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COMMUNICATION

A Screening Technique to Study the Mechanical Strength of Gelatin Formulations

Sriram Vemuri*

SciClone Pharmaceuticals, San Mateo, California

ABSTRACT

A semiquantitative method for measuring the mechanical strength of gelatin ribbons was demonstrated using a universal tensile testing machine (Instron, model 1122). Molten gelatin formulations comprised of acid-bone gelatin, limed-hide gelatin, or their combinations were made, pored as gelatin films, and aged at 50% relative humidity (RH). Viscoelastic properties (mechanical strength) of five gelatin formulations were evaluated by determining elastic modulus, tensile strength, and ratio of tensile strength to elastic modulus of gelatin ribbons. This study demonstrated that a 3 : 1 ratio of acid-bone to limed-hide gelatin combination showed better viscoelastic properties than the other formulations studied.

Key Words: *Elastic modulus; Gelatin films; Mechanical strength; Tensile strength; Universal tensile testing machine.*

INTRODUCTION

Viscoelastic properties of gelatin formulations are the result of physical arrangement and chemical structures, which are characterized by a number of rheological parameters. This complex mechanical behavior has interested several investigators (1–3), and they have employed mechanical models to depict these phenomena.

Nonaqueous, liquid pharmaceutical formulations are often packaged in soft elastic gelatin (SEG) capsules, which are made by entrapping drug formulations between two freshly made gelatin ribbons. The firmness and strength of gelatin ribbons at the time of manufacture and on storage can be related to the gelatin formulation.

There is no standard test to determine the mechanical behavior of gelatin ribbons at this time. I have investigated the use of the universal tensile testing machine (Instron, Instron Engineering Corp., Canton, MA) to study the behavior of capsules on storage (4). As recently as 1993, it was reported that the tensile properties of free

* Telephone: (650) 358-1443.

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films of ethylcellulose dispersions were evaluated using the universal tensile testing instrument (5). This study reports a screening technique to evaluate, using load-time profiles, the mechanical strength of gelatin in different formulations of gelatin ribbons cast from five different formulations. Such an evaluation can help in screening formulations of gelatin for their mechanical strength.

EXPERIMENTAL

Materials

Limed-hide and acid-bone gelatin of 150 bloom strength (Hormel, Minnesota, MN), glycerin USP (Witco Corp., New York, NY), sunflower oil, and purified water were obtained from commercial sources.

Preparation of Samples

To the crystalline gelatin in a flask, a mixture of glycerin and water was added. The flask was then placed in an 85°C water bath. Contents of the flask were stirred until the gelatin melted completely. The molten gelatin was then poured on a leveled glass plate, carefully avoiding air bubbles, and another glass plate was pressed on top of it. Spacers were put on the corners of the plate so that a uniform thickness was achieved. The wet gelatin film was dried at room temperature overnight between two glass plates. The gelatin film was then placed in a 50% relative humidity (RH) and room temperature desiccator (50% RH was achieved by placing a saturated solution of sodium chloride and magnesium nitrate in the bottom of a desiccator) for 5 days (both sides of the film were exposed). The moisture content of cured gelatin films was determined as 16% $\pm$ 2% (w/w) by loss on drying method. At the end of this initial curing period, the gelatin film was cut into 1 inch by 3 inch ribbons and submerged in sunflower oil in a closed jar, which was stored at 25°C. Before the measurement of mechanical strength, gelatin ribbons were taken out of the oil, and the oil on the surface was removed by wiping with paper napkins.

Mechanical Strength Evaluation

The mechanical strength of gelatin ribbons was tested on a universal tensile testing instrument (Instron model 1122). The instrument was mounted with a 500-N capacity load cell, and it has a moving crosshead with a strain gauge attached. Clamps were attached to the movable crosshead and to the base of the machine. The gelatin ribbon was clamped between the stationary clamp and the movable crosshead clamp. The gelatin ribbon between the clamps was subjected to pull by moving the crosshead upward at a rate of 1 inch per min (strain rate). The resistance offered by the gelatin to the free movement of the crosshead is sensed by an elastic bonded-wire strain gauge. The output was recorded on a high-speed strip chart recorder, which is driven synchronously with the crosshead. Averages of at least five measurements were made for each formulation at all the time points.

The behavior of this elastic model under an applied load can be used to describe the viscoelastic response of undried gelatin under these pulling conditions. The mechanical strength of the ribbons was measured from their load-time profiles, and this procedure is consistent with the ASTM guidelines (D-638-89) (6). Three different mechanical properties were calculated from the load-time profiles collected: elastic modulus, tensile strength, and the ratio of tensile strength to elastic modulus.

Viscoelasticity of materials can be described by a simplified Maxwell-type equation that represents the changes in elastic modulus as a function of time (7,8). Elastic modulus is the term that has been used to describe the measure of ductility of gelatin ribbon by a tension test, as elucidated in this report. It is the measure of extended length of gelatin strip by taking the value of slope from the load-time profiles. A typical example of a load-time profile is shown in Fig. 1. Breaking load was obtained by recording the load required to cause fracture in gelatin ribbon during the torsion test. Tensile strength is the maximum stress applied to a point at which the gelatin specimen breaks. Tensile strength can be calculated from the applied load at rupture and the cross-sectional area of a fractured strip as described here: Tensile strength is equal

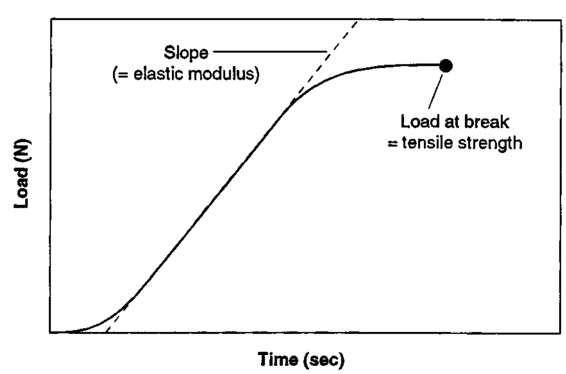

Figure 1. A typical load-versus-time curve for a fully hydrated gelatin strip on a universal tensile testing instrument.

to load at break divided by the thickness of the product and the width of the gelatin strip. When the thickness and width of gelatin strips are kept constant throughout the experiments, the tensile strength can simply be defined as load at break with appropriate units.

RESULTS AND DISCUSSION

Weak polymers are characterized by low elastic modulus, low tensile strength, and low strain at break, whereas a soft and tough polymer film is characterized by low elastic modulus, moderate tensile strength, and high strain at break. Tensile strength is an indicator of the gelatin strength, with a larger value corresponding to the stronger gelatin formulation. The slope in Fig. 1, elastic modulus, is an indicator of the film elasticity, with lower values corresponding to higher elasticity. Ideally, a gelatin formulation intended for SEG capsule preparation must be tough and elastic and maintain its properties throughout the storage period.

Five different gelatin formulas were used in this study. The composition of each of the formulas is given in Table 1. The gelatin ribbon thickness was carefully controlled at the time of preparation to reduce variations in mechanical strength evaluation on a universal tensile testing machine. Processing conditions and aging affect the viscoelastic properties of gelatin. Viscoelastic properties affect material handling, processing, and storage conditions of formulations. For example, a higher degree of shearing produces a lower elastic modulus in viscoelastic products. Different processes exert different types of shear on products. As the shearing increases, the elastic modulus of the product decreases. To minimize this variability, necessary precautions (e.g., heating rate, duration of heating) were taken in making gelatin ribbons.

Figure 2 shows the effect of variations in the gelatin formulations on mechanical strength measured by elastic modulus. Each point in the figure is an average of five determinations, and the vertical bars denote one standard deviation from the mean. Each line in the figure represents a different formulation and its behavior on storage. Table 2 shows the data for this figure. Formulation B, which was acid-bone gelatin alone, showed the lowest elastic modulus, and formulation C, which was a combination of acid-bone and limed-hide gelatin in 1 : 1 ratio, showed the largest value of elastic modulus throughout the stability period compared to the remaining formulations under study. Smaller elastic modulus values observed for formulation B are statistically different from the values of formulation C when compared using a two-sided Student *t* test at the 5% level. Initial time point values of formulations A and C, when compared with formulation B, are not statistically different. This observation also suggests that formulations A, B, and C were

Table 1

Gelatin Formulas Used to Determine the Mechanical Strength

Formula Designation	Formula Ingredients	Percentage (w/w)
A	Limed-hide gelatin (bloom strength 150)	36
	Glycerin	15
	Water	49
B	Acid-bone gelatin (bloom strength 150)	36
	Glycerin	15
	Water	49
C	Limed-hide gelatin	18
	Acid-bone gelatin	18
	Glycerin	15
	Water	49
D	Limed-hide gelatin	27
	Acid-bone gelatin	9
	Glycerin	15
	Water	49
E	Limed-hide gelatin	9
	Acid-bone gelatin	27
	Glycerin	15
	Water	49

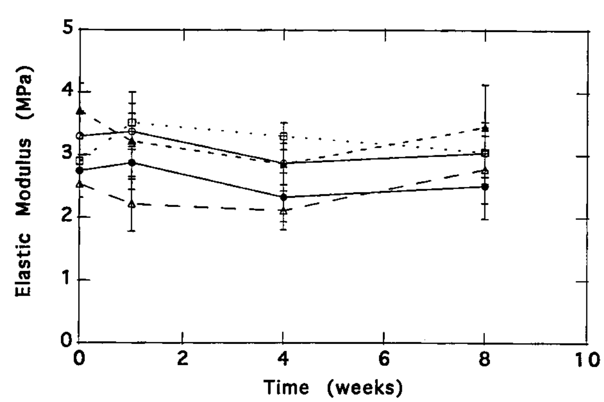

Figure 2. Plot of elastic modulus of fully hydrated gelatin ribbon strip as a function of storage time. Each point in the plot is an average of five determinations. The error bars represent one standard deviation on mean. ●, formulation A; △, formulation B; □, formulation C; ▲, formulation D; ○, formulation E.

Table 2

Viscoelastic Properties of Five Gelatin Formulas on Stability

Formulation Designation	Storage Time (weeks)	Elastic Modulus (MPa)	Tensile Strength (MPa)
A	0	2.750 ± 0.242	1.752 ± 0.261
	1	2.875 ± 0.259	1.645 ± 0.386
	4	2.325 ± 0.390	1.447 ± 0.321
	8	2.508 ± 0.529	1.553 ± 0.494
B	0	2.538 ± 0.216	1.480 ± 0.404
	1	2.220 ± 0.438	1.260 ± 0.318
	4	2.117 ± 0.308	1.192 ± 0.318
	8	2.775 ± 0.543	1.643 ± 0.397
C	0	2.900 ± 0.412	1.982 ± 0.674
	1	3.513 ± 0.309	2.699 ± 0.607
	4	3.300 ± 0.212	2.257 ± 0.199
	8	3.050 ± 0.397	2.347 ± 0.716
D	0	3.700 ± 0.442	2.945 ± 0.278
	1	3.225 ± 0.776	2.382 ± 0.833
	4	2.858 ± 0.330	2.066 ± 0.369
	8	3.450 ± 0.680	2.431 ± 0.715
E	0	3.300 ± 0.394	2.633 ± 0.558
	1	3.375 ± 0.286	2.359 ± 0.292
	4	2.867 ± 0.442	1.961 ± 0.593
	8	2.038 ± 0.492	2.155 ± 0.449

Means of five determinations along with the standard deviation (SD) are shown.

less elastic compared to the others, which is evidenced by larger elastic modulus values.

Figure 3 shows the tensile strength of the five formulations on storage over an 8-week period. The tensile strengths of the five formulations were different immediately after their preparation. Table 2 shows the data for this figure. The top curve in the figure represents the stability of formulation C, whereas the bottom curve is for formulation B, over an 8-week stability period. The larger values of tensile strength represent the mechanical strength of the formulation. On storage in sunflower oil, all formulations under study maintained their stability reasonably well.

Elastic modulus and tensile strength are good independent parameters to study two entirely different aspects of mechanical properties of a material. A ratio of these two parameters provides valuable information and may be useful in selecting one formulation from the other. Figure 4 shows the plot of the ratio of tensile strength to elastic modulus as a function of storage time. It is apparent that this ratio yielded the largest values for formulation C. The highest value indicates that the gelatin ribbons made with formulation C are more elastic as well as strong.

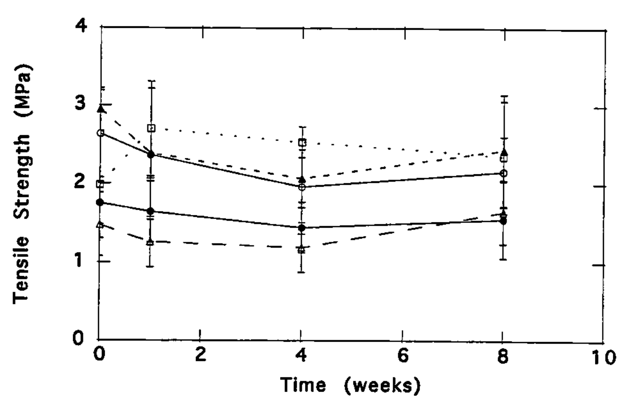

Figure 3. Plot of tensile strength of fully hydrated gelatin ribbon strip as a function of storage time in sunflower oil. Each point in the plot is an average of five determinations. The error bars represent one standard deviation on mean. ●, formulation A; △, formulation B; □, formulation C; ▲, formulation D; ○, formulation E.

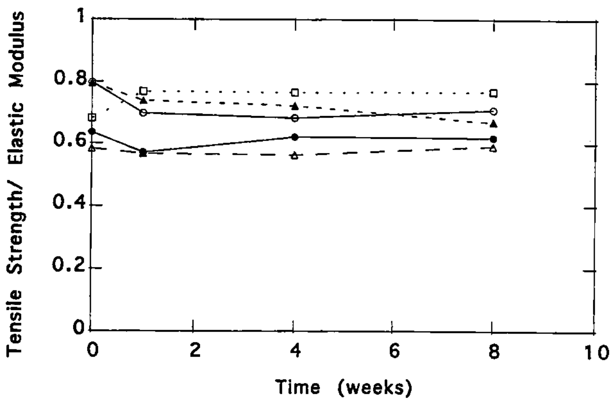

Figure 4. Plot of the ratio of tensile strength to elastic modulus of fully hydrated gelatin ribbon strip as a function of storage time in sunflower oil. ●, formulation A; △, formulation B; □, formulation C; ▲, formulation D; ○, formulation E.

This formulation contains both acid-bone and limed-hide gelatins.

The degree of elongation that occurs in a material is related to its macromolecular structure and the mechanical properties of polymeric materials. Figure 5 presents the tensile strength of wet gelatin as a function of elastic modulus immediately after the curing process. Stretching it to obtain better molecular alignment can increase the gelatin ribbon tensile strength. Contrary to my expectations, gelatin ribbon made with acid-bone gelatin alone is neither stronger nor elastic compared to the other formulations.

This study showed that the tensile strength properties could be enhanced by the combination of two different

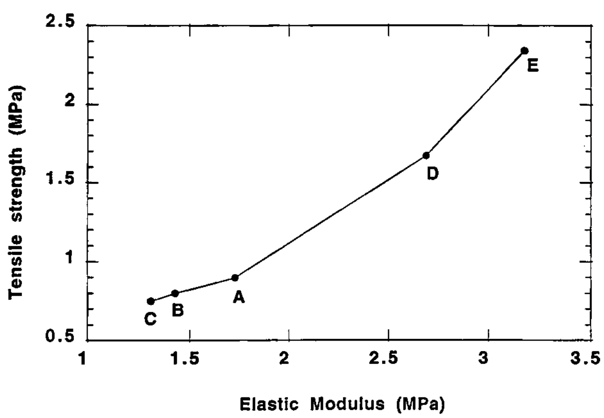

Figure 5. Mechanical strength and elasticity of gelatin formulations are compared in this plot. Each letter on the plot denotes a different formulation.

types of gelatin. Further, this study demonstrated a 3:1 ratio of acid-bone to limed-hide formulation exhibited superior viscoelastic properties compared to the other formulations investigated. This technique can be adopted to screen various gelatin formulations, film-coating formulations, and transdermal patches.

CONCLUSION

In summary, microstructure of the film influences the mechanical properties of gelatin formulations during their storage. Utilization of both acid-bone and limed-hide gelatin in the same formulation offered better mechanical properties (mechanical strength) compared to the noncombination formulations. Viscoelastic properties inherent to gelatin dictate the eventual mechanical properties of the gelatin formulations. This technique can also be adapted to other film-forming polymers of pharmaceutical interest.

THEORY

Viscoelasticity of materials can be described by a simplified Maxwell-type equation, which represents the changes in elastic modulus as a function of time:

$$E(t) = s(t)/e_0 = E_0 e^{-t/T_{rel}}$$

where $E(t)$ is elastic modulus, $s(t)$ is stress, e_0 is initial strain, E_0 is initial elastic modulus, t is time, and T_{rel} is relaxation time. When a material is purely viscous, the elastic modulus remains constant, and relaxation time becomes infinite. Most polymeric materials have a time-dependent elastic modulus. The degenerative elastic Maxwell model, when applied to polymeric systems, can adequately describe stress relaxation of a single polymer chain. Polymeric systems such as gelatin preparations are described as being composed of several (n) polymeric chains. Such a system was explained as a number of Maxwell models combined in parallel or series to express the viscoelasticity.

The behavior of this elastic model under an applied load can be used to describe the viscoelastic response of undried gelatin under pulling condition. *Elongation ratio* is the term that has been used to describe the measure of ductility of gelatin strip by a tension test, as elucidated in this report. It is the measure of the extended length of gelatin strip divided by its original length. Higher elongation indicates higher ductility. The *tensile strength* is defined as the strength of a material subjected to tensile loading. It is the maximum stress developed in a material in a tension test. In this study, this parameter was calculated by dividing breaking load by the area of gelatin ribbon. Breaking load was obtained by recording the load required to cause fracture in gelatin ribbon during the torsion test.

Figure 1 shows a typical stress deformation curve obtained with a universal testing machine. Tangents were drawn at inflection points of the curve. The perpendicular length between the tangents is defined as an elongation at break.

REFERENCES

1. J. D. Ferry, *Viscoelastic Properties of Polymers*, John Wiley and Sons, New York, 1961.
2. R. A. Castello and J. E. Goyan, Rheology of gelatin films, J. Pharm. Sci., 53, 777–782 (1964).
3. I. W. Kellaway, C. Marriott, and J. A. J. Robinson, The mechanical properties of gelatin films, Can. J. Pharm. Sci., 13, 87–90 (1978)
4. S. Vemuri, Measurement of soft elastic gelatin capsule firmness with a universal testing machine, Drug Dev. Ind. Pharm., 10(3), 409–423 (1984).
5. N. H. Parikh, S. C. Porter, and B. D. Rohera, Tensile properties of free films cast from aqueous ethylcellulose dispersions, Pharm. Res., 10(6), 810–815 (1993)
6. American Society of Testing and Materials (ASTM), *Guidelines, D-638-89: Standard Test Method for Tensile Properties of Plastics*, Author.
7. F. W. Billmeyer, *Textbook of Polymer Science*, John Wiley, New York, 1984, pp. 246–247.
8. A. V. Tobolsky, *Properties and Structures of Polymers*, John Wiley and Sons, New York, 1960, pp. 107–112.