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**United States Patent** [19]  
**Bahal et al.**

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[54] **STABILIZED NALOXONE FORMULATIONS**  
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[21] Appl. No.: **673,601**  
[22] Filed: **Jun. 25, 1996**

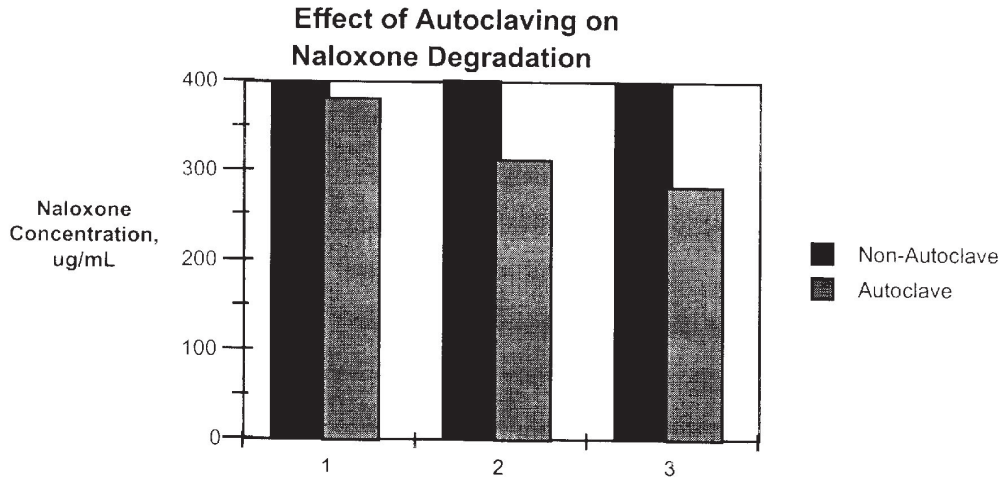
**Related U.S. Application Data**

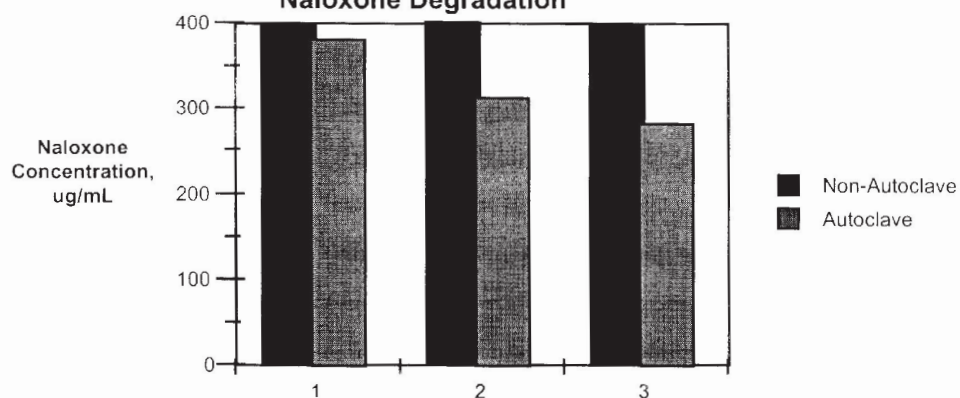
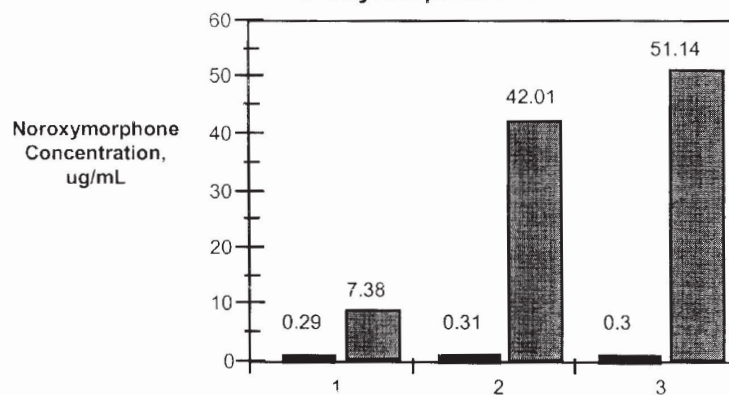
[63] Continuation of Ser. No. 319,920, Oct. 7, 1994, abandoned.  
[51] **Int. Cl.<sup>6</sup>** ..... **A61F 2/02; A61K 31/70**  
[52] **U.S. Cl.** ..... **424/423; 514/23**  
[58] **Field of Search** ..... **514/23; 424/423**

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*Primary Examiner*—Carlos A. Azpuru  
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[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****Effect of Autoclaving on  
Naloxone Degradation****Figure 1b****Effect of Autoclaving on  
Noroxymorphone Formation**

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.

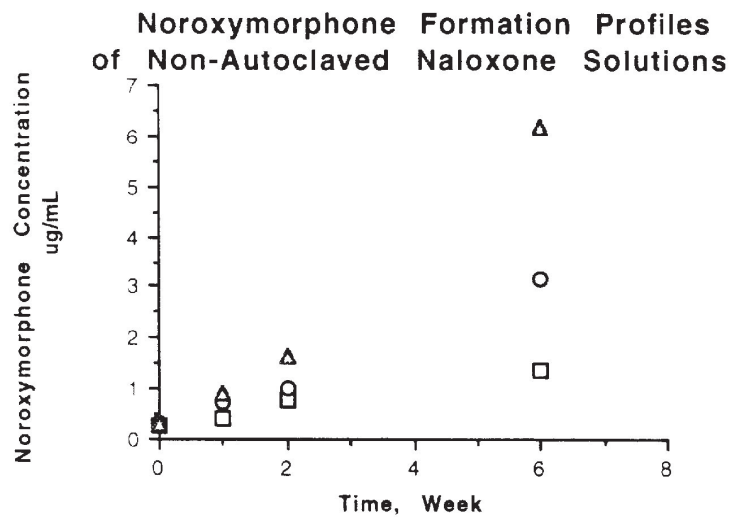


Figure 2 Noroxymorphone formation profiles of non-autoclaved naloxone solutions stored at 60°C.

- Δ Oxygen sparged sample (~100% oxygen in headspace)
- Non-sparged sample (18% oxygen in headspace)
- Nitrogen sparged sample (3-5% oxygen in headspace)

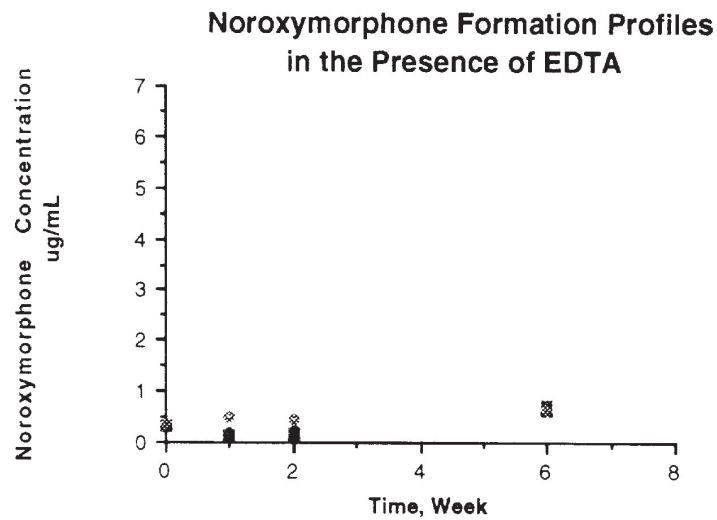


Figure 3 Noroxymorphone formation profiles of solutions with EDTA added and stored at 60°C.

- θ Nitrogen sparged, non-autoclaved sample
- F Nitrogen sparged, autoclaved sample
- n Non-sparged, non-autoclaved sample
- v Non-sparged, autoclaved sample

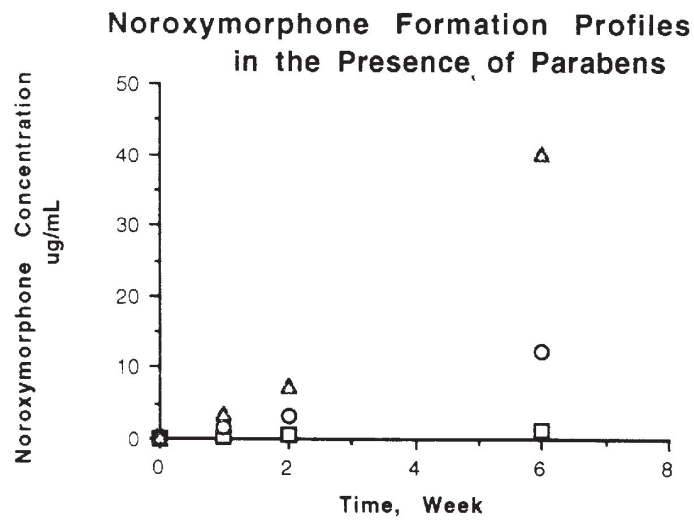


Figure 4 Noroxymorphone formation profiles of samples with parabens added and stored at 60°C.  
Δ Oxygen sparged sample;  
O Non-sparged sample;  
□ Nitrogen sparged sample.

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