Development of tramadol hydrochloride rectal gel preparations and evaluation of analgesic activity in experimental animals

Reanmongkol, W. a, Kaewnopparat, N. b, Ratanajamit, C. a

a Department of Clinical Pharmacy, Faculty of Pharmaceutical Sciences, Prince of Songkla University, Hat Yai, Songkhla 90110, Thailand
b Department of Pharmaceutical Technology, Faculty of Pharmaceutical Sciences, Prince of Songkla University, Hat Yai, Songkhla 90110, Thailand

Abstract
Tramadol rectal gel preparations were developed using poloxamer or hydroxyethylcellulose as a gel base. The tramadol rectal gel using poloxamer has a gel point at 36°C and was more bioadhesive (65.5 ± 2.4 × 10^{-2} dyne/cm²) to the rectal mucous membrane than was the gel with the hydroxyethylcellulose base (37.4 ± 2.2 × 10^{-2} dyne/cm²) with the gel strength of 87 ± 2 and 70 ± 2 s, respectively. All rectal gel formulations were colorless, clear, viscous liquid with a pH range of 6.65-7.13. In an in vitro release study, the release profiles of the drug from both rectal gels were similar and the cumulative amount of drug release was about 97 and 98% in 5 h for the mucoadhesive gel and thermoreversible gel, respectively. Analysis of the release kinetics revealed that the drug might be released from the rectal gels by non-Fickian diffusion. In an in vivo analgesic study, administration of tramadol (0.25, 0.5, and 1.0 mg) rectal gel using poloxamer as the gel base, exerted a marked increase in the latency of the nociceptive response in mice. Similar results were also observed when using hydroxyethylcellulose as the base. These results indicated that tramadol rectal gels prepared using poloxamer or hydroxyethylcellulose as a gel base showed a complete release of the drug from the bases, as well as prolonging the latency of a nociceptive response in experimental animals.

Author keywords
Pain; Physicochemical; Rectal gel; Release study; Tramadol

Indexed keywords
EMTREE drug terms: hydroxyethylcellulose; poloxamer; tramadol
EMTREE medical terms: analgesic activity; animal cell; animal experiment; animal model; article; controlled study; experimental animal; gel; male; mouse; mucosa; nociceptive stimulation; nonhuman; pH; rectum

Chemicals and CAS Registry Numbers: hydroxyethylcellulose, 9004-62-0; poloxamer, 9003-11-6; tramadol, 27203-92-5, 36282-47-0

Manufacturers: Drug manufacturer: Biolab, Thailand.

ISSN: 17732247 CODEN: JODSA Source Type: Journal Original language: English Document Type: Article

References (25)
Clinical pharmacology of tramadol
doi: 10.2165/00003088-200443130-00004

Enhanced rectal absorption of insulin-loaded Pluronic® F-127 gels containing unsaturated fatty acids
doi: 10.1016/S0378-5173(99)00090-3

Modulation of the rheological and mucoadhesive properties of thermosensitive poloxamer-based hydrogels intended for the rectal administration of quinine
doi: 10.1016/j.ejps.2005.11.001

In vitro and in vivo characteristics of a thermogelling and bioadhesive delivery system intended for rectal administration of quinine in children
doi: 10.1016/j.ejpb.2007.09.017

Enhanced rectal bioavailability of ibuprofen in rats by poloxamer 188 and menthol

Effect of sodium chloride on the gelation temperature, gel strength and bioadhesive force of poloxamer gels containing diclofenac sodium
doi: 10.1016/S0378-5173(01)00809-2

Development of in situ gelling and mucoadhesive mebeverine hydrochloride solution for rectal administration

**Pluronic gels for nasal delivery of Vitamin B\(_{12}\). Part I: Preformulation study**


**Preparation of ibuprofen-loaded liquid suppository using eutectic mixture system with menthol**

Woolfe, G., MacDonald, A.D.

**The evaluation of the analgesic action of pethidine hydrochloride (Demerol)**

Barakat, N.S.

**In vitro and in vivo characteristics of a thermogelling rectal delivery system of etodolac**


**Increased bioavailability of propranolol in rats by retaining thermally gelling liquid suppositories in the rectum**


**Effect of additives on the physicochemical properties of liquid suppository bases**

Martin, A.


4th ed., Lea & Febiger, Philadelphia


**Effect of sodium chloride on the release, absorption and safety of diclofenac sodium delivered by poloxamer gel**

Hewitt, W.D.

**Compounded suppositories and pharmaceutical care**


**Trials of in situ-gelling and mucoadhesive acetaminophen liquid suppository in human subjects**
Peppas, N.A.  
**Analysis of Fickian and non-Fickian drug release from polymers.**  

Fawaz, F., Koffi, A., Guyot, M., Millet, P.  
**Comparative in vitro-in vivo study of two quinine rectal gel formulations**  
doi: 10.1016/j.ijpharm.2004.05.002

Le Bars, D., Gozariu, M., Cadden, S.W.  
**Animal models of nociception**  

Sacerdote, P., Bianchi, M., Manfredi, B., Panerai, A.E.  
**Effects of tramadol on immune responses and nociceptive thresholds in mice**  
doi: 10.1016/S0304-3959(97)00055-9

Reanmongkol, W.; Department of Clinical Pharmacy, Faculty of Pharmaceutical Sciences, Prince of Songkla University, Hat Yai, Songkhla 90110, Thailand; email: wantana.r@psu.ac.th  
© Copyright 2012 Elsevier B.V., All rights reserved.