

The Investigation of the Anti-Inflammatory and Immunomodulatory Effects of İşgın (Rheum Ribes L.) Extract on Macrophage

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Introduction: *Rheum ribes L.*, commonly known as İşgın, is a perennial herb from the Polygonaceae family, native to mountainous regions of Turkey. Recent studies highlight its antioxidant, antimicrobial, antidiabetic, anticancer, antiulcer, and antitrichomonas activities. However, limited research has been conducted on its immunomodulatory and anti-inflammatory effects, and the underlying mechanisms remain unclear. This study aims to demonstrate the anti-inflammatory and immunomodulatory effects of *Rheum ribes L.* extract in lipopolysaccharide (LPS)-Stimulated RAW264.7 Macrophages.

Methods: Fresh *Rheum ribes L.* (İşgın) dried at 40°C. The plant was then extracted using ultrasound-assisted extraction with 80% ethanol. The total flavonoid and phenolic contents of *Rheum ribes* extract were determined using quercetin and gallic acid standards, respectively. The extract's effect on macrophage cell viability was analyzed via the MTT assay. An inflammation model was established in RAW 264.7 macrophages using lipopolysaccharide (LPS), and its confirmation was achieved by measuring nitric oxide levels in the cell culture medium with Griess reagent. The extract's effects on pro-inflammatory cytokines were evaluated using ELISA method. In the subsequent experimental setups, the effect of *Rheum ribes* extract on the inflammation marker NF-κB protein will be analyzed using Western blot and immunofluorescence staining methods.

Results: The extract was found to contain 161 mg/g gallic acid equivalents of total phenols and 40mg/g quercetin equivalents of total flavonoids. It exhibited cytotoxic effects on macrophage cells at doses above 75 µg/mL, while demonstrating significant proliferative effects at doses below this threshold. In the LPS-induced inflammation model, the extract notably reduced IFN-γ and TNF-α levels at 60 µg/mL and 75 µg/mL doses, while suppressing the pro-inflammatory cytokine IL-1β starting from a dose of 5 µg/mL.

Conclusion: *Rheum ribes*, characterized by its high phenolic and flavonoid content, has been identified as a promising agent for the suppression of inflammation. Its dose-dependent efficacy suggests significant potential for its application in the management of inflammation and inflammation-related diseases, highlighting its therapeutic value as a natural anti-inflammatory agent.

Keywords: rhubarb, Inflammation, Immunomodulatory, In vitro, *Rheum ribes L.*