Ottawa, Canada
K1A 0C9

(43) 1990/05/31

(52) 167-209

(51) INTL.CL.[5] A61K-31/00

(19)(CA) **APPLICATION FOR CANADIAN PATENT** (12)

5,103,2/64

(54) Sustained Release Diltiazem Formulation

(72) Chang, Richard R. - U.S.A. ;
Pereira-Rosario, Ronald - U.S.A. ;
Rudnic, Edward M. - U.S.A. ;

(73) Schering Corporation - U.S.A. ;

(30) (US) 278,057 1988/11/30

(57) 12 Claims

Notice: The specification contained herein as filed

A sustained release diltiazem tablet is disclosed which exhibits a unique dissolution profile due in large measure to the inclusion of the drug into a hydrophobic matrix. In particular, the sustained release diltiazem formulation disclosed herein is suitable for once-a-day administration.

SUSTAINED RELEASE DILTIAZEM FORMULATION

SUMMARY

The present invention encompasses sustained release oral dosage forms and formulations for medicinal agents, and in particular for diltiazem.

One such oral dosage form is a sustained release tablet, comprising an effective amount of active ingredient and excipients which may be compressed into a suitable oral dosage form, and which may be coated with one or more coating agents. The tablet coating may optionally contain diltiazem for immediate release.

In a particular formulation described herein, a sustained release tablet may contain diltiazem or a pharmaceutically acceptable salt thereof in combination with excipients such as glyceryl monostearate, sucrose, microcrystalline cellulose and povidone.

The matrix formed by tablet compression is hydrophobic in nature.

BACKGROUND OF THE INVENTION

Numerous references disclose diltiazem in sustained release formulations which utilize microencapsulation technology. Examples are the following:

et al. on September 17, 1985;

U.S. Patent no. 4,462,982, issued to Samejima et al. on July 31, 1984;

U.S. Patent no. 4,443,497 issued to Samejima et al. on April 17, 1984; and

U.S. Patent 4,411,933, issued to Samejima et al. on October 25, 1983.

Similarly, numerous publications have disclosed devices which rely upon an osmotically regulated membrane for the controlled delivery of pharmaceuticals, such as diltiazem. For example are the following:

Belgian Application 900817, published on February 1, 1985 discloses a device comprising a semipermeable wall, an osmopolymer, such as poly(ethylene oxide) and an active ingredient.

Belgian Appl. No. 900,824 also published on February 1, 1985 discloses a core and a membrane having variable permeability;

Belgian Appl. No. 898,819, published on May 30, 1984, discloses a device for controlled drug delivery containing two compositions, including poly(ethyleneoxide);

Belgian Appl. No. 903,540 published February 17, 1986 discloses a sustained release powder, which can be formulated into an ointment, suspension etc.

Belgian Appl. No. 901,359 published April 16, 1985 discloses a controlled release diltiazem formulation containing granules and a semipermeable external membrane.

Japanese Appl. No. 175,144 published on April 13, 1984, discloses a sustained release thermoset or thermoplastic resin;

Japanese Appl. No. 170,440 published on April 5, 1984, discloses a sustained release tablet which utilizes hardened oil;

1987, discloses diltiazem in combination with an acrylic acid resin;

Japanese Kokai 61/212517, published September 20, 1986 discloses the use of diltiazem in combination with hydrogenated oils;

Japanese Kokai 59/10512 published January 20, 1984, discloses diltiazem microencapsulated in ethylcellulose;

Panoz and Geohagan, U.S. Patent 4,721,619 discloses an alternating arrangement (between 50 and 200 layers) of diltiazem, organic acid and lubricant layers and polymeric material layers built upon a central inert core.

However, none of the references disclose a sustained release diltiazem tablet formulation utilizing a uniformly dispersed hydrophobic matrix.

DETAILED DESCRIPTION

The present invention relates to a novel sustained release tablet, useful in that it exhibits unexpectedly prolonged activity, a uniform dissolution rate, and formulation stability over an extended period of time. The sustained release diltiazem tablets described herein will be suitable for once a day and twice daily administration.

The tablets of the invention utilize a hydrophobic matrix, into which the active ingredient is incorporated. As used herein, the term "hydrophobic matrix" refers to the nature of the major pharmaceutically acceptable excipients into which the active ingredient such as diltiazem is incorporated prior to tableting. The components of the hydrophobic matrix are generally recognized as non-therapeutic, and are useful to impart the required dissolution characteristics to the sustained release tablets.

DOCKET ALARM

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.