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Scaffold Silk Fibroin

DEFINITION

Scaffold Silk Fibroin is a surgical scaffold device made from the silk of the *Bombyx Mori* silkworm. Raw silk filaments are comprised of a fibroin protein core that is naturally coated with the globular protein sericin. The sericin is removed from the fiber by aqueous extraction leaving the fibroin protein behind, consisting of layers of anti-parallel beta sheets, which give the fiber strength. The fiber is then assembled into a three dimensional patterned scaffold. The scaffold is a mechanically strong, flexible, single use device that can be produced in a variety of shapes, sizes, and thicknesses, and is terminally sterilized.

IMPURITIES

• **Nonpolar Solvent Extraction**

Positive control: 20 mg of mineral oil[1]

Negative control: 45 mL of *n*-hexane

Sample: Scaffold Silk Fibroin

Analysis: [Note—Gloves should be worn throughout the procedure as natural skin oil may affect the results. Glassware preparation: Each sample or control requires one 60-mL bottle and cap and one glass Petri dish. Wash glass Petri dishes (10 cm × 2 cm) and a corresponding number of 60-mL glass jars with lids with liquid detergent and rinse well with tap water. Rinse again with deionized water. Transfer glassware in the chemical hood and rinse all glassware with hexane. Air-dry glassware in the chemical hood for at least 15 min. Transfer dried glassware to a desiccator for NLT 30 min before weighing.] Ensure the relative humidity of the room is between 30% and 80% before weighing or labeling bottles and petri dishes. Label and pre-weigh 60-mL bottles. For the *Positive control*, add 20 mg of mineral oil to a 60-mL bottle and for the *Negative control*, add 45 mL of hexane to a 60-mL bottle. For the *Sample*, use stainless steel tweezers to place one device per 60-mL bottle and cap. Re-weigh bottles and calculate the sample weight (SW) by subtracting the initial mass of the bottle from the mass of the sample-containing bottle. In the chemical hood, open the bottles and add 45 mL of *n*-hexane to each, then re-close making sure that the hexane does not come in contact with the caps. Prepare an ultrasonic water bath for sample processing by degassing it. For this, use the “degas” setting of the equipment for 10 min. Place all 60-mL bottles, prepared as above, in the water bath. Ensure that the water level is 0.5-cm below the lids of the bottles. Sonicate bottles for 5 min on the “sonication” setting (frequency of 40 KHz). Label Petri dishes so that each bottle has a correspondingly labeled Petri dish. Weigh each dish individually and record the mass ($m_{initial}$). Pour the hexane solution from each bottle into the corresponding pre-labeled Petri dish. Add 15 mL of *n*-hexane to each bottle, rinse then pour in the corresponding Petri dish. Repeat this rinsing step and collect the solution. The final hexane volume in each of the Petri dishes should be approximately 75 mL (45 mL from extraction + 15 mL from first rinse + 15 mL from second rinse). Leave Petri dishes uncovered in the chemical hood for 12 h to evaporate the *n*-hexane. Re-weigh each Petri dish after hexane evaporation and record mass (m_{final}).

Calculate the recovery of the *Positive control* in percentage with the following formula:

$$\text{Result} = [(m_F - m_I)/W_O] \times 100$$

m_F = final mass of Petri dish after *n*-hexane evaporation in mg

m_I = initial mass of empty Petri dish in mg

W_O = weight of oil added, mg

Calculate the concentration of organic residuals, in ppm, in each tested device:

$$\text{Result} = [(m_F - m_I)/W_S] \times F$$

m_F = final mass of Petri dish after *n*-hexane evaporation in mg

m_I = initial mass of empty Petri dish in mg

W_S = sample weight, g (calculated by subtracting the initial mass of the bottle from the mass of the sample-containing bottle)

F = conversion factor for kg to g, 1000

System suitability criteria: The determined m_F for the *Negative control* should be NMT 0.2 mg and the *Positive control* recovery should be 95%–105%.

Acceptance criteria: Hexane extractable residues should be NMT 1106 ppm per tested device.

- **Elemental Impurities—Limits ⟨232⟩** and **Elemental Impurities—Procedures ⟨233⟩**

Nitric acid solution: 2% (v/v) nitric acid in water

Sample solution: Weigh 3–4 g of Scaffold Silk Fibroin, record the mass, then place in a 50-mL conical tube. Add 25 mL of *Nitric acid solution* to the tube. Incubate for 16 h at room temperature.

Analysis: Transfer 5 mL of the *Sample solution* to a tube that is compatible for testing. The levels of chromium, cadmium, nickel, vanadium, lead, and arsenic are determined by an inductively coupled plasma–atomic emission spectroscopy (ICP-AES) (see *Plasma Spectrochemistry ⟨730⟩*) normalized to the mass of the tested device and reported in parts per million (ppm).

Acceptance criteria: Meets the requirements of the Parental Daily Dose PDE (µg/day) in *Elemental Impurities—Limits ⟨232⟩*

SPECIFIC TESTS

- **Fibroin Content**

Digestion solution: 6 N hydrochloric acid

Reconstitution solution: 0.02 N hydrochloric acid

Borate buffer: 0.2 M sodium borate, pH 8.8 with 5 mM calcium disodium ethylenediaminetetraacetic acid (EDTA). Prepare the buffer by dissolving 124 g boric acid in 80 mL of deionized water; add 187 mg calcium disodium EDTA then titrate with 1 N sodium hydroxide to a pH of 8.8. Add deionized water to a final volume of 100 mL.

Derivatization reagent: 10 mM of 6-aminoquinolyl-*N*-hydroxysuccinimidyl carbamate in acetonitrile. Vortex for 10 s at 2700 rpm. Incubate the solution for 10 min at 55°, and vortex occasionally until the powder dissolves.

Preparation of hydrolysis sample vials and tubes: Clean glass acid hydrolysis sample vials (30 × 120 mm) and hydrolysis tubes (6 × 50 mm) used for sample preparation with a phosphate-free detergent[2], rinse with purified water then pyrolyze at 220° for 24 h. Allow vials to cool to room temperature then add 200 µL of constant boiling 6 N hydrochloric acid[3] to each hydrolysis tube along with a single phenol crystal.[4] Cap tubes with a polytetrafluoroethyl (PTFE) cap with a chlorotrifluoroethylene (CTFE) screw type on-off valve until needed.

System suitability solution: 25 µM in water from commercially available amino acid standard[5]

Fibroin solution: Bring 2 L of water to a boil in a glass beaker, then add 4.24 g of sodium carbonate. Add 5 g of raw silk yarn[6] and boil for 1 h. Remove yarn containing fibroin with a spatula and rinse in 2 L of water. Squeeze yarn with gloved hands to remove excess water. Rinse yarn 3 more times in 2 L of water for 20 min under agitation (use a stir bar for agitation and set the stir plate to 250 rpm). Squeeze yarn with gloved hands to remove excess water, place the fibroin yarn on a clean sheet of aluminum foil and dry for 16 h in a chemical hood. Transfer 1 mg of the fibroin yarn to a hydrolysis tube to obtain 5 mg/mL of fibroin in 6 N hydrochloric acid. Prepare three replicates. Incubate at 115° for 16 h. Allow the tubes to cool for 1 h at room temperature. Remove acid with a speed vacuum. Add 20 µL of *Reconstitution solution* to each tube and incubate at 50° for 10 min. Dilute each solution 5-fold (to 0.1 µg/µL) with *Reconstitution solution*.

Sericin solution: Add 1 mg of sericin[7] per hydrolysis tube to obtain 5 mg/mL sericin in 6 N hydrochloric acid. Prepare three replicates. Incubate at 115° for 16 h. Allow the tubes to cool for 1 h at room temperature. Remove acid with a speed vacuum. Add 20 µL of *Reconstitution solution* to each tube and incubate at 50° for 10 min. Dilute each solution 5-fold (to 0.1 g/µL) with *Reconstitution solution*.

Standard solutions: Prepare amino acid standards at the following concentrations: 600, 500, 400, 300, 200, 100, 50, 10, 5, and 1 µM in water from commercially available amino acid standard.[8]

Sample solutions: Add 1 mg of Scaffold Silk Fibroin per hydrolysis tube to obtain 5 mg/mL of Scaffold Silk Fibroin in 6 N hydrochloric acid. Prepare six replicates. Incubate at 115° for 16 h. Allow the tubes to cool for 1 h at room temperature. Remove acid with a speed vacuum. Add 20 µL of *Reconstitution solution* to each tube and incubate at 50° for 10 min. Dilute each solution 5-fold (to 0.1 µg/µL) with *Reconstitution solution*.

Amino acid derivatization: *Standard solutions* and reconstituted *Fibroin solution*, *Sericin solution*, and *Sample solutions* are derivatized. *Borate buffer* (70 µL) is added to 12- × 32-mm screw neck total recovery vials (the number of vials needed is equal to the number of Standards, samples, fibroin and sericin solutions, and one blank solution). An aliquot of 10 µL of each amino acid standard (one standard sample for each concentration) and each control (triplicates of *Fibroin solution* and *Sericin solution*) and sample (one sample per finished Scaffold Silk Fibroin) are added to the respective vials. The vials are vortexed for 5 s at 2700 rpm, followed by the addition of 20 µL of *Derivatization reagent*. The vials are capped and vortexed again for 5 s. The vials are then heated for 10 min at 55°. A blank is also prepared using 10 µL of *Reconstitution solution* instead of amino acid standard.

Solution A: Prepare a mixture of acetonitrile, formic acid, and 100 mM ammonium formate (10:6:84). Dilute this mixture with water (5:95).

Solution B: Acetonitrile and formic acid (98:2)

Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	99.9	0.1
0.54	99.9	0.1
5.74	90.9	9.1
7.74	78.8	21.2
8.04	40.4	59.6
8.64	40.4	59.6
8.73	99.9	0.1
9.5	99.9	0.1

Chromatographic system

(See *Chromatography ⟨621⟩, System Suitability*.)

Mode: LC

Detector: UV 260 nm

Column: 2.1-mm × 10-cm; L1 with particle size 1.7 µm and pore size 130 Å

Column temperature: 55°

Flow rate: 0.7 mL/min

Injection volume: 1 µL

Run time: 10 min

System suitability

Sample: *System suitability solution*

Suitability requirements

Plate count: NLT 2000 for all the amino acids

Tailing factor: NMT 2

Resolution: NLT 2

Signal-to-noise ratio: NLT 10 for all the amino acids

Analysis

Samples: *Fibroin solution*, *Sericin solution*, *Standard solutions*, and *Sample solutions*

Create a calibration curve for each amino acid by integrating the peak area obtained from the chromatograph for each concentration of *Standard solution* then plot the integrated peak area as a function of concentration. Run each replicate of *Fibroin solution* and *Sericin solution*. Perform one run for each of the six *Sample solutions*. Determine the concentration of each constituent amino acid of each control solution and *Sample solution* from the calibration curves of the amino acid standards.

A mathematical algorithm development software is used to set up a matrix based calculation for fibroin purity.[9] The algorithm uses 7 out of the 16 detected amino acids: glycine (Gly), alanine (Ala), tyrosine (Tyr), serine (Ser), asparagine (Asx), glutamate/glutamic acid (Glx), and threonine (Thr). [Note—The 7 amino acids were selected because the magnitude difference in weight percent of each found in sericin compared to fibroin is at least 2-fold.]

Convert the fibroin and sericin reference data into a [7 × 2] matrix (*Matrix A*), with 7 (columns) representing each of the selected amino acids and 2 (rows) representing the number of Reference Standards analyzed. Represent the amino acid composition of the silk samples being analyzed as a [7 × 6] matrix (*Matrix B*), where 7 (columns) represent each of the selected amino acids and 6 (rows) for each of the total number of samples analyzed. Specifically,

$$\text{Matrix A} = \begin{bmatrix} Gly & Ala & Tyr & Ser & Glx & Asx & Thr \\ Gly & Ala & Tyr & Ser & Glx & Asx & Thr \end{bmatrix}$$

- the first row is the sericin reference amino acid average from the three runs
- the second row is the fibroin reference amino acid average from the three runs

$$\text{Matrix B (1 to 6)} = \begin{bmatrix} Gly_1 & Ala_1 & Tyr_1 & Ser_1 & Glx_1 & Asx_1 & Thr_1 \\ \vdots & \vdots & \vdots & \vdots & \vdots & \vdots & \vdots \\ Gly_6 & Ala_6 & Tyr_6 & Ser_6 & Glx_6 & Asx_6 & Thr_6 \end{bmatrix}$$

Where:

- the rows indicated the amino acid averages for the six samples analyzed

The mass proportion of fibroin and sericin from each *Sample solution* is calculated by performing the matrix operation $B \times (A^{-1})$. The percent weight compositions of fibroin and sericin for each analyzed *Sample solution* are calculated by the software from the mass proportions.

Acceptance criteria: NLT 95% for fibroin content and NMT 5% for sericin content

- **Dimensional Analysis**

Sample: Scaffold Silk Fibroin

Analysis: Measure the length and width of intact Scaffold Fibroin Silk devices with a NIST traceable caliper with an accuracy of at least 0.02 mm.[10] Take three measurements at the top, the center, and the bottom of the device for each parameter. Measure the length of the scaffold in the longest direction. Measure the width of the scaffold along the shortest direction. Measure the thickness of the sample (single measurement) using a NIST traceable thickness gauge with accuracy of at least 0.01 mm.[11] Place the sample (either intact scaffold or sectioned piece) between the gauge feelers taking care to avoid creases and folds. Close the feelers and take the measurement. [Note—Test between 13 and 50 devices.]

Acceptance criteria: Each device is NLT 15 ± 1.5 cm in length and NLT 5 ± 0.5 cm wide, with a thickness range of 0.6–1.0 mm.

- **Density Determination**

Sample: Scaffold Silk Fibroin

Analysis: Determine the mass of the sample by a single measurement using a scientific calibrated balance that can be read to at least 0.1 mg.[12] The average length and width is determined by averaging the three measurements from the *Dimensional Analysis*. The thickness is measured as described in the *Analysis* of the *Dimensional Analysis*.

Calculate the density, mg/mm^3 of each sample by using the equation:

$$\text{Result} = M/(L \times W \times T)$$

M = mass, mg

L = average length, mm

W = average width, mm

T = thickness, mm

Acceptance criteria: NLT 0.14 mg/mm^3 and NMT 0.18 mg/mm^3

- **Pore Characterization**

Sample: Scaffold Silk Fibroin

Analysis: The assembled scaffold has a lattice-like appearance, with open spaces (pores) between the length and width constituent fibers that run perpendicular to each other. Measure the pore dimensions of the scaffold by using a stereo microscope with sufficient magnification and image capture capability. Select a magnification based upon the resolution of the pore in the scaffold pattern being examined (typical range is 0.5–2×). Take images under magnification. Randomly select eight pore images, determine the pore area and average the results. Measure pore size and analyze with a suitable image analysis software package.

Acceptance criteria: The pore area of each device is NLT 1×10^4 μm^2.

- **Ball Burst Testing**

0.01 M phosphate buffered saline: Dissolve 8 g of sodium chloride, 0.2 g of potassium chloride, 1.44 g of monobasic sodium phosphate, and 0.24 g of dibasic potassium phosphate in 800 mL of deionized water. Adjust with 1 N hydrochloric acid to a pH of 7.4, add deionized water to a final volume of 1000 mL.

Sample: Sections (40 × 40 mm) that are cut from the full sized, Scaffold Silk Fibroin. [Note—Test one section per device. Test between 13 and 50 devices.]

Analysis: Submerge the *Sample* fully in *0.01 M phosphate buffered saline* and incubate at 37° for 2 h. Use a suitable mechanical testing [illegible] and test frame.[13] Compress each device sample tested between the two circular fixation brackets (inner diameter of 18.6 mm)

of the mechanical testing instrument. Secure the *Sample* with a torque wrench to a value of 0.2 ± 0.1 N/m.[14] Ensure that the lattice structure of the *Sample* is evenly distributed across the inner fixture diameter and not skewed or sheared (the *Sample* should remain taut within the fixation brackets with even distribution of tension). Attach the ball burst fixture (10 mm diameter) to the mechanical testing instrument with a calibrated load cell. Insert the fixture ball through the center of the fixation brackets at a constant rate of 60 mm/min until the *Sample* fails. The resulting instrument output represents the maximum load sustained by the test sample.

Calculate the ultimate burst stress of the *Sample* in MPa:

$$\text{Result} = [B/(E_A)] \times F$$

B = maximum burst load, N

E_A = exposed area, m^2

F = conversion factor, 10^{-6}

The exposed area is the circular area of the test article covering the radius (r) of the inner fixture diameter and is calculated using the equation below:

$$\text{Exposed area} = \pi r^2$$

An additional sample parameter, burst stiffness that is reflective of elastic properties and indicative of the scaffold's capacity to withstand anatomical forces before failure is calculated by determining the slope of the middle of the linear region of the compressive load versus extension curve.

Acceptance criteria: The ultimate burst stress for each tested sample is NLT 0.5 MPa. The burst stiffness for each tested sample is NLT 30 N/mm.

- **Tensile Testing**

Sample: Cut two sample sections of 10 × 60 mm from each Scaffold Silk Fibroin tested, one in length direction and one in the width direction. Fully immerse samples in phosphate buffered saline and incubate at 37° for 2 h.

Analysis: Use a suitable mechanical testing instrument.[15] The tensile testing is done following the same principles as outlined in *Tensile Strength* ⟨881⟩, but modified as specified below. Clamp device samples in the mechanical test frame. Mount the upper clamp to the load cell, which is attached to the actuator. Mount the lower clamp to the support plate. Align the upper clamp to make the faces of both clamps parallel to each other. Adjust the height of the mechanical equipment crosshead so that the actuator is positioned to allow for a defined amount of upward movement and a specific sample gauge length resides between the upper and lower sample clamps.

Given a device sample of 60-mm long by 10-mm wide, load the sample by clamping the first 10 mm length of the *Sample* into the upper clamp and allowing the remainder of the *Sample* to fall unrestrained into the bottom clamp opening. Fix the last 10 mm of the *Sample* with the bottom clamp. Avoid pre-straining the *Sample*. Once the *Sample* is clamped, adjust the actuator height so that the *Sample* has a preload of 2 Newtons. Adjust the actuator position to achieve a 40-mm gauge length then reset to the zero-position. Strain the test sample at a rate of 2400 mm/min until it experiences ultimate tensile failure. The instrument output will provide maximum load value that was sustained by the *Sample*. [Note—The straining rate represents 100% of the gauge length/s and ensures that the *Sample* fails within 1 s (40 mm × 60 s = 2400 mm/min). Depending on the manufactured lot size, test between 13 and 50 devices. Use the maximum load value to calculate the ultimate tensile stress and percent elongation at break.]

Calculate the ultimate tensile stress in MPa using the equation:

$$\text{Result} = [M_L/(S_W \times S_T)] \times F$$

M_L = maximum load, N

S_W = sample width, m

S_T = sample thickness, m

F = conversion factor mm^2 to m^2, 10^{-6}

The sample width (S_W) is equal to 10 mm, and the sample thickness is determined as described in the *Analysis* section of the *Dimensional Analysis*.

The elongation at break in percentage is determined using the equation:

$$\text{Result} = [(L_B - O_L)/O_L] \times 100$$

L_B = length at break, mm

O_L = original length, mm

The numerator (length at break − original length) is measured and indicated by the instrument length = 40 mm (60 mm total length − 10 mm held by the upper clamp − 10 mm held by the lower clamp). Tensile stiffness is calculated by determining the slope of the trend line of the linear portion of the tensile load vs. elongation curve bound by an upper and lower tensile load.

Acceptance criteria: The maximum load for each tested sample along the scaffold length is NLT 31 N. The ultimate tensile stress (the force at which the device fails) for each tested sample is NLT 5 MPa. The percent elongation at break for each tested sample is NLT 35% in the direction of length. In the same direction, the tensile stiffness for each tested sample is NLT 0.8 N/mm.

- **Suture Retention Force**

Sample: Cut two sample sections of 20 × 40 mm from each Scaffold Silk Fibroin tested, one in the length direction and one in the width direction. Rehydrate all samples by completely submerging in phosphate buffered saline and incubating for 2 h at 37°.

Analysis: Use a suitable mechanical testing instrument.[16] Insert the upper part of the *Sample* into the upper clamp with the top 10 mm of the *Sample* gripped by the clamp with a pressure of 85 psi. Assess the overall suture retention strength of the samples in both orientations.

Using 2-0 polypropylene,[17] guide the first suture 10 mm from both sides of the *Sample* and approximately 3 mm from the lower edge. Loop the suture through a pore. Guide two more polypropylene sutures through the same way, but at a distance of 6 mm to the left and right of the center suture loop. Lower the upper actuator to maintain a distance of 10 mm between bottom edge of the *Sample* and lower clamp. Clamp the ends of the three sutures into the bottom clamp with a pressure of 85 psi. The created gauge length is 27 mm. Preload the *Sample* with 1 Newton. Strain the *Sample* at a constant rate of 1620 mm/min until the device sample breaks from the sutures or the sutures pull through the *Sample*. The instrument output represents the maximum load at failure. [Note—The straining rate represents 100% of the gauge length/s (27 mm × 60 s = 1620 mm/min) and ensures that the *Sample* fails within 1 s. Depending on the manufactured lot size, test between 13 and 50 devices.]

Calculate the average suture retention strength using the equation:

$$\text{Average Maximum Strength per Suture} = \frac{\text{Maximum Load}\,[N]}{3\,[\text{suture}]}$$

Acceptance criteria: The average suture retention force is NLT 13 N/suture in both vertical and horizontal orientations.

- **Tear Testing**

Sample: Cut two sample sections of 20 × 40 mm from each Scaffold Silk Fibroin tested, one in the length direction, and one in the width direction. Make a small cut one fourth the size of the test sample width in the center of the sample perpendicular to the length. Submerge all samples completely and incubate for 2 h in phosphate buffered saline at 37°.

Analysis: Use a material characterization mechanical testing instrument.[18] Affix clamps to the test frame of the mechanical testing equipment with tear testing capability. Mount the upper clamp to the actuator and the lower clamp to the load cell that is attached to the base support plate. Align the two clamps parallel to each other. Adjust the height of the mechanical equipment crosshead to position the actuator to allow for a defined amount of upward movement (minimum of 57 mm) and to ensure that a sample gauge length of 40 mm resides between the upper and lower clamps. Place the device sample in the upper clamp. The clamp should cover the top 10 mm of the *Sample*. Align the *Sample* perpendicular with the clamp before the clamp is closed. Allow the bottom portion of the *Sample* to fall unrestrained into the bottom clamp opening. Close the clamp and preload the *Sample* with 2 Newtons. Strain the *Sample* at a constant rate 2400 mm/min until it tears at the cut point. The maximum tear resistance load is calculated by the software of the mechanical instrument.[19] [Note—The strain rate represents 100% of the gauge length/s and was chosen to ensure that the *Sample* fails within 1 s (40 mm × 60 s = 2400 mm/min). Depending on the manufactured lot size, test between 13 and 50 samples.]

Acceptance criteria: The tear strength for each sample is NLT 109 N.

- **Sterility Tests ⟨71⟩:** Meets the requirements
- **Bacterial Endotoxins Test ⟨85⟩**

Sample: Scaffold Silk Fibroin

Analysis: Using depyrogenated forceps, place a 70-cm^2 sample of Scaffold Silk Fibroin in a depyrogenated 250-mL Erlenmeyer flask. Add 27 mL of limulus amebocyte lysate reagent water and 3 mL of tetrahydrofuran to the flask and cover with parafilm. Place on an orbital shaker at 250 rotations/min for 1 h at room temperature. Collect 0.5-mL samples from each flask and further dilute 20-fold with limulus amebocyte lysate reagent water. Analyze each sample in duplicate for bacterial endotoxin following *Turbidimetric Technique* in the chapter.

Acceptance criteria: Each sample should contain NMT 20.0 USP Endotoxin Units/device.

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Package in single-use, peel-open pouches that are gas permeable for sterilization purposes. Store under clean, dry conditions at room temperature, between 15° and 25°.

• **Labeling:** The package label indicates the dimensions of the enclosed Scaffold Silk Fibroin, the lot number, the expiry date, the required storage conditions, the trade name, the product manufacturer, and the manufacturer's contact information. In addition, the label indicates the product has been sterilized by EO and provides a date when the sterilization has taken place. It also lists some precautionary statements such as the product should not be reused, it should not be re-sterilized, or used if the package is damaged or open upon receipt. The instructions for use are included with each unit.

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[1] A suitable mineral oil can be obtained from Avantor Performance Materials, Inc. (Mallinckrodt Chemicals, Inc.), Center Valley, PA or equivalent.

[2] A suitable detergent can be obtained from EMD Biosciences, Inc., Darmstadt, Germany or equivalent.

[3] Suitable acid can be obtained from Pierce Biotechnology, Inc., Rockford, IL or equivalent.

[4] Suitable phenol crystals can be obtained from Sigma-Aldrich, St. Louis, MO or equivalent.

[5] Suitable amino acid standards can be obtained from Pierce Biotechnology, Inc., Rockford, IL or equivalent.

[6] Suitable raw silk yarn can be obtained from Bratac S.A, Londrina, Brazil or equivalent.

[7] A suitable sericin standard/reference can be obtained from Silk Biochemical Co., Ltd., Zhejiang, China or equivalent.

[8] Suitable amino acid standards can be obtained from Pierce Biotechnology, Inc., Rockford, IL or equivalent.

[9] A suitable software can be obtained from MathWorks, Natick, MA or equivalent.

[10] A suitable ruler can be obtained from Mitutoyo American Corporation, Aurora, IL or equivalent.

[11] A suitable thickness gauge can be obtained from Käfer Messuhrenfabrik GmbH & Co. KG, Villingen-Schwenningen, Germany or equivalent.

[12] A suitable balance can be obtained from Denver Instrument, Bohemia, NY or equivalent.

[13] Suitable mechanical testing instrument can be obtained from Instron Corporation, Norwood, MA or equivalent.

[14] A suitable torque wrench can be obtained from CDI Torque Products, City of Industry, CA or equivalent.

[15] A suitable mechanical testing instrument can be obtained from Instron Corporation, Norwood, MA or equivalent.

[16] Suitable mechanical testing equipment and data processing software can be obtained from Instron Corporation, Norwood, MA or equivalent.

[17] A suitable suture (2-0 FiberWire, cat # AR-7220) can be obtained from Arthrex, Inc., Naples, FL or equivalent.

[18] Suitable mechanical testing equipment can be obtained from Instron Corporation, Norwood, MA or equivalent.

[19] Suitable data processing software can be obtained from Instron Corporation, Norwood, MA or equivalent.

Auxiliary Information - Please check for your question in the FAQs before contacting USP.

Topic/Question	Contact	Expert Committee
SCAFFOLD SILK FIBROIN	Rebecca C. Potts Associate Scientific Liaison	BIO32020 Biologics Monographs 3 - Complex Biologics and Vaccines
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	BIO32020 Biologics Monographs 3 - Complex Biologics and Vaccines

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