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A Systematic Review of the Efficacy and Safety of Anti-aging Herbs in Animals and Human

[1]Shirin Hasani-Ranjbar, [1]Somayeh Khosravi, [1]Neda Nayebi, [1]Bagher Larijani and [1,2]Mohammad Abdollahi

[1]Endocrinology and Metabolism Research Institute, Faculty of Medicine, Tehran University of Medical Sciences, Tehran, Iran

[2]Faculty of Pharmacy and Pharmaceutical Sciences Research Center, Tehran University of Medical Sciences, Tehran, Iran

Corresponing Author: Mohammad Abdollahi, Faculty of Pharmacy and Pharmaceutical Sciences Research Center, Tehran University of Medical Sciences, Tehran, 1417614411, Iran

ABSTRACT

This review focuses on the efficacy and safety of medicinal plants which have been utilized in traditional medicine for anti-aging purpose. All relevant databases were searched for the terms "anti-aging" and "herbs" or "medicinal plant" without limitation up to 30th January 2011. All the clinical and non-clinical studies with the outcome of change in aging process were included. Search in databases resulted in 1733 articles that on the basis of inclusion/exclusion criteria, 67 studies were finally included. Six human and 61 animal studies were reviewed for the effect of anti-aging herbs on aging process. Most of the studies showed significant improvement in brain function (memory, cognitive, anxiety), sexual disorder and skin wrinkle. From the performed studies, the exact mechanism of anti-aging action and side effect cannot be concluded and thus further studies would be helpful.

Key words: Aging, aging process, anti-aging herbs, medicinal plants, herbal medicine

INTRODUCTION

Aging is a biological phenomenon of life that leads to progressive and deadly changes in organisms. Approximately 100,000 people worldwide die every day because of age-related problems (De Grey, 2007). Though neuron loss is minor after 20 years of age, there is a 10% decrease each decade in the total length of the brain's myelinated axons (Marner *et al*., 2003). A lot of theories propose that aging results from the accumulation of damage at different levels of organ, cell and cell nucleus. Various theories have been proposed in the aging process but the general ones refer to free-radicals, cross-linkage, reliability theory of aging and longevity, somatic mutation, accumulative-waste, aging-clock, the viral theory and etc. Amongst these theories, most of scientists are in favor of free radical theory (Momtaz and Abdollahi, 2012). Studies show that increasing Reactive Oxygen Species (ROS) has a key role in oxidative damage of major cellular elements such as protein, lipid and DNA resulting in deterioration of energy production, multi-organ failure, aging and death. The antioxidant defense system consists of free radical scavenging enzymes such as catalase (CAT), glutathione peroxidase (GPx), superoxide dismutase (SOD) and antioxidants such as vitamin C, vitamin E and etc. An imbalance that is caused by increased

generation of free radicals or reduced functional efficiency of antioxidant defense system is believed as one of the primary factors contributing to aging (Momtaz and Abdollahi, 2012). From ancient time, people were interested and tried to keep themselves young. Therefore, anti-aging study is certainly not a new research area and has traditional links. Nowadays, the meaning of anti-aging has changed from simply prolonging lifespan to increasing health span which emphasizes more on the quality of life. Herbal medicine has a long history in Asian countries. It is believed that many of the medicinal herbs have anti-aging properties. Recent studies have shown that some medicinal herbs are effective in intervention or prevention of aging-related disorders. In this review, we have focused on anti-aging herbs and their characteristics in different clinical or experimental models.

MATERIALS AND METHODS

All relevant databases like Google scholar, Scopus, Iranmedex and Pubmed were searched up to 30th January 2011 for studies examined effect of anti-aging herbs on aging process. The search terms were anti-aging and herbs, medicinal plants or herbal medicine without any limitation. A flow diagram of search process has been demonstrated in Fig. 1. Among the studies, 6 were on human and 61 on animals. Two reviewers independently examined all papers to ensure the title, abstract and references of each article to eliminate duplication. The reference list of each article was reviewed for additional relevant studies. Letter to editor, review articles, or dissertations were not included. The included papers were summarized according to dose, treatment duration, grouping, main outcome, probable mechanism and side effects (Table 1).

RESULTS

The initial search identified 1733 articles, from which 67 studies met inclusion criteria and were reviewed (Table 1). The search process is shown in Fig. 1. Herbs such as *Lycium barbarum* (wolfberry {goji berry}), Nardostachys jatamansi, Phragmites communis, Ginkgo (total lactone), Astragalus membranaceus (hairy root), Curcumin pointed to have anti-oxidant effects. Wolfberry (*Lycium barbrum*) is the fruit of the plant *Lycium barbarum* that grows in China or Vietnam contains powerful antioxidant with anti-aging properties such as vitamins B1, B6 and E. Anti-oxidant effect of Licuim barbarm (wolfberry or gojiberry) was demonstrated by its ability to improve body antioxidant power and immune function and reduction of Lipid Peroxides (LPO).

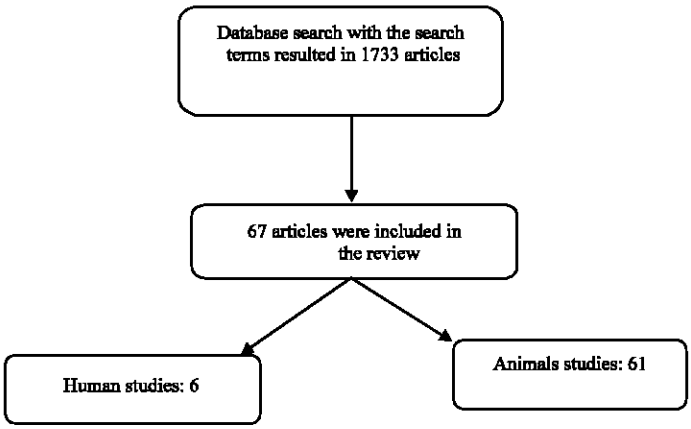

Fig. 1: Flow diagram of the search process.

Table 1: Human and animal studies considering anti-aging effects of medicinal plants

Animal studies

Author	Target	Herb	Dose/duration	Groups	Components	Anti-aging effect/Noted mechanisms	Outcomes in herbal treatment group
Mizoguchi *et al.* (2010)	Rats (young and aged)	Yokukansan (YKS) (a kampo drug)	3% (wt/wt)/oral/3 m	C: standard food T: YKS-treated aged rats	Atractylodin Eburicoic acid Cnidilide Rhynchophylline Ligustilide Saikosaponin a, c, d, e Glycyrrhizin	Anxiolytic by enhancing serotonergic and dopaminergic transmissions in the aged PFC	Sig improvement of anxiety-related responses; decrease of serotonin and dopamine in the PFC; improve of plasma increase in NH (3); but did not change in AST, ALT
Kang *et al.* (2009)	Mice (hairless)	Panax ginseng (red ginseng)	0/5%/2.5%/oral	C: control diet±UV irradiation T: extract±UV	Ginsenoside Rb1	Anti-wrinkle by the inhibition of collagen degradation rather than its synthesis	Sig inhibition of wrinkle formation, level of mRNA of procollagen type I decreased but its protein level increased; sig decreased either in mRNA or protein levels of MMP-1
Ichihashi *et al.* (2008)	Rats (female)	Nanpao (a kampo medicine)	0, 30 or 100 mg/kg/ oral/21, 31w	C: young and aged T: aged+ nanpao		Maintenance of normal embryo-fetal development	Inhibition of loss of regular estrous cycles; decrease in delivery and pregnancy rates and mean fetal wt; decrease in the numbers of mean live offspring and fetuses in the 100 mg/kg/d group
Makarova *et al.* (2007)	Rats (male)	Epimedium koreanum	300, 750 mg/kg/ oral/10 d	C: young and aged+olive oil T: aged+ two compositions (E-01 and E-02)	Icariin	Improved erectile function (sexual behavior)	Increase in the number of complete intromissions and ejaculations, decrease in latent period of ejaculation
Qin *et al.* (2008)	Rats (liver cancer model)	Antioxin (extract of Huangqi (Radix Astragali), Danggui (Radix Angelicae Sinensis), Danshen (Radix Salviae Miltiorrhizae), Dangshen (Radix Codonopsis) and Gouqizi (Fructus Lycii)	60 mg /kg /intra gastric/8 w	C: normal and model rats+saline injection T: model rats+adriamycin, saline, Antioxin		Protection on oxidative stress by multiple antioxidative effects	Sig higher survival than the chemotherapy group and antagonistic effect on chemotherapy-induced changes: (increase in level of MDA, NO and decrease of the activities of total SOD, manganese SOD, CAT, GSH and TAOC
Deng and Tang (2006)	Mice	Renshen Yangrong (RY)	High, middle, low dose	C: young and model (D-galactose induced subacute senile) T: (RY)		Membrane fluidity of mitochondrion protection and MDA decrease	Sig reduction of the MDA concentration in mitochondrion and marked increase of the membrane fluidity of mitochondrion in hepatic and cerebral cells in a dose-dependent manner

Table 1: Continued

Animal studies

Author	Target	Herb	Dose/duration	Groups	Components	Anti-aging effect/Noted mechanisms	Outcomes in herbal treatment group
Li *et al*. (2007)	Mice	*Lycium barbarum* (wolfberry or gojiberry)	200, 350, 500 mg/kg/oral/30d	C: young and aged±vit C T: aged+extract ±vit C		Compensating the decline in TAOC, immune function and antioxidant enzymes activities and reduction of lipid peroxidation	Restoration of increased endogenous lipid peroxidation and decreased antioxidant activities (SOD), (CAT), glutathione peroxidase (GSH-Px) and (TAOC) and immune function to normal levels
Yao *et al*. (2006)	Mice	Resveratrol: a natural phenol derived from several plants		D-galactose induced subacute senile mice	Resveratrol	Antioxidative and some immunity effects	Increased SOD and decreased MDA contents in serum, no change in spleen index, but thymus index increased; no change in the quantity of CD4+, but CD8+ increased and the ratio of CD4+/CD8+ was decreased, decrease in IL-6 and IL-8
Joshi and Parle (2006a)	Mice	Njatamansi	50, 100 and 200 mg/kg/oral/8 d	C: young, natural and induced (by diazepam and scopolamine) aged mice T: same mice+extract		Facilitation of cholinergic transmission in the brain and possible antioxidant property	200 mg/kg sig improved learning and memory (by the elevated plus maze and the passive avoidance paradigm) in young mice and also reversed both the natural and induced amnesia
Joshi and Parle (2006b)	Mice	*Ocimum sanctum* Linn.	50, 100 and 200 mg/kg/oral/8 d	C: young, aged, piracetam, amnestic induced by scopolamine, diazepam and induced aged T: same groups+extract		Effective improvement of aged learning and memory thus beneficial in cognitive disorders (dementia and Alzheimer's disease)	Sig decreased transfer latency and increased step down latency
Miao *et al*. (2004)	Mice (aged)	*Phragmites communis* polysaccharide				Antioxidative effect	Obvious increase of the activity of CAT, SOD, GSH-PX in blood; lowered level of LPO in plasma
Dong *et al*. (2004)	Mice	Ginkgo (total lactones)	D-galactose: 150mg/kg	Group: control D-galactose TLG	Total lactones	Attenuating lipid peroxidation and NO and apoptosis of cerebral cells	Increased GSH-Px activities, reduced NO content and MAO activity; decreased apoptosis in the brain, reduced lipofuscin content in liver and heart and increased liver hydroxyprolin

Table 1: Continued

Animal studies

Author	Target	Herb	Dose/duration	Groups	Components	Anti-aging effect/Noted mechanisms	Outcomes in herbal treatment group
Lei *et al.* (2003)	Mice	Astragalus root extract: astragalosides (AST)	40 mg/kg/ intragastric/10 w	(D-gal)-induced senescent mice and the middle-aged mice	Astragalosides	Improvement of brain function and immunomodulatory effects	Ameliorated age-related alterations in both motor response and memory (by rotating rod and step-down type passive avoidance tests); enhanced the deterioration of cellular immunity
Yang *et al.* (2000)	Rats	Qiangshengye liquid	3.3, 6.6 g/ kg/oral/21 d			Antagonizing lipid peroxidation	Sig increase of SOD activity in red blood cells and decrease of LPO in plasma and in liver and improvement of the fluidity of erythrocyte membrane
Jin *et al.* (1999)	Mice/Rats	*Astragalus membranaceus* (hairy root)	10 g/kg/oral/12, 50 d	1-D-gal induced aged mice 2-immuno-suppression induced mice by cyclo-phosphamide 3-rats (with anti-ischemia -reperfusion kidney model)		Antioxidizing and immunomodulating functions	Improved the memory, raised SOD activity in brain and liver; decreased MDA content in the liver of aged mice; promoted the activity of NK cells in immunosuppressed mice; reduced the MDA kidney content and creatinine level in blood
Furuya *et al.* (2002)	Mice (autoimmune diseases)	Hachimi-jio-gan (contains: Rehmannia root, Poria whole plant, Chinese yam root, Asiatic dogwood aerial part, Barrenwort aerial part, water plantain aerial part, Astragalus root and Cassia bark	1000 mg/kg gastric intubation/ 5 week			Decline in IL-12R expression, amelioration of MRL/lpr auto immune diseases, suppression of Th1 predominance via STAT4/STAT6 signaling	Down-regulated phosphorylated STAT4 and up-regulated phosphorylated STAT6 in CD4 T cells; in T cells, suppressed IL-12Rbeta1 and IL-12Rbeta2 mRNA expression; in antigen-presenting cells (CD45R-MHC class II+cells) decreased cell number of cells expressing co-stimulatory molecules; increased IL-12 and 18 mRNA expression
Utsuyama *et al.* (2001)		Mice	1-Hochu-ekki-to (TJ-41) 2-Juzen-taiho-to (TJ-48)	TJ-41: C: young and old mice+ saline T : same groups+ herbal drug TJ-48: C: young and old mice with injected B16 melanoma cells + control diet T: same groups+ herbal drug		Restoration of impaired immune functions of old mice in terms of number of T cells and NK cells and antibody response	(TJ-41)= sig increased number of T cells and NK cells and antibody response in old mice, (TJ-48)= sig increased T cells and slightly increased NK cells in aged mice but not effective in young mice; increased NK activity and sig decreased metastatic pulmonary colonies in both young and aged mice

Table 1: Continued

Animal studies							
Author	Target	Herb	Dose/duration	Groups	Components	Anti-aging effect/Noted mechanisms	Outcomes in herbal treatment group
		(TJ-48)	TJ-41:		herbal drug TJ-48: C: young and old mice with injected B16 melanoma cells+ control diet T: same groups+ herbal drug		
Bhattacharya *et al.* (2000)	Rats	*Withania somnifera* (WS) (roots)	20, 50 mg/kg/oral/5 d	C: lorazepam, imipramine± anxiogenic agent T: extract± anxiogenic agent	Bioactive glycowithanolides	Mood stabilizing in clinical conditions of anxiety and depression	Anxiolytic comparable to lorazepam, reduction of rat brain levels of tribulin; antidepressant comparable with imipramine
Drieu *et al.* (2000)	Rats	*Ginkgo biloba* extract (EGb 761)	50, 100 mg/kg/ intra gastric/10, 15d	C: water, fish oil T: extract		Increasing effects on circulating and cellular PUFAs	Compared to water sig increased circulating and erythrocyte membranes PUFAs, the fish oil increased only EPA; No effect on TG and Chol; improvement of the oxidative stress response of erythrocytes
Currier and Miller (2000)	Mice (aged)	*Echinacea purpurea* (root)	0.45 mg/14 d	C: control diet, thyroxin injected mice T: extract		Stimulating de novo production of NK cells, as well as augmenting their cytolytic function	Increased new NK cell production in bone marrow leading to an increase of NK cells in the spleen, paralleled by an increase in their anti-tumor, lytic functional capacity
Currier *et al.* (2000)	Mice (aged)	*Echinacea purpurea* (root)	0.45 mg/14 d	C: control diet, thyroxin injected mice T: extrac		Stimulating de novo production of NK cells, as well as augmenting their cytolytic function	Increased new NK cell production in bone marrow leading to an increase of NK cells in the spleen, paralleled by an increase in their anti-tumor, lytic functional capacity
Pardon *et al.* (2006)	Mice	*Ginkgo biloba* (Egb 761)	50 mg/kg/oral/7m	C: stressed and unstressed young and aged mice T: same groups+ extract		Anti-stress effects by regulation of MAO regulation regulation	Reductions in cerebral MAO activity in 18-month-old, but not in 17-month-old mice; increase in cerebral MAO activity; No difference in MAO-A and -B activities of stressed and treated 18-month-old mice from unstressed and untreated 17-m-old mice

Table 1: Continued

Animal studies

Author	Target	Herb	Dose/duration	Groups	Components	Anti-aging effect/Noted mechanisms	Outcomes in herbal treatment group
Komatsu *et al.* (1999)	Mice	Toki-Shakuyaku-San (Paeoniaeradix, atractylodis lanceae rhizoma, alismatis rhizoma, Hoelen, Cnidii Rhizoma, Angelicae Radix.)	0.125g/kg/oral/3m	C: male and male mice (SAMP8 and ddY)+water T: same mice+ extract		Stimulation of secreted estrogen on neurons	In the female elevation in SAMP8, T group, concentrations of gamma-aminobutyric acid, alanine and glycine were elevated in three brain regions
Rabin *et al.* (1998)	Gerbils	*Ginkgo biloba* (Egb 761)	50, 150 mg/kg/14d	C: vehicle± stroke mode T: stroke model +extract		Anti-ischemic effect by acceleration of AA reincorporation, reducing neurotoxic effects of AA brain exposure	Further augmented reincorporation of AA compared with palmitic acid into brain phospholipids following ischemia
Bhattacharya *et al.* (1997)	Rats	*Withania somnifera*	10, 20 mg/kg/ip/21d	C: deprenyl T: Active glycowithanolid	Glycowithanolides: sitoindosides VII-X and withaferin A	Anti oxidative effect	Sig dose-related increase in SOD, CAT and GSH-Px activity in brain, comparable to controls
Moriguchi *et al.* (1997)	Mice (senescence accelerated mouse (SAM))	Aged garlic	2% (wt/wt)/oral/3m	C: control diet T: extract		Prevents physiological brain ageing	Prevented the increase in score of senescence, improved learning and memory deficits; prevented the decrease in brain weight and the atrophic changes in frontal brain
Deng and Zhang (1991)	Rats	Ginsenoside (Rb1)	50, 25 mg/kg/ip/3d		Ginsenoside (Rb1)	Antioxidative effect	Sig inhibition of MDA formation in liver and increase of the activities of CAT and GSH- Px; no change in the activity of SOD in liver cytosol
Gorgi *et al.*(2010)	Mice	Spinach leaves extract powder	0.05, 0.10 and 0.15 g/1 m	C: water, sucrose T: extract		Higher doses decreaseed anxiety.	Sig anxiolytic effect (by elevated plus maze in doses of 0.10 and 0.15g by increase of the percentage of open time and decrease of the number of SAP
Naderi (2010)	Rats (male)	*Acorus calamus* L.	6.25%/oral /2 w and 25, 50, 100 mg/kg/ip	C: control diet, saline T: extract		Memory improvement by increase of spatial recognition and recalling the data	Sig difference in the step through latency (STL) time in oral and 100 mg/kg injected dose groups and sig increase of alternation behavior in oral T group (by Y maze and shuttle box tests)

Table 1: Continued

Animal studies

Author	Target	Herb	Dose/duration	Groups	Components	Anti-aging effect/Noted mechanisms	Outcomes in herbal treatment group
Shariati and Kaveh (2007)	Rats (male)	*Phoenix dactylifera* (Date- palm) Pit Powder	0.05, 0.1, 0.2 mg/kg/21d	C: no treatment, saline T: powder	Palmitic, stearic, linoleic and oleic acids.	Increased testosterone level and decreased dihydrotestosterone level via inhibiting of 5-α-reductase enzyme	Sig increase of the testosterone level and significant decrease of dihydrotestosterone level; no significant change in serum FSH and LH levels; increase in sperm density in seminiferous tubules
Ataie *et al.* (2010)	Rats (neurotoxic by homocysteine)	Curcumin	5, 15, 45 mg/ kg/ip/ 10 d	C: vehicle T: Curcumin	Polyphenols	Protecting the nervous system against oxidative stress	Sig decrease of MDA and SOA in brain and learning and memory improvement; cell death and apoptosis in hippocampi was inhibited
Joshi and Parle (2006c)	Mice	*Hibiscussabdariffa* Linn (calyces)	100 and 200 mg/kg/oral /8d	C: young and aged ±Piracetam ± scopolamin T: same mice + extract± scopolamin		Useful memory restorative agent in elderly due to anti Ach-E property	Sig attenuated amnestic deficits induced by scopolamine & natural aging; significant decrease of transfer latencies and increase of step down latencies in aged & induced amnesic mice as compared with piracetam; significant decrease of the whole brain Ach-E activity
Mahesh and Begum (2007)	Rats	*Terminalia chebula*	200mg/kg oral/4 w	C: young and aged+sterile water T: same rats+extract		Modulation of antioxidants activities and lipid peroxidation	Prevented the depletion of SOD, CAT, GSH-Px activities and GSH, vitamin C and E contents decrease in, MDA content in heart tissues in aged rats
Tanaka and Mizoguchi (2009)	Rats	Yokukansan (YKS)	3% wt/wt with food pellets /3 m	C: young and aged+control diet T: drug		Proliferation and migration of neural stem/progenitor cells	Decreased the age-related increase in aggrecan expression as well as normal expression in young rats; improvement of the decrease of the proliferation and migration of neural stem/progenitor cells in PFC and hippocampus; increased their numbers in young rats
Liu *et al.* (2007)	Mice (subacute senile induced)	Semen Cassia (protein and glucosides)	Low dose: 1,0.25 mg/kg/day High dose: 20, 5 mg/kg/day	group: control Model Group 2,3 Positive group Treatment group Group 6,7	Protein and anthraquinone glucosides	Antioxidative effect	Inhibited the increase of MDA; enhanced the level of SOD in cerebrum and lessened the lipofuscin (LF) in liver
Rho *et al.* (2005)	Rats (male)	Yukmijihwang-tang derivatives (YMJd): Rehmannia radix, Lycii fructus, Discoreae radix, Corni fructus, Hoelen, Mountain cortex radicis, Alismatis radix	400 mg 100 g^{-1} of body wt 10 d^{-1}	C: Ginkgo biloba, Soya lecithin, water T: extract		Differentially expressing genes may have memory enhancing effects	Sig delay of memory retention time compared to controls; Sig expression radix, Corni fructus, Hoelen, Mountain of transthyretin and PEP-19 (a neuron-specific cortex radicis, Alismatis radix protein inhibiting apoptosis) whereas sig expression of neuronal genes involved in neurodegeneration in the control water group

Table 1: Continued

Animal studies							
Author	Target	Herb	Dose/duration	Groups	Components	Anti-aging effect/Noted mechanisms	Outcomes in herbal treatment group
Chan *et al.* (2007)	Rats (with ocular hypertension model)	*Lycium barbarum* Lynn (fruits) (wolfberr y or gojiberry)	0.01, 0.1, 1, 10, 100, 1000 mg/kg/oral/ 21, 35 d	C: unoperated left eyes T: photocoagulated right eyes	Polysaccharides	Therapeutic function against neurodegeneration in the retin	Sig reduced the loss of retinal ganglion cells although no ateration in elevated IOP, rats fed with the 1 mg kg^{-1} extract could nearly totally escape from pressure-induced loss of retinal ganglion cells
Li *et al.* (2007)	Rats	Lycium barbarum Lynn (wolfberry)	A single injection dose STZ: 50 mg kg^{-1}	C: nondiabetic, streptozotocin induced diabetic T: same rats+extract	Polysaccharides	Antioxidative effect	Restored abnormal oxidative indices in blood, liver and kidney near normal levels
Liu *et al.* (2003)	Mice	('FTDA'): cuscutae semen, Schisandrae Fructus, Dioscoreae Rhizoma, Lonicerae Flos, Nelumbinis Semen, Angelica Radix and Poria		C: D-galactose aged induced T: D-galactose aged induced+ extract		Antioxidative effect	High and medium-dose exhibited higher levels of SOD, GSH-Px and TAOC in blood, lower levels of MDA activity; In the liver sig increases in SOD activity and a decrease in MDA activity; in medium-dose increased SOD activity in the brain
Liu *et al.* (1996)	Rats (aged)	Ginseng			Ginsenoside Rg1	Immunmodulatory and Antioxidative effect	Selectively enhanced the deteriorated immune function, ameliorate age-related alterations in both behavior and motor response; promote hippocampal neuronal function; provide partial protection against the excitotoxic effect of glutamate
Moon *et al.* (2009)	Mice	Gongjin-dan (GJD)	0.1, 1, 10, 100, 250 μg mL^{-1} GJD for 1 day			May improve memory and learning tasks via nerve growth factor (NGF) regulation and potential multiple function neuroprotection via NGF regulation	The number of entries, the time spent and the distance moved in the center area of the test region (by novel object test)
Vidal *et al.* (2010)	Mice (young and aged)	*Lycium barbarum*: a milk-based wolfberry formulation (lacto-wolfberry)		0.5% wt./volume/ 44 d	C: controlled diet T: Lacto-Wolfberry	Modulation of the poor responsiveness to antigenic challenge observed with aging	Sig increase of in vivo systemic immune markers that are known to decline with aging, enhance in both antigen specific humoral response and cell-mediated immune responses; no sig effect on ex vivo spleen cells proliferative response to mitogens and on splenocyte T cell subsets

Table 1: Continued

Animal studies							
Author	Target	Herb	Dose/duration	Groups	Components	Anti-aging effect/Noted mechanisms	Outcomes in herbal treatment group
Zhang *et al.* (2004)	Mice (aged female BALB/c)	VI-28, a TCM formula: radix ginseng, cornu Cervi pantotrichum & radix Salvia miltiorrhizae	0.5, 2% /oral 18 w^{-1}	C: normal diet T: VI-28		Immunoboosting effect by correction of the hyporesponsiveness of T lymphocytes in aged mice Enhancement of stem cell Production	T group were much healthier, stronger and more alert and their thymuses were sig bigger and heavier; the microstructure of their thymuses was comparable to that of mice of a much younger age
Kiss *et al.* (2010)	Mice (with induced liver damage), rats (with induced myocardial infarction)	A dietary supplement, olimpiq stemxcell (crystal Institute Ltd., Eger, hungary)		C: normal diet T: normal diet + extracts		Enhancement of stem cell production	Sig improvement of organ regeneration
Cui *et al.* (2010)	Mice (immunocosspressed)	*Polgonum cillinerve* (nakai) ohwi crude polysaccharides (pccp)	PCCP dasage:100, 200 300, 400, 500, 600 polygonon cillinerve: 0.2 g kg Utilized in folk Madicine for Human	C: saline T: pccp		Pronouncedfree radical-scavenging and antoxidant activities and prevention of oxidative damage in immunological system	Sig raise of the TAOC, CAT, SOD and GSH-Px levels; It also raised the liver, spleen and thymus indices; and decreased the MDA level
Hiramatsu *et al.* (1999)	Rats	Toki-shakuyaku-san" (TJ-23)		C: adult rat T: aged rat+ TJ-23		Cholinergic function in the striatum of aged rats	Decrease in Cholineacetyl transferase activity in the cortex and striatum; decreased Ach-E activity in the hippocampus, mid-brain and pons-medulla oblongata and increased in the striatum; increased muscarinic receptor binding in the cortex and striatum
Majlessi *et al.* (2011)	Rats (with induced Alzheimer's disease)	*Zataria multiflora* boiss (ZM) essential Oil	50, 100, 200 iL/kg	C: normal diet T: ZM oil			Increased in escape latency, traveled distance, heading angle; decreased in target quadrant entries were reversed by ZM essential oil
Kim *et al.* (2000)	Mice (senescence accelerated (SAM-P/8) with induced liver oxidant damage	Yukmi (decoction of six plants including rehmannia),	Oral/ 6 d			Antioxidative effect	Effectively blocked the oxidant induced effects on liver (MDA) levels; inhibited induced damage to the hepatic mitochondria and their membranes

Table 1: Continued

Animal studies							
Author	Target	Herb	Dose/duration	Groups	Components	Anti-aging effect/Noted mechanisms	Outcomes in herbal treatment group
Satoh *et al.* (2004)	Mice (SAM)	kangen-karyu and carthami flos	100 mg/kg/10 w	C: Carthami Flos T: Kangen-karyu		Antioxidative effect and ameliorating tissue damage	Inhibited generation of nitric oxide, superoxide and the hydroxyl radical (*OH), while Carthami Flos extract showed only *OH-scavenging activity; both groups enhanced the activities of SOD in hepatic tissue and GSH-Px in renal tissue; reduced the hepatic lipid peroxidation level and hepatic and renal dysfunction with aging was also ameliorated but the effects of the T group was more evident
Shin *et al.* (2009)	Mice (with induced memory impairment)	kyung-ok-ko (KOK) contains: ginseng radix, rehmanniae radix, hoelen, honey, lycium fructus and aquilaria lignum	1 or 2 g/kg/oral/ single treatment 30 min before induction of memory impairment			Useful in treatment of cognitive impairment, mediated, in part, by enhancing the cholinergic neurotransmitter system	Sig prevention of induced cognitive impairments in the passive avoidance task and the Y-maze task; improvement of escape latency in the Morris water maze; inhibition of Ach-E activity in a dose-dependent manner
Chiu *et al.* (2009)	Rats (with ocular hypertension)	Wolfberry (lycium barbarum) extract	1, 10, 100, 1, 000 mg/kg/oral/ 7 d before the first laser treatment and continued until euthanization		Lycium barbarum polysaccarides	Ueuroprotective effects of LBP partly due to modulating the activation of microglia	1 to 100 mg kg^{-1} dosage exerted the best neuroprotection and elicited moderately activated microglia in the inner retina
Gao *et al.* (1996)	Mice	Alcohol extraction from *Lycium barbarum*	500 mg/kg/day and 100 mg/kg/day/ 50day			Effectively increase the decreased ability of the passive avoidance reaction in the model animals induced by D-Galactose	Cleares away the free-radicals and improves the brain function
Jiang and Zhang (2010)	Mice	Fructus Lycii PFL	PFL: 200, 400, 800 mg/ kg/d VitE: 100 mg/kg/d D-gal: 10 mg/kg/d/ 5 w	C: D-galactose aged induced T: D-gal induced model group		Improvement in learning and memory ability by increasing SOD activity	PFL have anti-aging effect on D-gal induced aging mice, decrease MDA content in serum, heart, liver and brain of D-gal aging mice; increase of telomerase activity in serum and heart
Zhang and Zhang (2005)	Amnestic mice	Ce	D-galactose: 120 mg/kg NaNO_ (2): 90 mg/kg CE: 2.5, 5, 10mg/oral/kg			Effectiveness was induced by D-galactose and NaNO_	CE could exert protect effects on the aging mice of consecutive injection of D-galactose and NaNO

Table 1: Continued

Animal studies

Author	Target	Herb	Dose/duration	Groups	Components	Anti-aging effect/Noted mechanisms	Outcomes in herbal treatment group
He and Qiu (2005)	Mice	*Dipsacus asperoides* (DA)	DA's n-bectanol extract: 7.5 g kg^{-1}, 10 g kg^{-1}, water extract: 20 g kg^{-1}			Anti-oxidation	DA's n-butanol extract and water extract can improve the learning-memory abilities of D-galactose induced mice
Zhao *et al.* (2004)	Mice	*Agaricus blazei* murill	40, 80, 160 mg kg^{-1}			Inflammation action were inhibited obviously	Agaricus Blazei Murill polysaccharide has anti-inflammatory effects
Zhu and Tang (1987)	Mice	*Acorus rhizome*	0.1 g/10 g			Antagonizing sodium nitrite induced, cyanide-induced oxygen deficit and oxygen deficit of ligation of common carotid artery in mice	Improved impairment of acquisition of memory produced by scopolamine and disruption of consolidation of memory caused by sodium nitrite
Ganzhong (1998)	Mice	*Codonopsis pilosula* (franch.) nannf	30 g/kg/d /5 d				Act on both side of the cerebrum
Chu and Chen (1989)	Rat	Ginsenosides	100 mg/kg /iv/ 30 min			Inhibiting free radicals and subsequent lipid peroxidation	Ginseno-sides have protective effect on cerebral ischemia/reperfusion injury
Mao *et al.* (1996)	Mice	Atractylis macrocephal Koidz	1~20 mg L^{-1}			This regulation was related to the β adrenergic receptor agonist isoproterenol (ISO)	Sig enhancement of lymphocyte proliferation alone or with ConA/PHA; and promoted the production of interleukin 2 (IL 2) simultaneously
Xu and Sun (1989)	Mice	Dang Sheng fu fang (DSFF)	10mg/kg/ ip alcohol (40% 0.1 mL/10 g/ po) reserpine 0.15 mg kg^{-1} /sc /8 d			Antagonize change of EEG caused by scopolamine, increase the level of serotonin in mice brain	Antiamnestic effect of DSFF might involve serotonin metabolism and muscarinic receptor of Ach

Authors	Target	Herb	Study/dose, duration	Groups	Active component	Suggested tested mechanism	Outcomes
Human studies							
Gim *et al.* (2009)	Healthy volunteers	Tianwang Buxin Pills (TBPs)	TPS 8 g, 3 times/day/ 4w	C: placebo (n: 20) T: TBPs (n: 19)		Antioxidative and anti-stress effects	No sig difference in the blood reactive oxygen metabolites and the stress response inventory and the Korean version of the WHO quality of life scale abbreviated version values between the two groups

Table 1: Continued

Animal studies

Author	Target	Herb	Dose/duration	Groups	Components	Anti-aging effect/Noted mechanisms	Outcomes in herbal treatment group
Tian *et al.* (1997)	Human	TJ: Tong Jiang oral liquid with Da Huang (radix et Rhizoma rhei)	20 mL administrated orally 3 times daily/ 6 weeks	C: QY: Qi Yin oral liquid without Da Huang T: TJ		Anti senility action and mentality improvement	Sig better effects on shortening the duration and the interval between defecations and on improving senile persons' memory ability
Yonei *et al.* (2008)	Human (healthy n: 35 aged 40 to 60 sec)	L-carnitine and Garcinia cambogia	L-carnitine: 600 mg/d, Garcinia cambogia extract 500 mg/d as hydroxycitric acid/8 w	C: placebo T: supplement		Antioxidative effect without dietary efficacy	Sig improvement of blood LPO But sig rise in total cholesterol, FBS and HbA1c, physical symptoms improved but not sig
Sugiyama (2006)	Human (n: 5)	Gambir	10 g in the evening, at midnight and before breakfast				Four of the subjects reported feeling well in the morning
Harunobu *et al.* (2008)	Human (healthy)	Lycium barbarum: as (Goji) juice (GoChi™) (wolfberry or gojiberry)	Each group consumed 60 mL of the sample twice daily total 120 mL/d/30 day	C: placebo (n: 18) T: GoChi™ (n: 16)			Increase subjective feelings of general well-being and improve neurologic/psychologic performance and gastrointestinal functions
Lee *et al.* (2008)	Patients with Alzheimer disease (AD)	Panax ginseng powder	4.5 g/d/ 12 w	C: controlled die (n: 39) T: ginseng (n: 58)		Effective cognitive performance of AD patients	Improvement of cognitive subscale (by the mini-mental state examination (MMSE) and Alzheimer disease assessment scale (ADAS)) after discontinuing ginseng, scores declined to the levels of controls

Abréviations: d: Day, w: week, m: month, g: Gram, sc: Subcutaneus, Sig: Significant, PFC: prefrontal cortex, MMPs: Matrix Metalloproteinases, Inj: Injection, MDA: malondialdehyde, NO: nitrogen oxide. NH(3): Amonia, SOD: superoxide dismutase, CAT: catalase, GSH: glutathione, TAOC: total antioxidant capacity, GSH-Px: glutathione peroxidase, LPO: Lipid Peroxide, MAO: Monoamine oxidase, SAMP8: senescence accelerated mice, AA: arachidonic acid, SI: the saturation index saturated/polyunsaturated species), SAP: (Stretched Attend Posture), SAM: a novel strain of Senescence Accelerated Mouse, ip: intraperitoneal, SOA: Super Oxide Anion, wt: weight, FBS: fasting blood sugar, HbA1c: Glycated Hemoglobin, Chol: Cholesterol, Tg: Triglyceride, PUFA: poly unsaturated fatty acid, EPA: eicosa pantaenoic acid, NK cell: natural killer cell, Ach-E: acetyl cholinesterase, Ach: acetyl choline

Lycium barbarum (wolfberry or gojiberry) has been considered in anti-aging trials more than other herbs. Some studies pointed to mood stabilizing and anti-anxiety effects and effective improvement of cognitive disorders (dementia and Alzheimer's disease) (Joshi and Parle, 2006a; Bhattacharya *et al*., 2000; Pardon *et al*., 2006; Naderi *et al*., 2010; Shin *et al*., 2009). Eight studies noticed enhancement of stem cell production, restoration of impaired immune functions of old mice in terms of number of T cells and Natural Killer (NK) cells and antibody response. One animal study showed that Panax ginseng (red ginseng) significantly inhibits wrinkle formation (Kang *et al*., 2009). This herb inhibits degradation of collagen. Another study on sexual behavior showed that Epimedium koreanum improved erectile function (Makarova *et al*., 2007).

Human studies consisted of 6 articles (Gim *et al*., 2009; Tian *et al*., 1997; Yonei *et al*., 2008; Sugiyama, 2006; Amagase and Nance, 2008; Lee *et al*., 2008). Two studies revealed improvement of blood LPO, fasting blood sugar and glycated hemoglobin (HbA1c) (Tian *et al*., 1997; Yonei *et al*., 2008) while three studies (Sugiyama, 2006; Amagase and Nance, 2008; Lee *et al*., 2008) referred to subjective feeling of well-being and improvement in neurologic/psychologic performance of cognitive subscale confirmed by Mini-mental State Examination (MMSE) and Alzheimer disease assessment scale (ADAS).

DISCUSSION

Most of included studies concluded that some of herbs can significantly delay process of aging mostly in the organs like brain, vascular systems, skin and sex. Number of studies performed in humans is too few in comparison to that of animals. If the included papers are detailed, they can be divided into four categories in terms of proposed mechanism of action of the tested herb such as anti-oxidant effect, anti-inflammatory effect, effect on (memory, cognitive and mood) and stimulatory effect on sex hormones (Fig. 2). The most effective herb that had anti-oxidant effect

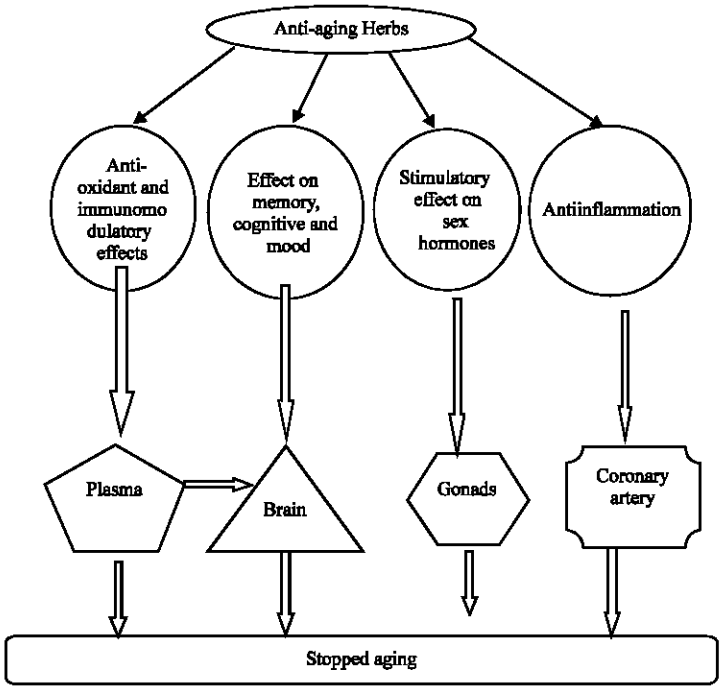

Fig. 2: Suggested machanisms of action of herbs in reducing aging process

was Licium barbarum (wolfberry or gojiberry) that significantly raised body SOD, CAT and reduced LPO (Li, 2007). Diseases which increase in frequency with age include arthritis, osteoporosis, heart disease, cancer, Alzheimer's, diabetes, etc. Animal cells have three important enzymes to deal with the free radicals including SOD, GPx and CAT.

Other herbs that showed anti-aging effect with the same mechanism includes Phragmites communis polysaccharide (Qin *et al*., 2008; Miao *et al*., 2004; Dong *et al*., 2004; Yang *et al*., 2000) and Garcinia cambogia Tianwang Buxin Pills (TBPs) that significantly improved blood LPO but raised total cholesterol, Fasting Blood glucose (FBS) and Hemoglobin A1c (HbA1c). In addition, physical symptoms improved but not significantly.

Yokukansan (YKS) significantly Improved anxiety-related responses and decreased serotonin and dopamine in the Prefrontal Cortex (PFC) and reduced plasma ammonia (NH3) (Mizoguchi *et al*., 2010).

Kami-Untan-To (KUT) significantly increased brain Acetylcholine (ACh) and the density of Choline Acetyltransferase (ChAT) immunoreactive cells (Wang *et al*., 2000).

Hibiscus sabdariffa Linn (calyces) decreased whole brain acetyl cholinesterase (AChE) activity (Joshi and Parle, 2006c). In two human studies, use of Panax ginseng powder and Tong Jiang oral liquid with Da Huang (radix et Rhizoma rhei) improved cognitive subscale (MMSE) and ADAS. After discontinuing ginseng, scores declined to the levels of controls (Tian *et al*., 1997; Lee *et al*., 2008).

Besides in some studies, herbs such as Hachimi-jio-gan a traditional Japanese herbal medicine (Furuya *et al*., 2002), Hochu-ekki-to (TJ-41) (Utsuyama *et al*., 2001), Echinacea purpurea (Currier and Miller, 2000), gerbils (Rabin *et al*., 1998) and Atractylis macrocephal Koidz (Mao *et al*., 1996) totally caused immunoboosting effect by increasing the number of T cells and NK cells and antibody response.

Toki-Shakuyaku-San (PaeoniaeRadix) (Komatsu *et al*., 1999) in the females elevated senescence-accelerated mice (SAMP8), concentrations of gamma-aminobutyric acid (GABA), alanine and glycine.

Taking collectively, most of anti-aging herbals have antioxidant components. In the recent years, role of oxidative stress and benefit of antioxidants in most of aging-related illnesses have been reviewed. For instance diabetes (Rahimi *et al*., 2005; Hasani-Ranjbar *et al*., 2009; Mohseni-Salehi-Monfared *et al*., 2009; Larijani *et al*., 2011), osteoporosis (Abdollahi *et al*., 2005; Yousefzadeh *et al*., 2006), illnesses from chronic exposure to environmental toxins (Abdollahi *et al*., 2004; Malekirad *et al*., 2005), inflammatory bowel disease (Rahimi *et al*., 2009; Rezaie *et al*., 2007), hyperlipidemia (Hasani-Ranjbar *et al*., 2010; Momtaz and Abdollahi, 2010) can be exampled.

Our study had some strengths and limitations. As an advantage, we conducted this review for the first time by examining all studies which tested herbs as anti-aging. Unfortunately, adverse effects have not been described in most of these studies. We acknowledge that there are really few number of clinical trials and those existing have low quality or are not homogeny and thus reaching a definitive conclusion is hard. Of course results of this study clarified these limitations and may help researchers to better design future trials.

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REFERENCES

Abdollahi, M., A. Ranjbar, S. Shadnia, S. Nikfar and A. Rezaie, 2004. Pesticides and oxidative stress: A review. Med. Sci. Monit., 10: RA141-RA147.

Abdollahi, M., B. Larijani, R. Rahimi and P. Salari, 2005. Role of oxidative stress in osteoporosis. Therapy, 2: 787-796.

Amagase, H. and D.M. Nance, 2008. A randomized, double-blind, placebo-controlled, clinical study of the general effects of a standardized *Lycium barbarum* (Goji) Juice, GoChi™. J. Altern. Complementary Med., 14: 403-412.

Ataie, A., M. Sabetkasaei, A. Haghparast, A.H. Moghaddam, R. Ataie and S.N. Moghaddam, 2010. An investigation of the neuroprotective effects of curcumin in a model of homocysteine-induced oxidative stress in the rat's brain. DARU J. Pharm. Sci., 18: 128-136.

Bhattacharya, S.K., A. Bhattacharya, K. Sairam and S. Ghosal, 2000. Anxiolytic-antidepressant activity of Withania somnifera glycowithanolides: An experimental study. Phytomedicine, 7: 463-469.

Bhattacharya, S.K., K.S. Satyan and S. Ghosal, 1997. Antioxidant activity of glycowithanolides from *Withania somnifera*. Int. J. Exp. Biol., 35: 236-239.

Chan, H.C., R.C.C. Chang, A.K.C. Ip, K. Chiu, W.H. Yuen, S.Y. Zee and K.F. So, 2007. Neuroprotective effects of *Lycium barbarum* Lynn on protecting retinal ganglion cells in an ocular hypertension model of glaucoma. Exp. Neurol., 203: 269-273.

Chiu, K., H.C. Chan, S.C. Yeung, W.H. Yuen, S.Y. Zee, R.C. Chang and K.F. So, 2009. Erratum: Modulation of microglia by Wolfberry on the survival of retinal ganglion cells in a rat ocular hypertension model. J. Ocular Biol. Dis. Inform., 2: 127-136.

Chu, G.X. and X. Chen, 1989. Protective effect of ginsenosides on acute cerebral ischemia/reperfusion injury of rats. Chin. J. Pharrnacol. Toxicol., 3: 18-23.

Cui, J.J., J.F. Yuan and Z.Q. Zhang, 2010. Anti-oxidation activity of the crude polysaccharides isolated from *Polygonum cillinerve* (Nakai) Ohwi in immunosuppressed mice. J. Ethnopharmacol., 132: 512-517.

Currier, N.L. and S.C. Miller, 2000. Natural killer cells from aging mice treated with extracts from Echinacea purpurea are quantitatively and functionally rejuvenated. Exp. Gerontol., 35: 627-639.

De Grey, A.D.N.J., 2007. Life span extension research and public debate: Societal considerations. Stud. Ethics Law Technol., 1: 1-13.

Deng, H. and F. Tang, 2006. Protective effect of renshen yangrong decoction on membrane fluidity of mitochondrion in brain and liver of subacute senile mice. Zhongguo Zhong Xi Yi Jie He Za Zhi, 26: 30-33.

Deng, H.L. and J.T. Zhang, 1991. Anti-lipid peroxilative effect of ginsenoside Rb1 and Rg1. Chin. Med. J., 104: 395-398.

Dong, L.Y., L. Fan, G.F. Li, Y. Guo, J. Pan and Z.W. Chen, 2004. Anti-aging action of the total lactones of ginkgo on aging mice. Yao Xue Xue Bao, 39: 176-179.

Drieu, K., R. Vranckx, C. Benassayad, M. Haourigi and J. Hassid *et al*., 2000. Effect of the extract of Ginkgo biloba (EGb 761) on the circulating and cellular profiles of polyunsaturated fatty acids: Correlation with the anti-oxidant properties of the extract. Prostaglandins Leukotrienes Essent. Fatty Acids, 63: 293-300.

Furuya, Y., T. Kawakita and K. Nomoto, 2002. Participation of contrasting changes in IL-10 and IL-12 production in the reduction of Th1-predominance by Hachimi-jio-gan in autoimmune MRL/MP-lpr/lpr mice. Immunopharmacol. Immunotoxicol., 24: 17-29.

Ganzhong, W.H.L., 1993. The effect of Dangshen (*Codonopsis pilosula* (Franch.) Nannf.) on learning and memory. Pharmacol. Clin. Chinese Mater. Med.

Gao, N., Z. Tian, L. Li and L. Xu, 1996. Beneficial effect of alcohol extraction from lyciumbarbarum on some aging disorders induced by D-galactose in mice. Pharmacol. Chin. Chinese Mater. Med.

Gim, G.T., H.M. Kim, J. Kim, J. Kim, W.W. Whang and S.H. Cho, 2009. Antioxidant effect of tianwang buxin pills a traditional Chinese medicine formula: Double-blind, randomized controlled trial. Am. J. Chin. Med., 37: 227-239.

Gorgi, H.M., H.A. Safakhah and S. Haghighi, 2010. Anxiolytic effects of the aqueous extracts of spinach leaves in mice. Sci. J. Kurdistan Univ. Med. Sci., 15: 43-50.

Hasani-Ranjbar, S., N. Nayebi, B. Larijani and M. Abdollahi, 2009. A systematic review of the efficacy and safety of herbal medicines used in the treatment of obesity. World J. Gastroenterol., 15: 3073-3085.

Hasani-Ranjbar, S., N. Nayebi, B. Larijani and M. Abdollahi, 2010. A systematic review of the efficacy and safety of *Teucrium* species; from anti-oxidant to anti-diabetic effects. Int. J. Pharmacol., 6: 315-325.

He, X. and J. Qiu, 2005. Effects of extract from dipsacus asperoides on anti-oxidation and learning-memory abilities in D-galactose-induced mice. China Pharm., 3: 185-187.

Hiramatsu, M., M. Komatsu, T. Yuzurihara, K. Saitoh, A. Ishige and Y. Komatsu, 1999. Enhanced cholinergic function in aged rats treated with TJ-23. J. Anti-Aging Med., 2: 51-57.

Ichihashi, M., A. Matsuda, T. Honda, C. Kokubun and Y. Hashimoto *et al*., 2008. Anti-aging effects of nanpao, a kampo medicine, on reproductive functions in female rats. Am. J. Chin. Med., 36: 873-887.

Jiang, W.Z and H.Q.J. Zhang, 2010. Anti-aging effect of polypeptides from Fructus Lycii on D-gal induced aging model mice and the possible mechanism. Int. Pharm. Res., 37: 47-50.

Jin, R., X. Zhang, C. Chen, Z. Sun, Y. Shen, D. Liu and Z. Hu, 1999. Studies on pharmacological junctions of hairy root of Astragalus membranaceus. Zhongguo Zhong Yao Za Zhi, 24: 619-621.

Joshi, H. and M. Parle, 2006a. Evaluation of nootropic potential of Ocimum sanctum Linn. in mice. Indian J. Exp. Biol., 44: 133-136.

Joshi, H. and M. Parle, 2006b. Nardostachys jatamansi improves learning and memory in mice. J. Med. Food, 9: 113-118.

Joshi, H. and M. Parle, 2006c. Nootropic activity of calyces of *Hibiscus sabdariffa* linn. Iranaian J. Pharmacol. Ther., 5: 15-20.

Kang, T.H., H.M. Park, Y.B. Kim, H. Kim and N. Kim *et al*., 2009. Effects of red ginseng extract on UVB irradiation-induced skin aging in hairless mice. J. Ethnopharmacol., 123: 446-451.

Kim, J.S., C.S. Na, S.C. Pak and Y.G. Kim, 2000. Effects of yukmi, an herbal formula, on the liver of senescence accelerated mice (SAM) exposed to oxidative stress. Am. J. Chin. Med., 28: 343-350.

Kiss, I., A. Tibold, R. Halmosi, E. Bartha and K. Koltai *et al*., 2010. Enhancement of organ regeneration in animal models by a stem cell-stimulating plant mixture. J. Med. Food., 13: 599-604.

Komatsu, M., Y. Ueda and M. Hiramatsu, 1999. Different changes in concentrations of monoamines and their metabolites and amino acids in various brain regions by the herbal medicine/Toki-Shakuyaku-San between female and male senescence-accelerated mice (SAMP8). Neurochem. Res., 24: 825-831.

Larijani, B., M. Salimi, N. Pourkhalili, A. Mohammadirad, M. Baeeri, A. Nili-Ahmadabadi and M. Abdollahi, 2011. Positive response of isolated rat pancreatic islets to IMOD; hopes for better transplant outcome and graft function. Asian J. Anim. Vet. Adv., 6: 1019-1025.

Lee, S.T., K. Chu, J.Y. Sim, J.H. Heo and M. Kim, 2008. Panax ginseng enhances cognitive performance in Alzheimer disease. Alzheimer Dis. Assoc. Disord., 22: 222-226.

Lei, H., B. Wang, W.P. Li, Y. Yang, A.W. Zhou and M.Z. Chen, 2003. Anti-aging effect of astragalosides and its mechanism of action. Acta Pharmacol. Sin., 24: 230-234.

Li, X.M., 2007. Protective effect of Lycium barbarum polysaccharides on streptozotocin-induced oxidative stress in rats. Int. J. Biol. Macromol., 40: 461-465.

Li, X.M., Y.L. Ma and X.J. Liu, 2007. Effect of the Lycium barbarum polysaccharides on age-related oxidative stress in aged mice. J. Ethnopharmacol., 111: 504-511.

Liu, J.H., S.C. Ho, T.H. Lai, T.H. Liu, P.Y. Chi and R.Y. Wu, 2003. Protective effects of Chinese herbs on D-galactose-induced oxidative damage. Methods Find Exp. Clin. Pharmacol., 25: 447-452.

Liu, J.Z., X. Lin, X.E. Li and B.J. Guo, 2007. Effect of protein and anthraquinone glucosides from Semen Cassia on learning and memory capacity and related substances of senile mice induced by D-galactose. Zhongguo. Zhong. Yao. Za. Zhi., 32: 516-519.

Liu, M., 1996. Studies on the anti-aging and nootropic effects of ginsenoside Rg1 and its mechanisms of actions. Sheng. Li. Ke. Xue. Jin. Zhan., 27: 139-142.

Mahesh, R. and V.M.H. Begum, 2007. Begum, 2007. Antioxidant effect of terminalia chebula aqueous extract on age-related oxidative stress in heart. Iran J. Pharmacol. Ther., 6: 197-201.

Majlessi, N., S. Choopani, M. Kamalinejad and Z. Azizi, 2011. Amelioration of amyloid â-induced cognitive deficits by *Zataria multiflora* Boiss. essential oil in a rat model of Alzheimer's disease. CNS Neurosci. Ther., 10.1111/j.1755-5949.2011.00237.x

Makarova, M.N., O.N. Pozharitskaya, A.N. Shikov, S.V. Tesakova, V.G. Makarov and V.P. Tikhonov, 2007. Effect of lipid-based suspension of Epimedium koreanum Nakai extract on sexual behavior in rats. J. Ethnopharmacol., 114: 412-416.

Malekirad, A.A., A. Ranjbar, K. Rahzani, A.A. Pilehvarian, A. Rezaie, M.J. Zamani and M. Abdollahi, 2005. Oxidative stress in radiology staff. Environ. Toxicol. Pharmacol., 20: 215-218.

Mao, J., Z. Lu, Q. Zeng and H. Ruan, 1996. Effects of the polysaccharide of atractylis macrocephala Koidz on the function of mouse T lymphocyte. Immunol. J., 4: 233-235.

Marner, L., J.R. Nyengaard, Y. Tang and B. Pakkenberg, 2003. Marked loss of myelinated nerve fibers in the human brain with age. J. Comp. Neurol., 462: 144-152.

Miao, M.S., L.Y. Gu, X.Y. Fang and Y.Y. Miao, 2004. Effect of Phragmites communis polysaccharide on the aged-model mice. Zhongguo Zhong. Yao. Za. Zhi., 29: 673-675.

Mizoguchi, K., Y. Tanaka and T. Tabira, 2010. Anxiolytic effect of a herbal medicine, yokukansan, in aged rats: involvement of serotonergic and dopaminergic transmissions in the prefrontal cortex. J. Ethnopharmacol., 127: 70-76.

Mohseni-Salehi-Monfared, S.S., B. Larijani and M. Abdollahi, 2009. Islet transplantation and antioxidant management: A comprehensive review. World J. Gastroenterol., 15: 1153-1161.

Momtaz, S. and M. Abdollahi, 2010. An update on pharmacology of Satureja species; from antioxidant, antimicrobial, antidiabetes and anti-hyperlipidemic to reproductive stimulation. Int. J. Pharmacol., 6: 454-461.

Momtaz, S. and M. Abdollahi, 2012. A comprehensive review of biochemical and molecular evidences from animal and human studies on the role of oxidative stress in aging: An Epiphenomenon or the Cause. Asian. J. Anim. Veterinary Adv. 7: 1-19.

Moon, E., Y. Her, J.B. Lee, J.H. Park and E.H. Lee *et al.*, 2009. The multi-herbal medicine Gongjin-dan enhances memory and learning tasks via NGF regulation. Neurosci. Lett., 466: 114-119.

Moriguchi, T., H. Saito and N. Nishiyama, 1997. Anti-aging effect of aged garlic extract in the inbred brain atrophy mouse model. Clin. Exp. Pharmacol. Physiol., 24: 235-242.

Naderi, G.A., K. Mohsen, K. Mehrdad and S. Maryam, 2010. The effect of oral and intraperitoneal administration of *Acorus calamus* L. Extract on Learning and Memory in Male Rats. J. Med. Plants, 9: 46-56.

Pardon, M.C., C. Joubert, F. Perez-Diaz, Y. Christen, J.M. Launay and C. Cohen-Salmon, 2006. *In vivo* regulation of cerebral monoamine oxidase activity in senescent controls and chronically stressed mice by long-term treatment with Ginkgo biloba extract (EGb 761). Mech. Ageing. Dev., 113: 157-168.

Qin, X.J., W. He, C.X. Hai, X. Liang and R. Liu, 2008. Protection of multiple antioxidants Chinese herbal medicine on the oxidative stress induced by adriamycin chemotherapy. J. Applied Toxicol., 28: 271-282.

Rabin, O., K. Drieu, E. Grange, M.C. Chang, S.I. Rapoport and A.D. Purdon, 1998. Effects of EGb 761 on fatty acid reincorporation during reperfusion following ischemia in the brain of the awake gerbil. Mol. Chem. Neuropathol., 34: 79-101.

Rahimi, R., S. Nikfar, B. Larijani and M. Abdollahi, 2005. A review on the role of antioxidants in the management of diabetes and its complications. Biomed. Pharmacother., 59: 365-373.

Rahimi, R., S. Mozaffari and M. Abdollahi, 2009. On the use of herbal medicines in management of inflammatory bowel diseases: A systematic review of animal and human studies. Dig. Dis. Sci., 54: 471-480.

Rezaie, A., R.D. Parker and M. Abdollahi, 2007. Oxidative stress and pathogenesis of inflammatory bowel disease: An epiphenomenon or the cause. Dig. Dis. Sci., 52: 2015-2021.

Rho, S., M. Kang, B. Choi, D. Sim, J. Lee and E. Lee, 2005. Effects of Yukmijihwang-tang derivatives (YMJd), a memory enhancing herbal extract, on the gene-expression profile in the rat hippocampus. Biol. Pharm. Bull., 28: 87-93.

Satoh, A., T. Yokozawa, E.J. Cho, T. Okamoto and Y. Sei, 2004. Antioxidative effects related to the potential anti-aging properties of the Chinese prescription Kangen-karyu and Carthami Flos in senescence-accelerated mice. Arch. Gerontol. Geriatr., 39: 69-82.

Shariati, M.S.E. and M. Kaveh, 2007. The effect of phoenix dactylifera (date-palm) pit powder on testosterone level and germ cells in adult male rats. ZUMS J., 15: 21-28.

Shin, B.Y., Y.H. Lee, D.H. Kim, C.S. Park, Y.W. Lee and H. Cho, 2009. Ameliorating effect of a herbal medicinal prescription, Kyung-Ok-Ko, on scopolamine-induced memory impairment in mice. J. Tradit. Med., 26: 35-43.

Sugiyama, S., 2006. The health benefits of gambir. Yakushigaku. Zasshi., 41: 47-49.

Tanaka, Y. and K. Mizoguchi, 2009. Influence of aging on chondroitin sulfate proteoglycan expression and neural stem/progenitor cells in rat brain and improving effects of a herbal medicine, yokukansan. Neuroscience, 164: 1224-1234.

Tian, J., H. Du, H. Yang, X. Liu and Z. Li, 1997. A clinical study on compound da huang (radix et *Rhizoma rhei*) preparations for improvement of senile persons' memory ability. J. Tradit. Chin. Med., 17: 168-173.

Utsuyama, M., H. Seidlar, M. Kitagawa and K. Hirokawa, 2001. Immunological restoration and anti-tumor effect by Japanese herbal medicine in aged mice. Mech. Ageing. Dev., 122: 341-352.

Vidal, K., J. Benyacoub, J. Sanchez-Garcia, F. Foata and I. Segura-Roggero *et al*., 2010. Intake of a milk-based wolfberry formulation enhances the immune response of young-adult and aged mice. Rejuvenation Res., 13: 47-53.

Wang, Q., K. Iwasaki, T. Suzuki, H. Arai, Y. Ikarashi and T. Yabe, 2000. Potentiation of brain acetylcholine neurons by Kami-Untan-To (KUT) in aged mice: Implications for a possible antidementia drug. Phytomedicine, 7: 253-258.

Xu Q.P. and J.N. Sun, 1989. Deng Sheng Fu Fang improve chemical-induced Amnesia in mice. Pharmacol. Clin. Chinese Mater. Med.

Yang, Q.S., H.L. Zhao and L. Chen, 2000. Studies on senility retarding effect of qiangshengye liquid. Zhongguo Zhong. Yao. Za. Zhi., 25: 367-369.

Yao, Y., T. Tian and K.J. Nan, 2006. Research on resveratrol's mechanism of immunity in anti-aging. Zhong Yao. Cai., 29: 464-467.

Yonei, Y., Y. Takahashi, S. Hibino, M. Watanabe and T.Yoshioka, 2008. Effects on the human body of a dietary supplement containing L-carnitine and *Garcinia cambogia* extract: A study using double-blind tests. J. Clin. Biochem. Nutr., 42: 89-103.

Yousefzadeh, G., B. Larijani, B. Mohammadirad R. Heshmat, G. Dehghan, R. Rahimi and M. Abdollahi, 2006. Determination of oxidative stress status and concentration of TGF?â1 in the blood and saliva of osteoporotic subjects. Ann. N. Y. Acad. Sci., 1091: 142-150.

Zhang, D. and J.J. Zhang, 2005. Effects of CE on immuno-organ index and neurosystem changes of subacute aging mice. Chinese J. Neuroimmunol. Neurol., Vol. 12.

Zhang, L., Y. Wang, L.Z. Wang and X.M. Gao, 2004. Immunopotentiating effect of a Yang-promoting formula of traditional Chinese medicine on aged female BALB/c mice. Phytother. Res., 18: 857-861.

Zhao, R.J., Z.L. Zhao, D. Wang, L.B. Li and Z.N. Jin, 2004. Anti-inflammatory effects of Agaricus Blazei *Murill polysaccharide*. J. Med. Sci. Yanbian Univ., 27: 19-22.

Zhu, X.D. and X.C. Tang, 1987. Facilitatory effects of huperzine A and B on learning and memory of spatial discrimination in mice. Yao. Xue. Xue. Bao., 22: 812-817.