Potential Effects of Traditional Chinese Medicine in Anti-Aging and Aging-Related Diseases: Current Evidence and Perspectives

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Abstract: Aging and aging-related diseases present a global public health problem. Therefore, the development of efficient anti-aging drugs has become an important area of research. Traditional Chinese medicine is an important complementary and alternative branch of aging-related diseases therapy. Recently, a growing number of studies have revealed that traditional Chinese medicine has a certain delaying effect on the progression of aging and aging-related diseases. Here, we review the progress in research into using traditional Chinese medicine for aging and aging-related diseases (including neurodegenerative diseases, cardiovascular diseases, diabetes, and cancer). Furthermore, we summarize the potential mechanisms of action of traditional Chinese medicine and provide references for further studies on aging and aging-related diseases.

Keywords: aging and aging-related diseases, traditional Chinese medicine, potential mechanisms

Introduction

Advances in antibiotics, medicine, hygiene, housing, and lifestyle and economic development have led to an increase in human life expectancy. Aging has come to the fore and represents a worldwide focus in the life sciences. By 2050, the proportion of the world's population aged over 60 will double to 22%, and 80% of older people will be living in low- and middle-income countries.[1] All countries face major challenges to ensure that their health and social systems are adequately prepared for this demographic shift. Aging results from the effects of various types of molecular and cellular damage that accumulate over time, leading to a gradual decline in physical and mental abilities, an increased risk of disease, and eventually to death. Aging-Related Diseases (ARDs) affect human health and life, bring with them physical, psychological and economic burden, not only for older people and their families, but also for societies. However, the pathological mechanisms of ARDs have not been adequately elucidated, which greatly limits the efficacy of available treatment for these diseases in clinical practice.

Traditional Chinese medicine (TCM) has a profound theoretical basis and deep cultural heritage. Under the guidance of TCM theory, herbal medicines have been used effectively to combat disease and save lives. TCM was described as a cure for aging for the first time over 3000 years ago in *Huangdi Neijing*, in which the concept of health preservation was described. A classical TCM book named *Shanghan Lun*, written by Zhang Zhongjing, describes applications of *Shenqi Wan* for anti-aging. Japanese Kampo medicine advocates for *Shenqi Wan* as an "anti-aging recipe" for treating senile diseases that has achieved effective treatment results.[2]

TCM formulations used against aging feature multiple components, multiple targets and multiple pathways. Herbal medicines such as quercetin and resveratrol have been shown to extend the lifespan of model organisms.[3] *Sijunzi* decoction has an anti-aging effect and can reduce the effects of aging of the spleen and brain in mice through the mTOR pathway.[4,5] *Shenqi* pills protect nerves and improve memory by improving energy metabolism, reducing oxidative damage, and increasing the

number and morphology of nerve cells.[6] Meanwhile, *Shenqi* can alleviate the damage of tight junctions in senescent sertoli cells via a mechanism potentially related to the down-regulation of the p38MAPK signaling pathway.[7] Notably, recent studies have shown that TCM can stimulate the oxidative stress response and attenuate the aging process,[8,9] suggesting that TCM may be strongly associated with anti-aging and making the impact of TCM on aging and ARDs a promising and far-reaching topic. In this review, we discuss the close relationship between herbal medicine and ARDs by the effects of herbal medicine in anti-aging and ARDs, and the mechanisms underlying the role of herb medicine in IRDs.

TCM and Aging

Preliminary evidence from preclinical studies has revealed the anti-aging potential of TCM. Chinese herbal preparations delay intestinal aging through three pathways: anti-inflammatory, improving intestinal metabolites, and intestinal flora, which may be related to the decrease of telomerase mRNA in elderly mice.[10] Herb extracts increased activity during aging and improved heart function, while increase the healthy lifespan of aging flies.[11] TCM can ameliorate age-related reductions in brain performance, including memory, cognitive, and motor functions, via the preservation of redox homeostasis and telomere integrity, and inhibition of apoptosis.[12] NF-κB activation is associated with age-associated pathologies and symptoms.[13] Curcumin, a polyphenolic compound isolated from *Curcuma longa*, has been shown to prolong the mean lifespan of some aging model organisms. Curcumin has been proposed to improve immune cell chemotaxis, inhibit NF-κB signaling, and have antioxidative and anti-inflammatory biological activity.[14] This implies that TCM may exert beneficial regulatory effects on immune function during aging. Additionally, mulberry leaves have been identified to increase the lifespan of *Caenorhabditis elegans*.[8] These studies collectively support the anti-aging potential of TCM and hold the potential for better treatment regimens in the battle against aging.

TCM and Age-Related Diseases

Common conditions associated with aging include diabetes, cognitive impairment, chronic obstructive pulmonary disease, diabetes, depression, dementia and cancer.[1,8] As people age, they are more likely to experience several conditions at the same time. Despite ongoing research and progress in the field, cures for such chronic afflictions have not yet been found. Herbs have massive therapeutic potential in treating common conditions associated with aging and the mechanisms of action are shown in Figure 1.

TCM and Neurodegenerative Diseases

As lifespans are increasing, aging is most prevalent risk factor for neurodegenerative diseases and their associated cognitive dysfunction.[15] Alzheimer's disease (AD), the most common cause of dementia, has become a global health threat to older adults. In the United States, an estimated 6.2 million people aged ≥65 years are living with Alzheimer's disease while adults aged >70 years will experience a rapid increase of dementia; this number could grow to 13.8 million by 2060 and has become the fifth leading cause of death.[16,17] Globally, AD is the leading cause of cognitive impairment, with Parkinson's disease (PD) being second, seriously affecting the quality of life of the elderly.[18,19] Amyotrophic lateral sclerosis (ALS) is an age-related neurodegenerative disease that increases in prevalence and incidence with age until the age of 70–79 years.[20,21] However, effective treatment strategies for age-related degeneration are lacking, leading to its irreversible progression.

At present, there are no drugs that can effectively prevent the pathological progression of AD.[22] Evidence has been presented that TCM contains multiple active ingredients that could act on multiple targets simultaneously and have good clinical efficacy in the treatment of AD.[23] For example, oral administration of *Polygoni Multiflori Radix Praeparata* (*ZhiHeShouWu*) and *Acori Tatarinowii Rhizoma* (*ShiChangPu*) or their traditional combination has been reported to enhance synaptic-related proteins in mice, thereby offering the potential to alleviate cognitive deficits in AD patients.[24] Chinese herbal extracts demonstrated similar alleviative effects in an AD-like rat model induced with scopolamine, which may be through modulation of the dopaminergic synapse and apoptosis signaling pathway.[25] Additionally, the potential effects of TCM on ALS were explored in another study; TCM can prolong the lifespan, extend the disease duration, and prevent the loss of spinal motor neurons in mice with ALS, which was associated with reduction in atrophy of gastrocnemius muscles and improved levels of apoptosis and inflammation.[26] Meanwhile, TCM can delay the decline
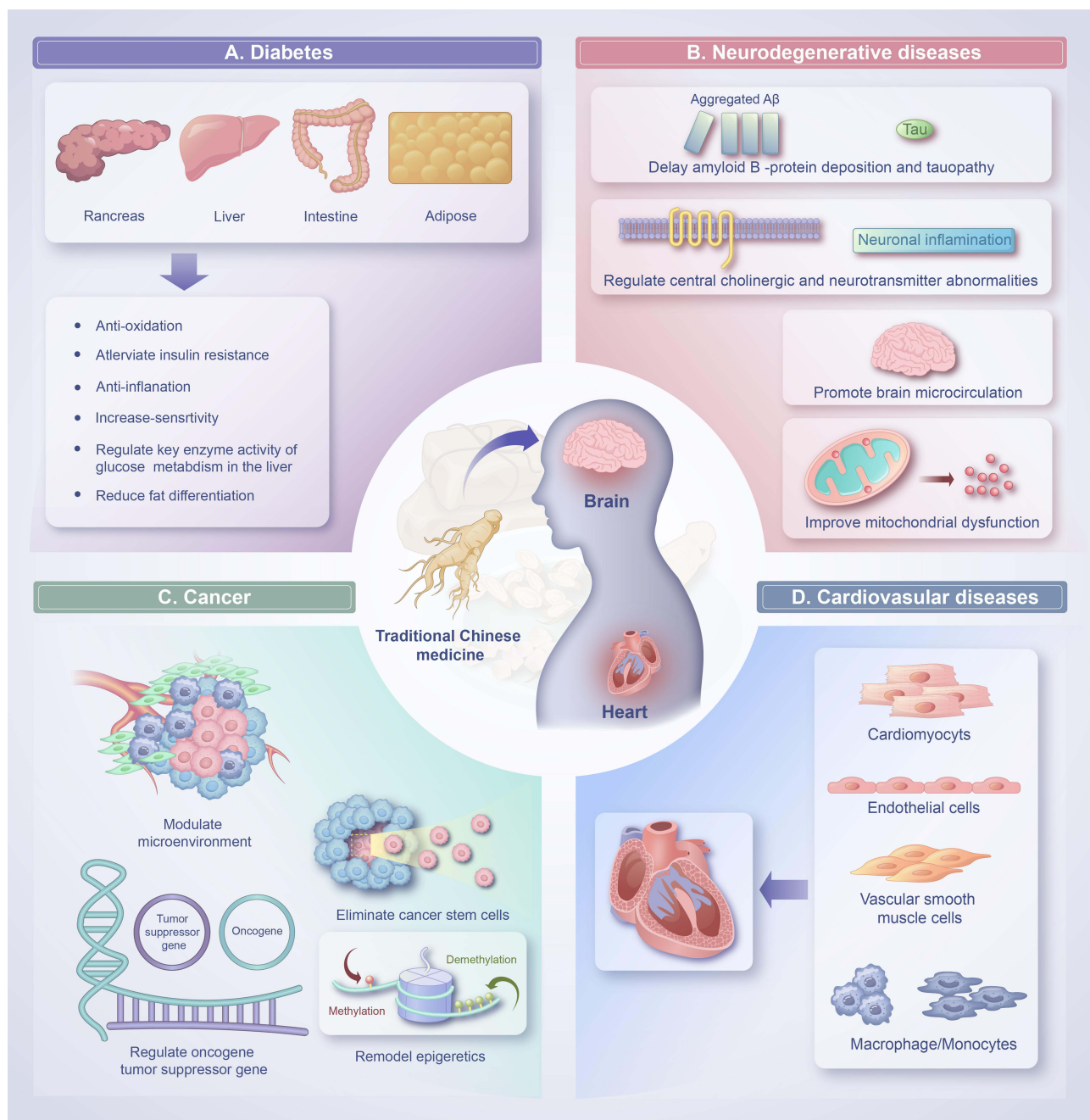
Figure 1 The effects of traditional Chinese medicine (TCM) with regards to the improvement of common conditions associated with aging and the mechanisms of action. (**A**) The mechanism of TCM in the treatment of diabetes is related to anti-oxidation, alleviate insulin resistance, anti-inflammation, increase insulin sensitivity, regulate key enzyme activity of glucose metabolism in the liver, reduce fat differentiation. (**B**) TCM can delay amyloid β-protein deposition and tauopathy, regulate central cholinergic and other neurotransmitter abnormalities, promote brain microcirculation, improve mitochondrial dysfunction. (**C**) Application of TCM in cancer therapy based on regulate genes (oncogenes and tumor suppressor genes), epigenetic modification (DNA and histone modification), the microenvironment, and cancer stem cells. (**D**) TCM have a protective effect on cardiovascular diseases by attenuate damage in cardiomyocytes, endothelial cells, vascular smooth muscle cells and macrophages/monocytes.

of motor function in ALS-model mice by alleviating the degeneration of neurons.[27] The results of preclinical tests and a previous clinical study support TCM as a novel therapeutic approach for AD and ALS patients. However, the potential of TCM to treat ALS should be assessed in a clinical trial.

The pathogenesis of PD is complex and is characterized as the progressive loss of dopaminergic neurons in the substantia nigra pars compacta. Oxidative stress, defective autophagy-lysosomal pathway, mitochondrial dysfunction,

endoplasmic reticulum stress, microglia reactivity and neuroinflammation are recognized to be features of PD.[28] However, no currently used therapeutic agent is known to slow down neuronal cell loss.

PD is closely related to mitochondrial dysfunction, which is a key factor in the occurrence and development of dopaminergic degeneration.[29] A study explored the mechanisms of *huangqin* decoction on attenuation of mitochondrial dysfunction, finding that *huangqin* decoction improved mitochondrial dysfunction, alleviated metabolic abnormality of mitochondria, and improved motor coordination and muscle strength in a rotenone-induced mice model of PD.[30] Andrographolide (andro) is a diterpenoid lactone isolated from *Andrographis paniculata*. Administration of andrographolide improved behavioral deficits and attenuated loss of dopaminergic neurons in mice with MPTP-induced PD via targeting mitochondrial fission mediated by dynamin-related protein 1.[31] *Duzhong fang* is a TCM formula that can alleviate neuroinflammation and regulate microglia morphology and reactivity by downregulating POMC expression in PD mice model.[32] Sinomenine, the main component of alkaloids, can augment the autophagy of dopaminergic neurons via inhibiting the PI3K/AKT/mTOR pathway and exerts a neuroprotective effect in PD mice.[33] *Zishenpingchan* granules can alleviate dopaminergic neuron apoptosis in PD mice induced by 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine by suppressing the over-activation of the c-Jun N-terminal protein kinase pathway in the substantia nigra. In addition, moxibustion can alleviate oxidative stress injury of the nigrostriatal system in mice with PD by activating the Nrf2/ARE pathway and protecting the dopamine neurons.[34] In a multicenter, randomized, double-blind, placebo-controlled study, 292 participants were included and followed for 9 months, the results showed that the TCM-treated group had significantly better improvement than participants in the control group in Movement Disorder Society Unified Parkinson's Rating Scale III motor score and its domain scores for axial symptoms, bradykinesia, rigidity, and tremor, indicating that TCM might be a viable alternative in the management of PD.[35]

TCM can protect dopaminergic neurons via multiple pathways. At present, great progress has been made in research into the mechanisms of TCM in the prevention and treatment of PD. However, it seems premature to conclude that TCM is associated with protective effects against deterioration of PD. There are several concerns that remain unresolved. First, the pathogenesis of PD is complex, which is the result of the mutual influence and interaction of multiple pathogenic factors, and the therapeutic advantage of TCM lies in the role of multiple components affecting multiple targets. Related studies focus on one or two molecular mechanisms, and rarely discuss the interactions between multiple molecular mechanisms from a multi-dimensional perspective. Second, in studies exploring the improvement of PD by TCM, the mechanisms of motor symptoms in model animals rarely involve non-motor symptoms. Third, there is a lack of corresponding large sample clinical studies to verify the experimental results. Therefore, extensive investigation is required to answer these questions.

TCM and Cardiovascular Diseases

At the age of 65 years or older, cardiovascular diseases (CVDs) are the leading pathological conditions, causing 40% of all deaths.[36] Calcium transient amplitude decreases gradually with age, increasing the risk of arrhythmias in the older population.[37] Accumulation of senescent cells within the vascular wall and heart can contribute to changes in cardiac structure and function, including progressive myocardial remodeling, left ventricular hypertrophy, decreased systolic and diastolic function, and aggravates pathophysiological processes of cardiovascular diseases, such as atherosclerosis, myocardial infarction, and cardiac fibrosis.[38,39]

Recent studies have confirmed that TCM has strong beneficial effects in the prevention and treatment of CVDs.[40] Accumulating evidence in model organisms and humans links cardiac aging to mitochondrial regulation.[41] Qishen granules promote PGC-1α-mediated mitochondrial biogenesis by coordinating mdm2-p53 mediated mitochondrial autophagy and Mitoch, and improve the degradation and protection of p53 protein in mice.[42] In atherosclerotic mice, TCM can suppress the inflammatory response, ameliorate endothelial growth/function and improve blood lipid levels, leading the effect of anti-atherosclerosis.[43] Similarly, berberine (BBR) in *Coptis chinensis* and other Berberis plants has been shown to attenuate trimethylamine/trimethylamine-N-oxide production and mitigate atherosclerotic lesion areas in mice via manipulation of the gut microbiome.[44] Dehydrocorydaline, an alkaloidal compound isolated from *Corydalis yanhusuo*, inhibits macrophage inflammation by targeting macrophage p65- and ERK1/2-mediated pathways to ameliorate atherosclerosis in mice.[45] Ethanol

extracts from *Schisandra chinensis* fruit significantly reduced atherosclerosis in rats by regulating serum lipid levels, enhancing the antioxidant enzyme activities, and improving endothelial dysfunction.[46]

There are several successive and interrelated steps in the development of atherosclerosis that have served as excellent models for evaluating atherosclerotic protective drugs, and TCM acts on one or more of these steps: (1) Low-density lipoprotein (LDL) oxidation activates endothelial cells and initiates the vicious cycle of atherosclerotic plaque progression.[47] Chinese herb compounds contribute to antioxidant activities and inhibit LDL oxidation.[48] Oxymatrine, a quinolizidine alkaloid isolated from *Sophora flavescens*, may attenuate oxidized low-density lipoprotein in vitro cell model by inhibiting NLRP3 inflammasome-mediated pyroptosis via activating the SIRT1/Nrf2 signaling pathway.[49] (2) Endothelial dysfunction, reduced elasticity of blood vessels and enhanced development of vascular plaque are central in the pathophysiologic processes of CVDs.[50] Astragaloside IV, the primary active ingredient of the Chinese herb *Huangqi*, prevents endothelial dysfunction by reducing apoptosis, oxidative stress, and inflammatory response in vitro.[51] (3) Vascular smooth muscle cell (VSMC) dysfunction, promoting extracellular matrix formation in atherosclerosis plaque areas, is the early form of atherosclerosis.[52] BBR significantly inhibits angiotensin II and heparin-bound epidermal growth factor by delaying or partially inactivating the Akt signaling pathway, thereby inhibiting the proliferation and migration of VSMCs.[53] (4) Macrophage-derived foam cell formation and inflammation is the hallmark of atherosclerosis.[54] Increased ox-LDL flow and the accumulation of cholesterol esters in endometrial macrophages are the main factors. Clematichinenoside AR (AR), a major active ingredient extracted from the traditional Chinese herb *Clematis chinensis*, inhibits foam cell formation by increasing cholesterol efflux and reduces the production of inflammatory cytokines by passivating the activation of the NLRP3 inflammasome in macrophages.[55] (5) Platelet activation and thrombus formation is the primary clinical presentation of atherothrombotic events.[56] Administration of *Tanshinone IIA* inhibited platelet activation more effectively via downregulating the CD36 and MKK4/JNK2 signaling pathways.[57] Simultaneous administration of *Ginkgo biloba* extract 50 and aspirin exert both synergistic and additive effects in restraining platelet aggregation, which enhance the antiplatelet effects.[58] Therefore, it is reasonable to believe that there is a crucial link between TCM and age-related CVDs.

TCM and Diabetes

Diabetes is considered a disease of aging. The abundance of senescent cells in various tissues increases with age and diabetes. Aging contributes to the development of diabetes and its complications.[59,60] Senescent adipocytes can induce macrophages to enter visceral adipose tissue and release chemokines, which aggravate the development of type 2 diabetes mellitus (T2DM).[61] The high glucose and fat environment in diabetic patients has been identified as the main cause of cellular senescence.[62] The main mechanisms of T2DM and aging are insulin resistance caused by hyperglycemia, the decrease of insulin-like growth factor-1 (IGF-1) levels, lipotoxicity and a series of senescence-associated secretory phenotype (SASP) and hyperglycemia is a key trigger of aging.[63]

TCM can prevent and treat diabetes through multiple targets and pathways. For example, BBR prolongs high glucose-dependent cell membrane depolarization by blocking KCNH6 currents and stimulates insulin secretion in mice with hyperglycemia induced by a high-fat diet. A Phase 1 clinical trial in humans found that compared with placebo treatment, BBR significantly promotes insulin secretion under a hyperglycemic state without side effects and did not affect basal insulin secretion.[64] Tetrahydroxystilbene glucoside (TSG), a main component of *Polygonatum multiflorum*, can improve memory ability and prolong the lifespan via reduced levels of neural insulin or insulin-like growth factor-1 and upregulation of neural klotho in mice.[65] *Gegen* is a Chinese herbal medicine that is often combined with other herbs to treat diabetes and other chronic metabolic diseases, and the isoflavone puerarin is the main active component of *gegen*. The combination of canagliflozin and puerarin can alleviate the oxidative stress and renal inflammation induced by lipotoxicity.[66] In the process of aging, senescent cells secrete pro-inflammatory cytokines and other factors, collectively known as SASP. SASP secretion, by contributing to inflammation, is a key risk factor for the development of aging-related diseases. Psoralen, with prenylflavonoids (PF) as the main bioactive components, can delay aging. There is insufficient evidence to prove that these PF can be used as anti-aging drugs (via modifying SASP components), but they can block certain aging-related signaling pathways by entering cells and play an anti-inflammatory and anti-aging role (such as in diabetes).[67] These results indicate that TCM can be an important entry point to treating diabetes and

preventing or delaying aging. However, related research should focus on the basic mechanisms and continue to explore how best to provide precision medicine for elderly and diabetic patients.

TCM and Cancer

The global population is growing older. Malignant tumors are closely related to aging, and the incidence is much higher in the population aged over 60 years, more than double that in the younger population.[68] Most elderly patients with malignant tumors are complicated with multiple chronic diseases, and the mortality rate is higher in these patients. The mechanisms of both cancer and aging are based on the time-dependent accumulation of cellular damage, and many of the characteristics of aging are shared with cancer. Recent research has shown that aging can affect the tumor microenvironment (TME) in normal cells, fibroblasts, and immune cells, which contributes to the progression and metastasis of tumors.[69]

Fibroblasts are the most common stromal component within tissues across the body and play a major role in tissue homeostasis. Cancer-associated fibroblasts (CAFs) are activated fibroblasts associated with cancer and play an important role in tumor growth and metastasis. Studies over the past two decades have provided important information on the ways TCM may suppress CAFs, indicating that TCM may also be effective cancer therapeutic treatment.[70] *Qingyihua* is a TCM prescription that has an anti-cancer effect on pancreatic cancer and is related to changes in the TME. It may inhibit the tumor-promoting ability of CAFs and weaken the invasion of pancreatic cancer cells in vivo and in vitro.[71] Artemisinin derivatives have been reported to inhibit CAF-induced growth and metastasis in an orthotopic model of breast cancer, possibly by inhibiting TGF-β signaling to inactivate CAFs fibroblasts and inhibit cancer metastasis.[72]

The interaction between tumor cells and the TME plays a decisive role in the progression of tumors. Solamargine (SM), a TCM compound, has been reported to reduce the proliferation of hepatocellular carcinoma and effectively induce hepatocellular carcinoma cell apoptosis and autophagy via inhibiting LIF/miR-192-5p/CYR61/Akt signaling pathways and eliciting an immunostimulatory tumor microenvironment in vitro and in vivo.[73] *Yi-Yi-Fu-Zi-Bai-Jiang-San* is a CH from *Synopsis of Prescriptions of the Golden Chamber* that has been reported to inhibit colorectal tumorigenesis by increased immune responses in the tumor microenvironment through its hypoxia-associated anti-cancer activities in a mouse model.[74] In the TME, the activation of the programmed death-1 (PD-1)–programmed death ligand-1 (PD-L1) pathway is one of the main signals of immune escape and tumor deterioration. Platycodon grandiflorum (PG), a medicine and food homology herb, can improve antitumor immunity by downregulating PD-1 expression of CD8+ T cells in the TME.[75]

The activation of the PD-1/PD-L1 pathway is one of the main signals of immune escape and tumor deterioration. Recently, studies have shown the importance of TCM combined with anti-PD-L1 antibodies in cancer therapy.[76–78] Analyses of the relationship between the therapeutic efficacy of immune checkpoint inhibitors and TCM in patients with different cancers have found that CH could facilitate immune checkpoint blockade therapy or CAR-T cell therapy for cancer treatment. Furthermore, TCM can modulate adaptive immunity by activating T effector cells mainly through its action on SHP1/2.[79] In another study, baicalein and baicalin blockade of the PD-L1/PD-1 pathway to prevent the immune evasion of tumor cells by decreasing STAT3 activity and downregulating IFN-γ subsequently restored T cell sensitivity to promote antitumor immunity.[80] Neobavaisoflavone (Neo), as a traditional Chinese medicine, inhibited the growth and lung metastasis of tumors in vivo. In addition, Neo enhanced anti-PD-1 efficacy in anti-PD-1-insensitive tumors.[78] The above results indicate that combining cancer immunotherapy with TCM may soon achieve better clinical results for patients.

Mechanisms of TCM Against Aging and Age-Related Diseases

TCM has been widely used in the treatment of aging and age-related diseases and achieved satisfactory clinical effect. With the development of the modernization of TCM, researchers have explored the specific mechanisms of TCM in view of its multi-target and multi-component advantages. There are several main models based on the available evidence (Figure 2).

Epigenetic regulation is used to classify heritable changes in gene expression that are not attributable to changes in DNA sequences.[81] Mounting evidence suggests that epigenetic dysregulation is a driver of cellular senescence and can accelerate the progression of age-associated disease.[82,83] As a major epigenetic modification, DNA methylation is one of the important markers of aging.[84,85] The role of TCM in DNA methylation has been widely reported. For example, Tanshinone IIA, the main fat-soluble component of *Salvia miltiorrhiza*, can prevent rifampicin-induced liver injury
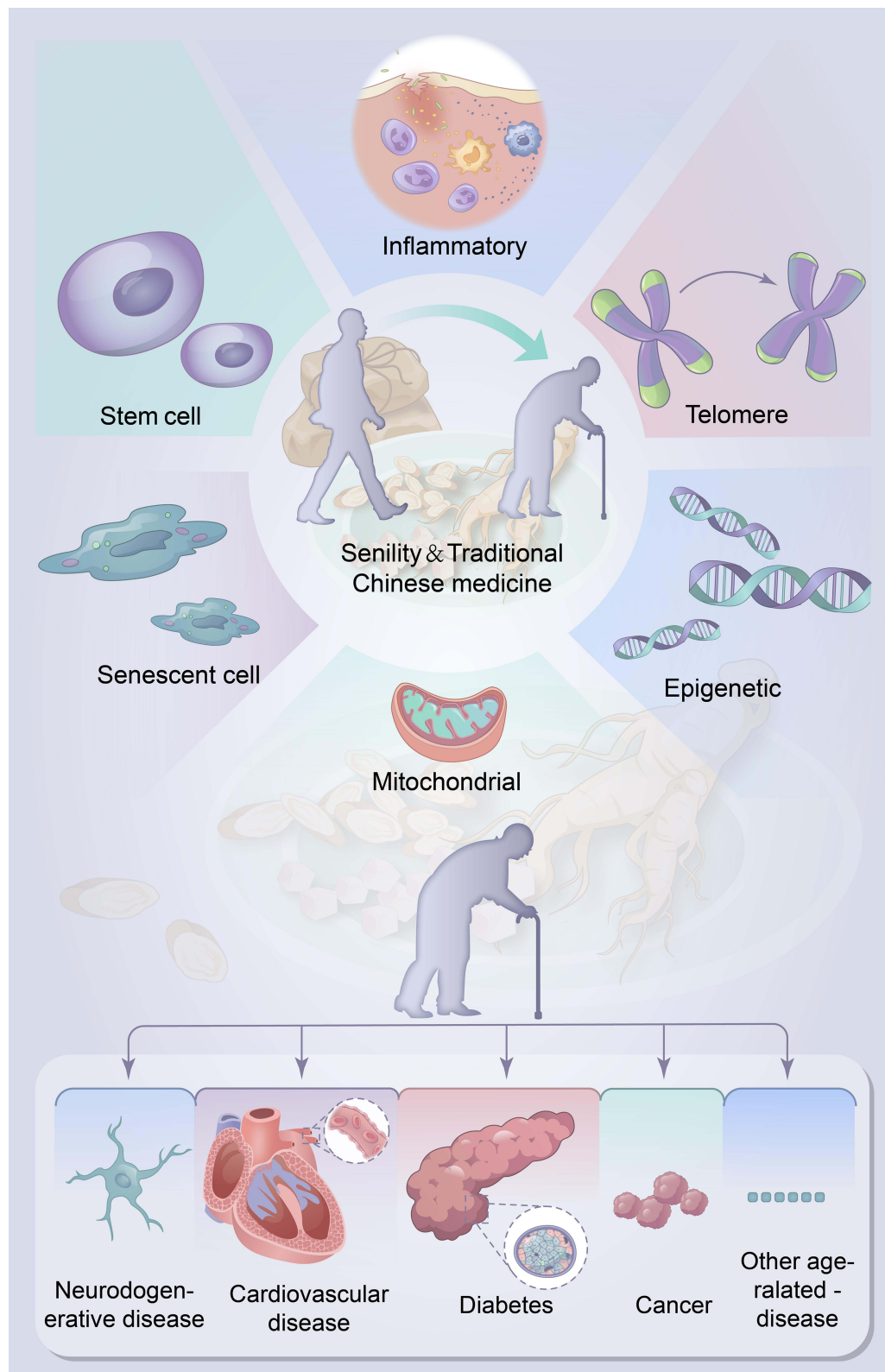
Figure 2 Potential role and major mechanisms of traditional Chinese medicine on Aging and aging-related diseases. Administration with traditional Chinese medicine may be an effective project for aging and aging-related diseases. The potential possible mechanisms of traditional Chinese medicine to control the aging and aging-related diseases are (a) increase the length of telomere; (b) Modulating epigenetics; (c) Maintenance of mitochondrial homeostasis. (d) Reduce the senescent cells; (e) Maintenance of stem cell viability; (f) Improve the intestinal flora.

through the DNA demethylation by ten-eleven translocation 2.[86] *Bazi bushen* (BZBS), a TCM prescription, significantly restored the methylation age of aging mice and trimmed the methylation pattern to that of young mice, and the extract has a direct effect on the regulation of methylase during cell aging in vitro.[87]

Telomere shortening and damage are recognized causes of cellular senescence and aging. Some aging and age-related diseases associated with accelerated telomere dysfunction.[88] Similarly, a range of evidence reveals the benefits of TCM for aging and age-related diseases. The effects of TCM on telomere dysfunction have been reported. BZBS can delay premature senescence by keeping redox homeostasis and telomere integrity, and inhibition of apoptosis in D-galactose and NaNO 2-induced aging mice.[12]

Autophagy plays important roles in regulating cell homeostasis and aging processes. Decreased autophagic capacity has been observed in animal models of aging, and some CH exert an important role in prolonging life via autophagy.[89,90] An herbal drink can maintain stem cell homeostasis and provide cytoprotection.[91] *Dendrobium nobile var. Lindl.*, used as an anti-aging herb, can exert anti-aging activity via reducing oxidative stress, and by enhancing autophagy through the Sch9/Rim15/Msn2 signaling pathway.[92]

Senescent cells trigger a low chronic inflammatory state, leading to changes in the microenvironment, thus inducing cellular senescence in neighboring cells and playing an important role in tissue and organ aging and ARDs.[14,93] With aging, stem cells show decreased self-renewal capacity and decreased function. TCM can reduce the number of senescent cells, reduce the level of cell cycle arrest protein, and maintain the cell repair ability. Studies have shown that CH play a role in maintaining the viability of stem cells, including inhibit aging, improve differentiation and promote proliferation.[94] *R. glutinosa*, an anti-aging Chinese

Table 1 The Link Between Chinese Herbal Medicine with Age-Related Disease

Age-Related Disease	Chinese Herbal Medicine	Composition	Potential Mechanisms	Ref.
Atherosclerosis	Qing-Xue-Xiao-Zhi formula	Reynoutria japonica Houtt., Rheum palmatum l., Typha angustifolia l., Curcuma longa l., Alisma plantago-aquatica Linn., Dioscorea septem loba Thunb. Artemisia capillaris Thunb., Atractylodes macrocephala Koidz., Acori tatarinowii Rhizoma, Carthamus tinctorius l.	Regulate TLR4/MyD88/NF-κB pathway	[98]
Parkinson's disease	Yiguanjian decoction	Glehniae Radix, Toosendan Fructus, Angelicae Sinensis Radix, Rehmanniae Radix Praeparata, Lycii Fructus, Ophiopogon japonicus,	Regulate the PI3K-Akt pathway, modulate endocrine resistance of the central nervous	[99]
Osteoporosis	Qing'e Pill	Eucommia ulmoides Oliv., Psoralea corylifolia L., Juglans regia L., and Allium sativum L.	Inhibit ferroptosis and promoting cell survival via the PI3K/AKT pathway and ATM	[100]
Osteoarthritis	Gubitong Recipe	Davallia mariesii Moore ex bak, Epimedium brevicornu Maxim., Psoralea corylifolia Linn., Eucommia ulmoides Oliver, Lycium chinense Miller, Rhizoma Bolbostematis, Stephania tetrandra S. Moore, Spatholobus suberectus Dunn	Inhibit the NF κB pathway	[101]
Chronic kidney disease	Jian-Pi-Yi-Shen Formula	Astragalus membranaceus, Dioscorea opposita Thunb. Rehmannia glutinosa, *Cistanche deserticola Ma, Amomum kravanh Pierre ex Gagnep. Salvia miltiorrhiza Bunge*, Rheum palmatum L., Glycyrrhiza uralensis Fisch	Modulate QPRT/NAD+/SIRT3/ Mitochondrial Dynamics Pathway and regulate Tryptophan Metabolism and Aryl Hydrocarbon Receptor Signaling.	[102,103]
Type 2 diabetes	Qijian mixture	Astragalus membranaceus, Ramulus euonymi, Coptis chinensis and Pueraria lobata,	Acte through TP53, AKT1 and PPARA proteins	[104]
Chronic obstructive pulmonary disease	Bufei Yishen formula	Ginseng Radix et Rhizoma, Astragali Radix, Corni Fructus, Lycii Fructus, Schisandra Chinensis Fructus, Fritillariae Thunbergii Bulbus, Perillae Fructus, Citri Reticulatae Pericarpium, Epimedii Folium, Paeoniae Rubra Radix, Pheretima, Ardisiae Japonicae Herba	Restore Th17/Treg balance via reciprocally modulating the activities of STAT3 and STAT5	[105]

medicine, has been shown to reduce cell senescence and increase survival in a mouse model, possibly by maintaining the quiescence of hematopoietic stem cells and downregulating the cellular senescence-related proteins p53 and p16.[95] Allicin, a chemical extracted from garlic, has been reported to alleviate the ameliorated aging phenotype in hematopoietic stem cells by up-regulating PKM2 expression.[96]

With aging, the gut homeostasis changes, and the imbalance of intestinal homeostasis contributes to many age-related degenerative diseases and unhealthy aging. CH can adjust the level of intestinal flora and improve the species diversity of intestinal flora and its metabolites, thereby improving the intestinal microecology. In one study, 104-week-old mice fed with ginsenoside Rb1 (GRb1) for 6 weeks showed characteristics of improved intestinal aging. GRb1 could reduce the senescent cells that are increased in the intestinal crypts of older mice. An increase in the protein levels of CLDN 2, 3, 7, 15, SIRT1, SIRT3, SIRT6 and Tert, Lgr5, mKi67, and c-Myc with changes in the composition and functions of the gut microbiota were evident. Thus, GRb1 was shown to improve intestinal aging, with an important role in regulating the expression of the sirtuin family.[97]

Conclusions and Perspectives

Convincing evidence has supported a strong link between TCM and aging. In terms of anti-aging, Chinese herbal has its unique advantages, and more evidence points to beneficial aspects (Table 1). Furthermore, there is a correlation between Chinese herbal and the prevention and control of age-related diseases (Table 2). TCM can enhance the ability to resist external stimuli and play a role in delaying aging through anti-inflammation and anti-oxidation. Meanwhile, TCM has shown improvement effects on cardiovascular, nervous system diseases and age-related diseases. However, there remain some deficiencies in the relevant studies on the use of TCM in anti-aging treatment. First, most of the studies on TCM remain at the level of in vitro experiments, and the relevant animal experimental studies are few, so further in vivo evaluations and clinical trials are needed to verify their reliability. In addition, although the anti-aging effect of TCM is

Table 2 Chinese Herbs and Its Anti-Aging Effects

Chinese Herbs	Type of Bioactive Components	Potential Mechanisms	Models	Ref.
Ginseng	Ginsenoside Rg1	Antioxidant enzymes GSH-Px and SO↑, telomere lengths and telomerase activity↑, the levels of proinflammatory cytokines↓	D-galactose induced aging rats	[106]
R. Astragali	Astragalosides, Astragalan, TA-65	Immunomodulatory effects↑, lengthens telomeres↑, the lifespan of daf-2 and age-1 mutants↑	Aging and the middle-aged rats, Caenorhabditis elegans Relatively healthy cytomegalovirus-positive subjects aged 53–87 years old	[107–109]
Ganoderma lucidum	Total water extract of G. lucidum	Anti-oxidative stress↑, mTOR/S6K signaling pathway,	Caenorhabditis elegans	[110]
Astragalus membranaceus	Polysaccharides, flavonoids, and saponins	Telomerase activity↑, antioxidant, anti-inflammatory and immunoregulatory	Myocardial ischemic rat, aging rats	[111]
Resveratrol	NR	Prevent inflammation and oxidative stress by activating Nrf2 and SIRT1 signaling↑	Male 18-month-old C57BL/6 mice	[112]
Psoralea corylifolia	Corylin	Gtr1 protein	Yeast, aging mice fed with a high-fat diet	[113]
Schisandra chinensis	Schisandra chinensis lignans	The mRNA expression level of p19, p53, and p21 ↓	Aging rats	[114]
Dendrobium officinale	NR	Antioxidation, immunoregulatory. Serum levels of SOD, GSH-Px and T-AOC, and restored SOD levels ↑	Aging rats	[115]

Abbreviation: NR, Not Report.

better, research into its efficacy and safety is inevitably limited by factors such as its complex composition. Furthermore, there is a lack of support for the development of scientific research in this field, such that the public lacks a comprehensive understanding of TCM in anti-aging. In conclusion, TCM provide a vast resource that may be therapeutically useful in anti-aging. Further research on the role of TCM in anti-aging therapy is important to explore.

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Disclosure

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