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The use of Red Onion (Allium Cepa L.) Skin Extract as an Antioxidant and Anti-Inflammatory in Rats: A Literature Review Study

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Abstract

Red onion peel (*Allium cepa* L.) is an agricultural by-product that contains high levels of bioactive compounds, particularly flavonoids and quercetin, which are known to possess antioxidant and anti-inflammatory properties. This systematic literature review aims to analyze the scientific evidence regarding the effects of red onion peel extract on antioxidant and anti-inflammatory activities in mouse models. Data were collected from international databases and selected based on relevance to in vivo and in vitro studies published between 2020 and 2025. The findings indicate that red onion peel extract significantly enhances antioxidant defense mechanisms by increasing the activity of superoxide dismutase (SOD), catalase, and total antioxidant capacity (ORAC), while reducing oxidative stress markers such as nitric oxide (NO) and inducible nitric oxide synthase (iNOS). In addition, the extract exhibits strong anti-inflammatory effects through the suppression of pro-inflammatory cytokines, including IL-1α, IL-1β, IL-6, and TNF-α, as well as inhibition of key signaling pathways such as JAK-STAT, NF-κB, and NLRP3/caspase-1. The effectiveness of the extract is influenced by dosage, duration of administration, and extraction method, with higher doses and longer exposure generally producing stronger biological effects. Overall, red onion peel extract shows promising potential as a natural source of antioxidant and anti-inflammatory agents for nutraceutical and therapeutic applications.

Keywords *Allium Cepa* L.; Antioxidant Activity; Anti-Inflammatory; Flavonoids, Mice Model; Red Onion Peel; Quercetin; Systematic Literature Review

INTRODUCTION

Agricultural by-products are increasingly recognized as valuable sources of bioactive compounds with potential therapeutic applications (Brito et al., 2022). One such underutilized resource is the outer peel of Allium cepa L. (red onion), which is commonly discarded as waste despite its rich phytochemical composition. Recent scientific attention has highlighted that onion peels contain high concentrations of

flavonoids, particularly quercetin, a compound known for its strong antioxidant and anti-inflammatory properties. These bioactive constituents contribute to the neutralization of free radicals and the modulation of inflammatory pathways, positioning onion peel as a promising candidate for natural therapeutic development (Marefati et al., 2021). Oxidative stress and chronic inflammation are closely associated with the pathogenesis of various degenerative diseases, including cardiovascular disorders, cancer, and inflammatory bowel diseases (Leyane et al., 2022; Sahoo et al., 2023). Natural antioxidants derived from plant sources have gained considerable interest due to their safety profile and multifunctional biological activities. In this context, onion peel extract has demonstrated significant antioxidant capacity by reducing oxidative damage and enhancing endogenous defense systems. Experimental findings indicate that its phenolic compounds can effectively scavenge reactive oxygen species (ROS) and inhibit lipid peroxidation (H.-S. Lee et al., 2023).

In vivo studies further support the therapeutic potential of onion peel extract. An experimental study using rat models of ulcerative colitis induced by acetic acid revealed that administration of onion peel extract at doses of 50 and 100 mg/kg body weight significantly reduced both macroscopic and microscopic colon damage. The treatment also resulted in decreased activity of myeloperoxidase (MPO), an enzyme associated with neutrophil infiltration, and lowered levels of pro-inflammatory cytokines such as tumor necrosis factor-alpha (TNF-α), interleukin-6 (IL-6), and interleukin-1 beta (IL-1β). These findings indicate a substantial anti-inflammatory effect of onion peel extract (Motavallian et al., 2025). The underlying mechanisms of these biological effects are thought to involve the inhibition of key inflammatory signaling pathways, particularly the Janus kinase-signal transducer and activator of transcription (JAK-STAT) pathway. Research has demonstrated that onion peel extract can suppress JAK-STAT activation in lipopolysaccharide (LPS)-stimulated macrophage cells (RAW264.7), leading to reduced production of pro-inflammatory mediators. This mechanism highlights its potential as a natural anti-inflammatory agent targeting molecular pathways involved in immune response regulation (H.-S. Lee et al., 2023).

In addition to its antioxidant and anti-inflammatory activities, onion peel extract has also shown potential applications in dermatological protection. Studies report its effectiveness as a natural sunscreen agent due to its ability to absorb ultraviolet (UV) radiation and prevent skin damage. This multifunctional property further enhances its value as a bioresource for pharmaceutical and cosmetic industries (Motavallian et al., 2025). Despite the promising findings, most existing

studies are limited to experimental models, particularly in rodents, and there remains a need for comprehensive evaluation regarding optimal dosage, duration of administration, and long-term safety. Therefore, further investigation is essential to validate the therapeutic efficacy of onion peel extract and to explore its potential translation into practical pharmaceutical formulations.

METHODS

This study employed a literature review design aimed at systematically collecting, evaluating, and synthesizing scientific evidence related to the antioxidant and anti-inflammatory effects of red onion peel (*Allium cepa* L.) extract in rodent models. A literature review approach was selected due to its effectiveness in summarizing existing knowledge, identifying research gaps, and providing a comprehensive understanding of a specific scientific topic without conducting primary experimental procedures. This method is widely used in biomedical research to integrate findings from multiple studies into a coherent analytical framework (Snyder, 2019). The research process consisted of three main stages: literature searching, article screening, and data synthesis. The literature search was conducted using several international electronic databases, including PubMed, Google Scholar, ScienceDirect, and ResearchGate. Relevant studies were identified using a combination of keywords and Medical Subject Headings (MeSH), such as "*Allium cepa* L.," "red onion peel extract," "antioxidant," "anti-inflammatory," and "rat" or "mice model." Boolean operators (AND, OR) were applied to refine the search strategy and ensure the retrieval of relevant articles. This structured searching approach enhances reproducibility and minimizes selection bias in review studies (Xiao & Watson, 2019).

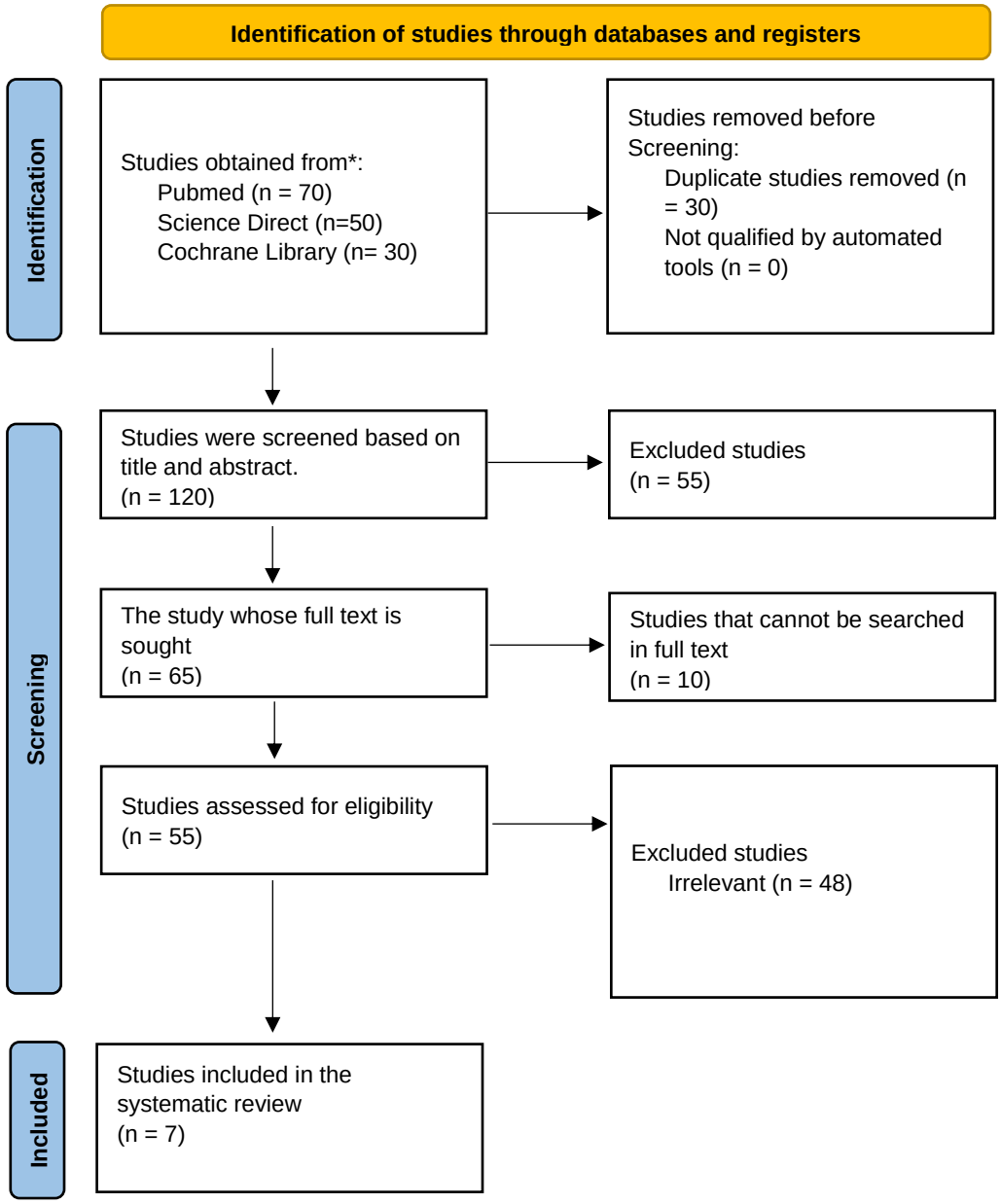
Following the initial search, a screening process was carried out to select articles that met the predefined inclusion criteria. The screening involved reviewing titles, abstracts, and full-text articles, as well as removing duplicate records. Inclusion criteria comprised experimental in vivo studies conducted on rats or mice that investigated the antioxidant and/or anti-inflammatory effects of red onion peel extract. Articles were further limited to publications between 2020 and 2025 to ensure the relevance and currency of the data. Studies that did not focus on onion peel extract or did not involve animal models were excluded from the analysis. This selection process aligns with standard systematic review procedures to ensure the validity and reliability of the included evidence (Page et al., 2021). The final stage involved data synthesis and interpretation. Selected articles were analyzed to extract key information, including dosage, duration of treatment, experimental models,

mechanisms of action, and outcomes related to antioxidant and anti-inflammatory activities. The synthesis process focused on identifying patterns, consistencies, and variations across studies. Findings were then organized into a systematic narrative and supported by summary tables to facilitate comparison between studies. This approach allows for a deeper understanding of the therapeutic potential of red onion peel extract and supports evidence-based conclusions (Snyder, 2019). The overall research workflow included several sequential steps: identification of relevant literature, selection of eligible studies, synthesis of findings, conclusion drawing, and preparation of the scientific manuscript for publication. The expected outputs of this study include a structured summary of scientific evidence, a comprehensive analysis of the effectiveness of *Allium cepa* peel extract, and a publishable scientific article in an international journal.

FINDINGS AND DISCUSSION

The article selection process for the literature study on the use of shallot skin extract (Allium cepa L.) as an antioxidant and anti-inflammatory in mice can be explained based on the flowchart that has been prepared: The process begins with the identification of articles from three databases, namely PubMed with 70 articles, ScienceDirect with 50 articles, and Cochrane Library with 30 articles. From the total of 150 articles, duplicate articles and articles that do not meet the initial criteria, such as multiple studies or those that do not match automatic tools, were removed, so that most irrelevant articles were immediately removed before the screening process.

The next stage was screening based on titles and abstracts, where an initial assessment of the 120 remaining articles was conducted for their relevance to the research topic. From this stage, 55 articles were excluded because they did not align with the research focus. Next, a full-text review was conducted on 65 articles deemed to have potential. From this stage, 10 articles were unable to access their full text and were therefore excluded from the analysis. Of the 55 articles available for eligibility assessment, a more detailed evaluation was conducted regarding the relevance and quality of the information presented. A total of 48 articles were then excluded because they were not relevant to the topic of the use of onion peel extract in mice as an antioxidant or anti-inflammatory. Ultimately, seven articles met all inclusion criteria and were further evaluated in a systematic literature review. These articles served as the basis for synthesizing data on the dosage, mechanism of action, and antioxidant and anti-inflammatory efficacy of onion peel extract in rat models.



Picture 1 Effect of red onion skin extract on antioxidant activity in mice

Effect of red onion skin extract on antioxidant activity in mice

Table 1 The effect of red onion skin extract on antioxidant activity in mice

No	Author & Year	Model & Dosage	Duration	Antioxidant Activity
1	(H. S. Lee et al., 2023)	RAW264.7 in vitro, AP50E	—	Reduces NO & iNOS; increases cell defense
2	(Sobanke et al., 2025)	Male rats, 1 ml/100 gBW orally	3 weeks	Increase antioxidant activity
3	(Chernukha et	Old Wistar rats, 2 ml/tail	188 days	Liver catalase & SOD +44–79%, brain 3x; high

	al., 2021)			antioxidant capacity
4	(Kim et al., 2025)	Immunosuppressed mice, HW/30E/50E extraction	—	30E superior radical scavenging; HW restores immunity
5	(B. Lee et al., 2022)	Sprague–Dawley rats, 5% skin/meat diet	4 weeks	Liver SOD, GPx, catalase & ORAC increased; MDA decreased

Based on the findings summarized in Table 1, red onion peel (*Allium cepa* L.) extract demonstrates a significant capacity to enhance antioxidant activity across various experimental models, including both in vitro and in vivo systems. Antioxidant activity was evaluated using multiple biochemical parameters, indicating consistent protective effects against oxidative stress. In an in vitro study using RAW264.7 macrophage cells, the extract significantly reduced the production of nitric oxide (NO) and the expression of inducible nitric oxide synthase (iNOS), which are key mediators of oxidative and inflammatory responses (H.-S. Lee et al., 2023). This finding suggests that onion peel extract can modulate oxidative pathways at the cellular level by suppressing reactive nitrogen species.

In vivo studies further support these observations. Administration of red onion peel extract in male rats at a dose of 1 ml per 100 g body weight for three weeks resulted in a measurable increase in antioxidant activity, indicating improved systemic defense against oxidative damage (Sobanke et al., 2025). A more extended study involving aged Wistar rats demonstrated even more pronounced effects. Daily administration of 2 ml extract per animal over 188 days significantly enhanced antioxidant enzyme activity, with catalase and superoxide dismutase (SOD) levels increasing by 44–79% in the liver and up to threefold in the brain. These findings highlight the potential neuroprotective and hepatoprotective roles of onion peel extract through the عزيز ment of endogenous antioxidant systems (Chernukha et al., 2021).

Further evidence from dietary intervention studies showed that supplementation with 5% onion peel or flesh in Sprague–Dawley rats for four weeks led to increased levels of key antioxidant enzymes, including SOD, glutathione peroxidase (GPx), and catalase, along with higher oxygen radical absorbance capacity (ORAC) in liver tissue. Concurrently, levels of malondialdehyde (MDA), a marker of lipid peroxidation, were reduced, indicating decreased oxidative damage at the cellular level (B. Lee et al., 2022). These biochemical changes confirm the ability

of onion peel extract to both enhance antioxidant defenses and reduce oxidative stress markers.

The effectiveness of the extract was also found to depend on the extraction method. A comparative study demonstrated that 30% ethanol extract (30E) exhibited the highest radical scavenging activity, while hot water extract (HW) showed superior efficacy in restoring immune function in immunosuppressed rats (Kim et al., 2025). This variation suggests that different extraction solvents selectively isolate distinct bioactive compounds, influencing the overall antioxidant and immunomodulatory potential of the extract.

The observed antioxidant effects are largely attributed to the high content of flavonoids, particularly quercetin, present in onion peel. These compounds act as free radical scavengers, metal chelators, and modulators of antioxidant enzyme activity. The enhancement of antioxidant enzymes in vital organs such as the liver and brain indicates a protective role against long-term oxidative damage, which is often associated with aging and degenerative diseases (Chernukha et al., 2021).

Overall, these findings confirm that red onion peel is a promising natural source of antioxidants with significant therapeutic potential. Its consistent effects across different experimental models support its possible application in the development of nutraceutical products and pharmaceutical formulations aimed at preventing or mitigating oxidative stress-related disorders.

Effect of red onion skin extract on inflammation in mice

Table 2 The effect of red onion skin extract on inflammation in mice

No	Author & Year	Model & Dosage	Duration	Anti-inflammatory Effects / Biomarkers	Conclusion
1	(H.-S. Lee et al., 2023)	RAW264.7 in vitro, AP50E	—	Decreases IL-1α, IL-1β, IL-6, IL-27; inhibits the JAK-STAT pathway	Potent anti-inflammatory effects via the JAK-STAT pathway
2	(Sobanke et al., 2025)	Male rats, 1 ml/100 gBW orally	3 weeks	Reduces TNF-α; improves hematological and lipid changes due to heat stress	Anti-inflammatory potential, limited protection under extreme stress

3	(Ali et al., 2024)	Ulcer model mice, T1/T2/P1/P2/S1/S2	—	Suppresses HMGB-1/NF-κB, NOX1/4, inflammatory cytokines; repairs gastric mucosa	Dose-dependent anti-inflammatory, gastroprotective activity
4	(Mounir et al., 2023)	Rat wounds & skin infections, RO & YO	—	Suppresses NO, NLRP3/caspase-1, inflammatory cytokines; YO enhances angiogenesis	Supports wound healing & modulates inflammation

The findings presented in Table 3 demonstrate that red onion peel (*Allium cepa* L.) extract exhibits substantial anti-inflammatory activity across both in vitro and in vivo models. These effects are reflected in the modulation of key inflammatory mediators, signaling pathways, and tissue repair processes, indicating a multifaceted mechanism of action. At the cellular level, an in vitro study using RAW264.7 macrophage cells revealed that a 50% ethanol extract (AP50E) significantly reduced the expression of pro-inflammatory cytokines, including interleukin-1 alpha (IL-1α), interleukin-1 beta (IL-1β), interleukin-6 (IL-6), and interleukin-27 (IL-27). The extract also inhibited the Janus kinase-signal transducer and activator of transcription (JAK-STAT) signaling pathway, which plays a central role in mediating immune and inflammatory responses. This evidence highlights a direct molecular mechanism by which onion peel extract suppresses inflammation at the cellular level (H.-S. Lee et al., 2023).

In vivo studies further confirm these anti-inflammatory properties. Oral administration of *Allium cepa* extract at a dose of 1 ml per 100 g body weight for three weeks in male rats significantly reduced tumor necrosis factor-alpha (TNF-α), a major pro-inflammatory cytokine. The treatment also improved hematological parameters and lipid profiles altered by heat stress, suggesting that the extract not only attenuates inflammation but also mitigates systemic physiological disturbances associated with stress conditions (Sobanke et al., 2025). More complex mechanisms were observed in disease-specific models. In a mouse model of gastric ulcer, onion peel extract and its fractions suppressed critical inflammatory signaling pathways, including high mobility group box-1 (HMGB-1)/nuclear factor kappa B (NF-κB) and

NADPH oxidase (NOX1/4). These pathways are known to regulate oxidative stress and inflammatory gene expression. Their inhibition resulted in significant improvement in gastric mucosal structure, indicating both anti-inflammatory and gastroprotective effects. The study also demonstrated a dose-dependent response, suggesting that higher concentrations of the extract yield stronger therapeutic outcomes (Ali et al., 2024).

In addition, studies involving wound healing and skin infection models showed that onion peel extract effectively suppressed nitric oxide (NO) production, the NLRP3 inflammasome/caspase-1 pathway, and pro-inflammatory cytokines. Notably, yellow onion peel extract (YO) was found to enhance angiogenesis, a critical process in tissue regeneration. This dual function—reducing inflammation while promoting tissue repair—suggests that onion peel extract may be particularly valuable in treating inflammatory skin conditions and accelerating wound healing (Mounir et al., 2023). Collectively, these findings indicate that the anti-inflammatory activity of red onion peel extract is mediated through multiple biological pathways, including inhibition of pro-inflammatory cytokines, suppression of key signaling cascades such as JAK-STAT and NF-κB, and regulation of oxidative stress-related enzymes. The extract's ability to act on both upstream signaling mechanisms and downstream inflammatory mediators highlights its potential as a natural therapeutic agent.

The observed effects are largely attributed to the presence of bioactive compounds, particularly flavonoids such as quercetin, which are known to possess strong anti-inflammatory and antioxidant properties. These compounds can modulate immune responses, inhibit enzyme activity involved in inflammation, and protect tissues from damage caused by oxidative stress. Overall, the evidence supports the conclusion that *Allium cepa* peel extract has significant anti-inflammatory potential across various experimental conditions. Its consistent efficacy in reducing inflammatory biomarkers and improving tissue integrity suggests promising applications in the development of nutraceuticals and pharmaceutical agents targeting inflammatory diseases. However, further studies are required to establish optimal dosing, long-term safety, and clinical applicability in humans.

Relationship between Dose & Duration with Antioxidant and Anti-inflammatory Effectiveness

Table 3 Relationship between Dose & Duration with Antioxidant and Anti-inflammatory Effectiveness

N	Study &	Dosage / Extract	Duration of Administrati	Antioxidant	Anti-inflammato	Vital

o	Year	Form	on	Effectiveness	ry Effectiveness	Records
1	(Chernukha et al., 2021)	2 ml/head	188 days	★★★★☆ (heart & brain)	☆ (insignificant blood)	Dosage & long duration → vital organ antioxidants increase
2	(Sobanke et al., 2025)	1 ml/100 gBW	3 weeks	★★★☆	★★☆	Short duration is quite effective; severe heat stress reduces protection.
3	(Ali et al., 2024)	Variables (fractions & extracts)	—	★★★☆	★★★	Effectiveness depends on dose & type of extract
4	(Kim et al., 2025)	HW / 30E / 50E	—	★★★★ (30E) / ★★★ (HW)	★★★ (30E/50E differs)	Extraction method affects the effectiveness of metabolites
5	(B. Lee et al., 2022)	5% skin/meat diet	4 weeks	★★★☆	—	A 4-week diet is enough to increase antioxidant defenses.

Star symbol (★) description:
★☆☆☆☆→ low effectiveness
★★☆☆☆→ moderate effectiveness
★★★☆☆→ quite high effectiveness
★★★★☆→ high effectiveness

★★★★★→ very high effectiveness

The analysis of studies summarized in Table 3 indicates that the antioxidant and anti-inflammatory effectiveness of red onion peel (*Allium cepa* L.) extract is strongly influenced by dosage, extraction method, and duration of administration. Overall, the evidence suggests that biological responses are not only compound-dependent but also highly time- and dose-sensitive, particularly in in vivo experimental models. Long-term administration appears to produce more pronounced systemic antioxidant effects. A study conducted on aged Wistar rats demonstrated that supplementation with 2 ml per animal over 188 days significantly increased antioxidant enzyme activity, particularly catalase and superoxide dismutase (SOD), in both liver and brain tissues. However, no significant improvement was observed in blood antioxidant parameters, indicating that prolonged exposure preferentially enhances protection in vital organs rather than systemic circulation. This finding suggests that extended administration may be necessary to achieve organ-specific oxidative protection, especially in tissues with high metabolic activity such as the brain and liver (Chernukha et al., 2021).

In contrast, shorter intervention periods may still yield measurable but more limited biological effects. Oral administration of 1 ml/100 g body weight for three weeks in male rats was sufficient to enhance antioxidant activity and reduce tumor necrosis factor-alpha (TNF-α) levels. However, the protective effects were less robust under conditions of severe physiological stress, such as heat exposure. This indicates that while short-term treatment can initiate antioxidant and anti-inflammatory responses, its capacity to counteract strong pathological stressors may be limited compared to long-term intervention (Sobanke et al., 2025). Variability in extract composition and dosage also plays a critical role in determining biological outcomes. Studies involving different fractions and extract types demonstrated that the efficacy of onion peel extract is highly dependent on its phytochemical composition and concentration. Certain fractions exhibited stronger suppression of inflammatory responses, while others showed greater antioxidant activity, confirming that both dose and chemical profile jointly determine therapeutic potential (Ali et al., 2024).

Furthermore, extraction method significantly influences bioactivity. A comparative analysis showed that 30% ethanol extract (30E) exhibited the highest radical scavenging activity, whereas hot water extract (HW) was more effective in restoring immune function in immunosuppressed animal models. These differences suggest that solvent polarity affects the extraction efficiency of flavonoids and other phenolic compounds, thereby altering antioxidant and immunomodulatory outcomes (Kim et al., 2025). Dietary supplementation studies further support the

importance of moderate duration exposure. A 4-week dietary intake of 5% onion peel or flesh in Sprague–Dawley rats significantly increased antioxidant enzyme activity, including SOD, glutathione peroxidase (GPx), catalase, and oxygen radical absorbance capacity (ORAC), while reducing oxidative damage markers. These results indicate that intermediate exposure durations may be sufficient to activate endogenous antioxidant defense systems effectively (B. Lee et al., 2022).

Collectively, these findings demonstrate a clear dose–duration–response relationship in the biological activity of red onion peel extract. Higher doses and longer administration periods generally enhance antioxidant effects, particularly in metabolically active organs such as the brain and liver. However, optimal outcomes also depend on the extraction method and phytochemical composition, which influence both antioxidant and anti-inflammatory pathways. These results highlight the importance of optimizing administration strategies when considering red onion peel extract for nutraceutical or therapeutic applications. Appropriate selection of dose, duration, and extraction method is essential to maximize its pharmacological potential while ensuring consistent and targeted biological effects.

CONCLUSION

This systematic literature review concludes that red onion peel (*Allium cepa* L.) extract demonstrates strong antioxidant and anti-inflammatory potential in various in vitro and in vivo mouse models. The antioxidant effects are evidenced by the enhancement of endogenous defense enzymes, including superoxide dismutase (SOD), catalase, and total antioxidant capacity (ORAC), along with a reduction in nitric oxide (NO) and inducible nitric oxide synthase (iNOS) in RAW264.7 macrophage cells. These effects are primarily attributed to bioactive compounds such as flavonoids and quercetin, which play a crucial role in reducing oxidative stress and protecting vital organs, particularly the liver and brain. In terms of anti-inflammatory activity, onion peel extract significantly suppresses inflammatory responses through multiple molecular mechanisms. In vitro studies show reduced expression of pro-inflammatory cytokines, including IL-1α, IL-1β, IL-6, and IL-27, along with inhibition of the JAK-STAT signaling pathway. In vivo studies further confirm reductions in TNF-α levels and modulation of key inflammatory pathways such as HMGB-1/NF-κB, NOX1/4, and NLRP3/caspase-1, contributing to improved tissue integrity and enhanced wound healing. Overall, the effectiveness of onion peel extract is highly dependent on dosage, duration, and extraction method. Higher doses and longer treatment periods generally enhance antioxidant defense, while

specific extraction techniques improve targeted biological activities. These findings highlight its promising potential for nutraceutical and therapeutic development.

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