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Some Skeletons in the Mature Silkworm Larvae: Not only Spinning Silk Threads but also Preventing Parkinson's Disease

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Overview

Innovations in medicine and improvement in hygiene in developed countries significantly increased the life expectancies of humans (http://gamapserver.who.int/gho/interactive_charts/mbd/life_expectancy/atlas.html). However, increased life expectancies do not guarantee extension of survival duration without suffering from various chronic diseases (a.k.a. healthspan) [1,2]. Although the life expectancies in most developed countries are now more than 80 years, healthspans in those countries are still around 70 years [2,3]. Thus, most of peoples have suffered from various chronic diseases including neurodegenerative disorders, cancers, metabolic syndromes and cardiovascular diseases at least for their last 10 years. Therefore, health costs for treating elderly peoples are enormously increased and caused severe economic crisis in healthcare systems in most of developed countries [4]. There are several simple but difficult and tedious ways to extend healthspan in humans. It has been shown that calorie restriction and moderate exercise regimen while healthy could extend healthspan in humans and animal models [5,6].

One of most important goals in nutrient and health improvement supplement researches is to find calorie restriction mimetics which induce the similar physiological effects which were accomplished by calorie restriction or moderate exercise. Even though many calories restriction mimetic candidates were suggested, most of them were not proven to be effectives in humans or animal models [2,5,6].

Health Benefits from Mulberry Silkworm Products

Mulberry silkworms have been used to weave silk fabrics and provided pupae which are valuable protein and lipid sources for many years [7]. Since 1980's, unknown health improvement effects of mulberry silkworm products have been investigated. The most well-known health improvement effect of silkworm products is hyperglycemic effects induced by uptake of freeze-dried 3rd day of 5th instar silkworm larval powder (FDSP) [8,9]. In addition, peptides derived from silk proteins have been shown to improve cognitive functions in animal models [10]. These two products are sold as human health supplementary materials in several countries including Korea.

Previous researches in mulberry silkworms suggested that mature silkworm larvae might have several unknown health improvement effects since they have enlarged silk glands enriched with silk proteins and other functional materials. However, it was not possible to eat mature silkworm larvae because their silk glands became too hard to chew if not processed properly. Recently, we developed and patented the protocol make silk glands in mature silkworm larvae chewable [7]. If mature silkworm larvae were steamed 130 min at 100°C, their silk glands were became crunchy and edible. Steamed mature silkworm larvae were immediately freeze-dried at −50°C and then grinded to make powders for easy intake [7].

The most significant health benefits from steamed and freeze-dried mature silkworm larval powder (SMSP, a.k.a. boiled and freeze-dried mature silkworm larval powder) was increased life expectancy and extension of healthspan [11]. More flies raised with SMSP food (SMSPf) retained their locomotor ability significantly longer than normal food (Nf) raised flies.

SMSP Increased Resistance to Rotenone, a PD Causative Chemical

PD is a movement disorder caused by loss of dopaminergic neurons in Substantia nigra pas compact in human central nervous system [12]. PD could be divided into familial or sporadic forms based on their causes. Familial PDs are known to be caused by mutations in certain specific genes. Sporadic PDs are known to be caused by combinations of genetic and/or environmental risk factors. One of known environmental risk factors in PD is chronic exposure to pesticides [13]. Drosophila has been extensively used to investigate molecular and cellular mechanisms underlying familial and sporadic PDs [14]. Exposure to rotenone was known to faithfully replicate PD's symptoms in Drosophila [15]. We followed the rotenone treatment protocol published by Coulom and Birman [15]. We found that SMSPf flies showed significantly enhanced motor control and life expectancy compared with Nf flies when they were treated with various concentration of rotenone. We used 100 flies for each treatment and used Kaplan-Meier survival analyses for performing statistical analyses. We also found that integrity of mitochondria that was measured by mitochondrial citrate synthase activities was increased in SMSPf flies compared with Nf flies [11]. In addition, SMSP increased PD resistance in flies by enhancing expression of olfactory genes and olfaction. The loss of olfaction is one of common symptoms observed from PD patients [16] and other neurodegenerative disorders. These results suggested that SMSP could prevent onset of PD in Drosophila by maintaining integrity of mitochondria and enhancing olfaction.

Nutrient Composition of SMSP Suggested Various Health Improvement Effects in Humans

To elucidate unknown nutritional basis of SMSP in health

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improvement effects, we investigate the nutrient compositions of SMSP [17]. Proximate analysis showed that crude proteins were most abundant components followed by crude lipids. The amino acid composition analysis showed that ASP, SER, GLY, ALA and TYR contents in SMSP were significantly higher compared with those of FDSP. Those amino acids are known to have unique health improvement effects such as enhancing secretion of ammonia (ASP), immune system (SER, GLY), and metabolisms (ALA) and production of dopamine in brains (TYR) [18]. In addition the contents of Ω-3 (n-3) fatty acids, which are one of the most popular health improvement supplements, were ~4 times more than those of Ω-6 (n-6) fatty acids. Recent studies suggested that the very low ratio of n-3 fatty acids to n-6 fatty acids in the Western diet (1/15~1/16) might cause various cardiovascular diseases in humans [19]. Indeed, mulberry silkworm chrysalis oil which has similar n-3 fatty acid to n-6 fatty acid ratio to SMSP has shown to improve hyeprlipidaemia and hyperglycaemia [20]. Furthermore, it contained very high amounts of essential minerals with a very high ratio of K/Na (71.4). It has been shown that ingesting high K/Na ratio food could make blood pressure lower in humans [21]. Because SMSP might contain other chemicals known to give health benefits in humans, such as flavonoids, polyphenols, carotenoids, etc., we are now investigating what kinds of mulberry originated chemicals are present in SMSP and their contribution to health benefits.

Another interesting finding we obtained was that SMSPf flies had reduced expression of carbohydrate and amino acid metabolism related genes [11]. Decreased expression of metabolism related genes suggested that SMSP could mimic several benefits from calorie restriction and moderate exercises at gene levels.

Conclusion

Is SMSP not only preventing PD, but also being a good candidate for calorie restriction mimetics?

Since the SMSP production protocol was recently developed [7], there was only few reports [11,17]. However, previous studies investigating various health benefits from mulberry silkworm larvae [8,9], pupae [20], and silk proteins [10] provided strong evidences supporting their positive effects in hyperglycemia [8,9,20], hyperlipidaemia [20], mild cognition defects [10] in animal models. Since SMSP shared ingredients with 3rd day of 5th instar larvae, pupae and silk proteins, the synergistic health improvement effects of its ingredients could extended healthspans and prevent onset of PD in fly models.

Taken together, SMSP could be a good candidate for a calorie restriction mimetic food and preventing onset of PD in humans. Performing further researches confirming those benefits in humans are utmost important.

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