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Comprehensive Review of Bioactive Compounds in Loquat and Their Pharmacological Mechanisms

Xiuying Zhao
Traditional Chinese Medicine Research Center, Cuixi Academy of Biotechnology, Zhuji, 311800, Zhejiang, China
Corresponding email: xiuying.zhao@cuixi.org

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Abstract Loquat (*Eriobotrya japonica* Lindl.) is a subtropical fruit tree with significant medicinal value that has been widely used in traditional Chinese medicine throughout history. Various parts of the loquat plant, including its leaves and fruits, contain numerous bioactive compounds that exhibit a wide range of pharmacological activities. This study comprehensively summarizes the bioactive compounds found in loquat and elucidates their pharmacological mechanisms. Research indicates that the main bioactive compounds in loquat include phenolics, terpenes, kaempferol, ursolic acid, oleanolic acid, and quercetin, which possess strong antioxidant, anti-inflammatory, antidiabetic, antitumor, and antibacterial properties. The bioactive compounds in loquat can improve conditions such as diabetes, non-alcoholic fatty liver disease (NAFLD), and hyperlipidemia by inhibiting cytochrome P450 2E1, reducing oxidative stress, and regulating metabolic pathways. Additionally, studies have found that loquat leaves and fruits have high antioxidant capacities, which are closely related to their phenolic content. These findings highlight the potential of loquat as a source of bioactive compounds with significant health benefits. Further research into the bioavailability, metabolism, and toxicity of these compounds is crucial for fully realizing their therapeutic potential.

Keywords Loquat (*Eriobotrya japonica* Lindl.); Bioactive compounds; Phenolics; Terpenes; Pharmacological mechanisms; Traditional medicine

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1 Introduction

Loquat (*Eriobotrya japonica* Lindl.) is a subtropical evergreen tree native to China and widely cultivated in various regions, including the Mediterranean (Liu et al., 2016; Khouya et al., 2022). Loquat is renowned for its small, round fruits that are sweet and tangy, rich in vitamins and minerals, as well as its large, glossy leaves (Dhiman et al., 2021). The leaves of the loquat tree have a long history of use in traditional medicine. And the fruits are typically consumed fresh but can also be processed into products such as jams and jellies.

In traditional medicine, loquat is highly valued for its various therapeutic effects. The leaves, seeds, and fruits of the loquat are used in different forms, such as tea, syrup, and poultices, to treat respiratory ailments, digestive issues, and skin diseases (Liu et al., 2016; Fu et al., 2020). Traditional Chinese medicine particularly emphasizes the benefits of loquat leaves, which are effective in relieving coughs, reducing phlegm, and soothing the throat. The medicinal use of loquat is not limited to China; for instance, in Morocco, loquat leaves are traditionally used to manage diabetes and its complications (Khouya et al., 2022).

Bioactive compounds are naturally occurring chemical constituents in plants that have biological activity in the body. These compounds are significant because they can influence health positively by providing antioxidant, anti-inflammatory, and other therapeutic effects (Liu et al., 2016). In loquat, bioactive compounds such as phenolics, terpenoids, and flavonoids have been identified and studied for their health benefits (Liu et al., 2016; Dhiman et al., 2021). The general health benefits associated with bioactive compounds include the reduction of oxidative stress, improvement of metabolic functions, and enhancement of immune responses (Ibrahim et al., 2021). For instance, phenolic compounds in loquat have been shown to exhibit antidiabetic, antihyperlipidemic, and antioxidative properties (Liu et al., 2016; Khouya et al., 2022). These compounds can help manage blood sugar levels, reduce lipid profiles, and protect against cellular damage caused by free radicals.

This study provides a comprehensive analysis of the bioactive compounds found in loquat and their associated pharmacological mechanisms. It systematically reviews existing research findings, highlighting the health benefits and potential therapeutic applications of loquat-derived compounds. The study further emphasizes the significance of these compounds in both traditional medicine and modern pharmacology, offering valuable academic insights into the nutritional and medicinal value of loquat. This study leverages an in-depth understanding of the bioactivities and mechanisms of loquat to further showcase its potential as a functional food and natural therapy, inspiring future research advancements in this field.

2 Phytochemical Composition of Loquat

2.1 Bioactive compounds in loquat

Loquat (*Eriobotrya japonica* Lindl.) is rich in various bioactive compounds that confer its pharmacological properties. The fruits, leaves, and seeds of loquat contain high levels of vitamins, minerals, and phytochemicals. The main bioactive compounds identified in loquat include flavonoids, phenolic acids, triterpenes, vitamins, carotenoids, and polysaccharides (López-Lluch et al., 2020). Loquat leaves are particularly rich in flavonoids such as quercetin, kaempferol, and rutin, which exhibit strong antioxidant, anti-inflammatory, and anticancer activities. Phenolic acids, including chlorogenic acid and caffeic acid, also contribute to the antioxidant capacity of loquat and play a role in protecting cells from oxidative damage (de Almeida Lopes et al., 2018; López-Lluch et al., 2020; Dhiman et al., 2021).

Triterpenoids, another significant group of compounds found in loquat, include ursolic acid and oleanolic acid. These compounds have demonstrated anti-inflammatory, hepatoprotective, and anticancer effects. Vitamins, particularly vitamin C, are present in loquat fruits, enhancing its nutritional value and contributing to its overall antioxidant properties. Carotenoids, such as beta-carotene and lutein, are also present and play a role in eye health and immune function (Ahn and Kim, 2021). Polysaccharides in loquat have been studied for their immunomodulatory and antidiabetic effects, highlighting the broad spectrum of bioactive compounds in this versatile plant (Chen et al., 2021).

2.2 Identification and quantification of phytochemicals

The identification and quantification of phytochemicals in loquat have been extensively studied using various analytical techniques. For instance, Silva et al. (2020) analyzed the chemical composition of loquat leaves using paper spray mass spectrometry (PS-MS) and identified 49 compounds, including organic acids, phenolic acids, flavonoids, sugars, quinones, and terpenes. The study also explored the impact of different dehydration temperatures and extraction methods on the phenolic compounds in the extracts, as well as their antioxidant and antimicrobial activities. The results showed that ultrasonic ethanol extraction from loquat leaves dehydrated at 40 °C yielded the best results, demonstrating significant antioxidant and antimicrobial activities (Silva et al., 2020). Another study analyzed loquat leaf extracts collected from southern Tunisia using liquid chromatography-electrospray ionization-tandem mass spectrometry (LC–ESI–MS), revealing that different extraction methods significantly affected the phenolic acid and flavonoid content, as well as the antioxidant activity of the extracts. This study further confirmed the potential of loquat leaves in pharmaceutical and food applications (Yahia et al., 2020).

High-performance liquid chromatography (HPLC), ultra-performance liquid chromatography (UPLC), and high-resolution mass spectrometry (HRMS) have also been used to quantify phenolic compounds, flavonoids, and antioxidant activity in loquat leaves and fruits (Hasibuan et al., 2020; Yan et al., 2023). Yan et al. (2023) conducted a qualitative and quantitative analysis of 22 phenolic compounds and 2 terpene compounds in the peel and pulp of different loquat varieties using UPLC and HRMS. The study found that loquat peel extracts exhibited higher antioxidant capacity compared to pulp extracts. Additionally, the methanol extracts of loquat leaves, containing alkaloids, flavonoids, and steroids/terpenes, showed significant antioxidant activity.

2.3 Seasonal and geographical variation in phytochemical content

The phytochemical composition of loquat varies depending on seasonal and geographical factors. Studies have shown that the concentration of bioactive compounds in loquat fruit changes during different ripening stages and across various production locations. For instance, one study evaluated the bioactive compounds in loquat fruits during the ripening process from three different production areas in northeastern Peru. The results indicated significant differences in the total phenolic and flavonoid content among loquat fruits from different regions, with the highest levels found in ripe fruits. In some cases, the phenolic compound content in fruits from certain areas was up to five times higher in ripe fruits compared to unripe ones (Castillo-Chuquizuta et al., 2023). Another study assessed the dynamic changes in phytochemical composition and antioxidant activity in loquat fruits at different ripening stages. It was found that ripe loquat fruits had significantly higher levels of phenolic and flavonoid compounds than unripe fruits, particularly antioxidant components like chlorogenic acid, which were present in higher concentrations during the early stages of fruit development. The study also revealed significant differences in these compounds' levels depending on the growing location, indicating that geographical factors play a crucial role in the accumulation of bioactive compounds in loquat fruits (Zhang et al., 2023).

Additionally, the genotype, harvest date, and storage conditions of loquat significantly affect its phytochemical properties. Research has shown that different loquat varieties (such as 'Karantoki' and 'Morphitiki') exhibit significant variations in mechanical properties, storage performance, and phytochemical attributes (including free and bound phenolic compounds and antioxidant capacity) depending on the harvest date. Fruits harvested early displayed higher flesh firmness and phenolic content, while late-harvested fruits showed a significant decrease in titratable acidity and an increase in maturity index (SSC/TA) (Hadjipieri et al., 2020). The study also noted that the harvest date had no significant impact on bound phenolic content, but the contribution of bound phenolics to total phenolics varied between 21.6% and 37.5% under different varieties and storage conditions.

3 Pharmacological Mechanisms of Loquat Bioactive Compounds

3.1 Antioxidant activity

Loquat leaves contain various bioactive compounds, including flavonoids and sesquiterpene glycosides, which exhibit significant antioxidant properties. These compounds act by scavenging free radicals, reducing lipid peroxidation, and enhancing the activity of antioxidant enzymes such as superoxide dismutase (SOD) (Jian et al., 2018; Jian et al., 2020a; Chen et al., 2021). For instance, sesquiterpene glycoside 3 (SG3) from loquat leaves has been shown to alleviate oxidative stress by inhibiting cytochrome P450 2E1 (CYP2E1) and enhancing SOD activity (Figure 1) (Chen et al., 2021). Similarly, total flavonoids (TF) from loquat leaves inhibit oxidative stress by downregulating CYP2E1 and upregulating SOD-2 expression (Jian et al., 2020a).

In vitro studies have demonstrated that loquat leaf extracts can significantly reduce oxidative stress markers in cell models. For example, SG3 and total sesquiterpene glycosides (TSG) from loquat leaves were found to decrease malondialdehyde (MDA) levels and increase SOD activity in HepG2 cells (Jian et al., 2018; Chen et al., 2021). *In vivo* studies using animal models, such as db/db mice and cigarette smoke (CS)-induced COPD mice, have shown that loquat leaf extracts can reduce oxidative stress and improve antioxidant enzyme activities (Jian et al., 2020a; 2020b; Chen et al., 2021). These findings suggest that loquat bioactive compounds have potent antioxidant effects both *in vitro* and *in vivo*.

3.2 Anti-inflammatory effects

Loquat leaves contain bioactive compounds such as triterpene acids and flavonoids that exhibit strong anti-inflammatory properties. These compounds act by inhibiting pro-inflammatory cytokines and signaling pathways. For instance, triterpene acids (TAs) from loquat leaves suppress the generation of pro-inflammatory cytokines like interleukin 1β (IL-1β), IL-6, and tumor necrosis factor α (TNF-α) by regulating AMP-activated protein kinase (AMPK)/nuclear factor erythroid-2-related factor-2 (Nrf2) and nuclear factor kappa B (NFκB) pathways (Figure 2). Similarly, TF from loquat leaves inhibit inflammation by downregulating transient receptor potential vanilloid 1 (TRPV1) and NFκB signaling pathways (Jian et al., 2020b).

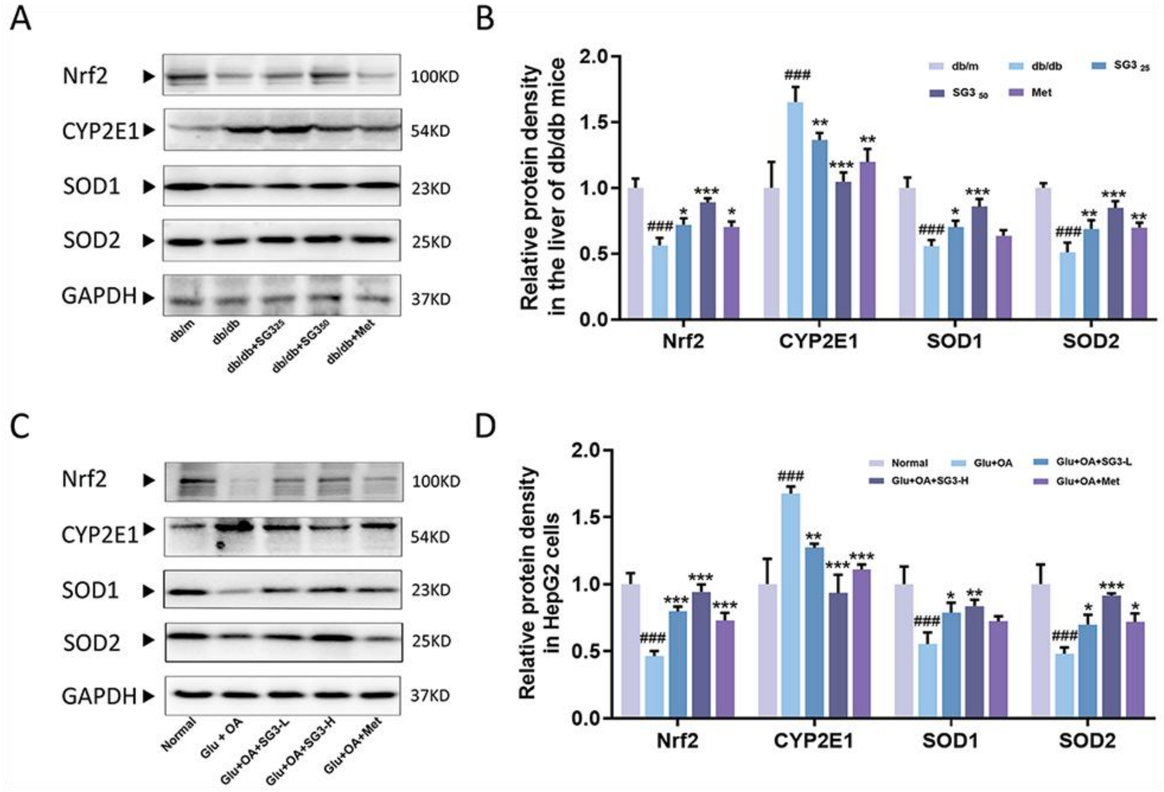

Figure 1 SG3 suppressed oxidative stress via modulating Nrf2, CYP2E1, SOD1, and SOD2 in diabetic db/db mice and HepG2 cells treated with high glucose in combination with OA (Adopted from Chen et al., 2021)

Image caption: Figures A and C show that SG3 treatment significantly increased the expression of nuclear factor Nrf2, superoxide dismutase 1 (SOD1), and superoxide dismutase 2 (SOD2), while reducing the expression of cytochrome P450 2E1 (CYP2E1). The quantitative analysis in Figures B and D further validated these changes in protein expression. These results indicate that SG3 exerts its antioxidant effects by modulating key proteins such as Nrf2 and CYP2E1, providing effective protection in diabetes-related non-alcoholic fatty liver disease (NAFLD) and supporting its potential application in antioxidant therapy (Adapted from Chen et al., 2021)

Clinical studies on the anti-inflammatory effects of loquat bioactive compounds are limited, but preclinical studies provide promising results. In CS-induced COPD mouse models, TAs and TF from loquat leaves significantly reduced lung inflammation and histological changes (Jian et al., 2020a; 2020b). These findings suggest potential therapeutic applications of loquat bioactive compounds in treating inflammatory diseases such as COPD and other chronic inflammatory conditions.

3.3 Anticancer properties

Loquat leaves contain bioactive compounds with potential anticancer properties, including pentacyclic triterpenes and flavonoids. These compounds exert their anticancer effects by inducing apoptosis, inhibiting cell proliferation, and modulating signaling pathways involved in cancer progression. For example, pentacyclic triterpenes such as oleanolic acid (OA) inhibit the differentiation of T helper 17 (Th17) cells and reduce the expression of pro-inflammatory cytokines, which are implicated in cancer development (Zhou et al., 2019). Additionally, flavonoids from loquat leaves have been shown to inhibit oxidative stress and inflammation, which are key factors in cancer progression (Jian et al., 2020a).

Preclinical studies have demonstrated the anticancer potential of loquat bioactive compounds. For instance, OA from loquat leaves significantly reduced serum anti-dsDNA antibody levels and alleviated renal pathological damage in lupus nephritis (LN) mouse models, indicating its potential application in cancer therapy (Zhou et al., 2019). Although clinical studies are still needed, these preclinical findings suggest that loquat bioactive compounds could be promising candidates for anticancer therapies.

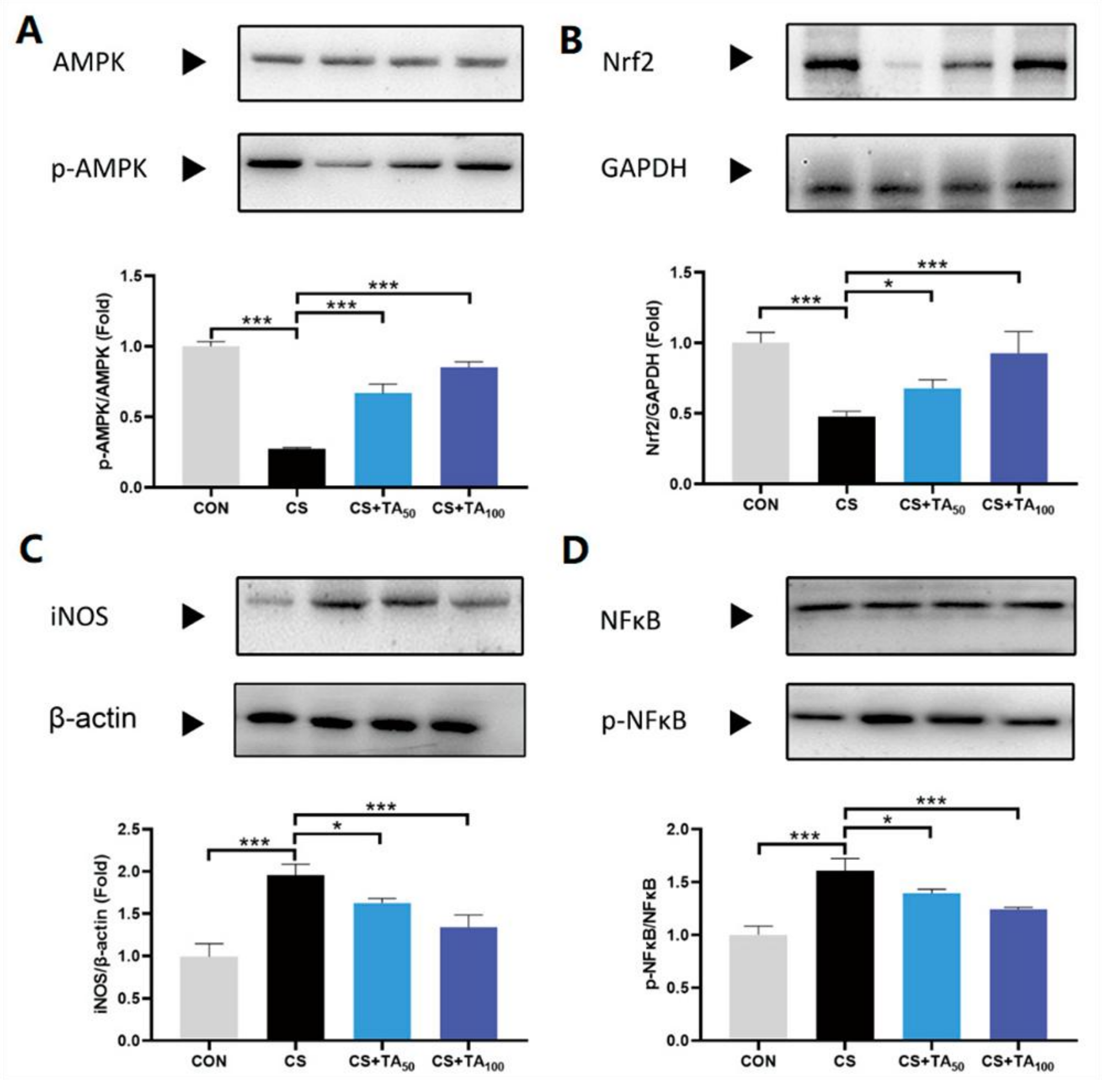

Figure 2 Effects of TA supplementation on AMPK and NFκB signaling pathways in the lungs of CS-exposed induced-COPD mice. Expression of (A) AMPK and p-AMPK, (B) Nrf2, (C) iNOS, and (D) NFκB and p-NFκB in lung tissues from each group were measured by Western blot. * $p < 0.05$, *** $p < 0.001$ (Adopted from Jian et al., 2020b)

Image caption: The figure demonstrates the effects of triterpene acids (TA) on the AMPK/Nrf2 and NFκB/iNOS signaling pathways in the lung tissues of mice with cigarette smoke-induced chronic obstructive pulmonary disease (COPD). The figure shows that the phosphorylation level of AMPK and the expression of Nrf2 in the lung tissues of the COPD model group significantly decreased, while the phosphorylation of NFκB and the expression of iNOS significantly increased. After TA treatment, the phosphorylation of AMPK and the expression of Nrf2 were significantly restored, while the phosphorylation of NFκB and the expression of iNOS were significantly reduced. The results indicate that TA inhibits inflammation and oxidative stress by modulating these key signaling pathways, revealing its potential mechanism in COPD treatment (Adapted from Jian et al., 2020b)

4 Health Benefits and Therapeutic Applications

4.1 Cardiovascular health

Loquat (*Eriobotrya japonica*) contains several bioactive compounds that contribute to cardiovascular health. These include flavonoids, carotenoids, and phenolic acids, which are known for their antioxidant properties (de Almeida Lopes et al., 2018; Silva et al., 2020; Dhiman et al., 2021). The presence of these compounds helps in reducing oxidative stress, which is a significant factor in cardiovascular diseases.

Studies have shown that the antioxidant properties of loquat can help in reducing low-density lipoprotein (LDL) oxidation, a key process in the development of atherosclerosis (Silva et al., 2020; Dhiman et al., 2021). Additionally, the anti-inflammatory properties of loquat compounds such as kaempferol and quercetin contribute to cardiovascular health by reducing inflammation in blood vessels (de Almeida Lopes et al., 2018; Dhiman et al., 2021). These mechanisms collectively help in maintaining heart health and preventing cardiovascular diseases.

4.2 Metabolic disorders

Loquat has been traditionally used in Chinese medicine for managing diabetes and obesity. The fruit and leaves of loquat contain bioactive compounds such as sesquiterpene glycosides, triterpenoids, and flavonoids, which have shown potential in regulating blood glucose levels and reducing body weight (Jian et al., 2018; de Almeida Lopes et al., 2018; Ibrahim, 2021). Studies have found that the total sesquiterpene glycosides (TSG) in loquat leaves significantly improve insulin resistance and metabolic disorders induced by a high-fat diet through the regulation of the IRS-1/GLUT4, TRPV1, and SIRT6/Nrf2 signaling pathways. Additionally, these compounds help reduce body weight, lower blood glucose levels, and improve liver damage (Wu et al., 2021).

Research indicates that loquat extracts can improve insulin sensitivity and reduce blood glucose levels by enhancing the activity of insulin receptors and glucose transporters (Jian et al., 2018; Ibrahim, 2021). Additionally, the anti-obesity effects are attributed to the inhibition of lipid accumulation and the promotion of lipid metabolism, as demonstrated in studies involving loquat leaf extracts (de Almeida Lopes et al., 2018). These effects are mediated through the downregulation of enzymes involved in lipid synthesis and the upregulation of those involved in lipid breakdown.

4.3 Neuroprotective effects

Loquat contains several bioactive compounds, including ursolic acid, oleanolic acid, and various flavonoids, which have been shown to possess neuroprotective properties (Silva et al., 2020; Dhiman et al., 2021; Castillo-Chuquizuta et al., 2023). These compounds help in protecting the brain from oxidative stress and inflammation, which are common in neurodegenerative diseases.

The neuroprotective effects of loquat are primarily due to its antioxidant and anti-inflammatory properties. Studies have shown that loquat extracts can reduce the levels of reactive oxygen species (ROS) and inhibit the activity of pro-inflammatory cytokines in the brain (Silva et al., 2020; Dhiman et al., 2021; Castillo-Chuquizuta et al., 2023). Additionally, the presence of compounds like quercetin and kaempferol helps in enhancing cognitive functions and protecting against neuronal damage (de Almeida Lopes et al., 2018; Dhiman et al., 2021). These mechanisms make loquat a potential therapeutic agent for neurodegenerative diseases such as Alzheimer's and Parkinson's.

5 Traditional and Modern Uses of Loquat

5.1 Historical usage in traditional medicine

Loquat (*Eriobotrya japonica*) has been utilized in traditional medicine for centuries, particularly in China and other parts of Asia. The leaves, fruits, and flowers of the loquat tree have been employed in various formulations to treat a range of ailments. Traditional Chinese medicine has extensively used loquat leaves to alleviate coughs and respiratory conditions such as chronic bronchitis and asthma (Su et al., 2021). Additionally, loquat leaves have been used in Moroccan traditional medicine to manage diabetes and its complications (Khouya et al., 2022). The historical use of loquat in these traditional systems underscores its significance in ethnomedicine.

Ethnobotanical studies reveal that loquat has been a staple in folk medicine across different cultures. In African traditional medicine, loquat extracts have been noted for their beneficial health effects, including antifungal properties against *Cryptococcus neoformans* (Bisso et al., 2022). The plant's widespread use in various traditional medical systems highlights its versatility and the rich ethnobotanical knowledge surrounding its applications. The bioactive compounds in loquat, such as sesquiterpene glycosides, have been identified as key contributors to its medicinal properties, particularly in managing hyperglycemia and inflammation (Wu et al., 2022).

5.2 Modern pharmaceutical applications

In modern times, the pharmacological potential of loquat has been harnessed in the development of nutraceuticals and functional foods. The leaves of loquat are rich in polyphenols and other bioactive compounds, which have been shown to possess antioxidant, anti-inflammatory, and antimicrobial properties (Silva et al., 2020). These properties make loquat an attractive candidate for inclusion in health-promoting products. For instance, loquat flower water extracts have been evaluated for their potential use in tea, demonstrating significant antioxidant and anti-inflammatory activities (Chen et al., 2023). Such developments indicate the growing interest in loquat as a functional ingredient in the food and pharmaceutical industries.

The transition from traditional use to modern pharmaceutical applications has also seen loquat being subjected to clinical trials to validate its efficacy. Studies have shown that loquat leaf extracts can ameliorate hyperglycemia, insulin resistance, and hyperlipidemia in animal models, suggesting potential benefits for managing diabetes (Khouya et al., 2022). Additionally, the antifungal activity of loquat extracts against clinical isolates of *Cryptococcus neoformans* points to its potential in developing new antifungal agents (Bisso et al., 2022). These findings provide a theoretical foundation for the commercialization of loquat-based products. Currently, there are dietary supplements and herbal medicines on the market that are derived from loquat.

6 Case Studies

6.1 Protective effects of loquat extracts on alcohol-induced liver injury

In recent years, with the increase in global alcohol consumption, alcohol-induced liver injury (ALI) has become a serious public health issue, leading to numerous liver diseases and related deaths. Traditional treatments have limited effectiveness and are often accompanied by significant side effects, making the search for low-toxicity, highly effective natural antioxidants a key research focus for the prevention and treatment of ALI. Loquat fruit, rich in bioactive compounds such as phenolics and terpenoids, has shown significant antioxidant and anti-inflammatory effects, making it a potential source of natural antioxidants (Li et al., 2019; Yan et al., 2023).

Yan et al. (2023) conducted a comprehensive analysis of six loquat varieties, comparing the distribution of their phenolic and terpenoid compounds and evaluating their antioxidant capacities through various in vitro and in vivo models. The results indicated that the concentrations of phenolics and terpenoids in loquat peels were significantly higher than in the flesh, endowing the peel with stronger antioxidant properties. The study further revealed that loquat extracts have a significant protective effect on liver cells against ethanol-induced oxidative damage, with loquat peel extracts notably enhancing cell viability and activating antioxidant enzymes, indicating their potential therapeutic role in preventing alcohol-related liver injury (Figure 3). These findings highlight the important value of loquat as a natural antioxidant and provide a scientific basis for developing health products aimed at alleviating alcohol-induced liver damage.

6.2 The multifaceted protective effects of loquat extract on diabetes-associated fatty liver disease

Non-alcoholic fatty liver disease (NAFLD) is a common liver disease closely associated with metabolic syndrome, often occurring alongside type 2 diabetes mellitus (T2DM). Plant extracts, as natural products, have garnered widespread attention for their role in treating metabolic syndrome. Loquat leaves, rich in bioactive compounds, have been found to possess potential antioxidant, anti-inflammatory, and metabolic improvement properties.

Chen et al. (2021) explored the effects of a novel sesquiterpene glycoside (SG3) from loquat leaves on T2DM mice with NAFLD. The study results showed that SG3 significantly improved insulin resistance, reduced oxidative stress, alleviated inflammation, and modulated gut microbiota composition. In the diabetic mouse model, SG3 not only effectively reduced body weight and liver lipid accumulation but also significantly decreased levels of inflammatory factors (Figure 4). Additionally, SG3 exhibited multifaceted protective effects by regulating insulin signaling pathways, inhibiting CYP2E1/NLRP3 pathways, and improving gut microbial communities.

The study revealed that SG3 provides protective effects against T2DM-associated NAFLD through multiple mechanisms. It not only inhibits key inflammatory pathways and oxidative stress responses but also restores gut microbiota balance, ultimately reducing liver damage and metabolic disorders in diabetic mice. This research provides a scientific basis for new therapeutic strategies for NAFLD, suggesting that SG3 could be a potential therapeutic natural product for liver diseases induced by diabetes (Chen et al., 2021).

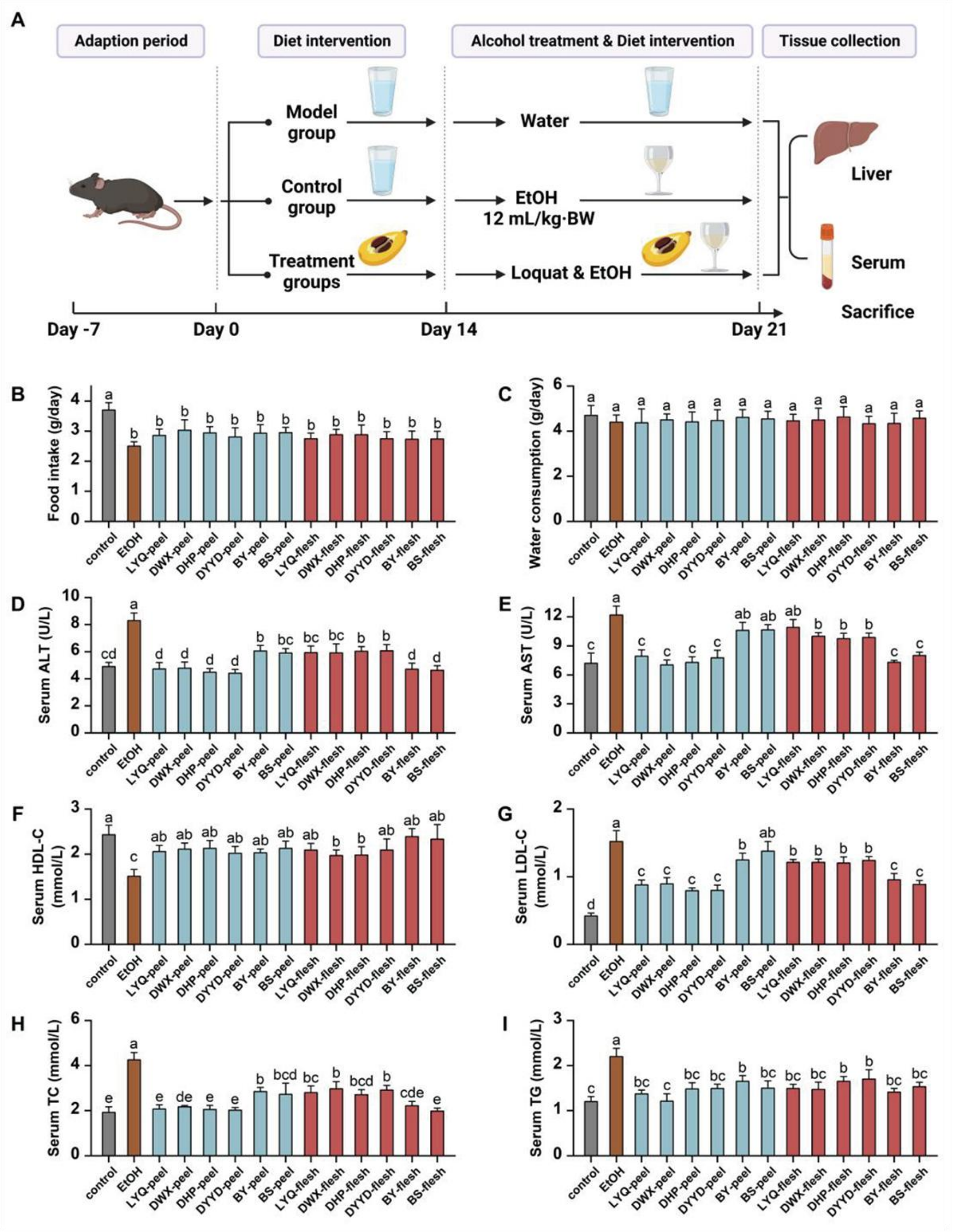

Figure 3 Effects of loquat extracts on serum markers of C57/BL6 mice fed with alcohol (Adopted from Yan et al., 2023)

Image caption: (A) Experimental schematic; (B) average food intake amount; (C) water consumption amount; (D) serum alanine aminotransferase (ALT) activity; (E) serum aspartate aminotransferase (AST) activity; (F) serum high-density lipoprotein cholesterol (HDL-C) level; (G) serum low-density lipoprotein cholesterol (LDL-C) level; (H) serum total cholesterol (TC) level; (I) serum triglyceride (TG) levels. EtOH, ethanol; BW, body weight; columns with different letters indicate significant difference at $p < 0.05$. The figure shows that loquat extracts significantly reduced the ethanol-induced elevation of ALT and AST levels and improved lipid metabolism disorders, with the effects being more pronounced in the peel extracts. The results reveal the protective role of loquat extracts in alleviating alcohol-induced liver damage and regulating lipid levels, validating their potential application in the prevention and treatment of alcoholic liver disease (Adapted from Yan et al., 2023)

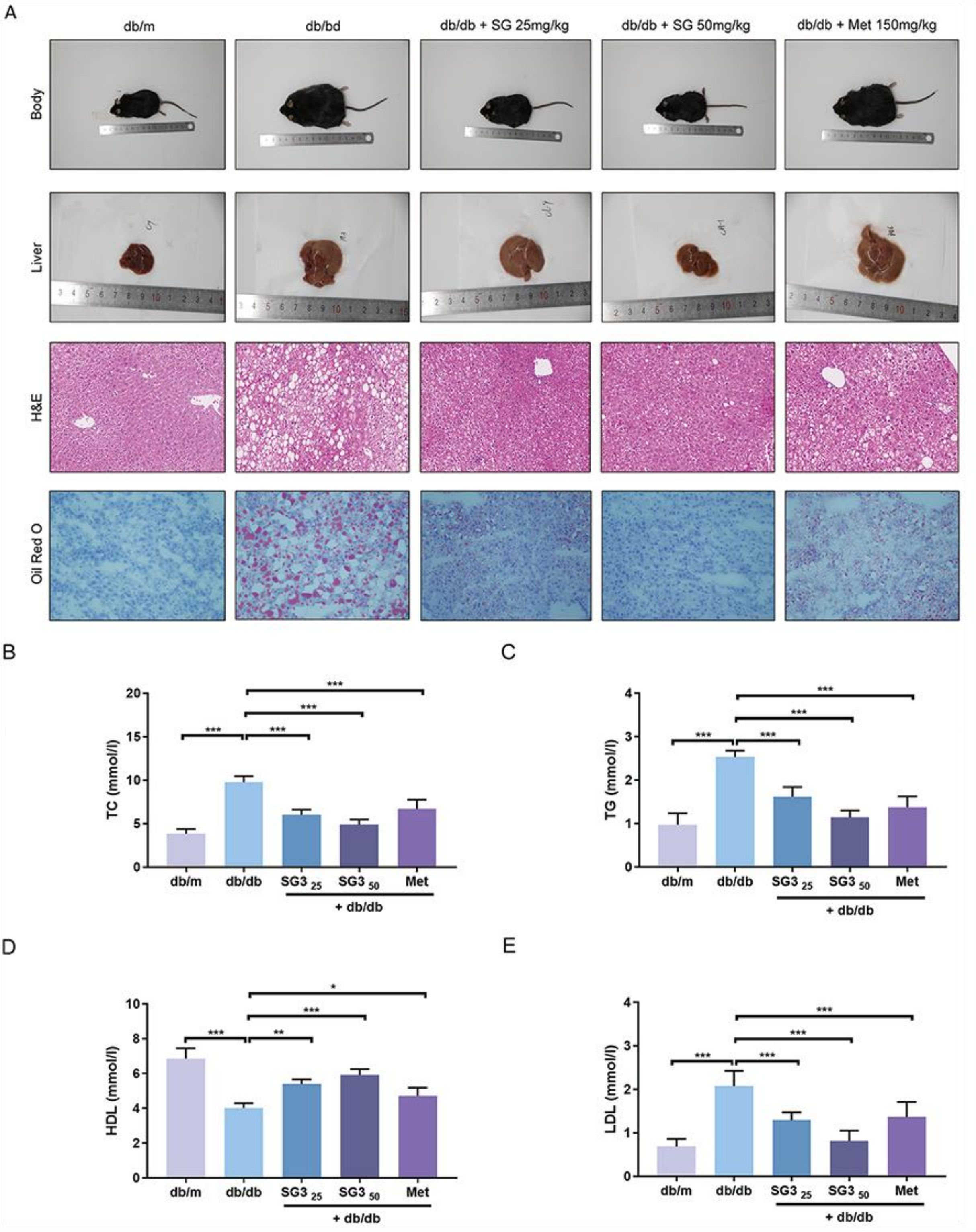

Figure 4 Effects of SG3 (25 and 50 mg/kg/day) on liver pathological changes and serum steatosis metabolism in diabetic db/db mice; 150 mg/kg of Met was used as a positive control (Adopted from Chen et al., 2021)

Image caption: Figure A shows the appearance of mouse liver, H&E staining, and Oil Red O staining results, indicating that SG3 treatment significantly reduced liver steatosis and inflammatory cell infiltration, thereby improving liver tissue structure. Figures B-E demonstrate the effects of SG3 on serum total cholesterol (TC), triglycerides (TG), high-density lipoprotein (HDL), and low-density lipoprotein (LDL) levels, showing that SG3 lowered TC, TG, and LDL levels while increasing HDL levels. These results confirm the efficacy of SG3 in alleviating fatty liver and regulating lipid metabolism, supporting its potential as a therapeutic approach for diabetes-related NAFLD (Adapted from Chen et al., 2021)

7 Genetic Studies and Breeding

7.1 Genetic diversity and germplasm

The genetic diversity and germplasm of loquat (*Eriobotrya japonica*) have been extensively studied to understand the evolutionary history and domestication processes of this fruit. A high-quality chromosome-level genome assembly of wild loquat has revealed significant genetic resources that are crucial for breeding improved varieties. Comparative genomics analysis indicates that loquat shares a common ancestor with apple and pear, and a recent whole-genome duplication event occurred before its divergence. The genome resequencing of loquat germplasms has shown distinct classifications between wild and cultivated groups, with commercial cultivars experiencing allelic admixture. Wild loquats exhibit higher genetic diversity and fewer selected genomic regions compared to cultivated loquats, which have undergone selective sweeps related to fruit quality, size, and flesh color during domestication (Jing et al., 2022).

7.2 Breeding for bioactive compounds

Breeding efforts in loquat have focused on enhancing bioactive compounds, which are essential for the fruit's nutritional and pharmacological properties. For instance, the dynamic changes in organic acid (OA) content during fruit development and ripening have been studied in common loquat and its interspecific hybrid. The predominant OA compound, malic acid, along with other acids like succinic and tartaric acid, are regulated by key enzymes such as PEPC and NAD-MDH. These findings provide a fundamental basis for future breeding programs aimed at improving loquat's nutritional quality (Deng et al., 2023).

Additionally, Wang et al. (2021) developed a qPCR system for detecting the genotype of polyploid loquat, particularly focusing on the genotype related to flesh color. This method, by analyzing the DNA ratios of different genotypes, enables accurate identification of tetraploid and triploid loquat genotypes, providing a powerful tool for selecting superior breeding lines. In another study, Wen et al. (2020) developed a detection method combining simple sequence repeat (SSR) markers with qPCR, known as SSR-qPCR, for detecting the aneuploid molecular karyotype of loquat. This method effectively identifies and constructs the molecular karyotype of aneuploid individuals, offering a new tool for genetic research in polyploid plants.

7.3 Future directions in genetic research

Future genetic research in loquat should focus on several key areas to further enhance the understanding and improvement of this fruit. One promising direction is the exploration of the molecular mechanisms underlying heterosis in triploid loquats. Studies have shown that triploid loquats exhibit greater growth vigor compared to diploids and tetraploids, potentially due to altered circadian rhythms. The expression levels of circadian clock genes and their output genes in triploid loquats have been found to be higher than in their parental types, suggesting a link between circadian rhythms and heterosis (Liu et al., 2019).

Another important area is the identification and functional analysis of genes involved in the biosynthesis of bioactive compounds. For example, the transcriptional activator EjMYB4 has been identified as a key regulator of lignin biosynthesis in loquat, providing insights into the genetic control of this important structural compound (Zhang et al., 2018). Continued research in these areas will be essential for developing new loquat varieties with enhanced nutritional and pharmacological properties.

8 Challenges and Future Perspectives

8.1 Research gaps

Despite the promising pharmacological activities of bioactive compounds in loquat, several research gaps remain. One significant gap is the limited understanding of the specific mechanisms through which these compounds exert their effects. While studies have demonstrated the anti-tumor, antibacterial, anti-inflammatory, and antioxidant activities of loquat extracts, the precise molecular pathways involved are not fully elucidated (Silva et al., 2020; Xiao et al., 2023). Additionally, there is a lack of comprehensive clinical trials to validate the efficacy and safety of these bioactive compounds in human populations. Most of the current evidence is derived from in vitro and animal studies, which may not fully translate to human health outcomes (Giordano et al., 2021; Shrinet et al., 2021).

8.2 Technological and methodological challenges

The extraction and characterization of bioactive compounds from loquat present several technological and methodological challenges. Traditional extraction methods, such as liquid-liquid and solid-liquid extraction, often result in low yields and may not efficiently isolate all active components (Shrinet et al., 2021). Advanced techniques like pressurized-liquid extraction, subcritical and supercritical extractions, and microwave- and ultrasound-assisted extractions have been developed, but their application to loquat compounds is still in its infancy (Silva et al., 2020; Shrinet et al., 2021). Furthermore, the stability of these bioactive compounds during extraction and processing is a concern, as they are susceptible to degradation, volatilization, and oxidation (Tavares et al., 2022). This instability can affect the efficacy of the compounds and complicate their use in pharmaceutical and nutraceutical applications.

8.3 Future research directions

Future research should focus on several key areas to address the existing challenges and gaps. More detailed studies are needed to elucidate the molecular mechanisms of action of loquat bioactive compounds. This could involve advanced techniques such as omics technologies and molecular docking studies to identify target pathways and interactions (Dehelean et al., 2021; Xiao et al., 2023). Carefully designed clinical trials to evaluate the therapeutic potential and safety of these compounds in humans are also a future research direction. Such studies should include diverse populations and consider long-term effects (Giordano et al., 2021; Shrinet et al., 2021).

Additionally, improving extraction and stabilization techniques will be crucial. Research should explore the optimization of advanced extraction methods and the development of novel encapsulation techniques to protect bioactive compounds from degradation (Fu et al., 2019; Tavares et al., 2022). Interdisciplinary collaborations between botanists, pharmacologists, and technologists will be essential to advance the understanding and application of loquat bioactive compounds in medicine and industry. By addressing these research gaps and technological challenges, the full potential of loquat bioactive compounds can be realized, providing theoretical basic for new therapeutic agents and functional products.

9 Concluding Remarks

The comprehensive review of bioactive compounds in loquat (*Eriobotrya japonica*) and their pharmacological mechanisms has revealed several significant findings. Loquat leaves contain a variety of bioactive compounds, including sesquiterpene glycosides, phenolic acids, flavonoids, and polysaccharides, which exhibit a range of pharmacological activities. These compounds have demonstrated anti-tumor, antibacterial, anti-inflammatory, and antioxidant properties. Specifically, sesquiterpene glycosides such as SG1 and SG3 have shown promising effects in alleviating metabolic syndromes like non-alcoholic fatty liver disease (NAFLD) and type 2 diabetes mellitus (T2DM) by improving insulin resistance, reducing oxidative stress, and modulating gut microbiota composition. Additionally, loquat leaf extracts have been found to possess significant antifungal activity against Cryptococcus neoformans and other pathogens, highlighting their potential in managing infectious diseases.

The bioactive compounds in loquat leaves offer substantial potential for health and disease management. Their antioxidant and anti-inflammatory properties can be harnessed to develop therapeutic agents for chronic diseases such as diabetes, NAFLD, and cardiovascular diseases. The ability of these compounds to modulate gut microbiota further underscores their potential in managing metabolic disorders and enhancing overall gut health. Moreover, the antimicrobial and antifungal activities of loquat leaf extracts suggest their use as natural alternatives or adjuncts to conventional antimicrobial therapies, particularly in the treatment of infections caused by resistant pathogens. The diverse pharmacological activities of loquat bioactive compounds also open avenues for their application in functional foods and nutraceuticals, providing a natural means to promote health and prevent disease.

In conclusion, the bioactive compounds found in loquat leaves exhibit a wide range of pharmacological activities that hold promise for the development of novel therapeutic agents and health-promoting products. Future research should focus on elucidating the precise mechanisms of action of these compounds, optimizing extraction and purification methods, and conducting clinical trials to validate their efficacy and safety in humans. The integration of loquat bioactive compounds into pharmaceutical and nutraceutical formulations could significantly contribute to the management of chronic diseases and the enhancement of overall health. Continued exploration and utilization of these natural compounds will provide references for innovative and sustainable health solutions.

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Conflict of Interest Disclosure

The author affirms that this research was conducted without any commercial or financial relationships that could be construed as a potential conflict of interest.

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