

**Wissenschaftliche Publikationen aus dem Institut für  
Ernährungswissenschaften veröffentlicht von Januar bis Mai 2021**

*Front Nutr 2021; 7:608854. doi: 10.3389/fnut.2020.608854*

**A study protocol for a parallel-designed trial evaluating the impact of plant-based diets in comparison to animal-based diets on health and prevention of non-communicable disease - the Nutritional Evaluation (NuEva) study**

Dawczynski C

**Abstract**

**Background and Aims:** Currently, there is a continuing upward trend for plant-based lifestyles in Germany and Europe. The implementation of vegetarian and vegan lifestyles is characterized by omitting defined food groups such as fish, meat, sausage (vegetarians), or dairy products and honey (vegans). This carries the risk of an undersupply of valuable nutrients. The NuEva study is designed to examine this hypothesis and to evaluate the impact of plant-based diets on health status and disease risk.

**Methods:** The NuEva study is a parallel-designed trial with at least 55 participants for each diet (vegetarian, vegan, flexitarian [rare meat/sausage consumption, once or twice per week]), and participants who consume a traditional Western diet as the control group. In the screening period critical nutrients are identified for the studied diets by analysis of a broad spectrum of nutrients in the human samples (fatty acids, vitamins, minerals, trace elements, nutrient metabolites).

**Results:** Based on the data from the screening period, defined menu plans, ensuring an adequate nutrient intake in accordance with the nutritional guidelines are prepared for each group. The plans are adapted and personalized to individual energy requirements based on the basal metabolic rate and physical activity level. The compliance with the NuEva concept and their impact on nutrient status and cardiovascular risk factors are validated during the intervention period of the NuEva study over 1 year. To investigate the impact of the studied diets on the microbiome, feces samples are collected at the beginning and after the 12 months intervention period (follow up: 12 months).

**Conclusion:** The NuEva study is designed to investigate the impact of common diets on health and disease status, with focus on prevention of cardiovascular diseases. In addition, the effectiveness of the prepared nutritional coaching strategy, ensuring optimal nutrient intake in accordance with the guidelines, is validated during the intervention period of the NuEva study.

**Clinical Trial Registration:** Registered under [ClinicalTrials.gov](https://clinicaltrials.gov) Identifier no. NCT03582020.

**A study protocol of a randomized trial evaluating the potential of an intensive personal nutritional counselling program using defined menu plans on cardiovascular risk factors: The MoKaRi trial**

Dawczynski C, Cullen P, Schlattmann P, Lorkowski S

**Abstract**

Changes in dietary habits and lifestyle can reduce the risk of cardiovascular disease which is the leading cause of death worldwide. Objectives of the MoKaRi study The MoKaRi (modulation of cardiovascular risk factors) intervention study is designed to evaluate the effectiveness and potential of the developed MoKaRi concept. The MoKaRi concept comprises three components, each designed to improve dietary behavior. The first component entails using daily menu plans to implement a defined “cardioprotective diet”. This diet consists of seasonal menu plans which are characterized by:

- (i) a personalized energy supply depending on his or her age, gender, level of physical activity.
- (ii) an adequate intake of carbohydrates, protein, fat, vitamins, minerals, and trace elements according to the guidelines of the German Society of Nutrition (DGE).
- (iii) a recommended intake of saturated fatty acids (SFA; < 7% of caloric intake (En%)), monounsaturated fatty acids (MUFA; > 10 En%), polyunsaturated fatty acids (PUFA; approx. 10 En%), and long-chain n-3 PUFA (≥500 mg per day).
- (iv) measures to encourage consumption of vegetables and fruits, and.
- (v) eating more than 40 g dietary fiber every day.

Half of the participants will be scheduled to consume an additional 3 g of long-chain n- 3 PUFA every day in the form of fish oil.

The second component consists of regular one-on-one nutritional counseling, while a variety of further incentives make up the third component of the MoKaRi concept.

The MoKaRi study will provide essential insights into the relationship between defined nutrient intake, markers of food intake and health status. Our specific aim is to investigate the influence of dietary and lifestyle choices have on cardiovascular health.

The information and practical tools suitable for daily use, such as the personalized menu plans, could help to transfer knowledge on nutritional facts to the general population. In this way, the validated MoKaRi concept may contribute to the prevention and therapy of cardiovascular diseases.

*Ernährungs Umschau 2021; 68(2): 26-35.*

## **Personalisierte Ernährung zur Gewichtsreduktion: wissenschaftlicher Standpunkt aus verschiedenen Perspektiven**

Holzapfel C, Dawczynski C, Henze A, Simon MC

### **Abstract**

Das Thema personalisierte Ernährung ist in aller Munde und wird sowohl von Laien als auch in der Fachwelt vielfach diskutiert, obwohl es keine einheitliche Definition für den Begriff der personalisierten Ernährung gibt. Verschiedene Ansätze, unter Berücksichtigung von Genetik, Mikrobiom sowie Stoffwechsel, werden diskutiert und zum Teil von kommerziellen Anbietern als personalisierte Ernährungskonzepte angeboten. Betrachtet man die verschiedenen Aspekte der personalisierten Ernährung bezüglich ihrer wissenschaftlichen Evidenz und klinischen Relevanz etwas genauer, so wird deutlich, dass personalisierte Ernährungsempfehlungen, wie sie derzeit primär von kommerziellen Unternehmen angeboten werden, nicht evidenzbasiert sind. Derzeit ist es nicht möglich, basierend auf z. B. der genetischen Ausstattung eines Menschen oder der Zusammensetzung der Darmmikrobiota personalisierte evidenzbasierte Ernährungsempfehlungen zu geben. Die Berücksichtigung phänotypischer Merkmale, wie z. B. Alter, Geschlecht, körperliche Aktivität, Gesundheitsstatus und Alltagssituation, ist durchaus sinnvoll und wird von qualifizierten Ernährungsfachkräften angewandt. Dies ist ein möglicher Ansatz der personalisierten Ernährung, an dem weiterhin festgehalten werden soll.

*Toxics. 2021 Apr 27;9(5):96. doi: 10.3390/toxics9050096*

## **Cellular Uptake and Toxicological Effects of Differently Sized Zinc Oxide Nanoparticles in Intestinal Cells**

Mittag A, Hoera C, Kämpfe A, Westermann M, Kuckelkorn J, Schneider T, Gleis M

### **Abstract**

Due to their beneficial properties, the use of zinc oxide nanoparticles (ZnO NP) is constantly increasing, especially in consumer-related areas, such as food packaging and food additives, which is leading to an increased oral uptake of ZnO NP. Consequently, the aim of our study was to investigate the cellular uptake of two differently sized ZnO NP (<50 nm and <100 nm; 12-1229 µmol/L) using two human intestinal cell lines (Caco-2 and LT97) and to examine the possible resulting toxic effects. ZnO NP (<50 nm and <100 nm) were internalized by both cell lines and led to intracellular changes. Both ZnO NP caused time- and dose-dependent cytotoxic effects, especially at concentrations of 614 µmol/L and 1229 µmol/L, which was associated with an increased rate of apoptotic and dead cells. ZnO NP < 100 nm altered the cell cycle of LT97 cells but not that of Caco-2 cells. ZnO NP < 50 nm led to the formation of micronuclei in LT97 cells. The Ames test revealed no mutagenicity for both ZnO NP. Our results indicate the potential toxicity of ZnO NP after oral exposure, which should be considered before application.

*Food Funct.* 2021 Mar 1;12(4):1452-1457. doi: 10.1039/d0fo02842h

## **Impact of pH changes on metal oxide nanoparticle behaviour during artificial digestion**

Schneider T, Mittag A, Westermann M, Gleis M

### **Abstract**

The physicochemical properties of orally ingested metal nanoparticles can be influenced by the conditions prevailing in the digestive tract. In our work, we demonstrate the strong influence of the pH value on particle fate using a simplified digestion approach to analyze magnesium oxide, copper oxide and zinc oxide nanoparticles and show why a separate consideration of the digestion parameters is necessary.

*Int J Food Sci Nutr.* 2021 Feb;72(1):57-69. doi: 10.1080/09637486.2020.1772205

## **Chemopreventive effects of raw and roasted oat flakes after *in vitro* fermentation with human faecal microbiota**

Gleis M, Zetzmann S, Lorkowski S, Dawczynski C, Schlörmann W

### **Abstract**

The aim of the present study was to analyse chemopreventive effects of oat flakes under consideration of processing. Thin and thick flakes were roasted and subjected to an *in vitro* digestion and fermentation. Fermentation supernatants (FS) were characterised and chemopreventive effects were analysed in LT97 colon adenoma cells. Compared to the fermentation control, pH values were decreased (from pH 6.3 to pH 5.0) and concentrations of SCFA, in particular butyrate, were increased in oat FS (2.6-fold, on average). Ammonia levels were not altered. Oat FS significantly decreased cell growth time- and dose-dependently. Caspase 3 activity was significantly increased (9.7-fold, on average). Oat FS slightly increased the mRNA expression of *CAT* (2.0-fold), *SOD2* (1.7-fold) and *GSTP1* (2.8-fold), on average, while *GPX1* mRNA (0.3-fold) was decreased. The results indicate a chemopreventive potential of *in vitro* digested oat flakes regarding colon cancer development mediated mostly by growth inhibition and apoptosis, unaffected by roasting.

## **Impact of processing degree on fermentation profile and chemopreventive effects of oat and waxy barley in LT97 colon adenoma cells**

Schlörmann W, Keller F, Zetzmann S, Lorkowski S, Dawczynski C, Gleis M

### **Abstract**

The chemopreventive effects of  $\beta$ -glucan-rich cereals such as oat and barley (beta@barley) have been examined previously, but studies comparing fermentation characteristics and chemopreventive effects of oat and barley of different processing stages are rare. Therefore, the present study aims at investigating the fermentation end points (pH values, concentrations of short-chain fatty acids (SCFA) and ammonia) in fermentation supernatants (FS) obtained from differently processed oat and barley samples (kernels, thick and thin flakes). Chemopreventive effects of FS, such as growth inhibition, apoptosis, and induction of cell cycle- and redox-relevant genes (*p21*, *SOD2*), were analysed in LT97 colon adenoma cells. After fermentation, pH values were reduced ( $\Delta$  pH - 1.3, on average) and SCFA concentrations were increased ( $\Delta$  + 59 mmol/L, on average) with a shift towards butyrate formation in FS obtained from oat and barley samples compared to the fermentation negative control (FS blank). Ammonia was reduced more effectively in FS obtained from barley ( $\Delta$  - 4.6 mmol/L, on average) than from oat samples ( $\Delta$  - 1.0 mmol/L, on average). Treatment of LT97 cells with FS resulted in a time- and dose-dependent reduction of cell number, an increase in caspase-3 activity (up to 9.0-fold after 24 h, on average) and an induction of *p21* (2.1-fold, on average) and *SOD2* (2.3-fold, on average) mRNA expression, while no genotoxic effects were observed. In general, the results indicate no concrete effect of the type of cereal or processing stage on fermentation and chemopreventive effects of oat and barley.

*Pharmacol Res* 2021;167:105556. doi: 10.1016/j.phrs.2021.105556

## **Anti-inflammatory celastrol promotes a switch from leukotriene biosynthesis to formation of specialized pro-resolving lipid mediators**

Pace S, Zhang K, Jordan PM, Bilancia R, Wang W, Börner F, Hofstetter RK, Potenza M, Kretzer C, Gerstmeier J, Fischer D, Lorkowski S, Gilbert NC, Newcomer ME, Rossi A, Chen X, Werz O

### **Abstract**

The pentacyclic triterpenoid quinone methide celastrol (CS) from *Tripterygium wilfordii* Hook. f. effectively ameliorates inflammation with potential as therapeutics for inflammatory diseases. However, the molecular mechanisms underlying the anti-inflammatory and inflammation-resolving features of CS are incompletely understood. Here we demonstrate that CS potently inhibits the activity of human 5-lipoxygenase (5-LOX), the key enzyme in pro-inflammatory leukotriene (LT) formation, in cell-free assays with  $IC_{50} = 0.19-0.49 \mu M$ . Employing metabololipidomics using ultra-performance liquid chromatography coupled to tandem mass spectrometry in activated human polymorphonuclear leukocytes or M1 macrophages we found that CS (1  $\mu M$ ) potently suppresses 5-LOX-derived products without impairing the formation of lipid mediators (LM) formed by 12-/15-LOXs as well as fatty acid substrate release. Intriguingly, CS induced the generation of 12-/15-LOX-derived LM including the specialized pro-resolving mediator (SPM) resolvin D5 in human M2 macrophages. Finally, intraperitoneal pre-treatment of mice with 10 mg/kg CS strongly impaired zymosan-induced LT formation and simultaneously elevated the levels of SPM and related 12-/15-LOX-derived LM in peritoneal exudates, spleen and plasma in vivo. Conclusively, CS promotes a switch from LT biosynthesis to formation of SPM which may underlie the anti-inflammatory and inflammation-resolving effects of CS, representing an interesting pharmacological strategy for intervention with inflammatory disorders.

## **The role of biofactors in the prevention and treatment of age-related diseases**

Frank J, Kisters K, Stirban OA, Obeid R, Lorkowski S, Wallert M, Egert S, Podszun MC, Eckert GP, Pettersen JA, Venturelli S, Classen HG, Golombek J

### **Abstract**

The present demographic changes toward an aging society caused a rise in the number of senior citizens and the incidence and burden of age-related diseases (such as cardiovascular diseases [CVD], cancer, nonalcoholic fatty liver disease [NAFLD], diabetes mellitus, and dementia), of which nearly half is attributable to the population  $\geq 60$  years of age. Deficiencies in individual nutrients have been associated with increased risks for age-related diseases and high intakes and/or blood concentrations with risk reduction. Nutrition in general and the dietary intake of essential and nonessential biofactors is a major determinant of human health, the risk to develop age-related diseases, and ultimately of mortality in the older population. These biofactors can be a cost-effective strategy to prevent or, in some cases, even treat age-related diseases. Examples reviewed herein include omega-3 fatty acids and dietary fiber for the prevention of CVD,  $\alpha$ -tocopherol (vitamin E) for the treatment of biopsy-proven nonalcoholic steatohepatitis, vitamin D for the prevention of neurodegenerative diseases, thiamine and  $\alpha$ -lipoic acid for the treatment of diabetic neuropathy, and the role of folate in cancer epigenetics. This list of potentially helpful biofactors in the prevention and treatment of age-related diseases, however, is not exhaustive and many more examples exist. Furthermore, since there is currently no generally accepted definition of the term biofactors, we here propose a definition that, when adopted by scientists, will enable a harmonization and consistent use of the term in the scientific literature.

*Biochim Biophys Acta Mol Cell Biol Lipids 2021; 1866(4):158875. doi: 10.1016/j.bbalip.2021.158875*

## **The vitamin E long-chain metabolite $\alpha$ -13'-COOH affects macrophage foam cell formation via modulation of the lipoprotein lipase system**

Kluge S, Schubert M, Börmel L, Lorkowski S

### **Abstract**

The  $\alpha$ -tocopherol-derived long-chain metabolite ( $\alpha$ -LCM)  $\alpha$ -13'-carboxychromanol ( $\alpha$ -13'-COOH) is formed via enzymatic degradation of  $\alpha$ -tocopherol ( $\alpha$ -TOH) in the liver. In the last decade,  $\alpha$ -13'-COOH has emerged as a new regulatory metabolite revealing more potent or even different effects compared with its vitamin precursor  $\alpha$ -TOH. The detection of  $\alpha$ -13'-COOH in human serum has further strengthened the concept of its physiological relevance as a potential regulatory molecule. Here, we present a new facet on the interaction of  $\alpha$ -13'-COOH with macrophage foam cell formation. We found that  $\alpha$ -13'-COOH (5  $\mu$ M) increases angiopoietin-like 4 (ANGPTL4) mRNA expression in human THP-1 macrophages in a time- and dose-dependent manner, while  $\alpha$ -TOH (100  $\mu$ M) showed no effects. Interestingly, the mRNA level of lipoprotein lipase (LPL) was not influenced by  $\alpha$ -13'-COOH, but  $\alpha$ -TOH treatment led to a reduction of LPL mRNA expression. Both compounds also revealed different effects on protein level: while  $\alpha$ -13'-COOH reduced the secreted amount of LPL protein via induction of ANGPTL4 cleavage, i.e. activation, the secreted amount of LPL in the  $\alpha$ -TOH-treated samples was diminished due to the inhibition of mRNA expression. In line with this, both compounds reduced the catalytic activity of LPL. However,  $\alpha$ -13'-COOH but not  $\alpha$ -TOH attenuated VLDL-induced lipid accumulation by 35%. In conclusion, only  $\alpha$ -13'-COOH revealed possible antiatherogenic effects due to the reduction of VLDL-induced foam cell formation in THP-1 macrophages. Our results provide further evidence for the role of  $\alpha$ -13'-COOH as a functional metabolite of its vitamin E precursor.

## **Modified bacterial cellulose dressings to treat inflammatory wounds**

Beekmann U, Zahel P, Karl B, Schmölz L, Börner F, Gerstmeier J, Werz O, Lorkowski S, Wiegand C, Fischer D, Kralisch D

### **Abstract**

Natural products suited for prophylaxis and therapy of inflammatory diseases have gained increasing importance. These compounds could be beneficially integrated into bacterial cellulose (BC), which is a natural hydropolymer applicable as a wound dressing and drug delivery system alike. This study presents experimental outcomes for a natural anti-inflammatory product concept of boswellic acids from frankincense formulated in BC. Using esterification respectively (resp.) oxidation and subsequent coupling with phenylalanine and tryptophan, *post*-modification of BC was tested to facilitate lipophilic active pharmaceutical ingredient (API) incorporation. Diclofenac sodium and indomethacin were used as anti-inflammatory model drugs before the findings were transferred to boswellic acids. By acetylation of BC fibers, the loading efficiency for the more lipophilic API indomethacin and the release was increased by up to 65.6% and 25%, respectively, while no significant differences in loading could be found for the API diclofenac sodium. *Post*-modifications could be made while preserving biocompatibility, essential wound dressing properties and anti-inflammatory efficacy. Eventually, *in vitro* wound closure experiments and evaluations of the effect of secondary dressings completed the study.

## **Inflammatory diseases and vitamin E - What do we know and where do we go?**

Wallert M, Börmel L, Lorkowski S

### **Abstract**

Inflammation-driven diseases and related comorbidities, such as the metabolic syndrome, obesity, fatty liver disease, and cardiovascular diseases cause significant global burden. There is a growing body of evidence that nutrients alter inflammatory responses and can therefore make a decisive contribution to the treatment of these diseases. Recently, the inflammasome, a cytosolic multiprotein complex, has been identified as a key player in inflammation and the development of various inflammation-mediated disorders, with nucleotide-binding domain and leucine-rich repeat pyrin domain (NLRP) 3 being the inflammasome of interest. Here an overview about the cellular signaling pathways underlying nuclear factor "kappa-light-chain-enhancer" of activated B-cells (NF- $\kappa$ B)- and NLRP3-mediated inflammatory processes, and the pathogenesis of the inflammatory diseases atherosclerosis and non-alcoholic fatty liver disease (NAFLD) is provided; next, the current state of knowledge for drug-based and dietary-based interventions for treating cardiovascular diseases and NAFLD is discussed. To date, one of the most important antioxidants in the human diet is vitamin E. Various *in vitro* and *in vivo* studies suggest that the different forms of vitamin E and also their derivatives have anti-inflammatory activity. Recent publications suggest that vitamin E-and possibly metabolites of vitamin E-are a promising therapeutic approach for treating inflammatory diseases such as NAFLD.

## **Are trace element concentrations suitable biomarkers for the diagnosis of cancer?**

Lossow K, Schwarz M, Kipp AP

### **Abstract**

Despite advances in cancer research, cancer is still one of the leading causes of death worldwide. An early diagnosis substantially increases the survival rate and treatment success. Thus, it is important to establish biomarkers which could reliably identify cancer patients. As cancer is associated with changes in the systemic trace element status and distribution, serum concentrations of selenium, iron, copper, and zinc could contribute to an early diagnosis. To test this hypothesis, case control studies measuring trace elements in cancer patients vs. matched controls were selected and discussed focusing on lung, prostate, breast, and colorectal cancer. Overall, cancer patients had elevated serum copper and diminished zinc levels, while selenium and iron did not show consistent changes for all four cancer types. Within the tumor tissue, mainly copper and selenium are accumulating. Whether these concentrations also predict the survival probability of cancer patients needs to be further investigated.

*Redox Biol.* 2021 Apr 15;43:101972. doi: 10.1016/j.redox.2021.101972

## **A coupled enzyme assay for detection of selenium-binding protein 1 (SELENBP1) methanethiol oxidase (MTO) activity in mature enterocytes**

Philipp TM, Will A, Richter H, Winterhalter PR, Pohnert G, Steinbrenner H, Klotz LO

### **Abstract**

Methanethiol, a gas with the characteristic smell of rotten cabbage, is a product of microbial methionine degradation. In the human body, methanethiol originates primarily from bacteria residing in the lumen of the large intestine. Selenium-binding protein 1 (SELENBP1), a marker protein of mature enterocytes, has recently been identified as a methanethiol oxidase (MTO). It catalyzes the conversion of methanethiol to hydrogen sulfide (H<sub>2</sub>S), hydrogen peroxide (H<sub>2</sub>O<sub>2</sub>) and formaldehyde. Here, human Caco-2 intestinal epithelial cells were subjected to enterocyte-like differentiation, followed by analysis of SELENBP1 levels and MTO activity. To that end, we established a novel coupled assay to assess MTO activity mimicking the proximity of microbiome and intestinal epithelial cells in vivo. The assay is based on in situ-generation of methanethiol as catalyzed by a bacterial recombinant l-methionine gamma-lyase (MGL), followed by detection of H<sub>2</sub>S and H<sub>2</sub>O<sub>2</sub>. Applying this assay, we verified the loss and impairment of MTO function in SELENBP1 variants (His329Tyr; Gly225Trp) previously identified in individuals with familial extraoral halitosis. MTO activity was strongly enhanced in Caco-2 cells upon enterocyte differentiation, in parallel with increased SELENBP1 levels. This suggests that mature enterocytes located at the tip of colonic crypts are capable of eliminating microbiome-derived methanethiol.



## **Regulation of GC box activity by 8-oxoguanine**

Müller N, Khobta A

### **Abstract**

The oxidation-induced DNA modification 8-oxo-7,8-dihydro-2'-deoxyguanosine (8-oxodG) was recently implicated in the activation and repression of gene transcription. We aimed at a systematic characterisation of the impacts of 8-oxodG on the activity of a GC box placed upstream from the RNA polymerase II core promoter. With the help of reporters carrying single synthetic 8-oxodG residues at four conserved G:C base pairs (underlined) within the 5'-TGGGCGGGAGC-3' GC box sequence, we identified two modes of interference of 8-oxodG with the promoter activity. Firstly, 8-oxodG in the purine-rich (but not in the pyrimidine-rich) strand caused direct impairment of transcriptional activation. In addition, and independently of the first mechanism, 8-oxodG initiated a decline of the gene expression, which was mediated by the specific DNA glycosylase OGG1. For the different 8-oxodG positions, the magnitude of this effect reflected the excision preferences of OGG1. Thus, 8-oxodG seeded in the pyrimidine-rich strand was excised with the highest efficiency and caused the most pronounced decrease of the promoter activity. Conversely, 8-oxodG in the symmetric position within the same CpG dinucleotide, was poorly excised and induced no decline of the gene expression. Of note, abasic lesions caused gene silencing in both positions. By contrast, an uncleavable apurinic lesion in the pyrimidine-rich strand enhanced the GC box activity, suggesting that the AP endonuclease step provides a switch between the active versus repressed promoter states during base excision repair.

**Carotenoids: Considerations for their use in functional foods, nutraceuticals, nutricosmetics, supplements, botanicals, and novel foods in the context of sustainability, circular economy, and climate change**

Meléndez-Martínez AJ, Böhm V, Borge GIA, Cano MP, Fikselová M, Gruskiene R, Lavelli V, Loizzo MR, Mandić AI, Mapelli Brahm P, Mišan AČ, Pinteá AM, Sereikaitė J, Vargas-Murga L, Vlaisavljević SS, Vulić JJ, O'Brien NM

**Abstract**

Carotenoids are versatile isoprenoids that are important in food quality and health promotion. There is a need to establish recommended dietary intakes/nutritional reference values for carotenoids. Research on carotenoids in agro-food and health is being propelled by the two multidisciplinary international networks, the Ibero-American Network for the Study of Carotenoids as Functional Foods Ingredients (IBERCAROT; <http://www.cytel.org>) and the European Network to Advance Carotenoid Research and Applications in Agro-Food and Health (EUROCAROTEN; <http://www.eurocaroten.eu>). In this review, considerations for their safe and sustainable use in products mostly intended for health promotion are provided. Specifically, information about sources, intakes, and factors affecting bioavailability is summarized. Furthermore, their health-promoting actions and importance in public health in relation to the contribution of reducing the risk of diverse ailments are synthesized. Definitions and regulatory and safety information for carotenoid-containing products are provided. Lastly, recent trends in research in the context of sustainable healthy diets are summarized.

## **From carotenoid intake to carotenoid blood and tissue concentrations – Implications for dietary intake recommendations**

Böhm V, Lietz G, Olmedilla-Alonso B, Phelan D, Reboul E, Bánati D, Borel P, Corte-Real J, de Lera AR, Desmarchelier C, Dulinska-Litewka J, Landrier J-F, Milisav I, Nolan J, Porrini M, Riso P, Roob JM, Valanou E, Wawrzyniak A, Winklhofer-Roob BM, Rühl R, Bohn T

### **Abstract**

There is uncertainty regarding carotenoid intake recommendations, because positive and negative health effects have been found or are correlated with carotenoid intake and tissue levels (including blood, adipose tissue, and the macula), depending on the type of study (epidemiological vs intervention), the dose (physiological vs supraphysiological) and the matrix (foods vs supplements, isolated or used in combination). All these factors, combined with interindividual response variations (eg, depending on age, sex, disease state, genetic makeup), make the relationship between carotenoid intake and their blood/tissue concentrations often unclear and highly variable. Although blood total carotenoid concentrations <1000nmol/L have been related to increased chronic disease risk, no dietary reference intakes (DRIs) exist. Although high total plasma/serum carotenoid concentrations of up to 7500nmol/L are achievable after supplementation, a plateauing effect for higher doses and prolonged intake is apparent. In this review and position paper, the current knowledge on carotenoids in serum/plasma and tissues and their relationship to dietary intake and health status is summarized with the aim of proposing suggestions for a “normal,” safe, and desirable range of concentrations that presumably are beneficial for health. Existing recommendations are likewise evaluated and practical dietary suggestions are included.