



REVIEW ARTICLE

Fruits and Herbs as Potential Human Anti-Aging Compounds - A Review

Sanjay Kumar¹, Reenu Yadav^{2*}, Vikas Kumar Singh³, Phool Singh Yaduvanshi⁴, Gaurav Jain⁵, Kavita R Loksh⁶, Samisha Sharma⁷

^{1,3,4,5,6,7} IES Institute of Pharmacy, IES University, Bhopal (M.P.)

^{*2}Department of Pharmacy, Prestige Institute of Management and Research, Bhopal (M.P.)

Author for Correspondence:

Reenu Yadav ^{2*}

Department of Pharmacy, Prestige Institute of Management and Research, Bhopal (M.P.)

Abstract

Due to the world's population's increasing aging, age-related disorders and increased life expectancy require attention and research. It is commonly acknowledged that aging is an unavoidable process impacted by lifestyle, environmental and genetic variables. The aging process begins the moment we are born and becomes distinctly apparent on our skin as we age. Collagenase, elastase, and hyaluronidase are among the enzymes that exhibit increased activity in relation to skin aging. These enzymes are associated with extracellular matrix deterioration, which has been directly connected to skin aging. ROS, or reactive oxygen species, are essential to many biological activities. The skin absorbs UV light, which increases reactive oxygen species (ROS) and oxidative stress. Skin aging can be accelerated by activated hyaluronidase, collagenase, and elastase, which are all brought on by elevated ROS. Ageing can also be caused by intrinsic factors like hormones, cellular metabolism, and heredity, in addition to external elements like pollution, smoking, food, and sun exposure. In this day of advanced science, many would like to look younger and avoid issues by using natural herbs over plastic surgery or laser therapy. Herbs provide the nutrients needed for healthy skin and assist the skin's biological functions. Herbs include a wide category of phytochemicals, including carotenoids, terpenoids, and polyphenols, that have anti-aging qualities. The antioxidative properties of many different plants and plant extracts are being investigated. Plants' flavonoids, proanthocyanidins, and phenolic chemicals are what give them their antioxidative properties. This article focuses on readily available fruits and herbs that have anti-aging properties.

Keyword: Anti-ageing, Reactive oxygen species, Antioxidants, Herbs, Fruits Phytochemicals, Phenolic Compounds.

1. INTRODUCTION

The ability of various tissues to sustain homeostasis, self-repair, regeneration, performance, and fitness declines with age.¹ This is a hallmark of aging. According to World Health Organization (WHO) projections, 2 billion individuals, or 22 percent of the global population, will be over 60 by the year 2050. As a result of rising life expectancy and an increase in age-related diseases, the issue of degenerating health in old age is projected to worsen dramatically.² All living things inevitably experience the aging process. Ageing is a process that begins from birth and becomes noticeably apparent on the skin as we age.³ There are two kinds of ageing of the skin: photoaging or premature ageing and age-dependent/chronological ageing. Extrinsic factors are the source of photoaging, which manifests as deep furrows, dark/light pigmentation, and a leathery appearance. Skin wrinkles are a sign of natural ageing.⁴ Fibroblasts, collagen, and elastin comprise the extracellular matrix (ECM), the skin's outermost layer. Degeneration of the extracellular matrix (ECM), which has been positively associated with aging skin, is concomitant with increased activity of several age-related enzymes, including collagenase, elastase, and hyaluronidase. Collagen, one of the essential components of skin, gives skin its resilience, suppleness, and continuous flexibility. The structure, flexibility, and hydration of the skin are all preserved in part by hyaluronic acid. In addition, it promotes the quick proliferation, regeneration, and repair of tissue while also facilitating the interchange of nutrients and waste products. Hyaluronic acid, elastin, and Collagen levels decrease with ageing, causing the skin to lose strength and flexibility. This causes wrinkles to become visible, which are linked to thicker epidermis, as well as mottled discoloration, laxity, dullness, and roughness.⁵



Reactive oxygen species (ROS) are crucial to numerous biological processes. The skin absorbs UV light, which rise the manufacturing of induces oxidative stress and ROS. Lipid peroxide production, damage to DNA and mitochondria, and modifications to proteins and genes that alter their structure and function are all possible outcomes of oxidative damage. Elevated reactive oxygen species (ROS) cause hyaluronic acid, elastin, and Collagen to become activated, which can more distinct exacerbate skin aging.⁶ The realization that aging is a treatable disorder has resulted from longer life expectancies and the goal of "healthy aging," which is maintaining excellent health into aging for as long as is feasible. As a result, the area of study known as "Anti-aging Medicine" is growing in popularity. Cosmetic surgeries, laser rejuvenation, and many surgical operations are made possible by current science and technology. In contrast to invasive procedures, which are more unpleasant and time-consuming, noninvasive approaches are risk-free, rarely have side effects, and rarely require any kind of difficulties. Scientists have become more interested in finding ways to minimize the signs of aging within the past ten years.⁷

The usage of herbs and plant extracts dates back thousands of years; the earliest known accounts come from ancient China and Egypt.⁸ Healthy food that is high in dietary antioxidants and a robust lifestyle are crucial for enhancing general well-being and reducing the rate at which people age. Dietary antioxidants such anthocyanins, adaptogens, isoflavones and vitamins A, D, C, and E, prolong the life of living things by slowing the aging process by lowering ROS generation in the cells. The antioxidative properties of many different plants and plant extracts are being investigated^{9,10} state that phenolic substances such as hesperidin derivatives and flavonoids such as rutin also possess anti-tumor, antiviral, antibacterial, antiradical, and antioxidative qualities. An aromatic ring is a distinguishing phenolic compounds feature due to its exceptional capacity to donate electrons and hydrogen connected to a hydroxyl group in their chemical structure.¹¹ Secondary metabolites responsible for anti-ageing effects of some common available fruits are given in table no.1.

Table 1. Common Herbs/Fruits and their anti-aging activity

S.no	Herbs/Fruits	Phytoconstituents	Mechanism of action	References
1	<i>Aloe barbadensis</i> (Aloevera)	-Vitamins A, C and E -Aloin A and B	Neutralizes -Antioxidant free radicals. - Inhibit the activity of collagenase	(Surjushe et al.,2008). (Chakraborty et al.,2018)
2	<i>Emblica officinalis</i> (Indian Goose berry)	Branch contains -mainly sinapic and ferulic acids Fruits -Ascorbic acid emblicanin A -emblicanin B hydrolyzable tannins	-antioxidant, anti-melanogenesis, and MMP-2inhibitory activities -Antioxidant -Reduce catalase and glutathione peroxidase activity -Reduce lipid peroxidation	(Yan et al.,2022) (Fernando &Kananke, 2020).
3	<i>Musa paradisiaca</i> (Banana)	-Dopamine, L-dopa, and catecholamines, norepinephrine, Vitamin C	-Antioxidant and chelating properties	(Faizan et al., 2022). (Gonzalez et al.,2010).



4	<i>Cameliasinensis</i> (Green tea)	-Epicatechingallate and epigallocatechingallate	-inhibition of matrix metalloproteinase-2, inhibition of tyrosinase and tyrosinase-related protein-2 activities to reduce the formation of melanin	(Chaikul et al., 2020).
5	Citrus fruits <i>Citrus sinensis</i> <i>Citrus reticulata</i> <i>Citrus bergamia</i>	-Alpha-hydroxy acids/ Beta-hydroxy acids	-Reduce signs of skin aging -Antioxidants	(Fernando & Kananke, 2020).
6	<i>Vacciniumcorymbosum</i> (Blueberries)	Resveratrol	-Anti- oxidant activity -Down-regulating the Methuselah (MTH) gene and up-regulating the genes for superoxide dismutase (SOD) catalase (CAT), and Rpn11	(Cheng et al., 2012)
7	<i>Macaluspumila</i> (Apple)	-Procyanidins Polymerized(-)- epicatechins and (+)- catechins make	-anti-oxidative, anti-protein aggregation, and pro-longevity effects	(Palermo et al., 2012).

Thus, an effort has been made to shed light on the common available herbs and fruits utilized for anti-aging activities in this article.

- ***Aloe barbadensis miller* (Aloe Vera)**

Aloe vera is known by its botanical name, Aloe barbadensis miller. Its family is Asphodelaceae [Liliaceae]. Aloe vera has seventy-five potentially active compounds, including salicylic acids, vitamins, minerals, enzymes, carbohydrates, lignin, and saponins. Aloe vera's mucopolysaccharides aid in keeping the skin hydrated. Aloe vera encourages fibroblasts to create collagen and elastin fibers, which reduce wrinkles and enhance skin suppleness. Additionally, it possesses cohesive activities that keep the seemingly peeling epidermal cells together, softening the skin. As an astringent, zinc tightens pores, and amino acids soften hard skin cells. Aloe vera gel gloves' moisturizing properties have been studied for the treatment of dry skin brought on by occupational contact, where they enhanced the skin's (Byeon et al., 1988). The effects of aloe gel on the biochemical changes and clinical signs of aging skin were studied by Cho et al. The treated groups showed a significant ($p < 0.05$) improvement in facial wrinkles after consuming aloe gel, while the lower-dose group showed an increase in face elasticity. Type I procollagen mRNA levels in the photoprotected skin were marginally greater in both groups, whereas MMP-1 mRNA levels were significantly lower in the group that received the higher dose. In both groups, there was a notable increase in type I procollagen immunostaining across the dermis. By upregulating the expression of the MMP-1 gene, which breaks down collagen, and promoting the synthesis of new collagen in the photoprotected skin, aloe gel considerably reduces wrinkles and enhances suppleness in photoaged human skin. But there was no discernible dose-response connection (Cho et al., 2009).

- ***Emblica officinalis* (Amla)**

Emblica officinalis (EO) or Amla, is a plant that native to the Phyllanthaceae family. Nutrients include alkaloids, phenolic acids, carbohydrates, vitamin C, and amino acids are abundant in it. Numerous phenolics, primarily sinapic and ferulic acids, were found in the amla branch extract and have demonstrated biological activity against skin aging



in in vitro, cellular, and clinical studies. Using assays that inhibited matrix metalloproteinase-2 (MMP-2), antioxidant, anti-tyrosinase, and anti-melanogenesis properties, the extract of amla branches was studied for its potential to prevent skin aging. reductions in skin aging both in vivo and in vitro, as well as MMP-2 inhibition, antioxidant, and anti-melanogenesis properties, were closely linked to better skin conditions in experiments. After applying PE gel, there was a correlation found between the qualities of younger skin, such as lighter skin tone, increased skin flexibility and moisture, and fewer wrinkles. The findings imply that amla branch might be used in cosmetics as an anti-aging ingredient.¹² A multitude of stress-induced conditions that hasten the aging process are associated with free radical accumulation in many tissues.¹³ Because of their antioxidant properties, tannins from *E. officinalis* also exhibit a protective effect against the tardive dyskinesia rat model.¹⁴ To look into the hypothesis that EO can shield human retinal pigment epithelial (RPE) transmittochondrial cells and age-related macular degeneration (AMD) from cellular damage caused by mitochondria, another investigation was conducted. After treating these RPE, AMD cells with extract EO, the effects of the treatment were assessed utilizing cellular and molecular tests. In this instance, EO markedly increased the number of living cells and mitochondrial membrane potential, decreased oxidative stress and apoptosis, down-regulated Vascular endothelial growth factor (VEGF) and PGC-1 α , a receptor-gamma coactivator activated by peroxisome proliferator, were upregulated. In conclusion, EO had a major cytoprotective effect on AMD in vitro via enhancing cellular and mitochondrial health.¹⁵

- ***Musa paradisiaca* (Banana)**

One important tropical fruit is the banana (*Musa sapientum*, *Musa cavendish*, and *Musa paradisiaca*, all belonging to the Musaceae family). A wide range of bioactive chemicals found in bananas are antioxidants that work to strengthen the body's defenses by scavenging free radicals. The most common antioxidants in bananas include bioactive substances including phenols, carotenoids, and vitamin C. Antioxidant-rich components found in banana pulp include vitamin C, carotenes, dopamine, and norepinephrine. During the oxidation process, proteins, lipids, and nucleic acids can sustain damage from reactive oxygen species (ROS) generated within cells. Numerous substances with chelating and antioxidant qualities can be found in bananas. It's also clear that bananas are one of the often consumed fruits with powerful antioxidant qualities that work wonders to strengthen immunity by delaying the oxidation of free radicals. Bananas' antioxidant qualities are particularly useful in preventing diseases including cancer, CVDS, aging, and neurological illnesses that are brought on by reactive oxygen species (ROS).¹⁶ Dopamine, L-dopa, and catecholamines are abundant in banana peels, and they also have strong antioxidant properties.¹⁷ Antioxidants and vitamin C, which are rich in banana peels, assist to keep skin supple and minimize the visibility of fine wrinkles and lines. Moreover, it eliminates dark spots and leaves the skin looking younger and more uniform.¹⁸ Clinical trials validated the anti-wrinkle effectiveness of a lotion containing banana leaf extract. The anti-wrinkle properties of the leaf extract from *Musa sapientum* L. (banana) were found in the chloroform fraction, and corosolic acid was found to be the active ingredient. Banana leaf extract also showed anti-oxidative action using the DPPH free radical scavenging assay, with an IC50 value of 67.91 ppm.¹⁹

An assessment was conducted on the anti-aging and antioxidant properties of a cream formulation that included a lyophilized banana peel extract. The impact of the inhibitory action of the elastase enzyme on anti-aging was investigated. Comparing the extract from banana peels to the standards, it showed a strong anti-aging and antioxidant activity. Despite the extract's 1% addition, the cream exhibited about 80% of the extract's anti-aging properties and antioxidant. Results for Total Total Flavonoid Content and Phenolic Content further demonstrated that phenolic and flavonoid molecules were responsible for this outcome.²⁰

- ***Camellia sinensis* (Green Tea)**

Because of its many advantages for health The tea plant known as *Camellia sinensis* (L) Kuntze, or green tea, is processed that is utilized in natural products and traditional remedies. In one study, green tea was shown to have anti-aging effects on melanoma cells, B16F10 human skin fibroblasts, and B16F10 cells. using collagen content analysis, antioxidant activity, melanogenesis, and matrix metalloproteinase-2 inhibitory test tests, the cytotoxicity and anti-aging properties in cell culture were assessed. In this investigation, the primary components of green tea were epicatechin gallate, epigallocatechin gallate, and epigallocatechin gallate. Green tea shown anti-aging properties for the skin, such as a strong antioxidant, a notable suppression of melanin formation because matrix metalloproteinase-2 was significantly inhibited, tyrosinase and tyrosinase-related protein-2 activities were inhibited ($p < 0.001$).²¹ Green tea's primary ingredient is called epigallocatechin gallate, or EGCG. There has been a suggestion that EGCG and EGC can both traverse the blood-brain barrier. Green tea contains the free amino acids arginine and theanine, which have the ability to reduce stress. The anti-stress properties of theanine and arginine slow down the aging process



of the brain, whereas prolonged stress speeds up this process. The anti-stress effect of green tea depends on the ratios between these components because EGCG and caffeine negate this effect.²²

- **Citrus fruits**

In a controlled, double-blind, and randomized experiment, 110 Asian and Caucasian participants were given 100 mg/day of *Citrus sinensis*, a red orange extract, to assess its photoprotective and antiaging effects. The product was taken for 56 days, and during that time, the skin responded better to UV radiation; it had more antioxidant capacity; and UVA-induced lipid peroxidation was lessened; The brightness, suppleness, and moisture of the skin were increased; and the Transepidermal water loss (TEWL), wrinkle depth, and melanin staining intensity inside dark spots were all decreased. The findings imply that the test product works well to mitigate the negative effects of UVR exposure as well as the indications of aging.²³ The ability of *Citrus reticulata* Blanco peel to delay the skin aging process and it was evaluated through the use of in vitro antioxidant and anti-enzyme assays. The anti-aging potential of the extracts was suggested by²⁴ who reported that the extracts exhibited strong anti-collagenase and anti-elastase capabilities in their in vitro enzyme inhibitory activities. In another study, the effects of a citrus-based juice mixture and its bioactive components on human dermal fibroblasts and hairless mice were examined, as well as the regulation of antioxidant enzymes and the mitogen-activated protein kinase pathway. The citrus-based juice mixture reduced the production of intracellular reactive oxygen species and H₂O₂-induced cell damage in human dermal fibroblasts. Following pretreatment with a variety of citrus juices, matrix metalloproteinases and activator protein 1 were generated and inhibited.²⁵ In the other study, Human red blood cells (RBCs) subjected to the aging model D-Galactose (DGal) are used to study the potential preventative effects of bergamot peel and juice extract. (*Citrus bergamia*). Based on the information provided, bergamot fruit peel and juice extracts high in polyphenols may shield human red blood cells' structural and functional integrity by affecting lipid and protein cellular components and oxidative stress-induced alterations, such as the body's own proteins and antioxidant system involved in enzymatic metabolism and ion transport. According to this study, bergamot is a functional food that is high in antioxidants. It also shows that adding bergamot or its derivatives to one's diet may help avoid or lessen pathophysiological events that are connected to RBC malfunction during aging.²⁶

- ***Vaccinium corymbosum* (Blueberries)**

Flavonoids, stilbenes, tannins, and phenolic acids are only a few of the phytochemicals that are abundant in berries and provide a wide variety of phenolic antioxidants.²⁷ Blueberries are more powerful antioxidants than most other vegetables and fruits due to their increase polyphenol content.²⁸ According to²⁹ eating blueberries has been shown to delay age-related physiological and functional impairments³⁰ proposed that a diet supplemented with blueberries could counteract the age-related decline in rats' hippocampal heat shock protein (HSP) neuroprotection, based on research in animal models. The current study examined the underlying mechanism of blueberry extracts' ability to extend fruit flies' lifespans. The findings showed that dietary additions of 5 mg/ml blueberry extract might significantly raise fruit fly mean lifespans by 10%. Additionally, this was linked to the Methuselah (MTH) gene being down-regulated and up-regulating the genes for catalase (CAT), Rpn11, and superoxide dismutase (SOD).³¹ In 2018, a study examined how *Caenorhabditis Legans*' lifespan and stress tolerance were affected by supplementing with blueberries. Given at 50, 100, and 200 mg/mL for four days, blueberry extract was found to significantly extend the mean longevity of *Caenorhabditis Legans* in a dose-dependent manner. The increases were 22.2%, 36.5%, and 44.4%, respectively. Additionally, *Caenorhabditis* worms fed with blueberries show increased stress tolerance (heat, paraquat, and UV-B radiation) in comparison to untreated *Caenorhabditis* worms.³²

- ***Malus pumila* (Apples)**

In apple fruit (*Malus pumila* Mill, Family: Rosaceae) polyphenols are primarily composed of procyanidins (PCs), also called as Polymerized (–) condensed tannins-epicatechins and (+)-catechins make up procyanidins (PCs). In addition, apples are a better source of minerals, vitamin B, citric acid, and malic acid, all of which can support healthy digestion and preserve the natural acidity of the digestive tract. Dietary Apple Polyphenols (AP) prolonged the longevity of the mutant mice by considerably slowing the development of heart fibrosis. Additionally, dietary APs reduced the generation of oxidative ROS and DNA damage in the mutant mice's enzymatically-dissociated cardiomyocytes. Notably, using patch clamp techniques, dietary APs also improved the electrophysiological abnormalities in the cardiomyocytes of the mutant mice, including changes in the action potential and inwardly rectifier potassium current. Additionally, using a burst ventricular pacing protocol, APs decreased the incidence of ventricular tachycardia or the induction of fibrillation. Moreover, APs significantly reduced the aggregation of amyloid- β protein 42 (A β 42) and separated A β 42 clumps in vitro, suggesting that APs are strong inhibitors of A β



aggregation. Additionally, APs greatly reduced A β neurotoxicity and promoted the growth of neuronal PC12 (pheochromocytoma-12) cells. It's interesting to note that AP therapy decreased polyglutamine aggregation in the Huntington's disease model *C. elegans* Q40 strain as well.³³ These results clearly suggest that, when applied to model organisms, APs demonstrated anti-aging properties, including anti-oxidative, anti-protein aggregation, and pro-longevity effects. A promising functional food to prevent age-related diseases is apple procyanidins. Another study examines the in vivo effectiveness of whole apples and its constituent parts, including the flesh, skin, and polyphenolic fraction, in influencing oxidative stress and aging. Yeast is a unicellular eukaryotic creature. The findings show that all apple components lengthen life, with the whole fruit producing the best effect, suggesting that all apple components work together.³⁴

2. CONCLUSION

The effectiveness of some fruits that have anti-aging qualities was the main topic of this review article. It's crucial to keep in mind that chronic stress can increase cell aging and speed up the aging process. These fruits have been shown to have a range of bioactive substances with antiaging qualities. Fruits, herbs, and phytochemicals derived from them have many properties that are good for the skin, such as antioxidant action, UV protection, matrix protection, and skin hydration. Many fruits and herbs contain antioxidant molecules that have been shown to have beneficial effects on aging. Additionally, they benefit the digestive tract rather than causing undesirable symptoms. Oxygen free radicals, which primarily harm different cells and tissues, are the primary cause of ageing.

Many phytochemicals derived from plant extracts have been studied in the last ten years, with a detailed in vitro examination of their biological activity. When taken as a whole, the current review supported the theory that antioxidant-rich herbs could slow down the aging process, as suggested by several anti-aging models. More clinical research is therefore constantly needed, with a focus on the safety, formulation, and duration of the anti-aging impact of herbal remedies as well as the ingredient's concentration.

Conflicts of interest:

The authors declare that they have no conflicts of interest.

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