesity
614 and type 2 diabetes', *Experimental and Clinical Endocrinology & Diabetes*, 120, pp. 1–
615 6.

616 Vázquez-Sánchez, K. *et al.* (2015) 'Antioxidant coffee dietary fiber for gastrointestinal
617 health and diabetes', *20th International Conference of FFC - 8th International*
618 *Symposium of ASFFBC*,. Boston.

619 Verma, S. and Hussain, M. E. (2017) 'Obesity and diabetes: An update', *Diabetes &*

620 *Metabolic Syndrome: Clinical Research & Reviews*, 11(1), pp. 73–79. doi:
621 10.1016/j.dsx.2016.06.017.

622 Vlassara, H. and Uribarri, J. (2014) ‘Advanced glycation end products (AGE) and
623 diabetes: cause, effect, or both?’, *Current Diabetes Reports*, 14(1), p. 453. doi:
624 10.1007/s11892-013-0453-1.

625 Voigt, J. and Fink, H. (2015) ‘Serotonin controlling feeding and satiety’, *Behavioural*
626 *Brain Research*. Elsevier B.V., 277, pp. 14–31. doi: 10.1016/j.bbr.2014.08.065.

627 World Health Organization (2003) *Diet, nutrition and the prevention of chronic diseases.*
628 *Report of a Joint WHO/FAO Expert Consultation.* Geneva.

629 World Health Organization (2014) *Global status report on noncommunicable diseases*
630 *2014.* Geneva.

631 Xiao, J. *et al.* (2013) ‘Advance in dietary polyphenols as α -glucosidases inhibitors: a
632 review on structure-activity relationship aspect.’, *Critical reviews in food science and*
633 *nutrition*, 53(8), pp. 818–36. doi: 10.1080/10408398.2011.561379.

634 Yabe, D. and Seino, Y. (2011) ‘Two incretin hormones GLP-1 and GIP: Comparison of
635 their actions in insulin secretion and beta cell preservation’, *Progress in Biophysics and*
636 *Molecular Biology.* Elsevier Ltd, 107(2), pp. 248–256. doi:
637 10.1016/j.pbiomolbio.2011.07.010.

638

639 **Website citations**

640 Bai Brands www.drinkbai.com

641 KonaRed® www.konared.com

642 CoffeeFlour® www.coffeeflour.com