Review

EFFECTS OF ADVANCED GLYCATION END (AGE) AND ACRYLAMIDE COMPOUNDS, AND FAST FOOD CONSUMPTION HABITS ON HEALTH

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ABSTRACT

Background: Food safety has become an area of primary concern over the past several decades, especially since sociological statistics show a linear association between increased incidence of chronic and the level of industrialization, which is associated with environmental pollution, and the scale of industrially processed foods. Many studies have shown that the formation of polluting and harmful compounds including acrylamides and advanced glycation end products (AGEs) in foods processed at high temperatures is incompatible with unhealthy lifestyles such as the consumption of high-sugar products and alcoholic foods increase the risk of diseases such as diabetes, obesity, non-alcoholic fatty liver disease (NAFLD), alcoholic liver disease (ALD), cirrhosis, etc., and even cancers.

Scope and approach: This article summarizes the formation aspects of AGEs and acrylamide, the source of the formation of acrylamide, AGEs related to food processing and preservation has become an object of research and a significant concern for consumers, health authorities, food safety regulators, and the food industry. Phytochemicals derived from various plant species inhibit the formation of endogenous AGEs, contributing to health protection.

Key findings and conclusions: The study of AGEs and acrylamides is significant in food and human health. Understanding the impact of phytochemicals, lifestyle behaviors, food processing methods, and epigenetic mechanisms on AGE and acrylamide helps us better understand how to protect health in the future.

Keywords: *processed foods, acrylamide, AGEs, Maillard reaction, unhealthy lifestyle, disease risk.*

I. INTRODUCTION

Acrylamide and advanced glycation end (AGE) are formed through many complex reaction pathways, most notably the Maillard reaction, discovered by the French scientist Louis-Camille Maillard in 1912. The Maillard reaction appears to be universal in the food processing patterns of today's diet, especially heat-processed foods such as cookies, bread, tea, coffee, fried foods, baked foods, and fast food products [1, 2].

On the other hand, bioactive plant compounds such as aminoguanidine, chlorogenic acid, genistein, and melatonin can inhibit acrylamide and AGE formation. Some other unique biologically active compounds, for example chlorogenic acid, are widely found in herbs that significantly benefit human health, such as anti-inflammatory, anti-cancer, antipyretic, and treatment of diabetes, lower blood pressure, and anti-neurodegeneration.

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In addition, genistein in soybeans has anti-inflammatory and antioxidant properties and inhibits angiogenesis and metastasis, preventing cancer. Melatonin found in coffee beans, black pepper, turmeric, cardamom, star anise, white radish, almonds, etc., also can inhibit inflammatory responses by inhibiting eicosanoid signaling pathways.

The overview article pointed out that an unhealthy lifestyle and diet are the leading cause of human diseases, including tobacco, alcohol, and Western-style fast foods rich in saturated fat, processed food, and refined sugar. High-temperature food processing and dry heating increase AGEs and acrylamides, increasing the risk of chronic diseases and accelerated aging. It is necessary to study scientifically, make statistics, summarize, and give proper warnings to improve it. By choosing foods that are low in AGEs and high in fiber, such as fresh fruits and vegetables, cooked with moist heat methods such as boiling, steaming, or stewing, we can enjoy the benefits of a high-fiber diet and reduce the risks of AGEs. AGEs inhibit the differentiation of adipose-derived stem cells and increase the risk of osteoporosis by an epigenetic mechanism. The overview article also gives readers a new perspective on the effects of AGE and acrylamide compound, and consumption habits of fast food on health.

II. METHODS

We conducted a thorough review of existing literature on the relationship between the harmful effects of AGEs, acrylamides, and unhealthy eating behaviors, including consuming energy-rich foods, high-sugar drinks, alcoholic beverages, and high-fructose corn syrup on health related to chronic diseases and metabolic diseases. The following keywords were used to search for relevant literature: processed foods, acrylamide, AGEs, Maillard reaction, unhealthy lifestyle, and disease risk. Researchers systematically searched reputable specialized databases with different filters, such as PubMed, Web of Science and Scopus, Google Scholar, ScienceDirect, and credible research books on the topic of interest. Out of 100 references and books that have passed filter selection, the author continues to select 55 concerns and books ranging from 2003 to 2022 suitable for the article's opinion academic research. Forty-five pieces were excluded due to: being written in a language other than English or Vietnamese, unrelated to the research problem, inability to read and refer to freely, and the source version is not considered reliable.

III. RESULTS

3.1. Acrinamide

Acrylamide is a contamination product in foods processed at temperatures greater than 120°C, especially in fried foods such as french fries, crackers, toast, bread crackers, cookies, and canned breakfast cereals [3]. Acrylamide was discovered in food by the Swedish National Food Service and Stockholm University in 2002. Acrylamide has the chemical formula C_3H_5NO and is a water-soluble, colorless, odorless compound susceptible to damage by bases, acids, oxidizing

agents, and iron salts [4]. Acrylamide is formed through many complex reaction pathways, of which two main paths include the generic amino acid pathway and the specific amino acid pathway) (Figure 1).

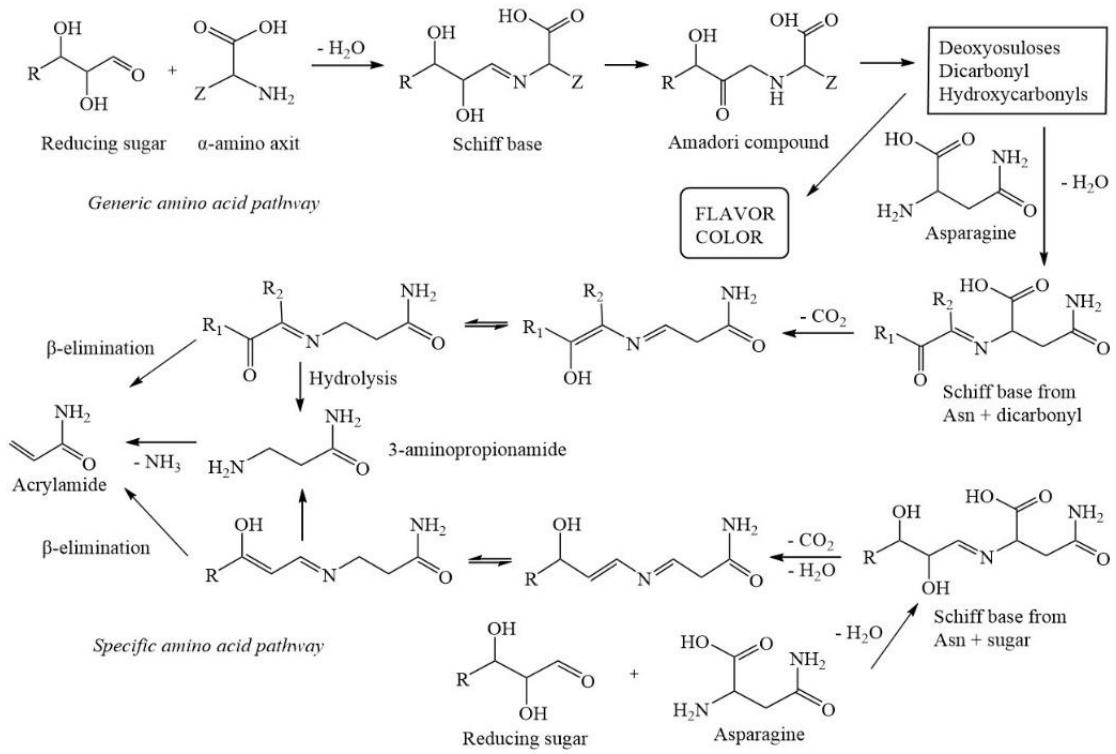


Figure 1. *The process of acrylamide formation via the general amino acid pathway and the specific amino acid pathway [2].*

With a common amino acid pathway, acrylamide is formed by the Maillard reaction between a reducing sugar (glucose/fructose) and an α-amino acid to form a Schiff base. Schiff base undergoes Amadori intramolecular rearrangement for glucose and Heyns intramolecular rearrangement for fructose to form Amadori and Heyns compounds [5]. Compounds Amadori and Heyns undergo multiple reaction stages, forming intermediate compounds, including deoxyosuloses, dicarbonyls, and hydroxycarbonyls. These intermediate compounds will react with asparagine to contribute to acrylamide formation. A specific amino acid pathway is formed between a reducing sugar (glucose/fructose) and a specific amino acid (asparagine) to create a Schiff base. The precise amino acid pathway that differs from the general amino acid pathway is the formation of azomethine ylide, skipping the intramolecular rearrangement of Amadori and Heyns to form Amadori and Heyns compounds. Azomethine ylide is an intermediate in the formation of acrylamide and 3-oxopropanamide (Strecker aldehyde) (Figure 2) [2, 6].

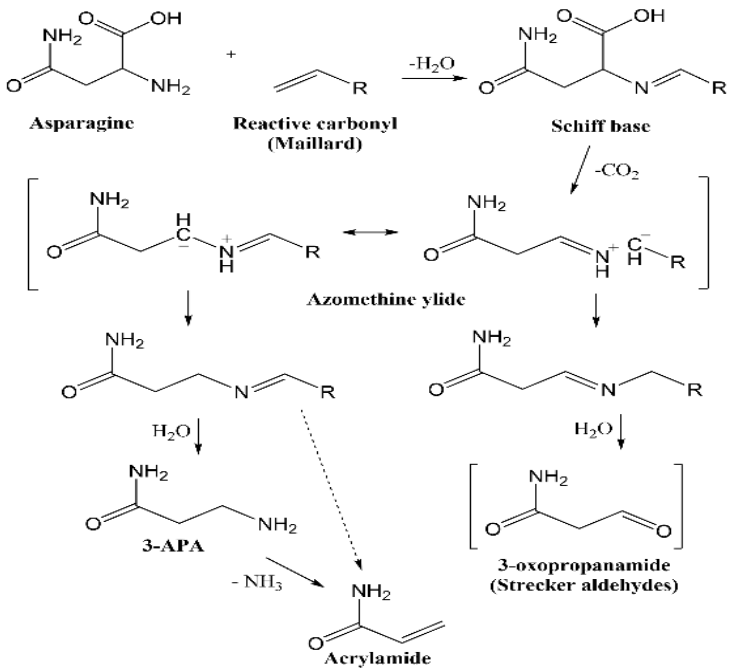


Figure 2. *Acrylamide formation pathway via azomethine ylide [6].*

In addition to the Maillard reaction between a reducing sugar (glucose/fructose)-α-amino acid and reducing sugar (glucose/fructose)-specific amino acid (asparagine), acrylamide is also formed by hydrolysis of triacylglycerol and oxidation at high temperature (Figure 3) [7].

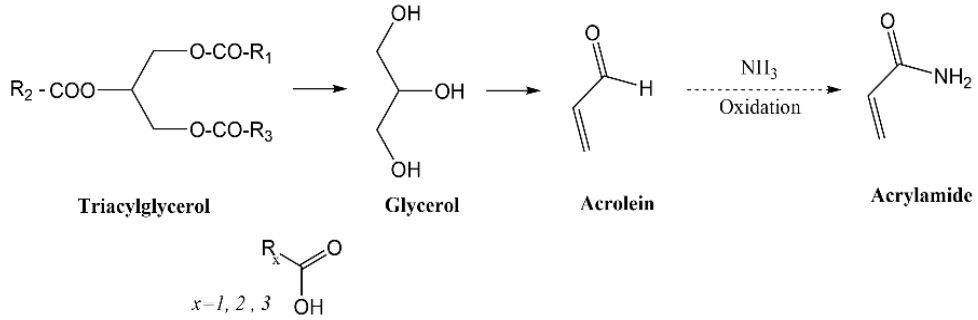


Figure 3. *Formation of acrylamide by hydrolysis of triacylglycerol and oxidation at high temperature [7].*

The amount of acrylamide formed is affected by the type of food, temperature, and processing time. Gertz et al. in 2003 found that at temperatures of 175°C and above, the acrylamide content in french fries increased markedly compared to that control sample at the temperature of 160°C, 165°C, and 170°C. Similar results were observed when using other oils for frying [7].

According to the International Agency for Research on Cancer, acrylamide is listed as a Category 2A substance possibly carcinogenic to humans. Acrylamide is a hydrophilic substance that crosses the blood-brain barrier to cause direct neurotoxicity. In animal studies, including dogs, cats, guinea pigs, rabbits, and rodents, acrylamide is neurotoxic at repeated

exposure levels between 0.5 and 50 mg/kg/day. Acrylamide was also found to alter the balance of the intestinal microflora, reducing the number of beneficial bacteria and increasing the harmful bacteria leading to the formation of lipopolysaccharides (LPS). LPS quickly enters the bloodstream causing damage to the blood-brain barrier and participating in the inflammatory signaling pathway that activates microglia, contributing to the formation of inflammatory cytokines (TNF-α, IL-6, and IL-1β). The consequences of this process promote cell death (apoptosis), leading to a degeneration of the nervous system, causing Alzheimer's disease, Parkinson and Lou Gehrig [8]. Simultaneously under the action of cytochrome P450 and cytochrome P450 2E1 (CYP2E1) enzyme systems, acrylamide is converted to glycidamide linked to purine groups (guanine and adenine) of DNA, forming DNA fragments associated with a chemical that causes cancer (DNA adduct) changes the structure of DNA. This process also increases cancer risk and promotes apoptosis (Figure 4) [9, 10]. Another study also showed that acrylamide and glycidamide cause mutations in the tumor suppressor gene TP53, leading to an increased risk of cancers, including breast, ovarian, colorectal, and lung cancer [11].

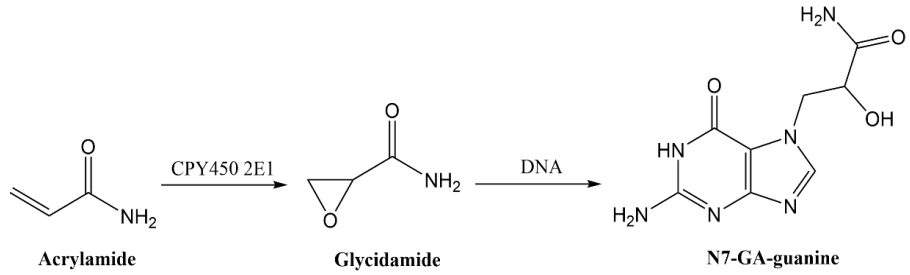


Figure 4. *DNA adduct formation under the action of acrylamide and cytochrome P450 2E1 (CYP 2E1) [10]*

Catherine Shanahan, the author of the book "Deep Nutrition", also said that the fats commonly used in the industry could not withstand heat during processing, such as canola oil, soybean oil, sunflower oil, cottonseed oil, corn oil, grapeseed oil, safflower oil... are classified as "bad fats" to avoid. Eating high-fat foods from the processed industry causes terrible effects on the body, such as weight gain, pressure on the cardiovascular system, psychological disorders, and newborn babies having to face facial deformities, etc. [12]. Traditional fats such as olive oil, peanuts oil, animal butter, macadamia nut oil, coconut oil, animal fat (lard), and palm oil can withstand temperatures during processing.

It can be seen that the use of canola oil and "bad fats" for food processing at high temperatures will promote the formation of acrylamide, which converts to glycidamide, binds to DNA, and forms DNA adduct, changes the structure of DNA, thereby increasing the risk of cancer. That is why "Why your genes need traditional food". From there, priority should be given to fresh foods and limited to processed foods.

3.2. Advanced glycation end products (AGEs)

AGEs give food products yellow color-aroma to a black-burnt smell. AGE compounds form many complex chemical reaction pathways [5, 13]. The most typical is the Maillard reaction pathway, which reduces sugars (glucose/fructose) - the protein forming Schiff base. Schiff base undergoes Amadori intramolecular rearrangement for glucose and Heyns intramolecular rearrangement for fructose to form Amadori and Heyns compounds. Compounds Amadori and Heyns undergo multiple reaction stages, forming intermediate compounds, including α-dicarbonyl. The compounds α-dicarbonyls (glyoxal, methylglyoxal, and 3-deoxyglycosone) bind with amino acids (lysine, arginine, and cysteine) to form stable glycation products, including carboxyethyl lysine, argpyrimidine, and carboxyethyl cysteine (Figure 5) [14].

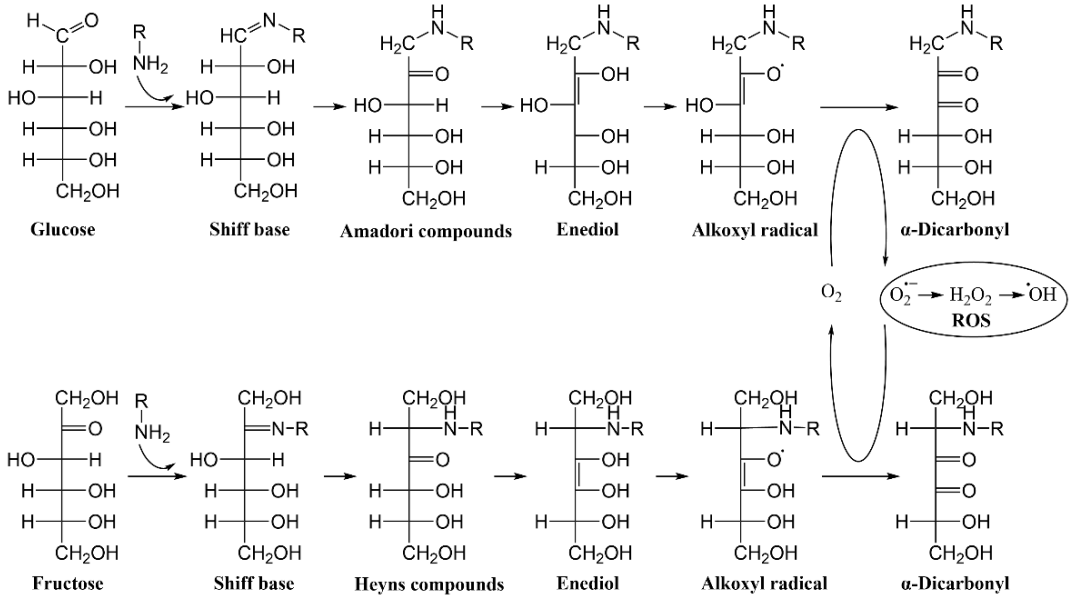


Figure 5. *Pathway for the formation of α-dicarbonyls from the Maillard reaction [5]*

In addition to the Maillard reaction pathway, the lipid peroxide reaction pathway occurs when lipids at elevated temperatures increase free radicals, taking away the charge of lipid structures and increasing their instability. This reaction, together with oxidation, promotes the breakdown of the structure from large molecules to chemical compounds with smaller molecules such as malonic dialdehyde, and trans-4-hydroxy-2-nonenal (4-HNE), glyoxal, methylglyoxal, acrolein, crotonaldehyde, hexanal... Glyoxal and methylglyoxal belong to chemical compounds of the α-Dicarbonyl group. The intermediate compounds α-Dicarbonyl are precursors of AGE (Figure 6).

Glyoxal combines with the cysteine-type protein, contributing to the formation of the s-(carboxymethyl) cysteine compound (CMC), and the lysine-type protein contributes to the formation of the Nε-(1-Carboxymethyl)-L-lysine (CML) compound. Both of these compounds are classified as AGEs [15]. Fast foods are often processed products derived from grains and starches, belonging to high-energy foods, including much sugar, saturated fatty acids, and salt, poor in nutrients, and low in fiber and micronutrients. Fat is the

most calorie-dense ingredient in fast foods like chips, pizza, and cheeseburgers [16]. Fast food processing at high temperatures (reducing sugars/α-amino acids, asparagine) and lipids both promote the formation of acrylamide and AGEs (Figure 7) [17, 18].

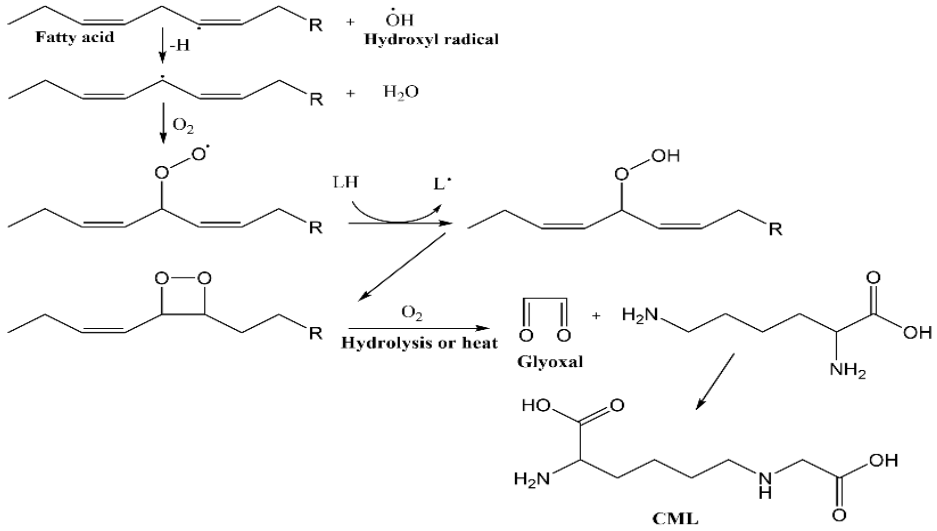


Figure 6. *The formation of AGEs from hydroxyl radicals destabilizes the structure with oxidation leading to glyoxal formation. Glyoxal combines with lysine to form CML [15].*

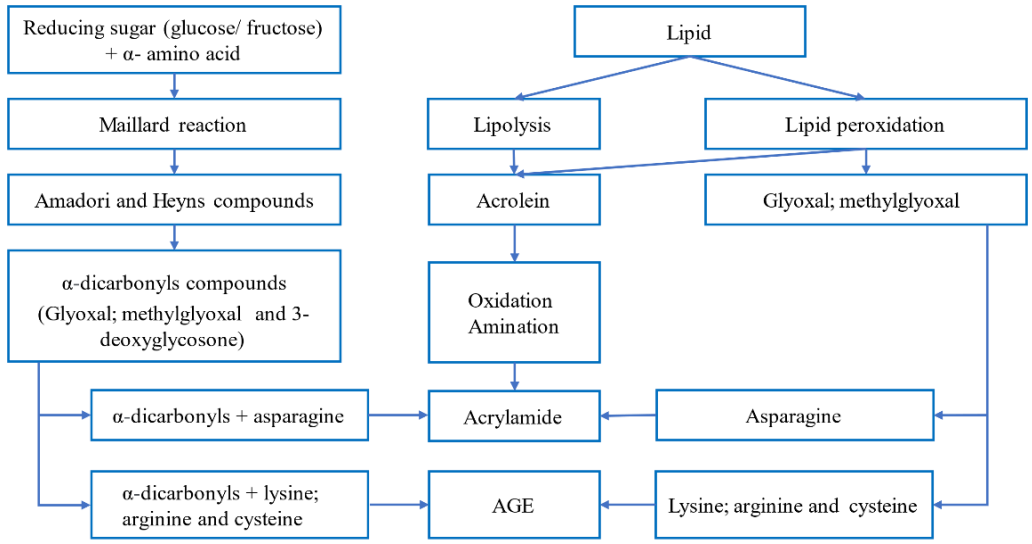


Figure 7. *Acrylamide and AGEs formation pathways during food processing.*

In 2020, Jale Çatak investigated glyoxal (GO) and methylglyoxal (MGO) by HPLC in french fries purchased from different fast food restaurants in Istanbul, Turkey Turkey. The results showed that high temperatures of french fries promote the formation of GO and MGO intermediate compounds, which are precursors to AGE formation. The content of GO and GMO measured ranged from 2 to 428 µg and 122 to 340 µg/100 g in the samples, respectively

[19]. The results show that the accumulation of AGEs in the body through an unhealthy diet, including fast foods, high-fat, and heat processing [19], and junk food - confectionery [20] is the cause of many diseases, in which the accumulation of AGE is high that promotes the aging rapidly. Figure 8 shows that patients with complications of diabetes age much faster than the general population [21].

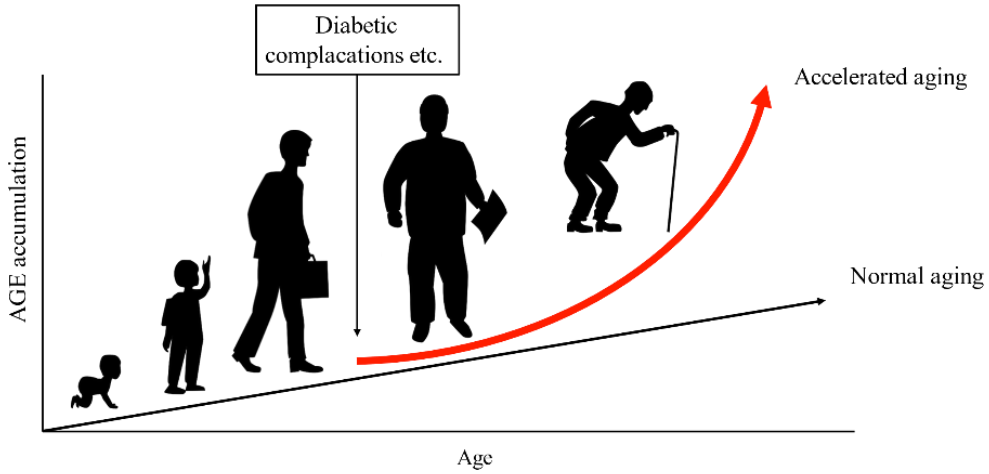


Figure 8. *AGE accumulation in the body with age, unhealthy lifestyle, and diabetes complications contribute to an accelerated aging process compared to ordinary people [21].*

AGEs have a common nature, which are toxic substances that are not beneficial to the body, more or less, and is associated with inflammatory reactions, damage to cell tissues, and stress to the body [12]. AGEs bind to the AGE receptor (RAGE), forming the NF-kB signaling pathway that produces inflammatory cytokines (IL-1β, TNF-α) and inducible nitric oxide synthase (iNOS) activation. Microglia causes nerve cell damage and degeneration, increasing the risk of Alzheimer's disease [22].

According to the US Census in 2020, the number of people with Alzheimer's disease accounts for 6.2 million Americans aged 65 and over and is expected to increase by 2060 (13.8 million people). In 2021, total healthcare costs will be $355 billion for Alzheimer's patients 65 and older [23].

As mentioned above, lipid peroxidation occurs when lipids at high temperatures promote structural breakdown from large molecules to more minor molecular mass chemical compounds, including α-Dicarbonyl compounds (glyoxal and methylglyoxal), malonic dialdehyde, trans-4-hydroxy-2-nonenal (4-HNE), glyoxal, methylglyoxal, acrolein, crotonaldehyde, hexanal,... Many studies show that 4-HNE causes hepatocellular carcinoma due to gene mutations, tumor suppressor p53 at codon 249. 4-HNE binds to the guanine (G) of DNA to form a 6-(1-hydroxyhexanyl)-8-hydroxy-1, N(2)-propano-2'-deoxyguanosine (4-HNE-dG) DNA adduct at the DNA adduct the third position of codon 249 (–AGG) of p53, leading to G-to-T conversion, leading to gene mutation, tumor suppressor p53 [24-26].

3.3. AGEs - The cause of many diseases

Dr. Paul Clayton's publication, "Let your food be your pharmaco-nutrition, the new road to health, healing, and happiness" explains that inflammation is a common bodily reaction with both beneficial and detrimental effects. Inflammation helps to heal damaged tissues and remove harmful pathogens such as bacteria and viruses from the external environment. This is known as acute inflammation, occurring over a short period. However, chronic inflammation is the prolonged process of tissue destruction and damage in the heart, brain, cartilage, bone, or other areas, ultimately resulting in pathological conditions [27]. Consuming a Western-style diet high in fat, consuming excessive amounts of sugary foods and beverages, and consuming processed foods heated at high temperatures for extended periods can increase the AGEs formation and their accumulation in the body. This can lead to increased chronic inflammation over time [28].

The prevalence and increasing prevalence of type 2 diabetes is a significant challenge in the 21st century. A report indicates that the number of patients with diabetes will reach about 439 million people by 2030, accounting for 7.7% of the world's adult population (aged 20-79 years) [29]. The incidence of diabetes in Vietnam has risen significantly, particularly in urban areas. National survey data on diabetes prevalence in Vietnam, conducted by the Ministry of Health and international health organizations, reported rates of 2.7% in 2002, 5.4% in 2012, and 7.3% in 202 [30-32].

Red blood cells comprise hemoglobin (Hb), which is responsible for transporting oxygen to tissues through the blood circulation system. Consumption of high-sugar foods and beverages (soft drinks, fruit juices) increases the risk of type 2 diabetes. Hb binds with glucose to form a glycoproteinated hemoglobin product called HbA1c [33]. HbA1c is an essential measure of the risk of diabetes: normal (3-5%), pre-diabetes (5.7-6.4%), and diabetes (≥ 6.5%). Markers of early glycation, such as HbA1c, fructosamine, and glycated albumin, were associated with atherosclerosis risk in diabetes; HbA1c undergoes many processes to form α-dicarbonyl intermediates as precursors of AGE [34, 35].

AGEs bind to the AGE receptor and activate an inflammatory response that increases the risk of microvascular and macrovascular diseases. Microvascular diseases include diabetic retinopathy, diabetes mellitus, and diabetic nephropathy. Macrovascular diseases include cardiovascular disease, cerebrovascular accident, and peripheral artery stenosis (Figure 9) [34].

In addition, consuming a lot of glucose, alcoholic beverages (beer, wine, ...), and high-fructose corn syrup (HFCS) increases AGE formation. AGEs cause inflammation and participate in lipogenesis, appearance, and adipose tissue accumulation, increasing body mass and causing obesity. Long-term collection of fatty tissue in the liver also reduces liver function, causing non-alcoholic fatty liver disease (NAFLD), alcoholic fatty liver disease (ALD), and cirrhosis [36]. In essence, these diseases reduce the effect of genes involved in β fat oxidation (very long-chain acyl-CoA dehydrogenase (ACADVL), medium-chain acyl-CoA dehydrogenase (ACADM)) and increase the impact using genes involved in the formation and

accumulation of adipose tissue (acetyl-CoA carboxylase (ACC) and stearoyl-CoA desaturase-1 (SCD1)) [37]. Patients with NAFLD are at increased risk for dementia [38].

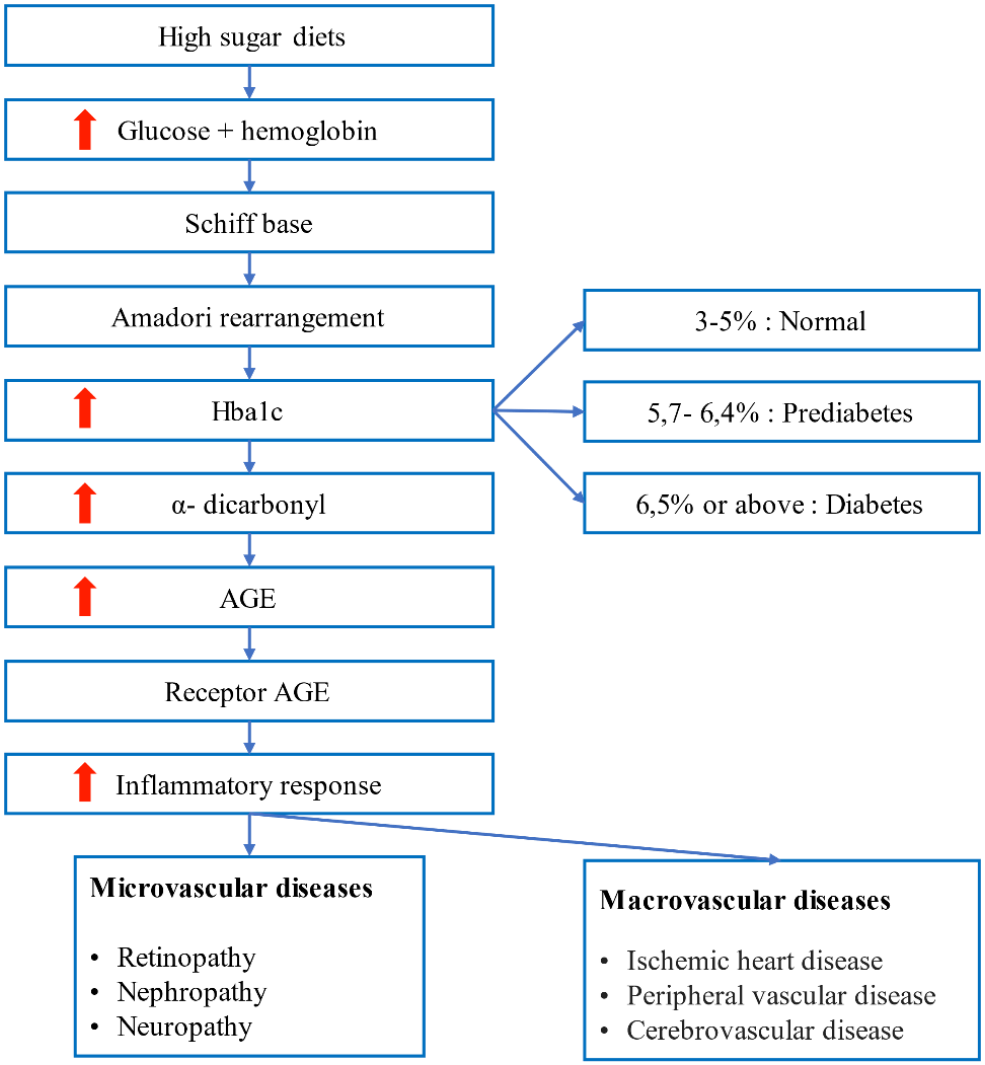


Figure 9. *Relationship between HbA1c-AGE-related high-sugar diet and drinks for microvascular and acrovascular diseases.*

A team of researchers from Japan looked at the concentrations of AGEs in beverages and foods commonly consumed in daily meals in Japan in 2015. More than 1,650 common beverages and foods can be obtained from vending machines, convenience stores, supermarkets, fast food stores (including doughnut or hamburger shops), or family restaurants (including lunch boxes, burgers, etc.). The following experiment showed that a significant proportion of inflammatory AGEs were present in the foods tested, namely some lactic acid bacteria drinks, carbonated drinks, canned fruit juices, etc. HFCS, sports drinks, confectionery (snacks), dried fruit, pastries, fried cereals, condiments, and processed foods have higher levels of AGEs than mushrooms, fresh vegetables,

tubers, and fruits, algae, nuts, and whole grains [20].

About 10% of AGEs in foods and beverages are absorbed into the human body. Of these, ~33% is excreted in the urine within 48 hours of consumption, while ~67% accumulates in the body [39]. Processed foods and refined sugars, along with high-temperature food processing, roasting, grilling, broiling, and dry heat, have increased AGEs and acrylamides, which accelerate aging and worsen aging, increasing the risk of chronic diseases [40].

The experiment conducted by Yong Li and colleagues in 2020 on C57BL/6 mice revealed that AGEs inhibit the differentiation of adipose-derived stem cells (ASCs) by modulating the Wnt/β-catenin signaling pathway. AGEs were found to promote the expression of DNA methyltransferase enzymes (DNMT1/3A/3B), leading to the methylation of promoter regions of genes such as Alkaline Phosphatase (*ALP*), Osteopontin (*OPN*), Osteocalcin (*OCN*), and Runt-related transcription factor 2 (*RUNX2*) [41]. These genes play a crucial role in promoting bone formation and mineralization. Thus, AGEs are implicated in increasing the risk of osteoporosis [42].

Through the above results, we can conclude that the use of fresh fruit is better than dried one. At the same time, recommendations to reduce AGE formation in food and endogenous formation in the body include [43]:

(1) Use low rather than high temperatures in cooking;
(2) Steaming, stewing, and boiling are better cooking methods than frying, grilling, and roasting;
(3) Adding acids (vinegar, lemon juice) to foods to reduce AGE levels;
(4) Limit consumption of processed foods;
(5) Use foods with low glycemic index and low in fat;
(6) Limit sugary drinks (soft drinks);
(7) Consume plant-based foods rich in antioxidant compounds.

3.4. Phytochemical - The gift of creation

Bioactive compounds derived from plants (fruits, vegetables, tubers, and berries) are diverse worldwide. To date, about 200,000 compounds have been known, and about 20,000 of them have been shown to have the ability to prevent and reduce inflammatory symptoms, providing excellent value for human health [44]. Biological active compounds include: aminoguanidine, chlorogenic acid, genistein, and melatonin can inhibit AGEs formation from Maillard reaction, and intermediate compounds α-dicarbonyls (glyoxal, methylglyoxal, and 3-deoxyglycosone) extracted from Coffee silverskin Arabica (*Coffea arabica*) and Robusta (*Coffea canephora*) from a study by Miguel Rebollo-Hernanz et al. in 2019 (Figure 10 and 11) [45].

Chlorogenic acid is one of the bioactive compounds widely found in herbs, and the human diet, including apples, artichokes, betel, carrots, coffee beans, eggplant... brings significant benefits to human health, including anti-inflammatory, prevention of cancer, antipyretic, diabetes treatment, lower blood pressure, and anti-neurodegeneration. At the same time, chlorogenic acid is also used as a food additive with antibacterial properties including gram (-) bacteria including *Enterobacter aerogenes, Pseudomonas aeruginosa, Salmonella typhimurium*;...

gram (+) bacteria including *Bacillus cereus, Enterococcus faecalis,* etc. antifungal including *Candida albicans, Malassezia furfur,* etc. and resistance to *Penicillium chrysogenum* [46].

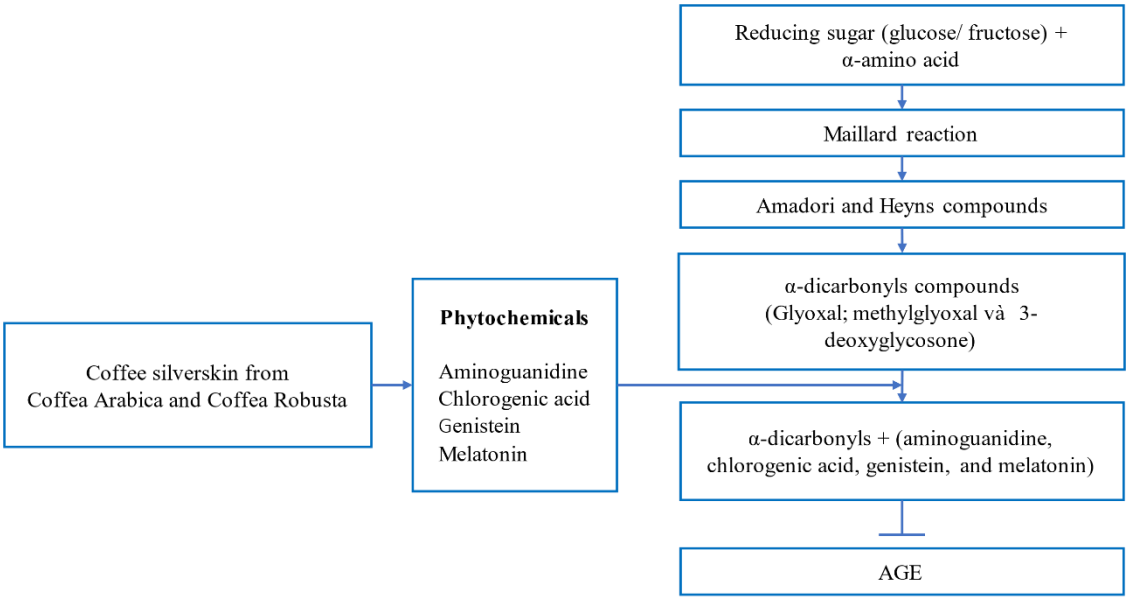


Figure 10. *Biologically active compounds (aminoguanidine, chlorogenic acid, genistein, and melatonin) inhibit the formation of AGEs.*

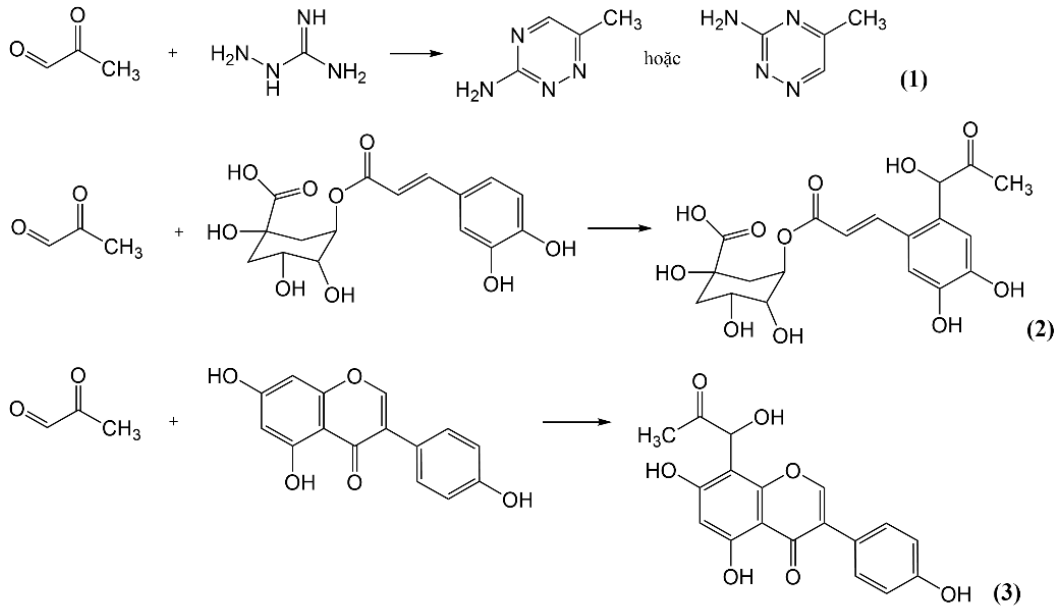


Figure 11. *The reaction between methylglyoxal and bioactive compounds (aminoguanidine (1); chlorogenic acid (2); genistein and melatonin (3)) inhibits AGE formation [45].*

Genistein is a natural isoflavone found in soybeans. Concentrations of most food ingredients derived from soybeans ranged from 1 to 2 mg/g. Studies have shown that anti-inflammatory genistein effectively inhibits NF-kB and Akt signaling pathways, and genistein has antioxidant properties and inhibits angiogenesis and metastasis, considered potential bioactive compounds in the fight against cancer [47].

Melatonin is one of the bioactive compounds found in coffee beans (coffee robusta and coffee arabica), black pepper, turmeric, cardamom, star anise, celery, turnip, almonds, etc. Melatonin is not only found synthetically in plants but also humans. Melatonin inhibits the inflammatory response through inhibition of the Eicosanoids signaling pathway by inhibiting prostaglandin-endoperoxide synthase 2 (cyclooxygenase-2; COX2) (Figure 12) [48].

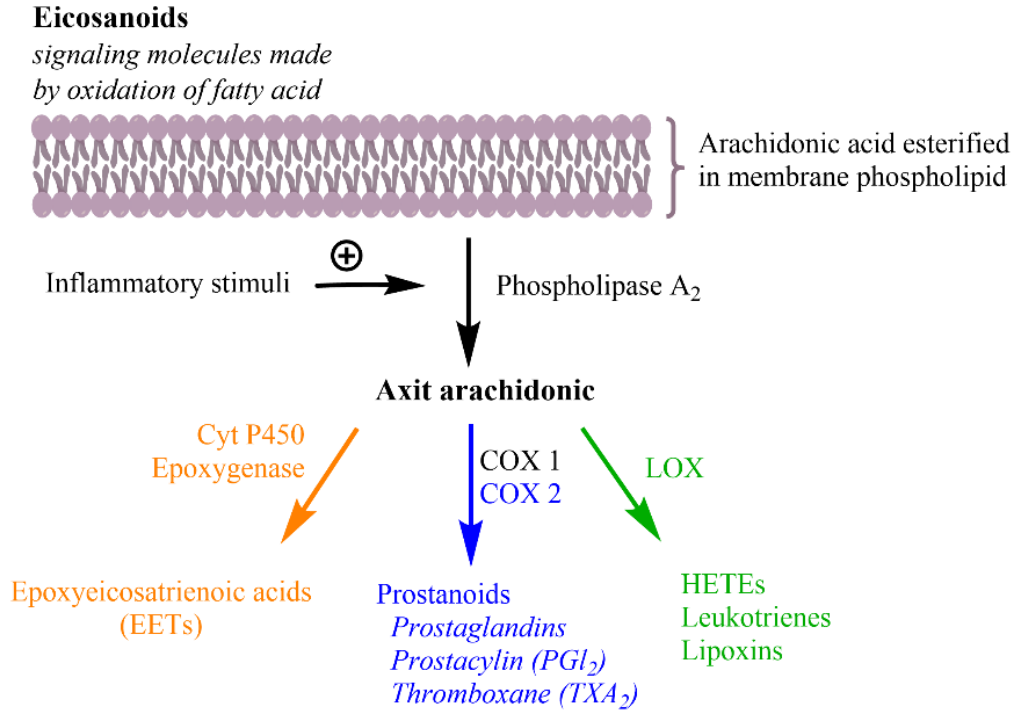


Figure 12. *Eicosanoids signaling pathway. Hydroxy Eicosatetraenoic (HETE); Prostaglandin-endoperoxide synthase 1/2 (COX1; COX2).*

Source: (https://tmedweb.tulane.edu/pharmwiki/doku.php/introduction_to_eicosanoids)

The benefits of a healthy plant-based diet are evident in inhibiting endogenous AGE formation, which helps prevent diseases such as diabetes, Alzheimer's, fatty liver, etc. [43, 49]. In particular, the latest studies also show that plant-based foods help prevent and improve symptoms caused by COVID-19, including fatigue, headaches, cognitive disorders, trouble sleeping, anxiety, depression, joint pain, muscle weakness, and shortness of breath, chest pain [50].

Phytochemicals are essential in protecting health by combating inflammation caused by advanced glycation end products (AGEs) and fighting harmful pathogens due to their antibacterial and antiviral properties.

They also contribute to improving symptoms caused by COVID-19. An anti-inflammatory diet is considered an effective way to prevent various diseases, is easy to follow, and includes foods that are rich in fiber, polyphenols, 1,3-β-glucan, 1,6-β-glucan, and omega-3, along with minimally processed and high-heat-treated foods. This explains why Victorian-era men lived three years longer on average than their modern counterparts with the same social and economic status [27]. Over 52 years (1961-2013), the average per capita food consumption in kilograms per year has undergone significant changes, increasing from 45.0 kg (1961) to 116.6 kg (2013) for vegetables, from 36.4 kg (1961) to 71.7 kg (2013) for fruits, and from 15.7 kg (1961) to 33.3 kg (2013) for fish and seafood [51].

3.5. The cycle life: "Another perspective of how we need to eat more fruits, veggies, roots, fruits"

According to the old-fashioned way of thinking, we eat fruits, vegetables, tubers, and fruits because of their health benefits: oranges because they provide vitamin C, tomatoes because they have lycopene, which has an anti-free radical effect [52]. Their biological activities help prevent aging and disease. However, from a different perspective Wang Tao, the author of the book *"The lost nutrition studies: Away from Disease"* [53], has stated that "The eternal nature of the Earth is the cycle of nutrition... For the most part, the nutrition we are in contact with today does not place it on the heights of nature to assess the situation, not to stand on the heights of the inorganic and organic worlds to develop themselves". Our world is an analogy from the micro to the macro level [54]. The life-forming nature of the Earth is the cycles of living things, the perfect cycles. Every 24 hours, a similar new day with many elements is repeated. After every 12 months consisting of 365 days (or 366 days), the spring, summer, autumn, and winter of the year are almost repeated. Water undergoes evaporation, condensation, and rain and returns to rivers and seas. The life cycle from the macro-natural perspective is a large cycle of nutrients known as the food chain.

Weeds that absorb nutrients in the soil grow and thrive as a food source for wildebeest and some herbivores. Herbivores are a food source for tigers, lions, and other carnivorous predators. Plants and animals, while growing, fighting, getting old, and dying from dead bodies, form a source of decomposition of microorganisms in the soil, providing nutrients for weeds to grow. The process continues, forming a closed cycle: plants are food sources for animals, animals are food sources for microorganisms, and microorganisms provide plant nutrients (Figure 13a).

Humans are also part of nature, so a life cycle exists. Human life is a cycle of birth, old age, illness, and death. The life cycle of micro nature is a small nutrient cycle called the human body (Fig. 13b).

Plant-based foods, which include fibers and biologically active compounds, form a food source for intestinal microorganisms. Bioactive compounds help balance intestinal bacteria and inhibit the growth of harmful bacteria to protect the gut [55]. Fiber provides the raw material for microbial growth called prebiotics, which helps form short-chain fatty acids that help fight inflammation and protect the body from disease [56, 57], starting a perfect cycle for the human

body. Thus all life on Earth is a cycle of nutrition which, in the author's deeper perspective, is the cycle of life between nature and man.

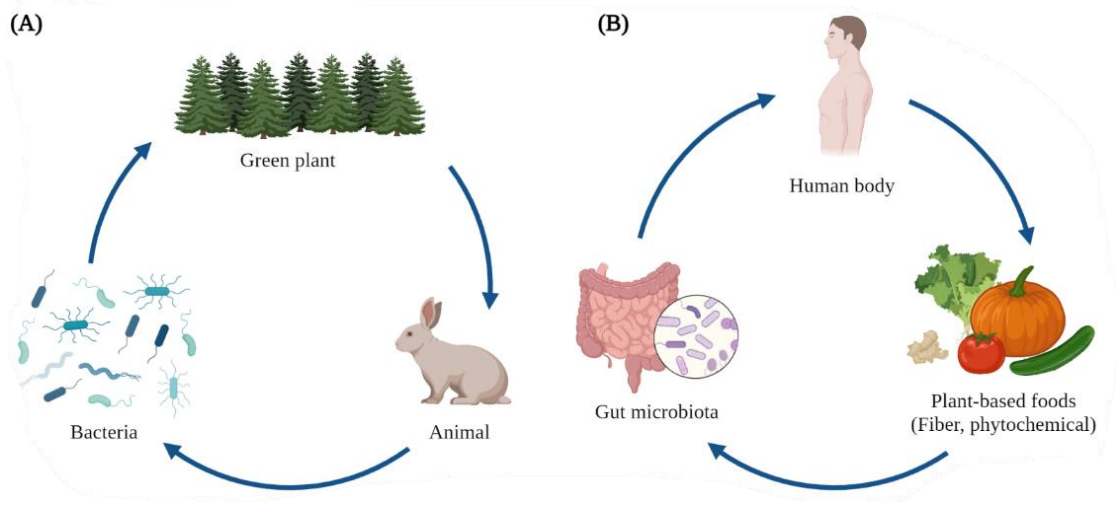


Figure 13. *The world is analogous. (a) - Life cycle in terms of macro-nature - food chain, (b) - The life cycle in terms of micro-nature - the human body.*

Nutritional health problems arise when people consume a lot of sweets and processed foods rich in fat. The formation of acrylamide and AGEs have changed the life cycle of our body. We always fall into a state of illness due to an unhealthy lifestyle (addiction to smoking, drinking alcohol, and even addiction to processed foods rich in energy and fat). The way to eliminate illness is through lifestyle and dietary changes that help restore the life cycle. Restoring the cycle of life means healing the body both nutritionally and spiritually.

V. CONCLUSION

AGEs and acrylamide are not beneficial to the body. An unhealthy lifestyle, and consumption of Western-style fast food rich in saturated fat, processed foods, and refined sugars, together with high-temperature food processing such as deep frying, baking, and drying under high temperatures, increases the production of AGEs and acrylamides, which accelerate aging and increase the risk of chronic diseases. To reduce the accumulation of AGEs and acrylamide, and prolong their health, we need to change the processing method, such as low-temperature heating for a long time, boiling, steaming, blanching, stewing, etc., and at the same time, change our lifestyle and healthy eating habits, increase more vegetables, tubers, fruits. "Your life is all about genes, not genes for life" changing behavior, perception and thinking in eating contributes to changing the epigenetic mechanism of genes, thereby reversing metabolic disorders related to chronic diseases to help individuals and communities lead healthy lives.

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