Application Note

H1: Microgels and Hydrogel Beads Mechanical Testing

In collaboration with ChitoLytic

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H2: Why are microgels important in the biomedical field?

H3: Introduction

Microgels and hydrogel beads are increasingly used in biomedical and pharmaceutical applications due to their injectability, high surface-area-to-volume ratio, and modular size control. These small-scale hydrogels enable precise spatial delivery in controlled drug release, cell encapsulation, 3D bioprinting, and minimally invasive therapies. For an in-depth overview of emerging applications and performance factors in microgel-based systems, see ***How are microgels used in regenerative medicine?***. In these applications, viscoelastic properties directly influence material performance—for example, how fast a drug is released, whether encapsulated cells survive, or how a printed structure holds its shape post-extrusion. Shear storage modulus (G'), in particular, provides insight into the gel's stiffness and ability to resist deformation, which can impact drug diffusion rates, mechanical protection of cells, or structural integrity during and after delivery.

H2: Challenges in mechanical testing of microgels and hydrogel beads

Soft, irregularly shaped hydrogels—such as microgels and hydrogel beads—play an important role in biomedical applications, yet their mechanical characterization remains challenging. Traditional tools like uniaxial compression testers, tensile rigs, rheometers, or atomic force microscopy (AFM) often involve direct contact and can be difficult to adapt for small, delicate samples. Challenges may include sample slippage, difficulties in mounting soft gels into grips or fixtures without deformation, or wall slip effects during rheological measurements.

To address these issues, researchers often turn to bulk hydrogel analogs as mechanical stand-ins. However, bead and bulk formulations may differ in their mechanical behavior. This distinction becomes especially relevant when injectable beads are designed for clinical use, yet mechanical data for regulatory or quality control purposes are derived solely from bulk samples. Testing methods that more closely replicate physiologically relevant conditions can help ensure that performance assessments accurately reflect the intended application.

H2: Non-contact solution for microgels and beads mechanical testing

The **ElastoSens™ Bio** provides a valuable solution—enabling non-destructive, contactless, and geometry-independent mechanical testing under hydrated, physiologically relevant conditions. The ElastoSens™ Bio allows real-time tracking of viscoelastic properties within the same sample over time. This makes it particularly well suited for studying degradation behavior, drug release kinetics, or cell–matrix interactions.

For example, researchers developing chitosan-based hydrogel beads can compare the impact of molecular weight or crosslinking pH while ensuring that each bead type retains its desired stiffness over multiple days in buffer. With rapid test cycles, built-in temperature and photostimulation control, ElastoSens™ Bio offers a unique advantage for researchers working in tissue engineering, drug delivery, and soft scaffold development—where subtle mechanical differences can have significant biological consequences.



For a broader overview of hydrogel formulation strategies and how ElastoSens™ Bio supports viscoelastic testing across biomaterial types, see our article on ***Formulation of Hydrogels***.

H2: Case Study: Beads and Bulk Hydrogel Mechanical Testing

To illustrate the value of geometry-independent mechanical testing, we prepared medium molecular weight chitosan hydrogels in both bead and bulk formats using an alkaline gelation method. By keeping all formulation and crosslinking parameters consistent between the two formats, we aimed to isolate the effect of geometry on viscoelastic properties. The ElastoSens™ Bio was then used to compare the stiffness (G') of each sample under identical, temperature-controlled conditions.

H2: Chitosan beads and bulk hydrogels preparation

p: Materials and Methods

To prepare a 2% (w/v) chitosan solution, 1.0 g of **medium molecular weight chitosan** (250–300 kDa, ~95% degree of deacetylation, derived from mushrooms; product code C-M-85-401132, ChitoLytic) was gradually added to 50 mL of a 1% (v/v) acetic acid solution, prepared by mixing 0.5 mL of glacial acetic acid with

49.5 mL of demineralized water. The chitosan powder was added slowly under continuous magnetic stirring at room temperature (20–25 °C) to prevent clumping and ensure even dispersion. The solution was stirred for 18–24 hours, covered with parafilm to minimize evaporation, until it became visibly uniform and free of undissolved particles. The resulting 2% chitosan solution was then subjected to alkaline gelation in a 2 M NaOH bath using two different methods:

- **Bead method:** The chitosan solution was loaded into a micropipette and dispensed dropwise from a height of 2–3 cm into the NaOH bath, resulting in the formation of uniform spherical beads.

- **Bulk method:** The full 50 mL volume of chitosan solution was gently poured into the NaOH bath without agitation, forming a single monolithic hydrogel.

In both cases, the gels were left undisturbed in the NaOH solution for 30 minutes to allow complete physical crosslinking. Following gelation, the samples were rinsed repeatedly with demineralized water until neutral pH was reached and excess surface liquid was drained. The bead and bulk samples were then weighed to ensure equal mass (3.0 ± 0.3 g) prior to testing. Mechanical testing was performed using the ElastoSens™ Bio system for 3 minutes with 10-second intervals at 25 °C.

For readers seeking a deeper overview of chitosan formulation parameters—including molecular weight, degree of deacetylation, and various gelation methods—please refer to our related article on ***Chitosan Hydrogels Formulation and Testing***.

H2: Beads vs Bulk Hydrogel Mechanical Properties

p: Results and Discussion

Figure 1 shows a visual comparison of chitosan hydrogels prepared using bead and bulk gelation methods. Bead gels appeared as closely packed spherical aggregates, while bulk gels formed continuous, monolithic structures.

Quantitative measurements of gel properties are presented in Figure 2. The **shear storage modulus (G')**—which reflects the material's ability to store elastic energy and resist deformation—was slightly higher in bead gels (~3200 Pa) compared to bulk gels (~3000 Pa), indicating marginally greater stiffness. However, this difference was not statistically significant. The slightly higher G' in bead gels may result from more uniform NaOH diffusion during their formation, potentially leading to denser or more homogeneous crosslinking.

Both gel types exhibited low loss tangent ($\tan\delta$) values (~0.2), indicating predominantly elastic (solid-like) behavior with minimal viscous dissipation, which is characteristic of well-formed physical gels.

Final sample heights were also consistent between groups, with average values of 7.0 ± 1.0 mm for beads and 7.2 ± 0.8 mm for bulk gels, supporting the validity of direct mechanical comparison.

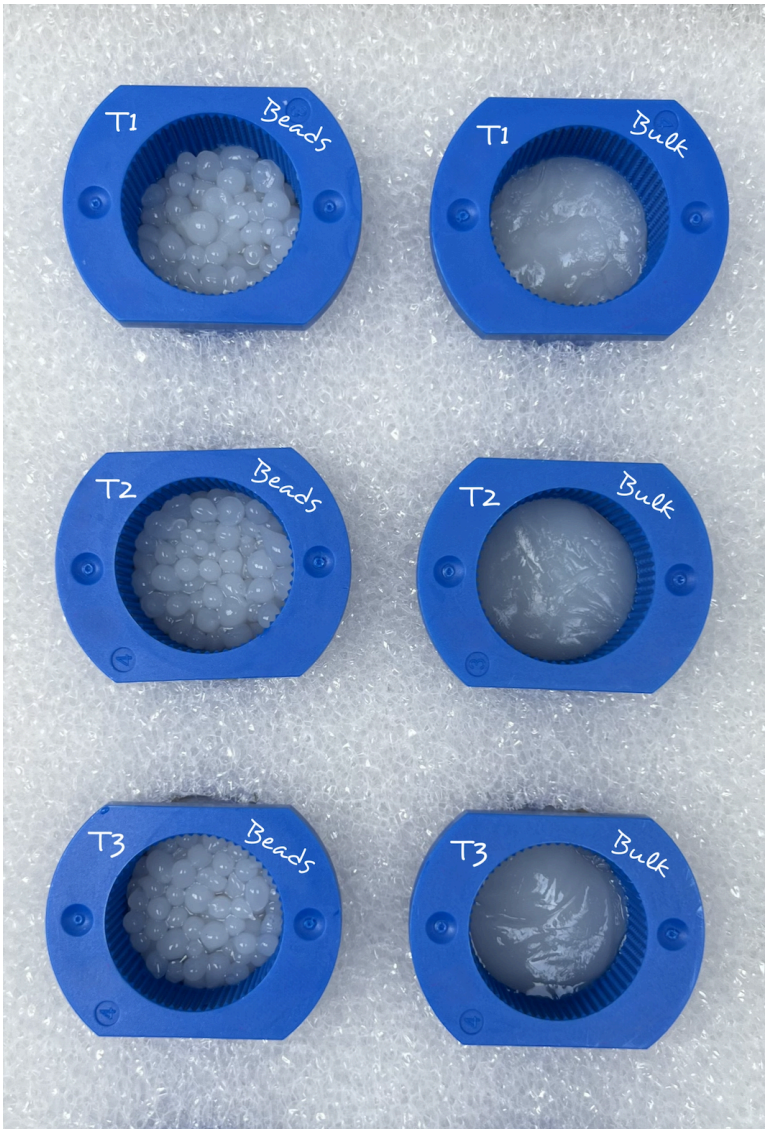


Figure 1: Visual comparison of 2% (w/v) medium molecular weight chitosan samples prepared by bead and bulk gelation methods. Each row represents one trial (T1–T3).

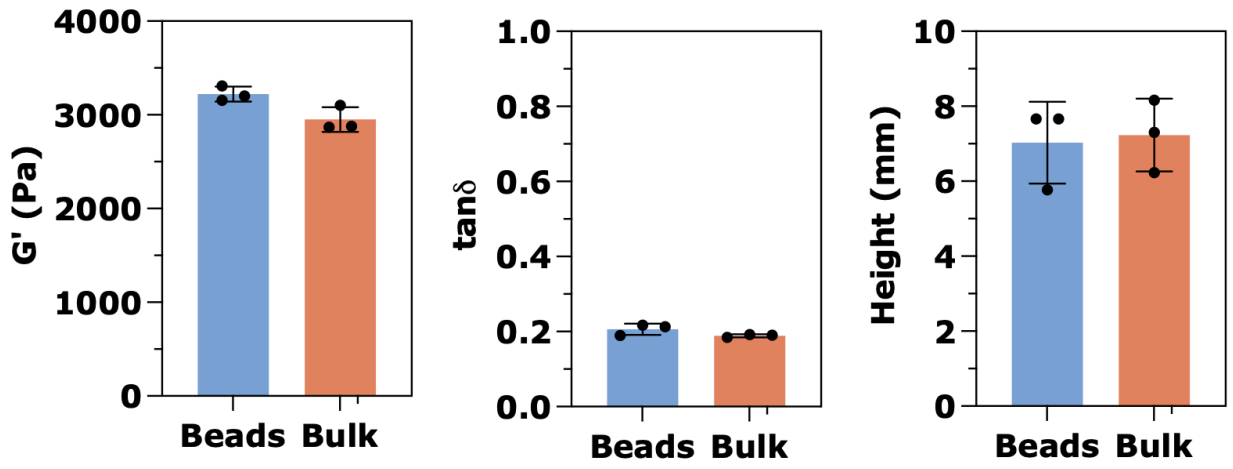


Figure 2: Viscoelastic and dimensional properties of 2% (w/v) medium molecular weight chitosan gels prepared by bead and bulk gelation methods. Shear storage modulus (G′), shear loss tangent (tan δ), and gel height were measured using ElastoSens™ Bio. Each bar represents the mean ± SD (n = 3).

Conclusions

This study demonstrates the advantages of using the **ElastoSens™ Bio** system to characterize the viscoelastic properties of chitosan hydrogels formed via bead and bulk gelation. Although no statistically significant difference in shear storage modulus (G′) was observed between the two formats under the tested conditions, the ElastoSens™ Bio effectively captured subtle mechanical variations. Importantly, mechanical differences may become more pronounced under different formulation parameters—such as polymer concentration, molecular weight, or crosslinking conditions—where structure and processing can significantly influence final properties.

These potential variations underscore the importance of format-specific mechanical testing. Relying solely on bulk analogs may overlook critical differences that affect drug release rates, cell viability, or scaffold performance in vivo. The ElastoSens™ Bio provides a powerful solution: its non-destructive, contactless, and geometry-independent platform enables real-time monitoring of viscoelastic properties in the same sample, under physiologically relevant conditions. This capability makes it especially valuable for applications in injectable therapies, tissue engineering, and soft biomaterial design, where small changes in stiffness or degradation behavior can have meaningful biological consequences.