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Chen et al.

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(54) **CONTROLLED RELEASE METFORMIN COMPOSITIONS**

(75) Inventors: **Chih-Ming Chen**, Davie, FL (US); **Xiu-Xiu Cheng**, Davie, FL (US); **Steve Jan**, Coral Springs, FL (US); **Joseph Chou**, Manassas, VA (US)

(73) Assignee: **Andrx Labs, LLC**, Davie, FL (US)

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 162 days.

This patent is subject to a terminal disclaimer.

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(52) U.S. Cl. **424/468; 424/457; 424/474; 424/480**

(58) Field of Search **424/473, 468, 424/474, 475, 479, 480, 482; 514/635, 588, 591, 592, 593**

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Primary Examiner—Thurman K. Page

Assistant Examiner—Micah Paul Young

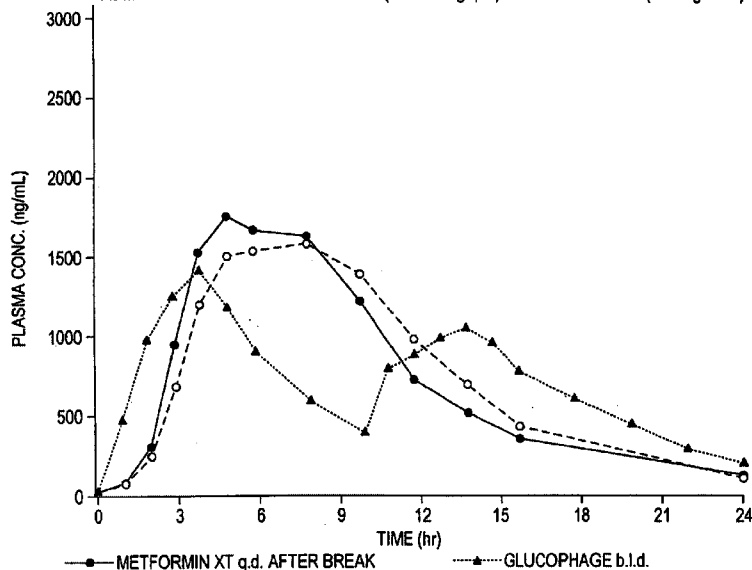
(74) *Attorney, Agent, or Firm*—Davidson, Davidson & Kappel, LLC

(57) **ABSTRACT**

A composition for treating patients having non-insulin-dependent diabetes mellitus (NIDDM) by administering a controlled release oral solid dosage form containing preferably a biguanide drug such as metformin, on a once-a-day basis. The dosage form provides a mean time to maximum plasma concentration (T_{max}) of the drug which occurs at 5.5 to 7.5 hours after oral administration on a once-a-day basis to human patients. Preferably, the dose of drug is administered at dinnertime to a patient in the fed state.

25 Claims, 8 Drawing Sheets

MEAN PLASMA CONCENTRATION-TIME PROFILES OF METFORMIN IN ELEVEN SUBJECTS AFTER AN ORAL ADMINISTRATION OF METFORMIN XT (2 x 850 mg q.d.) OR GLUCOPHAGE (850 mg b.i.d.)



MEAN PLASMA CONCENTRATION-TIME PROFILES OF METFORMIN IN ELEVEN SUBJECTS AFTER AN ORAL ADMINISTRATION OF METFORMIN XT (2 x 850 mg q.d.) OR GLUCOPHAGE (850 mg b.i.d.)

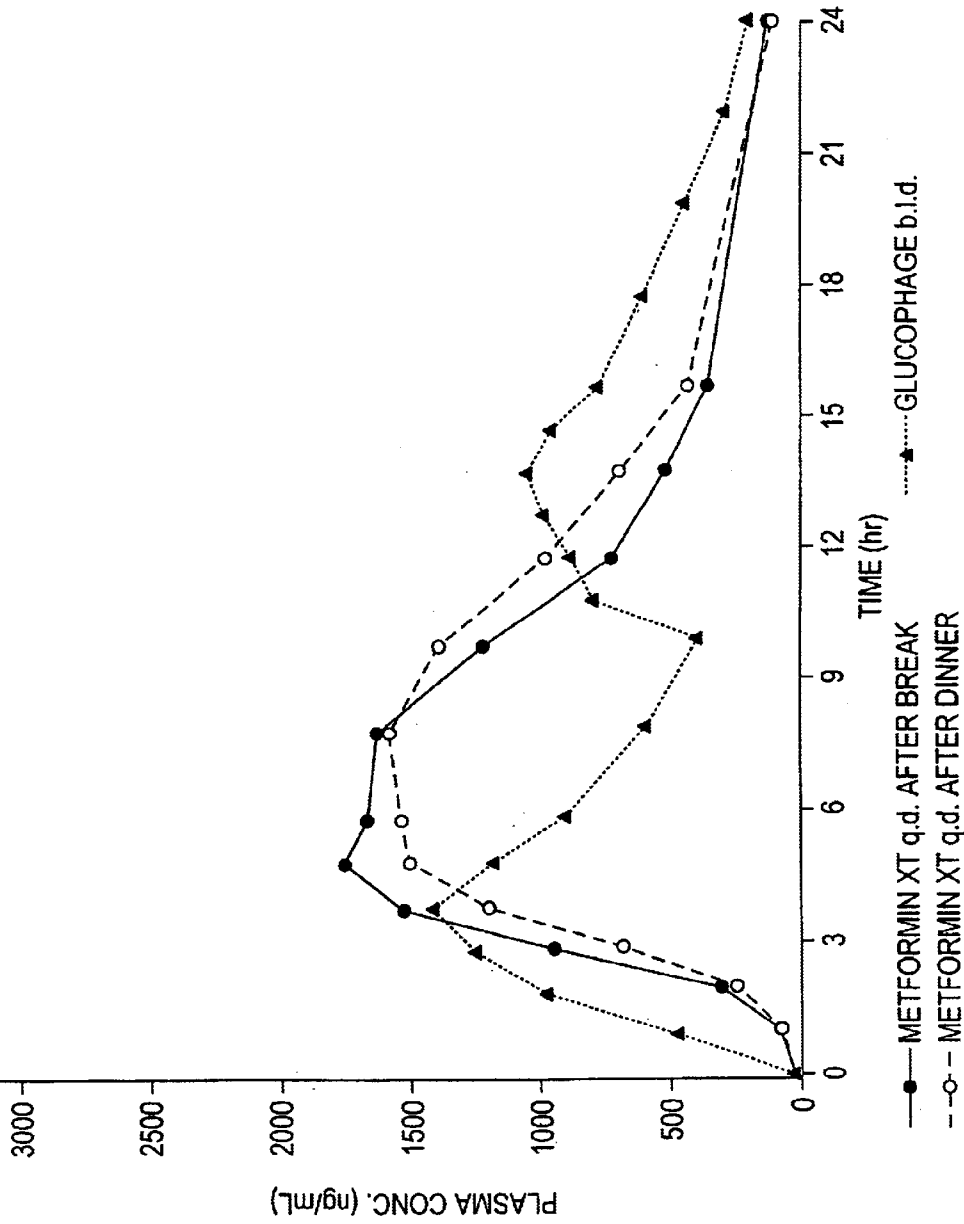


FIG. 1

MEAN PLASMA CONCENTRATION-TIME PROFILES OF METFORMIN IN TWELVE SUBJECTS AFTER AN ORAL ADMINISTRATION OF METFORMIN XT (4 x 500 mg q.d.) OR GLUCOPHAGE (2 x 500 mg b.i.d.)

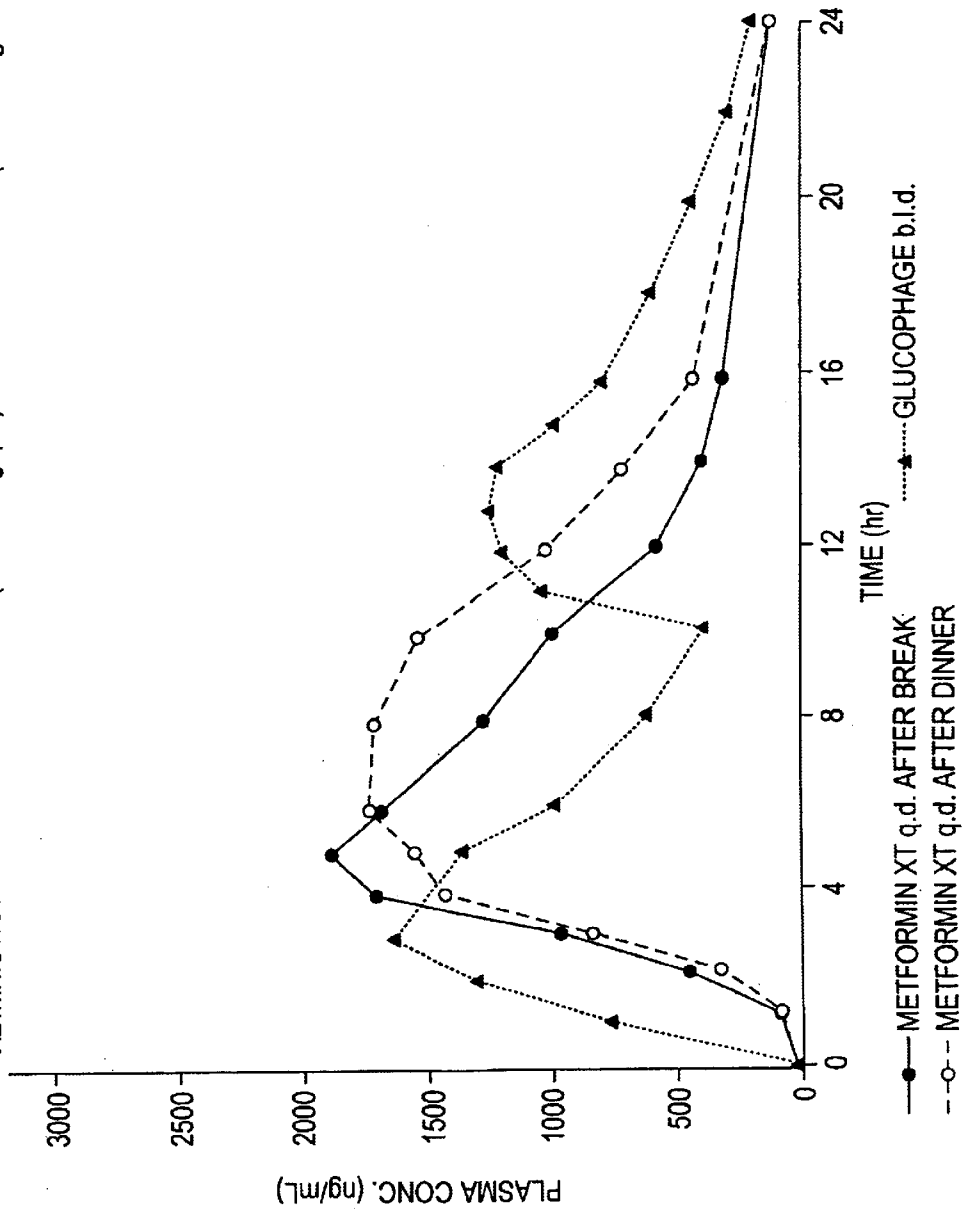


FIG. 2

MEAN PLASMA CONCENTRATION-TIME PROFILES OF METFORMIN IN EIGHT HEALTHY SUBJECTS AFTER MULTIPLE ORAL DOSES OF METFORMIN XT (4 x 500 mg q.d.)

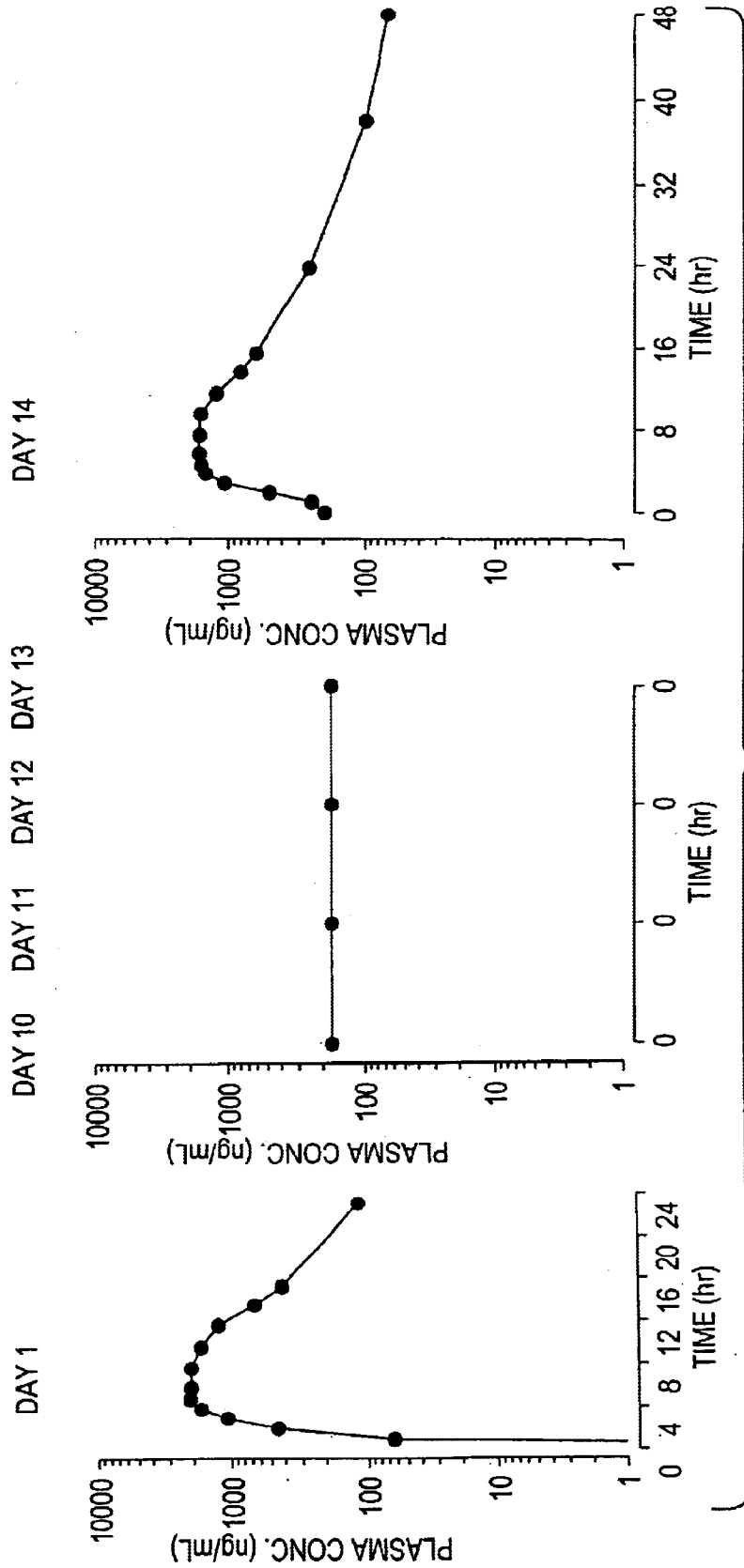


FIG. 3

MEAN STEADY-STATE PLASMA CONCENTRATION-TIME PROFILES OF METFORMIN IN NIDDM PATIENTS (n=23) AFTER MULTIPLE ORAL DOSES OF METFORMIN XT (2 x 1000 mg q.d. WITH DINNER) OR GLUCOPHAGE (1x1000 mg b.i.d.) FOR 4 WEEKS

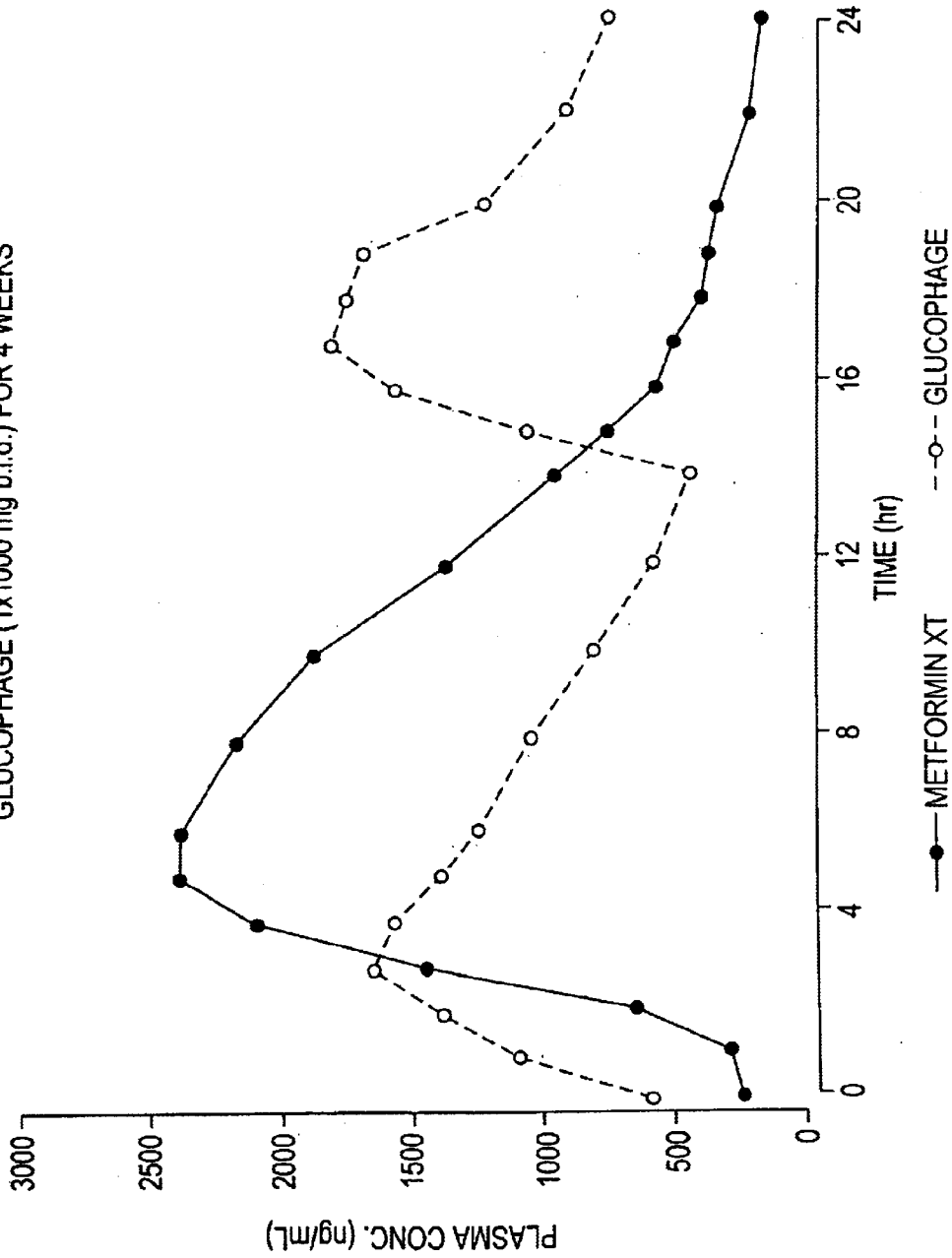


FIG. 4

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