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Non-extractable Polyphenols:
Important Dietary Polyphenols That Have Been Ignored

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Abstract

Polyphenols are a type of phytochemical widely consumed in the human diet which have been linked to health benefits including the prevention of several major chronic diseases, such as cancer.

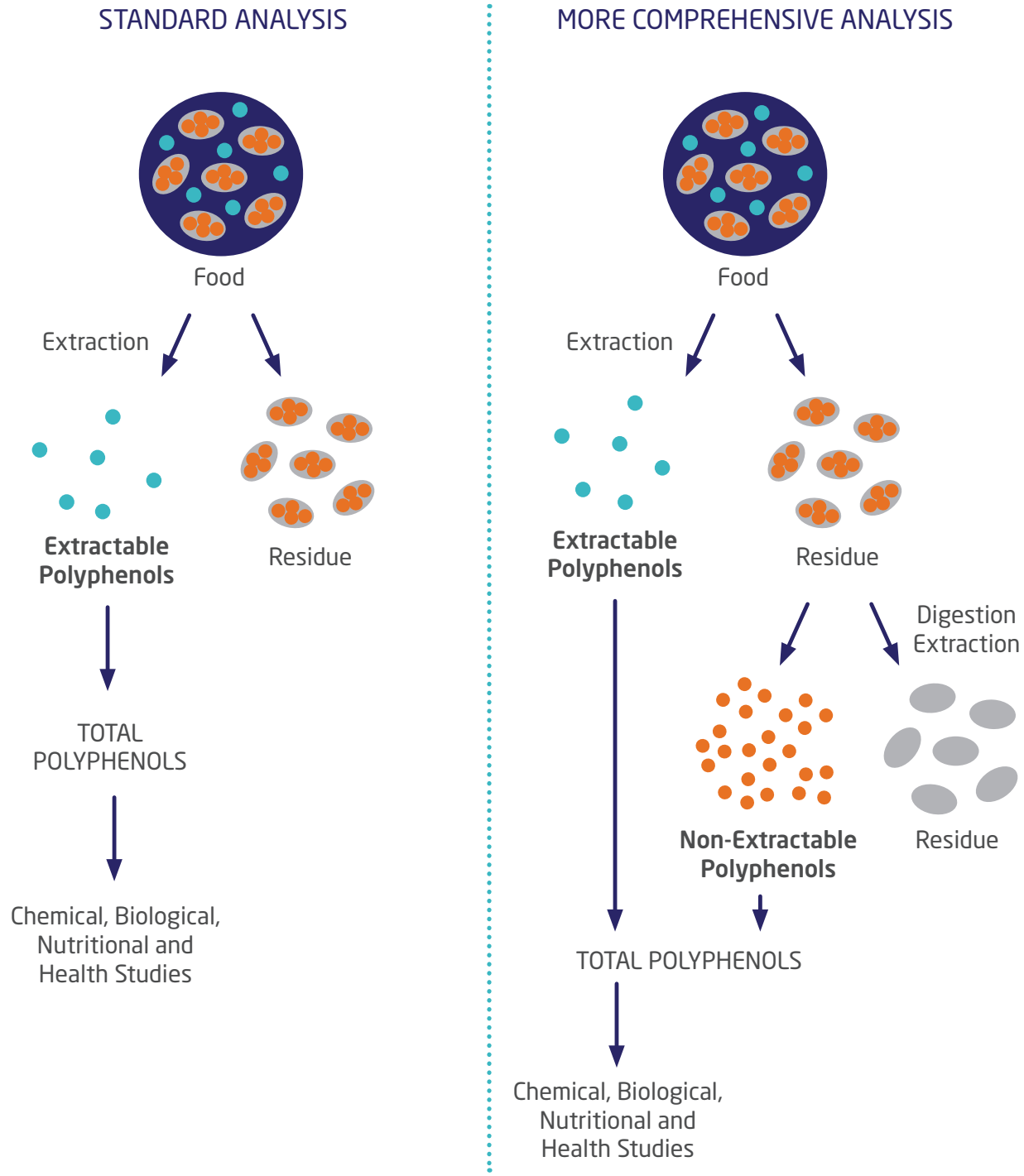
However, current chemical, biological, nutritional and health research has focused mainly on extractable polyphenols (EPPs) only, due to analytical limitations, and so non-extractable polyphenols (NEPPs) have effectively been ignored to date.

NEPPs are dietary polyphenols trapped in the food matrix, and thus are not soluble during aqueous and organic solvent extraction.

Evidence is accumulating to support the beneficial biological functions of NEPPs from a wide range of foods. NEPPs are bioavailable in the colon and have been shown to improve gastrointestinal health by modulating gut microbiota and gene expression.

More research is warranted on the potential health benefits of NEPPs in relation to their chemical and biological properties, which will, in turn, facilitate the use of underutilized food by-products, such as fruit peels, that contain a high abundance of NEPPs.

Graphical Abstract



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Polyphenols

Polyphenols, which include a variety of chemical structures with multiple phenol groups, are the most commonly consumed dietary antioxidants [1,2]. Their consumption has been associated with the prevention of several major chronic diseases [3,4].

Epidemiological studies have suggested that polyphenols may be a major factor responsible for the protective effects of fruits and vegetables against chronic diseases, such as cardiovascular disease and cancer [6-9]. Therefore, polyphenols have been subjected to extensive studies.

> Consumption has been associated with the prevention of several major chronic diseases

Extractable and Non-Extractable Polyphenols

Current biological, chemical, nutritional and health studies of polyphenols typically consider the polyphenols that can be extracted by aqueous and/or organic solvents from food matrices, namely the extractable polyphenols (EPPs)[10-12]. EPPs usually have relatively low molecular weight and dissolve in the stomach and small intestine after oral administration. Some examples of EPPs are hydrolysable tannins, stilbenes, flavonoids, extractable proanthocyanidins and hydroxycinnamic acids [12].

On the other hand, non-extractable polyphenols (NEPPs) are also present in food matrices, but they are not soluble during aqueous/organic solvent extraction. These NEPPs generally have high molecular weight and low solubility, and are physically or chemically bound to macromolecules in foods, such as fiber, which renders them non-extractable [10-12]. The majority of NEPPs are resistant to digestion and absorption in the stomach and small intestine, and therefore reach the colon intact. However, the microbiota in the colon produce enzymes that release and/or breakdown NEPPs, thus making them bioavailable in the colon, and so realize their potential health effects [11,12].

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Importance of Non-Extractable Polyphenols

NEPPs were discovered during a study on carob pods that revealed their existence in the residue that was obtained after extraction of soluble components12. Since then, further studies have been carried out on various fruits, vegetables, nuts and grains to characterize the NEPPs in these foods [10-12].

Some foods contain more NEPPs than EPPs [2,13]. Acai fruit, cranberry pomace and banana are some examples of foods with a high content of NEPPs. In banana, the NEPP content is 100-fold higher than that of EPP [11,14-16]. Ripeness affects the level of NEPPs in plums, with contents peaking during initial stages of ripening and then decreasing as the end of the process is reached [17].

Studies have examined the levels of NEPPs in Spanish Mediterranean and rural Mexican diets. Both diets contain different types of foods, but NEPPs were found to be a major part of the dietary antioxidants in both diets [2,11,18]. These results attest to the relevancy of NEPPs in human diets and highlight the importance of including NEPPs in health research.

Metabolic Fate of Non-Extractable Polyphenols

Unlike EPPs, NEPPs are insoluble and thus not bioavailable in the stomach or small intestine [12,19]. When NEPPs reach the colon, however, they can be released from the food matrix by gut microbiota fermentation and/or colonic enzyme activities [11,12].

Some NEPPs released in the colon include non-extractable proanthocyanidins (NEPA), hydrolysable phenolics, and hydrolysable tannins. These released NEPPs are then subjected to further metabolism by gut microbiota to produce various metabolites. Some metabolites of NEPA include epicatechins, valerolactones, flavanols, hippuric acids, hydroxyphenylpropionic acids, and hydroxyphenylacetic acids. Most of the hydrolysable phenolics are made up of ferulic acid that can be metabolized further to yield dihydroferulic acid and other phenolic acids. Hydrolysable tannins can be converted to ellagitannins that can be further metabolized to ellagic acid and urolithins [12]. Metabolites of NEPPs have been found in the colon of both animals and humans.

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After being produced in the colon, NEPP metabolites are transported through the portal vein to the liver where further metabolism can occur. The metabolites are then circulated in the bloodstream or transported back to the intestine through bile secretion. The metabolites are ultimately secreted via feces and urine.

This suggests that there are different timings associated with the circulation of NEPP and EPP metabolites both locally (in the gastrointestinal tract) and in different sites such as liver and lung [11,12].

Health Benefits of Non-Extractable Polyphenols

The bioavailability of NEPPs in the colon warrants examination of their biological effects in this location, for example their interaction with gut microbiota, and effects on colon endothelial function and related diseases such as colon cancer [10,12].

While clinical trials on NEPPs are still scarce, animal studies have reported potential health benefits, especially with respect to gastrointestinal health and cardiovascular disease.

NEPPs have been reported to increase intestinal antioxidant activity [20-22], enhance lipid secretion, modulate Lactobacillus growth [22,23], increase stool weight, and reduce stool transit time as well as exposure to toxic compounds [19,19,24,25].

NEPPs have also shown potential chemopreventive effects against colon cancer by reducing the abnormal crypts in the colon [26], down-regulating genes associated with tumor development, and up-regulating tumor-suppressing genes [27]. During those animal studies, no toxicity of NEPPs was reported [11].

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Conclusion

NEPPs are important dietary polyphenols with high potential for producing health benefits. However, only very limited understanding of NEPPs is available due to the fact that NEPPs have been largely ignored by the most studies on dietary polyphenols in favor of EPPs.

A greater number of in-depth investigations is necessary to elucidate the health benefits of NEPPs as well as their mechanisms of action; this will then encourage the utilization of NEPPs from various food products, especially NEPP-rich by-products such as pomace.

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