

Tragacanth Gum Facilitates Cutaneous Wound Healing Through Bioactive Polysaccharide-Driven Molecular Mechanisms

Soraya Agha Mohammadkhan¹, Somayyeh Meskarha¹, Hamid Babavalian² and Mohammad Reza Nourani³

1. Department of Basic Sciences, Science and Research Branch. Islamic Azad University, Tehran, Iran.
2. Applied Biotechnology Research Center, New Health Technologies Institute, Baqiyatallah University of Medical Sciences, Tehran, Iran
3. Tissue Engineering and Regenerative Medicine, New Health Technologies Institute, Baqiyatallah University of Medical Sciences, Tehran, Iran.

* corresponding author: Mohammad Reza Nourani 'r.nourani@yahoo.com



Soraya Agha Mohammadkhan

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Abstract

Tragacanth gum is a promising natural polysaccharide exudate from *Astragalus* species that presents bioactive properties to enhance cutaneous wound healing. This review discusses its molecular mechanisms in all phases of the healing process: hemostasis, inflammation, proliferation, and remodeling. Tragacanth consists of water-soluble tragacanthin (arabinogalactans) and swellable bassorin, conferring properties such as high viscosity, moisture retention, and pH stability that enable various hydrogel, film, and composite biomaterials. It modulates inflammation by downregulating TNF- α , IL-1 β , and NF- κ B while scavenging ROS. It also enhances fibroblast proliferation, collagen I/fibronectin synthesis via TGF- β , promotes M2 macrophage polarization, induces VEGF-driven angiogenesis through PI3K/Akt, and accelerates the migration of keratinocytes for re-epithelialization. In vitro and rodent in vivo studies have shown its biocompatibility along with reduced inflammation, enhanced granulation, and faster closure in full-thickness wounds. Compared to chitosan, alginate, hyaluronic acid, and collagen, tragacanth demonstrates better rheological properties and sustainability with less immunogenicity. Challenges include composition variability and a lack of clinical trials. Future combinations with nanoparticles, stem cells, or smart polymers may result in smart dressings with multiple functionalities. Being a GRAS, traditionally used biopolymer, tragacanth has the potential for translation in clinical applications of regenerative wound therapies, which requires further standardized studies and human trials.

Keywords: Tragacanth , Wound Healing , Molecular Mechanisms

Introduction

Wound healing is a dynamic and highly regulated biological process that is important in the restoration of integrity to damaged skin and deeper tissues. It consists of four overlapping, yet distinct, phases: hemostasis, inflammation, proliferation, and remodeling.

The hemostasis phase, starting immediately after injury, involves vasoconstriction and the aggregation of platelets that form a fibrin clot to prevent further bleeding. Next, the inflammatory phase involves the infiltration of neutrophils and macrophages into the wound site, which phagocytose

pathogens and debris while producing cytokines and growth factors that coordinate subsequent stages. The proliferation stage includes the proliferation and migration of fibroblasts, keratinocytes, and endothelial cells for the reconstruction of the ECM, re-epithelialization of the wound surface, and angiogenesis. Finally, during the remodeling phase, the maturation of collagen and reorganization of the ECM lead to the restitution of tensile strength and functional architecture to the skin. (1–3).

In recent years, natural biopolymers have gained prominence in regenerative medicine due to their biocompatibility, biodegradability, and structural similarity to native ECM. These materials, derived from polysaccharides, proteins, and other plant or microbial sources, offer multifunctional benefits such as moisture retention, antimicrobial activity, and controlled drug release (4). Biopolymers like chitosan, alginate, hyaluronic acid, and collagen have been extensively studied and commercialized for wound dressing applications. Their ability to mimic biological scaffolds and interact with cellular components makes them ideal candidates for enhancing wound healing outcomes(5).

In this context, the fact that among these biopolymers, the naturally occurring exuded compound from the *Astragalus* species, the Tragacanth gum, presents appealing physico-biological characteristics makes it deserving of analysis from a biomedical perspective, given its high viscosity, film forming capability, and polysaccharides content. In particular, the Tragacanth gum's chemical composition, based on arabinogalactans and tragacanthic acid, presents promising properties for the modulation of inflammatory processes, fibroblasts stimulation, and ECM remodeling (6,7). Preliminary studies suggest that Tragacanth-based hydrogels and composites may serve as effective wound healing platforms, especially when combined with other bioactive agents. Given its historical use, favorable safety profile, and emerging molecular evidence, a comprehensive review of Tragacanth gum's role in cutaneous wound healing is both timely and necessary.

Botanical and Biochemical Profile of Tragacanth

Tragacanth gum is a natural exudate obtained from the dried sap of several species of the genus *Astragalus*, particularly *A. gummifer*, *A. microcephalus*, and *A. kurdicus*, which are native to arid and semi-arid re-

gions of Iran, Turkey, and parts of Central Asia(6). The gum is harvested by making incisions in the root or stem of the plant, allowing the viscous exudate to dry into flakes or ribbons that are later purified and processed for biomedical or industrial use (8).

Chemically, Tragacanth is a complex, heterogeneous polysaccharide composed primarily of two fractions: tragacanthin (water-soluble) and bassorin (water-insoluble but swells in water). Tragacanthin consists of arabinogalactans and acidic polysaccharides rich in galacturonic acid, while bassorin contributes to the gum's high viscosity and gel-forming capacity (9). This dual-phase composition gives Tragacanth its unique rheological properties, making it suitable for hydrogel formation, film casting, and controlled drug delivery systems(10).

The biofunctional properties of Tragacanth gum are closely tied to its molecular structure. Its high molecular weight and branched polysaccharide chains enable strong water retention, shear-thinning behavior, and stability across a wide pH range (11). These features are particularly advantageous in wound healing applications, where moisture balance, mechanical protection, and bioactivity are critical. Moreover, the presence of uronic acids and hydroxyl groups allows for chemical modification and crosslinking, facilitating the development of composite biomaterials with tailored properties (12).

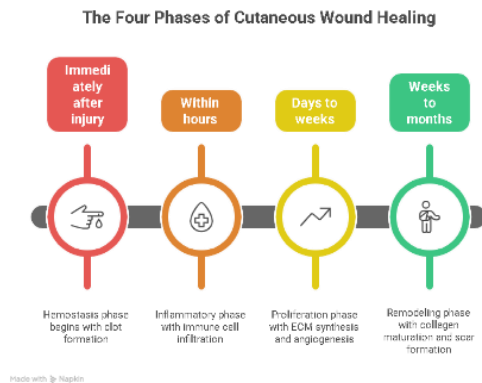
Apart from its physiochemical qualities, Tragacanth displays biological activities pertinent to skin repair. Its anti-inflammatory, antioxidant, and antibacterial properties have been reported in studies. important for controlling the wound microenvironment. Further emphasizing its potential as a regenerative agent is its ability to promote fibroblast growth, collagen formation, and epithelial cell migration.(13,14).

Cutaneous Wound Healing: Molecular Overview

Wound healing is a complex and dynamic biological process that restores the integrity of injured skin through a coordinated cascade of cellular and molecular events. It is traditionally divided into four overlapping phases: hemostasis, inflammation, proliferation, and remodeling(15).

The hemostasis phase begins immediately after injury, where platelets aggregate at the wound site and release clotting factors such as thrombin and fibrinogen to form a fibrin clot. This clot not only prevents hemorrhage but also serves as a provisional matrix for cell migration and growth factor release, including platelet-derived growth factor (PDGF) and transforming growth factor-beta (TGF- β)(2,16).

The inflammatory phase follows within hours and is characterized by the infiltration of neutrophils and monocytes. Neutrophils clear pathogens and debris through phagocytosis and release reactive oxygen species (ROS) and proteases. Monocytes differentiate into macrophages, which play a dual role: pro-inflammatory (M1) macrophages secrete cytokines such as TNF- α and IL-1 β , while anti-inflammatory (M2) macrophages promote tissue repair by releasing IL-10, VEGF, and TGF- β (3,4).



During the proliferation phase, fibroblasts migrate into the wound bed and begin synthesizing extracellular matrix (ECM) components, including collagen types I and III, fibronectin, and hyaluronic acid. Concurrently, keratinocytes proliferate and migrate to re-epithelialize the wound surface, while endothelial cells form new capillaries through angiogenesis, driven by VEGF and angiopoietins (5). This phase is also regulated by matrix metalloproteinases (MMPs), which remodel the ECM and facilitate cell migration (6).

The final remodeling phase can last for weeks to months and involves the replacement of immature collagen (type III) with mature collagen (type I), restoring tensile strength to the skin. Fibroblasts undergo apoptosis, and the vascular network regresses. TGF- β continues to play a central role in ECM maturation,

while MMPs and their inhibitors (TIMPs) balance matrix turnover(7).

At the molecular level, wound healing is orchestrated by a network of signaling pathways including NF- κ B, MAPK, PI3K/Akt, and Wnt/ β -catenin. These pathways regulate inflammation, cell proliferation, migration, and differentiation. Dysregulation of these signals can lead to chronic wounds or excessive scarring (17).

Mechanisms of Tragacanth Gum in Wound Healing

With important molecular events in cutaneous wound healing, tragacanth gum displays complex bioactivity. Its impacts encompass anti-inflammatory modulation, fibroblast activation, angiogenesis, and epithelial regeneration, so making it a promising applicant for therapeutic regenerative treatments and bioactive wound coverings.

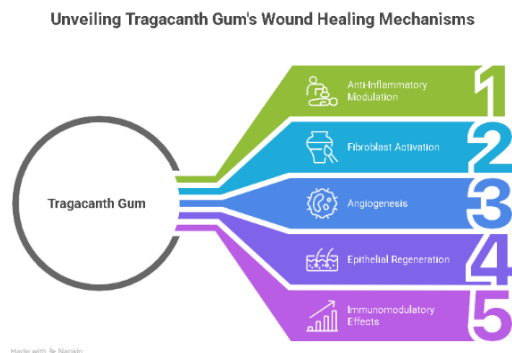
Tragacanth gum modulates inflammation by downregulating pro-inflammatory cytokines such as TNF- α and IL-1 β and inhibiting NF- κ B signaling(18). Its polysaccharide components also scavenge reactive oxygen species (ROS), reducing oxidative stress and protecting cellular integrity (19). These actions help transition the wound microenvironment from a pro-inflammatory to a reparative state.

In vitro studies have shown that Tragacanth gum enhances fibroblast proliferation and upregulates the expression of collagen type I and fibronectin(20). This is mediated through TGF- β signaling, which promotes myofibroblast differentiation and matrix synthesis. The gum's hydrophilic nature also supports cell adhesion and migration, facilitating granulation tissue formation.

Tragacanth gum has been reported to stimulate endothelial cell migration and tube formation, likely through VEGF induction and modulation of the PI3K/Akt pathway(21). Concurrently, it promotes keratinocyte proliferation and migration, accelerating re-epithelialization and barrier restoration(22).

Its immunomodulatory effects include promoting M2 macrophage polarization, which enhances tissue repair and suppresses chronic inflammation (23). Additionally, its acidic polysaccharides exhibit mild al activity

against common wound pathogens, contributing to infection control without disrupting host cells (24).



Tragacanth-Based Biomaterials and Formulations

With important molecular events in cutaneous wound healing, tragacanth gum displays complex bioactivity. Its impacts encompass anti-inflammatory modulation, fibroblast activation, angiogenesis, and epithelial regeneration, so making it a promising applicant for therapeutic regenerative treatments and bioactive wound coverings.(25).

Tragacanth-based hydrogels have demonstrated excellent biocompatibility, mechanical stability, and controlled drug release profiles. When crosslinked with agents like glutaraldehyde or genipin, Tragacanth hydrogels exhibit enhanced elasticity and degradation rates suitable for chronic wound management(26).

Tragacanth gum can be cast into thin films that serve as protective barriers over wounds. These films are breathable, flexible, and capable of incorporating bioactive compounds such as antimicrobial agents, growth factors, or herbal extracts. Studies have shown that Tragacanth films loaded with silver nanoparticles or plant-derived antioxidants accelerate wound closure and reduce microbial colonization (27,28).

Combining Tragacanth with other natural or synthetic polymers, such as chitosan, alginate, polyvinyl alcohol (PVA), or gelatin, results in composite scaffolds with improved mechanical strength, porosity, and cell adhesion properties(29). These scaffolds support fibroblast infiltration, angiogenesis, and epithelial regeneration.

Recent advances have explored injectable Tragacanth-based hydrogels and sprayable formulations for irregular or deep wounds. These systems conform to

wound geometry and deliver therapeutic agents directly to the site, offering minimally invasive treatment options (30).

Tragacanth's anionic nature and high surface area allow for efficient encapsulation and sustained release of drugs, including antibiotics, anti-inflammatory agents, and growth factors (31).

Comparative Analysis with Other Biopolymers

Wound healing has been much investigated using natural biopolymers including chitosan, alginate, hyaluronic acid, and collagen. Tragacanth gum has distinct advantages when contrasted to these. in terms of viscosity, pH stability, and sustainability(32).

Chitosan is known for its antimicrobial activity and ability to form porous scaffolds, but may trigger allergic reactions in shellfish-sensitive individuals (33). Alginate forms ionically crosslinked hydrogels with excellent moisture retention but limited cell adhesion (34). Hyaluronic acid promotes cell migration and angiogenesis but is mechanically weak and expensive (35). Collagen supports fibroblast attachment and tissue remodeling but may cause immunogenic responses depending on its source(36,37).

Tragacanth gum supports fibroblast proliferation, modulates inflammation, and integrates well into composite biomaterials, making it a competitive alternative in wound care(25).

Clinical and Translational Implications

Tragacanth gum is generally recognized as safe (GRAS) and exhibits excellent biocompatibility in vitro (38). Cytotoxicity assays have shown minimal adverse effects on fibroblasts, keratinocytes, and endothelial cells.

When Tragacanth-based hydrogels or films were used to full-thickness wounds in in vivo experiments with rodent models, accelerated wound closure, greater collagen deposition, and decreased inflammatory indicators were seen. (39). Histological analyses revealed improved epithelialization and granulation tissue formation.

Despite its favorable safety profile, Tragacanth gum has not yet been widely evaluated in clinical trials for wound healing. Regulatory approval will require

standardized extraction methods, reproducible formulation protocols, and comprehensive toxicological data (40).

Its compatibility with existing wound care technologies and potential for drug delivery make it a strong candidate for commercial development, especially in resource-limited settings (41).

Most studies on Tragacanth gum focus on its physicochemical properties and general bioactivity, with few exploring its precise molecular mechanisms in wound healing. The roles of key signaling pathways, such as NF- κ B, PI3K/Akt, and TGF- β , remain underexplored (42).

The composition of tragacanth gum varies greatly depending on the *Astragalus* species, geographical origin, and extraction process. This variation influences its viscosity, bioactivity, and reproducibility in formulations. Standardized procedures for gum harvesting, purification, and characterization are urgently required. (43).

While several in vitro and animal studies have demonstrated promising results, human clinical trials evaluating Tragacanth-based wound dressings are virtually nonexistent. Rigorous preclinical models, including diabetic wounds, burns, and chronic ulcers, should be prioritized (44).

Tragacanth's compatibility with other biopolymers and bioactive agents opens avenues for multifunctional wound healing platforms. Future research should explore its integration with stem cells, exosomes, nanoparticles, and smart polymers (20,45). Given its botanical origin and historical use in Persian and Ayurvedic medicine, Tragacanth gum offers a sustainable and culturally relevant alternative to synthetic materials.

Conclusion

With great potential in wound healing, tragacanth gum is a versatile, plant-based biopolymer. Its capacity to regulate inflammation, foster ECM remodeling, and fit into several biomaterial systems makes it a great prospect for next-generation regenerative medicine. Unlocking its whole therapeutic potential will need ad-

ressing present knowledge gaps by means of mechanistic, translational, and clinical research.

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