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Mini-Review

# Coffee Phenolics and Their Interaction with Other Food Phenolics: Antagonistic and Synergistic Effects

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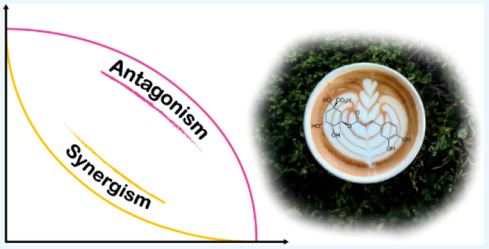
**ABSTRACT:** Due to its strong aroma and stimulating effect, coffee is the most consumed beverage worldwide, following water. Apart from being a luscious food product, its contents of high phenolic compounds dominated by chlorogenic acid, caffeic acid, and their derivatives have caused coffee to be consumed by individuals at higher ratios and have also encouraged the number of varying research studies for its health-promoting properties. However, it should be noted that these desirable beneficial actions of coffee phenolics are in dynamic behaviors, highly dependent on the roasting process parameters and presence of different types of phenolic compounds in the media. Interactions between coffee phenolics and other phenols might end up with induced or reduced biological activities, which is called synergism or antagonism, respectively. In this paper, bioactive properties such as antioxidant, enzyme inhibition, and chelating power are reviewed in terms of synergism and antagonism of coffee phenolics and other bioactive compounds that are introduced into the matrix, such as cacao, ginger, cinnamon, willow bark, cardamom, and chili pepper. Furthermore, how these properties are affected after in vitro digestion and potential reasons for the outcomes are also briefly discussed with the aim of providing a better understanding of these interactions for the food industry. Revealing the synergistic and antagonistic interactions of the phenolics between coffee and different ingredients in a food matrix and their effects on bioactivity mechanisms is not only important for scientific studies but also for conscious food consumption of individuals.




## 1. INTRODUCTION

Recently, the demand for nutrition has changed with an increasing awareness of the health-promoting properties of the diet. The revelation of the relation of a healthy life and balanced nourishment has led people to fresh, less processed, and/or additive-free natural foods for consumption. In this regard, nonalcoholic, low-calorie drinks are becoming one of the most important components of our diet with respect to their easy consumption with high nutritional properties. Even though there are many options in this category, coffee is the most preferred beverage after water, with consumption of approximately 500 billion glasses per year worldwide.[1] Coffee might be consumed in many different types depending on the consumer preference, such as with or without milk and/or the addition of sugar, cinnamon, cacao, or different aromas.

Although the reasons for individual consumption of coffee are mostly its strong stimulating aroma and flavor, its health benefits have also been known for many years. Coffee has various health-promoting effects such as antioxidant, anticarcinogenic, antimutagenic, and anti-inflammatory activities. In addition, coffee consumption has been associated with the prevention of many chronic diseases including diabetes, Parkinson's disease, or certain types of cancer.[2] Even though coffee has a complex structure with varying types of chemicals, significant contents of phenolic compounds are responsible for the above-mentioned health-promoting properties of coffee.

Phenolic compounds might interact with many components in the food matrix. These components could be macrocomponents such as carbohydrates, proteins, or lipids as well as microcomponents such as vitamins, minerals, and other phenolic compounds.[3] As a result of the interaction of phenolic compounds with other components, the bioactivity that they provide in the food system might also be affected.[4] The combination of different phenolic compounds might induce a synergistic effect as well as an antagonistic effect in varying circumstances.[3] Phenolic compounds of coffee might also induce these synergistic/antagonistic effects when they are introduced to other phenolic compounds in different food matrices due to varying consumption conditions. This study aims to discuss the interaction of phenolic compounds in coffee with other phenolic compounds and the effects of this interaction on the antioxidant properties of coffee.

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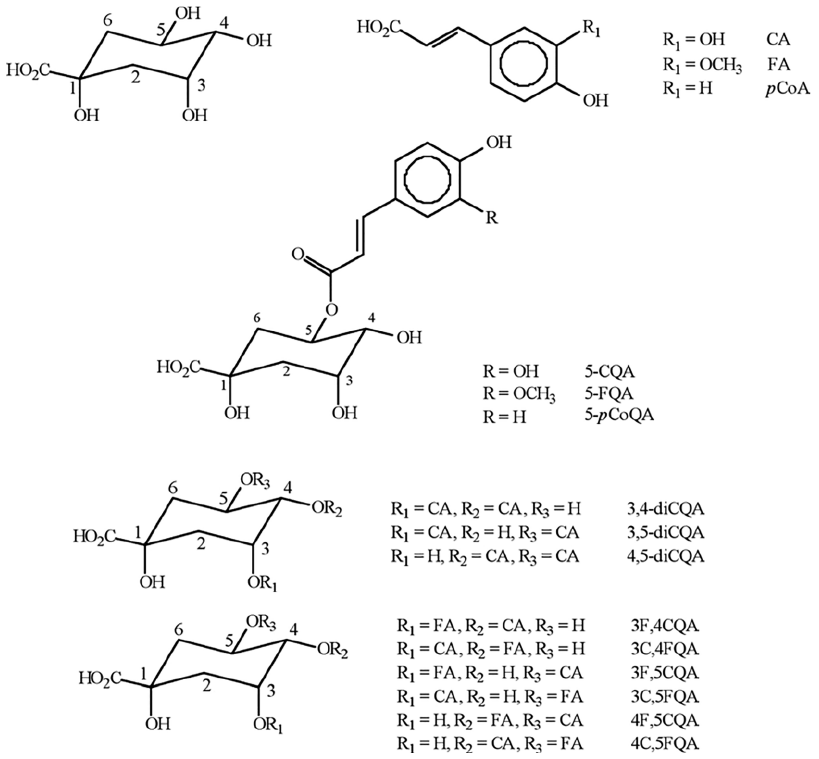


**Figure 1.** Chlorogenic acid and its isomers found in coffee.[5] Reprinted with permission from ref 5. Copyright 2006 SciELO. This work is licensed under a Creative Commons Attribution-NonCommercial 4.0 International License.

## 2. PHENOLIC COMPOUNDS IN COFFEE

Almost every type of coffee from green to roasted beans contains several common phenolic compounds. For example, chlorogenic acid and its derivatives are known as major phenolic compounds in coffee, and they are found in every type of coffee variety. The main groups of chlorogenic acids including caffeoylquinic acids (CQA), dicaffeoylquinic acids (diCQA), feruloylquinic acids (FQA), *p*-coumaroylquinic acids (pCoQA) and their isomers, and six mixed diesters of caffeoylferuloylquinic acids (CFAQ) found in coffee are presented in Figure 1.[5] In addition to the chlorogenic acids, gallic acid, hydroquinone, 3,4-dihydroxybenzoic acid, 4-hydroxybenzoic acid, 3,5-dihydroxybenzoic acid, 2,3-dihydroxybenzoic acid, benzoic acid, salicylic acid, and ferulic acid have also been found in different extracts of coffee.[6] Although many coffee types contain similar phenolic compounds, the phenolic content and their composition might vary depending on factors such as the cultivation method, agricultural practices, and degree of roasting.

There are more than 85 different known coffee species worldwide. However, only two of them, Arabica and Robusta, are the most known, produced, and consumed species among all.[2] The phenolic compositions of these two species are similar; however, the ratio of phenolics they contain are different from each other. For instance, Arabica coffee has a higher chlorogenic acid content, whereas Robusta coffee has a higher amount of caffeic acid.[6] Overall, Robusta coffee was indicated for having a phenolic content higher than that of Arabica coffee.

Green coffee beans are rich in phenolic and antioxidant compounds. They contain predominantly chlorogenic acids such as dicaffeoylquinic acids, feruloylquinic acids, and *p*-coumaroylquinic acids. Despite their rich phenolic content, green coffee beans are poor in aroma when directly brewed. Therefore, they are roasted at different temperatures for specified times prior to consumption. For the roasting process, hot air at 200−260 °C passes through the beans, and several reactions might occur, resulting with the possible changes of chemical composition and bioactivity of phenolic compounds. It leads to the transformation of natural substances that are present in green coffee, as well as the formation of new chemical structures throughout the Maillard reaction, caramelization of carbohydrates, and pyrolysis of some organic compounds. Some types of phenolic compounds are newly formed, while some of them are decomposed by the effect of heat. For instance, total chlorogenic acid contents of both Arabica and Robusta coffee were observed to decrease after roasting. Moreover, 5-*O*-feruloylquinic acid, 4-*O*-feruloylquinic acid, and 4-*O*-coumaroylquinic acid are totally degraded after roasting, whereas 3-*O*-coumaroylquinic acid is newly formed.[6] Consequently, the chosen parameters for the roasting process are critically important in terms of types and moieties of phenolic compounds, as well as their biological activities.

## 3. INTERACTION OF COFFEE PHENOLICS AND OTHERS AND ITS EFFECT ON BIOACTIVE PROPERTIES

There is limited information on the interactions of coffee phenolics with those of other commonly paired food matrices in the literature. Although coffee itself is a considerably popular beverage, its pairing with other aromatic ingredients has the potential to not only enhance the aroma and flavor of the drink but to also significantly increase its antioxidant capacity. Additionally, there is a trend toward functional coffee-based beverages such as herbal coffee, bulletproof coffee, as well as well-known brands launching products of the kind, for


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example, Starbucks "Coffee with More" range and Laird Superfood. These fortified coffee products currently available in the market seem to be focused on added ingredients such as cinnamon, ginger, and even mushrooms, which provide additional antioxidant properties, supplying coffee with added benefits to the consumers. However, the potential synergistic or antagonistic effects of these added compounds have not been explored yet. The focus of this study is to investigate interactions between coffee and added ingredients to better understand the real situation in a food matrix rather than evaluating the components individually, which would be beneficial for the industry and also for the literature to pinpoint the combinations with the most beneficial outcomes in this sense.

Durak et al.[7] studied the interaction of coffee and cinnamon, carrying out their research in two different parts. In the first part, researchers focused on how individual bioactive phenolics of coffee and cinnamon interacted with each other, with both of those obtained from the extracts and standard chemicals for comparison. Second, it was investigated how these compounds interacted during in vitro gastrointestinal digestion and determined their bioavailabilities. Cinnamon is rich in cinnamic acid and coumarin, providing antioxidant properties as well as defense against lipoxygenase (LOX) activity and can be used in coffee to enhance flavor and taste. The ABTS (2,2′-azinobis(3-ethylbenzothiazoline-6-sulfonic acid)) method for free-radical-scavenging activity and spectrophotometry for LOX inhibition were used, and both were expressed as $EC_{50}$ − extract concentration (mg dry weight (dw)/mL) provided 50% of activity. For inhibition capability, half-maximal inhibitory concentration ($IC_{50}$) values were assessed and were further confirmed by determining the interaction factor (IF). In coffee extracts, the predominant phenolic acids were found to be caffeoylquinic acid and its isomers, whereas for cinnamon, they were cinnamic acid, proanthocyanidins, and coumarin. Chlorogenic acid (CGA) for coffee extract and cinnamic acid for cinnamon were chosen as model compounds. The antiradical scavenging and lipoxygenase (LOX)-inhibitory activities of cinnamon and coffee extracts were on par; however, in terms of their respective standard model compounds, coffee showed greater capacity in both. For both coffee and cinnamon, antiradical scavenging and LOX inhibitory activity increased after simulated gastrointestinal digestion, with their notably decreased $EC_{50}$ values. In terms of their interaction, the antiradical scavenging activity of coffee and cinnamon was shown to be antagonistic, before and after digestion. The same applied to their standard model compounds, as well. The opposite situation was observed for LOX inhibition ability, with their extracts and model compounds displaying synergistic effects. However, antagonism in LOX inhibition was observed for their mixture after digestion.

Similar to the study discussed above, coffee and ginger were investigated with respect to both the interaction of individual compounds in comparison with their standard equivalents, along with the influence of in vitro gastrointestinal simulation.[8] The antiradical scavenging activity of coffee extracts was found to be higher than that of ginger, and both increased with in vitro digestion. The opposite situation was observed for their model compounds, with caffeic acid for ginger exhibiting antioxidant capacity higher than that of chlorogenic acid (5-caffeoylquinic) for coffee. For extracts and standard compounds, ginger was shown to have a greater LOX inhibition capacity, and both foods showed an increase in this sense after simulated digestion. Antiradical scavenging activity of coffee and ginger combinations displayed synergism, though this turned into an additive effect after in vitro digestion. Antagonism was also observed for their standard compounds. LOX inhibitory activity showed the exact opposite of this situation and was antagonistic before digestion and synergistic afterward. The synergism of the pure compounds was higher than that of the extracts. These interactions evaluated via isobolographic analysis were further confirmed by IF.

Willow bark is considered as an aspirin substitute by some due to not having the unfavorable side effects of aspirin, as well as being a natural alternative.[9] A study investigated the interaction of coffee with purple willow, *Salix purpurea*, and dark-leaved willow, *Salix myrsinifolia*. The main phenolics of coffee extracts were found to be caffeoylquinic acid and its isomers. The phenolic glycosides found in willow were expressed as salicin equivalent, with *S. myrsinifolia* having a significantly higher content than that of *S. purpurea*. In terms of LOX inhibition, CSm (coffee extracts with *S. myrsinifolia*) and CSp (coffee extracts with *S. purpurea*) clearly had the highest inhibition ability, with $IC_{50}$ values lower than others on par with each other. It was noted that the active compounds present in the two components acted in synergy with each other. These were followed by coffee, *S. myrsinifolia* and *S. purpurea*, respectively. A similar pattern was observed for OH• scavenging activity, with CSp and CSm achieving high levels of synergy, thus exhibiting a greater capability than coffee alone. This showed that the interaction of coffee compounds with willow contributed to the neutralization of the hydroxyl radical. The opposite was observed for ABTS scavenging activity and ferric reducing antioxidant power (FRAP), where the mixtures exhibited antagonism. Chelating power resulted in a synergistic effect for CSp and additive effect for CSm. Another study conducted with the same material showed that while ABTS scavenging activity was antagonistic for both species, FRAP and LOX inhibition was synergistic.[10]

Cardamom as a potential roasted coffee supplement was studied to determine the interaction of their compounds along with the influence of in vitro digestion on the bioavailability of their interaction.[11] For the water extract of cardamom, four phenolic compounds were identified: protocatechuic acid, vanillic acid, *p*-coumaric acid, and ferulic acid. Vanillic acid was chosen as its standard model compound as it was the most predominant compound for cardamom, and CGA was used for coffee, in line with the studies mentioned above. Coffee extracts were recorded to have higher antioxidant capacity, and cardamom extracts showed greater LOX inhibition ability, while both properties were increased with in vitro digestion for both of the materials. Coffee had a significantly high FRAP value, which was decreased after in vitro digestion, while the opposite was observed for cardamom, with FRAP values increasing after simulated digestion. Chelating ability was decreased and OH• scavenging activity was increased after digestion for both. In terms of their interaction, water-extractable antiradical compounds and LOX inhibition capability were observed to be synergistic, though both changed to antagonistic in vitro. FRAP, SOD (superoxide dismutase)-like activity, and XOi (xanthine oxidase inhibiting activity) were synergistic both before and after digestion, and their strongest positive interaction was noted for raw extracts rather than their corresponding standard chemicals. Chelating ability was synergistic before and additive after in vitro


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digestion. The outcomes of the standard model compounds were observed to be similar to those above. OH• radical neutralization potential was notably antagonistic before and additive after in vitro digestion. Their model compounds, however, were synergistic, indicating that while CGA and vanillic acid may be strong OH• radical scavengers, they are not the leading compounds present in the analyzed materials contributing to this property. Overall high bioaccessibility for cardamom and low capacity for coffee was observed. Furthermore, a consumer acceptance test was carried out with 50 participants, and its results showed that cardamom at 0.5% was the most favored ratio, although addition of 1−2.5% did not exert a critical change in terms of sensory profile.

A study carried out with coffee and dried coconut meat (DCM) showed that while coffee contained a significant amount of caffeoylquinic acid and its isomers, coconut's leading phenolics were catechin, epicatechin, vanillic acid, and gallic acid.[12] Coffee was observed to show a high antiradical activity compared to that of DCM; however, they had similar LOX inhibition activities. The authors further studied the interaction of the two materials and how they affected these parameters after simulated gastrointestinal digestion. Synergism was observed between their antiradical compounds, both before and after in vitro digestion. The opposite situation was observed for LOX inhibition activity; in fact, the observed antagonism became significantly stronger after in vitro digestion. This was somewhat interesting that simulated gastrointestinal digestion was certainly influential in regards to interactions between compounds while performing high LOX inhibitory activity of the materials before digestion.

In contrast to the studies above, Gawlik-Dziki et al.[13] explored coffee as a functional additive to bread and focused on the interactions of green coffee beans and whole meal wheat flour. Their major phenolics, CGA for green coffee beans and ferulic acid for wheat flour, are known to have multiple positive effects on human health including antioxidative properties and were investigated to understand if they could potentially be a natural alternative for gastrointestinal medication such allopurinol, a prevalent urate-lowering drug with numerous side effects. The results of the study showed that XO inhibitory activity for green coffee was significantly higher than that for wheat flour, which was suggested to derive from starch and protein interaction with ferulic acid. It was also noted that their respective standard chemical compounds showed higher inhibition activity. The main parameter investigated was XO inhibition, and it was observed that there was a synergistic interaction between the inhibitors from green coffee beans and wheat flour. Complementary results were observed for their standard chemical compounds as well as after in vitro digestion. It was further stated that supplanting wheat flour with 3% green coffee beans was accepted by the consumers and was reported to have a substantial positive impact on XO inhibitory activity.

An unconventional combination with coffee was applied using chili peppers.[14] As chili peppers contain bioactive compounds, with capsaicin being the most predominant phenolic, they have the potential to have a positive impact on the overall antioxidant properties of coffee. Interactions between their individual compounds as well as the effect of simulated gastrointestinal digestion were observed. It was noted that coffee had higher antiradical power than chili, and this ability was observed to increase for both before and after in vitro digestion. FRAP activity was higher in coffee and decreased after digestion, while the activity of chili was increased. Chelating ability was approximately the same for coffee and chili and increased after simulated digestion for both. Chili had the highest OH• radical neutralization ability which was decreased after in vitro digestion, while that of coffee was observed to increase. Synergism was observed in antiradical scavenging activity and OH• radical neutralization; however, these both changed to an antagonistic effect after stimulated digestion. Chelating and FRAP activities were antagonistic in all tests. SOD-like and SASA (superoxide anion scavenging) activities were only able to be evaluated before in vitro digestion and were observed to have a synergistic effect.

Cocoa is one of the most commonly added ingredients to coffee, for the most part due to its favorable flavor. Acosta-Otálvaro et al.[15] investigated the interaction of coffee and cocoa phenolics with regard to bioavailability and radical scavenging power. As with other studies, CGA was found to be the main phenolic acid for coffee, while for cocoa, flavan-3-ols (catechins and epicatechins), anthocyanins, and procyanidins were identified. Antioxidant capacity was measured through the 2,2-diphenyl-1-picrylhydrazyl (DPPH) radical scavenging and oxygen radical absorbance capacity (ORAC) assays, while Caco-2 cells were used to create an in vitro standard model to investigate the bioavailability of the present phenolic compounds. These were carried out with various blend ratios of cocoa and coffee (0:100, 25:75, 50:50, 75:25, and 100:0). Radical scavenging activity increased as the ratio of cocoa in the mixtures was increased, showing that cocoa had a higher antioxidant activity, even at lower doses. Comparing their $IC_{50}$ values (lowest with 100% cocoa at 9.976 mM TE/g dw and highest with 100% coffee at 15.030 mM TE/g dw), it was stated that almost 5 times more coffee extract would be required to obtain an inhibition activity similar to that of cocoa. The ORAC values displayed a similar outcome, and it was stated that the antioxidant capacity of cocoa extracts was greater than those of coffee. Although the bioavailability of the individual compounds was assessed, their potential synergism/antagonism was not further discussed. A combination index was used to evaluate the interactions of the extracts. As the ratio of cocoa in the blend increased, the antioxidant activity also increased, displaying a slight synergism between the compounds for the ratio of 75:20 cocoa−coffee. Moderate antagonism and nearly additive outcomes were observed for 25:75 and 50:50 ratios, respectively. While it was evident that cocoa was linked with increased antioxidant activity in cocoa−coffee mixtures, there was no substantial evidence of their definite synergism.

A study by Çelik and Gökmen[16] was conducted in two parts: interactions of insoluble fractions of coffee infusions with major cocoa free antioxidants, catechin and epicatechin, as well as interaction of coffee infusions with dark chocolate containing 60% cocoa, in terms of antioxidant capacity. Four different types of coffee infusions were utilized; espresso, filtered coffee, French press, and Turkish coffee. Turkish coffee was found to have the highest antioxidant activity, closely followed by French press, with espresso prepared in a moka pot (moka) containing the lowest activity in terms of insoluble fractions. Here, it was also important to note that the brewing process improved the antioxidant capacity, as the results of the coffee infusions were higher than that of coffee beans. When looking at the interactions of insoluble fractions of coffee infusions with catechin/epicatechin, synergism was observed for espresso and additive and/or antagonistic outcomes for the


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Table 1. Interaction Outcomes of Coffee with Other Food Materials[a]

| material | polyphenols | synergistic attributes | antagonistic/additive attributes | ref |
|---|---|---|---|---|
| cinnamon | cinnamic acid, coumarin proanthocyanidins | LOXi | RSA, RSA,[b] LOXi[b] | 7 |
| ginger | caffeic acid | RSA, LOXi[b] | RSA,[b] LOXi | 8 |
| willow: *Salix myrsinifolia* | salicin/salicylic glycosides | LOXi, OH | RSA, CHEL, FRAP | 9 |
| willow: *Salix purpurea* | | LOXi, CHEL, OH | RSA, FRAP | 9 |
| willow: *Salix myrsinifolia* and *Salix purpurea* | | LOXi, FRAP | RSA | 10 |
| cardamom | protocatechuic acid, vanillic acid, *p*-coumaric acid, ferulic acid | FRAP, CHEL, SOD, LOXi, XOi | CHEL,[b] SOD,[b] OH, LOXi[b] | 11 |
| coconut | catechin, epicatechin, vanilic acid, gallic acid | RSA, RSA[b] | LOX | 12 |
| whole meal wheat flour | *trans*- and *cis*-ferulic acids | XOi | | 13 |
| chili pepper | capcaicin | RSA, OH, SOD, SASA | RSA,[b] CHEL, OH,[b] FRAP | 14 |
| cocoa | catechins, epicatechins, anthocyanins, and procyanidins | RSA | | 15 |
| *Ginkgo biloba* L., *Scutellaria baicalensis*, and quercetin-3-*O*-rutinoside | hydroxycinnamic acid, caffeoylquinic acid, etc. | $H_2O_2$ | AChE | 17 |
| N/A | $\alpha$-tocopherol vs chlorogenic acid | | antioxidant capacity | 23 |
| N/A | $\alpha$-tocopherol vs caffeic acid/ferulic acid | antioxidant capacity | | 23 |

[a]LOXi, lipoxygenase inhibition activity; RSA, radical scavenging activity; CHEL, chelating power; OH, OH• scavenging assay; FRAP, ferric reducing antioxidant power; XOi, xanthine oxidase inhibiting activity; SOD, superoxide dismutase-like activity; SASA, superoxide anion scavenging activity; $H_2O_2$, hydrogen peroxide scavenging activity; AchE, acetylcholinesterase inhibition. [b]Outcome after in vitro digestion.

other infusions. This could be due to a regeneration reaction between the bound antioxidants of espresso and catechin/epicatechin; however, it could not be the sole explanation as the content of bound antioxidants in espresso was noted to be the lowest of all investigated coffees. In terms of coffee infusions and chocolate, synergism for French press and Turkish coffee, additive/antagonistic for moka, and additive for espresso and filtered coffee were observed. This was suggested to be caused by the free soluble antioxidants in French press and Turkish coffee or the antioxidants in dark chocolate.

A study by Delerue et al.[17] examined a combination of two Chinese medicinal plants, *Ginkgo biloba* L. and *Scutellaria baicalensis* in varying ratios with respect to their potential neuroprotective impact on Alzheimer's disease. These were further compared with a commercial pill purchased online consisting of these plants with unroasted *Coffea arabica* L. and quercetin-3-*O*-rutinoside, along with a prepared version with the same ratio of each component. The investigated parameters were acetylcholinesterase inhibition and hydrogen peroxide scavenging, and interactions of compounds were also evaluated using the combination index (CI). It was observed that the above-mentioned plants were more effective when utilized by themselves individually, but their mixtures generally showed antagonism. With respect to the results of the commercial pill containing coffee, a low synergism against $H_2O_2$ scavenging activity and additive interaction against acetylcholinesterase inhibition was reported. The prepared blend showed antagonism against both parameters. Therefore, it could not be concluded that the assessed materials induced synergistic effects.

Riberio et al.[18] compared commercial coffee blends to a newly prepared mixture consisting of roasted coffee powder with a total of 6% cocoa powder, coffee silverskin, and minimally processed green coffee. It was stated that it had higher phenolics content and radical scavenging power than the commercial types; nevertheless, the potential synergism/antagonism of the blend was not evaluated. Sęczyk et al.[19] studied the antioxidant activity of soymilk fortified with green coffee extract at various ratios. Total phenolic content (TPC), antiradical capacity, and FRAP were elevated, and although no interaction analysis was carried out, synergism between the compounds was briefly suggested. Another herbal coffee blend was coffee fortified with white turmeric and wild ginger, where the TPC and antioxidant capacity of the beverage increased with their addition and reached its inhibition peak at 60% for both.[20] The potential effect of bulletproof coffee on cognition has also been investigated, although studies conducted so far have not indicated any benefits in contrast to black coffee.[21,22]

Unlike the studies above, Neunert et al.[23] examined the interaction of three major coffee phenolics, caffeic acid, chlorogenic acid, and ferulic acid, with $\alpha$-tocopherol to evaluate their antioxidant abilities in L-$\alpha$-phosphatidylcholine liposomes but not in a food matrix. The locations of these compounds within the liposomes were explored along with their partition coefficients (lipophilicity). It was observed that ferulic acid had the strongest interaction with L-$\alpha$-phosphatidylcholine liposomes and was fractionally embedded in the membrane, which was attributed to the nonpolar group ($-CH_3$) in its structure. The interaction with caffeic acid and chlorogenic acid was in the hydrophilic range since both compounds are more polar than ferulic acid. Protection coefficients (PCF) were calculated to evaluate the ability of phenolic acids to prevent AAPH-induced lipid oxidation in the liposomes. In terms of their individual antioxidant capacity, $\alpha$-tocopherol resulted in the highest PCF, with the values increasing with the concentration of the compound. It was suggested that this was due to $\alpha$-tocopherol being embedded inside the membrane. Even though higher antioxidant capacities were expected for caffeic acid and chlorogenic acid, ferulic acid had the highest PCF, indicating that in liposomes there were other impacting factors for the antioxidant capacity of phenolic acids rather than individual capacities of the compounds. These values only increased up to a certain point and were not concentration-dependent afterward. When investigating the interaction of the phenolics, the strongest synergism was observed between ferulic acid and $\alpha$-tocopherol, followed by caffeic acid and $\alpha$-tocopherol. This may be location related as both ferulic acid and $\alpha$-tocopherol


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were embedded in the membrane. It was speculated that the interaction could arise from regeneration or sacrificial oxidation, both of which have been previously observed for polyphenol−tocopherol interactions. There seemed to be no interaction between chlorogenic acid and $\alpha$-tocopherol with regard to lipid peroxidation inhibition.

Table 1 presents the interaction outcomes of coffee with other food materials, specifically looking into the parameters investigated within these studies. As can be seen, in a majority of studies, antagonism was observed after in vitro digestion, with the exception of ginger and coffee for LOXi, and a continued synergism between the water-extractable components of coffee and DCM for RSA. It is evident that in vitro digestion played a crucial role, mainly steering toward an antagonistic interaction of the compounds. These changes during or after digestion can be related to the conditions that affect phenolic compounds in terms of their quantity or profile. Each phenolic compound may be affected differently during gastrointestinal digestion; some phenolic compounds may lose their stability, while others are metabolized or interacted with other components.[24,25] In this case, the ratio of the interacting phenolic compounds changes, and accordingly, the bioaccessibility and bioavailability of these compounds are also affected.[26]

## 4. CONCLUSION

Coffee, being one of the most preferred and consumed nonalcoholic hot/cold beverages worldwide, is also highly compatible for blending/mixing with some accompanying food components such as cacao, ginger, cinnamon, willow bark, cardamom, and even chili pepper in order to obtain an enhanced flavor and/or to tailor novel tastes. However, aromatic compounds are not the only encountering components for flavor, but the phenolics of coffee and its accompanier would also possibly be interacting. From the health-promoting points of view, phenolic−phenolic interactions of coffee and the accompanier matrix might induce or reduce the biological activities of coffee phenolics and sometimes do not even affect them. This review provides a short but concise summary of the research conducted so far on the interactions of coffee phenols with those of other food products, while also touching briefly on the role of in vitro digestion on the interaction outcomes. Even though there has been a certain amount of research carried out in this regard, to the best of our knowledge, these have not been reviewed comparing the data so far available.

Phenolic interactions are of importance for designing novel food products, particularly functional foods. It is a matter of fact that the results of mentioned interactions are significantly different at lab-scale calculations using purified standard phenolic compounds rather than in-matrix interactions of real food systems. For instance, estimations indicated synergism for the antioxidant activity in samples (coffee−cinnamon phenolic interaction), while real phenolic extracts might reveal distinctive and even opposite results for bioactive properties. Furthermore, food matrix exposure to gastrointestinal digestion (in vitro) will end up with varying biological activities of interacted coffee and accompanier food phenolics. For health-promoting activities of coffee-based food/beverage products and also for all complex food matrices, phenolic−phenolic interactions before and after digestion require further consideration. In the literature, still there is a lack of information covering the mentioned synergism/antagonism phenomena of phenolic−phenolic interactions for different food products, which is a significant subject not only for the food industry but also for individual household consumptions targeting conscientious, healthy and balanced diets.

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### Notes

The authors declare no competing financial interest.

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Beyza Vahapoglu obtained her B.S.c in Food Engineering from the Istanbul Sabahattin Zaim University. Currently, she is continuing her master's degree in Food Science and Technology at Istanbul Technical University.

Dr. Esra Capanoglu received her Ph.D. from Istanbul Technical University in 2008. She became an Associate Prof. in 2014 and Professor in 2019. Her research areas include the investigation of antioxidant activity and in vitro bioaccessibility of bioactive materials, effect of food matrix and processing on the content and bioaccessibility of phenolics and carotenoids, and waste valorization of fruits and vegetables.

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*ACS Omega* 2022, 7, 1595−1601