Interactions between nutrition and medicine in effect and law

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Summary and general discussion

The main objective of the studies presented in this thesis was to elucidate the shift of nutrition and pharmaceutics in both effect and subsequent legislation. **Chapter 1** introduces legislation upon nutrition and medicinal products and showed the shift of these concepts towards each other, by nutrition focussing on maintaining and improving health next to provide sufficient nutrients. **Chapter 2 and 3** analyse the implementation of the nutrition and health claim regulation in the field of food products containing antioxidants. The enforcement strategies of national enforcement authorities throughout the European Union are reviewed in **chapter 4**. **Chapter 5** reviews international pieces of legislation upon nutrition and health claims. The shifting perception of nutrition and medicinal products in effect are studied in **chapter 6 and 7**. **Chapter 8** applies the nutritional and toxicological knowledge to the characterisation of active ingredients under the nutrition and health claim regulation[i] (NHCR). The research presented in this thesis shows that it is necessary to scientifically unravel both the effects of nutrition and pharmaceutics as well as legislation surrounding these types of products to increase the clarity upon both.

Main findings

The implementation of the NHCR leads to discussion on its effectiveness

In **chapter 2** the consequences of the implementation of the NHCR in the field of food products containing antioxidants or claiming antioxidant activity are analysed. The origin and the creation of the NHCR as well as the involvement of EFSA in the implementation of this legislative act are reviewed. The assessment procedure of the scientific substantiation of health claims is studied by analysing opinions provided by EFSA on this evidence provided for putative health claims. Three criteria are shown to

[i] Regulation (EC) No 1924/2006 of the European Parliament and of the Council on nutrition and health claims made on foods (Consolidated version 13 December 2014).

be crucial in the health claim assessment by EFSA: (i) the food or functional ingredient must be well defined and characterised; (ii) the claimed effect must be well defined and be physiologically beneficial; and (iii) a cause and effect relationship between intake of the food or functional ingredient and the claimed effect must be established. The described criteria are shown to have various implications for research focussed on substantiating health claims. These implications however do not all seem to fit nutrition research as it is currently executed. The definition of health is highly debated, leading to the development of new methodologies to assess the effects of dietary components on health. This should be taken into consideration in assessing the scientific substantiation of health claims. In the case of antioxidants specifically, the complexity of the mechanisms and actions of these bioactives has not been recognised by the evaluating criteria, nor by the methodologies used to assess antioxidant effects on health. A clear divergence in claim authorisation (with eight authorised claims) versus claim submission (over 200 claims on antioxidants were proposed) highlights this.

Chapter 3 analyses the perception of stakeholders (industrials, regulatory experts, nutritional scientists and consumer representatives) on the implementation of the NHCR, to unravel the grounds of disproving the putative health claims on food products containing antioxidants or claiming antioxidant activity. Most health claims were considered to be refused based on the quality of the scientific evidence substantiating the proposed claims. The interviewed stakeholders attributed this to the use of scientific methods in substantiating evidence on which no general consensus had been reached, as well as a difference in expectations of submitting bodies and required criteria concerning the evidence in the assessment procedure. Three themes are identified on which the application of the NHCR should be improved: (i) enforcement; (ii) methodology in nutrition; and (iii) perceived impact of the NHCR on innovation, research, the market and consumers. The stakeholders are shown to have highly diverging perceptions, which gives rise to the question whether the NHCR in its current form is effective. The views expressed by the interviewed stakeholders on the

different themes could be valuable in focussing the discussion on the NHCR in capturing health effects.

Similar enforcement strategies for the NHCR throughout the EU are crucial for its effectiveness

With the NHCR aiming to protect consumers against false or incorrect claims as well as establish a level playing field in the internal market for all food producers, enforcement of the regulation is crucial. European food regulations, as the NHCR, are required to be enforced by national authorities. Due to Regulation (EC) No 882/2004[ii], when controlling compliance with feed and food law requirements the national authorities are obligated to adopt a risk-based enforcement approach. Our analysis in **chapter 4** however shows fragmented national enforcement practices. This is depicted by the development of 13 different guidance documents on the flexibility of wording and/or general compliance with the NHCR developed by 18 member states. In the meantime also diverging actions have been taken by member state authorities in correcting non-compliance, ranging from punitive measures as imposing fines to persuasive measures as naming and shaming. The NHCR is therefore currently shown to be unable to establish a level playing field. We call for the development of an EU-wide approach in enforcement to ensure fair competition in the internal market.

The global landscape of nutrition and health claim legislation is highly divergent

The European legislation on nutrition and health claims is compared with international pieces of legislation dealing with these types of claims in **chapter 5**. Thereby we depict the global diversity in approaches and envisioned ways to optimise procedures from a scientific perspective. Pieces of legislation of 28 jurisdictions are reviewed. Three

[ii] Regulation (EC) No 882/2004 of the European Parliament and of the Council of 29 April 2004 on official controls performed to ensure the verification of compliance with feed and food law, animal health and animal welfare rules (Consolidated version 30 June 2014).

prominent differences are discerned, concerning (i) the classification of different types of nutrition and health claims and their permitted use; (ii) variations arising in the (pre-marketing) authorisation procedures; and (iii) the use of the scientific minority opinion in substantiating claims. Although various studied approaches displayed positive aspects in their regulation of nutrition and health claims, no optimal approach has been identified to be implemented yet. It would be preferable to permit similar types of claims throughout jurisdictions and to permit the use of emerging evidence in the substantiation of claims that have lower probability to mislead consumers (as nutrition claims), with requiring pre-marketing approval for claims having higher impact. By harmonising these aspects globally, improved pieces of legislation could be developed that stimulate industrial efforts concerning functional foods and enhance the opportunity for consumers to use health-enhancing products.

The interactions between foods and medicinal products have either positive or negative effects

The shifting perception of the roles and effects of nutrition and medicinal products are studied in chapter 6 and 7. By evaluating the potential positive effects elicited by dietary components on chronic inflammatory lung diseases in **chapter 6**, we demonstrated several components that can decrease inflammatory markers in the lung and thereby improve lung function in patients. Taking into account the number of weighed articles in this literature review, n-3 PUFAs and vitamin E seem to beneficially influence both inflammatory and immunological markers as well as lung function of patients suffering from chronic inflammatory lung diseases. Many other dietary components show only small or no effects on inflammation and/or lung function, although the number of weighted studies is often too small for a reliable assessment. The potential beneficial influence of various dietary components on chronic inflammatory lung diseases might lead to improved quality of life of patients suffering from these diseases. We conclude that optimal dietary elements might reduce the required amounts of anti-inflammatory treatments, thereby decreasing both side effects and development of resistance.

In **chapter 7** the adverse events occurring due to concomitant intake of health-enhancing products and drugs that were reported to the Netherlands Pharmacovigilance Centre Lareb are studied. With the increased popularity of food supplements and herbal products, the risks of interactions occurring between prescribed drugs and these bioactive products increase. The 55 notified adverse events are suspected to be caused by the concomitant intake of bioactives and drugs. Most of these suspected interactions seem to occur during the metabolism of xenobiotics or in the pharmacodynamics stage. Where legislation is seen to distinct food and medicine, legislation concerning these different bioactive products is less clear-cut. This can only be resolved by increasing the molecular knowledge on bioactive substances and their potential interactions. Thereby potential interactions can be better understood and prevented on an individual level. By considering the dietary pattern and use of bioactive substances with prescribed medication, both health professionals and consumers will be increasingly aware of interactions and these interactive adverse effects can be prevented.

Characterisation of functional foods and ingredients should be based on their bioactive constituent

The first criterion in the assessment procedure of EFSA in reviewing scientific substantiation of health claims under the NHCR is the definition and characterisation of the active ingredient responsible for the claimed health effect. In **chapter 8** we analyse three health claims in which the active ingredient responsible for the health effect is directly connected to a specific food item containing this bioactive, either in the wording of the claim or in the specified conditions of use. Since the bioactive itself is held responsible for the health effect, the association of the food item with the bioactive component is not always justifiable. Two elements were shown to influence whether the bioactive ingredient would be linked to a specific food component: (i) the type of claim considered, differing between generic health claims (Article 13.1 claims) and new function health claims (Article 13.5 claims); and (ii) the substantiating evidence available and submitted in the dossier substantiating the proposed claim. We argue

that it would be preferable to chemically define the active ingredients for subsequent use in standardising the real bioactive substance in the claim. Along these lines, claims can be based on a bioactive constituent without the necessity to connect the claim to a specific matrix. Thereby health claims become more transparent upon the active ingredient that elicits the proposed health benefit, which makes the claims more relevant to both the industry and consumers. Therefore characterisation and defining the active ingredient should be central in the health claim assessment.

Implications and suggestions

The consumer's perspective

As described in the studies within this thesis, the focus of nutrition shifts more to the enhancement and maintenance of health, touching upon the application of medicinal products. The difference between both types of products is thereby narrowing. Consumers are seen to be more interested in maintaining and increasing their health by using more products as vitamins and dietary supplements or other health and wellness products, products for which growth is predicted in most European countries in the upcoming years[1–3]. Health consciousness of consumers is especially highly correlated to their interest in functional products[4]. The health-consciousness of consumers is not only shown in the expanded sales of health products, it is also exemplified by the popularity of the information on the Internet concerning health and healthy foods. Consumers thereby try to increase their knowledge on health and bioactive substances[5]. The elevated importance of health is however also suggested to lead to increased uncertainty of consumers on health[6].

The increased availability of information and increased amount of products lead to new opportunities for consumers in managing their health, as exemplified in chapter 6 and 7 on the combination of nutrition and medicinal products. Where in some cases combining different products can elicit beneficial effects on health as described in

chapter 6, chapter 7 depicts the risk of combining bioactive substances without professional advice. This demonstrates the need for health professionals as doctors, dietitians and nutritionists to give truthful and personal information to consumers. With increased information about bioactives and bioactive containing products, consumers will be better able to make well-informed decisions. Stakeholders as the food industry, nutritional scientists and legislators are seen to respond differently to the consumer's demand for safety, trust and truth upon health and health enhancing products.

The food industrial's perspective

Producers of food products focus on the development of new products that carry effect claims, claims on their naturalness, carry logos or focus on other unique selling points as taste or price of the product[7,8]. Various studies on purchasing behaviour identified health as an important factor for consumers in buying food products[7,8]. The increased interest in bioactive ingredients as potential health enhancing products resulted in the development of various product categories, including not only food supplements, but also other categories as functional foods, nutra- and cosmoceuticals and foods for special use are increasingly found on the market[1,2,9]. The legal boundaries set by the legislator on the communication of health enhancing effects on e.g. homeopathic medicinal products and foods are challenged by industrials by repositioning these products as medical devices. This enables producers to carry claims on the products that are not allowed under the nutrition and health claim regulation[10].

The scientist's perspective

Nutritional academics on the other hand focus on how the effects of nutrition should be tested, by discussing used methodology in assessing the effects on health and how health should actually be defined. The WHO definition of health as *'a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity'* was developed right after the Second World War in 1948[11]. Since this absolute approach did not result in a very practical definition, efforts have been made to develop a new definition of health recently[12]. An example of a definition more often

used to define health is 'the dynamic ability to adapt'[13]. This ability to adapt is also referred to as 'increased resilience': successful adaptation to adversity via recovering from the challenge and sustainability of the state of well-being[14]. This new definition is less static and more personal than the first definition Such a new definition of health also requires new measurements of health and health-enhancing compounds. Newly developed biomarkers and integrating the different (smaller) effects of one substance into one measure should be part of such approach[15,16]. The integration of pleiotropic effects of substances on health could also describe the effect of a substance as a 'risk on health': the higher the effects elicited, the higher the risk that the substance will show health enhancing effects[17]. The scientific community is however quite rigid in changing and accepting new definitions and subsequently new methodologies. Therefore the integration of these evolving concepts will take time; its applicability in legislation will take place in an even lower speed.

The legislator's perspective

As put forward in chapter 1, historically nutrition and medicinal products were regulated locally. Legally a distinction has been made between nutrition, that focussed on supplying sufficient macro- and micronutrients and to alleviate hunger, with pharmaceuticals aiming to cure diseases or alleviate their symptoms[18,19]. Following various food scares in the 1990s, European food law was highly reformed and not only focussed on harmonising the internal market, but also addressed consumer interests[20]. To regain the trust of consumers in both science and politics, independent agencies were established to advise on scientific issues and transparency was increased in the risk management process[20–22]. The reform of European Food Law also resulted in the development of new pieces of legislation as the NHCR, aiming to not only increase harmonisation but also to protect consumers from misleading by false and inaccurate claims[23,24].

The NHCR was however developed without awaiting the results of the academic discussion on how health should be defined and assessed. As described in chapter 2

and 3, only Terms of Reference were provided to the independent agency assessing the proposed health claims and the assessment procedure was not clear for bodies submitting health claims. The assessment procedure of generic health claims (Article 13.1 claims) resulted in the development of a positive list of authorised claims in the Annex of Regulation 432/2012[iii]. Within this procedure however claims describing health effects from botanicals used in foods were not included. The assessment of these health effects is still highly debated and often connected to the approach taken in medicinal products, where traditional herbal medicinal products are reviewed through the so called simplified procedure. This again depicts the shift of food products towards more health enhancing, medicine like products.

Where foods and medicinal products are seen to overlap in effect and law, the question arises whether regulating these concepts separately is still justifiable. The definitions of a medicinal product described in Directive 2001/83/EC[iv] already take into account the concept of intended use: when either the presentation or the function of a product shows that it is aimed to treat or cure a disease, it automatically becomes a medicinal product[25,26]. As described in chapter 7, the definition of food is also based on the intended use by defining food as any substance or product that is intended or can be expected to be ingested by humans[27]. In the current market of health enhancing products these definitions however give rise to uncertainty in which category the

[iii] Commission Regulation (EU) No 432/2012 of 16 May 2012 establishing a list of permitted health claims made on foods, other than those referring to the reduction of disease risk and to children's development and health (Consolidated version 27 January 2015).

[iv] Directive 2001/83/EC of the European Parliament and of the Council of 6 November 2001 on the Community code relating to medicinal products for human use (Consolidated version 16 November 2011).
The definitions of medicinal product by function and medicinal product by presentation were amended by Directive 2004/27/EC of the European Parliament and of the Council of 31 March 2004 amending Directive 2001/83/EC on the Community code relating to medicinal products for human use.

different types of products should fall. Focussing on the bioactive components of these different products and their mechanisms of action might result in more certainty.

Future perspectives and advice

This thesis describes the interactions between nutrition and medicine in effect and law and depicts the shift of nutrition in both effect and legal status towards a medicinal product. Where this gives rise to increased opportunities to treat diseases with less use of medicinal products, it is also seen to create confusion amongst consumers and increases complexity in law. With the involvement of a multitude of stakeholders in this process, an interdisciplinary approach is required to deal with all uncertainties surrounding this shift. We tried to unravel uncertainties and create understanding among all involved stakeholders as a first step in increasing the acceptance and effectiveness of functional foods and related legislation.

Although this research does not provide sufficient details to draw up new legislation upon bioactive substances and their commercial outings, we highlighted various elements that are important to be taken into consideration for medicinal and food law and more specifically the NHCR. The NHCR can be considered as an example of legislating before general consensus has been reached in the academic setting. A new definition of health can result in new methodologies to assess the multifactorial effects of nutrition, but also other bioactive substances. The use of emerging evidence in communicating health effects should be thoroughly discussed, as it can drive innovation and improve health of consumers. When these elements can be incorporated in legislation, enforcement should ensure the creation of a level playing field throughout the European Union. Increased knowledge upon effects of foods and pharmaceutical products should be used in legislation, leading to interactions between effect and law.

The differences and similarities between nutrition and medicinal products as well as the various other product categories should be taken into consideration when drafting new legislation on nutrition or medicinal products. Although the different intermediate legal categories can result in the repositioning of products in the markets by industrials that are looking to use unauthorised claims on food products, more pieces of legislation might create a confusing and unclear situation for all players in the field. By reviewing active compounds as bioactives rather than focussing on the different legal categories, a new opportunity may arise to draft legislation that can stimulate innovation, protect consumers from false and misleading claims and ensure safety.

Unravelling the effects of nutrition on one hand and medicinal products on the other increases the clarity about what can be expected from the different types of products. Separating the legal concepts of food and pharmaceutics improves transparency upon the positioning of different health enhancing products. However, the increased understanding of both aspects separately helps to understand the other aspect: the effects of food and pharmaceuticals clarify their legal constructs and legal constructs of food and pharmaceuticals can help to show what effect can be expected. The interaction between effect and law is required to clarify both. When the legal concepts and the biochemical effects correspond more closely to each other, not only understanding of consumers on nutrition and pharmaceutical products will increase, also more possibilities to innovate will arise.

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Samenvatting en algemene conclusie

In het verleden werd er geen onderscheid gemaakt tussen voeding en geneesmiddelen. Zowel voedingsmiddelen als geneeskrachtige middelen werden gevonden in de natuur. In diverse culturen met traditionele geneeskunde wordt nog altijd geen fundamenteel verschil gemaakt tussen voeding en geneesmiddelen. In de Westerse wereld zijn beide concepten echter uit elkaar gegroeid: voeding is vooral gericht op het voorkomen van honger en het voorzien in benodigde macro- en micronutriënten, terwijl geneesmiddelen zijn bedoeld om ziekten te genezen of symptomen van ziekten te verminderen. Dit onderscheid wordt ook concreet gemaakt in voedings- en geneesmiddelenwetgeving.

In de ruim 200 jaar dat geneesmiddelen gereguleerd worden, is er echter wel een verschuiving te zien. Door de economische en technologische vooruitgang is voeding niet alleen meer belangrijk bij het voorkomen van honger. Inmiddels gebruiken we voedingsmiddelen ook om ziekten te voorkomen en de gezondheid te bevorderen. Hierdoor verschuift de definitie van voeding richting medicijnen. Een voorbeeld hiervan is de toegenomen interesse in en het gebruik van functionele voedingsmiddelen; voedingsmiddelen die positieve effecten op de gezondheid hebben die verder gaan dan de voedingswaarde van het product. Om met deze verschuiving van voedingsproducten richting geneesmiddelen om te gaan, is wetgeving ontwikkeld om bijvoorbeeld de beweringen die over deze functionele voedingsmiddelen gemaakt worden te reguleren; de Europese verordening inzake voedings- en gezondheidsclaims voor levensmiddelen[i] (NHCR). Het onderzoek gepresenteerd in dit proefschrift laat zien dat het belangrijk is om zowel de effecten van voeding en geneesmiddelen als bijbehorende wetgeving op een wetenschappelijke manier te ontrafelen, om beiden ondanks de verschuiving van voeding en geneesmiddelen te kunnen begrijpen.

[i] Verordening (EG) Nr. 1924/2006 van het Europees Parlement en de Raad van 20 december 2006 inzake voedings- en gezondheidsclaims voor levensmiddelen (Geconsolideerde versie 13 December 2014).

Belangrijkste bevindingen

De toepassing van de NHCR leidt tot een discussie over de effectiviteit

In **hoofdstuk 2** zijn de consequenties bestudeerd van de toepassing van de NHCR bij voedingsmiddelen met antioxidanten. Hierin zijn de aanleiding van het ontwikkelen van de NHCR beschreven als ook de betrokkenheid van de Europese Autoriteit voor Voedselveiligheid (EFSA) bij deze wetgeving. Drie criteria blijken essentieel te zijn in de beoordeling van de wetenschappelijke onderbouwing van gezondheidsclaims door EFSA: (i) het voedingsmiddel of functioneel ingrediënt moet goed worden gedefinieerd en gekarakteriseerd; (ii) het geclaimde effect moet goed worden gedefinieerd en moet fysiologisch gunstig zijn; en (iii) een oorzakelijk verband moet worden vastgesteld tussen de inname van het voedingsmiddel of functioneel ingrediënt en het geclaimde effect. De implicaties van deze criteria, zoals het *in vivo* kunnen meten van het effect, zouden toegepast moeten worden in het onderzoek dat gedaan wordt om gezondheidsclaims te onderbouwen. Deze implicaties lijken echter niet allemaal toepasbaar op voedingsonderzoek zoals het nu uitgevoerd wordt, waarbij men nog uitgaat van de statische definitie van gezondheid en methoden gebruikt worden die daarbij aansluiten zoals de gerandomiseerde klinische studie. De huidige discussie rondom de definitie van gezondheid geeft aanleiding tot het ontwikkelen van nieuwe methoden om gezondheidseffecten van voedingscomponenten vast te stellen. Deze nieuwe methoden moeten meegenomen worden bij het beoordelen van de wetenschappelijke onderbouwing van gezondheidsclaims. In het specifieke geval van antioxidanten doen de gebruikte evaluatiecriteria en gewenste methoden om effecten op gezondheid te meten, geen recht aan de complexiteit van de mechanismen en effecten van deze bioactieve stoffen. Dit wordt benadrukt door het opmerkelijke verschil in het aantal voorgestelde claims (meer dan 200) ten opzichte van de acht claims die zijn toegekend.

In **hoofdstuk 3** zijn 14 personen met vier verschillende invalshoeken (fabrikanten, wetgevingsdeskundigen, voedingswetenschappers en consumentenvertegenwoordi-

gers) geïnterviewd, die in aanraking komen met de NHCR. Door middel van interviews hebben we geanalyseerd hoe deze belanghebbenden naar de toepassing van de NHCR kijken. Hiermee hebben we geprobeerd te ontrafelen waarom vele voorgestelde gezondheidsclaims op voedingsmiddelen met antioxidanten zijn afgewezen. De kwaliteit van het wetenschappelijke bewijs dat voorgestelde claims moest onderbouwen wordt gezien als belangrijkste reden voor het afwijzen van voorgestelde gezondheidsclaims. De geïnterviewde belanghebbenden wijten dit allereerst aan het gebruik van wetenschappelijke methoden waarover nog geen consensus is bereikt. Ook geeft men aan dat er een groot verschil was tussen wat indienende instanties dachten aan te moeten leveren als bewijs en hoe het bewijs uiteindelijk in de beoordelingsprocedure gewogen werd Hierbij hebben we drie elementen geïdentificeerd waarin de toepassing van de NHCR zou kunnen worden verbeterd: (i) de handhaving, (ii) de gebruikte methoden in voedingswetenschappen, en (iii) de visie op het effect van de NHCR op innovatie, onderzoek, de markt en consumenten. De belanghebbenden blijken zeer uiteenlopende opvattingen te hebben, waardoor de effectiviteit van de NHCR in zijn huidige vorm betwijfeld kan worden. De standpunten van de geïnterviewde belanghebbenden geven richting aan de discussie rondom de NHCR in het beschrijven van effecten op de gezondheid.

Voor de effectiviteit van de NHCR zijn vergelijkbare nalevingsstrategieën in de gehele EU cruciaal

Naleving is cruciaal om de doelstellingen van de NHCR te behalen: consumenten beschermen tegen misleiding door valse of onjuiste beweringen, maar ook een gelijk speelveld op de Europese interne markt te creëren voor alle levensmiddelenfabrikanten. Europese voedingswetgeving zoals de NHCR moet worden gehandhaafd door de nationale handhavingsautoriteiten. Als gevolg van

Verordening (EG) 882/2004[ii] moeten nationale handhavingsautoriteiten bij het controleren van de naleving van (dier)voedingswetgeving hun handhavingsaanpak baseren op risico's. Onze analyse in **hoofdstuk 4** laat echter zien dat de handhaving van de NHCR gefragmenteerd is binnen de EU. Dit wordt duidelijk door de 13 verschillende richtlijnen over de flexibiliteit van bewoording van claims en/of de algemene naleving van de NHCR die zijn ontwikkeld door 18 lidstaten. Intussen zijn uiteenlopende acties ondernomen door de nationale handhavingsautoriteiten bij het corrigeren van schending van naleving. Deze acties variëren van strafmaatregelen als het opleggen van boetes tot overredende maatregelen als *'naming and shaming'*. Door deze fragmentatie is de NHCR momenteel niet in staat een gelijkwaardig speelveld te creëren. Wij pleiten voor de ontwikkeling van een EU-brede aanpak bij het handhaven van de NHCR om eerlijke concurrentie op de interne markt te waarborgen.

Het wereldwijde landschap van voeding en gezondheidsclaims verordeningen is zeer divers

De Europese verordening inzake voedings- en gezondheidsclaims voor levensmiddelen wordt vergeleken met internationale regelgeving rondom deze claims in **hoofdstuk 5**. We beschrijven de wereldwijde diversiteit in benaderingen en schetsen manieren om de procedures te optimaliseren vanuit een wetenschappelijk perspectief. Regelgeving in 28 jurisdicties zijn bediscussieerd, waarbij drie prominente verschillen aan het licht komen, namelijk: (i) de indeling en het toestaan van verschillende typen voedings- en gezondheidsclaims, (ii) variaties in (pre-marketing) vergunnings-procedures, en (iii) het gebruik van het wetenschappelijke minderheidsstandpunt in te onderbouwen claims. Diverse benaderingen hebben positieve aspecten, maar er kan er geen optimale aanpak geïdentificeerd worden in de huidige werkwijzen. Door wereldwijd een gelijke aanpak te kiezen voor deze drie aspecten kan wet- en

[ii] Verordening (EG) nr. 882/2004 van het Europees Parlement en de Raad van 29 april 2004 inzake officiële controles op de naleving van de wetgeving inzake diervoeders en levensmiddelen en de voorschriften inzake diergezondheid en dierenwelzijn (Geconsolideerde versie 30 juni 2014).

regelgeving worden ontwikkeld die fabrikanten stimuleert functionele voeding te ontwikkeling en consumenten meer kansen biedt om gezondheidsbevorderende producten te gebruiken.

De interacties tussen voeding en geneesmiddelen hebben positieve of negatieve effecten

Het verschuiven van de beleving van de rol en de effecten van voeding en geneesmiddelen wordt bestudeerd in hoofdstukken 6 en 7. In **hoofdstuk 6** hebben we mogelijke positieve effecten van de inname van voedingscomponenten geëvalueerd bij chronische inflammatoire longziekten. We tonen aan dat diverse componenten ontstekingsfactoren in de longen kunnen verminderen en daarmee de longfunctie van patiënten verbeteren. Gezien het aantal gewogen artikelen in deze review lijken in het bijzonder omega-3 vetzuren en vitamine E zowel de inflammatoire en immunologische markers als ook de longfunctie van patiënten met chronische inflammatoire longziekten positief te beïnvloeden. Veel andere voedingscomponenten tonen weinig tot geen effecten op ontstekingen of longfunctie, hoewel het aantal gewogen studies vaak te klein is voor een betrouwbare beoordeling. De potentiële gunstige effecten van verschillende voedingscomponenten op chronische inflammatoire longziekten kunnen leiden tot een verbeterde kwaliteit van leven van patiënten. Door zulke voedingscomponenten te gebruiken, kunnen anti-inflammatoire en bronchodilatoire therapieën teruggebracht worden waardoor zowel bijwerkingen als de ontwikkeling van resistentie tegen deze medicatie afnemen.

In **hoofdstuk 7** worden bijwerkingen tussen voedingssupplementen of kruiden en geneesmiddelen zoals die zijn gemeld bij het Nederlands Bijwerkingen Centrum Lareb bestudeerd. Door de toegenomen populariteit van voedingssupplementen en kruidengeneesmiddelen verhoogt ook het risico op interacties tussen voorgeschreven medicatie en deze bioactieve producten. Van 55 gemelde bijwerkingen wordt gedacht dat deze veroorzaakt worden door de gelijktijdige inname van bioactieve stoffen en

medicijnen. Het grootste deel van deze vermoedelijke interacties lijken te ontstaan tijdens het metabolisme van de stoffen en bij de uiting van het effect. Waar in de wetgeving voeding en medicijnen als verschillende concepten worden gezien, is de wetgeving rondom de verschillende bioactieve producten minder duidelijk. Dit kan alleen worden opgelost door de moleculaire kennis van biologisch actieve stoffen en interacties te verhogen. Hiermee kunnen potentiële interacties beter begrepen en voorkomen worden.

Functionele voedingsmiddelen en ingrediënten moeten gekarakteriseerd worden op basis van hun bioactieve bestanddelen

Bij het beoordelen van de wetenschappelijke onderbouwing van een gezondheidsclaim onder de NHCR is het eerste criterium de definitie en karakterisering van de werkzame stof. Deze werkzame stof is verantwoordelijk voor het geclaimde effect. In **hoofdstuk 8** analyseren we drie gezondheidsclaims waarin deze werkzame stof rechtstreeks verbonden is aan een specifiek levensmiddel met deze bioactieve stof. Deze verbinding wordt beschreven in de formulering van de claim of in de gespecificeerde gebruikscondities. De bioactieve stof zelf wordt echter verantwoordelijk gehouden voor het gezondheidseffect, waardoor de associatie met het specifieke levensmiddel niet altijd te rechtvaardigen lijkt. Wij laten zien dat twee elementen bepalen of de bioactieve stof in een claim als stof op zich wordt gezien of gekoppeld wordt aan een specifiek voedingsmiddel: (i) het type claim, waarbij het doorslaggevend is of het een generieke claim is (artikel 13.1 claim) of een claim is die gebaseerd is op nieuwe, en dus beperktere hoeveelheid wetenschappelijke gegevens (artikel 13.5 claim), en (ii) het beschikbare en ingediende wetenschappelijke bewijs voor de voorgestelde claim, waarbij vaak de koppeling met een specifiek voedingsmiddel gemaakt wordt in de uiteindelijke claim als dit ook gedaan is in de wetenschappelijke studies ter onderbouwing van de claim. Het zou echter onze voorkeur hebben om ingrediënten specifieker chemisch te definiëren, zodat de daadwerkelijke bioactieve stof benoemd wordt in de claim en diens beoordeling. Nu wordt in de gezondheidsclaims vaak een generieke term gebruikt of verwezen naar het voedingsmiddel als geheel, terwijl de

bioactieve stoffen verantwoordelijk zijn voor het gezondheidseffect. Als deze stoffen chemisch gedefinieerd kunnen worden, hoeven de bioactieve stoffen niet meer gelinkt te worden aan een specifieke matrix. Zo wordt het transparanter welk ingrediënt het gezondheidsvoordeel beschreven in de claim veroorzaakt en wordt de claim relevanter voor zowel de industrie als de consument. Daarom zouden karakterisering en definiëring van de werkzame stof centraal moeten staan in het beoordelen van de gezondheidsclaim.

Conclusie

Bij het ontwikkelen van nieuwe wet- en regelgeving op voeding en geneesmiddelen zou rekening gehouden moeten worden met de verschillen en overeenkomsten tussen voeding en geneesmiddelen en de intermediaire productcategorieën die zich richten op gezondheid en gezondheidsbevordering. Hoewel fabrikanten de intermediaire categorieën van gezondheidsproducten zouden kunnen misbruiken bij het presenteren van hun product, creëert het ontwerpen van meer wetgeving op deze categorieën alleen maar meer onduidelijkheid bij alle spelers op de markt. Door in de beoordeling de bioactieve stoffen centraal te stellen in plaats van de rechtspositie van producten, kan er meer eenduidige wetgeving worden geformuleerd. Daarmee ontstaat de mogelijkheid tot het ontwerpen van nieuwe wetgeving, die zowel innovatie stimuleert alsook consumenten beschermd.

Door de effecten van zowel voeding als geneesmiddelen te kunnen ontrafelen, kan er duidelijkheid geschapen worden over wat men mag verwachten van de verschillende typen producten. Het scheiden van de juridische begrippen van voeding en medicijnen verbetert de transparantie over het positioneren van verschillende gezondheidsbevorderende producten. Toegenomen begrip van beide aspecten afzonderlijk helpt bij het begrijpen van beide aspecten: het effect van voeding en geneesmiddelen verduidelijkt hun juridische positie, waar de juridische positie van

voeding en geneesmiddelen kunnen helpen om aan te geven welk effect verwacht mag worden. Deze interactie tussen effect en wetgeving vereist dat beiden verduidelijkt worden. Wanneer de juridische begrippen en biochemische effecten duidelijker met elkaar overeen komen, zal niet alleen kennis van consumenten over voeding en medicijnen toenemen maar zullen ook meer mogelijkheden ontstaan om te innoveren.