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Perspective

Nutrition and Food Science Research Propelled by Healthy Aging

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The human lifespan has increased substantially in the past decades. Simultaneously, we have also witnessed a rapid rise in metabolism-related disorders such as obesity and chronic diseases. According to the CDC National Center for Chronic Disease Prevention and Health Promotion (NCCDPHP), approximately 90% of US annual healthcare expenditurehas been onpeople with chronic and mental health conditions. Because chronic diseases have created such significant health and economic costs in the United States,preventing chronic diseases not onlycan benefit the people but also reduce these costs. It is reported that the four chronic diseases-heart disease, cancer, stroke, and diabetes-account for almost two-thirds of all deaths each year. Other diseases including obesity, arthritis, Alzheimer's disease, epilepsy, and tooth decay also affectmany olderadults. Risk factors such as cigarette smoking, lack of physical activity and alcohol abuse further deteriorate their quality of life [1].Therefore, the role of nutrition and food science research is not onlyforsearching the truth and sustaining human life, butalso for alleviatingthe chronic diseases and promoting a healthy aging process.

Aging is a natural process that is not avoidable.The human body can be viewed as a very sophisticated machine that may generate harmful components such as free radicals thatdisruptsits normalfunctions. Pastbiomedical research has revealed many critical targets (biomarkers) involved in the aging process. Bioactive compounds capable of intervening with their functions can be viewed as the "elixir of life" that people havelonged for since ancient times [2]. For example, the manganosalen complexes which are the coordination compounds that possess a chelating salen-type ligand (for example, EUK-207 from researchgate.net; Figure 1A), may act as catalytic antioxidants mimicking both the structure and the reactivity of the active site of native antioxidant enzymes. Thus, they could potentially facilitate the scavenging of excess reactive oxygen species (ROS)and restore the redox balance in damaged cells and organs [2]. Several studies have indicated that NAD (nicotinamide adenine dinucleotide; Figure 1B) levels decrease with age, and the decline of NAD metabolism may induce several aging-associated diseases including metabolic and neurodegenerative diseases and various cancers [3]. It has also been discovered that compounds such as sirtuins (SIRT; Figure 1C), which are NAD^+-dependent deacetylases, are involved in stress response, anti-oxidative defense, and longevity via post-translational modifications [4]. The reduced sirtuin function and reduction of the cofactor NAD^+ were found to be closely associated with aging. These protective effects have been demonstrated through the activation of a NAD-dependent histone deacetylase family member sirtuin-1 (SIRT-1) protein [5]. In addition, recent studies have shown that xanthohumol (Figure 1D) and its derivatives may be able to reduce obesity and metabolic syndrome in part by changing the gut microbiota and modulating the bile acid metabolism (Figure 1E) [6].

There is no doubt that a healthy lifestyle and diet are the best means of sustaining life and alleviating various chronic diseases.

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Meanwhile, by intervening the biological systems, such as nutrient sensing, cellular senescence, and the gut microbiome, phenotypes of aging can be slowed down. These interventions can also delay the onset of many chronic diseases, including cancer, cardiovascular disease and neurodegeneration, in animal models. Many preclinical results have also indicatedthe beneficial effects of several compounds such as rapamycin, metformin, and NAD^+ enhancers [7]. Among them, metformin (Figure 1E) is a first-line therapy that has been used successfully to treat diabetes for more than 60 years. Studies have already shown that metformin can delay aging in animals. It may also influence the fundamental aging factors that underlie multiple age-related conditions in humans. Therefore, the"Targeting Aging with Metformin (TAME) Trial", a series of nationwide, six-year clinical trials(still waiting for visionary donors) was initiatedby the American Federation for Aging Research (AFAR).In fact, metforminwas chosen mainly because of its multiple functions: it decreases insulin level, decreases IGF-1 signaling, reduces DNA damage and inhibits mTOR pathway, in addition to its safety and low cost [8].

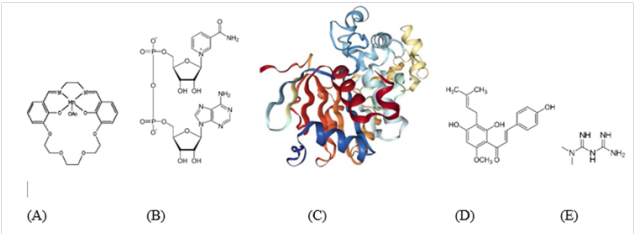

Figure 1: Molecular structures of (A) Manganosalen EUK-207 (B) NAD+ (C) Sirtuin-1 (D) Xanthhumol (E) Metformin

Though there are a few candidates on the list of anti-aging clinical trials, the best and easiest way for the general public to age healthily could simply be to maintain a good lifestyle, including eatingfoods not only taste good, but also rich in the critical components capable of slowing down the aging process. The discovery of bioactive pharmaceutics from food ingredients can be accelerated by three major target-based drug discovery strategies: high throughput screening, phage display technique, and virtual screening techniques [9]. The

in silico target prediction and mass spectroscopy based proteomics, efficient strategies to identify and further validate cellular targets are also available. However, these powerful strategies rely heavily upon the availability and completeness of libraries of potential drug candidates, especially compounds from food ingredients. To achieve these very promising research goals by targeting the critical proteins involved in many chronic diseases and the aging process, the establishment of an International Food Ingredients Consortium (IFIC) is thus proposed [9]. This endeavor is important for people around the world to livelonger and healthier lives. Indeed, now is the time to unravel the precious anti-agingcomponents hiding within the food ingredients!

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