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Mundgesunde Ernährung im Alter - Empfehlungen für den Praxisalltag.
Schulze-Späte U, Dawczynski C, Bär AK.
Quintessenz Zahnmedizin 2024;4:255-263.

Ernährung und Mundgesundheit sind eng miteinander verknüpft. Vor dem Hintergrund der jüngsten demographischen Entwicklung, die eine deutliche Alterung der Gesellschaft beinhaltet, beschäftigten sich jüngste Untersuchungen mit der Rolle der Ernährung beim gesunden Altern. Zudem hat die World Health Organisation (WHO) gesundes Altern zu einer Priorität im Bereich des Alterns erklärt [1]. Dabei liegt eine bidirektionale Beziehung zwischen der Ernährung und der Mundgesundheit vor. So führen eine unzureichende Nährstoffzufuhr und ungünstige Ernährungsgewohnheiten zu einem erhöhten Risiko für orale Erkrankungen wie Karies und Parodontitis. Umgekehrt kann ein therapiebedürftiges Gebiss erheblich die Nahrungszufuhr beeinträchtigen. Dies führt besonders in der vulnerablen Gruppe der älteren Senioren zu einem erheblichen Problem und kann zur Ausbildung von Nährstoffmangelerkrankungen führen, die wiederum mit Gebrechlichkeit, vermehrten Krankenhausaufenthalten und einer erhöhten Morbidität und Sterblichkeit verbunden sein können. Daher sind eine gute Mundgesundheit und ein funktionsfähiges Gebiss im Alter unerlässlich, um eine ausreichende Nährstoffzufuhr zu gewährleisten und somit eine wichtige Säule eines gesunden Alterungsprozesses dazustellen [1].

Validation of Nutritional Approaches to Modulate Cardiovascular and Diabetic Risk Factors in Patients with Hypertriglyceridemia or Prediabetes – The MoKaRi II Randomized Controlled Study.
Braun TS, Drobner T, Kipp K, Kiehntopf M, Schlattmann P, Lorkowski S, Dawczynski C.
Nutrients 2024, 16, 1261. https://doi.org/10.3390/nu16091261.

Hypertriglyceridemia and diabetes mellitus type 2 are among the most important metabolic diseases globally. Diet plays a vital role in the development and progression of both clinical pictures. For the 10-week randomized, controlled, intervention study, 67 subjects with elevated plasma triglyceride (TG) concentrations (≥1.7 mmol/L) and 69 subjects with elevated fasting glucose concentrations (≥5.6 < 7.0 mmol/L) were recruited. The intervention groups received specially developed, individualized menu plans and regular counseling sessions to lower (A) TG or (B) fasting glucose and glycated hemoglobin A1c as well as other cardiovascular and diabetic risk factors. The hypertriglyceridemia intervention group was further supplemented with fish oil (3.5 g/d eicosapentaenoic acid + docosahexaenoic acid). The two control groups maintained a typical Western diet. Blood samples were taken every 2 weeks, and anthropometric data were collected. A follow-up examination was conducted after another 10 weeks. In both intervention groups, there were comparable significant reductions in blood lipids, glucose metabolism, and anthropometric parameters. These results were, with a few exceptions, significantly more pronounced in the intervention groups than in the corresponding control groups (comparison of percentage change from baseline). In particular, body weight was reduced by 7.4% (6.4 kg) and 7.5% (5.9 kg), low-density lipoprotein cholesterol concentrations by 19.8% (0.8 mmol/L) and 13.0% (0.5 mmol/L), TG concentrations by 18.2% (0.3 mmol/L) and 13.0% (0.2 mmol/L), and homeostatic model assessment for insulin resistance by 31.8% (1.1) and 26.4% (0.9) ($p < 0.05$) in the hypertriglyceridemia and prediabetes intervention groups, respectively. Some of these changes were maintained until follow-up. In patients with elevated TG or fasting glucose, implementing individualized menu plans in combination with regular counseling sessions over 10 weeks led to a significant improvement in cardiovascular and diabetic risk factors.

Potenziell kritische Nährstoffe bei vegetarischer und veganer Ernährung, Empfehlungen zur bedarfsgerechten Zufuhr – Teil 1

Dawczynski C.

Ernährungs Umschau 2024; 2: M90-M105.

Im Rahmen einer vegetarischen bzw. veganen Ernährungsweise stehen Getreide, Hülsenfrüchte, Gemüse, Obst, Beeren, Nüsse, Samen, Makro- und Mikroalgen sowie hochprozessierte Fleisch-, Wurst- und Milchersatzprodukte zur Verfügung. Dieses Sortiment wird bei Vegetariern durch den Verzehr von Eiern, Milch und Milchprodukten erweitert.
Die genannten Lebensmittelgruppen bieten ein großes Spektrum an nährstoffreichen Lebensmitteln. Mit Ausnahme von Vitamin B12 in der veganen Ernährung kann durch eine vielfältige Lebensmittelauswahl eine bedarfsgerechte Energie- und Nährstoffzufuhr sichergestellt werden. Dennoch zeigen aktuelle Untersuchungen zur Energie- und Nährstoffzufuhr von Vegetariern und Veganern in Deutschland und Europa, dass ausgewählte Nährstoffe nicht bedarfsgerecht aufgenommen werden. Der vorliegende Teil 1 der zertifizierten Fortbildung zeigt anhand der Datenlage, dass n-3-LC-PUFA, Vitamin B12 und Vitamin A zu den kritischen Nährstoffen zählen. Bei Veganern kommt das Risiko einer verminderten Zufuhr von Protein und unentbehrlichen Aminosäuren sowie Vitamin B2 hinzu. Gründe dafür liegen in einer einseitigen Lebensmittelauswahl, niedrigeren Gehalten dieser Nährstoffe in pflanzlichen Lebensmitteln sowie einer eingeschränkten Bioverfügbarkeit
durch weitere Inhaltsstoffe. Um die bedarfsgerechte Versorgung mit kritischen Nährstoffen im Rahmen einer langfristigen vegetarischen oder veganen Ernährung zu kontrollieren, wird empfohlen, die Versorgung mit kritischen Nährstoffen regelmäßig (1-mal im Jahr) durch den Hausarzt prüfen zu lassen, wobei die Messung der in Tabelle 6 aufgeführten Laborwerte empfohlen wird. Zu den Limitationen der Studiendaten, die auf Ernährungsprotokollen beruhen, zählt die Nutzung von Standardportionsgrößen, die Verwendung von Nährstoffdaten aus Datenbanken (keine direkte Nährstoffanalyse) sowie das Risiko von Under- oder Overreporting. In diesem Zusammenhang muss die Unvollständigkeit der zur Verfügung stehenden Nährstoffprofile in den Datenbanken (z. B. Bundeslebensmittelschlüssel
BLS 3.02) berücksichtigt werden.
Für die Betrachtungen zum Nährstoffstatus zählt die limitierte Verfügbarkeit aussagekräftiger Biomarker, welche den Versorgungsstatus abbilden, zu den Schwachpunkten.
Durch die kombinierte Betrachtung von Nährstoffzufuhr und -status können die Schwächen beider Ansätze minimiert werden.

Chemopreventive effects of α-tocopherol and its long-chain metabolites α-13'-hydroxy- and α-13'-carboxychromanol in LT97 colon adenoma cells.
Schlörmann W, Liao S, Dinc T, Lorkowski S, Wallert M, Glei M.
Food Funct. 2024 Jan 2;15(1):183-195. doi: 10.1039/d3fo02826g.

Anticancer effects of vitamin E (tocopherols) have been studied extensively. While *in vitro* and animal studies showed promising results regarding anticancer effects of tocopherols, human intervention studies failed to reproduce these results. *In vivo*, α-tocopherol (α-TOH) is metabolized to the long-chain metabolites (LCM) 13'-hydroxychromanol (α-13'-OH) and 13'-carboxychromanol (α-13'-COOH), which likely reach the large intestine. The LCM showed antiproliferative effects in different colon cancer cell lines, but the exact mechanism of action remains unclear. To further clarify the chemopreventive action of the LCM, premalignant LT97 colon adenoma cells were treated with α-TOH, α-13'-OH and α-13'-COOH to study their impact on growth, apoptosis, antigenotoxicity, and ROS-scavenging capacity as well as expression of selected genes involved in detoxification and the cell cycle. Growth inhibitory potential was observed for α-13'-OH (IC_{50}: 37.4 µM) and α-13'-COOH (IC_{50}: 5.8 µM) but not for α-TOH in the tested concentrations. Levels of caspase-3 activity and expression of genes regulating the cell cycle and detoxification remained unchanged. However, α-TOH, α-13'-OH and α-13'-COOH exhibited antigenotoxic and partly ROS-scavenging capacity. The results indicate that the LCM exert chemopreventive effects *via* ROS-scavenging capacity, the protection against DNA damage and the induction of cell death *via* caspase-independent mechanisms in premalignant colon cells.

Targeted nuclear irradiation with a proton microbeam induces oxidative DNA base damage and triggers the recruitment of DNA glycosylases OGG1 and NTH1.
Robeska E, Lalanne K, Vianna F, Sutcu HH, Khobta A, Busso D, Radicella JP, Campalans A, Baldeyron C.
DNA Repair (Amst), 2024 Jan; 133:103610. doi: 10.1016/j.dnarep.2023.103610.

DNA is the major target of radiation therapy of malignant tumors. Ionizing radiation (IR) induces a variety of DNA lesions, including chemically modified bases and strand breaks. The use of proton beam therapy for cancer treatment is ramping up, as it is expected to reduce normal tissue damage. Thus, it is important to understand the molecular mechanisms of recognition, signaling, and repair of DNA damage induced by protons in the perspective of assessing not only the risk associated with human exposure to IR but also the possibility to improve the efficacy of therapy. Here, we used targeted irradiation of nuclear regions of living cells with controlled number of protons at a high spatio-temporal resolution to detect the induced base lesions and characterize the recruitment kinetics of the specific DNA glycosylases to DNA damage sites. We show that localized irradiation with 4 MeV protons induces, in addition to DNA double strand breaks (DSBs), the oxidized bases 7,8-dihydro-8-oxoguanine (8-oxoG) and thymine glycol (TG) at the site of irradiation. Consistently, the DNA glycosylases OGG1 and NTH1, capable of excising 8-oxoG and TG, respectively, and initiating the base excision repair (BER) pathway, are recruited to the site of damage. To our knowledge, this is the first direct evidence indicating that proton microbeams induce oxidative base damage, and thus implicating BER in the repair of DNA lesions induced by protons.

Long-term suboptimal dietary trace element supply does not affect trace element homeostasis in murine cerebellum.

Friese S, Ranzini G, Tuchtenhagen M, Lossow K, Hertel B, Pohl G, Ebert F, Bornhorst J, Kipp AP, Schwerdtle T.

Metallomics. 2024 Feb 7;16(2):mfae003. doi: 10.1093/mtomcs/mfae003.

The ageing process is associated with alterations of systemic trace element (TE) homeostasis increasing the risk, e.g. neurodegenerative diseases. Here, the impact of long-term modulation of dietary intake of copper, iron, selenium, and zinc was investigated in murine cerebellum. Four- and 40-wk-old mice of both sexes were supplied with different amounts of those TEs for 26 wk. In an adequate supply group, TE concentrations were in accordance with recommendations for laboratory mice while suboptimally supplied animals received only limited amounts of copper, iron, selenium, and zinc. An additional age-adjusted group was fed selenium and zinc in amounts exceeding recommendations. Cerebellar TE concentrations were measured by inductively coupled plasma-tandem mass spectrometry. Furthermore, the expression of genes involved in TE transport, DNA damage response, and DNA repair as well as selected markers of genomic stability [8-oxoguanine, incision efficiency toward 8-oxoguanine, 5-hydroxyuracil, and apurinic/apyrimidinic sites and global DNA (hydroxy)methylation] were analysed. Ageing resulted in a mild increase of iron and copper concentrations in the cerebellum, which was most pronounced in the suboptimally supplied groups. Thus, TE changes in the cerebellum were predominantly driven by age and less by nutritional intervention. Interestingly, deviation from adequate TE supply resulted in higher manganese concentrations of female mice even though the manganese supply itself was not modulated. Parameters of genomic stability were neither affected by age, sex, nor diet. Overall, this study revealed that suboptimal dietary TE supply does not substantially affect TE homeostasis in the murine cerebellum.

Determination of copper status by five biomarkers in serum of healthy women.

Chillon TS, Tuchtenhagen M, Schwarz M, Hackler J, Heller R, Kaghazian P, Moghaddam A, Schomburg L, Haase H, Kipp AP, Schwerdtle T, Maares M.

J Trace Elem Med Biol. 2024 Mar 22;84:127441. doi: 10.1016/j.jtemb.2024.127441.

Background: The essential trace element copper is relevant for many important physiological processes. Changes in copper homeostasis can result from disease and affect human health. A reliable assessment of copper status by suitable biomarkers may enable fast detection of subtle changes in copper metabolism. To this end, additional biomarkers besides serum copper and ceruloplasmin (CP) concentrations are required.
Objectives: The aim of this study was to investigate the emerging copper biomarkers CP oxidase (CPO) activity, exchangeable copper (CuEXC) and labile copper in serum of healthy women and compare them with the conventional biomarkers total serum copper and CP.
Method and main findings: This observational study determined CPO activity, the non CP-bound copper species CuEXC and labile copper, total serum copper and CP in sera of 110 healthy women. Samples were collected at four time points over a period of 24 weeks. The concentrations of total serum copper and CP were within the reference ranges. The comparison of all five biomarkers provided insight into their relationship, the intra- and inter-individual variability as well as the age dependence. The correlation and Principal Component Analyses (PCA) indicated that CP, CPO activity and total copper correlated well, followed by CuEXC, while the labile copper pool was unrelated to the other parameters.
Conclusions: This study suggests that the non-CP-bound copper species represent copper pools that are differently regulated from total copper or CP-bound copper, making them interesting complementary biomarkers to enable a more complete assessment of body copper status with potential relevance for clinical application.

Fostering healthy aging through selective nutrition: A long-term comparison of two dietary patterns and their holistic impact on mineral status in middle-aged individuals-A randomized controlled intervention trial in Germany.

Pellowski D, Heinze T, Tuchtenhagen M, Müller SM, Meyer S, Maares M, Gerbracht C, Wernicke C, Haase H, Kipp AP, Grune T, Pfeiffer AFH, Mai K, Schwerdtle T.

J Trace Elem Med Biol. 2024 Apr 22;84:127462. doi: 10.1016/j.jtemb.2024.127462.

Aging is associated with a decline in physiological functions and an increased risk of age-related diseases, emphasizing the importance of identifying dietary strategies for healthy aging. Minerals play a crucial role in maintaining optimal health during aging, making them relevant targets for investigation. Therefore, we aimed to analyze the effect of different dietary pattern on mineral status in the elderly. We included 502 individuals aged 50-80 years in a 36-month randomized controlled trial (RCT) (NutriAct study). This article focuses on the results within the two-year intervention period. NutriAct is not a mineral-modulating-targeted intervention study, rather examining nutrition in the context of healthy aging in general. However, mineral status might be affected in an incidental manner. Participants were assigned to either NutriAct dietary pattern (proportionate intake of total energy consumption (%E) of 35-45 %E carbohydrates, 35-40 %E fats, and 15-25 %E protein) or the German Nutrition Society (DGE) dietary pattern (proportionate intake of total energy consumption (%E) of 55 %E carbohydrates, 30 %E fats, and 15 %E protein), differing in the composition of macronutrients. Data from 368 participants regarding dietary intake (energy, calcium, magnesium, iron, and zinc) and serum mineral concentrations of calcium, magnesium, iron, copper, zinc, selenium, iodine, and manganese, free zinc, and selenoprotein P were analyzed at baseline, as well as after 12 and 24 months to gain comprehensive insight into the characteristics of the mineral status. Additionally, inflammatory status - sensitive to changes in mineral status - was assessed by measurement of C-reactive protein and interleukin-6. At baseline, inadequate dietary mineral intake and low serum concentrations of zinc and selenium were observed in both dietary patterns. Throughout two years, serum zinc concentrations decreased, while an increase of serum selenium, manganese and magnesium concentrations was observable, likely influenced by both dietary interventions. No significant changes were observed for serum calcium, iron, copper, or iodine concentrations. In conclusion, long-term dietary interventions can influence serum mineral concentrations in a middle-aged population. Our findings provide valuable insights into the associations between dietary habits, mineral status, and disease, contributing to dietary strategies for healthy aging.

Nutrigenomics and redox regulation: Concepts relating to the Special Issue on nutrigenomics.
Klotz LO, Carlberg C.
Redox Biol. 2023 Dec;68:102920. doi: 10.1016/j.redox.2023.102920.

During our whole lifespan, from conception to death, the epigenomes of all tissues and cell types of our body integrate signals from the environment. This includes signals derived from our diet and the uptake of macro- and micronutrients. In most cases, this leads only to transient changes, but some effects of this epigenome programming process are persistent and can even be transferred to the next generation. Both epigenetic programming and redox processes are affected by the individual choice of diet and other lifestyle decisions like physical activity. The nutrient-gene communication pathways have adapted during human evolution and are essential for maintaining health. However, when they are maladaptive, such as in long-term obesity, they significantly contribute to diseases like type 2 diabetes and cancer. The field of nutrigenomics investigates nutrition-related signal transduction pathways and their effect on gene expression involving interactions both with the genome and the epigenomes. Several of these diet-(epi)genome interactions and the involved signal transduction cascades are redox-regulated. Examples include the effects of the NAD^+/NADH ratio, vitamin C levels and secondary metabolites of dietary molecules from plants on the acetylation and methylation state of the epigenome as well as on gene expression through redox-sensitive pathways via the transcription factors NFE2L2 and FOXO. In this review, we summarize and extend on these topics as well as those discussed in the articles of this Special Issue and take them into the context of redox biology.

Selenium-Enriched *E. coli* Bacteria Mitigate the Age-Associated Degeneration of Cholinergic Neurons in *C. elegans*.
Zytner P, Kutschbach A, Gong W, Ohse VA, Taudte L, Kipp AP, Klotz LO, Priebs J, Steinbrenner H.
Antioxidants (Basel). 2024 Apr 20;13(4):492. doi: 10.3390/antiox13040492.

Selenium (Se) is an essential trace element for humans and animals, but high-dose supplementation with Se compounds, most notably selenite, may exert cytotoxic and other adverse effects. On the other hand, bacteria, including *Escherichia coli* (*E. coli*), are capable of reducing selenite to red elemental Se that may serve as a safer Se source. Here, we examined how a diet of Se-enriched *E. coli* bacteria affected vital parameters and age-associated neurodegeneration in the model organism *Caenorhabditis elegans* (*C. elegans*). The growth of *E. coli* OP50 for 48 h in medium supplemented with 1 mM sodium selenite resulted in reddening of the bacterial culture, accompanied by Se accumulation in the bacteria. Compared to nematodes supplied with the standard *E. coli* OP50 diet, the worms fed on Se-enriched bacteria were smaller and slimmer, even though their food intake was not diminished. Nevertheless, given the choice, the nematodes preferred the standard diet. The fecundity of the worms was not affected by the Se-enriched bacteria, even though the production of progeny was somewhat delayed. The levels of the Se-binding protein SEMO-1, which serves as a Se buffer in *C. elegans*, were elevated in the group fed on Se-enriched bacteria. The occurrence of knots and ruptures within the axons of cholinergic neurons was lowered in aged nematodes provided with Se-enriched bacteria. In conclusion, *C. elegans* fed on Se-enriched *E. coli* showed less age-associated neurodegeneration, as compared to nematodes supplied with the standard diet.

Copper Homeostasis in the Model Organism *C. elegans*
Ohse VA, Klotz LO, Priebs J.
Cells. 2024 Apr 23;13(9):727. doi: 10.3390/cells13090727.

Cellular and organismic copper (Cu) homeostasis is regulated by Cu transporters and Cu chaperones to ensure the controlled uptake, distribution and export of Cu ions. Many of these processes have been extensively investigated in mammalian cell culture, as well as in humans and in mammalian model organisms. Most of the human genes encoding proteins involved in Cu homeostasis have orthologs in the model organism, *Caenorhabditis elegans* (*C. elegans*). Starting with a compilation of human Cu proteins and their orthologs, this review presents an overview of Cu homeostasis in *C. elegans*, comparing it to the human system, thereby establishing the basis for an assessment of the suitability of *C. elegans* as a model to answer mechanistic questions relating to human Cu homeostasis.

Selective activation of cellular stress response pathways by fumaric acid esters.
Erler K, Krafczyk N, Steinbrenner H, Klotz LO.
FEBS Open Bio. 2024 (in press). doi: 10.1002/2211-5463.13833.

The cellular response to oxidants or xenobiotics comprises two key pathways, resulting in modulation of NRF2 and FOXO transcription factors, respectively. Both mount a cytoprotective response, and their activation relies on crucial thiol moieties. Using fumaric acid esters (FAEs), known thiol-reactive compounds, we tested for activation of NRF2 and FOXO pathways in cultured human hepatoma cells by dimethyl/diethyl as well as monomethyl/monoethyl fumarate. Whereas only the diesters caused acute glutathione depletion and activation of the stress kinase $p38^{MAPK}$, all four FAEs stimulated NRF2 stabilization and upregulation of NRF2 target genes. However, no significant FAE-induced activation of FOXO-dependent target gene expression was observed. Therefore, while both NRF2 and FOXO pathways are responsive to oxidants and xenobiotics, FAEs selectively activate NRF2 signaling.

In vitro bioactivity evaluation of hydrangenol extracted from Hydrangea macrophylla leaves.
Al-Yafeai A, Schmitt B, Malarski A, Böhm V.
Int. J. Second. Metab. 2024; 11:78-92. doi.org/10.21448/ijsm.1390183.

Hydrangea macrophylla plant, native to Japan and Korea, has been attracting scientific attention due to its potential applications in both food science and health-related research. In this investigation, dry *Hydrangea* leaves were utilized as the source material. Subsequent to comminution and thermal treatment at 70 °C for an 18-hour duration, followed by a 30-minute ultrasonic bath extraction and a 5-minute centrifugation at 5000 rpm, hydrangenol was isolated through preparative HPLC. The investigation involved assessing the antioxidant capacity of hydrangenol, its impact on the activity of α-amylase and α-glucosidase enzymes, and its ability to prevent enzymatic browning. Quantification of antioxidant capacity, determined through TEAC (Trolox Equivalent Antioxidant Capacity), showed values from 1.8 to 3.2 mmol TE/mmol. Likewise, the ORAC (Oxygen Radical Absorbance Capacity) values were in the range of 16.5-27.0 mmol TE/mmol. Total phenolics content (Folin-Ciocalteu test) yielded a range of 7.1-11.2 g GAE (Gallic Acid Equivalents) per 100 g. Examining α-amylase inhibition, hydrangenol demonstrated a 52% inhibition (IC50: 3.6 mg/mL), whereas acarbose (positive control) displayed a higher inhibition of 99% (IC50: 0.51 mg/mL). Regarding α-glucosidase inhibition, hydrangenol exhibited a 51% inhibition (IC50: 0.97 mg/mL), while acarbose displayed a 46% inhibition (IC50: 2.1 mg/mL). Additionally, the activity of PPO was suppressed by 61% at hydrangenol concentrations of 1 mg/mL and 2 mg/mL, and by 46% at a concentration of 4 mg/mL.

High-Pressure processing of fruit smoothies enriched with dietary fiber from carrot discards: effects on the contents and bioaccessibilities of carotenoids and vitamin E.
Donda Zbinden, M, Schmidt M, Vignatti C I, Pirovani M E, Böhm V.
Molecules 2024; 29:1259. doi.org/10.3390/molecules29061259.

The effects of high-pressure processing (HPP) (450 MPa/600 MPa/3 min) on the carotenoid and vitamin E contents of smoothies made from strawberry, orange juice, banana and apple, and the same smoothies enriched with dietary fiber from discarded carrots were compared. The contents and bioaccessibilities of these compounds were also evaluated over the course of 28 days at 4 °C. The application of HPP in the formulations significantly increased the contents of β-cryptoxanthin, α-carotene and β-carotene and retained the contents of lutein, zeaxanthin and vitamin E compared to untreated samples. A decreasing trend in the content of each compound was observed with an increase in storage time. The application of HPP initially led to reductions in the bioaccessibility of individual compounds. However, overall, during storage, there was an increase in bioaccessibility. This suggests that HPP influences cell structure, favoring compound release and micelle formation. HPP is a sustainable method that preserves or enhances carotenoid extractability in ready-to-drink fruit beverages. Furthermore, the incorporation of dietary fiber from carrot processing discards supports circular economy practices and enhances the health potential of the product.

Characterization and application of a microemulsion as model system for lipophilic phytochemicals in high pressure processing.

Tauber S, Fehn S, Schmidt M, Schwarzenbolz U, Böhm V.

Appl. Res. 2024; 3:e202400016. doi.org/10.1002/appl.202400016.

High-pressure processing (HPP) is considered as gentle preservation technique for especially heat-sensitive food ingredients. So far, the focus has been on the fact that it is called a nonthermal process and high pressure can affect bioavailability, but it is questionable whether the high pressure affects the ingredients themselves. By using an o/w-microemulsion (ME) as a model system, it was possible to investigate the influence of pressure, especially on lipophilic compounds (e.g., carotenoids and vitamin E), without the complexity of a food matrix. The ME consisted of Capryol® TM 90, Tween® 80 or 20, Transcutol® HP and distilled water. Lipophilic and hydrophilic compounds were introduced to the oil phase and to the aqueous phase, respectively. Storage experiments confirmed the applicability for β-carotene and α-tocopherol. HPP of MEs, performed for 10 min at room temperature (RT) and up to 600 MPa, resulted in pressure stability of β-carotene (exceptional at 400 MPa; −11%) and α-tocopherol. Multicomponent ME showed that both had a positive effect on the stability of chlorophyll a/b during HPP. An ME environment was used to facilitate co-oxidation of β-carotene via lipoxygenase (LOX) from an Edamame-based crude enzyme extract and lyophilized LOX-1 from soybeans during storage (RT and 4 °C, dark conditions) and HPP treatment. A loss of β-carotene occurred after addition of linoleic acid, whereas effects of added α-tocopherol could be related to β-carotene protection. Overall, the introduced ME for studying HPP effects on lipophilic food ingredients showed promising results as versatile model system for future investigations regarding interactions of phytochemicals.

Protein intake and cancer: an umbrella review of systematic reviews for the evidence-based guideline of the German Nutrition Society.
Kühn T, Kalotai N, Amini AM, Haardt J, Lehmann A, Schmidt A, Buyken AE, Egert S, Ellinger S, Kroke A, Lorkowski S, Louis S, Schulze MB, Schwingshackl L, Siener R, Stangl GI, Watzl B, Zittermann A, Nimptsch K; German Nutrition Society.
Eur J Nutr 2024; im Druck. doi: 10.1007/s00394-024-03380-4

Purpose: It has been proposed that a higher habitual protein intake may increase cancer risk, possibly via upregulated insulin-like growth factor signalling. Since a systematic evaluation of human studies on protein intake and cancer risk based on a standardised assessment of systematic reviews (SRs) is lacking, we carried out an umbrella review of SRs on protein intake in relation to risks of different types of cancer.
Methods: Following a pre-specified protocol (PROSPERO: CRD42018082395), we retrieved SRs on protein intake and cancer risk published before January 22th 2024, and assessed the methodological quality and outcome-specific certainty of the evidence using a modified version of AMSTAR 2 and NutriGrade, respectively. The overall certainty of evidence was rated according to predefined criteria. **Results:** Ten SRs were identified, of which eight included meta-analyses. Higher total protein intake was not associated with risks of breast, prostate, colorectal, ovarian, or pancreatic cancer incidence. The methodological quality of the included SRs ranged from critically low (kidney cancer), low (pancreatic, ovarian and prostate cancer) and moderate (breast and prostate cancer) to high (colorectal cancer). The outcome-specific certainty of the evidence underlying the reported findings on protein intake and cancer risk ranged from very low (pancreatic, ovarian and prostate cancer) to low (colorectal, ovarian, prostate, and breast cancer). Animal and plant protein intakes were not associated with cancer risks either at a low (breast and prostate cancer) or very low (pancreatic and prostate cancer) outcome-specific certainty of the evidence. Overall, the evidence for the lack of an association between protein intake and (i) colorectal cancer risk and (ii) breast cancer risk was rated as possible. By contrast, the evidence underlying the other reported results was rated as insufficient.
Conclusion: The present findings suggest that higher total protein intake may not be associated with the risk of colorectal and breast cancer, while conclusions on protein intake in relation to risks of other types of cancer are restricted due to insufficient evidence.

Cardiovascular mortality attributable to dietary risk factors in 54 countries in the WHO European Region from 1990 to 2019: an updated systematic analysis of the Global Burden of Disease Study.
Pörschmann T, Meier T, Lorkowski S.
Eur J Prev Cardiol 2024; im Druck. doi: 10.1093/eurjpc/zwae136

This study aimed to estimate the association between single dietary risk factors and cardiovascular diseases (CVDs) in the WHO European Region (WHO ER) by age and sex using the data of the Global Burden of Diseases Study (GBD) from 1990 to 2019. For this purpose, 13 dietary risks and 13 forms of CVDs were included in the study, and the comparative risk assessment framework of the GBD was used to estimate the deaths attributable to them. The study included four regions, with a total of 54 countries. In 2019, 1.55 million (95% UI, 1.2-1.9 million) people in the WHO ER died from CVDs attributable to suboptimal diet. Diet-related CVD deaths (DRCDs) accounted for 16.4% of total deaths and 36.7% of CVD deaths in 2019. Between 1990 and 2019, there was a DRCDs reduction of 8.1% and the age-standardised death rate decreased. The deaths were almost equally distributed between women (777,714 deaths) and men (772,519 deaths). The distribution of death numbers between the sexes has changed only slightly over the study period. The largest percentage across the age groups were found in the group 85+ years (32.1%). Most DRCDs in the WHO ER were caused by a diet low in whole grains (326,755 deaths), followed by a diet low in legumes (232,918 deaths) and a diet high in sodium (193,713 deaths). Overall, 80.3% of deaths were due to ischaemic heart disease, which was the most common cause of death in all countries.

Dietary protein and blood pressure: an umbrella review of systematic reviews and evaluation of the evidence.

Boeing H, Amini AM, Haardt J, Schmidt A, Bischoff-Ferrari HA, Buyken AE, Egert S, Ellinger S, Kroke A, Lorkowski S, Louis S, Nimptsch K, Schulze MB, Schutkowski A, Schwingshackl L, Siener R, Zittermann A, Watzl B, Stangl GI; German Nutrition Society.

Eur J Nutr 2024; im Druck. doi: 10.1007/s00394-024-03336-8

Introduction: This umbrella review aimed to investigate the evidence of an effect of dietary intake of total protein, animal and plant protein on blood pressure (BP), and hypertension (PROSPERO: CRD42018082395).
Methods: PubMed, Embase and Cochrane Database were systematically searched for systematic reviews (SRs) of prospective studies with or without meta-analysis published between 05/2007 and 10/2022. The methodological quality and outcome-specific certainty of evidence were assessed by the AMSTAR 2 and NutriGrade tools, followed by an assessment of the overall certainty of evidence. SRs investigating specific protein sources are described in this review, but not included in the assessment of the overall certainty of evidence.
Results: Sixteen SRs were considered eligible for the umbrella review. Ten of the SRs investigated total protein intake, six animal protein, six plant protein and four animal vs. plant protein. The majority of the SRs reported no associations or effects of total, animal and plant protein on BP (all "possible" evidence), whereby the uncertainty regarding the effects on BP was particularly high for plant protein. Two SRs addressing milk-derived protein showed a reduction in BP; in contrast, SRs investigating soy protein found no effect on BP. The outcome-specific certainty of evidence of the SRs was mostly rated as low.
Discussion/conclusion: This umbrella review showed uncertainties whether there are any effects on BP from the intake of total protein, or animal or plant proteins, specifically. Based on data from two SRs with milk protein, it cannot be excluded that certain types of protein could favourably influence BP.

Characterization of different inflammatory skin conditions in a mouse model of DNCB-induced atopic dermatitis.

Riedl R, Kühn A, Hupfer Y, Hebecker B, Peltner LK, Jordan PM, Werz O, Lorkowski S, Wiegand C, Wallert M.

Inflammation 2024; 47(2):771-788. doi: 10.1007/s10753-023-01943-x

The mouse model of 2,4-dinitrochlorbenzene (DNCB)-induced human-like atopic dermatitis (hlAD) has been widely used to test novel treatment strategies and compounds. However, the study designs and methods are highly diverse, presenting different hlAD disease patterns that occur after sensitization and repeated challenge with DNCB on dorsal skin. In addition, there is a lack of information about the progression of the disease during the experiment and the achieved pheno- and endotypes, especially at the timepoint when therapeutic treatment is initiated. We here examine hlAD in a DNCB-induced BALB/cJRj model at different timepoints: (i) before starting treatment with dexamethasone, representing a standard drug control (day 12) and (ii) at the end of the experiment (day 22). Both timepoints display typical AD-associated characteristics: skin thickening, spongiosis, hyper- and parakeratosis, altered cytokine and gene expression, increased lipid mediator formation, barrier protein and antimicrobial peptide abnormalities, as well as lymphoid organ hypertrophy. Increased mast cell infiltration into the skin and elevated immunoglobulin E plasma concentrations indicate a type I allergy response. The DNCB-treated skin showed an extrinsic moderate sub-acute hlAD lesion at day 12 and an extrinsic mild sub-acute to chronic pheno- and endotype at day 22 with a dominating Th2 response. A dependency of the filaggrin formation and expression in correlation to the disease severity in the DNCB-treated skin was found. In conclusion, our study reveals a detailed classification of a hlAD at two timepoints with different inflammatory skin conditions and pheno- and endotypes, thereby providing a better understanding of the DNCB-induced hlAD model in BALB/cJRj mice.

Global, regional, and national burden of disorders affecting the nervous system, 1990-2021: a systematic analysis for the Global Burden of Disease Study 2021.
GBD 2021 Nervous System Disorders Collaborators.
Lancet Neurol 2024; 23(4):344-381. doi: 10.1016/S1474-4422(24)00038-3

Background: Disorders affecting the nervous system are diverse and include neurodevelopmental disorders, late-life neurodegeneration, and newly emergent conditions, such as cognitive impairment following COVID-19. Previous publications from the Global Burden of Disease, Injuries, and Risk Factor Study estimated the burden of 15 neurological conditions in 2015 and 2016, but these analyses did not include neurodevelopmental disorders, as defined by the International Classification of Diseases (ICD)-11, or a subset of cases of congenital, neonatal, and infectious conditions that cause neurological damage. Here, we estimate nervous system health loss caused by 37 unique conditions and their associated risk factors globally, regionally, and nationally from 1990 to 2021.
Methods: We estimated mortality, prevalence, years lived with disability (YLDs), years of life lost (YLLs), and disability-adjusted life-years (DALYs), with corresponding 95% uncertainty intervals (UIs), by age and sex in 204 countries and territories, from 1990 to 2021. We included morbidity and deaths due to neurological conditions, for which health loss is directly due to damage to the CNS or peripheral nervous system. We also isolated neurological health loss from conditions for which nervous system morbidity is a consequence, but not the primary feature, including a subset of congenital conditions (ie, chromosomal anomalies and congenital birth defects), neonatal conditions (ie, jaundice, preterm birth, and sepsis), infectious diseases (ie, COVID-19, cystic echinococcosis, malaria, syphilis, and Zika virus disease), and diabetic neuropathy. By conducting a sequela-level analysis of the health outcomes for these conditions, only cases where nervous system damage occurred were included, and YLDs were recalculated to isolate the non-fatal burden directly attributable to nervous system health loss. A comorbidity correction was used to calculate total prevalence of all conditions that affect the nervous system combined.
Findings: Globally, the 37 conditions affecting the nervous system were collectively ranked as the leading group cause of DALYs in 2021 (443 million, 95% UI 378-521), affecting 3·40 billion (3·20-3·62) individuals (43·1%, 40·5-45·9 of the global population); global DALY counts attributed to these conditions increased by 18·2% (8·7-26·7) between 1990 and 2021. Age-standardised rates of deaths per 100 000 people attributed to these conditions decreased from 1990 to 2021 by 33·6% (27·6-38·8), and age-standardised rates of DALYs attributed to these conditions decreased by 27·0% (21·5-32·4). Age-standardised prevalence was almost stable, with a change of 1·5% (0·7-2·4). The ten conditions with the highest age-standardised DALYs in 2021 were stroke, neonatal encephalopathy, migraine, Alzheimer's disease and other dementias, diabetic neuropathy, meningitis, epilepsy, neurological complications due to preterm birth, autism spectrum disorder, and nervous system cancer.
Interpretation: As the leading cause of overall disease burden in the world, with increasing global DALY counts, effective prevention, treatment, and rehabilitation strategies for disorders affecting the nervous system are needed.

Global burden of cardiovascular diseases and risks, 1990-2022.
Mensah GA, Fuster V, Murray CJL, Roth GA; Global Burden of Cardiovascular Diseases and Risks Collaborators.
J Am Coll Cardiol 2023; 82(25):2350-2473. doi: 10.1016/j.jacc.2023.11.007

Kein Abstract verfügbar.

Protein intake and body weight, fat mass and waist circumference: an umbrella review of systematic reviews for the evidence-based guideline on protein intake of the German Nutrition Society.

Ellinger S, Amini AM, Haardt J, Lehmann A, Schmidt A, Bischoff-Ferrari HA, Buyken AE, Kroke A, Kühn T, Louis S, Lorkowski S, Nimptsch K, Schulze MB, Schwingshackl L, Siener R, Stangl GI, Volkert D, Zittermann A, Watzl B, Egert S; German Nutrition Society.

Eur J Nutr 2024; 63(1):3-32. doi: 10.1007/s00394-023-03220-x

Purpose: This umbrella review aimed to assess whether dietary protein intake with regard to quantitative (higher vs. lower dietary protein intake) and qualitative considerations (total, plant-based or animal-based protein intake) affects body weight (BW), fat mass (FM) and waist circumference (WC).

Methods: A systematic literature search was conducted in PubMed, Embase and Cochrane Database of Systematic Reviews for systematic reviews (SRs) with and without meta-analyses of prospective studies published between 04 October 2007 and 04 January 2022. Methodological quality and outcome-specific certainty of evidence of the retrieved SRs were assessed by using AMSTAR 2 and NutriGrade, respectively, in order to rate the overall certainty of evidence using predefined criteria.

Results: Thirty-three SRs were included in this umbrella review; 29 were based on randomised controlled trials, a few included cohort studies. In studies without energy restriction, a high-protein diet did not modulate BW, FM and WC in adults in general (all "possible" evidence); for older adults, overall certainty of evidence was "insufficient" for all parameters. Under hypoenergetic diets, a high-protein diet mostly decreased BW and FM, but evidence was "insufficient" due to low methodological quality. Evidence regarding an influence of the protein type on BW, FM and WC was "insufficient".

Conclusion: "Possible" evidence exists that the amount of protein does not affect BW, FM and WC in adults under isoenergetic conditions. Its impact on the reduction in BW and FM under hypoenergetic conditions remains unclear; evidence for an influence of protein type on BW, FM and WC is "insufficient".

Protein intake and type 2 diabetes mellitus: an umbrella review of systematic reviews for the evidence-based guideline for protein intake of the German Nutrition Society.

Schulze MB, Haardt J, Amini AM, Kalotai N, Lehmann A, Schmidt A, Buyken AE, Egert S, Ellinger S, Kroke A, Kühn T, Louis S, Nimptsch K, Schwingshackl L, Siener R, Zittermann A, Watzl B, Lorkowski S; German Nutrition Society.

Eur J Nutr 2024; 63(1):33-50. doi: 10.1007/s00394-023-03234-5

Purpose: Protein-rich foods show heterogeneous associations with the risk of type 2 diabetes (T2D) and it remains unclear whether habitual protein intake is related to T2D risk. We carried out an umbrella review of systematic reviews (SR) of randomised trials and/or cohort studies on protein intake in relation to risks of T2D.

Methods: Following a pre-specified protocol (PROSPERO: CRD42018082395), we retrieved SRs on protein intake and T2D risk published between July 1st 2009 and May 22nd 2022, and assessed the methodological quality and outcome-specific certainty of the evidence using a modified version of AMSTAR 2 and NutriGrade, respectively. The overall certainty of evidence was rated according to predefined criteria.

Results: Eight SRs were identified of which six contained meta-analyses. The majority of SRs on total protein intake had moderate or high methodological quality and moderate outcome-specific certainty of evidence according to NutriGrade, however, the latter was low for the majority of SRs on animal and plant protein. Six of the eight SRs reported risk increases with both total and animal protein. According to one SR, total protein intake in studies was ~ 21 energy percentage (%E) in the highest intake category and 15%E in the lowest intake category. Relative Risks comparing high versus low intake in most recent SRs ranged from 1.09 (two SRs, 95% CIs 1.02-1.15 and 1.06-1.13) to 1.11 (1.05-1.16) for total protein (between 8 and 12 cohort studies included) and from 1.13 (1.08-1.19) to 1.19 (two SRs, 1.11-1.28 and 1.11-1.28) (8-9 cohort studies) for animal protein. However, SRs on RCTs examining major glycaemic traits (HbA_{1c}, fasting glucose, fasting insulin) do not support a clear biological link with T2D risk. For plant protein, some recent SRs pointed towards risk decreases and non-linear associations, however, the majority did not support an association with T2D risk.

Conclusion: Higher total protein intake was possibly associated with higher T2D risk, while there is insufficient evidence for a risk increase with higher intakes of animal protein and a risk decrease with plant protein intake. Given that most SRs on plant protein did not indicate an association, there is possibly a lack of an effect.