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United States Patent [19]
Bahal et al.

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[54] **STABILIZED NALOXONE FORMULATIONS**
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Related U.S. Application Data

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

[56] **References Cited**
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Primary Examiner—Carlos A. Azpuru
Attorney, Agent, or Firm—Karen H. Kondrad

[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

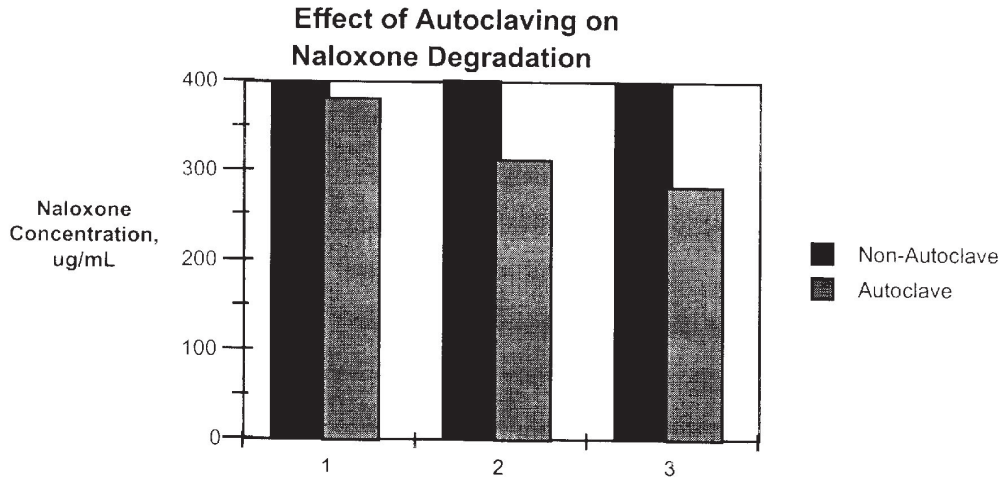


Figure 1a

Effect of Autoclaving on Naloxone Degradation

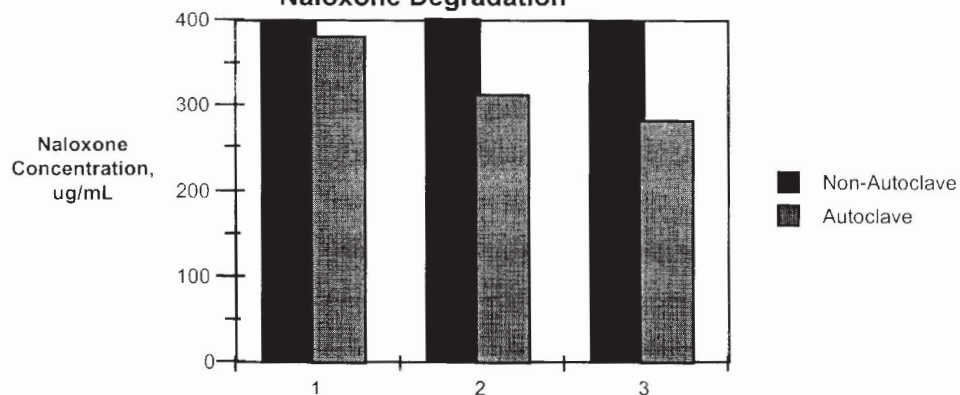
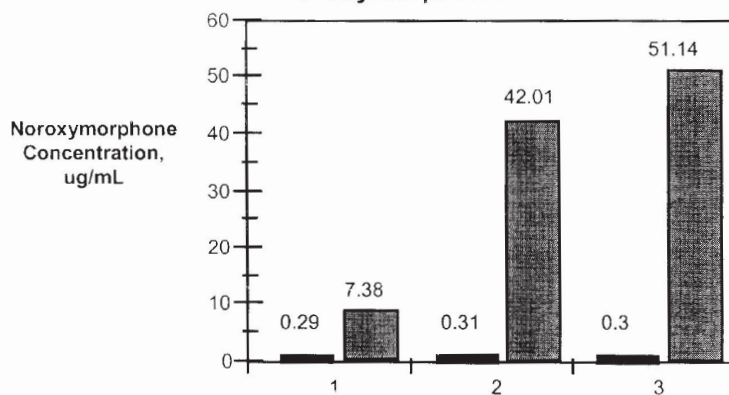


Figure 1b

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.

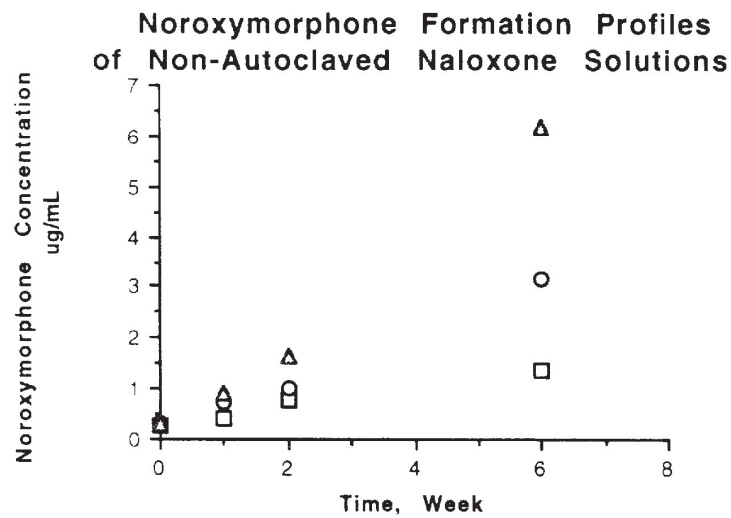


Figure 2 Noroxymorphone formation profiles of non-autoclaved naloxone solutions stored at 60°C.

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

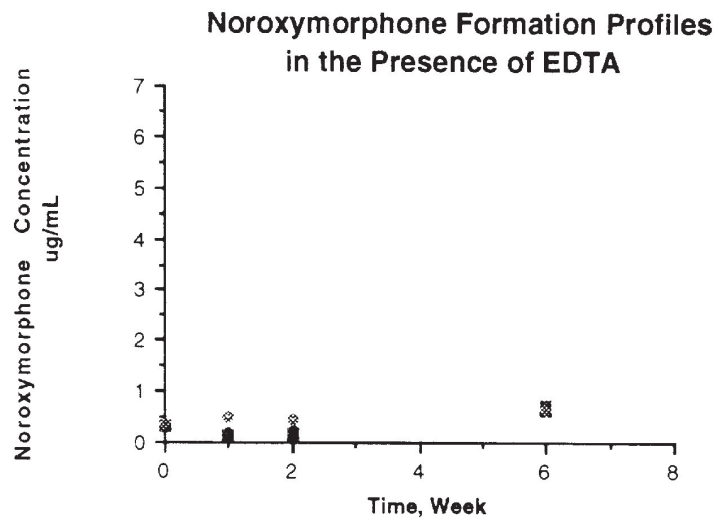


Figure 3 Noroxymorphone formation profiles of solutions with EDTA added and stored at 60°C.

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

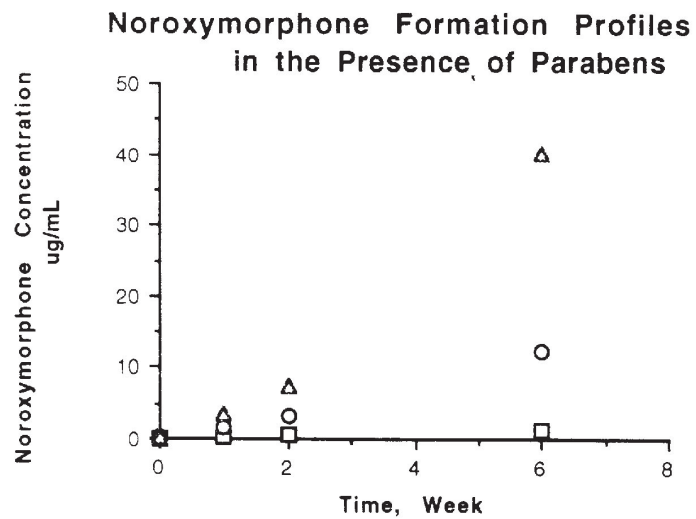


Figure 4 Noroxymorphone formation profiles of samples with parabens added and stored at 60°C.
Δ Oxygen sparged sample;
O Non-sparged sample;
□ Nitrogen sparged sample.

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