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# Coffee Silverskin: A Low-Cost Substrate for Bioproduction of High-Value Health Promoting Products

*Amaia Iriondo-DeHond[1], Beatriz Fernandez-Gomez[1], Nuria Martinez-Saez[1], Danik M Martirosyan[2], María Dolores Mesa Garcia[3]** and María Dolores del Castillo[1]**

[1]Department of Bioactivity and Food Analysis, Universidad Autónoma de Madrid, Spain

[2]Functional Food Center/Functional Food Institute, USA

[3]Deparment of Biochemistry and Molecular Biology II, University of Granada, Spain

## Abstract

In the last decade, the valorization of food wastes has become a priority research line in order to achieve a sustainable food industry. Large amounts of by-products are generated during the coffee industrial processing. Coffee Silverskin (CS) is a thin tegument of the outer layer of the coffee bean and it is the only by-product of the roasting process. This agricultural by-product causes an environmental impact in countries dedicated to its cultivation and processing. Our research group patented an aqueous extract of coffee silverskin (CSE) (P201131128) that is rich in different phytochemicals possessing multifunctional properties such as antioxidant capacity and potential for several applications in nutrition, health and cosmetic. Another priority of our society is to find natural and sustainable strategies to reduce the risk of chronic diseases, in particular those considered epidemics of the 21st century: obesity and diabetes. The aim of the present review is to provide scientific evidence of the usefulness of CSE as a sustainable natural bioproduct for chronic diseases.

**Keywords: Antioxidants; Chronic diseases; Coffee by-products; Coffee silverskin; Obesity; Oxidative stress; sustainability**

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***Correspondence:***

*Dolores del Castillo, Department of Bioactivity and Food Analysis, Institute of Food Science Research (CIAL, UAM-CSIC), Nicolás Cabrera, 9 Campus Cantoblanco, Universidad Autónoma de Madrid, 28049 Madrid, Spain, Tel: +34 91 0017900 Ext. 953; E-mail: mdolores.delcastillo@csic.es

**María Dolores Mesa Garcia, Department of Biochemistry and Molecular Biology II, Institute of Nutrition and Food Technology, Centre of Biomedical Research, Laboratory 123, University of Granada, Avenida del Conocimiento s/n, 18100 Armilla, Granada, Spain, Tel: +34 958242334; E-mail: mdmesa@ugr.es

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## Introduction

Today, 415 million people have diabetes and this alarming number is expected to reach 642 million by 2040. Type 2 Diabetes (T2D) is the most common type of diabetes representing 90% to 95% of all cases. This disease is growing rapidly worldwide in both developed and developing nations. This rise is associated with economic development, ageing populations, increasing urbanization, dietary changes, reduced physical activity and changes in other lifestyle patterns [1].

The term T2D designates not a single disease but a heterogeneous collection of hyperglycemic syndromes resulting from the interaction between a genetic predisposition and behavioral and environmental risk factors. There is strong evidence that obesity and physical inactivity are the main non-genetic determinants of the disease. Usually, T2D occurs in adults, but it is increasingly seen in children and adolescents. The development of T2D is usually associated with a combination of insulin resistance and beta cell failure leading to high blood glucose levels. Insulin resistance is defined as a pathophysiological condition in which a normal insulin concentration does not adequately produce a normal insulin response in peripheral tissues, such as adipose, muscle and liver tissues [2]. Under these conditions, pancreatic beta cells secrete more insulin (i.e. hyperinsulinemia) to overcome the hyperglycemia among insulin-resistant individuals. Although hyperinsulinemia may compensate maintaining normoglycemia, it may cause the over-expression of other insulin activities [3,4].

Nowadays, experimental and clinical studies support the role of oxidative stress in the pathogenesis of T2D [5]. In diabetes, free radical formation by non-enzymatic glycation of proteins, glucose oxidation and increased lipid peroxidation, leads to the damage of enzymes and cellular machinery and also increased insulin resistance [6]. Oxidative stress and free radicals play a major role in the onset and progression of late diabetic complications such as coronary artery disease, neuropathy, nephropathy and retinopathy [7]. *In vivo* studies support the role of hyperglycemia in the enhancement of oxidative stress leading to endothelial dysfunction in blood vessels of diabetic patients [8].

Food has a vital role in maintaining our health properly and in helping in the prevention and

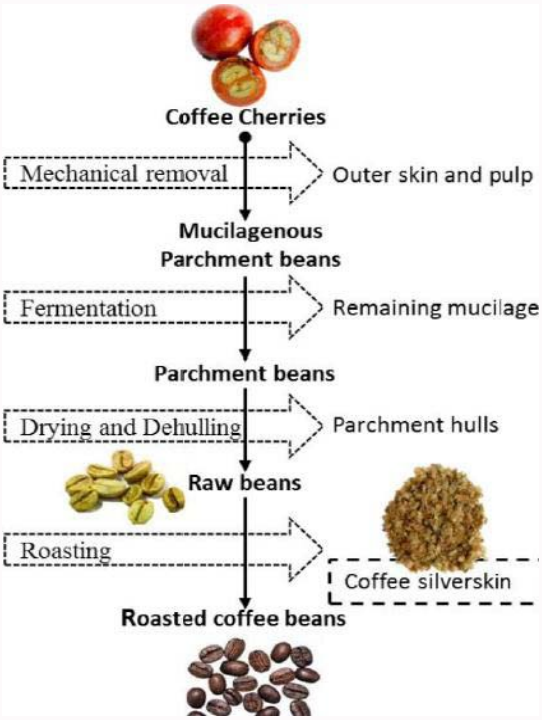


**Figure 1:** Diagram of coffee silverskin production from wet processing.

cure of some diseases. Nowadays, more than 95% of all chronic disease is caused by food choice, toxic food ingredients, nutritional deficiencies and lack of physical exercise. Many plant extracts and natural compounds are emerging as functional candidates for the reduction of risk of non-communicable chronic diseases, such as T2D [9].

Coffee is considered as an antioxidant beverage with potential beneficial effects on human health [10]. This antioxidant property is due to the presence of bioactive compounds such as caffeine, hydroxycinnamic acids including Chlorogenic Acid (CGA), and melanoidins [11]. Several epidemiological studies have documented the protective effect of coffee components against the risk of chronic diseases due to oxidative stress and inflammation including diabetes [12].

Coffee consumption has been associated with a lower risk of T2D, which may influence different mechanisms such as glucose tolerance, insulin sensitivity, insulin resistance, glucose-6-phosphatase, intestinal glucose absorption, antioxidant activity, inflammatory biomarkers, glucose uptake, glucose homeostasis, glucose metabolism and insulin secretion [13,14]. Although these physiological effects of coffee are related to different components present in the beverage and to the cumulative effects of each compound, most studies on coffee and diabetes clearly associate the observed biological effects to caffeine and CGA [10,13,14].

Coffee silverskin is the thin tegument of the outer layer of the coffee beans and represents about 4.2% (w/w). It is the only by-product produced during the roasting process (Figure 1). This coffee by-product presents phenolic compounds, mainly CGA, and other phytochemicals and bioactive compounds that contribute to its high antioxidant capacity. Our research group patented a CSE from Arabica (*Coffea arabica*) and Robusta (*Coffea canephora*) coffee silverskin (WO 2013004873 A1) enriched in caffeine and CGA [15]. This CSE is extracted with 2 volumes of water per gram of CS at 100°C for at least 10 min, and does not use organic solvents. Thus, CSE is obtained using an environment-friendly technology [15]. The extraction of bioactive compounds from natural products like CS is increasingly being used to prepare dietary supplements (nutraceuticals), food ingredients and some pharmaceutical products (Figure 2) [16].

The patented CSE is rich in total dietary fiber (28% to 36%), which includes about 4% to 9% insoluble dietary fiber and 24% to 26% soluble dietary fiber. CSEs are a good source of polyphenols, particularly CGA (1% to 6%); the most relevant are 5-O-, 3-O- and 4-O-caffeoylquinic acids [9]. CSE is also a good source of caffeine (3%), and melanoidins (17% to 23%) which are formed during the roasting process [17]. The chemical composition of the patented CSE has been described by [9]. Recent studies [18] have shown that CSE contained 11.42 µg/L of acrylamide; which is approximately 10 times lower than that reported in coffee beverages. After *in vitro* digestion under mimicked human conditions acrylamide was not bioaccesible. Therefore, CS may be used as a safe and natural source of health promoting compounds for chronic diseases.

## Coffee Silverskin Extract, Oxidative Stress and Aging

Generally, cells are able to balance the production of oxidants and antioxidants. However, when cells are subjected to excessive levels of ROS or as a result of antioxidant depletion, oxidative stress occurs [19]. Under normal conditions, ROS are natural byproducts produced in mitochondria, peroxisome and in the plasma membrane which have positive physiological effects on cells, such as killing microorganisms, acting as a second messenger ($H_2O_2$) in cellular differentiation and proliferation and regulating signal transduction [20]. However, ROS are also induced by exogenous sources (UV radiation or chemical agents) and cause DNA, protein and lipid damage. The combination of DNA mutations, protein oxidation and lipid peroxidation induces a cellular progressive decline as a result of insufficient supply of energy leading to oxidative stress-induced aging [21]. In the process of aging, there is a deficiency of the endogenous antioxidant defenses of cells and the residual ROS generate oxidative stress, even in physiological conditions [22]. Large epidemiological studies support the relationship between oxidative state and global health, while high consumption of foods rich in antioxidants is associated with lower disease rates and preventive protection [23]. The anti-aging effect of CSE has been investigated *in vivo* employing as an animal model *Caenorhabditis elegans* [24].

Chlorogenic acid has been described as an anti-aging compound in *C. elegans*. A recent study has demonstrated that CGAs, caffeine, melanoidins and other bioactive compounds all together in the CSE may act in a synergic manner when protecting from UV-induced accelerated aging on *C. elegans* [24]. The nematodes that were treated with CSE (1 mg/mL) showed a significantly increased longevity compared to those cultured on a standard diet. The increased longevity observed was similar to that of the nematodes fed on CGA or vitamin C (0.1 µg/mL). The antiaging properties of the CSE observed in this study are due to its antioxidant character caused by phenols among other bioactive compounds present in the botanical material. Some plant extracts containing CGA and other polyphenols are able to exert an antiaging effect on *C. elegans*. For instance, crude blueberry extract and blueberry polyphenols (including an hydroxycinnamic ester fraction containing CGA) have lengthened the nematode's mean lifespan by 28% [25]. Moreover, Vayndorf et

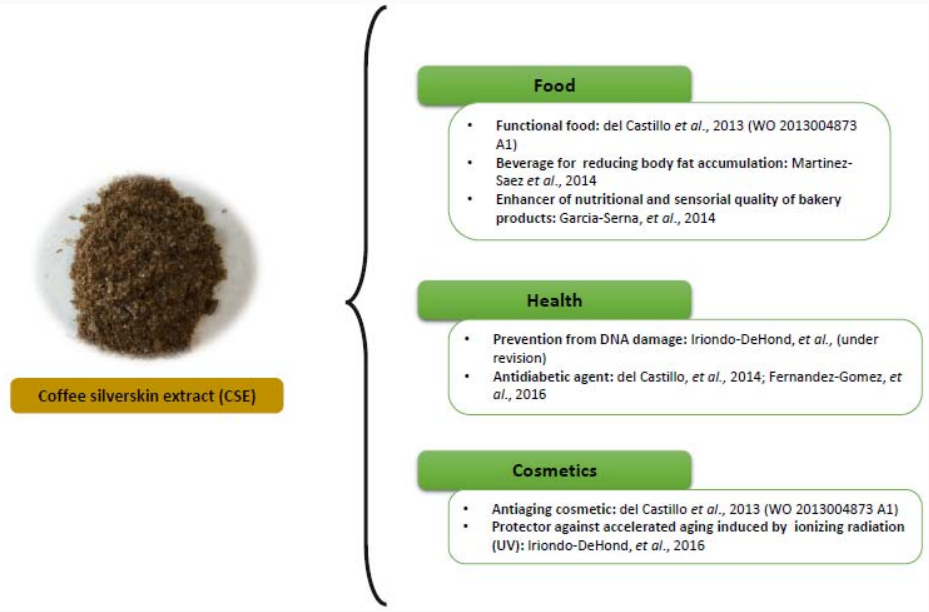


**Figure 2:** Applications of the patented CSE (WO 2013004873 A1) in food, health and cosmetics.

al. [26] observed that when *C. elegans* was pre-treated with whole apple extracts, worms were more resistant to stresses such as heat, UV radiation and pathogenic infection, suggesting that cellular defense and immune system functions were improved. The authors suggest a possible antioxidant mechanism underlying the antiaging effects of whole apple phytochemicals [26]. Coffee silverskin extract has the potential to be used as an ingredient in skin care products for topical use and as nutricosmetic to prevent accelerated skin aging induced by oxidative stress caused either by exogenous sources (photoaging).

Oxidative stress can also lead to DNA lesions such as DNA strand breaks and oxidized bases [27]. Considering the high antioxidant power of CSE, this extract could protect cells from DNA damage when induced by an oxidative agent. Benzo(a)pyrene (B(a)P) is a carcinogenic Polycyclic Aromatic Hydrocarbon (PAH) found in air, water, soils and in thermally processed foods and cigarette smoke [28,29]. Benzo(a)pyrene induces the production of ROS in cells during the metabolism of this food mutagen, which leads to DNA damage [30].

Have evaluated the protective effect of CSE and CGA against B(a)P induced DNA damage (strand breaks and oxidized purines/pyrimidines) in HepG2 cells. Results showed a significant decrease ($p \leq 0.05$) in DNA strand breaks when cells were pretreated with CSE and CGA [31]. Several authors have confirmed the protective effect of roasted coffee consumption on DNA integrity in humans [32,33]. The reduction of spontaneous DNA strand breaks observed may be attributed to the presence of antioxidants with chemo preventive properties (such as CGAs and roast-associated constituents) [32]. Considering that CS keeps part of the polyphenolic compounds that are normal constituents of coffee beans, such as CGA, it is likely that this effect described for coffee brews is also maintained in CS. These results indicate that CSE protects human cells from DNA strand breaks and oxidative DNA damage effects of B(a)P, and that free CGA or linked to other chemical structures seem to be contributors to the observed chemo protective effect of CSE [31]. This extract presents potential as a natural and sustainable food ingredient.

## Coffee Silverskin, Obesity and Dyslipidemia

Overweight and obesity are the major cause of the metabolic syndrome, which is increasing rapidly in modern societies [34]. Therefore, treatment should focus on weight loss by increasing exercise and improving dietary habits; and medical treatment can be used if lifestyle changes are insufficient. Novel foods from natural sources have attracted much attention as potential therapeutic agents in the prevention and treatment of obesity [35].

Recently, the impact of CSE on obesity and diabetes has been evaluated. CSEs from Arabica and Robusta coffees have been used for the preparation of antioxidant novel beverages to study the inhibitory effect on fat accumulation *in vivo* using as animal model *C. elegans* [36]. A significant dose-response effect on reducing accumulation of body fat was found for pure CGA (3.54 mg/L) and caffeine (4.85 mg/L), achieving 30% and 29% reduction of lipid deposits, respectively. The brews of Arabica and Robusta CSE (100 µg/mL), which contained physiologically active doses of CGA and caffeine, were effective reducing body fat 21% and 24%, respectively. Furthermore, similar results in body fat reduction by Robusta CSE beverage were found when a commercial dietary supplement made from Robusta decaffeinated green coffee extract was studied. Therefore, CSE is a natural alternative to dietary supplements for the prevention of overweight and obesity [18,36].

In addition, CSE reduced total cholesterol and triglycerides plasma levels in rats after 45 days of treatment with CSE (2.2 mg caffeine/kg body weight and 0.8 mgCGA/kg body weight). CSE also reduced 41.73% the activity of pancreatic lipase *in vitro* at concentration of 36 mg/mL. This could explain the mechanism of action of the observed reduction of total cholesterol and triglycerides, since pancreatic lipase is a key enzyme in fat digestion [37]. These results support the lyporegulatory character of CSE through the inhibition of pancreatic lipase and therefore its preventive and therapeutic effect in the obesity disease.

The anti-obesity effect of coffee may be due to its bioactive compounds, such as caffeine, CGAs and melanoidins, which are

also present in coffee silverskin [17,37]. CGA and caffeine can regulate lipid metabolism by modulating cell signaling, reducing lipid accumulation and size of adipocytes [38], inhibiting pancreatic lipase [39], regulating hepatic lipid metabolism-related enzymes [40], and by down regulating genes involved in adipogenesis [41]. The combination of these effects leads to the suppression of body fat accumulation [42]. In addition, coffee melanoidins have showed to protect against non-alcoholic fatty liver disease by reducing the hepatic fat accumulation in the rat model [43].

## Coffee Silverskin and Diabetes

Type 2 diabetes is usually associated to a combination of insulin resistance and beta cell failure leading to high blood glucose levels. Hyperglycemia is a major factor contributing to accelerated protein glycation and the formation of Advanced Glycation End Product (AGEs) [44]. In diabetes, free radical formation by non-enzymatic glycation of proteins, glucose oxidation and increased lipid peroxidation, leads to damage of enzymes, cellular machinery and also increases insulin resistance [6]. Oxidative stress plays a major role in the development of late diabetic complications such as coronary artery disease, neuropathy, nephropathy, and retinopathy [7].

Studies suggest that moderate intake of coffee may lower risk of T2D [45]. The effects observed on diabetes biomarkers may be associated to the synergic effect of different bioactive compounds present in coffee such as CGA, caffeine, their metabolites and others coffee components. Some of these compounds are also present in CSE [9] and have an effect in diabetes biomarkers.

Caffeine concentrations present in CSE range between 3% and 3.4% [9]. Studies performed in rats suffering streptozotocin-induced diabetes showed that caffeine in CSE was metabolized and the metabolites protected the pancreas against oxidative stress [46]. In addition, caffeine can also reduce glucose levels and insulin sensitivity [47,48]. Other authors have also observed a protective effect of caffeine in pancreatic beta cells [49,50].

Coffee silverskin extract also contains CGA in a range of 1.1% to 6.8% [9]. Results obtained by our research group suggest that CGA and its metabolites have a greater effect on T2D biomarkers than caffeine. CGA and its roasting-formed derivates present in CSE have been proposed as the main contributors to the beneficial effects of CSE on T2D [14,51]. The different mechanisms by which CGA exerts its antidiabetic effect are: a) regulation of glucose metabolism [45,52], b) enhancement of insulin action [52,53]. c) Inhibition of α-glucosidase activity [54,55], d) protection against oxidative stress [56] and e) inhibition of AGEs formation [57]. Different studies demonstrate that the formation of fluorescent AGEs is inhibited by different pathways such as carbonyl trapping, antioxidant effect and the formation of protein-phenols conjugates [57-59].

Other coffee constituents relevant in the prevention of T2D are melanoidins, melatonin, lignans and lignin, tannic acid, isoflavones and trigonelline, all of which may be present in CSE. These compounds may exert synergic effects being responsible for the health-promoting properties of CSE. Further research should be carried out in order to confirm the presence of these compounds in CSE and to prove their effect in the prevention of T2D.

In conclusion, CSE contains a number of coffee components able to reduce the risk of accelerated aging and chronic metabolic disorders such as T2D. These effects may be associated to its antioxidant power and capacity to inhibit enzymes involved in the metabolism of nutrients.

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