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CHEMOPREVENTIVE MOLECULES OF COFFEE AND BENEFICIAL METABOLIC EFFECTS

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Abstract

Among all the plant species examined, together with the food products that derive from it, coffee has a reputation that over the course of history has had a rather controversial evolution: some episodes are emblematic of the mistrust that, in the first decades of its diffusion in Europe and in the World, accompanied the drink. Coffee is obtained by infusing the powder obtained by grinding the toasted seeds of some species of tropical shrubs belonging to the genus Coffea, practiced through various techniques; although there are over 100 species, those used for food consumption are very few, and almost all of the market is aimed at only two of them: *Coffea arabica* and *Coffea canephora*, better known commercially (but improperly) with the name of Robusta. Today it can be said that the antioxidant activity of coffee, intended both as a vegetable and as a drink, has been known for some time and has been evaluated through different methods; various studies have shown that the high content of polyphenols in coffee plays an important role in its strong antioxidant action. Since 1997, the year in which the first works on this activity were presented, the concern about the potential risks related to coffee intake has rapidly diminished and a line of research has originated aimed at evaluating its therapeutic effects, especially chemopreventive, antidiabetic and anticarginogenic effects.

It was immediately proposed that, at the head of the wide family of active polyphenolic compounds, there were chlorogenic acids, whose remarkable ability to prevent oxidative cell damage was immediately determined.

Keywords: Coffee,Polyphenols, Chlorogenic acids, Chemopreventive effects.

Introduction

Over the centuries, the spread of coffee has been promoted and hindered much more by political and social factors than for reasons related to its real characteristics, at least until the latter have been rigorously observed thanks to an evaluation based on a scientific approach [1]. Although coffee has been mentioned in modern scientific publications since the beginning of the eighteenth century (and, absolutely, by the Persian scientists Rasis and Avicenna, who lived between the ninth and eleventh centuries), it is only with the advent of chemistry that descriptions cease to be related only to symptoms and physiological aspects in general.

As in all foods, the substances most present in coffee powder belong to the well-known categories of macronutrients: carbohydrates, proteins and lipids, as well as inorganic substances such as water and minerals (expressed as Ash). As for the drink, however, water constitutes from 97.8% of espresso coffee to 99.4% of the notoriously diluted American long coffee, and the macronutrient content is negligible [2].

The amount of total carbohydrates present in ground coffee is 71%, and their composition changes considerably following the roasting process. In fresh coffee grains there are both low molecular weight sugars (especially sucrose: 8.2% in Arabica and 3.7% in Robusta) and polysaccharides (mostly galactans, mannans, responsible for the remarkable hardness of coffee grains , arabans and arabinogalactans) [3-5].Following the roasting process there is an almost total loss of low molecular weight sugars, including sucrose [6], while the polysaccharides undergo much smaller reductions (from a minimum of 19% for glucans to a maximum of 60% for arabans), but associated with some structural modifications that make them more soluble in water than those present in green coffee [4]. Roasting leads to a caramelization of sucrose, favored by the presence of substances of a protein or aminoacid nature [7]; another part is converted into carbon dioxide and water. In general, the pyrolysis processes of carbohydrates are accompanied by the formation of largely water-soluble brown pigments as well as polymers called condensation complexes, which tend to bind with protein fragments to form melanoidins according to the Maillard reaction, but also with products from chlorogenic acids.

Methods and Results

The family of chemical compounds containing nitrogen present in coffee is enormously vast and its components contribute heterogeneously to the properties of coffee. Caffeine is certainly the most famous of them: this purine compound is accompanied, even if only in trace amounts, by its two demethylated analogues theobromine and theophylline (Figure 1).The caffeine content varies significantly between the two main species (1.2%in Arabica and 2.2% in Robusta).A fact that may be surprising, if we take into account that the sublimation temperature of caffeine is 178 ° C, is that following the roasting process, which is due both to external heating and to exothermic reactions that occur in the inside of the bean reaches and exceeds a temperature of 200 °C, the presence of caffeine does not decrease but increases by about 10%. This is not only due to the fact that roasting produces a decrease in the mass of the product up to 20% (of which about half of water and half of other volatile substances) and that therefore the caffeine present is related to a total mass less, but also at the minimum loss of this during the process, a phenomenon that is justified by the impermeability of the outermost layer of the beans, which not only prevents them from escaping but, following the increase in pressure inside them, it also raises the caffeine sublimation temperature[8,9].

In addition to purine alkaloids, coffee contains numerous other alkaloids, which can be divided according to the stability they show during the roasting process. Those stable at high temperatures are ammonia, betaine (trimethylglycine) and choline [10,11]: these compounds are present in traces, even if the choline after roasting reaches a presence of about 1% due to the thermal degradation of the lecithins; those that, on the other hand, decompose during roasting produce volatile substances that contribute to the aroma of the coffee: this category is basically made up of trigonelline and serotonin amides(Figure 2A and 2B). Trigonelline should be a compound of little interest: its toxicity and physiological activity are decidedly poor when compared with those of caffeine, and also from an organoleptic point of view its vaguely bitter taste and its concentration lower than that of caffeine seem to relegate it to the role of a minor substance [12], but the importance of the products formed by its thermal degradation, mainly N-methylpyridinium and nicotinic acid, indirectly makes it a compound of interest.The extent of these degradation processes is strictly correlated with the conditions under which the roasting is carried out: it has long been known [13]that at high temperatures (230 °C) there is a rapid degradation which reduces the presence of trigonelline at 15% of the initial value already within 15 minutes, while procedures at more moderate temperatures (180 °C) keep 40% of trigonelline intact even after 45 minutes. In an attempt to identify quantitative correlations between the presences of the various substances, it was found that the logarithm of the ratio between the concentrations of nicotinic acid, a compound whose almost exclusive origin is the degradation of trigonelline, and of trigonelline itself, is directly proportional to the fraction of mass lost from a generic sample following roasting [14-16]. Regarding the protein part contained in green coffee, it is made up half of a water-soluble fraction, composed of albumins, and half of a water-insoluble one [17-20]. The lipid fraction of green coffee is mainly composed of triacylglycerols, sterols and tocopherols, for example the typical compounds of all edible vegetable oils [21-23].In addition, green coffee oil contains a considerable amount of diterpenes analogous to *ent*-Kaurene (Figure 2C)[24,25]. The total lipid content is 15% in the Arabica species and 10% in the Robusta, and is almost entirely located in the endosperm of the drupes, while only the so-called coffee wax is located on the outside.Coffee is an important source of chlorogenic acids, a family of esters whose structure is that of (-)-quinic acid linked to one or more cinnamic residues, for example those of caffeic acid, ferulic acid and p-coumaric acid [26-28]. Among them, the name chlorogenic acid (Figure 2D) refers in particular to the 3-quinic ester of caffeic acid [29]; also present are quinic acids esterified in other positions or polyesterified[30-31].

In nature, chlorogenic acids are present in a wide variety of plants: apples, pears, plums, cabbages, American potatoes, blueberries, blackberries, broccoli, and are an important source of polyphenols for human nutrition [32-34].

The total content of chlorogenic acids in green coffee ranges from 6.5% by weight of the Robusta variety to 14% of Arabica, but during the roasting process about 70% is lost with the obtainment of a commercial powder blend. whose content is about 3%; however the content of chlorogenic acids does not significantly depend on the cultural or climatic conditions [35-37].

Discussion

It has been observed that coffee extracts are capable of mitigating oxidative damage to tissues, and that the common roasted coffee has an antioxidant power (determined on the basis of the value of ORAC (Oxygen Radical Absorbance Capacity) of its extracts 30 times better than green coffee [38,39]. *In vivo* it has been observed that coffee is able to mimic the action of the neurotransmitter acetylcholine [40], producing the same effects as cholinesterase inhibitor drugs, which by slowing down the activity of the enzyme acetylcholinesterase, which destroys the neurotransmitter acetylcholine, cause the increase of this substance in the brain by compensating for the loss of cholinergic neurons observed in subjects with Alzheimer's [41,42].

Coffee also counteracts the activity of betamiloid, the main constituent of neural plaques, both by slowing down the formation of the latter [43], and by favoring the destruction of betamyloid itself [44]. Studies aimed at the single substances contained in coffee have shown that various extracts act as neuroprotectors by intervening on cholinergic degeneration [45] and on oxidative damage to neurons [46].Dozens of epidemiological studies have shown that regular coffee consumption is correlated with a low incidence of Parkinson's [47]. The neuroprotective effect is largely due to caffeine: doses of pure caffeine show a greater effect than doses of decaffeinated coffee [48], but not only: studies on tea have shown that black tea has a very strong effect. higher than green tea, while having the same amount of caffeine [49]. The stimulating action of coffee on motor activities is known, which is expressed with an antagonism on the A2A and A1 receptors of the striated muscles: this action attenuates the symptoms of Parkinson's [50] in a similar way to what is obtained with a dopaminergic stimulation [51].

Habitual consumption of coffee leads to a low level of liver enzymes aspartate aminotransferase (AST) and alanine aminotransferase (ALT) in the blood [52]: they, normally contained within the hepatocytes, are released into the blood as a result of damage to these, and their blood content is used as an index of liver damage. It is believed that the hepatoprotective activity of coffee is exerted through the antioxidant action, which limits the formation and permanence in the organism of reactive oxygen species (ROS, Reactive Oxygen Species), a family of free radicals that includes the superoxide anion (O_2^-), hydrogen peroxide (H_2O_2) and hydroxyl radical (·OH): the production of these chemical species is instead stimulated both by a chronic consumption of alcoholic beverages and by the proteins of the hepatitis B and C viruses , primary causes of liver fibrosis and cirrhosis [53].

The same caffeine exerts an antioxidant action similar to that of glutathione and considerably higher than that of ascorbic acid [54], and is flanked by phenols, melanoidins, phenylindanes and hundreds of other substances isolated and evaluated for the their antioxidant action [55]. In addition, it has been found that the action of coffee is also due to the action of two diterpenes, cafestol and cafeol, which exert a chemoprotective action especially against liver carcinogenesis [56,57].

The incidence of adult diabetes mellitus is notoriously related to obesity and an unhealthy diet, and its incidence has grown enormously in recent decades, especially in wealthier nations. In addition of course to interventions on the two main triggers, regular coffee consumption can have preventive effects on the incidence of this disease [58].

The results of taking coffee consist in a better regulation of the glucose and insulin levels and a reduction in hyperinsulinemia; the beneficial action has been extensively evaluated with epidemiological studies and has shown that it occurs in countries with different diets, from the Netherlands [59] to Spain [60], to Finland [61,62], to Japan [63], and also regardless of the usual lifestyle: in drinkers as in abstainers, in sedentary personsas in sportsmen, in obese as in normal weight, even if obviously the protective effect it is more evident in the subjects most at risk [64]. As with other actions, it has been observed that decaffeinated coffee is much less effective than normal coffee [65].

Diseases affecting the cardiovascular system, as the leading cause of mortality in the World (in 2004 they caused 29% of the total number of deaths: 10% from heart attacks and 13% from coronary heart disease), are subject to enormous attention from the scientific community[66].

There are numerous substances contained in coffee that show an activity related to these pathologies, in particular: the polyphenolic compounds, in particular chlorogenic acids, prevent damage to the endothelium cells, show an antioxidant activity that acts on the production of LDL and VLDL, act on the plasma levels of homocysteine and improve the conditions of heart myocytes [67]; caffeine regulates blood pressure and heart rate, intervenes on the balances of norepinephrine and epinephrine, increases resistance to deformation of the arterial walls, improves insulin sensitivity, increases metabolic speed and promotes diuresis [68]; diterpenes, among which the aforementioned cafestol and cafeol, intervene on the blood concentration of cholesterol [69]. Given the multiple mechanisms by which the various types of cancer originate and spread, the relationships between the substances contained in coffee (and other foods) and the possible protective effects can be many and varied [70]. Cafestol and cafeol possess anticarcinogenic properties, intensify the activities of phase II enzymes involved in detoxification [71] and stimulate defense mechanisms based on the presence of intracellular antioxidants [72]. Coffee is also a source of polyphenols, among which flavonoids and lignanic-type phytoestrogens have shown anticarcinogenic properties in various epidemiological and laboratory studies [73-76]. Chlorogenic acid is able to lower blood glucose and its catabolic products increase insulin sensitivity, lowering those that are risk factors for some types of cancer [77], while caffeic acid is capable of inhibiting DNA methylation in human cell cultures [78], one of the mechanisms of action by which tumors defend themselves from the body's defensive processes by blocking the regulatory systems of cell cycles and apoptosis.

Conclusions

Although in some cases the current knowledge regarding the ability of coffee to act on the prevention of certain diseases is vague and sometimes reach conclusions in disagreement with each other, from a general point of view it is clear that regular coffee consumption involves this type, especially in the case of degenerative syndromes of the nervous system such as Alzheimer's and Parkinson's diseases, diseases affecting the cardiovascular system, adult diabetes and some types of neoplasms, especially those of the colon and rectum, prostate and liver.The bibliographic study carried out has brought to light some gaps in the complex of research conducted so far, especially as regards the laboratory studies whose number is very small compared to that of epidemiological studies. Especially considering the presence in coffee of different types of substances that contribute to the maintenance of a physiological state of the organism, a nascent line of research is expected to determine, for each of them, the real effectiveness, the mechanism of action, and later the possibility of being used for therapeutic purposes: the fact that studies of this type are starting to appear in the journals in recent years, however, bodes well for the future.

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Figure 1. Caffeine (left) and its demethylated analogues theobromine (middle) and theophylline (right).

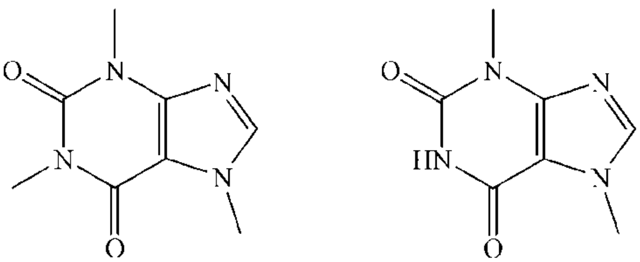
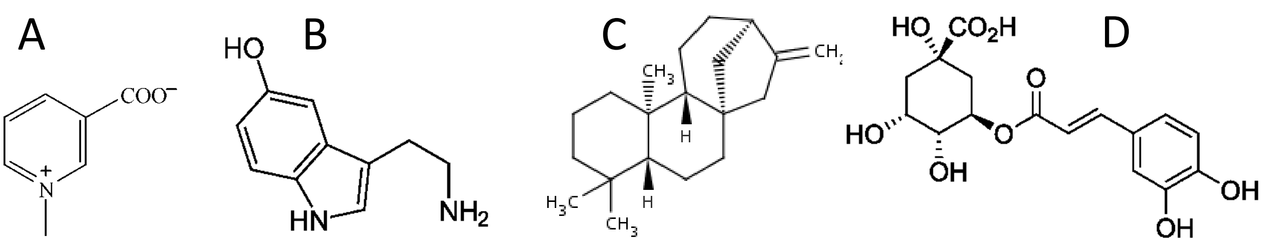


Figure 2. Structure of: A) trigonelline;B) serotonin; C) *ent*-kaurene;D) chlorogenic acid.



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