

US005866154A

## **United States Patent** [19]

Bahal et al.

[11] Patent Number: 5,866,154 [45] Date of Patent: Feb. 2, 1999

[54]	STABILIZED NALOXONE FORMULATIONS	
[75]	Inventors:	Surendra Mohan Bahal, Wayne, Pa.; Lei-Shu Wu, Wilmington, Del.
[73]	Assignee:	The DuPont Merck Pharmaceutical Company, Wilmington, Del.
[21]	Appl. No.: 673,601	
[22]	Filed:	Jun. 25, 1996
Related U.S. Application Data		

[63] Continuation of Ser. No. 319,920, Oct. 7, 1994, abandoned.

[52] U.S. Cl. 424/423; 514/23 [58] Field of Search 514/23; 424/423 Primary Examiner—Carlos A. Azpuru Attorney, Agent, or Firm—Karen H. Kondrad

[56]

[57] ABSTRACT

Physically and chemically stable pharmaceutical compositions useful for administering naloxone by injection are described. These compositions are essentially aqueous solutions having a pH between 3.0–3.5, and containing naloxone, an acidic or buffer component, a tonicity-adjusting agent, and a stabilizing agent, said composition being optionally sterilized by autoclaving.

9 Claims, 8 Drawing Sheets

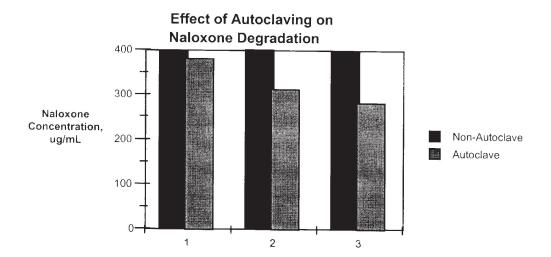




Figure 1a

Feb. 2, 1999

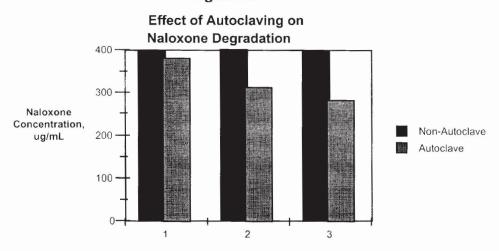


Figure 1b

#### Effect of Autoclaving on Noroxymorphone Formation 60 51.14 50 42.01 Noroxymorphone 40 Concentration, ug/mL 30 20 7.38 10 0.29 0.31 0.3

The degradation of naloxone (Figure 1a) and formation of noroxymorphone (Figure 1b) for nitrogen sparged (1), non-sparged (2), and oxygen sparged (3) samples under autoclaving and non-autoclaving conditions.

2

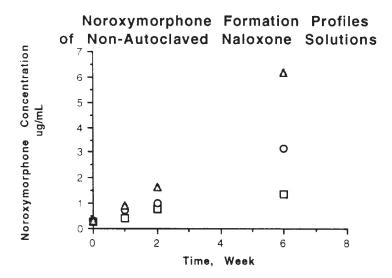


Figure 2 Noroxymorphone formation profiles of non-autoclaved naloxone solutions stored at 60°C. Oxygen sparged sample (~100% oxygen in headspace) Non-sparged sample (18% oxygen in headspace) 0 

headspace)

Nitrogen sparged sample (3-5% oxygen in



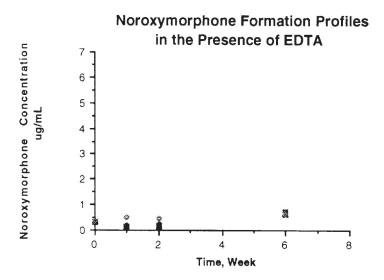


Figure 3 Noroxymorphone formation profiles of solutions with EDTA added and stored at 60  $^{\circ}\text{C}\,.$   $\theta$  Nitrogen sparged, non-autoclaved sample

F Nitrogen sparged, autoclaved sample
Non-sparged, non-autoclaved sample
V Non-sparged, autoclaved sample

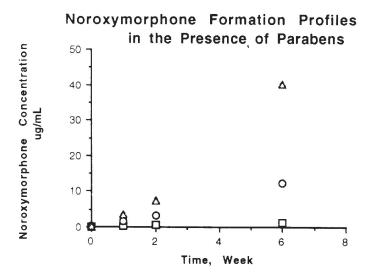


Figure 4 Noroxymorphone formation profiles of samples with parabens added and stored at  $60^{\circ}\text{C}$ .  $\Delta$  Oxygen sparged sample;

O Non-sparged sample;

Nitrogen sparged sample.

# DOCKET

# 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.

