Rheolution Article

H1: Chitosan Hydrogels Formulation and Testing

In collaboration with ChitoLytic

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H2: What is chitosan?

Chitosan is a natural, biodegradable polymer derived from chitin—the structural material found in the shells of crustaceans like shrimp and crabs. Through a process known as deacetylation, chitin is converted into chitosan, which in its conventional form dissolves in mildly acidic solutions and can form hydrogels under suitable conditions. Because of its biocompatibility, tunable properties, and mild processing requirements, chitosan is widely used in drug delivery, wound healing, and tissue engineering.

Commercial sources, such as **ChitoLytic**, offer chitosan in various grades and specifications; ChitoLytic specializes in producing high-quality chitosan from sustainably sourced crustacean shells for research and industrial applications.

H2: What are the different types of chitosan?

Chitosan is available in a variety of grades based on two main parameters:

- Molecular Weight (MW):
    - *Low MW chitosan* (<100 kDa): Typically more soluble, lower viscosity, and well-suited for injectable formulations or blending with other polymers.
    - *Medium MW chitosan* (~200–400 kDa): A balance between mechanical strength and processability.
    - *High MW chitosan* (>400 kDa): Can produce stronger gels and films but may be more challenging to dissolve.
- Degree of Deacetylation (DDA):
    - Ranges from 70–95%, indicating how many acetyl groups have been removed from chitin.
    - Higher DDA generally corresponds to more free amino groups, which can enhance positive surface charge, mucoadhesion, and gelation efficiency.

Different chitosan types are selected depending on the application and desired mechanical or biological behavior.

H2: What are common methods to make chitosan gels?

Chitosan gels can be formed using several mild, tunable techniques:

- pH-Induced Gelation: Raising the pH (e.g., via NaOH bath) leads to gel formation by neutralizing chitosan's positive charges.
- Ionic Crosslinking: Using multivalent anions like sodium tripolyphosphate (TPP) to form ionic bonds between chitosan chains.
- Thermal Gelation: Combining chitosan with thermosensitive agents like β-glycerophosphate enables gelation at body temperature.
- Chemical Crosslinking: Aldehydes or genipin are sometimes used for stronger, more permanent gel networks—often in tissue engineering.

H2: How do formulation parameters affect chitosan gel mechanics?

Changes in formulation dramatically influence the viscoelastic behavior of chitosan hydrogels. For example, low-MW chitosan tends to form softer, faster-degrading gels, while high-MW chitosan creates stiffer networks with slower degradation profiles. Similarly, the crosslinking mechanism (e.g., alkaline gelation vs. heat-induced gelation) affects gelation kinetics, stiffness, porosity, and final morphology. These differences directly impact clinical performance, influencing factors like drug release profiles, cell migration, and injectability. However, soft and irregular gel shapes—such as chitosan beads or films—are difficult to assess using conventional mechanical tools.

H2: What are the limitations to traditional mechanical testers?

Characterizing soft hydrogels like chitosan benefits from testing methods that capture their behavior under conditions relevant to their intended use. Traditional instruments—such as rheometers, tensile testers, or atomic force microscopy (AFM)—can present handling challenges for delicate gels, including deformation during loading, slippage in grips, and wall slip effects. In addition, continuous monitoring under physiologically relevant conditions is often limited, making it more difficult to track mechanical changes, such as those occurring during degradation. These factors can make it more challenging to detect subtle differences between formulations when tested under conventional setups.

H2: Optimizing Chitosan: How ElastoSens™ Bio Enhances Mechanical Testing

Chitosan's mechanical properties are highly sensitive to processing variables such as pH, molecular weight, and ionic strength. Accurately comparing formulations—like chitosan gelled at pH 10 versus pH 12, or medium versus high molecular weight—requires a system capable of detecting subtle differences in G′ without damaging the sample. ElastoSens™ Bio offers a non-contact, easy-to-use solution that preserves sample integrity while enabling precise, real-time measurement of gelation and degradation. Its compatibility with physiologically relevant conditions—including pH-, ion-, and temperature-triggered gelation—makes it ideal for developing injectable chitosan hydrogels, mucoadhesive coatings, or tissue scaffolds. The system supports reproducible testing and streamlined formulation optimization under conditions that closely mimic the biological environment.

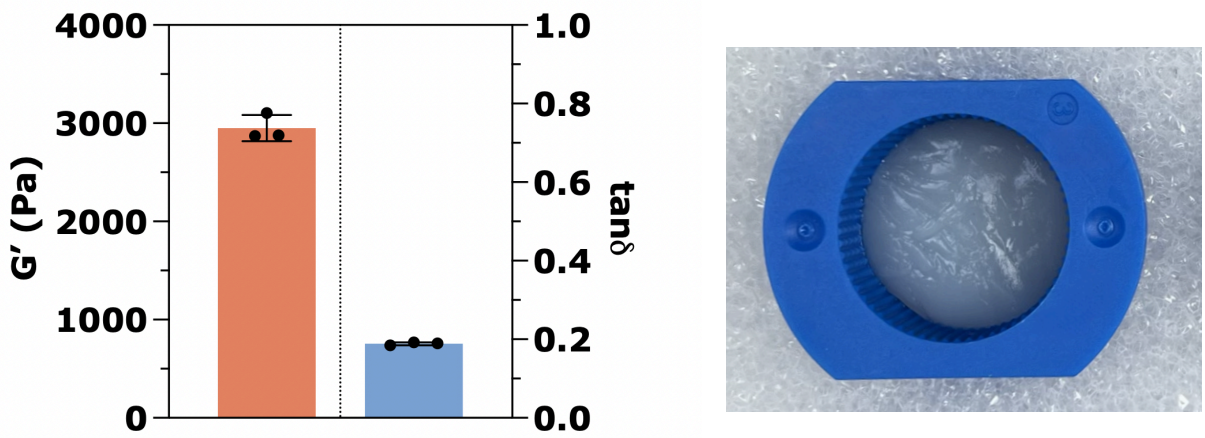
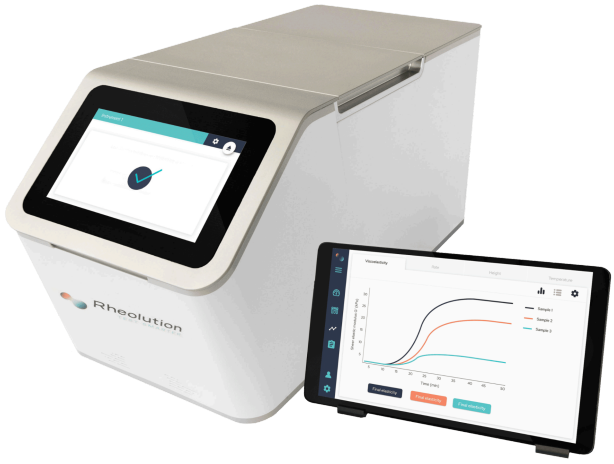


Figure 1: *Viscoelastic characterization of 2% (w/v) medium molecular weight chitosan gel.* Left: Shear storage modulus (G′, orange) and shear loss tangent (tan δ, blue) measured using ElastoSens™ Bio. Data are presented as mean ± SD (n = 3). Right: Representative image of the gel formed inside the sample holder. High G′ and low tan δ values indicate a predominantly elastic and stable hydrogel network.



To explore how ElastoSens™ Bio supports mechanical testing across a variety of hydrogel formulations and application areas, refer to our broader overview: **Formulation of Hydrogels**.

H3: Examples of chitosan applications that the ElastoSens™ Bio can support

- **Monitoring the Softening of Injectable Chitosan Gels Loaded with Enzymes**
  - In regenerative medicine, chitosan gels loaded with enzymes like lysozyme or collagenase are used to remodel tissue. ElastoSens™ Bio allows researchers to track progressive softening of the same gel sample over days, simulating in vivo degradation.
- **Comparing Mucoadhesive Strength Across Acid Sources**
  - Chitosan is commonly dissolved in acetic, lactic, or citric acid, each influencing final gel behavior. ElastoSens™ Bio enables high-throughput comparison of gels formed with different acid types, measuring G′ and tan δ to correlate with expected *adhesiveness* in nasal or buccal delivery systems, where minor formulation shifts can change performance.
- **Validating Vaginal Chitosan Gels for pH-Triggered STI Prevention**
  - Some chitosan-based vaginal gels are designed to remain fluid at neutral pH and rapidly gel under acidic vaginal conditions, forming a protective barrier against pathogens. ElastoSens™ Bio can monitor *in situ gelation kinetics* and *final stiffness* under controlled pH and temperature, enabling real-time assessment of performance-critical transitions without disrupting the sample.
- **Evaluating Chitosan-Based Ocular Inserts That Soften After Insertion**

    - Some ophthalmic chitosan inserts are engineered to *soften gradually* after contact with tears for comfort and controlled drug release. ElastoSens™ Bio's hydration-compatible, time-resolved testing can simulate this transition, helping researchers tune the formulation to reach a target softness after a defined period.
- **Testing Heat-Induced Chitosan Gelation for Thermo-Gelling Nasal Sprays**
    - In thermo-sensitive nasal sprays, chitosan gels are liquid at room temp but gel at 32–34 °C. ElastoSens™ Biocan simulate *nasal cavity conditions* and quantify the exact *onset temperature* of gelation, allowing *developers to select or adjust formulations to match the physiological window and avoid early or delayed gelling.*
- **Characterizing In-Situ Forming Chitosan Gels for Bone Fillers**
    - In orthopedic applications, injectable chitosan gels are combined with calcium phosphate or other fillers and gel in vivo. ElastoSens™ Biosupports testing these composite formulations as they set over time, ensuring the final stiffness aligns with that of surrounding tissue (e.g., 10–50 kPa for cancellous bone) without premature drying or sample failure.

Conclusion: A versatile platform for a versatile polymer

Chitosan's tunability—shaped by its molecular weight, degree of deacetylation, and crosslinking approach—makes it a useful material for biomedical applications ranging from drug delivery to tissue repair. These same adjustable properties make it important to characterize gelation kinetics, stiffness, and long-term mechanical behavior under conditions that reflect the intended use. The ElastoSens™ Bio system offers a uniquely compatible platform for studying chitosan-based hydrogels because it supports real-time, contactless, and non-destructive measurement of viscoelastic properties under physiologically relevant conditions.

Whether researchers are comparing pH- or ion-induced gels, screening formulation variables, or validating that bead properties match their bulk counterparts, ElastoSens™ Bio provides the precision and ease of use needed to accelerate development. By enabling faster iteration, clearer insights, and more confident quality control, it empowers teams to refine chitosan systems more efficiently—and bring translational products to life with greater mechanical assurance.

For an in-depth overview of emerging applications and performance considerations in microgel-based systems, see ***How are microgels used in regenerative medicine?***. For a detailed example of bead-versus-bulk comparisons, refer to our application note ***Microgels and Hydrogel Beads Mechanical Testing***.