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**Chen et al.**

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(54) **CONTROLLED RELEASE METFORMIN COMPOSITIONS**

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(\* ) 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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(51) Int. Cl.<sup>7</sup> ..... **A61K 9/22**; **A61K 9/52**

(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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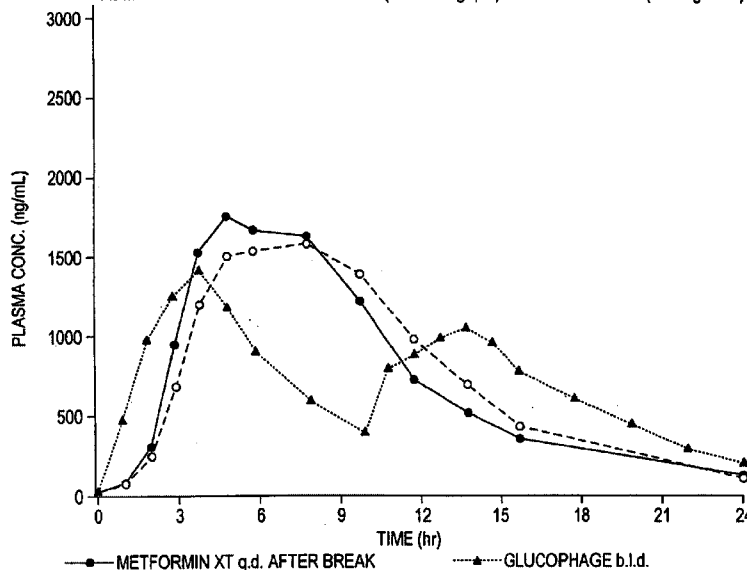
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(57) **ABSTRACT**

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.)

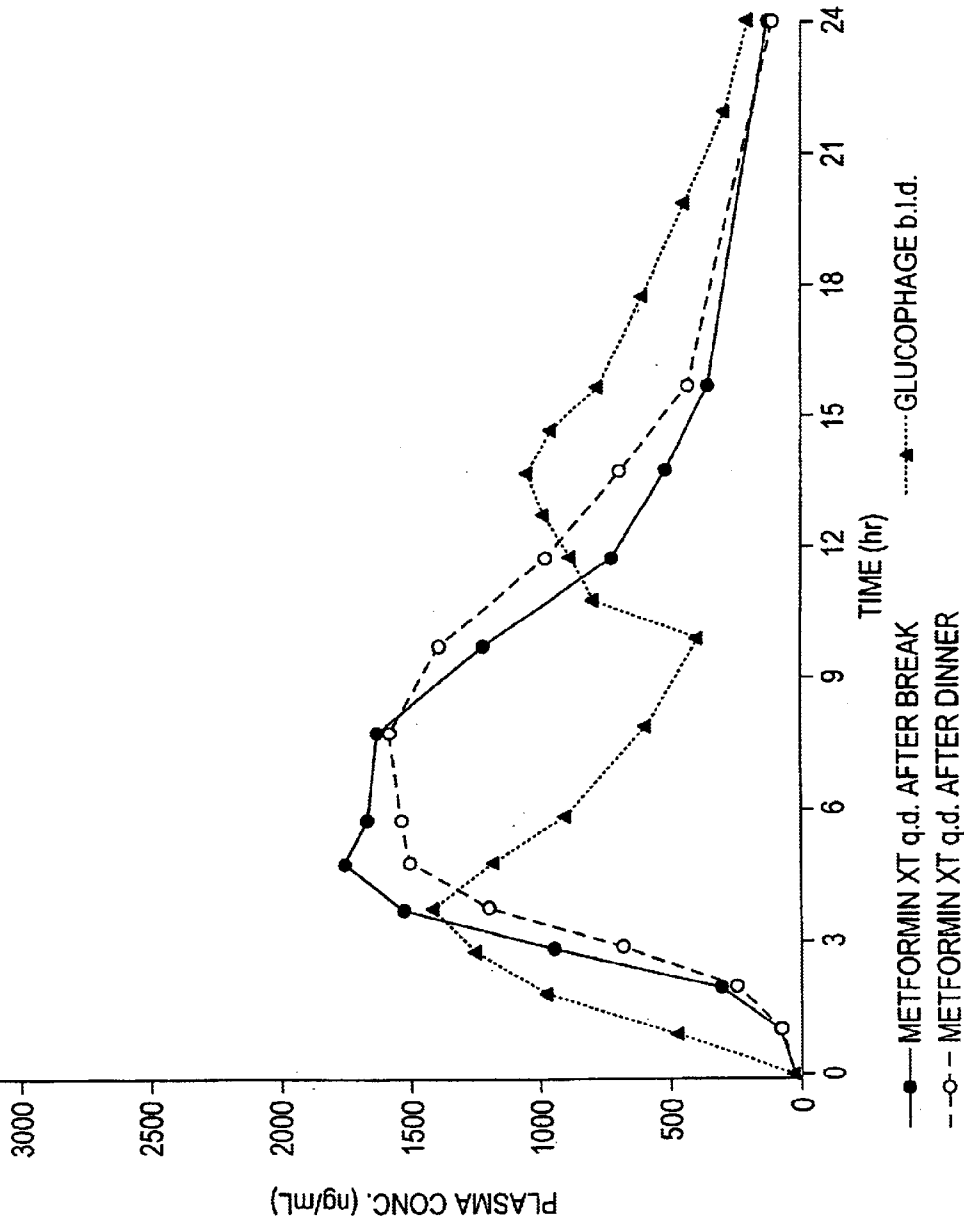


FIG. 1

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.)

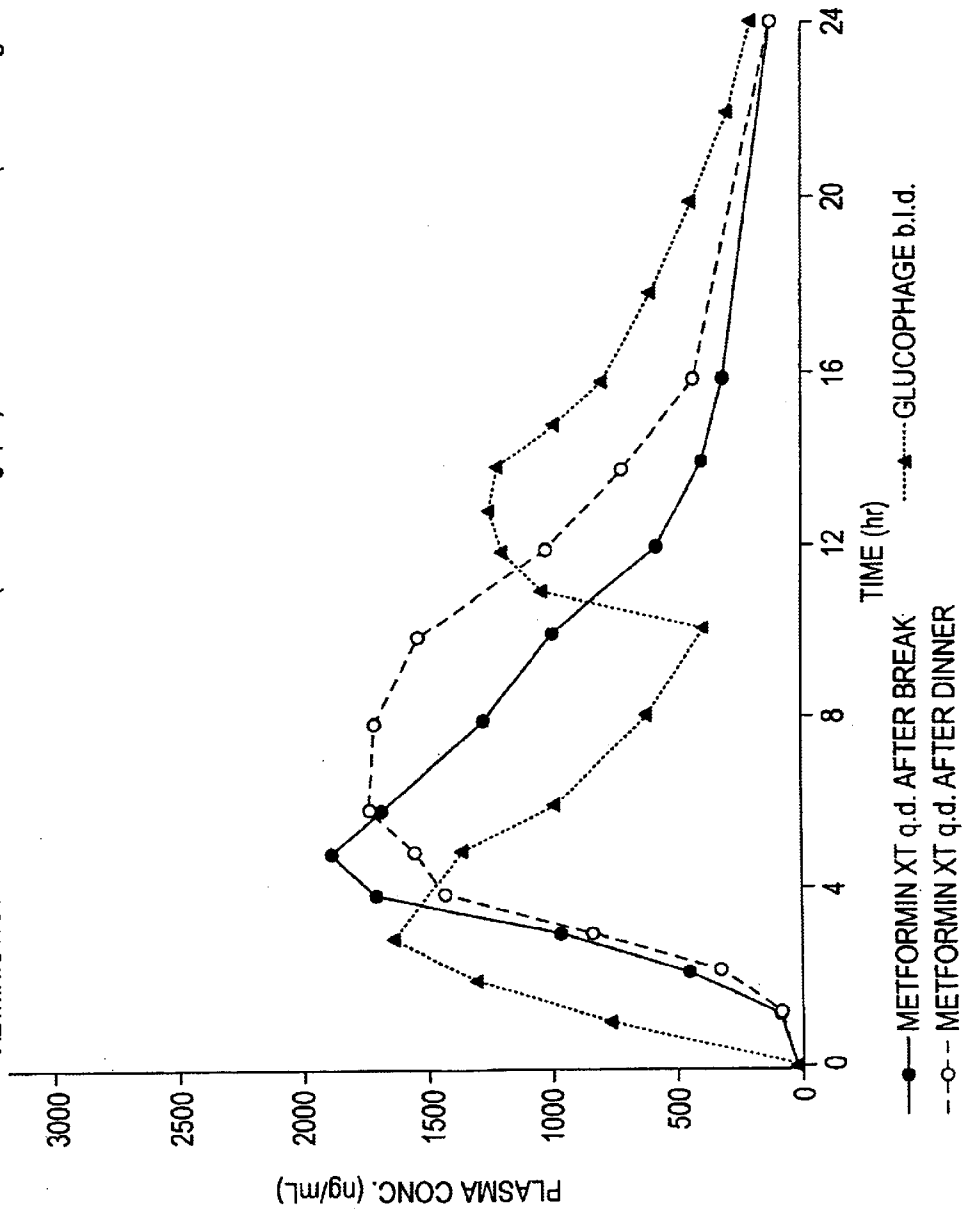


FIG. 2

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

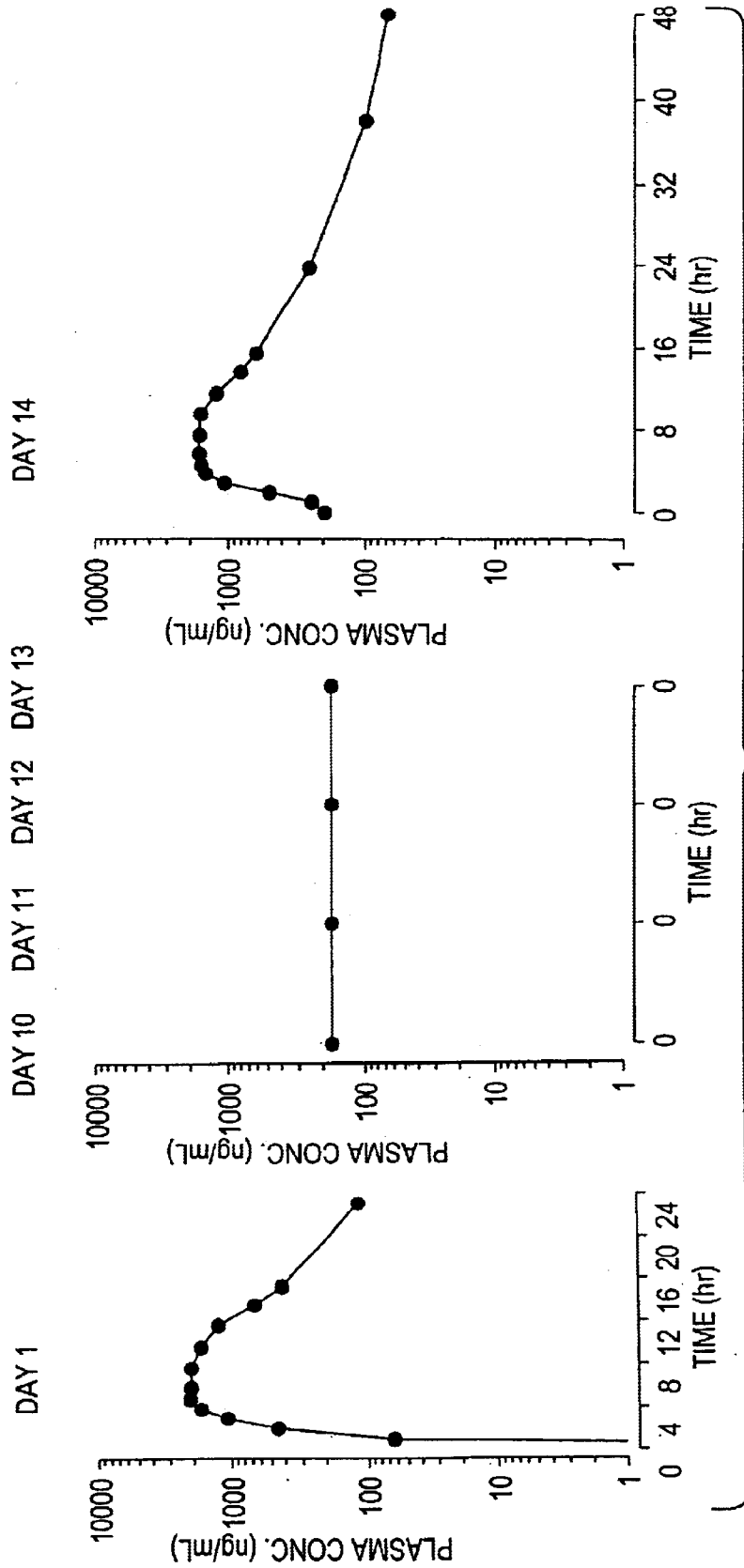


FIG. 3

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

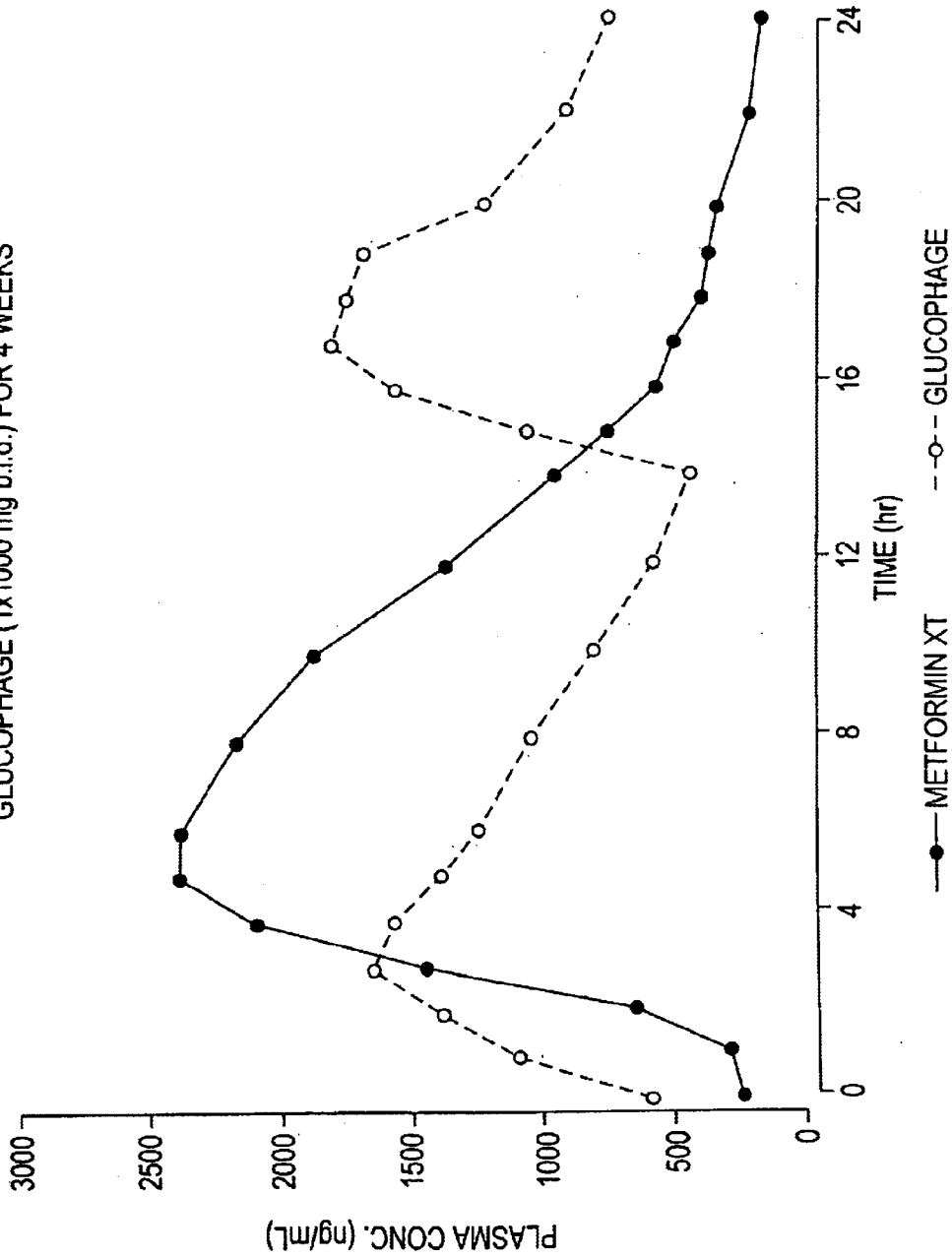


FIG. 4

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