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EXPERIMENTAL EVALUATION OF FLAVONOIDS FROM SOPHORA JAPONICA AS PROSPECTIVE ACTIVE COMPONENTS FOR REGENERATIVE MEDICINE

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Abstract

Background. The identification of bioactive compounds with antioxidant and cytoprotective properties is a key objective of modern regenerative medicine and the development of multifunctional therapeutic agents and biomaterials. Natural flavonoids are of particular interest due to their ability to reduce oxidative stress and create favorable conditions for tissue repair.

Objective. To experimentally evaluate the antioxidant and cytoprotective activity of quercetin and rutin isolated from Sophora japonica as prospective active components for regenerative medicine.

Materials and Methods. The study was performed using experimental models of gastric injury in rats induced by immobilization stress and indomethacin. Quercetin and rutin were administered intragastrically at a dose of 150 mg/kg. Antioxidant activity was assessed by measuring serum malondialdehyde (MDA) levels and catalase activity. Statistical analysis was conducted using standard medical statistics methods, with $p < 0.05$ considered statistically significant.

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Results. Pretreatment with quercetin and rutin significantly reduced the severity of gastric mucosal injury, decreased the number of ulcerative lesions, lowered MDA levels, and increased catalase activity. These antioxidant and cytoprotective effects were confirmed in both experimental models.

Conclusion. Quercetin and rutin isolated from Sophora japonica exhibit pronounced antioxidant and cytoprotective properties, supporting their potential use as active components in the development of therapeutic agents and biomaterials for regenerative medicine, including collagen-based wound dressings.

Keywords: Sophora japonica; flavonoids; quercetin; rutin; antioxidant activity; cytoprotection; regenerative medicine; wound dressings.

Introduction

The development of modern regenerative medicine products, including wound dressings and pharmaceutical forms for tissue repair, requires the identification of bioactive components with antioxidant, anti-inflammatory, and pro-regenerative properties. A critical factor determining the effectiveness of such products is the ability of the active component to suppress oxidative stress, stabilize cellular membranes, and promote reparative processes under conditions of tissue injury of various etiologies.

One promising approach in this field is the creation of multifunctional wound dressings based on biopolymers, particularly collagen, combined with natural bioactive compounds. Plant-derived flavonoids have attracted considerable attention due to their strong antioxidant activity and their ability to modulate cell proliferation and angiogenesis [1].

Quercetin and its glycoside rutin are among the most extensively studied flavonoids and are known to possess antioxidant, anti-inflammatory, and cytoprotective properties. Experimental studies have shown that these

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compounds reduce tissue damage induced by stress, inflammation, and ischemia and activate endogenous antioxidant defense systems, thereby creating favorable conditions for tissue regeneration. *Sophora japonica* is an accessible and valuable source of flavonoids and represents a promising raw material for the development of biomedical products [2].

However, despite extensive pharmacological data, the potential of quercetin and rutin as active components of regenerative medicine products, including collagen-based wound dressings, remains insufficiently explored. Therefore, the present study aimed to evaluate the antioxidant and cytoprotective activity of flavonoids from Sophora japonica using experimental models of tissue injury.

Materials and Methods

Experiments were conducted on male outbred rats weighing 150–180 g, housed under standard vivarium conditions with free access to food and water. All experimental procedures complied with accepted ethical standards for laboratory animal research.

Quercetin and rutin were isolated from Sophora japonica buds at the Pharmaceutical Institute of the Ministry of Health of the Republic of Uzbekistan. Two experimental models of gastric injury were used: immobilization stress-induced ulcers and indomethacin-induced ulcers.

In the stress-induced model, rats were immobilized for 24 h. Rutin was administered intragastrically at a dose of 150 mg/kg for 9 days prior to injury induction. In the indomethacin-induced model, indomethacin was administered intragastrically at a dose of 60 mg/kg, and quercetin was administered at 150 mg/kg for 9 days prior to ulcer induction.

Gastric mucosal damage was assessed macroscopically. Antioxidant activity was evaluated by measuring serum catalase activity and malondialdehyde (MDA) levels using spectrophotometric methods.

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Statistical analysis was performed using SPSS and STATISTICA software, with $p < 0.05$ considered statistically significant.

Results and Discussion

In the immobilization stress-induced gastric injury model, control animals exhibited pronounced mucosal damage characterized by multiple ulcerative lesions. Pretreatment with rutin resulted in a significant reduction in the number and severity of gastric ulcers compared with the control group (Figure 1).

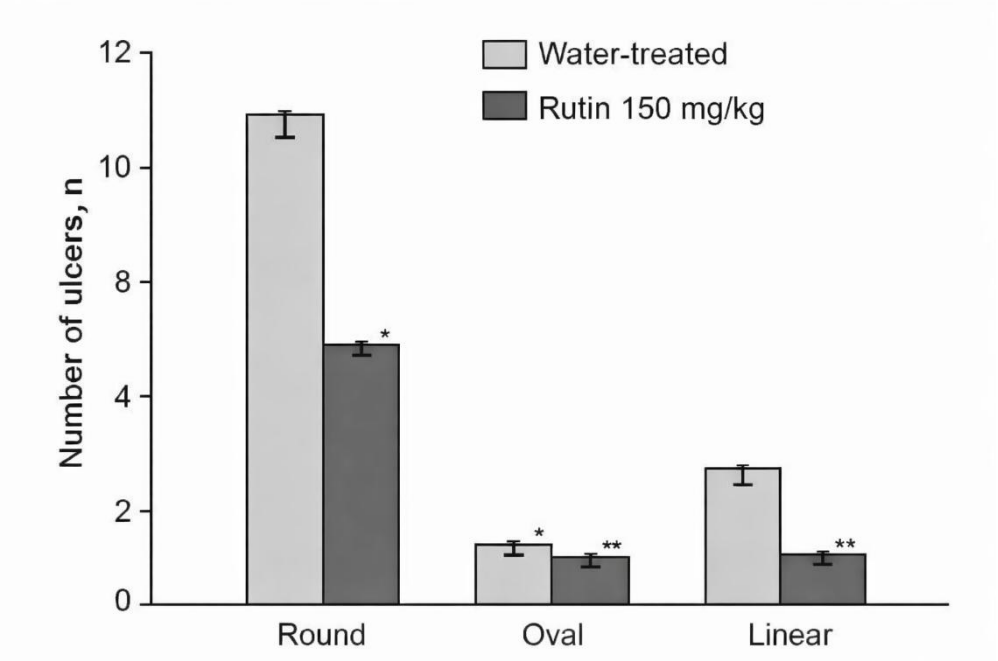

Figure 1. Number of gastric ulcers in rats subjected to immobilization stress–induced gastric injury compared with the water-treated control group: *P≤0,01; **P≤0,001.

Rutin administration was also associated with a significant increase in catalase activity and a decrease in serum MDA levels, indicating suppression of oxidative stress (Figure 2).

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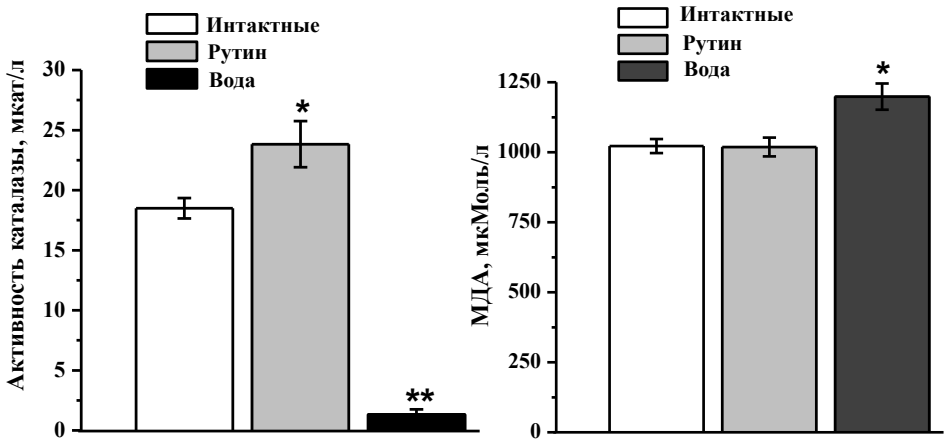

Figure 2. Catalase activity and malondialdehyde (MDA) levels in the serum of rats with immobilization stress–induced gastric injury treated with rutin: statistically significant differences compared with intact animals: *P≤0,005; **P≤0,001.

In the indomethacin-induced gastric injury model, quercetin pretreatment significantly reduced the number of ulcerative lesions relative to control animals (Figure 3).

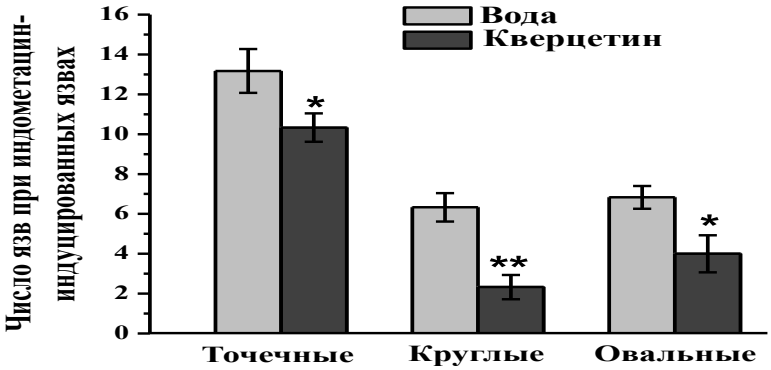

Figure 3. Number of gastric ulcers in rats subjected to indomethacin-induced gastric injury compared with the placebo (water-treated) group:*P≤0,05; **P≤0,01.

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This protective effect was accompanied by enhanced antioxidant defense, as evidenced by increased catalase activity and reduced MDA levels (Figure 4).

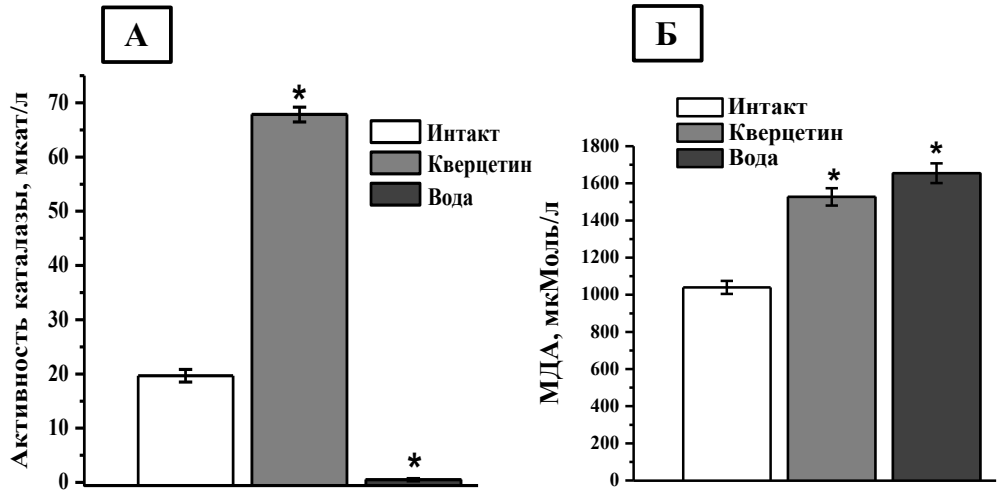

Figure 4. (A) Catalase activity and (B) malondialdehyde (MDA) levels in the serum of rats with indomethacin-induced gastric injury compared with intact animals:*P≤0,001.

The results of the present study demonstrate that the flavonoids quercetin and rutin isolated from *Sophora japonica* exhibit pronounced antioxidant and cytoprotective activity in experimental models of gastric injury induced by immobilization stress and indomethacin. The observed reduction in ulcer formation, together with normalization of oxidative stress markers, indicates that these compounds effectively counteract tissue damage mediated by reactive oxygen species and impaired endogenous antioxidant defense.

Oxidative stress plays a central role in the pathogenesis of tissue injury of various etiologies, including stress-related and nonsteroidal anti-inflammatory drug (NSAID)-induced gastric damage. Excessive production of reactive oxygen species leads to lipid peroxidation, disruption of cell membranes, mitochondrial dysfunction, and activation of inflammatory cascades, ultimately impairing tissue

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https://eurekaoa.com/index.php/5

integrity and regeneration [3]. In the present study, the significant decrease in malondialdehyde (MDA) levels and the concomitant increase in catalase activity observed after treatment with quercetin and rutin clearly indicate suppression of lipid peroxidation and activation of endogenous antioxidant mechanisms.

The gastroprotective effects of quercetin observed in the indomethacin-induced ulcer model are consistent with previous reports demonstrating that quercetin mitigates NSAID-induced gastric injury by attenuating oxidative stress, modulating prostaglandin-dependent pathways, and stabilizing the gastric mucosal barrier [4,5]. Importantly, indomethacin-induced gastric damage is considered a robust experimental model reflecting impaired cytoprotection and reduced prostaglandin synthesis, conditions that are also relevant to chronic inflammatory and ischemic tissue injuries.

The ability of quercetin to reduce ulcer severity under these conditions highlights its broad cytoprotective potential. Similarly, rutin demonstrated a strong protective effect in the immobilization stress-induced gastric injury model. Stress exposure is known to activate hypothalamic–pituitary–adrenal axis signaling, induce ischemia-reperfusion-like injury in gastric tissues, and exacerbate oxidative damage [4,6]. The significant reduction in ulcer number and area observed in rutin-treated animals, together with improved antioxidant parameters, suggests that rutin effectively mitigates stress-induced tissue injury by enhancing antioxidant defense and preserving cellular integrity.

The findings of the present study are in good agreement with experimental and review data indicating that flavonoids possess multifunctional biological activity, including antioxidant, anti-inflammatory, vasoprotective, and cytoprotective effects [2,7]. These properties are particularly relevant for regenerative medicine, where excessive oxidative stress is recognized as a major limiting factor for effective tissue repair and wound healing. Persistent oxidative damage has been shown to impair fibroblast proliferation, collagen synthesis, angiogenesis, and re-epithelialization, thereby delaying wound closure and tissue regeneration. From

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a translational perspective, the mechanisms identified in this study are not limited to gastric mucosal protection. Suppression of lipid peroxidation and activation of antioxidant enzymes represent universal protective pathways that contribute to tissue regeneration in various organs and tissues. In this context, quercetin and rutin may be considered promising active components for incorporation into biomaterials designed for regenerative applications.

Collagen-based wound dressings represent a cornerstone of modern regenerative medicine due to their biocompatibility, biodegradability, and ability to support cell adhesion and extracellular matrix remodeling. However, the regenerative potential of collagen scaffolds can be significantly enhanced by the inclusion of bioactive compounds capable of modulating oxidative stress and inflammatory responses. Flavonoids such as quercetin and rutin are attractive candidates for this purpose, as they may provide local antioxidant protection, reduce inflammatory damage, and create a microenvironment favorable for cell proliferation and tissue remodeling.

Previous studies have shown that flavonoid-enriched biomaterials improve wound healing outcomes by accelerating granulation tissue formation, enhancing angiogenesis, and promoting collagen deposition [2]. The antioxidant and cytoprotective effects demonstrated in the present study provide a strong experimental rationale for further investigation of *Sophora japonica* flavonoids as functional additives in collagen-based wound dressings and other regenerative biomaterials.

In addition, the dose used in this study (150 mg/kg), which demonstrated pronounced biological activity without reported toxic effects, is consistent with literature data indicating a favorable safety profile for both quercetin and rutin [8]. This further supports the feasibility of their translational application in biomedical products intended for repeated or prolonged use.

Taken together, the present findings extend existing knowledge on the biological activity of *Sophora japonica* flavonoids and highlight their potential relevance

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beyond gastroprotection. By demonstrating effective suppression of oxidative stress and enhancement of endogenous antioxidant defense, this study provides a scientific basis for the development of multifunctional therapeutic agents and biomaterials for regenerative medicine, including collagen-based wound dressings with incorporated natural flavonoids.

Conclusions

Quercetin and rutin isolated from Sophora japonica exhibit pronounced antioxidant and cytoprotective activity in experimental models of gastric injury. These properties provide a strong scientific basis for their further investigation and application as active components of therapeutic agents and biomaterials for regenerative medicine, including collagen-based wound dressings.

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