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A STUDY OF FORMULATIONS FOR THE CONTROLLED RELEASE OF AQUATIC HERBICIDES

by

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<p>Three aquatic herbicides--diquat, fluridone, and endothall--were formulated into controlled-release systems. These systems were in the form of fibers or pellets with polycaprolactone, cellulose acetate, polyethylene glycol, and hydroxypropyl cellulose being used as the biodegradable polymeric excipients.</p> <p>The first herbicide investigated was diquat. It was incorporated into two fibrous systems. One was monolithic with diquat distributed throughout the fiber. Diquat appeared to be released from these fibers by a dissolution mechanism. The other system was a reservoir fiber with a core of diquat and excipient surrounded by a rate-controlling membrane. These fibers were prepared by solution coating monolithic fibers or by melt spinning coaxial fibers.</p> <p style="text-align: right;">(Continued)</p>			
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Biodegradable polymers	Endothall	Pellets
Cellulose acetate	Fibers	Polycaprolactone
Controlled release	Fluridone	Polyethylene glycol

19. ABSTRACT (Continued).

Coaxial fibers with poly(ethylene glycol) as the core matrix and highly oriented polycaprolactone as the sheath material were expected to provide the desired zero-order release kinetics and the required release period of 270 to 360 days.

Fluridone, the second herbicide to be evaluated, was incorporated into both fibers and pellets. These released fluridone by a solution-diffusion mechanism. The monolithic fibrous system contained only fluridone and polycaprolactone, and the release characteristics were controlled by altering the fluridone concentration and fiber diameter. Large-scale production processes were developed, and large quantities of fibers were provided for field trials. Release durations of 20 and 40 days were targeted and achieved. Specifications for the fibers were a 25 percent (by weight) loading of fluridone and a diameter of 0.08 cm for 20 days of release or a diameter of 0.11 cm for 40 days of release. The fibers were effective in the field in slow-moving but not fast-moving water. Studies were also conducted with fluridone-loaded reservoir fibers. These studies indicated that controlled-release systems that provide a constant rate of fluridone release instead of exponential release were also feasible.

The fibers were difficult to apply in the field, and this difficulty led to the development of a pellet system containing fluridone, polycaprolactone, and hydroxypropyl cellulose. Release was controlled by pellet composition and geometry. Large-scale production processes were developed, and several hundred pounds of pellets were provided for field trials. Release studies conducted in the laboratory indicated that the targeted 20-day release period was achieved, and the targeted 40-day release period was very close to being attained. Additional 25-lb (11-kg) lots of pellets with release durations of 12 and 20 days were also prepared for field trials.

Only preliminary studies were conducted with the third aquatic herbicide, endothall. A solid salt form of endothall was prepared, and a method of quantifying endothall by high-performance liquid chromatography was developed. Endothall was incorporated into monolithic pellets containing polycaprolactone and either hydroxypropyl cellulose or clay. The pellet system that contained clay was expected to provide the targeted release periods of 7 and 14 days.

PREFACE

This report was prepared under Contract No. DACW39-80-C-0073 dated 1 May 1980, as part of the Aquatic Plant Control Research Program (APCRP), Work Unit 32352 entitled "Herbicide Concentration/Exposure Time Relationships for Aquatic Plant Control." The APCRP is sponsored by the Office, Chief of Engineers (OCE), US Army, and is assigned to the US Army Engineer Waterways Experiment Station under the management of the Environmental Laboratory (EL). The OCE Technical Monitor for APCRP is Mr. E. Carl Brown.

The research was conducted by Southern Research Institute from 1 July 1980 to 16 February 1987. The project was carried out in the Polymer Technology Division under the general direction of Dr. Donald R. Cowsar, Director, Applied Sciences Research. Dr. Richard L. Dunn, Associate Director of the Applied Sciences Department and Head of the Polymer Technology Division, was Principal Investigator. Other project personnel were Dr. Danny H. Lewis; Dr. Terry E. Lawler; Mr. John Gibson; Dr. Gary S. Dagenhart, Head, Polymer Engineering Section; Mr. James P. English, Head, Polymer Development Section; Mr. W. Curtis Stoner, Jr., Senior Chemist; Dr. David P. Vanderbilt, Senior Polymer Chemist; Dr. Janna D. Strobel, Senior Biochemist; Mr. Thomas O. Dappert, Head, Capsular Products Section; Mr. Michael W. Price, Associate Chemist; Ms. Brenda H. Perkins, Associate Biomathematician; Ms. Amelia G. Potter, Associate Chemist; Mr. Christopher L. Clark, Assistant Chemist; Mr. Arthur J. Tipton, Assistant Chemist; Mr. W. David Fine, Assistant Chemist; Mr. Hai Nam Tran, Assistant Polymer Chemist; Mr. J. David Rotenberry, Research Chemical Technician; Mr. Ronnie E. Bayless, Research Chemical Technician; Ms. Teresa D. Price, Chemical Technician; Ms. Gloria Y. Doby, Chemical Technician; Mr. Archie Hopson, Jr., Chemical Technician; and Mr. Bernard J. Jenkins, Chemical Technician.

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CONVERSION FACTORS, NON-SI TO SI (METRIC)
UNITS OF MEASUREMENT

Non-SI units of measurement used in this report can be converted to SI (metric) units as follows:

<u>Multiply</u>	<u>By</u>	<u>To Obtain</u>
denier	0.00011	grams per metre
feet	0.3048	metres
gallons (US liquid)	3.785412	cubic decimetres
inches	2.54	centimetres
mils	0.0254	millimetres
pounds (force)	4.448222	newtons
pounds (force) per square inch	6.894757	kilopascals
pounds (mass)	0.4535924	kilograms

A STUDY OF FORMULATIONS FOR THE CONTROLLED RELEASE OF
AQUATIC HERBICIDES

PART I: INTRODUCTION

1. Aquatic weeds are a burden to the economy and health in many areas of the country. They present a hazard to navigation, reduce or prevent the use of recreational facilities, serve as a habitat for harmful insects, destroy fish life, and retard water flow in drainage channels.

2. There are four conventional methods that can be used singly or in various combinations to control aquatic weeds. The first and primary method is the application of chemical herbicides. The second is water management, which is effective only against certain weeds and can be used only under special circumstances. The third method is mechanical control, which is usually used in combination with chemical control. Mechanical control is limited in applicability and economic feasibility. Biological agents constitute the fourth method of weed control. Although progress is being made, the technology of biological control is still in its infancy.

3. In the past, research to improve the chemical method of weed control centered on the development of more potent herbicides. However, in practice, the biological response to these agents was often disappointing, primarily because an effective delivery system was lacking. A delivery system was needed to deliver the agents directly to their target for the optimum time and in optimum quantities. The purpose of this study, therefore, was to improve the delivery and efficacy of aquatic herbicides.

4. The approach used to improve delivery was to incorporate aquatic herbicides into controlled-release systems. A controlled-release system, which is a combination of an active agent (aquatic herbicide) and an excipient (usually a polymer), is designed to deliver an agent to the target at a controlled rate for a specified period. Controlled-release systems have several advantages over conventional formulations for aquatic herbicides. Much less herbicide is needed for the same duration of activity. Furthermore, the herbicide should be more efficient because the rate of release is controlled. If the biological half-life of the herbicide is short, the extended duration of

release will minimize the number of applications that are needed. The incorporation of a chemically reactive agent into a polymeric controlled-release system can increase an agent's stability. In addition, a potentially toxic compound incorporated into an inert excipient should also increase the safety in handling.

5. When a controlled-release formulation takes the form of a fiber, the primary shape that was investigated during this study, there are additional advantages. Fibers can be fabricated by low-cost processes. They are uniform in size, shape, and composition and offer a high surface area. Moreover, the shape of fibers can be easily altered. By changing their diameter, fibers can be prepared in the form of threads or pellets. They can also be packed into bundles or woven into membranes. However, the most important advantage of fibers for the delivery of aquatic herbicides is that they become entangled with the weeds and provide localized delivery to the target.

6. Monolithic diffusion-controlled systems, in which an active agent is evenly distributed throughout the polymeric matrix, exhibit exponential or pseudo-first-order kinetics. The agent is released from the surface layers of the device first, and the distance the agent must diffuse to reach the surface increases with time. Thus, the rate of release decreases in proportion to the amount of active agent remaining in the device. The profile of release is also affected by whether the agent is dissolved and diffuses through the bulk polymer phase or is dispersed within the device. At economical loadings for aquatic herbicides [≥ 5 percent active ingredient by weight ($\geq 5\%$ wt)], it is most likely that the agent will be dispersed and not dissolved in the device. Dispersed agents can be released by two mechanisms: solution diffusion or microporous diffusion. In solution diffusion, solid agent dissolves from the surface of the device first. This decrease in concentration causes more drug to dissolve, diffuse, and be released; the interface between dissolved and dispersed agent moves to the interior of the device with time. For devices with cylindrical geometry, such as fibers, the following expression of Fick's Law describes the release of active agent when the initial concentration of agent, C_0 , is much greater than that dissolved in the polymer, C_s :

$$\frac{dM_t/M_\infty}{dt} = \frac{-4DC_s}{r_0^2 C_0 \ln(1 - M_t/M_\infty)} \quad (1)$$

where

$$\frac{dM_t / M_\infty}{dt} = \text{fractional rate of release of herbicide}$$

t = time, sec

D = diffusion coefficient of the herbicide in the polymer, cm^2/sec

C_s = saturation solubility, g/cm^3

r_o = radius of the cylinder, cm

C_o = herbicide loading, g/cm^3

M_t/M_∞ = fraction of initial mass released at time t

By integrating the above equation and rearranging terms, the following expression is obtained:

$$\frac{C_o r_o^2}{4} \left\{ \left[1 - \frac{M_t}{M_\infty} \right] \left[\ln \left(1 - \frac{M_t}{M_\infty} \right) \right] + \frac{M_t}{M_\infty} \right\} = DC_s t \quad (2)$$

A plot of the terms on the left side of the equation versus time in seconds will yield a straight line with a slope that is the apparent permeability product, DC_s .

7. In microporous systems, the active agent, which is usually water-soluble, diffuses through solvent-filled pores in the polymeric matrix or membrane. The kinetics of release are also described by various expressions of Fick's Law. However, the diffusion equations must be modified to reflect the geometry of the pores. The introduction of two terms, porosity and tortuosity, accomplishes this. Porosity is the volume fraction of the device that is porous (i.e., the portion of the device through which diffusion can occur). Tortuosity is a measure of the path length the agent must travel to reach the exterior of the device. The effect of pore size is usually not incorporated into diffusion equations because this effect is essentially constant within limits that are useful, and because changes in this effect will be reflected as changes in the apparent diffusivity.

8. Reservoir controlled-release devices consist of a core of active agent and excipient surrounded by a membrane or sheath. To obtain a true reservoir system, the permeability of the sheath material to the agent must be much lower than the permeability of the core excipient; that is, the membrane must limit the rate of release of the agent. The release kinetics of reservoir devices are zero order (constant rate) as long as constant thermodynamic activity is maintained in the agent/matrix core. Furthermore, the rate of release depends on the thickness of the membrane. For reservoir devices with cylindrical geometry, the following expression of Fick's Law describes the steady-state release of an agent through the rate-controlling wall of the cylinder:

$$dM/dt = \frac{2\pi hDC_s}{\ln r_o:r_i} \quad (3)$$

where

dM/dt = rate of release, g/sec

h = length of cylinder, cm

D = diffusivity coefficient, cm^2/sec

C_s = saturation solubility of agent in sheath material, g/cm^3

r_o = outer radius of cylinder (sheath and core), cm

r_i = inner radius of cylinder (core), cm

9. One of the most important tasks in developing a controlled-release system is to match the properties of the active agent and excipient. Improper selection of the polymer excipient will result in release characteristics that are either too slow or too fast. Sometimes, however, there are restrictions on the excipient that can be used, such as the need for biodegradability or the need for materials already approved for use in humans. When problems such as these are encountered, a number of techniques can be used to modify and optimize release characteristics. These techniques include the addition of plasticizers or fillers; alterations in the molecular weight, crystallinity, or

degree of crosslinking of the polymeric excipient; and alterations in fabrication processes or conditions. Fortunately, a pilot study had indicated that polycaprolactone and cellulose acetate, both of which are biodegradable, were potential excipients for a controlled-release system for diquat, the first aquatic herbicide that was investigated.

10. Because this report covers work performed over approximately 7 years, the results are presented in chronological order. Descriptions of materials and methods accompany the discussion of each controlled-release system because different pieces of equipment and several fabrication methods were used during the course of the project, and each affected the release characteristics and physical properties of the controlled-release system. The rationale prompting each study or series of studies is also included in the discussion section because the research involved a continual development of each formulation from laboratory-scale studies to large-scale commercial processes. Therefore, the Conclusions and Recommendations section primarily summarizes the major considerations that governed development of each system and presents recommendations as to the direction of further work. For readability, the detailed descriptions of the fabrication and evaluation methods are presented in Appendix A.

11. Three different aquatic herbicides (diquat, fluridone, and endothall) were incorporated into controlled-release formulations during the project. Therefore, there is a natural division of the work with each herbicide. Research with fluridone has also been divided on the basis of the shape of the controlled-release system (fiber or pellet). Further subdivisions include the type of system under study (monolithic or reservoir) and the method of preparation.

Fibrous Controlled-Release Formulations for Diquat

12. The objective for this phase of the study was to develop and optimize a fibrous, controlled-release system of diquat and polycaprolactone (PCL) that a pilot project had indicated was feasible. Specific goals were a zero-order (constant) release of diquat, different rates of release, extended durations of release, and fibers that were strong and flexible enough to be applied in the field.

Preparation and characterization of monolithic fibers

13. An earlier feasibility study had indicated that PCL held promise as an excipient for controlled-release fibers that would deliver diquat for extended periods. Therefore, monolithic fibers containing diquat and PCL were prepared. Two types of extruders were used to produce the diquat/PCL fibers. Melt indexers were used in the initial studies to produce fibers with a low degree of orientation. In later studies, monolithic fibers more uniform in size and with a higher degree of orientation were produced on a ram extruder. The fibers produced on the melt indexers were prepared from diquat/PCL blends containing 30% wt diquat and 70% wt PCL. The extrusion temperature was 100° C. Detailed procedures for the preparation of diquat, PCL, and their blends, as well as the extrusion of fibers, are given in Appendix A. The release of diquat from these fibers was fast and essentially complete within 1 day (Figure 1).

14. The ram extruder was used to produce fibers with a greater degree of orientation and crystallinity in efforts to slow the release of diquat. Greater crystallinity can be obtained by changing the fiber-quenching conditions, exerting tension on the fiber as it is extruded, or drawing the fiber after spinning. The melt-spinning conditions of ram-extruded fibers are given in Table 1. The release characteristics of these fibers were not determined because similar fibers had been tested extensively in the pilot study. They

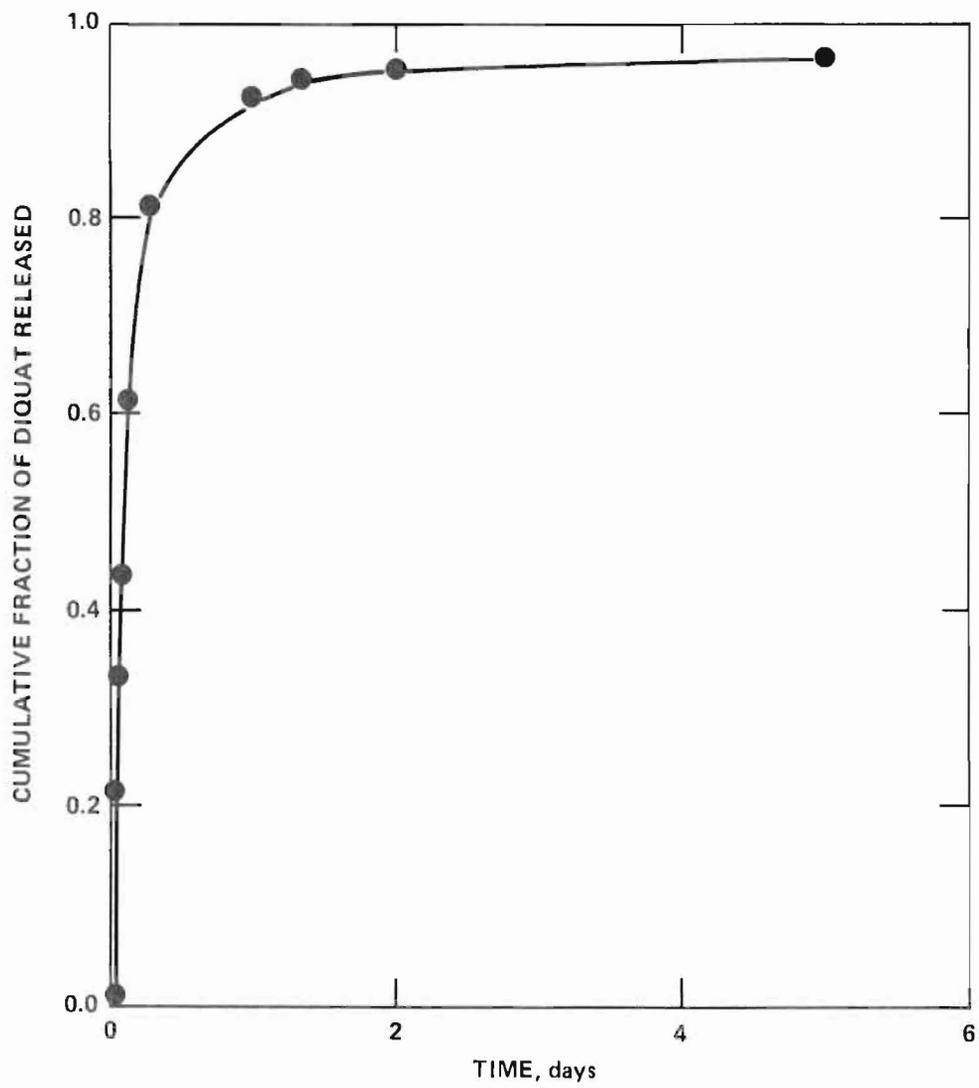


Figure 1. Release of diquat from 30-percent-loaded PCL fibers, Sample A222-3-1A

Table 1

Monolithic Diquat Fibers Prepared on the Ram Extruder

Sample No.	Spinning Conditions					Orienting Conditions, † Draw Ratio
	Block Temp. °C	Feed Rate cm ³ /min	Ram Pressure psi*	Take-Up Speed, ft/min**	Quench Condition	
A293-3	180	0.40	373	16	Air	0
A293-3-1	180	0.40	373	16	Air	2.1
A293-3-2	180	0.40	373	16	Air	4.1
A293-3-3	180	0.40	373	16	Air	4.1
A293-5	190	0.56	536	46	Water	0
A293-5-1	190	0.56	536	46	Water	3.0
A293-5-3	190	0.56	536	46	Water	5.0

* To convert pounds (force) per square inch to kilopascals, multiply by 6.894757.

** To convert feet to metres, multiply by 0.3048.

† Draw temperature, 65° C; delivery speed, 15 ft (4.6 m) per minute.

were, however, tested for mechanical properties. The results are summarized in Table 2. The tenacity values (measure of fiber strength) increased directly with the draw ratio, while the elongation values tended to decrease. The tensile factor, which incorporates both of these values, also increased with increasing draw ratio. These results indicate that drawing increased the overall strength and flexibility of the fibers. In addition, air-quenched fibers (Samples A293-3, -3-1, -3-2, and -3-3) appear to have better tensile properties than water-quenched fibers (Sample A293-5, -5-1, -5-2, -5-3).

15. The mechanical properties of drawn monolithic fibers were excellent even though they contained 30% wt diquat. The values for tenacity and tensile factor indicate that much higher loadings of diquat would be possible before a serious problem with fiber strength was encountered. Therefore, monolithic fibers with exponential release characteristics are a feasible alternative controlled-release system for diquat if a constant rate of release is not required.

16. The release characteristics of the monolithic diquat/PCL fibers can be described mathematically by Fick's Law of diffusion as expressed in Equations 1 and 2 for the release of a dispersed agent by a solution-diffusion mechanism. Equation 2 was used to calculate the apparent permeability product, DC_s , for the monolithic diquat/PCL fibers. An average value of 2.3×10^{-10} g/cm/sec was obtained. This was too high to achieve the desired 6- to 12-month duration of release without extensive modification of the monolithic system. Three parameters could be changed to slow the release of diquat from monolithic fibers and extend its duration of action: the fiber diameter could be increased, the diquat loading could be increased, or a membrane could be applied to form a coaxial or reservoir fiber. The third option, the use of a rate-controlling membrane, was selected as the means of achieving the required release characteristics. Therefore, further development of controlled-release diquat formulations was conducted with reservoir fibers.

Preparation and characterization of coaxial fibers

17. Coaxial fibers prepared by the melt-spinning process during the pilot study exhibited a large initial burst of diquat. This may have been caused by

Table 2
Mechanical Properties of Monolithic Diquat Fibers
Prepared on the Ram Extruder

<u>Sample No.</u>	<u>Draw Ratio</u>	<u>Denier*</u>	<u>Diameter mm</u>	<u>Tenacity g/day</u>	<u>Elongation at Break %</u>	<u>Initial Modulus g/day</u>	<u>Tensile Factor TE^{1/2}</u>
A293-3	0	--	0.294	--	--	--	--
A293-3-1	2.1	216	0.265	2.5	75	34	20
A293-3-2	3.1	196	0.167	3.1	90	42	30
A293-3-3	4.1	174	0.176	5.0	53	42	38
A293-5	0	--	0.333	--	--	--	--
A293-5-1	3.0	497	0.225	1.7	40	29	11
A293-5-2	4.0	252	0.245	2.4	24	44	12
A293-5-3	5.0	225	0.216	3.4	37	66	21

* To convert denier to grams per metre, multiply by 0.00011.

diquat migrating from the core matrix to the surface of the sheath material during the extrusion process or by incomplete sealing of the fiber ends. To eliminate these factors, monolithic fibers were solution coated to prepare the reservoir-type fibers, and the ends of the fibers were sealed with a thermo-setting resin. The composition of the monolithic fibers was 30:70 diquat/PCL, and they were coated with a polymer solution containing either PCL or cellulose acetate (CA). Several variables were examined in preparing these new reservoir-type or modified monolithic fibers. These variables included the fabrication method used to prepare the core material, the concentration of polymer in the coating solution, the coating solvent, and the thickness of the sheath.

18. A coating solution containing 30% wt polymer in acetone was ultimately used. The coated fibers that were suitable for release studies are described in Table 3. The release profiles for these fibers are plotted in terms of the cumulative fraction of diquat released versus time in Figures 2-9. None of the fibers released diquat at a constant rate, which was an objective for the fibrous diquat formulation. The duration of release also was not long enough. The time lag evident in Figures 4, 6, 7, 8, and 9 is typical of reservoir controlled-release systems and is indicative of the time required for an active agent to diffuse through the sheath material.

19. In Figure 10, the release profile of the unoriented monolithic fiber prepared on the melt indexer is compared with the release profiles of the PCL-coated fibers that were prepared from this same monolithic fiber. Coating with PCL did cause a reduction in the initial burst of diquat and an extension in the duration of release. However, a very thick sheath of PCL would be required to reduce the release rate to a level that would provide a release period of several months. (Note: The diameter of the monolithic core matrix fibers extruded on a melt indexer varied. This may account in part for the low fractional release for Sample A222-54-2, which does not correlate with the $r_o:r_i$ values as do the other fibers.)

20. In Figure 11, the release profile of the same monolithic fiber produced on the melt indexer is compared with reservoir fibers coated with CA or PCL. A thick sheath of CA ($r_o:r_i = 1.5$) modified the release profile

Table 3
Solution-Coated Diquat Fibers

Sample No.	Coating	Core	Core Preparation	Outer Diameter mm	Inner Diameter mm	Sheath Thickness mm	$r_o:r_i$
A222-15-1	PCL*	Monolithic**	Melt indexer	0.487	0.301	0.093	1.62
A222-15-2	PCL*	Monolithic**	Melt indexer	0.588	0.344	0.122	1.71
A222-54-2	PCL*	Monolithic**	Melt indexer	0.473	0.373	0.100	1.27
A222-54-5	CA†	Monolithic**	Melt indexer	0.559	0.373	0.186	1.50
A222-54-1	PCL*	Monolithic††	Ram extruder	1.516	0.373	0.143	1.38
A222-54-6	--	Coaxial‡	Ram extruder	0.530	0.480	0.050	1.10
A222-54-3	PCL*	Coaxial‡	Ram extruder	0.578	0.459	0.119	1.26
A222-54-4	CA†	Coaxial‡	Ram extruder	0.568	0.472	0.096	1.20

*PCL = polycaprolactone; inherent viscosity, 1.80 dL/g.

**Sample A222-3-1; 30:70 Diquat/PCL.

†CA = cellulose acetate; Eastman Organic Chemicals.

††Sample A293-3-1; 30:70 Diquat/PCL.

‡Sample 9337-71-2; 30:70 Diquat/PCL; sheath = PCL; inherent viscosity, 1.25 dL/g.

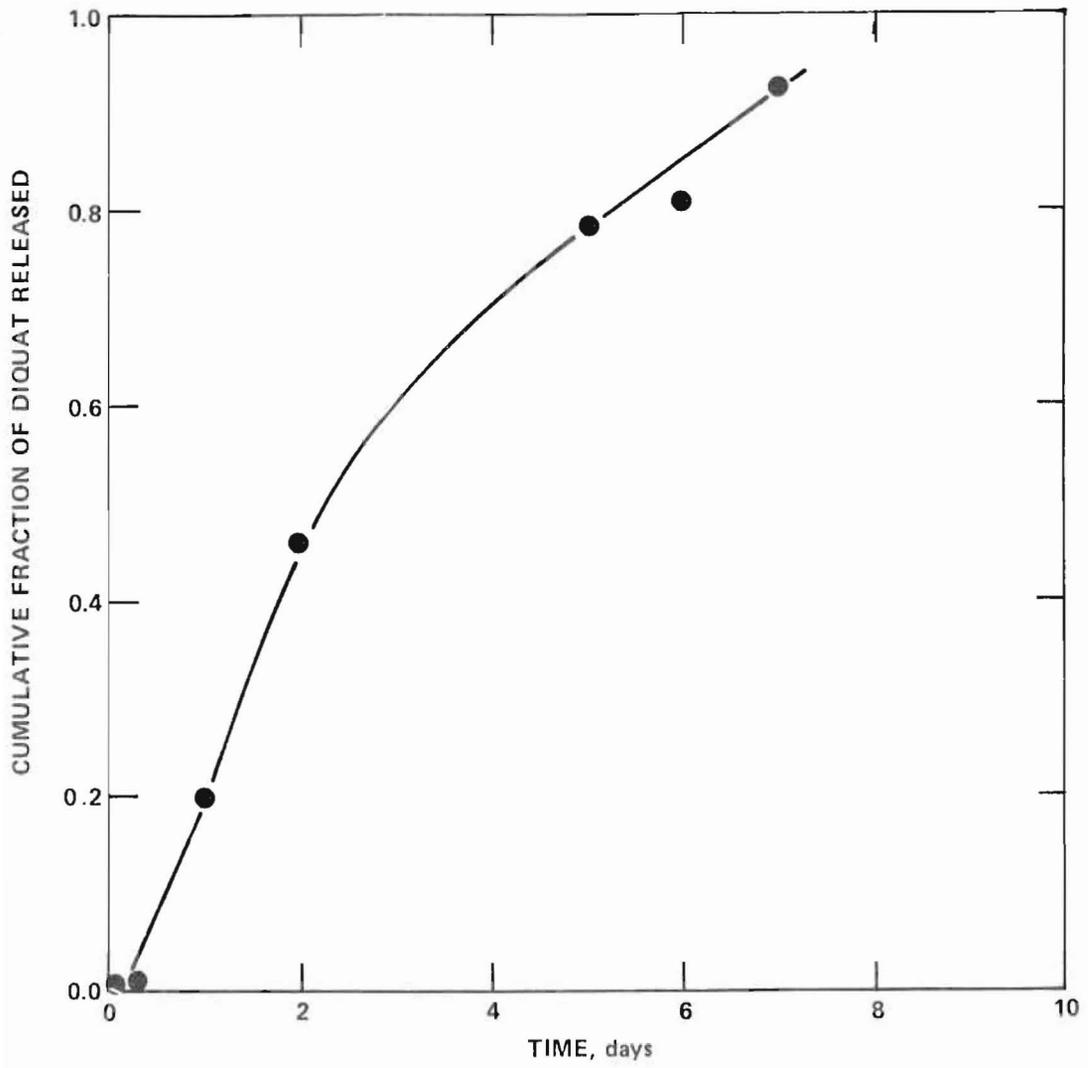


Figure 2. Release of diquat from fibers: PCL sheath, 30:70 diquat/PCL core, Sample A222-15-1

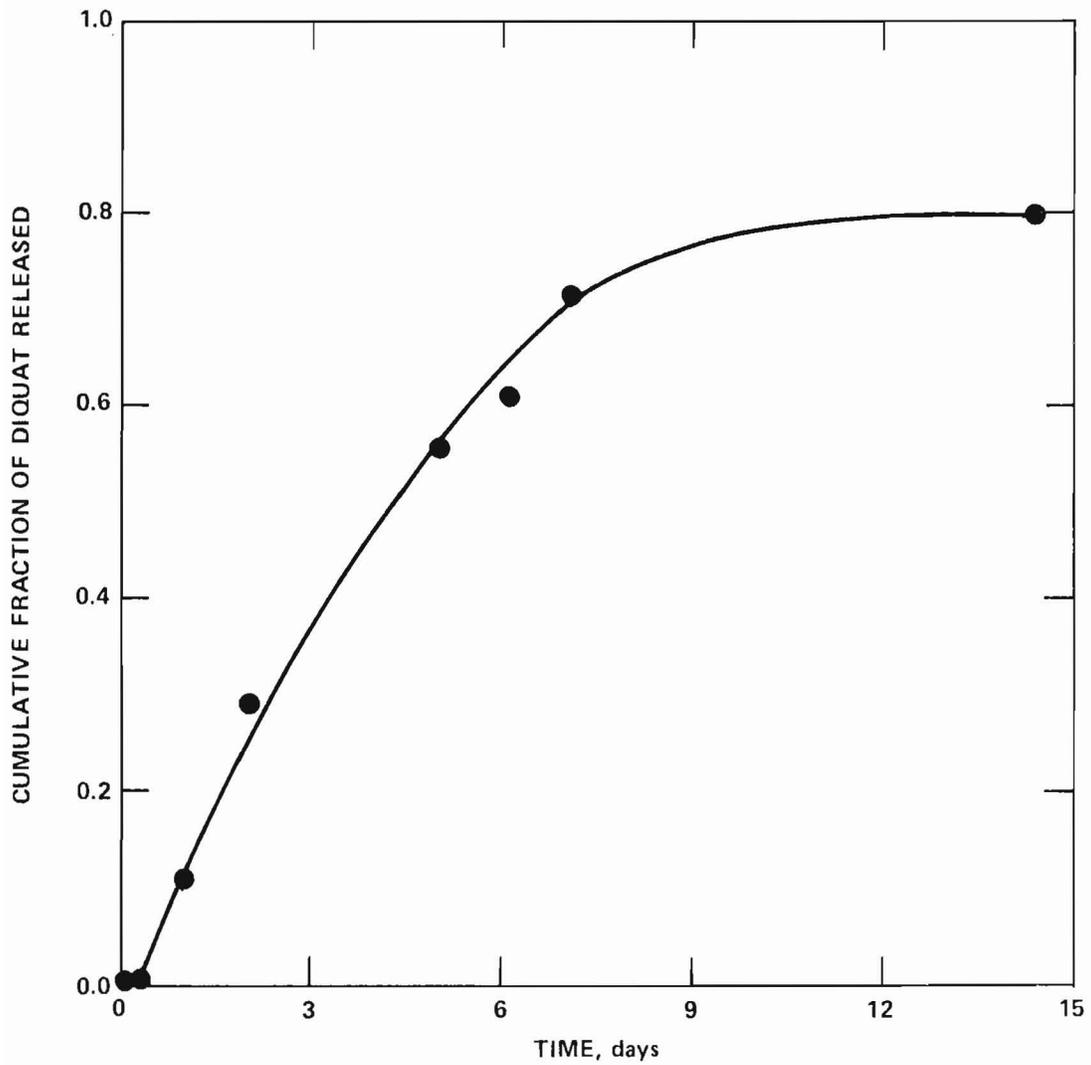


Figure 3. Release of diquat from fibers: PCL sheath, 30:70 diquat/PCL core, Sample A222-15-2

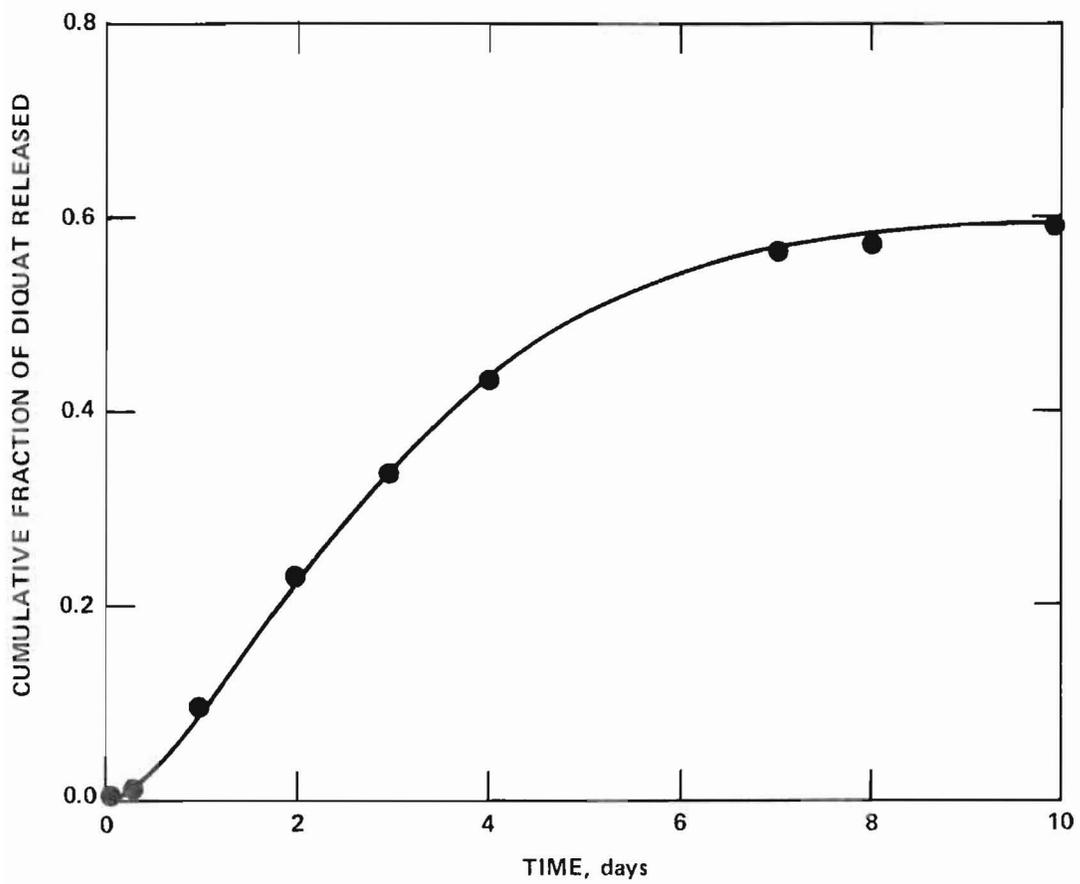


Figure 4. Release of diquat from fibers: PCL sheath, 30:70 diquat/PCL core, Sample A222-54-2

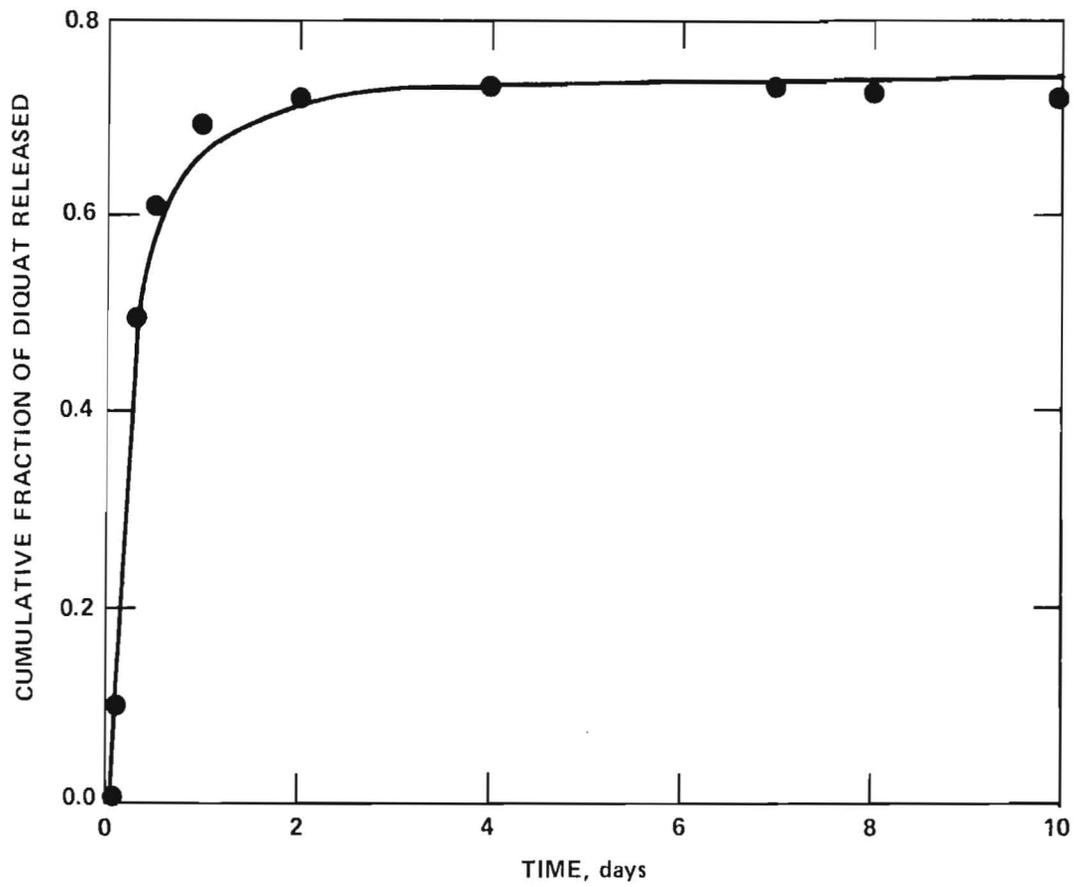


Figure 5. Release of diquat from fibers: CA sheath, 30:70 diquat/PCL core, Sample A222-54-5

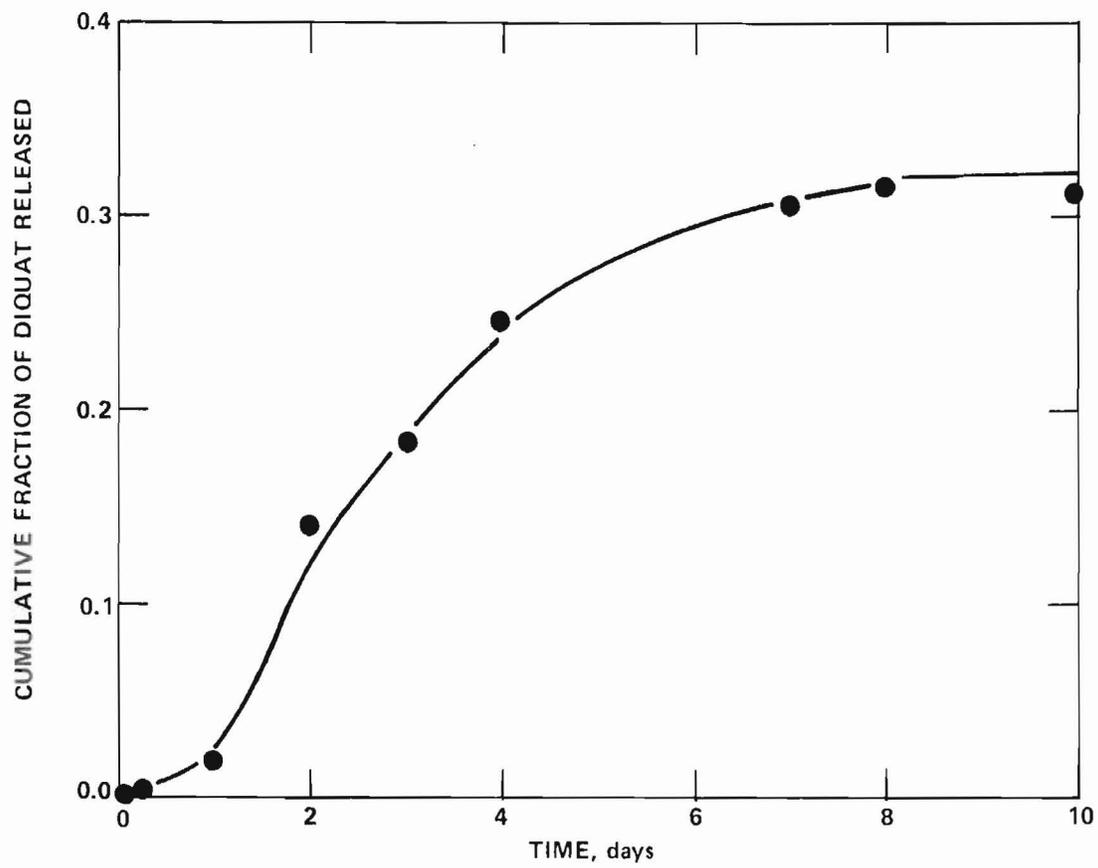


Figure 6. Release of diquat from fibers: PCL sheath, 30:70 diquat/PCL core, Sample A222-54-1

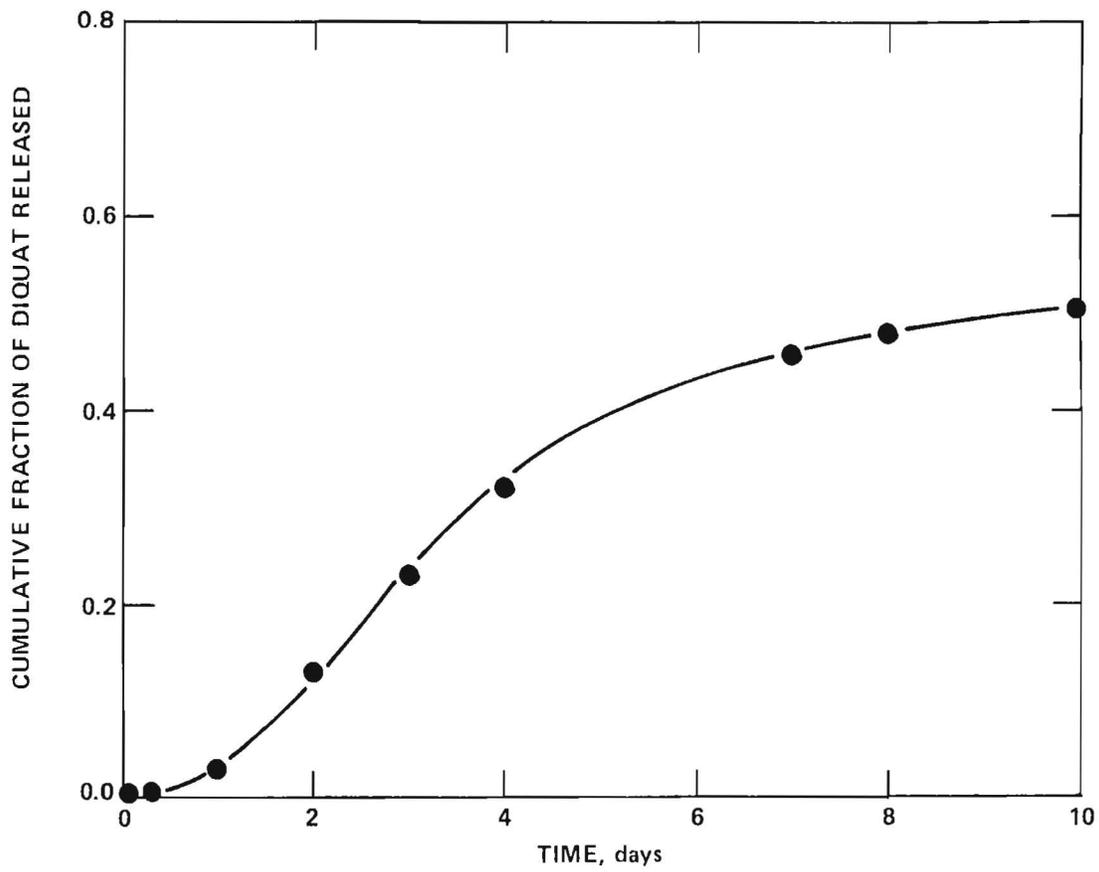


Figure 7. Release of diquat from fibers: PCL sheath, 30:70 diquat/PCL core, Sample A222-54-6

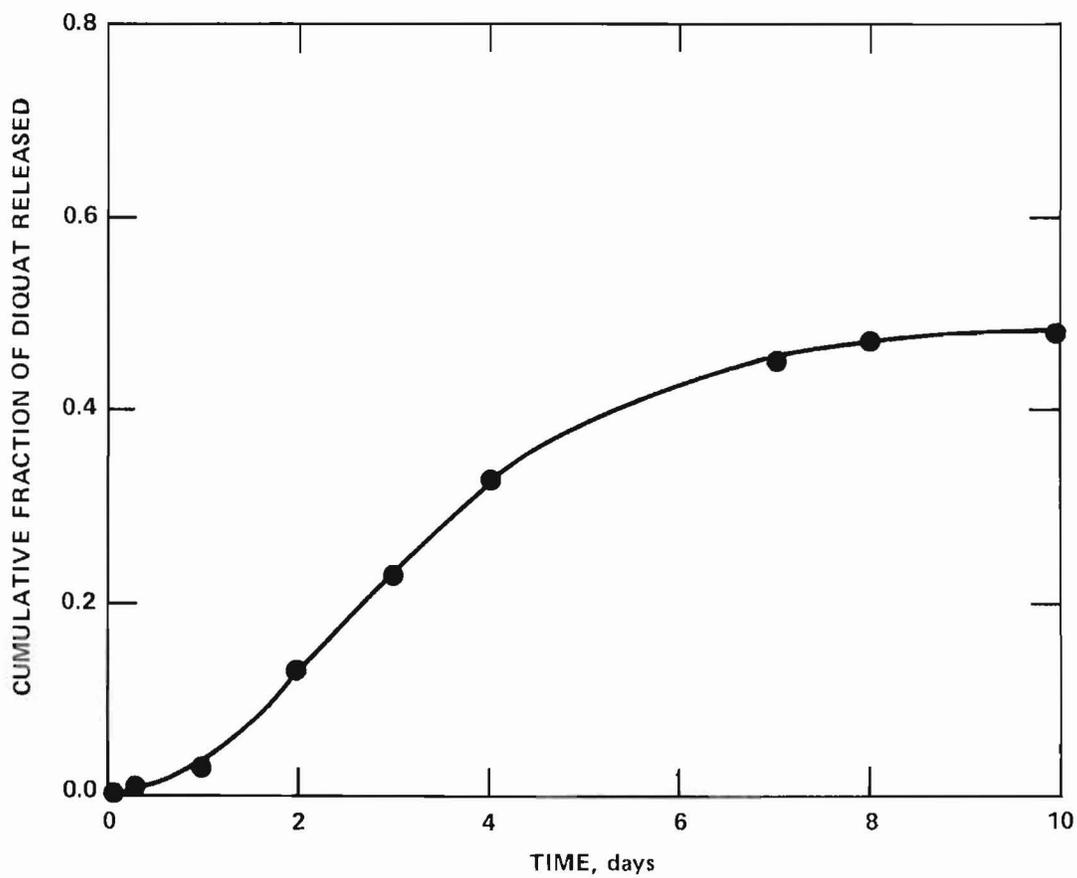


Figure 8. Release of diquat from fibers: PCL sheath, 30:70 diquat/PCL core, Sample A222-54-3

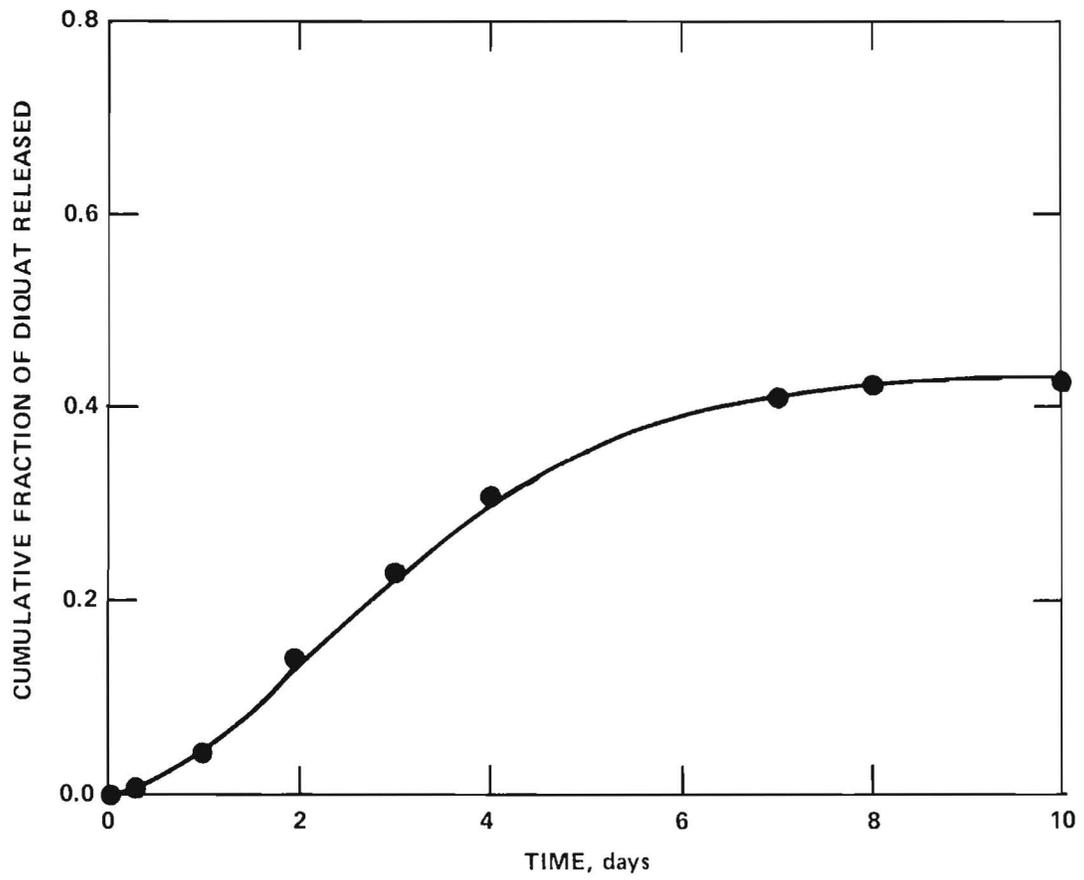


Figure 9. Release of diquat from fibers: CA sheath, 30:70 diquat/PCL core, Sample A222-54-4

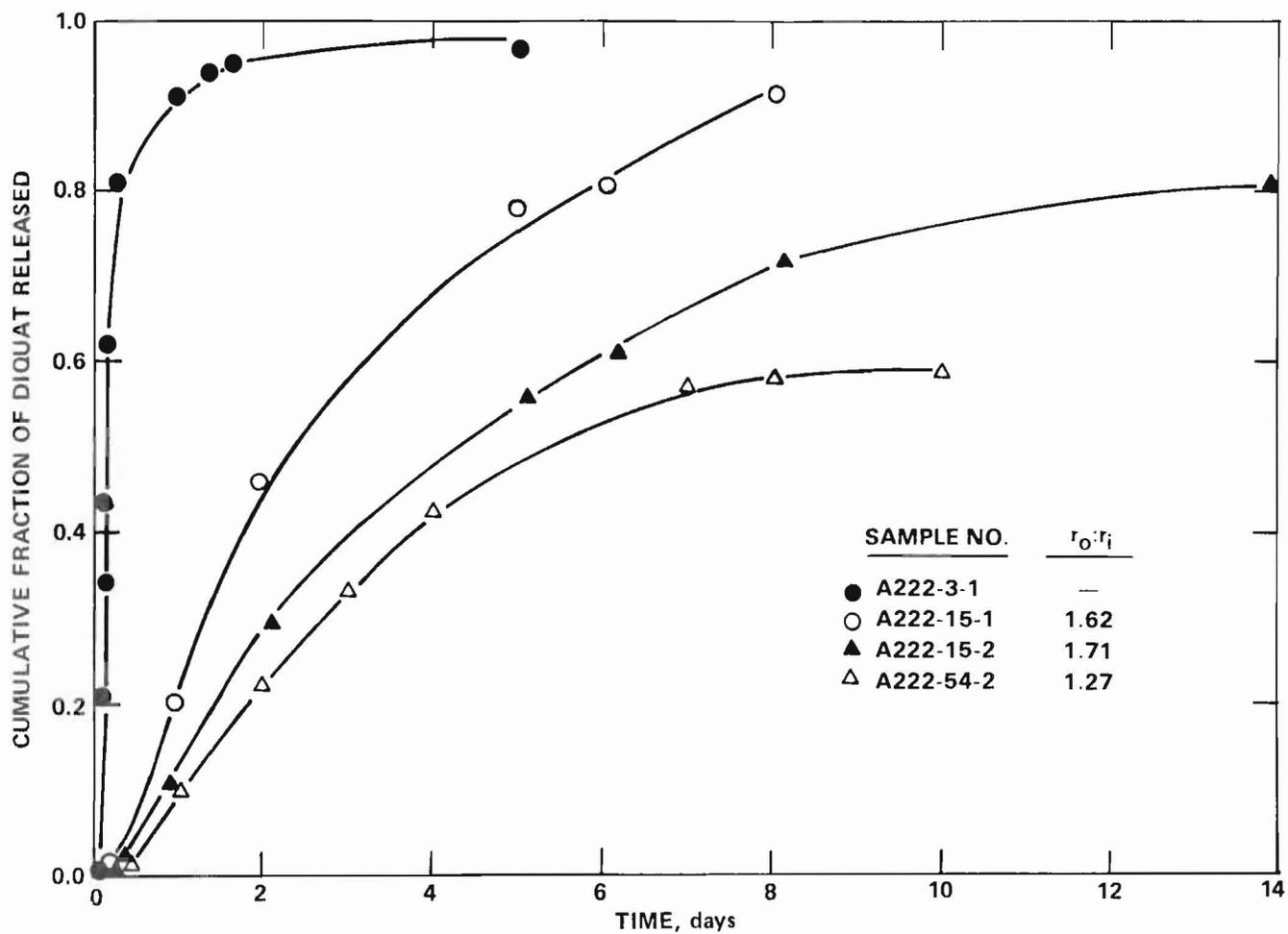


Figure 10. Effect of PCL coating on release of diquat from monolithic fibers prepared on melt indexer

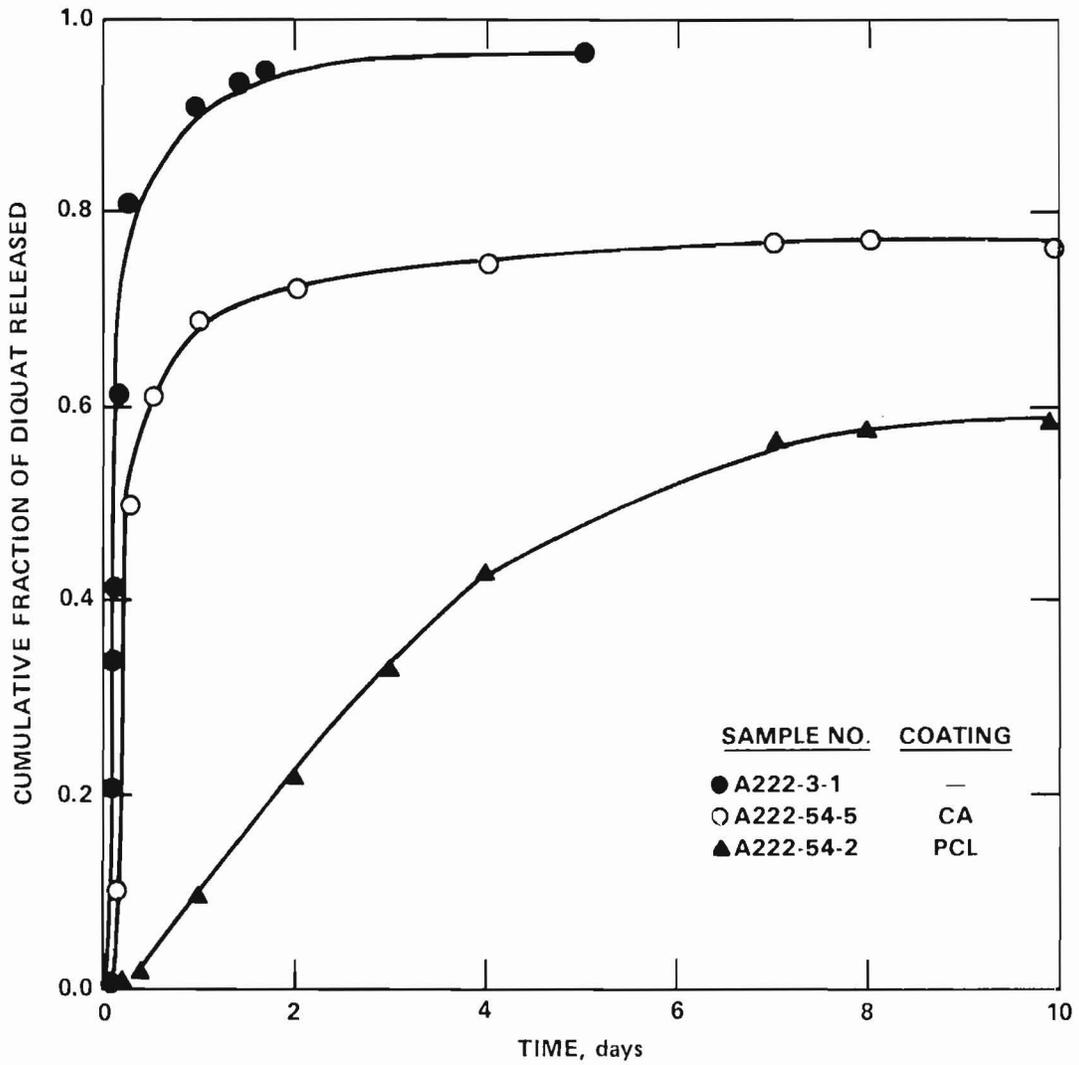


Figure 11. Effect of sheath polymer on release of diquat from monolithic fibers prepared on melt indexer

only slightly. This indicates that CA is even more permeable to diquat than PCL and can be eliminated as a candidate sheath material.

21. In Figure 12, the release profile of a melt-spun coaxial fiber is compared with the release profiles of fibers prepared by coating the coaxial fiber with PCL or cellulose acetate. The release profiles of the fibers are nearly identical. Therefore, it can be concluded that the coating material is not rate-limiting in these fibers and that release is controlled by the diffusion of diquat from the core matrix.

22. To obtain zero-order release rates in reservoir fibers requires a core excipient that is more permeable to diquat than the sheath material. Based on the results presented above, CA is a likely core excipient. However, it is not melt-spinnable. Polyethylene glycol (PEG), another hydrophilic polymer, is melt-spinnable at the same temperature as PCL and is likely to be highly permeable to diquat. In a preliminary study, coaxial fibers with a 30:70 diquat/PEG core and a PCL sheath were prepared on the ram extruder. Although satisfactory fibers were produced, they were not evaluated for mechanical properties or release characteristics because, at the time, diquat was replaced by fluridone as the aquatic herbicide of choice for the controlled-release formulation. The diquat release profile at the time was not considered sufficiently long, i.e., less than 4 to 8 days, to warrant further evaluation of the formulations. Recent information from ongoing research at the US Army Engineer Waterways Experiment Station (WES) suggests that 4- to 8-day release may be desired.

23. Two of the coaxial fibers were evaluated for conformity to the form of Fick's Law of diffusion given in Equation 3. The values for r_o and r_i were determined by measuring cross sections of the fibers under a microscope equipped with a calibrated scale. Two values were used for the apparent permeability product, DC_s . One had been previously determined in diffusion-cell studies in the pilot program; the other was obtained from the release studies with monolithic fibers. The predicted and actual release values are given in Table 4. The differences between the predicted and actual values for the release rates are not unusual and are explainable. The actual rate of release from coaxial fibers is normally faster than the rate predicted from diffusion-cell studies because diffusion in a cell is unaffected by fabrication

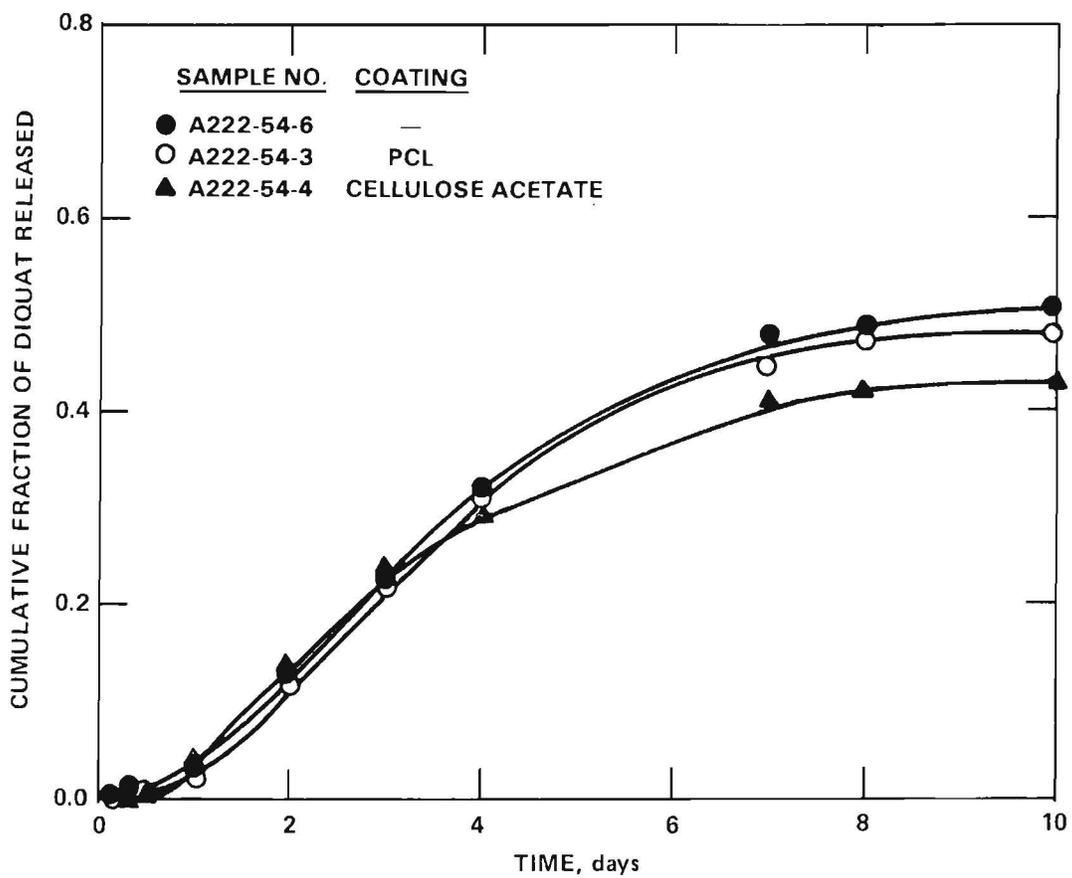


Figure 12. Effect of additional polymer coatings on release of diquat from a melt-spun coaxial fiber

processes. The actual rate is usually slower than the rate predicted from monolithic fibers because melt spinning and drawing can cause migration of an agent to the surface of the fiber. Consequently, more agent is released than can be accounted for from theoretical considerations. The actual release-rate value for the coaxial fibers is intermediate because they represent a combination of both systems. Overall, the values in Table 4 indicate that a much thicker sheath of PCL would be required to slow the release of diquat to provide the rate and duration desired.

Table 4
Release Data for Coaxial Fibers Prepared by Solution Coating

Parameter	Sample A222-15-1	Sample A222-15-2
Sheath	PCL	PCL
Core	30:70 diquat/PCL	30:70 diquat/PCL
r_o , mm	0.487	0.294
r_i , mm	0.301	0.172
Sheath thickness, mm	0.093	0.122
r_o/r_i	1.62	1.71
Predicted release rate, $\mu\text{g}/\text{cm}/\text{day}$		
Diffusion cell DCs	1.81	1.62
Monolithic DCs	259.00	232.00
Actual release rate, $\mu\text{g}/\text{cm}/\text{day}$	35.00	32.00
Predicted duration of action, days		
Diffusion cell	139.60	203.10
Monolithic	1.00	1.50
Actual duration of action, days	8.00	10.00

Fibrous Controlled-Release Formulations for Fluridone

24. Because our data indicated that a thick coating of PCL would be required for a long-term delivery system for diquat, and also at the sponsoring agency's request, diquat was replaced with fluridone as the aquatic herbicide in the fibrous controlled-release system. The targeted duration of release was also shortened from a period of 6 to 12 months to a period of 8 weeks. Because the properties of both the active agent and the polymeric excipient determine the release characteristics of controlled-delivery systems, the substitution of fluridone for diquat required adjustments in both fiber composition and fabrication conditions.

Monolithic fluridone/PCL fibers prepared on melt indexer

25. First, monolithic fibers with different loadings of fluridone were prepared to determine the mechanism of release that could be expected with fluridone and to obtain a first estimation of feasible fluridone loadings and fabrication conditions.

26. Solvent blends of fluridone and PCL with weight-to-weight ratios of 60:40, 50:50, 40:60, 30:70, 20:80, and 10:90 were prepared with methylene chloride. (The blending procedure was essentially the same as that given in paragraph 6, Appendix A, for diquat/PCL mixtures.) Monofilaments were spun on a melt indexer preset at 120° C. A spinneret with a diameter of 35 mils* was used. The sample designations and ram weights used in spinning each blend are given in Table 5.

* A table of factors for converting non-SI units of measurement to SI (metric) units is presented on page 7.

Table 5

Monolithic Fluridone Fibers Prepared on the Melt Indexer

<u>Sample No.</u>	<u>Fluridone/PCL Ratio</u>	<u>Ram Weight g</u>
A293-41-1	60:40	12,200
A293-33-1	50:50	7,084
A293-35-1	40:60	2,144
A293-35-2 and -3	40:60	4,945
A293-37-1-5 and -51-1	30:70	2,144
A293-49-1	20:80	4,945
A293-53-1	20:80	2,144
A293-47-1	10:90	2,144

27. The release characteristics of the fibers were determined in two *in vitro* release systems. In one, aqueous ethanol was used as the receiving solution; in the other, hard water. (A detailed description of the release systems and the method of analysis for fluridone is given in paragraphs 24-26, Appendix A.) With aqueous ethanol (50:50 wt/wt) as the receiving solution, fluridone was quantified by measuring its absorption at 237 nm. The release profiles of monolithic fibers with different loadings of fluridone are shown in Figure 13. The cumulative fractional release of fluridone was proportional to the fluridone loading. This behavior is typical of a controlled-release system containing a dispersed active agent that is released by a mechanism of solution-diffusion and is described by Equations 1 and 2. The apparent permeability product was calculated using Equation 2. An average DC_s value of 2.03×10^{-10} g/cm/sec was obtained (see following tabulation).

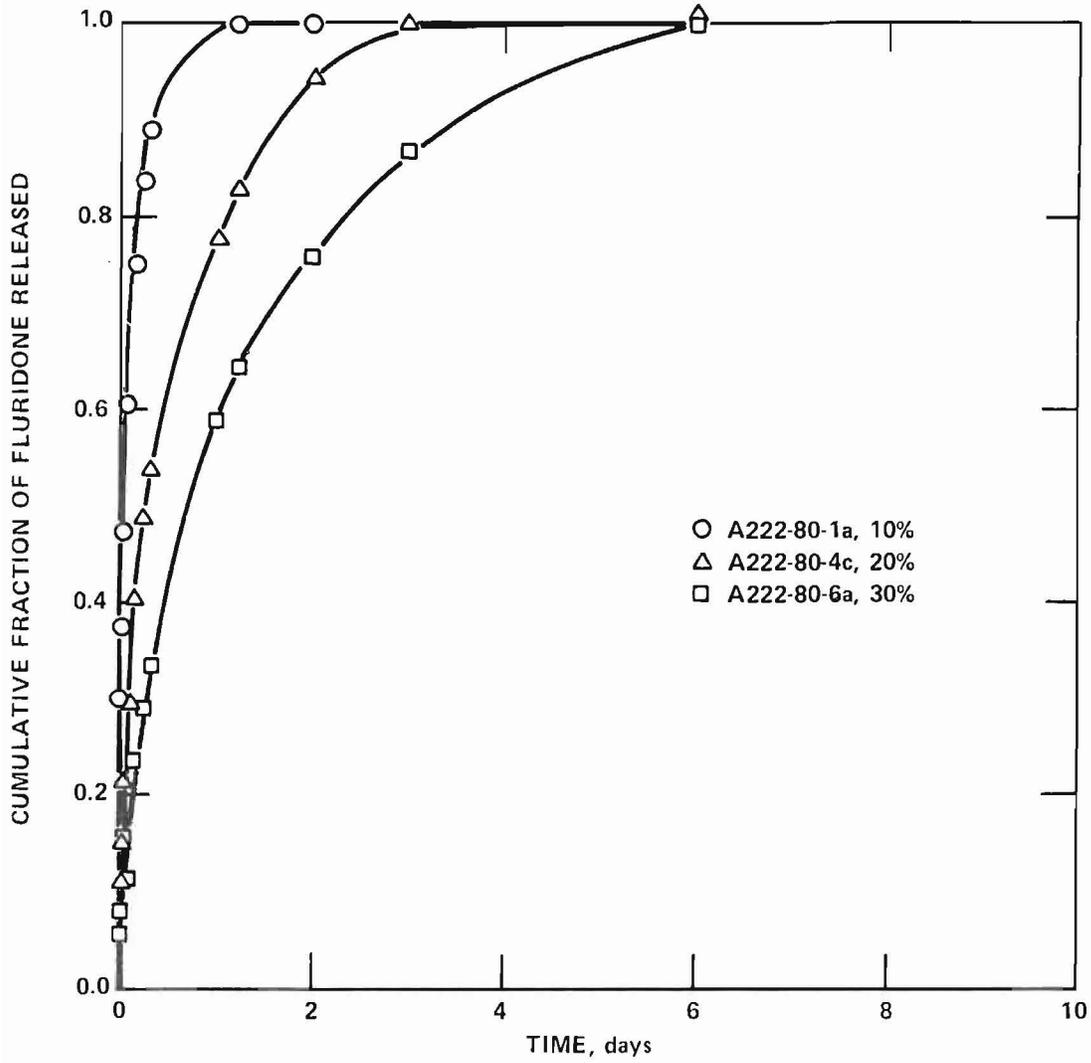


Figure 13. Cumulative fractional release of fluridone from PCL monolithic fibers into 50:50 ethanol/water

Herbicide Loading %	DS_s g/cm/sec
10	2.56×10^{-10}
20	1.55×10^{-10}
30	1.98×10^{-10}

28. Although the ethanolic water solution was convenient to use in the laboratory because larger amounts of fluridone could be measured under infinite-sink conditions, a receiving fluid was needed that would simulate field conditions more closely. Therefore, an artificially prepared medium of reconstituted hard water was selected and used in all further release studies. The hard water containing sodium carbonate, magnesium sulfate, calcium sulfate, and potassium chloride in deionized water gave a water hardness of 160 to 180 mg of calcium carbonate per litre. Release studies were performed in the usual manner, and fluridone was quantified by ultraviolet (UV) absorbance. Because fluridone is less soluble in hard water than in an ethanolic medium, the release rate can be expected to be slower in hard water. Figures 14-16 show this effect for 10-, 20-, and 30-percent-loaded monolithic fibers.

29. The cumulative fractional release of fluridone from monolithic fibers with different loadings of fluridone is shown in Figure 17. As in the ethanolic medium, fluridone release into hard water, when expressed in terms of cumulative fraction, was inversely proportional to the loading of fluridone. These data indicate that fluridone is dispersed within the polymeric matrix and that a solution-diffusion mechanism is operating. In Figure 18, release is expressed in terms of the cumulative mass of fluridone released from fibers, (as micrograms per centimetre). These data show that the quantity of fluridone released increases with increasing fluridone loadings. From Figures 17 and 18, it is evident that increasing the fluridone loading increases the amount of fluridone released and extends the duration of release. In Figure 19, the same data are plotted in yet another manner, as the amount of fluridone released per centimetre of fiber per day (or daily release rate) versus time in days. This method of presenting data emphasizes the high initial release rate or burst effect typical of monolithic controlled-release systems.

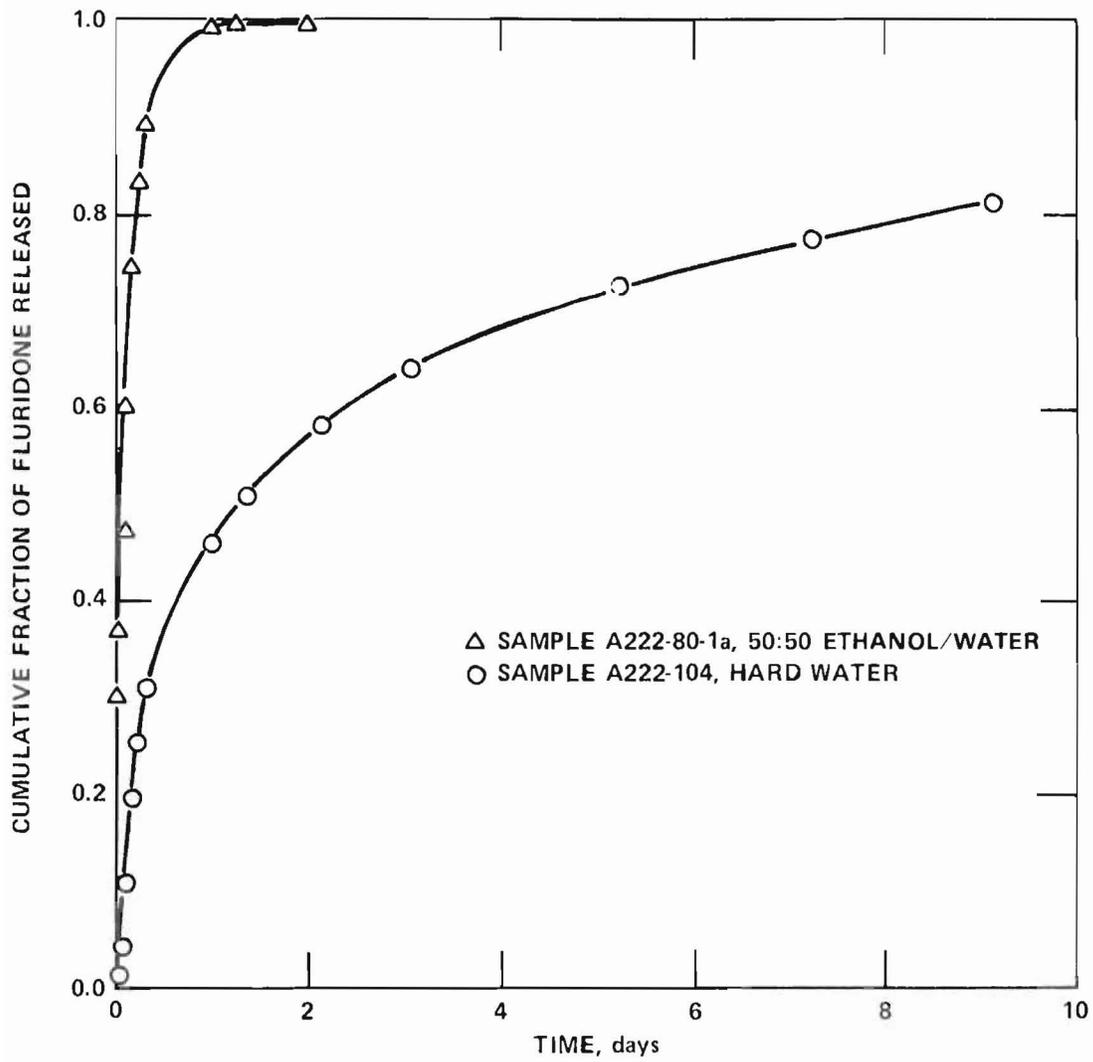


Figure 14. Comparison of *in vitro* release rates of fluridone/PCL monolithic fibers in different media, 10-percent-loaded

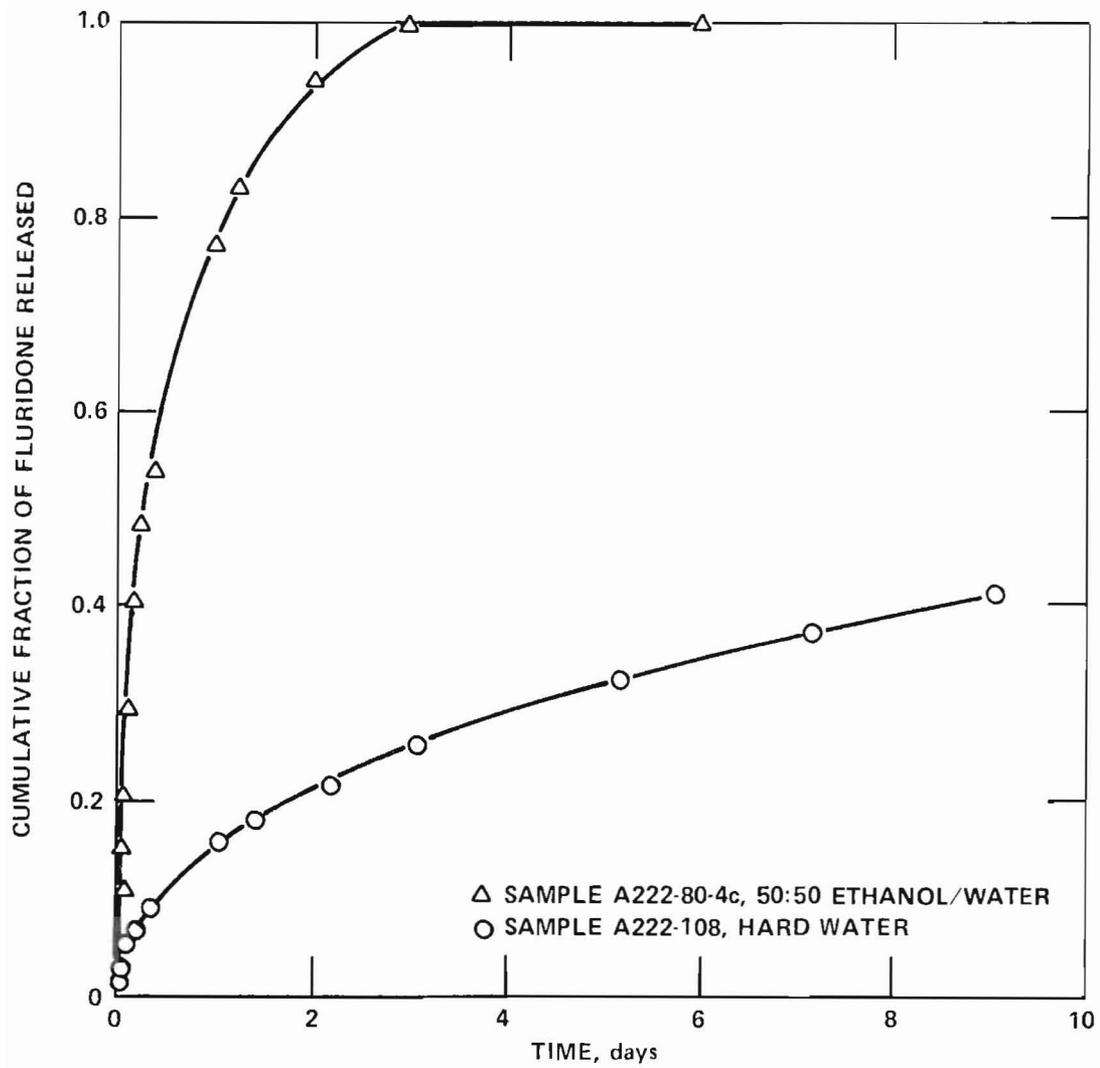


Figure 15. Comparison of in vitro release rates of fluridone/PCL monolithic fibers in different media, 20-percent-loaded

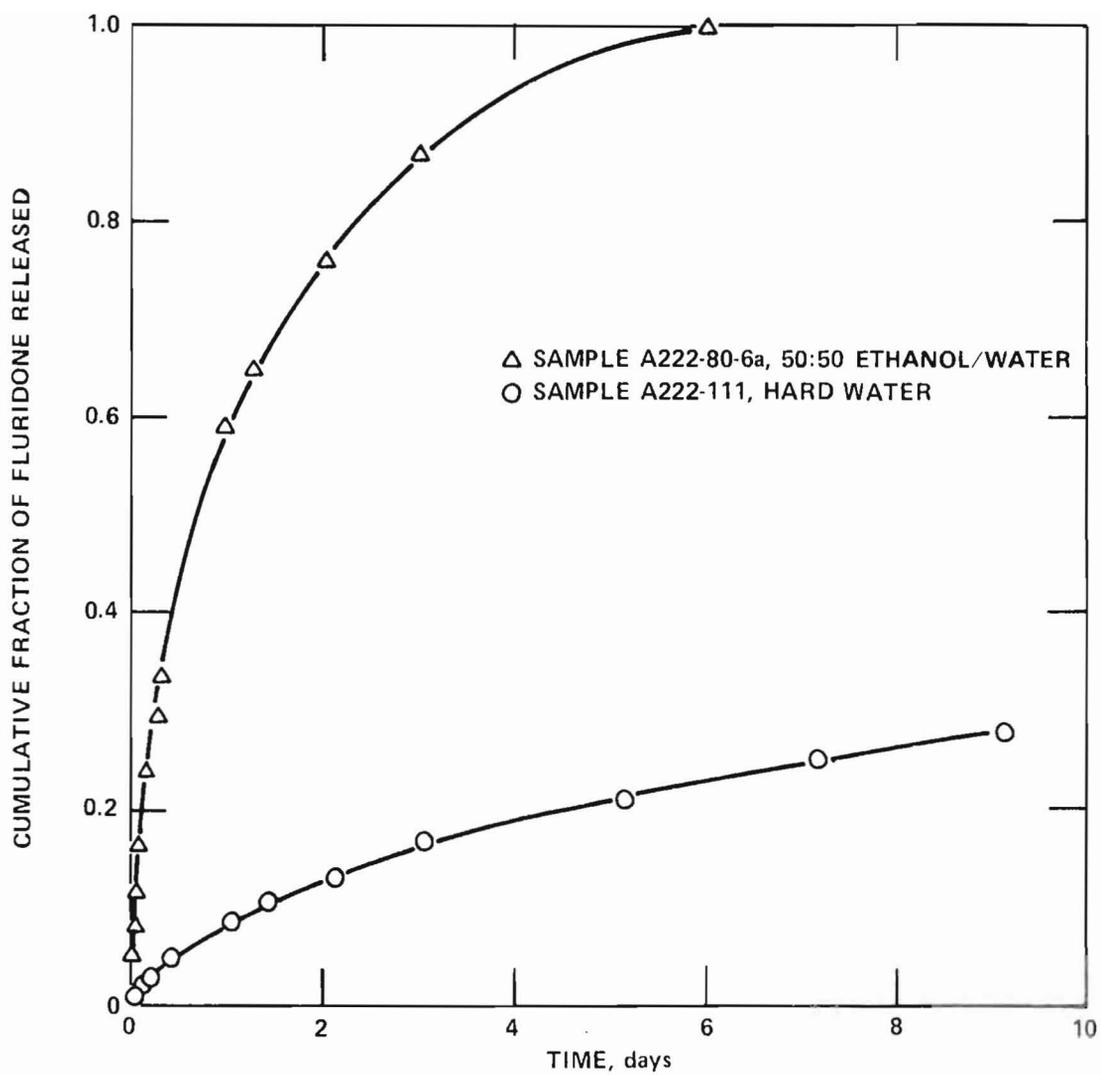


Figure 16. Comparison of *in vitro* release rates of fluridone/PCL monolithic fibers in different media, 30-percent-loaded

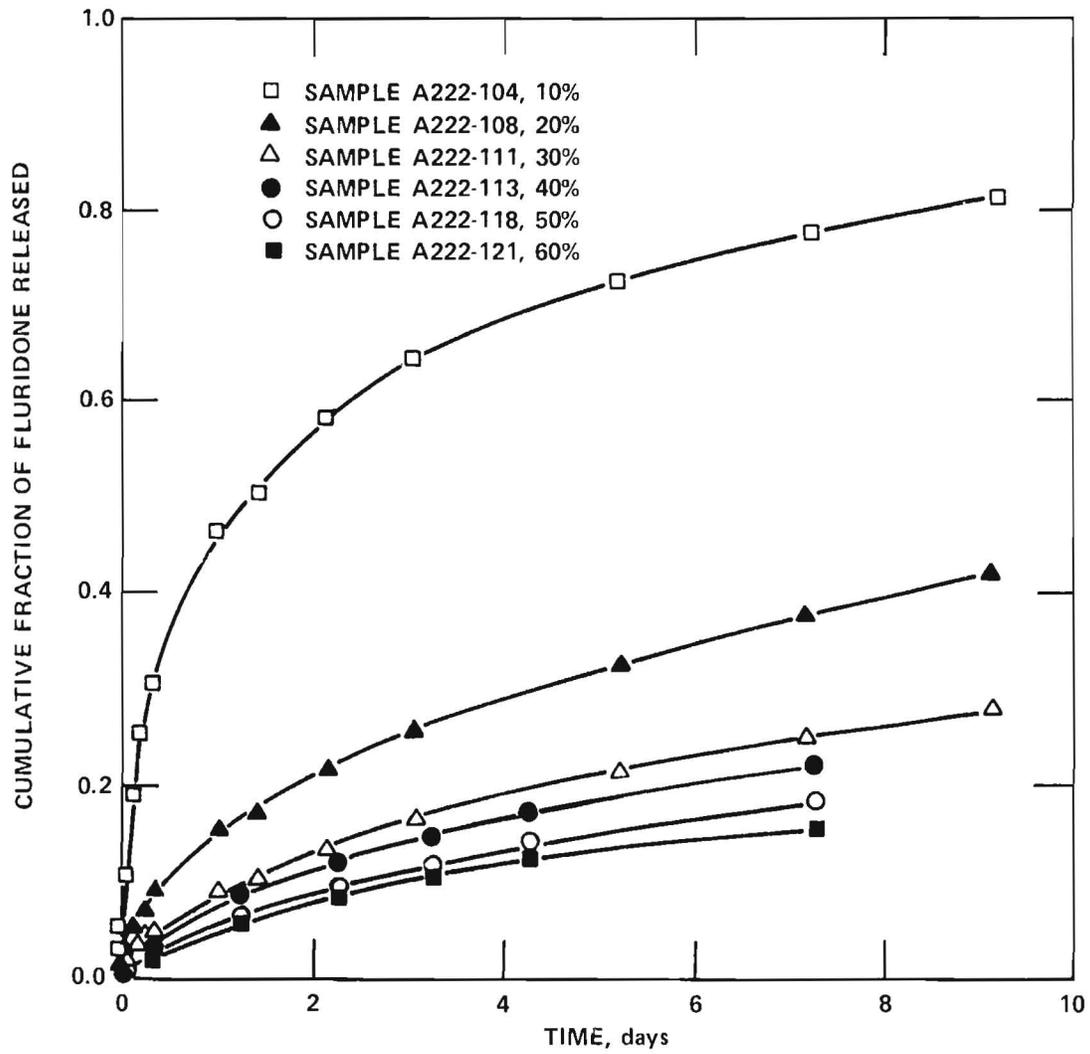


Figure 17. Cumulative fractional release of fluridone from PCL monolithic fibers into hard water, 0 to 10 days

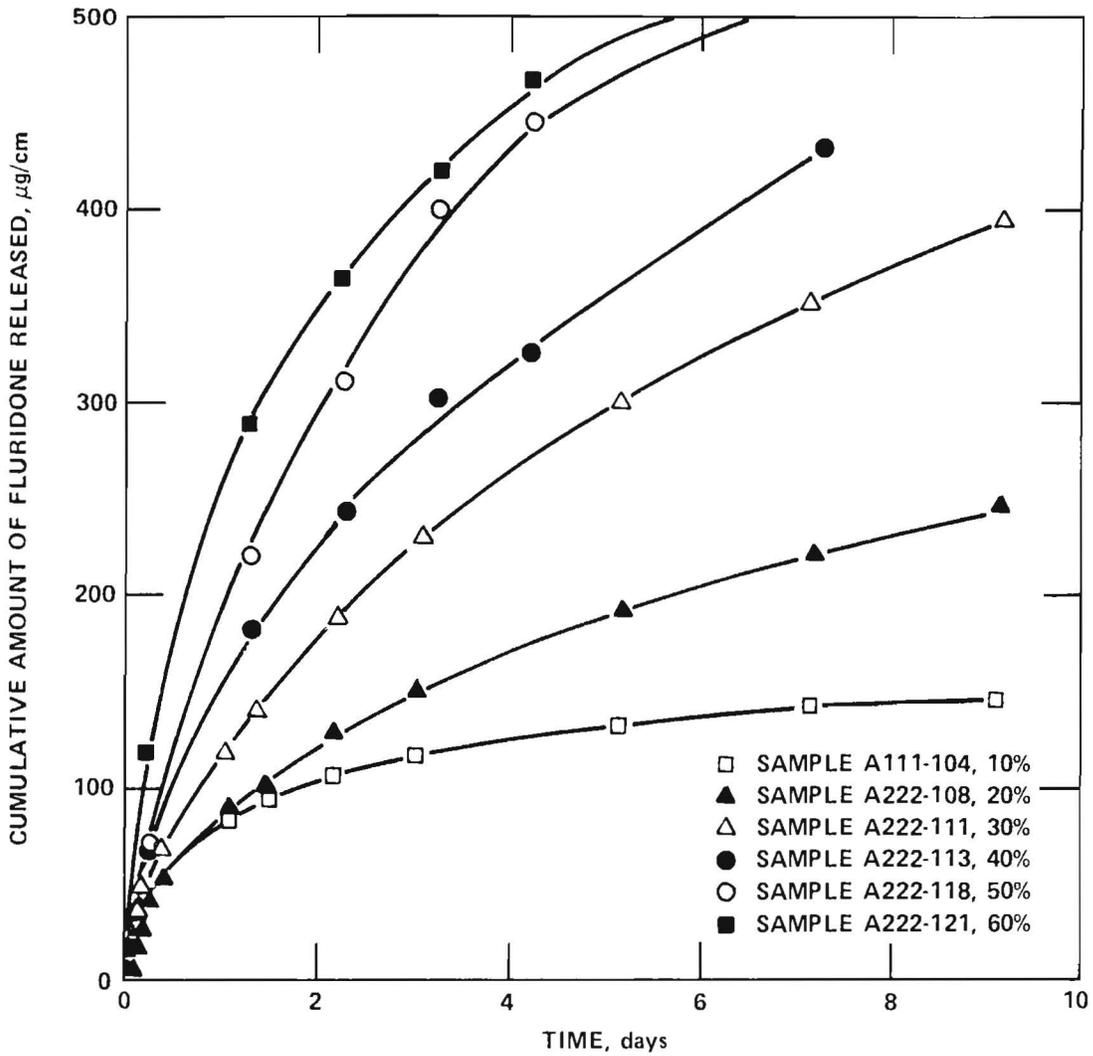


Figure 18. Cumulative release of fluridone from PCL monolithic fibers into hard water, 0 to 10 days

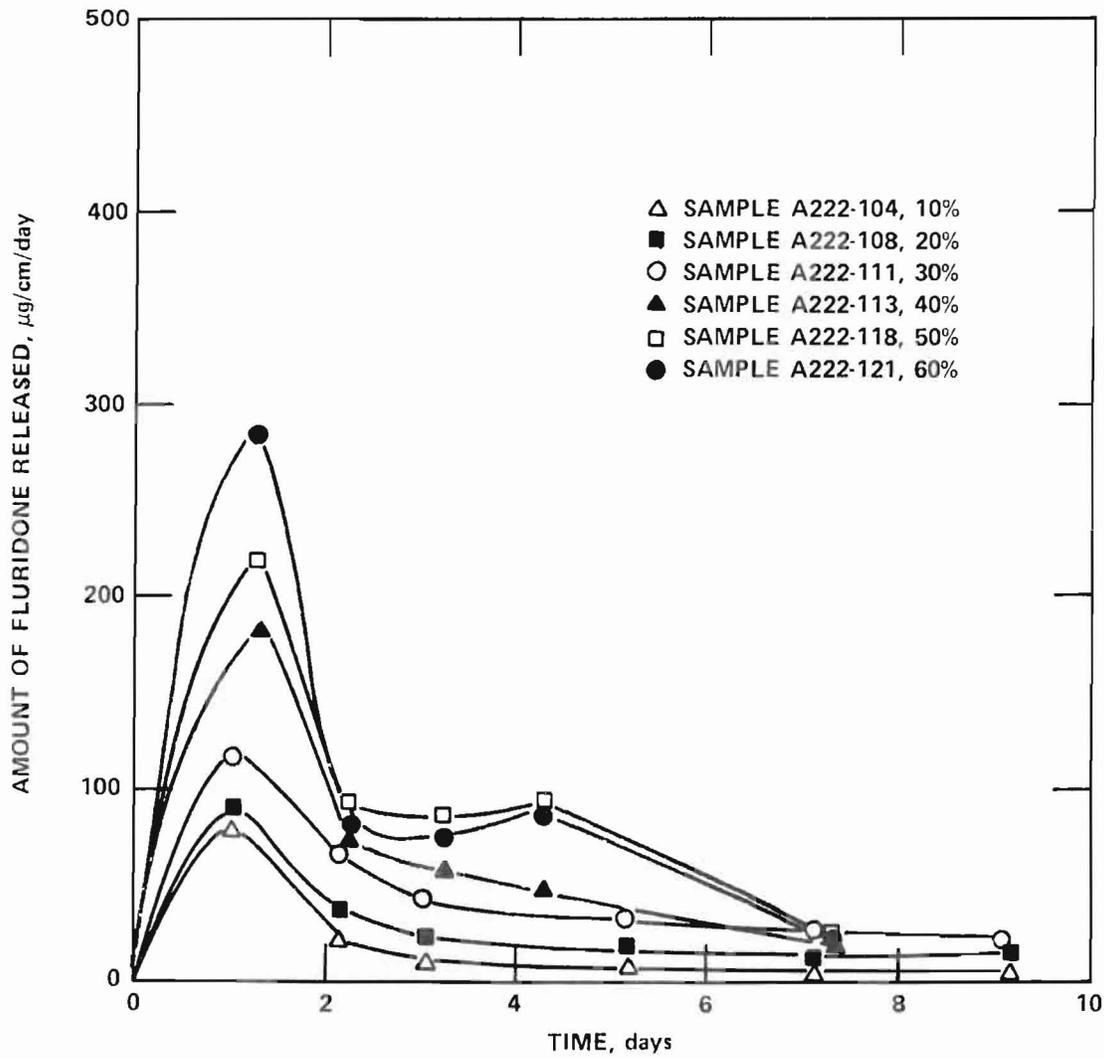


Figure 19. Daily release of fluridone from PCL monolithic fibers into hard water

30. The release studies with these fibers were extended to 110 days, and then the fluridone remaining in the fibers was extracted and quantified to determine the actual loading of fluridone in the fibers. The theoretical and experimentally determined fluridone loadings are given in Table 6. The experimental values were used to correct the values for the cumulative fraction of fluridone released with time, and the long-term release profiles with the corrected values are shown in Figure 20. For comparison, the cumulative mass of fluridone released during the 110-day release study is shown in Figure 21. Upon completion of the study, the apparent permeability product for fluridone release into hard water was calculated and compared with the values obtained with aqueous ethanol (see Table 7). The apparent permeability product (DC_s) was almost two orders of magnitude smaller when hard water was used as the receiving fluid. This result suggests that ethanol may have a plasticizing effect on PCL, may increase the solubility of fluridone in PCL, or both. Also, the DC_s value is slightly greater at the lower fluridone loadings of 10% and 20% wt. This difference is probably not significant, but if it were, it would suggest that the herbicide may itself act as a filler or may alter excipient crystallinity.

Table 6
Fluridone Loadings of Monolithic Fibers

Sample No.	Fluridone Content	
	Theoretical	Experimental
A293-47-1	10.0	9.0
A293-43-1	20.0	20.0
A293-51-1	30.0	31.2
A293-35-1	40.0	43.3
A293-67-1	40.0	38.7
A293-33-1	50.0	50.8
A293-41-1	60.0	69.4

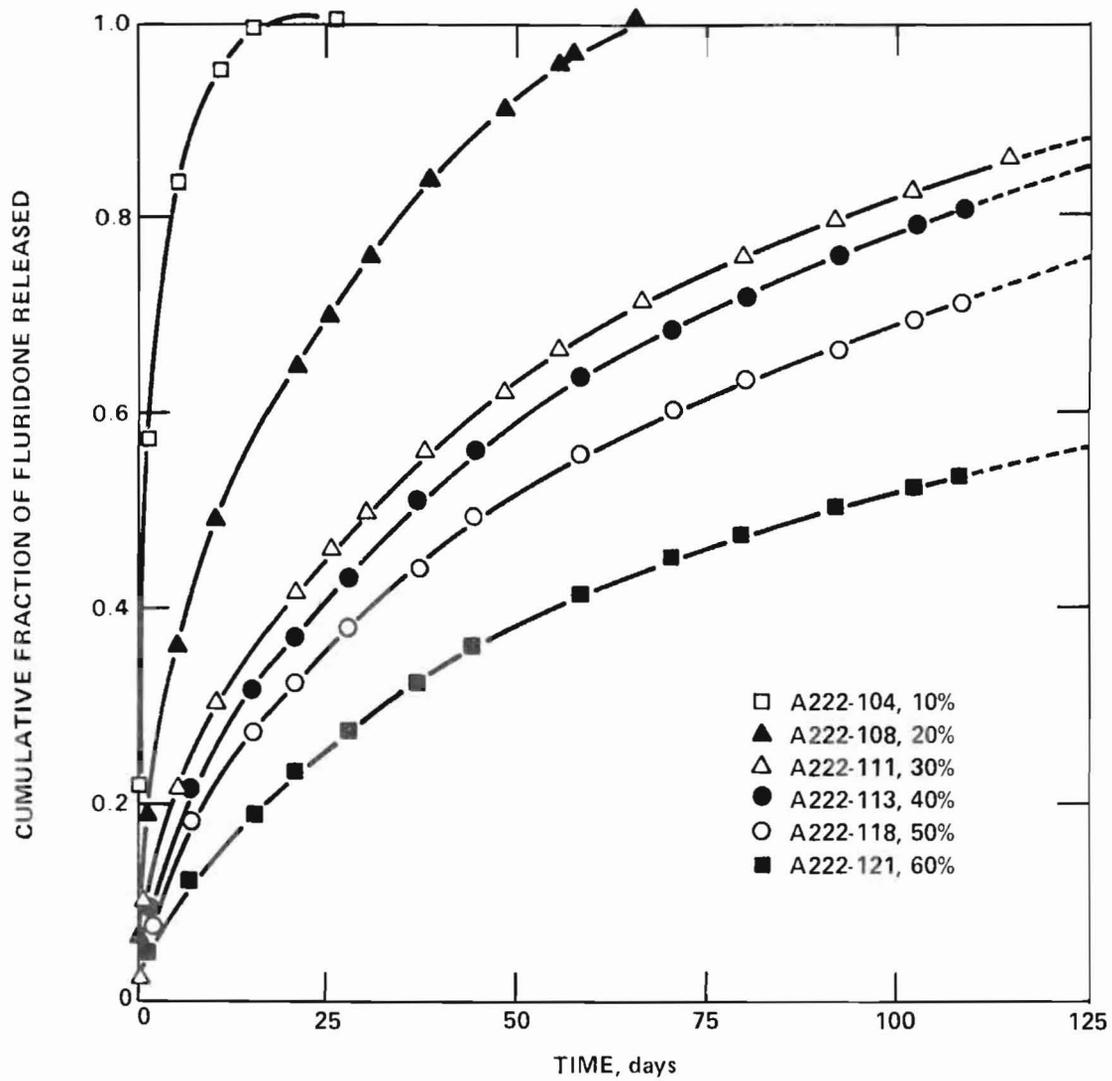


Figure 20. Cumulative fractional release of fluridone from PCL monolithic fibers into hard water, 0 to 110 days

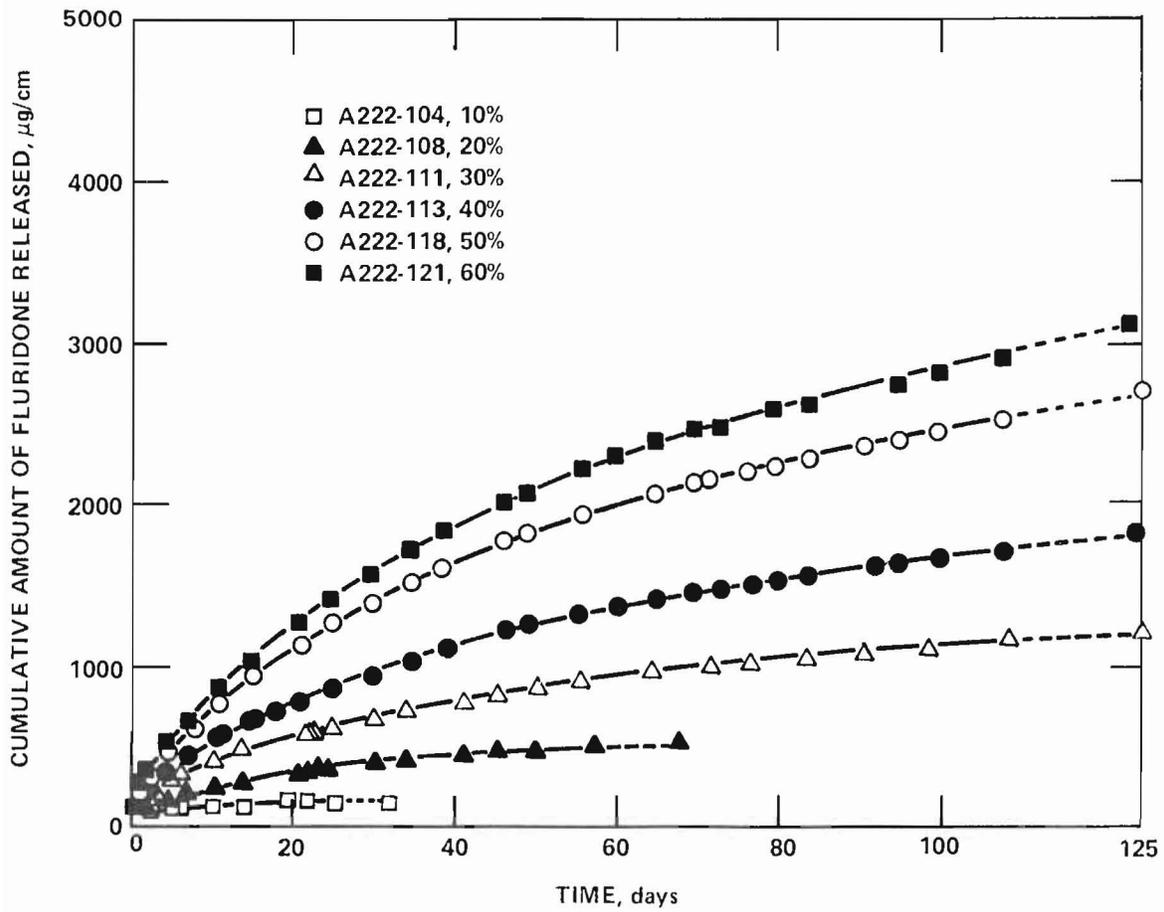


Figure 21. Cumulative release of fluridone from PCL monolithic fibers into hard water, 0 to 110 days

Table 7
Values of DC_s for Fluridone in PCL
in Various Solutions

Herbicide Loading %	DC_s , g/cm/sec	
	<u>50:50 Ethanol/Water</u>	<u>Hard Water</u>
10	2.56×10^{-10}	6.43×10^{-12}
20	1.55×10^{-10}	7.04×10^{-12}
30	1.98×10^{-10}	5.04×10^{-12}
40	Not determined	5.43×10^{-12}
50	Not determined	5.08×10^{-12}
60	Not determined	5.23×10^{-12}

31. To determine how much fluridone could be incorporated into a fiber that had acceptable mechanical properties, the melt indexer was used to prepare fibers from an 80:20 fluridone/PCL blend. At this loading of fluridone, the block temperature had to be increased from 120° to 150° C, and a ram weight of 12.2 kg had to be applied to produce fibers. The fibers, however, still had a rough surface and were brittle. These results indicate that the maximum fluridone loading lies between 60 and 80 percent, and careful adjustment of the extrusion temperature is needed to produce fibers with acceptable mechanical properties.

Coaxial fluridone-loaded fibers
 prepared by solution coating

32. Coaxial fibers of PCL and fluridone were prepared by solution coating monolithic fibers that had been extruded on the melt indexer. These coaxial or modified monolithic fibers were prepared to decrease the initial burst and smooth the overall release profile of monolithic fibers. The coating solution contained 21.5% wt PCL-700 in toluene, and two or four coats were applied to the monolithic fibers to give two different sheath thicknesses. A detailed description of the coating procedure is given in paragraph 14, Appendix A. The release profiles of the coaxial fibers are presented as cumulative fraction

released and cumulative mass released in Figures 22-25. In each figure, release from the uncoated fiber is presented for comparison with the coated fibers. The effect of coating on release characteristics was pronounced in fibers with both a 10- and a 60-percent core loading of fluridone. In both cases, the rate of release was slowed considerably and was very nearly zero order. The duration of release was also extended. However, the simpler monolithic fibers, which are more economical to produce in bulk quantities, were selected for further development in scaled-up fabrication processes.

Monolithic fluridone/PCL
fibers prepared on a ram extruder

33. The melt indexer is a piece of experimental equipment that can be used to evaluate the spinnability of various formulations and to produce small quantities of fibers. The preparation of uniform fibers in larger amounts required a ram extruder designed and built at Southern Research Institute (described in detail in paragraph 11, Appendix A). Because the ram extruder permits the control of more variables during extrusion than the melt indexer, including block temperature, ram drive force, fiber take-up rate, and quenching method, several adjustments in extrusion conditions were needed. Extrusions with the ram were begun with a 60:40 fluridone/PCL blend. At a block temperature of 155° C (the melting temperature of fluridone), extrusion occurred at a low ram force of only 25 lb. Although the extruded filament was quenched by several methods, none gave a fiber hard and strong enough for winding. In fact, the extruded material remained soft and tacky indefinitely at room temperature. The 155° C block temperature may have caused degradation of the fluridone or PCL. Consequently, the block temperature for subsequent extrusions was lowered.

34. Using block temperatures ranging from 98° to 112° C and ram forces ranging from 100 to 175 lb, blends containing 20% and 40% wt fluridone were extruded at a rate of about 15 linear feet per minute. The monolithic fibers were reasonably strong, flexible, and uniform with a smooth surface. Release studies were conducted with the 40-percent-loaded fibers, some of which had been subjected to drawing after extrusion. Figure 26 shows the data as cumulative fraction released, and Figure 27, as cumulative mass released.

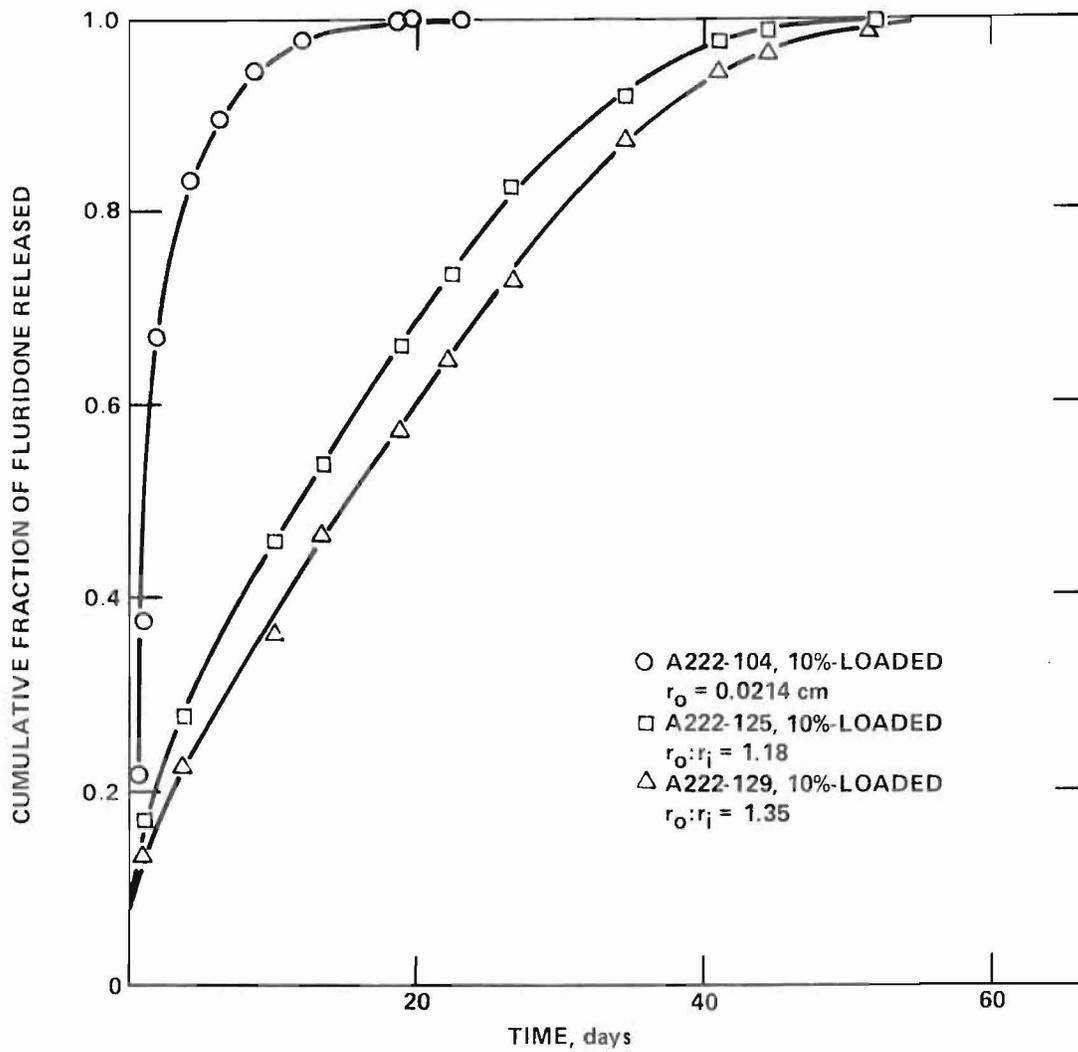


Figure 22. Cumulative fractional release of fluridone from 10-percent-loaded coaxial fibers into hard water

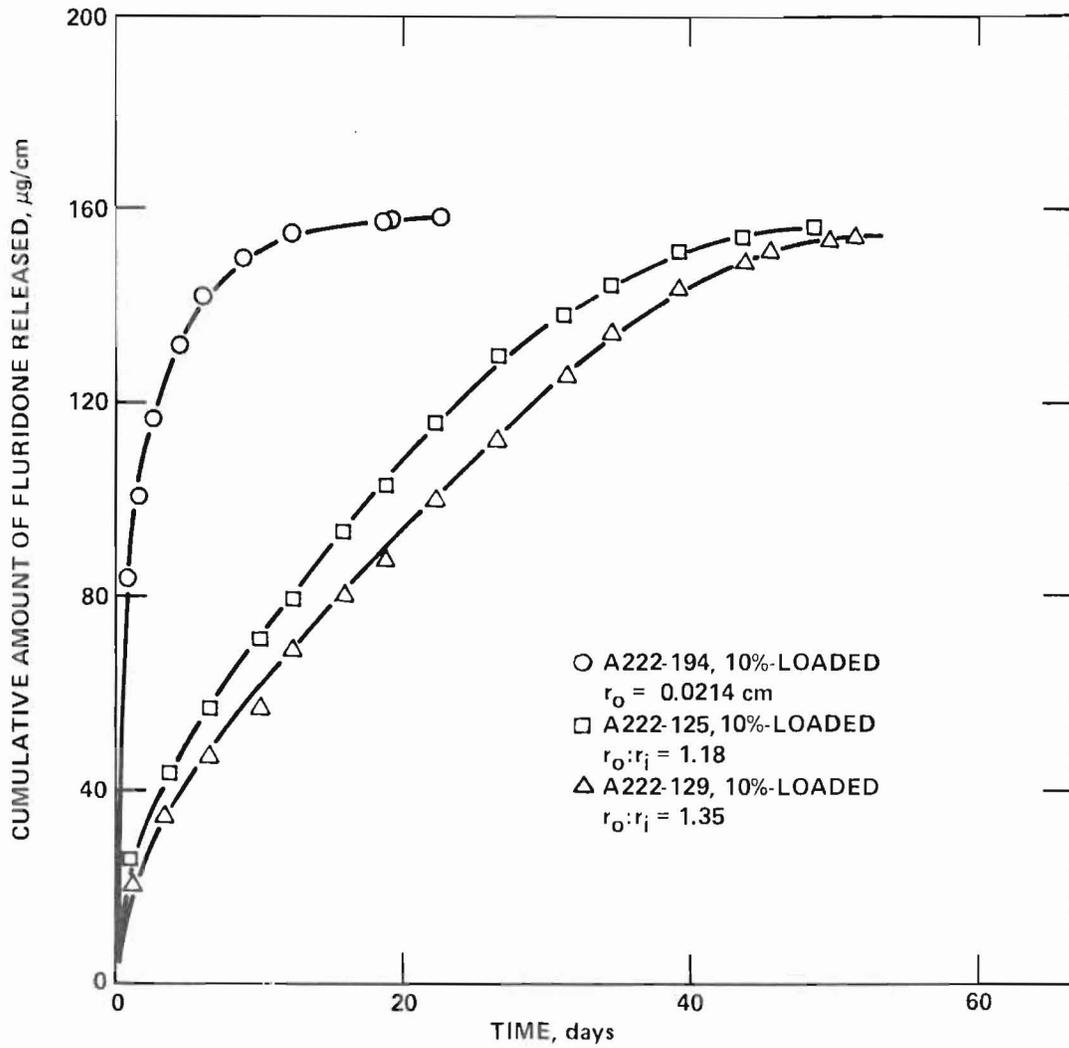


Figure 23. Cumulative release of fluridone from 10-percent-loaded coaxial fibers into hard water

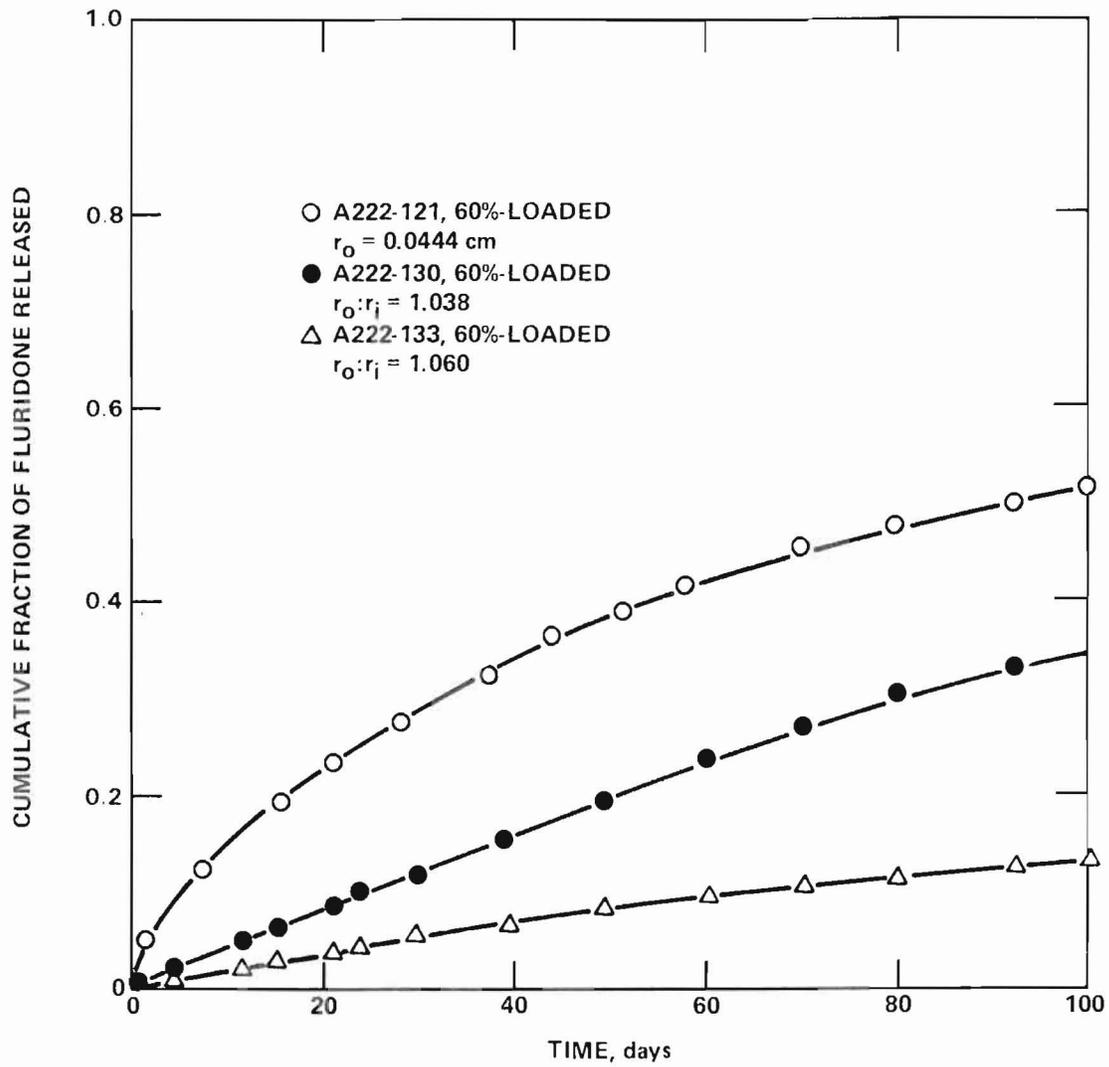


Figure 24. Cumulative fractional release of fluridone from 60-percent-loaded coaxial fibers into hard water

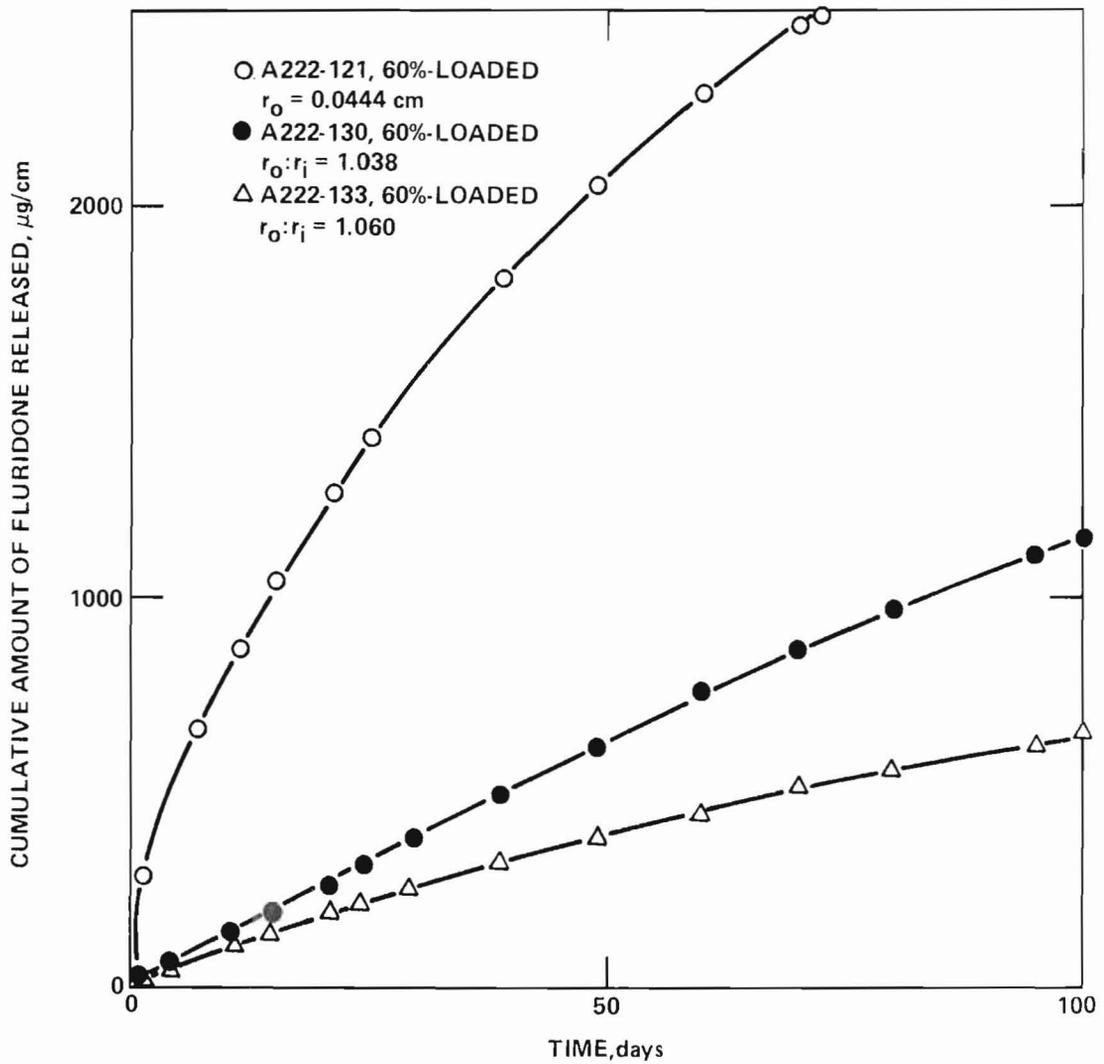


Figure 25. Cumulative release of fluridone from 60-percent-loaded coaxial fibers into hard water

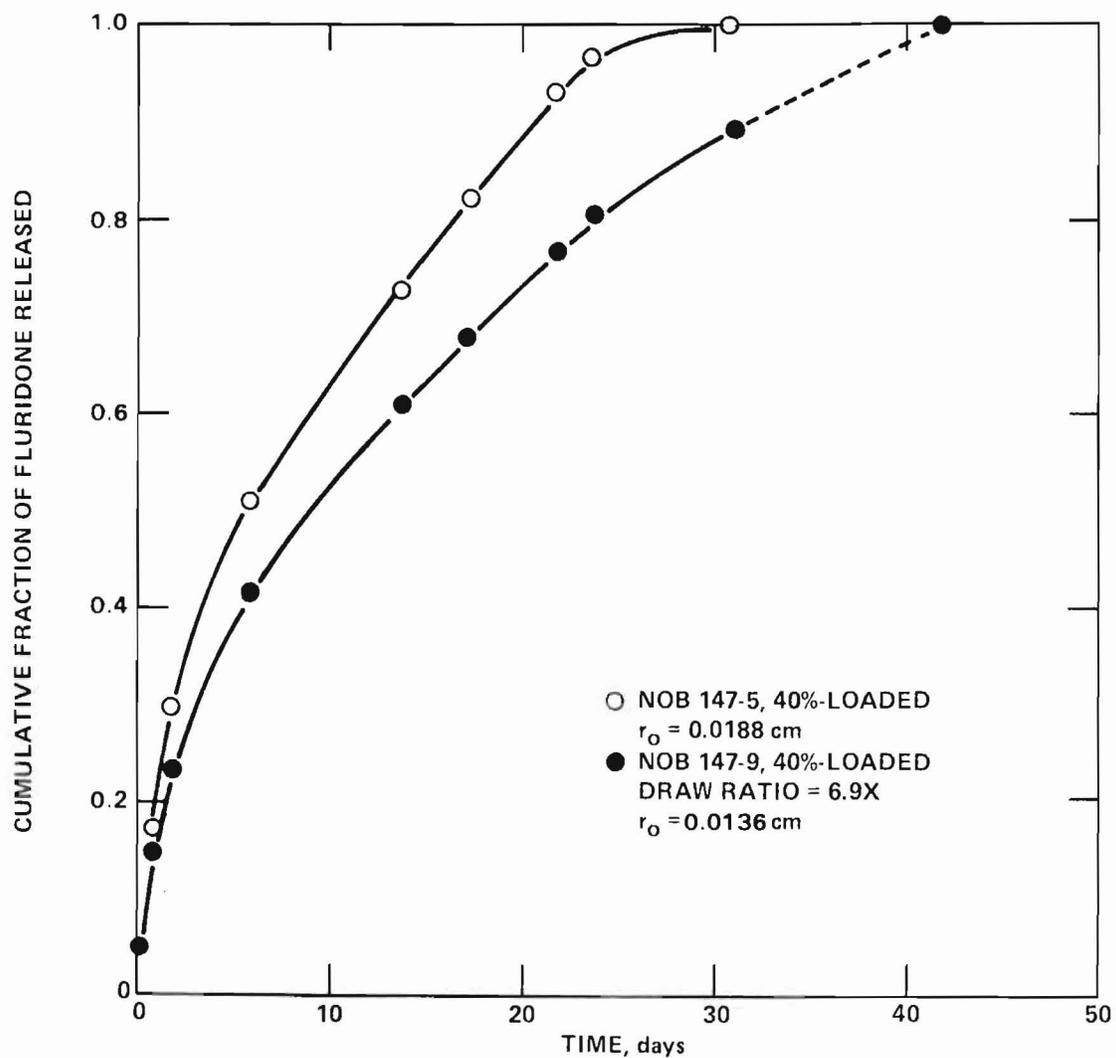


Figure 26. Cumulative fractional release of fluridone from 40-percent-loaded drawn and undrawn monolithic fibers

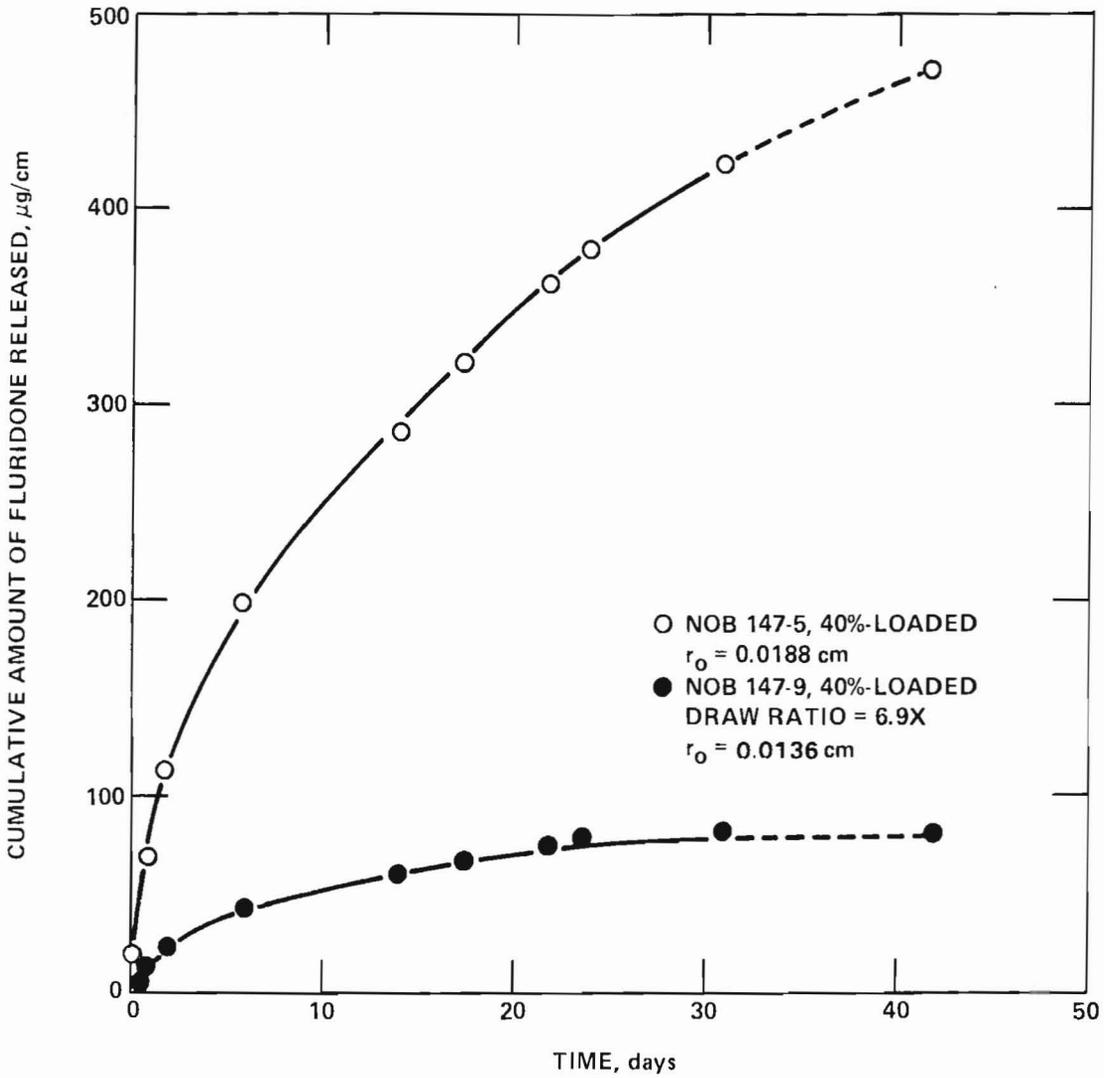


Figure 27. Cumulative release of fluridone from 40-percent-loaded drawn and undrawn monolithic fibers

Analysis of the release data gave a DC_s value of 9.14×10^{-12} g/cm/sec for the undrawn fibers and 2.57×10^{-12} g/cm/sec for the drawn fibers. The drawing of the extruded fibers, a process which increases molecular orientation and polymer crystallinity, gave the expected decrease in the DC_s value and in the rate of release of fluridone.

35. The targeted duration of release was changed from one period of 56 days to two periods of release, 20 and 40 days. The latter release rates were selected based on results from herbicide concentration/exposure time studies conducted at the WES. This change in project goals required the development of two different fiber formulations. Because diffusion-controlled release is governed by both the loading of active agent and the geometry of the system, the effects of both fluridone concentration and fiber diameter on release characteristics were now examined in detail. Fibers with two diameters (0.015 and 0.030 cm) that contained 10%, 20%, or 40% wt fluridone were prepared on the ram extruder. Feed stocks of each fluridone concentration were again prepared by solution blending, but toluene was used as the solvent instead of methylene chloride. The sheets of fluridone and PCL that formed upon evaporation of the solvent were cut into small strips for melt spinning. One batch of fibers 0.030 cm in diameter was also prepared from a melt blend of 10 percent fluridone and 90 percent PCL. Because larger quantities of fibers were now being extruded on the ram, PCL-700 (Lot 6322), which is commercially available from Union Carbide, was used as the excipient. The fluridone lot was No. X36950. The blends or feed stocks were melt spun at 90° C using a 20-mil-diam spinneret with feed rates of about 0.2 g/min. The extruded monofilaments were quenched in ambient air at fiber take-up rates of 5 to 15 ft/min.

36. The effect of fluridone concentration on cumulative fractional release from fibers with approximately the same diameter (0.015 to 0.020 cm) is shown in Figure 28. The fractional rate of release decreased, and the duration of release increased with increasing fluridone loading, which was expected on the basis of previous results. At this point, all of our data indicated that a

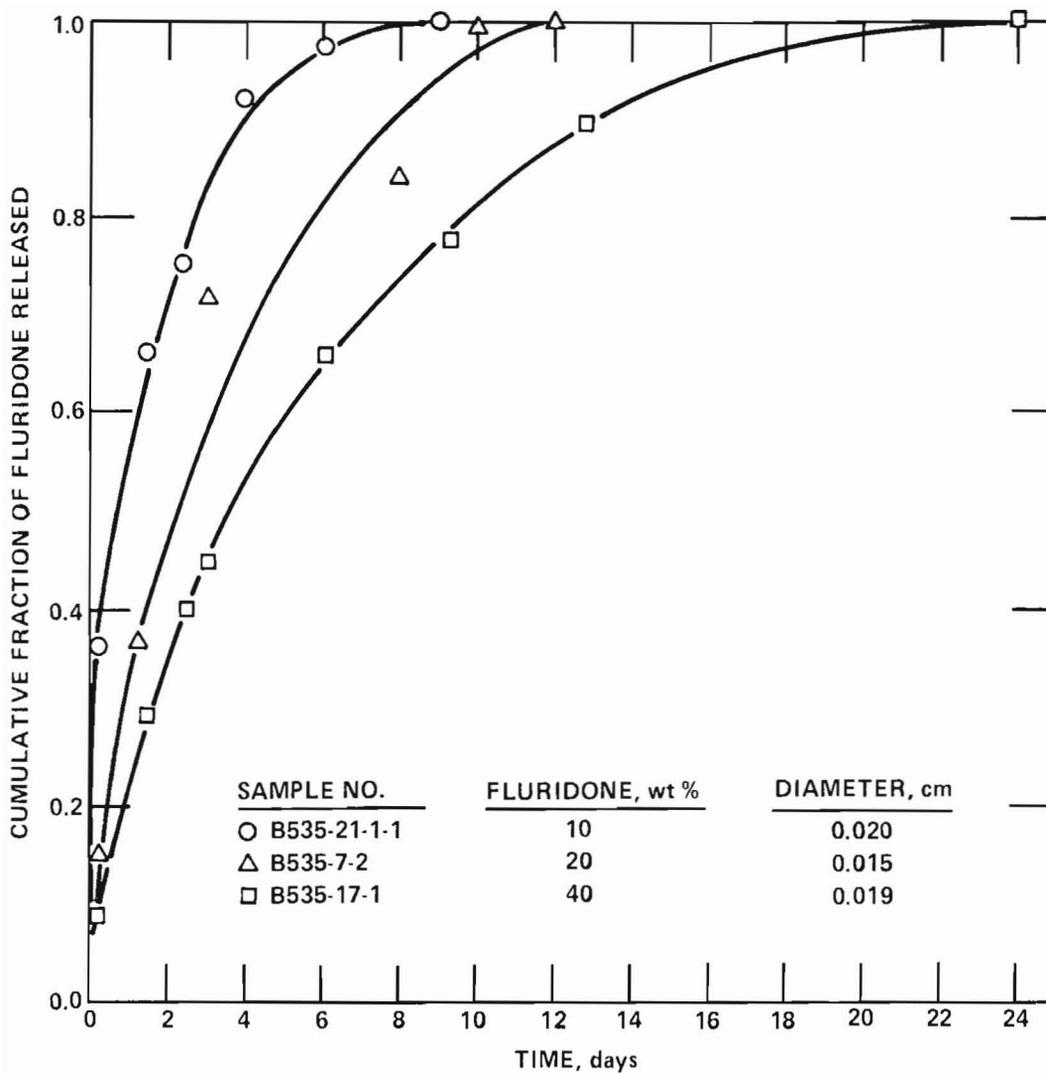


Figure 28. Effect of fluridone loading on release from monolithic PCL-700 fibers

fluridone concentration of 40% wt was too great to permit the release duration to be controlled satisfactorily by fiber diameter. Consequently, further studies were performed at a fluridone concentration of 20% wt. Figure 29 shows the effect of fiber diameter on the fractional release of fluridone at the 20% loading level. The release rate decreased with increasing fiber diameter as predicted by Fick's Law of diffusion for devices with cylindrical geometry (see Equation 1). These results, together with those obtained in the previous concentration study, indicated that the fiber diameter and fluridone loading could be varied to obtain the desired durations of release.

Scale-up of monolithic,
fluridone/PCL fiber production

37. Three field trials were scheduled during the summer of 1983 to determine the efficacy of fluridone-containing fibers under field conditions. Two pounds of active fluridone was to be applied per acre. One lot of fibers was to release fluridone for 20 days, and a second lot was to release fluridone for 40 days. On the basis of the previous laboratory studies, these conditions could be met with two 25-percent-loaded fibers, one with a diameter of 0.02 cm (20 days of release) and one with a 0.04-cm diameter (40 days of release).

38. Very few problems had been encountered in melt spinning small quantities of solution- or melt-blended feed stocks at low polymer feed rates on the ram extruder, but a number of difficulties arose in melt spinning dry blends on screw extruders at feed rates that were feasible for producing the quantities of fibers needed in field trials. The production of fibers for field trials was begun on pilot-plant equipment normally used for the production of continuous-filament yarns. This equipment consisted of a 0.75-in. screw extruder, air- or water-quench system, and a dual-godet take-up and Leeson winder.

39. Specifications for polycaprolactone. Considerable differences in melt-spinning characteristics and fiber properties can arise when different lots of excipient are used during fabrication. Therefore, a joint effort was made by Southern Research Institute and Union Carbide to establish the optimal

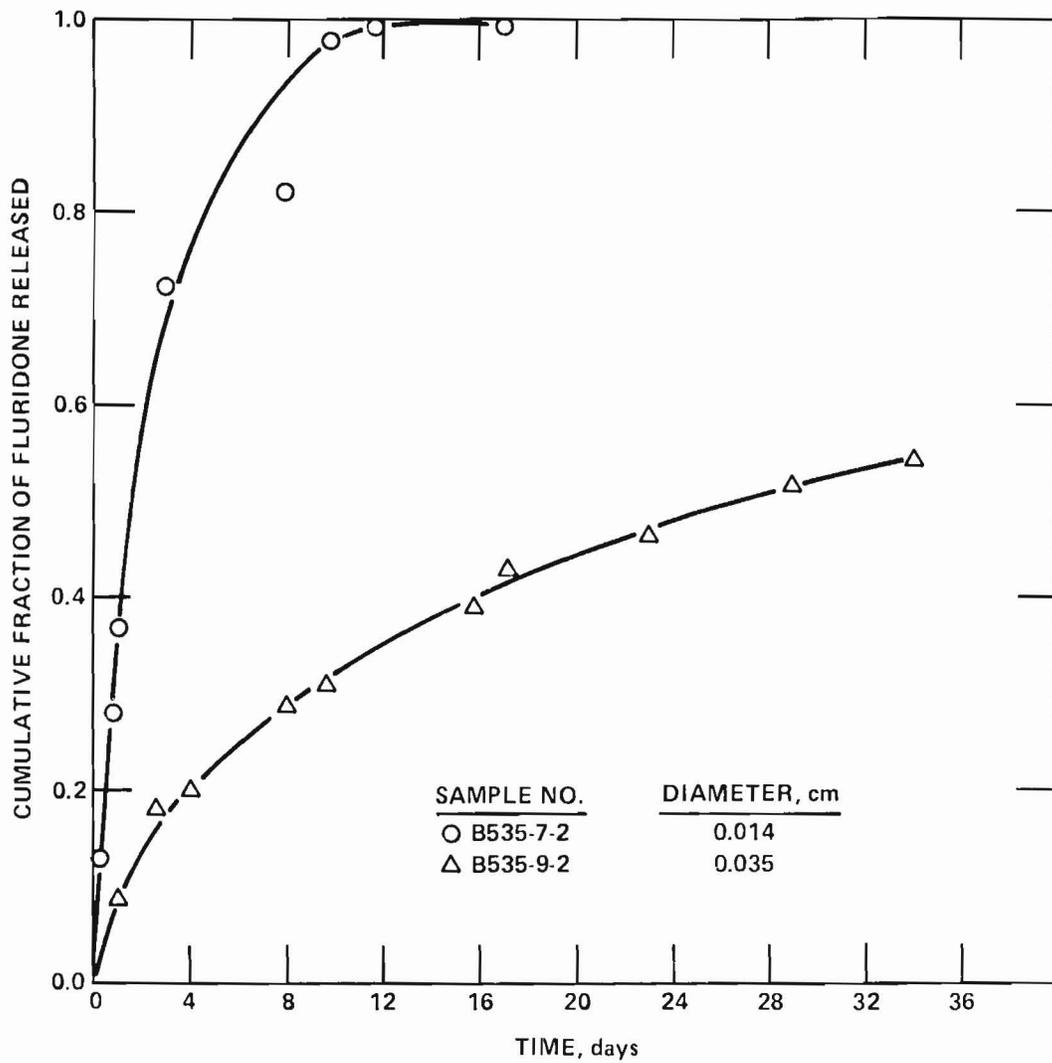


Figure 29. Effect of fiber diameter on fluridone release from undrawn monolithic PCL-700 fibers with 20-percent-weight-loadings of fluridone

melt-viscosity range of PCL-700 for fiber processing. Three PCL-700 samples of different viscosities were supplied by Union Carbide, and the melt index and melt-spinning characteristics were determined at Southern Research Institute.

40. The melt-index values given in Table 8 were determined on a Tinius Olsen plastometer according to ASTM D 1238-79. The melt-spinning characteristics, which were determined by extruding a portion of each sample on the ram extruder, are also reported in Table 8. Lot 6322 [viscosity of 210,000 centipoise (cps)] processed the most easily and formed strong fibers. Therefore, this lot and Lot 6361, with a reported viscosity of 225,000 cps, were used in preparing fibers for field trials.

Table 8
Melt Index and Extrusion Pressure of PCL-700 Polymers

<u>Union Carbide PCL-700 Lot No.</u>	<u>Viscosity cps</u>	<u>Melt Index 140° C*</u>	<u>Extrusion Pressure,** lb/in.² gage</u>
6311	280,000	1.07	1,224
6317	140,000	1.31	989
6322	210,000	1.35	770
6361	225,000	--	--

*Orifice diameter, 2 mm; weight, 2,160 g.
 **Extrusion pressure at 90° C and 0.18 cm³/sec through a 20-mil-diam by 40-mil-long orifice.

41. Preparation of feedstocks. To be economically feasible, large-scale fiber production requires an inexpensive method of blending an active agent and an excipient. The blend must also be in a convenient form for feeding the

extruder. Although solution and melt blending are excellent methods for obtaining uniform blends of small experimental quantities of fibers, these methods usually are not satisfactory for large-scale production. They are also relatively expensive because solvent and energy are required. Therefore, new and more efficient blending and pelleting processes were developed to fabricate the fluridone-releasing fibers for field trials. The most satisfactory feedstock proved to be a dry blend of finely ground PCL and the fluridone powder supplied by Eli Lilly and Company. However, special grinding techniques were necessary to reduce the PCL to a suitable size because of its low melting point (60° C) and its low glass-transition temperature (-70° C). The PCL used in the preparation of the first 80-lb lot of fibers for field testing (Samples C011-29-1 and C011-29-2) was ground to a particle diameter of about 2 mm before being mixed with fluridone. The preparation of this feedstock is described in detail in paragraphs 17-19, Appendix A. For the second and third field trials, PCL was cryogenically ground to a particle size of <850 μm (<20 mesh) by Wedco, Inc. (Bloomsbury, N.J.), prior to dry blending it with fluridone to form the feedstock.

42. Establishment of extrusion conditions. Feedstocks pelletized on the 1-in. extruder (see Paragraph 17, Appendix A) were melt spun first. Monofilaments were successfully extruded at temperatures below the melting point of fluridone with air quenching at low polymer feed rates (0.2 lb/hr). The air-quench system was used to avoid leaching of the fluridone into the water-quench bath. Extrusion conditions for four small lots of fibers produced on the 0.75-in. extruder are reported in Table 9. Because a feed rate of 0.2 lb/hr is not feasible for large-scale production, several modifications in the extrusion process were tried to increase the throughput. These modifications included increasing the feed rate, increasing the number of monofilaments extruded at a time, and increasing the extrusion temperature. None was successful. The fibers produced were either brittle and weak or were tacky and generally exhibited poor physical properties and caused processing problems.

Table 9
Conditions for Spinning Experimental Fluridone Fibers
on the 0.75-in. Melt Extruder*

Sample No.	Extrusion Temperatures, °C					Nominal Fiber Diameter cm	Fluridone Lot No.**
	Feed Zone	Metering Zone	Metering Pump	Spinneret	Melt		
B535-43-4	131	196	90	84	88	0.04	X36950
C011-11-1	133	196	128	121	126	0.06	X36950
C011-11-2	134	196	129	123	127	0.06	X36950
C011-25-1	133	196	129	121	126	0.04	827EG2

*PCL-700, Lot 6322; feed rate, 0.25 lb/hr.

**Sample B-535-43-4 contained 20 percent fluridone by weight; all other samples contained 25 percent fluridone.

43. Inadequate mixing of PCL with fluridone and insufficient quenching appeared to be the major causes of problems on the 0.75-in. extruder. Therefore, spinning trials were begun on a larger, 1-in. extruder that provided better mixing and was equipped with a long (10-ft) horizontal water-quench bath for more efficient quenching. It is important to note that spinning trials on the 0.75-in. extruder were performed with fluridone Lot X36950, and at this time new lots of fluridone (Lots 827EG2 and 944EG2) were received and used in all subsequent spinning trials. On the 1-in. extruder, fluridone-loaded monofilaments 0.04 cm in diameter were successfully extruded at temperatures above the melting point of fluridone at feed rates of about 3.5 lb/hr. The monofilaments were unusually difficult to quench, however, and it was necessary to maintain the water-quench bath at a temperature below 10° C. To obtain the smaller 0.02-cm-diam fibers for the shorter 20-day release period, the

0.04-cm-diam fibers were drawn through a 5.5-ft-long oven at 65°C using a draw ratio of 4X.

44. Effect of processing conditions on release characteristics. The effect of changes in processing conditions on the release characteristics of fibers was determined at the same time that scaled-up production procedures were being established.

45. First, the effects of different blending methods on the release characteristics of 10-percent-loaded fibers that had been melt spun on the ram extruder were determined. The release profiles in Figure 30 show that fibers prepared from melt blends release fluridone more slowly than fibers prepared from solution blends. One explanation for this effect is that residual solvent in the solution-blended fibers may act as a plasticizer and thereby increase the release rate. Because melt blending is simpler and more economical than solvent blending and because the release characteristics of the melt-blended fibers were within the range necessary to obtain the targeted release durations, all further blends were prepared by this method when experimental quantities of fibers were needed.

46. The release profiles of four fibers that were melt spun using the 0.75-in. screw extruder and pelletized feedstock are shown in Figure 31. Three variables were altered in preparing these fibers: the loading of fluridone, the fiber diameter, and the degree of orientation. In fibers with a 20% wt loading of fluridone, there was little difference in release from a 0.041-cm-diam fiber and a 0.020-cm-diam fiber produced by drawing the larger fiber. These results are explained as follows. When fibers with different diameters are extruded, the release rate is inversely proportional to fiber diameter. However, the postextrusion process of drawing (even though it decreases fiber diameter) increases the crystallinity of a fiber. This increase in crystallinity decreases permeability and consequently the rate of release. In the 20-percent-loaded fibers, these two effects (diameter and crystallinity) may have counteracted each other and resulted in release rates that were nearly identical for fibers with different diameters.

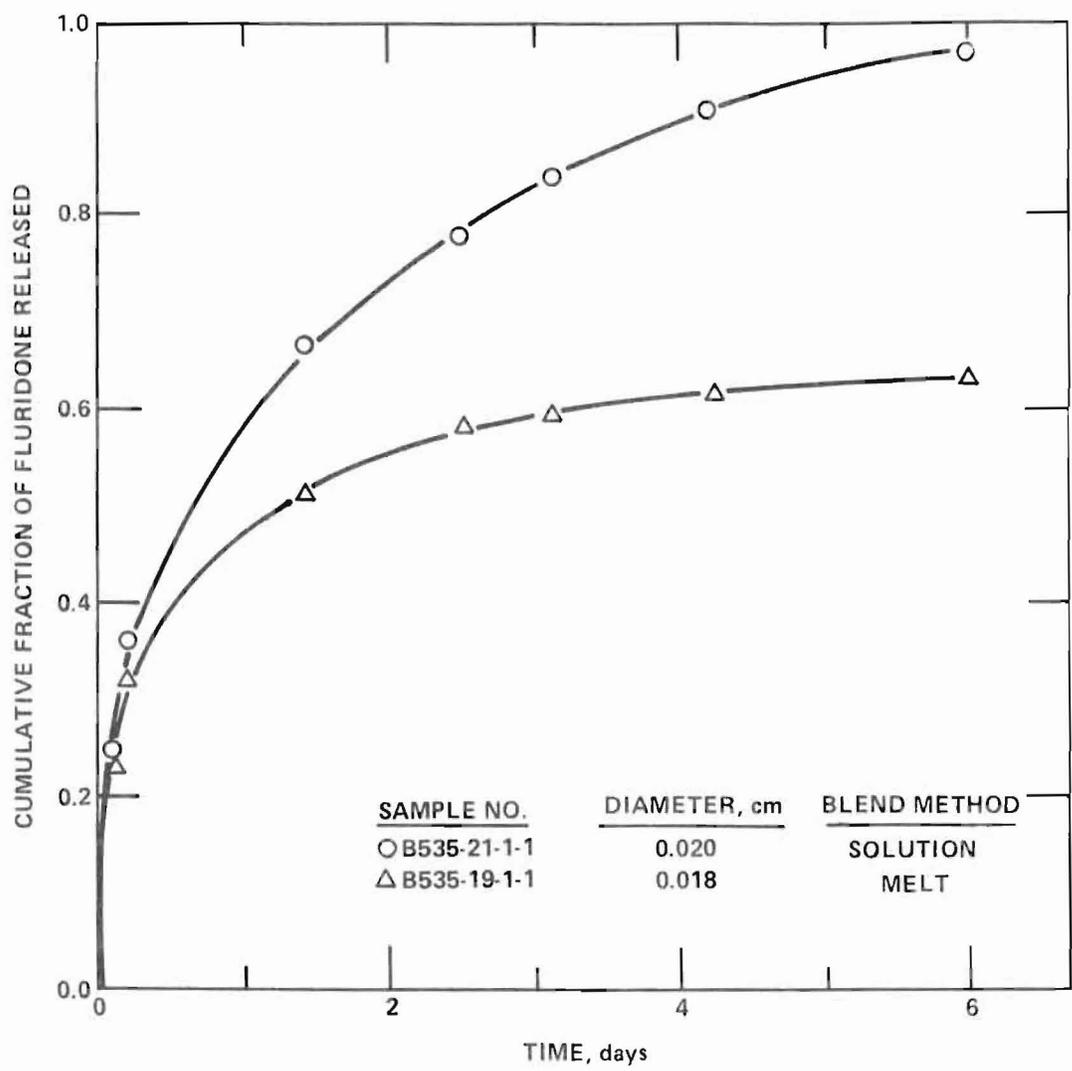


Figure 30. Effect of blending method on fluridone release from drawn monolithic PCL-700 fibers with 10-percent-weight-loadings of fluridone

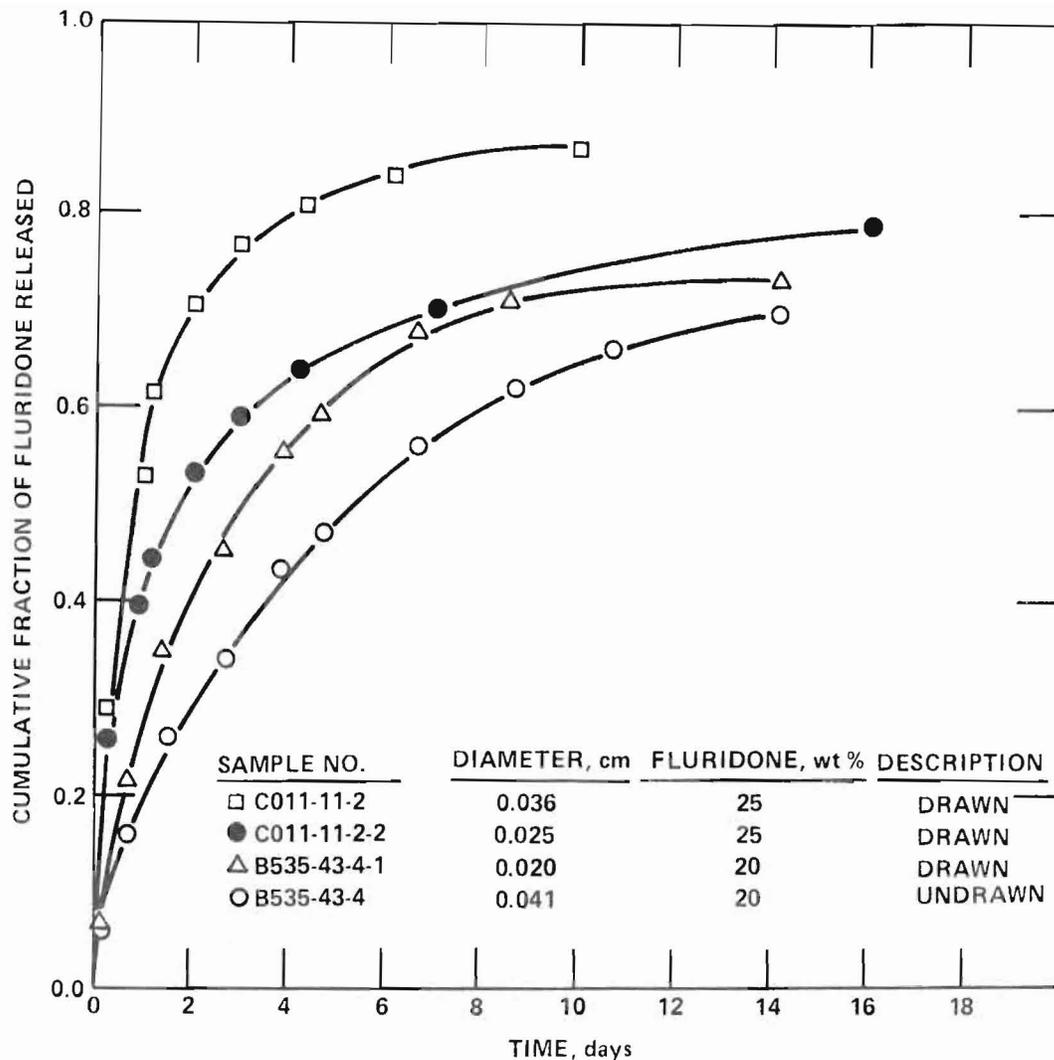


Figure 31. Fluridone release from monolithic PCL-700 fibers melt spun on the 0.75-in. extruder from pelletized feed stocks

47. The loading of fluridone was increased from 20% to 25% wt to increase the duration of release. Alterations in diameter should also have a greater effect on the release rate of fibers that contain a higher concentration of fluridone. A 0.036-cm-diam fiber and a 0.025-cm-diam fiber were prepared by drawing a 25-percent-loaded, 0.061-cm-diam fiber. Their release profiles are also shown in Figure 31. As predicted, the difference in the release rates of these two fibers was greater than the difference between the 20-percent-loaded fibers. Unexpectedly, however, the release rates of these fibers were greater than those of the 20-percent-loaded fibers. The opposite was expected on the basis of increased fluridone concentration, decreased diameter, and orientation. At the time of these experiments, problems in blending and feeding these blends to the 0.75-in. extruder were being encountered, which might have led to the anomalous results. In general, fibers prepared on the screw extruder released fluridone much more rapidly than fibers prepared on the ram extruder.

Production of monolithic fluridone/PCL fibers

48. Large-scale production of fibers for field trials was begun using the information gained from the spinning trials and release studies described in the preceding sections (paragraphs 39-47). However, during production, it was necessary to make further adjustments in the melt-spinning conditions and fiber geometry because different lots of PCL and fluridone were required to fabricate the large quantities of fibers. Short-term release studies were conducted with each lot of fibers produced for field trials to assess the effects of these adjustments on release characteristics and to correct for them in succeeding lots. The targeted durations of release were 20 and 40 days.

49. The first field trial was scheduled for Toledo Bend, La., in June 1983. Fifty pounds each of a 20-day-releasing fiber and a 40-day-releasing fiber were to be produced for this trial.

50. Fibers 0.04 cm and 0.02 cm in diameter were produced from 25:75 fluridone/PCL pellets. All fibers were melt spun on the Killion extruder equipped with a 1-in.-diam mixing screw (20:1 length/diameter), a Model KMB-100

melt blender, and a 0.075-in.-diam die (12:1 length/diameter). The extruded fiber passed through a 10-ft-long water-quench bath at a temperature of 5° to 10° C, through guides, and over dual-godet take-up rolls. Fiber was collected on paper spools using a Model 959 Leeson winder at rates that yielded a fiber 0.04 cm in diameter. Approximately 80 lb of fiber was produced. Forty pounds were shipped without further processing (Sample C011-29-1), and 40 lb were drawn to a 0.02-cm diameter (Sample C011-29-2). Both samples were provided in 2- to 3-in. lengths. Cutting was accomplished with a serrated blade while the fiber was held in place on the collecting spool with a metal holder designed and built at Southern Research Institute. The exact conditions used in processing Lots C011-29-1 and C011-29-2 are reported in Table 10. Approximately one half (20 lb) of Sample C011-29-2 was prepared directly from an unpelletized powder blend of fluridone and PCL. Because the appearance of the fibers did not change and only minor problems (occasional bridging) were encountered in feeding, the powder blend was also used for subsequent experimental samples.

51. The release of fluridone from the two lots of fibers prepared for the Toledo Bend field trials is illustrated in Figure 32. The duration of release of the 0.04-cm-diam fiber prepared from pelletized feedstock (C011-25-1 in Figure 32) was only 10 days instead of the targeted 40 days. Extruding the fibers above the melting point of fluridone and using a water quench instead of an air quench may have shortened the release period. Scanning electron microscopy showed fluridone crystals on the fiber surface (Figure 33), which indicates that a migration of fluridone occurred under these fabrication conditions. Release from this field-trial sample was compared with fluridone release from a 0.04-cm-diam sample that had been prepared from unpelletized feed stock (C011-29-1), and the field trial sample was found to release more slowly. In addition to the effects of slight alterations in extrusion conditions, it is possible that a porous diffusion mechanism may also contribute to fluridone release. This contribution would be more evident in a less compact fiber prepared from a powder blend. The 0.02-cm-diam fibers that had been provided for field trials released their fluridone in only 2 days. The release was so rapid that little difference could be seen between fibers that had been prepared from pelletized and powder blends. Fluridone crystals were also

Table 10
Conditions for Melt Spinning Fluridone Fibers Used in Field Trials*

Sample No.	Temperature, °C				Feed Rate lb/hr (approx.)	Nominal Fiber diam, cm	Quantity lb	Fluridone Lot No.	PCL-700 Lot No.
	Feed Zone	Metering Zone	Melt Blender	Die					
C011-29-1	76	217	162	140	3.5	0.04	40	827EG2	6322**
C011-29-2	62	186	158	120	3.5	0.02	40	827EG2	
C011-45-1	60	132	139	103	2.2	0.08	50	944EG2	6361†
C011-45-2	59	132	139	104	2.2	0.12	50	944EG2	
C011-45-3	60	130	138	106	2.2	0.08	50	944EG2	
C011-45-4	57	125	132	100	2.2	0.04	46	944EG2	

* All fibers contained 25-percent fluridone and 75 percent PCL-700 by weight and were in 2- to 3-in. lengths.

** Ground at SoRI on a Wiley mill with a 2-mm screen.

† Ground at Wedco, Inc., to <20 mesh.

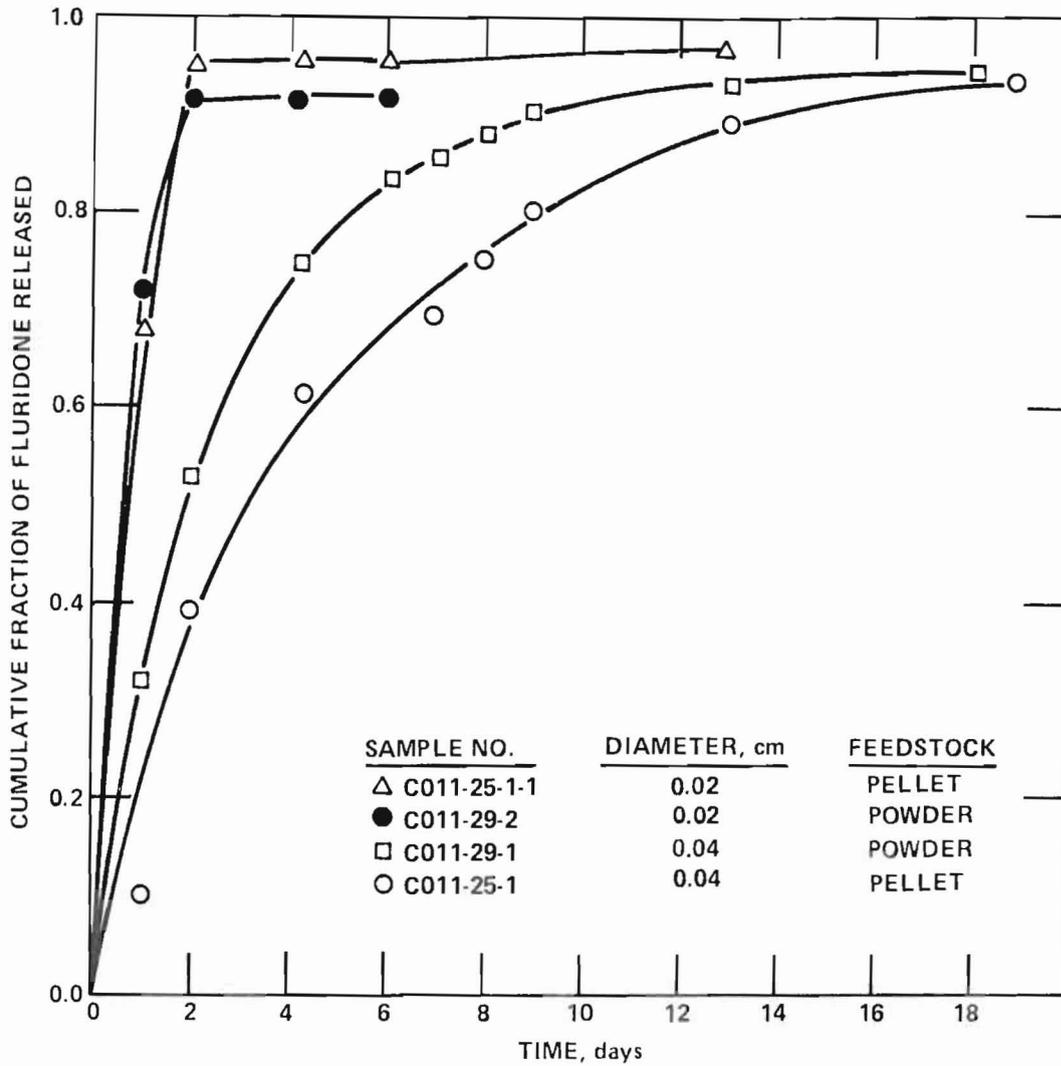
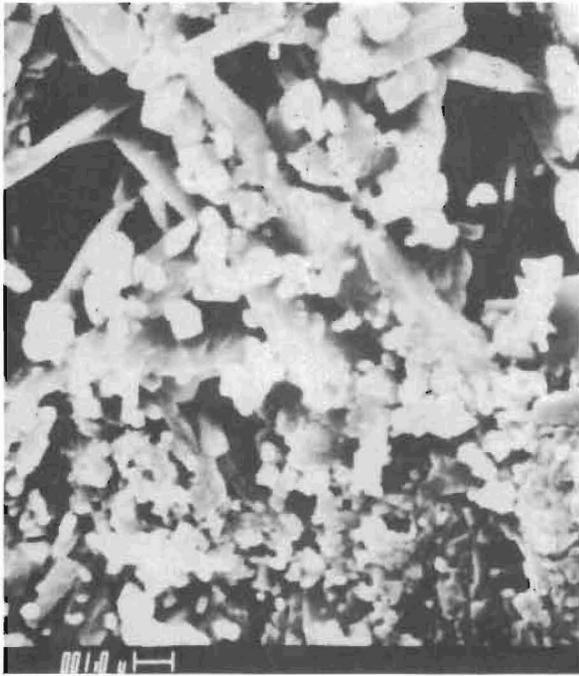


Figure 32. Fluridone release from monolithic fluridone/PCL-700 (25:75) fibers produced for the Toledo Bend field trials



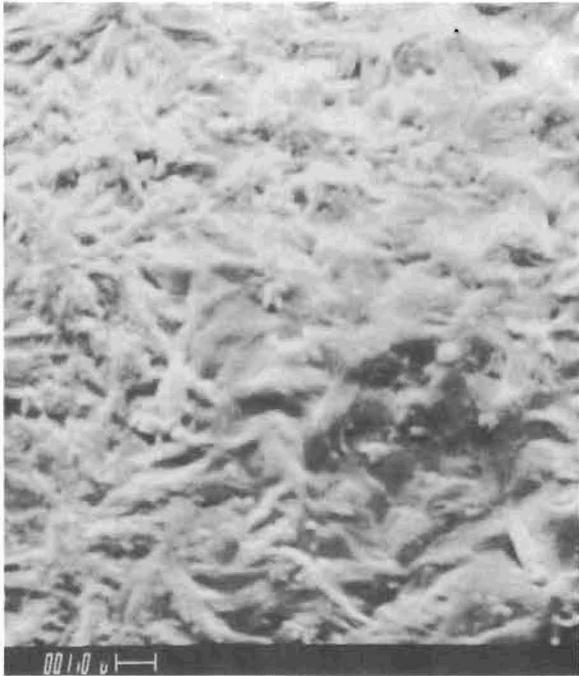
A. C011-29-1

0.04-cm DIAM



C011-29-2

0.02-cm DIAM



B. C011-45-1

0.08-cm DIAM



C011-45-2

0.12-cm DIAM

Figure 33. Scanning electron micrographs of the surfaces of fibers produced for (a) Toledo Bend (Fluridone Lot 827EG2, PCL Lot 6322) and (b) Florida (Fluridone Lot 944EG2, PCL Lot 6361) 5,000X magnification.

present on the surface of these fibers (Figure 33), which suggests that the drawing process enhanced the migration effect caused by the fabrication conditions.

52. The second field trial was scheduled for Florida in August 1983. Again the goal was 100 lb of fiber--half with a 20-day release period and half with a 40-day release period.

53. Several fabrication conditions were changed in preparing fibers for the last two field trials in Florida and Washington State. First, a different PCL lot (Lot 6361) was used, one that had been cryogenically ground to a particle size of $<850 \mu\text{m}$ at Wedco, Inc. Second, a different lot of fluridone (Lot 944EG2) was used. Third, the changes in the raw material lots required changes in the melt-spinning conditions. Last, fiber diameters were increased to extend the duration of fluridone release. Therefore, small quantities of test fibers with diameters of 0.05, 0.08, 0.11, and 0.15 were prepared and evaluated in release studies prior to the production of large quantities of fibers.

54. Release studies conducted for 1 week indicated that fibers 0.08 and 0.11 cm in diameter would provide approximately 20 and 40 days of release (Figure 34). Therefore, 50 lb of each fiber was prepared for the Florida field trials. Any alterations in the fabrication conditions that were used in preparing the 20-day fiber (0.08-cm diameter, Sample C011-45-1) and the 40-day fiber (0.12-cm diameter, Sample C011-45-2) are reported in Table 10.

55. Continuation of the release studies with the 0.08- and 0.11-cm-diam test fibers indicated that the release duration of the 0.08-cm fibers would be approximately 40 days instead of the 20- to 30-day release period initially predicted and that the 0.11-cm fibers would release fluridone for an even longer period (Figure 34). An additional concern with the larger 0.11-cm-diam fiber was that the quantity of fluridone released might be below the level needed to kill weeds. Therefore, for the field trials in Washington State, a 50-lb lot of 0.08-cm-diam fiber was supplied to provide the longer targeted release period of 40 days, and 0.12-cm-diam fibers were replaced with a 46-lb lot of 0.04-cm-diam fibers (see Figure 32) to provide a shorter release period of 10 to 20 days. The fabrication conditions for these field-trial samples

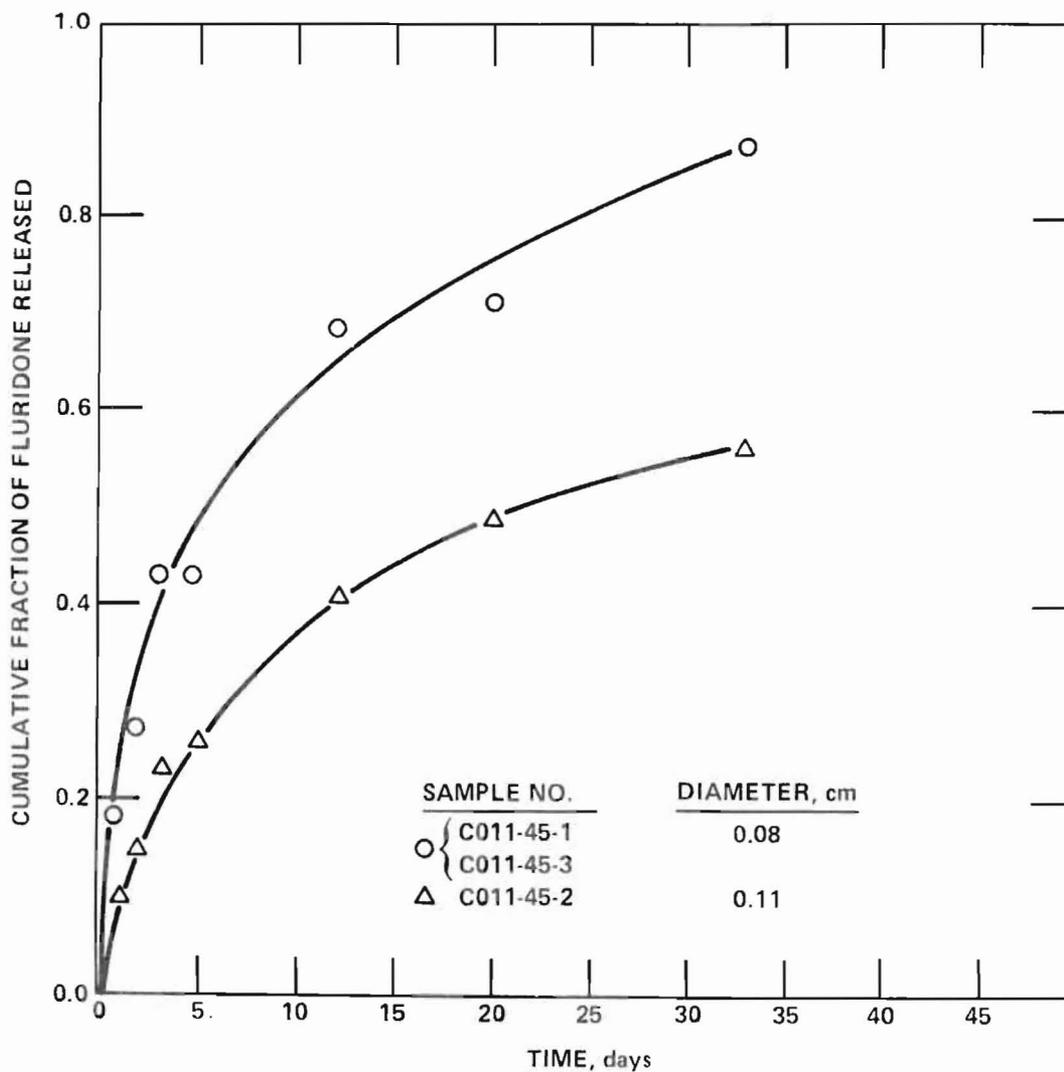


Figure 34. Fluridone release from monolithic fluridone/PCL-700 (25:75) fibers produced for the Florida and Washington field trials

(0.08-cm diameter, Sample C011-45-3 and 0.04-cm diameter, Sample C011-45-4) are also given in Table 10.

Effect of fluridone
lot and fiber diameter

56. During the preparation of fibers for field trials, it was noted that the lot of fluridone being used affected the melt-spinning characteristics of feedstocks and the release characteristics of fibers. These effects were now examined in more detail.

57. Three samples of fluridone, identified as Lots X36950 (97-percent active), 827EG2 (97.8-percent active), and 944EG2 (95-percent active), had been used thus far in the program. Lot X36950 was used in melt-spinning trials on the ram extruder in initial production studies on the 0.75-in. ram extruder. There were no major problems in feeding blends containing this lot to the extruder or in extruding the feedstocks below the melting point of fluridone. The second fluridone sample, identified as Lot 827EG2, was used to prepare the fibers for field trials in Toledo Bend. It was more difficult to feed the extruder when this lot was mixed with PCL powder or PCL pellets, and fibers could only be extruded above the melting point of fluridone. Also, the surface of large-diameter fibers was rough when this lot was used in a powdered feedstock. As shown in the scanning electron micrographs in Figure 33, fluridone from this lot migrated to the surface of fibers and appeared as crystals. This suggests poor blending of the fluridone and PCL, even at temperatures above the melting point of fluridone. The last fluridone lot (Lot 944EG2) was used to prepare fibers for the field trials in Florida and Washington State. It appeared to have a plasticizing effect on the PCL that the previous lot did not have. Tacky fibers formed that were difficult to quench, and consequently, the melt-spinning temperature was lowered (see Table 10, Samples C011-45-1, -2, -3, -4).

58. To confirm the differences in fluridone Lots 827EG2 and 944EG2, blends were prepared with PCL Lot 6361. The melting point of both blends was determined on a Perkin-Elmer thermal analyzer. The melting point of PCL alone was 53.7° C; the 827EG2 blend, 48.9° C; and the 944EG2 blend, 46.2° C. Each blend was then melt spun on the 1-in. extruder. Temperatures 40° to 80° C higher were required to extrude fibers with the blend containing Lot 827EG2

(see Table 11). The difference in melt temperature and in melt-flow characteristics between the two lots suggests that the inactive material present in a particular lot has a major effect on the melt-spinning characteristics of a feedstock.

59. The release profiles of the fibers prepared from these two lots of fluridone are shown in Figures 35 and 36. The effects of fluridone lot and fiber diameter were examined concurrently. The rate of fluridone release from fibers prepared with Lot 944EG2 was greater than that of fibers prepared from Lot 827EG2, and this difference was more pronounced in fibers with smaller diameters. Increased susceptibility to changes in raw materials and fabrication conditions is to be expected in fibers with smaller diameters and faster rates of release.

Pellet Formulations for Controlled Release of Fluridone

60. The fibers produced for field trials proved to be effective in killing aquatic weeds in Toledo Bend and in Florida canals with slow-moving water but were not as effective in Washington State where they were tested in fast-flowing water. The primary problems encountered under field conditions involved application. The fibers were difficult to apply with conventional equipment, and they remained on the surface of the water too long before sinking and entangling with the weeds.

61. To circumvent these application problems, large-diameter fibers or pellets were developed. Pellet diameter was restricted to 3 mm or greater because field applicators can accommodate formulations of this size. Increasing the diameter of the fluridone/PCL fibers decreases the release rate and extends the duration of release greatly. Extensive modifications of the fibrous system were therefore necessary to obtain the desired 20- and 40-day release periods. Three approaches were used. First, water-soluble additives were incorporated into the system. Water-soluble additives leach out of pellets when they are exposed to water, create a porous polymer matrix, and increase the release rate. Second, the geometry of the pellets was altered to optimize release characteristics. This approach was taken on the tenet that the ratio of surface area to volume plays a major role in determining release

Table 11
Effects of Fluridone Lot on Conditions for
Spinning Fibers on the 1.0-in. Melt Extruder

Sample No.	Extrusion Temperature, °C			Die	Nominal Fiber Diameter, cm	Fluridone Lot No.
	Feed Zone	Metering Zone	Melt Blender			
C011-33-1	112	208	194	200	0.11	827EG2
C011-33-2	112	208	194	175	0.08	(97.8%
C011-33-3	112	208	194	175	0.05	active
C011-33-4	112	208	194	175	0.15	ingredients)
C011-39-1	81*	128*	137*	110*	0.11	944EG2
C011-39-2	81	128	137	110	0.15	(95% active
C011-39-3	81	128	137	110	0.08	ingredients)
C011-39-4	81	128	137	110	0.04	

Note: Data for PCL-700, Lot No. 6361, powder/powder (type/blend),
at feed rate of approximately 3.5 lb/hr.

*Increasing spin temperature reduced melt viscosity rapidly,
and fiber production was not possible.

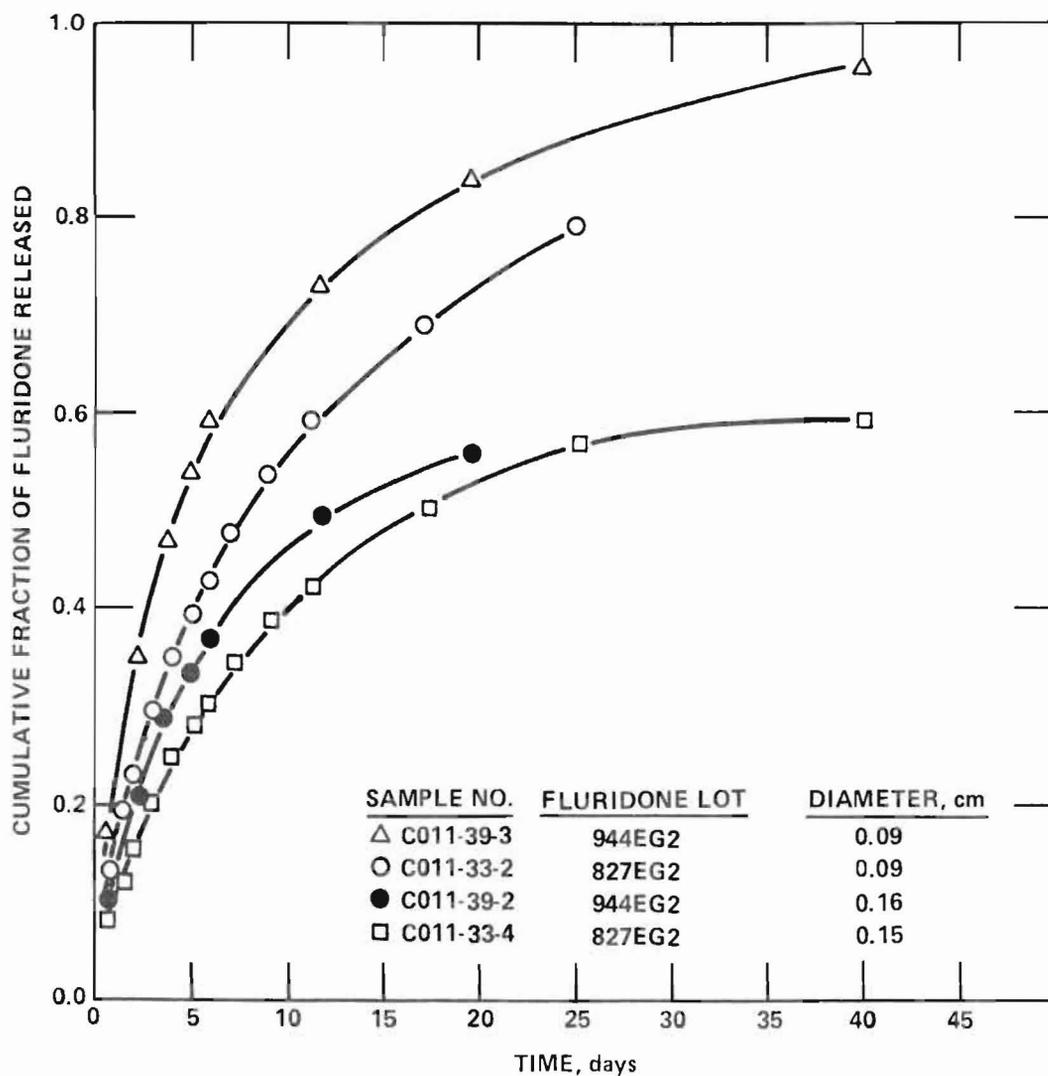


Figure 35. Effect of fluridone lot on release from monolithic fluridone/PCL-700 (25:75) fibers with nominal diameters of 0.08 and 0.15 cm

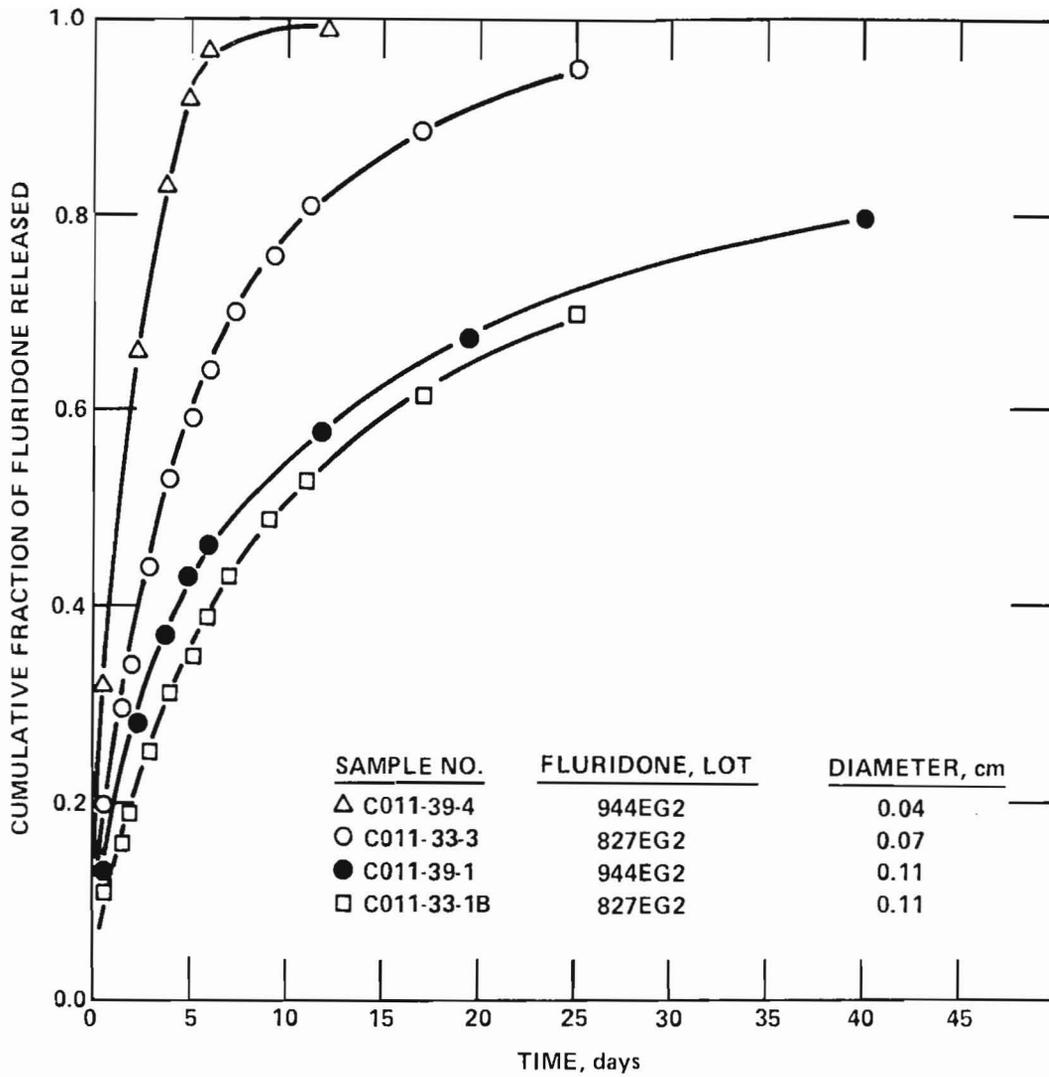


Figure 36. Effect of fluridone lot on release from monolithic fluridone/PCL-700 (25:75) fibers with nominal diameters of 0.05 and 0.11 cm

characteristics. A combination of these two approaches led to the development of one pellet system, which is disk shaped and contains hydroxypropyl cellulose, a water-soluble additive. The third approach was to modify previously prepared fibers with 20- and 40-day durations of release. This approach led to the development of a second pellet system that consists of a bundle of short fibers coated with a water-soluble mixture of polyethylene glycols. The diameter of this system is also large enough for easy application, and the coating dissolves readily after immersion in water.

Effect of pellet additives on fluridone release

62. Four water-soluble additives were evaluated for their effect on fluridone release: hydroxypropyl cellulose (Klucel, Type GF, Hercules, Inc., Wilmington, Del.), polyethylene glycol 8000 (Carbowax 8000, Union Carbide, Danbury, Conn.), triethyl citrate (Pfaltz and Bauer, Inc., Stanford, Conn.), and sodium chloride. Of the four additives, Klucel was studied the most thoroughly.

63. Large fibers or rods having three diameters (0.24, 0.32, and 0.40 cm) and containing fluridone, PCL, and Klucel, were melt spun on the 1-in. extruder. The composition and fabrication conditions for each lot of fibers are given in Table 12.

64. Release studies were conducted as usual in hard water. As shown in Figure 37, increasing the concentration of Klucel from 5% to 13% wt had little effect on the release rate of fluridone from pellets with a diameter of 0.24 cm. In the larger pellets (0.40-cm diameter), slightly more fluridone was released from the samples with a 13% wt loading. This effect, however, was small. Pellets containing 13% wt Klucel were tested further to determine the effect of rod length on fluridone release. The release profiles in Figure 38 show that decreasing the rod length increases the release rate.

65. Because fluridone is released from the fibrous PCL system by a solution-diffusion mechanism, a reduction in the fluridone loading will shorten the duration of release. Therefore, to compensate for the large diameter that was needed in pellets, the loading of fluridone was reduced to low, but still practical, levels. The effect of incorporating Klucel was then examined. For

Table 12
Extrusion Conditions, Composition, and Diameters of Fluridone Rod Samples

Sample No.	Composition	Extruder Temperature, °C				Rod Diameter* cm
		Feed Zone	Metering Zone	Melt Blender	Die	
C011-41-A	100% PCL**	108	152	158	110	0.40
C011-41-C		108	152	158	110	0.32
C011-41-B		108	152	158	110	0.24
C011-41-2	75% PCL**	108	152	158	110	0.40
C011-41-1	25% Fluridone†	108	152	158	110	0.32
C011-41-3		108	152	158	110	0.24
C011-41-6	5% Klucel††	145	203	187	150	0.40
C011-41-4	24% Fluridone†	145	203	187	150	0.32
C011-41-5	71% PCL**	145	203	187	150	0.24
C011-41-7	22% Fluridone†	118	152	137	110	0.40
C011-41-8	65% PCL**	118	152	137	110	0.32
C011-41-9	13% Klucel††	118	152	137	110	0.24

*Polymer feed rate = 3.5 lb/h.
 **Union Carbide PCL-700, Lot 6361.
 †Fluridone Lot 827EG2.
 ††Klucel (hydroxypropyl cellulose) Lot 3175.

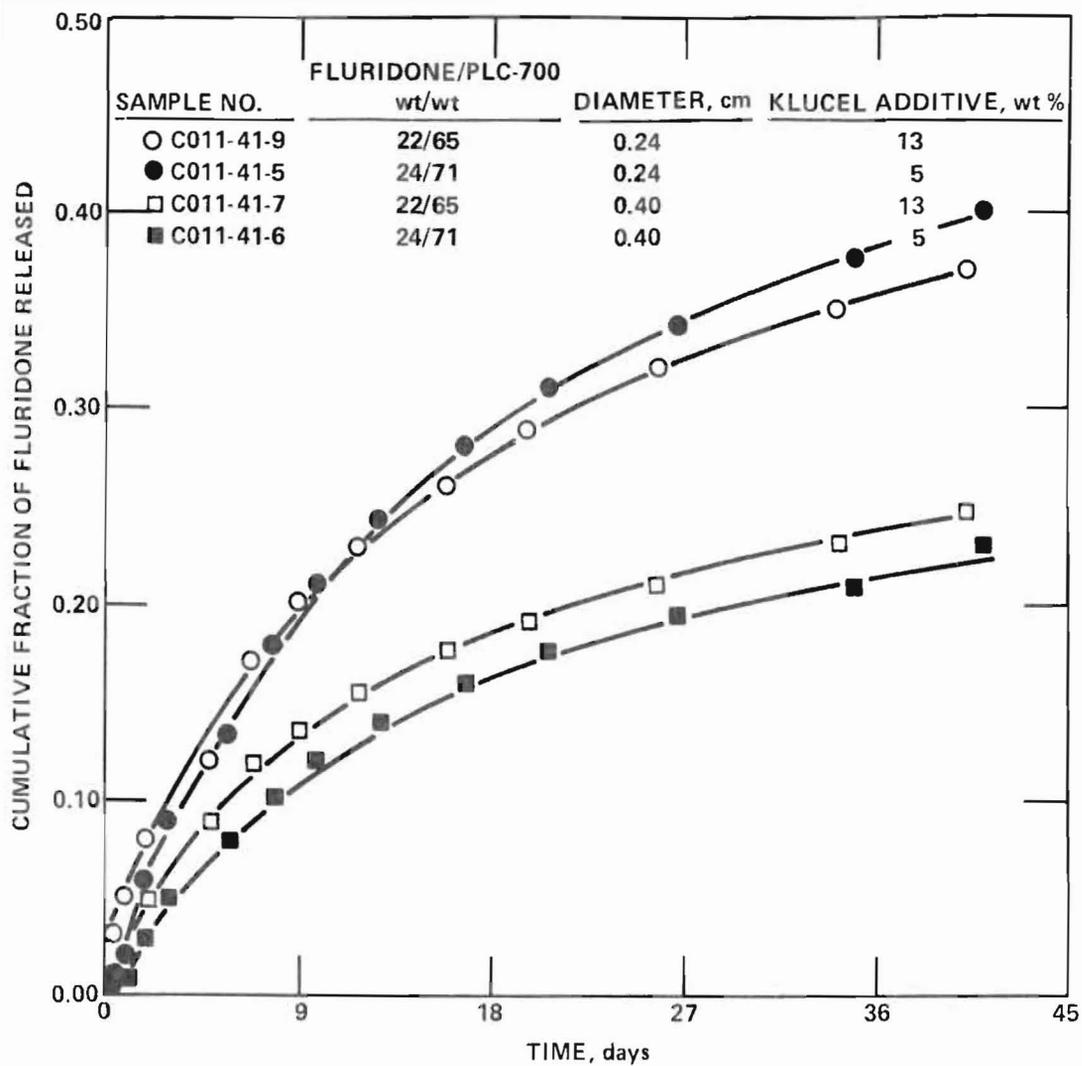


Figure 37. Effect of Klucel additive on fluridone release from monolithic fluridone/PCL-700 rods

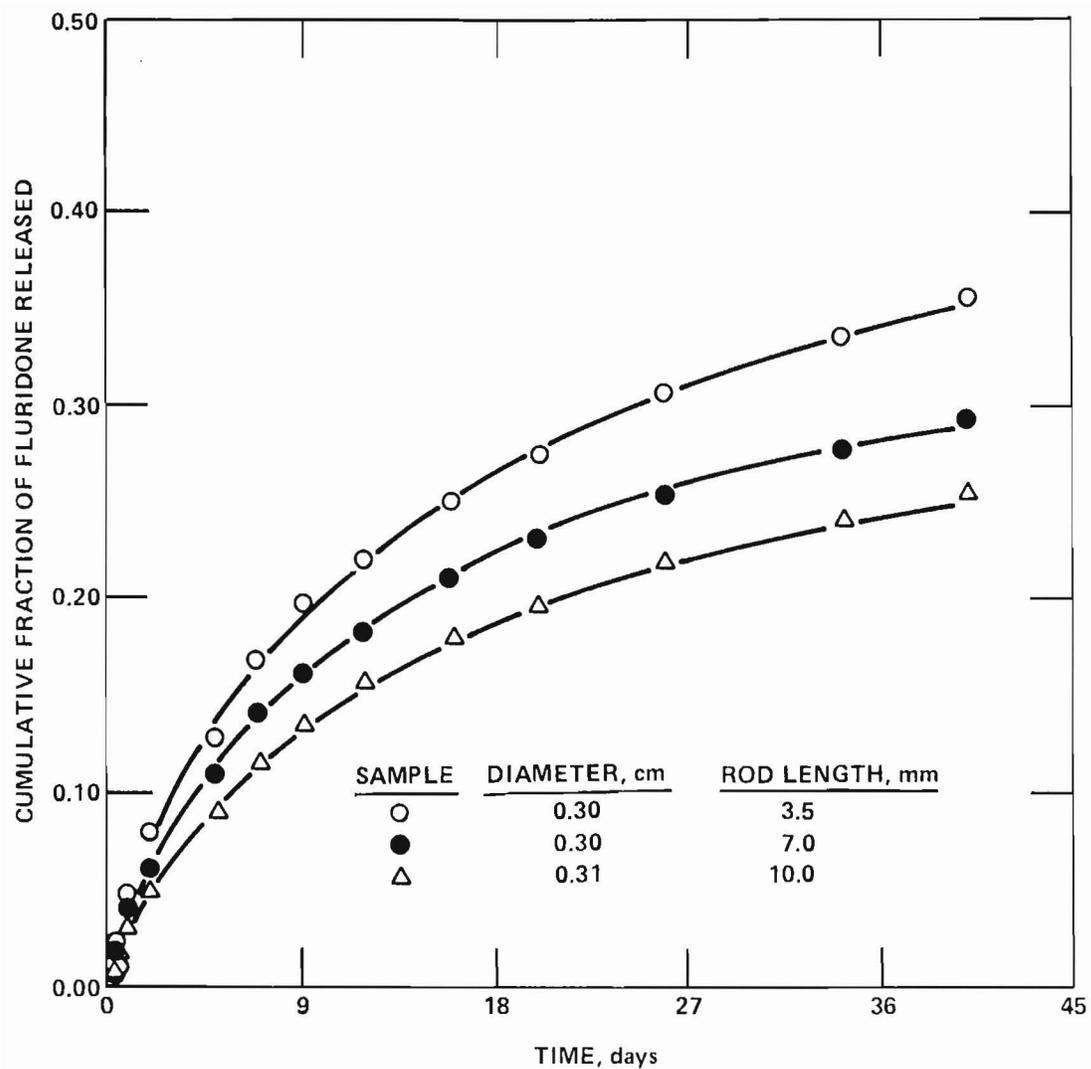


Figure 38. Effect of rod length on fluridone release from monolithic fluridone/PCL-700/Klucel(23:64:13) rods (Sample C011-41-8)

these studies, dry blends with particle sizes of 180 to 250 μ (60 to 80 mesh) were melt spun on the Tinius Olsen plastometer. The release profiles of pellets containing 10% wt fluridone and concentrations of Klucel (HPC) ranging from 20% to 90% wt are shown in Figure 39. (The diameter and length of the pellets were constant.) Although the samples that did not contain PCL exhibited the fastest release rate, they disintegrated within 1 week and therefore were not useful. The next fastest rate of release was observed in samples with the composition 10:40:50 fluridone/PCL/HPC. The HPC loadings that were higher and lower than 50 percent resulted in less release. This seemingly anomalous behavior may be caused by the partitioning of fluridone between the two excipients or by differences in pore structure at different HPC loadings.

66. Polyethylene glycol 8000 was not as effective as HPC in promoting fluridone release (see Figure 40). Moreover, these pellets were waxy at loadings greater than 50%, which could cause the pellets to stick together during storage.

67. Sodium chloride (NaCl) also had little effect on fluridone release (Figure 41). Scanning electron microscopy (SEM) was used to compare the effects of sodium chloride and HPC (the most promising additive) on the structure of the polymeric matrix. The SEM photographs (Figure 42) suggest that the pores that form when sodium chloride dissolves from the pellet matrix are discontinuous. These pores may act like pockets that trap and immobilize fluridone. Because fluridone must still diffuse through the bulk polymer phase, release is affected very little. On the other hand, HPC appears to form channels in the PCL matrix upon dissolution. These channels can increase the release rate by providing an alternative pathway for diffusional release.

68. One additional additive was tested, triethyl citrate (TEC). Unlike the other additives, however, TEC decreased the fluridone release rate. The release profiles of these pellets are shown in Figure 43, along with those of fluridone/PCL fibers with 20- and 40-day durations of release. The reduction in release upon addition of TEC may be caused by low fluridone solubility in TEC and partitioning of the fluridone into the polymer phase. In effect, these factors would increase the concentration of fluridone in PCL and decrease the release rate.

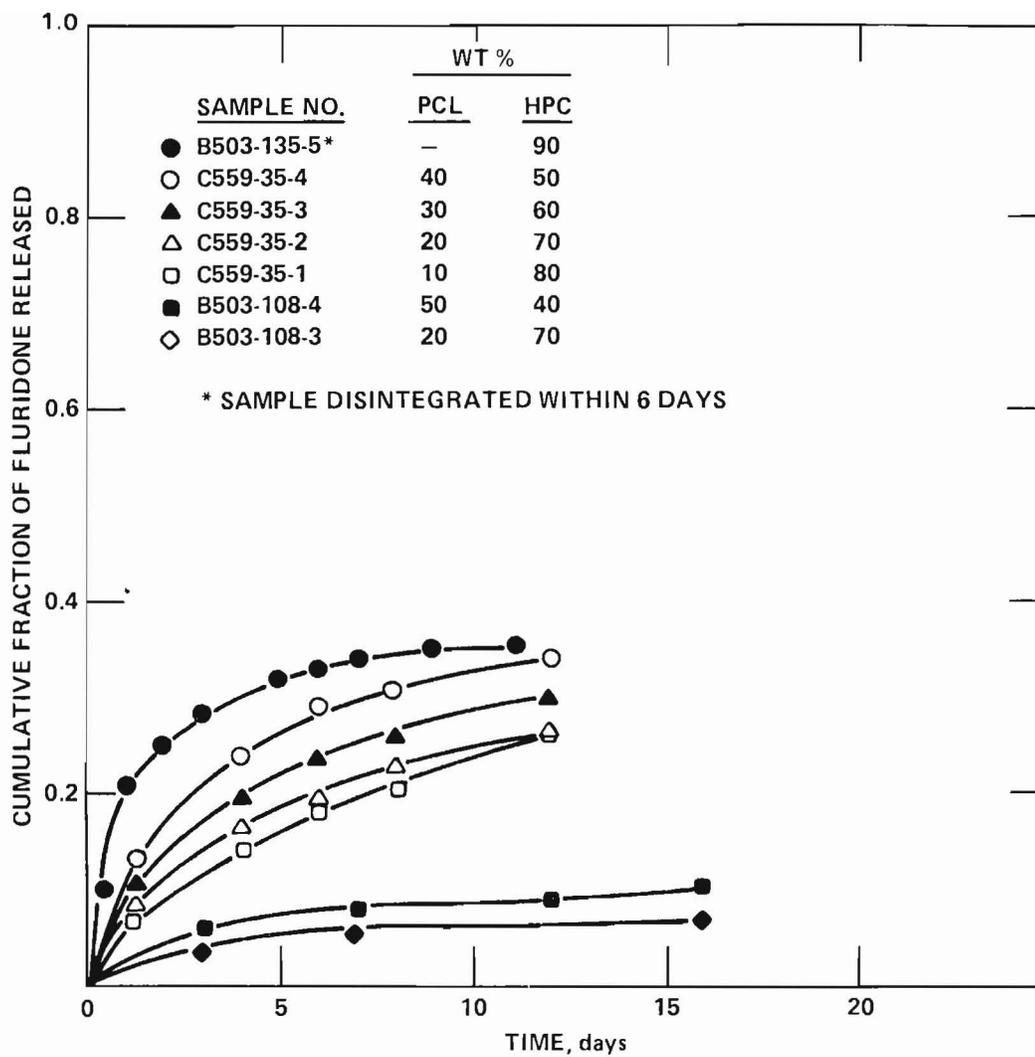


Figure 39. Effect of hydroxypropyl cellulose on fluridone release from monolithic pellets containing 10-percent-weight fluridone

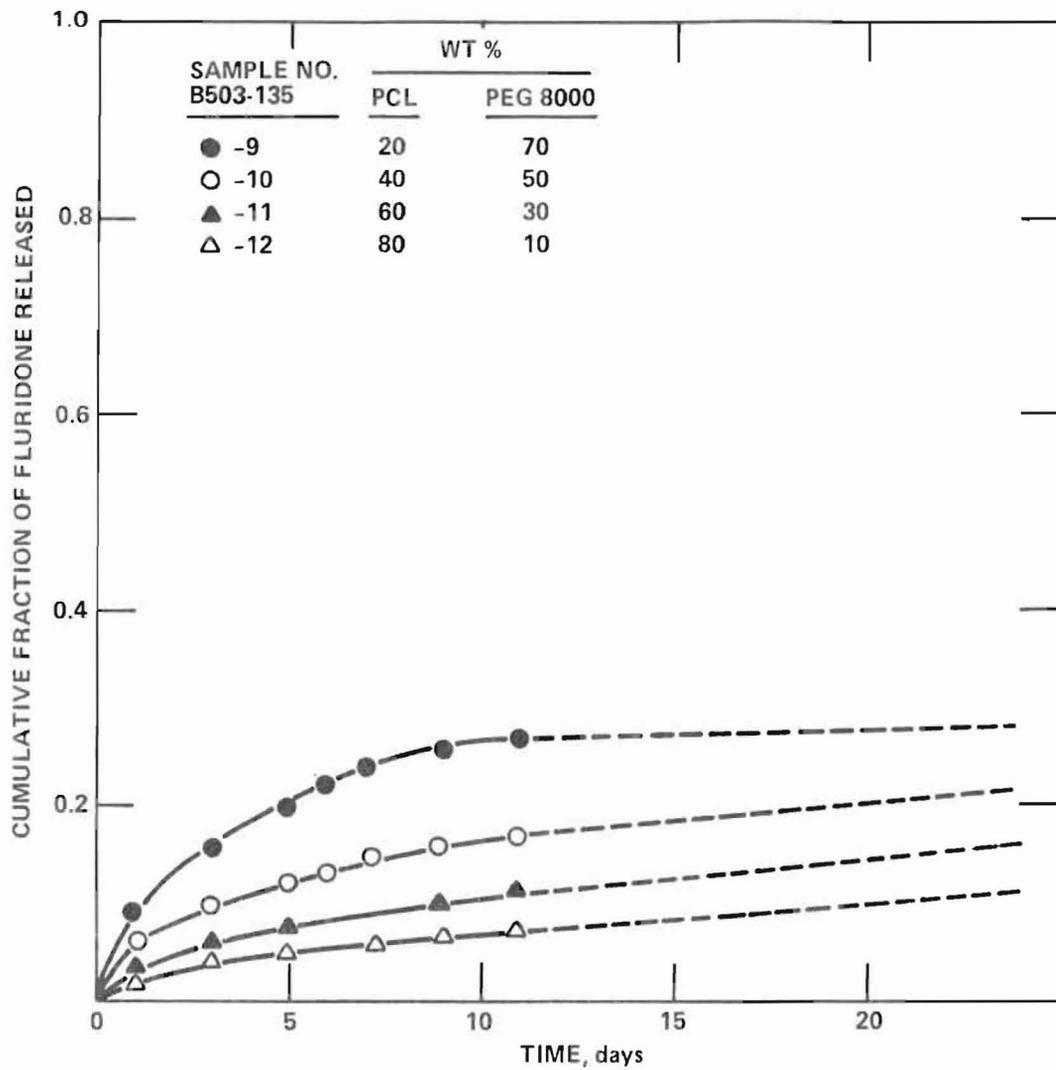


Figure 40. Effect of polyethylene glycol 8000 on fluridone release from monolithic pellets containing 10-percent-weight fluridone

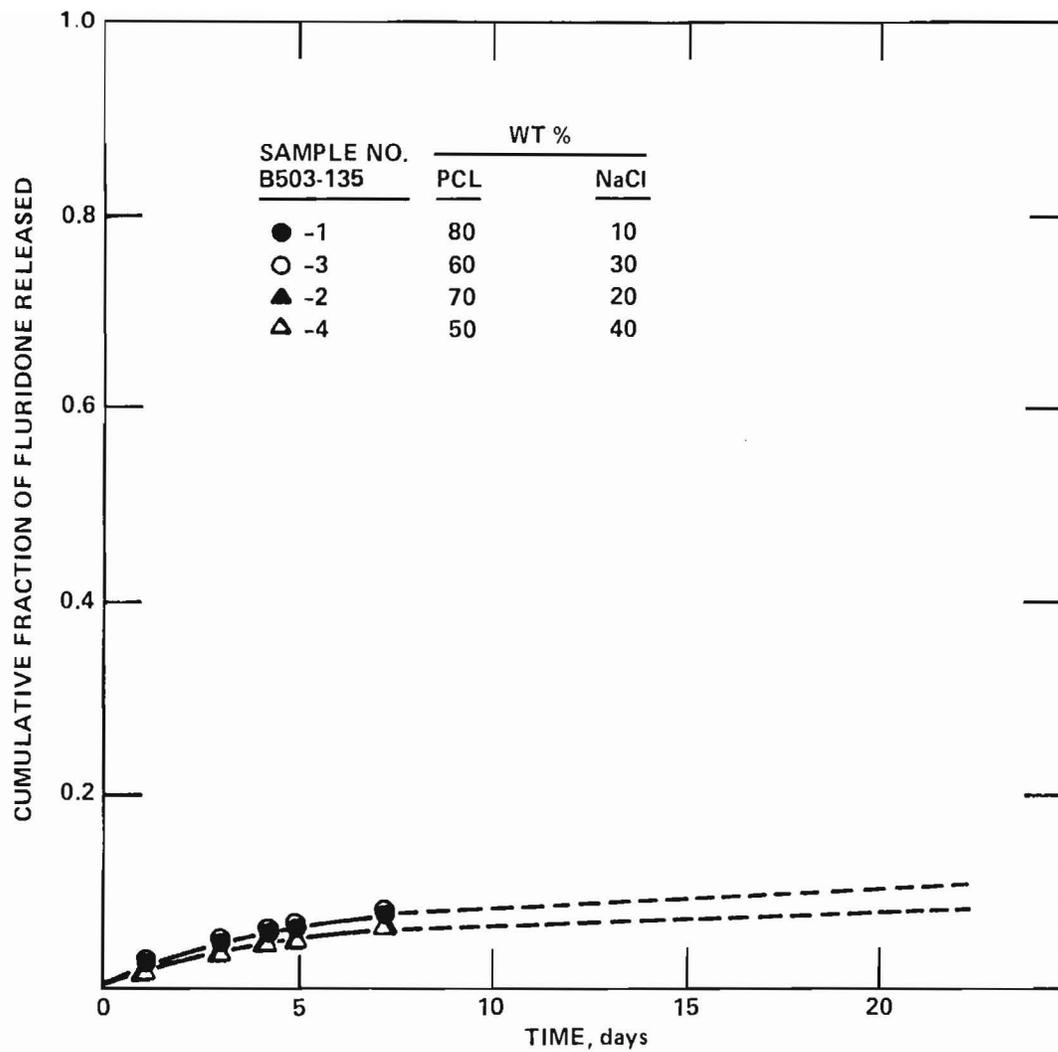
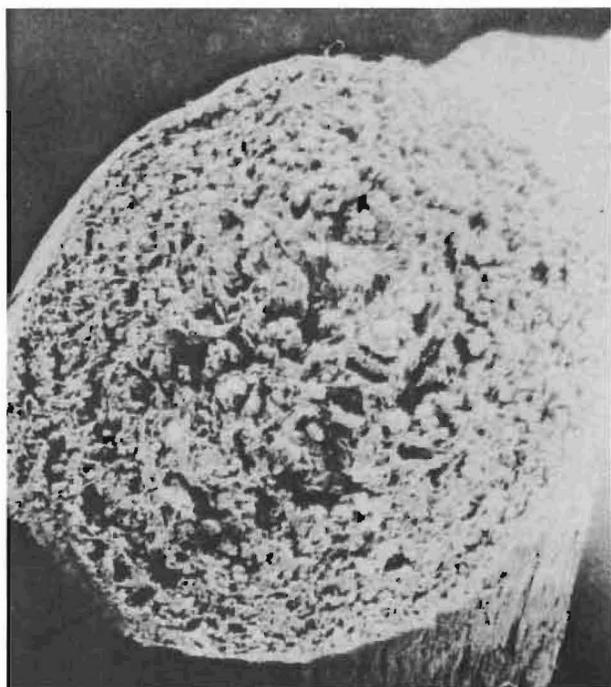
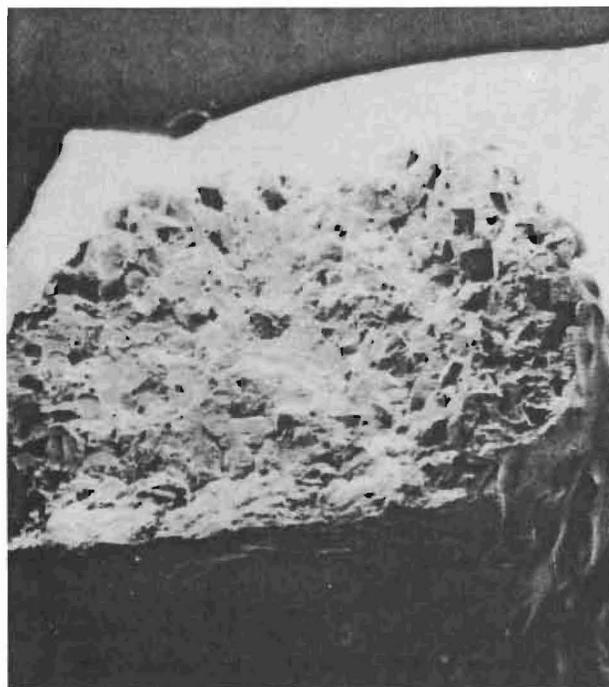


Figure 41. Effect of sodium chloride on fluridone release from monolithic pellets containing 10-percent-weight fluridone



a. SAMPLE B503-135-6



b. SAMPLE B503-135-4

Figure 42. Scanning electron micrographs of (a) fluridone/PCL/HPC (10:10:80) pellet and (b) fluridone/PCL/NaCl (10:50:40) pellet

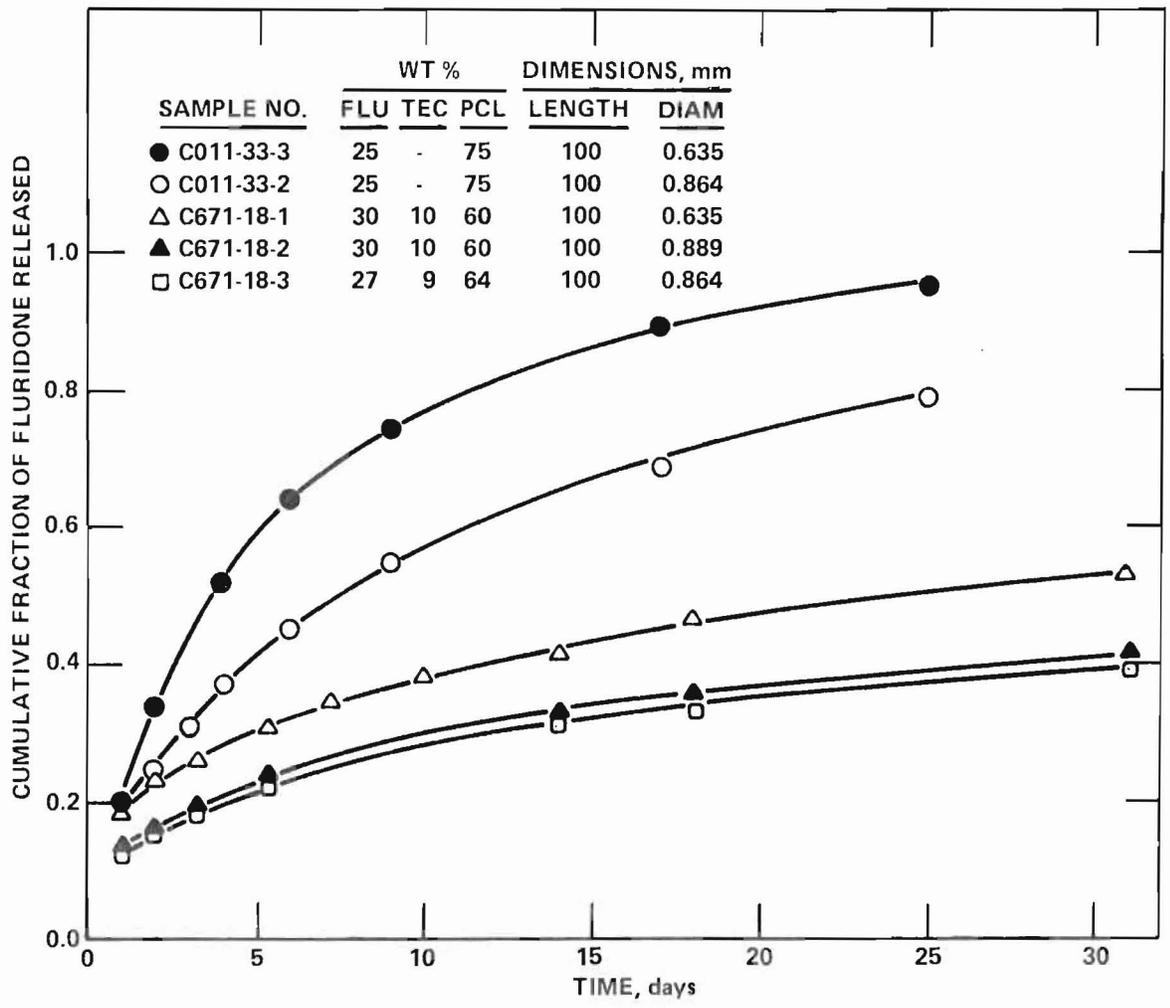


Figure 43. Effect of triethyl citrate on fluridone release from large-diameter monolithic fibers

69. Overall, HPC was the most promising water-soluble additive. Pellets with the composition 10:40:50 fluridone/PCL/HPC were selected for optimization.

Effect of pellet geometry
on fluridone release

70. In designing fibers for the controlled release of fluridone, the targeted durations of release could be achieved by varying the diameter of fibers once an optimal composition and proper extrusion conditions had been selected. The same rationale is appropriate for pellet-shaped devices.

71. Solid pellets and doughnut-shaped pellets of the composition 10:40:50 fluridone/PCL/HPC were prepared with different ratios of surface area to volume (SA/VOL). Dimensions, SA/VOL, and release profiles are given in Figure 44. Fluridone release increased consistently with increasing SA/VOL values ranging from 0.96 to 2.70.

72. The time required for 90 and 100 percent of the fluridone to be released from each pellet system represented in Figure 44 was calculated using Equation 2 (paragraph 6). These release periods were then plotted against the SA/VOL values to show the relationship between pellet geometry and release duration (Figure 45). By using Figure 45, an SA/VOL may be selected that will provide any duration of release ranging from approximately 20 days to 170 days for a pellet with the specified composition of 10:40:50 fluridone/PCL/HPC.

73. Preliminary experiments were also performed with trilobal or cloverleaf-shaped pellets in an effort to increase the SA/VOL value. Trilobal pellets were prepared by using a high-speed drill to reshape the disklike pellets. The release profiles of trilobal pellets are compared with their disk-shaped counterparts in Figure 46. Pellets with two different compositions were tested. Fluridone release from trilobal pellets containing only PCL was greater than release from disk-shaped pellets of the same composition. There was, however, little difference in the release characteristics of trilobal and disk-shaped pellets that also contained HPC. This lack of a geometrical effect may have been due to the crude method used to form the trilobal shape. To increase accuracy in forming trilobal pellets, the hand drill should be replaced with a trilobal spinneret.

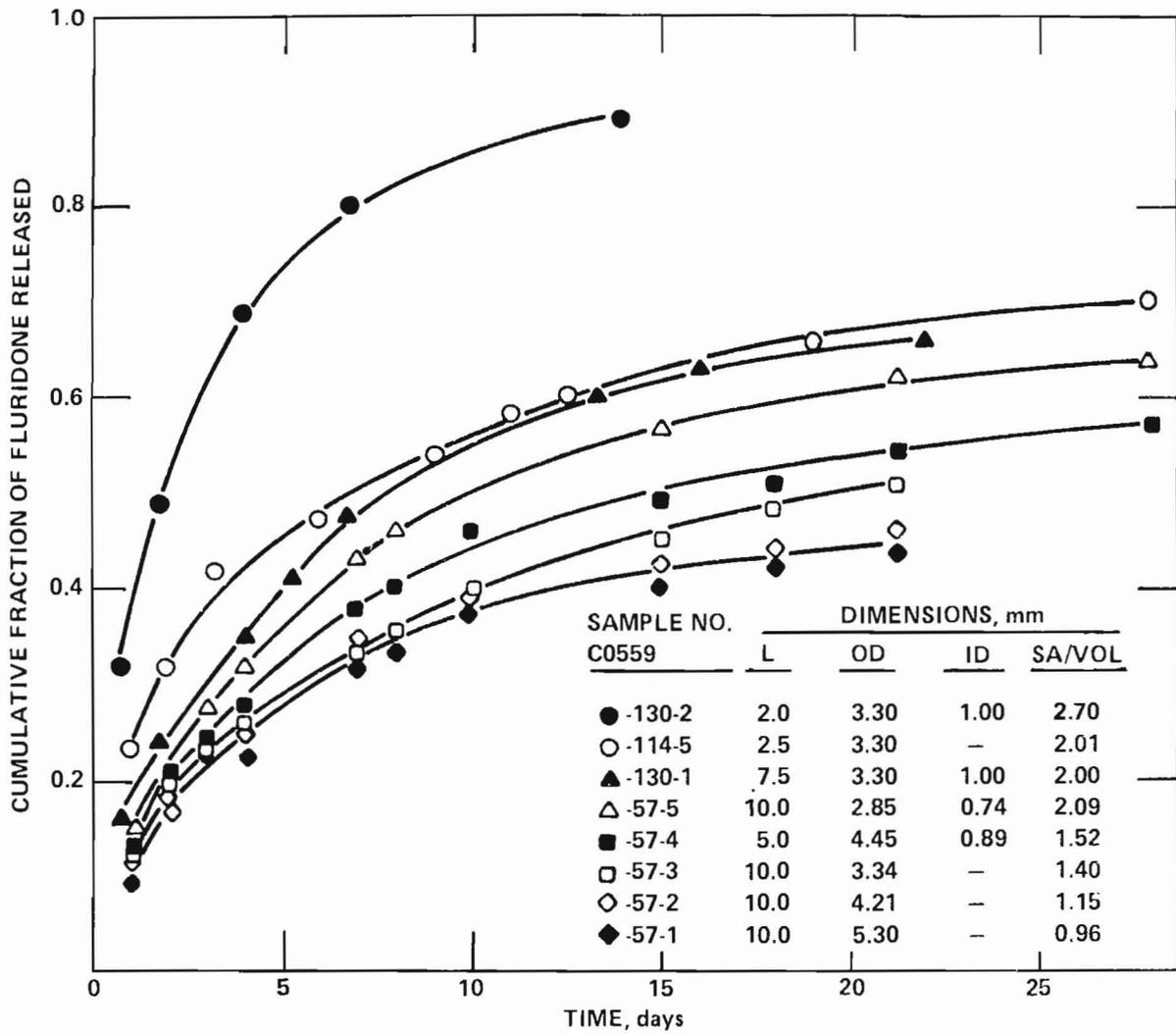


Figure 44. Effect of pellet geometry on fluridone release from monolithic fluridone/PCL/HPC (10:40:50) systems

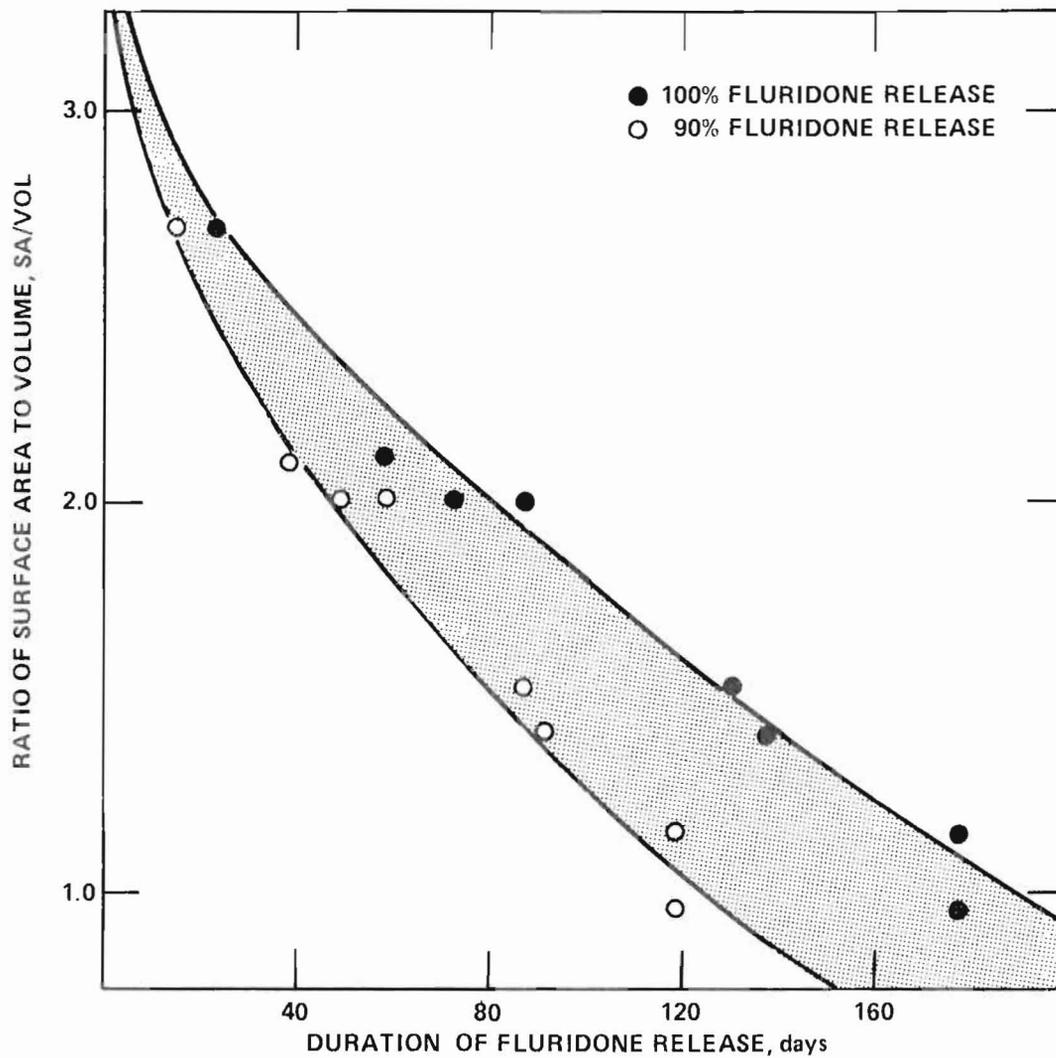


Figure 45. Duration of fluridone release from monolithic fluridone/PCL/HPC (10:40:50) pellets as a function of the ratio of surface area to volume

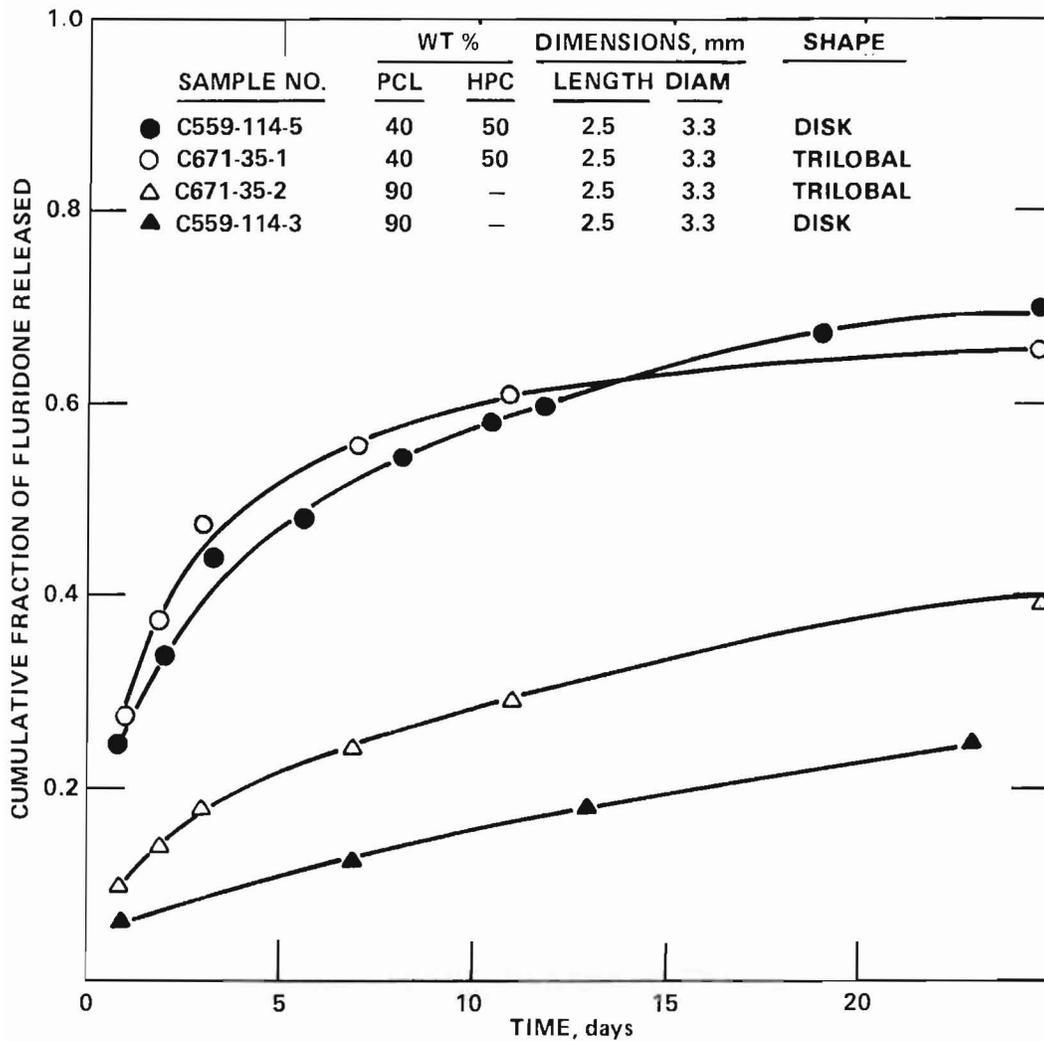


Figure 46. Fluridone release from trilobal and disk-shaped pellets containing 10-percent-weight fluridone

Development of coated fiber bundles

74. A third approach was used to develop a large-diameter, controlled-release system for fluridone that was easy to apply in the field. This approach entailed the use of the fibers that had been prepared previously and that already possessed the desired release characteristics. The system that was eventually developed consisted of a bundle of five to seven fluridone-releasing fibers coated with a water-soluble excipient. The coating procedure was simple. First, the coating material was melted in a U-shaped glass tube about 1 in. in diameter. The fiber bundle was then pulled through the melt and air-dried. This procedure was repeated until the required diameter of 3 mm for the entire pellet system was obtained. Several water-soluble coating materials were examined. A 95:5% wt blend of PEG 3350 and PEG 600 had the best coating properties. These pellets were supple and did not flake or adhere to each other at room temperature. The release profiles of 1-cm lengths of this pellet system and the fibers from which they were prepared are shown in Figure 47. Fluridone release from the pellets closely paralleled that from the original fibers (see also Figures 35 and 36). The small differences that are apparent may have been caused by the crystallization of fluridone in fibers during storage, the heat encountered in the coating bath, or slight changes in release conditions between studies.

Scaled-up production of pellets

75. The pellets containing fluridone, PCL, and HPC were selected for further development in a large-scale production process. This pellet system was preferred to the coated fiber bundles because fewer steps were needed in the fabrication process, i.e., no coating operation was required. Large-scale processing was to be used in preparing two lots of pellets with 20- and 40-day durations of release for field trials.

76. A Berstorff twin-screw extruder located at Berstorff Corporation (Charlotte, N.C.) was used to obtain the high throughput rates and optimal mixing needed in a commercial process. For the initial trials, two formulations of fluridone/PCL/HPC (10:40:50 and 15:35:50) were blended in drums and then fed to the extruder with an Acrison auger feeder. The feedstocks were extruded at a rate of 50 lb/hr through a multifilament die that produced five

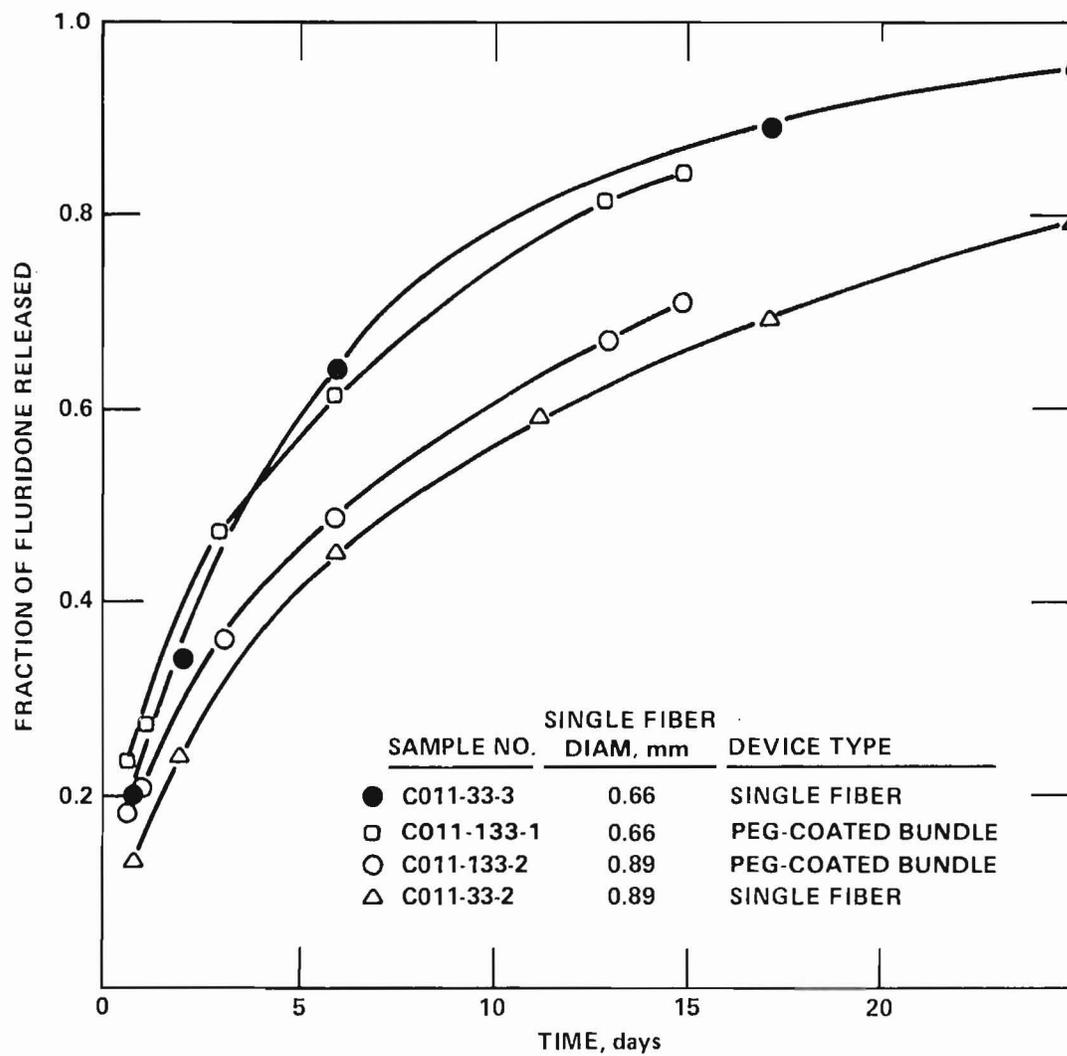


Figure 47. Fluridone release from fluridone/PCL (25:75) fibers coated with a mixture of polyethylene glycol 3350 and 600 (95:5)

rods. Rods were air-cooled on a 20-ft-long conveyor, fed into drums, and allowed to cool further overnight under ambient conditions. A Conair pelletizer was used to chop the rods into pellets about 3 mm long.

77. The twin-screw extruder and auger feeder permitted the use of the raw materials (powdered fluridone, PCL pellets, and Klucel) without additional processing prior to extrusion. The only problem encountered was in quenching the extruded strands sufficiently for pelletizing. Water quenching resulted in tacky fibers and could not be used. Air quenching required additional time for cooling. This would add to the cost of a commercial process.

78. Release studies were conducted with pellets produced on the twin-screw extruder after determining the SA/VOL. The composition, dimensions, and SA/VOL value are presented along with the release profiles in Figure 48. As previous studies have shown, the release characteristics of pellets controlled by a solution-diffusion mechanism are affected by both the fluridone loading and the SA/VOL. The duration of release decreases as the fluridone loading is decreased and the SA/VOL is increased. Samples C0671-50-1 and C0671-40-1, which contained 20% wt fluridone and had respective SA/VOL values of 3.21 and 2.57, were the best candidates for field trials. However, the Conair pelletizer could not be adjusted to give the short pellet length of 1.63 mm required for a 20-day release period. Altering the pellet diameter was considered, but the adjustment was too fine for reliable control on the extruder. Another alternative was to decrease the fluridone loading and maintain the same length and diameter as pellets with a 40-day release duration. A loading of 5% wt fluridone was estimated as being close to the level that would provide 20 days of release, and this loading was selected for large-scale production.

Production of pellets for field trials

79. Pellets for field trials were prepared on the twin-screw extruder. The two formulations (5:45:50% wt fluridone/PCL/HPC and 10:40:50% wt fluridone/PCL/HPC) were blended in a Day strand mixer prior to extrusion. Extrusion conditions were the same as in the trial runs. The air-quenching process consisted of air cooling the rods with fans as they passed over the 20-ft-long conveyor, then a 20-ft-long metal guide, and finally a second 8-ft-

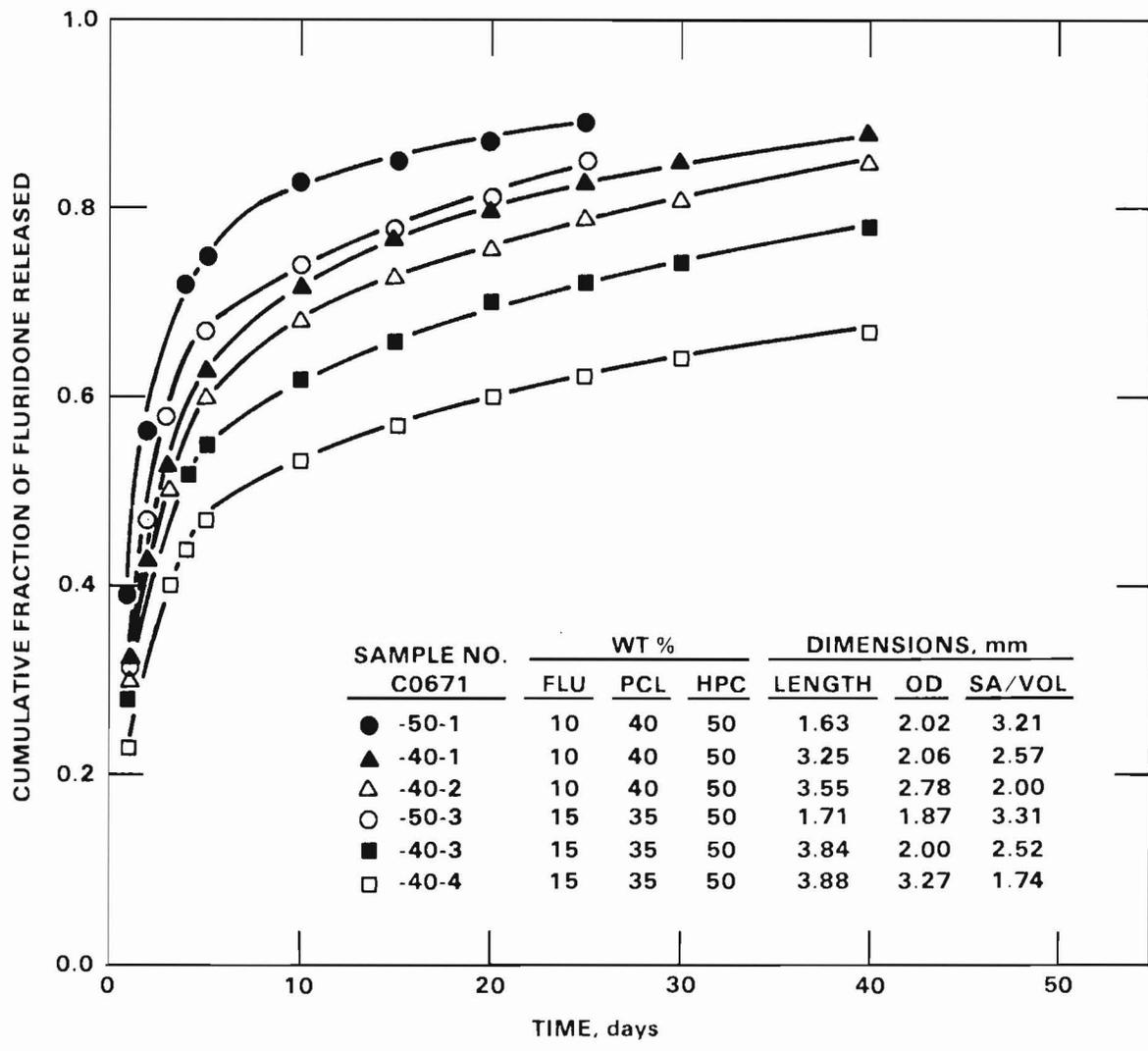


Figure 48. Fluridone release from fluridone/PCL/HPC pellets produced on a twin-screw extruder

long conveyor. A pressure-type idle roll was applied to the rods as they passed over the second conveyor to provide a more uniform draw rate. The idle roll, however, also flattened the rods because they had not cooled completely. This problem may be alleviated in the future by using a cold air quench and cooled conveyors, or by using nucleating agents to promote crystallization of the PCL resin. The rods were collected in boxes and allowed to cool for about 30 min at room temperature before being pelletized.

80. The identification number, composition, lot size, and expected duration of release of the pellets shipped to the WES are given below. Release profiles obtained in the laboratory are shown in Figure 49. Pellets that contained 5% wt fluridone released 80 to 90 percent of their loading within the estimated 20 days and consequently were close to target. Pellets that contained 10% wt fluridone, however, did not release fluridone as rapidly as expected. Only 70 percent of their fluridone was released within 40 days. The longer release duration may have been caused by a lower SA/VOL than was required or by more thorough blending during the production run.

<u>Sample No.</u>	<u>Description</u>	<u>Weight lb</u>	<u>Expected Duration of Release days</u>
A293-75-1	10:40:50 fluridone/PCL/HPC	306	40
A293-75-2	5:45:50 fluridone/PCL/HPC	460	20

Modification of pellet release characteristics for field trials

81. After receiving the large lots of pellets for field trials by the large-scale production process, the WES requested two additional 25-lb lots of pellets. One lot was to have a release duration of 20 days as was targeted previously. The second lot was to have a release duration of 12 days. Control pellets containing only PCL were also to be provided.

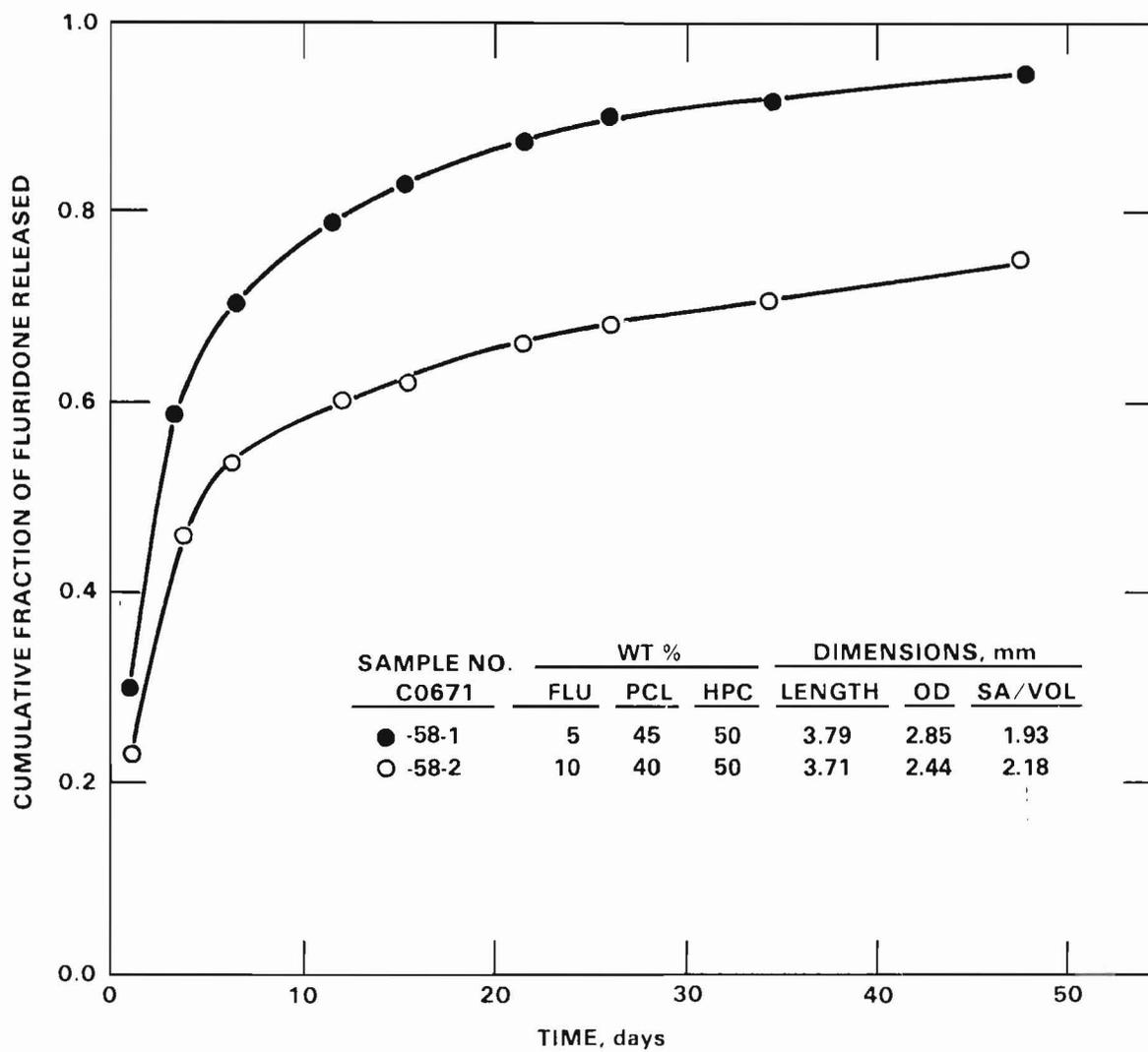


Figure 49. Fluridone release from large-scale production of fluridone/PCL/HPC pellets

82. A 20-day release period required pellets that were approximately 2.85 mm in diameter and 3.79 mm in length, with a composition of 5:45:50 fluridone/PCL/HPC. It was estimated that a diameter of 1.8 to 2.0 mm would be required to obtain a 12-day-release period with pellets of the same composition and length.

83. Because 25-lb lots were small enough to be prepared readily on equipment at Southern Research Institute, the pellets were melt spun on the Killion extruder under conditions similar to those described for large-scale fiber production in paragraph 50 and Table 10. Feed stocks were prepared by first blending fluridone and PCL in a two-roll rubber mill under ambient conditions. The roll temperatures were then increased to 135° C, and the HPC was added. The sheets that formed were cut into manageable pieces for grinding in a Wiley mill fitted with a 6-mm mesh screen. These feedstocks were melt spun on the extruder using a rod die with a single 0.125-in.-diam orifice. Because adequate quenching had been a problem previously, the extruded rods were air-cooled with fans for 9 ft before 10 wraps were made around a metal cooling roll. The rod was then passed through fan-cooled air an additional 6 ft to pressure-type, take-off rolls and finally to a pelletizer. No major difficulties were encountered during the fabrication process. Sample identification numbers and extrusion conditions are given in Table 13.

84. A small quantity of each lot was retained by Southern Research Institute for laboratory release studies. The release profiles are presented in Figure 50. Pellets from both lots released approximately 80 percent of their fluridone content in 10 to 12 days, one of the two targeted release periods. One reason for the rapid release of fluridone from the large-diameter pellets with an expected release duration of 20 days was the variation in pellet length. The pelletizer did not cut the rather hard, large-diameter rods into uniform lengths. Also, some pellets were cracked and had uneven ends. All of these defects could lead to a shortened duration of release, based on

Table 13

Conditions for Melt Spinning Fluridone Pellets with Modified
Release Characteristics for Field Trials

Sample No.	Composition	Extrusion Temperature °C			Polymer Feed Rate lb/hr	Cooling and Take-Up Roll Rate, ft/min	Chopper Speed rpm	Pellet Diameter mm
		Feed Zone	Metering Zone	Melt Blender and Die				
A293-83-1	5% fluridone* 45% PCL** 50% Klucel (HPC)†	61	120	141	3.0	15	1,143	2.8
A293-85-1	100% PCL	53	98	116	3.5	15	1,143	2.8
A293-89-1	5% fluridone 45% PCL 50% Klucel (HPC)	77	115	133	2.4	18.5	1,263	1.9
A293-87-1	100% PCL	66	115	142	2.4	17.3	1,262	1.9

*Union Carbide Tone-700, Lot 6672.

**Elanco fluridone, Lot 827EG2.

†Hercules Klucel (hydroxypropyl cellulose), Lot 1444.

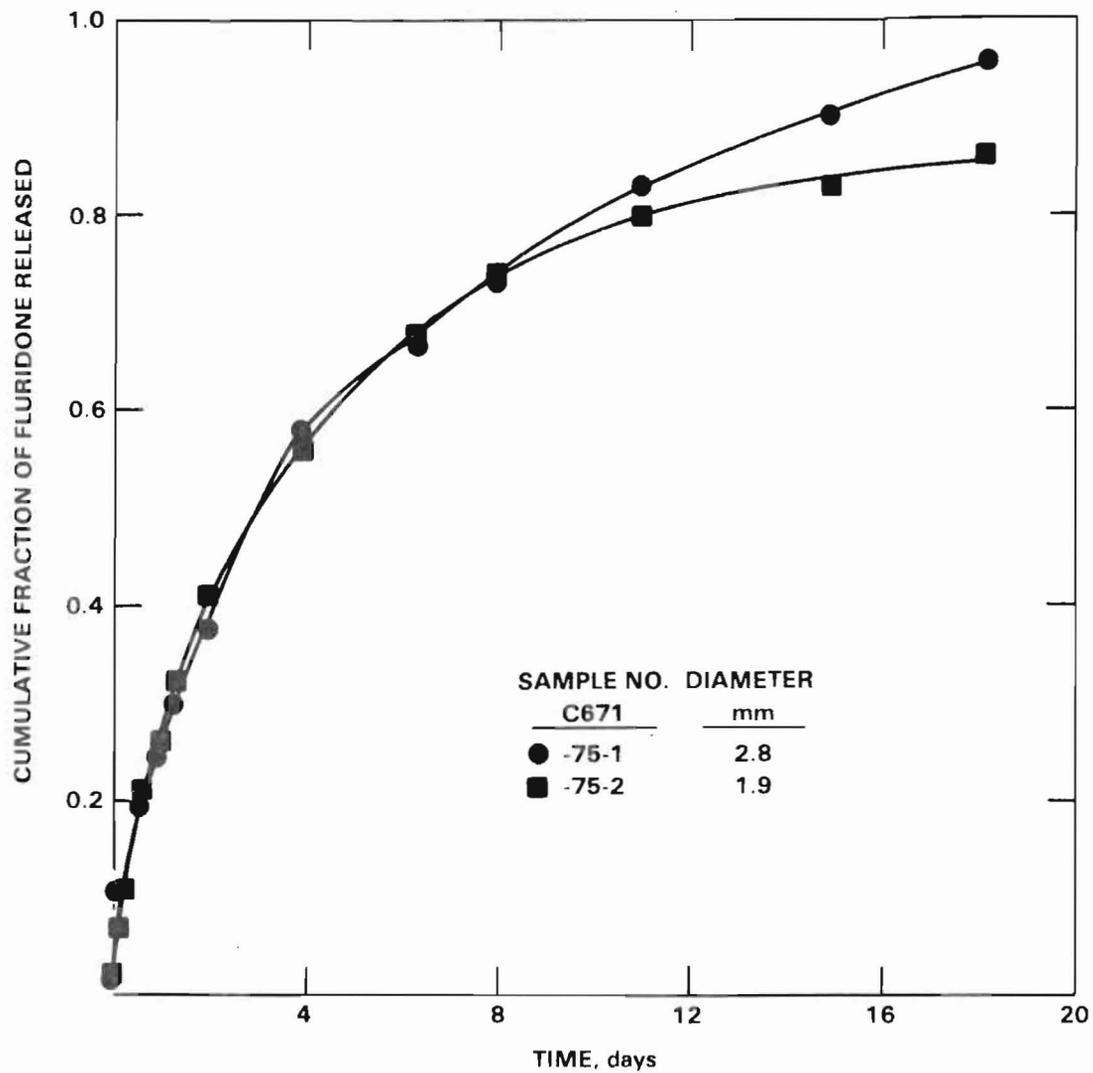


Figure 50. Cumulative fraction of fluridone released from 5:45:50 fluridone/PCL/HPC pellets produced on a Killion screw-type extruder for field trials

Fick's Law and the surface-area dependency on release rate. The change in extrusion equipment and fabrication conditions also cannot be discounted as possible factors responsible for the shorter-than-expected release period.

Pellet Formulations for Controlled Release Of Endothall

85. In the last phase of the project, development was begun on controlled-release pellet formulations for endothall with targeted release durations of 7 and 14 days.

Preparation of solid endothall salt

86. Before controlled-release pellets containing endothall could be prepared, a method of converting the aqueous solution of endothall acid supplied by the Pennwalt Corporation to a solid salt was needed. Precipitation in methanolic potassium hydroxide proved to be suitable for forming a solid potassium salt of endothall. A detailed description of the procedure is given in paragraph 106. Thermogravimetric analysis indicated that the solid form of endothall contained approximately 6.5% wt water. Elemental analysis of the solid was not performed.

Analysis of endothall

87. A rapid and simple assay method for endothall was also required before a controlled-release system could be developed. Endothall is normally analyzed by gas/liquid chromatography after derivatization to an imide. Because this involves a rather lengthy and complicated procedure and requires an expensive piece of equipment with limited share time at the Institute, an assay method utilizing high-performance liquid chromatography was developed. Although this assay requires further refinement, it proved adequate for the quantification of endothall in the initial release studies that were performed. (See paragraph 27, Appendix A for a detailed description of the analytical method.)

Preliminary studies with
endothall-containing pellets

88. In the first study with endothall, pellets approximately 2.75 mm in diameter and 3.8 mm in length were melt spun on the ram extruder. Four compositions were tested: 5:45:50 and 10:40:50% wt endothall/PCL/HPC and 5:45:50 and 10:40:50% wt endothall/PCL/clay. In the first two pellet systems, endothall was simply substituted for fluridone in previously successful formulations to provide a starting point. The second two pellet systems that contained clay were included for reasons of cost. As an excipient, clay is less expensive than HPC. Release studies with hard water indicated that all four formulations released endothall too rapidly to be of use in controlled-release formulations. In addition, the formulations containing HPC were difficult to blend. Formulations containing HPC were, therefore, eliminated from immediate consideration.

89. In the second study, the effects of endothall particle size and the presence of the clay excipient on pellet release characteristics were investigated. Again, four formulations were tested. Two contained 50% wt clay, 5% wt endothall, and 45% wt PCL. These formulations differed only in the particle size (coarse and fine) of endothall used in blending. The second two formulations contained no clay and had the composition 5:95 endothall/PCL. Again, the only difference between these two formulations was the particle size (coarse or fine) of the endothall used. The release profiles of the pellets prepared from these formulations are shown in Figure 51. These results show that clay increases the release rate of endothall markedly. It is possible that the clay, even though it is not water soluble, increases the release of endothall by increasing the porosity of the pellets. Alternatively, the clay may, in effect, increase the loading of endothall in the pellets by forcing the endothall into the PCL phase. If this is the case, the results suggest that endothall is released by a mechanism of microporous diffusion, and not solution diffusion as was observed for fluridone. Further studies would, however, be required to establish the mechanism of release for endothall.

90. One would also expect the particle size of the endothall to affect release characteristics if microporous diffusion were involved. Figure 51 shows that pellets containing coarsely ground endothall released endothall more

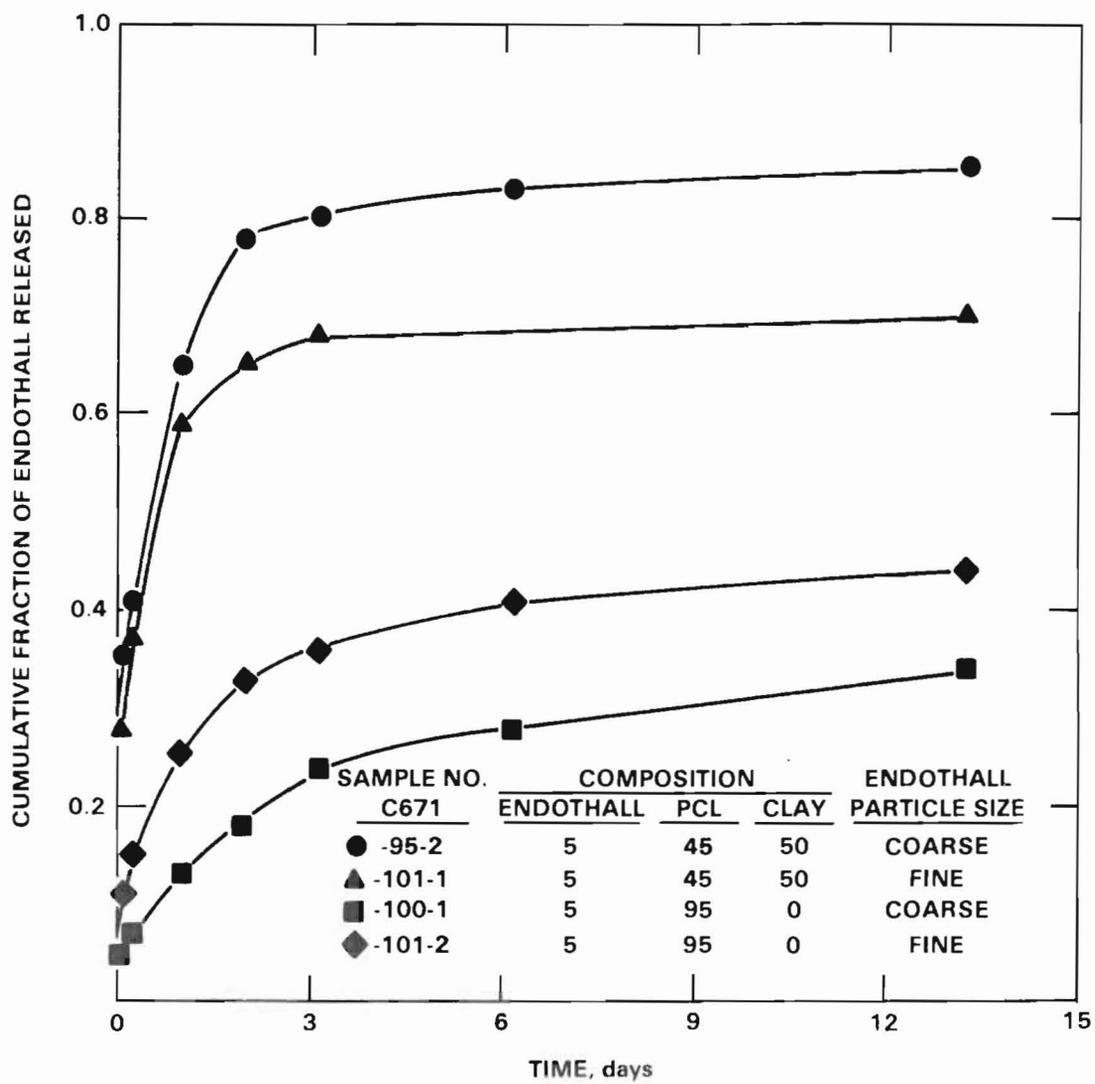


Figure 51. Cumulative fraction of endothall released from controlled-release pellet formulations for endothall

rapidly than pellets containing fine particles of endothall. This effect may be expected in the case of microporous diffusion when extrusion of coarsely ground material results in a pellet with a less compact, more porous structure. However, in pellets that contained only endothall and PCL, the endothall particle size had the opposite effect: pellets containing coarse endothall released more slowly than pellets with fine endothall. Further investigations would be needed to define the cause of this effect.

91. None of the pellet formulations released their entire endothall content based on the theoretical loading of 5% wt. Therefore, at the end of 13 days, the endothall was extracted by prolonged incubation in hard water at elevated temperatures (60° C for 24 hr and 37° C for 1 week). Very little additional endothall was recovered, and the relationship of the release profiles in Figure 51 did not change. Less than 100 percent recovery of endothall suggests that there was a poor distribution of endothall within the extruded rods. However, the difference in release characteristics among duplicate samples was small. Unless endothall was preferentially excluded from the charge placed in the extruder or was segregated in a portion of the extruded rod, it is unlikely that triplicate samples would contain approximately the same concentration of endothall. This suggests that the low recovery may have been due to incomplete extraction of endothall from the pellets or a lack of sensitivity in the analytical method.

92. Future studies should therefore include improvements in the blending method and fabrication process, and also refinements in the extraction procedure and analytical method. Overall, the results obtained thus far with endothall/PCL/clay pellets indicate that the duration of release can easily be altered to achieve the desired release durations of 7 and 14 days by adjusting either the concentration of clay or the concentration of endothall.

PART III: CONCLUSIONS AND RECOMMENDATIONS

Fibrous Controlled-Release System for Diquat

Conclusions

93. The objectives of the studies with diquat were to obtain zero-order release, different rates of release, extended durations of release, and good mechanical properties in a fibrous controlled-release system containing PCL as an excipient. Two fabrication methods, solution coating of monolithic fibers and direct extrusion of coaxial fibers, were used to obtain a reservoir system. The coaxial melt-spinning process gave fibers with the most promising release characteristics. Release studies conducted in the laboratory indicated that a coaxial fiber consisting of a core of diquat and a hydrophilic polymer (such as a polyethylene glycol or a cellulosic) surrounded by a membrane of oriented and crystalline PCL would yield the desired delivery system. The PCL sheath membrane, oriented by a drawing process after extrusion of the coaxial fiber, would not only provide the permeability characteristics necessary for extended durations of release but also the tensile strength necessary for field application.

Recommendation

94. For diquat, the coaxial fiber described briefly above is the controlled-release system to be preferred. The thickness and orientation of the sheath can be altered to provide the rates and durations of release that are needed under field conditions. Prototype fibers should first be evaluated in the laboratory for the following: release characteristics in hard water, mechanical strength, and density (to assess their ability to sink and reach submersed weeds).

Fibrous Controlled-Release System for Fluridone

Conclusions

95. Monolithic fluridone/PCL fibers with exponential release characteristics were prepared on several types of equipment. The equipment ranged from a laboratory-scale melt indexer yielding 0.5-g lots to a commercial twin-screw extruder producing lots from several hundred to thousands of pounds in size. The fibers release fluridone by a solution diffusion mechanism, and their

release characteristics can be predicted by using appropriate expressions of Fick's Law of diffusion. The duration of release of the monolithic fibers is controlled by the fluridone loading and fiber diameter. Fabrication processes and raw materials will alter release characteristics and should be carefully monitored. Among the production variables that affect the release characteristics of fibers are PCL viscosity and particle size, fluridone purity, feed-stock blending method, extrusion temperature, fiber take-up rate and extent of drawing, and the quench method. Changing the lot of fluridone and PCL used during fabrication will also alter release characteristics. The effects of all of these variables, however, may be compensated for by making the proper adjustments. The targeted release periods for the fluridone/PCL fibers of 20 and 40 days were achieved.

96. The fluridone-releasing fibers proved to be effective in the field in all but the fastest moving water. For a slow-acting herbicide such as fluridone, the concentration of fluridone in the immediate vicinity of the weeds may have been insufficient to arrest biosynthetic processes in fast-flowing water. Therefore, in water systems with high flow, a contact herbicide may be more appropriate.

Recommendation

97. In those water systems where fluridone is effective, a coaxial or reservoir fiber would provide more efficient delivery of fluridone. A zero-order rate of release would require less fluridone and ensure a prolonged, constant delivery of the aquatic herbicide. Preliminary laboratory studies with coaxial fluridone-loaded fibers were conducted during the project. These studies indicated that a fibrous reservoir system of fluridone is feasible.

Pellet Formulations for Controlled Release of Fluridone

Conclusions

98. The major problem encountered with the fibrous fluridone/PCL system was not lack of effectiveness but difficulty in dispersing the fibers in the field with conventional application equipment. Other than designing a new method of application, the only alternative was to alter the geometry of the fluridone/PCL system for compatibility with field equipment already in use. As a result, the fibrous fluridone/PCL system was converted to a pellet system.

99. Fluridone-containing pellets were made by the same melt-spinning process as the fibrous system. However, the large increase in diameter that accompanied the change in geometry made it necessary to modify the composition and fabrication conditions to obtain the desired release characteristics. As a result, two different pellet delivery systems were developed. One was a monolithic pellet much like the fibrous system except that the fluridone concentration was markedly reduced and a water-soluble excipient (HPC) was added to shorten the duration of release to the targeted periods of 20 and 40 days. Both the loading of fluridone and the geometry of the device were critical in achieving the desired release characteristics. The second pellet system consisted of a fiber bundle coated with a water-soluble excipient to increase the diameter of the fibers for field application. After immersion in water, the water-soluble coating would dissolve slowly (in about 20 min) and release the fibers. Because the first pellet system of fluridone, PCL, and HPC involved fewer production steps and was therefore considered more economical, it was selected for scale-up in production and field trials.

100. Two lots of fluridone-releasing pellets, totaling close to 800 lb, were produced on a commercial twin-screw extruder and sent to the WES for field tests. One lot (460 lb) was to have a release period of 20 days. This pellet system had the following specifications: 5:45:50% wt fluridone/PCL/HPC; length, 3.79 mm; diameter, 2.85 mm; SA/VOL, 1.93. Release studies conducted in the laboratory indicated that this lot was very close to target, with about 85 percent of the fluridone being released in 20 days.

101. The second pellet system (306 lb) was to have a release period of 40 days. The specifications of this lot were as follows: 10:40:50% wt fluridone/PCL/HPC; length, 3.71 mm; diameter, 2.44 mm; SA/VOL, 2.18. Release studies indicated that the release period of this lot was slightly longer than the required 40 days, with only about 70 percent of the fluridone being released during this period. Only minor adjustments in composition are needed to achieve the targeted release duration of 40 days.

Recommendation

102. The release durations of the monolithic pellet system can be varied widely. Using pellets of one composition, release durations ranging from 20 to 170 days are possible. The system is, therefore, adaptable to a number of different field conditions. For more efficient use of fluridone, a reservoir system would be appropriate, for the same reasons mentioned with regard to the

fibrous, fluridone-releasing system. Unless a new method of applying fibers in the field is developed, the pellet system is more promising than the fibrous system.

Pellet Formulations for Controlled Release of Endothall

Conclusions

103. In the last phase of the project, development studies were begun with endothall, a third aquatic herbicide. This controlled-release system was also to be in the form of pellets. The endothall was first received as an aqueous solution of the acid and other ingredients, and later as solid endothallic acid. Because a solid powder form of the herbicide was needed, the endothall was precipitated from solution as a potassium salt. Surprisingly, the salt is more soluble than the acid in organic solvents, which suggested that the salt form would be more compatible with PCL. Gas/liquid chromatography is normally used to analyze for endothall after it has been derivatized to an imide. However, a more convenient high-performance liquid chromatography (HPLC) assay was developed. Although the HPLC method may require further development, it was sufficient to examine the release characteristics of endothall-containing pellets prepared in the first trials on the ram extruder. Clay, in combination with endothall and PLC, was found to be a useful and economical additive for altering the release characteristics of the pellets. It appears that the clay additive may act by altering the porosity of the pellets.

Recommendation

104. These preliminary studies suggest that, within limits, the release characteristics of the monolithic endothall/PCL/clay pellets can be altered to provide release durations ranging from 2 days to several months. Further refinement of a endothall-releasing system would involve the fabrication of reservoir-type controlled-release system to give a constant rate of endothall release.

APPENDIX A: EXPERIMENTAL PROCEDURES

Preparation of Anhydrous Diquat Dibromide

1. Anhydrous diquat dibromide was prepared by precipitation from an aqueous formulation obtained from Chevron (Lot 21237A03). The diquat solution (300 ml) was added to a 3-ℓ beaker that contained 1,500 ml of absolute ethanol. Then 500 ml of acetone was added to complete the precipitation. The crystalline diquat was collected and washed with 200 ml of absolute ethanol using vacuum filtration. The crystals were transferred to a 2-ℓ beaker, and boiling water was gradually added until the diquat was dissolved (about 125 ml of water was required). About 15 g of decolorizing carbon was then added. After 15 min of magnetic stirring, the solution was vacuum filtered and allowed to cool to room temperature. The filtrate was then placed in a refrigerator. After 18 hr, the large diquat crystals that had formed were collected by vacuum filtration. These crystals were dissolved at room temperature in a minimum amount of deionized water, and the resulting solution was added by drops to 1,200 ml of stirred absolute ethanol. The very small crystals that formed were collected by vacuum filtration and dried in vacuo at 120° C for 24 hr.

Preparation of Solid Endothall Salt

2. First, an aqueous solution of endothall and other ingredients (Aquathol-K, Pennwalt Corporation) was evaporated overnight at 65° to 70° C to remove the solvent and obtain a solid form of endothall suitable for melt spinning. When this method proved to be unsatisfactory, advantage was taken of the difference in the water solubility of the acid and salt forms of endothall to prepare a solid potassium salt of the aquatic herbicide. Solid endothallic acid (Technical Grade) supplied by the Pennwalt Corporation was dissolved in methanol on a stirring plate. Pellets of potassium hydroxide were added to the solution such that the mole ratio of potassium hydroxide to endothall was about 2:1. (A slight excess of the water-soluble endothallic acid was used so that the base would react completely.) The solution was stirred until the pellets dissolved. A precipitate of the potassium salt of endothall formed upon reaction in the methanol. The reaction was complete in approximately 2 hr.

The precipitate was collected on a filter and washed several times with methanol and then with acetone. The precipitate was transferred to a tray lined with Teflon and dried overnight at 58° C in a vacuum oven that had been purged with nitrogen.

Preparation of Polycaprolactone

3. The polycaprolactone that was commercially available from Union Carbide Corporation (PCL-700) was a relatively low-molecular-weight polymer (inherent viscosity of approximately 0.7 dl/g. Although this material could be melt spun into fibers, their strength and uniformity were poor. Better fibers can be produced from polycaprolactone with inherent viscosity values greater than 1.0 dl/g. Therefore, polymers with these viscosities were prepared by a ring-opening polymerization of purified ϵ -caprolactone using stannous octoate as a catalyst.

4. The following procedure for the purification of ϵ -caprolactone was employed. A 2- ℓ distillation flask, Vigreux distillation column, condenser, and a 1- ℓ receiving flask were dried overnight in an oven at 200° C and then cooled in a glove box filled with dry nitrogen. The glassware was assembled and flame-dried under vacuum. The system was flushed with nitrogen, and 1,000 g of ϵ -caprolactone from Aldrich Chemical Company was placed in the distillation flask. The liquid caprolactone was heated to reflux, and an impure fraction was collected and discarded. The main fraction was collected at a distillation temperature of 64° to 68° C and a vacuum of 0.5 mm Hg. This fraction of pure ϵ -caprolactone (590 g) was transferred to a dried bottle in a glove box filled with nitrogen.

5. For the polymerization reaction, 100 g of purified ϵ -caprolactone and 0.03 g of stannous octoate catalyst were placed into a 250-ml, three-neck flask equipped with a mechanical stirrer and gas-inlet adapter. All glassware had been dried in an oven at 200° C and cooled and assembled in a glove box filled with nitrogen. The reaction flask was attached to a nitrogen bubbler system and placed in an oil bath at room temperature. The stirrer was started, and the monomer was heated slowly to 140° C over 2 hr. The reaction mixture was maintained at 140° C with stirring for 3 hr, one drop of lauryl alcohol was added to the mixture, and heating and stirring were continued for an additional 2 hr. The flask was removed from the oil bath and cooled to room temperature

under a nitrogen atmosphere. The polymer mass was dissolved in methylene chloride and precipitated into methanol. It was then dried in a vacuum oven at approximately 40° C to remove residual solvents. The inherent viscosity of the polymer was 2.5 dl/g in chloroform at 30° C.

Preparation of Diquat/PCL Mixtures for Coaxial Fibers

6. Two methods were used to prepare the 30:70 mixture of diquat and PCL for the coaxial-spinning process. In the first procedure, 42 g of PCL (inherent viscosity of 1.80 dl/g) was dissolved in 300 ml of methylene chloride. Then, 80 g of diquat was dispersed in 180 ml of methylene chloride by sonification with a Fisher Sonic Dismembrator. The diquat dispersion was added to the PCL solution and stirred with a magnetic stirrer. The uniformly dispersed mixture was poured into a large glass container, and the methylene chloride was allowed to evaporate in a hood. The diquat/PCL mixture was then dried in a vacuum oven, and the dry blend was subsequently cut into small pieces for melt spinning.

7. In the second procedure, PCL was melted at 80° C, and diquat powder was added with stirring. Small portions of the uniform mixture were removed with a spatula and allowed to cool. Upon cooling, these portions solidified to form small pieces suitable for melt spinning.

Preparation of Diquat/PEG Mixtures for Coaxial Fibers

8. To prepare diquat/PEG mixtures for coaxial spinning, polyethylene glycol from Union Carbide Corporation with a molecular weight of 20,000 was melted at 65° C. Diquat powder was added to the molten PEG with stirring. Small portions of the melt were removed and solidified by cooling to give small particles adequate for melt spinning.

Preparation of Monolithic Fibers on Melt Indexers

9. Two melt indexers were used to extrude small lots of monolithic fibers that contained diquat or fluridone. One was manufactured by the F. F. Slocumb Corporation, Wilmington, Del. The other, a Tinus Olsen plastometer, was manufactured by the Tinus Olsen Testing Machine Company, Inc., Willow

Grove, Pa. Only the Tinius Olsen plastometer will be described in detail because the construction and dimensions of the two melt indexers were nearly the same. The Tinius Olsen plastometer consists of a cylindrical, electrically heated metal block that is 2 in. in diameter and 7 in. in length. The block is hollow and has an orifice, 0.375 in. in diameter, located in the center. Prior to the spinning process, a spinneret is positioned in the bottom of the orifice. A spinneret is a hollow metal cylinder. Spinnerets with different inner diameters are used to obtain fibers with different diameters. For example, to prepare monolithic diquat-loaded fibers, a spinneret 328 mils long with a hole 12 mils in diameter was used. During the spinning process, a metal piston 0.375 in. in diameter and about 9.25 in. in length forces the polymer through the spinneret upon the addition of various metal weights. The temperature of the cylinder is regulated by a solid-state controller with continuous digital display.

10. To melt spin a fiber, the plastometer was switched on and the temperature preset. After the temperature stabilized, about 5 g of the aquatic herbicide/polymer mixture was added to the melt chamber, and a charging tool was used to remove trapped air. The piston was inserted into the chamber, and the sample was allowed to melt and equilibrate for about 5 min. Weights were then added to the piston to extrude the fiber. The fiber was cooled in air and collected in loose coils.

Preparation of Monolithic Fibers on the Ram Extruder

11. In the later studies with diquat and in studies with fluridone and endothall, a ram extruder designed and built at Southern Research Institute was used to prepare either fibers or pellets. The essential parts of the ram extruder are a 4-in.-diam, 8-in.-long, cylindrical, electrically heated metal block with a 0.6-in.-diam bore through the center. A spinneret and a metal screen filter are fitted to the bottom of the block. A ram with a nominal diameter of 0.6 in. that is driven by a variable-speed motor is used to force the polymer through the spinneret. A pressure gage located directly above the ram is used to measure the applied ram force. A take-up winder is located about 3 ft below the spinneret for collection of fibers onto paper spools. For monolithic fibers, a single-orifice spinneret with a 0.040-in. orifice length and a 0.020-in. orifice diameter (2:1 length-to-diameter ratio) was used.

12. The melt-spinning procedure was similar to that used with the Tinius Olsen. The aquatic herbicide/polymer blend was charged into the barrel of the extruder and allowed to equilibrate at the extrusion temperature that had been selected. The blend was then forced through the spinneret by the ram. The extruded fibers were cooled in air or quenched in water before being collected on paper spools.

Drawing of Ram-Extruded Fibers

13. To draw ram-extruded fibers, the fibers were passed from a feed spool through tensioning devices to a feed godet. After several turns around the feed godet, the fibers were passed over a heated platen (45° C), 10 in. in length, to a second godet called the draw godet. The draw godet was set at speeds faster than the feed godet, and the ratio of the godet speeds was used to set the fiber draw ratio. The drawn fibers were collected on paper spools with a surface-driven winder.

Fabrication of Coaxial Fibers by Solution Coating

14. Two fabrication methods, solution coating and coaxial melt spinning, were used to prepare coaxial fibers. In solution coating, monolithic herbicide-loaded fibers were coated with a polymer solution devoid of herbicide. The coating equipment consisted of disposable plastic hypodermic syringe barrels with 16- and 18-gauge needles. The coating solution was placed in the syringe barrel, and the fiber was pulled vertically downward through the barrel and needle. Repeat applications of polymer coatings were made with fresh needles and with fresh polymer solutions when acetone was used as the solvent. After the fibers dried, the ratio of the coated fiber radius to the initial fiber radius was determined to provide an $r_o:r_i$ (outer/inner) value. This coating equipment was simple and useful for preparing small samples of experimental fibers. Precision-coating dies can be used to prepare larger quantities of coated fibers.

Preparation of Coaxial Fibers by Melt Spinning

15. The melt extruder used for preparing coaxial fibers was designed and built at the Institute. It consists of a cylindrical, electrically heated metal block that is 4 in. in diameter and about 8 in. in length. The block has two orifices, 0.375 in. in diameter, located near the center of the block. A coaxial spinneret consisting of an inner tube (47 mils inner diameter, 59 mils outer diameter) and an outer tube (74 mils inner diameter, 375 mils outer diameter) fits into the block directly below the two orifices. The extruder was designed to feed the core material from one block orifice and the sheath material from the other block orifice. Two metal rams (about 0.375 in. in diameter) driven by a variable-speed motor were used to force the herbicide/polymer blends through the spinneret. A pressure gage measured the force applied to the rams. A surface-driven winder located about 5 ft below the spinneret was used to collect the fibers.

16. The spinning procedure was similar to that used for the monolithic fibers. The herbicide/polymer blend and neat PCL were pulverized. About 10 g each of the polymer and the blend were charged into the extruder and allowed to equilibrate. The core and sheath materials were then forced through the spinneret by the rams. The coaxial fiber was cooled in air as it passed from the spinneret through guides to the winder, and then it was collected on paper spools.

Preparation of PCL/Fluridone Blends for Large-Scale Fabrication Processes

17. The PCL used in preparing the first 80 lb of fibers for field trials in Toledo Bend, La., was ground at Southern Research Institute according to the following procedure. The PCL-700 pellets obtained from the Union Carbide Company were mixed with finely crushed dry ice, cooled for about 1 hr, and then ground on a Wiley Mill. The granulation was passed through a 4-mm screen first. Second and third passes were made through 3- and 2-mm screens. After the granulation was vacuum-dried for about 40 hr at 40° C and <1 mm Hg pressure, a portion of it was mixed with fluridone in a 30-gal drum on ball-mill rolls. This blend was then pelletized by extrusion on a 1-in. Killion

10-ft-long water-quench bath, through take-up rolls, and then through a extruder equipped with a mixing screw, a Model KMB 100C Koch melt blender, and a rod die having a 0.125-in.-diam orifice. The extruded rod passed through a pelletizer. A rotary vacuum-drier was used to dry the pellets further for about 12 hr at 40° C and <1 mm Hg pressure. The PCL particles produced were approximately 2 mm in diameter.

18. Several unsuccessful attempts were made to air-quench the extruded rod on a chilled roll to avoid exposing the rod to water, but the rod did not cool sufficiently for pelletizing at practical throughput rates (i.e., about 3 lb/hr).

19. For subsequent field trials with fibers in Florida and Washington State, PCL was cryogenically ground to a particle size of <850 μ (<20 mesh) at Wedco, Inc. (Bloomsbury, N.J.) to eliminate the labor-intensive procedure described above.

Large-Scale Fabrication of Fibers and Pellets

20. The large-scale screw extruders used to fabricate fluridone-releasing fibers and pellets are described in detail in Part II of the main text because the processing conditions employed while using this equipment greatly affected release characteristics.

Determination of Mechanical Properties

21. The mechanical properties of fibers were measured on an Instron by standard ASTM procedures. Values for the tenacity (g/d), elongation at break (percent), initial modulus (g/d), and tensile factor ($TE^{1/2}$) were obtained to assess fiber strength and flexibility.

Determination of Diquat Release

22. Triplicate samples of each diquat-loaded fiber were cut to a length that would give approximately 10 μ g of diquat release per day based on theoretical calculations. Each sample was weighed, and the fiber ends were sealed with poly(methyl methacrylate), a thermosetting resin. Each fiber sample was then immersed in a vessel containing 50 ml of deionized water. The vessels were sealed and agitated at 25° C on a mechanical shaker. Portions of water

were periodically assayed for diquat on a Perkin-Elmer spectrophotometer at a wavelength of 310 nm.

23. The following equation, which is a linear least-squares fit of absorbance at 310 nm to diquat concentration (micrograms of anhydrous diquat dibromide per millilitre of solution) in standards, was used to quantify diquat in experimental samples:

$$C = 16.367A + 0.4926$$

Determination of Fluridone Release

24. Laboratory release studies with fluridone were conducted with two receiving solutions. In early release studies, the receiving fluid was 50:50 ethanol/water (wt/wt). This receiving fluid was selected because fluridone is highly soluble in aqueous ethanol, and fluridone could be quantified simply and easily by UV absorbance measurements at 237 nm under infinite-sink conditions. A standard curve of fluridone concentration in aqueous ethanol absorbance at 237 nm is shown in Figure A1.

25. Although aqueous ethanol was suitable for determining the diffusional mechanisms that controlled the release of fluridone, a receiving fluid was needed that would more closely imitate field conditions. Therefore, for the majority of release studies with fluridone and all of the release studies with endothall, the receiving fluid consisted of an artificially prepared solution of hard water. The reconstituted hard water contained 3.84 g of sodium bicarbonate, 0.16 g of potassium chloride, 2.4 g of magnesium sulfate, and 1.89 g of calcium sulfate in 20 l of deionized water. A standard curve for fluridone was also constructed for this receiving fluid (Figure A2). Standards were prepared by first dissolving fluridone in a minute quantity of methanol and diluting with hard water to give a stock solution containing 10 ml of methanol in 2 l of hard water. This stock solution was then diluted serially to obtain additional standards.

26. Release studies with fibers and pellets were conducted in the same manner. Triplicate samples were immersed in individual vessels containing hard water. Each sample consisted of enough fiber, fiber staple, or pellets for fluridone to be measurable in the receiving fluid while still maintaining infinite-sink conditions (one-tenth saturation or less). The vessels were sealed and agitated on an Eberbach shaker at room temperature. The receiving

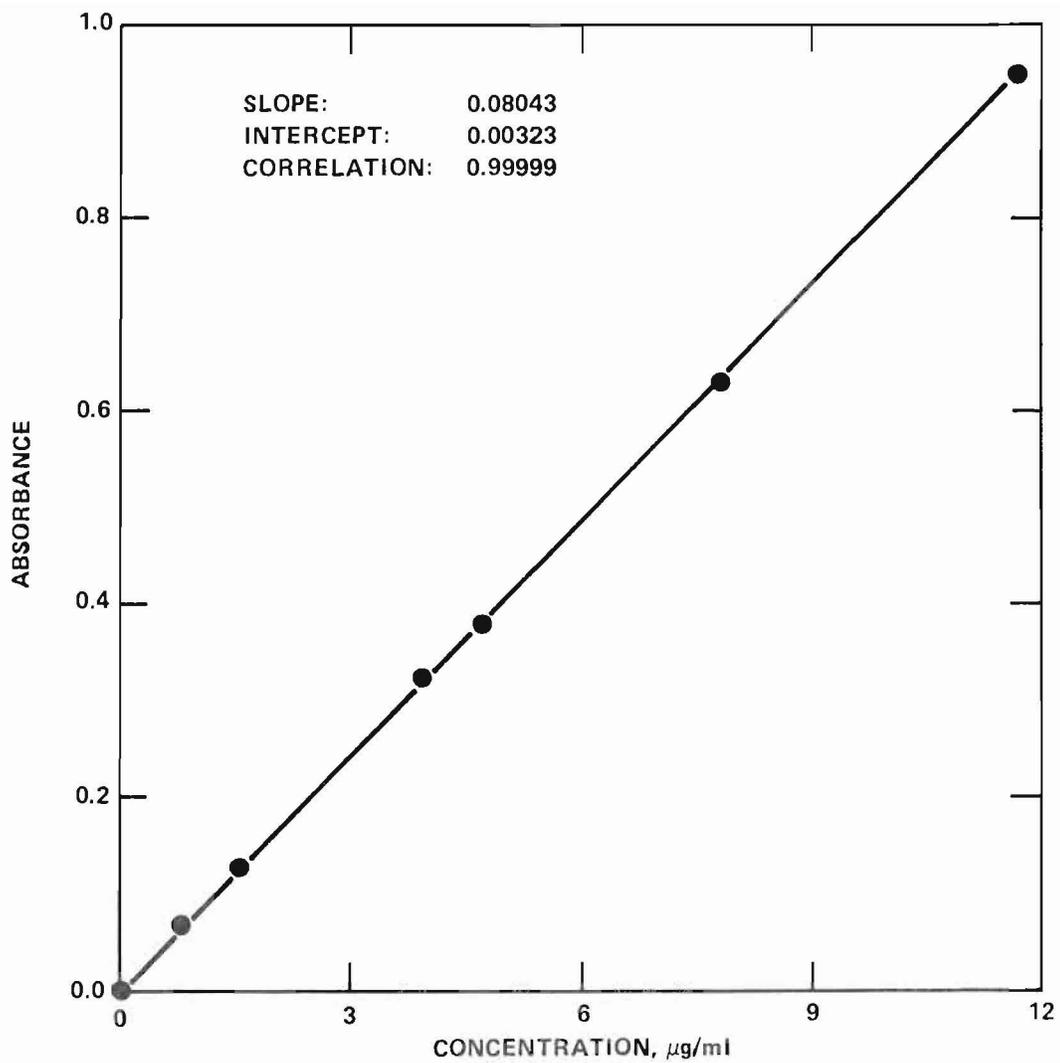


Figure A1. Calibration curve for UV absorbance at 237 nm versus fluridone concentration in 50:50 ethanol/water

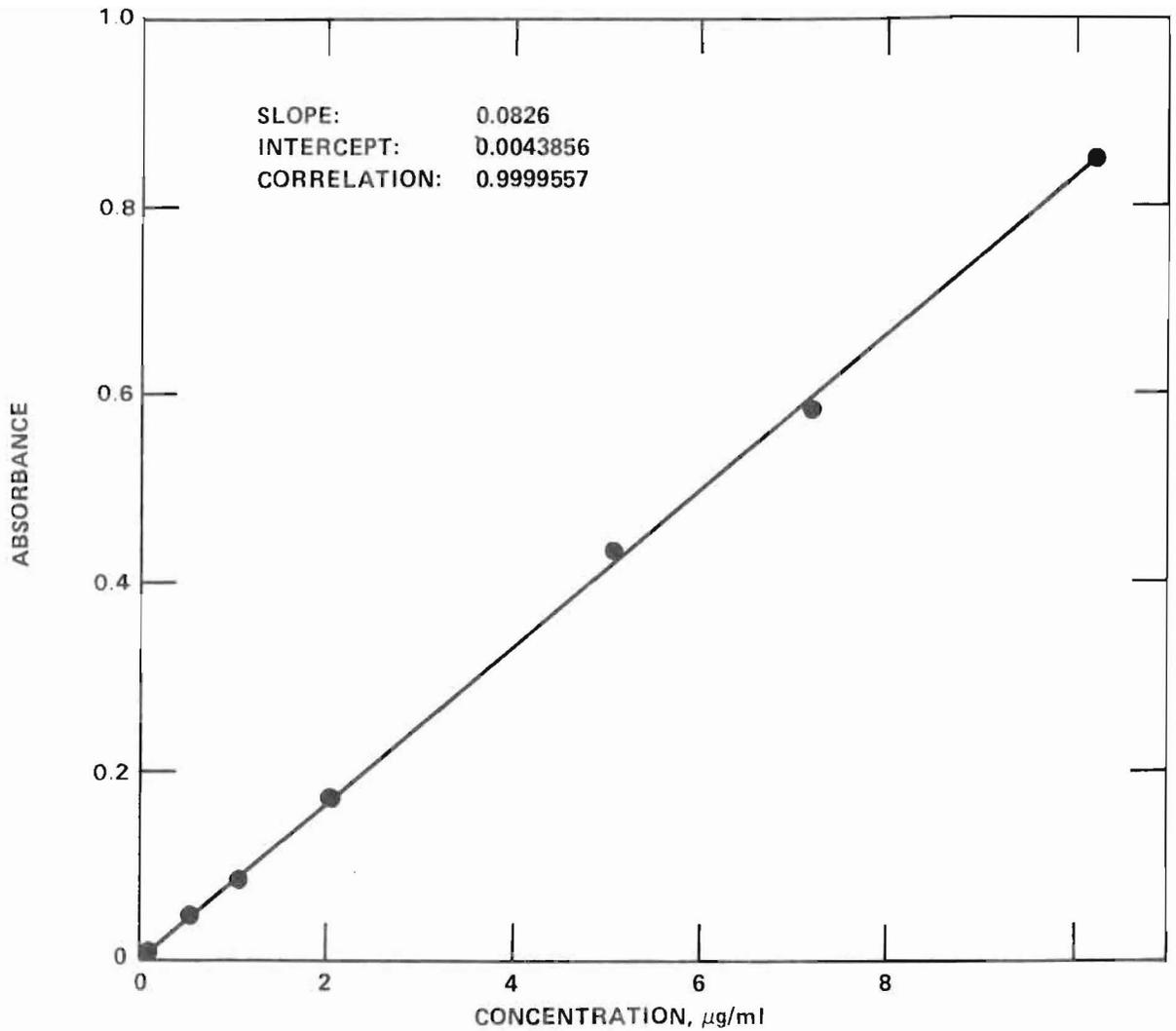


Figure A2. Calibration curve for UV absorbance at 236 nm versus fluridone concentration in hard water

fluid was periodically exchanged for fresh receiving fluid and assayed for fluridone.

Determination of Endothall

27. Endothall was quantified by high-performance liquid chromatography. The chromatographic system consisted of a Hewlett-Packard (HP) Model 1090 liquid chromatograph equipped with a diode-array detector and an auto sampler, an HP Model 85B computer equipped with a dual disk drive, an HP Model 3392A integrator, and an HP Model 7470A printer/plotter. A 10- μ Partisil ODS-3 column (Phenomenex) was used, and endothall was eluted with 83:17 phosphate buffer (pH 2.7)/methanol (v/v) at a flow rate of 0.8 ml/min. Endothall was detected at a wavelength setting of 225 ± 4 nm. Each set of samples from a release study was accompanied by endothall standards prepared from the same lot of endothall used in preparing pellets. The sensitivity of the assay ranges from approximately 20 to 200 μ g/ml receiving fluid. A typical standard curve is shown in Figure A3.

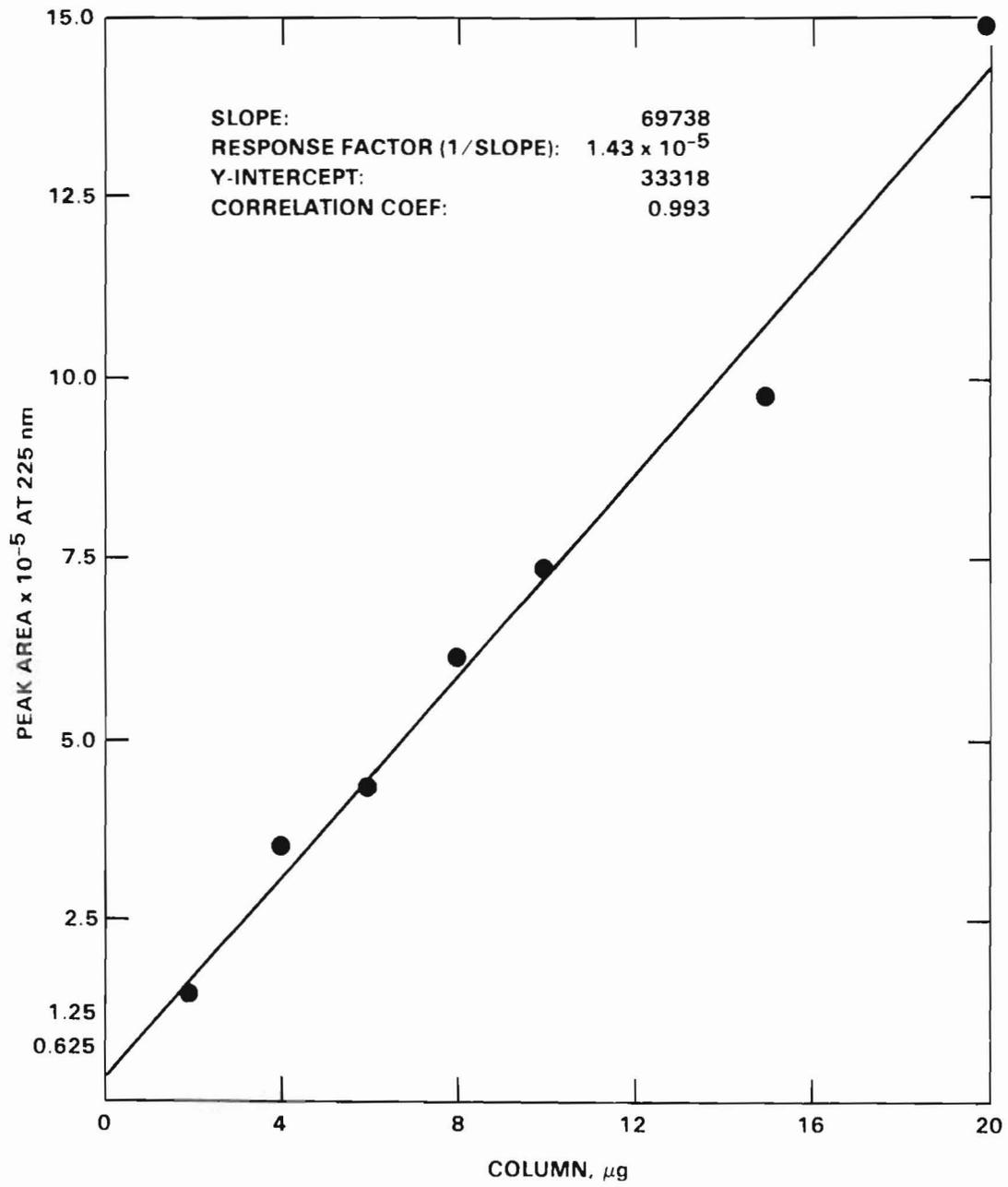


Figure A3. Standard curve for endothall