Current Clinical and Medical Education

Received 05 Apr 2023 | Revised 06 Apr 2023 | Accepted 05 Jun 2024 | Published Online 08 Jun 2024

Published By: Vision Publisher

ISSN 2942-0776

CCME 02 (6), 63-76

Natural Products with Health Benefits, Mass Spectrometry in Phytonutrient and Methods with Mass spectrometry (MS) [Liquid Chromatography Mass Spectrometry (LC-MS) and Gas Chromatography Mass Spectrometry (GC-MS)

Russul Ali Hashim [1], Shahad Salman Ahmed [2], Maryam Abbas Hassoon [3], Rafal Handhal Bandar [4], Walaa Falih Mahdi [5]

[1]Al-Qasim Green University, College of Food Sciences, Department of Food Science and Technology, Iraq.

[2]Al-Qasim Green University, College of Food Sciences, Department of Dairy Science and Technology, Iraq.

[3]Al-Qasim Green University, College of Food Sciences, Department of Dairy Science and Technology, Iraq.

[4]Al-Qasim Green University, College of Food Sciences, Department of Food Science and Technology, Iraq.

[5]Al-Qasim Green University, College of Food Sciences, Department of Dairy Science and Technology, Iraq.

Abstract: Now more than ever, nutritious eating is essential, as many inflammatory disorders can be prevented with a well-rounded, minimally processed diet. Here, ascomycetous fungus, truffles, and edible hypogeous (10-30 cm below ground) fungi show promise. Their culinary and nutritional worth is already well-known. The nicknames "underground gold" and "diamond of the kitchen" attest to their great esteem in the haute cuisine (gourmet) community. Nevertheless, they have a very small customer base. Because of their low production, they are pricey and beyond of reach for most people around the globe. The current world truffle production of hundreds of metric tonnes is woefully inadequate. White truffles, which are in extremely high demand but supply is severely lacking, can cost as much as $5,000 USD per kilogramme (but other varieties, particularly desert truffles, can be far less expensive). Because of its prohibitive cost, this gourmet treat is reserved for the most affluent diners. More people will be able to afford truffles and enjoy their advantages if their yield can be increased globally. To achieve this goal, integrative methods like fermentation and artificial inoculation can be used. This revised evaluation is an attempt to make a contribution in this area. Thus, this study aims to For thousands of years, early humans relied on gut feelings, intuition, and trial and error to determine which natural substances would be most effective in treating common health problems. In terms of biodiversity, India is among the top countries in the world. Its botanical diversity exceeds 47,000 species. Of these, approximately 20,000 are considered to have therapeutic significance. The World Health Organisation found that traditional medicine is the main source of health treatment for 80% of the people in underdeveloped nations. At the present time, the herbal medicine market is worth more than $60 billion worldwide. The medical plant based industry has great promise and has immense economic growth potential due to the significant role that medicinal plants play in human health through their therapeutically active compounds and nutritional supplements. In industrialised nations, nutraceuticals, also known as health foods, are in high demand

Keyword: Natural Products, Mass Spectrometry, Liquid Chromatography GC-MS.

Corresponding Author: Russul Ali Hashim †, Al-Qasim Green University, College of Food Sciences, Department of Food Science and Technology, Iraq.

Supplementary information The online version of this article (https://doi.org/xx.xxx/xxx.xx) contains supplementary material,which is available to autho-rized users.

Introduction

A wide variety of secondary metabolites with low molecular weights that are chemically and physiologically varied are grouped together as phytonutrients, also known as phytochemicals. Not only may you find these NPs in fruits and vegetables, but also in spices and other traditional seasonings; they aren't strictly necessary for human nutrition. Many NPs are ingested by people on a daily basis in many forms, including food, spices, traditional ingredients, and medicinal plants. These substances can all have positive or negative impacts on the body. Due to their diverse physiochemical characteristics, these chemicals necessitate specialised analytical techniques for profiling, identification, and quantification in either their native matrices or bodily fluids [1-3]. Functional foods are those that are abundant in bioactive components; this category includes foods like fruits, vegetables, and whole grains. While the exact meaning of a "functional food" is up for debate, the International Food Information Council uses the term to describe foods that have additional health advantages beyond their nutritional value. The American Dietetic Association defines functional foods as "foods that have a potentially beneficial effect on health when consumed as part of a varied diet on a regular basis, at effective levels." This includes both whole foods and those that have been fortified, enriched, or enhanced. Phytonutrients, which are secondary metabolites found mostly in plants, are among the most common bioactive dietary components. Zoonutrients, which are derived from animals, and products of some microorganisms can also contain these components. Like vitamins, the concentration of bioactive components in food varies with the genotype of the plant or animal, growing circumstances, and processing techniques; therefore, only analysis can reveal the precise concentration of these components in a particular food. Supplemental sextracts or concentrates, in contrast to whole foods, may provide detailed analytical information [4], albeit this is not yet mandated. In addition to having positive effects on human health when consumed in food, bioactive NPs have served as a model for the majority of pharmaceutical active ingredients. They likely have a lot in common chemically, evolved to produce physiologically active compounds, or have structural similarities with protein targets across many species, all of which contribute to their effectiveness in drug discovery. Up until 1996, natural products were the source of inspiration for or directly derived from over 80% of pharmaceutical drugs. Newer research shows that natural products are still important for drug discovery [5, 6]. There has to be improved regulation of the safety and effectiveness of phytopreparations and herbal medications, which are becoming increasingly popular among the general population as natural medicines. The fact that several of these plant extracts have potential applications in the production of functional foods raises concerns about their appropriate application. There are various sources from which bioactive NPs are sourced. Depending on the countries they could potentially reach, they could be sold as phytomedicines, dietary supplements, or functional foods, all of which have the potential to bear health claims and be utilised for disease treatment. It should come as no surprise that different categories of products make varying safety and effectiveness claims.

Time-Honored Recipe Items (Essential Meals)

Foods and dietary components that are said to have health benefits beyond basic nutrition are called functional foods or neutraceuticals. These nutrients are present in many different diets, including regular foods, foods that have been fortified or enhanced, and even some dietary supplements. But there is still no comprehensive regulation, even though herbal products are becoming increasingly popular. It is true that there are various methods for delivering phytonutrients derived from herbs and botanicals, and these methods may provide varying degrees of control. One side of the coin is that they can be legally sold as nutritional supplements in the form of tablets, powders, or capsules. However, they can be consumed as additives in traditional foods (such as teas, juices, chips, and energy bars) and can thereafter be regulated accordingly [8, 9]. Problems with quality control and standardisation requirements, as well as a lack of clarity between phytopharmaceuticals and nutraceuticals, arise from the fact that laws governing the use of traditional ingredients and phytopharmaceuticals differ greatly from one country to another. As an extreme example, in the US, you can find chocolate energy bars containing Hypericum perforatum (Saint John's wort) extracts, but in Switzerland, you can only find this preparation in pharmacies due to serious issues with drug interactions.

The Most Important Groups of All-Natural Health Foods

Primary and secondary metabolites are the two most common types of NPs found in plant and vegetable sources. In contrast to primary metabolites, which play an essential role in an organism's development and reproduction, secondary metabolites are organic chemicals that play no such role. Secondary metabolite deficiency does not cause instant death as primary metabolite deficiency does; instead, it may lead to impaired fertility, aesthetics, or survivability [9–11] or maybe no change at all. To entice pollinators and insects that disperse seeds, as well as to shield themselves from predators and harmful ultraviolet (UV) rays, plants produce these compounds. Plants also rely on phytochemicals, which serve as flavour and colour indicators, to signal to nitrogen-fixing bacteria to establish root nodules. Rare secondary metabolites are typically found only in a small number of closely related species. Therefore, phytonutrients include a wide variety of plant chemicals with different structures and physiological functions.

Polyphenols

Having a minimum of one aromatic ring and a maximum of one or more hydroxyl groups attached makes polyphenols secondary metabolites from plants. At now, we know of around 8,000 phenolic structures. Tannins and proanthocyanidins are examples of complex high-molecular-weight chemicals, while phenols, phenolic acids, and flavonoids are examples of more basic molecules. You can find them conjugated to sugars and organic acids; they originate biogenetically in plants through the shikimate and acetate synthesis pathways.

Extensive study on the health benefits of polyphenols in the diet has been conducted over the past 15 years, providing strong evidence that polyphenols can help avoid degenerative diseases, especially cancer and cardiovascular disease. Although polyphenols have long been known for their antioxidant capabilities and their ability to neutralise free radicals produced during cell oxidation, it is now apparent that polyphenols' mechanisms of action extend well beyond this. 12 There is no nutrient that contributes more to the antioxidant capacity of the human diet than polyphenols. Their daily consumption might reach 1 g, which is ten times more than the recommended daily allowance for vitamin C and one hundred times more than the recommended daily allowance for vitamin E and carotenoids combined. Fruits and drinks made from plants, including tea, coffee, red wine, and fruit juices, are the primary food sources of polyphenols [12–15]. A person's overall polyphenol intake can be increased by eating more vegetables, cereals, chocolate, and dry beans. The following is a quick rundown of the many types of phenolic compounds found in plants.

Essential Oils

Many plant species contain simple C6 -phenols, including phenol, cresol, thymol, and resorcinol. The hydroxybenzoic and hydroxycinnamic acid classes are two of the most abundant subgroups of phenolic acids. All hydroxybenzoic acids share the same C6-C1 structure as phenolic acids and aldehydes; these acids include gallic, p-hydroxybenzoic, protocatechuic, vanillic, and syringic acids. Conversely, hydroxycinnamic acids [16, 17] are aromatic molecules that often have a three-carbon side chain (phenylpropanoid derivatives, C6-C3). The most prevalent of these acids are caffeic, ferulic, p-coumaric, and sinapic acids. There is a lack of information regarding phenylacetic acids and acetophenones (C6-C2).

Flavonoids

High amounts of flavonoids (C6-C3-C6) are found in fruit and leaf skins, and these secondary metabolites play significant and diverse activities. They are commonly consumed by humans because they can be found in a variety of foods such as fruits, vegetables, cereals, tea, wine, roots, stems, and flowers. Flavones, flavonols, iso-flavones, flavanones, and anthocyanidins are the primary subclasses of flavonoids. Less important from a dietary standpoint are the other flavonoid families, which include dihydroflavones, flavan-3,4-diols, coumarins, chalcones, dihydrochalcones, and aurones [18, 19]. There are a lot of possible constituents for the basic flavonoid skeleton, although hydroxyl groups are typically found at positions 4, 5, and 7. Glycosides are the natural form of most flavonoids. Flavonoids are water-soluble due to the presence of sugars and hydroxyl groups; yet, they are lipophilic due to other constituents like methyl or isopentyl groups.

To classify flavonoids, which are benzo-g-pyrones, one can look at their precursors. One way to classify flavonoids is as benzo-g-pyrones; these compounds can be further classified according to the pre- To classify flavonoids, which are benzo-g-pyrones, one can look at the amount of benzo-g-pyrone ring saturation as well as the kinds of substituents that are present. A chain reaction involving condensation between malonyl residues (A-ring) and hydroxycinnamic acid (B-ring) produces these compounds; the C-ring's carbons 2, 3, and 4 are carbons of the hydroxycinnamic acid residue. In pure flavonoids, the B-ring is located at C-ring position 2, whereas in iso-flavonoids, it is at C-ring position 3. Flavones, flavonols, and their dihydroderivative [20–14] counterparts, as well as flavanones and flavanolols, can have g-pyrone as their C ring. Flavonoids can be found in a variety of plant types. The aglycones of flavonoids can be connected at various places by C- or C-O-C bonds, allowing them to exist as dimers (biflavonoids).

Nevertheless, glycosylation, which can take the form of O-glycosides or C-glycosides, is the most common alteration. Plants store flavonoids in cell vacuoles efficiently, and glycosylation makes them more polar. A sugar is attached to the aglycone in C-glycosides through an acid-resistant C-C bond, whereas in O-glycosides the aglycone is connected to the sugar through an acid-labile hemiacetal bond [25]. Anthocyanidins, flavonols, and flavanols have 3-and 7-hydroxyl groups, flavones, flavanones, and isoflavones have 7-hydroxyl groups, and flavonols and flavanols have 3- and 5-hydroxyl groups that are glycosylated most frequently in O-glycosides. Rarely glycosylated because the 5-hydroxyl group hydrogen bonds with the carbonyl group in the majority of flavonoids. It has been documented that C-glycosylation exclusively takes place at the C-6 and C-8 sites on the B-ring. Flavonoid glycosides primarily include glucose as their sugar, although they may also contain galactose, rhamnose, xylose, and arabinose; mannose, fructose, and glucuronic and galacturonic acids are uncommon [26, 27]. It is not uncommon to find disaccharides like neohesperidose [rhamnosyl-(a1-42)-glucose] and rutinose [rhamnosyl-(a1-46)-glucose]. Rarely, higher oligosaccharides may also be present. Acetylation and coupling with malonyl residues are two ways the sugars can be changed.

Insect food dyes

Anthocyanins are pigments that give many natural foods their red, blue, and purple hues. They are most commonly found in the flesh of fruits and flowers. The plant parts that contain them include the stems, leaves, seeds, and roots. They shield the plant's mesophyll cells from direct sunlight by drawing the shade down from the leaves. They also help bring in pollinating insects, which is a crucial function they do. The anthocyanins used in this study are derived from the flavylium cation (2-phenylbenzopyrylium) and are O-glycoside and acylglycoside conjugates of anthocyanidins [28]. As sugar conjugates, the most common anthocyanidins in plants are pelargonidin, cyanidin, delphinidin, peonidin, petunidin, and malvidin. The most common sugars in plants are arabinose, D-glucose, L-rhamnose, D-galactose, and D-xylose.

Vitamin A

The carotenoids, which comprise the more specific compounds carotenes and xanthophylls, are a subset of the terpenoids and isoprenoids, two broader classes of plant chemicals. As pigments, carotenoids may soak up light and give the illusion of colour. Plants create carotenoids as photosynthetic pigments and as photoprotective entities[29,30], however their functional significance in human nutrition is mostly associated with molecular defence against free radical assault. There are two ways in which carotenoids contribute to photosynthesis. Carotenoids transmit energy from light to chlorophyll by first acting as photoreceptors. Plants often use carotene as part of their light-harvesting system, while xanthophylls may have a more general function in this regard. Secondly, carotenes seem to act as a "sink" for the triplet states generated during light stimulation of chlorophyll, safeguarding biological membranes and other molecules in plant tissue; this suggests that their primary function is more protective in nature. Chromoplasts are specialised organelles found in plants, particularly fruits and vegetables. This is when they start to make a wide range of carotenoids, including yellow, red, and orange pigments, but they also stop being able to make chlorophyll. For instance, in order to alter the visual traits of the fruit bearing seeds, a tomato's chloroplasts transform into chromoplasts as it ripens, resulting in a decrease in chlorophyll and photosynthetic enzyme production and an increase in the red carotenoid pigment lycopene. 18 Among the several functions shared by provitamin A carotenoids, b-carotene was first identified in humans as a precursor to vitamin A [31, 32]. As biological antioxidants, carotenoids shield human cells and tissues from free radicals and singlet oxygen, two potentially harmful substances. When exposed to singlet oxygen, lycopene effectively neutralises its damaging potential. It is thought that lutein and zeaxanthin serve as antioxidant defences in the human retina's macular area. Carotenoids also help the immune system work better, shield the skin from the sun's rays, and even prevent some cancers from developing (lycopene, for example, is protective against prostate cancer).

Glucosinolates and Thiosulfinates

Glucosinolates are a type of secondary metabolite that is unique to the Capparales plant order and contains sulphur and nitrogen. Originally discovered in mustard seeds, they were first isolated in the 1830s. Approximately 500 species, including many edible ones, contain over 120 glucosinolates; the majority of these species are members of the Brassicaceae family. The sulfur-linked b-D-glucopyranose and amino acid derived side chains make up the b-thioglycosyl N-hydroxysulfate moiety of glucosenolates. Aliphatic, alkenylic, aromatic, hydroxyalkyl benzoated, indolic, sulfur-containing, and ketoderivative side chains are all possible, as are a variety of structures that can be glycosylated several times. In their inert form, glucosinolates found in spices and cruciferous vegetables including cabbage, broccoli, cauliflower, cress, mustard, and horseradish can be transformed into hazardous compounds when plant cells are damaged and their contents combine. The odour of certain cruciferous vegetables, such radishes, cabbage, and broccoli, is caused by these chemicals, which may discourage animals from eating them. Plant tissue trauma permits glucosinolates from certain cells to mix biotics with enzymes in other cells, creating the derived compounds such as isothiocyanates, thiocyanates, and nitriles. In addition to protecting against herbivores and diseases, intact glucosinolates and their degradation products attract specialised toxin-tolerant insects and perform other chemo-ecological tasks. The cancer-preventive effects of specific breakdown products, such sulforaphane (produced from glucoraphanin, broccoli's active ingredient), have piqued interest in the function of dietary glucosinolates. In animal models, isothiocyanates like sulforaphane inhibit cell cycle progression and enhance apoptosis, hence preventing cancer growth. For the most part, desulfo-glucosinolates are analysed using reversed phase high performance liquid chromatography (HPLC). These methods involve adsorbing the extracted glucosinolates onto a solid substrate, usually Sephadex A-25, and then eluting the desulfoglucosinolates after enzymatic desulfation.22 Recently, LC-ESI-MS (liquid chromatography-electrospray ionization-mass spectrometry) has been used to examine these components in their whole. Thiosulfinates, which are present in a number of Allium species, are another sulfur-containing molecule that has a number of positive health effects. In this regard, two of the first domesticated plants, garlic (Allium sativum) and onion (Allium cepa), have dual culinary and therapeutic uses. Enzymatic cleavage of S-alk(en)yl- L -cystein S-oxides (e.g., alliin in garlic) produces thiosulfinates, such as allicin from garlic, which are present in whole plants. The prevention of hypertension, type 2 diabetes, cancer, and coronary heart disease are only a few of the health benefits associated with Allium species, which are thought to be caused by them. The pungency of these veggies is also caused by these volatile chemicals. A thorough evaluation of the examination of these volatile components has been compiled by Lanzotti.

Mixtures of Hyphenated and MS Techniques (GC-MS and LC-MS)

When it comes to the online identification of phytonutrients, LC-MS is a crucial approach. In addition to detecting, mass spectrometers can produce molecular ions with a nominal mass or precise mass readings that can be used to find empirical formulas. Moreover, by fragmenting the molecular species through collision-induced dissociation (CID) processes, in-depth structural information can be obtained using tandem or hybrid MS equipment. Online NP identification is discussed in several reviews, covering topics such as screening and dereplication, quality control, biomarker identification, and fingerprinting for authentication or standardisation. Determining the molecular weight is significant for online identification. The challenge here is distinguishing protonated or deprotonated molecules from adducts or fragments using MS data collected with various detection settings. By utilising high-resolution instruments like a Fourier transform ion cyclotron resonance (FTICR) mass spectrometer system or a time-of-flight (ToF) mass spectrometer, the chemical formula of crude mixes can be directly determined. Dereplication searches of natural product libraries can be fine-tuned with the use of this strategic data. 33 With CID, investigations using multi-stage mass spectrometry (MS n) or liquid chromatography tandem mass spectrometry (LC-MS/MS) can produce complementary structural information. However, it is not possible to directly use the typical EI-MS libraries for dereplication purposes because the produced CID spectra do not match those recorded by electron ionisation (EI). One limitation of this strategy is that automated dereplication procedures require custom MS/MS libraries based on laboratory standards. The ability to record MS/MS spectra with high mass precision has been made possible by the advent of hybrid instruments that combine with high-resolution spectrometers like ToF, FTICR, or Orbitrap analyzers. This makes it easier to understand the spectra that are produced. To name a few applications of MS/MS spectra, there's partial sugar sequence determination for glycosides, identifying characteristic losses like those of prenylated compounds [35], classic flavonoid fragmentation for substituent position determination on A or B rings, isomer differentiation, and so on. To extract structurally significant information and build guidelines that can be utilised for structure prediction, the interpretation of the MS/MS spectra in other research generally involves the examination of many related products 46. Combining this method with other online resources is frequently necessary for analyses of completely unknown components because it typically cannot give enough information to determine the structure. Online nuclear magnetic resonance (NMR) techniques like liquid chromatography-solid phase extraction-nuclear magnetic resonance (LC-SPE-NMR) or CapNMRTM could potentially fill in the gaps in our structural knowledge in this area. Structure identification often requires this approach, which is slower and less sensitive than MS.

Extract Profiling from Plants, Fruits, and Vegetables

Nutraceutical registration does not necessitate the profiling of all food product components, as contrast to herbal medications or phytopharmaceuticals. However, in order to comprehend the health advantages of these substances, it is necessary to analyse a large number of bioactive food components in order to fully identify or quantify them in vegetable, fruit, or plant matrices. This is particularly crucial when it comes to herbal additions used in food items from a safety and compliance standpoint. It is common practice to macerate dried plant material with either polar (e.g., CH_3OH) or non-polar (e.g., CH_2Cl_2) solvents in order to create crude extracts for use in herb and vegetable sample preparation. These extracts are complicated combinations, and there can be hundreds of different components in them. It is possible to use liquid-liquid partitioning techniques for analysing fresh vegetable matrices. Particular procedures requiring extraction with heated solvents are required for classes of compounds that are susceptible to enzymatic degradation, such as glucosinolates. It is possible to utilise SPE pre-purification before HPLC in some situations when sample enrichment is required.

Health Advantages from Proper Diet

Access to nutrients

Many types of micronutrients, and phytochemicals in particular, have had their bioavailability studied at length. Biological effects and mechanisms of action are determined by the lowest concentration of bioactive food compounds that reach the target organ. Numerous intervention trials that did not use validated bioavailability measurements failed to show the expected outcomes, because food intake of a bioactive substance does not always correspond to the dose reaching the target tissue [36]. A bioavailable dosage of an active ingredient may have varying degrees of impact in various individuals due to individual predispositions (such as genetics, medication, and age). A biomarker of exposure can only be considered valid if the key events that characterise the nutrients' destiny can be understood. A high-level overview of these occurrences is shown in Figure 6.18. Endogenous factors include mucosal mass, intestinal transit time, rate of gastric emptying, metabolism, and extent of conjugation; exogenous factors include things like: • the chemical form of the compound; • the structure and amounts of co-ingested compounds; and complexity of the food matrix are examples of exogenous factors.

The complexity of these elements causes significant variations in bioavailability, both between and within individuals. These variances can range from 0% to 100% of the ingested dose. Similar metabolic pathways (common transport systems) govern the absorption and metabolism of both phytochemicals and pharmaceuticals. When thinking about phytochemicals, though, the following distinctions must be kept in mind. To start, compared to pharmaceutical formulations, the food matrix is quite intricate. Hence, the biomarker needs to be component-specific, meaning that variations in the concentration of the biomarker should only be caused by changes in the consumption of the component-of-interest in the diet. Factors such as plant and animal genetics, environmental factors, and processing techniques all have a role in determining the precise concentration of bioactive components in different foods. We have studied potential polyphenol consumption biomarkers generated from the small intestine and liver's phase I and II metabolism of flavonoids and other polyphenols. An great way to gauge the amount of polyphenol absorption in human subjects is with metabolites like glucuronide and sulphate conjugates, as well as related O-methylated forms. Cellular metabolites of polyphenols, notably glutathionyl and cysteinyl conjugates, have a lot of promise in addition to these well-studied metabolic forms because of the high concentrations of these compounds in blood and urine. The second point is that different parts often work together in a complementary or synergistic way. The bioavailability of a purified component may also vary significantly from that of the identical component in its original food matrix (61). Thirdly, phytochemicals contend for the same transporters and enzymes in metabolism as other dietary components. Lastly, in contrast to greater (acute) dosages of medications, dietary components are present at lower concentrations and exert their effects through chronic applications, which last for a longer period of time. It has been suggested that many phytochemicals do not directly scavenge radicals but rather activate adaptive cellular response pathways to oxidative stress and environmental toxins. This is supported by the fact that tissue concentrations of phytonutrients are lower than those of endogenous antioxidants. Quantification methods for biomarkers should be both quantitatively and qualitatively robust, and biomarker concentrations in the target tissue or biofluid should be responsive to small changes in the dietary component's consumption. To detect and measure molecular changes in the body with great specificity and sensitivity, as well as to identify and quantify bioactive chemicals in food, which can be present in minute amounts, suitable analytical instruments are crucial to the development and assessment of biomarkers. For these reasons, LC-MS and LC-MS/MS have replaced other analytical methods as the gold standard for calculating phytochemical bioavailability. It is possible to approach markers for bioavailability either holistically, without making any presumptions, or in a hypothesis-driven, targeted method. After its introduction, LC-MS and LC-MS/MS became the analytical gold standard for LADME determination of phytochemicals. On top of that, proteomics and metabolomics are being used in the field of nutrition to find biologically active food components, measure their bioavailability at various organ sites, and determine their site-specific and overall health benefits. The kinetics and extent of polyphenol absorption in adults following a single dosage of polyphenol supplied as a pure chemical, plant extract, or entire food/beverage were examined in a review by Manach et al. The scientists demonstrated that bioavailability varies significantly among polyphenols; hence, the polyphenols that are most plentiful in our diet may not be the ones that cause target tissues to have the largest concentrations of active metabolites. Digestive and hepatic processes produce metabolites in the blood that are distinct from their source components. While quercetin glucosides, catechins, flavanones, and gallic acid had variable absorption kinetics, iso-flavones and gallic acid were the most efficiently absorbed polyphenols. These polyphenols—anthocyanins, galloylated tea catechins, and proanthocyanidins—are the least absorbed of the bunch. Scholz and Williamson looked into what makes polyphenols, especially flavanols, flavonols, flavanones, and flavones, bioavailable.

According to the research, the single most critical component in determining absorption in the gut is bioaccessibility, which is the quantity of chemical that reaches the enterocyte in an absorbable state. Flavonols, especially quercetin and its metabolites, are absorbed more efficiently when the attached sugar is of a certain kind and when their solubility is altered by the presence of ethanol, fat, or emulsifiers. The absorption of flavanols in green tea catechins is influenced by processing-related epimerization processes, lipids, and carbohydrates; however, piperine and tartaric acid enhance this absorption. The type of connected sugar has a substantial impact on flavanones like hesperidin. Polyphenols that are not well absorbed by humans include proanthocyanidins, galloylated tea catechins, and anthocyanins. Since proanthocyanidins do not undergo stomach-based depolymerization, they pass intact into the small intestine and are absorbed sparingly due to their high molecular weight.

after taking the pill. The specifics and processes of anthocyanin absorption and transport are less well understood than those of other classes of flavonoids, like flavonols. Given the complex nature of foodstuffs, it is possible for substances to have synergistic effects on one another, but it is also possible for interactions to occur that reduce bioavailability. Concerning the impact of milk proteins on the bioavailability of polyphenols, there is ongoing debate. There have been reports of interactions between polyphenols and proteins, and milk contains a variety of proteins. Depending on the culture, some foods and drinks are customarily drunk with or without milk. Products like tea and chocolate are good examples of how people in different nations enjoy them. The world's second-most-popular beverage is tea, behind water. Many people in the United Kingdom, Ireland, Canada, and India drink their tea with milk. Milk is not typically added to tea in Japan and China. In the US, chocolate—specifically milk chocolate—contributes significantly to the antioxidants consumed by the average American, ranking as the third-highest source of antioxidants consumed daily per capita. Milk chocolate is more popular in the United Kingdom and Germany, whereas dark chocolate is more popular in France. Some studies have attempted to resolve the polyphenol-milk protein interactions in light of the advantages linked with tea catechins and cocoa proanthocyanidins (discussed further below), but the findings are still up for debate. The catechins in green and black tea, according to van Het Hof et al., were fast absorbed and were unaffected by milk in terms of bioavailability. Similarly, Leenen et al. showed that adding milk to tea did not remove the considerable increase in plasma antioxidant activity in vivo that was generated by consuming only one dosage of either green or black tea. Milk, however, mitigates the beneficial benefits of tea on vascular function, as demonstrated more lately by Lorenz and colleagues. Sixteen fit female volunteers participated in the study, and they were given 500 millilitres of either unsweetened black tea, black tea sweetened with 10% skimmed milk, or water that had been boiled. Before and 2 hours after ingestion, high-resolution vascular ultrasonography was used to quantify endothelial function as determined by flow-mediated dilation (FMD). When given to people, black tea considerably increased FMD compared to water, but when milk was added, the tea's effects were entirely muted.136A study conducted by Nature137 indicated that when comparing milk chocolate to dark chocolate—or even dark chocolate mixed with milk—the bioavailability of epicatechin was much lower in the milk chocolate. The working theory was that polyphenols would be less accessible once milk proteins bound to them. In line with these findings, a bioefficacy study examined the impact of white and dark chocolate bars on healthy volunteers' blood pressure, glucose and insulin responses to an oral glucose tolerance test, and overall health. Following a seven-day period in which the individuals did not consume any cocoa, the healthy volunteers were given a random assignment to either consume 100 g of dark chocolate bars containing 500 mg of polyphenols or 90 g of white chocolate bars serving as a negative control, devoid of polyphenols, for a duration of fifteen days. After a seven-day washout period without cocoa, individuals were transferred to the opposite condition. To determine the homeostasis model assessment of insulin resistance and the quantitative insulin sensitivity check index, an oral glucose tolerance test was administered at the conclusion of each session in order to evaluate the polyphenol bioefficacy. Researchers observed that healthy individuals' blood pressure and insulin sensitivity were both improved by dark chocolate, but not by white chocolate. Nevertheless, in 2007, Roura et al. investigated whether or not milk interfered with healthy humans' absorption of cocoa powder's (-)-epicatechin. In a randomised crossover design with a one-week interval, 21 volunteers were placed in one of three groups: the control group, which received 250 mL of whole milk; the experimental group, which received 40 g of cocoa powder dissolved in 250 mL of whole milk; and the comparison group, which received 40 g of cocoa powder dissolved in 250 mL of water. Following a solid-phase clean-up method, the concentration of (-)-epicatechin in plasma was determined by LC-MS/MS analysis. Researchers found that polyphenols' bioavailability was unaffected by milk, suggesting that milk may help protect against chronic and degenerative diseases. Ultimately, understanding how bioavailable dietary polyphenols are is crucial for determining their health benefits. Although there has been a lot of work done in this field, broad concepts that can be used for prediction cannot be proposed at this time. Additional research is needed to thoroughly examine the numerous kinds of interactions that impact the bioavailability of distinct phytonutrient groups.

Tea

The world's second-most-popular beverage is tea, behind water. Green tea, which is defined as "non-fermented," has a higher catechin content than its black and oolong counterparts. Green tea has a long history of positive associations with health in traditional Chinese medicine. Recent human studies have shown that green tea has a number of potential health benefits, including a lower risk of cardiovascular disease and some types of cancer, better oral health, protection from sun UV rays, increased bone mineral density, anti-fibrotic properties, neuroprotective power, and a reduction in the risk of hypertension and obesity. In fact, polyphenols found in tea have a wide range of beneficial benefits, including antioxidant, antiviral, antibacterial, anti-inflammatory, and anti-carcinogenic capabilities. They can also alter signalling pathways including nuclear factor-kB activation. In a number of inflammatory bowel disease models, the polyphenols found in green tea were effective. Green tea is now considered one of the beverages with functional characteristics due to the growing interest in its health benefits. The majority of green tea's health benefits are attributed to epigallocatechin-3-gallate, one of the several polyphenols found in tea. Furthermore, the antioxidant capacity of green tea is enhanced by the presence of specific minerals and vitamins. Although tea polyphenols can have biological effects in vitro, the concentrations needed to do so are often 10–100 times higher than what is achieved in blood and tissues. Furthermore, reactive oxygen species are produced in the majority of cell culture conditions, and tea polyphenols are not stable. If these responses take place in living organisms, it is unclear. Lastly, results in cell culture systems and animal models of obesity are supported by multiple human studies that show decreased body weight and body fat, enhanced thermogenesis, and fat oxidation. These results highlight the importance of conducting well planned clinical trials to determine the benefits of green tea on obesity. Additionally, since EGCG is considered the most active ingredient in green tea, its effects on this condition should be investigated in human trials.

Coffee

Caffeoylquinic acids are mostly found in coffee, a beverage that is drunk by many and produces an average of six million tonnes annually. The average daily intake of cinnamates for coffee drinkers is 500 mg to 1 g (complemented by other food sources like bran), while the average daily intake for coffee abstainers is less than 100 mg. The addition of 25% milk to coffee resulted in the binding of up to 40% of the coffee chlorogenic acid to dairy proteins. Beverage antioxidant power is unaffected by the inclusion of milk, though. There may not be any substantial impact on the antioxidant activity of coffee either before or after intake due to interactions between chlorogenic acid and milk proteins in milk beverages and coffee, especially since these interactions diminish during in vitro stomach and intestinal digestion. After roasting, the antioxidant activity of green Robusta coffee beans was no longer significantly higher than that of Arabica coffee, which was twice as high. To sum up, these popular drinks are packed with antioxidants, with soluble coffee ranking first per cup.

Fruits and Healthy Foods

Dietary antioxidants including vitamin C, carotenoids, and flavonoids in produce may reduce the likelihood of cardiovascular disease by blocking the oxidation of cholesterol in arterial walls. The chance of developing chronic diseases is increased by oxidative stress. Antioxidant phytochemicals found in abundance in fruits and vegetables help to reduce the harmful effects of oxidative stress. It is widely acknowledged that carotenoids play a significant role in human health promotion and disease prevention. Not only are certain carotenoids powerful antioxidants, but they also add vitamin A to your diet. The function of lycopene in human health has recently attracted attention to carotenoids. The provitamin A characteristics of lycopene are absent, in contrast to those of other carotenoids. The unsaturated fatty acid chain makes lycopene an effective antioxidant and singlet oxygen quencher. Researchers have found that lycopene, a pigment found in tomatoes, reduces oxidative stress biomarkers in healthy individuals and carcinogenesis biomarkers in people with type II diabetes and prostate cancer, respectively. Tomato lycopene levels in the blood are increased relative to the starting point when consumed processed tomato products including tomato juice, tomato paste, puree, ketchup, and oleoresin, since these foods contain bioavailable lycopene. It is recommended to ingest dietary fats alongside foods that contain lycopene, as they increase this process. Having said that, in vivo evidence of lycopene's health effects is scarce. Clinical studies including tomato products have shown that lycopene, when combined with other nutrients, can reduce oxidative stress and carcinogenesis indicators more effectively. The combination of lycopene and other naturally occurring elements in tomatoes makes processed tomato products a very healthy food choice. The association between the consumption of individual carotenoids and the risk of cardiovascular disease needs further investigation, even though a diet rich in fruits and vegetables can help reduce the mortality and morbidity caused by heart disease.

References

1. Butler MS. Natural products to drugs: natural product-derived compounds. (2008).
2. Hobden AN, Harris TJR. Proc. R. Soc. Edinburgh. Sect. B. 1992; 99: 37-45.
3. Davis J. New chemical entities disappoint in 1992, Scrip Review, 1992, PJB publications, Richmond. 1993; 20-21.
4. Suffness M, Douros J. J. Nat. Prod., 45: 1-14.the last 25 years. J. Nat. Prod. 1982; 70: 461–477.
5. Wu S. Multi-channel counter-current chromatography for highthroughput. 2007; 11: 480–484.
6. Harvey AL. Natural products as a screening resource. Curr. Opin. Chem. Biol. Helminthostachys zeylanica in mice". Journal of Tropical Medicinal Plants. 2007; 3: 191–195.
7. Quinn RJ. Developing a drug-like natural product library. J. Nat. Prod. 2008; 71: 464–468
8. Hamberger M, Marston A and Hostettmann KK. Advances in Drug Research, 20, B., ed., Academic Press, London. (1991) 167-215.
9. Wagner H, Fransworth NR.Economic and Medicinal Plant Research. 1990; 4: 3-16.
10. Kalia AN. Textbook of Industrial Pharmacognosy. CBS Publishers, New Delhi. (2000).
11. Kinghorn AD, Balandrin MF. Human Medicinal Agents from Plants. American Chemical Society, Washington, DC. (1993).
12. Jachak SM, Saklani A. Challenges and opportunities in drug discovery from plants.Current science. 2007: 92 (9).
13. Knowles J, Gromo G. Target selection in drug discovery. Nature Review on Drug Discovery. 2003; 2: 63-69.
14. Kramer R, Cohen D. Functional genomics to new drug targets. Nature Review on Drug Discovery. 2004; 3: 965-972.
15. Walters WP, Namchuk M. Designing screens: How to make your hits a hit. Nature Review on Drug Discovery. 2003; 2: 259-266.
16. Kamboj VP. Herbal Medicine. Current Science. 2000; 78 (1): 35-39.
17. Krishnan R. Indian Drug Manufactured Association Bulletin. 1998; 13: 318- 320

18. Kokate CK, Purohit AP and Gokhale SB. Pharmacognosy. Nirali Prakashan, 30th Edn. (2005).
19. Inamdar N, Edalat VB, and Kotwal SP. Herbal Drugs in Milieu of Modern Drugs. Int. J. Green Pharm. 2008; 2 (1): 2-8.
20. Calixto JB. Efficacy, Safety, Quality Control, Marketing and Regulatory Guidelines for Herbal Medicines (Phytotherapeutic Agents). Braz. J. Med. Biol. Res. 2000; 33(2): 179-189.
21. Prajapti ND, Purohit SS, Sharma AK and Kumar A. Handbook of Medicinal Plants. Agrobios, India. (2003).
22. Raskin I, Ribnicky DM, Komarnytsky S, Ilic N, Poulev A, Borisjuk N, Brinker A, Moreno DA, Ripoll C, Yakoby N, O'Neal JM. Cornwell T, Pastor I, and Fridlender B. Plants and Human health in the twenty first century. Trends in biotechnology. 2002; 20 (12): 522-531.
23. Schippmann U, Leaman DJ and Cunningham AB. Impact of cultivation and gathering of medicinal plants on biodiversity: Global trends and issues. Biodiversity and the Ecosystem Approach in Agriculture. Proc. 9thsession of the Commission on Genetic Resources for Food and Agriculture. 2002; 12–13.
24. Gadre AY, Uchi DA, Rege NN and Daha SA. Nuclear Variations in HPTLC (2001).
25. Borris J. Natural Products Research Perspectives from a Major Pharmaceutical. 1996.
26. Austin DF. Evolvulus alsinoids (Convolvulaceae), An American herb in the whole world. J. Ethnopharmacology. 2008; 117 (2): 185-198.
27. Sarine YK. Quality control of herbal drugs, Indian journal of natural products. 1993; 10: 35.
28. Gogtay NJ, Bhatt HA, Dalvis SS and Kshirsagar NA. The use of non-allopathic Indian medicines, Drug Safety. 2002; 25: 1005-1019.
29. Pal SK, Shukla Y. Herbal medicine: current status and the future Asian Pacific Journal of Cancer Previous. 2003; 281-288.
30. De Smet PAGM. Aristolochia species, in Adverse Effects of Herbal Drugs, vol.1 Spinger Verlag, Berlin. (1992) 79-89.
31. Raina MK. Specification for Herbal drugs, Indian Journal of natural products. 1993; 9:12
32. Sethi PD. HPTLC quantative analysis of pharmaceutical formulation 1st Edition, CBS Publishers, New Delhi. (2001) 1-57.
33. Ali M. Textbook of Pharmacognosy, CBS Publications & Distributors, New Delhi. (1998).
34. Chaterrjee TK. "Medicinal Plants with Hepatoprotective Properties". Herbal Options. Books and Applied Allied (P) Ltd, Calcutta. (2000) 143.
35. Handa SS, Sharma A and Chakraborti KK. Natural products and plants as liver protecting drugs. Fitoterapia. 1986; 57(5): 307-352.

36. Harborne JB. Textbook of phytochemical methods 3rd edition, Chapman and Hill Publishers, 11 New Fetter Lane, London. (1998) 1-6; 56-99.

37. Subramonium A, Pushpangadan P. “Development of Phytomedicines for liver diseases”. Indian J. Pharmacol. 1999; 3: 166-175.

38. Thyagarajan SP, Jayaram S, Gopalakrishnan V, Hari R, Jeyakumar P and Sripathi MS. Herbal medicines for liver diseases in India. J Gastroenterol Hepatol. 2002; 17; S: 370-376 .

39. World Health Organization (WHO). WHO traditional medicine strategy, Geneva.2002.