Simplifying Progress

# Advancing Gene Therapy: Stabilization of Viral Formulations with Recombumin® Human Albumin

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## Introduction

Gene and cell therapy using viral vectors - particularly adeno-associated viruses (AAVs) — is transforming the treatment landscape for a range of genetic and chronic conditions. However, a critical bottleneck remains: preserving AAV stability during storage and handling. AAVs are highly sensitive to temperature fluctuations and can degrade rapidly above -80°C, leading to loss of biological activity and compromised therapeutic efficacy.

We demonstrate that Recombumin®, a high-purity recombinant human albumin, significantly enhances the stability of AAVs across a wide range of storage conditions, ensuring superior preservation and reliability. As a multifunctional excipient, Recombumin® provides several key benefits:

- Prevents surface adsorption
- Minimizes particle aggregation
- Protects against mechanical shear stress
- Acts as a powerful antioxidant

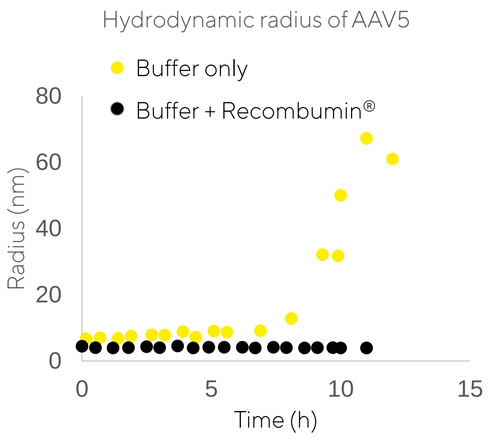
Unlike serum-derived or other recombinant albumins, Recombumin® offers superior purity, high stability and a minimal aggregation profile. This ensures that there will be no confounding results from a degrading albumin. High stability albumin is a critical property, proven to maintain consistent protection of AAV capsid integrity and concurrent functionality.

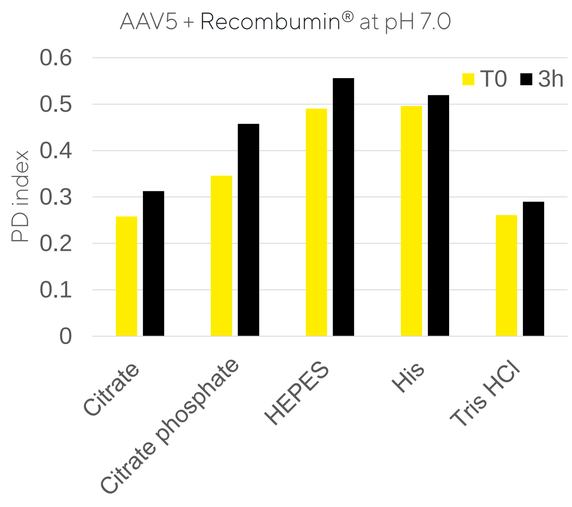
Furthermore, when formulated with specific anions, buffers, salts and excipients, Recombumin® provides enhanced viral stability. This leads to extended shelf life, more flexible storage conditions, and reduced product waste. Improved preservation of viral titers may also enable lower dosing requirements, ultimately decreasing manufacturing costs and increasing the accessibility of gene and cell therapies.

## Optimizing AAV Formulation: The Critical Role of Buffer Selection

Analysis of the hydrodynamic radius revealed that buffers alone were not sufficient to prevent AAV5 aggregation. However, with Recombumin®, the formulation demonstrated a significant reduction in aggregation and improved size uniformity.

We evaluated the impact of buffer composition on AAV5 stability by measuring the polydispersity (PD) index using dynamic light scattering (DLS) following a 3-hour incubation at 25°C, pH 7.0. Various buffer systems were tested, all incorporating **Recombumin®**. The results show that **Tris** and **Citrate** buffers yielded the lowest PD indices, indicating greater particle uniformity and enhanced formulation stability.

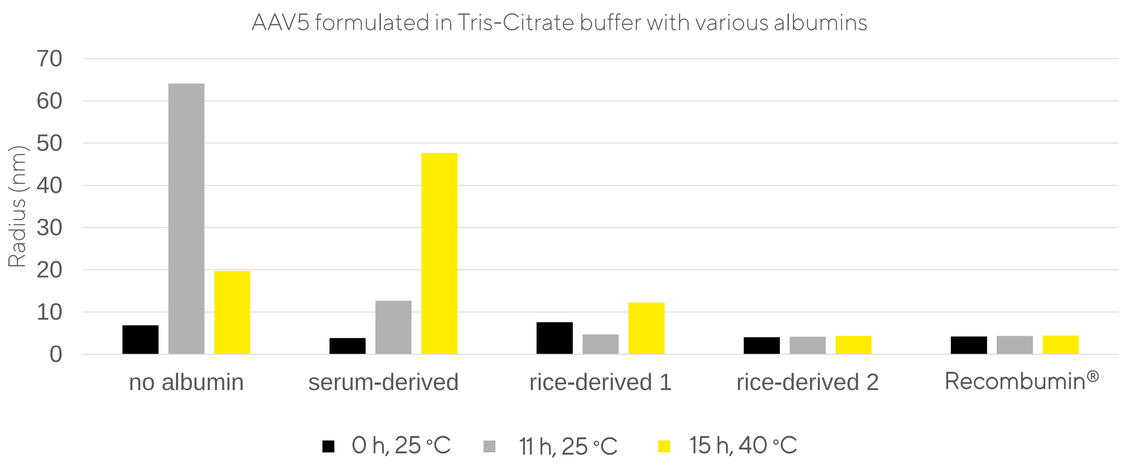



## The Importance of Albumin Source: Superior Results with High-Quality Recombinant Albumin

To assess the impact of different albumin sources on AAV stability, we examined changes in hydrodynamic radius of AAV5 formulated in Tris-Citrate buffer over time and under thermal stress. **Recombumin®** consistently outperformed other albumin types, maintaining a stable radius at 0 hours and 25°C, and showing minimal changes even after 15 hours at 40°C.

In contrast, **serum-derived** and **rice-derived** albumins exhibited significant fluctuations in Rh under the same conditions, suggesting reduced stability and increased aggregation risk. These results highlight the superior stabilizing properties of Recombumin®, reinforcing the critical role of high-quality recombinant albumin in maintaining AAV integrity for effective and reliable gene therapy formulations.



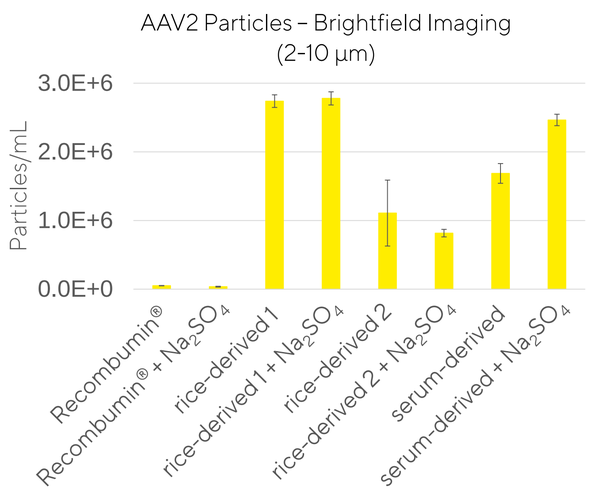

## Recombumin®: Enabling Exceptional Long Term AAV Stability Without Cryopreservation

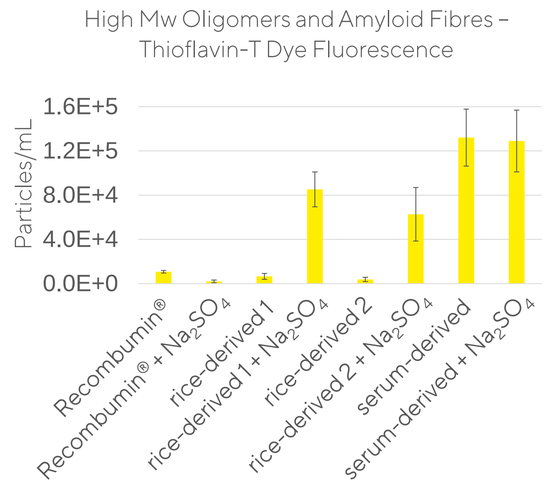
We evaluated subvisible particle formation in AAV2 formulations **stored at 4 °C** for **two months** using the Halo® Aura instrument for background membrane imaging. AAV2 was maintained at a concentration of $1.0 \times 10^{12}$ GC/mL. Analysis focused on: 1) Brightfield imaging to quantify subvisible particles. 2) Thioflavin-T dye fluorescence to detect high molecular weight (Mw) oligomers and amyloid-like aggregates.

**Two buffer conditions were tested:**

- Tris/Citrate: Tris-HCl (pH 6.8), Citrate, $MgCl_2$
- Tris/Citrate + supplemented with sodium sulfate ($Na_2SO_4$)
- Formulations included various albumin sources.

The data below demonstrates that Recombumin®, particularly in the presence of $Na_2SO_4$, exhibited an exceptionally low aggregation profile after two months—highlighting its effectiveness in maintaining AAV2 stability under refrigerated conditions.




## Conclusion

Our data demonstrate that **Recombumin®**, a high-purity recombinant human albumin, plays a pivotal role in enhancing the stability of AAV formulations. When used in optimized buffer systems such as **Tris-Citrate**, **Recombumin®** significantly reduces particle aggregation, preserves hydrodynamic radius, and protects AAV vectors under both thermal and mechanical stress.

Compared to serum-derived and rice-derived albumins, Recombumin® consistently delivers superior protection against degradation—maintaining structural integrity even at elevated temperatures and over extended periods. This is further supported by **lower subvisible particle counts** and **reduced formation of high molecular weight oligomers and amyloid structures**, underscoring its stabilizing effect.

Crucially, this formulation removes the need for **ultra-low temperature storage** (e.g., –80 °C freezers), which are costly, logistically challenging, and impractical in many **hospital and clinical settings**. In contrast to several marketed AAV therapies that suffer from **poor stability and strict frozen storage requirements**, Recombumin®-based formulations offer a **more robust and flexible alternative**—facilitating easier transport, simplified handling, and improved accessibility for gene therapy delivery.

These findings position Recombumin® as a **key enabling excipient** for next-generation viral vector therapeutics, advancing both **formulation resilience** and **clinical practicality**.

## Recombumin®: Quality, Consistency and Performance for Advanced Therapies

- Manufactured in Nottingham, UK, in accordance with ICH Q7 current Good Manufacturing Practice (cGMP) for Active Pharmaceutical Ingredients and certified by the UK Medicines and Healthcare products Regulatory Agency (MHRA) ensuring adherence to the highest standards of quality and safety.
- Recombumin® is the only recombinant human albumin in compliance for the USP-NF for rAlbumin (Human).
- Global master file access (DMF), comprehensive non-clinical studies, Phase I safety data
- Validated through extensive use in multiple marketed life science products.
- Utilized in the manufacture of over 200 million doses of Merck® (MSD) ProQuad® and M-M-R® II paediatric vaccines worldwide.
- Entirely free from animal and human origin components, providing unparalleled safety.
- Quality documents available on request (CoA, CoO, TSE/BSE , B lactam , cGMP, Melamine, Elemental impurities, Nitrosamines statements)
- Vial presentations meet USP<71> sterility standards, ensuring the highest level of sterility and safety.

## Sampling Information

Free samples available for evaluation.

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