proceedings

MDPI

Proceedings

Critical Evaluation of Coffee Pulp as an Innovative Antioxidant Dietary Fiber Ingredient: Nutritional Value, Functional Properties, and Acute and Sub-Chronic Toxicity †

Silvia Cañas [1,2,*], Miguel Rebollo-Hernanz [1,2,*], Paz Cano-Muñoz [1,2], Yolanda Aguilera [1,2], Vanesa Benítez [1,2], Cheyenne Braojos [1,2], Andrea Gila-Díaz [3], Pilar Rodríguez-Rodríguez [3], Ignacio Monedo Cobeta [3], Ángel L. López de Pablo [3], Maria del Carmen González [3], Silvia M. Arribas [3] and Maria A. Martin-Cabrejas [1,2]

[1] Department of Agricultural Chemistry and Food Science, Universidad Autónoma de Madrid, 28049 Madrid, Spain; paz.cano@estudiante.uam.es (P.C.M.); yolanda.aguilera@uam.es (Y.A.); vanesa.benitez@uam.es (V.B.); cheyenne.braojos@uam.es (C.B.); maria.martin@uam.es (M.A.M.C.)
[2] Institute of Food Science Research, CIAL (UAM-CSIC), 28049 Madrid, Spain
[3] Department of Physiology, Universidad Autónoma de Madrid, 28029 Madrid, Spain; andrea.gila@uam.es (A.G.D.); pilar.rodriguezr@uam.es (P.R.R.); ignacio.monedero@uam.es (I.M.C.); angel.lopezdepablo@uam.es (Á.L.L.d.P.); m.c.gonzalez@uam.es (M.C.G.); silvia.arribas@uam.es (S.M.A.)
* Correspondence: silvia.cannas@uam.es (S.C.); miguel.rebollo@uam.es (M.R.H.)
† Presented at the 1st International Electronic Conference on Food Science and Functional Foods, 10–25 November 2020; Available online: https://foods_2020.sciforum.net/.

Abstract: Coffee pulp is a by-product generated during coffee processing, producing environmental pollution when discarded in rivers. The revalorization of coffee by-products is currently being studied due to their high potential as new value-added food ingredients. This work aims to explore the chemical composition and functional properties of coffee pulp and validate its safety for use as a novel food ingredient. Coffee pulp composition was assessed following the standard methods (AOAC). Physicochemical properties, total phenolic compounds (TPC), antioxidant capacity, hypoglycemic and hypolipidemic properties were determined using in vitro techniques. Acute and subchronic oral toxicity experiments were carried out following OECD Test Guidelines 452 and 408. Coffee pulp showed a high content of dietary fiber (51.2%), highlighting the insoluble fraction. Proteins (9.2%) and lipids (2.6%) were considered a min fraction. Coffee pulp presented high content of TPC (40.6 mg g^{-1}), of which 29% were linked to DF, giving coffee pulp its antioxidant potential (102.3 mg Trolox eq g^{-1}). The by-product showed good physicochemical properties. Coffee pulp reduced the absorption of cholesterol (84%) and bile salts (85%), inhibited pancreatic lipase (64%), and presented the capacity to diminish the diffusion of glucose (34%). The intake of coffee pulp did not cause significant lesions in vital organs. In conclusion, the coffee pulp could be used as a potential ingredient with beneficial health properties.

Keywords: coffee by-products; coffee pulp; dietary fiber; physicochemical properties; hypolipidemic properties; hypoglycemic properties; toxicity

Citation: Cañas, S.; Rebollo-Hernanz, M.; Cano-Muñoz, P.; Aguilera, Y.; Benítez, V.; Braojos, C.; Gila-Díaz, A.; Rodríguez-Rodríguez, P.; Cobeta, I.M.; de Pablo, L.; et al. Critical Evaluation of Coffee Pulp as an Innovative Antioxidant Dietary Fiber Ingredient: Nutritional Value, Functional Properties and Acute and Sub-Chronic Toxicity. *Proceedings* **2021**, *70*, 65. https://doi.org/10.3390/foods_2020-07623

Published: 9 November 2020

1. Introduction

The coffee processing industry produces vast quantities of by-products every year, causing enormous economic and environmental problems when they are discarded. Furthermore, in recent years, the steady growth of the world population and the threat of reduced food sources has increased the interest in reusing materials that are currently considered waste [1].

Coffee by-products, including husk, skin, pulp, coffee mucilage, coffee parchment, coffee silverskin, and spent coffee grounds, can be obtained by wet or dry processing. Coffee pulp is one of the by-products obtained during the wet processing, representing

43.2% of the whole fruit. The coffee pulp can be used as food for animals or as a substrate for microbiological processes, but few studies explore its potential as a new ingredient for human food [2].

Several reports have shown that coffee pulp is a source of bioactive compounds of high value and attractive nutritional value, such as dietary fiber (DF) and phenolic compounds [3,4]. DF has several physiological benefits, and its intake provides health benefits, such as reducing the risk of coronary heart disease, type 2 diabetes, and intestinal disorders. The physiological effects of DF depend on physicochemical properties. Therefore, the coffee pulp study as a source of DF is necessary to estimate its potential health benefits and its technological properties [5].

The purpose of this work was to determine the chemical composition and functional properties of coffee pulp, including potential antioxidant, hypoglycemic and hypocholesterolemic effects, and to validate the by-product as a novel sustainable and safe food ingredient.

2. Materials and Methods

2.1. Materials

Coffee pulp from Arabica species was obtained by the wet method and kindly supplied by AORA HEALTH S.L (Spain). The coffee pulp was milled to obtain coffee pulp flour.

2.2. Chemical Composition

The AOAC Official methods [6] were used to determine lipid and nitrogen contents. Protein content was calculated as nitrogen ×6.25. Total dietary fiber (TDF), insoluble dietary (IDF), and soluble dietary fiber (SDF) were determined by enzymatic–gravimetric assay according to AOAC-991.4 and AACC-32.07.01 methods [6,7].

2.3. Extraction and Analysis of Total Phenolic Compounds and Antioxidant Capacity

2.3.1. Extraction of Free and Bound Phenolic Compounds

Free and bound phenolic compounds were extracted using organic solvents according to the method described by Rebollo-Hernanz et al. [8].

2.3.2. Total Phenolic Compounds

Total phenolic compounds were analyzed by the Folin–Ciocalteu method [9]. The experiment was performed in a 96-well microplate. Briefly, 10 µL of the sample, 150 µL of Folin–Ciocalteu reagent (diluted 1: 14, *v*/*v* in Milli-Q water), and 50 µL of Na_2CO_3 20% were added to each well. The plate was incubated in the dark at room temperature for 2 h. Absorbance was measured at 750 nm in a microplate reader. A standard gallic acid curve (0.01–0.2 mg mL^{-1}) was performed, and the results were expressed as mg gallic acid equivalents per gram (mg GAE g^{-1}).

2.3.3. In Vitro Antioxidant Capacity

Antioxidant capacity was assessed by the $ABTS^+$ assay [10]. 2.2′-Azino-bis(3-ethylbenzothiazoline-6-sulfonic) acid radical cations ($ABTS^+$) were obtained by reacting 7 mmol L^{-1} ABTS solution with 2.45 mmol L^{-1} potassium persulfate and stirring it in the dark at room temperature for 16 h before use. The $ABTS^+$ solution obtained was diluted in 5 mmol L^{-1} PBS, pH 7.4 by adjusting the solution to an absorbance of 0.70 at 734 nm. The assay was carried out in a 96-well microplate by adding 30 µL of the sample and 270 µL of the diluted solution $ABTS^+$ to each well. After 10 min of incubation, the absorbance was read at 734 nm on a microplate reader. A calibration curve was made using Trolox as a standard solution (0–0.06 mg mL^{-1}). The results were expressed as mg Trolox equivalent per gram (mg TE g^{-1} extract).

2.4. Physicochemical and Techno-Functional Properties

Bulk density, water holding capacity, oil holding capacity, water absorption capacity, swelling capacity, emulsifying activity, foaming capacity, and gelation capacity (last gelation concentration), were measured according to published protocols [11].

2.5. In Vitro Hypoglycemic Effect of Coffee Pulp

2.5.1. Glucose Absorption Capacity

Glucose absorption capacity was determined by mixing the sample (1 g) with 100 mL of glucose solution (10, 50, 100, 300 mmol L^{-1}), then, the coffee pulp flour was incubated (37 °C, 6 h) and centrifuged (3500× *g*, 15 min) [5]. The supernatant's glucose content was measured using an enzymatic kit (Megazyme K-GLUC, Wicklow, Ireland).

2.5.2. In Vitro Glucose Diffusion Retardation

In vitro glucose dialysis retardation capacity was determined by assessing the glucose dialysis retardation index (GDRI)[11]. The sample (0.5 g) was mixed with 25 mL of a glucose solution (50 mmol L^{-1}). The samples were dialyzed using a dialysis membrane (cut-off molecular weight of 12,000–14,000 Da) against 80 mL of Milli-Q water at 37 °C for 150 min, taking aliquots at 15, 30, 60, 90, 120, and 150 min of incubation. The amount of glucose in the dialysate was measured using the K-GLUC Enzyme Kit (Megazyme, Wicklow, Ireland).

2.5.3. In Vitro Residual α-Amylase Activity

The residual amylase activity was determined by mixing 1 g of the sample or controls (pectin or cellulose) with α-amylase (4 mg) and potato starch solution (4% *w*/*v*, 40 mL). The mixture was incubated (37 °C, 60 min), then 80 mL of NaOH 0.1 mol L^{-1} was added, and centrifuged (3500× *g*, 15 min). Finally, the glucose content was evaluated using the K-GLUC test kit [11].

2.5.4. In Vitro Starch Digestibility Retardation

The retardation of in vitro starch digestibility was studied by mixing 0.2 g of sample, 4 mg of α-amylase, and 10 mL of potato starch solution (4% *w*/*v*). The solution was dialyzed (cut-off molecular weight of 12,000–14,000 Da) against 200 mL of distilled water at 37 °C. After 10, 30, 60, 120, and 150 min of incubation, the dialysate's glucose content was quantified using the glucose test kit [5].

2.6. Evaluation of the In Vitro Hypolipidemic Properties of Coffee Pulp

2.6.1. Cholesterol Binding Capacity

Fresh egg yolks were diluted nine times their weight with Milli-Q water and beaten to obtain an emulsion. The mixture was divided into two equal parts and adjusted to pH 2.0 and 7.0. The sample (0.4 g) was mixed with 10 mL of egg yolk diluted at pH 2.0 and 7.0. The samples were then incubated under agitation at 37 °C for 2 h and centrifuged at 800× *g* for 15 min. The supernatant obtained (0.1 mL) was mixed with 0.6 mL of pure acetic acid, 0.2 mL of H_2SO_4 (96%), and 0.1 mL of *o*-phthalaldehyde (0.6 mg Ml^{-1}). The mixture was incubated (60 °C, 30 min) with continuous stirring for color development. Absorbance was finally measured at 550 nm [11].

2.6.2. Bile Salts Binding Capacity

For the evaluation of the binding capacity of bile salts, the sample (0.2 g) was mixed with 5 mL of NaCl solution (100 mL, 0.15 mol L^{-1}, pH 7.0) and sodium cholate (0.2 g). The samples were incubated while stirring at 37 °C for 1, 2, and 3 h, and centrifuged at 800× *g* for 20 min. The supernatant (0.1 mL) was mixed with 0.6 mL H_2SO_4 (45%) and 0.1 mL

furfural (0.3%). The mixture was incubated (30 min, 65 °C) under agitation for color development, and then, the absorbance was measured at 620 nm [11].

2.6.3. Inhibitory Activity against Pancreatic Lipase

For the determination of the inhibitory activity against pancreatic lipase, 2 mL of olive oil, 10 mL of sodium phosphate buffer (0.1 mol L^{-1}, pH 7.2), and 2 mL of pancreatic lipase (0.75 mg mL^{-1}) were added to the sample (0.1 g). Afterward, the samples were shaken and incubated (37 °C, 1 h). They were placed in a water bath at 100 °C to stop the reaction, followed by centrifugation (800× *g*, 15 min). Tween™ 20 was added to the supernatants containing olive oil to obtain an emulsion. The amount of free fatty acid released was evaluated by titration with NaOH (0.05 mol L^{-1}) and phenolphthalein [11].

2.7. Acute and Sub-Chronic Toxicity Experiments

Acute toxicity and Sub-chronic toxicity assays were performed following the guidelines of the OECD (Organization for Economic Co-operation and Development) Test Guidelines 452 and Test Guidelines 408, respectively. Adult male and female C57BL/6 mice were obtained from the Animal House Facility of the Universidad Autónoma de Madrid (Madrid, Spain). The mice were placed in cages with free access to water and a standard chow diet *ad libitum*. Treatment for the study of acute toxicity (2000 mg kg^{-1}) was administered in a single oral dose to each animal. After administration, the mice were observed for 24 h, and once a day for the next 14 days to identify changes in body weight, signs of toxicity, behavior, and mortality. For the sub-chronic toxicity test, a dose of 1000 mg kg^{-1} was administered orally every day for 90 days. The weight of animals and food consumption were measured daily. At the end of the study, the mice were sacrificed, and the collected organs (liver, spleen, and kidney) were subjected to a histopathological study.

2.8. Statistical Analysis

Statistical analysis was carried out using the statistical program SPSS 26.0. The results were expressed as mean ± standard deviation (SD) ($n = 3$). The data were analyzed by one-way analysis of variance (ANOVA) and *post hoc* Tukey's test. Differences were significant at $p < 0.05$.

3. Results

3.1. Chemical Composition

Coffee pulp contained a high amount of DF. The TDF in coffee pulp represented 51% of its composition. The IDF and SDF fractions represented 89% and 11% of the total DF. Proteins (9.2%) and lipids (2.6%) were considered a minor fraction.

3.2. Phenolic Compounds and Antioxidant Capacity

Coffee pulp presented a significant amount of total phenolic compounds (46.6 mg g^{-1} GAE). The fractions of free and bound phenolic compounds represented 70.8 and 29.2%, respectively. The antioxidant capacity of the coffee pulp was remarkably high (102.3 mg^{-1} TE). The antioxidant capacity linked to the fraction of free and bound phenolic compounds represented 68.6 and 31.4%, respectively.

3.3. Physicochemical and Techno-Functional Properties

Coffee pulp flour had a pH of 3.7. Compared to the control samples (cellulose and pectin) the water and oil holding capacities and bulk density of coffee pulp were adequate. On the other hand, the coffee pulp flour did not exhibit right swelling, gelation, emulsifying, and foaming capacities.

3.4. In Vitro Hypoglycemic Effects of Coffee Pulp

Concerning glucose adsorption, the coffee pulp was able to retain glucose in its structure. The results show that the coffee pulp can adsorb glucose at all the concentrations studied (10–300 mmol L^{-1}). Determination of glucose diffusion showed that all samples (cellulose, pectin, and coffee pulp flour) increased the dialysate's glucose concentration over time (150 min). Coffee pulp flour decreased glucose diffusion compared to a control sample (without sample). Pectin showed the highest retention rate of dialyzed glucose (40%), followed by coffee pulp flour (34%) and cellulose (22%). The presence of coffee pulp reduced glucose production ($p < 0.05$) by inhibiting the α-amylase enzyme activity. The study of starch digestibility revealed that the sample containing coffee pulp exhibited lower amounts of glucose in the dialysate than the control sample and cellulose. Starch digestion was affected in the presence of coffee pulp.

3.5. In Vitro Hypolipidemic Effects of Coffee Pulp

The determination of the binding capacity of cholesterol to the by-product (Figure 1A) was carried out at pH 2.0 and pH 7.0. Coffee pulp flour and cellulose showed an increased capacity to bind cholesterol to its matrix at pH 7.0. Pectin and coffee pulp at pH 7.0 proved to be good matrices for cholesterol binding. Regarding the bile salt absorption capacity (Figure 1B), coffee pulp flour exhibited a significantly higher bile salt absorption capacity than cellulose and the same as pectin ($p < 0.05$). During incubation, cellulose showed a significant increase ($p < 0.05$) in bile salt absorption. The study of inhibitory activity against pancreatic lipase (Figure 1C) reported higher values for coffee pulp flour (64%) and pectin (55%). Cellulose had the lowest value (28%) ($p < 0.05$) of pancreatic lipase inhibition.

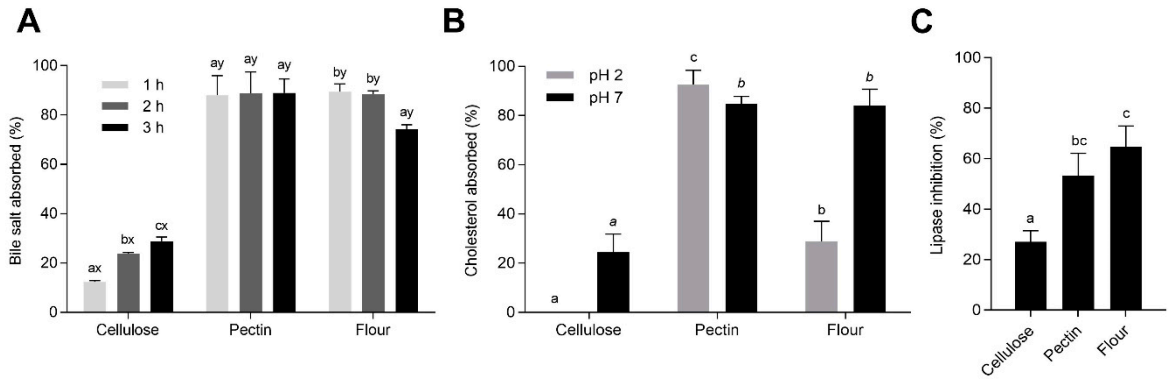

Figure 1. Effect of cellulose, pectin, and coffee pulp flour on cholesterol absorption capacity (%) at pH 2.0 and pH 7.0 (**A**), bile salts absorption capacity (%) after 1, 2, and 3 h of incubation (**B**), and pancreatic lipase activity (%) (**C**). The results are expressed as mean ± SD ($n = 3$). Different letters among columns indicate significant ($p < 0.05$) differences between samples.

3.6. Food Toxicity of Coffee Pulp

Oral intake of a single acute dose (2000 mg kg^{-1}) and sub-chronic doses (1000 mg kg^{-1}) of coffee pulp did not cause visible signs of toxicity, unusual behavior, or mortality. No significant changes in histological parameters or lesions in vital organs (liver, spleen, and kidney) were shown, ensuring this sustainable food ingredient's safety.

4. Discussion

Coffee production generates high quantities of by-products, including coffee pulp, which could be valorized for use as new functional ingredients due to their high content of bioactive compounds [12]. We present a critical evaluation of coffee pulp for its use in human food for the first time. To date, the coffee pulp was reported to be dangerous for animal consumption due to its high caffeine content [13]. In this work, coffee pulp proved

to be a DF source, mainly composed of IDF, which may give volume to feces and increases bowel emptying, favoring intestinal health [14]. The water and oil retention capacity and the coffee pulp's apparent density were adequate for using coffee pulp as flour. Coffee pulp's physiochemical and techno-functional properties may influence foods' nutritional and sensory characteristics and play a significant role during food preparation, processing, and storage [15]. The coffee pulp contained many phenolic compounds, which proved to possess in vitro antioxidant capacity. FPC was the main fraction. BPC was a considerable fraction linked to the DF, which cannot be released or absorbed in the small intestine but released in the colon by the action of bacterial enzymes and metabolized by the microbiota, leading to beneficial effects on human health [16]. As observed, coffee DF may be a natural vehicle for transporting antioxidant compounds into the large intestine [17]. Coffee pulp was able to adsorb glucose and delay its diffusion, which may result in diminished intestinal glucose absorption. This effect could be related to insoluble fiber, which can pose a physical obstacle, keeping glucose trapped within the network formed by fibers. Coffee pulp inhibited α-amylase activity, delaying starch's digestibility. DF can trap the enzyme and reduce its access to starch. Likewise, inhibitors in coffee pulp and its DF matrix (such as phenolics) can interact with the enzyme's active site, hindering its activity [18]. Therefore, coffee pulp could lower postprandial plasma glucose through different mechanisms [19]. Similarly, pancreatic lipase could be inhibited by the DF and the phenolic compounds released from coffee pulp [20]. Cholesterol and bile salts can bind to the coffee pulp DF, impeding its absorption. As a result, the liver synthesizes more bile salts from circulating cholesterol, reducing cholesterol levels [20]. Hence, coffee pulp's DF may exert hypolipidemic effects through diverse mechanisms. These hypoglycemic and hypolipidemic effects have also been observed in other coffee by-products [11]. Previous studies in our research group also provided evidence of the biological activity of phytochemicals released from the coffee pulp, reducing lipid accumulation, inflammation, oxidative stress, and insulin resistance in vitro [21,22]. The intake of acute and sub-chronic coffee pulp doses showed no toxicity, abnormal behavior, or mice mortality. Other coffee by-products, such as coffee silverskin, were previously validated [23]. Evaluating the nutritional value, biological properties, and safety of food products are the first steps leading to their commercialization and use as a food ingredient. Future studies will assess the in vivo biological activity of coffee pulp in different animal models. If its health-promoting effects are validated, human clinical studies will be necessary to corroborate in vitro and in vivo results. This work motivates coffee pulp's use as a novel ingredient with a high antioxidant DF content and great potential to be safely incorporated into functional foods.

5. Conclusions

In summary, the coffee pulp is mainly composed of insoluble dietary fiber. This fraction, along with phenolic compounds, was associated with the reduction of intestinal glucose and lipid absorption. Coffee pulp did not exert toxic acute and sub-chronic effects. Therefore, the coffee pulp could be validated as a new antioxidant dietary fiber, with hypoglycemic and hypoglycemic effects and good physicochemical and techno-functional properties, which would allow for its incorporation into foods with potential health benefits.

Author Contributions: Conceptualization, M.R.H., V.B., Y.A., and M.A.M.C; methodology, M.R.H., S.C., and Y.A.; formal analysis, S.C. and M.R.-H.; investigation, S.C., M.R.H, P.C.M., C.B., A.G.D., P.R.R., I.M.C., Á.L.L.d.P., and M.C.G.; data curation, S.C. and M.R.H.; writing—original draft preparation, S.C. and M.R.-H.; writing—review and editing, S.C., M.R.H., and V.B.; visualization, M.R.H.; supervision, Y.A., S.M.A., and M.A.M.C; funding acquisition, S.M.A. and M.A.M.C. All authors have read and agreed to the published version of the manuscript.

Funding: This research was funded by the COCARDIOLAC project from the Spanish Ministry of Science and Innovation (RTI 2018-097504-B-I00). M. Rebollo-Hernanz received funding from the FPU program of the Ministry of Science, Innovation, and Universities for his predoctoral fellowship

(FPU15/04238). P. Cano-Muñoz received funding from the Universidad Autonoma de Madrid for her predoctoral fellowship (Fomento de la Investigación en Estudios de Máster-UAM 2020).

Institutional Review Board Statement: Not applicable.

Informed Consent Statement: Not applicable.

Data Availability Statement: The data presented in this study are available from the corresponding author on reasonable request.

Conflicts of Interest: The authors declare no conflict of interest.

References

1. Klingel, T.; Kremer, J.I.; Gottstein, V.; Rajcic de Rezende, T.; Schwarz, S.; Lachenmeier, D.W. A Review of Coffee By-Products Including Leaf, Flower, Cherry, Husk, Silver Skin, and Spent Grounds as Novel Foods within the European Union. *Foods* **2020**, *9*, 665.
2. Esquivel, P.; Jiménez, V.M. Functional properties of coffee and coffee by-products. *Food Res. Int.* **2012**, *46*, 488–495.
3. Moreno, J.; Cozzano, S.; Mercedes Pérez, A.; Arcia, P.; Curutchet, A. Coffee Pulp Waste as a Functional Ingredient: Effect on Salty Cookies Quality. *J. Food Nutr. Res.* **2019**, *7*, 632–638.
4. Delgado, S.R.; Arbelaez, A.F.A.; Rojano, B. Antioxidant capacity, bioactive compounds in coffee pulp and implementation in the production of infusions. *Acta Sci. Pol. Technol. Aliment.* **2019**, *18*, 235–248.
5. Mudgil, D.; Barak, S. Composition, properties and health benefits of indigestible carbohydrate polymers as dietary fiber: A review. *Int. J. Biol. Macromol.* **2013**, *61*, 1–6.
6. AOAC (Association of Official Analytical Chemists)). *Official Methods of Analysis II*; EUA: Washington, DC, USA, 2002; Volume 32.
7. AACC International. *Approved Methods of the Americcan Association of Cereal Chemists*, 11th ed.; AACC International: St. Paul, MN, USA, 2008.
8. Aguilera, Y.; Rebollo-Hernanz, M.; Cañas, S.; Taladrid, D.; Martín-Cabrejas, M.A. Response surface methodology to optimise the heat-assisted aqueous extraction of phenolic compounds from coffee parchment and their comprehensive analysis. *Food Funct.* **2019**, *10*, 4739–4750.
9. Rebollo-Hernanz, M.; Aguilera, Y.; Herrera, T.; Cayuelas, L.T.; Dueñas, M.; Rodríguez-Rodríguez, P.; Ramiro-Cortijo, D.; Arribas, S.M.; Martín-Cabrejas, M.A. Bioavailability of melatonin from lentil sprouts and its role in the plasmatic antioxidant status in rats. *Foods* **2020**, *9*, 330.
10. Rebollo-Hernanz, M.; Fernández-Gómez, B.; Herrero, M.; Aguilera, Y.; Martín-Cabrejas, M.A.; Uribarri, J.; Del Castillo, M.D. Inhibition of the Maillard reaction by phytochemicals composing an aqueous coffee silverskin extract via a mixed mechanism of action. *Foods* **2019**, *8*, 438.
11. Benítez, V.; Rebollo-Hernanz, M.; Aguilera, Y.; Bejerano, S.; Cañas, S.; Martín-Cabrejas, M.A. Extruded coffee parchment shows enhanced antioxidant, hypoglycaemic, and hypolipidemic properties by releasing phenolic compounds from the fibre matrix. *Food Funct.* **2021**, *12*, 1097.
12. Aristizábal-Marulanda, V.; Chacón-Perez, Y.; Cardona Alzate, C.A. The biorefinery concept for the industrial valorization of coffee processing by-products. In *Handbook of Coffee Processing By-Products: Sustainable Applications*; Academic Press, Cambridge, United States, 2017; ISBN 9780128112915.
13. Murthy, P.S.; Madhava Naidu, M. Sustainable management of coffee industry by-products and value addition—A review. *Resour. Conserv. Recycl.* **2012**, *66*, 45–58.
14. Lattimer, J.M.; Haub, M.D. Effects of Dietary Fiber and Its Components on Metabolic Health. *Nutrients* **2010**, *2*, 1266–1289.
15. Huang, Y.L.; Hsieh, I.T. Physicochemical properties and intestinal health promoting water-insoluble fiber enriched fraction prepared from blanched vegetable soybean pod hulls. *Molecules* **2019**, *24*, 1796.
16. Rebollo-Hernanz, M.; Cañas, S.; Taladrid, D.; Benítez, V.; Bartolomé, B.; Aguilera, Y.; Martín-Cabrejas, M.A. Revalorization of Coffee Husk: Modeling and Optimizing the Green Sustainable Extraction of Phenolic Compounds. *Foods* **2021**, *10*, 653.
17. Tao, B.; Ye, F.; Li, H.; Hu, Q.; Xue, S.; Zhao, G. Phenolic Profile and in Vitro Antioxidant Capacity of Insoluble Dietary Fiber Powders from Citrus (*Citrus junos* Sieb. ex Tanaka) Pomace as Affected by Ultrafine Grinding. *J. Agric. Food Chem.* **2014**, *62*, 7166–7173.
18. Sun, L.; Miao, M. Dietary polyphenols modulate starch digestion and glycaemic level: A review. *Crit. Rev. Food Sci. Nutr.* **2020**.
19. Chau, C.F.; Chen, C.H.; Lin, C.Y. Insoluble fiber-rich fractions derived from Averrhoa carambola: Hypoglycemic effects determined by in vitro methods. *LWT-Food Sci. Technol.* **2004**, *37*, 331–335.
20. Daou, C.; Zhang, H.; Daou, C.; Zhang, H. Functional and physiological properties of total, soluble, and insoluble dietary fibres derived from defatted rice bran. *J. Food Sci. Technol.* **2014**, *51*, 3878–3885.
21. Rebollo-Hernanz, M.; Zhang, Q.; Aguilera, Y.; Martín-Cabrejas, M.A.; Gonzalez de Mejia, E. Phenolic compounds from coffee by-products modulate adipogenesis-related inflammation, mitochondrial dysfunction, and insulin resistance in adipocytes, via insulin/PI3K/AKT signaling pathways. *Food Chem. Toxicol.* **2019**, *132*, 110672.

22. Rebollo-Hernanz, M.; Zhang, Q.; Aguilera, Y.; Martín-Cabrejas, M.A.; de Mejia, E.G. Relationship of the phytochemicals from coffee and cocoa by-products with their potential to modulate biomarkers of metabolic syndrome in vitro. *Antioxidants* **2019**, *8*, 279.
23. Iriondo-DeHond, A.; Aparicio García, N.; Fernandez-Gomez, B.; Guisantes-Batan, E.; Velázquez Escobar, F.; Blanch, G.P.; San Andres, M.I.; Sanchez-Fortun, S.; del Castillo, M.D. Validation of coffee by-products as novel food ingredients. *Innov. Food Sci. Emerg. Technol.* **2019**, *51*, 194–204.