Seminar Proceedings

The innovation of functional foods in Asia: IFFA 2018

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Functional foods (FF) are commonly consumed by Asians, and this trend has increased in recent years. Despite the reported health benefits of FF, it is necessary scrutiny and updates of the underpinning research are important. The first international conference on functional food innovation in Asia (IFFA 2018) took place on January 22nd-24th, 2018, at the University of Phayao, Thailand. Domestic and international speakers, researchers, nutritionists, dieticians, research scholars and students shared their knowledge and experience in FF research. Key features were the potential beneficial roles of FF in health and disease, the current situation with FF in Asia and innovative trends. The IFFA 2018 involved 2 keynote speakers, 34 invited speakers and 10 sessions. About 250 people from across Asia participated. Key themes, discussions, innovative opportunities, and future directions to link research in academia with health-directed applications as FF are summarised.

Key Words: functional foods, probiotics, cognitive health, food technology, SFRR-Thai

Background and key concepts of IFFA 2018

The IFFA 2018 was held on January 22nd-24th, 2018, at the University of Phayao, Phayao province, Thailand. The conference was organized and hosted by University of Phayao, and supported by the Society for Free Radical Research-Thai (SFRR-Thai) and Food Innopolis, Thailand (http://iffa.up.ac.th/). The Asian functional food (FF) market is large and increasing. However, innovative research and development are limited and could be promoted.[1] This informed the organisation of the 1st IFFA conference. Its aim was to gather domestic and international, particularly Asian, FF stakeholders together to share knowledge and experience (Figure 1). The conference provided a platform for basic and innovative applied research and for indicative trends. These embraced health promotion and disease prevention in fields such as cognitive impairment and Alzheimer disease, diabetes, cancer and more; the role of probiotics, prebiotics and synbiotics; trends in the use of traditional and functional foods in Asia; and food preferences related to health benefits.

Personal behaviours, which include unhealthy dietary patterns, contribute to the prevailing disease spectrum, increasingly characterised by the so-called non-communicable diseases (NCDs) and their associated mortality. Cardiovascular, neoplastic, metabolic (particularly those body compositional and diabetes-related) and respiratory disease are the major adverse health outcomes.[2,3] That premature NCD-related disability and mortality can be mitigated by addressing dietary pattern is a benefit-risk-cost consideration in novel food development.

Current situation and innovative trends of functional foods

FF can be defined as foods and drinks containing active ingredients that potentially exert a positive influence on health. In the first keynote lecture, N Bunyapraphatsara presented her understanding of the development of FF. She stated that in recent times, a definition and guideline for FF registration have been introduced in Europe, the USA, and Japan. The Ministry of Health and Welfare of Japan established the "Foods for Specified Health Use (FOSHU)" in 2001 (https://www.mhlw.go.jp) and, in

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Figure 1. Group photo of speakers and guests at the IFFA opening ceremony, Jan 22nd, 2018.

2015, "Food with Functional Claims (FFC)", was introduced to provide a labeling system for FF and its claims, where suitable physiological evidence and a safety assessment in humans are required. In the USA, FF is broadly defined as nutraceuticals and dietary supplements that reduce the risk of disease or improve health. The Food and Drug Administration (FDA) is responsible for creating regulations and approving the use of health claims on foods supported by scientific agreement on biological activity.[4] In the European Union, Functional Food Science in Europe (FUFOSE) has been established. FUFOSE has published the "Scientific Concepts of Functional Food Science in Europe", which sets out the evidence needed for functional food products. FF legislation for health claims is evolving in other countries. In Thailand, a national policy on promoting food and herbal product innovation has been initiated.

Kanjana-Opas, CEO of Food Innopolis, Thailand, spoke about the expanding FF industry. The global market value of FF and functional beverages have reached US$ 2.7 billion. Natakankitkul talked about nutraceutical and cosmeceutical market trends; these products come in various forms like capsules or tablets, beverages, foods, serum, gels and masks. The global market in 2018 was estimated to be about US$500 billion, with over three fourths of sales in the USA, Europe, Japan and China combined. A key concept driver of sector growth is the concept of "beauty from within". This approach combines the notion of nutrition and beauty in a single ingestible fortified food or supplement. The conference focused on "improving the lifestyle of the 'needy' to prevent the growing health challenges" through FF developments. This agenda has implicit public health nutrition ethical dilemmas.

Potential active ingredients for functional foods

Probiotics, prebiotics and synbiotics

Gut microbial metabolism regulates human and animal health by modulating the immune system, improving nutrient utilisation and preventing adhesion of pathogens to the intestinal mucosa. According to Kang and Im (2015), the failure to maintain intestinal normal flora homeostasis is closely linked to the development of host immune disorders. This group found a probiotic strain, *Bifidobacterium bifidum*, which induced the expression of host regulatory T cells. The interaction between the probiotic strain and the host could re-establish immunological homeostasis in the gut.[5] . There is global concern about the widespread microbial resistance to antibiotics, related to the overuse of antibiotics in food-producing animals, agriculture and human medicines. WHO underscores the relevance to food safety and security as well as the health issues such as antibiotic resistance.[6,7] Probiotics and prebiotics may reduce antibiotic dependency. 'Prebiotics' refers to indigestible food materials that are selectively metabolised by intestinal microbes and may assist probiotics colonization of the gastrointestinal tract with benefit to the host.[8] Sivamaruthi and Chaiyasut discussed the potential complementary and alternative treatment strategies for metabolic disorders and gastrointestinal (GI) disease using probiotic based formulations.[9]

Gänzle, a keynote speaker from Canada, explained the potential for the development of prebiotic carbohydrates as functional foods. Although there is controversy about whether dietary oligosaccharides exert beneficial or adverse effects on host health (e.g. FODMAPs in irritable bowel syndrome), functional foods containing prebiotics are already in a fast growing market, as reported by Global Market Insights. Any advantages that prebiotics may have for an individual depends on the genetic background of the host, the presence of plant secondary metabolites

and the functional features of the colonic microbiota.[10] The uncertainties associated with prebiotics and dietary fiber have affected health claims about them. That prebiotics, probiotics and synbiotics, may enhance immunity was the conclusion drawn by Gänzle.

Local plants and their extracts as a source of global FF products

Sesamin

Sesamin is a lignan dominantly found in the seed of *Sesamum indicum* Linn. Kongtaweelert reported chondroprotective and anti-inflammatory effects of sesamin, protective against the degradation of cartilage (cartilage degradation is induced by a combination of tumor necrosis factor-alpha and oncostatin)[11] and anti-osteoporosis in terms of differentiation and function in M-CSF and RANKL induced human PBMCs.[12] Sesamin is a promising phytochemical with anti-inflammatory, cartilage-protective, chondroprotective, and exhibit osteoclast differentiation inhibitory activity.

Astaxanthin

Ramesh, representing Vincent of Astra Real Pte Ltd., talked about astaxanthin, a group of red-orange xanthophyll carotenoids that naturally occurs in microalgae and certain fish. Astaxanthin is a powerful antioxidant. How these effects translate into claims about it as an ingredient in foodstuffs or supplements is sub judice given the regulatory embargoes in this area of antioxidant claims. Considerable circumspection is required about wide ranging assertions to do with benefits for "improved blood circulation, cardiovascular protection, neuroprotection, anti-metabolic syndrome, carpal tunnel syndrome, dyspepsia, male infertility, symptoms of menopause, and rheumatoid arthritis. Clinical trials are underway and awaited with interest.[13]

Traditional and herbal foods in Asia

Current trends are towards healthier plant-based diets where meat and meat-product intake is limited. However, vegetarians may have a greater risk of developing vitamin B12 deficiency than those who consume mixed diets, with adverse haematological and neurological consequences.[14] Vitamin B-12 serves as a cofactor for enzymic methylation (NIH fact sheet). Vitamin B-12 ultimately comes from micro-organisms and is only found in animal-based foods, fermented foods like tempeh or fortified products.[15] Indonesian tempe, a traditional food made from soybean, has become a valuable source of vitamin B-12 and isoflavones.[16] Tseng reported that lacto-ovo-vegetarians treated with tempe cereal could retain their normal level of serum vitamin B-12 and homocysteine. Methionine synthase requires vitamin B-12 as cofactor in the process of THF methylation and conversion of homocysteine to methionine. Vitamin B-12 deficiency induces hyperhomocysteinemia, which is a risk factor of circulatory health problems.[17]

Han talked about red ginseng, a health functional product of Korea (*Panax ginseng* C. A. Meyer), which accounted for 46.6% of overall functional health product sales in South Korea in 2016.[18] Ginseng has a long history as a medicinal plant, which dates back thousands of years in Asia. Ginseng and its active components, ginsenosides have been reported to have a wide range of health applications.[19-21] A search with the keyword 'Korean ginseng' yielded more than 260 research articles published during the period 2017-2018, as stated in Web of Science (wcs.webofknowledge.com). It is commonly assumed to promote health for both the young and elderly. It is not without serious side effects; some cultivars cause insomnia, skin eruptions, elevate BP and nervousness (Ginseng Abuse Syndrome).

Numerous Thai herbs, such as roselle, ginger, rice and banana, have potential roles in disease prevention and could be developed into nutraceutical products, as reported by Itharat A. The formula of a Thai traditional remedy called Benjakul (BJK) is composed of 5 plants: fruits of *Piper retrofractum* Vahl., roots of *Piper sarmentosum* Roxb, stem of *Piper interruptum* Opiz., roots of *Plumbago indica* L., and rhizome of *Zingiber officinale* Roscoe. The clinical efficacy of BJK extract in treating primary osteoarthritis of the knee was shown to be comparable to the western drug, diclofenac, without renal and liver toxicity.[22]

Dejian, discussed bioactive compounds in plant materials. He talked about the development of new fluorescent probes and analytical methods for activity-guided isolations, structural characterizations, and the mechanistic study of natural products. He highlighted his group's findings regarding the discovery of starch hydrolase inhibitors in edible plants (such as Malay cherry, okra, and 'dragon's blood') from Southeast Asia. By applying this high throughput assay to screen, fractionate, and isolate compounds that inhibit alpha-amylase and alpha-glucosidase, their food applicability to wheat and rice-based products were determined. The results provide promise for FF with low glycemic indices. Sivakumar reviewed FF in India.

Functional foods for health promotion and disease prevention

Diabetes

There are FF with the potential to prevent or improve DM status. The place of rice and its products in Asia is of food cultural relevance. In a session on FF and diabetes management, rice bran hydrolysate (RBH), a byproduct of rice milling was considered. Kukongviriyapan V had found that RBH improved insulin sensitivity and lipid profiles by activating AMPK and Akt as well as increasing PPAR-γ expression; lipogenic genes, including SREBP-1c, FASN and CPT-1 are down-regulated. RBH also suppresses the expression of inflammatory cytokines, such as IL-6, TNF-α, MCP-1 and NOS-2.[23,24] Apart from starch in the rice grain core, the germ and bran contain dietary fiber, vitamins, minerals and phytochemicals. However, less refined brown rice has an unpleasant texture, which reduces its popularity. The most popular rice type is white, but it has a greater glycaemic index and results in high blood glucose level especially in type 2 DM. Yamamoto S discussed the benefits of germinated brown rice. Germination increases metabolic functions in the whole grain and, thus, activates biosynthetic pathways for bioactive components, such as γ-aminobutyric acid (GABA) and γ-oryzanols. Long-term consumption of

germinated black rice (GBR) as a part of the diet can reduce blood glucose concentration in women with impaired glucose tolerance.[25]

Kuppusamy used the term 'diabesity' with reference to the pathophysiological link between diabetes and obesity. Her presentation focused on the benefits of β-glucan rich polysaccharides from mushrooms, which are common food sources for humans and may play a role in diabetes management. The *in vivo* efficacy of β-glucan polysaccharides rich *Pleurotus sajor-caju* (GE) and *Ganoderma neo-japonicum* (PF) against 'diabesity' was tested in high-fat-diet-induced diabetic mice (C57BL/6J). High-fat diets decrease anti-inflammatory adiponectin and increase proinflammatory cytokines, including TNF-α and IL-6, which then amplify insulin resistance in adipose tissue. In this setting, β-glucan polysaccharides can act as AMPK activators, increasing expression of GLUT-4 and adiponectin genes while suppressing the expression of NF-κB and other inflammatory responses.[26,27]

Starchy food in diabetes

Siriamornpun discussed how diet affects the risk of type 2-diabetes, obesity and other related non-communicable diseases. Food products can be developed reducing added sugar together with refined carbohydrate, and increasing whole grain, nuts, legumes, vegetables, and fruit. FF products can be developed using the plant based ingredients that exhibits potential antioxidant and anti-glycation properties.

Starch structure and digestion

Starch is the main source of exogenous glucose in the human diet and is an important macromolecule. In recent years, refined starch consumption has been linked to a range of chronic cardiometabolic conditions. Warren explored the structural variation in food starch and how it affects its passage through the digestive tract. He discussed the *in vitro* kinetic models for measuring the rate and extent of starch digestion, allowing us to understand the mechanisms underpinning the differences in starch digestion rate between different forms of starch. He also discussed *in vitro* fermentation, which allows us to understand the differences in microbial communities and microbial metabolite production that result from changing the structure of starch delivered to the colon.

Stevioside, a non-nutritive sweetener

Chandrapatya, a representative of the Sugavia company, introduced stevia (Ya Wan in Thai, *Stevia rebaudiana* bertoni), now popular in Thailand. Stevia sweetness is due to the presence of steviol glycosides, at least 300 or more times sweeter than sucrose by weight. The glycosides are considered safe and stable by the food industry. Some studies suggest that steviosides may have therapeutic utility in certain diseases, such as diabetes, hypertension and types of inflammation, but long term effects on complications and survival are largely unknown. Three types of products based on this plant (dry leaf, granulated powder, and concentrated syrup) have been commercialized, and other products are being developed. Their safety and quality assurance require caution.

Cancer

Cancers are the leading causes of death worldwide. Their reliable recognition and management require close professional engagement. While biodiverse plant-based diets and avoidance of obesity and diabetes are associated with reduced risk for some cancers, there is no convincing evidence for single food components or foods for prevention or management. The world literature on diet, physical activity and cancer is regularly updated on-line by the World Cancer Research Fund (WCRF).

Various phytochemicals such as flavonoid and phenolic compounds have been widely investigated for their potential anti-cancer properties.[28] Green tea has attracted interest as a source of potential cancer protectives.[29] Epigallocatechin gallate (EGCG) is a major bioactive catechin compound in green tea and reported for potential cancer preventive and therapeutic effects.[30] Suganuma referred to EGCG's ability to inhibit cancer cell motility through the inhibition of Slug and vimentin expression. Tyrosine protein kinase (AXL) plays a role in cell softening, motility and cancer cell stemness. EGCG inhibits the binding of the AXL receptor to its ligand, leading to a decrease in cancer cell motility and spheroid formation (cancer cell stemness).[31] Upon administration of EGCG, the expression of program death-ligand (PD-L1) is down-regulated in cancer cells.[32] The expression of PD-L1 allows escape from the immune system, and is induced by secreted cytokines from cancer cells. Therefore, blockage of PD-L1 expression may provide an approach to cancer immunotherapy.

Watanabe reported the synergistic effects of EGCG and anti-cancer drugs, including tamoxifen and cyclooxygenase-2 (COX-2) inhibitors. Srichairatanakool indicated that green tea extract has inhibitory effects on the growth of *Plasmodium falciparum* culture and reduced parasitemia. Green tea chelates iron and has antioxidant action in iron-loaded cells and in β-thalassemia mice. Toyokuni reviewed the carcinogenicity of iron both *in vitro* and *in vivo* studies. Iron storage management may contribute to cancer prevention.

Gastrointestinal (GI) disease

The consumption of omega-3 polyunsaturated fatty acids (PUFAs), especially docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA) has health benefits. Diets supplemented with omega-3 PUFAs may offer disease prevention by their anti-inflammatory and other actions. Omega-3 PUFAs may have a role in the changing spectrum of gastroenterological disease according to a study by Hahm KB et al. Omega-3 PUFAs and N-IgY, alone or in combination, could mitigate against high fat diet (HFD)-induced fatty liver by the activation of cholesterol catabolism to bile acids and by decreasing cholesterol-induced fibrosis.[33] Omega-3 PUFAs prevent GI-epithelial cell damage by NSAIDs through their anti-inflammatory and perhaps other actions.[34] *Helicobacter pylori* is associated with gastric carcinogenesis, and long-term administration of omega-3 PUFAs might suppress *H. pylori*-induced gastric tumorigenesis through the inhibition of inflammation and proliferation.[35]

Brain health

Various phytonutrients may be neuroprotective.[36-39] The PUFAs, especially omega-3 fatty acids DHA and EPA, are the principal components of brain cellular structure. The cis-double bond configuration of omega-3 fatty acids contributes to membrane fluidity and permeability for membrane transportation, cell signaling, memory and cognitive behaviour.[40,41] Earlylife attention to brain nutrition is likely to prevent or delay the onset of Alzheimer's, Parkinson's diseases, which are more prevalent in aging populations; the onset of neuropsychiatric disorders. Evidence that biodiverse dietary pattern intervention can maintain brain health is accumulating. Sittiprapaporn presented his findings about long-term intakes of long-chain polyunsaturated fatty acids (LCPUFA) and brain development.[42] Children who have been supplemented with LCPUFA in early childhood develop coherent synchronized brain activation involving a wider frontal lobe; brain electrophysiology revealed that LCPUFA supplementation could impact individual developmental programming.

Evidence for effects of alpha-linolenic acid (ALA), one of the LCPUFA, was presented by Suttajit. ALA is an omega-3 fatty acid abundantly found in the seed oil of *Perilla frutescens* (Ngamon in Thai). ALA exhibits *in vitro* antioxidant and anti-inflammatory activities. Memory-impaired mice treated with perilla seed oil show a decrease in latency period for memory in the Morris Water Maze test.[43] Perilla is not only an essential oil source, but perilla leaves also contain healthful bioflavonoids and rosmarinic acid. Both perilla seed oil and leaf extract produce a marked decrease in NO production and mRNA expression of markers including IL-1, IL-6, TNF-α, iNOS and COX-2.[44] Therefore, perilla seed oil and leaf extracts are potentially anti-inflammatory and might be used as functional foods.

Daily consumption of polyphenols-rich foods can prevent the onset of Alzheimer's disease and improve cognitive performance in normal aging. Suganthy reported that dietary polyphenols are promising molecules for AD therapy due to their blood brain barrier permeability and multiple neuropharmacological actions. Dietary polyphenols attenuate oxidative stress by scavenging reactive oxygen/nitrogen species, chelating metal ions and modulating the expression of antioxidant enzymes. Dietary polyphenols combat inflammatory process by regulating the expression of the NF-κB signaling pathway. The dual cholinergic effect of polyphenols plays a key role in ameliorating cholinergic function. Dietary polyphenols also maintain calcium homeostasis and inhibit glutamate mediated excitotoxicity of neurons, thereby preventing neuronal death. Dietary polyphenols attenuate aggregation of β amyloid peptide, the key pathogenic step in AD, and destabilize preformed mature plaques. The findings suggest that the regular consumption of plant foods rich in polyphenols might prevent the onset of AD and improve cognitive performance in at-risk individuals.

Sripanidkulchai found that adult male Wistar rats treated with aged garlic extract for 56 days withstood β-amyloid-induced neurotoxicity in regard to short-term spatial memory, working memory and reference memory. This could be attributed to anti-inflammatory responses through reduced microglial activation and IL-1β production. Synchronously, aged garlic extract strengthened hippocampal neurotransmitter systems to do with memory.[45,46]

Toida pointed out that brain health depends on a blood supply capable of transporting needed oxygen and nutrients. In stroke, blood flow is interrupted, leading to brain cell damage and death in association with oxidative stress. The environmental pollutant acrolein increases oxidative stress in stroke.[47] Thus, inhibition of oxidative stress by antioxidative treatment might minimise stroke complications. Polyphenols in the *Phellinus igniarius* mushroom can prevent acrolein toxicity in a mouse neuroblastoma cell line. Moreover, *P. igniarius* extract can reduce brain infarction volume in mice with experimentally-induced stroke.[48]

Stress and anxiety

Aengwanich discussed how FF might support mental health and prevent neuronal and brain disorders. Stress and anxiety are some of the main risk factors of neuropsychiatric disorders. According to WHO in 2010, neuropsychiatric disorders are the third leading contributor of global disability-adjusted life years (DALYs) (258 million).[49] Long-term exposure to stress can lead to adverse consequences such as insomnia; losing the ability to learn, memorize, and socialize; and suicide in the worst-case scenarios. Various micronutrients have been canvassed in regard to impaired brain function, often on arguable mechanistic grounds, and with little convincing evidence. Among the more robust studies are those to do with iron in children and, in later years, B group vitamins and n-3 PUFA (polyunsaturated fatty acids). Insofar as phytonutrients are concerned, the evidence favours biodiverse food patterns rather than isolated compounds. Amino acid profiles that might alter neurotransmission, as with tryptophan, might conceivably which alter mood.[50-53,40] Active components such as L-carnosine, L-anserine and taurine found in Chicken Essence (CE) may modulate cognitive function after mental stress.[54] Kotchabhadi argued that CE can promote 'optimal health' and wellness as well as support healthy brain function.

A trend to link nutrition to 'inner beauty' has also been evident in Asia and parts of South America. This has led to a demand for drinks and supplements containing hydrolyzed collagen and so-called antioxidants, a disturbing food trend where the evidence that does exist has more to do with food patterns and their complexity.

Adverse effects and health risks of functional foods

There are few studies which are designed to report the limitations and adverse effects of functional foods. They are available for nutrient supplements among healthy people, as with the Iowa Women's study or the 3rd report of the World Cancer Fund in 2018. No study of this type provides evidence of benefit. Rather, adverse outcomes on survival are seen. That said, health risks associated with the use of functional foods may indeed arise through inaccurate health claims, and idiosyncratic adverse effects (e. g., allergic reactions.), and poor-quality control.[55] Sivamaruthi BS reviewed the adverse effects reported with probiotics such as dry cough, unwarranted immune stim-

ulation, overt sepsis, bacteremia, endocarditis, and fungemia in vulnerable patients with inflammatory bowel disease.[9] Evivie et al reviewed the limitations of lactic acid bacteria in particular.[56] Ameratunga et al explored the lack of attention to adverse effects and health risk in health claim regulations for functional foods and those that are available.[55] Further research on FF regulatory frameworks is needed. The IFFA conference heightened is awareness of these deficiencies in the FF domain.

The future for functional foods

Plant-based foods

The Chairman of the Hong Kong Vegan Association, Ms Shara Ng, talked about the functionality of plant-based foods and daily life. A plant-food orientation has characterised many food cultures since time in memoriam, occasionally as vegetarianism or veganism. Its imprimaturs now include new ethical frameworks like animal rights and climate change. People are changing their behaviour accordingly. Global food technology can be expected to follow more plant-based foods that should be available for those who want to benefit from such technology. New and practical recipes based on plant-based foods are increasingly available, in print, in the media and on-line. The question is to what extent should these reflect the notion of functionality.

Conclusions

The IFFA-2018 conference, created more awareness about functional foods, their potential health benefits, limitations and risks, as they emerge from advances in functional food research, especially among Asian countries. IFFA-2018 was hosted by University of Phayao (UP) and SFRR-Thai. About 250 people participated in the conference, including invited speakers, academicians, researchers and graduate students. Information sharing took place through scientific discussions, oral and poster presentations. IFFA-2018 has built connections between cognate researchers and industrialists in ways that will, hopefully, ensure that product development will address food and health insecurity, be evidence-based, be cost-effective for consumers and be environmentally sustainable. IFFA-2018 should play a part in the nutritional betterment of Asia.

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AUTHOR DISCLOSURES

The authors declare no conflict of interest.

REFERENCES

1. Vicentini A, Liberatore L, Mastrocola D. Functional foods: Trends and development of global market. Ital J Food Sci. 2016;28:338-51. doi: 10.14674/1120-1770/ijfs.v211.
2. WHO. Global status report on noncommunicable diseases. 2014. [cited 2018/8/3]; Available from: www.who.int/nmh/publications/ncd-status-report-2014/en/.
3. WHO. Global report on diabetes. 2016. Available from: www.who.int/diabetes/global-report/en/.
4. International food information council foundation. Functional foods. [cited 2018/07/09]; Available from: http://foodinsight.org.
5. Kang HJ, Im SH. Probiotics as an immune modulator. J Nutr Sci Vitaminol. 2015;61:S103-5. doi: 10.3177/jnsv.61.S103.
6. Tang K, Caffirey NP, Nóbrega DB, cork SC, Ronksley PE, Barkema HW et al. Restricting the use of antibiotics in food-producing animals and its associations with antibiotic resistance in food-producing animals and human beings: a systematic review and meta-analysis. Lancet Planet Health. 2017;1:e316-27. doi: 10.1016/S2542-5196(17)30141-9.
7. WHO. Implementation of the global action plan on antimicrobial resistance. WHO GAP AMR Newsletter 2017:32. [cited 2018/8/6]; Available from www.who.int/antimicrobial-resistance.
8. Bindels LB, Delzenne NM, Cani PD, Walter J. Towards a more comprehensive concept for prebiotics. Nat Rev Gastroenterol Hepatol. 2015;12:303-10. doi: 10.1038/nrgastro.2015.47.
9. Sivamaruthi BS. 2018. A comprehensive review on clinical outcome of probiotic and synbiotic therapy for inflammatory bowel diseases. Asian Pac J Trop Biomed. 2018;8:179-86. doi: 10.4103/2221-1691.228000.
10. Yan YL, Hu Y, Ganzle MG. Prebiotics, FODMAPs and dietary fiber - conflicting concepts in development of functional food products?. Curr Opin Food Sci. 2018;20:30-7. doi: 10.1016/j.cofs.2018.02.009.
11. Phitak T, Pothacharoen P, Settakorn J, Poompimol W, Caterson B, Kongtawelert P. Chondroprotective and anti-inflammatory effects of sesamin. Phytochemistry. 2012;80:77-88. doi: 10.1016/j.phytochem.2012.05.016.
12. Wanachewin O, Pothacharoen P, Kongtawelert P, Phitak T. Inhibitory effects of sesamin on human osteoclastogenesis. Arch Pharm Res. 2017;40:1186-96. doi: 10.1007/s12272-017-0926-x.
13. Fassett RG, Coombes JS. Astaxanthin: a potential therapeutic agent in cardiovascular disease. Mar Drugs. 2011;9:447-65. doi: 10.3390/md9030447.
14. O'Leary F, Samman S. Vitamin B12 in health and disease. Nutrients. 2010;2:299-316. doi: 10.3390/nu2030299.
15. National Institutes of Health (NIH). Vitamin B12 fact sheet for health professionals. [cited 2018/08/08]; Available from: https://ods.od.nih.gov/factsheets/Vitamin%20B12-HealthProfessional/.
16. Nout MJR, Kiers JL. Tempe fermentation, innovation and functionality: update into the third millenium. J Appl Microbiol. 2005;98:789-805. doi: 10.1111/j.1365-2672.2004.02471.x.
17. Pawlak R. Is vitamin B12 deficiency a risk factor for cardiovascular disease in vegetarians?. Am J Prev Med. 2015;48:e11-26. doi: 10.1016/j.amepre.2015.02.009.
18. Statista. Distribution of health functional product sales in the South Korean market in 2016 by type. [cited 2018/08/08]; Available from: https://www.statista.com/statistics/791667/south-korea-health-functional-food-bestseller-mark et-share/.
19. Ahuja A, Kim JH, Kim JH, Yi YS, Cho JY. Functional role of ginseng-derived compounds in cancer. J Ginseng Res. 2018;42:248-54. doi: 10.1016/j.jgr.2017.04.009.
20. Kim KH, Lee D, Lee HL, Kim CE, Jung K, Kang KS. Beneficial effects of *Panax ginseng* for the treatment and prevention of neurodegenerative diseases: past findings and future directions. J Ginseng Res. 2018;42:239-47. doi: 10.1016/j.jgr.2017.03.011.
21. Kim JH. Pharmacological and medical applications of *Panax ginseng* and ginsenosides: a review for use in

cardiovascular diseases. J Ginseng Res. 2018;42:264-9. doi: 10.1016/ j.jgr.2017.10.004.
22. Rachawat P, Pinsornsak P, Kanokkangsadal P, Itharat A. Clinical efficacy and safety of Benjakul remedy extract for treating primary osteoarthritis of knee compared with diclofenac: double blind, randomized controlled trial. Evid Based Complement Alternat Med. 2017;2017:Article ID 9593580. doi: 10.1155/2017/9593580.
23. Boonloh K, KukongviriyapanU, PannangpetchP, Kongyingyoes B, Senggunprai L, PrawanA, et al. Rice bran protein hydrolysates prevented interleukin-6 and high glucose-induced insulin resistance in HepG2 cells. Food Funct. 2015;6:566-73. doi: 10.1039/c4fo00872c.
24. Boonloh K, Kukongviriyapan V, Kongyingyoes B, Kukongviriyapan U, Thawornchinsombut S, Pannangpetch P. Rice bran protein hydrolysates improve insulin resistance and decrease pro-inflammatory cytokines gene expression in rats fed a high carbohydrate-high fat diet. Nutrients. 2015; 7:6313-29. doi: 10.1039/c4fo00872c.
25. Bui TN, Le TH, Nguyen DH, Tran QB, Nguyen TL, Le DT et al. Pre-germinated brown rice reduced both blood glucose concentration and body weight in Vietnamese women with impaired glucose tolerance. J Nutr Sci Vitaminol. 2014;60: 183-7. doi:10.3177/jnsv.60.183.
26. Knagasabapathy G, Kuppusamy UR, AbdMalek SN, Abdulla MA, Chua KH, Sabaratnam V. Glucan-rich polysaccharides from *Pleurotussajor-caju* (Fr.) Singer prevents glucose intolerance, insulin resistance and inflammation in C57BL/6J mice fed a high-fat diet. BMC Complement Altern Med. 2012;12:261. doi: 10.1186/1472-6882-12-261.
27. Kanagasabapathy G, Chua KH, Malek SN, Vikineswary S, Kuppusamy UR. AMP-activated protein kinase mediates insulin-like and lipo-mobilising effects of -glucan-rich polysaccharides isolated from Pleurotussajor-caju (Fr.), Singer mushroom, in 3T3-L1 cells. Food Chem. 2014;145: 198-204. doi: 10.1016/j.foodchem.2013.08.051.
28. Rajesh E, Sankari LS, Malathi L, Krupaa JR. Naturally occurring products in cancer therapy. J Pharm Bioallied Sci. 2015;7(Suppl 1): S181-3. doi: 10.4103/0975-7406.155895.
29. Wang H, Khor TO, Shu L, Su ZY, Fuentes F, Lee JH, et al. Plants vs. cancer: a review on natural phytochemicals in preventing and treating cancers and their druggability. Anticancer Agents Med Chem. 2012;12:1281-305. doi: 10. 2174/187152012803833026.
30. Rady I, Mohamed H, Rady M, Siddiqui IA, Mukhtar H. Cancer preventive and therapeutic effects of EGCG, the major polyphenol in green tea. Egypt J Basic Appl Sci. 2018;5:1-23. doi: 10.1016/j.ejbas.2017.12.001.
31. Iida K, Sakai R, Yokoyama S, Kobayashi N, Togo S, Yoshikawa HY et al. Cell softening in malignant progression of human lung cancer cells by activation of receptor tyrosine kinase AXL. Sci Rep. 2017;7:17770. doi: 10.1038/s41598-017-18120-4.
32. Rawangkan A, Iida K, Sakai R, Fujiki H, Suganuma M. Abstract 2665: Green tea catechin, EGCG, enhances antitumor immunity by down-regulation of PD-L1 expression in non-small human lung cancer cell lines. Cancer Res 2017;77(Suppl 13):2665. doi: 10.1158/1538-7445.AM2017-2665.
33. Bae JS, Park JM, Lee J, Oh BC, Jang SH, Lee YB et al. Amelioration of non-alcoholic fatty liver disease with NPC1L1-targeted IgY or n-3 polyunsaturated fatty acids in mice. Metabolism. 2017;66:32-44. doi: 10.1016/j.metabol. 2016.10.002.
34. Han YM, Park JM, Kang JX, Cha JY, Lee HJ, Jeong M et al. Mitigation of indomethacin-induced gastrointestinal damages in fat-1 transgenic mice via gatekeeper action of omega-3-polyunsaturated fatty acids. Sci Rep. 2016;6:33992. doi: 10.1038/srep33992.
35. Han YM, Kim KJ, Jeong M, Park JM, Go EJ, Kang JX et al. Suppressed *Helicobacter pylori*-associated gastric tumorigenesis in Fat-1 transgenic mice producing endogenous omega-3 polyunsaturated fatty acids. Oncotarget. 2016;7:66606-22. doi: 10.18632/oncotarget. 11261.
36. Aquilano K, Baldelli S, Rotilio G, Ciriolo MR. Role of nitric oxide synthases in Parkinson's disease: a review on the antioxidant and anti-inflammatory activity of polyphenols. Neurochem Res. 2008;33:2416-26. doi: 10.1007/s11064-008-9697-6.
37. Singh M, Arseneault M, Sanderson T, Murthy V, Ramassamy C. Challenges for research on polyphenols form foods in Alzheimer's disease: bioavailability, metabolism, and cellular and molecular mechanisms. J Agric Food Chem. 2008;56:4855-73. doi: 10.1021/jf0735073.
38. Feng Y, Wang X. Antioxidant therapies for Alzheimer's disease. Oxid Med Cell Longev. 2012;2012:Article ID: 472932. doi: 10.1155/2012/472932.
39. Hussain D, Cossette MP, Brake WG. High oestradiol replacement reverses response memory bias in ovariectomised female rats regardless of dopamine levels in the dorsal striatum. J Neuroendocrinol. 2016;28:1-10. doi: 10.1111/jne.12375.
40. Husted KS, Bouzinova EV. The importance of n-6/n-3 fatty acids ratio in the major depressive disorder. Medicina. 2015;52:139-47. doi: 10.1016/j.medici.2016.05.003.
41. Lukiw WJ, Cui JG, Marcheselli VL, Bodker M, Botkjaer A, Gotlinger K et al. A role for docosahexaenoic acid-derived neuroprotectin D1 in neural cell survival and Alzheimer disease. 2005;115:2774-83. J Clin Invest. 2005;115:2774-83. doi: 10.1172/JCI25420.
42. Liao K, McCandliss BD, Carlson SE, Colombo J, Shaddy DJ, Kerling EH et al. Event-related potential differences in children supplemented with long-chain polyunsaturated fatty acids during infancy. Dev Sci. 2017;20:e12455. doi: 10. 1111/desc.12455.
43. Nunez J. Morris water maze experiment. J Vis Exp. 2008; 19:897. doi: 10.3791/897.
44. Lee HA, Han JS. Anti-inflammatory effect of *Perilla frutescens* (L.) Britton var. *frutescens* extract in LPS-stimulated RAW 264.7 macrophages. Prev Nutr Food Sci. 2012;17:109-15. doi: 10.3746/pnf.2012.17.2.109.
45. Thorajak P, Pannangrong W, Welbat JU, Chaijaroonkhanarak W, Sripanidkulchai K, Sripanidkulchai B. Effects of aged garlic extract on cholinergic, glutamatergic and GABAergic systems with regard to cognitive impairment in Aβ-induced rats. Nutrients. 2017;9: pii:E686. doi: 10.3390/nu9070686.
46. Nillert N, Pannangrong W, Welbat JU, Chaijaroonkhanarak W, Sripanidkulchai K, Sripanidkulchai B. Neuroprotective effects of aged garlic extract on cognitive dysfunction and neuroinflammation induced by β-amyloid in rats. Nutrients. 2017;9:24. doi: 10.3390/nu9010024.
47. Tomitori H, Usui T, Saeki N, Ueda S, Kase H, Nishimura K et al. Polyamine oxidase and acrolein as novel biochemical markers for diagnosis of cerebral stroke. Stroke. 2005;36: 2609-13. doi: 10.1161/01.STR.0000190004.36793.2d.
48. Suabjakyong P, Saiki R, Van Griensven LJ, Higashi K, Nishimura K, Igarashi K et al. Protects against acrolein toxicity *in vitro* and provides protection in a mouse stroke model. PLoS One 2015;10: e0122733. doi: 10.1371/journal. pone.0122733.

49. Whiteford HA, Ferrari AJ, Degenhardt L, Feigin V, Vos T. The global burden of mental, neurological and substance use disorders: an analysis from the global burden of disease study 2010. PLoS One 2015;10:e0116820. doi: 10.1371/journal.pone.0116820.
50. Keservani RK, Singh S, Singh V, Kesharwani RK, Sharma AK. Nutraceuticals and functional foods in the prevention of mental disorders. In: Bagchi D, Preuss HG, Swaroop A, editors. Nutraceuticals and functional foods in human health and disease prevention. New York: CRC Press Taylor & Francis Group; 2016. pp. 255-68
51. Letenneur L, Proust-Lima C, Gouge AL, Dartigues JF, Barberer-Gateau P. Flavonoid intake and cognitive decline over a 10-year period. Am J Epidemiol. 2007;165;1364-71. doi: 10.1093/aje/kwm036.
52. Hellhammer J, Hero T, Franz N, Contreras C, Schubert M. Omega-3 fatty acids administered in phosphatidylserine improved certain aspects of high chronic stress in men. Nutr Res. 2012;32:241-50. doi: 10.1016/j.nutres.2012.03.003.
53. Kroes MCW, van Wingen GA, Wittwer J, Mohajeri MH, Kloek J, Fernández G. Food can lift mood by affecting mood-regulating neurocircuits via a serotonergic mechanism. NeuroImage. 2014;84:825-32. doi: 10.1016/j.neuroimage.2013.09.041.
54. Chan L, Wang HM, Chen KY, Lin YC, Wu PJ, Hsieh WL et al. Effectiveness of essence of chicken in improving cognitive function in young people under work-related stress. Medicine (Baltimore) 2016;95:e3640. doi: 10.1097/MD.0000000000003640.
55. Ameratunga R, Crooks C, Simmons G, Woon ST. Health risks and adverse reactions to functional foods. Crit Rev Food Sci Nutr. 2016;56:318-25. doi: 10.1080/10408398.2012.751895.
56. Evivie SE, Huo GC, Igene JO, Bian X. Some current applications, limitations and future perspectives of lactic acid bacteria as probiotics. Food Nutr Res. 2017;61:1318034. doi: 10.1080/16546628.2017.1318034.