



Redox ingredients for oxidative stress prevention: the unexplored potentiality of coffee

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Abstract Plant-based foods (such as fruit and vegetables, wine, nuts, natural vegetable oils, and whole grains) are an important component of traditional diets in Mediterranean regions. A large, consistent body of scientific evidence demonstrates that diets rich in plant foods provide protection against degenerative diseases; however, despite the consensus of the evidence about the health effect of plant foods, it is unclear which components of plant-based foods are protective and what their mechanism of action is. One of the hypotheses postulated to explain the protective effect of plant food, the antioxidant hypothesis, is based on their high content of bioactive molecules. Recent evidence suggests that it is the variegate composition of the plant food, an optimal mixture of different antioxidants endowed with complementary mechanism of action and different redox potential, which is at the basis of their effect on health. The global antioxidant efficiency of complex matrixes can be assessed by measuring their total antioxidant capacity (TAC) representing the result of variables such as redox potentials of the compounds present in the matrix and their cumulative and synergistic interaction. In the last years different databases for TAC of plant foods have been developed. Results suggest that coffee might represent a potential contributor to dietary antioxidant intake. In this contribution after describing the main contributors to dietary TAC for different plant food group, we will discuss the potentiality of coffee as a source of “ready to drink” reducing equivalents.

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Introduction

Plant-based foods (such as fruit and vegetables, wine, nuts, natural vegetable oils, and whole grains) are an important component of traditional diets in Mediterranean regions. A large, consistent body of scientific evidence demonstrates that diets rich in plant foods provide protection against cardiovascular disease, several common types of

cancer, and other chronic diseases¹; however, despite the consensus of the evidence about the health effect of plant foods, it is unclear which components of plant-based foods are protective and what their mechanism of action is.²

One of the hypotheses postulated to explain the protective effect of plant food, the antioxidant hypothesis, is based on their high content of bioactive molecules. Dietary antioxidants reduce the risk of diseases by preventing oxidative cellular damage; however, results from clinical trials with antioxidants have given contrasting results which have raised strong concerns on the use of galenic antioxidants in disease prevention.^{3,4}

Recent evidence suggests that it is the variegate composition of the plant food, an optimal mixture of different antioxidants endowed with complementary mechanism of

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action and different redox potential, which is at the basis of their effect on health.² Cooperation among different antioxidants provides protection against free radicals injury greater than any single compound, which highlights the importance of the synergic action of the redox network.² The global antioxidant efficiency of complex matrixes can be assessed by measuring their total antioxidant capacity (TAC), which is defined as the tested extract's ability to neutralize oxidants.⁵ TAC represents the result of many variables, such as redox potentials of the compounds present in the matrix, their cumulative and synergistic interaction, the kind of stress, the nature of the oxidizing substrate, and antioxidants localization.

The use of TAC in epidemiological studies represents a new approach (that has been proposed for the first time) for investigating the relationship between the dietary antioxidant network and gastric cancer risk in a population-based case-control study.⁶ Results from this study showed that the intake of dietary TAC through plant food was inversely associated with the risk of gastric cancer with a significant dose-response trend. In the gastric cancer study, a TAC database of only 12 food items was used. To properly study the association between dietary TAC and disease incidence in selected groups of population at the epidemiological level, a specific TAC database for plant food has been developed.^{7,8} Results showed that espresso coffee is one of the "top five" plant food rich in antioxidants.

In this contribution, we describe the main contributors to dietary TAC for each vegetable food group (vegetables, fruits, alcoholic and non-alcoholic beverages, pulses, nuts, dried fruits, sweets, and spices) and the potentiality of coffee as a source of "ready to drink" reducing equivalent.

Total antioxidant capacity of vegetables foods

The growing interest in determining the TAC of plant foods emerges from the large number of articles published in the last 15 years on the TAC of almost all foods consumed in the human diet.⁹⁻¹¹ Among these, a significant number of articles focused on the assessment of TAC in different varieties of a single food item grown and/or stored in different conditions, showing that the TAC values of food items vary considerably from variety to variety and are deeply affected by cultivation and storage conditions.^{12,13}

Three databases that focused on the main food contributors to dietary TAC were analyzed and have been published.^{7,8,14-16} The database published by Halvorsen et al¹⁴ includes data on the ferric reducing antioxidant power (FRAP), which measures the reducing power of 32 vegetables, 23 fruits, 19 berries, 11 tubers, 18 cereals, 10 pulses, 6 nuts, and 4 dried fruits from different countries all around the world. In the Wu et al¹⁶ database, 24 fruits, 22 vegetables, 10 nuts, 4 dried fruits, 16 spices, 19 breakfast cereals, breads, and snack foods from the United States were measured by

the oxygen radical absorbance capacity (ORAC) assay. In our Italian database, 34 vegetables, 30 fruits, 34 beverages, 5 pulses, 6 vegetable oils, 11 spices, 5 dried fruits, 7 sweets, and 6 nuts were evaluated with three different methods: total radical-trapping antioxidant potential (TRAP), FRAP, and trolox equivalent antioxidant capacity (TEAC), which are assays for measuring, respectively, the chain-breaking antioxidant potential, reducing power, and the quenching ability.^{7,8} Results from this study showed that, between the food vegetables, spinach had the most antioxidants in the FRAP (26.94 mmol Fe⁺²/Kg) and TEAC (16.98 mmol/Kg) assays, followed by peppers (red bell, 20.98 mmol Fe⁺²/Kg and 16.80 mmol/Kg, and chili pepper, 23.54 mmol Fe⁺²/Kg and 15.24 mmol/Kg), turnip tops (17.77 mmol Fe⁺²/Kg and 11.04 mmol/Kg), and mushroom (16.39 mmol Fe⁺²/Kg and 9.86 mmol/Kg) or beet (13.13 mmol Fe⁺²/Kg and 10.42 mmol/Kg), respectively for FRAP and TEAC assay. TRAP assays furnish a slight difference ranking; asparagus had the highest TAC value (19.42 mmol/Kg), followed by beetroot (15.34 mmol/Kg), artichoke (13.70 mmol/Kg), turnip tops (13.24 mmol/Kg), and chilli pepper (12.84 mmol/Kg).

As far as the TAC values of fruits are concerned, blackberries were the most effective for all three assays (FRAP 51.53 mmol; Fe⁺²/Kg; TRAP 42.02 mmol/Kg and TEAC 40.48 mmol/Kg), followed by redcurrant (44.86 mmol Fe⁺²/Kg), raspberry (43.03 mmol Fe⁺²/Kg), black olive (39.99 mmol Fe⁺²/Kg), and strawberry (28.00 mmol Fe⁺²/Kg) for FRAP. The ranking for TRAP was slightly different, with black and green olives (36.16 mmol/Kg and 29.28 mmol/Kg) in second and third position, followed by redcurrant and raspberry (24.28 mmol/Kg and 20.96 mmol/Kg). Raspberry showed the second TAC value for TEAC (33.58 mmol/Kg) before black olive (29.46 mmol/Kg), redcurrant (28.10 mmol/Kg) and strawberry (22.68 mmol/Kg).

Among soft beverages, orange juice (9.44 mmol Fe⁺²/L), lemon juice (7.34 mmol/L), and grapefruit juice (6.60 mmol/L) were at the top of ranking for FRAP, TRAP, and TEAC, respectively.

In agreement with literature, herbs and spices were characterized with the highest overall values of TAC between the different food groups, with bay leaf (FRAP 204.50 mmol Fe⁺²/Kg; TRAP 178.60 mmol/Kg and TEAC 95.80 mmol/Kg) and saffron (FRAP 739.40 mmol Fe⁺²/Kg; TRAP 748.00 mmol/Kg and TEAC 106.00 mmol/Kg) at the top of the ranking in all three methodologies for herbs and spices. Of the six nuts analyzed, walnuts displayed a very high TAC score for all three assays (FRAP 412.30 mmol Fe⁺²/Kg; TRAP 55.20 mmol/Kg and TEAC 239.80 mmol/Kg). Between pulses, lentils for FRAP and TRAP (8.60 mmol Fe⁺²/Kg and 2.60 mmol/Kg) and broad bean for TEAC (15.40 mmol/Kg) displayed the highest TAC value. Among the dried fruits analyzed, prunes exhibited the highest value (60.5 mmol Fe²⁺/kg, 46 mmol/Kg and 29.6 mmol/Kg respectively for FRAP, TRAP and TEAC) in all three methodologies.

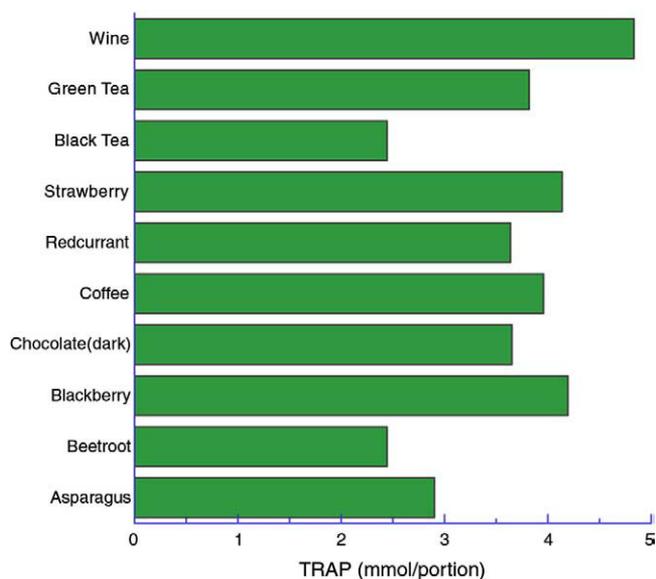


Fig. 1 Values of total radical-trapping antioxidant potential (TRAP)^a standardized for portion for the selected foods^{b,c}. ^aTRAP, expressed as millimoles of peroxy radicals neutralized per serving (mmol/portion). ^bFoods (n = 10) considered are at the top of TRAP values for each selected category. ^cBay leaf, chilli pepper and saffron excluded for lack of portion size.

All chocolates analyzed were far higher than the other sweets measured (ie, honey, ice creams and jam). In agreement with the literature¹⁷ dark chocolate showed the highest TAC value for all the three assays (FRAP 182.18 mmol Fe⁺²/Kg; TRAP 183.20 mmol/Kg and TEAC 189.62 mmol/Kg), followed by gianduja (FRAP 108.12 mmol Fe⁺²/Kg; TRAP 97.30 mmol/Kg and TEAC 100.68 mmol/Kg) and milk chocolate (FRAP 42.13 mmol Fe⁺²/Kg; TRAP 23.1 mmol/Kg and TEAC 72.32 mmol/Kg) characterized by a lower concentration in phenolic antioxidants.

Between beverages, as expected, red wine showed a higher TAC (FRAP 30.53 mmol Fe⁺²/L; TRAP 32.18 mmol/L and TEAC 24.28 mmol/L) with respect to white (FRAP 5.04 mmol Fe⁺²/L; TRAP 4.64 mmol/L and TEAC 3.88 mmol/L) and rosé wines (FRAP 7.22 mmol Fe⁺²/L; TRAP 6.40 mmol/L and TEAC 4.36 mmol/L). Green tea (FRAP 18.00 mmol Fe⁺²/L; TRAP 15.26 mmol/L and TEAC 12.02 mmol/L) was stronger than black tea (FRAP 10.09 mmol Fe⁺²/L; TRAP 9.74 mmol/L and TEAC 7.20 mmol/L). Espresso coffee displayed the highest TAC for alcoholic and nonalcoholic drinks independently of the applied assays (FRAP 129.38 mmol Fe⁺²/L; TRAP 132.00 mmol/L and TEAC 73.08 mmol/L). Caffeine removal in the decaffeinated espresso coffee determined a decrease of TAC values of about 25-30% (FRAP 93.01 mmol Fe⁺²/L, TRAP 91.64 mmol/L and TEAC 53.92 mmol/L). Apart from the leadership of the beverages groups, the results for coffee are interesting if we consider that, on the basis of *in vitro* TAC, espresso is among the five foods at high antioxidant content with saffron, bay leaf, walnuts, and chocolate. If we express the

results on the basis of their portion size, coffee is still in the first five foods with high TAC (Figure 1).

Antioxidant properties of coffee

Coffee is one of the most widely consumed nonalcoholic beverages in Western Society, although research on its health properties is highly controversial.¹⁸⁻²⁰ During coffee making, the roasting process leads to profound changes in the chemical composition and biological activities of the coffee bean, leading to the generation of compounds deriving from the Maillard reaction, carbohydrate caramelization, and pyrolysis of organic compounds.²¹ During the process of roasting (even though despite most of the polyphenols are destroyed), Maillard reaction products are generated²² with an increase in the antioxidant activity of coffee.²¹ Coffee also contains antioxidant phenolics of the hydroxycinnamic acids family, such as caffeic, coumaric, chlorogenic, and ferulic acids.²⁰ Moreover, caffeine and its catabolic products (theobromine and xanthine) might contribute to the overall antioxidant capacity of coffee.²³

In vivo evidences in humans are scarce, with only one study showing that plasma antioxidant capacity increased following coffee drinking (200 mL); however, the effect was limited (+7%).²⁴ Statistical significance was reached by assessing jointly the different time points of antioxidant peaks for the different subjects, suggesting that, because of the limited bioavailability of coffee antioxidants, only a small fraction of the antioxidant equivalents is delivered in the body.

Effect of coffee drinking on cardiovascular disease and cancer

The effects of coffee consumption on the risk of cardiovascular disease and cancer are limited and extremely contrasting. In people who are not used to drinking coffee, coffee consumption has been shown to raise diastolic and systolic blood pressure.²⁵ The effect on blood pressure does not seem to be dose-dependent and does not display a large interindividual variability. In people who regularly drink coffee, the effect on pressure is much smaller than in people who abstain from coffee. Stamler et al²⁶ showed an inverse association between coffee consumption and blood pressure in 12,000 men in the Multiple Risk Factor Intervention Trial (MRFIT); however, if we look at the body of epidemiological evidences, the effects of coffee consumption on blood pressure is highly inconsistent, with studies showing no effect and positive and inverse associations.²⁷

Epidemiological studies examining the association between coffee consumption and cardiovascular morbidity and mortality have been controversial and inconclusive. In

the study from Jick et al,²⁸ subjects drinking more than six cups of coffee a day doubled the risk of myocardial infarction. Grobbee et al²⁹ studied more than 45,000 Americans and found that the risk for cardiovascular diseases was slightly increased in persons who drank four or more cups of coffee a day. A retrospective on the Nurse's Health Study showed no correlation between coffee consumption and cardiovascular diseases in 85,747 women.³⁰ On the contrary, in 230 men enrolled in Sweden, an inverse correlation was found between coffee consumption (more than seven cups a day) and the risk for cardiovascular disease.³¹ A very recent case-control study was conducted on 4018 subjects, matched for age, sex, and area of residence in Costa Rica. The study showed that intake of coffee was associated with an increased risk of nonfatal myocardial infarction only among individuals who had slow caffeine metabolism.³² Meta-analyses investigating the relationship between coffee intake and the risk of coronary heart disease have observed a positive association in case-control studies but not among prospective cohort studies.^{33,34}

Evidence is scarce and contrasting regarding the effect of coffee drinking on cancer development. Kubik et al³⁵ found that cigarette smoking was directly associated with the development of cancer and that drinking coffee was inversely associated with lung cancer risk. In contrast with this evidence, Mendilaharsu et al³⁶ showed no effect of coffee drinking on lung cancer risk in smokers when compared in a matched control group. One of the explanations for these contrasting results is the strong association between chronic coffee consumption and other risk factors, such as smoking.¹⁸ The contrasting evidence from epidemiological studies might arise from the fact that coffee drinking often is associated with cigarette smoking, which is a clear risk factor for cancer and cardiovascular diseases and makes it difficult to understand if the coffee mitigates the negative effect of smoking or if it represents a further risk factor. Detailed protocols should be developed for splitting the potential antioxidant effects of coffee consumption from the bias lead by cigarette smoking.

Conclusions

The experimental evidence shows that coffee has higher potential as an *in vitro* antioxidant among the different plant foods, which may suggest the inclusion of coffee in the list of foods able to exert an antioxidant effect in humans. Despite the promising evidence *in vitro*, *in vivo* studies are scarce and inconclusive, and they do not allow any conclusions on the possibility of coffee to strengthen antioxidant defenses in humans. At epidemiological levels, evidence regarding a possible preventive effect on cardiovascular disease and cancer are strikingly contrast-

ing. The reason might be the confounding effect of the association with well known risk factors, such as smoking and alcoholic drinking.

Despite the strong *in vitro* antioxidant properties, further and more detailed evidence is needed in well-tailored human intervention studies and epidemiological studies before formulating any hypotheses regarding the active role of coffee in oxidative stress and disease prevention.

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