Introduction and perspective

Coffee is arguably one of the most studied components of our diet, with an extensive range of research published in areas of mental performance, sports performance, fluid balance, type 2 diabetes, liver function, neurodegenerative disorders, pregnancy, cancer, and cardiovascular disease (CVD). Research investigating associations between coffee intake and the risk of CVD presents an interesting overview suggesting that a moderate intake of coffee is associated with a reduced mortality from CVD\textsuperscript{1–4}.

Polyphenols are plant-based compounds. There is much interest in their potential role in health through antioxidant and anti-inflammatory effects. Coffee is one of the main sources of polyphenols in the diet, and polyphenols in coffee contribute to the unique flavours and aromas that typify coffee beverages\textsuperscript{5}. Additionally, there is growing interest in the role of polyphenols in health.

A moderate intake of coffee is associated with a reduced risk of developing type 2 diabetes, metabolic syndrome, and certain cancers as well as CVD. Research suggests that a moderate intake of coffee of 3–5 cups a day is associated with a 15% reduced risk of CVD\textsuperscript{1–4}. Although the precise mechanism of action is still not clarified, it is suggested that polyphenols in coffee could exert antioxidant and anti-inflammatory effects including having pivotal roles on lipid and glucose metabolism, thereby contributing to the reduced risk of CVD\textsuperscript{6–8}.

This report gives a brief outline of the current research on polyphenols, coffee and CVD highlighting a potential role for these compounds in reducing the risk of CVD. Although there are a number of studies available, further research is required to understand the associations and mechanisms of action in more detail.

This report is suitable for healthcare professionals, researchers and medical journalists. It is not intended as a scientific review of the literature, rather as a general overview of current scientific research, and where this research could be developed in future.

“Research suggests that a moderate intake of coffee of 3–5 cups a day is associated with a 15% reduced risk of CVD\textsuperscript{1–4}.”
What are polyphenols and where are they found?

Nutrients comprise of macronutrients (carbohydrate, fat and protein), which are digested and stored or used in the body and micronutrients (vitamins and minerals) which are stored or temporarily retained in the body and facilitate basic biochemical processes. They also comprise of numerous other compounds that are not stored in the body and do not contribute directly to basic chemical processes. The latter group helps to fine tune cells, protect against stress and to improve long-term health in various ways — polyphenols are a diverse group of molecules that belong to this group.

Polyphenols are plant based substances and include compounds such as flavonoids, tannins and phenolic acids. They are the largest group of phytochemicals (plant based chemicals) and are found in a variety of foods including fruit, vegetables, whole grains, tea, coffee, cocoa and wine\(^5\) (Table 1).

### Table 1 Types of polyphenols in foods and beverages

<table>
<thead>
<tr>
<th>CHEMICAL CLASS</th>
<th>MOST COMMON EXAMPLES</th>
<th>RICH SOURCES</th>
</tr>
</thead>
<tbody>
<tr>
<td>Flavanols</td>
<td>Catechins, gallicatechins (monomeric and oligomeric)</td>
<td>Tea (epicatechins, gallicatechins, theaflavins), cocoa (epicatechin, procyanidins), apples, broad beans (epicatechin)</td>
</tr>
<tr>
<td>Flavanones</td>
<td>Hesperidin</td>
<td>Citrus fruit</td>
</tr>
<tr>
<td>Flavonols</td>
<td>Quercetin, rutin</td>
<td>Tea, apples, onions</td>
</tr>
<tr>
<td>Hydroxycinnamic acids</td>
<td>Chlorogenic acids (caffeoylquinic acids)</td>
<td>Coffee, chicory, artichoke, plum, pears</td>
</tr>
<tr>
<td>Anthocyanins</td>
<td>Cyanidin</td>
<td>Berry fruits</td>
</tr>
<tr>
<td>Stilbene</td>
<td>Resveratol</td>
<td>Grape skins</td>
</tr>
</tbody>
</table>

Adapted from Williamson G 'The role of polyphenols in modern nutrition'\(^5\)

Stilbene information from Reinisalo\(^9\)
Polyphenols in the diet

The types of polyphenols found in the diet depend on the type and variety of plant based foods consumed.

In Japanese women, the main source of polyphenols in the diet was found in coffee, followed by green tea, black tea, chocolate, beer and soya sauce. Cereals/noodles, vegetables, fruits, beans, seeds and seasonings also contributed to polyphenol intake in this cohort.

Epidemiological studies in a European cohort suggested that the main sources of polyphenols were coffee, tea, and fruits. The authors commented on the high variability of intakes between European populations, particularly between Mediterranean and non-Mediterranean countries. In Spanish adults cherries, chocolate, coffee, apples, and olives were the major sources of variability in polyphenol intake across the diet.

Results from a cohort of UK women suggested that flavanols and hydroxycinnamic acids were the most important polyphenols, provided by tea and coffee. Other major polyphenol sources included fruits, vegetables and processed foods. Interestingly, older women consumed more polyphenol-containing foods and beverages, because of their higher coffee and tea consumption.

Coffee and Polyphenols

Coffee is a valuable source of polyphenols in the diet, and research suggests that it is a key provider of antioxidants in the diet of the populations of some European countries, including Italy, Finland, France and Spain.

Chlorogenic acids, members of the group of hydroxycinnamic acids, are the main types of polyphenols found in coffee making up 7–9% of coffee by weight. Chlorogenic acids are degraded by heat so that levels in roast coffee beans are lower than green coffee. Levels of chlorogenic acids in coffee vary depending on the type of coffee bean and the intensity and length of the roasting process. The metabolism of chlorogenic acids from coffee is now quite well understood, involving a critical action of the gut microbiota, and knowledge on the plasma metabolites of chlorogenic acids. Polyphenols from coffee are highly bioavailable; about 30% are absorbed in the circulation.
Coffee consumption and health

Habitual consumption of 3–5 cups of coffee per day is associated with a 15% reduction in the risk of CVD\textsuperscript{1–4}. Importantly, a higher coffee consumption is not associated with elevated CVD risk. In people who have already suffered a CVD event, a typical consumption of 1–5 cups/day is associated with a lower risk of death compared to those who do not consume coffee, suggesting that habitual consumption does not increase the risk of a recurrent CVD or death\textsuperscript{4}.

Data from the Health Survey of São Paulo suggests that a coffee intake of 1–3 cups/day is associated with a reduced risk of elevated blood pressure and hyper-homocysteinaemia, a risk factor for CVD\textsuperscript{16}.

What are the roles of polyphenols in the body?

Epidemiological research suggests that there is an association between the consumption of polyphenol rich vegetables and a reduction in CVD prevalence\textsuperscript{6}.

Research has suggested that those with a higher intake of flavonoids had a 47% lower incidence of cardiovascular events compared to those with the lowest intake after adjusting for potential confounders. No significant associations were seen for other polyphenol types\textsuperscript{12}.

It was found in Polish adults that body mass index (BMI), waist circumference (WC), blood pressure, and triglycerides were significantly lower among individuals with a higher polyphenol intake, although a linear association was found only for BMI and WC\textsuperscript{7}. The researchers also investigated the potential effects of individual classes of polyphenols suggesting that hydroxycinnamic acids, flavanols, and dihydrochalcones had the most relevant role\textsuperscript{7}.
How might polyphenols reduce the risk of CVD?

Whilst there may be an association between the consumption of polyphenol-rich plant foods and a reduced risk of CVD, the precise mechanisms are not fully understood.

Polyphenols may have a range of cardio protective functions. They may alter hepatic cholesterol absorption, triglyceride biosynthesis and lipoprotein secretion, the processing of lipoproteins in plasma, and inflammation. Polyphenols have also been shown to decrease the activity of specific enzymes, to improve endothelial function and blood pressure, and to counteract the development of atherosclerosis.$^{6,8,17,18}$

Chlorogenic acids are of special interest due to their wide spectrum of potential health benefits e.g. antioxidative, anti-diabetic, anti-carcinogenic, anti-inflammatory, and anti-bacterial effects$^8$. The different pathways and their potential interaction in the generation of diseases are illustrated in Figure 1.

Figure 1 Putative mechanisms of action of chlorogenic acids and their effects on physiological systems on health (adapted from Tajik et. al 2017)$^8$. 

<table>
<thead>
<tr>
<th>Molecule</th>
<th>Function</th>
</tr>
</thead>
<tbody>
<tr>
<td>HMGR</td>
<td>3-hydroxy-3-methylglutaryl coenzyme A reductase</td>
</tr>
<tr>
<td>PPAR-α</td>
<td>peroxisome proliferator-activated receptor-α</td>
</tr>
<tr>
<td>CPT</td>
<td>carnitine palmitoyl transferase</td>
</tr>
<tr>
<td>AMPK</td>
<td>AMP-activated protein kinase</td>
</tr>
<tr>
<td>GIP</td>
<td>glucose-dependent insulinotropic peptide</td>
</tr>
<tr>
<td>G-6-Pase</td>
<td>glucose-6-phosphatase</td>
</tr>
<tr>
<td>ROS</td>
<td>reactive oxygen species</td>
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</table>
Potential effects of polyphenols and coffee on men and women

Health evaluations often identify differences between men and women, and there is some evidence this is the case for polyphenols too.

As previously mentioned Polish adults with a higher polyphenol intake had a lower risk of a high waist circumference, high blood pressure, high lipoprotein cholesterol, and triglycerides in women, and fasting plasma glucose in both men and women7.

Postmenopausal women specifically noted that a higher dietary polyphenol intake was associated with a reduced risk of CVD, suggesting that an increased intake of polyphenols may be valuable for this group of women19. Further research is, however, required to understand the association in more detail, and to compare with men. Some benefits have been seen in a group of Japanese women in relation to polyphenol levels and diabetes incidence20. However, it should be noted that a recent meta-analysis did not find a significant difference between coffee consumption and risk of type 2 diabetes between women and men21.

Whilst chlorogenic acids are one of the main components of coffee that is potentially associated with the reduced risk of CVD, there are very few specific intervention studies looking at pure chlorogenic acids in humans. One small study where chlorogenic acid-rich green coffee extract was administered for 12 weeks decreased both systolic and diastolic blood pressure, but did not affect body mass index or pulse rate in patients with mild hypertension22.

One of the main difficulties in drawing conclusions on the effect of coffee polyphenols on CVD risk is separating out the effects of the various components of coffee including caffeine. Further evidence is necessary to understand the potential roles for polyphenols on CVD prevention and treatment18.

“Postmenopausal women specifically noted that a higher dietary polyphenol intake was associated with a reduced risk of CVD, suggesting that an increased intake of polyphenols may be valuable for this group of women19.”
Practical advice for Health Care Professionals on coffee consumption

Coffee drinking is an enjoyable part of the daily routine for many, a cup of coffee provides a range of compounds including caffeine and polyphenols.

Research suggests that a regular moderate coffee intake can help to reduce the risk of various diseases including CVD.

A moderate intake of coffee is approximately 3–5 cups of coffee a day\(^\text{23}\).

Pregnant women should limit their caffeine intake to 200mg caffeine per day (EFSA 2015) [a cup of coffee provides 75–100mg caffeine].

Individual advice is best, and health care professionals can help their patients by providing tailor made advice specific to their lifestyle and health.
About Professor Kjeld Hermansen

Kjeld Hermansen graduated in medicine from Aarhus University and became DrMedSci from Aarhus University 1981 (“Secretion of somatostatin from the normal and diabetic pancreas: studies in vitro”). He is chief physician at Department of Endocrinology and Internal Medicine, Aarhus University Hospital and professor in clinical nutrition at Copenhagen University. Prof Hermansen has been primary investigator in a number of national and international nutritional and pharmaceutical projects. He has been president of the Danish Endocrine Society and the of the Diabetes and Nutrition Group under EASD. He is member of “The Council on Health and Disease Prevention” and has served as chairman in developing the report “Coffee, Health and Diseases” (2015). He has more than 330 peer reviewed publications, has given more than 500 oral presentations and has 4 patents (incl on cafestol as antidiabetic treatment).

EXPERT REPORT
Coffee, polyphenols and cardiovascular disease

About ISIC

The Institute for Scientific Information on Coffee (ISIC) is a not-for-profit organization, established in 1990 and devoted to the study and disclosure of science related to “coffee and health.” Since 2003 ISIC also supports a pan-European education programme, working in partnership with national coffee associations in nine countries to convey current scientific knowledge on “coffee and health” to health care professionals.

ISIC’s activities are focused on:

- the study of scientific matters related to “coffee and health”
- the collection and evaluation of studies and scientific information about “coffee and health”
- the support of independent scientific research on “coffee and health”
- active dissemination of balanced “coffee and health” scientific research and knowledge to a broad range of stakeholders.

ISIC respects scientific research ethics in all its activities. ISIC’s communications are based on sound science and rely on scientific studies derived from peer-reviewed scientific journals and other publications.

ISIC members are six of the major European coffee companies: illycaffè, Jacobs Douwe Egberts, Lavazza, Nestlé, Paulig, and Tchibo.

About coffeeandhealth.org

The website www.coffeeandhealth.org is a science-based resource developed for health care and other professional audiences and provides the latest information and research into coffee, caffeine and health.

Follow us on twitter: @coffeeandhealth
References


18. EFSA Panel on Dietetic Products, Nutrition and Allergies (NDA) (2015) Scientific Opinion on the substantiation of health claims related to caffeine and increased fat oxidation leading to a reduction in body fat mass (ID 735, 1484), increased energy expenditure leading to a reduction in body weight (ID 1487), increased alertness (ID 736, 1101, 1187, 1485, 1491, 2063, 2103) and increased attention (ID 736, 1485, 1491, 2375) pursuant to Article 13(1) of Regulation (EC) No 1924/20061. EFSA Journal, 9(4):2054.