



US006024976A

**United States Patent [19]****Miranda et al.****[11] Patent Number: 6,024,976****[45] Date of Patent: \*Feb. 15, 2000**

- [54] **SOLUBILITY PARAMETER BASED DRUG DELIVERY SYSTEM AND METHOD FOR ALTERING DRUG SATURATION CONCENTRATION**

[75] Inventors: **Jesus Miranda; Steven Sablotsky**, both of Miami, Fla.

[73] Assignee: **Noven Pharmaceuticals, Inc.**, Miami, Fla.

[\*] Notice: This patent is subject to a terminal disclaimer.

[21] Appl. No.: **08/907,906**

[22] Filed: **Aug. 11, 1997**

**Related U.S. Application Data**

[62] Continuation of application No. 08/178,558, Jan. 7, 1994, Pat. No. 5,656,286, which is a continuation-in-part of application No. 07/722,342, Jun. 27, 1991, which is a continuation-in-part of application No. 07/671,709, filed as application No. PCT/US90/01750, Mar. 28, 1990, which is a continuation-in-part of application No. 07/295,847, Jan. 11, 1989, Pat. No. 4,994,267, which is a continuation-in-part of application No. 07/164,482, Mar. 4, 1988, Pat. No. 4,814,168.

[51] **Int. Cl.<sup>7</sup>** ..... **A61F 13/02**

[52] **U.S. Cl.** ..... **424/449; 424/448**

[58] **Field of Search** ..... **424/448, 449**

**[56] References Cited****U.S. PATENT DOCUMENTS**

3,969,308	7/1976	Penneck .....	260/37 SB
3,972,995	8/1976	Tsuk et al. ....	424/28
4,291,015	9/1981	Keith et al. ....	424/28
4,292,301	9/1981	Keith et al. ....	424/28
4,390,520	6/1983	Nagai et al. ....	424/28
4,438,139	3/1984	Keith et al. ....	424/28
4,542,013	9/1985	Keith .....	424/28
4,585,452	4/1986	Sablotsky .....	604/896
4,593,053	6/1986	Jevne et al. ....	523/111
4,668,232	5/1987	Cordes et al. ....	604/897

(List continued on next page.)

**FOREIGN PATENT DOCUMENTS**

2027053	4/1991	Canada .
0-201-828	11/1986	European Pat. Off. .
208395	1/1987	European Pat. Off. .
0-272-045	6/1988	European Pat. Off. .
0-343-807	11/1989	European Pat. Off. .
0 371 496	6/1990	European Pat. Off. .
0-416-842	3/1991	European Pat. Off. .
A 0529123	3/1993	European Pat. Off. .
54-89017	7/1979	Japan .
58-225010	12/1983	Japan .
2 105 990	4/1983	United Kingdom .
91/05529	5/1991	WIPO .
WO 93/08795	5/1993	WIPO .
WO		
97/116689	4/1997	WIPO .

**OTHER PUBLICATIONS**

Sloan, K. B. et al., "Use of Solubility Parameters of Drug and Vehicle to Predict Flux Through Skin", *The Journal of Investigative Dermatology*, vol. 87 (No. 2) pp. 244-252 (Aug. 1986).

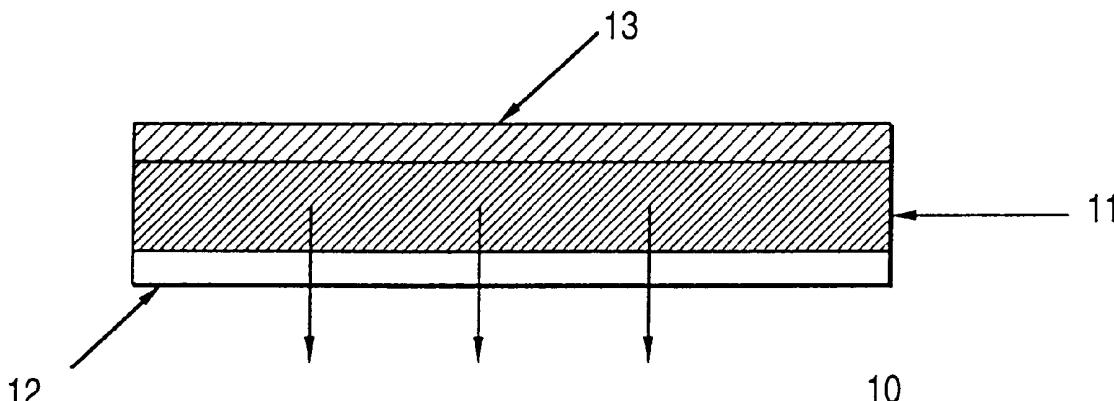
Yu et al., "Transdermal Dual-Controlled Delivery of Testosterone and Estradiol: (I) Impact of System Design," *Drug Devel. Indust. Pharm.* 17(14): 1883-1904 (1991).

(List continued on next page.)

*Primary Examiner—Jyothsna Venkat  
Attorney, Agent, or Firm—Foley & Lardner*

**[57]****ABSTRACT**

A blend of at least two polymers, or at least one polymer and a soluble polyvinylpyrrolidone, in combination with a drug provides a pressure-sensitive adhesive composition for a transdermal drug delivery system in which the drug is delivered from the pressure-sensitive adhesive composition and through dermis when the pressure-sensitive adhesive composition is in contact with human skin. According to the invention, soluble polyvinylpyrrolidone can be used to prevent crystallization of the drug, without affecting the rate of drug delivery from the pressure-sensitive adhesive composition.

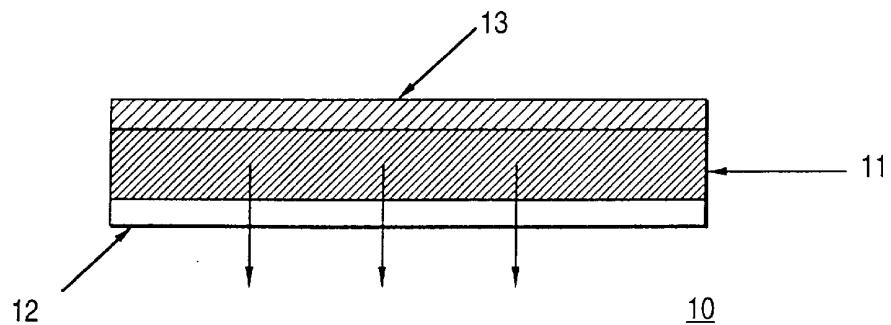
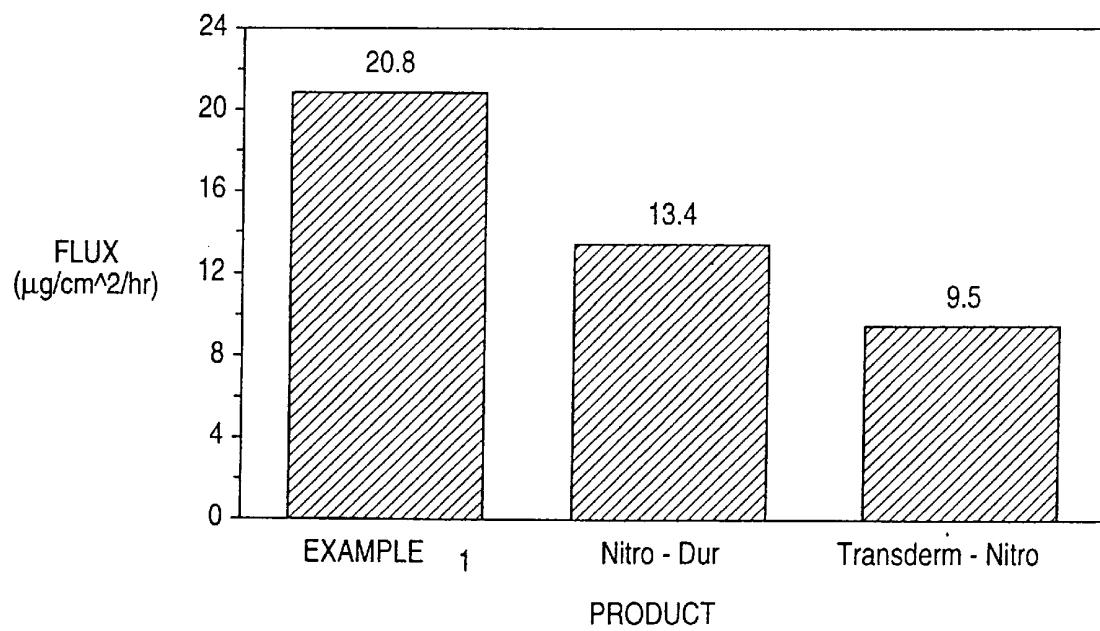
**66 Claims, 19 Drawing Sheets**

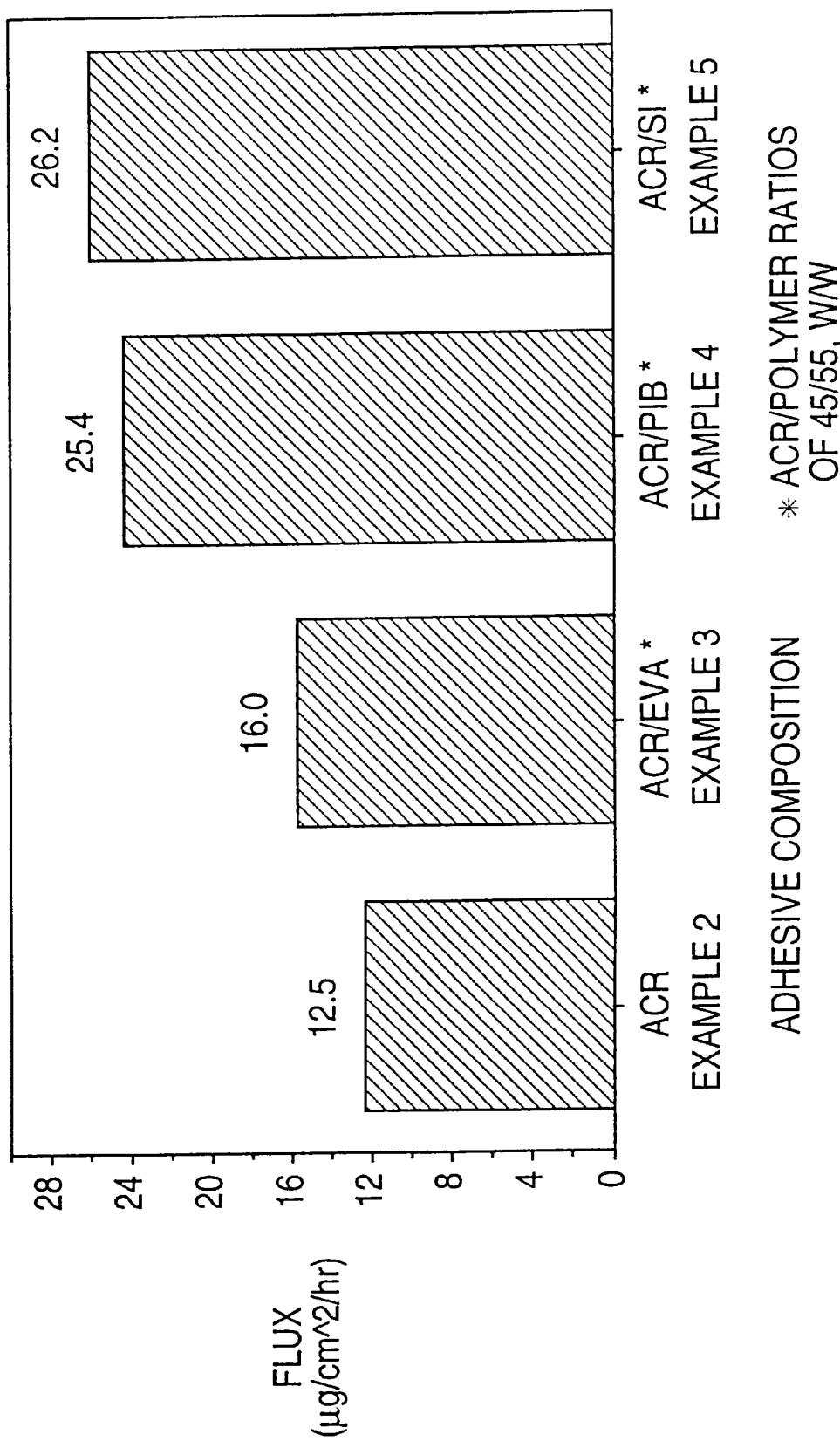
## U.S. PATENT DOCUMENTS

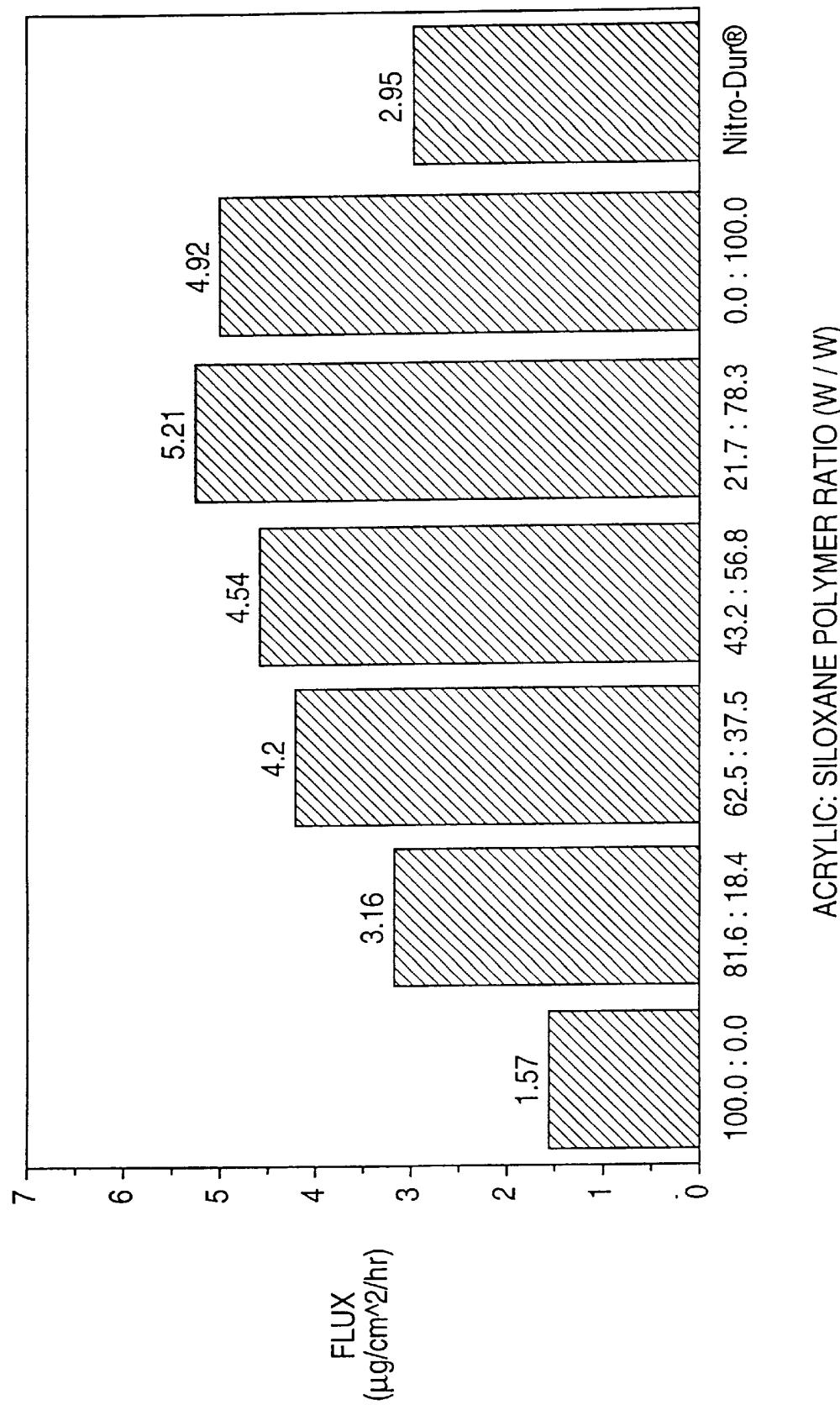
4,690,683	9/1987	Chien et al.	604/896	5,230,896	7/1993	Yeh et al.	424/443
4,693,887	9/1987	Shah	424/19	5,230,898	7/1993	Horstmann et al.	424/449
4,696,821	9/1987	Belsole	424/448	5,232,702	8/1993	Pfister et al.	424/448
4,699,146	10/1987	Sieverding	128/640	5,232,703	8/1993	Blank	424/449
4,750,482	6/1988	Sieverding	128/156	5,252,334	10/1993	Chiang et al.	424/448
4,769,013	9/1988	Lorenz et al.	604/265	5,260,064	11/1993	Nakagawa et al.	424/448
4,814,168	3/1989	Sablotsky et al.	424/78	5,262,165	11/1993	Govil et al.	424/448
4,845,081	7/1989	Sloan	514/232.2	5,393,529	2/1995	Hoffmann et al.	424/445
4,883,669	11/1989	Chien et al.	424/448	5,676,968	10/1997	Lip et al.	424/448
4,906,169	3/1990	Chien et al.	424/448				
4,911,916	3/1990	Cleary	424/449				
4,931,281	6/1990	Kim et al.	424/448				
4,987,893	1/1991	Salamone et al.	128/156				
4,994,267	2/1991	Sablotsky	424/78				
5,032,403	7/1991	Sinnreich	424/448				
5,059,189	10/1991	Cilento et al.	604/307				
5,071,656	12/1991	Lee et al.	424/448				
5,122,543	6/1992	Khanna	514/772.5				
5,128,138	7/1992	Blank	424/449				
5,141,750	8/1992	Lee et al.	424/448				
5,151,271	9/1992	Otsuka et al.	424/443				
5,154,922	10/1992	Govil et al.	424/448				

## OTHER PUBLICATIONS

- Ziller et al., "Control of Crystal Growth in Drug Suspensions," *Pharm. Ind.* 52(8):1017–1022 (1990).
- Kuhnert–Brandstätter et al., "Kristalisationsvorgänge in Suspensionen von Steroidhormonen," *Sci. Pharm.* 35(4):287–297 (1967).
- English translation of Japanese patent application No. 2-48859, filed Feb. 27, 1990.
- English translation of European Patent Application No. 0-201-828 (1986).
- English translation of WO 93/08795 (PCT/EP92/02478).

**FIG. 1****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.