

**CENTER FOR DRUG EVALUATION AND  
RESEARCH**

*APPLICATION NUMBER:*  
**74657**

**BIOEQUIVALENCY REVIEW(S)**

JAN 5 1996

**Terazosin Hydrochloride**

1, 2, 5, and 10 mg Tablets  
ANDA #74-657  
Reviewer: Kuldeep R. Dhariwal

**Invamed Inc.**

2400 Rt. 130 North  
Dayton, New Jersey 08810  
Submission Date:  
April 8, 1995

**Review of Bioequivalence Study, Dissolution Data,  
and Waiver Request**

The firm has submitted a single-dose *in vivo* bioequivalence study under fasting conditions and dissolution data comparing its terazosin hydrochloride tablets, 5 mg with Abbott's Hytrin® tablets, 5 mg. The firm has also requested waivers of *in vivo* bioequivalence study requirements for its 1, 2, and 10 mg tablets. To support the request, the firm has submitted comparative dissolution profiles on 1, 2, and 10 mg strengths of its product and reference listed drug Hytrin®.

**Introduction:**

Terazosin Hydrochloride is chemically defined as 1-(4-amino-6,7-dimethoxy-2-quinazolinyl)-4-[(tetra-hydro-2-furanyl)carbonyl]-, monohydrochloride and is indicated for the treatment of symptomatic benign prostatic hyperplasia (BPH) and hypertension.

Terazosin Hydrochloride administered as tablets is essentially completely absorbed in man. Food had little or no effect on the extent of absorption but food delayed the time to peak concentration by about one hour. The plasma levels peak about one hour after dosing, and then decline with a half-life of approximately 12 hours. The drug is highly bound to plasma proteins. Approximately, % of an orally administered dose is excreted as parent drug in the urine and approximately % is excreted in the feces. The remainder is eliminated as metabolites.

The reference product is Hytrin® by Abbott Laboratories and is available in four dosage strengths: 1, 2, 5, and 10 mg. Its starting dose is 1 mg given at bedtime. The dose should be increased in a stepwise fashion to 2 mg, 5 mg, or 10 mg once daily. Doses of 10 mg once daily are generally required for the clinical response.

## **Bioavailability of Terazosin Tablets, 5 mg under Fasting Conditions:**

### **A. Objective:**

The objective of this study is to compare the relative bioavailability of 5 mg terazosin hydrochloride tablets (Invamed) with that of Hytrin® 5 mg tablets (Abbott) in healthy adult male volunteers under fasting conditions.

### **B. Study Sites and Investigators:**

Clinical Site:

Analytical Site:

Principle Investigator:

Sub-Investigator:

Analytical Director: Paul Likhari

Protocol #B-02214; "A Relative Bioavailability

Study of Terazosin (5 mg) Tablets" was approved by the Institutional Review Board for

Consent Form: A copy of volunteer informed consent form used in the study is given on page 779 vol. 1.2.

Study Dates: Phase I January 14-16, 1995

Phase II January 21-23, 1995

Analysis Dates: 2/15 to 3/3, 1995

### **C. Study Design:**

The study was a single-dose, randomized, two-way crossover design involving thirty-eight healthy male subjects. The subjects were housed 10 hours before dosing until 36 hours after dosing each period. The study was executed in two phases with seven day washout period between doses. The subjects were assigned to two groups at random as follows:

Group	Subject number	Phase I	Phase II
1	3, 8, 11, 12, 14, 15, 16, 17, 18, 20, 21, 24, 25, 27, 32, 33, 34, 36, 37	A	B
2	1, 2, 4, 5, 6, 7, 9, 10, 13, 19, 22, 23, 26, 28, 29, 30, 31, 35, 38	B	A

A: Terazosin Hydrochloride, 1 x 5 mg, Invamed, Inc.; Lot

#D941201; Lot size: Theoretical Yield: Actual Yield:

Expiration Date: N/A; Manufacture Date: 12/1994; Assay: 101.2%; Uniformity of dosage units: 99.9%.

B: Hytrin®, 1 x 5 mg, Abbott Laboratories: Lot #92-198-AA-21; Expiration Date: 10/1997; Assay: 100.5%; Uniformity of dosage units: 100.2%.

The subjects fasted for 10 hours prior to dosing until 4 hours after dose administration during each study period. No fluid except that given with drug administration was allowed from 1 hour before dosing until 2 hours after dosing. The drug products were administered with 240 mL of water. After administration of the product, the subject's oral cavity was checked to confirm complete medication and fluid consumption. The subjects were sequentially dosed. After dose administration, subjects were placed in a sitting or supine position until all symptoms of dizziness or lightheadedness had resolved. Two hours after dosing, all subjects consumed 240 mL of water. Four hours after dose administration, water was allowed ad lib, if requested, but generally controlled during confinement and limited to approximately 4740 mL from the time of dosing until release from the study site. Subjects were served standardized meals and beverages. Meals were the same in content and quantity during each study period.

Blood pressure and heart rate were measured prior to dosing and at 1,2,3,4,6,8,12,24, and 36 hours after each dose. Physical examination and diagnostic blood and urine analysis were also done at the end of the study.

#### **D. Subject Selection:**

Thirty-eight healthy male subjects were recruited for the study. Following inclusion criteria were used in selecting the subjects:

- 18-40 years of age
- no more than  $\pm 10\%$  from normal for height and body frame as per Desirable Weights for Men - 1983 Metropolitan Height and Weight Table
- good health as determined by medical histories and physical examinations. Blood chemistry, hematology, and urinalysis within clinically acceptable limits completed within 21 days prior to period I dosing.

Subjects were excluded from this study based on the following criteria:

- history of chronic alcohol consumption, drug addiction, or serious gastrointestinal, renal, hepatic, neurological, respiratory, endocrine, ocular, hematological, psychological or cardiovascular disease
- positive hepatitis B surface antigen screen or a reactive HIV 1 and 2 antibody screen
- history of an allergic response to the class of drug tested
- use of tobacco in any form

- blood or plasma donation within 30 days prior to starting the study
- positive urine test for drugs of abuse
- intake of any investigational drug within 30 days prior to the start of the study
- diastolic blood pressure lower than 60 mmHg
- exposure to any drug known to induce or inhibit hepatic drug metabolism within 30 days prior to dosing

Subjects were imposed with following restrictions:

- no prescription or over-the-counter medications in the 14 days prior to period I dosing and throughout the study
- no caffeine and/or xanthine containing products for at least 3 days prior to days on which they were dosed, and during the periods when blood samples were drawn
- no alcohol for at least 48 hours prior to dosing and during the periods when blood samples were obtained
- no strenuous physical activity will be permitted during the confinement

#### **E. Sample Collection:**

Ten milliliters of venous blood were obtained in EDTA-Vacutainers at 0 (predose), 0.17, 0.33, 0.50, 0.75, 1, 1.5, 2, 3, 5, 8, 10, 12, 16, 24, 36, 48, and 60 hours. The samples remained at the blood collection station until all samples had been collected for one collection period (about 10 minutes). The Vacutainer samples were then transferred to the processing laboratory. The blood was centrifuged at 2400 rpm for 15 minutes at 4°C and the plasma separated. The plasma samples were frozen immediately and stored at -20°C until shipment.

#### **F. Analytical Methods:**

## G. Pharmacokinetics/Statistical Analysis:

The analytical data were used to calculate the pharmacokinetic parameters:  $AUC_{0-t}$ ,  $AUC_{0-inf}$ ,  $C_{max}$ ,  $T_{max}$ , half life and elimination rate constant. The pharmacokinetic parameters and drug plasma concentrations were evaluated statistically by ANOVA for differences due to treatments, study days, dosing sequence, and subjects within sequence. The statistical analysis was performed using SAS version 6.08. The SAS GLM procedure was used for the analysis of variance. The study power calculations and 90% confidence interval calculations were based on the least-squares means values generated by the SAS LSMEANS option to the SAS GLM procedure and the standard error of the estimate as given by the GLM procedure.

## H. Results:

### 1. Clinical:

Thirty-eight subjects entered the study. Thirty-seven subjects completed the study. Subject #35 dropped from the study prior to period II dosing for personal reasons. The plasma samples from 37 subjects were assayed for terazosin. Blood pressure and heart rate were measured prior to dosing and at 1,2,3,4,6,8,12,24, and 36 hours after dosing. After dosing, subjects had a decrease in diastolic blood pressure of 10 mmHg or greater by study hour 8. All blood pressures returned to baseline values prior to subject release from the clinical research unit. The mean heart rate increased by 20 bpm 8 hours postdose. The analysis of blood pressure and heart rate data show that there were no statistically significant differences between the two products in the baseline, minimum or drop from baseline for diastolic pressure, systolic pressure, or heart rate. A significant difference for baseline systolic blood pressure was detected between dosing periods. In general, the blood pressure readings were lower by about 5 mmHg for the second period. This is attributed by the firm to factors like the subjects were more relaxed and less anxious during the second period. The differences in blood pressure was small (5 mmHg), but could be detected as significant due to high study power. Similarly, a small difference in the minimum heart rate values between dosing periods was detected as significant, again due to the high study power.

Adverse events:

Fifty-four adverse events were reported in twenty-two of thirty-eight subjects dosed over the course of the study. Of the fifty-four reported adverse events, thirty-seven were probably or possibly related to the study drug. None of the adverse events were considered to be serious in nature.

Subject #	Phase	Product	Sign/Symptom
1	1	ref	Dizziness
2	1	ref	Syncope (fainted)
5	1	ref	hematoma
5	2	test	stuffy nose
6	1	ref	headache
8	1	test	nose bleed
10	1	ref	sore throat, muscle aches
16	1	test	dizziness
17	2	ref	stuffy nose
18	1	test	dizziness, headache, stiff neck
19	1	ref	dizziness, anorexia
19	2	test	abdominal pain
21	2	ref	dizziness, stuffy nose, pale, sore throat, cough, chills, bodyache
22	1	ref	stuffy nose
22	2	test	sore throat
24	1	test	dizziness
26	1	ref	dizziness, stuffy nose, headache
27	1	test	dizziness, nausea, headache, pale
28	1	ref	dizziness
31	1	ref	headache
33	1	ref	stuffy nose
34	1,2	test,ref	headache
35	1	ref	nausea, vomiting, headache, stuffy nose, sweating
37	2	ref	stuffy nose, cough

Following subjects showed poststudy laboratory results outside of the reference range but were considered clinically not significant:

Subject #	Test result
16	low hematocrit
26	low WBC
29	low hematocrit
36	low RBC
1,2,7,10,15,31,33,34,37	high total protein
4,32	high glucose

12	low glucose
9,23,30,	high SGPT
25	high creatinine
27	high total bilirubin
32	high alkaline phosphatase

Deviations in the study:

a) A few deviations from the scheduled phlebotomy time occurred during the study:

Subject #	Product	Time of Blood Collection Scheduled	Collection Actual	Deviation
Phase I				
24	test	0:10	0:13	+0:03
30	reference	0:10	0:17	+0:07
07	reference	0:20	0:23	+0:03
33	test	0:30	0:33	+0:03
05	reference	0:45	0:47	+0:02
26	reference	8:00	8:04	+0:04
04	reference	60:00	57:35	-2:25
Phase II				
33	reference	0:20	0:22	+0:02

Actual collection times were used in the pharmacokinetic calculations.

b) There were five deviations from the protocol restriction of no non-prescription medications within 14 days of period I dosing. One subject had vitamin C 11 days prior to the study, one subject had multivitamin 5 days prior to the study. Seven days before the study, one subject took Motrin, one subject took Tylenol, and one subject took Benadryl.

c) Reassays: A total number of 1332 samples were analyzed. Following 8 samples were reanalyzed for reasons shown against them:

# of samples	reason for reassay
6	value above high standard
2	anomalous value

2. Analytical:

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### 3. Pharmacokinetics/Statistics:

The mean plasma concentrations of terazosin at each time point after test and reference products are shown in Table 1. These data indicate that with the exception of 60 hour, terazosin plasma concentration following administration of test product were within 20% of that of the reference product. The time courses of terazosin after the two products are plotted in Figures 1 and 2. The pharmacokinetic parameters are summarized in Table 2. There is no statistical significant difference between the two formulations for any parameter.  $AUC_{0-t}$  and  $AUC_{0-inf}$  were about 3% higher for test product compared to reference product.  $C_{max}$  in test product occurred about 8 minutes earlier and was about 4% higher compared to reference product.

The reviewer performed some calculations to determine the accuracy of the values given in the application:

Drug Product: Terazosin Hydrochloride (Test)

Subject#	Reviewer		Firm	
	$AUC_{0-t}$	$AUC_{0-inf}$	$AUC_{0-t}$	$AUC_{0-inf}$
1	985.4	1034.7	985	1035
20	1142.9	1199.2	1143	1199
36	1098.5	1143.1	1099	1143

The results of these calculations indicate good agreement between reviewer's calculations and the data reported by the firm.

The individual mean ratios for  $AUC_{0-t}$ ,  $AUC_{0-inf}$ , and  $C_{max}$  are given in Table 3. The test/reference ratio for  $AUC_{0-t}$  ranged from 0.72 to 1.69 (mean 1.04),  $AUC_{0-inf}$  ranged from 0.71 to 1.68 (mean 1.05) and for  $C_{max}$  ranged from 0.73 to 1.97 with a mean of 1.04.

Table 4 shows the  $AUC_{0-t}/AUC_{0-inf}$  ratios for individual subjects. The ratios ranged from 0.84 to 0.98.

The following are the 90% confidence intervals provided by the firm along with those calculated by the reviewer:

Parameter	90% Confidence Interval	
	Firm's Values	Reviewer's Values
LAUC <sub>0-t</sub>	98.9-107.0	98.9-107.2
LAUC <sub>0-inf</sub>	99.4-108.0	99.4-108.1
LC <sub>max</sub>	98.1-110.0	98.1-109.8

The 90% confidence intervals for AUC<sub>0-t</sub>, AUC<sub>0-inf</sub>, and C<sub>max</sub> are within the acceptable range of 80-125. Statistical analysis of data did not show any significant treatment, period, or sequence effect for AUC<sub>0-t</sub>, AUC<sub>0-inf</sub>, and C<sub>max</sub>. A period difference was detected for the log transformed C<sub>max</sub> (p=0.0354) but not for the non-transformed C<sub>max</sub>.

**In Vitro Dissolution Testing:**

The firm has submitted comparative dissolution data for test and reference products (1, 2, 5, and 10 mg). The dissolution testing was done in 900 mL water using apparatus 2 (paddle) at 50 rpm. The 5 mg tablets used in the dissolution tests were from the same lot used in the *in vivo* bioequivalence study. The assay methodology was detection at 245 nm. The dissolution data are acceptable. The firm has demonstrated that % of the test products are dissolved in 30 minutes. The dissolution profiles for the test and reference drugs are similar (Table 6).

**Waiver Request:**

The firm is requesting for a waiver of *in vivo* bioequivalence study for its 1 mg, 2 mg, and 10 mg terazosin tablets. The comparative quantitative compositions of all strengths are shown in Table 5. The 1 mg, 2 mg, and 10 mg tablets are proportionally similar in their active and inactive ingredients to the 5 mg strength. However, the lactose content varied from % to % which is considered a minor difference. There are also some differences in the contents of the dye between different strengths. The dissolution profiles of all strengths of the test products are similar to their respective strengths of the reference products.

## Comments:

1. Thirty-eight subjects entered the study. One subject did not complete the study because of personal reasons. The plasma samples from 37 subjects were assayed for terazosin. Twenty subjects experienced adverse effects; none of them were considered clinically significant. No medication was required for any adverse events. Twenty-one subjects showed poststudy laboratory results outside of the reference range but were considered clinically not significant.

2. Blood pressure and heart rate were measured prior to dosing and at 1,2,3,4,6,8,12,24, and 36 hours after dosing. The analysis of blood pressure and heart rate data show that there were no statistically significant differences between the two products in the baseline, minimum or drop from baseline for diastolic pressure, systolic pressure, or heart rate.

3.  $AUC_{0-t}$  and  $AUC_{0-inf}$  was about 3% higher for test product compared to reference product.  $C_{max}$  in test product occurred about 8 min earlier and was about 4% higher compared to reference product. The 90% confidence intervals for log transformed data for  $AUC_{0-t}$ ,  $AUC_{0-inf}$ , and  $C_{max}$  are within the acceptable range of 80-125.

4. Statistical analysis of data did not show any significant treatment, period, or sequence effect for  $AUC_{0-t}$ ,  $AUC_{0-inf}$ , and  $C_{max}$ . A period difference was detected for the log transformed  $C_{max}$  ( $p=0.0354$ ) but not for the non-transformed  $C_{max}$ .

5. The dissolution testing was done using FDA method. No USP dissolution method for this drug product is available at this time. The firm has demonstrated that greater than % of the test products are dissolved in 30 minutes, and have met agency's specifications. The *in vitro* data are acceptable.

6. The 1 mg, 2 mg, and 10 mg tablets are proportionally similar in their active and inactive ingredients to the 5 mg strength. However, the lactose content varied from % to % which is considered a minor difference. The *in vivo* bioequivalence study on 5 mg tablet is acceptable. The comparative dissolution profiles of the test and reference products are similar. The test products dissolve greater than % in 30 minutes. The waiver can be granted.

## Recommendations:

1. The *in vivo* bioequivalence study conducted under fasting conditions by Invamed Inc. on its terazosin hydrochloride, 5 mg tablets, lot # D941201, comparing it to the reference product Hytrin® 5 mg tablets, lot #92-198-AA-21, manufactured by Abbott

Laboratories has been found acceptable to the Division of Bioequivalence. The study demonstrates that under fasting conditions, Invamed's terazosin hydrochloride 5 mg tablet is bioequivalent to the reference product Hytrin® 5 mg tablet manufactured by Abbott Laboratories.

2. The dissolution testing conducted on terazosin hydrochloride, 1 mg, 2 mg, 5 mg, and 10 mg tablets is acceptable. The dissolution testing should be incorporated into firm's manufacturing controls and stability programs. The dissolution testing should be conducted in 900 mL of water at 37°C using apparatus 2 (paddle) at 50 rpm. The test products should meet the following specifications:

Not less than % of the labeled amount of terazosin hydrochloride in the dosage form is dissolved in 30 minutes.

3. The formulations for the 1 mg, 2 mg, and 10 mg terazosin hydrochloride tablets are proportionally similar to the 5 mg tablet which underwent a bioequivalence study. The waiver of the *in vivo* bioequivalence study requirements for Invamed's 1 mg, 2 mg, and 10 mg tablets is granted. The 1 mg, 2 mg, and 10 mg terazosin hydrochloride tablets from Invamed Inc. are therefore deemed bioequivalent to the 1 mg, 2 mg, and 10 mg Hytrin® tablets manufactured by Abbott Laboratories.

4. From bioequivalence standpoint the firm has met the *in vivo* bioavailability and *in vitro* dissolution testing requirements and the application is approvable.

/S/

10/25/95

Kuldeep R. Dhariwal, Ph.D.  
Review Branch II  
Division of Bioequivalence

RD INITIALED R.PATNAIK  
FT INITIALED R.PATNAIK

/S/

Date 10/25/95

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Concur:

Dr. Keith Chan, Ph.D.  
Director  
Division of Bioequivalence

Date

1/5/96

cc: ANDA #74657 (original, duplicate), HFD-600 (Hare), HFD-630,  
HFD-344 (CViswanathan), HFD-655 (Patnaik, Dhariwal), Drug File,  
Division File

Table 1

Mean Terazosin Plasma Concentrations (ng/mL) and Pharmacokinetic Parameters (N=37): Arithmetic Means and Standard Deviation (SD)

Time (h)	Test		Reference		Test/Ref
	Mean	SD	Mean	SD	
<b>Plasma Concentrations</b>					
0	0		0		
0.17	15.76	16.03	16.71	16.96	0.94
0.33	60.50	33.37	54.43	29.58	1.11
0.50	78.17	32.35	75.74	30.77	1.03
0.75	84.92	26.61	86.31	28.21	0.98
1.00	84.96	22.03	86.39	25.79	0.98
1.50	83.06	19.74	84.46	24.47	0.98
2.00	83.32	21.55	82.47	23.21	1.01
3.00	75.17	18.25	74.74	18.56	1.00
5.00	62.50	14.75	60.87	13.60	1.03
8.00	47.28	11.08	46.36	11.22	1.02
10.0	37.75	8.99	36.74	9.03	1.03
12.0	31.25	8.08	30.47	8.80	1.03
16.0	21.61	5.96	20.48	6.29	1.06
24.0	12.43	3.55	12.05	3.89	1.03
36.0	6.05	1.91	5.89	2.20	1.03
48.0	3.48	1.32	3.59	2.22	0.97
60.0	2.49	2.16	2.04	0.96	1.22
<b>Pharmacokinetic Parameters</b>					
AUC <sub>0-t</sub> (ng/mLxh)	1125	253	1099	296	1.02
AUC <sub>0-inf</sub> (ng/mLxh)	1182	275	1146	310	1.03
C <sub>max</sub> (ng/mL)	99.92	25.8	96.3	26.2	1.04
T <sub>max</sub> (h)	0.9289	0.63	1.0562	0.69	0.88
T <sub>1/2</sub> (h)	14.785	2.37	14.592	2.80	1.01
KELM (1/h)	0.0481	0.008	0.0492	0.009	0.98

KELM: Terminal elimination constant

Table 2

**Terazosin Plasma Concentrations: Pharmacokinetic Parameters  
Least Square Means  $\pm$  Standard Error**

Parameter	Test	Reference	Test/Ref	90% Confidence Interval
AUC <sub>0-t</sub> (ng/mLxh)	1126 $\pm$ 21.3	1100 $\pm$ 21.3	1.02	97.7-107
AUC <sub>0-inf</sub> (ng/mLxh)	1183 $\pm$ 23.5	1147 $\pm$ 23.5	1.03	98.3-108
C <sub>max</sub> (ng/mL)	99.91 $\pm$ 2.59	96.49 $\pm$ 2.59	1.04	97.1-110
T <sub>max</sub> (h)	0.93 $\pm$ 0.086	1.06 $\pm$ 0.086	0.88	68.6-108
LNAUC <sub>0-t</sub>	7.003 $\pm$ 0.017	6.974 $\pm$ 0.017	1.00	98.9-107
LNAUC <sub>0-inf</sub>	7.051 $\pm$ 0.017	7.015 $\pm$ 0.017	1.00	99.4-108
LNC <sub>max</sub>	4.573 $\pm$ 0.023	4.536 $\pm$ 0.023	1.01	98.1-110

Table 3

Test/Reference Ratios for Pharmacokinetic Parameters for  
Individual Subjects

Subject	Sequence	Ratio		
		AUC <sub>0-t</sub>	AUC <sub>0-inf</sub>	C <sub>max</sub>
1	2			
2	2			
3	1			
4	2			
5	2			
6	2			
7	2			
8	1			
9	2			
10	2			
11	1			
12	1			
13	2			
14	1			
15	1			
16	1			
17	1			
18	1			
19	2			
20	1			
21	1			
22	2			
23	2			
24	1			
25	1			
26	2			
27	1			
28	2			
29	2			
30	2			
31	2			
32	1			
33	1			
34	1			
36	1			
37	1			
38	2			
Mean		1.04	1.05	1.04
Range		0.72-1.69	0.71-1.68	0.73-1.97

Table 4

**AUC<sub>0-t</sub>/AUC<sub>0-inf</sub> Ratio for Individual Subjects**

Subject	AUC <sub>0-t</sub> /AUC <sub>0-inf</sub> Ratio	
	Test	Reference
1		
2		
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Table 5

## Comparative Quantitative Composition of Terazosin Hydrochloride Tablets

Ingredient	1 mg		2 mg		5 mg		10 mg	
	mg/tablet	%	mg/tablet	%	mg/tablet	%	mg/tablet	%
✓Terazosin Hydrochloride								
✓Microcrystalline Cellulose, NF 18								
✓Pregelatinized Starch, NF 18								
✓Lactose Monohydrate, NF 18								
✓Magnesium Stearate, NF 18								
Yellow 10 Iron Oxide								
Red 30 Iron Oxide								
✓D&C Red #27, Aluminum Lake								
Total Tablet Weight	140	100%	140	100%	140	100%	140	100%

1.094 mg Terazosin Hydrochloride equals 1 mg Terazosin  
2.188 mg Terazosin Hydrochloride equals 2 mg Terazosin  
5.470 mg Terazosin Hydrochloride equals 5 mg Terazosin  
10.94 mg Terazosin Hydrochloride equals 10 mg Terazosin

**Table 6. In Vitro Dissolution Testing**

Drug (Generic Name): Terazosin Hydrochloride Tablets  
 Dose Strength: 1 mg, 2 mg, 5 mg, 10 mg  
 ANDA No.: 74-657  
 Firm: Invamed Inc.  
 Submission Date: April 8, 1995  
 File Name: 74657SDW.495

**I. Conditions for Dissolution Testing:**

USP XXII Basket: Paddle: X RPM: 50  
 No. Units Tested: 12  
 Medium: Deionized deaerated water Volume: 900 mL  
 Specifications: NLT % (Q) in 30 minutes  
 Reference Drug: Hytrin Tablets (Abbott)  
 Assay Methodology:

**II. Results of In Vitro Dissolution Testing:**

Sampling Times (Minutes)	Test Product Lot # D941203 Strength(mg) 1			Reference Product Lot # 91-101-AA-21 Strength(mg) 1		
	Mean %	Range	%CV	Mean %	Range	%CV
10	96.8		2.6	89.9		9.3
20	98.8		2.4	95.8		3.2
30	99.5		2.2	96.6		2.8
40	99.3		1.6	97.2		2.4
Sampling Times (Minutes)	Test Product Lot # D941204 Strength(mg) 2			Reference Product Lot # 92-231-AA-21 Strength(mg) 2		
	Mean %	Range	%CV	Mean %	Range	%CV
10	96.2		3.5	94.0		5.6
20	97.7		2.3	99.5		3.1
30	98.7		1.6	100.8		2.4
40	98.4		2.0	101.6		2.0

Table 6. continued						
Sampling Times (Minutes)	Test Product Lot # D941201 Strength(mg) 5			Reference Product Lot # 92-198-AA-21 Strength(mg) 5		
	Mean %	Range	%CV	Mean %	Range	%CV
10	95.2		2.0	89.2		7.6
20	97.5		1.3	97.5		1.5
30	97.8		1.5	98.5		1.7
40	98.4		1.5	98.9		1.2
Sampling Times (Minutes)	Test Product Lot # D941205 Strength(mg) 10			Reference Product Lot # 90-047-AA-21 Strength(mg) 10		
	Mean %	Range	%CV	Mean %	Range	%CV
10	94.0		1.6	94.2		2.5
20	95.1		1.2	97.5		1.6
30	95.7		1.4	99.0		1.2
40	95.7		1.4	99.4		1.7

TERAZOSIN HCl (5 MG) TABLET STUDY  
INVAMED B-02214  
SECTION 4

Figure 4.5.1 Linear Plot of Mean Plasma Terazosin Concentrations vs Time

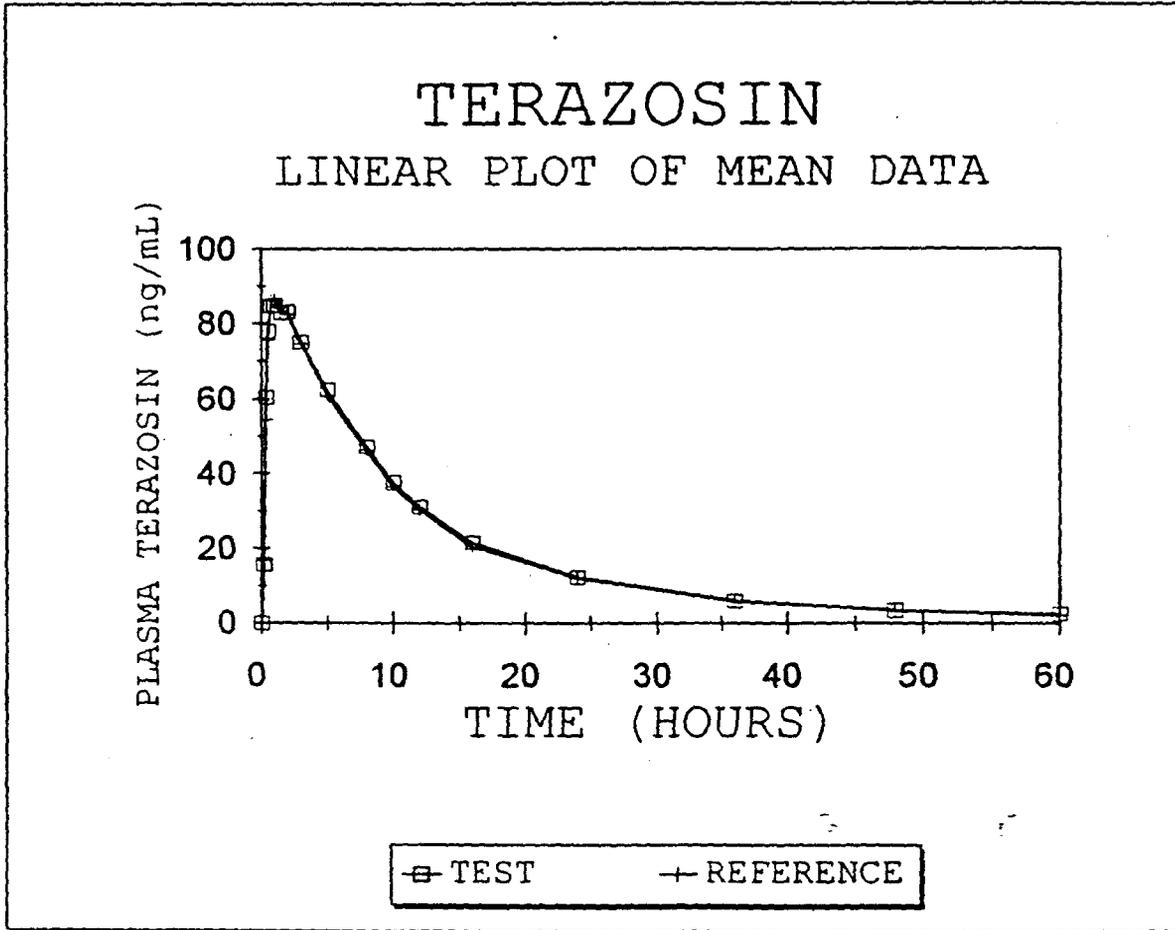


FIG 1

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Figure 4.5.2 Semi-logarithmic Plot of Mean Plasma Terazosin Concentrations vs Time

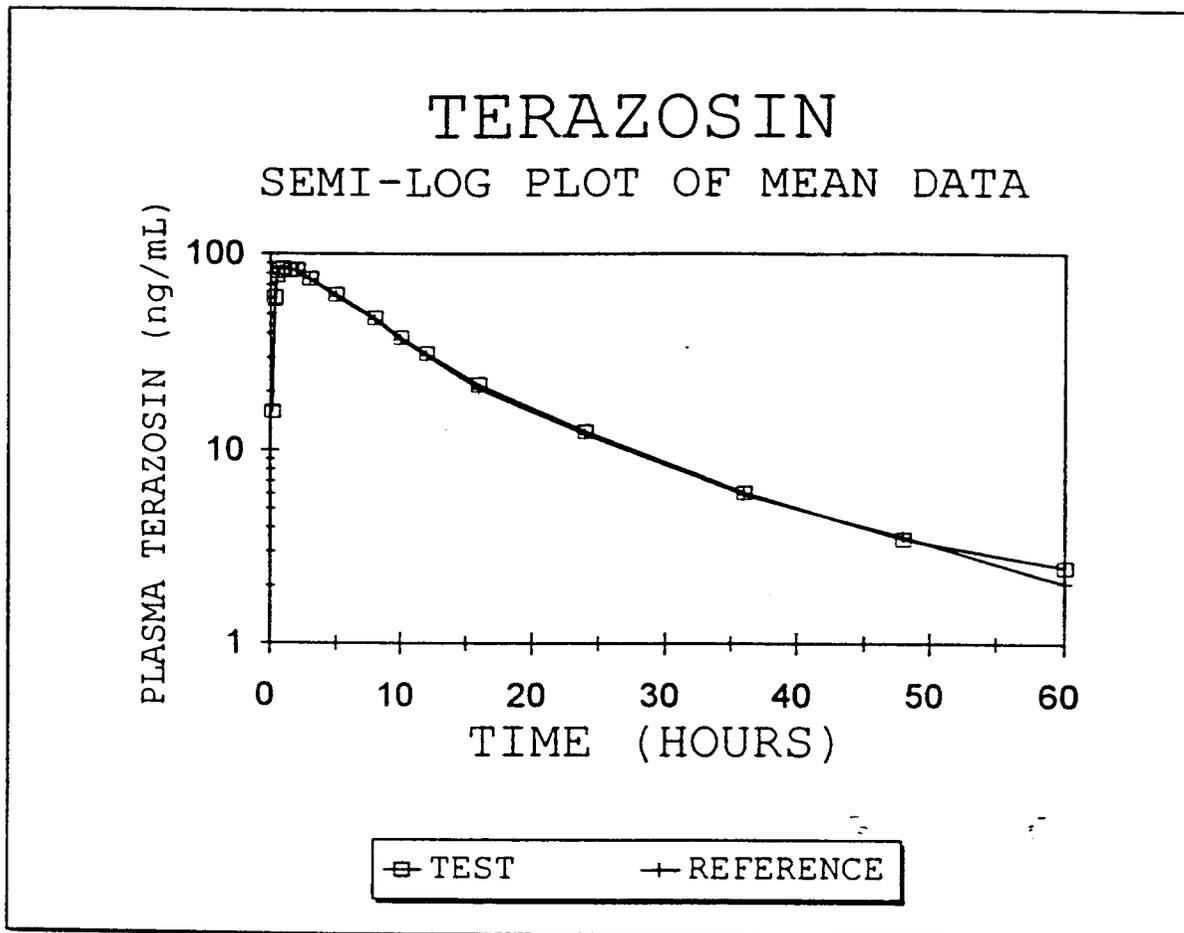
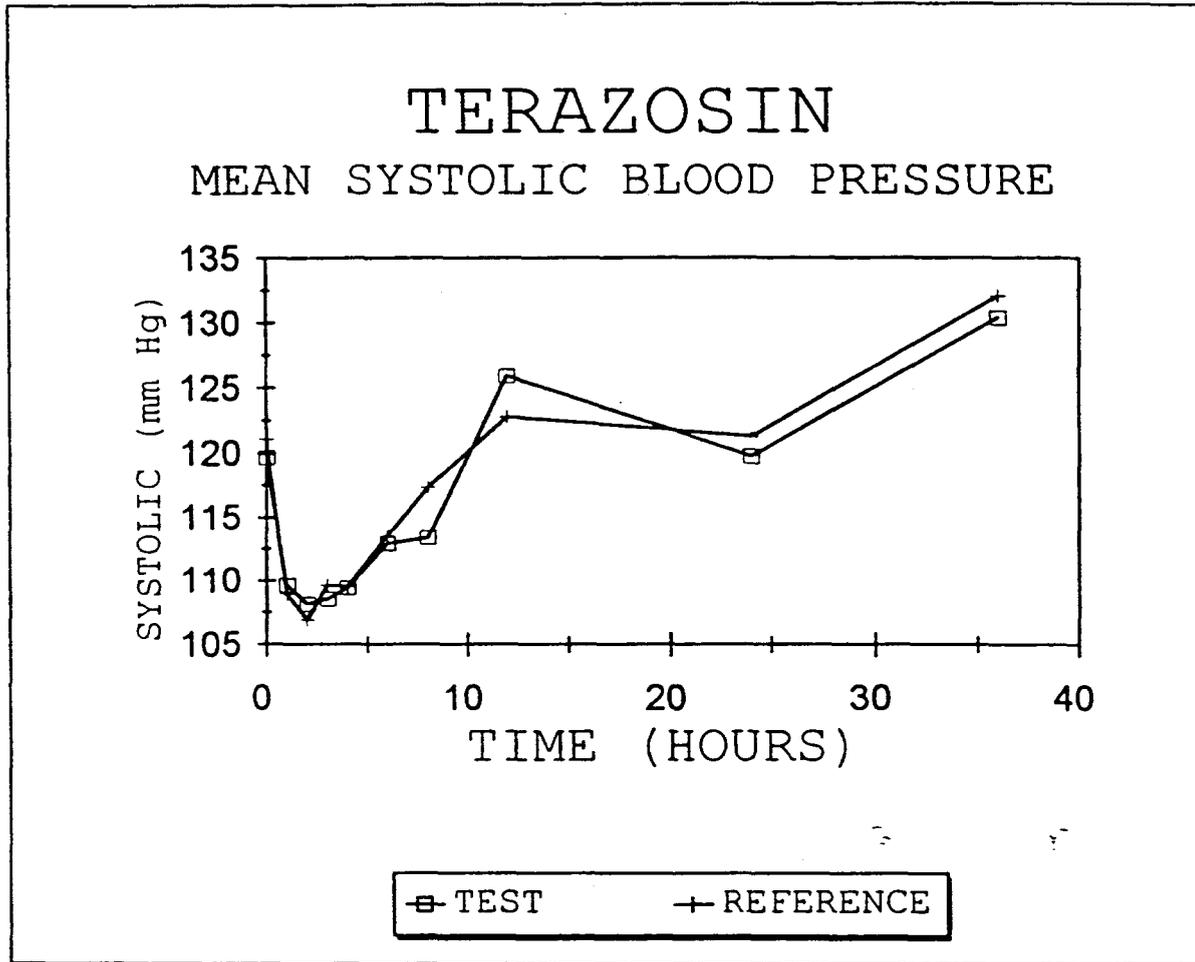


FIG. 2

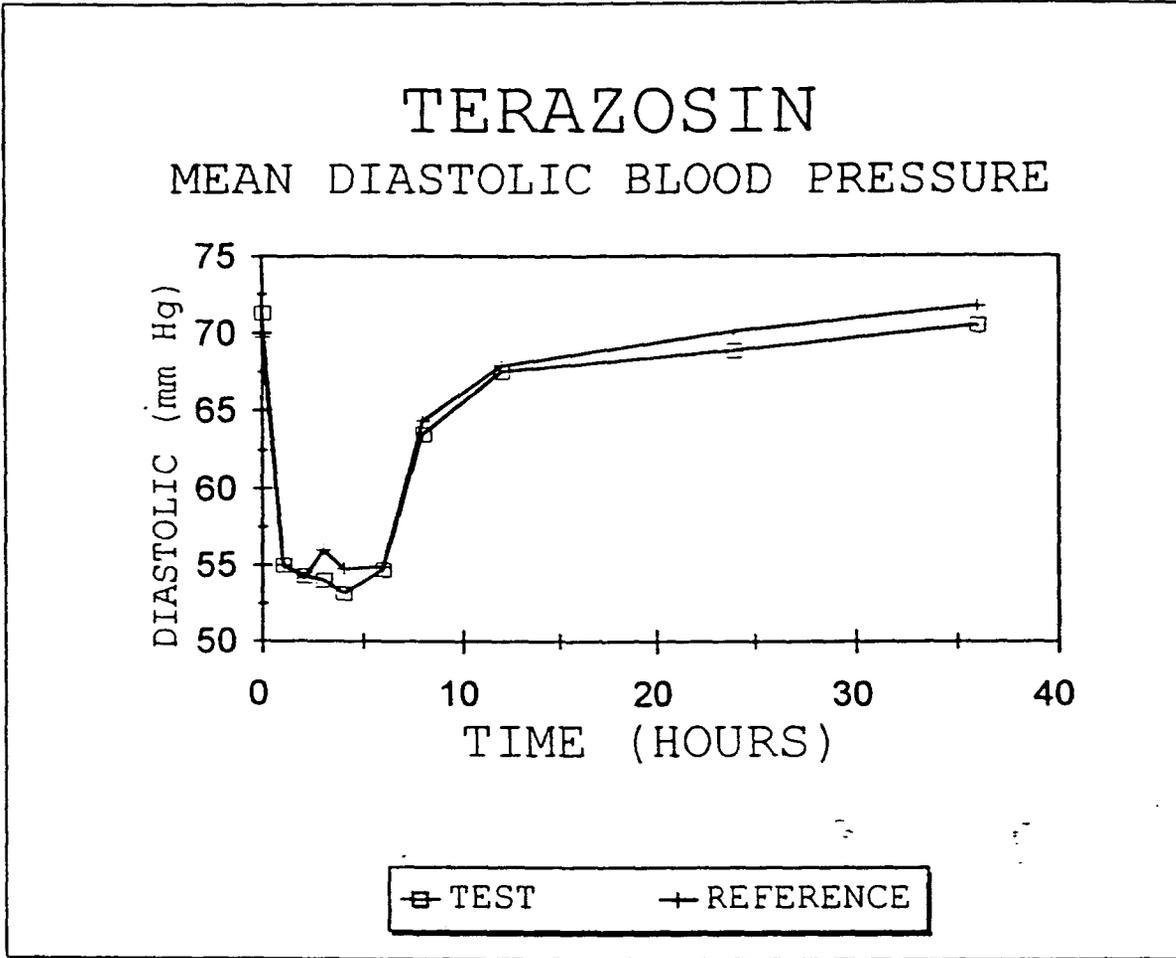
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Figure 4.5.3 Linear Plot of Mean Systolic Blood Pressure vs Time.



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Figure 4.5.4 Linear Plot of Mean Diastolic Blood Pressure vs Time



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Figure 4.5.5 Linear Plot of Mean Heart Rate vs Time

