



US005868720A

United States Patent [19]
Van Antwerp

[11] **Patent Number:** **5,868,720**
[45] **Date of Patent:** **Feb. 9, 1999**

- [54] **INDWELLING CATHETER WITH STABLE ENZYME COATING**
- [76] Inventor: **William P. Van Antwerp**, 7809 Airport Blvd., Westchester, Calif. 90045
- [21] Appl. No.: **127,839**
- [22] Filed: **Aug. 3, 1998**

Related U.S. Application Data

- [62] Division of Ser. No. 557,408, Nov. 13, 1995, Pat. No. 5,788,678, which is a division of Ser. No. 428,944, Apr. 25, 1995, Pat. No. 5,538,511, which is a division of Ser. No. 221,934, Apr. 1, 1994, Pat. No. 5,506,713.
- [51] **Int. Cl.⁶** **A61M 5/32**
- [52] **U.S. Cl.** **604/265**; 604/266; 604/890.1; 427/2.3
- [58] **Field of Search** 604/264, 265, 604/266, 890.1, 891.1, 892.1; 424/422, 423, 426, 499; 435/177, 178, 180; 427/2.12, 2.28, 2.3

References Cited

U.S. PATENT DOCUMENTS

- 4,305,926 12/1981 Everse et al. .
- 4,378,425 3/1983 Schnoering et al. .
- 4,592,920 6/1986 Murfeldt .
- 4,879,135 11/1989 Greco et al. .
- 4,906,237 3/1990 Johansson et al. .
- 5,001,062 3/1991 Larsson et al. .

- 5,019,393 5/1991 Ito et al. .
- 5,061,237 10/1991 Gessler et al. .
- 5,102,402 4/1992 Dior et al. .
- 5,126,140 6/1992 Ito et al. .
- 5,167,960 12/1992 Ito et al. .
- 5,182,317 1/1993 Winters et al. .
- 5,217,492 6/1993 Guire et al. .
- 5,244,799 9/1993 Anderson .
- 5,258,041 11/1993 Guire et al. .
- 5,263,992 11/1993 Guire .
- 5,298,255 3/1994 Sawamoto et al. .
- 5,304,121 4/1994 Sahatjian .
- 5,324,261 6/1994 Amundson et al. .
- 5,470,307 11/1995 Lindall .
- 5,531,716 7/1996 Luzio et al. .
- 5,554,147 9/1996 Batich et al. .

FOREIGN PATENT DOCUMENTS

- 366564A3 6/1993 European Pat. Off. .

Primary Examiner—John D. Yasko
Attorney, Agent, or Firm—Minimed Inc.

[57] **ABSTRACT**

An improved indwelling catheter adapted for long-term usage includes a stable enzyme coating to prevent occlusion of the catheter lumen. The enzyme coating includes a fibrinolytic and/or lipolytic enzyme incorporated in a catheter coating to resist or control proteolytic degradation, thereby maintaining the enzyme in an active state for dissolving clots and occlusions within the catheter lumen over an extended period of time.

19 Claims, 3 Drawing Sheets

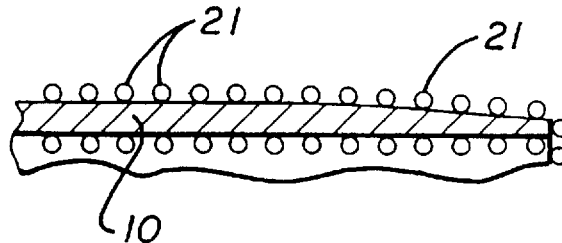


FIG. 1

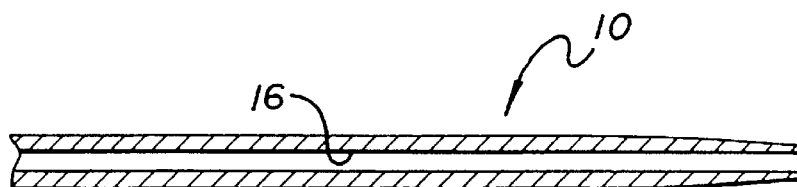
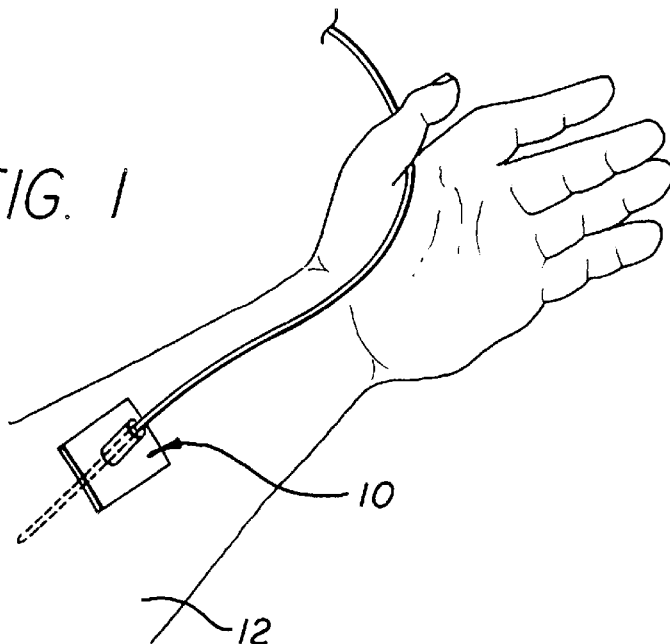


FIG. 2

FIG. 3

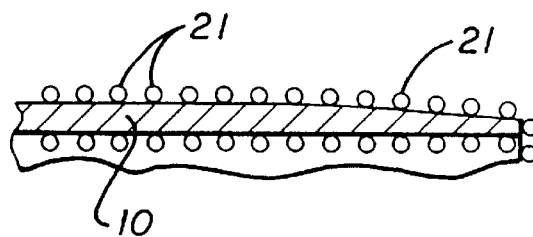
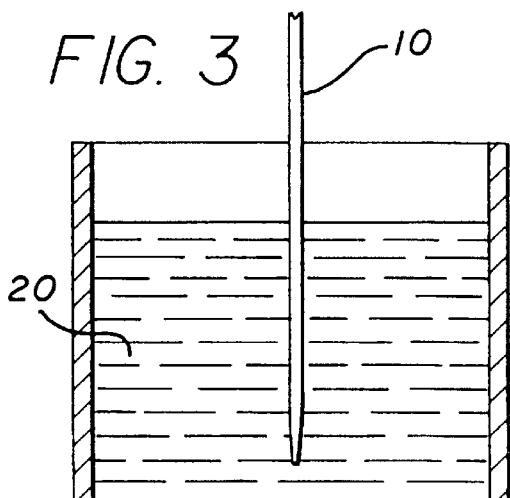


FIG. 4

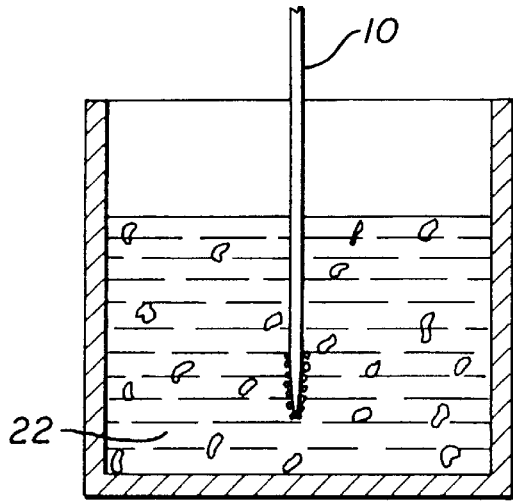


FIG. 5

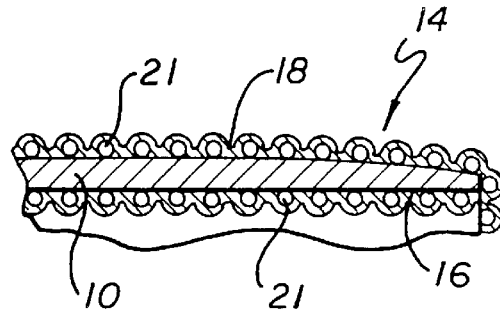


FIG. 6

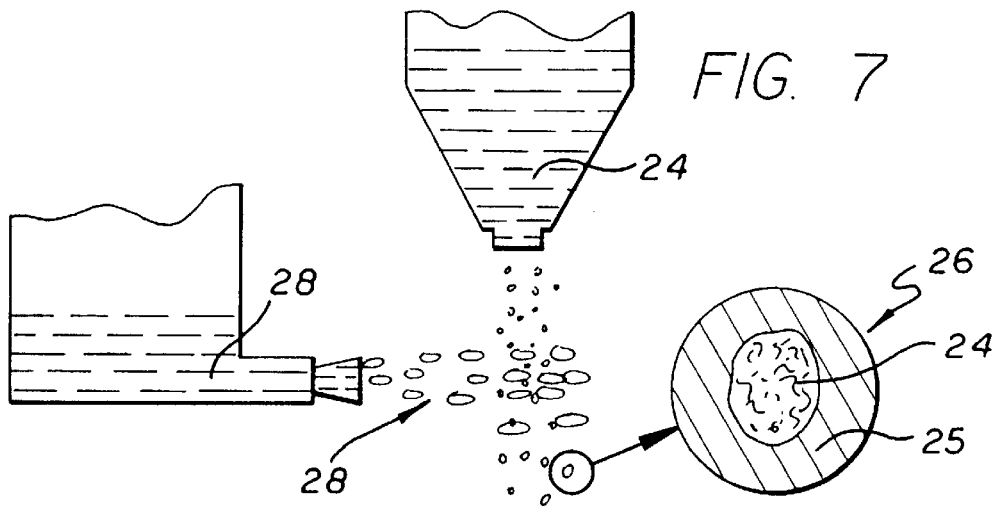


FIG. 7

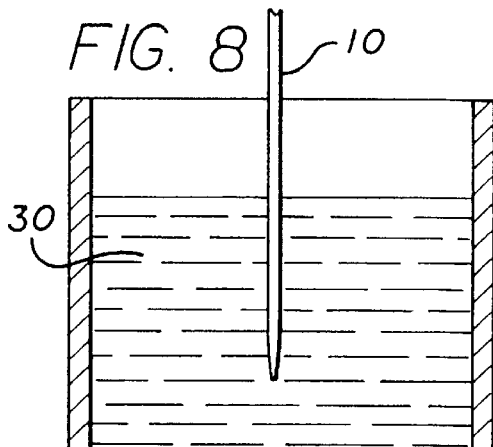


FIG. 8

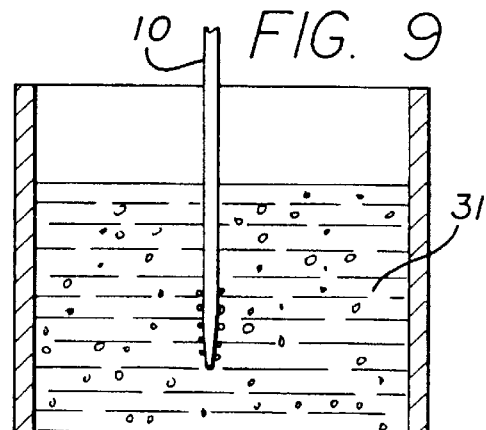
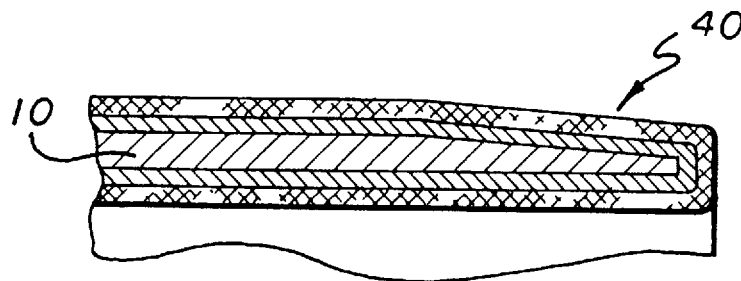
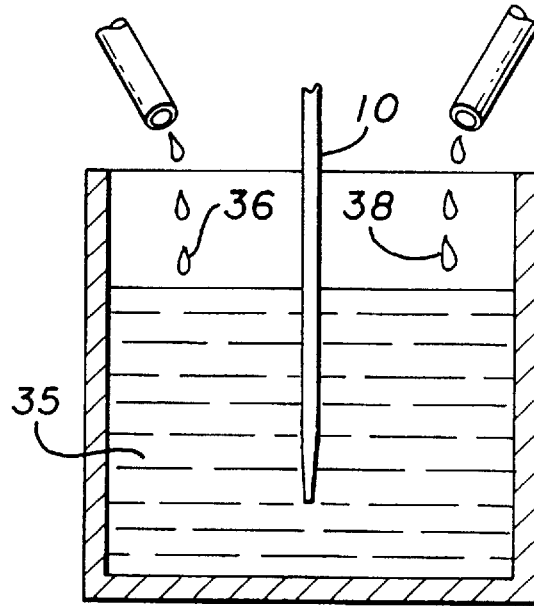
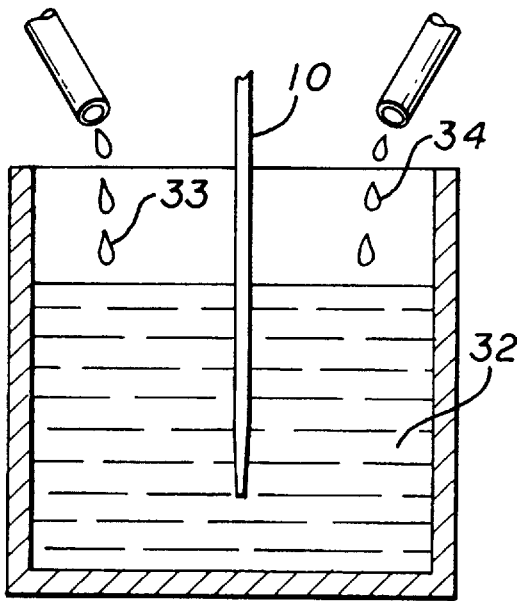
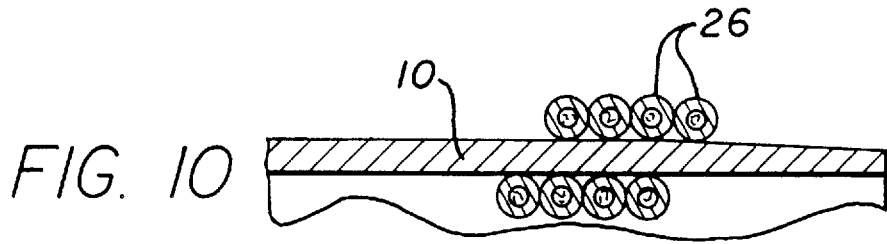


FIG. 9



INDWELLING CATHETER WITH STABLE ENZYME COATING

This is a divisional application of U.S. patent application Ser. No. 08/557,408 filed Nov. 13, 1995, now U.S. Pat. No. 5,788,678 which is a divisional application of U.S. patent application Ser. No. 08/428,944 filed Apr. 25, 1995, now U.S. Pat. No. 5,538,511, which is a divisional application of U.S. patent application Ser. No. 08/221,934 filed Apr. 1, 1994, now U.S. Pat. No. 5,505,713.

BACKGROUND OF THE INVENTION

This invention relates generally to improvements in catheters for use in delivering medical fluids to a patient. More particularly, this invention relates to an improved catheter and related methods of manufacture, wherein the improved catheter has a stabilized enzyme coating for long-term interaction with body fluids to prevent and/or dissolve clots and occlusions within the catheter lumen.

Catheters are well-known in the medical arts for use in delivering medical fluids to or drawing body fluids from a patient. In one typical form, the catheter comprises an elongated tubular element adapted for transcutaneous placement, normally with the assistance of a withdrawable stylet needle. The catheter defines a narrow lumen or passage permitting transcutaneous fluid transfer to or from the patient. In another typical application, the catheter is implanted into the patient in association with an implantable infusion pump or similar instrument for programmed delivery of a selected medication such as insulin over an extended period of time. One such implantable infusion pump including an implantable catheter is shown, by way of example, in U.S. Pat. Nos. 4,373,527 and 4,573,994. In either case, the catheter is commonly constructed from a biocompatible polymer material, such as a medical grade silicone rubber.

In many patient treatment applications, it is necessary or desirable for the catheter to remain in place for an extended period of time which may range from several days to several years. Such long-term indwelling catheters are routinely used, for example, for monitoring patient blood components, dialysis and hemodialysis, parenteral feeding, delivery of certain medications, etc. However, the catheter lumen is susceptible to occlusion which occurs as a result of complex interactions involving the catheter material, and the simultaneous presence of infusion and body fluids. In some forms, catheter occlusions appear to consist primarily of fibrin-based clots, whereas in other forms the occlusions include lipid-based substances. When an occlusion occurs, the catheter must be replaced or the lumen otherwise cleared before infusion of the medical fluids can be resumed. Occlusion removal in an implanted catheter can be difficult, and removal is not a desirable alternative.

In the past, several methods have been proposed in an effort to prevent catheter occlusions or otherwise to clear the catheter lumen after a blockage has occurred. More specifically, heparin is well-known for its anticoagulant characteristics, and is frequently used to prevent clot formation within the catheter lumen. In one approach, the catheter lumen is simply dipped in a heparin solution before patient placement, with the dip coating being generally effective to prevent localized clotting over a relatively short period of time until the heparin is degraded upon contact

Unfortunately, heparin is ineffective to dissolve clots and/or other occlusions after formation thereof, whereby heparin usage has not provided satisfactory catheter occlusion control. Moreover, heparin has not been approved for use with some medications, such as insulin.

Alternative occlusion control methods have utilized a fibrinolytic enzyme such as a kinase enzyme known to be effective in dissolving fibrin-based clots. In this regard, dip coating of the catheter in a solution containing a fibrinolytic enzyme has been shown to be effective in preventing and/or dissolving clots along the narrow catheter lumen. However, in the presence of body fluids, the fibrinolytic enzyme degrades rapidly and is thus ineffective for long-term occlusion control. Any clots formed subsequent to enzyme degradation are extremely difficult to dissolve, since it is difficult to deliver additional enzyme solution to the blockage site along the catheter lumen.

In addition, it is believed that occlusions forming along the catheter lumen are frequently attributable at least in part and perhaps primarily to accumulation of lipid-based substances, with fibrin-based clotting having a lesser role in formation of the blockage. Previous occlusion control methods involving the use of heparin or fibrinolytic enzymes are ineffective to break down and dissolve a lipid-based occlusion.

There exists, therefore, a significant need for further improvements in indwelling catheters and related methods for preventing and/or dissolving catheter occlusions, particularly for use in providing occlusion control over an extended period of time. The present invention fulfills these needs and provides further related advantages.

SUMMARY OF THE INVENTION

In accordance with the invention, an improved indwelling catheter and related production method are provided, wherein the catheter includes a stable and substantially immobilized enzyme coating to prevent formation of and/or to dissolve occlusions along the catheter lumen. The enzyme coating comprises a selected fibrinolytic and/or lipolytic enzyme applied to the catheter, in combination with means for preventing or otherwise regulating proteolytic degradation in response to enzyme interaction with body fluids. The thus-protected enzyme exhibits relatively stable characteristics, with long-term effectiveness in the prevention and/or dissolution of catheter occlusions.

In one form, the selected enzyme is applied to indwelling surfaces of the catheter as a thin micellar coating. A porous encapsulant such as a porous silicone rubber film is then applied to the catheter to cover and encapsulate the micellar enzyme. The porosity of the encapsulant film is controlled to isolate the enzyme from significant interaction with proteolytic body fluids, while permitting diffusion of other body fluid constituents to activate the enzyme for purposes of preventing or dissolving an occlusion. For example, by controlling the porosity of the encapsulant film, a fibrinolytic enzyme can be protected against proteolytic degradation yet interact with plasminogen to produce plasmin which is effective in dissolving fibrin-based clots.

In an alternative form, the selected enzyme in particulate form is coated with an encapsulant shell of starch-based material or the like, and variable coating thickness. The resultant capsules are bonded to the polymeric surface of the catheter by silicone chemistry, such as coating the capsules

Explore Litigation Insights

Docket Alarm provides insights to develop a more informed litigation strategy and the peace of mind of knowing you're on top of things.

Real-Time Litigation Alerts



Keep your litigation team up-to-date with **real-time alerts** and advanced team management tools built for the enterprise, all while greatly reducing PACER spend.

Our comprehensive service means we can handle Federal, State, and Administrative courts across the country.

Advanced Docket Research



With over 230 million records, Docket Alarm's cloud-native docket research platform finds what other services can't. Coverage includes Federal, State, plus PTAB, TTAB, ITC and NLRB decisions, all in one place.

Identify arguments that have been successful in the past with full text, pinpoint searching. Link to case law cited within any court document via Fastcase.

Analytics At Your Fingertips



Learn what happened the last time a particular judge, opposing counsel or company faced cases similar to yours.

Advanced out-of-the-box PTAB and TTAB analytics are always at your fingertips.

API

Docket Alarm offers a powerful API (application programming interface) to developers that want to integrate case filings into their apps.

LAW FIRMS

Build custom dashboards for your attorneys and clients with live data direct from the court.

Automate many repetitive legal tasks like conflict checks, document management, and marketing.

FINANCIAL INSTITUTIONS

Litigation and bankruptcy checks for companies and debtors.

E-DISCOVERY AND LEGAL VENDORS

Sync your system to PACER to automate legal marketing.