Bioactive plant foods: plant substances against cancer stem cells

Many findings indicate that the consumption of cruciferous vegetable plants rich in mustard oil glycosides has a cancer-inhibiting effect. Researchers from Heidelberg have now shown that sulforaphane, a broccoli mustard oil, blocks a signalling pathway that makes tumour stem cells resistant to cytotoxic drugs. The administration of sulforaphane can prevent therapy resistance and metastasis of pancreatic cancer in animal models.

Cruciferous vegetables have a high mustard oil glycoside content.

The large Brassicales plant order, which includes the mustard family (Brassicaceae, formerly referred to as Cruciferae, meaning 'cross-bearing') and others, is characterised by the production of sulfur-containing compounds known as mustard oil glycosides (glucosinolates). Cabbage is the prototype of the genus Brassica to which also cauliflower, broccoli, Brussels sprouts and other cabbage species belong.

These cruciferous glucosinolates, which are stored in the vacuoles of special leaf, stem and root cells, serve as natural pesticides and help plants fend off predators. Damage to the cells caused, for example, by rot, insects and caterpillars, triggers myrosinases, enzymes found in the cytoplasm of plant cells, to cleave off the glucose group from a glucosinolate that is released from the vacuoles. The remaining sulfur-containing molecule converts to an isothiocyanate. Isothiocyanates are responsible for the bitterness, pungent taste and sometimes also pungent smell of cabbage plants.

More than 150 different glucosinolates have been identified in cruciferous vegetables. These glucosinolates occur in different compositions and quantities. Many cruciferous plants are used as food or spices, including mustard, horseradish, peppercress, rocket (arugula), radishes, kohlrabi, broccoli, cauliflower and other cabbage varieties.

The healing power of cruciferous plants was already recognised in ancient Greek and Roman medicine and in traditional Chinese medicine, and has been confirmed by modern medicine through nutrition studies and experimental pharmacological investigations. Of the many compounds tested, the mustard oil glycoside glucoraphanin proved to be a particularly interesting compound. The enzyme myrosinase transforms glucoraphanin into sulforaphane. The compound was isolated from broccoli, which has the highest concentration of sulforaphane of all cruciferous vegetables, for the first time in 1992.

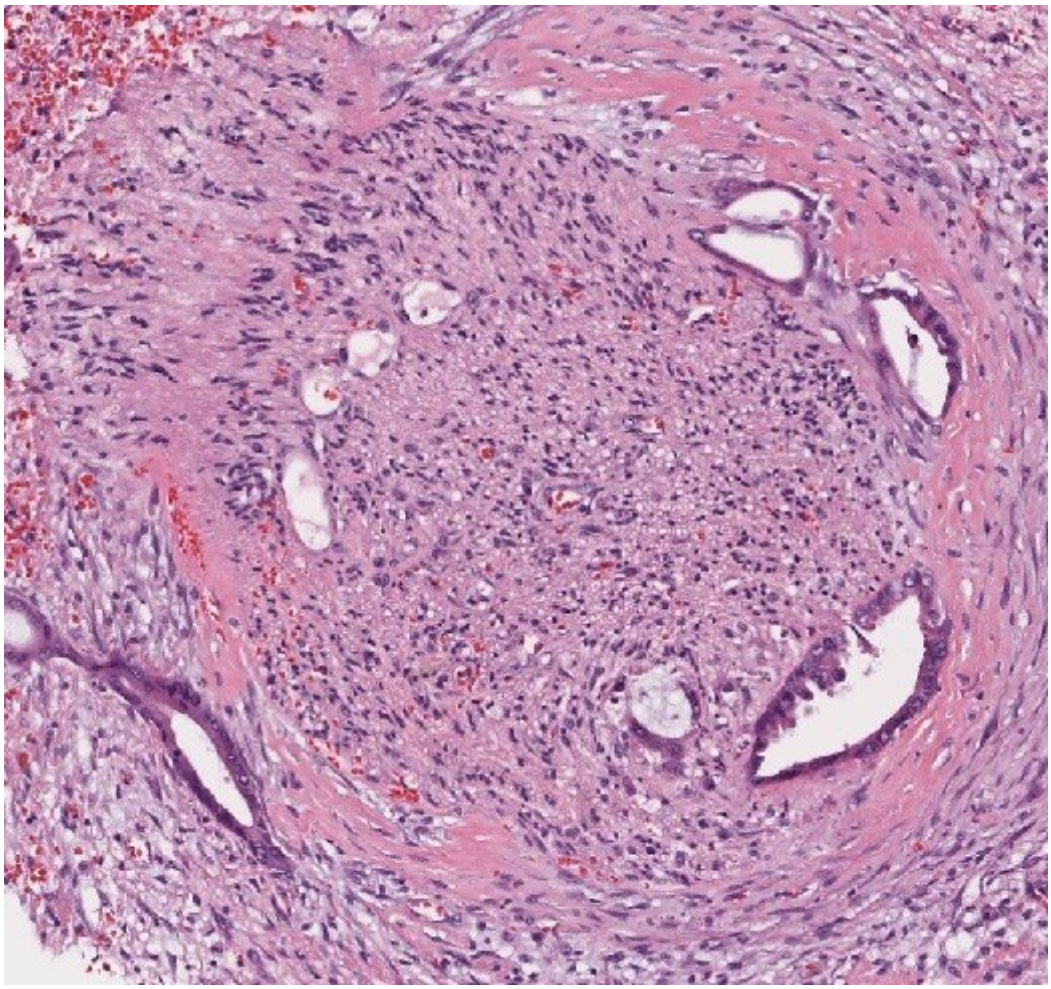
Sulforaphane has a broad range of protective effects

Prof. Dr. Ingrid Herr and her "Molecular OncoSurgery" research group, a cooperation unit between the Department of Surgery at Heidelberg University Hospital and the German Cancer Research Center, are specifically focussed on the effect the broccoli compound sulforaphane has in the treatment of cancer. Over the last ten years, numerous studies have focussed on the anti-cancer effect of the compound, including in the treatment of leukaemias, melanomas, colon and lung cancers. These findings are also in line with nutrition studies, which found that the weekly consumption of broccoli and other cruciferous vegetables significantly reduces the risk of developing breast cancer. Other studies have shown that the weekly consumption of broccoli or cauliflower reduces the metastasis of tumours in patients with prostate carcinoma by 50 percent. However, no agreement exists on the molecular mechanisms underlying the effect of sulforaphane.

Researchers agree that sulforaphane, which is a strong antioxidant, interferes at different points in the metabolism, for example by stimulating programmed cell death (apoptosis), blocking the division of cells, activating detoxification enzymes in the liver (so-called phase II enzymes involved in the biotransformation of chemical compounds into nutrients, amino acids, etc. in the body) and by stimulating the biosynthesis of glutathione and antioxidant enzymes that are responsible for the neutralisation of free radicals. All these mechanisms can play a role in the processes that have been shown to cause cancer.

Ingrid Herr and her colleagues have shown in cancer cell and mouse experiments that sulforaphane blocks the NF-κB (nuclear factor kappa-light-chain-enhancer of activated B cells) signalling pathway, whose incorrect regulation has been linked to cancer and other diseases. NF-κB is a transcription factor that occurs in almost all cell types. It affects the expression of numerous genes due to its ability to bind to regulatory DNA sequences. In addition to its importance in the immune response of B lymphocytes, cell division and apoptosis, NF-κB also plays a crucial role in inflammatory processes.

Synergistic effects in pancreatic cancer



Pancreatic cancer; histological preparation.

The Department of General, Visceral and Transplantation Surgery at Heidelberg University Hospital is home to the European Pancreas Centre and is aimed at pooling efforts to improve the therapy of patients with pancreatic cancer.

Pancreatic cancer has an extremely poor prognosis. It is often not diagnosed until it is at an advanced stage. Around 95% of patients die within a year of diagnosis. The tumour is largely resistant to treatments involving established chemotherapeutic drugs and has a strong tendency to form metastases. According to Ingrid Herr, the precursor cells of the tumour, i.e. cancer stem cells, are the sole cause of the uncontrolled growth of the tumour, its spread into other organs and for creating resistances to standard cancer therapies. The investigations of the Heidelberg scientists have shown that the activity of the NF-κB signalling pathway protects these cancer stem cells against cytotoxic drugs. Herr and her team were able to block the signalling pathway with sulforaphane and make the pancreatic cancer stem cells sensitive to chemotherapeutic treatment.

Mice transplanted with stem cells of human pancreatic cancer were used to test whether sulforaphane weakens the effect of chemotherapeutic treatment, an effect that is currently being discussed for antioxidant vitamins. In fact, the animal experiments showed that exactly the opposite was the case: sulforaphane enhanced the effect of the drugs on the cancer stem cells without affecting healthy cells or organs. The researchers also found that sulforaphane administered in combination with a cytostatic drug (e.g. sorafenib) increased the effectiveness of the drug, the tumour stopped growing and did not spread to other organs. However, clinical studies need to be carried out in order to find out whether these promising results can be transferred to patients with pancreatic cancer.

Food against cancer

Broccoli contains high concentrations of sulforaphane.

Experimental studies, along with the aforementioned nutrition studies, suggest that the uptake of broccoli sulforaphane has an anti-cancer effect in pancreatic as well as other types of cancer. Sulforaphane also exhibits properties that may prevent cancer. In addition, numerous other studies show that plant mustard oil glycosides and their derivatives such as sulforaphane have an antibacterial and antiviral effect.

In a patient information brochure published by the Heidelberg University Hospital (see link in the top right-hand corner), Prof. Ingrid Herr provides advice on how people can take up sufficient active substances by eating broccoli and other cruciferous vegetables. Herr gives advice on how broccoli sprouts, which are much richer in sulforaphane than the vegetables, can be grown using broccoli seeds.

Sulforaphane preparations (extracts and cryoconserved sprouts) can also be purchased through the Internet. But people are well advised not to limit consumption to only one particular source or dosage form. In addition to sulforaphane, a broad range of other plant compounds have been shown to be effective against tumour stem cells. One of these compounds is quercetin, a polyphenol that is also found in cruciferous vegetables (but also in many other fruit and vegetables). The Heidelberg researchers therefore advise people to eat a well balanced, mainly plant-based diet including a high proportion of raw vegetables in order to take up a broad range of compounds that are effective against tumour stem cells.

Publication:
Kallifatidis G, Labsch S, Rausch V, Mattern J, Gladkich J, Moldenhauer G, Büchler MW, Salnikov AV, Herr I: Sulphoraphane increases drug-mediated cytotoxicity toward cancer stem-like cells of pancreas and prostate. Molecular Therapy (2011), 19 (1), 188-195.

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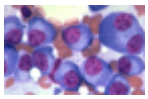
Bioactive plant foods – more than just filling



Cancer therapy and cancer diagnostics