Chapter 1

Introductory Chapter: Design of an Ideal Diet Using Common Foods

Naofumi Shiomi

Additional information is available at the end of the chapter

http://dx.doi.org/10.5772/intechopen.77100

1. Introduction

In recent times, lifestyle-related diseases, such as diabetes and heart disease, are increasing due to changes in lifestyle and dietary habits. Rapid increase in type 2 diabetes is becoming a serious problem, especially in South Asian countries [1]. There is also an increase in the number of patients with cancer and dementia worldwide. In addition, the elderly population in the world is increasing, while dementia is becoming a serious social problem in Japan. The risk associated with these diseases can be decreased by improving eating habits, and the best way is to control total calorie intake and eat foods containing active ingredients to prevent these diseases.

Many active ingredients in food to prevent these diseases have been discovered a long time ago, and effective consumption methods for dairy food have been developed. For instance, active ingredients extracted from food or artificially synthesized are found in the form of tablets for use as a dietary supplement. Many people living in Europe and the United States prefer dietary supplements, while the Japanese people prefer food-type to tablet-type supplements. Consequently, "functional foods" have been developed that comprise artificial foods in which active ingredients are added [2]. Currently, various functional foods are developed and sold in Japan.

Recently, superfoods, instead of dietary supplements or functional foods, are considered an effective mode of intake of active ingredients. The word "superfood" is a marketing term and is not correctly defined. The idea of superfood was first proposed by Platt [3] and Wolfe [4]. According to the concept of Platt, superfood can be defined as a low-calorie food containing active ingredients that decrease the risk of diseases, such as cancer and dementia. Wolfe defined the word "superfood" as a food that contains extremely high concentrations of active ingredients or important nutrients. Foods shown in **Table 1** have been selected as typical superfoods based on these concepts, and their characteristics have been previously examined [5, 6].

Superfoods	Active ingredients or important nutrients at extremely high concentrations
Açaí	Anthocyanin
Black Garlic	Cycloalliin and S-allyl-L-cysteine
Broccoli (Super Sprout)	Sulforaphane
Cacao/Cocoa powder	Cocoa polyphenols
Camu camu	Vitamin C
Chia seeds	Glucomannan
Goji berries	β-Carotene
Hemp seeds	α-Linolenic acid
Maca	Minerals (iron and calcium)
Mangosteen	Xanthone
Coconut oil	Lauric acid (Medium Chain Triglyceride)
Spirulina	Various nutrients

Table 1. Typical superfoods and their respective main active ingredient or important nutrients.

On the other hand, several common foods consumed on a daily basis contain sufficient amounts of active ingredients, and therefore, they should also be considered "superfoods." A diet with a well-balanced combination of those foods is the most effective method to consume active ingredients because the ingredients are easily available, used on a daily basis, and can be used in several different recipes. However, there are few reviews on this approach. Thus, in the introductory chapter of this book, I introduced the concept of an ideal diet using common superfoods. I recommend that the interested readers read the other chapters of this book on the development of superfoods because the purpose of this book is to introduce both the current topics on the development of superfoods and diet using superfoods.

2. Superfoods generally used in Japanese cuisines

Before discussing an ideal diet using common foods, I introduced the active ingredients included in common foods that decrease the risk of lifestyle-related diseases, such as cancer and dementia. I selected foods that are consumed on a daily basis in Japan, with active ingredients that have been precisely examined previously.

2.1. Foods that decrease the risk of lifestyle diseases

Type-2 diabetes, high blood pressure, hyperlipidemia, and heart failure are the common lifestyle-related diseases in Japan. These diseases can occur in conjunction with each other, like a domino effect, and sometimes, more than two diseases can often occur simultaneously, and is referred to as the "metabolic syndrome." The main causes of the metabolic

syndrome are insulin resistance and high glucose consumption induced by obesity [7, 8]. Therefore, reducing obesity is the best countermeasure to decrease the risk of lifestyle-related diseases.

The choice of oil is most impactful in reducing obesity because fatty acid composition strongly influences the triglyceride characteristics. Docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA) of ω-3 polyunsaturated fatty acids (PUFAs) are present in high concentrations in fish such as Pacific saury, sardine, mackerel and eel, which are popular fish in Japan. DHA is most effective in enhancing the fluidity of fat. Rapid degradation of fat can be achieved by positive and frequent eating of these fish, consequently reducing obesity [9]. Oleic acid has an effect similar to DHA because it increases the ratio of ω-3/ω-6 by decreasing the number of ω-6 fatty acids [10, 11]. Olive oil contains high concentrations of oleic acid. Since people living in the Mediterranean region frequently use olive oil, the risk of lifestyle-related diseases is lower than that in people living in other European regions [12].

Positive consumption of compounds that can inhibit the absorption of triglycerides or enhance the secretion of cholesterol is also effective in reducing obesity. Triglycerides are degraded to glycerol and fatty acids by lipases at the small intestine. To inhibit absorption, compounds can interact with those fatty acids in the small intestine. Calcium, which is mainly contained in milk, small fish, and soybean, converts fatty acids to fatty acid calcium salt and inhibits absorption. A study on rats showed that absorption of triglycerides could be decreased if high concentrations of calcium are ingested with triglycerides [13]. Intake of polyphenols, such as quercetin, is also effective in inhibiting absorption of triglycerides [14, 15]. Catechins contained in green tea [16] can inhibit both intake and degradation of glucose, thereby decreasing the levels of glucose, total cholesterol, and LDL in the blood. Alginate, a component of seaweeds such as *Wakame* and *Kombu*, promotes release of cholesterol from the body by enhancing of the secretion of bile. Taurine, which is present in octopus and shellfish, is a feedstock of bile and enhances the production rate from cholesterol to bile. Therefore, positive and frequent eating of foods containing these compounds decrease triglyceride and LDL cholesterol levels, consequently preventing arteriosclerosis [17, 18].

Degrading triglycerides or inhibiting absorption is effective in reducing obesity. Fatty acids are degraded via two pathways: (1) to produce energy in the mitochondria and (2) to produce glucose in the case of low blood glucose levels. In the former, fatty acids must be transported, assisted by carnitine, to the inner membrane of the mitochondria before degradation. Several studies have suggested that positive consumption of carnitine enhances the degradation of triglyceride [19]. As carnitine is contained in fish muscle, consumption of fish is the best way of consuming this ingredient without unfavorable intake of animal fat.

Meanwhile, recent studies have estimated that increase or activation of brown adipocytes (or bright adipocytes) is the most effective way to enhance degradation of triglycerides. Uncoupling protein 1 (UCP1) in brown adipocytes is activated by noradrenaline and produces heat by decreasing the potential energy of the inner membrane of mitochondria. The energy decrease results in the degradation of fatty acids via the TCA cycle to reconstitute the energy gradient. Several studies have shown that obesity and type-2 diabetes reduced by the enhancement of UCP1 in humans [20–22]. Capsaicin and shogaol, which are spicy ingredients of red

pepper and ginger, respectively, can activate UCP1 via the TRPV1 receptor, producing heat. Therefore, continuous intake of these ingredients reduces obesity [23].

2.2. Foods to prevent aging

Recent studies have elucidated the mechanism of aging. One important factor that accelerates aging is oxidation of lipids, proteins, and telomeres by reactive oxygen species (ROS). Superoxide dismutase and catalase enzymes degrade ROS from mitochondria, preventing the harmful effects of ROS. The activity of these enzymes in the elders is much lower than those in the young people. Therefore, the increase in oxidation in lipids, proteins, and DNAs in the elderly results in aging [24]. Antioxidants are effective in preventing the harmful effects of ROS. Vitamin C, vitamin E, and β-carotene are known antioxidants; many polyphenols and other compounds have been discovered as novel antioxidants with increased activity [25, 26], for example, catechin (component of green tea), anthocyanin (berries), daidzein and genestin (soybean), sesaminol (sesame), and lycopene (tomato). Eating foods containing sufficient amounts of these antioxidants daily is expected to delay aging, although this effect on humans has not been elucidated.

Foods that have antiaging effects based on another mechanism are present. Rutin, a component of buckwheat and onion, improves blood circulation and insulin secretion [27, 28]. Sesamin protects many kinds of tissues. Allicin, contained in garlic and green onions, improves the secretion of several hormones and the reproductive function, and allithiamine promotes fatigue recovery [29]. Taurine, from octopus and shellfish, has effects of fatigue recovery and decrease of stress. Therefore, positive and frequent eating of buckwheat, sesame, garlic, and octopus may delay aging by controlling homeostasis. These foods are frequently used in the Japanese cuisine.

Moreover, important genes related to aging were discovered by the progress of recent studies [30]. One is the sirtuin gene, which restricts gene transcription and results in delay of aging. The sirtuin gene can be induced by caloric restriction. For instance, a group of researchers from Wisconsin University investigated the effects of caloric restriction on aging using rhesus monkeys; the aging effect was decreased in monkeys fed a low-calorie diet compared to the control group [31]. Other researchers suggested that resveratrol, component of red wine, is capable of enhancing the sirtuin gene [32]. The effect of polyamine on aging is also remarkable [33]. A previous study reported that the mice fed a high polyamine diet appeared much younger than the control. Another study reported that polyamine secreted by *Bifidobacteria* in yogurt is responsible for increasing longevity. Although the study on foods that have a capacity of rejuvenation is at a primary stage, such foods will become one of the targets as superfoods in the near future.

2.3. Foods to prevent cancer

Deaths caused by cancer are increasing worldwide, despite development of several technologies to discover the early stages of cancer. Among the various causes of cancer, dietary habits account for approximately 30%, while genetic factors have a less contribution. Therefore,

positive and frequent eating of foods containing anti-cancer ingredients might be effective in preventing cancer.

The effectiveness of green tea [34], garlic [35], and soybean [36] in preventing cancer has been experimentally and statistically estimated. For instance, the rate of gastric cancer is much lower in Chinese and Italian people, who commonly eat garlic, and in Japanese people, due to the consumption of green tea. The rate of breast cancer in Oriental people, who commonly eat soybean, is lower than that in the Western people. These results suggest that allicin, daidzein (or genestin), and catechin are effective in preventing cancer.

It has also been reported that isocyanate, a component in cabbages, can prevent cancer by degrading nitrosamine compounds. DHA and oleic acids can inhibit the growth of cancer cells at the primary stage [37, 38]. Moreover, many kinds of seafood and mushrooms, which are frequently used in Japan, show anti-cancer effects. Fucoidan is a component of seaweeds, such as *Mozuku*, *Wakame* and *Hijiki*, and can inhibit both growth of cancer cells and formation of new blood vessels. β-Glucan contained in mushrooms, such as *Shitake* and *Maitake*, induces apoptosis of cancer cells by activating immune cells, for example, NK cells [39, 40].

Although many compounds have been discovered as anti-cancer agents, it is difficult to determine the most effective ingredient because various causative genes are also responsible for the disease. The National Cancer Institute in the United States conducted the "Designer Foods Project" in the 1990s. The purpose of this project was to categorize the importance of foods to cancer. As a result, approximately 40 foods with strong anticancer effect were selected, divided into three categories based on their importance, and arranged into a pyramidal shape. The foods belonging to the most important category are garlic, soybean, cabbage, ginger and plants belonging to the family Umbelliferae.

2.4. Foods to prevent dementia

The proportion of elderly people is rapidly increasing in Japan. Consequently, dementia, such as Alzheimer's disease (AD), is a serious social issue in Japan. Although studies have elucidated why AD is developed, effective treatment to cure dementia has not been established yet. Therefore, good dietary habits and lifestyle are the best ways to prevent the onset of AD.

DHA is one of key compounds effective in preventing AD. Phospholipids of the nerve cell membranes are rich in ω-3 PUFAs, and 11% of PUFAs are DHA, keeping a healthy network between nerve cells in hippocampus where new information is remembered by reconnecting a neural network. The conversion rates from α-linolenic acid to EPA and from EPA to DHA in humans are only 5 and 0.5%, respectively. Humans are unable to synthesize DHA in the brain. Therefore, the healthy function of the brain is strongly disturbed by the shortage of DHA. In fact, DHA content in the brain of AD patients is much lower than that of younger people [41]. Several studies have reported that the brain functions can be improved by frequent intake of DHA [42–45]. These results suggest that positive and frequent eating of fish, which contains DHA, is necessary to delay the onset of AD.

Inhibition of amyloid β (Aβ) accumulation and aggregation is also effective to prevent AD. Neprilysin (NEP) and insulin-degrading enzyme (IDE) function as Aβ degrading enzymes [46, 47]. They preferentially function to degrade insulin, under high levels insulin, and, therefore, the incidence of AD is high in patients with diabetes whose insulin levels are constantly high [48]. Active ingredients, which can control the blood glucose level, are also effective against AD, that is, green tea [49].

In addition to the abovementioned compounds, several active ingredients are also effective. For instance, the effect of olive oil was discovered when the relationship between the diet and dementia was investigated in the Mediterranean region, where the rate of dementia is low. Some studies suggest that oleocanthal, from extra virgin olive oil, is the active ingredient effective in preventing AD [50, 51]. Dipropyl trisulfide (DPTS), contained in onions, is an antioxidant, whose preventive effect on dementia is expected because DPTS can be transferred to brain through the blood brain barrier. The rate of dementia in India is much lower than in America, probably due to consumption of curcumin, a component of turmeric [52]. Several studies have demonstrated the effectiveness of curcumin with regard to AD. Japanese frequently eat "curry rice" containing high amounts of turmeric.

3. Ideal diet using common foods containing active ingredients

Foods and active ingredients described in Section 2 were summarized in **Table 2**. These foods are commonly used in Japanese cuisines. As shown in **Table 2**, most of the active ingredients can prevent two or more diseases. A well-balanced diet containing these foods would be ideal to prevent lifestyle-related diseases, aging, cancer, and dementia. In Japanese food as well as in other cuisines, many kinds of fish, seaweeds, shellfish, and mushrooms are used. Therefore, well-balanced intake of active ingredients in a variety of dishes is a characteristic of Japanese food, and I believe that Japanese food is one of the ideal diets.

The Mediterranean diet is also noteworthy, since the risk factors of lifestyle-related diseases in people living in this region are low. Furthermore, many studies have elucidated that the Mediterranean diet is effective in preventing dementia as well as lifestyle-related diseases [53–55]. The Mediterranean diet is a good combination of fish, olive oil, shellfish, seafoods, and plant-based foods, such as vegetables, fruits and beans. Recently, a Mediterranean–DASH Intervention for Neurodegenerative Delay (MIND) diet was developed by a group of the Rush University [56–58]. The concept of the MIND is based on the combination of both advantages of the DASH and Mediterranean diets. In the MIND diet, positive intake of 10 kinds of foods and negative intake of 5 kinds of foods are recommended.

A remarkable aspect is that the active ingredients in Mediterranean diet and MIND diet are similar to those in Japanese food, and all of them utilize well-balanced intake of these active ingredients in common foods. Therefore, these active components are essential factors to realize an ideal diet. Foods and taste preferences are different for each country, and eating Japanese or Mediterranean foods every day can be difficult or unacceptable for people of

Active ingredients	Effectiveness to				Foods	Japanese cuisine
Contained in food	A	B	C	D		
Unsaturated fatty acid						
DHA and EPA	○	○	○	○	Saury, mackerel, horse mackerel etc.	Sushi
Oleic acid	○	—	○	○	Olive oil	Anthocyanin
Antioxidants						
Anthocyanin	○	○	—	○	Berries	
Catechin	○	○	○	○	Green tea	Japanese tea
Daidzein and genestin	○	○	○	—	Soybean	Tofu, Miso
Rutin	○	○	—	○	Buckwheat	Soba
Lycopene	○	—	—	—	Tomato	
Resveratrol	—	○	—	—	Red wine	
Curcumin	—	—	○	○	Turmeric	Curry
Other compounds						
Allicin	○	○	○	—	Garlic, green onions	
Taurine	○	○	—	—	Octopus, turban shell	Takoyaki
Sesaminol	○	○	○	—	Sesame	
Alginate	○	—	—	—	Kelp, wakame	Miso soup
Fucoidan	—	—	○	—	Mozuku	
β-Glucan	—	—	○	—	Shiitake, maitake etc.	

A, Obesity and metabolic syndrome; B, aging; C, cancer; D, Alzheimer's disease; ○, effective; —, effectiveness is unknown or low effective.

Table 2. Active ingredients and foods commonly used in Japanese cuisines and their respective effectiveness to some diseases.

other countries. It is important to use local foods and cuisines for designing the ideal diet containing active ingredients.

4. Conclusion

Superfoods listed in **Table 1** have excellent effects on nutritional supplementation or on prevention diseases. Therefore, they are useful for the people who are short of medicine. Moreover, the study on the development of novel superfoods including genetically modified one is useful for food shortage, which may occur in the near future. On the other hand, several common foods that are frequently eaten daily contain sufficient amounts of active ingredients. These can be found in ideal diets, such as Japanese food, the Mediterranean diet, and the MIND diet. A well-balanced diet combination of these foods may be more effective in preventing diseases.

Author details

Naofumi Shiomi

Address all correspondence to: n-shiomi@mail.kobe-c.ac.jp

Kobe College, Japan

References

[1] Waisundara V, Shiomi N. Diabetes miletus in South Asia. In: Ahmed RG editors. Diabetes and Its Complications. Rijeca: InTech; 2018. p. 1-21. DOI: 10.5772/intechopen.76391

[2] Williamson C. Functional foods: What are the benefits? British Journal of Community Nursing. 2009;**14**(6):230-236. DOI: 10.12968/bjcn.2009.14.6.42588

[3] Pratt SG, MK. SuperFoods Rx: Fourteen Foods That Will Change Your Life. New York: Harper Collins; 2005

[4] Wolfe D. Superfoods: The Food and Medicine of the Future. California: North Atlantic Books; 2009

[5] Waisundara V, Shiomi N, editors. Superfood and Functional Foods – An Overview of Their Processing and Utilization. Rejeca: InTech; 2017. DOI: 10.5772/63180

[6] Shiomi N, Waisundara V, editors. Superfood and Functional Foods – The Development of Superfoods and their Roles as Medicine. Rejeca: InTech; 2017. DOI: 10.5772/65088

[7] Samson SL, Garber AJ. Metabolic syndrome. Endocrinology and Metabolism Clinics of North America. 2014;**43**(1):1-23. DOI: 10.1016/j.ecl.2013.09.009

[8] Chan JM, Rimm EB, Colditz GA, Stampfer MJ, Willett WC. Obesity, fat distribution, and weight gain as risk factors for clinical diabetes in men. Diabetes Care. 1994;**17**(9):961-969. DOI: 10.2337/diacare.17.9.961

[9] Huang CW, Chien YS, Chen YJ, Ajuwon KM, Mersmann HM, Ding ST. Role of n-3 polyunsaturated fatty acids in ameliorating the obesity-induced metabolic syndrome in animal models and humans. International Journal of Molecular Sciences. 2016;**17**(10). pii: E1689. DOI: 10.3390/ijms17101689

[10] Picklo MJ, Murphy EJ. A high-fat, high-oleic diet, but not a high-fat, saturated diet, reduces hepatic α-linolenic acid and eicosapentaenoic acid content in mice. Lipids. 2016;**51**(5): 537-547. DOI: 10.1007/s11745-015-4106-9

[11] Picklo Sr MJ, Idso J, Seeger DR, Aukema HM, Murphy EJ. Comparative effects of high oleic acid vs high mixed saturated fatty acid obesogenic diets upon PUFA metabolism in mice. Prostaglandins, Leukotrients and Essential Fatty Acids. 2017;**119**:25-37. DOI: 10.1016/j.plefa.2017.03.001

[12] Mitjavila MT, Fandos M, Salas-Salvadó J, et al. The mediterranean diet improves the systemic lipid and DNA oxidative damage in metabolic syndrome individuals. A randomized, controlled, trial. Clinical Nutrition. 2013;**32**(2):172-178. DOI: 10.1016/j.clnu.2012.08.002

[13] Murata T, Kuno T, Hozumi M, Tamai H, Takagi M, Kamiwaki T, ITOH Y. Inhibitory effect of calcium (derived from eggshell) -supplemented chocolate on absorption of fat in human males. Journal of Japan Society of Nutrition and Food Sciences (Japanese). 1998;**51**(4):165-174

[14] Fraga CG, Galleano M, Verstraeten SV, Oteiza PI. Basic biochemical mechanisms behind the health benefits of polyphenols. Molecular Aspects of Medicine. 2010;**31**(6):435-445. DOI: 10.1016/j.mam.2010.09.006

[15] Yang J, Kim CS, Tu TH, Kim MS, Goto T et al. Quercetin protects obesity-induced hypothalamic inflammation by reducing microglia-mediated inflammatory responses via HO-1 induction. Nutrients. 2017;**9**(7). pii: E650. DOI: 10.3390/nu9070650

[16] Singh BN, Shankar S, Srivastava RK. Green tea catechin, epigallocatechin-3-gallate (EGCG): Mechanisms, perspectives and clinical applications. Biochemical Pharmacology. 2011;**82**(12):1807-1821. DOI: 10.1016/j.bcp.2011.07.093

[17] LGeorg Jensen M, Kristensen M, Astrup A. Effect of alginate supplementation on weight loss in obese subjects completing a 12-wk energy-restricted diet: A randomized controlled trial. The American Journal of Clinical Nutrition. 2012;**96**(1):5-13. DOI: 10.3945/ajcn.111.025312

[18] Borck PC, Vettorazzi JF, Branco RCS et al. Taurine supplementation induces long-term beneficial effects on glucose homeostasis in ob/ob mice. Amino Acids. 2018 (in press). DOI: 10.1007/s00726-018-2553-3

[19] Shiomi N, Maeda M, Mimura M. Compounds that inhibit triglyceride accumulation and TNFα secretion in adipocytes. Journal of Biomedical Science and Engineering. 2011;**4**(11):684-691. DOI: 10.4236/jbise.2011.411085

[20] Kontani Y, Wang Y, Kimura K, Inokuma K, et al. UCP1 deficiency increases susceptibility to diet-induced obesity with age. Aging Cell. 2005;**4**(3):147-155. DOI: 10.1111/j.1474-9726.2005.00157.x

[21] Kozak LP, Anunciado-Koza R. UCP1: Its involvement and utility in obesity. International Journal of Obesity (London). 2008;**32**(Suppl 7):S32-S38. DOI: 10.1038/ijo.2008.236

[22] Shiomi N, Ito M, Watanabe K. Characteristics of beige adipocytes induced from white adipocytes by *Kikyo* extract. Journal of Biomedical Science and Engineering. 2016;**9**(7):342-353. DOI: 10.4236/jbise.2016.97029

[23] Ono K, Tsukamoto-Yasui M, Hara-Kimura Y, Inoue N, Nogusa Y, Okabe Y, Nagashima K, Kato F. Intragastric administration of capsiate, a transient receptor potential channel agonist, triggers thermogenic sympathetic responses. Journal of Applied Physiology (1985). 2011;**110**(3):789-798. DOI: 10.1152/japplphysiol.00128.2010

[24] Liochev SI. Reactive oxygen species and the free radical theory of aging. Free Radical Biology and Medicine. 2013;**60**:1-4. DOI: 10.1016/j.freeradbiomed.2013.02.011

[25] Fusco D, Colloca G, Lo Monaco MR, Cesari M. Effects of antioxidant supplementation on the aging process. Clinical Interventions in Aging. 2007;**2**(3):377-387

[26] Sadowska-Bartosz I, Bartosz G. Effect of antioxidants supplementation on aging and longevity. BioMed Research International. 2014;**2014**:404680. DOI: 10.1155/2014/404680

[27] Li T, Chen S, Feng T, Dong J, Li Y, Li H. Rutin protects against aging-related metabolic dysfunction. Food and Function. 2016;**7**(2):1147-1154. DOI: 10.1039/c5fo01036e

[28] Jyrzanowska J, Piechal A, Blecharz-Klin K, Joniec-Maciejak I, Zobel A, Widy-Tyszkiewicz E. Influence of long-term administration of rutin on spatial memory as well as the concentration of brain neurotransmitters in aged rats. Pharmacological Reports. 2012;**54**:818-816

[29] Rahman MS. Allicin and other functional active components in garlic: Health benefits and bioavailability. International Journal of Food Properties. 2007;**10**:245-268. DOI: 10.1080/10942910601113327

[30] Shiomi N. Introductory chapter: Recent studies on cellular aging and rejuvenation. In: Shiomi N, editor. Molecular Mechanisms of the Aging Process and Rejuvenation. Rijeca: InTech; 2016. pp. 1-11. DOI: 10.5772/63897

[31] Mattison JA, Roth GS, Beasley TM, et al. Impact of caloric restriction on health and survival in rhesus monkeys from the NIA study. Nature. 2012;**489**(7415):318-321. DOI: 10.1038/nature11432

[32] Baur JA, Pearson KJ, Price NL, et al. Resveratrol improves health and survival of mice on a high-calorie diet. Nature. 2006;**444**(7117):337-342. DOI: 10.1038/nature05354

[33] Kibe R, Kurihara S, Sakai Y, Suzuki H, et al. Upregulation of colonic luminal polyamines produced by intestinal microbiota delays senescence in mice. Scientific Reports. 2014;**4**:4548. DOI: 10.1038/srep04548

[34] Fujiki H, Watanabe T, Sueoka E, Rawangkan A, Suganuma M. Cancer prevention with green tea and its principal constituent, EGCG: From early investigations to current focus on human cancer stem cells. Molecules and Cells. 2018;**41**(2):73-82. DOI:10.14348/molcells.2018.2227

[35] Luo R, Fang D, Hang H, Tang Z. The mechanism in gastric cancer chemoprevention by allicin. Anticancer Agents in Mediclinical Chemistry. 2016;**16**(7):802-809

[36] Sarkar FH, Li Y. Soy isoflavones and cancer prevention. Cancer Investigation. 2003;**21**(5):744-757. DOI: 10.2174/187152061666615111111544 3

[37] Newell M, Baker K, Postovit LM, Field CJ. A critical review on the effect of docosahexaenoic acid (DHA) on cancer cell cycle progression. International Journal of Molecular Sciences. 2017;**18**(8). pii: E1784. DOI: 10.3390/ijms18081784

[38] Boss A, Bishop KS, Marlow G, Barnett MP, Ferguson LR. Evidence to support the anti-cancer effect of olive leaf extract and future directions. Nutrients. 2016;**8**(8). pii: E513. DOI: 10.3390/nu8080513

[39] Atashrazm F, Lowenthal RM, Woods GM, Holloway AF, Dickinson JL. Fucoidan and cancer: A multifunctional molecule with anti-tumor potential. Marine Drugs. 2015;**13**(4): 2327-2346. DOI: 10.3390/md13042327

[40] Akramiene D, Kondrotas A, Didziapetriene J, Kevelaitis E. Effects of beta-glucans on the immune system. Medicina (Kaunas, Lithuania). 2007;**43**(8):597-606

[41] de Wilde MC, Vellas B, Girault E, Yavuz AC, Sijben JW. Lower brain and blood nutrient status in Alzheimer's disease: Results from meta-analyses. Alzheimers and Dement (New York, NY) 2017;**3**(3):416-431. DOI: 10.1016/j.trci.2017.06.002

[42] Hashimoto M. N-3 fatty acids and the maintenance of neuronal functions. Nihon Yakurigaku Zasshi. 2018;**151**(1):27-33. DOI: 10.1254/fpj.151.27

[43] Su HM. Mechanisms of n-3 fatty acid-mediated development and maintenance of learning memory performance. Journal of Nutritional Biochemistry. 2010;**21**(5):364-373. DOI: 10.1016/j.jnutbio.2009.11.003

[44] Newton W, McManus A. Consumption of fish and Alzheimer's disease. The Journal of Nutrition, Health and Aging. 2011;**15**(7):551-4552

[45] Wu S, Ding Y, Wu F, Li R, Hou J, Mao P. Omega-3 fatty acids intake and risks of dementia and Alzheimer's disease: A meta-analysis. Neuroscience and Biobehavioral Reviews. 2015;**48**:1-9. DOI: 10.1016/j.neubiorev.2014.11.008

[46] Wang S, Wang R, Chen L, Bennett DA, Dickson DW, Wang DS. Expression and functional profiling of neprilysin, insulin-degrading enzyme, and endothelin-converting enzyme in prospectively studied elderly and Alzheimer's brain. Journal of Neurochemistry. 2010;**115**(1):47-57. DOI: 10.1111/j.1471-4159.2010.06899.x

[47] Hüttenrauch M, Baches S, Gerth J, Bayer TA, Weggen S, Wirths O. Neprilysin deficiency alters the neuropathological and behavioral phenotype in the 5XFAD mouse model of Alzheimer's disease. Journal of Alzheimers Diseases. 2015;**44**(4):1291-1302. DOI: 10.3233/JAD-142463

[48] Schilling MA. Unraveling Alzheimer's: Making sense of the relationship between diabetes and Alzheimer's disease. Journal of Alzheimers Disease. 2016;**51**(4):961-977. DOI: 10.3233/JAD-150980

[49] Yasutake Tomata Y, Sugiyama K, Kaiho Y, et al. Green tea consumption and the risk of incident dementia in elderly Japanese: The Ohsaki cohort 2006 study. The American Journal of Geriatric Psychiatry. 2016;**24**(10):881-889. DOI: 10.1016/j.jagp.2016.07.009

[50] Rigacci S. Olive oil phenols as promising multi-targeting agents against Alzheimer's disease. Advances in Experimenta Medicine and Biology. 2015;**863**:1-20. DOI: 10.1007/978-3-319-18365-7_1

[51] Qosa H, Mohamed LA, Batarseh YS, Alqahtani S, Ibrahim B, LeVine 3rd H, Keller JN, Kaddoumi A. Extra-virgin olive oil attenuates amyloid-β and tau pathologies in the brains of TgSwDI mice. Journal of Nutritional Biochemistry. 2015;**26**(12):1479-1490. DOI: 10.1016/j.jnutbio.2015.07.022

[52] Mishra S, Palanivelu K. The effect of curcumin (turmeric) on Alzheimer's disease: An overview. Annals of Indian Academy of Neurology. 2008;**11**(1):13-19. DOI: 10.4103/0972-2327.40220

[53] Sanches Machado d'Almeida K, Ronchi Spillere S, Zuchinali P, Corrêa Souza G. Mediterranean diet and other dietary patterns in primary prevention of heart failure and changes in cardiac function markers: A systematic review. Nutrients. 2018;**10**(1). pii: E58. DOI: 10.3390/nu10010058

[54] Salas-Salvadó J, Guasch-Ferré M, Lee CH, Estruch R, Clish CB, Ros E. Protective effects of the mediterranean diet on type 2 diabetes and metabolic syndrome. Journal of Nutrition. 2016;**146**(4):920S-927S. DOI: 10.3945/jn.115.218487

[55] Radd-Vagenas S, Duffy SL, Naismith SL, Brew BJ, Flood VM, Fiatarone Singh MA. Effect of the mediterranean diet on cognition and brain morphology and function: A systematic review of randomized controlled trials. American Journal of Clinical Nutrition. 2018;**107**(3):389-404. DOI: 10.1093/ajcn/nqx070

[56] Morris MC, Tangney CC, Wang Y, Sacks FM, Barnes LL, Bennett DA, Aggarwal NT. MIND diet slows cognitive decline with aging. Alzheimer's and Dementia 2015;**11**(9):1015-1022. DOI: 10.1016/j.jalz.2015.04.011. (Epub Jun 15, 2015)

[57] Morris MC, Tangney CC, Wang Y, Sacks FM, Bennett DA, Aggarwal NT. MIND diet associated with reduced incidence of Alzheimer's disease. Alzheimer's and Dementia. 2015;**11**(9):1007-1014. DOI: 10.1016/j.jalz.2014.11.009

[58] Morris MC. Nutrition and risk of dementia: Overview and methodological issues. Annals of New York Academy of Sciences. 2016;**1367**(1):31-37. DOI: 10.1111/nyas.13047