I'm not a bot

Hydrogels have gained popularity due to their unique properties and applications in various fields, including medicine, agriculture, and personal care. This guide explores hydrogel testing, focusing on quality analysis, composition, testing methods, and regulatory requirements. Hydrogel testing maintains product quality, ensures safety, and adheres to regulatory requirements across various industries. | Credit: OpenAI (2024) Hydrogels are three-dimensional polymeric networks that absorb and retain significant amounts of water. They consist of hydrophilic polymer chains, which give them the ability to hold water and maintain a gel-like structure. Due to their biocompatibility, flexibility, and tunable properties, hydrogels serve a variety of applications, including wound care, drug delivery, tissue engineering, agriculture, and personal care products. Their high water content makes them particularly suitable for biomedical applications, as they mimic the natural environment of biological tissues. Hydrogel testing includes a range of analytical processes that evaluate the physical, chemical, and mechanical properties of hydrogels. These tests ensure that hydrogels meet the requirements of their intended applications in industries like medicine, agriculture, and personal care. Hydrogel testing helps determine the properties that make these materials suitable for specific applications. In medical uses, such as wound dressings or drug delivery systems, testing ensures that the hydrogel remains biocompatible, non-toxic, and absorbs water appropriately. In agriculture, hydrogels undergo testing to verify their water retention properties, which help improve soil quality. Overall, testing confirms that hydrogels meet performance expectations and comply with industry standards and regulations. Quality testing of hydrogels assesses their structural, physical, and chemical characteristics to ensure they meet the desired performance criteria. Here are the key aspects of quality testing: Swelling Capacity and Water Content Purpose: Swelling capacity determines the hydrogel's ability to absorb and retain water. Testing this characteristic helps evaluate how effectively a hydrogel performs in its intended application. Procedure: The hydrogel is immersed in water or a saline solution, and its weight before and after swelling is measured. The swelling ratio is calculated to determine its water absorption capabilities. Mechanical Strength Purpose: Mechanical strength testing confirms that the hydrogel maintains its integrity under different conditions, such as compression, stretching, or adhesion. This is particularly important for hydrogels used in tissue engineering, wound care, or medical devices. Procedure: The hydrogel sample undergoes several mechanical tests: Compression Testing: Compression testing measures the hydrogel's ability to withstand compressive forces. The sample is compressed between two plates, and the force needed to deform the hydrogel is recorded. This test determines the hydrogel's mechanical stability and resistance to deformation under pressure. Tensile Testing: Tensile testing evaluates the hydrogel's ability to withstand stretching forces. The sample is pulled until it breaks, and the force required to break it is recorded. This test is crucial for applications where the hydrogel must remain intact under tension, such as in tissue scaffolds. Skin Adhesion Testing: For hydrogels used in wound care, skin adhesion testing measures how well the hydrogel adheres to biological surfaces. The hydrogel is applied to a simulated skin surface, and the force required to peel it off is recorded. This ensures that the hydrogel provides sufficient adhesion without causing skin irritation or damage upon removal. Biocompatibility Testing Purpose: For medical applications, it is critical that hydrogels remain non-toxic and do not cause adverse reactions when in contact with biological tissues. Procedure: Biocompatibility is assessed through in-vitro cytotoxicity tests or in-vivo animal studies, where the hydrogel's interaction with cells or tissues is monitored. Purity and composition testing confirms the chemical makeup of hydrogels and detects any impurities that might impact performance or safety. Key aspects of this type of testing include: Fourier Transform Infrared Spectroscopy (FTIR) Purpose: FTIR identifies the functional groups present in the hydrogel, helping confirm its chemical composition and detect unwanted impurities. Procedure: The hydrogel is analyzed using FTIR, and the resulting spectrum is compared to reference spectra to verify its composition. Thermogravimetric Analysis (TGA) Purpose: TGA assesses the thermal stability of hydrogels, as well as their water content and overall purity. Procedure: A hydrogel sample is gradually heated, and the changes in its weight are measured to determine the presence of water, residual solvents, and other volatile substances. Elemental Analysis Purpose: Elemental analysis determines the presence and concentration of elements like carbon, hydrogen, nitrogen, and others in the hydrogel. Procedure: The hydrogel sample is analyzed using elemental analyzers to detect and quantify key components, ensuring it meets compositional specifications. Several analytical methods test the quality and properties of hydrogels, depending on their intended applications: Rheological Testing Description: Rheological testing evaluates the viscoelastic properties of hydrogels, including their ability to flow or deform under stress. This helps us understand how the hydrogel performs in different conditions. Scanning Electron Microscopy (SEM) Description: SEM provides detailed images of the hydrogel's surface morphology. This analysis helps understand the porosity and structural integrity of the hydrogel, which is important for applications in tissue engineering or controlled drug release. Gel Fraction and Sol Fraction Analysis Description: Gel fraction analysis determines the proportion of crosslinked polymer within the hydrogel, while sol fraction analysis assesses the amount of soluble polymer that has not formed crosslinks. These tests evaluate the stability and crosslinking efficiency of hydrogels. Hydrogel testing must adhere to various regulatory requirements, depending on the application. Here are some of the major regulations that govern hydrogel testing: ISO Standards Hydrogels used in medical applications must comply with specific ISO standards to ensure quality and safety. ISO 10993, for example, provides guidelines for biocompatibility testing of medical devices, including hydrogels. Food and Drug Administration (FDA) In the United States, the FDA regulates hydrogels used in medical devices and drug delivery systems. Hydrogels must meet requirements for safety, efficacy, and biocompatibility, as outlined in FDA guidance documents for medical devices and pharmaceutical products. European Medicines Agency (EMA) The EMA oversees hydrogels used in medicinal products within the European Union. For hydrogels used in drug delivery, compliance with EMA guidelines for safety, quality, and efficacy is mandatory. Good Manufacturing Practices (GMP) Manufacturers of hydrogels must follow GMP guidelines to ensure consistent production quality. GMP includes testing raw materials, maintaining proper documentation, and adhering to standard operating procedures to guarantee product safety and efficacy. Hydrogel testing maintains product quality, ensures safety, and adheres to regulatory requirements across various industries. Quality testing, composition analysis, and performance testing help verify that hydrogels meet the necessary standards for their intended applications. Whether used in medical devices, agriculture, or personal care, rigorous testing helps provide reliable and safe products for consumers. If you are a manufacturer, supplier, or distributor of hydrogels and require assistance finding a qualified third-party testing partner, Submit a Testing Request or Contact Us for more information.

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Synthetic tough hydrogels have received attention because they could mimic the mechanical properties of natural hydrogels, such as muscle, ligament, tendon, and cartilage. Many recent studies suggest various approaches to enhance the mechanical properties of tough hydrogels. However, directly comparing each hydrogel property in different reports is challenging because various testing specimen shapes/sizes were employed, affecting the experimental mechanical property values. This study demonstrates how the specimen geometry—the lengths and width of the reduced section—of a tough double-network hydrogel causes differences in experimental tensile mechanical values. In particular, the elastic modulus was systemically compared using eleven specimens of different shapes and sizes that were tensile tested, including a rectangle, ASTM D412-C and D412-D, JIS K6251-7, and seven customized dumbbell shapes with various lengths and widths of the reduced section. Unlike the rectangular specimen, which showed an inconsistent measurement of mechanical properties due to a local load concentration near the grip, dumbbell-shaped specimens exhibited a stable fracture at the reduced section. The dumbbell-shaped specimen with a shorter gauge length resulted in a smaller elastic modulus. Moreover, a relationship between the specimen dimension and measured elastic modulus value was derived, which allowed for the prediction of the experimental elastic modulus of dumbbell-shaped tough hydrogels with different dimensions. This study conveys a message that reminds the apparent experimental dependence of specimen geometry on the stress-strain measurement and the need to standardize the measurement of of numerous tough hydrogels for a fair comparison. Keywords: double-network hydrogel, tough hydrogel, tensile testing, mechanical properties Hydrogels are a significant component of the human body, consisting primarily of three-dimensional polymer networks and water. Natural hydrogels, such as muscle, ligament, tendon, cartilage, and so on, commonly suffer from mechanical damage due to repetitive exercise of tension and compression. For that reason, soft yet tough synthetic hydrogels, including double-network (DN) and polyampholyte (PA) hydrogels [1,2,3,4], are emerging to support/replace biological tissues (natural hydrogels) and to further bridge human–machine interfaces as adhesives and surface coating materials. Since a mechanical match between the synthetic hydrogel and surrounding tissues is one of the primary considerations in the development of the practical use of synthetic hydrogels [5,6,7,8,9], many researchers have focused on improving the hydrogel mechanical performance. The hydrogel mechanical properties are usually evaluated through tensile testing using a universal testing machine (UTM) that uses values such as the yield strength, fracture strength, elastic modulus, work of fracture, and fracture toughness. However, because previous reports indicate that hydrogels have a wide variety of specimen shapes and sizes, the improvement of hydrogel mechanical properties compared with the values in previous reports is unclear. Despite this, studies regarding the standardization of hydrogel specimens for a fair comparison of their mechanical properties are lacking. In this study, considering the hypothesis that the mechanical property values vary with the test specimen shapes/sizes, we used tensile testing to investigate the influence of the specimen shapes and sizes of a tough hydrogel on the experimental tensile mechanical properties. To systemically compare the values, we prepared variously shaped alginate/polyacrylamide (Alg/PAM) double-network hydrogels as tough-hydrogel models. We found that the rectangular specimen is inappropriate for measuring accurate mechanical properties owing to the stress concentration near the grip, whereas the dumbbell-shaped specimen is more suitable for obtaining consistent mechanical property values owing to stable stretching up to the occurrence of a fracture at a reduced section rather than near the grip. Furthermore, we derived a relationship between the specimen dimensions and measured elastic modulus values using dumbbell-shaped specimens, allowing for the prediction of the elastic moduli based on the hydrogel specimen dimensions. Alginic acid sodium salt from brown algae (Alg, medium viscosity, Sigma A2033, Sigma-Aldrich, St. Lois, MO, USA), acrylamide (AM, Sigma A8887), N,N′-methylenebisacrylamide (MBAA, Sigma M7279), N,N,N′,N′-tetramethylethylenediamine (TMEDA, Sigma T7024), ammonium persulfate (APS, Sigma A7460), and calcium sulfate dihydrate ($CaSO_4·2H_2O$, Samchun C0227, Samchun Chemical Co., Ltd., Seoul, Republic of Korea) were purchased and used without any purification. The Alg and AM were first dissolved in distilled water. Subsequently, MBAA (0.07% wt/wt of AM), a covalent crosslinker for AM; TMEDA (0.28% wt/wt of AM), an accelerator for AM; APS (4% wt/wt of AM), an initiator for AM; and $CaSO_4$ (15% wt/wt of Alg), an ionic crosslinker for Alg were added to the Alg/AM solution to obtain a 1.83 wt% Alg and 12 wt% AM mixture. The obtained mixture was poured into a rectangular mold with a thickness of 3 mm and polymerized under 254 nm ultraviolet light for an hour. The resulting double network (DN) hydrogel composed of Ca^{2+}-crosslinked alginate and covalently crosslinked polyacrylamide (Alg/PAM) hydrogel was then stored overnight in a cooler maintained at approximately 5 °C. In the case of Fe-crosslinked DN hydrogels, the Alg/PAM hydrogel was soaked in 100 mM $FeCl_3$ solution for one day. Eleven specimens of different shapes and sizes were prepared, including a rectangle, ASTM-standard ASTM D412-C and D412-D, Japan-standard JIS K6251-7, and seven customized dumbbell shapes (#1–#7) with various lengths and widths of the reduced section, by cutting a large and wide hydrogel into the specific geometry. The detailed specimen shapes and sizes are depicted in the main figures. Tensile testing was conducted using a Comtech QC548 M1F-M (Comtech, Testing Machines Co., Ltd., Taichung City, Taiwan) universal testing machine with a 100 N load cell. The tests were performed at a load speed of 100 mm min^{-1}. The elastic modulus was measured using the slope of the linear elastic region. The mechanical testing of each hydrogel was performed at least five times, and the consequent data were presented as the average ± standard deviation. Statistical significance was conducted using Student's t-test (one-sided test); ** $p < 0.01$; *** $p < 0.001$; **** $p < 0.0001$; n.s., not significant. The double-network (DN) hydrogels, which are composed of two interpenetrating polymer networks, a rigid first-network and a stretchable second-network, with contrasting mechanical properties, have a significant ability to absorb mechanical energy that is incomparable to single-network (SN) hydrogels [9,10]. Among many kinds of DN tough hydrogels, the Alg/PAM hydrogel, consisting of physically Ca-crosslinked Alg and chemically covalent-crosslinked PAM, is a representatively widely used DN hydrogel due to the easy one-pot synthesis method [2]. The Alg, a natural polysaccharide polymer, which has G residues (G blocks), can be coordinated with metal cations, forming rigid polymer networks. These relatively rigid Alg networks can be combined with relatively stretchable PAM networks, becoming tough DN hydrogels. Based on the same principle and fabrication procedure as for the Alg/PAM DN hydrogel, other kinds of DN tough hydrogels that are composed of a different first-network polymer, such as agar, chitosan, cellulose, polyvinyl alcohol (PVA), i.e., Agar/PAM [11,12], Chitosan/PAM [13,14,15,16], Cellulose/PAM [17], and PVA/PAM [18] DN hydrogels, were also proposed. In addition, post-treatments to enhance the mechanical properties of the Alg/PAM DN hydrogel were usually also demonstrated [6,19,20,21,22,23,24,25]. Meanwhile, a wide variety of specimen geometries (shapes and sizes) used in each research paper hinder a direct comparison of how much mechanical improvement was achieved compared to the previous hydrogels (Table 1). Accordingly, herein, we would like to figure out to what extent the hydrogel specimen geometry affects the tensile mechanical testing results, mainly, an elastic modulus value that is one of the most important factors in judging the material's usability. Comparison of specimen shapes and sizes, and tensile testing speeds of representative tough hydrogels in the literature. Hydrogels Specimen Shapes Specimen Size a Width × Length × Thickness[mm3] Test Speed [mm min−1] Strain Rate b[min−1] Ref. Alg/PAM Rectangle 75 × 5 × 3 10 2.0 [2] Alg/PAM Rectangle 10 × N.M. × N.M. 60 N.M. [6] Alg/PAM Dumbbell 2 × 12 × 2 100 8.3 [19] Alg/PAM Rectangle 5 × N.M. × 3 60 N.M. [20] Alg/PAM Rectangle 5 × 30 × 3 60 N.M. [21] Alg/PAM Rectangle 45 × 40 × 2 5 0.5 [22] Alg/PAM Dumbbell 2 × 35 × 1.8 100 2.9 [23] Alg/PAM Dumbbell 5 × 10 × 5 60 6 [24] Agar/PAM Dumbbell 4 × 30 × 1 50 1.7 [11] Agar/PAM Dumbbell 4 × 25 × 1 100 4.0 [12] Chitosan/PAM Rectangle 5 × N.M. × 2 50 N.M. [13] Chitosan/PAM Rectangle 5 × N.M. × 1.5 10 N.M. [14] Chitosan/PAM Rectangle 5 × 35 × 1.5 10 N.M. [15] Chitosan/PAM Rectangle N.M. × 10 × N.M. N.M. 0.1 [16] Cellulose/PAM Dumbbell 4 × 16 × 4 40 2.5 [17] PVA/PAM Rectangle 75 × N.M. × 3 N.M. 2 [18] First, we prepared four types of hydrogels with frequently used standardized shapes: rectangular, ASTM standard ASTM D412-C and D412-D, and Japan-standard JIS K6251-7 (Figure 1a). The rectangular shape is the most frequently used shape to measure the tensile mechanical properties of hydrogels, including tough gels, owing to the ease of specimen preparation. In the case of a dumbbell shape, the ASTM D412-C is one of the most frequently used dumbbell shapes to measure stretchable materials such as rubbers and elastomers, and it has a width of 6 mm and a gauge length of 33 mm in a reduced section [26]. ASTM D412-D is also typically used to measure such stretchable materials, with a width of 3 mm and a gauge length of 33 mm in a reduced section [26]. JIS K6251-7 has one of the smallest sizes, and its width and gauge length in a reduced section are 2 and 12 mm, respectively [27]. (a) Specimen dimensions of the rectangle, ASTM D412-C, ASTM D412-D, and JIS K6251-7. (b) Stress-strain curves for rectangular specimen under different clamping conditions. Photographs depicting (c) rectangular hydrogel and (d) ASTM D412-C hydrogel mounted in the testing machine and broken after the test. In the rectangular hydrogel, a stress concentration near the grip usually provokes an early fracture of the hydrogel (dashed box). (e) Stress-strain curve and (f) elastic moduli of the hydrogel with different shapes. ** $p < 0.01$; **** $p < 0.0001$.Since hydrogels are soft and weak, measuring rectangular hydrogels in tensile tests requires special care. When the hydrogel was weakly clamped, causing the hydrogel to slip from the grip, the stress-strain curves were not accurate (Figure 1b, dotted line). Some cases exhibited irregular stress values at large strain regions because of gradual slipping from the grip, whereas others demonstrated low final stress and strain values because the hydrogel abruptly came out of the grip early. Such challenges consequently led to large deviations in the elastic modulus values. On the other hand, when the hydrogel was adequately clamped without any scope for it to slip from the grips, the stress-strain curves and elastic moduli were evenly obtained (Figure 1b, solid line). However, in many cases, a stress concentration near the grip caused an early fracture of the hydrogel (Figure 1c), obscuring an accurate evaluation of the hydrogel fracture strength and strain. In most reports on tough hydrogels, rectangular specimens were used; therefore, the assessment of the mechanical properties of newly developed hydrogels by comparing them with those of previously reported hydrogels can be limited. In contrast to the rectangular hydrogel, all dumbbell-shaped Alg/PAM tough hydrogels, which contained a reduced section where almost all of the load was gathered, exhibited more consistent stress-strain curves with a large strain until fracture occurred at the reduced section in different samples with the same shape when compared with that of the rectangular shape (Figure 1d). Since the stress was concentrated in the narrower region rather than in the wider clamping region, the fracture was consistently observed in the reduced section. Therefore, dumbbell-shaped hydrogels are more suitable than rectangular hydrogels for accurately and consistently evaluating hydrogel tensile properties. However, a notable issue exists in the result for dumbbell-shaped specimens. The stress-strain curves and resultant mechanical property values, particularly the elastic modulus and yield strength, which are the most essential parameters for determining the practical utility of the material, vary significantly according to the specimen dimensions (Figure 1e,f). Therefore, comparing the mechanical properties of tough hydrogels, even when dumbbell-shaped specimens are measured, remains a challenge. To the best of our knowledge, not enough studies have been conducted on the influence of dumbbell-shaped specimen shape and size on the measured mechanical properties of hydrogels. To better understand the variation in the elastic modulus values according to the gauge length and width, we investigated the effect of the gauge length when maintaining other dimensions of the specimen at a constant value based on ASTM D412-C, which is a very frequently used dumbbell shape (Figure 2a). The tensile test results indicated that the overall slope of the stress-strain curve varied significantly according to the specimen gauge length (Figure 2b). Although almost no difference was observed in yield strength, the shorter gauge length resulted in a gentle slope; that is, the elastic modulus value decreased with a decrease in the gauge length (Figure 2c). This trend was consistently observed in other specimens, similar to ASTM D412-C, but with a much broader entire width. In this case, hydrogels with the same 6 mm narrow width of the reduced section, but with a 50 mm entire width (to accentuate the narrow reduced section with a wider clamping region), were prepared (Figure 2d). When the gauge length of the hydrogel was gradually reduced from 33 to 17 mm, the elastic modulus value gradually decreased (Figure 2e,f). (a,d) Specimen dimensions of dumbbell shape with a different gauge length. (b,e) Stress-strain curve and (c,f) elastic modulus of hydrogels with different dimensions.We hypothesized that there must be a more qualitative method to predict the measured elastic modulus values, depending on the dimensions of the dumbbell-shaped specimens. Thus, the modulus data depicted in Figure 2 were plotted using the mathematical expression of specimen dimensions, (a + b)/ac, where a, b, and c are the narrow width of the reduced section, entire width of the specimen, and gauge length, respectively (Figure 3). Notably, the data points in Figure 3 are linearly regressed. The difference between the two linear plots obtained from the specimens depicted in Figure 3 was expressed using the b/a ratio; the b/a values for each plot were 4.2 and 8.3 for the data points obtained from Figure 2a–c and Figure 2d–f, respectively. Under the same b/a ratio, a decrease in c leads to a reduced elastic modulus value. For a given (a + b)/ac, the specimen with a larger b/a ratio exhibited a higher modulus value. Taken together, we inferred that specimens with a longer (larger c and smaller (a + b)/ac) and narrower reduced section (smaller a and larger b/a) exhibited a larger elastic modulus value. In other words, when the significance of the reduced section is high, the elastic modulus is measured as a large value. Elastic modulus value of hydrogels with a different gauge length and width, represented along (a + b)/ac.We further hypothesized that (a + b)/ac and b/a could be used as a parameter pair to estimate the experimental elastic modulus value of the hydrogel, where the widths and gauge lengths are associated with the accumulated stress in the reduced section. To test this idea, we prepared three dumbbell-shaped tough hydrogels with different dimensions but the same (a + b)/ac and b/a parameters (Figure 4a). All three specimens exhibited an almost similar pattern in the early region of the tensile stress-strain curve (Figure 4b) and the same elastic modulus value (Figure 4c). This result was consistent with our hypothesis that the experimental elastic modulus of tough hydrogels with different specimen dimensions is the same when they have the same (a + b)/ac and b/a parameters, despite having different specimen dimensions (Figure 4d). (a) Specimen dimensions of three dumbbell shapes with a fixed entire width/narrow width ratio of 4.17 and the same gauge length of 8 mm. (b) Stress-strain curve and (c) elastic modulus of each hydrogel. (d) Elastic modulus value of the hydrogel along (a + b)/ac.In addition to the elastic modulus values that varied based on the specimen dimensions, the overall stress-strain curve pattern differed (Figure 5). The specimen with a narrower and longer reduced section relative to the entire width/length (i.e., larger b/a and smaller (a + b)/ac) exhibited a much steeper stress-strain curve (Figure 5a,b) and larger tangent modulus and tensile strength values at each strain point compared with those of other specimens (Figure 5d,e). The specimens with the same (a + b)/ac and b/a parameters exhibited almost overlapping stress-strain curves with a similar fracture strain, which led to similar strength values (Figure 5c,f). It is also notable that only tiny deviations were observed in the mechanical property values obtained from the different specimens with the same (a + b)/ac and b/a parameters (Figure 4c and Figure 5f). Owing to there being almost no deviations between the curves of each sample, particularly below a strain of 10, which is an elongation range for the practical use of soft materials, the well-designed dumbbell-shaped specimens with the same (a + b)/ac and b/a parameters that we propose are, in practice, favorable for evaluating and comparing the hydrogel mechanical properties. (a–c) Stress-strain curves of each hydrogel with a different specimen shape/size. (d–f) Tensile strength values at a strain of 10 or 20. In the previous sections, we demonstrated the importance of fabricating dumbbell-shaped specimens and the change in stress-strain curves based on the dimensions of dumbbell-shaped specimens. Thus, the significant differences caused by specimen shapes/sizes require attention to understand and accurately interpret the hydrogel mechanical properties. In this section, we revealed which specimen shape/size could be appropriate for evaluating soft/tough hydrogels by accessing the load-focusing region of the hydrogel specimen (Figure 6). To clearly visualize the change in the hydrogel during stretching, Alg/PAM hydrogels additionally crosslinked in $FeCl_3$ solution were used as model hydrogels. Because the brown Fe-crosslinked Alg/PAM hydrogel displays a color change during stretching, distinguishing the region that gathers maximum load is easy. Photographs and stress-strain curves of Fe-crosslinked hydrogels with different shapes. (a,d) Photographs of a different stretching process for each hydrogel. Arrows in the photographs indicate the stress concentration near the grip resulting in the abrupt hydrogel rupture. (b,c) Stress-strain curves of each hydrogel. All five dumbbell-shaped specimens exhibited notably stable measurements, whereas rectangular specimens always exhibited different measurements.A rectangular hydrogel distinctly exhibited a stress concentration near the grip (Figure 6a), similar to the previous result (Figure 1c); the bright yellow area near the grip indicates hydrogel deformation during polymer network stretching. The applied load should be evenly distributed over an area of 15 × 33 mm2; however, the load was locally concentrated in the area near the grip. Furthermore, the load was often considerably accumulated between the grips, which resulted in the abrupt failure of the hydrogel (Figure 6a arrows). Such an irregular stress distribution obscures the determination of material fracture elongation, as depicted in the stress-strain curves (Figure 6b). In the case of ASTM D412-C dumbbell-shaped hydrogels, a tall UTM machine with a high crosshead travel capacity is required; in particular, for highly stretchable double-network hydrogels that can stretch over a strain of 20–30, many testing machines may not be able to meet this capacity. Therefore, a dumbbell-shaped specimen with a short gauge length can be a good alternative. Representatively, the specimen #5, with a reduced section with a 6 mm width and 17 mm length, exhibited highly consistent stress-strain curves with a stable stretching process (Figure 6c,d). The wide clamping region was stably fixed between the grips, and the applied load effectively gathered at the reduced section, which yielded highly similar stress-strain curves without deviations. Accordingly, while evaluating the mechanical performance of soft/tough hydrogels, the use of a rationally designed dumbbell-shaped specimen (such as a dumbbell with a wide clamping region and a properly narrow and long reduced section) is recommended, and accurate experimental results can be obtained and compared with previous results. Numerous efforts have led to many advances in mechanically robust tough hydrogels over the last two decades. Given such a development, comparing the mechanical properties of the reported tough hydrogels in a fair way is a necessity. We demonstrated the effect of the test specimen dimensions (width and gauge length) on the mechanical properties of tough hydrogels. In particular, the elastic moduli, a critical value for assessing hydrogel performance, of hydrogels with different shapes and sizes were systemically compared. A relationship between the specimen dimensions and measured elastic modulus value was derived, enabling the experimental elastic modulus value of the dumbbell-shaped tough hydrogel with different specimen dimensions to be estimated. Moreover, visual photographic materials exhibiting how the applied load transferred onto the hydrogel and gathered at the reduced section distinctly demonstrated the necessity for dumbbell-shaped specimens. This finding suggests that there is a need to start a discussion on how to evaluate the mechanical properties of soft/tough hydrogels and compare newly developed and previously developed hydrogels. Although further studies are mandated to firmly establish the conclusion, this finding provides baseline information regarding the testing method and the development of a standardized method for soft/tough hydrogels. Furthermore, since here we only used the tensile testing method, a comparison of experimental results obtained from different testing methods, including compression, indentation, and rheology tests, should be performed in order to reach a specific, true value of the material mechanical properties. D.J. and J.K. conceived the concepts and ideas. D.J. and P.I. prepared the experimental samples, and D.J. collected and analyzed the experimental data. D.J., S.S. and J.K. discussed the data and wrote the manuscript. All authors have read and agreed to the published version of the manuscript. The data supporting the findings of this study are available from the corresponding author. The authors declare no conflict of interest. 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Mechanical Property Testing of Hydrogels Hydrogels have a wide range of applications from biomedicine to food science, due to their water-rich composition and biocompatibility. However, most hydrogels are soft materials that exhibit poor mechanical properties, which greatly limit their applications in various fields. Therefore, it is very necessary to design hydrogels with excellent mechanical properties. Mechanical property testing of hydrogels is an important part of evaluating the success of hydrogel improvement, and has significance in evaluating the failure degree and life of hydrogels. Alfa Chemistry is committed to providing our customers with professional mechanical property testing services for hydrogels. Our team has many years of experience and is capable of delivering reliable results to our customers.Testing MethodsAlfa Chemistry provides consumers with professional mechanical property testing services for hydrogels using the most common testing methods, including but not limited to the following.The most common method to evaluate the mechanical properties of hydrogels is uniaxial tensile testing, which is widely accepted by the scientific community to determine the mechanical toughness and ultimate tensile strength of various hydrogels. Furthermore, uniaxial tensile testing plays an important role in inferring the mechanical toughening mechanism for anisotropic filler-embedded nanocomposite hydrogels.Bulge testing can reflect the plastic flow behavior of hydrogels. In this method, the sample architecture is circular in shape (diaphragm-like), tightly held at the outer fringe of the sample holder, followed by uniform stretching via an external force applied laterally. One restriction to sample preparation is that the thickness to bulge diameter ratio should be small enough to eradicate the bending effect of hydrogels during clamping.Compressive testing is another destructive experiment to evaluate the load-bearing and compressive fracture toughness of hydrogels. This testing is generally carried out by placing the hydrogel sample between parallel plates. The main advantages of compressive testing are the ease of sample preparation and the unconditional limitation of sample geometry.Indentation testing is actually a single-point compressive testing where the surface deflection has been quantified. In this method, a force displacement transducer is connected to an indentation probe. This arrangement results in a force displacement plot from which the elastic modulus of hydrogels can be calculated, while the residual impression can be measured after the test has been completed.Our AdvantagesWe offer mechanical property testing for a wide range of hydrogels, ranging from pure hydrogels to composite hydrogels.We have reliable testing methods to ensure the accuracy of mechanical property data.We provide flexible and targeted technical support 24 hours a day, 7 days a week to reduce your time costs.We offer a complete analysis report, including method interpretation, data, result files and other information you need.Service Process Please kindly note that our products and services are for research use only.

A universal method to easily design tough and stretchable hydrogels Hydrogels are flexible materials that have high potential for use in various applications due to their unique properties. However, their applications are greatly restricted by the low mechanical performance caused by high water content and inhomogeneous networks. This paper reports a universal strategy for easily preparing hydrogels that are tough and stretchable without any special structures or complicated processes. Our strategy involves tuning the polymerization conditions to form networks with many polymer chain entanglements to achieve energy dissipation. Tough and stretchable hydrogels can be prepared by free radical polymerization with a high monomer concentration and low cross-linker content to optimize the balance between physical and chemical cross-links by entanglements and covalent bonds, respectively. The strategy of using polymer chain entanglements for energy dissipation allows us to overcome the limitation of low mechanical performance, which leads to the wide practical use of hydrogels. Article Open access 12 August 2020 Article Open access 05 October 2020 Hydrogels are soft materials that consist of physically or chemically cross-linked polymer networks and a large quantity of water. Hydrogels have a high water content and low elastic modulus (~100 kPa) and exhibit stimulus-responsive behavior, similar to biological tissues; thus, hydrogels have many potential applications as biomaterials for drug delivery systems, biosensors, and cell culture[1,2,3,4,5]. Although hydrogels are soft and flexible, they are also weak and brittle[6]. Standard hydrogels can be easily broken when subjected to a sub-MPa tensile stress or large deformation. The fracture energy of hydrogels is only approximately one hundredth that of biological tissues such as cartilage[7,8]. Recently, to overcome the low mechanical properties of hydrogels, some researchers have strategically designed network structures of hydrogels, such as sliding-ring hydrogels[9,10], nanocomposite hydrogels[11], double network (DN) hydrogels[12,13,14], and other structures[15,16,17,18,19,20,21,22]. DN hydrogels, which consist of a densely cross-linked and brittle polyelectrolyte 1st network and a sparsely cross-linked and ductile neutral 2nd network, exhibit high mechanical strength (tensile fracture stress of ~10 MPa and tensile fracture strain of 1000–2000%) and toughness (fracture energy of ~4000 J m^{-2})[13,14]. The superior mechanical properties of DN hydrogels are attributed to energy dissipation through the internal fracture of the brittle 1st network. In addition, dynamic cross-links that reversibly dissociate and form in response to stimuli such as temperature, molecules, and stress are useful tools for designing not only responsive hydrogels but also tough hydrogels[23,24,25,26,27,28]. The abovementioned studies suggest that structural design is required to achieve effective energy dissipation in hydrogels.During deformation, hydrogels exhibit viscoelastic behavior, which includes both viscous and elastic characteristics[29]. While hydrogels are deformed by the application of stress, part of the total energy, which is based on loaded stress, is stored as elastic energy because of the elastic characteristic; however, the other part dissipates because of the viscous characteristic. The use of a large amount of chemical cross-linker results in the formation of rigid hydrogel networks in which the elastic characteristic contributes to their mechanical properties more predominantly than the viscous characteristic. In addition, we reported that hydrogels with a high cross-linker content have an inhomogeneous structure[30], in which stress concentration within weak regions causes low fracture stress and strain. Therefore, to design tough hydrogels, we focused on the viscous characteristic to allow the applied stress to be relaxed by energy dissipation. A decrease in the cross-linker content enhances the contribution of the viscous characteristic to the mechanical properties of the hydrogels. Using our approach, it is possible to produce hydrogel networks with a high polymer chain density; the large molecular weight between cross-links enables effective energy dissipation by viscous characteristics because hydrogel networks have many entanglements that act as mobile cross-links. Herein, we report a simple and versatile method to produce tough and stretchable hydrogels by conventional radical polymerization without complicated structures or special preparation methods. Our strategy uses structural design to achieve effective energy dissipation. Specifically, the use of a high monomer concentration and low cross-linker content allows the formation of hydrogel networks with many entanglements, which produce physical cross-links (Fig. 1). In the obtained networks containing many entanglements, polymer chains can easily creep owing to the presence of minute amounts of chemical cross-links, enabling energy dissipation. To demonstrate that our strategy is universal, we used polyacrylamide (PAAm) and poly(2-methacryloyloxyethyl phosphorylcholine) (PMPC) as the main chains of the hydrogels, which have been widely used as representative hydrophilic polymers in various fields and biocompatible zwitterionic polymers in the biomedical field, respectively. While there have been studies on tough hydrogels that have been designed using unique cross-linkers[9,10,11,17,18], this study demonstrates that tough and stretchable hydrogels can be prepared by conventional free radical polymerization without any special cross-linkers.Fig. 1: Schematics of hydrogels with physical and chemical cross-links.a Covalent and entanglement cross-links for energy storage and dissipation, respectively. b Chemically and physically cross-linked structures of brittle and tough hydrogels. c Fracture behavior of brittle and tough hydrogels with few and many entanglements, respectively.Acrylamide (AAm), N,N′-methylenebisacrylamide (MBAA), N,N,N′,N′-tetamethylethylenediamine (TEMED), and ammonium persulfate (APS) were purchased from Wako Pure Chemical Industries (Wako, Japan). 2-(Methacryloyloxy)ethyl phosphorylcholine (MPC) was supplied by NOF Corporation (Tokyo, Japan).Synthesis of poly(acrylamide) (PAAm) hydrogelsAAm, which was recrystallized from benzene prior to use, MBAA as a cross-linker, and TEMED were dissolved in deionized water to prepare a monomer solution with a total volume of 2.42 mL. In deionized water, APS, as an initiator, was also dissolved. The aqueous monomer and APS solutions were degassed using freeze-pump-thaw cycles and purged with Ar. After the freeze-pump-thaw cycles, the aqueous APS solution (0.08 mL) was added to the monomer solution in an ice bath to prevent premature gelation. The resulting mixture containing APS and TEMED in concentrations of 0.47×10^{-3} mol/L and 4.0×10^{-3} mol/L, respectively, was poured into a mold composed of two slides separated with a 5-mm-thick glass spacer (for compression tests) or a 1.76-mm-thick glass spacer (for tensile tests) (Fig. S1). The copolymerization of AAm and MBAA was performed at 25 °C for 1 day. As-prepared PAAm hydrogels were obtained by removing the molds. Swollen PAAm hydrogels were prepared by immersing the as-prepared hydrogels in water until their swelling ratio reached equilibrium.Synthesis of poly(2-methacryloyloxyethyl phosphorylcholine) (PMPC) hydrogelsMPC as the main monomer, MBAA as a cross-linker, and TEMED were dissolved in deionized water to prepare a monomer solution with a total volume of 0.92 mL. APS, as an initiator, was dissolved in deionized water to prepare an initiator solution. The aqueous monomer and initiator solutions were degassed using six freeze-pump-thaw cycles and purged with Ar. After the freeze-pump-thaw cycles, the aqueous APS solution (0.08 mL) was added to the monomer solution in an ice bath to prevent premature gelation. The resulting mixture of APS and TEMED at concentrations of 0.47×10^{-3} mol/L and 4.0×10^{-3} mol/L, respectively, was poured into a mold composed of two slides separated with a 5-mm-thick glass spacer (for compression tests) or a 1.76-mm-thick glass spacer (for tensile tests) (Fig. S1); copolymerization of MPC and MBAA was performed at 25 °C for 1 day. As-prepared PMPC hydrogels were obtained by removing the molds.Conversion measurementsThe as-prepared PAAm hydrogels were washed by immersion in deionized water for 2 weeks to completely remove unreacted monomers and initiators. Then, after the PAAm gels were dried at 70 °C in an oven for 2 days, their weight (Wdried gel) was measured. Wdried gel represents the total weight of polymerized AAm and MBAA in the resulting PAAm networks. The conversion of the monomers after gel formation was determined from the Wdried gel and the total weight (Wmonomer) of AAm and MBAA in a feed solution using Eq. (1).

$${\mathrm{Conversion}}\,({\mathrm{\% }}) = \frac{{W_{drie\,gel}}}{{W_{monomer}}} \times 100$$

Measurement of the water content of the hydrogelsPAAm hydrogels were immersed in deionized water until their swelling ratio reached equilibrium. Then, the weight (Wswollen gel) of the swollen hydrogels was measured. After they were dried at 70 °C in an oven for 2 days, the weight (Wdried gel) of the resulting dried gels was measured. The equilibrium water content of the PAAm hydrogels was determined using Eq. (2).

$$Water\,content\,({\mathrm{\% }}) = \frac{{W_{swollen\,gel} - W_{dried\,gel}}}{{W_{swollen\,gel}}} \times 100$$

Mechanical testsCompression tests of the as-prepared and swollen PAAm and PMPC hydrogels, which were prepared using the molds shown in Fig. S1, were performed using a mechanical testing instrument (SMT1-2-N, Shimadzu Co. Ltd., Kyoto) with a compression velocity of 10 mm/min−1. Tensile tests of the as-prepared and swollen PAAm and PMPC hydrogels were performed using a mechanical testing instrument with crosshead speeds of 5, 50, and 500 mm/min−1. The toughness of the hydrogels, which is the work to fracture, was determined from the area under the tensile stress–strain curve of an unnotched sample with a length of 20 mm.Determination of the cross-linking density of the hydrogelsThe elastic modulus of the hydrogels was determined from the strain-stress curves obtained by the compression tests using Eq. (3).

$$\sigma = G\left({\alpha - \alpha ^{ - 2}} \right)$$

where σ is the compression stress, G is the elastic modulus, and α is the ratio of the thickness of the gel before and after compression. The plot of σ vs. (α−α−2) showed a linear relationship. The slope of this line provided the G value. The effective cross-linking density, νe, of the gel was determined by Eq. (4).

$$G \approx RTu _e\phi ^{1/3}$$

Dynamic mechanical analysisDynamic mechanical analysis of the hydrogels was conducted using a nonresonance forced vibration viscoelastometer (Rheogel-E-4000F; UBM, Kyoto, Japan) in tension mode. The frequency and amplitude of the vibration were adjusted to 100 Hz and 50 μm, respectively. From the dynamic mechanical analysis, we determined the storage modulus (G′), loss modulus (G″) and loss factor (tanδ = G″/G′) to evaluate the viscoelastic properties of the hydrogels prepared under various conditions.First, to design polymer networks with many entanglements and a minute number of chemical cross-links, we prepared PAAm hydrogels, which are the most standard hydrogels, by the copolymerization of AAm as the main monomer and MBAA as a standard cross-linker using a wide range of monomer concentrations and cross-linker contents. The mechanical properties of the as-prepared PAAm hydrogels synthesized with various monomer concentrations and cross-linker contents were evaluated by compression and tensile tests (Fig. 2). Polymerization with high monomer concentrations (2.5 mol/L and 5.0 mol/L) allowed self-standing PAAm hydrogels with a cross-linker content of 0.001 mol% to form despite the low cross-linker content. As-prepared PAAm hydrogels with a cross-linker content greater than 0.1 mol% easily broke during compression (Fig. 2a–d and Movie S1b). However, the as-prepared PAAm hydrogels with a cross-linker content lower than 0.1 mol% did not break at up to 95% strain and 6-MPa stress (Fig. 2c and Movie S1a). From the work of Sakai et al.[31], the stress–strain curve of a four-arm poly(ethylene glycol) (tetra-PEG) hydrogel is replotted in Fig. 2a–c. The as-prepared tetra-PEG hydrogel is tough owing to its homogeneous network structure. Notably, although standard free radical polymerization results in the formation of an inhomogeneous network structure[30], the as-prepared PAAm hydrogels prepared under polymerization conditions with a high monomer concentration and a low cross-linker content were tougher than the tetra-PEG hydrogel with a homogeneous network structure.Fig. 2: Mechanical properties of PAAm hydrogels prepared under various conditions.a–c Stress–strain curves of as-prepared PAAm hydrogels during compression tests. Hydrogels with various cross-linker contents were prepared using AAm concentrations of a 1.0, b 2.5, and (c) 5.0 mol/L. d Photographs of as-prepared PAAm hydrogels with cross-linker contents of (i) 0.005 and (ii) 1.0 mol% during compression tests. The hydrogels were prepared at an AAm concentration of 5.0 mol/L. e–g Stress–strain curves of as-prepared PAAm hydrogels during tensile tests. The hydrogels were prepared using AAm concentrations of e 1.0, f 2.5, and g 5.0 mol/L. h Photographs of a swollen PAAm hydrogel during compression and shear tests. The PAAm hydrogel was swollen to equilibrium in water after it was prepared with an AAm concentration of 5.0 mol/L and a cross-linker content of 0.005 mol%. i Photographs of the as-prepared PAAm hydrogel during tensile tests. The hydrogel was prepared with an AAm concentration of 2.5 mol/L and a cross-linker content of 0.005 mol%.In the tensile tests, the as-prepared PAAm hydrogels with a high cross-linker content of more than 0.1 mol% could slightly extend, while the hydrogels prepared with a 2.5 mol/L monomer concentration and less than 0.01 mol% cross-linker content could be elongated by more than ten times and exhibited the highest fracture strain (Fig. 2e–g, i and Movie S2). The stress–strain curve of the hydrogel with a cross-linker content greater than 0.5 mol% is a straight line. Conventional polymer materials, such as elastomers, demonstrate S-shaped stress–strain curves because polymer chains result in extension from a thread-like shape. These results show that a large number of chemical cross-links cause brittleness of the PAAm hydrogels because the extension of the polymer chains is inhibited, and the stress is concentrated in weak chains within inhomogeneous networks. However, the fracture stress of the PAAm hydrogels was effectively improved with an increase in the monomer concentration during polymerization. The fracture stress of the PAAm hydrogels prepared with a 5.0 mol/L monomer concentration and 0.005 mol% cross-linker content was approximately 300 kPa. At the same cross-linker content, the initial slopes of the stress–strain curves of hydrogels synthesized with a 5.0 mol/L monomer concentration were steeper than those of hydrogels synthesized with a 2.5 mol/L monomer concentration. The steeper initial slopes indicate that the former hydrogels had a higher elastic modulus than the latter despite the same cross-linker content. For example, even though PAAm hydrogels were prepared using the same cross-linker content of 5.0 mol%, the Young's moduli of the hydrogels prepared with AAm concentrations of 1.0, 2.5, and 5.0 mol/L were determined to be 9.6, 40.0, and 196.7 kPa from the initial slopes of the stress–strain curves. These results suggest that the high monomer concentration during polymerization causes physical chain entanglements that act as mobile cross-links. Therefore, the improved fracture stress is attributed to the high polymer chain density in the hydrogel formed at a high monomer concentration. Of note, when only AAm was polymerized at a monomer concentration of 5.0 mol/L, a self-standing PAAm hydrogel formed despite the absence of a chemical cross-linker. Many polymer chain entanglements, which result from polymerization with a high monomer concentration, act as physical cross-links. However, when the strain of the PAAm hydrogel

without a chemical cross-linker was greater than 2, the stress was quickly relaxed by creeping of the polymer chains, and the hydrogel easily broke upon application of low stress. These results suggest that the conditions for preparing tough and stretchable hydrogels require polymerization with a high monomer concentration and a minute amount of cross-linker.Some papers have reported that as-prepared hydrogels designed using unique strategies exhibit high toughness; however, most of them do not exhibit the mechanical properties of swollen hydrogels after equilibrium swelling in aqueous media. In addition, the mechanical properties of swollen hydrogels are important because these hydrogels are typically utilized in aqueous media. Compression and tensile tests of swollen PAAm hydrogels demonstrated that their fracture strain and stress decreased after equilibrium swelling in aqueous media. The water content of the swollen PAAm hydrogels after equilibrium swelling decreased with increasing cross-linker content (Fig. S2). It should be noted that the swollen PAAm hydrogels prepared with a higher AAm concentration had a lower water content than those prepared with a lower AAm concentration even though they were prepared with the same cross-linker content. This means that polymerization with high monomer concentrations is likely to induce polymer chain entanglements in the resulting hydrogel networks. The decreased fracture stress and strain of swollen hydrogels are caused by an increase in the water content (Fig. S3). Because polymer chains are expanded in swollen hydrogels, they cannot be expanded further by applying stress. In addition, entanglements as physical cross-links are partially loosened during the swelling of hydrogels in aqueous media. Thus, swollen hydrogels break under a smaller strain than the as-prepared hydrogels because the applied stress is not effectively dissipated. However, the swollen PAAm hydrogels prepared under polymerization conditions of a high monomer concentration and low cross-linker content retain their high toughness despite equilibrium swelling (Figs. S2 and S3). For the swollen hydrogels with a 0.005 mol% cross-linker content, even if a large strain of more than 90% is applied during compression tests or a large elongation of more than seven times is applied during tensile tests, these hydrogels do not fracture despite the high water content of more than 90%, and they recover to their original shape after the stress is released (Fig. 2h, Figs. S2, S3 and Movie S3a). Of note, the swollen hydrogels prepared with a monomer concentration of 5.0 mol% and a cross-linker content of 0.005 mol% cannot be cut with a knife despite their swollen state (Fig. 2h and Movie S3b). Thus, the as-prepared and swollen PAAm hydrogels prepared with a high monomer concentration and a low cross-linker content demonstrate high mechanical toughness and high stretchability.Relationship between the cross-linked structure and toughness of PAAm hydrogelsTo elucidate the mechanism by which hydrogels become tough and stretchable, we determined the toughness of PAAm hydrogels from the stress–strain curve during tensile tests. In general, the fracture energies of polymeric materials are determined from the stress–strain curve of notched samples6,32,33. However, we were not able to notch the PAAm hydrogels synthesized in this study because they were very tough. In this study, we defined toughness from the area under the tensile stress–strain curve of an unnotched sample. The toughness is larger than the fracture energy determined using a notched sample because it includes energies not only for growing cracks but also for notching. The PAAm hydrogels prepared with a cross-linker content of more than 0.1 mol% have a much lower toughness than those prepared with a cross-linker content less than 0.1 mol% (Fig. 3a). An increase in the monomer content during the polymerization considerably enhanced the toughness of the resulting hydrogels. Of note, the PAAm hydrogel prepared with a monomer concentration of 5.0 mol/L and a cross-linker concentration of 0.005 mol% exhibited the maximum toughness of 1.6 MJ/m3, although the toughness could not be directly compared with the fracture energy of tough hydrogels prepared by different strategies13,15,33,34.Fig. 3: Toughness of PAAm hydrogels with various cross-linked structures.a Relationship between the cross-linker content and toughness of as-prepared PAAm gels prepared under various preparation conditions. The gels were prepared at AAm concentrations of 1.0 (○), 2.5 (◐), and 5.0 mol/L (●). b Effect of the cross-linker content on the cross-linking ratio between the experimental and theoretical cross-linking densities (νexp/νtheo) of the PAAm gels prepared under various conditions. c Relationship between νexp/νtheo and toughness of the PAAm gels prepared under various conditions.In general, the experimental cross-linking density (νexp) of hydrogels can be determined from their elastic modulus. For example, the νexp of the as-prepared PAAm hydrogels prepared with an AAm concentration of 1.0 mol/L increased gradually with an increase in the cross-linker content (Fig. S4). Although it is natural that an increase in the cross-linker content results in increasing νexp of the resulting PAAm hydrogels, not only chemical cross-links based on MBAA but also physical cross-links based on entanglements are included in the νexp determined from the elastic modulus. To evaluate the chemical and physical cross-links based on MBAA and entanglements, respectively, we determined the theoretical cross-linking density (νtheo)35 and νexp of the PAAm hydrogels prepared under various conditions. If the ratio of experimental to theoretical cross-linking densities (νexp/νtheo) is less than one, unreacted polymerizable groups of MBAA remain in the PAAm hydrogels, and not all MBAA is involved in chemical cross-links. The PAAm hydrogels with νexp/νtheo ratios greater than one contained physical cross-links that were based on polymer chain entanglements in addition to chemical cross-links based on MBAA. The νexp/νtheo ratio of the PAAm hydrogels monotonically decreased with an increase in the cross-linker content (Fig. 3b). The PAAm hydrogel prepared with a cross-linker content of approximately 0.1 mol% has a νexp/νtheo ratio of one, which means that the cross-linking density determined from the elastic modulus is equal to that based on a chemical cross-linker. Specifically, the PAAm hydrogels prepared with a cross-linker content of less than 0.1 mol% have physical cross-links that are based on entanglements because they have νexp/νtheo ratios greater than one, while the PAAm hydrogels with νexp/νtheo ratios less than one have a very low toughness, and the toughness increases considerably with an increase in νexp/νtheo to greater than one (Fig. 3c). These results suggest that the entanglement of polymer chains contributes to the high toughness of the PAAm hydrogel with a monomer concentration of 5.0 mol/L and a cross-linker content of 0.005 mol%. In polymer networks with many entanglements, because the applied stress is dissipated by creeping of the polymer chains entangled in the networks, the hydrogels become tough and stretchable. In fact, we observed creeping of the hydrogel prepared with AAm concentrations of 5.0 and 10 mol/L after they were elongated up to strains of 7 and 4, respectively (Fig. S5).Our strategy for preparing tough hydrogels uses the viscous characteristic to allow the applied stress to be relaxed by energy dissipation. In this strategy, a decrease in the cross-linker content enhances the contribution of the viscous characteristic to the mechanical properties of the hydrogels. Dynamic mechanical analysis is useful for evaluating the contribution of the elastic and viscous characteristics to the mechanical properties of hydrogels. We carried out dynamic mechanical analysis of PAAm hydrogels prepared with an AAm concentration of 2.5 mol/L and various cross-linker contents. When the cross-linker content of the PAAm hydrogels decreased, their storage modulus (G′) decreased, and the loss modulus (G″) increased (Fig. 4). As a result, the loss factor tanδ, which is the ratio of G″ to G′, of the PAAm hydrogels increased substantially with a decrease in the cross-linker content. In particular, the PAAm hydrogel with a cross-linker content of 0.005 mol% had an approximately twelve times greater tanδ than that with a cross-linker content of 1 mol%. As shown in Fig. 3b, the νexp/νtheo ratio of the PAAm hydrogels with a cross-linker content of less than 0.1 mol% was greater than one, revealing that the entanglements of the polymer chains increased in the hydrogel networks. Therefore, an increase in tanδ coincides with an increase in νexp/νtheo. In addition, the constant G′ in the regime of νexp > νtheo, as shown in Fig. 4a, indicates that the storage modulus of the PAAm hydrogels is determined by the density of the trapped entanglements. This implies that the PAAm hydrogels in the regime of νexp > νtheo were mainly cross-linked by the polymer chain entanglement. Although Fig. 4 might not be strong evidence, we think that an increase in G″ plays an important role in making hydrogels tough despite the slight increase in tanδ. From these results, we propose a possible mechanism by which the polymer chain entanglements enhance the contribution of the viscous characteristic, which enables energy dissipation, to the mechanical properties of the hydrogels. As a result, tough and stretchable hydrogels can be easily prepared by tuning the conditions for the preparation of networks with many entanglements. Further works about dynamic mechanical analysis and homogeneity of the networks will be performed to clarify the detailed mechanism.Fig. 4: Dynamic mechanical properties of PAAm hydrogels with various cross-linked structures.Effect of the cross-linker content on the storage modulus (G′) (a), loss modulus (G″) (b), and loss factor (tanδ) (c) of the as-prepared PAAm hydrogels prepared at an AAm concentration of 2.5 mol/L and various cross-liner contents.Tough and stretchable zwitterionic polymer hydrogelsTo demonstrate that the use of a high monomer concentration and low cross-linker content is a universal method for easily making hydrogels tough and stretchable, we used 2-methacryloyloxyethyl phosphorylcholine (MPC), which has been widely used as a biocompatible zwitterionic polymer in the biomedical field, instead of AAm to prepare hydrogels. In general, MPC has been widely utilized to prepare biocompatible polymers. Although hydrogels based on MPC have many potential applications in contact lenses, artificial joints, and other biomaterials36, they have a considerable disadvantage of low mechanical strength (i.e., they are brittle and weak). We tried to prepare tough and stretchable hydrogels using MPC by only tuning the preparation conditions of high monomer concentration and low cross-linker content. To optimize the conditions to prepare hydrogel networks with many entanglements, poly(2-methacryloyloxyethyl phosphorylcholine) (PMPC) hydrogels were prepared by the copolymerization of MPC and MBAA with a wide range of monomer concentrations and cross-linker contents. Similar to PAAm hydrogels, the PMPC hydrogels with a high cross-linker content easily broke upon application of a low stress in compression tests; however, the PMPC hydrogels with a cross-linker content of less than 0.1 mol% did not break at up to a 95% strain and 6-MPa stress (Fig. 5a, c and Movie S4). Of note, the PMPC hydrogel with a cross-linker content of 0.1 mol% could not be cut with a knife (Fig. 5d and Movie S5). In tensile tests, the PMPC hydrogels with many entanglements underwent large elongations and exhibited the highest fracture strain, differing from the general MPC-based hydrogels (Fig. 5b, e and Movie S6). The Young’s moduli of the PMPC hydrogels prepared with MPC concentrations of 2.5, 5, and 10 mol/L and with the same cross-linker content of 0.1 mol% were determined to be 16.6, 60.4, and 74.0 kPa from the initial slopes of the stress–strain curves, respectively. It should be noted that the PMPC hydrogel prepared with a higher MPC concentration exhibited a greater Young’s modulus than that prepared with a lower MPC concentration even though the PMPC hydrogels were prepared using the same cross-linker content. Similar to the formation of the PAAm networks, the preparation conditions with a high monomer concentration and a low cross-linker content resulted in the formation of networks with many entanglements of PMPC chains rather than chemical cross-links based on MBAA. Therefore, we conclude that preparation with a high monomer concentration and low cross-linker content is a universal method for preparing tough and stretchable hydrogels because the resulting networks have many physical cross-links based on polymer chain entanglements that act as mobile cross-links for energy dissipation. Thus, tough and stretchable hydrogels can be easily prepared by optimizing the preparation conditions to form many polymer chain entanglements without using complicated methods.Fig. 5: Mechanical properties of PMPC hydrogels prepared under various conditions.a Stress–strain curves of as-prepared PMPC hydrogels with various cross-linker contents during compression tests. The hydrogels were prepared using an MPC concentration of 5.0 mol/L. b Stress–strain curves of as-prepared PMPC hydrogels with MPC concentrations of 2.5, 5, and 10 mol/L during tensile tests. The hydrogels were prepared using a cross-linker content of 0.1 mol%. c Photographs of as-prepared PMPC hydrogels with cross-linker contents of (i) 0.1 and (ii) 1.0 mol% during compression tests. The hydrogels were prepared at an MPC concentration of 2.5 mol/L. d Photographs of as-prepared PMPC hydrogels with cross-linker contents of (i) 0.1 and (ii) 1.0 mol% during shear tests. The hydrogels were prepared at an MPC concentration of 2.5 mol/L. e Photographs of the as-prepared PMPC hydrogel during tensile tests. The hydrogel was prepared under an MPC concentration of 5.0 mol/L and a cross-linker content of 0.1 mol%.In summary, we have demonstrated a simple and versatile strategy for producing tough and stretchable hydrogels by free radical polymerization of standard hydrophilic monomers. Our strategy is to only tune the polymerization conditions without introducing a special structure or using complicated methods; we can optimize the network structures, which have many polymer chain entanglements for energy dissipation by polymerization conditions with a high monomer concentration and a low cross-linker content. The hydrogels prepared under the optimized conditions have a νexp/νtheo ratio greater than one, indicating that the hydrogels contain physical cross-links based on polymer chain entanglements in addition to chemical cross-links based on MBAA. The toughness of the hydrogels increased considerably with an increase in νexp/νtheo above than one. Although our strategy uses neither a special structure nor a complicated method, the hydrogels prepared using our strategy exhibited high toughness. Tough and stretchable nonionic PAAm and zwitterionic PMPC prepared under optimized polymerization conditions undergo large elongations, exhibit high fracture strain and cannot be cut with a knife because of the many entanglements as physical cross-links. Our strategy is applicable to preparing tough and stretchable hydrogels from a variety of polymers. Structural design using polymer chain entanglements for energy dissipation to overcome the limitation of low mechanical performance will lead to many practical uses of hydrogels.Hoffman, A. S. Hydrogels for biomedical applications. Adv. Drug Deliv. Rev. 54, 3–12 (2002).Article CAS Google Scholar Peppas, N. A., Hilt, J. Z., Khademhosseini, A. & Langer, R. Hydrogels in biology and medicine: from molecular principles to bionanotechnology. Adv. Mater. 18, 1345–1360 (2006).Article CAS Google Scholar Li, J. & Mooney, D. J. Designing hydrogels for controlled drug delivery. Nat. Rev. Mater. 1, 1–17 (2016). Google Scholar Zhang, Y. 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