Review

DOI: 10.5582/ddt.2025.01092

Food, medicine, and cosmetic homology: A comprehensive review of bioactive components, functions, and applications of *Torreya grandis*

Xiaoyan Cui[1,2], Chuanyin Shi[1,2,*], Yan Sun[2,3,*]

[1] Shanghai University Mengchao Cancer Hospital, Shanghai, China;
[2] Shanghai Cell Therapy Group Co., Ltd., Shanghai, China;
[3] School of Medicine, Shanghai University, Shanghai, China.

SUMMARY: *Torreya grandis* (*T. grandis*) is one of the evergreen tree species in China. The kernels of *T. grandis* have been used as traditional medicine and food for thousands of years in China. In recent years, it has also been developed as raw materials for cosmetics. *T. grandis* is rich in bioactive components, including unsaturated fatty acids, vitamins, protein, amino acids, trace elements, minerals, polyphenols, squalene, phytosterol, terpenes, *etc*. Therefore, *T. grandis* possesses a wide range of biological activities such as anti-oxidation, anti-inflammation, microbiota alteration, effects on blood pressure, blood glucose and lipids, neuroprotective effect, brightening, reducing uric acid (UA) level, ameliorating bone metabolism disorders, alleviating slow transit constipation, and antinociceptive activity. This review presents a comprehensive analysis of *T. grandis* on its active components and functions, and explores its existing and potential applications in food, medicine, and cosmetics.

Keywords: Anti-oxidation, anti-inflammation, unsaturated fatty acids, microbiota alteration

1. Introduction

Torreya grandis (*T. grandis*, Taxaceae) is an evergreen economic tree species in China. It is a tertiary relict plant and belongs to gymnosperms. With a cultivation history over 1,000 years (*1*), the kernels of *T. grandis* have been used as traditional medicine and food since ancient time. *T. grandis* is an important component of many classical prescriptions to expel intestinal parasites, prevent hair loss, and relieve cough (*2*). The first credible medical record of *T. grandis* appeared in the *Classic of the Materia Medica* during the Three Kingdoms era of China and dated back to the 3rd century AD (*3*). More than 400 years ago, the *Compendium of Materia Medica* listed *T. grandis* nuts as a prescription for repelling internal parasites, preventing hair loss, and relieving sudden hematemesis. For thousands of years, the components, biological activities and functions of *T. grandis* have been developed and applied (Figure 1).

T. grandis fruit includes a thick layer of soft peel (aril), seed coat, and kernel, each structure contains different bioactive components. *T. grandis* comprises abundant unsaturated fatty acids, tocopherol, amino acids, trace elements, minerals, polyphenol, squalene, phytosterol, terpenoid, *etc*. which accounts for its various beneficial functions (*4*) (Figure 2). Modern pharmacological studies showed that *T. grandis* extracts or its main components have biological activities such as anti-oxidation, anti-inflammation, microbiota regulation, angiotensin-converting enzyme inhibitory (ACE-I) activity, tyrosinase inhibition, lowering blood glucose, regulating blood lipids, and protecting nerve activities (*5-8*). This review summarizes recent research progresses of bioactive components and biological functions of *T. grandis*, providing theoretical basis for *T. grandis* in the development of related food, medicine, and cosmetics.

2. Bioactive components of *T. grandis*

It takes 17 months for the seed of *T. grandis* to reach maturity and the oil content of *T. grandis* kernel varies enormously in different *T. grandis* landraces (11.15%-59.47%) (*9,10*). In *T. grandis*, biotin carboxylase (BC), acyl-ACP thioesterase A (FATA), diacylglycerol acyltransferase (PDAT), and TgLBD40 exert significant influence on its oil accumulation (*9*). The expression level of TgLBD40 and oil concentration both increase during the kernel development and reach the highest level in September (*3,11*). Hence, the optimal harvest time of *T. grandis* fruits is mid-September (*11,12*) while

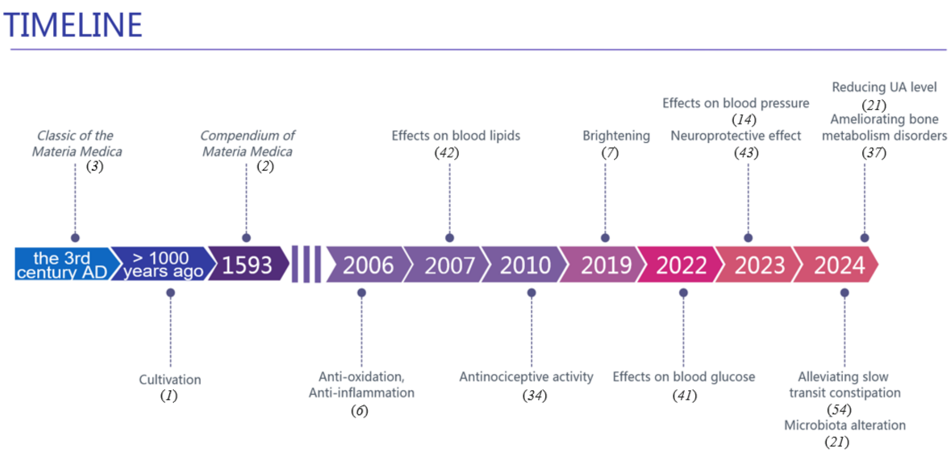

Figure 1. For thousands of years, the biological activities and functions of *T. grandis* have been developed and applied. Created with MedPeer (*medpeer.cn*)

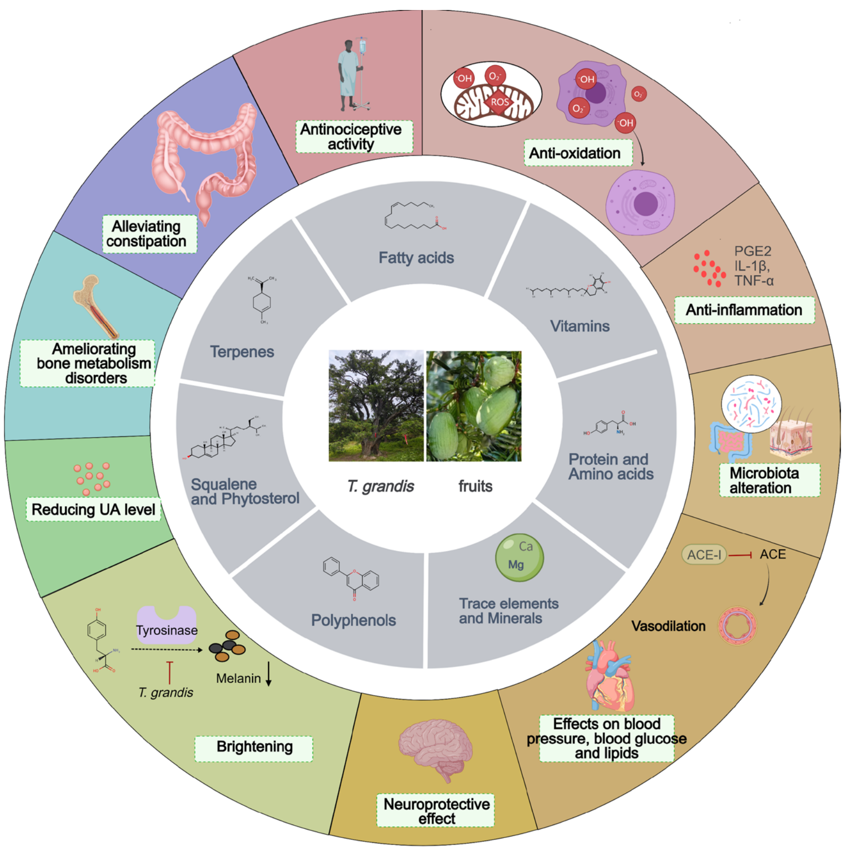

Figure 2. The bioactive components and functions of *T. grandis* have been developed and applied. Created with MedPeer (*medpeer.cn*)

the actual harvest time may still vary by weeks due to regional climate changes.

2.1. Fatty acids

T. grandis kernel is rich in unsaturated fatty acids, especially oleic acid, linoleic acid (*11*), and sciadonic acid (*3*). The total unsaturated fatty acid content is more than 80% in *T. grandis* kernel oil (*3,13*) among which linoleic acid is the highest (Table 1). The polyunsaturated fatty acids are the main bioactive components as they have multiple medicinal properties, including anti-inflammation and anti-atherosclerotic (*11*).

2.2. Vitamins

T. grandis contains several kinds of vitamins, including vitamin B_1, vitamin B_2, vitamin B_3, nicotinic acid, folic acid, and tocopherols. Tocopherols account for the highest content and possess potent antioxidant effects

Table 1. Major fatty acids in *T. grandis* kernel oil

Fatty acids	*T. grandis* kernel oil (%)	References
Palmitic acid (C16:0)	3.23-10.44	11; 5; 13; 57; 58
Stearic acid (C18:0)	2.20-6.07	11; 5; 13; 57; 58
Oleic acid (C18:1)	25.50-34.85	11; 5; 13; 57; 10
Linoleic acid (C18:2)	25.94-46.80	11; 5; 13; 57; 10
Linolenic acid (C18:3)	0.45- 17.12	11; 5; 13; 56; 10; 58
Eicosanoic acid (C20:0)	0.00-0.18	11; 5; 13; 56
cis-11-eicosenoic acid (C20:1)	0.50-1.33	11; 5; 13; 56; 58
cis-11,14-eicosadienoic acid (C20:2)	2.08-4.40	11; 5; 13; 56; 58
cis-5,11,14-eicosatrienoic acid (C20:3)	8.35- 13.93	11; 3; 5; 13; 10
Unsaturated fatty acid (UFA)	87.28-90.84	11; 5; 13
Monounsaturated fatty acid (MUFA)	26.00-35.44	11; 13
Polyunsaturated fatty acid (PUFA)	49.16-61.50	11; 13; 58
Saturated fatty acid (SFA)	11.33-16.80	11; 5; 13; 58
Free fatty acids (FFA)	0.23±0.02 mg/g	11

which can scavenge reactive oxygen species and free radicals as well as inhibit membrane lipid peroxidation (*11*). Therefore, tocopherols have a protective effect on cells. The total tocopherol contents vary enormously in different *T. grandis* cultivars (0.28-167.31 mg/100 g) (Table 2) and β-tocopherol is the major type. In the tocopherol accumulation of *T. grandis* kernels, homogentisate phytyltransferase coding gene (TgVTE2b) and γ-tocopherol methyltransferase coding gene (TgVTE4) may be highly associated (*12*).

2.3. Protein and amino acids

Protein is one of the main nutritional components in *T. grandis* kernel. The protein content of *T. grandis* seeds varies from 10.34% to 25.30% depending on the cultivar (*11,14*). *T. grandis* kernel proteins consist of 20 kDa to 43 kDa peptides. Bioactive peptides possess antioxidant and ACE-I activities (*15*).

T. grandis kernel contains 16 amino acids, with a total amino acid content of 12.3 g /100 g (*1*). It contains eight of the nine essential amino acids for human body: leucine, valine, lysine, isoleucine, phenylalanine, threonine, histidine, methionine. The mass proportion of essential amino acids accounts for 38.6% of the total amino acids in *T. grandis* kernels which meets the standards for high-quality protein stipulated by FAO/WHO.

2.4. Trace elements and minerals

Trace elements and minerals are essential nutrients that sustain fundamental physiological homeostasis in the human body, and are critically involved in metabolism, normal growth, and development. *T. grandis* is abundant in both Mg and Ca with similar concentration in the nut: 1,045.88~1,846.82 mg/kg (Mg) and 948.21~1,459.74 mg/kg (Ca) (*16*). Besides, *T. grandis* also contains Fe, Co, Cu, Zn, Se.

2.5. Polyphenols

Table 2. Tocopherol composition and content in *T. grandis* kernel oil

Tocopherols	$mg \cdot 100\ g^{-1}$	References
α-tocopherol	0.04 -33.30	11;12; 13; 56
β-tocopherol	0.23-133.75	11;12; 13; 56
γ-tocopherol	0.00-0.26	11;12; 13; 56
δ-tocopherol	*ND*	11;12; 13; 56
Total tocopherol	0.28-167.31	11;12; 56

T. grandis is rich in polyphenols, including flavonoids, phenolic acids, *etc*. Flavonoids are a very important class of bioactive compounds with high antioxidant, anti-inflammatory, and antibacterial activities in *T. grandis* kernels. Compounds in *T. grandis* kernels that highly correlated with antioxidant activity include hesperetin, naringenin, and quercetin (*17*). Hesperetin can inhibit oxidative stress, neuroinflammation, apoptotic cell death, and cognitive consolidation by regulating Toll-like receptor 4 (TLR4) / nuclear factor-kappa B (NF-κB) signal pathway (*18*). Naringenin and quercetin possess anti-inflammatory and antiallergic activities in mice and have therapeutic potential for sepsis, fibrosis, and cancer caused by inflammation (*19*). The main components of flavonoids vary among different varieties of *T. grandis*, and the content and diversity of flavonoids were more ample in *T. grandis* 'Shishengfei' compared to *T. grandis* 'Xifei' (*20*). The unigenes encoding chalcone synthase (CHS), dihydroflavonol 4-reductase (DFR), and anthocyanidin synthase (ANS) serve as critical regulators of flavonoids biosynthesis (*17*). Phenolic acids in *T. grandis* kernels include gallic acid, shikimic acid, sinapinic acid (*7*), 4-hydroxybenzoic acid, carnosic acid, and caffeic acid (*21*) which all possess high antioxidant activities.

2.6. Squalene and phytosterol

Squalene and β-sitosterol are considered pharmacologically significant in antimicrobial, anti-inflammatory, anti-oxidative, anticancer, and immunomodulating effects (*22*). Also, squalene is an important constituent of skin-care products, oxidation-resistant industrial lubricants, and numerous vaccines (*23*). Squalene is widely used in the cosmetic industry due to its moisturizing and antioxidant properties on the skin (*24*). Additionally, β-sitosterol is one of the most important phytosterols and is considered to reduce cholesterol level (*24*). The contents of squalene and β-sitosterol varies between cultivars (*22*) (Table 3).

Table 3. Squalene and β-sitosterol in *T. grandis* kernel

Compounds	Content (mg /kg)	References
Squalene	13-72	13; 22
β-sitosterol	900-4,100	13; 22; 56

2.7. Terpenes

The aroma components of the *T. grandis* differ with processing methods (fried, roasted, and raw) for nuts and shedding time of arils. The main aroma components are terpene, benzene, ether, ketone, aldehyde, esters, alkanes, and alcohol compounds (*25-27*). Terpenes have the highest portion (41.99%-86.7%) among the aroma substances of *T. grandis* kernel oil (*25,27,28*) and D-limonene is the highest terpene.

3. Biological functions

Since rich in components, various beneficial effects such as anti-oxidation, anti-inflammation, microbiota regulation, ACE-I activity, tyrosinase inhibitory activity have been discovered for *T. grandis*. Among the abundant contents, unsaturated fatty acids, flavonoids, phenolic acids, and terpenes account for the main functional components.

3.1. Anti-oxidation

Oxidation is essential for living organisms to generate energy which fuels biological processes. However, oxidative processes *in vivo* continuously generate free radicals and reactive oxygen species, and these excessive highly reactive species play an important role in aging, neurodegenerative diseases, and plentiful debilitating diseases, including diabetes, cirrhosis, and cancer (*29*).

The ethanol extracts from *T. grandis* seed have significant antioxidant effects. The 2,2-diphenyl-1-picrylhydrazyl (DPPH) radical scavenging activity of the ethanol extract at a high concentration (2 mg/mL) was close to that of vitamin C which has a half inhibitory concentration (IC_{50}) value of 0.43 ± 0.04 mg/mL (*21*). The 2,2'-azino-bis(3-ethylbenzothiazoline-6-sulfonic acid) (ABTS) radical scavenging ability of the ethanol extract increased rapidly as the concentration of the extract rised (0-6.25 mg dried material/mL), with IC_{50} value of 0.70 mg dried material/mL (*7*). Moreover, both raw extraction and purified 2-hydroxy-2-(4-hydroxyphenylethyl) malonic acid from seed coat demonstrated potent ABTS, DPPH, and hydroxyl radical-scavenging activity (*30*). The free radical scavenging ability of *T. grandis* seeds is greater than that of *T. grandis* arils. An essential oil extraction from the *T. grandis* cv. Merrillii arils can scavenge ABTS and DPPH radicals, with IC_{50} values of 4.14 ± 0.06 mg/mL and 20.73 ± 1.56 mg/mL, respectively (*31*).

Treatment of human dermal fibroblasts with the seed extract at 50 and 250 μg/mL demonstrated significant protection against hydrogen peroxide-induced oxidative stress (*6*). Under the same concentrations, it also demonstrated significant suppression of lactate dehydrogenase (LDH) enzyme leakage from fibroblasts. This reveals the antioxidant protective effect of *T. grandis* seed on hydrogen peroxide-induced fibroblast injury.

Bivariate correlation analysis demonstrated that flavonoids exhibited the strongest correlation with DPPH radical scavenging activity ($r = -0.805$), significantly surpassing that of phenolics ($r = -0.500$). This suggests that flavonoids likely serve as the primary contributors to the radical scavenging capacity of *T. grandis* kernels (*7*). The bioactive peptides from *T. grandis* nut protein extract also exhibited antioxidant effect which is higher than its protein extract, especially in DPPH radicals scavenging (*32*).

Furthermore, the antioxidant capacity and total flavonoid content were significantly higher in *T. grandis* kernels from 100- and 1000-year-old trees compared to those from 10-year-old trees. Flavonoids were strongly correlated with enhanced antioxidant activity in older trees, and seven genes were identified as potentially involved in age-dependent flavonoid biosynthesis. Additionally, the differential accumulation of flavonoids with tree age may be regulated by abscisic acid and gibberellin (*33*).

3.2. Anti-inflammation

T. grandis has huge potential to suppress the inflammatory response (Figure 3). Topical administration of the ethanol extracts from *T. grandis* seed exhibited dose-dependent inhibition against either arachidonic acid (AA)- or 12-O-tetradecanoylphorbol-13-acetate (TPA)-induced ear-edema in mice (*6*). The butanol fraction of *T. grandis* leaves reduced edema by 63.8% and 72.1% at the dose of 100 mg/kg and 200 mg/kg respectively. In comparison, aspirin at 200 mg/kg reduced edema 45.2% against the acute inflammation in xylene-induced ear edema (*34*). Moreover, *T. grandis* aril also exhibited anti-inflammatory activity where its extracts (torregrandin A, torregrandin B, methyl 12-hydroxy-7-oxodehydroabietate, and torreyagrandate) can inhibit nitric oxide (NO) production with IC_{50} values of 49.4,

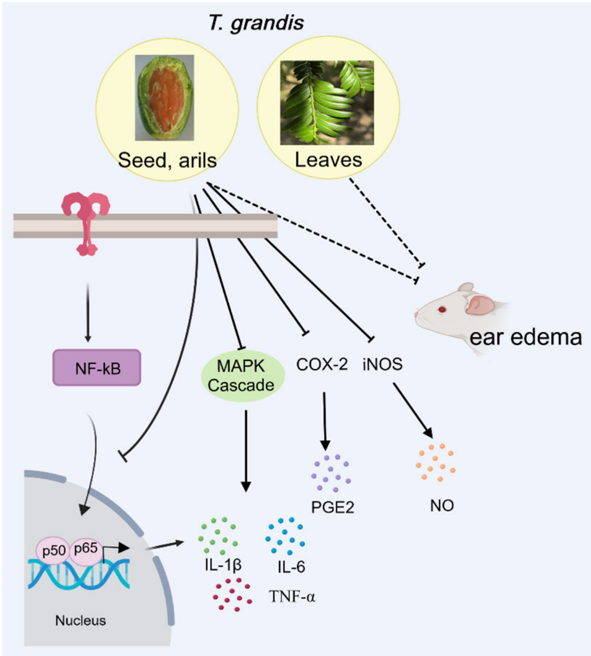

Figure 3. Anti-inflammatory property of *T. grandis*. Created with MedPeer (*medpeer.cn*)

41.9, 38.4, and 52.6 μM respectively. This demonstrated the anti-neuroinflammatory activity for *T. grandis* in LPS-induced BV-2 cells (*35*).

The ethanol extracts from *T. grandis* seed can effectively reduce the expression of kidney prostaglandin E2 (PGE2) and decrease the expression of kidney interleukin-1β (IL-1β) and tumour necrosis factor α (TNF-α) in a mouse model of hyperuricemia (*21*). *T. grandis* kernel contains sciadonic acid (SCA) which can decrease the production of PGE2, NO, TNF-a, and interleukin-6 (IL-6) in macrophages. When incubated under different concentrations of SCA (0, 10, 25, 50 or 100 μM) followed by LPS-stimulation, macrophages exhibited significantly reduced the production of PGE2, NO, TNF-a, and IL-6 by 29%, 31%, 14%, and 34%, respectively, as compared to the control groups (*36*). Moreover, SCA can decrease the production of proinflammatory factor IL-1β and TNF-α in high-fat diet mice. Both low and high doses of SCA significantly reduced the relative expression of IL-1β, and the high dose additionally suppressed TNF-α expression in high-fat diet mice (*37*). The suppression of pro-inflammatory mediators partly attributed to reduced expression of inducible nitric oxide synthase (iNOS) and cyclooxygenase-2 (COX-2). The reduction of PGE2 synthesis by SCA was probably due to its suppression of COX-2 expression and reducing proportions of phospholipid arachidonic acid (AA) in cell membrane. In addition, SCA also inhibited the expression of total mitogen-activated protein kinases (MAPK) and phosphorylated MAPK, and the translocation of NF-κB p65 (*36*).

Furthermore, water-soluble polysaccharides in *T. grandis* nuts possess strong anti-inflammatory activity (*38*). Heteropolysaccharide TGP-0a significantly lowered pro-inflammatory cytokines IL-1β and IL-6. Moreover, TGP-0a decreased the level of inflammatory mediators (NO and reactive oxygen species (ROS)) by reducing the levels of iNOS and COX-2.

3.3. Microbiota alteration

Extracts from *T. grandis* seeds play a dual role in microbiota alteration by increasing microbial diversity and beneficial bacteria while suppressing those harmful ones. This dual role mainly comes from the direct functions by its rich bio-active contents or through regulations under various microenvironments, and yet many of the detailed mechanisms remain to be fully addressed. The α-diversity index (the Shannon index) for the microbiota of the ethanol extracts from *T. grandis* seed group was elevated compared to that of the model group and the positive drug group (*21*). The ethanol extracts of *T. grandis* seed modulated the gut microbiota composition, significantly enriching beneficial bacteria including *Akkermansia muciniphila*, *Corynebacterium parvum*, *Enterorhabdus*, Muribaculaceae, *Marvinbryantia*, and *Blautia* (*21*). On the other hand, the defensin 4 protein from *T. grandis* nuts significantly suppressed the proliferations of *B. subtilis*, *E. coli* DH5α, *S. aureus*, and *P. aeruginosa*, *M. albican* and *S. cerevisiae* (*32*).

On the suppression side, dehydroabietinol and dehydroabietic acid from the arils of *T. grandis* significantly inhibited methicillin-resistant *Staphylococcus aureus* (MRSA), with MIC values (the lowest concentration of the tested compounds which completely inhibited the growth of bacteria) of 100 μM (*35*).

Furthermore, the abietane-type diterpenoids from the twigs and leaves of *T. grandis*, including torgranol E, 12-hydroxy-6,7-seco-abieta-8,11,13-triene-6,7-dial, 6,11,12-trihydroxyabieta-5,8,11,13-tetraen-3,7-dione, and 6α-hydroxysugiol, moderately inhibited *M. tb* H37v, demonstrating equivalent MIC values at 16 μg/mL (*39*). Moreover, both compounds (6,11,12-trihydroxyabieta-5,8,11,13-tetraen-3,7-dione and 6α-hydroxysugiol) demonstrated potent inhibition of the *S. aureus* ATCC 29213, exhibiting MIC of 16 and 4 μg/mL respectively (*39*). Dehydroabietinol, dehydroabietic acid, and abietane-type diterpenoids mainly exert their antibacterial effects through multiple mechanisms such as destroying microbial cell membranes and inhibiting key enzymes (*35,39*).

On the enriching part, SCA from the seeds of *T. grandis* can modulate the intestinal flora composition by selectively enriching beneficial bacteria (such as *Lactobacillus* and *Bifidobacterium*) and suppressing potentially detrimental bacteria (such as *Faecalibaculum*, *norank_f_Desulfovibrionaceae*, and *Romboutsia*). Such a dual role effect to the gut microbiota was suggested to be associated with short-chain fatty acids (SCFAs) and other metabolites from *T. grandis* (*40*). Intervention with SCA significantly increased the acetic acid content and slightly elevated the levels of propionic acid and butyric acid. Acetic, propionic, and butyric acids belong to SCFAs, and they can regulate hormone secretion and beneficially alter the structural composition of the gut microbiota (*40*). Therefore, SCA can stimulate the growth and proliferation of acid-producing bacteria, regulate the SCFAs contents, and improve gut microbiota composition. However, the potential mechanisms of SCA on the acid-producing bacteria remain unclear.

3.4. Effects on blood pressure, blood glucose and lipids

Hypertension is an important contributing factor to cardiovascular disease. Inhibition or inactivation of angiotensin-converting enzyme is considered an effective way to alleviate hypertension. ACE-I oligopeptides and peptides were identified in *T. grandis* nuts, and the former has been reported in the treatment of several diseases including cardiovascular disease, type 2 diabetes, increased blood pressure, increased level of triglycerides in the blood, and obesity (*32*). Moreover, a new ACE-I peptide (VW-7) identified from *T. grandis* meal protein has an IC_{50} value of 205.98 μM (*14*). These results indicate the blood pressure-lowering potential of *T. grandis* nuts.

T. grandis kernel extracts exhibit pronounced α-glucosidase inhibition effect in a dose-related manner. The 70% ethanol extract possesses the best α-glucosidase inhibition with the lowest IC_{50} value of 0.60 mg DM/mL and yields better activity than acarbose (0.76 mg/mL), a clinical drug treating diabetes (*7*). This suggests the hypoglycemic potential of *T. grandis* kernel.

T. grandis leaves also exhibit blood glucose regulating activity. When treated with the n-butanol fraction of the 75% ethanol extract of *T. grandis* leaves (BFTL), serum biochemical indexes exhibited a significant reduction while superoxide dismutase and glutathione peroxidase levels exhibited a significant increase as compared to the type 2 diabetes mellitus (T2DM) group without treatment (*41*). The BFTL treatment also ameliorated oral glucose tolerance and the pathological changes of the liver, kidney, and pancreas. It significantly reduced cytochrome and caspase-3 expression in pancreatic and augmented the Bcl-2/Bax ratio (*41*).

Dyslipidemia, especially the elevation of total cholesterol, triglycerides and low-density lipoprotein cholesterol (LDL-C), is another important risk factor for cardiovascular disease. Plasma triacylglycerol level was markedly lower in the *T. grandis* kernel oil group (113 ± 12 mg/dl) relative to both soybean (161 ± 15 mg/dl) and corn oil (179 ± 20 mg/dl) controls. The liver triacylglycerol level was also markedly lower in the *T. grandis* kernel oil group (15.4 ± 1.8 mg/g) relative to both soybean (29.9 ± 1.9 mg/g) and corn oil (30.7 ± 2.0 mg/g) controls (*42*).

SCA from the seeds of *T. grandis* can alleviate the increase of total cholesterol (TC), triacylglycerol (TG), and LDL-C levels and decrease of high-density lipoprotein cholesterol (HDL-C) level under high-fat diet in a dose-dependent manner (*37*). Both SCA treatment groups effectively suppressed body weight gain relative to the model group. SCA regulate lipid metabolism by activating the expression of the PPARα/SREBP-1C/FAS protein pathway (*40*). SCA, especially high dose group, decreased SREBP-1c and increased PPARα, compared with the high-fat diet group.

3.5. Neuroprotective effect

T. grandis oil possesses a neuroprotective effect on a scopolamine (SCAOP)-induced C57BL/6J mouse model (*43*). The administration of SCAOP impaired short-term non-spatial recognition memory and working memory while *T. grandis* oil can effectively reverse the trend. The *T. grandis* oil can attenuate the substantial decline in acetylcholine (ACh) activity and increase in acetylcholinesterase (AChE) activity in the cortex of the SCAOP group, therefore protecting against cholinergic dysfunction.

Neuroinflammation underlies various central nervous system (CNS) conditions, and it is central to the pathology of neurodegenerative diseases, including Parkinson's disease (PD) and Alzheimer's disease (AD) (*44*). The *T. grandis* oil can inhibit neuroinflammation and oxidative stress (*43*). The *T. grandis* oil alleviated the upregulation of microglia in the cortical and hippocampal CA1 regions and the mRNA expressions of TNF-α, IL-1β, IL-6, and iNOS in the cortex by SCAOP induction. Moreover, it alleviated the upregulation of malondialdehyde (MDA) and down-regulation of glutathione (GSH) and superoxide dismutase (SOD) by SCAOP induction.

The neuroprotective effects of the *T. grandis* oil are due to, in part, unsaturated fatty acids (UFAs) which can prevent the accumulation of lipoprotein-associated Aβ, alleviate neuroinflammation and oxidative stress (*45*). For example, oleic acid pretreatment strongly attenuated lipoteichoic acid (LTA)-induced IL-6 secretion in BV2 microglia (*46*). Prenatal oleic acid administration enhanced brain weight and the synthesis of postsynaptic density 95 in Down syndrome model mice (*47*). Oral α-linoleic acid administration suppressed neuroinflammation and TLR4 to ameliorate memory dysfunction (*48*). In addition, torregrandin A, torregrandin B, methyl 12-hydroxy-7-oxodehydroabietate, and torreyagrandate from *T. grandis* aril inhibited NO production, confirming their anti-neuroinflammatory activities (*35*).

T. grandis oil can also participate in the gut-brain axis regulation where its administration can effectively reverse the decrease of SCFA levels in SCOP mice. SCFAs are vital metabolites produced by gut microbiota and play a mediational role within the gut–brain axis

(*43*). SCFAs modulate CNS processes through direct and indirect patterns. In addition to crossing the blood-brain barrier (BBB) *via* endothelial monocarboxylate transporters, SCFAs strengthen BBB integrity through the upregulation of tight junction proteins. Furthermore, within the CNS, SCFAs modulate neuroinflammation *via* two primary mechanisms: by regulating glial cell morphology and function, and by controlling the levels of neurotrophic factors. These actions collectively enhance neurogenesis, support serotonin biosynthesis, and promote neuronal homeostasis and function. On the other hand, the activation of specific receptors on enteroendocrine cells by SCFAs mediates indirect communication with the brain through systemic circulation or vagal pathways. This is achieved by stimulating the release of signaling molecules, such as the gut hormones glucagon-like peptide 1 (GLP1) and peptide YY (PYY), alongside the neurotransmitters γ-aminobutyric acid (GABA) and serotonin (5-HT) (*49*). This indicates the treatment of *T. grandis* oil could regulate gut microbiota and it might be associated with the functions of *T. grandis* oil on cognitive impairment induced by SCOP.

3.6. Brightening

Tyrosinase is a key rate-limiting enzyme that can catalyze enzymatic browning and melanin synthesis (*31*). Tyrosinase exhibits monophenolase and diphenolase activities, which catalyze the hydroxylation of L-tyrosine to L-dihydroxyphenylalanine (L-DOPA) and the oxidation of L-DOPA to dopaquinone, leading to nonenzymatic polymerization and then dark pigments (*50,51*). In humans, the overexpression of tyrosinase will cause melanin overproduction in the skin, which can trigger hyperpigmentation effects such as freckles, melasma, age spots, and melanoma (*52*). *T. grandis* seed and aril demonstrate an inhibitory eaffect on the oxidation of L-DOPA and L-tyrosine. *T. grandis* seed oil inhibited the oxidation of L-DOPA and L-tyrosine with IC_{50} values of 237.42 ± 2.23 μg/mL and 849.42 ± 4.37 μg/mL, respectively (*10*). Ethanol extracts from *T. grandis* seed inhibited tyrosinase activity with IC_{50} value of 6.60 ± 0.15 mg DM/mL (*7*). The essential oil from *T. grandis* cv. Merrillii aril inhibited tyrosinase activity with IC_{50} value of 11.04 ± 0.76 mg/mL (*31,53*).

Total phenolics and total flavonoids are involved in tyrosinase inhibition (*54*), and correlation coefficients between tyrosinase inhibition and these two substances were −0.867 and −0.809, respectively in *T. grandis* seed (*7*). D-limonene and α-pinene are the predominant constituents of the essential oil from the *T. grandis* cv. Merrillii aril and they might account for the inhibitory effect on tyrosinase of this essential oil (*31*).

3.7. Reducing uric acid (UA) level

The ethanol extracts from *T. grandis* seed exhibit significant effects in reducing UA level and protecting the kidneys in hyperuricemia mice. The extract treatment decreased the serum UA level by 71.9%, exhibiting efficacy equivalent to that of xanthine. The mechanism of the extracts in reducing UA level is by inhibiting xanthine oxidase activity and promoting UA excretion (*21*).

3.8. Ameliorating bone metabolism disorders

SCA, the substance from *T. grandis* seeds, can regulate the bone formation-related OPG/RANKL/RANK signaling pathway through reducing inflammation and modulating the lipid metabolic state (*37*). SCA improves bone health by regulating the proportion of factors associated with bone resorption and formation and inhibiting fat vacuoles in bone (*37*).

3.9. Alleviating slow transit constipation

Slow transit constipation (STC) is mainly caused by weakened colonic motility and reduced intestinal peristalsis speed. *T. grandis* nuts have been used as a prescription for repelling internal parasites in traditional medicine. *T. grandis* kernel oil effectively mitigated constipation, rescued intestinal barrier damage, and ameliorated intestinal inflammation and intestinal flora *via* promoting the colonic expressions of Occludin/Claudin-1/zonula occludens-1 and 5-hydroxytryptamine 3R/4R (*55*).

3.10. Antinociceptive activity

T. grandis leaves exhibit antinociceptive activity. The extract and fractions of *T. grandis* leaves (100 and 200 mg/kg) significantly decreased acetic acid-induced writhing in mice. Especially, the writhing inhibition percentage of butanol fraction of *T. grandis* (200 mg/kg, 82.3%) was higher than that of the standard drug aspirin at the same dose (47.8%). Moreover, *T. grandis* extract and its fractions significantly inhibited the second phase of formalin-induced nociception and reduced the licking time in mice (*34*).

4. Applications

4.1. Food applications

The seed of *T. grandis* is rich in multiple types of nutrients including unsaturated fatty acids, vitamins, protein, essential amino acids, trace elements, and minerals. Unsaturated fatty acids, including oleic acid and linoleic acid, accounts for 87.28%-90.84% of all fatty acids in *T. grandis* kernel. It contains eight of the nine essential amino acids that cannot be synthesized by the human body. Moreover, *T. grandis* kernel contains anti-inflammatory or anti-oxidative bioactive components, such as sciadonic acid, tocopherols, polyphenols, squalene, and β-sitosterol, terpenes. Owing to these nutrients and bioactive components, *T. grandis* kernel is a suitable source for diverse food products, including nut snacks and edible oil.

The essential oil of *T. grandis* aril is rich in volatile compounds, such as limonene (35.6%-37.1%), *α*-pinene (20.1%-24.1%), and *δ*-carene (3.3%-3.9%) which exhibits typical flavors (*53*). Therefore, the essential oil can be helpful for the flavoring of foods. In addition, the essential oil possesses various bioactive functions, such as anti-oxidation, tyrosinase inhibition, antibacterial and antiseptic effects (*31*) and it can be used for food preservation. The decay index of the treatment with the essential oil of *T. grandis* aril was significantly reduced. The decline rate of the ascorbic acid, an important indicator for evaluating the nutritional quality of loquat fruits, was relatively slow under the treatment with *T. grandis* essential oil. The activities of catalase and peroxidase, important indicators for the postharvest storage quality of fruits, reached the peak in fruits treated with essential oil on the 12th day of storage (*31*).

4.2. Medicine applications

With records dated back to the ancient times and the long application history of *T. grandis* kernel in Traditional Chinese Medicine to expel intestinal parasites, prevent hair loss, and relieve cough, *T. grandis* exhibited various other beneficial functions on human health. In summary, *T. grandis* possesses anti-oxidation, anti-inflammation, microbiota alteration, reducing blood pressure, reducing blood glucose, reducing blood lipids, neuroprotective effect, reducing UA level, ameliorating bone metabolism disorders, alleviating slow transit constipation, and antinociceptive activity. With these exhibited functional activities, more potential values are to be discovered in future medicine development.

4.3. Cosmetic applications

T. grandis extract and *T. grandis* seed extract are both listed in the cosmetic raw material catalog. The essential oil of *T. grandis* aril exhibits a characteristic aroma like galbanum and can be added to the cosmetics, soap, and daily used perfume to impart a desirable fragrance. The essential oil of *T. grandis* aril and kernel oil possess anti-oxidation, anti-inflammation, brightening, hair care, and regulation of skin microecology. The ethanol extract of *T. grandis* seed exhibits a protective effect on fibroblast oxidative injury induced by H_2O_2 (*6*). The pinene and D-limonene in the essential oil exhibit an inhibitory effect on tyrosinase (*31*). *T. grandis* seed oil inhibits the oxidation of L-DOPA and tyrosinase (*10*). The extracts of *T. grandis* are included in skin care products such as creams, serums, and masks to enhance the moisturization and repair functions.

5. Conclusion and future perspectives

The fruit of *T. grandis* and its extracts possess a wide range of bioactive components and functions. Therefore, *T. grandis* has extensive application potential in food, medicine, and cosmetics. Although new mechanisms associated with their components were discovered in recent years, more were yet to be explored. The challenges encountered in *T. grandis* include: (1) *T. grandis* is rich in bioactive components, which is the key factor influencing its biological activities. Hundreds of components of *T. grandis* have been reported so far, including those unique ones, but its bioactive constituents and their targets are not fully understood. (2) The landrace, maturation stage, and extraction process of *T. grandis* have certain influences on its active components and biological activities. Therefore, it is important to conduct a systematic comparison of the effective components of different landraces, tree ages, harvest time, and extraction processes. (3) To formulate the quality control standards of the *T. grandis* extract, it is necessary to clarify the composition and content of the most critical bioactive compounds. Through comprehensive and in-depth research of *T. grandis*, new processing method development, exploration on non-traditional components such as exosome or RNA, more ingredients and more mechanisms and functions are expected to be found. In addition, further development and wider utilization of *T. grandis*, such as *T. grandis* leave, aril, bark, *etc*. may be realized.

Funding: None.

Conflict of Interest: The authors have no conflicts of interest to disclose.

References

1. Zhu J, Chai Z, Wu C, Huang Y, Wu X. Comprehensive research on the quality of *Torreya grandis* and its oil in Zhejiang Province. J Chin Cereals Oils Assoc. 2019; 34:67-73.
2. Li SZ. Fruit. In: Compendium of Materia Medica (Vol. 31). China, 1593; pp. 1080.
3. Lou H, Zheng S, Chen W, Yu W, Jiang H, Farag MA, Xiao J, Wu J, Song L. Transcriptome-referenced association study provides insights into the regulation of oil and fatty acid biosynthesis in *Torreya grandis* kernel. J Adv Res. 2024; 62:1-14.
4. Xiao M, Huang M, Huan W, Dong J, Xia J, Wu J, Wang D, Song L. Effects of *T. grandis* kernel oil on lipid metabolism and intestinal flora in C57BL/6J mice. Oxid Med Cell Longev. 2022; 4472751.
5. Dong D, Wang H, Xu F, Xu C, Shao X, Li H. Supercritical carbon dioxide extraction, fatty acid composition, oxidative stability, and antioxidant effect of *Torreya grandis* seed oil. J Am Oil chem Soc. 2014; 91:817-825.
6. Chen BQ, Cui XY, Zhao X, Zhang YH, Piao HS, Kim JH, Lee BC, Pyo HB, Yun YP. Antioxidative and acute antiinflammatory effects of *Torreya grandis*. Fitoterapia.

2006; 77:262-267.
7. Zhu MF, Tu ZC, Zhang L, Liao H. Antioxidant, metabolic enzymes inhibitory ability of *Torreya grandis* kernels, and phytochemical profiling identified by HPLC-QTOF-MS/MS. J Food Biochem. 2019; 43:e13043.
8. Laghari AH, Kandhro AA, Memon AA. Chapter 4 - Cold pressed *Torreya grandis* kernel oil. In: Cold pressed oils: Green technology, bioactive compounds, functionality, and applications (Ramadan MF eds.). Academic Press, 2020; pp. 31-38.
9. Ding M, Lou H, Chen W, Zhou Y, Zhang Z, Xiao M, Wang Z, Yang Y, Yang L, Zhang F, Wu J, Song L. Comparative transcriptome analysis of the genes involved in lipid biosynthesis pathway and regulation of oil body formation in *Torreya grandis* kernels. Ind Crops Prod. 2020; 145:112051.
10. Cui HX, Duan FF, Jia SS, Cheng FR, Yuan K. Antioxidant and tyrosinase inhibitory activities of seed oils from *Torreya grandis* Fort. ex Lindl. Biomed Res Int. 2018; 2018:5314320.
11. Wang Y, Yao X, Yang L, Fei X, Cao Y, Wang K, Guo S. Effects of harvest time on the yield, quality and active substance of *Torreya grandis* nut and its oil. J Oleo Sci. 2021; 70:175-184.
12. Lou H, Ding M, Wu J, Zhang F, Chen W, Yang Y, Suo J, Yu W, Xu C, Song L. Full-length transcriptome analysis of the genes involved in tocopherol biosynthesis in *Torreya grandis*. J Agric Food Chem. 2019; 67:1877-1888.
13. Ren C, Zhang Y, Tang F, Shen D, Mo R. Analysis of main chemical components in camellia oil, olive oil, walnut oil and *Torreya* seeds oil. J Food Saf Qual. 2015; 6:5011-5016.
14. Wu F, Luo X, Zhang Y, Wang P, Chang Y, He Z, Liu X. Purification, identification, and inhibitory mechanisms of a novel ACE inhibitory peptide from *Torreya grandis*. Nutrients. 2023; 15:2374.
15. Zongo AW, Jin C, Hao G, Yu N, Zogona D, Nie X, Lu Y, Ye Q, Meng X. Functional compounds of *Torreya grandis* nuts and their processing byproducts: Extraction process, health benefits, and food applications - A comprehensive review. Food Res Int. 2024; 197(Pt 1):115232.
16. Ni L, Shi WY. Composition and free radical scavenging activity of kernel oil from *Torreya grandis*, *Carya cathayensis*, and *Myrica rubra*. Iran J Pharm Res. 2014; 13:221-226.
17. Zhang F, Ma Z, Qiao Y, Wang Z, Chen W, Zheng S, Yu C, Song L, Lou H, Wu J. Transcriptome sequencing and metabolomics analyses provide insights into the flavonoid biosynthesis in *Torreya grandis* kernels. Food Chem. 2022; 374:131558.
18. Ikram M, Muhammad T, Rehman SU, Khan A, Jo MG, Ali T, Kim MO. Hesperetin confers neuroprotection by regulating Nrf2/TLR4/NF-κB signaling in an Aβ mouse model. Mol Neurobiol. 2019; 56:6293-6309.
19. Escribano-Ferrer E, Queralt Regué J, Garcia-Sala X, Boix Montañés A, Lamuela-Raventos RM. *In vivo* anti-inflammatory and antiallergic activity of pure naringenin, naringenin chalcone, and quercetin in mice. J Nat Prod. 2019; 82:177-182.
20. Tao H, Zhu M, Chen M, Liu K, Zhang Z, Song L, Gao F. Diversity of flavonoids in five *Torreya grandis* cultivars: Integrating metabolome and transcriptome to elucidate potential applications for health and metabolic engineering. Food Res Int. 2024; 198:115374.
21. Yao J, Bai E, Duan Y, Huang Y. Ethanol extracts from *Torreya grandis* seed have potential to reduce hyperuricemia in mouse models by influencing purine metabolism. Foods. 2024; 13:840.
22. Suo J, Tong K, Wu J, Ding M, Chen W, Yang Y, Lou H, Hu Y, Yu W, Song L. Comparative transcriptome analysis reveals key genes in the regulation of squalene and β-sitosterol biosynthesis in *Torreya grandis*. Ind Crop Prod. 2019; 131:182-193.
23. Fox CB. Squalene emulsions for parenteral vaccine and drug delivery. Molecules. 2009; 14:3286-3312.
24. Hu Y, Suo J, Jiang G, Shen J, Cheng H, Lou H, Yu W, Wu J, Song L. The effect of ethylene on squalene and β-sitosterol biosynthesis and its key gene network analysis in *Torreya grandis* nuts during post-ripening process. Food Chem. 2022; 368:130819.
25. Yang L, Zhao D, Hu Y, Suo J, Yu W, Wu J, Lou H, Song L. Comparative analysis of aroma components and oil quality of *Torreya grandis* 'Merrillii' nuts with different processing techniques. Zhejiang Nong Lin Da Xue Xue Bao. 2022; 39:22-31. (in Chinese)
26. Wei X, Hu Y, Zhu G, Yu W, Zhang Z, Wu J, Song L. Effects of different shedding time on aroma and nutrients of *Torreya grandis* 'Merrillii' seed kernel. Nanjing Lin Ye Da Xue Xue Bao. 2024; 48:51-60. (in Chinese)
27. Hu Y, Zhang Z, Hua B, Tao L, Chen W, Gao Y, Suo J, Yu W, Wu J, Song L. The interaction of temperature and relative humidity affects the main aromatic components in postharvest *Torreya grandis* nuts. Food Chem. 2022; 368:130836.
28. Zhang C, Fang X, Chen Z, Luo F, Zhong H, Du M. Effects of processing process on the composition of volatile substances in *Torreya* seed oil. China Oils Fats. 2024; 49:22-28.
29. Neagu E, Radu GL, Albu C, Paun G. Antioxidant activity, acetylcholinesterase and tyrosinase inhibitory potential of *Pulmonaria officinalis* and *Centarium umbellatum* extracts. Saudi J Biol Sci. 2018; 25:578-585.
30. Quan W, Xu Y, Xie Y, Peng F, Lin Y. *In vitro* antioxidant properties and phenolic profile of acid aqueous ethanol extracts from *Torreya grandis* seed coat. Molecules. 2022; 27:5560.
31. Wang H, Zheng Y, Tang X, Zhang T. Formulation of a stable oil-in-water microemulsion of *Torreya grandis* cv. Merrillii aril essential oil and its application in loquat fruit preservation. Foods. 2023; 12:4005.
32. Durrani R, Meiyun Y, Yang B, Durand E, Delavault A, Bowen H, Weiwei H, Yiyang L, Lili S, Fei G. Identification of novel bioactive proteins and their produced oligopeptides from *Torreya grandis* nuts using proteomic based prediction. Food Chem. 2023; 405(Pt A):134843.
33. Yan J, Zeng H, Chen W, Zheng S, Luo J, Jiang H, Yang B, Farag M, Lou H, Song L, Wu J. Effects of tree age on flavonoids and antioxidant activity in *Torreya grandis* nuts *via* integrated metabolome and transcriptome analyses. Food Frontiers. 2023; 4:358-367.
34. Saeed MK, Deng Y, Dai R, Li W, Yu Y, Iqbal Z. Appraisal of antinociceptive and anti-inflammatory potential of extract and fractions from the leaves of *Torreya grandis* Fort Ex. Lindl. J Ethnopharmacol. 2010; 127:414-418.
35. Gao Y, Yang J, Zhang Y, Gao L, Tian J, Han W, Gao J. Abietane-type diterpenoids from the arils of *Torreya grandis*. Molecules. 2024; 29:1905.
36. Chen SJ, Huang WC, Yang TT, Lu JH, Chuang LT. Incorporation of sciadonic acid into cellular phospholipids reduces pro-inflammatory mediators in murine

macrophages through NF-κB and MAPK signaling pathways. Food Chem Toxicol. 2012; 50:3687-3695.
37. Yao S, Lu H, Zhou T, Jiang Q, Jiang C, Hu W, Li M, Tan CP, Feng Y, Du Q, Shen G, Xiang X, Chen L. Sciadonic acid attenuates high-fat diet-induced bone metabolism disorders in mice. Food Funct. 2024; 15:4490-4502.
38. Yang L, Hu Y, Deng H, Li Y, Zhang R, Zhang Q, Yang L, Pang H, Liu F, Fu C. Water-soluble polysaccharides from *Torreya grandis* nuts: Structural characterization and anti-inflammatory activity. Int J Biol Macromol. 2025; 291:138935.
39. Cui JJ, Li WJ, Wang CL, Huang YQ, Lin W, Zhou B, Yue JM. Antimicrobial abietane-type diterpenoids from *Torreya grandis*. Phytochemistry. 2022; 201:113278.
40. Chen L, Jiang Q, Jiang C, Lu H, Hu W, Yu S, Li M, Tan CP, Feng Y, Xiang X, Shen G. Sciadonic acid attenuates high-fat diet-induced obesity in mice with alterations in the gut microbiota. Food Funct. 2023; 14:2870-2880.
41. Li XQ, Jia SS, Yuan K, Jin SH. Hypoglycemic effect of the n-butanol fraction of *Torreya grandis* leaves on type 2 diabetes mellitus in rats through the amelioration of oxidative stress and enhancement of β-cell function. Biomed Res Int. 2022; 2022:5648896.
42. Endo Y, Osada Y, Kimura F, Shirakawa H, Fujimoto K. Effects of Japanese Torreya (*Torreya nucifera*) seed oil on the activities and mRNA expression of lipid metabolism-related enzymes in rats. Biosci Biotechnol Biochem. 2007; 71:231-233.
43. Ma J, Yuan T, Gao Y, Zeng X, Liu Z, Gao J. *Torreya grandis* oil attenuates cognitive impairment in scopolamine-induced mice. Food Funct. 2023; 14:10520-10534.
44. Thakur S, Dhapola R, Sarma P, Medhi B, Reddy DH. Neuroinflammation in Alzheimer's disease: current progress in molecular signaling and therapeutics. Inflammation. 2023; 46:1-17.
45. Galloway S, Takechi R, Nesbit M, Pallebage-Gamarallage MM, Lam V, Mamo JCL. The differential effects of fatty acids on enterocytic abundance of amyloid-beta. Lipids Health Dis. 2019; 18:209.
46. Howe AM, Burke S, O'Reilly ME, McGillicuddy FC, Costello DA. Palmitic acid and oleic acid differently modulate TLR2-mediated inflammatory responses in microglia and macrophages. Mol Neurobiol. 2022; 59:2348-2362.
47. García-Cerro S, Rueda N, Vidal V, Puente A, Campa V, Lantigua S, Narcís O, Velasco A, Bartesaghi R, Martínez-Cué C. Prenatal administration of oleic acid or linolenic acid reduces neuromorphological and cognitive alterations in Ts65dn Down Syndrome mice. J Nutr. 2020; 150:1631-1643.
48. Ali W, Ikram M, Park HY, Jo MG, Ullah R, Ahmad S, Abid NB, Kim MO. Oral administration of alpha linoleic acid rescues Aβ-Induced glia-mediated neuroinflammation and cognitive dysfunction in C57BL/6N mice. Cells. 2020; 9:667.
49. Silva YP, Bernardi A, Frozza RL. The role of short-chain fatty acids from gut microbiota in gut-brain communication. Front Endocrinol (Lausanne). 2020; 11:25.
50. Ebanks JP, Wickett RR, Boissy RE. Mechanisms regulating skin pigmentation: the rise and fall of complexion coloration. Int J Mol Sci. 2009; 10:4066-4087.
51. Ramsden CA, Riley PA. Tyrosinase: the four oxidation states of the active site and their relevance to enzymatic activation, oxidation and inactivation. Bioorg Med Chem. 2014; 22:2388-2395.
52. Yamaguchi Y, Brenner M, Hearing VJ. The regulation of skin pigmentation. J Biol Chem. 2007; 282:27557-27561.
53. Feng T, Hu Z, Song S, Yao L, Sun M, Zhu X, Lu J. The antioxidant and tyrosinase inhibition properties of essential oil from the peel of Chinese *Torreya grandis* Fort. RSC Adv. 2019; 9:42360-42366.
54. Zolghadri S, Bahrami A, Hassan Khan MT, Munoz-Munoz J, Garcia-Molina F, Garcia-Canovas F, Saboury AA. A comprehensive review on tyrosinase inhibitors. J Enzyme Inhib Med Chem. 2019; 34:279-309.
55. Wang X, Guo R, Yu Z, Zikela L, Li J, Li S, Han Q. *Torreya grandis* kernel oil alleviates loperamide-induced slow transit constipation *via* up-regulating the colonic expressions of Occludin/Claudin-1/ZO-1 and 5-HT3R/5-HT4R in BALB/c mice. Mol Nutr Food Res. 2024; 68:e2300615.
56. Chen Z, Ni Z, Mo R., Zhong D, Tang F. Comprehensive evaluation on quality of oils from seven kinds of woody oilcrops. China Oils Fats. 2018; 43:80-85.
57. Wu F, Han Q, Yu Y, Ni S. GC-MS analysis of fatty acids from *Torreya grandis* and *Camellia oleifera* seed. Chin Wild Plant Res. 2014; 33:36-39.
58. Ni Q, Gao Q, Yu W, Liu X, Xu G, Zhang Y. Supercritical carbon dioxide extraction of oils from two *Torreya grandis* varieties seeds and their physicochemical and antioxidant properties. LWT Food Sci Technol. 2015; 60:1226-1234.

Received September 4, 2025; Revised October 14, 2025; Accepted October 18, 2025.

**Address correspondence to:*
Chuanyin Shi and Yan Sun, Shanghai Cell Therapy Group Co., Ltd., Shanghai, China.
E-mail: shicy@shcell.com (C. Shi), suny@shcell.com (Y. Sun)

Released online in J-STAGE as advance publication October 25, 2025.