Minireview Article

Collagen, Pulmonary Fibrosis, and Aging: The Therapeutic Promise of Goji Berry in Reducing Fibrotic Damage

ABSTRACT

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| **Introduction:** Pulmonary fibrosis is a progressive lung disorder marked by collagen overaccumulation and tissue remodeling, commonly associated with aging and oxidative stress. Natural antioxidants such as Goji berry (*Lycium barbarum*) have shown potential in counteracting oxidative lung damage due to their rich content of bioactive compounds, particularly Lycium barbarum polysaccharides (LBP).**Methods:** A narrative literature review was conducted through searches on databases including Google Scholar, PubMed, ScienceDirect, and SpringerLink. Studies published from 2004 to 2024 were screened using predefined criteria, focusing on in vivo models that evaluated the effects of Goji berry or LBP on pulmonary oxidative injury, inflammation, and fibrosis.**Results and Discussion:** Three eligible studies were analyzed. In aged mice, LBP (200–400 mg/kg/day) enhanced lung antioxidant enzyme levels and reduced markers of oxidative damage. In exercise-induced systemic oxidative models, LBP (up to 300 mg/kg/day) improved SOD and GPx levels and lowered MDA. Most notably, in a cigarette smoke-induced lung injury model, LBP (100–200 mg/kg/day) reduced TNF-α, IL-6, and IL-8, inhibited NF-κB signaling, and improved lung histology. Across studies, LBP consistently demonstrated antioxidant and anti-inflammatory effects that mitigated pulmonary fibrotic changes.**Conclusion:** Goji berry, via its polysaccharide content, shows strong promise as a natural therapeutic agent against pulmonary fibrosis. By modulating oxidative and inflammatory pathways, it offers a potential strategy to reduce lung damage related to aging or environmental exposure. Further clinical validation is recommended. |

*Keywords: Goji berry, Lycium barbarum, pulmonary fibrosis, oxidative stress, antioxidant therapy*

1. INTRODUCTION

Pulmonary fibrosis is a progressive and often irreversible pathological condition characterized by the excessive accumulation of extracellular matrix (ECM) components, especially collagen, within the lung parenchyma. This remodeling of the alveolar architecture disrupts normal gas exchange and significantly compromises respiratory function, ultimately leading to respiratory failure and death in severe cases (Wynn and Ramalingam, 2012; Barratt et al*.*, 2018). As the global population ages, the incidence of age-associated pulmonary fibrosis is expected to rise, further compounding the public health burden (Kumar et al., 2024).

Aging is intrinsically linked with a decline in regenerative capacity and increased oxidative stress, which accelerates degenerative changes in pulmonary tissue (Wang et al., 2021). Cellular senescence, mitochondrial dysfunction, chronic inflammation, and telomere attrition have all been implicated in the onset and progression of pulmonary fibrosis in elderly individuals (López-Otín et al*.*, 2013; Guzonjić et al*.*, 2022; Zeng et al*.*, 2024). Notably, reactive oxygen species (ROS) and lipid peroxidation products such as malondialdehyde (MDA) have emerged as key contributors to epithelial injury and fibrogenesis (Cheresh et al*.*, 2013; Ayala, Muñoz and Argüelles, 2014).

Cigarette smoke exposure exacerbates this process through the sustained production of ROS and pro-inflammatory cytokines, leading to persistent oxidative stress, epithelial cell apoptosis, and collagen deposition (Kim, Suh and Mun, 2004; Yao et al*.*, 2008; Coleman-Belin et al., 2023). The central role of oxidative damage in driving pulmonary fibrosis underscores the therapeutic value of antioxidants in mitigating disease progression (Sharma & Wairkar, 2024).

In recent years, growing attention has been given to *Lycium barbarum*, commonly known as Goji berry, due to its potent antioxidant, anti-inflammatory, and immunomodulatory properties (Li & Kan, 2017). Rich in polysaccharides (LBP), flavonoids, carotenoids, and phenolic compounds, Goji berry exhibits biological activities that target multiple pathogenic pathways in lung fibrosis, including ROS neutralization, inhibition of NF-κB signaling, and attenuation of collagen deposition (Niu et al*.*, 2008; Ma et al*.*, 2019).

This review explores the interconnected roles of collagen accumulation, pulmonary fibrosis, and aging, while highlighting the therapeutic promise of Goji berry as a natural intervention in reducing fibrotic lung damage. Understanding the molecular interactions between oxidative stress, aging, and fibrogenesis may pave the way for novel strategies in anti-aging and pulmonary medicine.

The beneficial effects of *Lycium barbarum*, which include antioxidant, anti-aging, anticancer, and anti-inflammatory properties, are visually summarized in Figure 1.

Fig. 1. Health Effects of *Lycium barbarum* (Kocyigit and Sanlier, 2017)

2. METHODS

This article is structured as a narrative literature review, aiming to synthesize existing scientific evidence and theoretical perspectives from previously published research articles. Relevant studies were obtained through systematic searches conducted on several scholarly databases including Google Scholar, PubMed, ScienceDirect, and SpringerLink.

The literature search employed a combination of keywords such as: “Goji Berry”, “Lycium barbarum”, “Pulmonary Fibrosis”, “Collagen”, “Oxidative Stress”, and “Aging Lung”. The selection focused on articles published within the last twenty years (2004 – 2024) to ensure relevance to current scientific developments.

Inclusion criteria for selected sources comprised: (1) peer-reviewed journal articles; (2) studies published in English; and (3) publications investigating the role of *Lycium barbarum* or its extracts in relation to oxidative stress, aging-related tissue degeneration, or pulmonary fibrosis. Articles that were inaccessible in full text, non-peer-reviewed conference proceedings, and case reports or case series were excluded.

Eligible articles were reviewed and analyzed for critical information regarding experimental models, biological mechanisms, outcome measures, and therapeutic implications. Emphasis was placed on extracting data concerning antioxidant activity, modulation of collagen deposition, and the attenuation of fibrotic markers. The findings were synthesized thematically to present a comprehensive overview of the potential of *Lycium barbarum* in mitigating collagen-associated pulmonary damage.

3. results and discussion

The initial literature curation, based on the specified keywords, yielded a total of 15 cited studies related to aging, oxidative stress, collagen remodeling, and *Lycium barbarum* (Goji berry). After screening for topic relevance and experimental focus, particularly regarding pulmonary fibrosis and antioxidant interventions, three (3) full-text articles were selected for final inclusion. These studies directly examined the protective effects of Goji berry extract or its bioactive polysaccharides (LBP) on lung oxidative injury, inflammation, and fibrotic remodeling.

The selected articles are summarized in Table 1, which outlines the experimental models, type of Goji berry intervention, key biological outcomes, and resulting conclusions.

**Table 1. Research investigates the effects of Goji berry extract on pulmonary fibrosis**

| **Author** | **Sample** | **Intervention** | **Result** | **Conclusion** |
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| Li, Ma and Liu (2007) | Male Kunming mice (20–22 months old), n=10 per group, divided into 4 groups: control and LBP-treated (200, 300, 400 mg/kg). Treatment duration: 20 days via oral gavage. | LBP was administered orally at doses of 200, 300, and 400 mg/kg/day for 20 consecutive days. Lung tissue was harvested for analysis of SOD, CAT, GSH-Px activities, and MDA and lipofuscin content as oxidative stress markers. | At 400 mg/kg LBP, SOD, CAT, and GSH-Px activities in lung tissue increased by 31.8%, 39.6%, and 44.5% respectively compared to control. MDA reduced by 27.3%, and lipofuscin content decreased significantly (p<0.05). | LBP at 400 mg/kg/day demonstrated strong antioxidant capacity in aged lungs, restoring enzymatic defenses and reducing peroxidative damage, suggesting potential for fibrosis prevention in age-related pulmonary degeneration. |
| Niu et al. (2008) | Male Wistar rats, n=10 per group, divided into 5 groups: sedentary control, exercise control, and LBP-treated (100, 200, 300 mg/kg/day) groups. Treadmill training: progressive overload to exhaustion for 30 days. | LBP was given orally at doses of 100, 200, and 300 mg/kg/day for 30 days. Treadmill regimen included 5 days/week exercise with progressive intensity. Antioxidant status measured via serum and muscle SOD, GPx, and MDA assays. | 300 mg/kg/day LBP increased SOD by 41.2% and GPx by 35.6%, while MDA and CK levels decreased by 29.8% and 22.7% compared to exercise-only group. Improvements were dose-dependent and statistically significant (p<0.01). | Systemic LBP administration at 300 mg/kg/day effectively mitigated exercise-induced oxidative stress, with implications for reducing risk of oxidative lung damage in high-stress physiological conditions. |
| Ma et al. (2019) | Male Wistar rats, n=10 per group, exposed to 12 unfiltered cigarettes/day (2×/day for 28 days). LBP treatment groups received 100 or 200 mg/kg/day orally during the same period. | Rats were exposed to cigarette smoke in a 27×18×14 cm chamber. LBP was administered orally at 100 mg/kg and 200 mg/kg/day. Lung samples analyzed for TNF-α, IL-6, IL-8 (via ELISA), MDA (via TBA method), SOD, GSH-Px, and histology. NF-κB expression assessed via immunohistochemistry. | 200 mg/kg/day LBP decreased TNF-α, IL-6, and IL-8 by 37.9%, 34.2%, and 31.6% respectively; MDA reduced by 42.8%, while SOD and GSH-Px increased by 45.7% and 40.3%. Lung histology showed reduced alveolar thickening and inflammatory infiltration. NF-κB expression downregulated significantly. | LBP at 200 mg/kg/day significantly suppressed inflammatory cytokines and oxidative damage in cigarette smoke-induced lung injury, confirming its therapeutic relevance in preventing or treating pulmonary fibrosis via NF-κB inhibition. |

As the human body undergoes the natural process of aging, significant structural and functional changes take place in the lungs. These changes include diminished pulmonary elasticity, thinning of alveolar walls, and a decline in the antioxidant defense system, which makes the lungs more susceptible to oxidative stress and chronic inflammation. One of the most concerning consequences is the excessive accumulation of extracellular matrix proteins, particularly collagen, which plays a central role in the development of pulmonary fibrosis. This condition is marked by irreversible scarring of the lung tissue and is commonly associated with aging, exposure to environmental toxins such as cigarette smoke, and the accumulation of reactive oxygen species (ROS) (Li, Ma and Liu, 2007; Ma et al*.*, 2019).

The imbalance between ROS generation and the antioxidant defense system in aging lungs leads to cellular damage, inflammatory signaling, and ultimately, fibrotic remodeling. ROS can activate nuclear factor-kappa B (NF-κB), a key transcription factor that promotes the release of pro-inflammatory cytokines like TNF-α, IL-6, and IL-8, all of which further stimulate fibroblast proliferation and collagen deposition (Ma et al*.*, 2019). In this context, enhancing the antioxidant capacity of lung tissue becomes a rational therapeutic strategy for preventing or attenuating fibrotic damage.

Among various natural antioxidant sources, Goji berry (Lycium barbarum) has attracted considerable attention due to its rich content of Lycium barbarum polysaccharides (LBP), carotenoids, flavonoids, and phenolic acids (Donno et al*.*, 2015; Kulczyński and Gramza-Michałowska, 2016). LBP is the most abundant and bioactive compound in Goji berry, making up approximately 5–8% of the fruit’s dry weight, and is known to enhance enzymatic antioxidant defenses, reduce lipid peroxidation, and modulate inflammation.

Li, Ma and Liu (2007) conducted one of the earliest studies examining the effects of LBP in aged mice, administering oral doses of 200, 300, and 400 mg/kg/day for 20 consecutive days. Their results demonstrated that LBP significantly elevated the activities of superoxide dismutase (SOD), catalase (CAT), and glutathione peroxidase (GSH-Px) in lung tissue while simultaneously reducing levels of malondialdehyde (MDA) and lipofuscin, key markers of oxidative damage. At the highest dose of 400 mg/kg, SOD activity increased by 31.8%, CAT by 39.6%, and GSH-Px by 44.5%, while MDA levels were reduced by 27.3%. These findings suggest that LBP is effective in restoring redox balance and protecting lung tissue from age-related oxidative injury.

While not focused specifically on pulmonary tissue, the study by (Niu et al*.*, 2008) explored systemic oxidative stress in Wistar rats subjected to exhaustive treadmill exercise and found that LBP supplementation at 100–300 mg/kg/day for 30 days significantly improved antioxidant status. In the 300 mg/kg group, SOD activity rose by 41.2%, and GPx by 35.6%, while MDA levels decreased by nearly 30%. These improvements imply a broad systemic antioxidant effect of LBP that may extend to lung tissues, especially under conditions of physiological stress.

More recently, Ma et al. (2019) provided direct evidence of LBP’s protective role in pulmonary fibrosis by using a cigarette smoke-induced lung injury model in rats. Over a 28-day period, LBP at doses of 100 and 200 mg/kg/day was administered concurrently with cigarette smoke exposure. The treatment led to significant reductions in TNF-α (−37.9%), IL-6 (−34.2%), and IL-8 (−31.6%) concentrations in lung tissue, alongside a 42.8% decrease in MDA levels. Additionally, SOD and GSH-Px levels increased by 45.7% and 40.3% respectively. Histopathological analysis revealed diminished inflammatory cell infiltration and alveolar wall thickening, while immunohistochemical studies confirmed the downregulation of NF-κB expression in lung tissues.

The consistency of these findings across diverse experimental models strengthens the conclusion that LBP plays a multifactorial protective role in the lungs. It restores antioxidant capacity, inhibits inflammatory signaling, and reduces fibrotic remodeling, all of which are critical in preventing the progression of pulmonary fibrosis. Although further studies, especially in human populations, are required to confirm these effects, the preclinical evidence presents a compelling case for considering Goji berry as a natural therapeutic agent against oxidative lung injury and age-related fibrosis.

4. Conclusion

Pulmonary fibrosis is closely linked to aging and oxidative stress, which impair lung structure through excessive collagen accumulation and chronic inflammation. The decline in endogenous antioxidants with age contributes to redox imbalance and activation of fibrotic pathways.

Goji berry (*Lycium barbarum*), particularly through its Lycium barbarum polysaccharides (LBP), has shown consistent protective effects in preclinical models. LBP enhances antioxidant enzyme activity, reduces oxidative damage, suppresses inflammatory cytokines, and inhibits NF-κB signaling. These mechanisms collectively attenuate lung tissue damage and fibrotic remodeling.

Findings from aging and smoke-induced lung injury models support the potential of Goji berry as a natural therapeutic agent against pulmonary fibrosis. While further human studies are needed, current evidence highlights its promise in reducing age-related and environmentally driven lung damage through antioxidant and anti-inflammatory action.

aConsent and ethical approval

It is not applicable.

disclaimer (Artificial intelligence)

The author(s) confirm that generative AI tools, including Large Language Models, were used in the process of writing or editing this manuscript.

**Details of AI usage:**

AI assistance was used only in approximately 2 to 3 instances. The tool utilized was ChatGPT, accessed via chatgpt.com. It was used specifically to paraphrase certain sentences in order to avoid direct plagiarism from the referenced journal texts.

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