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## Phytochemicals: Sources and biological functions

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### Abstract

Many plants are traditional sources for food and pharma products. Since the difference of a therapeutic and a toxic effect depends on the dose, there are fluent transitions between consumption, therapy and toxicity of nutraceuticals in food, medicines, or plants. The following review provides a classification of phytochemicals into categories according to their biosynthesis from carbohydrates, lipids and amino acids as well as an overview of epidemiologically important toxic phytochemicals affecting human health including examples from the terpenoids, phenolic compounds, and alkaloids families. Despite evidence indicating that phytochemicals can reduce the risk of chronic non-communicable diseases, research is still needed using new and precise methodologies to unravel the multitude of beneficial roles played by phytochemicals in human health.

**Keywords:** Phytochemicals, terpenoids, phenolic compounds, alkaloids, biosynthesis, bioavailability

### Introduction

Many plants and fungi are traditional sources for food and pharma products. Plant components are biosynthesized from primary metabolites and energy (light and temperature). For a maximal concentration, plants should be harvested at the right moment before the onset of degradation. Sprouts normally do not have many secondary metabolites because the time they are exposed to light and temperature will not do for biosynthesis. In addition, the yield depends on the choice of the right variation of the species. Classes of phytochemicals can often be recognized from the colors, e.g. blue and red berries are sources for anthocyanidins which are well estimated as antioxidant, or yellow – orange colored plants for their content of flavonoids and carotenoids. On the other hand, plants produce secondary metabolites for the survival of the own kind. Therefore, some ingredients are toxic for insects or grazing animals and prevent the species from getting caught in the predator-prey chain.

### Primary and secondary plant components

In the late Paleozoic, oxygen concentration may have reached a maximum of 35% and then dropped in the Triassic to 15% (compared with the present 21%). This oxygen pulse may have influenced the evolution markedly about 300 to 400 million years ago. CO<sub>2</sub> was converted by green algae to oxygen and decreased to the lowest concentrations in the Carboniferous and Permian periods. This change in oxygen atmosphere demonstrates the vital importance chlorophyll and plants have even today for the biosynthesis of oxygen and glucose and thus for human survival, and why tropic forests should be protected to limit the greenhouse effect.

Primary substances are essential for cell metabolism, whereas secondary metabolites are not. However, the plant has learnt with evolution to synthesize both. Their number is estimated to 80'000 components. Most likely, secondary metabolites are needed to defend against herbivorous predators, phytotoxic substances and microorganisms, UV irradiation, or to attract pollinators, thus to warrant the survival of the species. Meanwhile, some predators adapted to these new substrates by building up detoxifying enzymes such as cytochrome P450 isoenzymes in intestines and liver for phase I (monooxygenation) and for phase II (coupling, e.g. with glucuronic acid) to excrete xenobiotics efficiently. In turn, the plant has to do the next evolutionary step and modify its pattern of secondary metabolites.

Glucosinolates in Brassica species liberating anti-thyroid rhodanide, or *Claviceps purpurea* infecting rye and leading to gangrene with limb loss, have been examples of epidemiologically important toxic phytochemicals affecting human health. Since the difference of a therapeutic and a toxic effect depends on the dose, there are fluent transitions between consumption, therapy and toxicity of nutraceuticals in food, medicines, or plants. National legislations regulate the use as food or as phytochemical medicines according to the lead substances and their concentrations. In addition, processing can help degrade undesirable ingredients such as intact glucosinolates (by activation of myrosinase in the course of cutting the vegetable), lectins, or protease-inhibitors, and make foodstuff edible.

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### Biosynthesis of phytochemicals and their biological function

It is widely accepted to classify phytochemicals into categories according to their biosynthesis from carbohydrates, lipids and amino acids (Table 1).

**Table 1:** Relation of primary and secondary metabolism and biosynthesis of phytochemicals

<b>Phytochemicals issued from photosynthesis</b> (light reactions, dark reactions = Calvin cycle)
• Glycerate-3-P / Pyruvate derived
• Serine
• Cysteine
• Glycine
• Purine bases / Nucleic acids
• Purine alkaloids (Caffeine, Theobromine, Theophylline)
• Erythrose-4-P / Shikimate derived
• Phenylalanine
• Phenylpropanoids
• Cinnamic acid derivatives
• Phenolic compounds (C6-C1), Polyphenols, Phenolic glycosides
• Lignin, Lignan (condensed from two C6-C3)
• Coumarins (C6-C3)
• Flavonoids / Phytoestrogens (non-steroidal structure, partial similarity with 17 $\beta$ -estradiol)
• Flavonoids (C6-C3-C6, Flavanones, Flavones,
• Flavonoles, Isoflavones [e.g. daidzein and genistein], Anthocyanidins, Chalconoids [e.g. xanthohumol, 6-prenylnaringenin, 8-prenylnaringenin])
• Stilbenes (C6-C2-C6, decarboxylated derivatives of flavonoids [e.g. Resveratrol])
• <i>Phenylalkylamine</i> derivatives
• Isoquinoline alkaloids
• Papaver alkaloids
• Ipecac alkaloids
• Colchicum alkaloids
• Curare alkaloids
• Ephedra alkaloids
• Cyanoglycosides
• Glucosinolates
• Tryptophan
• Indole alkaloids
• Secale alkaloids
• Rauwolfia alkaloids
• Strychnos alkaloids
• Vinca alkaloids
• Catharanthus alkaloids
• Cinchona alkaloids
• Physostigmine
• Psilocybin
<b>Phytochemicals issued from activated sugars</b>
• Monosaccharides
• Polysaccharides
• Sugar unit of glycosides
<b>Phytochemicals issued from glycolysis</b>
• Pyruvate derived
• Shikimate (see photosynthesis)
• Alanine
• Leucine
• Valine
• Cyanoglycosides
<b>Phytochemicals issued from Acetyl CoA</b>
• Acetate-Malonate derived (Polyacetates)

• Anthraquinones
• Flavonoids (see photosynthesis)
• Cannabinoids
• Phloroglucin derivatives
• Polyacetylenes
• Acetate-Mevalonate derived
• Monoterpenoids (e.g. menthol, limonene, thymol)
• Iridoids
• Secoiridoids
• Valepotriates
• <i>Gentiana</i> bitter substances
• Indole alkaloids
• Isoquinoline alkaloids
• Sesquiterpenoids
• Matricaria components
• Artemisia bitter substances
• Diterpenoids
• Aconitum alkaloids
• Carotenoids
• Phenolic diterpenes (e.g. carnosol, carnosic acid)
• Triterpenoids
• Saponins (e.g. solanine, tomatine, diosgenin)
• Phytosterols
• Tetraterpenoids (carotenoids / xanthophylls, e.g. $\beta$ -carotene, lycopene, lutein, zeaxanthin)
<b>Phytochemicals issued from Citric acid cycle</b>
• Oxaloacetate derived
• Asparagine acid derived
• Methionine, C1 pool, Yang cycle
• Glucosinolates
• Indoles
• Isothiocyanates
• Pyridine alkaloids
• Piperidine alkaloids
• $\alpha$ -Ketoglutaric acid
• Glutamic acid derived (N donor)
• Lysine
• Quinolizidine alkaloids
• Areca alkaloids
• Lobelia alkaloids
• Arginine, Ornithine
• Tropa alkaloids
• Nicotiana alkaloids
• Proline

As phytochemicals have an impact on many metabolic functions, the term “pharmacognosy” is widely used to express the close relationship between food and medicines. Nature biosynthesizes enantiomeric phytochemicals which differ from one another in their pharmacological as well as olfactory effect. R-(+)-limonene has an aroma of orange, S-(-)-limonene one of lemon, S-(+)-carvone one of caraway, R-(-)-carvone one of mint, et cetera.

Terpenoids such as  $\beta$ -carotene are orange colored and components of carrots, oranges, tomatoes. They liberate vitamin A and have a high antioxidant potential. Saponins are surface-active foaming agents and thus hydrolyzing and fungicide. They are found in soy, legumes, *solanums* (tomatoes, potatoes, quinoa, *glycyrrhiza glabra*). Phytosterols (sitosterin, stigmaterin, campestrin) are 5 to 10 times worse absorbed as compared to cholesterol and can lower cholesterol plasma level due to this antagonistic mechanism. It is diversely discussed, if the absorption of fat-soluble vitamins is inhibited.

Phenolic compounds such as flavonoids, including anthocyanidins, are often found as glycosides in yellowish plants or in the skin of blue-red berries, e.g. arbutin in uva ursi or in blueberry. Their effects range from antioxidation to aromatase inhibition. Antioxidant effects are likely for o- and p-diphenol derivatives found in pomegranates, cranberry, blueberry, mangostane, or in red wine. Aromatase inhibition and estrogen receptor modulation is found for stilbenes such as resveratrol. The trans enantiomere has an estrogenic effect, the cis enantiomere is however antiestrogenic. Polyphenols serve as UV protectors for the plant and are therefore predominant in outer parts of fruits and vegetables.

Alkaloids are comprised in many plants and used for their pharmacological and psychotropic effects. Alliines are derivatives of cysteine and found in allium species such as onion or garlic. Bound as S-alkyl-L-cystein sulfoxides they are fragmented after decompartmentation of cells and tissues during processing. Alliines are associated with cholesterol decrease and inhibition of thrombocytes aggregation. Glucosinolates from broccoli, Brussels sprout, or cauliflower have been the reason for endemic goiter in countries and regions with low iodine content in the soil in times before iodine was supplemented in table salt. Available iodine was competitively inhibited from being trapped in the thyroid gland by the structurally sufficiently similar isothiocyanate (rhodanide). Another Brassica component is Glucobrassicin, derived from tryptophan, which liberates indol-3-carbinol, another phytoestrogen in addition to the flavonoid group. Lectins from *viscum album* (mistletoe) are likely to have immunomodulatory effects.

#### **No evidence or evidence of no effect?**

There is much evidence indicating that phytochemicals can reduce the risk of chronic non-communicable diseases. Many studies rely on food frequency questionnaires. They are not very reliable due to inherent information biases and confounding. Research with new and precise methodologies is needed, since many studies have been published with very poor added value and statistically insufficient significance. The main challenge in nutrition research is the involvement of numerous components as compared to relatively simple medicines comprising one or very few active ingredients.

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