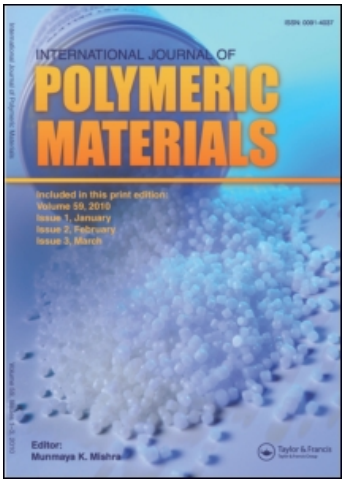

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Springy Polypropylene: A Novel Elastomeric Biomaterial†

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Polypropylene has been fabricated into a different molecular morphology which shows the usual stiffness and high strength indigenous to this polymer, but which also exhibits surprising elastic behavior. Fibers and films in this form are extensible to several hundred percent without rupture and yet show nearly complete recovery to their original length when the force is removed. No other biomaterial which is in present use has such a unique set of mechanical properties. This study has identified the nature and extent of the unusual springy behaviour; the stress–strain, recovery, and cyclic loading properties are now well documented. A stress-softening occurs as the result of the amount of the initial deformation: this means the fibers may be conditioned in order to produce a surprisingly wide spectrum of stiffnesses. Once exercised, the deformation is quite reproducible. Initial fatigue behavior is commendable, on a par with nylon tire yarn fibers. No change in properties has resulted from either long-term conditioning in physiological saline solution or sterilization by autoclaving. Since polypropylene is already an approved biomaterial, it is not surprising that the new and different arrangement of molecules has not elicited an undesirable response in either tissue culture studies or rabbit intramuscular implantation evaluations. Because of the variation possible in the unusual properties of springy polypropylene in the fiber form, a unique opportunity is at hand to design new prostheses to match more perfectly the replaced components.

MECHANICAL PROPERTIES OF SPRINGY POLYPROPYLENE

A typical stress–strain diagram of springy polypropylene (SPP) is represented in Figure 1. The extension at fracture (segment AE) varies from 300 to 700 percent of the gauge length as the latter is decreased from 6.0 to 0.125 inches. The normal morphological form of polypropylene fibers ruptures at 31.0 percent.

The stress–strain behavior of SPP when cyclically loaded at lower than fracture extensions is also remarkable. Figure 2 depicts the load cycling of SPP

†Presented at the Symposium on Elastomers in Medicine at the 105th Meeting of the Rubber Division, American Chemical Society, Toronto, Canada, May 9, 1974.

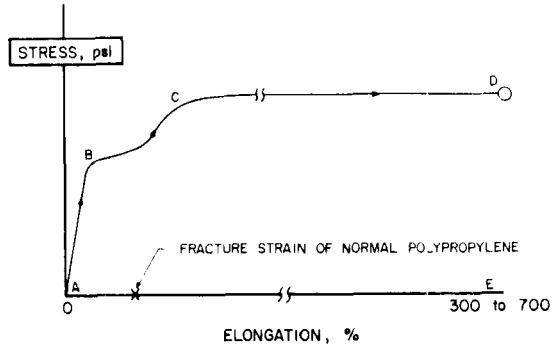

FIGURE 1 Typical stress-strain diagram for springy polypropylene.

at 50 percent extension. Four novel aspects of the mechanical behavior of SPP are clearly indicated.

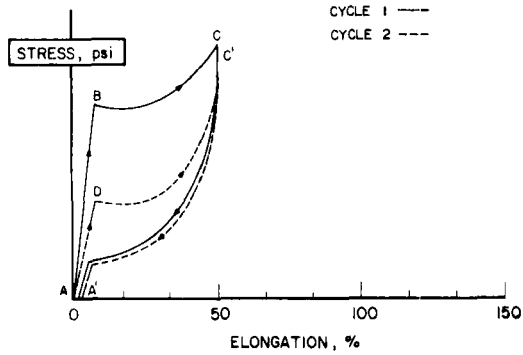

FIGURE 2 Cyclic loading to 50 percent extension.

Firstly, the second cycle yield stress (point D) is substantially less than that of the initial cycle (point B): a work softening effect produces more easy extensibility in the second cycle for the same applied load.

Secondly, the second cycle modulus of elasticity (slope of segment AD) is lower than that of the first cycle (slope of segment AB). The magnitude of this decrease is roughly the same as that of the yield point.

Thirdly, the recovery of deformation in excess of the yield point B (projection of curve BC upon the abscissa) is much greater than would be expected, i.e., the

projection of segment AB on the abscissa would constitute the amount of extension considered (classically) to be elastically recoverable. This elastic recovery is an energetic elasticity as contrasted to the normal entropic elasticity.

Fourthly, the ultimate load bearing capability after cyclic loading (point C') is only slightly reduced. Even though SPP work softens and experiences a comparable decrease in modulus, the ultimate strength is not significantly decreased.

The aforementioned decreases of yield point and modulus both increase in magnitude smoothly as the amount of first cycle extension is increased. Therefore, SPP may be conditioned by exercising at various extensions to produce a range of stiffnesses and extensibilities. After a few cycles the level of modulus and yield stress becomes quite constant and reproducible.

Not so clearly indicated by Figure 2 is another intriguing aspect of SPP: the set (segment AA') decreases with time as though it were anelastic. Figure 3 reveals the nature of this healing characteristic for four levels of initial strain. That the second cycle yield point and modulus values experience a concomitant restoration to their original values, i.e., point B and slope of AB in Figure 2, respectively, is truly amazing.

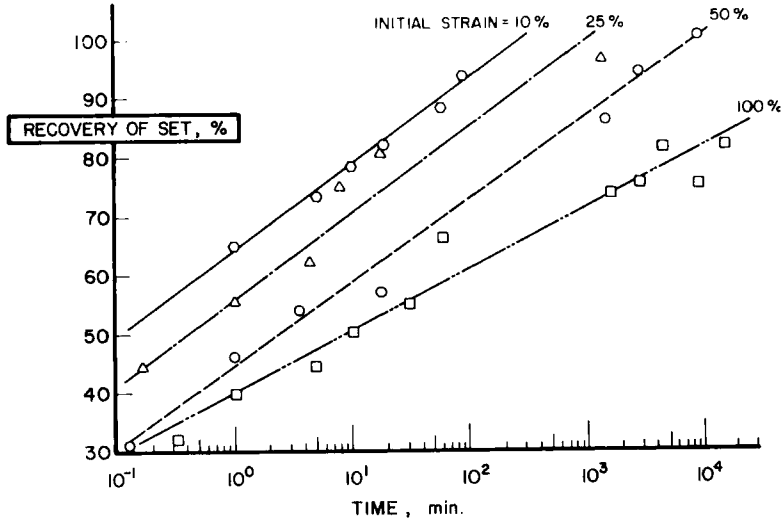

FIGURE 3 Healing behavior of SPP.

The degree to which the ultimate load bearing capability is reduced by cyclic loading is a factor of extreme importance in indicating whether a material is a bona fide candidate for prosthetic applications. SPP has an endurance limit at least as attractive as nylon and polyester tire yarns. Figure 4

indicates that SPP can withstand indefinitely cyclic loading at stresses of 20 or less percent of its tensile strength.

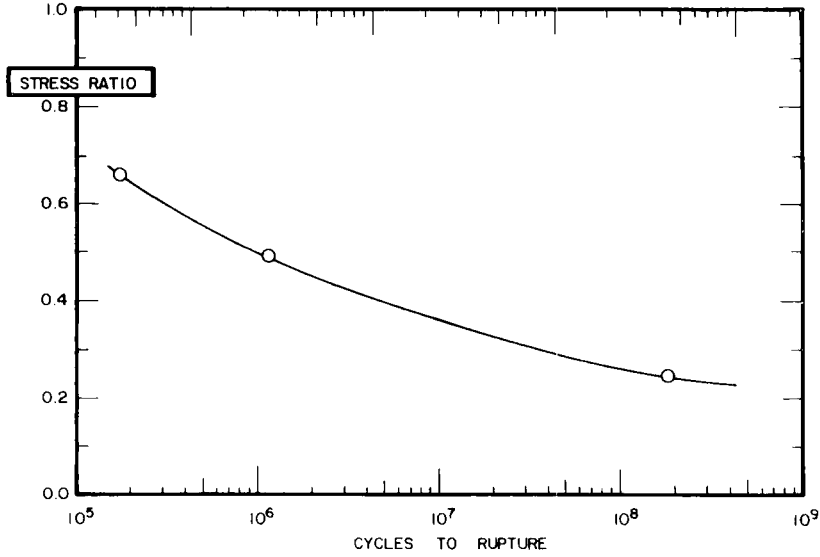

FIGURE 4 S-N diagram for SPP.

EFFECTS OF CONDITIONING TREATMENTS

The extensibility of SPP after various conditioning treatments is shown in Figure 5. No adverse effects result from conditioning in 0.15 N saline or autoclaving; this normality saline is roughly that of blood and autoclaving is a convenient and standard means of sterilization.

Since the yield stress healing behavior is similar to the modulus and recovery, Table I has been prepared to indicate that there is a negligible effect of conditioning in 0.15 N saline on these mechanical properties.

BIOCOMPATIBILITY TESTING OF SPP

Background

The advent and increasing popularity of polymeric materials has provided the engineer with an additional dimension and a wider latitude in the myriad of end-products and applications. In the field of prosthetic medicine alone, the impact of polymers has led to a voluminous number of reports which have been

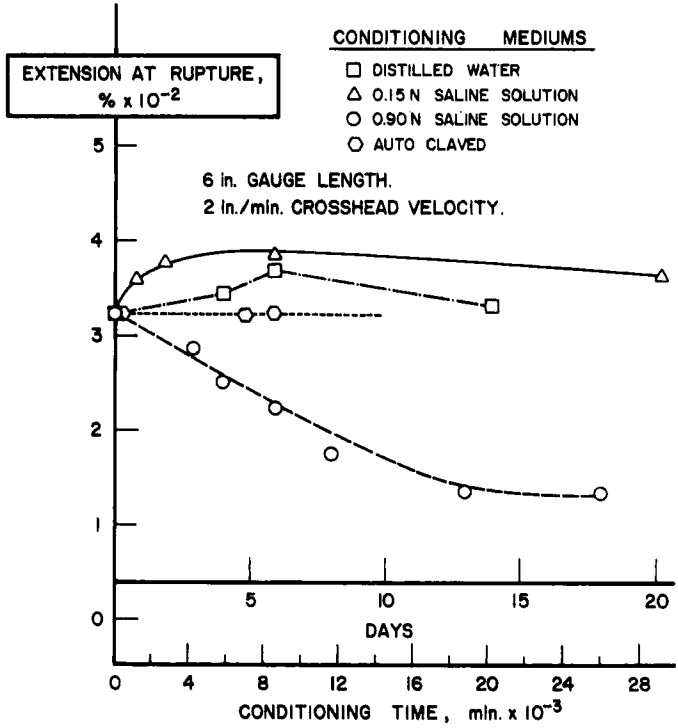

FIGURE 5 Extension at rupture versus conditioning time.

TABLE I

Percent decrease of yield point versus conditioning time

Cyclic extension (%)	Conditioning time (days)						
	Control	1	2	4	34	201	309
25	29.6	27.7	31.2	30.4	27.8	30.9	28.5
50	42.9	43.6	43.2	43.1	40.5	42.2	38.9
100	66.2	69.4	62.6	66.4	63.6	66.7	74.9

concerned with both prosthesis design and biocompatibility evaluation. Fortunately, a comprehensive review of the state of the art of using polymers as surgical implants has been published recently by Leininger.[1] This article acknowledges 214 papers and includes many of their salient data and conclusions.

Since this project has as its goal the characterization and evaluation of springy polypropylene as a prosthetic device, it is appropriate that we use the most effective biocompatibility testing of the implant candidate. It has been suggested that this testing be comprised of *in vivo* and *in vitro* methods.[2]

Although polypropylene has demonstrated an excellent degree of compatibility in implantation (both implanted fibers, films and sutures) and tissue culture studies,[2-5] it should be remembered that these studies have used the usual form of polypropylene. Although the sole difference between the ordinary and springy forms is one of morphology, it is felt that biocompatibility testing should be undertaken to remove any doubt that the material in this novel state can be a prime candidate for prosthesis fabrication.

High density polyethylene is the U.S.P. standard negative control because of the minimal tissue reaction which it elicits. This is due probably to factors indigenous to the material, e.g., high molecular weight with little or no branching, narrow molecular weight distribution, and pronounced hydrophobicity.[6] Since springy polypropylene is a material similar to the negative standard in both chemical composition and the aforementioned factors, it is logical that this polymer should behave favorably. Probably the major concern at this point then is whether the material contains any extractables of a toxic nature. Indeed, it has been stated that any resulting incompatibility is probably the result of the body fluid leaching soluble additives which were introduced in the production and processing of the polymer.[1]

Probably the simplest means of determining the toxicity of the implant is a tissue culture study. As early as 1945, Blum[7] stated, "The most sensitive index of tissue response to foreign bodies is their effect on explants of living embryonic tissue in tissue culture." In general the gross responses of the animal tissue to the implants were predictable from the corresponding results of the tissue culture study. Additional tissue culture work has been done by Rosenbluth[8] which has demonstrated agreement between the *in vitro* and *in vivo* methods and indicated that the former techniques are more sensitive in evaluating toxic reaction. Further corroboration of these findings has been provided by Powell.[9] Although a strong case has been made that the *in vitro* techniques are more sensitive than the implantation methods in determining toxicity and incompatibility, it is still thought advisable to evaluate the performance of the implant candidate in the body environment particularly since certain polymer additives are known to be extractable by blood but are unaffected by saline solutions.[10]

In vitro biocompatibility evaluations

Due primarily to the time consuming and expensive nature of *in vivo* testing of implant materials, Rosenbluth, *et al.*,[8] have developed a tissue culture method to facilitate the screening of plastic implant candidates. Although this technique was originally intended for speeding the examination of many test specimens, it was shown to be a more sensitive, effective procedure than the popular rabbit intramuscular implantation method offered by Brewer and Bryant.[11] It

is thought that a modified Rosenbluth procedure is adequate for the *in vitro* evaluation of springy polypropylene.

The evaluation of cellular toxicity by means of the above tissue culture studies has been completed. In addition to testing SPP fiber and film samples, Dacron® 62 and 68 fibers, normal polypropylene fibers, and Silastic® sheeting were also tested.

Tissue cultures of L-929 cells were grown as follows:

1. *Media*
   a) 1 *x* Eagles Minimal Medium Salts mixture
   b) 10 ml amino acid mixture
   c) 25 ml fetal calf serum
   d) 5 ml vitamin mixture
   e) 5 ml penicillin and streptomycin bacteria
   f) 5 ml glutamic solution.

2. Growth procedure The liquid medium described above was removed from a stock culture monolayer of L-929 cells. The cells were washed with phosphate-buffered saline solution. After washing, one ml of trypsin solution and five ml of the above nutrient mixture were added to the monolayer. After approximately five minutes incubation, the cells were released from the glass and from each other by trypsin hydrolysis to form a cell suspension. Five ml of suspension were added to 75 ml of medium, thoroughly mixed, and then dispensed into 25 mm plastic tissue culture petri dishes, two ml of suspension per dish. The dishes were incubated in a humidified CO_2 incubator at 37°C until a confluent cell monolayer had formed.

3. Toxicity test procedure The liquid medium was removed from the confluent monolayer and a mixture of agarose and the above-described media were layered over the monolayer. Small pieces of plastic (approximately 1 × 2 mm) were placed onto the agar overlay. Each plate received a known toxic plastic, a U.S.P. negatively toxic control plastic and the test sample. (Note: some of the samples were furnished as 1 cm discs, others as fibers. These were used as presented, i.e., the discs were placed intact on the surface of the agarose overlay, the fibers were cut and placed on the overlay as a small bundle).

4. Observations The plates were examined microscopically for cytopathology of the tissue culture cells surrounding the control materials and test samples. Where cytopathology was observable, there was usually a well-marked zone of cells which had been affected by the plastic or some of its components. The diameter of this zone was readily measured by centering the plastic in the microscopic field, then taking a reading on the mechanical stage micrometer. The

specimen was then moved horizontally until the edge of affected cell zone divided the microscopic field in half. The stage micrometer was read again. Thus the radius of the circular zone was established and the diameter calculated and reported. In the case of the discs, both the radius of the disc and the affected zone were taken into consideration.

5. *Results* The positively toxic control plastic was a polyvinyl small diameter tubing. A toxic zone was evident on every plate where tissue culture cells were exposed to this material. The zone sizes varied in size, but for what reason will require further study. It is proposed that sample size may play a role. The cells are very sensitive and a sample only slightly larger or smaller might result in larger or smaller zones. Also, even though an effort was made to have equal incubation times, these did vary by a few hours from time to time due to circumstances beyond control and this could have contributed to variation. Generally the positive control zones varied between 4 and 8 mm. Where a plastic test sample was not toxic, the zone size of the positive control is not critical. The tissue culture toxicity test results are listed in Table II.

6. *Conclusions* Of the seven types of submitted materials, none showed any toxic effect on the L-929 tissue culture cells. These results provide strong evidence that SPP fiber and film are tissue compatible.

In vivo tissue compatibility evaluations

Although a strong case has been made that the *in vitro* techniques are more sensitive than the implantation methods in determining toxicity and incompatibility, it was still thought advisable to evaluate the performance of the implant candidate in the body environment particularly since certain polymer additives are known to be extractable by blood but are unaffected by saline solutions.[10]

Two types of compatibility testing, subcutaneous and intramuscular implantation, have both enjoyed widespread applications; hoewver, Hopkins and Turner[12] report that "rabbit muscle implantation is a much more sensitive and valuable testing method for determining the toxicity of new materials than rat subcutaneous implants. The milder reaction evoked in the rat could lead to a false negative interpretation of toxicity." In addition, it has been observed that cancers have developed at the implant sites in rodents much more frequently than in other host species.[13-16] In fact the suggestion is that this phenomenon may be an artifact attributable to the host organism since the incidence of tumors has been shown to decrease as the implant is made smaller[17] or introduced in powder form[18] or the surface smoother.[19] Indeed, as late as 1967, no data were available which could implicate that prostheses of polymeric materials produce cancer in humans.[20]

TABLE II

Tissue culture toxicity test results

No.	Material	Test number 1	2	3	4	5	6
1	Celanese SPP fiber	+0	0	0	0	0	0
2	Dacron® 62 fiber	0	0	0	0	0	0
3	Dacron® 68 fiber	0	0	0	0	0	0
4	Normal polypropylene fiber	0	0	0	0	0	0
5	Hercules SPP fiber	0	0	0	0	0	0
6	SPP film	0	0	0	0	0	0
7	Silastic®	0	0	0	0	0	0

+0 = No toxic reaction.

Control results:

A. Negative Toxic U.S.P. Controls on each test plate showed no toxicity.

B. Positive Toxic Controls showed positive toxicity zones on each plate. Average zone size for all plates—9.85 mm.

In no case did the negative U.S.P. control materials show zones of CPE (cytopathological effect).

Although a number of different animals have served as implant hosts, rabbits offer some advantages *vis-à-vis* other species, e.g., easily handled, economically acquired and sustained, and multiple implants accommodated.[21] In fact, the paravertebral muscles provide six essentially homogeneous implant sites with isolation adequate to insure that the evaluation of implant compatibility will not be confounded by a site-to-site interaction. The fact that these sites are practically inaccessible to post-operative mechanical trauma inflicted by the host constitutes an additional bonus to the experimenter. For all of these reasons, the rabbit is thought to be an adequate subject for the *in vivo* study of the biocompatibility of springy polypropylene (SPP).

The two different forms of SPP which were implanted are specimens of film and multifilament yarn. For purposes of comparison, samples of Dow Corning Silastic®, and Dacron® polyester were implanted along with the SPP samples since the latter two materials have already achieved widespread recognition as surgical implants.

Although the U.S.P. recommended procedure[22] for implanting film specimens calls for 1 mm by 10 mm strips of material injected through a 19 mm, 15-gauge intravenous needle, Kaminski, *et al.*, [23,24] have demonstrated that a disc-shaped implant is preferable to the rod-type in that the tissue response is more uniform and hence more easily evaluated. The same investigators have found a disc 1.0 to 1.5 mm in thickness and 10 mm in diameter to be of suitable dimensions for rabbit implantation. In the case of the implanting of a fiber specimen, the A.S.T.M. procedure[25] recommends that the weight of sample

specimen be 50 mg; however, since the aforementioned disc weighs ca. 2 mg it is thought that a similar quantity of fiber specimen would be appropriate.

Coleman, King and Andrade of this Department have reported a protocol for implanting, harvesting, and evaluating polymeric materials and the nature of the foreign body reaction of the host which these specimens elicit.[21] This protocol is believed generally to be applicable to the studying of the biocompatibility of implant candidates and is therefore used with some modifications in this investigation.

Preliminary data were acquired for 7- and 15-day survival groups containing three rabbits each in order that expertise could be developed in the procedural details of the preparing, implanting, and sacrificing of the implant host. The resulting implant sections were subjected to a histopathological evaluation which indicated that the SPP discs elicited a mild response after the 7-day interval and a lesser reaction after 15 days. In both cases the degree of severity of these reactions was of the same order as that for the polyethylene negative standard. This fact is particularly significant in that SPP was tested in the form as received from the manufacturer, the only modification being an autoclaving procedure which is known not to affect adversely the polymer mechanical properties.

The 1-, 2-, 6-, 8-, and 26-week survival group raw data have been collected and evaluated. Subjective observations indicate that SPP in disc form is not significantly more toxic than the Silastic® and the fiber is no more toxic than a similar Dacron® polyester fiber implant. Since the subjective evaluations of the skin, subcutaneous, and muscle responses to the implant candidates are by nature somewhat arbitrary, high-speed Ektachrome® photographs were made of each host so that comparative assessments within and among survival group implant specimens could be accommodated. These results further corroborated the conclusion that SPP in fiber and film forms is highly compatible during both short- and long-term *in vivo* implantation.

CONCLUSIONS

A new class of polymeric properties has been disclosed for high strength films and fibers which also have very high extensibility and, surprisingly, nearly complete elastic recovery from large deformations. Because it is strong, tough dynamic, and resilient, the springy form of polypropylene (SPP) physically matches many of the components of the cardiovascular system more closely than polymers now in use. The aims of this research have been to learn the detailed properties of SPP, to find the appropriate match of properties in the cardiovascular or pulmonary systems, and to demonstrate the feasibility of new prostheses which exploit these novel properties.

Both dynamic and static loading measurements have been made of the mechanical properties of springy polypropylene, e.g., extension, recovery, and hysteresis for dry and wet testing at ambient temperatures. The wet testing has involved conditioning the polymer in aqueous and saline media for various intervals after which time mechanical evaluations were made on the immersed specimen. No adverse effects from sterilization via an autoclave exist. Fatigue behavior of SPP is excellent, i.e., on a par with nylon tire yarn.

Data from intramuscular implantation studies indicate that SPP film is not significantly more cytotoxic than Silastic® and the SPP fiber is no more cytotoxic than Dacron® 68 fiber or normal polypropylene fiber. Results of tissue culture studies on L-929 cells have provided strong evidence that SPP film and fiber are tissue compatible.

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