



US007977376B2

(12) **United States Patent**
Singh et al.

(10) **Patent No.:** **US 7,977,376 B2**
(45) **Date of Patent:** **Jul. 12, 2011**

(54) **OLOPATADINE FORMULATIONS FOR TOPICAL NASAL ADMINISTRATION**

(75) Inventors: **Onkar N. Singh**, Arlington, TX (US); **G. Michael Wall**, Fort Worth, TX (US); **Rajni Jani**, Fort Worth, TX (US); **Masood A. Chowhan**, Arlington, TX (US); **Wesley Wehsin Han**, Arlington, TX (US)

(73) Assignee: **Novartis AG**, Basal (CH)

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 228 days.

(21) Appl. No.: **11/703,373**

(22) Filed: **Feb. 7, 2007**

(65) **Prior Publication Data**

US 2007/0142458 A1 Jun. 21, 2007

Related U.S. Application Data

(63) Continuation-in-part of application No. 11/079,996, filed on Mar. 15, 2005, now Pat. No. 7,402,609, which is a continuation of application No. 10/175,106, filed on Jun. 19, 2002, now Pat. No. 6,995,186.

(60) Provisional application No. 60/301,315, filed on Jun. 27, 2001.

(51) **Int. Cl.**
A61K 31/335 (2006.01)

(52) **U.S. Cl.** **514/450; 424/810**

(58) **Field of Classification Search** None
See application file for complete search history.

(56) **References Cited**

U.S. PATENT DOCUMENTS

4,407,791 A 10/1983 Stark 424/80
4,749,700 A 6/1988 Wenig 514/225.2

4,778,596 A * 10/1988 Linder et al. 210/638
4,871,865 A 10/1989 Lever, Jr. et al. 549/354
4,923,892 A 5/1990 Lever, Jr. et al. 514/450
5,116,863 A 5/1992 Oshima et al. 514/450
5,164,194 A 11/1992 Hettche 424/489
5,443,833 A * 8/1995 Clark et al. 424/400
5,478,565 A * 12/1995 Geria 424/434
5,482,706 A * 1/1996 Igari et al. 424/85.7
5,641,805 A * 6/1997 Hayakawa et al. 514/450
6,054,462 A * 4/2000 François et al. 514/275
6,146,622 A 11/2000 Castillo et al. 424/78.02
6,174,914 B1 1/2001 Yanni et al. 514/450
6,207,684 B1 3/2001 Aberg 514/324

(Continued)

FOREIGN PATENT DOCUMENTS

EP 0 048 023 3/1982

(Continued)

OTHER PUBLICATIONS

PH Ratner, FC Hampel, NJ Amar, JH van Bevel, D Mohar, BF Marple, PS Roland, GM Wall, MJ Brubaker, M Drake, D Turner, LH Silver. Safety and Efficacy of Olopatadine Hydrochloride Nasal Spray for the Treatment of Seasonal Allergic Rhinitis to Mountain Cedar. *Annals Allergy Asthma Immunol.* 2005. vol. 95, pp. 474-479.*

(Continued)

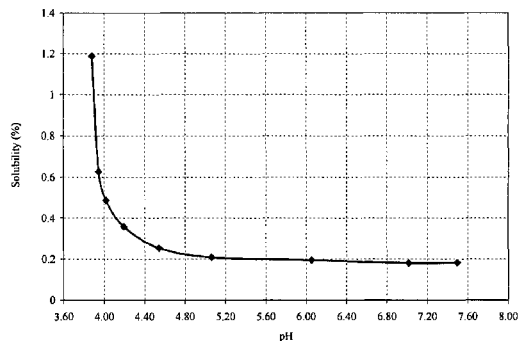
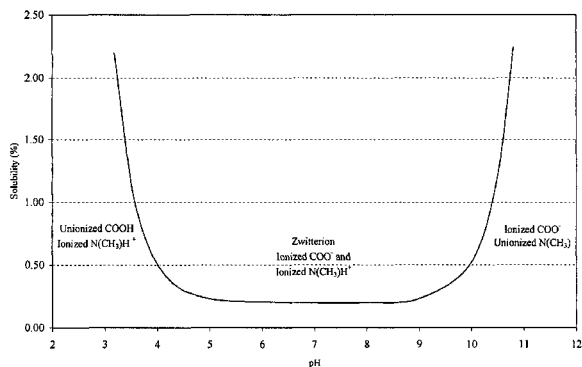
Primary Examiner — Patricia A Duffy
Assistant Examiner — Isaac Shomer

(74) *Attorney, Agent, or Firm* — Patrick M. Ryan

(57) **ABSTRACT**

Topical formulations of olopatadine for treatment of allergic or inflammatory disorders of the nose are disclosed. The aqueous formulations contain approximately 0.6% (w/v) of olopatadine.

2 Claims, 4 Drawing Sheets



U.S. PATENT DOCUMENTS

6,316,483	B1	11/2001	Hasiwanter et al.	514/401
6,333,044	B1	12/2001	Santus et al.	424/434
6,995,186	B2 *	2/2006	Castillo et al.	514/450
2001/0056093	A1	12/2001	Yanni	514/218
2006/0110328	A1	5/2006	Cagle et al.	424/45

FOREIGN PATENT DOCUMENTS

EP	0 214 779	3/1987
EP	0 235 796	9/1987
JP	61926	3/1995
WO	WO 00/03705	1/2000
WO	WO 01/21209	3/2001
WO	WO 01/21210	3/2001
WO	WO 01/35963	5/2001
WO	WO 01/54687 A1	8/2001
WO	WO 02/30395 A1	4/2002
WO	WO 03/002093	1/2003
WO	WO 03002093 A1 *	1/2003
WO	WO 2004/043470	5/2004

OTHER PUBLICATIONS

SM Berge, LD Bighley, DC Monkhouse. "Pharmaceutical Salts." *Journal of Pharmaceutical Science*, vol. 66, No. 1, pp. 1-19, Jan. 1977.*

Church, "Is Inhibition of Mast Cell Mediator Release Relevant to the Clinical Activity of Anti-allergic Drugs?," *Agents and Actions*, vol. 18, ¾, pp. 288-293 (1986).

Clegg et al., "Histamine Secretion from Human Skin Slices Induced by Anti-IgE and Artificial Secretagogues and the Effects of Sodium Cromoglycate and Salbutamol," *Clin. Allergy*, vol. 15, pp. 321-328 (1985).

Hamilton et al., "Comarison of a New Antihistaminic and Antiallergic Compound KW 46790 with Terfenadine and Placebo on Skin and Nasal Provocation in Atopic Individuals," *Clinical and Experimental Allergy*, vol. 24, pp. 955-959 91994).

Ikeda et al., "Effects of Oxatomide and KW-4679 on Acetylcholine-Induced Responses in the Isolated Acini of Guinea Pig Nasal Glands," *Int. Arch. Allergy Immunol.*, vol. 106, p. 157-162 (1995).

Irani et al., "Mast Cell Heterogeneity," *Clinical and Experimental Allergy*, vol. 19, pp. 143-155 (1989).

Kamei et al., "Effects of Certain Antiallergic Drugs on Experimental Conjunctivitis in Guinea Pigs," *Atarashii Ganka*, vol. 11(4), p. 603-605 (1994) (abstract only).

Kamei et al., "Effect of (Z)-11-[3-(Dimethylamino) propylidene]-6,11-dihydrodibenz[b,e]oxepin-2-acetic Acid Hydrochloride on Experimental Allergic Conjunctivitis and Rhinitis in Rats and Guinea Pigs," *Arzneimittelforschung*, vol. 45(9), p. 1005-1008 (1995).

Ohshima et al., "Synthesis and Antiallergic Activity of 11-(Am inoalkylidene)-6,11,dihydrodibenz[b,e]oxepin Derivatives," *J. Medicinal Chemistry*, vol. 35(11), p. 2074-2084 (1992).

Pearce et al., "Effect of Disodium Cromoglycate on Antigen Evoked Histamine Release in Human Skin," *Clinical Exp. Immunol.*, vol. 17, pp. 437-440 (1974).

Pujara et al., "Effects of formulation variables on nasal epithelial cell integrity: Biochemical evaluations," *International J. of Pharmaceutics*, vol. 114, pp. 197-203 (1995).

Sharif et al., "Characterization of the Ocular Antiallergic and Antihistaminic Effects of Olopatadine (AL-4943A), a Novel Drug for Treating Ocular Allergic Diseases," *J. of Pharmacology and Experimental Therapeutics*, vol. 278(3), p. 1252-1261 (1996).

Sharif et al., "Olopatadine (AL-4943A): Pharmacological Profile of a Novel Anti-histaminic/Anti-allergic Drug for Use in Allergic Conjunctivitis," *Investigative Ophthalmology & Visual Science*, vol. 37(3), p. 1027 (1996) (abstract only).

Siraganian, "An Automated Continuous Flow System for the Extraction and Fluorometric Analysis of Histamine," *Anal. Biochem.*, vol. 57, pp. 383-394 (1974).

Spitalny et al., "Olopatadine Ophthalmic Solution Decreases Itching and Redness Associated with Allergic Conjunctivitis," *Investigative Ophthalmology & Visual Science*, vol. 37(3), p. 593 (1996) (abstract only).

"The Lung," *Scientific Foundation*, Raven Press, Ltd., New York, Ch. 3.4.11 (1991).

Yanni et al., "The In Vitro and In Vivo Ocular Pharmacology of Olopatadine (AL-4943A), An Effective Anti-allergic/Anti-histaminic Agent," *Investigative Ophthalmology & Visual Science*, vol. 37(3), p. 1028 (1996) (abstract only).*

Zhang et al., "Optically Active Analogues of Ebastine: Synthesis and Effect of Chirality on Their Antihistaminic and Antimuscarinic Activity," *Chirality*, vol. 6(8), p. 631-641 (1994).*

Astelin® Nasal Spray Product Insert.*

Hamilton et al., "Comarison of a New Antihistaminic and Antiallergic Compound KW 46790 with Terfenadine and Placebo on Skin and Nasal Provocation in Atopic Individuals," *Clinical and Experimental Allergy*, vol. 24, pp. 955-959, (1994).

* cited by examiner

Fig. 1A

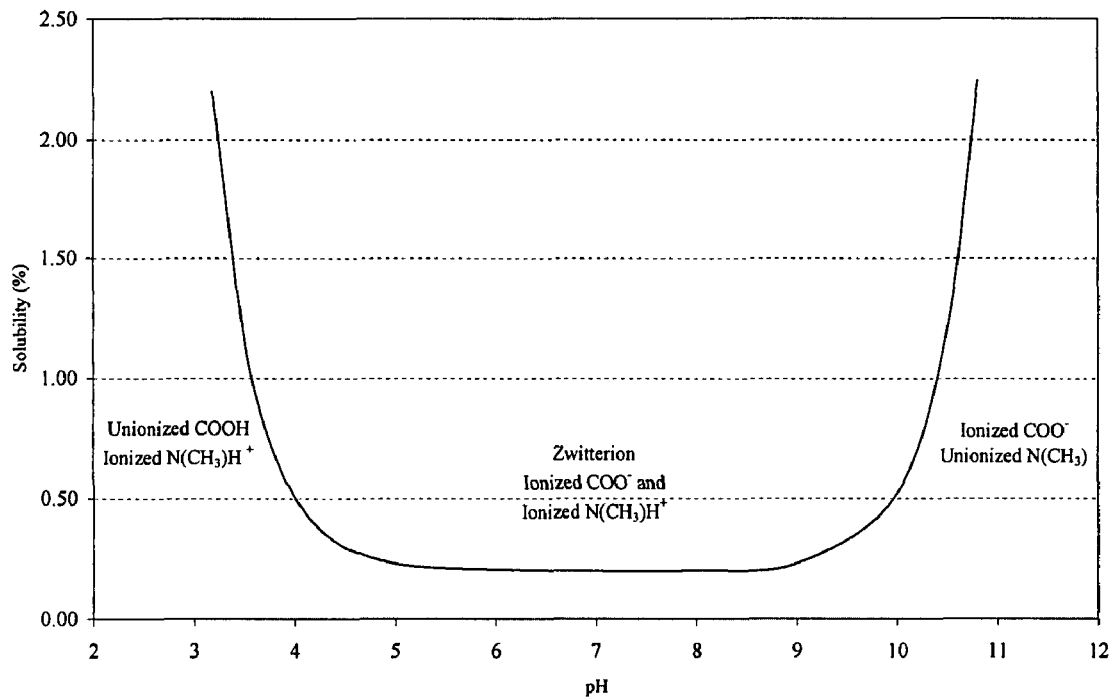


Fig. 1B

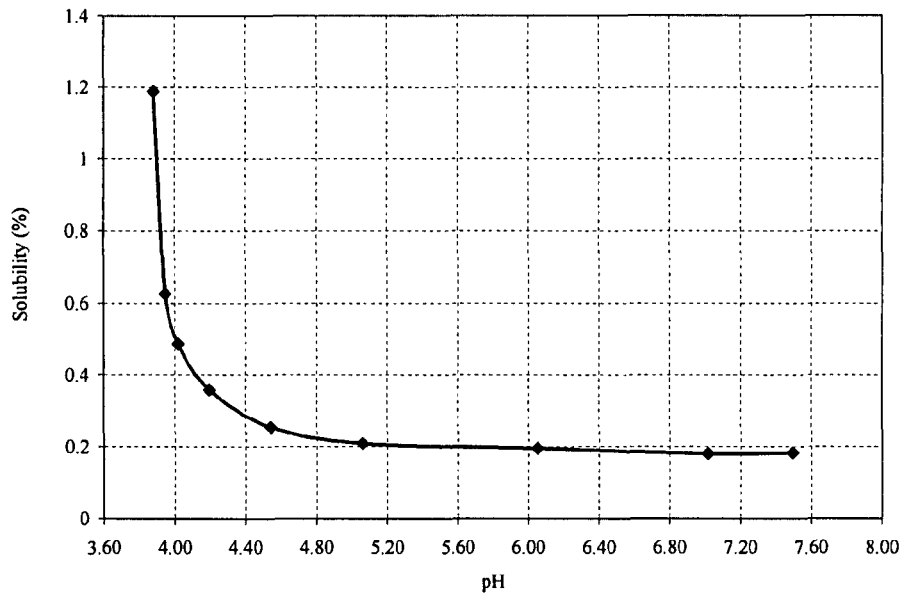


Fig. 2

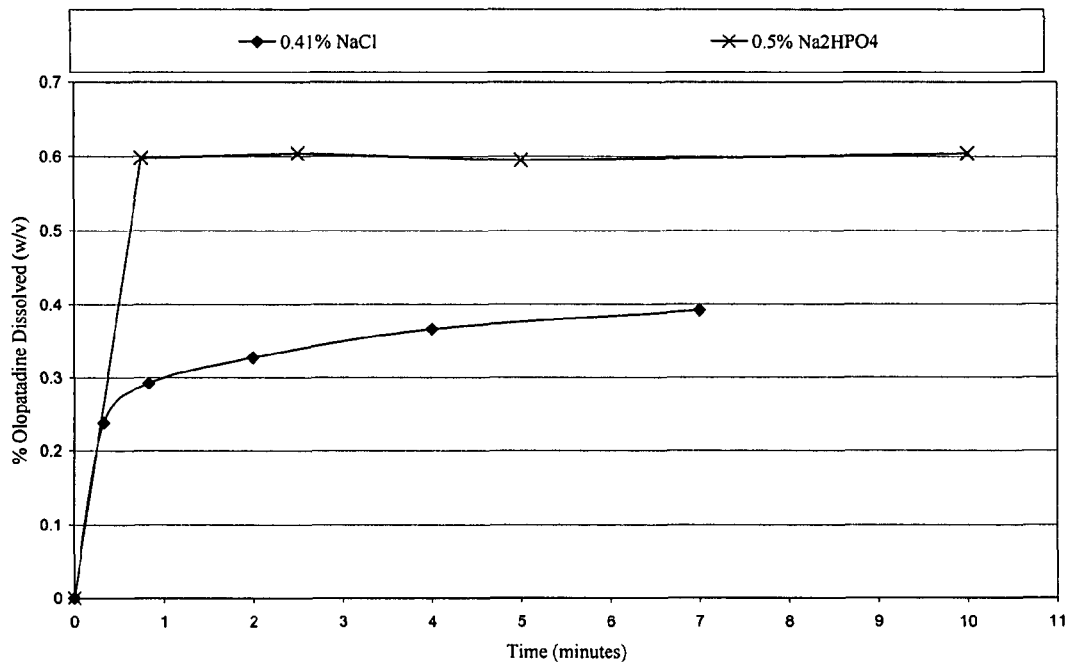


Fig. 3

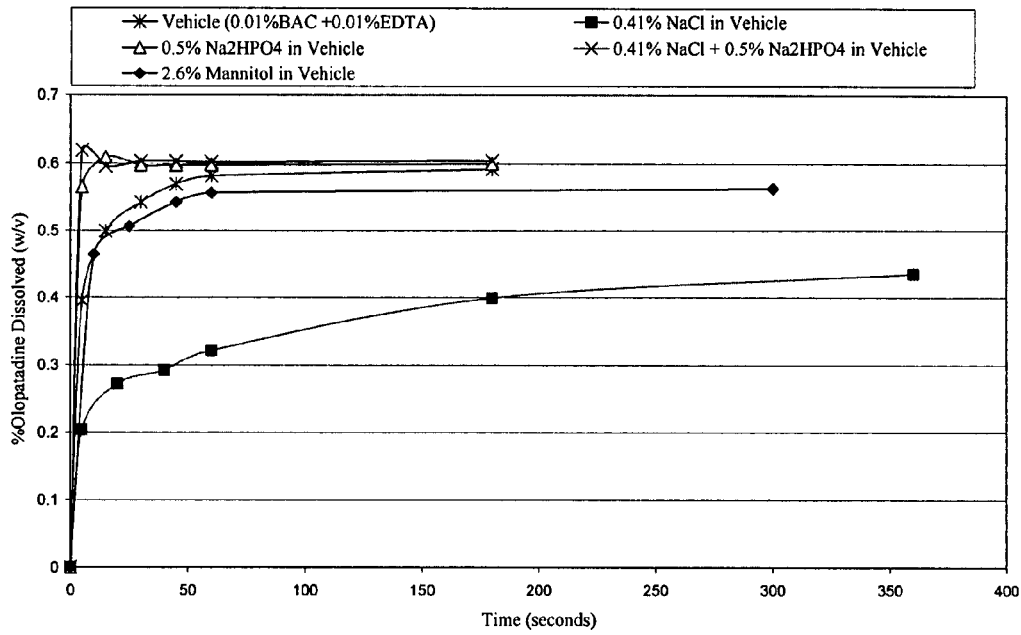
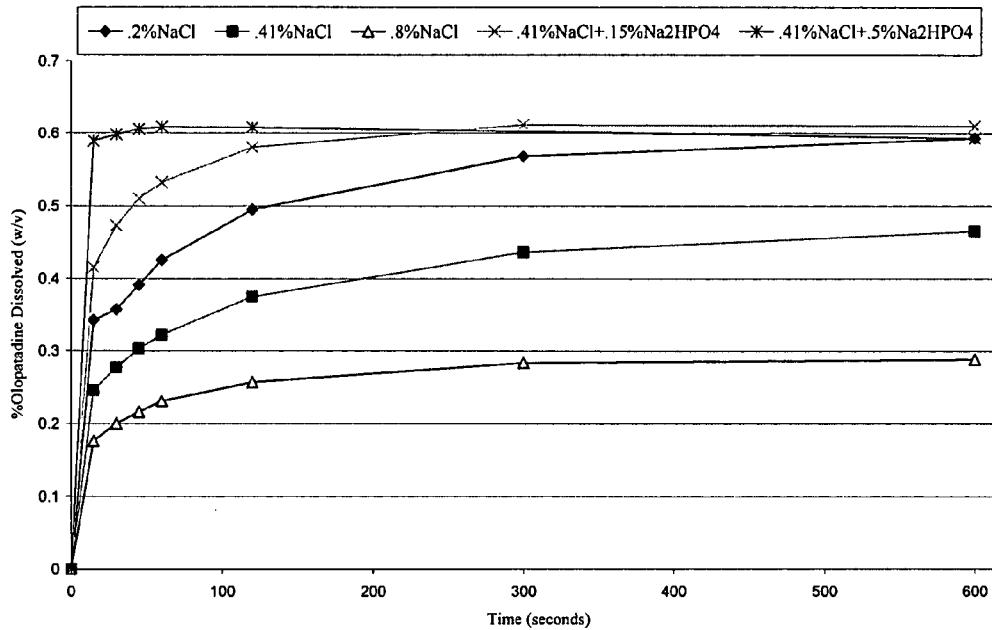


Fig. 4



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.