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Coffee by-products in topical formulations: A review

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ABSTRACT

Background: Coffee is of the most traded commodities in the world and its market has grown regularly over the last 150 years. During production and processing of coffee beans many by-products are generated such as skin, pulp, mucilage, parchment, silverskin, and immature /defective coffee beans. Around 50% of coffee fruit is discard and can contaminate the environment.

Scope and approach: The purpose of this review is to raise potential applications for coffee by-products in topical formulations. Besides, to present the main bioactive compounds responsible for their biological activity. With population changing habits, use and consumption of natural products has been growing, so there has been greater interest in research in this area. Added to this interest, is the concern caused by the environmental impact caused by tons of industrial waste discarded daily.

Key findings and conclusions: Coffee by-products have several biological activities, such as antioxidant, anti-inflammatory, antimicrobial, anti-aging, anti-cancer, anti-cellulite and sunscreen. Therefore, they are a good alternative for the composition of topical pharmaceutical and cosmetic formulations, because in addition to their numerous activities, they have low cost, and are sustainable, safe and effective. However, most studies are mainly focused on their antioxidant activity, and studies on the finished product are still lacking.

1. Introduction

Coffee is a beverage broadly consumed in the world with typical flavor, aroma, color and beneficial health effects and is one of the most traded commodities. A worldwide consumption of 3.5 billion cups of coffee is estimated every day (Blinová, Sirotiak, Bartosová, & Soldán, 2017; Murthy & Madhava Naidu, 2012). Coffee production and sales directly or indirectly affects millions of people (Blinová et al., 2017; Heeger, Kosinska-Cagnazzo, Cantergiani, & Andlauer, 2017; Murthy & Madhava Naidu, 2012).

Brazil is the largest producer and exporter in the world, followed by Vietnam, Colombia and Indonesia (ICO, 2020b). The international market is dominated by *Coffea arabica L.* (arabica) and *Coffea canephora Pierre* (robusta) species (Heeger et al., 2017).

In addition to the worldwide known caffeine, coffee has many others chemical compounds such as trigonelline, chlorogenic acids, vitamin B-3, volatile compounds, totaling about 2000 compounds (Alves, Casal, Alves, & Oliveira, 2009). Those compounds are responsible for its biological activities as antioxidant, anti-inflammatory, antimicrobial, antiviral, anti-aging, anticancer, anti-cellulite and sunscreen (Marto et al., 2016).

Coffee cherry is composed of bean, silverskin, parchment, mucilage, pulp and skin. During the production of coffee powder, the only part used is the bean, and all other parts, known as by-products, are discarded and can contaminate the environment. Therefore, more than 50% of coffee fruit is discarded when they could have potential use in pharmaceutical, food and cosmetic industries (Alves, Rodrigues, Nunes, Vinha, & Oliveira, 2017).

Concern with environment has grown encouraging industries to formulate more green and natural products focusing on sustainability.

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More and more consumers are aware of the type of products they are purchasing and demand better and more sustainable alternatives. The idea is to create innovative products rationally using resources, adding value to them and consequently reducing the environmental impact. Renewable resources used in formulations, such as those derived from plants or microorganisms, have bioactive ingredients that have greater biocompatibility when compared to synthetic substances (Carriço, Ribeiro, & Marto, 2018).

The purpose of the present study is to address biological activities of coffee by-products as well as their current applications in topical products. Although there are already some reviews on coffee, none focuses on the application of coffee by-products in topical formulations for cosmetic and pharmaceutical products. The existing literature addresses more the application of by-products for production of composting, biodiesel, alcohol, biogas, mushrooms, reusable cups, and animal feed (Blinová et al., 2017; Esquivel & Jiménez, 2012; Murthy & Madhava Naidu, 2012).

2. Methods

The most relevant articles in the coffee by-products area were selected from 2010 to 2020 in the Web of Science, Pubmed and Virtual Library of Heath (BVS) databases. The terms used in the data search were "coffee", "by-products", "formulation", "coffee bean", "dry method", "wet method", "skin", "pulp", "mucilage", "parchment", "silverskin", "husk", "spent coffee grounds", "caffeine", "trigonelline", "chlorogenic acids", "antioxidant", "antiaging", "anti-inflammatory", "sunscreen", "antimicrobial" and "anticellulite". Some older than 2010 references were included to describe methods and concepts.

3. Coffee production and consumption

Coffee was originated in Ethiopia and its market has grown regularly over the last 150 years (Murthy & Madhava Naidu, 2012). It is currently one of the most consumed beverages worldwide and its consumption continues to grow, being attributed to its excellent organoleptic characteristics, stimulating and beneficial health effect, besides being a social habit.

When ingested moderately, on average four cups a day, it improves attention and concentration, stimulates memory, and reduces the incidence of apathy and depression. Many practitioners of physical activity use coffee as a metabolism booster, thus increasing performance during physical activity (Alves, Casal, & Oliveira, 2009). Coffee is characterized as a functional food, since it provides, in addition to basic nutrition, health benefits. Several studies have been published in recent years on its pharmacological effects (Amano et al., 2019; Bosso et al., 2019).

Coffee belongs to Rubiaceae family, *Cincchonoideae* subfamily and genus *Coffea*. The genus *Coffea* contains over 80 species, *Coffea arabica* and *Coffea canephora* are the most important. (Alves, Casal, & Oliveira, 2009; Murthy & Madhava Naidu, 2012). Of the worlds production in 2018, arabica accounted for 58.91% of coffee production and robusta for 41.09% (ICO, 2020b). Arabica is original from Ethiopia, province of Kaffa and robusta comes from Central Africa (Murthy & Madhava Naidu, 2012). The two species differ in their sensory, physical and chemical characteristics, however arabica coffee has a more appreciated flavor and aroma compared to robusta, and consequently is more commercially valued (Alves, Casal, & Oliveira, 2009).

4. Coffee bean anatomy

Coffee bean is composed of skin and seed (Fig. 1) and its structure can be divided based on dry matter: the outside of the coffee bean is the skin, which is also known as pericarp, and when mature it has red or yellow color, depending on the variety; the pulp is right under the skin and is a by-product obtained after the coffee pulping process and contains both exocarp and part of mesocarp; and below the pulp is the mucilage, also called mesocarp. The next structure is the parchment or endocarp; followed by the silverskin. Inside of the coffee bean it is found the seed, also called endosperm (Esquivel & Jiménez, 2012; Heeger et al., 2017).

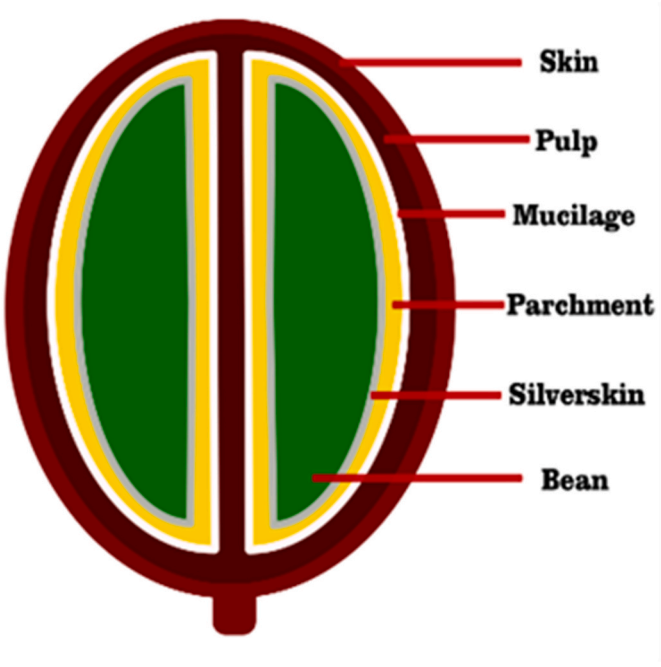

Fig. 1. Schematic structure of the coffee bean indicating the different structures, based on dry matter. Figure was created by authors.

5. Coffee processing

The main activity in coffee industry is the conversion process of coffee cherries into liquid. The process is carried out using two different techniques, dry and wet method, which differs from each other by its complexity and final product quality. It also influences the chemical constituents present in raw grains such as carbohydrates, lipids, proteins, minerals and secondary metabolites (Durán et al., 2017; Murthy & Madhava Naidu, 2012).

5.1. Dry method

Dry processing is technologically simpler and less expensive, being often used for robusta coffee (Esquivel & Jiménez, 2012). In this process, coffee cherries are dried right after harvest. Cherries can dry under the sun or mechanically, in ovens, affecting this stage time: under the sun it can last 3–4 weeks on average, while in ovens the time will depend on the used temperature. After this stage, the nuts have a moisture content of about 11% and acquire a dark brown tone (Bicho, Oliveira, Lidon, Ramalho, & Leitão, 2011; Esquivel & Jiménez, 2012). After drying, the coffee is hulled and the husks (skin, pulp and parchment) are generated, and usually discarded (Esquivel & Jiménez, 2012).

5.2. Wet method

The wet processing is more difficult, expensive, causes more environmental impact due to the amount of water required, and is generally used for coffee arabica. Right after harvest, coffee is immersed in water, where impurities, green beans and mature beans are separated (green beans float, skin sinks). Afterwards, skin and pulp are mechanically removed using a pulper (pulping step) (Esquivel & Jiménez, 2012; Murthy & Madhava Naidu, 2012).

The next step is fermentation, in which beans are stored in

fermentation tanks for approximately 12–48 h (or more depending on the varieties and local climate) for mucilage removal. Fermentation occurs and this stage ends with a washing process, which completely removes mucilage. (Esquivel & Jiménez, 2012).

Finally, beans are dried and parchment is removed. There is still the silverskin that can be optionally removed to obtain premium coffee using mechanical polishing. The coffee obtained in this method is called parchment coffee (Esquivel & Jiménez, 2012).

Dried fruit and pulped fruit remain in these forms until they are benefited, which should only occur shortly before they are marketed to maintain their original characteristics. In processing, these are transformed into coffee beans, called green coffee. At this stage the coffee beans undergo cleaning, impurities removal, peeling, polishing, shape and size calibration and classification (Fig. 2) (Bicho et al., 2011; Esquivel & Jiménez, 2012).

6. By-products

Skin, pulp, mucilage, parchment, silverskin, and also immature and defective coffee beans are by-products generated during agricultural production and agro-industrial processing (Heeger et al., 2017), which can affect economic, environmental and social sectors, and contribute to Green House Gas (GHG) emissions (Torres-León et al., 2018). Coffee by-products have an average composition of carbohydrates (35%), proteins (5.2%), fibers (30.8%) and minerals (10.7%). More than 50% of the coffee fruit is not used and, if not properly treated, can be a source of

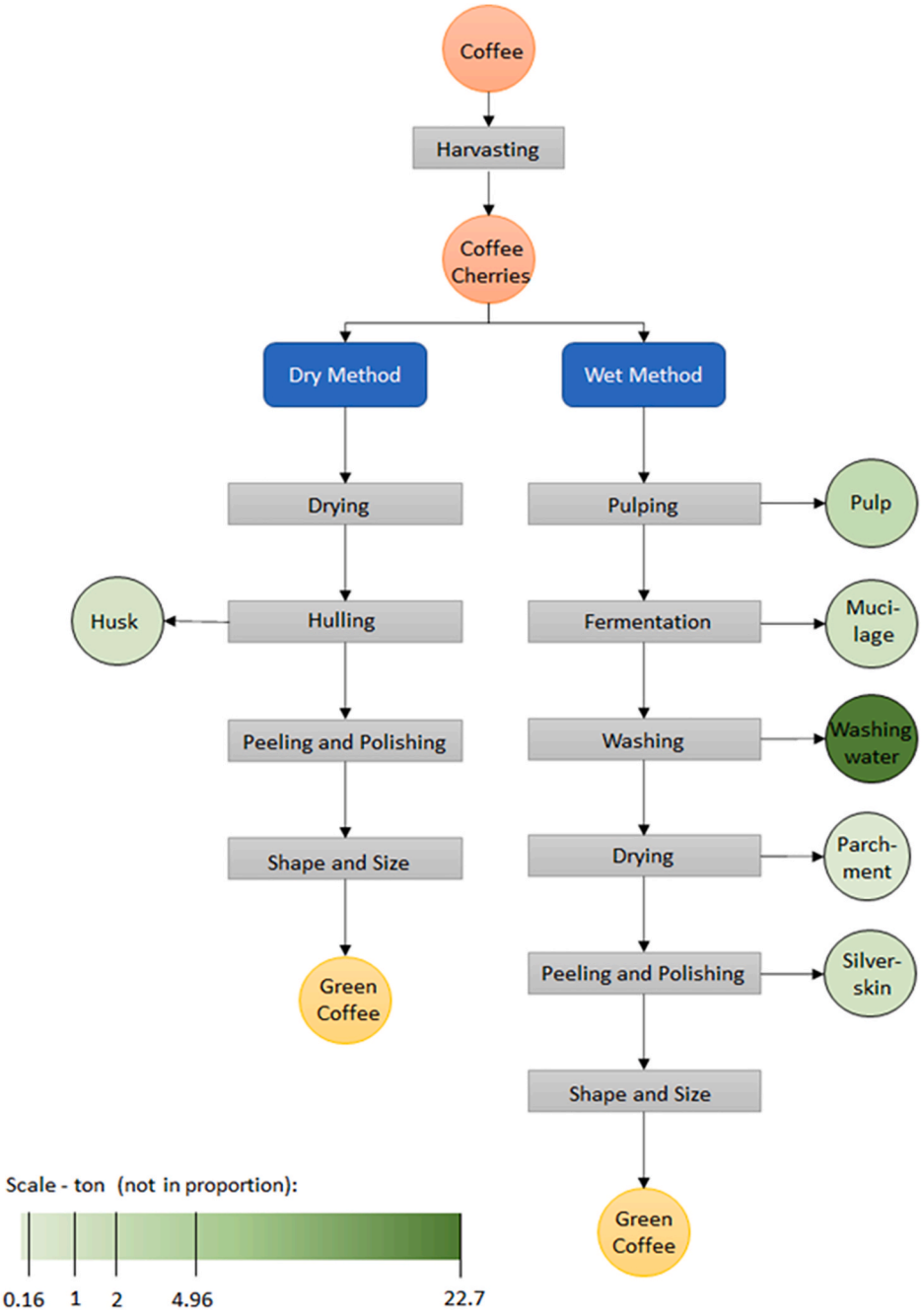

Fig. 2. Dry and wet coffee processing and its generated by-products. Process are represented as rectangles, and circles represent products and by-products generated at each stage. By-products (green circles) are presented in a color scale according with generated amounts to produce 1 ton of green coffee. Figure was created by authors. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

environmental contamination (Esquivel & Jiménez, 2012).

The wet method residues generally represent a greater damage to the environment, since the pulp pathway generates tannins, caffeine and polyphenols, considered antinutritional factors. If the water used in the washing steps is discharged directly into effluents, it can threaten aquatic life due to the high concentration of organic matter (high oxygen demand). In addition, the high content of sugars, proteins and minerals contribute to the environmental problem, since they offer an ideal medium for the proliferation of microorganisms (Durán et al., 2017).

A more sustainable chain around the entire coffee production process is necessary, and new initiatives should be implemented such as improving origin, recyclable packaging, reducing emissions, creating green facilities and above all creating new products from everything what is considered food waste (Iriondo-DeHond et al., 2019).

By-products available sources are in all coffee plantations if correctly processed. Considering that only in 2018, 174,897 thousand 60-kg bags were produced worldwide representing only 50% of what was harvested from cherry coffee, this indicates the availability of a great source of by-products (ICO, 2020b). Table 1 shows the main possible applications for components of coffee by-products, and Table 2 shows the main chemical compounds of coffee by-products.

However, natural products face a limitation in the development of topical products: its action depends on its chemical composition, which may vary according to its extractive method. In addition, several other factors such as, species of coffee, place of planting, time of harvest, storage period, among others influence their activity. Therefore, the same product made from coffee by-products may contain a greater or lesser presence of its bioactive compounds (Blinová et al., 2017).

Table 1
Coffee by-products and their application.

By-product	Application	References
Husk	Antioxidant	Andrade et al. (2012); Blinová et al. (2017); Iriondo-DeHond et al. (2019)
Pulp	Antioxidant	Ameca et al. (2018); Chaves-Ulate and Esquivel-Rodríguez (2019); Delgado et al. (2019); Geremu, Tola, and Sualeh (2016); Heeger et al. (2017)
	Antimicrobial	Chaves-Ulate and Esquivel-Rodríguez (2019); Duangjai et al. (2016)
	Anti-inflammatory	Magoni et al. (2018)
	Pigment	Alves et al. (2017)
Silverskin	Antioxidant	Ballesteros et al. (2014); Bessada et al. (2018); Blinová et al. (2017); Borrelli et al. (2004); Chaves-Ulate and Esquivel-Rodríguez (2019); Costa et al. (2018); Esquivel and Jiménez (2012); Janissen and Huynh (2018); Martinez-Saez et al. (2014); Murthy and Madhava Naidu (2012); Puga et al. (2017); Rodrigues et al. (2016); Rodrigues et al. (2015); Toschi et al. (2014)
	Antiaging	Castillo et al. (2013); Cho et al. (2017); Iriondo-DeHond et al. (2016)
	Antimicrobial	Chaves-Ulate and Esquivel-Rodríguez (2019); Rodrigues et al. (2015)
	Anticellulite	Rodrigues et al. (2016)
Spent coffee grounds	Antioxidant	Andrade et al. (2012); Ballesteros et al. (2014); Blinová et al. (2017); Campos-Vega et al. (2015);Mussatto, Ballesteros, Martins, and Teixeira (2011)
	Anti-inflammatory	Campos-Vega et al. (2015); López-Barrera et al. (2016)
	Sunscreen	Chiari et al. (2014); Marto et al. (2016)
	Antimicrobial	Campos-Vega et al. (2015)
	Emulsifying activity	Ballesteros et al. (2014)
	Emulsion stability	Ballesteros et al. (2014)
	Hydration	Ribeiro et al. (2013)

Table 2
Coffee by-products and their chemical compounds.

Chemical compounds (%)	Husk	Pulp	Silverskin	Spent coffee grounds
Protein	8–11	5–15	20	10.32
Lipids	0.5–3	2.0–7.0	3	16
Minerals	3–7	9	~8	0.82–3.52
Fat	0.5	2–7	2.2	2.29
Carbohydrate	58–85	21–32	0.25–6.35	–
Cellulose	43	63.0	17.8	8.6
Hemicellulose	7	2.3	13.1	36.7
Total pectic substances	1.6	6.5	0.02	0.01
Lignin	9	14.3–17.5	1.0	0.05
Caffeine	~1	1.5	0.6–1.1	0.02
Chlorogenic acid	~2,5	2.4	3.0	2.3
Tannins	~5	3	0.02	0.02
Total fiber	24.0–30.8	60.5	60.0	43.0
Moisture	13.0–15.0	82.4	5–7	74.72
Ash	5.4–6.2	7.3	7.34–10.5	0.47

From: Acevedo et al. (2013); Bessada et al. (2018); Blinová et al. (2017); Campos-Vega et al. (2015); Durán et al. (2017); Gouvea, Torres, Franca, Oliveira, and Oliveira (2009); Loyao, Villasica, Dela Peña, and Go (2018).

6.1. Husk

Coffee husk (composed of dried skin, pulp and parchment) is the main by-product obtained during the dry processing method of coffee cherries. It represents around 45% of the berry (Blinová et al., 2017; Brand et al., 2001; Iriondo-DeHond et al., 2019). For every 1 ton of coffee fruit, around 0.18 ton of husk is generated, yielding about 150–200 kg of green coffee (Blinová et al., 2017; Murthy & Madhava Naidu, 2012).

Coffee husk is rich in organic content with proteins (8–11%), carbohydrates (58–85%), cellulose (43%), hemicellulose (7%), lignin (9%), lipids (0.5–3%), minerals (3–7%), fibers (24–30.8%), minor amounts of bioactive compounds, such as caffeine (~1%) and chlorogenic acid (~2,5%) besides phytochemical compounds as tannins (5–9%) (Table 2) and cyanidins (20%) (Blinová et al., 2017; Brand et al., 2001; Durán et al., 2017; Iriondo-DeHond et al., 2019). In its composition high levels of 5-caffeoylquinic acid (commonly known as chlorogenic acid; 0.2–1.9 mg/g) can also be found, but other phenolics are also present in minor amounts (quercetin-3-rutinoside, quercetin-3-glucoside, quercetin-3-galactoside, catechin, epicatechin, and procyanidin dimers, trimers, and tetramers). According to the geographical origin, total procyanidin contents can vary from 1.3 to 534 μg/g and total flavonols from 5 to 261 μg/g (Mullen, Nemzer, Stalmach, Ali, & Combet, 2013).

The studies on coffee husk were focused on the production of composting, vermicomposting, detoxification, solid biofuel, ethanol, biogas, adsorbents, mushroom, energy drinks, energy bars and fermentation studies (Andrade et al., 2012; Brand et al., 2001). However, due to its concentration in caffeine, polyphenols and its good antioxidant activity, it is possible that this material is used in the study and development of new topical anti-inflammatory and healing formulations.

A study reported the antioxidant activity of coffee husk extracts obtained by low pressure extractions (LPE) using Soxhlet and ultrasound with different solvents, and supercritical fluid extraction (SFE) according to extraction, co-solvent, flow and pressure conditions. Antioxidant potential was determined by DPPH, ABTS and Folin-Ciocalteau methods and compared to the synthetic liposoluble antioxidant BHT (Andrade et al., 2012). the results showed that depending on extraction method and conditions, different phenolic content and antioxidant activities were observed. Coffee husk extracts presented good antioxidant potential, and sometimes with activities greater than BHT. The choice of extraction method for each substance is extremely important to obtain the best possible yield of active compounds and, consequently, a better antioxidant activity. In addition, it is necessary to pay attention to the solvent selection taking into account its physico-chemical characteristics

that should match those of the substances of interest in the extraction (Andrade et al., 2012).

The investigation of mycotoxins in the coffee husk is a major concern to ensure the safety of the material, since during the drying of the coffee cherries mycotoxins can be produced and lead to a toxicological problem (Klingel et al., 2020). One study reported that ochratoxin A (4.3 μg/kg) was found in the husk. However, when analyzing the acute toxicity of the husk in rats, they found no signs of toxicity, mortality or abnormal behavior with a single dose of 2000 mg/kg body weight (Iriondo-DeHond et al., 2019).

Phytochemicals are considerably safe and on the human body can have potential positive physiological effects. Therefore, considering its chemical composition and bioactive compounds, coffee husk has a great potential to be used in pharmaceutical and food industries as a natural source to obtain bioactive molecules.

6.2. Pulp

Pulp is the main by-product generated during the wet processing method, and corresponds to 29% of dry-weight of the whole berry. It still contains 6–8% of mucilage. During processing, for each 2 tons of produced coffee, 1 ton is coffee pulp. It is substantially rich in carbohydrates (21–32%), total pectic substances (6.5%), reducing sugars (12.4%), non-reducing sugars (2%), proteins (5–15%), minerals (9%) fats (2–7%), and also contains significant amounts of tannins (3%), chlorogenic acids (2.4%), caffeic acid (1.6%) and caffeine (1.5%) (Blinová et al., 2017; Bonilla-Hermosa, Duarte, & Schwan, 2014; Durán et al., 2017; Murthy & Madhava Naidu, 2012).

In coffee pulp, Ramirez-Coronel et al. (2004) identified four major classes of phenolic compounds (flavan-3-ols, hydroxycinnamic acids, flavonols and anthocyanidins) and, in another study, Ramirez-Martinez (1988) described 5-caffeoylquinic acid as the major phenolic, reporting also lower amounts of epicatechin, catechin, dicaffeoylquinic acids, rutin, protocatechuic acid and ferulic acid. Other phenolics have also been described in coffee pulp, namely 5-feruloylquinic acid, cyanidin-3-rutinoside, and cyanidin-3-glucoside (Esquivel, Kramer, & Carle, 2010). More recently, Rodríguez-Durán et al. (2014) analyzed the soluble and bound hydroxycinnamates in arabica coffee pulp from seven cultivars identifying chlorogenic acid as the major phenolic (94–98%) in the soluble fraction, while caffeic acid was the most abundant hydroxycinnamate in the bound fraction (72–88%). Ferulic and *p*-coumaric acids were also reported, although in lower amounts.

Extracts of coffee pulp presented a total polyphenol content between 254.62 and 453.21 mg GAE/100 g of pulp, higher when compared to other residues as white grape skin (239 mg GAE/100 g) and onion peel (422 mg GAE/100 g). The flavonoid content (132.61–784.76 mg CAE/100 g) was similar to other by-products such as apple peel (566 mg CAE/100 g) and olive tree leaves (858 mg CAE/100 g) (Delgado, Arbelaez, & Rojano, 2019).

A study determined the antioxidant capacity of the coffee pulp extracted with hot water by different methods. Some coffee varieties were analyzed and in the total polyphenols test the best result was for the bourbon variety from Congo with 9.17 mg GAE/g DM. Other samples showed values between 4.85 mg and 6.08 mg GAE/g DM. However, the literature shows better results when extraction is performed with 70% methanol/water with results between 11 and 20 mg/g. This difference is due to the fact that methanol/water and ethanol/water mixtures have the capacity to provide a higher extraction yield for phenolics than water. The antioxidant activity in the ABTS test and ORAC assay also obtained the best result in the bourbon variety from Congo with 92.2 μmol TE/g DM and 274 μmol TE/g DM, respectively. A good correlation between ABTS and total polyphenol content values ($R^2 = 0.95$) (Heeger et al., 2017).

Coffee pulp has proven to be a source of anthocyanins, which are flavonoid compounds responsible for pigmentation in plants, flowers, fruits and tubers. As an example, a study carried out the extraction of anthocyanins with a mixture of 0.01 HCl solutions in methanol for 18 h at low temperature (4 °C) and yielded 24 mg of monomeric anthocyanins/100 g of fresh pulp (Alves et al., 2017). Natural dyes are safer to be consumed even in high quantities when compared to synthetic dyes, and therefore coffee pulp is a potential source to be used as a natural color in foods, medicines and cosmetics. In addition, anthocyanins have value-added properties as nutraceutical, antioxidants, antimicrobial effect and prevention of chronic diseases (Khoo, Azlan, Tang, & Lim, 2017).

Currently, there are no studies reporting specific data on pulp toxicity. However, its composition due to its bioactive compounds, such as caffeine and tannins, mycotoxin contamination and microbial deterioration can pose a safety problem (Klingel et al., 2020).

It is already known that pulp can produce animal feed, biogas, bioethanol, substrate for mushrooms, composting, vermicomposting, enzymes, citric acid, gibberellic acid, aroma compounds and substrate for microbial processes (Ameca et al., 2018). On the other hand, unfortunately there are no studies with pulp application in the area of topical products, however due to its good antioxidant capacity and its bioactive compounds, it can be predicted that the coffee pulp has great potential to be used as adjuvants in topical formulations.

6.3. Silverskin

Coffee silverskin is a thin layer that is directly in contact with the coffee bean. Strongly adherent, it detaches from the bean when exposed to roasting high temperatures. Being the main by-product of coffee roasting industries, major efforts have been performed in order to characterize its chemical composition and develop new potential applications. Indeed, while till date, the majority of silverskin is used for direct combustion or dispatched into landfills as fertilizer, several publications have emerged suggesting the incorporation of coffee silverskin in beverages (Martinez-Saez et al., 2014), bakery products, bread (Mussatto, Machado, Martins, & Teixeira, 2011), or even in cosmetic products (Rodrigues, Matias, Ferreira, Amaral, & Oliveira, 2016; Rodrigues, Pereira, et al., 2015).

Although silverskin represents a minor fraction of the coffee fruit, it is obtained in very high amounts, based on the millions of coffee bags roasted around the world every year. For reference, in 2019/2020, the total world coffee consumption achieved 169,337 thousand 60 kg bags (ICO, 2020a).

Compared to other coffee by-products, silverskin seems to be a more stable material, and one of the reasons is its low moisture content (5–10%) (Bessada, Alves, Costa, Nunes, & Oliveira, 2018; Borrelli, Esposito, Napolitano, Ritieni, & Fogliano, 2004). The roasting temperatures can also reduce/eliminate microbial charge potentially associated to the raw coffee bean. In addition, silverskin can be easily gathered and collected in coffee roasting facilities, which is a great advantage for further processing.

Silverskin is particularly rich in dietary fiber (~60%), especially insoluble one, protein (~20%), minerals (~8%), and antioxidants (Bessada et al., 2018; Borrelli et al., 2004; Jiménez-Zamora, Pastoriza, & Rufián-Henares, 2015). Its dietary fiber includes cellulose and hemicellulose, being this last composed by xylose, arabinose, galactose and mannose (Carneiro, Silva, Mussatto, Roberto, & Teixeira, 2009). Within minerals, potassium (5%), magnesium (2%), and calcium (0.5%) are the major ones (Costa et al., 2018).

The main antioxidants of coffee silverskin are undoubtedly their phenolic compounds, which have been found to be mainly chlorogenic acids and related compounds. Indeed, a series of phenolics such as 5-caffeoylquinic acid (the major one), 4-caffeoylquinic acid, 3-caffeoylquinic acid, 5-feruloylquinic acid, 3-feruloylquinic acid, 4-feruloylquinic acid, dicaffeoylquinic acids, caffeoyltryptophan, caffeoylferuloylquinic acids, sinapoylquinic acid, among others, have been identified in silverskin (Puga, Alves, Costa, Vinha, & Oliveira, 2017). Bessada et al. (2018) quantified 5-caffeoylquinic acid in robusta silverskin from different

geographical origins and found amounts varying between 11 and 819 mg/100 g. Notice that this compound can be thermally degraded, so its content will also depend on roasting conditions to which samples were subjected. In general, total phenolics content can be expressed in chlorogenic acid equivalents (CAE) and values as 8–32 mg CAE/g (Bessada et al., 2018) and 20 mg CAE/g (Puga et al., 2017) have been reported. In addition, coffee silverskin also presents caffeine content ranging from 0.6 to 1.1% (Bessada et al., 2018).

Total lipid content is usually lower than 3% and the lipid profile can vary according to the geographical origin (Bessada et al., 2018). Toschi, Cardenia, Bonaga, Mandrioli, and Rodriguez-Estrada (2014) described triacylglycerols as the major components of silverskin fat (48%), followed by free fatty acids (21%), esterified sterols (15%), free sterols (13%), and diacylglycerols (4%). Although silverskin presents mainly saturated fatty acids (62–86%), followed by polyunsaturated (10–29%) and monounsaturated (5–10%) fatty acids, the profile was different among samples from different origins (Bessada et al., 2018). Coffee species and geographical origin also seem to have great influence in vitamin E vitamers profile of this by-product. A Brazilian robusta sample presented 2- to 5-fold higher amounts of α-tocopherol compared to other five geographical origins. Overall, total vitamin E ranged from 4 to 17 mg/100 g (Bessada et al., 2018; Costa et al., 2018).

The presence of other group of antioxidant compounds formed through Maillard reactions during roasting, such as melanoidins, has also been reported. The formation of melanoidins, together with polysaccharides (galactomannans and arabinogalactans) and proteins, can be due to chlorogenic acids and their thermal degeneration products (Alves, Casal, & Oliveira, 2009). In this by-product, the amount of water-soluble melanoidins present is comparable to cherry brews and about 4.5% (Borrelli et al., 2004).

Silverskin may also contain acrylamide and mycotoxins, mainly ochratoxin A (18.7–34.4 μg/kg) (Iriondo-DeHond et al., 2019; Toschi et al., 2014). Acute toxicity test was performed and no toxicity, mortality or abnormal behavior were observed within silverskin (Iriondo-DeHond et al., 2019). Rodrigues, Palmeira-de-Oliveira, et al. (2015) performed a cytotoxicity study with silverskin extract using two assays, the MTS and LDH with keratinocyte cell line (HaCaT) and human foreskin fibroblasts (HFF-1) cells. At concentrations tested up to 1000 μg/mL, no cytotoxicity was observed in the extracts.

In sum, the complex composition of coffee silverskin, rich in several antioxidants and bioactive compounds, is an interesting basis to develop natural extracts with high potential to be used as alternative functional ingredient or natural preservatives, including in the pharmaceutical and cosmetic field.

6.4. Spent coffee grounds

Spent coffee grounds (SCG) are a solid waste, one of the main ones in the coffee industry, generated during instant coffee production, on average 6 million tons per year. (Mussatto, Carneiro, Silva, Roberto, & Teixeira, 2011). During coffee processing, for each ton of green coffee is estimated the production of 650 kg of spent coffee, and for each kg of powder coffee is produced 2 kg of wet spent coffee (Murthy & Madhava Naidu, 2012).

The type of coffee beans will determine SCG composition, as well as roasting conditions and extraction processes (Acevedo et al., 2013). Their common composition in dry matter is neutral detergent fiber (86.60%), acid detergent fiber (78.50%), moisture (74.72%), crude fiber (36.87%), nitrogen-free extract (23.30%), protein (10.32%) and ash (0.47%) (Acevedo et al., 2013).

Ramalakshmi, Rao, Takano-Ishikawa, and Goto (2009) showed that the major antioxidant in spent coffee grounds is 5-caffeoylquinic acid (~6%) and Bravo et al. (2012) reported significant amounts of total caffeoylquinic acids (6–13 mg/g) and dicaffeoylquinic acids (3–6 mg/g). Monente, Ludwig, Irigoyen, De Peña, and Cid (2015) also detected caffeic acid, ferulic acid, p-coumaric acid, sinapic acid, and 4-hydroxybenzoic acid.

There is a growing interest in knowing SGC composition due to the fact that these by-products are expected to contain properties similar to coffee beans because they are derived from them and could be used in future industrial application in different areas due to its anti-inflammatory, antioxidant, anti-bacterial, antiviral and anti-carcinogenic activities (Ballesteros, Teixeira, & Mussatto, 2014; Campos-Vega, Loarca-Piña, Vergara-Castañeda, & Oomah, 2015).

The extraction of SCG with 40 mL 60% methanol/g during 90 min obtained an average 18 mg gallic acid equivalents (GAE)/g SCG, which is a high phenolic concentration when compared with ripe raspberry (12.0–15.3 mg GAE/g dry matter) and blackberry (12.1–14.8 mg GAE/g dry matter). SCG extract also contains high antioxidant activity (FRAP - 0.043–0.102 mM Fe(II)/g) when compared to other agro-industrial waste such mango residue (0.010 mM $FeSO_4$/g dry matter), passion fruit residue (0.034 mM $FeSO_4$/g dry matter) and pineapple residue (0.072 mM $FeSO_4$/g dry matter) (Ballesteros et al., 2014; Campos-Vega et al., 2015; Mussatto, Carneiro, et al., 2011).

Although caffeine amount in waste is lower than in coffee beans, SCG have still a large amount of caffeine. It is possible to obtain between 0.734 and 41.3 μg/mg of caffeine, extracted by low-pressure extraction as ultrasound and Soxhlet, or supercritical CO_2 extraction. Caffeine extracted by supercritical CO_2 from SCG corresponds to 18–48% of extracted compounds from coffee beans, and 8–31% from roasted coffee (Campos-Vega et al., 2015).

The emulsifying activity (EA) and emulsifying stability (ES) of SCG was evaluated according to Chau, Cheung, and Wong (1997). SCG shows EA of 54.72% and ES of 92.38%. These results are better than others compounds, as EA of chia fibrous (53.26%), lima bean (49.3%), mango peel flour (4.68%) and ES wheat straw (86.94%), corncobs (80%), mango peel flour (79.12%), papaya kernel flour (58%) an lima bean (28.25%) (Ballesteros et al., 2014; Noor, Siti, & Mahmad, 2015).

One study performed the extraction of oil from SCG with supercritical carbon dioxide, an environmentally friendly technique, and was incorporated into a non-ionic o/w cream. This formulation containing 10% of the lipid fraction of SCG presented hydration action proven by increase of skin barrier function with lowering TEWL (transepidermal water loss or intact epidermal barrier function). This emulsion was also able to increased sebum levels and consequently increased barrier properties of the skin, possibly by supplementation of skin lipids (Ribeiro et al., 2013).

As natural agent SGC oil can be used in sunscreens synergistically with synthetic filters increasing sun protection factor (SPF) by up to 20% besides being rich in antioxidants and polyphenols (Chiari et al., 2014). The effects caused by UV radiation on the skin can be prevented by phenolic compounds (Chiari et al., 2014; Marto et al., 2016). Therefore, it is possible to reduce the amount of chemical and physical filters when using SGC oil.

Spent coffee grounds can be contaminated by mycotoxins. In one study, ochratoxin A (2.31 μg/kg) was found in spent coffee grounds, but neither aflatoxin B1 nor enniatin B were detected, and indications of toxicity were not observed (Iriondo-DeHond et al., 2019).

Due to its chemical composition and antioxidant, emulsifying and emulsion properties, high content of lipids (mainly fatty acids) spent coffee grounds have the potential to be incorporated into topical products as creams and photoprotectors.

7. Bioactive compounds

Coffee has many compounds that drive aroma and flavor in a brewed coffee. Alkaloids, proteins, polymeric polysaccharides, caffeine, acids, lipids and carbohydrates (sucrose, glucose, fructose) add sensory characteristics to the beverage. The composition changes between coffee species and also before and after roast process (Barbosa, Scholz, Kitzberger, & Benassi, 2019; Sunarharum, Williams, & Smyth, 2014). Caffeine, trigonelline and chlorogenic acids (Fig. 3) are among the most

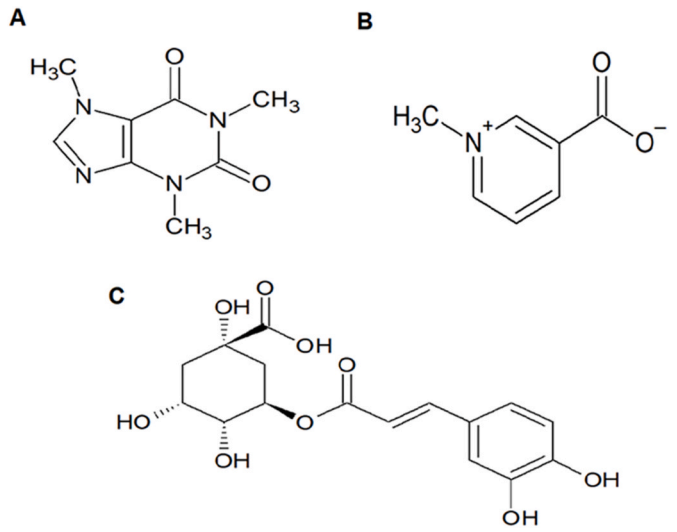

Fig. 3. Chemical structure of the main bioactive compounds of coffee (A) caffeine, (B) trigonelline and (C) chlorogenic acid. Figure was created by authors using ChemSketch 12.0.

important metabolites that regulate its quality and taste and may change during fruit maturation (Barbosa et al., 2019; Lemos et al., 2020). In this topic we focus on the molecule itself and its chemical properties. Properties and action of the compounds will be discussed more deeply below.

7.1. Caffeine

Caffeine (1,3,7-trimethylpurine-2,6-dione) is a secondary metabolite that accumulates during the coffee bean development. This compound, from the methylxanthine class, is highly affected by genotype and environmental conditions on its formation. Caffeine is a recognized stimulator of CNS and beneficial health effects have also been described. Organoleptically, it is associated with the bitterness of the beverage and robusta beans contain almost double amounts of this compound than arabica ones (Lemos et al., 2020; Sunarharum et al., 2014).

Its chemical structure is heat stable and provides many actions/properties related to anti-aging, photoprotective, antioxidant, cellulite treatment, acne treatment, amongst others. Besides its activity, another reason for using caffeine in dermocosmetics is as sunscreen adjuvant, acting in synergy as a photoprotector and a photostabilizer (Rosado et al., 2019). When in a topical formulation, it is important to consider that even though caffeine is a hydrophilic skin-permeation substance, it tends to precipitate depending on its vehicle and can form non redispersible clumps (Fernandes, Damasceno, Ferrari, & Azevedo, 2015).

7.2. Trigonelline

Trigonelline (N-methylpyridinium-3-carboxylate) is a heterocyclic alkaloidal phytochemical, with numerous health benefits and is principally found in the seeds of fenugreek coffee (Lone A, Malik A, NaikooH, RaghuR, & A.Tasduq, 2020). It is present in higher amounts in arabica than in robusta coffee beans (Lemos et al., 2020).

Trigonelline has several health benefits, its antioxidant, anti-inflammatory, antiglycation, anti-microbial, anti-carcinogenic properties (Costa et al., 2020; Nugrahini, Ishida, Nakagawa, Nishi, & Sugahara, 2020). It also causes attenuation of UV-B mediated photo-damage (Lone A et al., 2020).

Recent studies tested this alkaloid for anti-degranulation activity aiming a future product with anti-allergy effects. Trigonelline showed inhibition of mast cell degranulation in *in vitro* studies by modulating the intracellular signaling pathways involved in degranulation (Nugrahini et al., 2020).

7.3. Chlorogenic acids

Chlorogenic acids are a group of phenolic compounds known as the most prevalent in green coffee beans. The three major chlorogenic acids classes in coffee are caffeoylquinic acids (CQA), feruloylquinic acids (FQA) and dicaffeoylquinic acids (diCQA) (Duarte, Pereira, & Farah, 2010; Farah & Donangelo, 2006) with at least 3 isomers each. 3,4-Dicaffeoilquinic acid is related to good coffee cup quality, while 5-caffeolylquinic acid is related to poor cup quality and off flavors. In opposition to trigonelline, chlorogenic acids are present in higher concentrations in robusta than arabica beans (Lemos et al., 2020). Comparing to other beverages, coffee showed one of the highest content (Sunarharum et al., 2014).

Chlorogenic acids, mainly 5-caffeoylquinic acid, are also the main group of phenolic compounds in post-roasting coffee by-products. For instance, Puga et al. (2017) reported a total phenolic content of ~20 mg of chlorogenic acid equivalents per g of coffee silverskin, in which ~1 mg/g referred to 5-caffeoylquinic acid. Other phenolics were tentatively identified, such as 3-caffeoylquinic acid, 4-caffeoylquinic acid, 5-feruloylquinic acid, 3-feruloylquinic acid, dicaffeoylquinic acids, caffeoyltryptophan, and caffeoylferuloylquinic acid.

The roasting process can degrade around 93% of chlorogenic acids, which are converted into chlorogenic lactones, contributing for the bitter taste of a brewed coffee (Sunarharum et al., 2014).

This phenolic cluster possesses diverse health benefits. Boran (2018) showed a high collagenase inhibition with a IC_{50} value of 73.3 μg/mL for chlorogenic acids. It also has an antioxidant activity frequently reported (Cao et al., 2020; Chen et al., 2016) and anti-inflammatory properties (Bagdas et al., 2020).

Han et al. (2019) showed evidence that thermogenesis of brown adipocytes, a function that is deactivated in humans, can be stimulated by chlorogenic acid, through stimulation of mitochondria synthesis and function and promotion of glucose uptake. This finding could provide an effective method to treat metabolic diseases in humans.

8. Potential topical application for coffee by-products

8.1. Antioxidant

There is a natural dynamic balance *in vivo* between antioxidants and free radicals, in which antioxidant enzymes (superoxide dismutase or catalase), and antioxidant compounds (glutathione, vitamins C and E) can protect membrane lipids, proteins, DNA, and other macromolecules against several reactive species (e.g. hydroxyl radicals (·OH), superoxide anion radicals, (O2·−), nitroxide radicals (NO·), peroxyl radicals (ROO·−), and hydrogen peroxide (H_2O_2). Although oxygen and nitrogen reactive species play an important role in host defense and physiological processes, when in excess, they can disrupt the antioxidant protection and lead to a situation of oxidative stress. This condition has been associated to the development of several injuries, including skin accelerated aging and related injuries (e.g. dermatitis, eczema, vasculitis, sunburn, or even cancer) (Bessada et al., 2018; Wu et al., 2015). Thus, antioxidant-rich extracts can be useful in the preparation of formulations for topical application, aiming the protection of skin against oxidative damage mediated, for instance, by sunlight or pollution exposure (Pinnell, 2003). Moreover, the search for new and natural antioxidants to replace synthetic ones (e.g. butylated hydroxytoluene, butylated hydroxyanisole, tert-butylhydroquinone, propyl gallate) has increased in the last years, since this last group of compounds has to be used under stringent regulation to limit potential health hazards (Wu et al., 2015). Simultaneously, consumers are more aware to this and other issues, increasingly demanding more natural and environmentally friendly products, obtained by sustainable processes (Fonseca-Santos, Corrêa, & Chorilli, 2015).

Coffee by-products have been explored as sources of natural antioxidants, including for topical applications (Esquivel & Jiménez, 2012; Murthy & Madhava Naidu, 2012; Rodrigues, Palmeira-de-Oliveira, et al., 2015) once they are very rich in phenolics, namely chlorogenic acids and related compounds, widely recognized by their *in vitro* and *in vivo* antioxidant properties (Esquivel & Jiménez, 2012; Murthy & Madhava Naidu, 2012).

Besides phenolics, roasted by-products (silverskin and spent coffee grounds) also contain melanoidins, a group of antioxidant compounds that are formed through Maillard reactions during the thermal processing (Ballesteros et al., 2014; Borrelli et al., 2004). Moreover, they also contain vitamin E. The major vitamer in coffee silverskin is α-tocopherol (2.23 mg/100 g), followed by other vitamers present in minor amounts (0.03–0.59 mg/100 g) (Costa et al., 2018). Roasted coffee beans contain α-tocopherol (arabica: 2.4 mg/100 g dry weight (dw); robusta: 1.5 mg/100 g dw) and β-tocopherol (arabica: 7.3 mg/100 g dw; robusta: 1.6 mg/100 g dw) (Alves, Casal, Alves, & Oliveira, 2009), and the amount that remains in the coffee cake after the beverage preparation depends highly on the brewing method used. For instance, only 1% of tocopherols are effectively extracted into a classic espresso coffee, while an espresso prepared with a capsule can have a 5-fold higher amount of tocopherols (Alves et al., 2010). Nevertheless, being beverage preparation an aqueous extraction, most of the coffee lipids (including tocopherols) are retained in the coffee cake. Consequently, spent coffee grounds can be a great source of vitamin E.

Based on their chemical composition, it is expected that coffee by-products present a high antioxidant activity, being possible to extract such compounds and apply the extracts in innovative products in the cosmetic field, such as anti-aging or anti-stress ingredients, or even as natural preservatives replacing synthetic ones. In fact, several studies have confirmed the *in vitro* antioxidant properties of different coffee by-products, using diverse types of assays, such as DPPH· inhibition, ferric reducing antioxidant power, oxygen radical absorbance capacity, among others (Bravo et al., 2012; Costa et al., 2018; Ramalakshmi et al., 2009; Rodrigues, Gaspar, et al., 2016; Rodrigues, Palmeira-de-Oliveira, et al., 2015). Rodrigues, Gaspar, et al. (2016) also studied the physical stability and antioxidant activity of a hand cream formulation containing 2.5% (w/w) of a silverskin extract and observed a significantly higher anti-radical activity (using the DPPH· inhibition assay) compared to the base formulation.

The antioxidant activity of different coffee silverskin extract was evaluated by DPPH and FRAP assays. Antioxidant activity ranged from 206 to 287 μmol Trolox equivalent/g and 95–217 μmol Fe^{2+}/g by DPPH and FRAP methods, respectively, depending on the solvent system used. Authors also investigate extracts antimicrobial activity, which will be reported on a later section. Finally, extracts' effects on keratinocyte and fibroblast cells growth were investigated, and extracts did not affect *in vitro* cell viability in any tested concentration. Thus, all extracts could be used for topical application. Authors pointed that based on obtained results, ethanolic extract showed best performance, with higher antioxidant and antimicrobial activities (Rodrigues, Palmeira-de-Oliveira, et al., 2015).

Some of the chemical compounds present in coffee by-products also have been shown to have antioxidant potential *in vivo*. For instance, a study performed in hairless mice showed that skin can be protected from UV radiation with topical administration of α-tocopherol through up-regulation of a network of enzymatic and non-enzymatic antioxidants. Epidermal glutathione peroxidase and superoxide dismutase were protected against depletion and dermal superoxide dismutase activity increased by 30%, significantly reducing the formation of epidermal lipid hydroperoxides after UV irradiation (Lopez-Torres, Thiele, Shindo, Han, & Packer, 1998). Topical products containing antioxidants are able to contain oxidative stress, so they can improve the wound repair process (Chen, Liou, Tzeng, Lee, & Liu, 2013). Indeed, Chen et al. (2013) evaluated the therapeutic effects of topical chlorogenic acid on excision wounds in Wistar rats and reported an increase in several enzymes (i.e. superoxide dismutase, catalase, and glutathione), while simultaneously lipid peroxidation decreased.

Overall, the antioxidant properties of coffee by-products seem to be due to their complex chemical composition, in which antioxidant compounds are present as major bioactive components and can act in synergism. Therefore, the potential to explore these matrices as active ingredients in skin cosmetic products to reduce the production of intracellular reactive oxygen species and improve skin health should not be underestimated.

8.2. Antiaging

Antiaging potential of coffee by-products was first proposed in a patent by Castillo et al. (2013). The invention proposes a method for extracting coffee silverskin followed by extract use in cosmetics specially to prevent physiological aging process. Besides attributing results to antioxidants, such as caffeine and chlorogenic acid, inventors point out other important roles for the silverskin extract in the formulation: preservative, antioxidant, antiaging and anti-cellulite. As an example of application in cosmetics, researchers produced an emulsion with mild olive oil in water and added 0.4% of coffee powder husk extract, resulting in a formulation with pH 5.44, phenolic compounds content (around 11 mg Trolox/100 mL lotion) and high antioxidant capacity (around 118 mg Trolox/100 mL lotion). However, this patent did not present any further investigation in cosmetic activity.

Preclinical data regarding the antiaging properties of coffee silverskin extracts was reported employing human keratinocytes also showed that 1 mg/mL extracts promoted an antioxidant protection to skin cells when oxidative damage was induced by tert-butyl hydroperoxide. At the same concentration, extracts showed an increase in *C. elegans*' longevity compared with control conditions (nematode growth without UVC exposure), and similarly to vitamin C and chlorogenic acid positive controls (Iriondo-DeHond et al., 2016).

Mouse fibroblasts cells irradiated by ultraviolet radiation B (UVB) were used to investigate anti-wrinkle effects of chlorogenic acid, pyrocatechol and 3,4,5-tricaffeoyl quinic acid isolated from beans of *Coffea arabica*, by examining expression levels of matrix metelloproteinases (MMP-1, MMP-3 and MMP-9) and regulation of type-I procollagen. The three studied compounds were isolated and identified from coffee grounds. Initially authors investigate cell viability and a concentration up to 50 μg/mL maintained more than 90% viability. It was previously described that UVB exposure up-regulated MMPs and down regulate type-I collagen expression in skin fibroblasts, and treated cells showed a MMP's basal expression level similar to the control cells. Results also show that chlorogenic acid and 3,4,5-tricaffeoyl quinic acid at 50 μg/mL concentration significantly elevated type-I procollagen level, and no significant results were found for pyrocatechol. This study also analyzed sun protection factor of isolated compounds from coffee, which will be presented in a later section. Based on results, authors conclude that chlorogenic acid has potential as a therapeutic agent against induced photo-aging (Cho et al., 2017).

In summary, antiaging activity has been attributed to coffee by-products mainly due to the presence of compounds with antioxidant activity. Therefore, there is a potential to explore the cosmetic application of bioactive molecules found in coffee by-products.

8.3. Anti-inflammatory

Skin inflammation is a usual response to an injury, infection, or tissue destruction. Reactive oxygen species can contribute to pro-inflammatory cascades, inducing the production of specific cytokynes (e.g. interleukin-1) and tumor necrosis factor-α. Consequently, inflammatory enzymes and NADPH oxidase-dependent inflammation can also be induced, as well as keratinocyte proliferation and monocyte recruitment to the injured skin (Bessada et al., 2018).

The studies about the topical anti-inflammatory effect of coffee by-

products are still limited, but there is some evidence about their potential in this field. For instance, Chen et al. (2013) evaluated the therapeutic effects of topical chlorogenic acid on excision wounds in Wistar rats and found an acceleration of the wound healing due to its antioxidant activity and ability to increase collagen synthesis through upregulation of tumor necrosis factor-α and transforming growth factor-β1. Increased rates of epithelialization were also observed in the treated rats (Chen et al., 2013). More recently, Segheto et al. (2018) studied the anti-inflammatory activity *Coffee arabica* leaves and 5-caffeoylquinic acid in Swiss mice to which ear edema was previously induced. Both treatments decreased inflammatory parameters and the activity of myeloperoxidase and *N*-acetyl-β-d-glucosaminidase. In another study, Affonso et al. (2016) ascertained the effect of topical application of hydrogels containing chlorogenic acid or aqueous extracts of coffee beans residual press cake (produced after oil extraction) on skin wound healing, using an animal model. The enriched hydrogels contributed to wound healing process, revealing positive effects on the cutaneous tissue regeneration.

High molecular weight hyaluronic acid inhibits macrophage phagocytic ability, having an important role in the regulation of wound healing by significantly reducing the inflammatory response. Nevertheless, there may be an increase in collagen deposition, fibrosis, angiogenesis and inflammation in wound healing, resulting from the degradation products of hyaluronic acid (Lee, Kim, Cho, & Choi, 1999). Hyaluronidase promotes the degradation of high molecular weight hyaluronic acid and hyaluronidase inhibitors seem to be effective in suppressing inflammation (Furusawa, Narita, Iwai, Fukunaga, & Nakagiri, 2011; Lee et al., 1999). Furusawa et al. (2011) have shown that aqueous coffee silverskin extracts are able to inhibit hyaluronidase and that acidic polysaccharides mainly composed of uronic acid are responsible for that effect.

Although not focusing specifically on topical applications, some studies have also been highlighting the potential anti-inflammatory effects of coffee by-products, which can give more sustenance to the use of these matrices as sources of anti-inflammatory compounds. For instance, Hwang et al. (2016) tested the anti-inflammatory effect of caffeine on lipopolysaccharide-induced inflammation using RAW 264.7 macrophages. A decrease on inflammation, nitric oxide levels and expression of several pro-inflammatory genes were observed (Hwang et al., 2016). López-Barrera, Vázquez-Sánchez, Loarca-Piña, and Campos-Vega (2016) reported the ability of spent coffee grounds to prevent inflammation. According to the authors, human gut fermented and unabsorbed spent coffee grounds suppressed NO production (55%) in RAW 264.7 macrophages by modulating IL-10, CCL-17, CXCL9, IL-1β, and IL-5 cytokines. The anti-inflammatory activity was mediated by short chain fatty acids produced after prolonged (24 h) fermentation of its dietary fiber (López-Barrera et al., 2016). More recently, Magoni et al. (2018) described that coffee pulp extracts inhibit significantly the release of IL-8 (a relevant chemokine involved in gastric inflammation) in human gastric epithelial cells, at concentrations that can be reached *in vivo* in the gastric tract.

Although coffee by-products seem to be very promising in what concerns to their potential topical application, further *in vitro* and *in vivo* studies are still needed to better understand their anti-inflammatory effect and real efficacy.

8.4. Sunscreen

Choquenet, Couteau, Paparis, and Coiffard (2009) evaluated sunscreen effectiveness of various flavonoids and two polyphenols (caffeic acid and chlorogenic acid). They applied 2% and 10% concentration of studied molecules in oil-in-water emulsions and evaluated their effectiveness and photostability *in vitro* (polymethylmethacrylate plates). Caffeic and chlorogenic acids at 10% presented sun protection factor (SPF) around 6.2 and 10.1, maximum absorption wavelengths of 324 and 330 nm, and UVA protection around 3.8 and 5.9, respectively. However, polyphenols did not present good stability when compared to flavonoids and should be stabilized through combination with other filters (Choquenet et al., 2009). A further study was conducted to determine the photostability of chlorogenic acid (Rivelli et al., 2010).

In Rivelli et al. (2010) study, an aqueous solution of chlorogenic acid at 10 mg/mL concentration presented UVA protection factor around 92%, SPF around 146, critical wavelength of 372 nm and UVA/UVB ratio of 0.81. Authors analyzed by HPLC the chlorogenic concentration in the aqueous solution initially and after UVA and UVB radiation. Their results show that, in both cases, chlorogenic acid concentrations did not change and those molecules presented UVA/UVB photostability (Rivelli et al., 2010).

Wagemaker, Carvalho, Maia, Baggio, and Guerreiro Filho (2011) characterized the lipid fractions extracted from green coffee beans and determine their SPF. In this study, 10 different species of *Coffea* genus were analyzed. Even with the diversity found, all studied species presented suitable characteristics for a cosmetic products. *C. arabica* represents about 70% of all coffee grown in the world and presented mean SPF of 1.5, which was statistically different from the other species. Nonetheless, SPF above 2 was found for *C. eugenioides*, *C. heterocalyx*, *C. salvatrix* and *C. stenophylla* (Wagemaker et al., 2011).

Continuing previous study, Wagemaker et al. (2016) evaluated four plants of *C. arabica* and seven *C. canephora* cultivars for oil content and SPF variability. Toxic and cytotoxic effects, antioxidant and antimicrobial activities were also evaluated in unsaponifiable matter obtained from green *C. arabica* seed oil. According to results, although low, SPF values for *C. arabica* were higher than for *C. canephora*, and ranged between 1.5 and 2.8 in the two years of study.

Green coffee oil was then incorporated in topical formulations to evaluate the influence of its concentration in physical stability, *in vitro* SPF and *in vivo* protective effects. Green coffee oil content in formulations vary between 2.5 and 15%. All formulations were considered stable, even after 90-days storage. Formulations' *in vitro* SPF increased proportionally with the increase in oil concentrations, reaching a value of 2.3 with 15% of oil. Formulation were also *in vivo* evaluated using irradiated animal skins, and even high oil concentrations did not prevent erythema when compared to control, suggesting that green coffee oil effects may be linked to post-radiation protection (Wagemaker, Silva, Leonardi, & Maia Campos, 2015).

SPF of chlorogenic acid, pyrocatechol and 3,4,5-tricaffeoyl quinic acid isolated from beans of *Coffea arabica* were *in vitro* measured among with anti-wrinkle effect. A SPF around 16 was found for chlorogenic acid in a 40 μg/mL concentration. This result corroborates authors' conclusion that chlorogenic acid has potential to be used to prevent UV-induced photo-aging (Cho et al., 2017).

From the aforementioned studies, it can be seen that chlorogenic acid is a photostable UVA/UVB molecule and has a good photoprotective activity with SPF ranging from 10 to 140 depending on its concentration. Coffee oil has shown an interesting applicability in photoprotection and *C. arabica* has shown more promising results than other species, with an SPF ranging from 1.5 to 2.8 that proportionally increases with the extract contraction.

8.5. Antimicrobial

Antimicrobial activity of different coffee silverskin extracts was investigated against bacteria (gram positive and negative) and a yeast. Extracts did not present any activity against *C. albicans* or *P. aeruginosa*. However, they present positive results (ranging from 31.3 to 250 μg/mL) against all other tested microorganisms (*S. aureus*, *S. epidermidis*, *E. coli* and *K. pneumoniae*) depending on the solvent system used. Ethanolic extract present the lowest MIC (minimal inhibitory concentration) for *K. pneumoniae* (31.3 μg/mL) and the highest for *S. aureus* MRSA (250 μg/mL) (Rodrigues, Palmeira-de-Oliveira, et al., 2015).

Antimicrobial activity of unsaponified matter extracted from standard green *C. arabica* seed oil was reported by Wagemaker et al. (2016),

using the disc diffusion method. A 10 mg/mL of unsaponified matter inhibited the growth of all tested bacteria (*S. aureus*, *S. epidermidis*, *E. coli* and *P. aeruginosa*) with inhibition zone ranging between 9 and 19 mm, and the growth of C. albicans with inhibition zone of 22 nm (Wagemaker et al., 2016).

The bioprospection of 14 agro-industrial residues for their antimicrobial activity against pathogenic biofilms were reported, including straw, bark and dreg of *C. arabica*. Obtained residues were priory subject to hydroalcoholic extraction and tested against 12 different opportunistic pathogens. Coffee dreg inhibit the growth of *P. intermedia* (MIC 1000 μg/mL), *S. aureus* (MIC 1000 μg/mL) and *S. mutans* (MIC 250 μg/mL). *In vitro* inhibition of biofilm adhesion was conducted at MIC value and only for extracts showing MIC values lower than 500 μg/mL. Coffee dreg was tested at 250 μg/mL concentration against *S. mutans* and inhibit approximately 23% of biofilm formation. When compared to other extracts such as geopropolis and pomegranate, coffee did not show promising results (Rochelle et al., 2016).

Antibacterial activity using agar diffusion method and MIC were conducted in a coffee pulp extract with high total phenolic content. Compared to negative control, extract inhibit the growth of all tested bacteria. However, when compared among groups, extract presented a better result for gram-positive microorganisms than gram-negative. MIC ranged from 37.5 to 75 mg/mL of extract, and MBC was higher than 300 mg/mL in all tested bacteria, indicating that extract may act as a bacteriostatic agent only. Authors attributed this bacteriostatic activity to the presence of quinic acid, malic acid, chlorogenic acid, and caffeine in total ion current chromatograms (Duangjai et al., 2016). Studies to evaluate antimicrobial activity of natural substances for formulations use are important to validate activity, indicating their use as preservatives, reducing or eliminating the use of synthetic preservatives. In these studies, coffee showed potential use as preservative, after presenting relevant MIC data. Its bioactive compounds may be responsible for its bacteriostatic action and the different MIC results obtained for each bacteria may be related to different factors such as the active compounds and the structure of the bacterial envelope (Duangjai et al., 2016; Rochelle et al., 2016; Rodrigues, Palmeira-de-Oliveira, et al., 2015).

8.6. Anticellulite

Cellulite is an alteration in the surface of the skin that leaves it with an irregular and wavy appearance with an orange peel or cottage cheese type dimpling aspect (Byun et al., 2015; Hamishehkar et al., 2015). About 85–98% of women after puberty are affected by some degree of cellulite, appearing more frequently on the buttocks and thighs (Hamishehkar et al., 2015). One of the causes of this alteration is the accumulation of fat in the adipose tissue, therefore the promotion of lipolysis is one of the main ways to treat cellulite (Hexsel, Orlandi, & Zechmeister do Prado, 2005). There are several studies with caffeine for cellulite because it stimulates lipolytic activity (Byun et al., 2015; Hamishehkar et al., 2015).

A formulation was developed for cellulite treatment using caffeine extracted from silverskin and incorporated in nanostructured lipid carriers (NCL) formulated by a double emulsion. *In vivo* studies have proven the safety of the extract and the formulation. NCLs containing extract presented sizes <200 nm, low value of polydispersity index, high value of association efficiency for the hydrophilic components and high zeta potential. Caffeine associated with nanoparticles has the ability to cross the skin barrier. Therefore, this formulation presented a good topical delivery (Rodrigues, Alves, et al., 2016).

In another study using caffeine-loaded nanoparticles, solid lipid nanoparticles (SLN) were prepared and incorporated in hydrogel, compared to hydrogel containing caffeine, followed by stability and physical characteristics analyses. In the Franz test (flow rate 0–720 min), the hydrogel incorporated with caffeine nanoparticle showed a higher concentration of drug in the skin (0.0272 ± 0.0134 mg/cm^2/min) compared to the caffeine hydrogel (0.0171 ± 0.003 mg/cm^2/min). On the other hand, in a higher flow 720–1440 min, hydrogel with caffeine presented a concentration (0.1614 ± 0.0003 mg/cm^2/min) greater than the hydrogel incorporated with the caffeine nanoparticle (0.0492 ± 0.0017 mg/cm^2/min). Therefore, the nanoparticle increases caffeine local action without systemic absorption, because hydrogel incorporated with caffeine nanoparticle presented lower drug flux and higher drug accumulated in the skin compared to the caffeine hydrogel. Hydrogel with caffeine nanoparticle showed a deposition of caffeine on the skin 16 times more than the hydrogel with caffeine by itself. In histopathological studies, it was possible to observe the complete lysis of adipocytes with the hydrogel loaded with caffeine nanoparticle, but no lysis with the hydrogel with caffeine. The nanoparticles have more effect on white adipose tissue compared to the upper skin paste, revealing its potential application for the treatment of cellulite (Hamishehkar et al., 2015).

A slimming cream containing 3.5% water-soluble caffeine and xanthines was applied to volunteers with cellulite for 6 weeks, showing significant improvements. At week 3 there was an improvement in cellulite in ~36% of the volunteers, while at week 6, there was an improvement in ~86%. In the third and sixth week, transient flushing (57%) and slight itching (36%) occurred. On the other hand, no serious adverse events happened and no adverse events led to treatment interruption or decrease use of cream. This treatment can be considered safe and effective for cellulite. However, this study had some limitations, such as single-center intervention, small number of participants (n = 15) and no long-term tests were performed (Byun et al., 2015).

In the studies reported above, caffeine showed good results in cellulite treatment. These results may be due to the fact that caffeine is a hydrophilic molecule with low water solubility, so it is able to reach the dermis after penetrating the skin barrier, where it will play its role in lipolysis. There are still not many studies with coffee by-products for application in cellulite, however considering the effectiveness of caffeine for this treatment and its significant amount present in the by-products, it can be inferred that it is a good option to be used.

9. Conclusions

Based on their bioactive compounds, coffee by-products have numerous biological activities such as antioxidant, anti-inflammatory, anti-aging, sunscreen, antimicrobial and anti-cellulite. Therefore, it is possible to conclude that these waste products have a great potential to be used in topical formulations in the pharmaceutical and cosmetic industry. However, there are still few studies of finished products actually using these by-products, which makes necessary to continue these studies. Therefore, future research in this field is necessary to incorporate coffee by-products into topical formulations and validate their activity. Use of by-products promotes the valorization of residues from coffee industry, besides causing less environmental impact, generating new sources of income and adding value to commodities.

Declaration of competing interest

The authors declare no conflict of interest.

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