AM-230-03-0600

ANALYTICAL METHOD PROCEDURES

Total Number of Pages: 6

DISSOLUTION TEST
10 and 20mg Fluoxetine Capsules
By - HPLC determination

DISSOLUTION ASSAY

Release & Stability Studies

Ed. 04.

General Index:

Method is suitable for:

☒ In-process control
☑ Product Release
☑ Stability indicating analysis (Suitability - US/EU Product)

CAUTION

FLUOXETINE HYDROCHLORIDE IS A HAZARDOUS CHEMICAL AND SHOULD BE HANDLED ONLY UNDER CONDITIONS SUITABLE FOR HAZARDOUS WORK.

IT IS HIGHLY PRESSURE SENSITIVE AND ADEQUATE PRECAUTIONS SHOULD BE TAKEN TO AVOID ANY MECHANICAL FORCE (SUCH AS GRINDING, CRUSHING, ETC.) ON THE POWDER !

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FOR GENERAL PROCEDURE FOR ALIGNMENT OF EQUIPMENT & WITHDRAWAL OF SAMPLES REFER TO BP 2000 & RELEVANT SOP

DISSOLUTION TEST PROCEDURE

Equipment : 6 vessels for apparatus II (paddle)

Medium : : Water

Volume : : 900mL

Stirring rate : 50rpm

Temperature : 37°C ± 0.5°C

Note: Wrap each capsule in a wire helix to prevent the capsules from floating ! Make sure that each wire helix is not too tight.

Place one weighed capsule in each of the 6 vessels and immediately operate the apparatus.

Unless otherwise specified a 5mL sample is withdrawn from each vessel after 30 minutes and immediately filtered through filter tips (filter reagent CP07H245, cat. no. 178-3985-01 Technicon).

CHROMATOGRAPHIC SYSTEM

Column	:	Shandon Hypersil BDS C-8, 5µ, 150 x 4.6mm
Mobile phase	:	Solution A: Solution B (55:45)
Solution A	:	Triethylamine buffer*: acetonitrile: tetrahydrofuran (75:15:10)
Solution B	:	Triethylamine buffer*: acetonitrile: tetrahydrofuran (65:20:15)
Column Temperature	:	30°C
Flow rate	:	1.5mL/min
Injection volume	:	50µL
Detector	:	UV at 227nm, 10mm flow cell
Diluent A	:	Water:acetonitrile (70:30)
Diluent B	:	Water:acetonitrile (45:55
Diluent C	:	Water:acetonitrile (65:35)

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NOTE:

1. Wash the autosampler Injector with degassed solution of methanol.

2. Overnight conditioning with acetonitrile: water (70:30) for a *new* column is recommended.

3. The injection method is cut volume with a 100µL of lead volume and 80µL of wear volume (use 200µL loop)

4. Mobile phase proportions and flow rate may be varied in order to achieve the required system suitability

*** Triethylamine buffer**

Place 10mL triethylamine in a 1000mL volumetric flask. Add 900mL water. Adjust to pH 5.5 with concentrated Phosphoric Acid and make up to volume with water. Filter through 0.45µ membrane.

STANDARD PREPARATION

Standard stock Solution

Accurately weigh about 11mg of Fluoxetine HCl A.S. (equivalent to about 10mg fluoxetine) into a 100mL volumetric flask, dissolve and dilute to volume with water.

Working standard solution

Dilute 5mL of standard stock solution into 100mL volumetric flask with diluent A.

SYSTEM SUITABILITY SOLUTION

To a 20mL volumetric flask weigh about 1mg of Meta Fluoxetine Hydrochloride [N-methyl-γ-[3-(trifluoromethyl)phenoxy]benzenepropanamine hydrochloride], dissolve and dilute with water.

Transfer 5.0mL from this solution to a 50mL volumetric flask, add 2.5mL standard stock solution and adjust to volume with diluent A.

Note: Standard stock solution is usable for one week, if refrigerated.

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SYSTEM SUITABILITY TEST

Inject the System Suitability solution.

The tailing for Fluoxetine peak should be not more than 2.0. The resolution between the Fluoxetine and the Meta Fluoxetine peaks should be not less than 2.0.

Typical retention time of Fluoxetine peak is about 9.5 - 10 minutes.

Note: If the resolution is less than 2.0, increase the percent of solution A vs. percent of solution B (about 10%)

SAMPLE PREPARATION

Dilute the filtered sample solutions manually as follows:

Dose (mg/capsule)	Diluent	Dilution factor
10	B	2
20	C	4

Note: Sample solutions were considered stable for 3 days, if refrigerated.

Diluted sample solutions were considered stable in refrigerator or at room temperature conditions for about 48 hours.

PROCEDURE

Inject the dissolution medium twice.

Inject diluent A once.

Inject the standard working solution 5 times. The relative standard deviation for Fluoxetine peak area in the 5 replicate injections should be less than 2.0%.

The difference between the two standards should be less than 3.0%.

Inject the samples. Continue the chromatogram up to 1.6 times the retention time of Fluoxetine and determine the peak areas of Fluoxetine using a suitable integrator.

Note: A peak related to capsule shell with placebo might appear at RRT 1.3 (about 12.5 minutes)

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CALCULATIONS

CALCULATE using a validated in-house computer program for “Assay Calculations" or alternatively use the following equation:

$$\frac{\text{Smp. peak area x W. Std conc * * * (mg / mL) x 0.8944 * xDil. factor * *}}{\text{Std peak area x Dose (mg / cap)}} \times 900 \times 100 = \text{\% fluoxetine dissolved of labeled amount}$$

* Correction factor: $0.8944 = \frac{\text{MW Fluoxetine}}{\text{MW Fluoxetine HCl}} = \frac{309.29}{345.79}$

** Dil. Factor = dilution factor for 10mg/cap = 2, for 20mg/cap = 4

*** Take into account the % water and the % assay of Fluoxetine hydrochloride standard.

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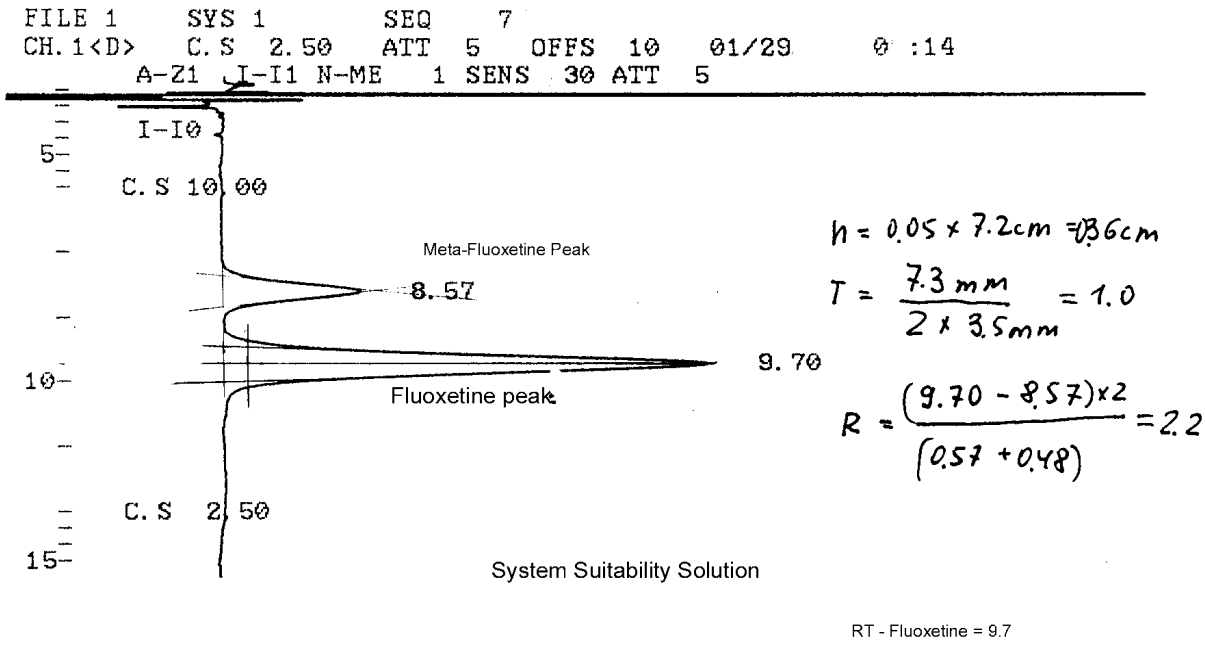
SYSTEM SUITABILITY CHROMATOGRAM



FLUOXETINE CAPS.
Hypersil BDS C-8, 5u, 4.6*150mm
DISSOLUTION-
55 A:45 B
Flow=1.5ml/min, Press=147

D-7500 INTEGRATOR REPORT

ANALYZED: 01/29 0 :14 REPORTED:
SYSTEM : 1 SAMPLE : Vial= 1 , Vol= 50.0 ul
METHOD : FLUOXETINE OPERATOR: G
CHANNEL : 1 <DIGITAL> SEQ : 7

FILE : 1 (01/23 6:28) MODULE T-PROG : DETECTOR= 1
CALC-METHOD: AR/HI% <AREA> COMPONENT TBL : 0

NO.	RT	AREA	CONC	HEIGHT	BC
1	8.57	77162	19.469	4319	BB
2	9.70	319176	80.531	15140	BB
TOTAL		396338	100.000	19459	
PEAK REJ :		0			

(RAW) STORAGE NO. 22 WRITTEN

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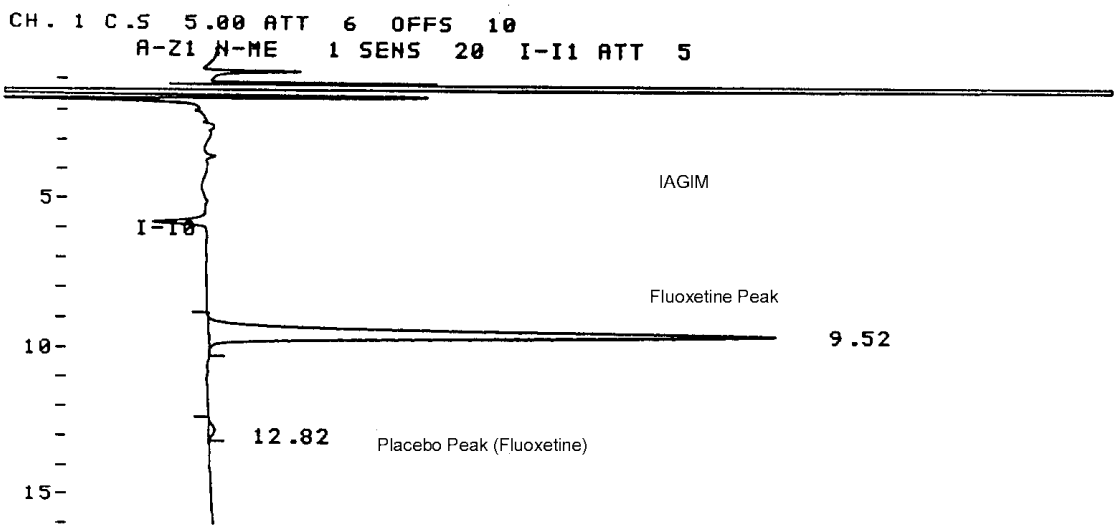
TYPICAL CHROMATOGRAM

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FLUOXETINE CAPS
VALIDATION
METHOD REPEATABILITY
K-21     20mg CAPS  DISSOLUTION
SAM-4  30min P-133atm MERCK 15

D-2500

METHOD: ADI            TAG:     14  CH: 1  VIAL:      9

FILE: 0  CALC-METHOD: AREA%     TABLE:    0  CONC: AREA

  NO.      RT         AREA       CONC     HEIGHT  BC
    1    9.52       316229     98.544      18241  BB
    2   12.82         4673      1.456        229  BB
TOTAL
                    320902    100.000      18470
PEAK REJ :             0
INJ-VOL  :      50.00

RAW DATA STORAGE NO.         14

DRIVE NO. 0 (RAW     )   STORAGE NO. 14   WRITTEN
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REFERENCE HISTORY:
IAG-SI-2337X-03/699 FLUOXETINE CAPSULES EU Containing: Fluoxetine HCl equivalent to 10mg or 20mg Fluoxetine per capsule DISSOLUTION TEST

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