US005407686A

United States Patent [19]

Patel et al.

[11] Patent Number: 5,407,686

[45] Date of Patent: Apr. 18, 1995

[54] **SUSTAINED RELEASE COMPOSITION FOR ORAL ADMINISTRATION OF ACTIVE INGREDIENT**

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[21] Appl. No.: **827,604**

[22] Filed: **Jan. 29, 1992**

Related U.S. Application Data

[63] Continuation-in-part of Ser. No. 799,344, Nov. 27, 1991, abandoned.

[51] **Int. Cl.**[6] **A61K 9/22**

[52] **U.S. Cl.** **424/468**; 424/494; 424/495; 424/480

[58] **Field of Search** 424/468, 476, 496, 475

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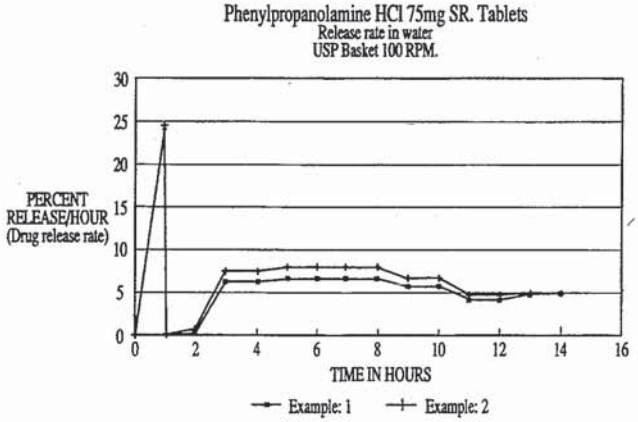
[57] **ABSTRACT**

A sustained release tablet adapted to provide an initial immediate release of an active agent, a period of no release of the active agent, followed by a substantially constant, rate of release of the active agent. The tablet includes (a) a compressed tablet core containing an active agent, an insoluble binder and an insoluble; (b) a barrier coating formed over the tablet core, the barrier coating including a mixture of soluble and insoluble polymers and a plasticizer; (c) an active coating deposited over the barrier coating, the active coating including an active agent, a soluble polymer and a plasticizer; and (d) a film coating formed over the active coating, the film coating containing a soluble polymer and plasticizer.

36 Claims, 3 Drawing Sheets



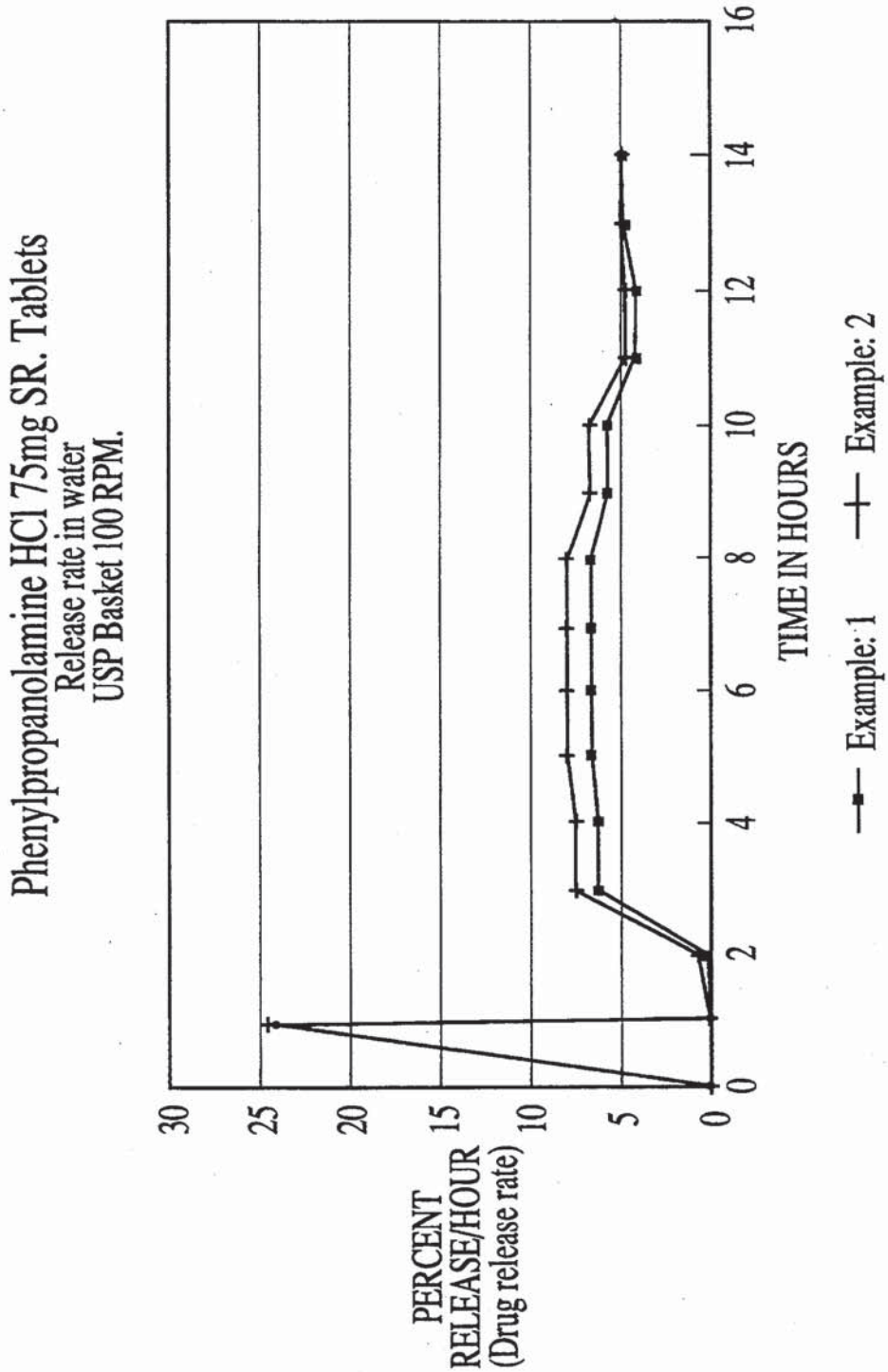


FIGURE 1

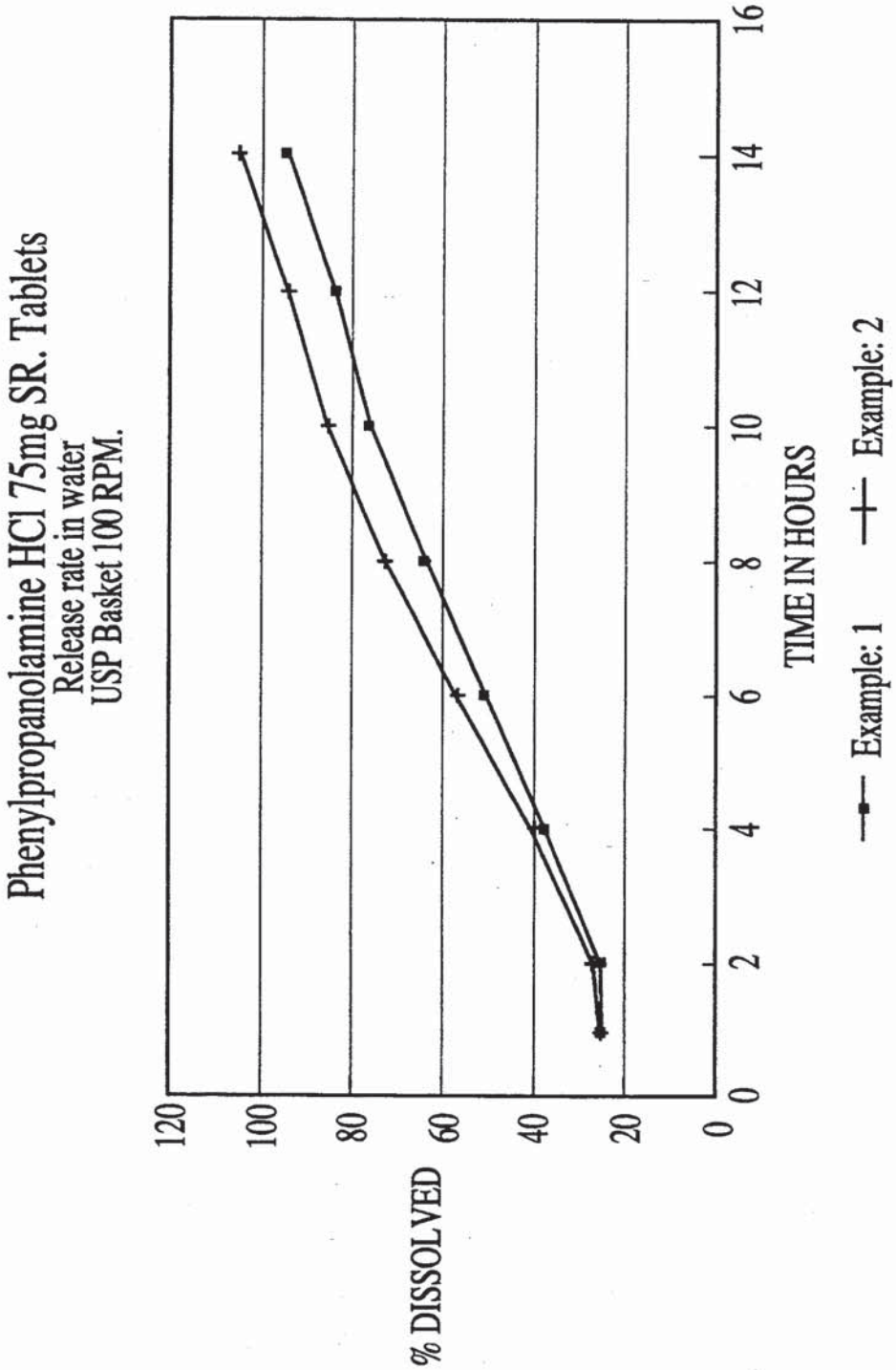


FIGURE 2

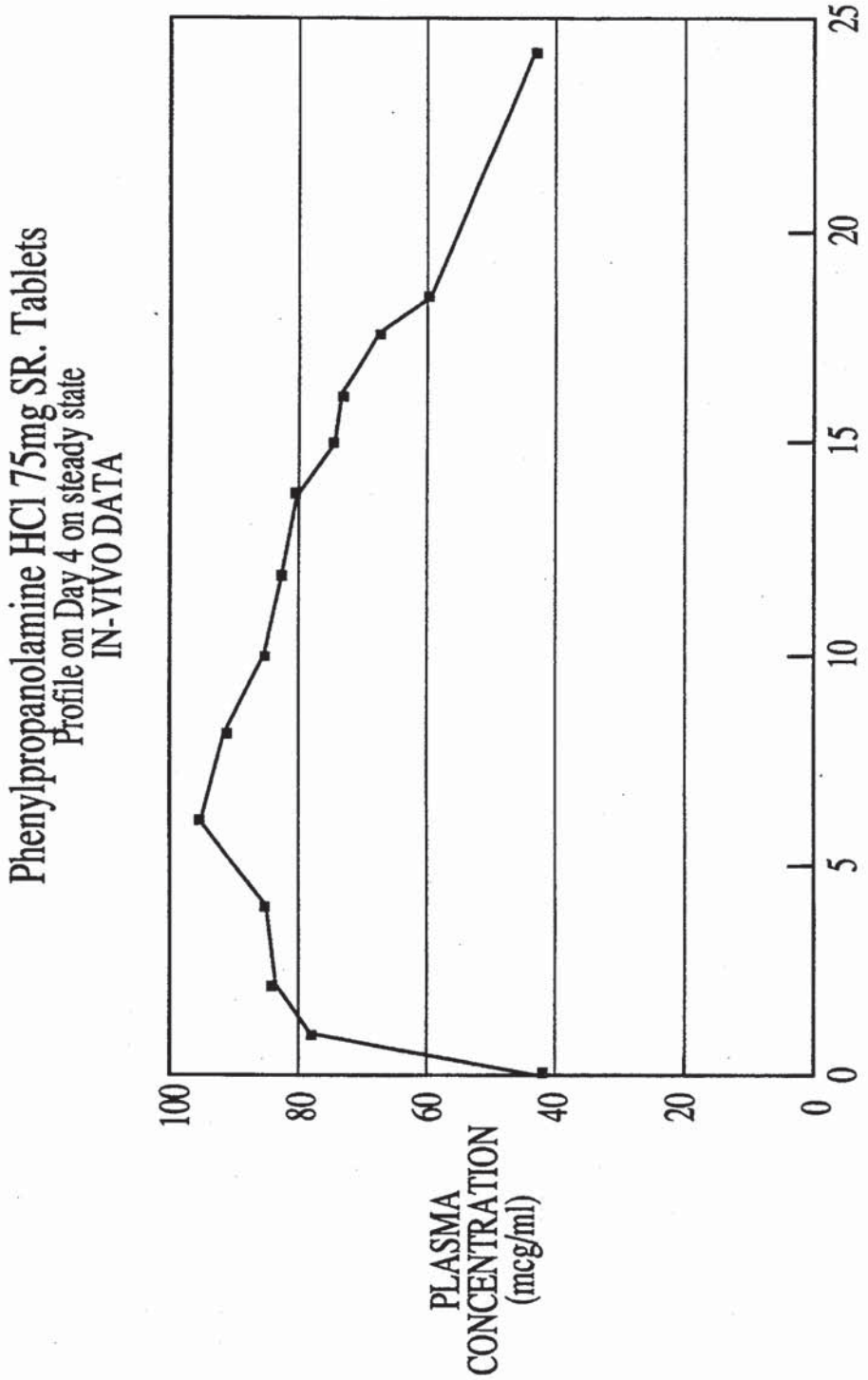


FIGURE 3

SUSTAINED RELEASE COMPOSITION FOR ORAL ADMINISTRATION OF ACTIVE INGREDIENT

REFERENCE TO RELATED APPLICATIONS

This application is a Continuation-In-Part application of application Ser. No. 07/799,344, filed Nov. 27, 1991, now abandoned the disclosure of which is incorporated by reference in its entirety.

BACKGROUND OF THE INVENTION

1. Field of the Invention

The present invention relates to a sustained release tablet designed or adapted to provide an immediate release of an active agent, a period of no release of an active agent, followed by a substantially constant release of the active agent.

2. Description of the Prior Art

Phenylpropanolamine hydrochloride α-(aminoethyl)benzyl alcohol hydrochloride, also known as dl-norephedrine hydrochloride, 2-amino-1-phenyl-1-propanol hydrochloride, and α-hydroxy-β-aminopropylbenzene hydrochloride), is a well-known sympathomimetic amine. Phenylpropanolamine hydrochloride is well documented as a therapeutic agent which is used as an anorexiant for control of obesity. In this capacity it has been marketed by, among others, SDA Pharmaceuticals, Inc. under the trademarks Anorexin ® and One-Span ®, and by Thompson Medical Company, Inc. under the trademark Dexatrim ®.

Phenylpropanolamine hydrochloride is also a bronchial dilator, and is accordingly used for the treatment of asthma, as well as being commonly employed as a decongestant for treatment of upper respiratory tract congestion. As an antiasthmatic, phenylpropanolamine hydrochloride has been marketed by Eaton Laboratories under the trademark Rymed ®.

U.S. Pat. No. 4,971,798 describes a slow-dissolving lozenge confection to provide slow sustained release of an antitussive, decongestant, antihistamine, or expectorant ingredient, which may be phenylpropanolamine.

U.S. Pat. No. 4,894,223 describes a novel drug delivery system for decongestants. The delivery system, which may be used to deliver phenylpropanolamine hydrochloride, is in dry particulate form, and includes a hydrophobic matrix and a coat.

It is an object of the present invention to provide a sustained release form of an active ingredient, such as Phenylpropanolamine hydrochloride, which is characterized by immediate release of the active ingredient, a period of no release of active agent, followed by release of the active ingredient at a uniform constant rate, independent of the drug concentration and/or gastrointestinal pH variation during the period of release

SUMMARY OF THE INVENTION

The object of the present invention is to provide a sustained release tablet adapted to provide an initial immediate release of an active agent, a period of no release of active agent, followed by a substantially constant, zero-order rate of release of the active agent.

The tablet of the present invention comprises:

(a) a compressed tablet core comprising an active agent, an insoluble binder and an insoluble filler;

(b) a barrier coating formed over the tablet core, the barrier coating comprising a mixture of soluble and insoluble polymers, and a plasticizer;

(c) an active coating formed over the barrier coating, the active coating comprising the active agent, a soluble polymer and a plasticizer; and

(d) a film coating formed over the active coating, the film coating comprising a soluble polymer and a plasticizer.

The active agent is contained in the active coating in an amount of from about 1 to about 35% by weight of the total dosage weight of the active agent in the sustained release tablet. Preferably, the active agent is phenylpropanolamine hydrochloride, which may be present in the active coating in an amount of from about 15 to about 33% by weight, of the total dosage weight of the phenylpropanolamine hydrochloride in the tablet. Other active agents may be employed, however, including, but not limited to, to adrenergic agents, anticholinergic agents; antispasmodic agents; curariform agents; tranquilizers; muscle relaxants; antihistamines; hypotensive agents; cardioactive agents; angiotensin converting enzyme inhibitors; bronchodilators; steroids; antibacterial agents; antimalarials; antibiotics; sedatives; and analgesics.

The sustained release tablet of the present invention has a typical release profile of the active agent in the tablet, as measured in the in-vitro dissolution method utilizing U.S.P. XXII, basket method at 100 RPM in water at 37° C., as follows:

1 hour	15–33%
2 hours	No release
3–4 hours	4–6%/hour
5–6 hours	4–6%/hour
7–8 hours	4–6%/hour
9–10 hours	4–6%/hour
11–12 hours	3–5%/hour
13–14 hours	3–5%/hour

The sustained release tablet according to the present invention comprises:

(a) a compressed tablet core comprising phenylpropanolamine hydrochloride, ethyl cellulose and calcium sulfate;

(b) a barrier coating formed over the tablet core, the barrier coating comprising a mixture of hydroxypropyl methyl cellulose, ethyl cellulose and glyceryl triacetate, wherein the hydroxypropyl methyl cellulose and the ethyl cellulose are utilized in a ratio by weight of about 1:3;

(c) an active coating formed over the barrier coating, the active coating comprising phenylpropanolamine hydrochloride, hydroxypropyl methyl cellulose and glyceryl triacetate, wherein the amount of phenylpropanolamine hydrochloride in the active coating is from about 15 to about 33% by weight of the total dosage weight of the phenylpropanolamine hydrochloride in the tablet; and

(d) a film coating formed over the active coating, the film coating comprising hydroxypropyl methyl cellulose and glyceryl triacetate.

The present invention also contemplates a method of preparing the novel sustained release tablet of the invention. According to a preferred method, a sustained release tablet adapted to provide an initial immediate release of an active agent, a period of no release of active agent, followed by a substantially constant, zero-

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