



US005342625A

**United States Patent** [19][11] **Patent Number:** 5,342,625

Hauer et al.

[45] **Date of Patent:** Aug. 30, 1994

- [54] **PHARMACEUTICAL COMPOSITIONS COMPRISING CYCLOSPORINS**
- [75] **Inventors:** Birgit Hauer, Lahr; Armin Meinzer, Freiburg/Munzingen; Ulrich Posanski, Freiburg, all of Fed. Rep. of Germany; Friedrich Richter, Schönbühl-Urtenen, Switzerland
- [73] **Assignee:** Sandoz Ltd., Basel, Switzerland
- [21] **Appl. No.:** 990,734
- [22] **Filed:** Dec. 15, 1992

**Related U.S. Application Data**

- [63] Continuation of Ser. No. 680,211, Apr. 4, 1991, abandoned, which is a continuation of Ser. No. 406,656, Sep. 13, 1989, abandoned.

**[30] Foreign Application Priority Data**

- |                    |                |         |
|--------------------|----------------|---------|
| Sep. 16, 1988 [GB] | United Kingdom | 8821754 |
| Feb. 9, 1989 [GB]  | United Kingdom | 8902900 |
| Feb. 9, 1989 [GB]  | United Kingdom | 8902903 |
- [51] **Int. Cl.<sup>5</sup>** ..... A61K 9/66; A61K 9/107; A61K 37/02; C07K 7/64
- [52] **U.S. Cl.** ..... 424/455; 424/456; 424/457; 424/489; 514/11; 514/885; 514/937; 514/938; 514/963; 514/964; 514/970; 514/974; 514/975; 530/321
- [58] **Field of Search** ..... 424/455, 456, 457, 489; 514/9, 11, 885, 937, 938, 970, 963, 964, 974, 975; 530/317, 321, 322

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

- |           |        |                 |         |
|-----------|--------|-----------------|---------|
| 4,108,985 | 8/1978 | Rüegger et al.  | 514/11  |
| 4,210,581 | 7/1980 | Rüegger et al.  | 530/321 |
| 4,220,641 | 9/1980 | Traber et al.   | 514/11  |
| 4,388,307 | 6/1983 | Cavanak         | 514/11  |
| 4,835,002 | 5/1989 | Wolf et al.     | 426/590 |
| 4,914,188 | 4/1990 | Dumont et al.   | 530/317 |
| 4,990,337 | 2/1991 | Kurihara et al. | 424/427 |
| 4,996,193 | 2/1991 | Hewitt et al.   | 514/11  |

**FOREIGN PATENT DOCUMENTS**

2098865 12/1992 United Kingdom .

**OTHER PUBLICATIONS**

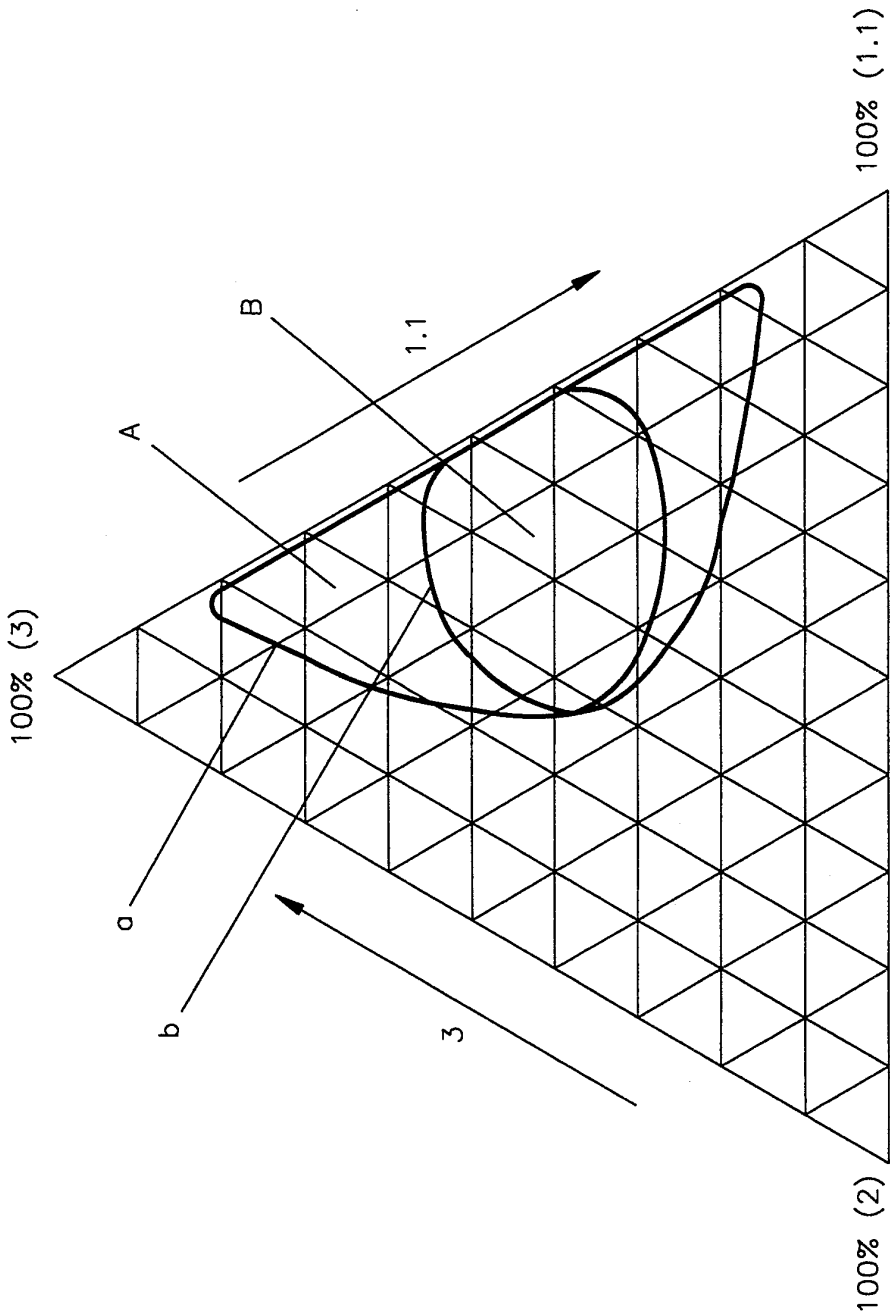
- W. A. Ritschel, et al., *Pharm. Res.*, 1988 (May 1910), Suppl. 108.
- Derwent No. 86/335072/51, (Apr. 26, 1985).
- Takada, et al., *J. Pharmacobia-Dyn.*, vol. 11, pp. 80-87 (1988).
- Bryan D. Tarr, et al., *Pharmaceutical Research*, vol. 6, No. 1, pp. 40-43 (1989).
- Reymond, et al., *Pharmaceutical Research*, vol. 5, No. 10, pp. 673-679 (1988).
- Remington's *Pharmaceutical Sciences*, 17th Edition, pp. 298-299 (1985).
- Derwent No. 87-086213/12 (1985).
- Takada, et al., *International Jour. of Pharmaceutics*, vol. 44, pp. 107-116 (1988).
- Derwent No. 89/088668/12 (Jul. 31, 1987).
- Derwent 87/024776/04 (Apr. 4, 1985).
- W. A. Ritschel, et al., *Meth. Find. Exp. Clin. Pharmacol.*, vol. 11, pp. 281-285 (1989).

*Primary Examiner*—Christina Y. Chan  
*Attorney, Agent, or Firm*—Robert S. Honor; Melvyn M. Kassenoff; Carl W. Battle

**[57] ABSTRACT**

Pharmaceutical compositions comprising a cyclosporin, e.g. Cyclosporin or [Nva]<sup>2</sup>-Cyclosporin, in "microemulsion pre-concentrate" and microemulsion form. The compositions typically comprise (1.1) a C<sub>1-5</sub>alkyl or tetrahydrofurfuryl di- or partial-ether of a low molecular weight mono- or poly-oxy-alkane diol, e.g. Transcutol or Glycofurol, as hydrophilic component. Compositions are also provided comprising a cyclosporin and (1.1) and, suitably, also a saccharide monoester, e.g. raffinose or saccharose monolaurate. Dosage forms include topical formulations and, in particular, oral dosage forms.

**26 Claims, 4 Drawing Sheets**



2  
FIG. 1

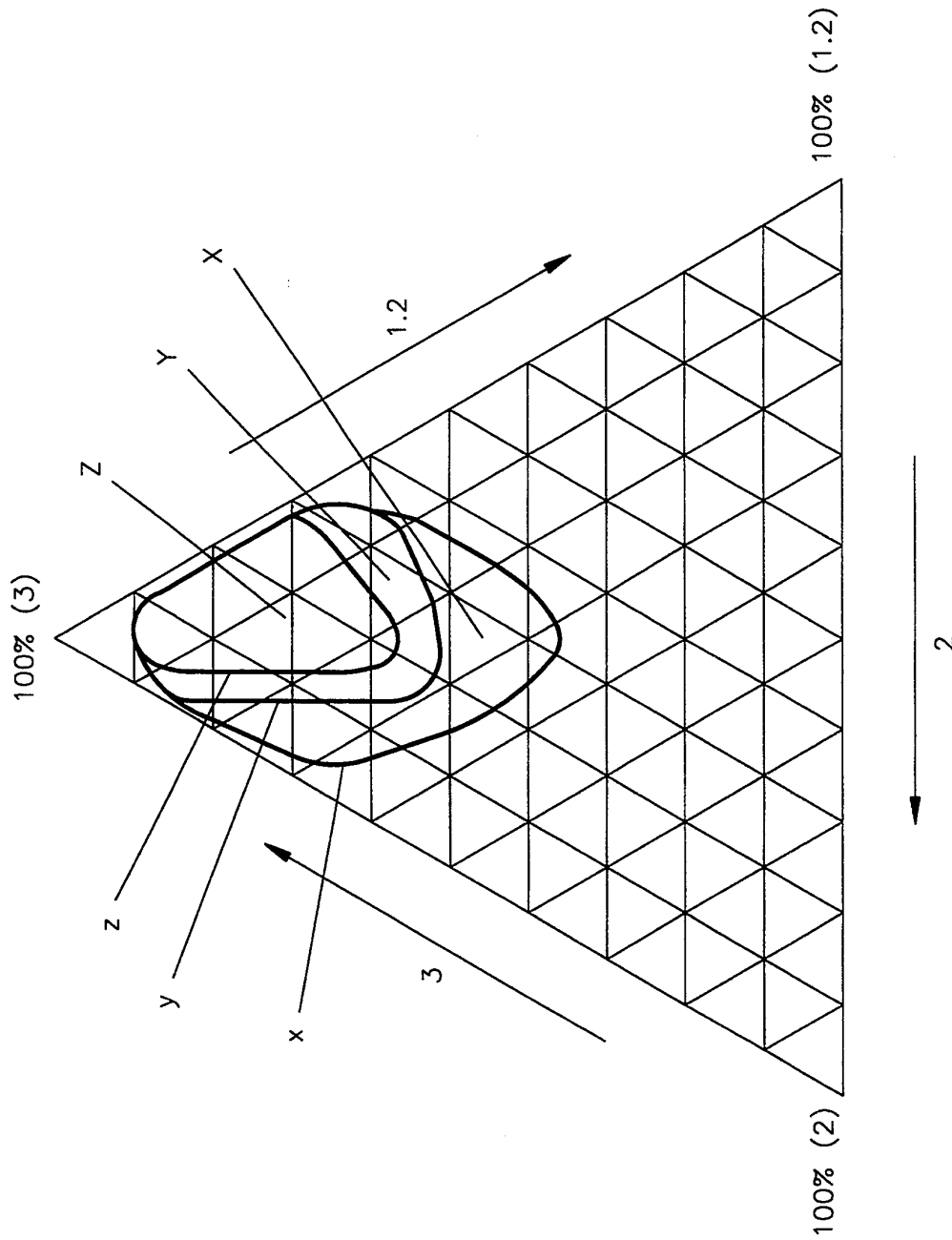


FIG. 2

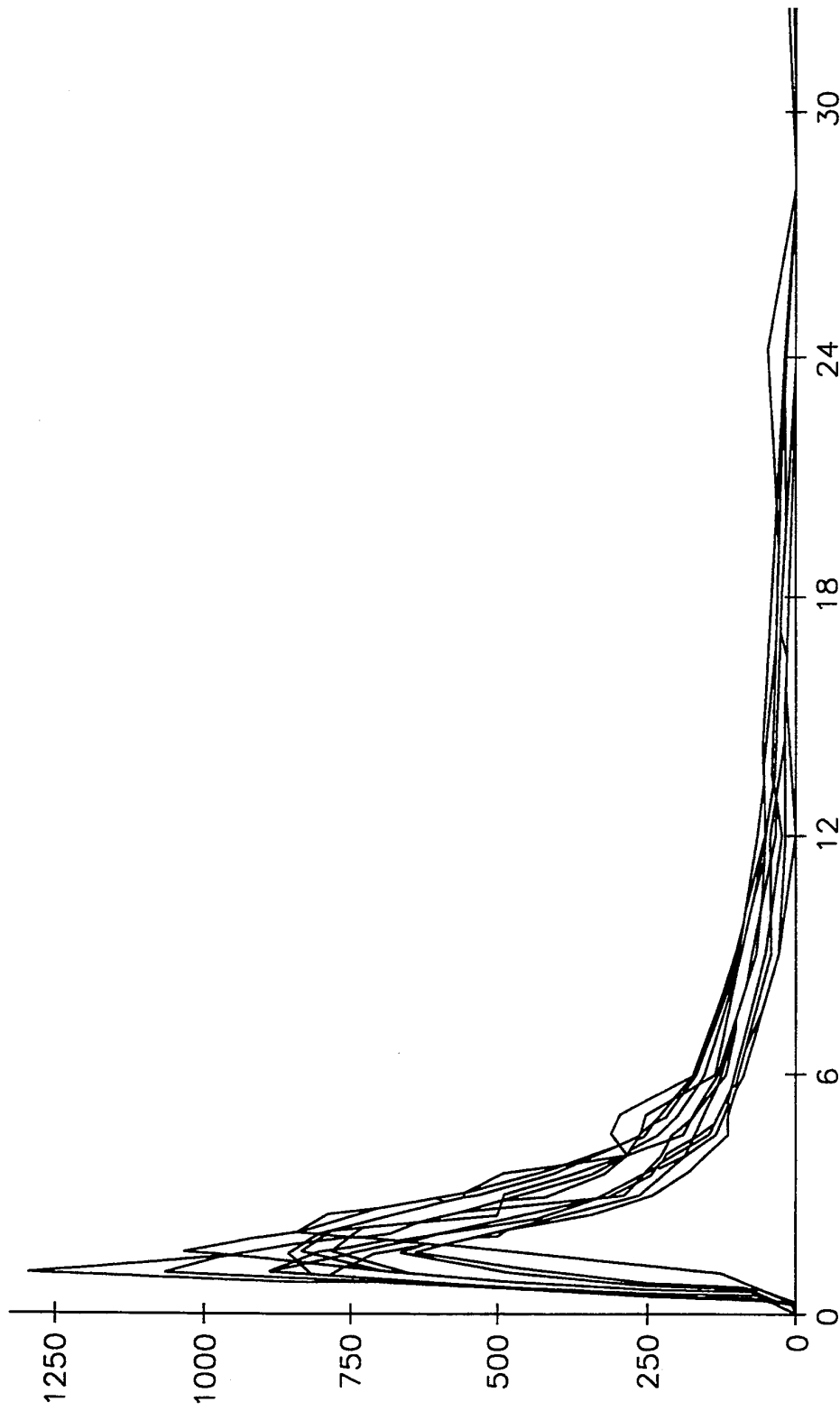


FIG. 3

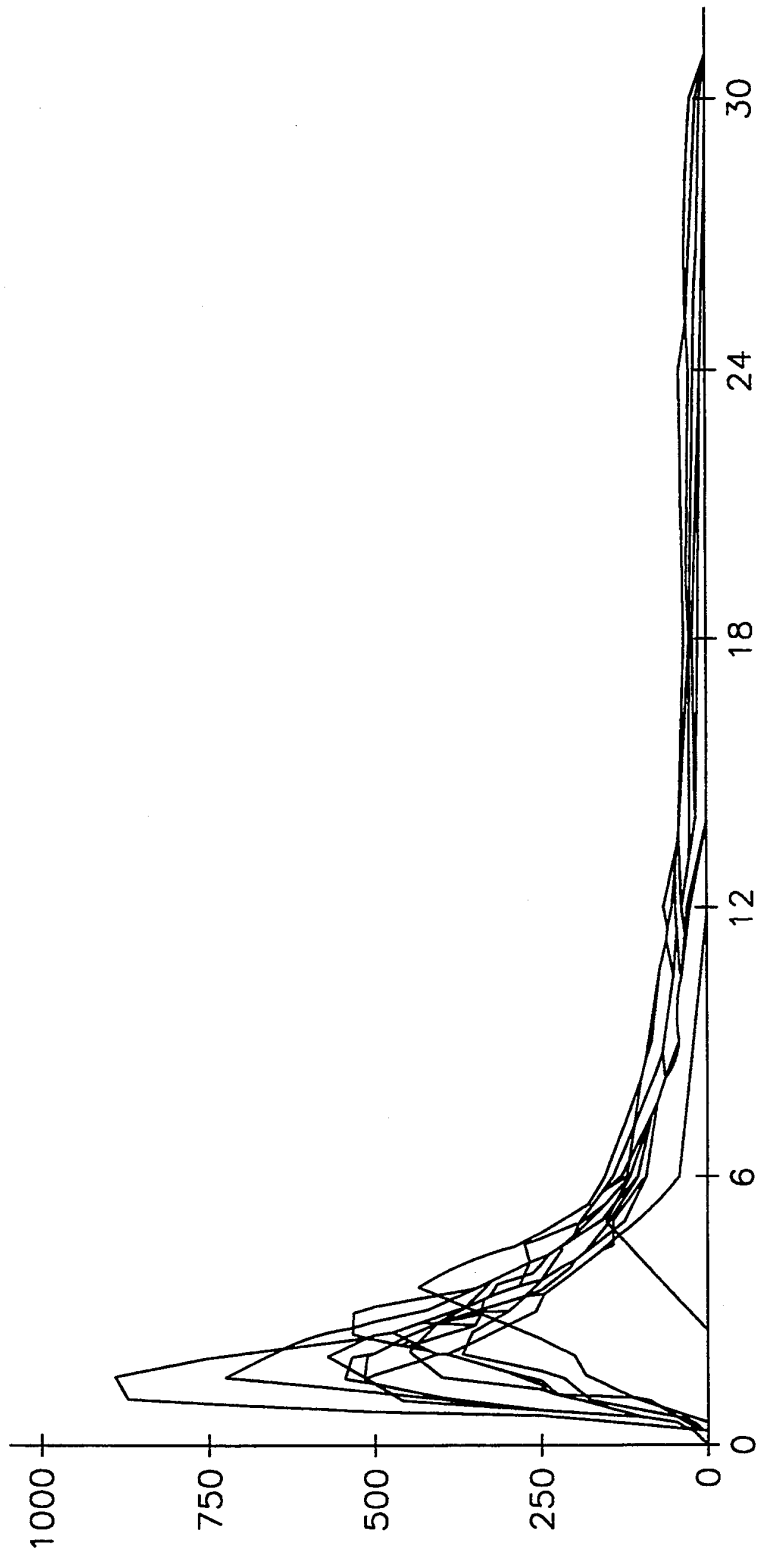


FIG. 4

# 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.