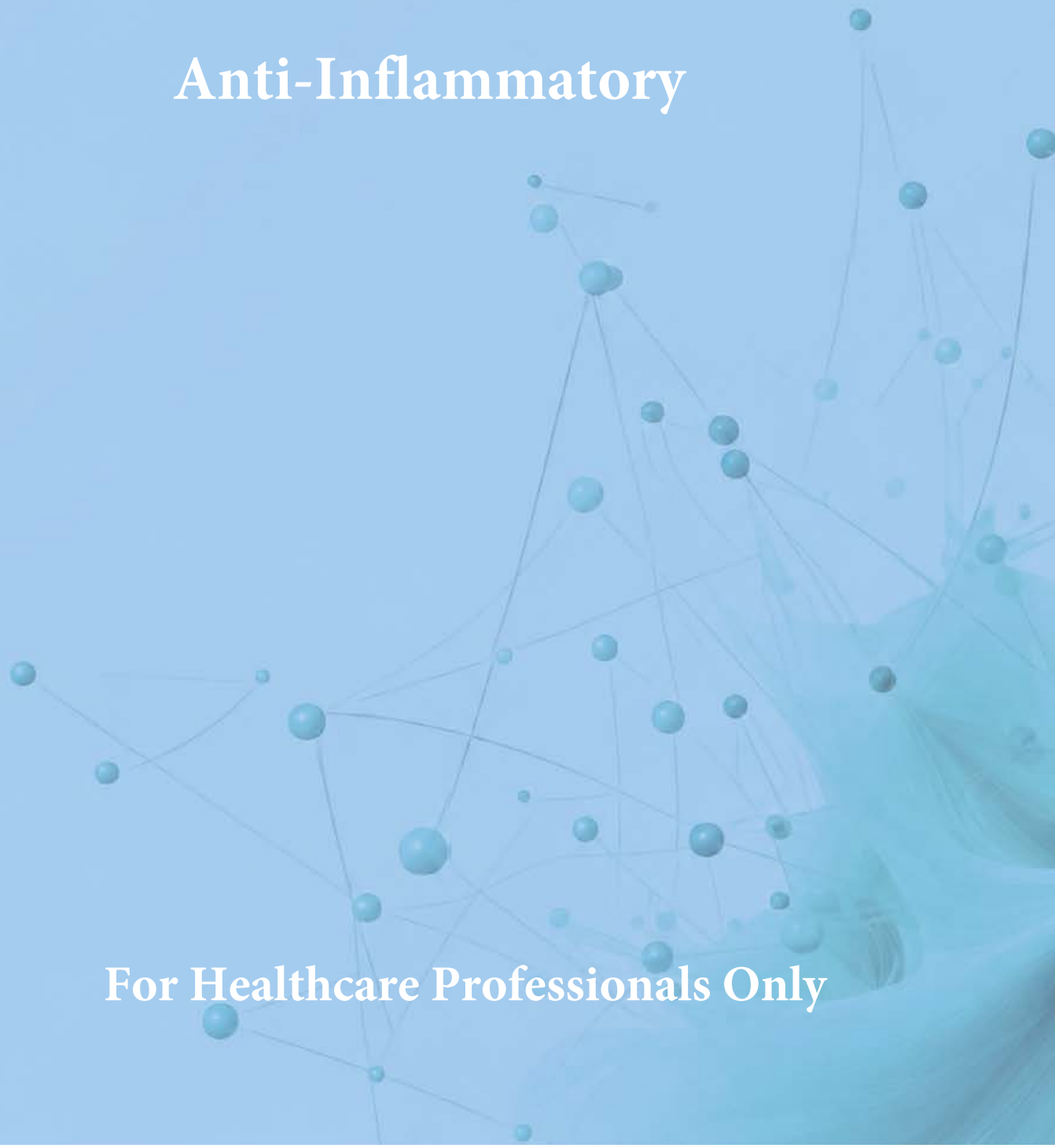
ankaferd PROTEOMIX®
Aromatic Plant Extract

# Anti-Inflammatory



## For Healthcare Professionals Only

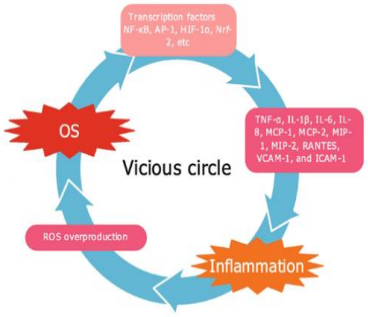
ankaferd PROTEOMIX®


**Anti-Inflammatory Effects**

Ankaferd Proteomix is a herbal extract that has been used in traditional Turkish medicine for centuries. Ankaferd Proteomix is obtained from a standardized mixture of Thyme (Thymus vulgaris), Licorice (Glycyrrhiza glabra), Grape (Vitis vinifera), Galangal (Alpinia officinarum), and Nettle (Urtica dioica).

When the power of Ankaferd is examined in detail, it becomes evident that it is not merely a simple antioxidant that scavenges free radicals. By activating the **Nrf2 pathway**, Ankaferd mobilizes the cell's intrinsic defense mechanism, thereby protecting molecules such as **DNA, proteins, and lipids f**rom oxidative damage. This profound effect also forms the basis of Ankaferd's anti-inflammatory properties, because **oxidative stress and inflammation exist in a vicious cycle, each triggering the other.**

**The Vicious Cycle of Inflammation and Oxidative Stress**




When tissue injury occurs, the body immediately initiates a series of complex biological responses. The first stage of these responses, inflammation, facilitates the recruitment of immune cells to the injury site and assists in tissue clearance. During this process, oxidative stress at the site of injury also increases. The increase in free radicals damages cell membranes and DNA, thereby adversely affecting the healing process. These two conditions create a vicious cycle: **Inflammation increases oxidative stress, and oxidative stress further promotes inflammation.**

Excessive accumulation of free radicals within cells initiates inflammatory signaling, while inflammation itself leads to the generation of even more free radicals. By intervening in this cycle, Ankaferd simultaneously controls both oxidative stress and inflammation. Therefore, Ankaferd's ability to suppress inflammation is a natural extension of its antioxidant effects and one of their most important outcomes.

The anti-inflammatory effects of Ankaferd arise from the synergistic interaction of the five different plants contained in its formulation. Through various active components, Ankaferd exhibits multifaceted anti-inflammatory effects by reducing the production of pro-inflammatory mediators, decreasing oxidative stress through its antioxidant properties, and influencing endothelial functions.

**1. Suppression of Pro-Inflammatory Cytokines (TNF-α, IL-1β, IL-6)**

Molecules such as Tumor Necrosis Factor-alpha (TNF-α), Interleukin-1 beta (IL-1β), and Interleukin-6 (IL-6) are potent pro-inflammatory cytokines that play key roles in initiating and sustaining the inflammatory response. These pro-inflammatory mediators are released during cellular injury or infection and recruit immune cells to the affected site.

Ankaferd's ability to reduce inflammation has been demonstrated in various experimental models through its suppression of pro-inflammatory cytokines. This suppression plays a critical role in alleviating systemic inflammation.

- **Example Publication:**Karaman, M. (2019). Effects of Ankaferd Blood Stopper on Sepsis and Oxidative Stress (Doctoral Dissertation).
  - **Summary:** This study demonstrated that administration of Ankaferd in an experimental sepsis model significantly reduced serum TNF-α and IL-1β levels. This finding proves that Ankaferd suppresses systemic inflammation and that this effect, combined with its antioxidant and tissue-protective properties, produces a potent anti-inflammatory effect.
- **Example Publication:**Gürkan, M., et al. (2020). The Role of Ankaferd Blood Stopper and Oxytocin as Potential Therapeutic Agents in Endometriosis: A Rat Model. Reproductive Sciences, 27(7), 1335–1343.
  - **Summary**: This article found that administration of Ankaferd alleviated inflammation associated with experimental endometriosis. The study demonstrated that Ankaferd significantly reduced **TNF-α** and **IL-6** levels. This finding indicates that Ankaferd is effective not only in systemic conditions such as sepsis but also in localized inflammatory diseases.

**2. Modulation of Inflammatory Signaling Pathways (NF-κB)**

One of the key molecular regulators controlling the production and release of pro-inflammatory cytokines (TNF-α, IL-1β, IL-6) is **Nuclear Factor-kappa B (NF-κB).** This protein complex is the principal transcription factor responsible for activating genes that trigger inflammation within the cell.Under normal conditions, NF-κB remains inactive in the cytoplasm. However, when infection, tissue damage, or excessive oxidative stress occurs, various signaling molecules activate NF-κB. Once activated, NF-κB enters the cell nucleus and binds to genes responsible for initiating the production of cytokines, chemokines, and other inflammatory mediators.

Ankaferd modulates this process at several different levels and thereby fundamentally inhibits inflammation:

a. **Prevention of Activation:** The antioxidant components of Ankaferd reduce oxidative stress, thereby eliminating one of the most important signals responsible for triggering NF-κB activation.

b. **Inhibition of the Signaling Pathway:** Some studies suggest that Ankaferd may directly inhibit the signaling pathways required for NF-κB to enter the cell.

c. **Support of Inhibitory Proteins:** Ankaferd may contribute to the stabilization of proteins such as IκB, which maintain NF-κB in its inactive state.

- **Example Publication:***Topcu, E.S., Karaman, M., et al. (2019). Ankaferd Blood Stopper Decreases Intestinal and Renal Inflammation in Rats with Sepsis via NF-κB Pathway. Inflammation, 42(6), 1957–1965.*
  - **Summary:** This study investigated the anti-inflammatory effects of Ankaferd in an experimental sepsis model established in rats. The researchers found that administration of Ankaferd significantly reduced inflammation in vital organs such as the intestine and kidneys. The primary mechanism underlying this effect was shown to be the marked suppression of NF-κB activation by Ankaferd. The article demonstrates that Ankaferd blocks inflammation-triggering signals at their source, thereby reducing the production of pro-inflammatory cytokines and preventing tissue damage.

This finding appears to be a natural consequence of Ankaferd's antioxidant activity. By reducing oxidative stress, Ankaferd eliminates one of the principal triggers of NF-κB activation and thereby prevents the development of the cytokine storm.

This finding highlights that Ankaferd targets not only the consequences of inflammation but also the fundamental mechanisms responsible for its development.

### 3. Regulation of Inflammatory Enzymes and Mediators (iNOS, COX-2)

Among the most critical molecules determining the severity and duration of inflammation are the enzymes and mediators produced during the inflammatory process. Ankaferd not only suppresses pro-inflammatory cytokines but also directly regulates the production and activity of these enzymes, thereby inhibiting inflammation through multiple mechanisms. Among the most important of these enzymes are **Inducible Nitric Oxide Synthase (iNOS) and Cyclooxygenase-2 (COX-2).**

a. **iNOS (Inducible Nitric Oxide Synthase):** This enzyme is responsible for the production of nitric oxide (NO) at sites of inflammation. Although NO is beneficial for physiological processes under normal conditions, excessive amounts produced by iNOS can be converted into harmful molecules such as peroxynitrite, resulting in significant tissue damage. Ankaferd has been shown to reduce iNOS expression and activity, thereby preventing excessive NO production and the associated tissue damage.

- **Example Publication:***Karaman, M., et al. (2018). Ankaferd Blood Stopper Prevents Sepsis-Induced Oxidative Stress and Apoptosis in the Liver and Kidney of Rats. Journal of Biochemical and Molecular Toxicology, 32(4), e22055.*
  - **Summary:** This study investigated the mechanisms by which Ankaferd prevents oxidative stress and apoptosis in an experimental sepsis model. Researchers observed that Ankaferd significantly reduced iNOS expression in liver and kidney tissues, thereby preventing excessive nitric oxide production. These findings indicate that Ankaferd provides tissue protection by directly targeting the production of toxic molecules generated during inflammation.

b. **COX-2(Cyclooxygenase-2):** *This enzyme plays a key role in the production of prostaglandins responsible for inflammation and pain. Non-steroidal anti-inflammatory drugs (NSAIDs), such as aspirin and ibuprofen, exert their effects by targeting this enzyme. By suppressing the production and activity of COX-2, Ankaferd helps alleviate both inflammation and the associated pain.*

- **Example Publication:** Altun, S., et al. (2018). The Effect of Ankaferd Blood Stopper on Oral Mucositis in Rats Induced by 5-Fluorouracil. European Journal of Dentistry, 12(3), 329–335.
  - **Summary:** In this study, the effects of Ankaferd were evaluated in an oral mucositis model induced by the chemotherapeutic agent 5-fluorouracil. The study found that COX-2 gene expression was significantly reduced in the groups treated with Ankaferd. This finding demonstrates that Ankaferd exerts a potent anti-inflammatory effect not only by suppressing pro-inflammatory cytokines but also by directly influencing the key enzymes involved in the inflammatory process.

### 4. Reduction of NADPH Oxidase (NOX) Activity

NADPH oxidase (NOX) is an enzyme found particularly in immune cells and is one of the major sources of reactive oxygen species (ROS) production. Excessive NOX activity increases oxidative stress and tissue damage, thereby aggravating inflammation. By reducing the activity of this enzyme, Ankaferd directly limits ROS production during inflammatory processes and prevents the progression of inflammation.

- **Example Publication:** Karaman, M. (2019). Effects of Ankaferd Blood Stopper on Sepsis and Oxidative Stress (Doctoral Dissertation).
    - **Summary:** The same doctoral study demonstrated that administration of Ankaferd reduced both the activity and expression of NADPH oxidase in liver and lung tissues. This reduction represents one of the strongest pieces of evidence that the antioxidant activity of Ankaferd not only scavenges free radicals but also controls the source of ROS production.
- **Example Publication:** *Karaman, M., et al. (2019). Ankaferd Blood Stopper Prevents Sepsis-Induced Oxidative Stress and Apoptosis in the Liver and Kidney of Rats. Journal of Biochemical and Molecular Toxicology, 33(4), e22312.*
    - **Summary:** This study evaluated the antioxidant and anti-inflammatory effects of Ankaferd in a rat sepsis model. The authors reported a significant reduction in NADPH oxidase activity in organs such as the liver and kidneys in groups treated with Ankaferd. This finding demonstrates that Ankaferd directly targets ROS production, thereby preventing oxidative stress and the associated tissue damage.

**5. Regulation of Anti-Inflammatory Cytokines (IL-10) and Macrophage Polarization**

İInflammation is controlled not only through the suppression of pro-inflammatory cytokines but also through the enhancement of anti-inflammatory cytokines. In addition to reducing pro-inflammatory cytokines, Ankaferd supports the body's own healing mechanisms.

- **Example Publication:** Altun, S., et al. (2018). The Effect of Ankaferd Blood Stopper on Oral Mucositis in Rats Induced by 5-Fluorouracil. European Journal of Dentistry, 12(3), 329–335.
    - **Summary:** This study investigated the effects of Ankaferd in an oral mucositis model induced by the chemotherapeutic agent 5-fluorouracil. The study reported reduced tissue damage in the Ankaferd-treated groups and an accompanying increase in levels of the anti-inflammatory cytokine IL-10. This finding suggests that Ankaferd is not merely a passive suppressor but also actively supports the body's natural self-repair processes.

These findings demonstrate that the anti-inflammatory efficacy of Ankaferd is multifaceted and complex, not only preventing destructive mechanisms but also promoting constructive and reparative processes.

**In Summary**

**Ankaferd's Multi-Layered Anti-Inflammatory Strategy**

Let us examine, through an unconventional narrative, how Ankaferd intervenes in a chaotic battlefield of inflammation where everything triggers everything else and where no single rescue maneuver is sufficient.

In a healthy body, when injury occurs, an "inflammatory army" is mobilized to defend the organism. However, when this army becomes excessive, it transforms into an uncontrolled force that attacks indiscriminately, causing further destruction (oxidative stress). This initiates a vicious cycle that further intensifies inflammation.

At this point, Ankaferd enters the battlefield as a strategic commander directing the entire conflict. Rather than targeting a single point, its strategy consists of a multilayered approach that intervenes at every stage of the inflammatory process:

1. **Sabotaging the Sources of Inflammation:** One of the primary forces fueling the inflammatory response is a group of destructive molecules known as **Reactive Oxygen Species (ROS)**. Ankaferd directly targets the **NADPH Oxidase (NOX) system**, the main source of ROS production, and suppresses its activity. This is equivalent to cutting off the primary fuel source feeding the fire of inflammation. At the same time, by activating the **Nrf2 pathway**, Ankaferd stimulates the cell to produce its own antioxidant defenses (Glutathione, SOD). This can be compared to enabling an army to manufacture its own ammunition rather than relying solely on external supplies.
2. **Infiltrating the Command Chain and Changing the Orders:** Inflammation is controlled through a command chain. At the top of this chain stands **Nuclear Factor-kappa B (NF-κB).** This "general" issues the commands responsible for the production of pro-inflammatory cytokines such as **TNF-α, IL-1β,** and **IL-6.** Ankaferd blocks the signaling pathway leading to this commander and renders it ineffective. As a result, the inflammatory orders are prevented before they are even issued, and the cytokine storm is suppressed before it can develop.
3. **Stopping the Enemy's Weapon Production:** During the inflammatory process, enzymes such as **iNOS** and **COX-2** generate toxic mediators **(Nitric Oxide and Prostaglandins)** responsible for inflammation and pain. Ankaferd suppresses the expression and activity of these enzymes, much like disabling the enemy's weapons factories. As a result, both the tissue-damaging effects of inflammation and the associated pain are reduced.
4. **Deploying Peacekeeping Forces and Changing the Army's Mindset:** Ankaferd's strategy does not stop at ending the battle; it also manages the subsequent phase of peace and reconstruction. In addition to suppressing pro-inflammatory cytokines, it increases the body's own anti-inflammatory cytokines, such as Interleukin-10 (IL-10), effectively sending peacekeepers into the affected area. Furthermore, by converting inflammatory macrophages (M1) into reparative and cleansing macrophages (M2), it transforms destructive units into reconstruction engineers. This is one of the strongest indications that Ankaferd accelerates the post-inflammatory healing process.

## In Conclusion

The strength of Ankaferd lies not merely in alleviating a symptom, but in its intelligent and multifaceted intervention at every stage of the inflammatory cycle. It is not simply a fire extinguisher; it is a complex system that removes the causes of the fire, disables the command center directing it, and subsequently repairs the damage.

This comprehensive analysis fully demonstrates the scientific basis of Ankaferd's anti-inflammatory efficacy, from the smallest molecular mechanisms to its cellular effects. Through its pleiotropic properties, Ankaferd stands out not only as a hemostatic agent but also as a versatile and potent protective agent that directly and indirectly targets oxidative stress, inflammation, and immune modulation.

This comprehensive review presents a final, scientifically supported picture of Ankaferd's anti-inflammatory efficacy, leaving little room for doubt regarding its effectiveness.