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**Singh et al.**

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

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**Related U.S. Application Data**

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

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

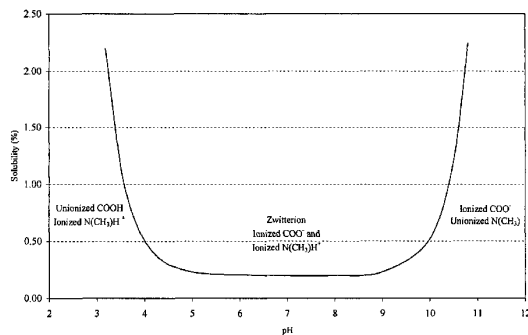
(52) **U.S. Cl.** ..... **514/450**; 424/810

(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

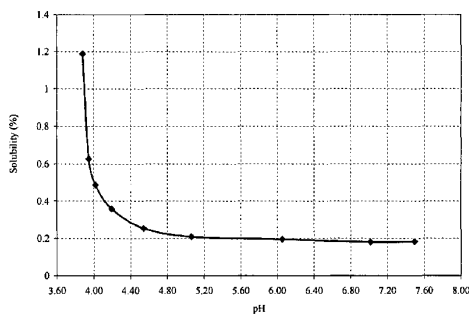
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(57) **ABSTRACT**

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

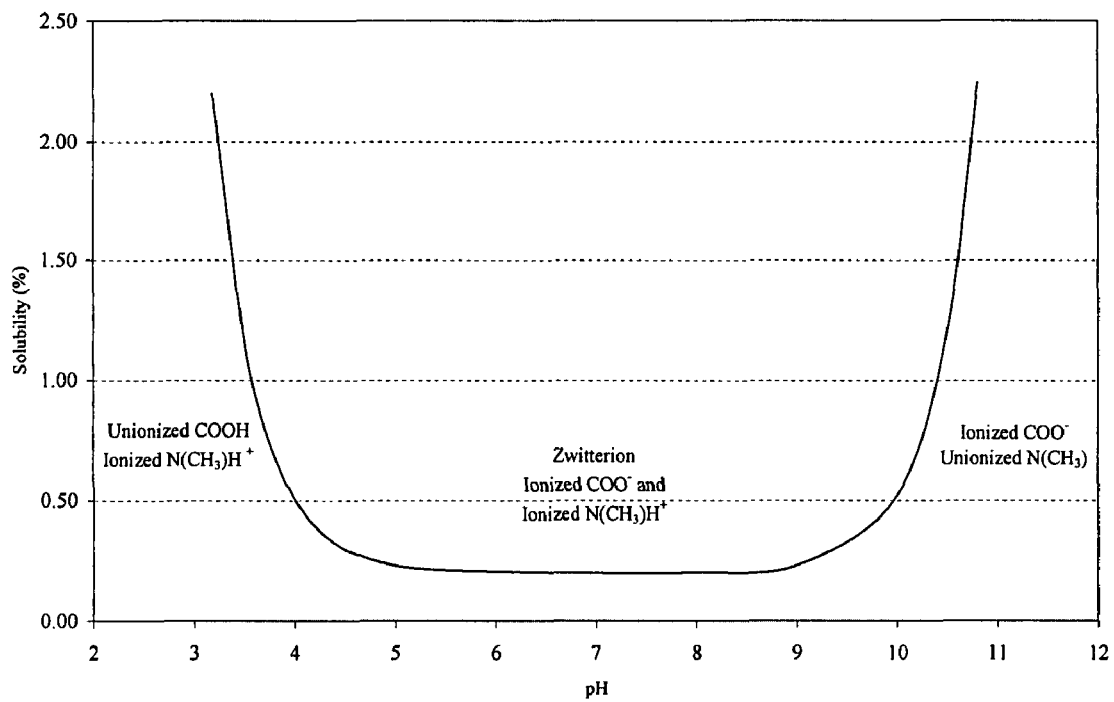


Fig. 1B

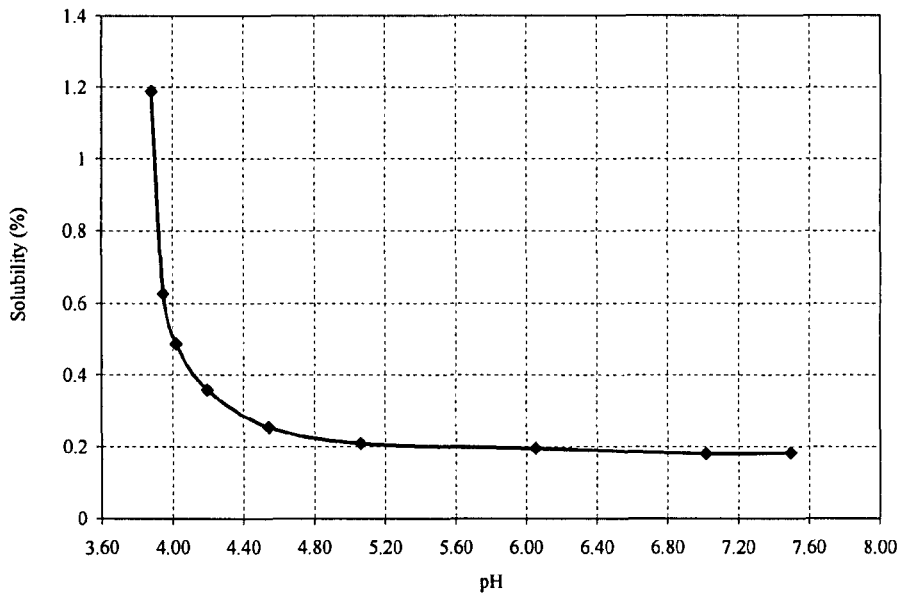


Fig. 2

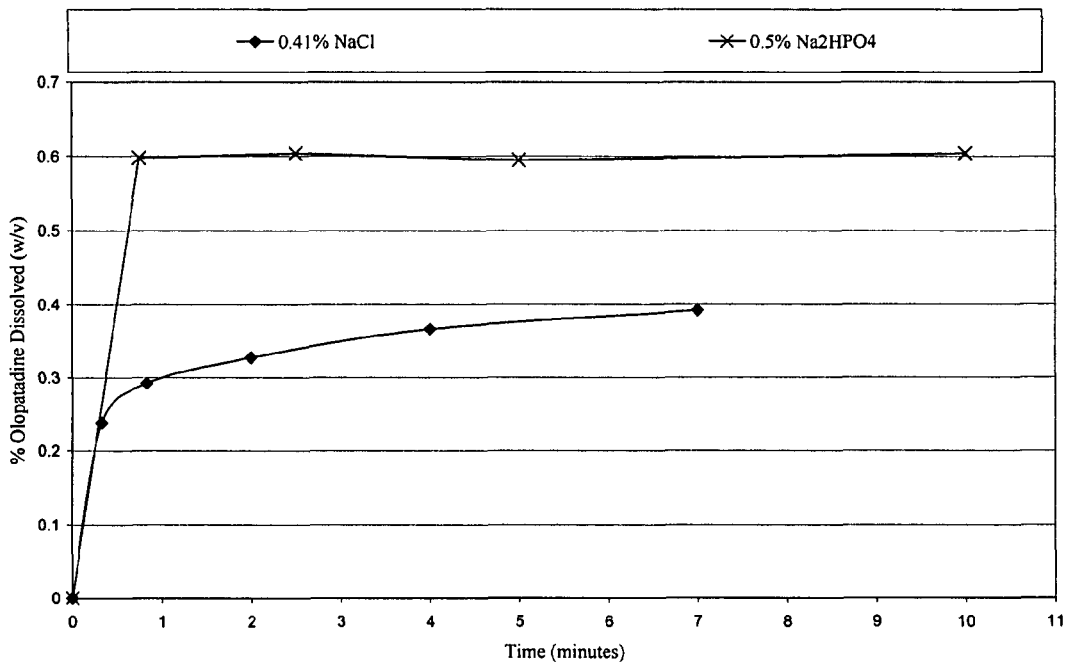


Fig. 3

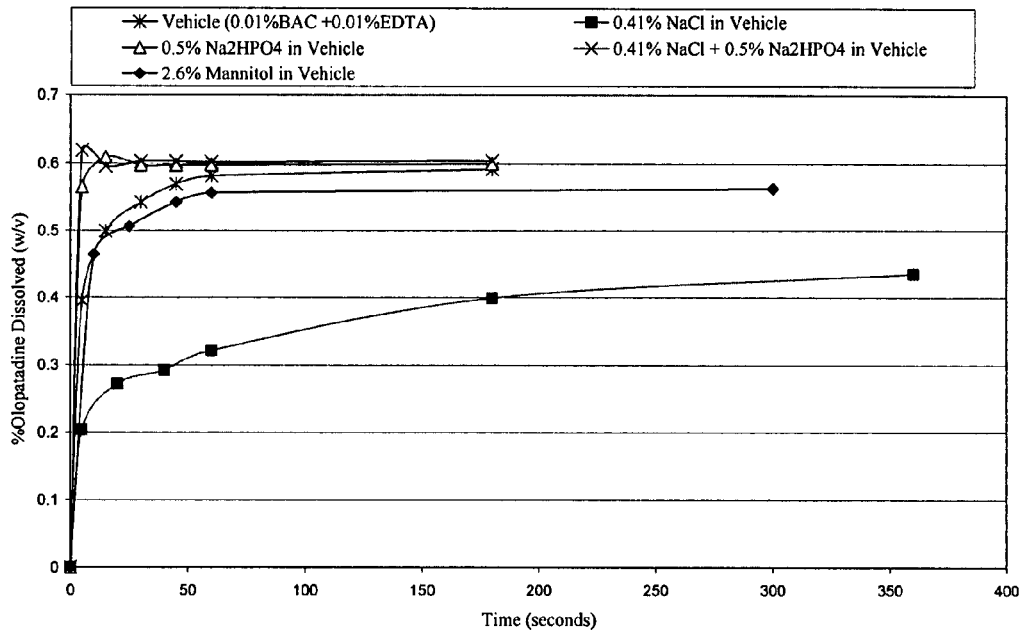
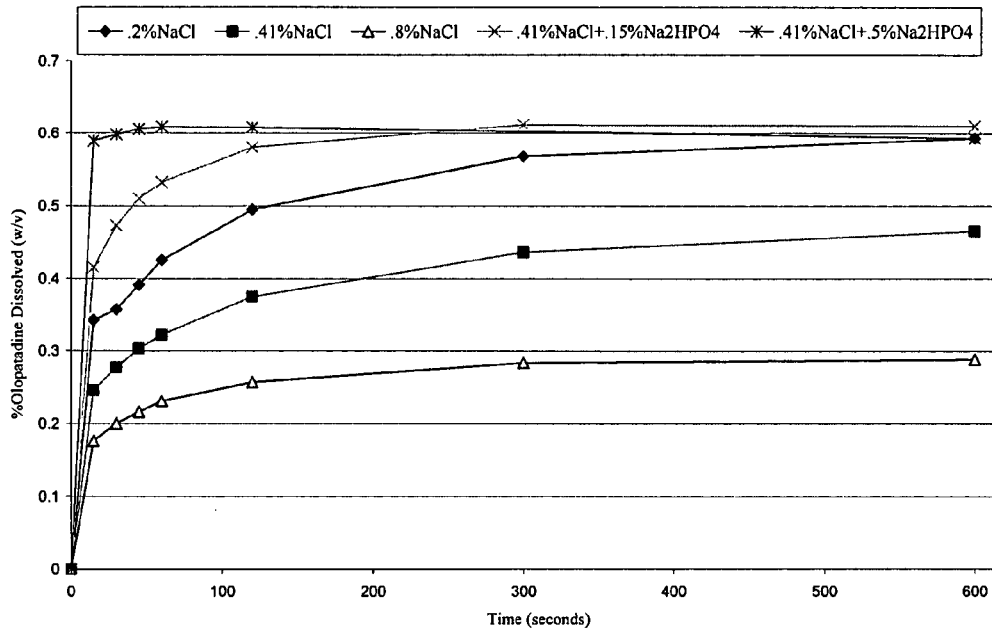


Fig. 4



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