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REPORT M 044

IN VITRO BIODEGRADATION OF GEL-FILLED MAMMARY IMPLANTS

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IN VITRO BIO0DEGRADATION OF GEL-FILLED MAMMARY IMPLANTS

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1.0 TITLE

IN VITRO BIODEGRADATION OF GEL-FILLED MAMMARY IMPLANTS

2.0 ABSTRACT

This report presents results of a study of in vitro biodegradation of Siltex® Round Moderate Profile Gel-Filled Mammary Implants. Whole devices were immersed in saline, the control solution, and porcine serum, the test solution, and incubated at 37 °C for sixty days. Periodically devices were sampled and weighed, dissected and gel and shell subjected to rheological and tensile testing respectively.

The study was intended to determine the effects of porcine serum immersion on gravimetric and mechanical properties of mammary implants. Weight measurements allowed for monitoring of changes associated with potential gel bleed and lipid infiltration. Mechanical testing of gel and shell facilitated assessment of the extent of crosslinking and potential degradation. Results indicate that no weight change was observed for either saline or porcine serum. In addition the tensile strength of shells and crossover modulus of gel showed no effects for either saline or porcine serum. Accordingly in vitro biodegradation of gel mammary implants was not observed.

3.0 INTRODUCTION

Mentor Corporation manufactures a variety of mammary prostheses including Smooth and Siltex Round Moderate and High Profile and Moderate Plus Profile Gel-Filled Mammary Implants. All devices are composed of a shell assembly and gel filler. The shell assembly is primarily a smooth low bleed envelope. The minor components include patches, fill reinforcement patch -------- -------------- --------- -----------and a Siltex® model --------- ----- -------------------------- -------------- ------- he raw materials o---------- -- -------s are highly crosslinked dimethylsiloxan----------- --------- -------------- polymers with silicone dioxide filler and the gel is a partially crosslinked dimethylsiloxane material.

In vitro biodegradation of polymers has been extensively studied and reported in the literature particularly for biocompatible implantable polymers.[1] Several mechanisms have been identified that may contribute to degradation and include hydrolytic, oxidative and enzymatic pathways, metal ion induced oxidation and environmental stress cracking and mineralization and plasticization.[2,3] Silicone elastomers have also been studied for infiltration of lipids and apparent effects on mechanical properties and implant aging.[4,5] Although explanted devices exhibited absorption of lipids no deterioration of mechanical strength has been reported. Mentor Corporation undertook a study to assess in vitro biodegradation of Siltex Saline-Filled Mammary Implants and obtained similar results.[6] The current study was designed to evaluate in vitro biodegradation of Gel-Filled Mammary Implant silicone elastomer shells and gel. Periodically devices were sampled and weighed, dissected and the shells subjected to tensile testing. Gel samples were also obtained and subjected to rheological characterization. Results will be used for partial fulfillment of Premarket Approval (PMA) application for Gel-Filled Mammary Implants.[7]

4.0 EXPERIMENTAL

A detailed description of the experimental procedure is compiled in Appendix A Protocol. A sample list including device traceability is compiled in Appendix B Sample Information. Analysis samples were selected from Siltex Round Moderate Profile Gel-Filled Mammary Implants (100 cc---------------g the minimum model volume. Devices were manufactured with -------------- raw materials and that had undergone all recommended manufa--------- processes for sterile finished product.

Immersion and Gravimetry

Whole devices were immersed in saline, the control solution, and porcine serum, the test solution, and incubated at 37 °C for approximately sixty days using mass-to-volume ratio m/v= 1/2.5. Each test solution was prepared with silver metal coil to provide an inert, nontoxic broad spectrum bactericide. Samples were obtained at 0, 1, 3, 7, 14, 21, 28, 35, 42, 49 and 56 days. Three device replicates were exposed for each solution and sample period and weighed prior to immersion. Upon completion of individual sample exposure period devices were removed, rinsed with water. weighed and dissected.

Electromechanical Testing

Electromechanical testing was performed to determine shell tensile properties. Samples were prepared as dog-bone specimens (2 per device shell) and subjected to electromechanical testing for determination of tensile properties. Instrumentation, (Instron 4200), grips, extensometer and experimental conditions are described in Test Method 000348.[8]

Rheological Testing

Rheology testing of gel was performed with oscillatory torsion dynamic frequency scan to measure crossover modulus.[9,10] Crossover modulus is directly proportional to extent of crosslinking. The rheometer (Rheometric Scientific, ARES) was equipped with parallel plate fixture and operated with constant strain (γ= 25 %) and temperature (T= 23 ± 2 °C). Smooth surface parallel plate fixture (25 mm diameter) was configured with automatic gap adjustment (1 mm thickness). A frequency scan (= 0.1-400 rad/s) was performed to measure complex (G^*), storage (G') and loss (G'') modulus. The crossover modulus (G'/G''= 1) was recorded for each test. Three devices representing each sample period and immersion medium were tested. Three replicate determinations were performed for each device.

5.0 RESULTS

Gravimetric test data are compiled in Appendix C Raw Data Section 1 (Gravimetric Test Raw Data). This includes weight measurements obtained prior to and following immersion in saline and porcine serum for each device. Statistical calculations for mean, standard deviation and coefficient of variation for replicate devices and evaluation of variance and mean for control and test samples (F-test and t-test) are listed in Appendix D Results and Calculations Section 1 (Gravimetric Test Results). In addition time dependents weight changes are presented graphically for saline and porcine serum.

Electromechanical test data are compiled in Appendix C Raw Data Section 2 (Electromechanical Test Raw Data). This includes ultimate tensile strength, elongation, stress at 100 %, 200 % and 300 % elongation, break energy and

Young's modulus (E). Load dependent displacement is plotted with modulus assignment. Statistical calculations for mean, standard deviation and coefficient of variation for replicate determinations and evaluation of variance and mean for control and test samples (F-test and t-test) are presented in Appendix D Results and Calculations Section 2 (Electromechanical Test Results). In addition time dependent ultimate tensile strength is plotted for saline and porcine serum.

Rheology test data is compiled in Appendix C Raw Data Section 3 (Rheology Test Raw Data). This includes a listing of experimental parameters for instrument control and data acquisition, raw data and plots of frequency dependent modulus. Rheological test results include storage (G′), loss (G″) and complex (G*) modulus and crossover modulus (G′/G″= 1). Statistical calculations of mean, standard deviation and coefficient of variation for replicate determinations and evaluation of variance and mean for control and test samples (F-test and t-test) are presented in Appendix D Results and Calculations Section 3 (Rheology Test Results). In addition time dependent crossover modulus is plotted for saline and porcine serum.

A summary of results is listed in Tables I-III and illustrated in Figures 1-6.

6.0 DISCUSSION

Gravimetric test results are listed in Table I and illustrated in Figures 1 and 2. The mean percent weight change for devices immersed in saline was -0.09-0.12 %. The mean percent weight change for devices immersed in porcine serum was -0.03-0.12 %. Weight changes observed for either immersion solution exhibited random fluctuations. Typical relative standard deviation of 75 % was characteristic of these measurements. Accordingly no weight loss was observed for either immersion solution that may be associated with gel bleed and no weight gain was observed for porcine serum that may be associated with lipid infiltration. Statistical comparison (F-test and t-test) of the initial devices with no immersion to devices sampled at various exposure times indicated the same population. In addition comparison of devices immersed in saline and porcine serum for the same sample period showed no statistical differences.

Electromechanical test results are listed in Tables IIA-D and illustrated in Figures 3 and 4. The mean ultimate tensile strength for shells from devices immersed in saline was 849-929 psi. The mean ultimate tensile strength for shells from devices immersed in porcine serum was 849-950 psi. Ultimate tensile strength changes observed for either immersion solution exhibited random fluctuations. Typical relative standard deviation of <11 % was characteristic of these measurements. The mean percent elongation for shells from devices immersed in saline was 450-532 %. The mean percent elongation for shells from devices immersed in porcine serum was 450-548 %. Percent elongation changes observed for either immersion solution exhibited random fluctuations. Typical relative standard deviation of <12 % was characteristic of these measurements. The mean break energy for shells from devices immersed in saline was 0.40-0.48 ftlb. The mean break energy for shells from devices immersed in porcine serum was 0.40-0.52 ftlb. Break energy changes observed for either immersion solution exhibited random fluctuations. Typical relative standard deviation of <20 % was characteristic of these measurements. The mean Young's modulus for shells from devices immersed in saline was 250-276 psi. The mean Young's modulus for shells from devices immersed in porcine serum was 240-277 psi. Young's modulus changes observed for either immersion solution exhibited random fluctuations. Typical relative standard deviation of <15 % was characteristic of these measurements. Statistical comparison (F-test and t-test) of the initial devices with no immersion to devices sampled at various exposure times indicated the same population. In addition comparison of devices immersed in saline and porcine serum for the same sample period showed no statistical differences. Accordingly immersion of devices in porcine serum did not affect the tensile properties of shells.

Rheology test results are listed in Table III and illustrated in Figures 5 and 6. The mean crossover modulus for gel from devices immersed in saline was 1438-1706 dyn/cm^2. The mean crossover over modulus for gel from devices immersed in porcine serum was 1464-1722 dyn/cm^2. Crossover modulus changes observed for either immersion solution exhibited random fluctuations. Typical relative standard deviation of 10 % was characteristic of these measurements. Statistical comparison (F-test and t-test) of the initial devices with no immersion to devices sampled at various exposure times indicated the same population. In addition comparison of devices immersed in saline and porcine serum for the same sample period showed no statistical differences. Accordingly immersion of devices in porcine serum did not affect the rheological properties of gel.

7.0 CONCLUSION

In vitro biodegradation has been investigated for Siltex Round Moderate Profile Gel-Filled Mammary Implants. This entailed immersion of devices in saline, the control solution, and porcine serum, the test solution, for 56 days at 37 °C. Gravimetric and mechanical tests were conducted to assess weight changes, tensile properties and rheological properties. Conclusions are summarized below.

- No device weight changes were observed following immersion in saline and porcine serum. No statistical differences were observed between saline and porcine serum immersion devices. Accordingly no gel bleed or lipid infiltration occurred during immersion.

- No shell tensile property changes were observed following immersion in saline and porcine serum. No statistical differences were observed between saline and porcine serum immersion device shells. Accordingly no mechanical property degradation of shells occurred during immersion.

- No gel rheological property changes were observed following immersion in saline and porcine serum. No statistical differences were observed between saline and porcine serum immersion device gels.

Accordingly no mechanical property degradation of gel occurred during immersion.

8.0 ACKNOWLEDGEMENTS

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Table I In Vitro Biodegradation Gravimetric Results of Gel-Filled Mammary Implants

Time (days)	Saline Immersion Solution	Porcine Serum Immersion Solution
	Mean Percent Change from Initial Weight	Mean Percent Change from Initial Weight
1	0.03	-0.03
3	0.06	0.06
7	-0.09	0.06
14	0.03	0.06
21	0.06	0.12
28	0.00	0.06
35	0.12	0.09
42	0.06	0.06
49	0.03	0.15
56	0.06	0.06

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Table IIA In Vitro Biodegradation Electromechanical Test Results of Gel-Filled Mammary Implants: Ultimate Tensile Strength

TIME (Days)	TENSILE STRENGTH MEAN (psi)	
	Saline Immersion Solution	Porcine Serum Immersion Solution
0	862.97	862.97
1	848.78	949.97
3	896.43	922.45
7	839.00	854.75
14	928.65	861.97
21	917.13	939.90
28	892.48	848.58
35	920.83	909.25
42	883.15	901.33
49	836.15	869.05
56	867.50	920.27

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Table IIB In Vitro Biodegradation Electromechanical Test Results of Gel-Filled Mammary Implants: Elongation

TIME (Days)	ULTIMATE ELONGATION MEAN (%)	
	Saline Immersion Solution	Porcine Serum Immersion Solution
0	450.18	450.18
1	462.23	490.47
3	480.87	482.10
7	471.00	456.53
14	484.68	470.42
21	532.12	548.15
28	500.70	477.33
35	505.05	485.20
42	494.65	507.48
49	502.08	513.20
56	502.20	524.92

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Table IIC In Vitro Biodegradation Electromechanical Test Results of Gel-Filled Mammary Implants: Break Energy

TIME (Days)	BREAK ENERGY MEAN (ft/lbs)	
	Saline Immersion Solution	Porcine Serum Immersion Solution
0	0.4001	0.4001
1	0.4048	0.4802
3	0.4314	0.4558
7	0.3998	0.4026
14	0.4643	0.4255
21	0.4760	0.5170
28	0.4592	0.4033
35	0.4621	0.4476
42	0.4344	0.4487
49	0.4373	0.4558
56	0.4337	0.4984

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Table IID In Vitro Biodegradation Electromechanical Test Results of Gel-Filled Mammary Implants: Young's Modulus

TIME (Days)	YOUNG'S MODULUS MEAN (psi)	
	Saline Immersion Solution	Porcine Serum Immersion Solution
0	266.75	266.75
1	255.54	276.78
3	267.43	275.32
7	248.65	266.22
14	276.20	259.65
21	251.21	243.36
28	255.52	249.90
35	257.01	262.08
42	249.92	240.14
49	237.48	235.55
56	240.30	250.22

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Table III In Vitro Biodegradation Rheology Results of Gel-Filled Mammary Implants

Time (days)	Saline Immersion Solution Mean Crossover Modulus G'/G" (dyn/cm^2)	Porcine Serum Immersion Solution Mean Crossover Modulus G'/G" (dyn/cm^2)
0	1391	1391
1	1438	1486
3	1463	1480
7	1508	1464
14	1456	1547
21	1429	1531
28	1557	1619
35	1706	1711
42	1663	1722
49	1717	1693
56	1634	1686

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Figure 1 In Vitro Biodegradation Gravimetric Test Results, Saline

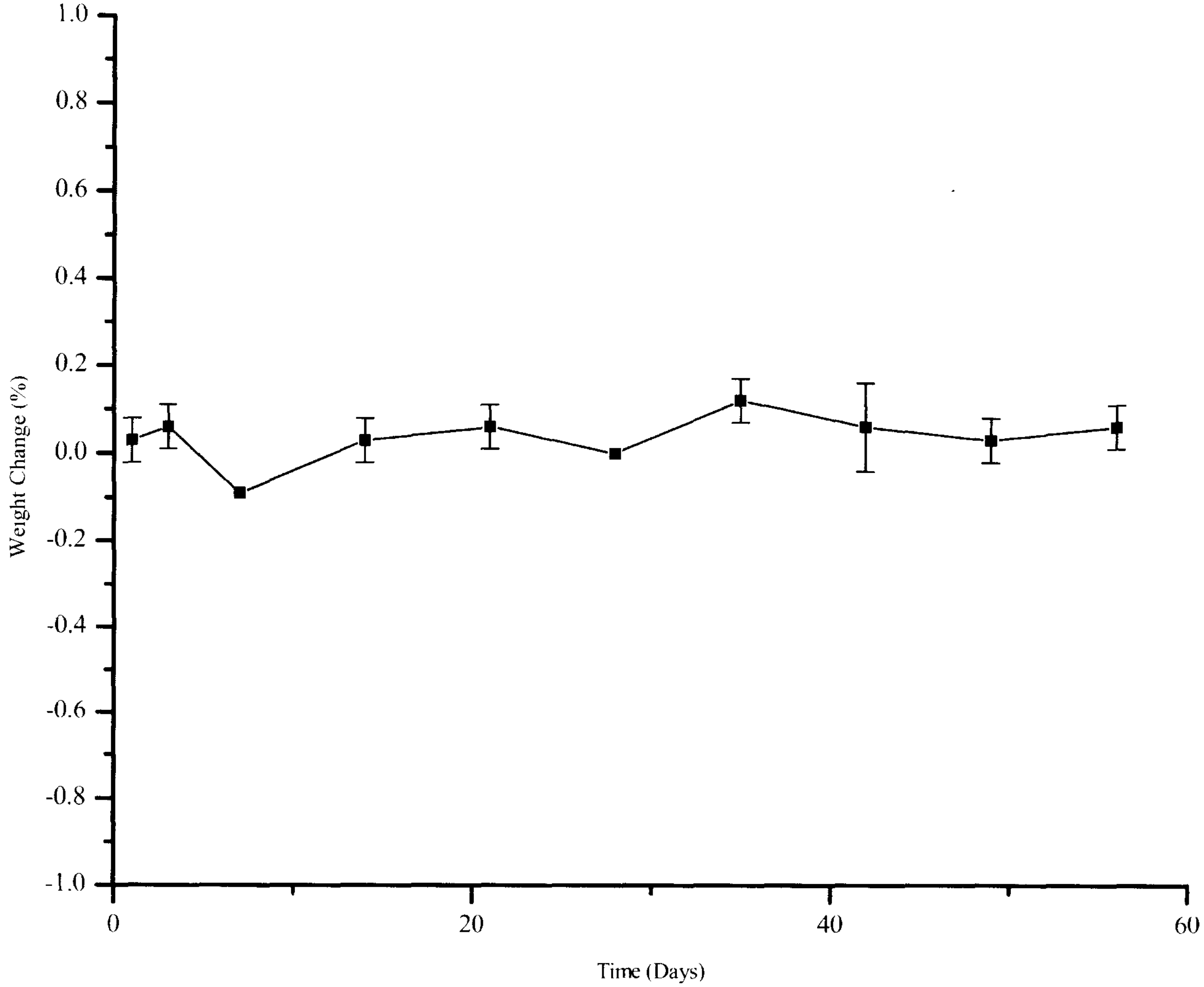

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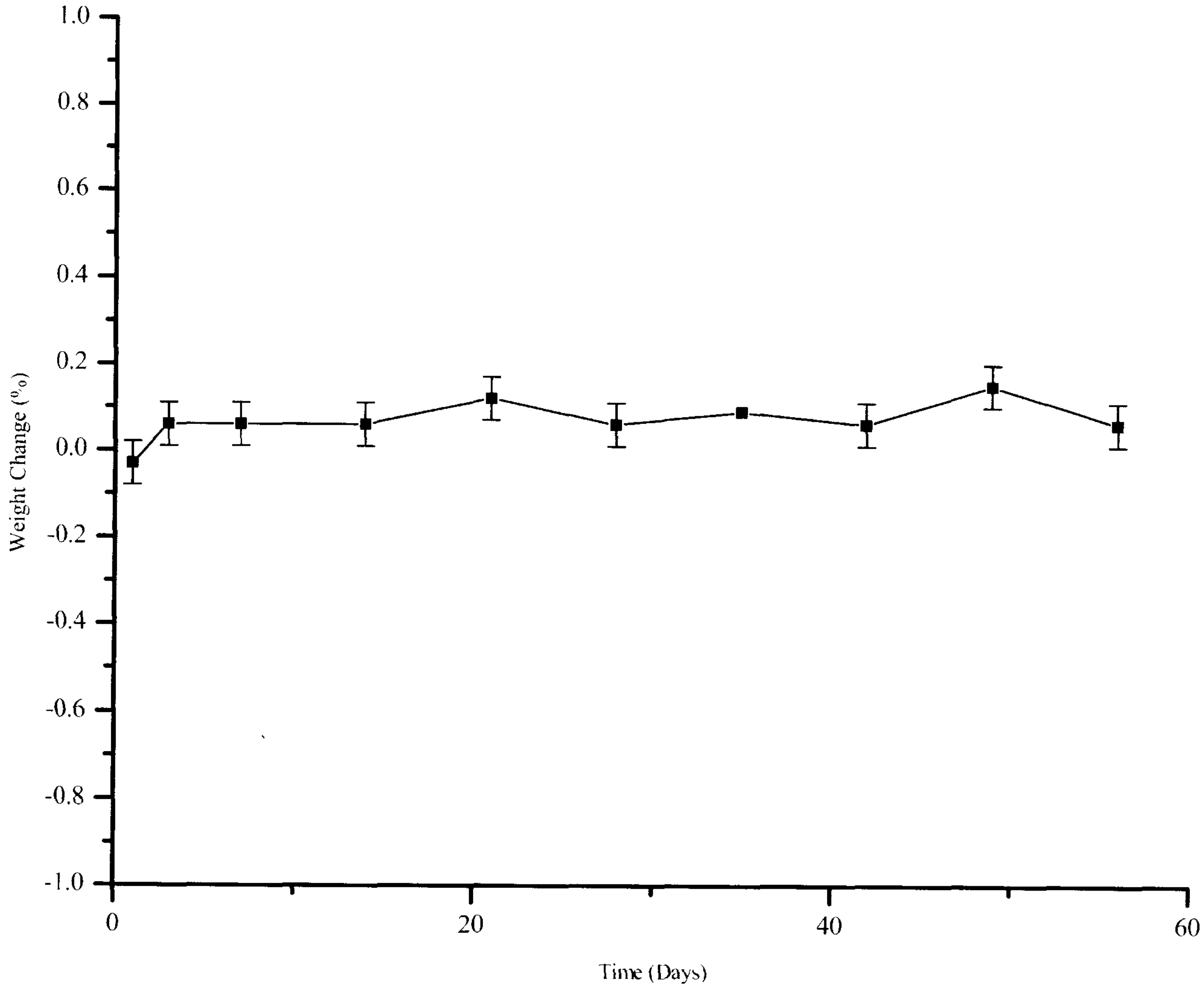
Figure 2 In Vitro Biodegradation Gravimetric Test Results: Porcine Serum



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Figurre 3 In Vitro Biodegradation Electromechanical Test Results: Saline

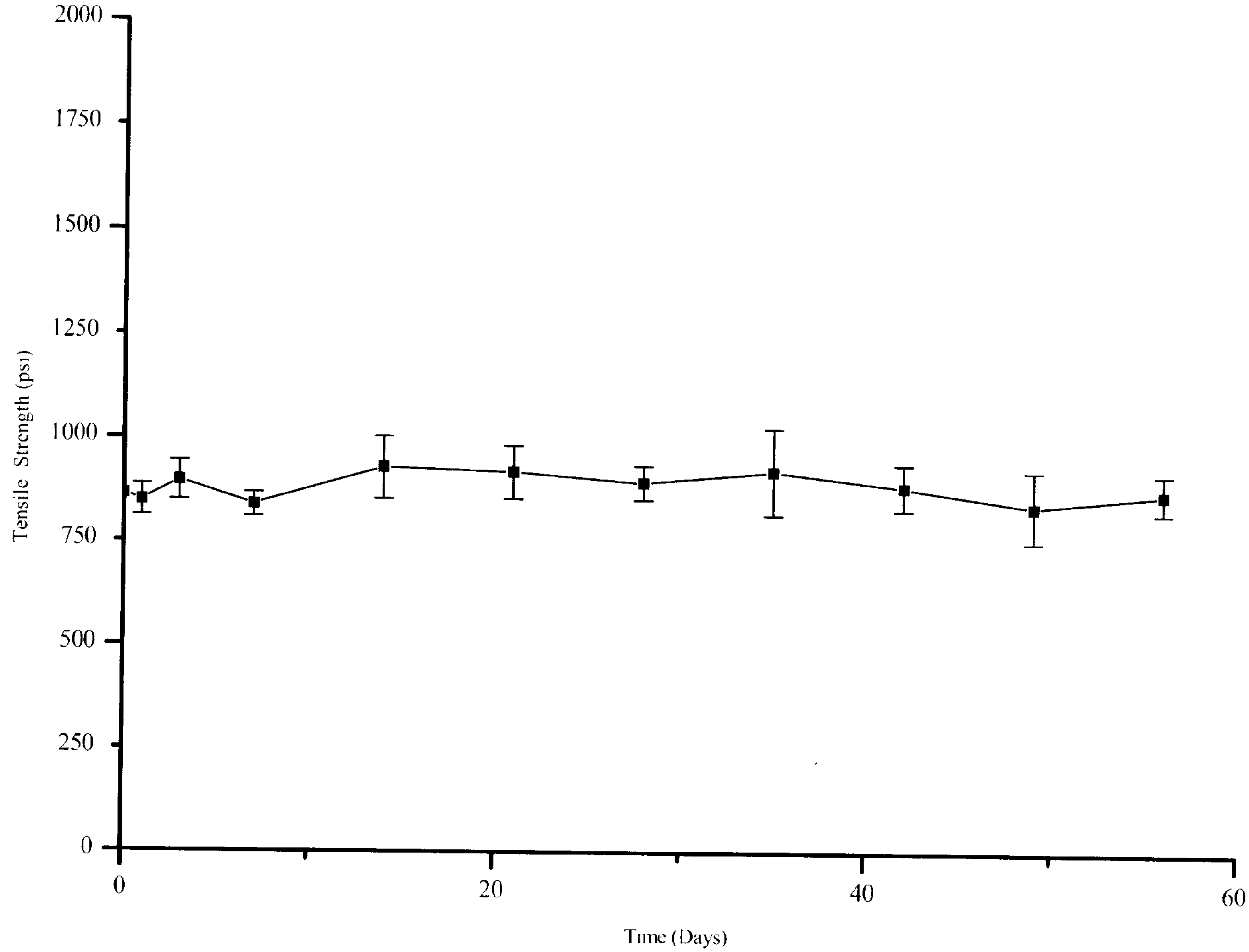

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Figure 4 In Vitro Biodegradation Electromechanical Test Results: Porcine Serum

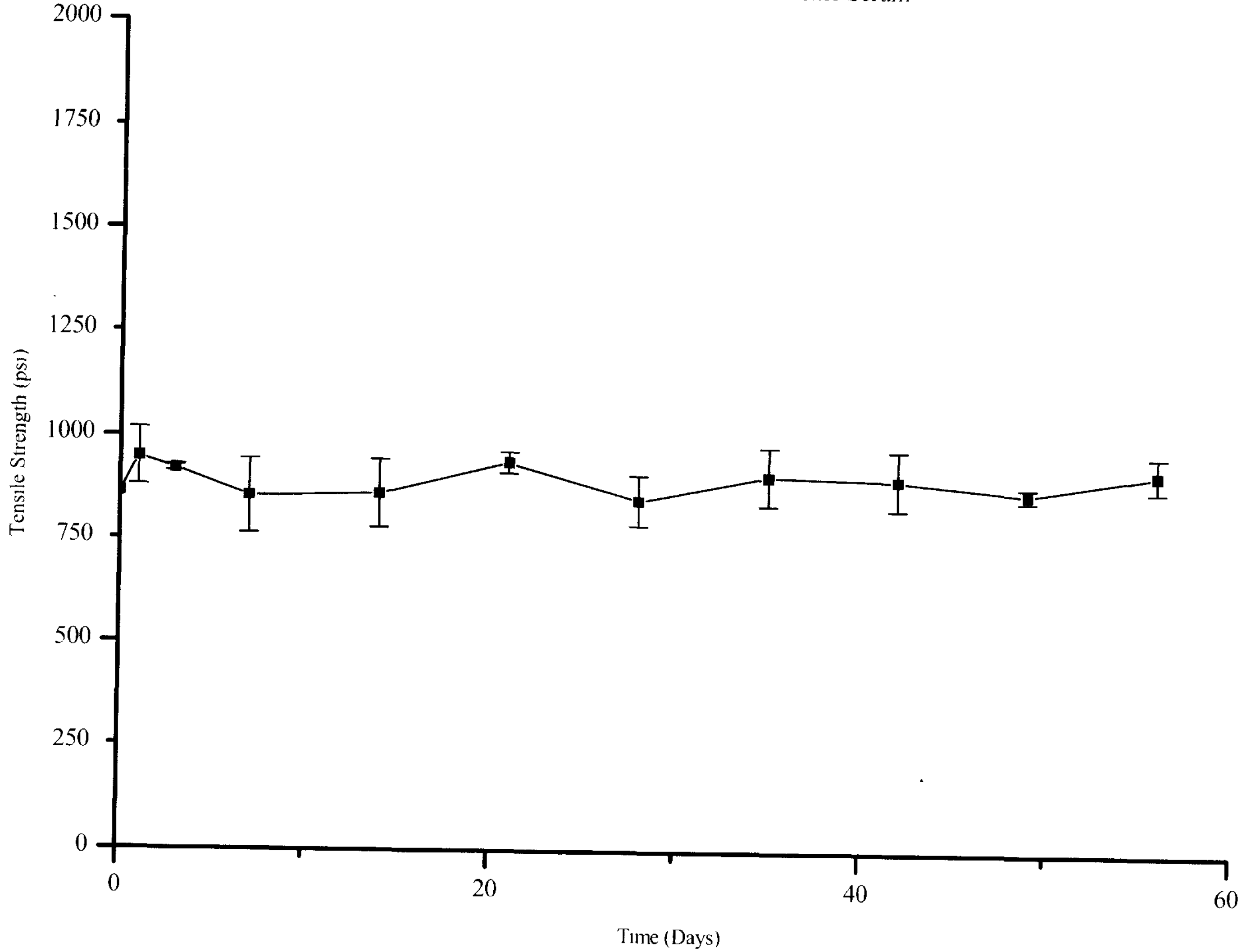

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Figure 5 In Vitro Biodegradation Rheology Test Results: Saline

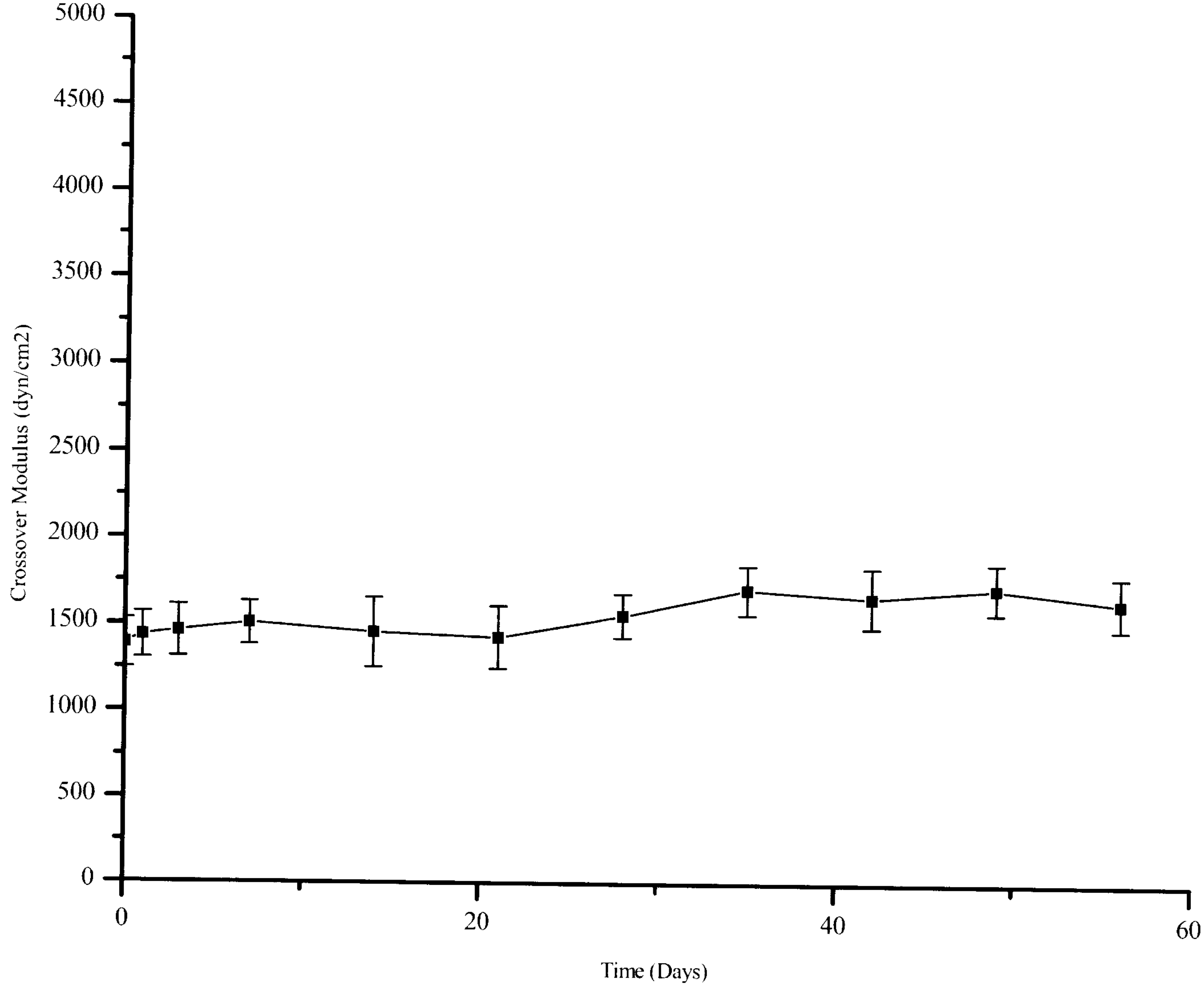

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Figure 6 In Vitro Biodegradation Rheology Test Results: Porcine Serum