FOR HEALTHCARE PROFESSIONALS

Acemannan & The Dalton Story

Why molecular weight is the variable that defines whether acemannan works.

Abstract

Acemannan, a mannose-rich polysaccharide derived from the inner-leaf gel of *Aloe vera*, has been the subject of more than four decades of peer-reviewed research and over 100 issued U.S. patents. Yet most acemannan-containing products available to consumers fail to produce the immunomodulatory effects documented in the literature. This white paper presents the reason: **molecular weight**. The bioactivity of acemannan depends on a specific molecular weight range — 50,000 to 400,000 daltons — identified in landmark research by Im et al. (2005) and corroborated by subsequent investigations. Products containing aloe-derived material outside this range deliver little or none of the immune, gut, and cellular benefits attributed to the molecule. TreoCare's acemannan formulation is sourced exclusively from aloe cultivated for this molecular weight fraction, stabilized to preserve its biological integrity, and distributed in partnership with Alovéa — a manufacturer with 22 countries of regulatory experience.

Authorship & Distribution

This white paper was prepared by TreoCare, an authorized educator and distributor of acemannan-based nutritional support. The product itself (Alovéa Immun) is manufactured by Alovéa under their established quality and regulatory frameworks. Scientific claims herein reference primary literature; no statement should be construed as a representation of disease treatment.

1. The Acemannan Question

In the late 1980s and early 1990s, researchers at Carrington Laboratories in Texas identified, isolated, and characterized a long-chain polysaccharide from the inner-leaf gel of *Aloe vera* and named it **acemannan**. In 1992, the United States Patent and Trademark Office granted U.S. Patent No. **5,106,616** for the administration of acemannan, naming Bill H. McAnalley, Ph.D., Robert H. Carpenter, D.V.M., and Harley R. McDaniel, M.D. as the inventors and Carrington Laboratories as the assignee.

In the years that followed, acemannan accumulated a regulatory and scientific track record that is unusual for a botanical compound:

- USDA recognition as an **immunomodulator** for veterinary use (immunostimulant therapy in small animals; vaccine adjuvant in poultry)
- Approval for use in topical wound care systems for both human and veterinary applications
- More than **200 peer-reviewed studies** documenting effects on macrophage activation, cytokine signaling, and gut microbiota

- More than **100 issued U.S. patents** covering extraction, stabilization, formulation, and therapeutic application

Despite this evidence base, acemannan-containing supplements available today produce highly inconsistent results in real-world use. Practitioners frequently report that one aloe-derived product appears to support patients meaningfully while another, marketed in similar language, produces no observable effect. The variable that explains this inconsistency is not dosage. It is not formulation strategy. It is not even purity.

THE CENTRAL INSIGHT

The bioactivity of acemannan is governed by **molecular weight**. A product can be labeled "acemannan" or "aloe vera inner-leaf extract" and contain a quantitatively significant amount of polysaccharide — and still fall outside the molecular weight range where biological activity occurs.

2. The Dalton Story

The molecular weight argument is not new. It is, however, systematically under-emphasized in commercial marketing.

2.1 The Im et al. (2005) Landmark Study

In 2005, Im SA and colleagues at Sookmyung Women's University in South Korea published a fractionation study in *International Immunopharmacology* that has since become the reference point for understanding acemannan bioactivity. The team separated *Aloe vera* gel polysaccharides into discrete molecular weight ranges and tested each fraction independently against human peripheral blood monocytes and macrophage cell lines.

The result was unambiguous. Polysaccharide fractions in the **50,000 to 400,000 dalton range** produced the strongest immunomodulatory effects — measurable increases in macrophage activation, cytokine signaling, and antigen-presentation behavior. Fractions outside this range — both smaller and larger — produced little or no detectable immune-cell response under the same conditions.

This finding was not an isolated artifact. Subsequent investigations (reviewed in Reynolds & Dweck, 1999; corroborated by Sheets et al. and others) have repeatedly confirmed that *Aloe vera* polysaccharide fractions exhibit a clear molecular-weight-dependent activity profile.

2.2 What This Means in Practice

Aloe is rarely processed with the molecular weight question in mind. A typical commercial aloe extraction yields polysaccharides distributed across a wide weight range:

- **Short-chain fragments (<50,000 daltons)** — absorbed systemically through the intestinal wall, contributing dietary mannose and supporting cellular signaling, but lacking the macrophage activation properties of the medium-chain range.

- **Medium-chain fractions (50,000 to 400,000 daltons)** — the immunoactive window. Activate macrophages via cell-surface receptors, support Th1/Th2 cytokine balance, and modulate inflammatory signaling.
- **Long-chain fractions (>400,000 daltons)** — function primarily as prebiotic substrates for the gut microbiome, supporting beneficial fermentation and short-chain fatty acid production, but largely too large to act directly on systemic immune cells.

A finished product whose polysaccharide content sits predominantly outside the 50–400 kDa window may still test positive for "acemannan content" on a label assay while delivering little of the immune-modulating activity that practitioners and patients expect.

WHY MOST PRODUCTS UNDERPERFORM

Most commercial aloe products optimize for yield, cost, and shelf stability — not molecular weight distribution. The result: a marketplace crowded with technically-acemannan-containing products that bear little functional resemblance to the molecule documented in the research literature.

3. Cultivation & Stabilization

Solving the molecular weight problem requires intervention at two stages: how the plant is grown and how the gel is processed.

3.1 Cultivation

TreoCare's acemannan is sourced from aloe cultivated specifically for the medium-chain molecular weight fraction. **Dr. Santiago Rodriguez**, a Mexican aloe agronomist whose operation supplies the raw material, has developed cultivation and harvest practices that consistently yield gel with the desired polysaccharide profile. Aloe destined for cosmetic applications — which typically prizes high-molecular-weight viscosity — is grown and sold separately. The 50–400 kDa fraction is reserved for immunological use.

3.2 Stabilization

Once harvested, *Aloe vera* inner-leaf gel begins to degrade rapidly. Within 24 to 48 hours under ambient conditions, unstabilized acemannan loses much of its immune-regulatory capacity through enzymatic depolymerization and oxidation. The 1992 Carrington patent (U.S. 5,106,616) and subsequent process patents address this with proprietary stabilization methods that preserve the polysaccharide's molecular structure during extraction, concentration, and encapsulation.

Without effective stabilization, even properly cultivated aloe yields an inert product by the time it reaches the consumer.

3.3 Regulatory Standing

Acemannan occupies an unusual regulatory position. Multiple attempts to classify it as a pharmaceutical drug for human therapy were unsuccessful — not because of safety concerns, but because acemannan does not appear to *alter* normal physiology. It supports and enhances inherent immune regulation. This places it firmly within the category of nutritional immune support rather than drug intervention.

Outcomes of this regulatory history include:

- USDA approval as an immunomodulator and vaccine adjuvant in veterinary medicine — a recognition extended to very few botanical compounds
- Approval for use in topical wound-care systems
- Distribution in 22 countries under various regulatory frameworks, all as a nutritional supplement rather than a drug

A NOTE ON COMPLIANCE

Acemannan supplements are not intended to diagnose, treat, cure, or prevent any disease. The statements in this paper have not been evaluated by the FDA. Practitioners considering acemannan should do so within the framework of nutritional and integrative care, not as a replacement for standard medical treatment.

4. Mechanisms of Action

The biological activity of stabilized acemannan operates through several pathways relevant to integrative practice. None of these mechanisms constitute treatment of disease; each describes a normal physiological process that the molecule supports.

4.1 Macrophage Activation

Macrophages are the principal phagocytic cells of the innate immune system and act as **master regulators of immune defense, repair, and regeneration**. Acemannan in the 50–400 kDa range engages macrophage cell-surface mannose receptors, activating downstream signaling that increases cytokine production, antigen presentation, and the modulation of pro- and anti-inflammatory responses.

4.2 Th1/Th2 Balance & Inflammatory Resolution

Rather than provoking an indiscriminate pro-inflammatory cascade — the mechanism of many herbal "immune boosters" — acemannan appears to support Th1/Th2 cytokine balance and the appropriate resolution of inflammatory episodes. This is consistent with the broader frame of **immune optimization** rather than **immune stimulation**: the goal is a response system that activates appropriately and resolves cleanly, not one that is chronically elevated.

4.3 Gut-Immune Axis Support

The long-chain polysaccharide fraction (>400 kDa) functions as a prebiotic substrate for beneficial gut bacteria. Fermentation produces short-chain fatty acids (SCFAs) — particularly butyrate — which support colonocyte nutrition, gut barrier integrity, and gut-mediated immune regulation (Koh et al., reviewed in *Nature Reviews Immunology*).

4.4 Cellular Communication

Acemannan is approximately 95% mannose by composition. Mannose participates in glycoprotein synthesis and serves as a substrate for cellular signaling molecules across multiple tissue types. The short-chain fragments that are absorbed systemically appear to contribute to this pool of cellular communication substrate.

4.5 Safety Profile

Stabilized acemannan derived from inner-leaf gel does not contain aloin — the anthraquinone laxative compound concentrated in aloe leaf latex. Properly extracted product is free of aloin, heavy metals, pesticides, and mycotoxins, and does not accumulate in tissues. Excess intake of the higher-molecular-weight fraction functions as prebiotic nutrition rather than producing toxicity.

5. Clinical Integration

Acemannan in the 50–400 kDa fraction is positioned as a foundational nutritional support within an integrative care model. It is appropriate for individuals experiencing immune dysregulation associated with stress, aging, environmental exposure, compromised gut function, or recovery from illness.

5.1 Practitioner Considerations

- **Mechanism category:** immune optimization via macrophage regulation (not stimulation)
- **System scope:** reinforces gut-immune axis integrity; supports Th1/Th2 balance and inflammatory resolution
- **Use horizon:** suitable for daily, long-term nutritional support rather than acute intervention
- **Drug interactions:** no clinically significant interactions reported in the available literature; standard caution applies for immunosuppressed patients, in whom adjustments to immune-modulating supplementation should be coordinated with the prescribing physician
- **Pregnancy / lactation:** insufficient data for specific recommendation; standard cautions apply

5.2 What Acemannan Is Not

It is worth being explicit about category boundaries. Acemannan is not an antibiotic. It is not an antiviral. It is not a treatment for autoimmune disease. It does not replace pharmaceutical therapy or standard-of-care medical management. It is a nutritional support — a substrate the immune system can use to operate more appropriately within its normal physiological range.

Patients seeking acute disease intervention should be directed to standard medical care. Patients seeking nutritional reinforcement of normal immune function — particularly in contexts of chronic stress, recovery from acute illness, or general systems-based wellness — may benefit from a stabilized acemannan formulation in the 50–400 kDa range.

5.3 Why TreoCare

Most acemannan-containing products on the market do not specify their molecular weight distribution. This is the single variable that determines whether the bioactivity documented in 40+ years of research is present in the bottle. TreoCare's acemannan is sourced from aloe cultivated by Dr. Santiago Rodriguez specifically for the immunoactive 50–400 kDa fraction, stabilized through processes developed and patented by Carrington Laboratories beginning in 1992, and manufactured to international standards by Alovéa, our distribution partner.

For practitioners, this means: the molecular weight question is resolved at the source. You are not relying on a generic aloe extract to deliver specific molecular weight bioactivity. You are recommending a product engineered around the variable that determines whether the molecule works.

References & Compliance

Scientific References

1. McDaniel HR, et al. Macrophage activation and immune modulation by acetylated mannans derived from *Aloe vera*. *International Immunopharmacology.*

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5. Koh A, et al. Role of short-chain fatty acids in gut health and immune regulation. *Nature Reviews Immunology.*

6. U.S. Patent No. 5,106,616. Administration of Acemannan. Inventors: McAnalley BH, Carpenter RH, McDaniel HR. Assignee: Carrington Laboratories, Inc. Granted April 21, 1992.

7. U.S. Department of Agriculture. Approval of acemannan as an immunostimulant and vaccine adjuvant in veterinary applications.

Disclaimer

The information in this white paper is provided for healthcare professional and educational purposes only. It is not intended to diagnose, treat, cure, or prevent any disease. These statements have not been evaluated by the U.S. Food and Drug Administration. Acemannan-containing nutritional supplements distributed by TreoCare are dietary supplements regulated under FDA structure-function rules; they are not pharmaceutical drugs.

TreoCare is an authorized distributor and educator. The acemannan-containing product referenced (Alovéa Immun) is manufactured by Alovéa under their established regulatory frameworks. No statement in this paper should be construed as a representation or warranty of any specific clinical outcome. Practitioners are encouraged to evaluate the primary literature and use professional judgment in any patient context.

Contact & Further Information

For practitioner inquiries, additional research summaries, or to request a sample for evaluation, contact TreoCare at **treocare.com**.