



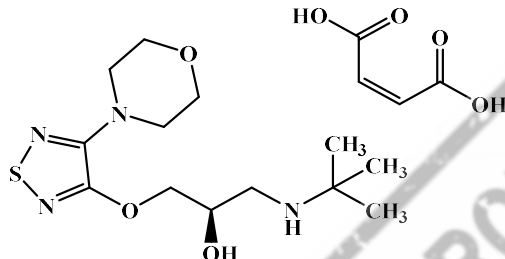
**GlobeSynth
Pharma Tech**

GlobeSynth Pharma Tech

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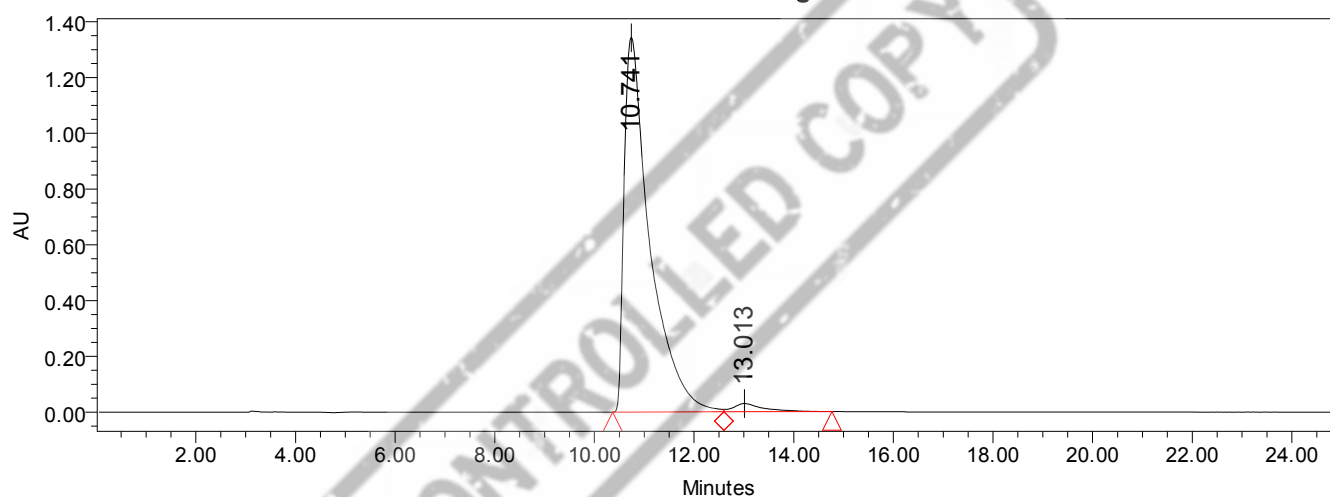
Certificate Of Analysis

Catalogue Name		Timolol USP Related Compound A ; (R)-Timolol Maleate					
Product Category		Timolol Maleate Ph. Eur. Impurity A / Timolol EP Impurity A					
Sub-Category		Chiral Standards, Pharmaceutical Standards, Intermediates, Fine Chemicals					
Chemical Name / Synonyms		(+) -Timolol Maleate; d-Timolol Maleate ; (R)-(+)-Timolol Maleate ; (2R)-1-[(1,1-Dimethyl ethyl)amino]-3-[[4-(morpholin-4-yl)-1,2,5-thiadiazol-3-yl]oxy]propan-2-ol Maleate ; (R)-1-(tert- Butylamino)-3-(4-morpholino-1,2,5-thiadiazol-3-yloxy)propan-2-ol, (Z)-2-butenedioate ; (R)-1-(tert- Butylamino)-3-(4-morpholino-1,2,5-thiadiazol-3-yloxy) propan-2-ol maleate ; 26839-76-9 (Free Base)					
Catalog Number		GS.38.TIO.01	Manufacturing Date		25.11.2024		
Batch Number		GS-TIO-02501M1	Date of Analysis (HPLC)		28.01.2025		
CAS Number		26839-77-0	Retest Date (HPLC)		28.01.2028		
Chemical Structure :			Mol. Weight		316.4 : 116.1		
			Mol. Formula		C13H24N4O3S : C4H4O4		
			Description		White to Off-White Solid		
			Solubility		DMSO, Water & Methanol		
			Storage conditions : Store in a tight container at room temperature . For long term storage keep in between 2-8°C temperature (Refrigerator).				
Applications:		(2RS)-3-[(1,1-Dimethylethyl)amino]-2-[[[4-(morpholin-4-yl)-1,2,5-thiadiazol-3-yl]oxy]propan-1-ol Maleate, it is one of the impurities of Timolol, which is used in the treatment of hypertension, arrhythmias, angina pectoris, and for the secondary prevention of myocardial infarctions.					
I. Identity							
S.No.	Test	Specification		Results			
1	HPLC Purity(%)	NLT 95.0%		97.46% (Chromatogram Attached) as per Ph. Eur. Method (0572)			
2	IR	To conform to structure		Conforms (Spectra Attached)			
3	HNMR	To conform to structure		Conforms (Spectra Attached)			
4	Mass/LC MS	To conform to structure		Conforms (Spectra Attached)			
5	TGA	NMT 2.0%		0.248%			
PO Reference No.:		2024MC -project 8100		Pack Size: Place :	120 GM Salem, TN	Vial Nos :	80 GM * 1 40 gm * 1
Shipment Condition & Date : Should be shipped under Amber vial, between 15° and 30° Centigrade & N/A				This certificate is valid for Three year from the date of shipment provided the substance is stored under the recommended conditions. (Note: Use for research and Analytical purpose only)			
Prepared By		Checked By		Approved By			
Mr. R. Mani (Sr. Executive)		Mr. Nand Lal (Jr. Scientist)		Mr. Bharat Patel (QC Head)			

SAMPLE INFORMATION

Sample Name:	GS-TIO-02501M1	Acquired By:	System
Sample Type:	Unknown	Sample Set Name:	28012025_HPLC_01
Vial:	58	Acq. Method Set:	ARAL_NP_HPLC_DEV
Injection #:	1	Processing Method:	HPLC_DEV
Injection Volume:	15.00 ul	Channel Name:	295.0nm
Run Time:	25.0 Minutes	Proc. Chnl. Descr.:	PDA 295.0 nm
Date Acquired:	1/28/2025 3:49:33 PM IST		
Date Processed:	1/28/2025 4:23:22 PM IST		

Auto-Scaled Chromatogram

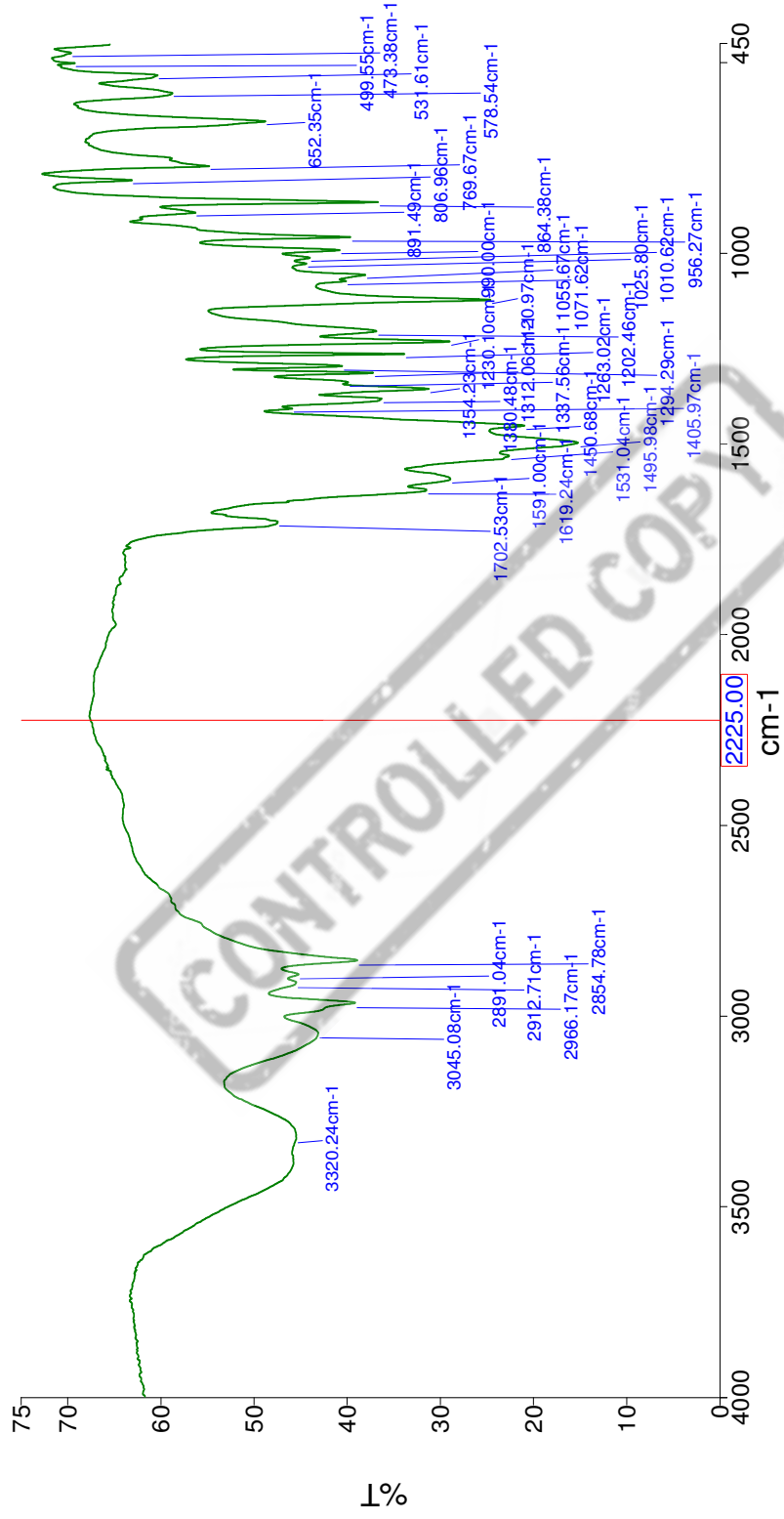


Peak Results

	Name	RT	Area	Height	% Area
1		10.741	48193452	1344544	97.46
2		13.013	1254036	29635	2.54

PEService
Monday, February 10, 2025 3:33 PM

Analyst
Date



GS-TIO-02501M1_001 Date Monday, February 10 2025

Source Spectra Results	
Spectrum Name	Number Of Peaks
GS-TIO-02501M1_001	37

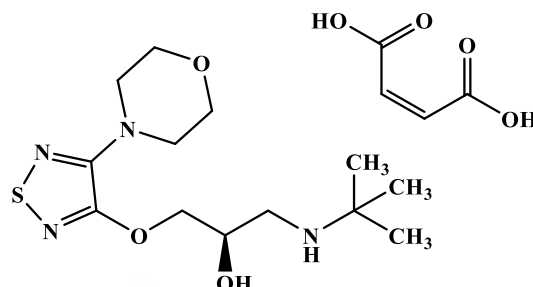
List of Peak Area/Height	
Peak Number	X (cm-1) (cm-1)
1	3320.24
2	3045.08
3	2966.17
4	2912.71
5	2891.04
6	2854.78
7	1702.53
8	1619.24
9	1591.00
10	1531.04
11	1495.98
12	1450.68
13	1405.97
14	1380.48
15	1354.23
16	1337.56
17	1312.06
18	1294.29
19	1263.02
20	1230.10
21	1202.46
22	1120.97
23	1071.62
24	1055.67
25	1025.80
26	1010.62
27	990.00
28	956.27
29	891.49
30	864.38
31	806.96
32	769.67

List of Peak Area/Height	
Peak Number	X (cm-1) (cm-1)
33	652.35
34	578.54
35	531.61
36	499.55
37	473.38

CONTROLLED COPY

IR INTERPRETATION OF TIMOLOL MALEATE Ph. Eur. IMPURITY A

Catalog Number : GS.38.TIO.01
CAS Number : 26839-77-0
Batch Number : GS-TIO-02501M1
Mol.Wt : 316.4 : 116.1
Mol. For : C₁₃H₂₄N₄O₃S : C₄H₄O₄



Timolol Maleate Ph. Eur. Impurity A ; Timolol EP Impurity A ; Timolol USP Related Compound A ; (+)-Timolol Maleate; d-Timolol Maleate ; (R)-(+)-Timolol Maleate ; (2R)-1-[(1,1-Dimethyl ethyl)amino]-3-[[4-(morpholin-4-yl)-1,2,5-thiadiazol-3-yl]oxy]propan-2-ol Maleate ; (R)-1-(tert-Butylamino)-3-(4-morpholino-1,2,5-thiadiazol-3-yloxy)propan-2-ol, (Z)-2-butenedioate ; (R)-1-(tert-Butylamino)-3-(4-morpholino-1,2,5-thiadiazol-3-yloxy)propan-2-ol maleate ; **26839-76-9** (Free Base); **26839-77-0** ; Chiral Standards, Pharmaceutical Standards, Intermediates, Fine Chemicals

S.No	Wave number (cm ⁻¹)	Group	Stretch
1	1120.97	Ether Linkage	C-O-C
2	1495.98	Aromatic Ring System	C=C-C
3	2966.14	Alkyl Group	H-C-H
4	3320.24	Hydroxy Group	O-H
5	3045.08	Carboxylic Acid from Maleic Acid	-COOH

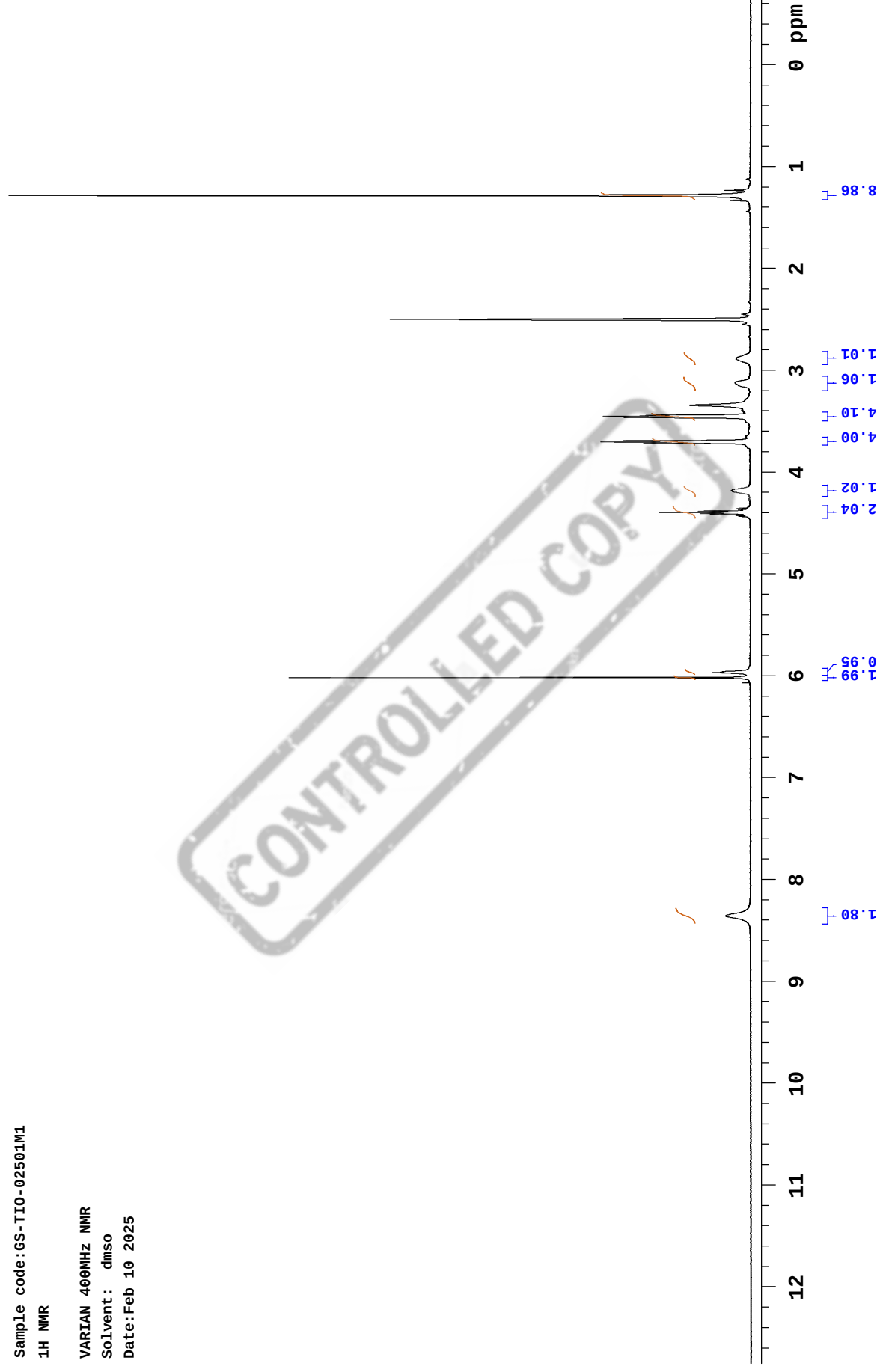
The signals of the IR spectrum and their interpretation are consistent with the structural formula.

Checked by

Approved by

Sample code:GS-TIO-02501M1
1H NMR

VARIAN 400MHz NMR
Solvent: dmso
Date:Feb 10 2025



Sample code:GS-TIO-02501M1
1H NMR

VARIAN 400MHz NMR
Solvent: dmso
Date:Feb 10 2025

8.358

CONTROLLED COPY

9.2 9.0 8.8 8.6 8.4 8.2 8.0 7.8 7.6 7.4 7.2 7.0 ppm

1.80

Plotname: GS-TIO-02501M1_PROTON_01_plot02

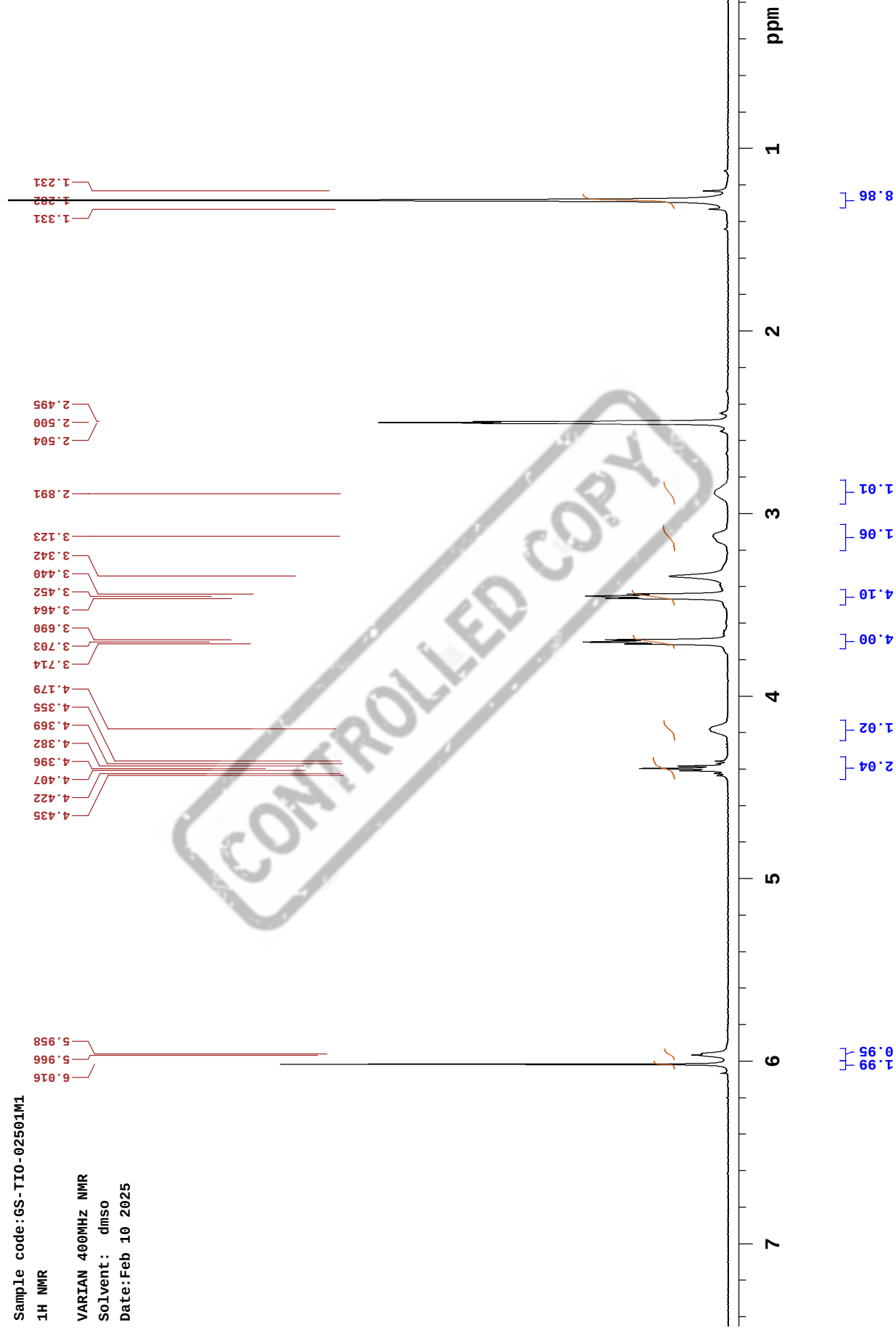
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¹H NMR

VARIAN 400MHz NMR

Solvent: dmso

Date:Feb 10 2025



Plotname: GS-TIO-02501M1_PROTON_01_plot03

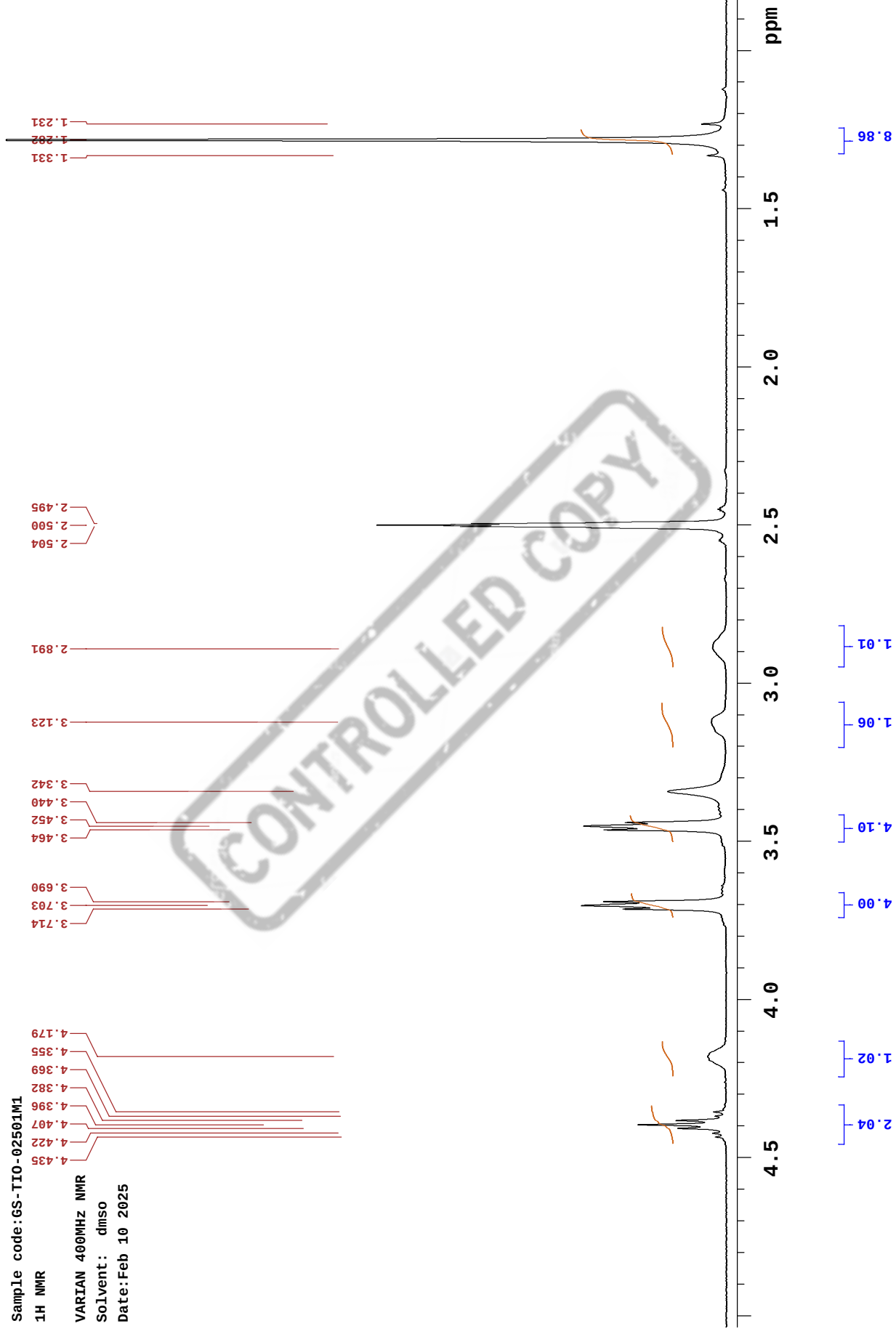
Sample code:GS-TIO-02501M1

¹H NMR

VARIAN 400MHz NMR

Solvent: dms

Date:Feb 10 2025



Sample code:GS-TIO-02501M1

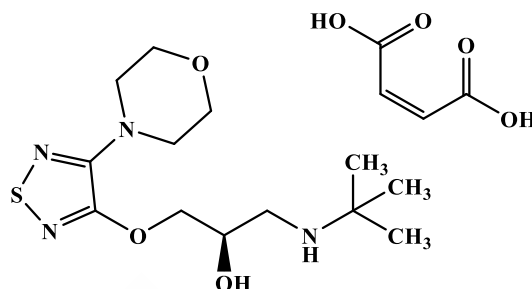
¹H NMR
VARIAN 400MHz NMR
Solvent: dmsd
Date:Feb 10 2025

INDEX	FREQUENCY	PPM	HEIGHT
1	3340.9	8.358	4.5
2	2404.6	6.016	83.8
3	2384.6	5.966	6.9
4	2381.6	5.958	5.1
5	1772.5	4.435	2.1
6	1767.7	4.422	2.6
7	1761.6	4.407	9.2
8	1757.0	4.396	16.6
9	1751.7	4.382	9.5
10	1746.2	4.369	2.2
11	1740.7	4.355	2.5
12	1670.6	4.179	3.5
13	1484.4	3.714	19.4
14	1480.1	3.703	27.2
15	1475.0	3.690	23.1
16	1384.5	3.464	23.0
17	1379.6	3.452	26.8
18	1375.0	3.440	18.9
19	1335.8	3.342	11.0
20	1248.1	3.123	2.8
21	1155.4	2.891	2.6
22	1001.0	2.504	49.8
23	999.3	2.500	65.5
24	997.3	2.495	47.8
25	532.1	1.331	3.6
26	512.4	1.282	171.7
27	492.2	1.231	4.7



HNMR INTERPRETATION OF TIMOLOL MALEATE Ph. Eur. IMPURITY A

Catalog Number : GS.38.TIO.01
CAS Number : 26839-77-0
Batch Number : GS-TIO-02501M1
Mol.Wt : 316.4 : 116.1
Mol. For : C₁₃H₂₄N₄O₃S : C₄H₄O₄



Timolol Maleate Ph. Eur. Impurity A ; Timolol EP Impurity A ; Timolol USP Related Compound A ; (+)-Timolol Maleate; d-Timolol Maleate ; (R)-(+)-Timolol Maleate ; (2R)-1-[(1,1-Dimethyl ethyl)amino]-3-[[4-(morpholin-4-yl)-1,2,5-thiadiazol-3-yl]oxy]propan-2-ol Maleate ; (R)-1-(tert-Butylamino)-3-(4-morpholino-1,2,5-thiadiazol-3-yloxy)propan-2-ol, (Z)-2-butenedioate ; (R)-1-(tert-Butylamino)-3-(4-morpholino-1,2,5-thiadiazol-3-yloxy)propan-2-ol maleate ; **26839-76-9** (Free Base); **26839-77-0** ; Chiral Standards, Pharmaceutical Standards, Intermediates, Fine Chemicals

SOLVENT USED: DMSO-D6

δ 1.231-1.331 ppm (9H, s, -3CH₃), δ 2.891 ppm (1H, s, -NCH),
δ 3.123 ppm (1H, s, -NCH), δ 3.440-3.464 ppm (4H, m, -2CH₂),
δ 3.690-3.714 ppm (4H, m, -2CH₂), δ 4.179 ppm (1H, s, -CH),
δ 4.355-4.435 ppm (2H, m, -OCH₂), δ 5.958-5.966 ppm (1H, d, -NH)
δ 6.016 ppm (2H, s, -Olefinic CH [Maleic Acid]), δ 8.358 ppm (2H, s, -COOH [Maleic Acid])

Note : Above Said Proton NMR spectrum, one OH proton was merged with DMSO-D6.

Checked by

Approved by

GS-TIO-02501M1

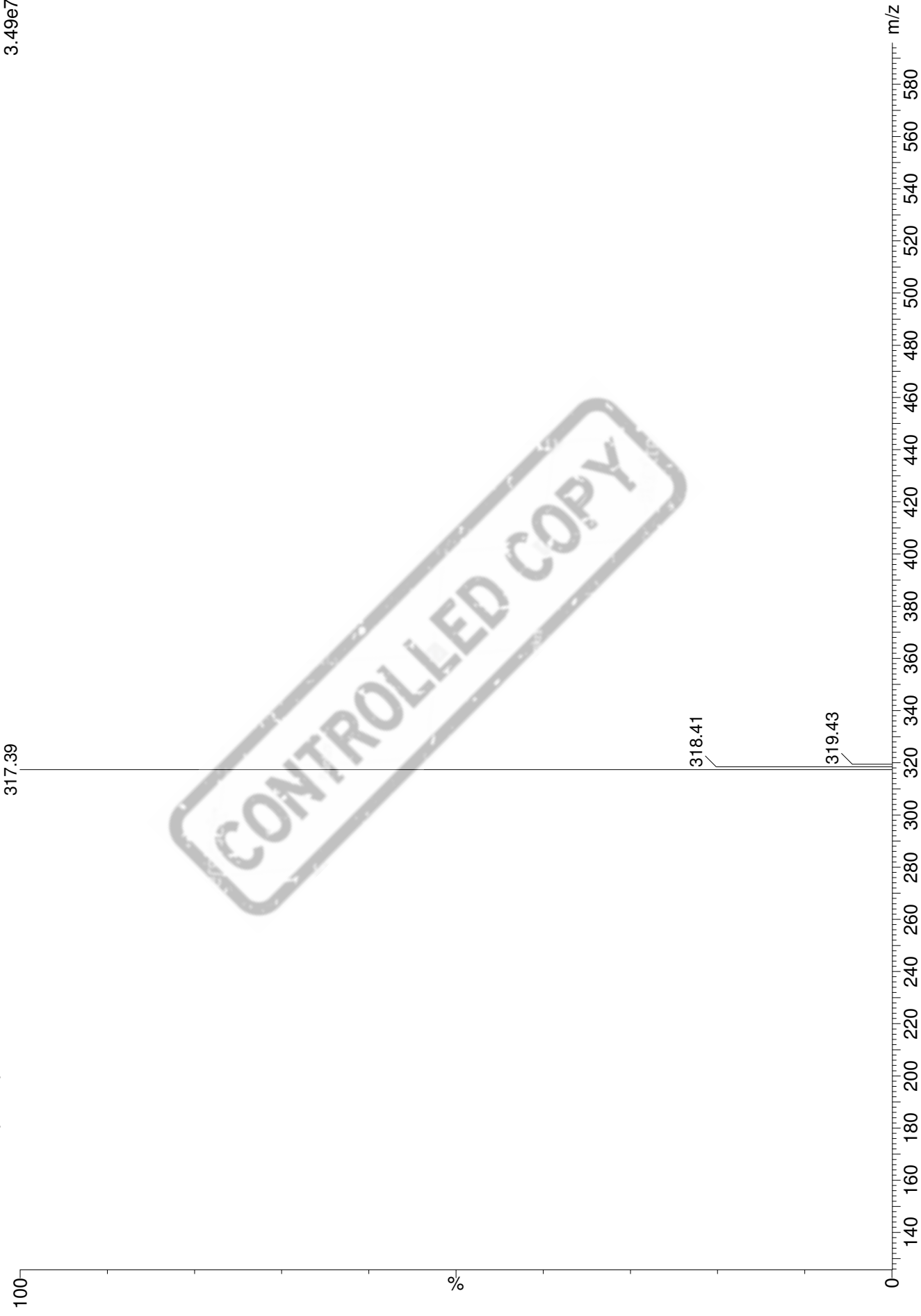
10-Feb-2025

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GS-TIO-02501M1 13 (0.321)

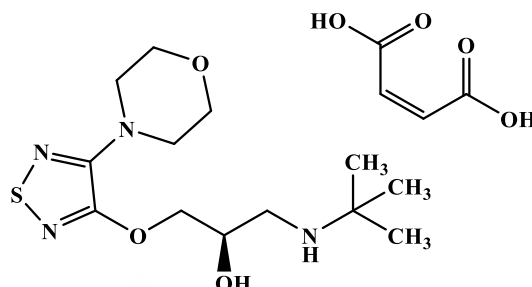
1: Scan ES+

3.49e7



MASS INTERPRETATION OF TIMOLOL MALEATE Ph. Eur. IMPURITY A

Catalog Number : GS.38.TIO.01
CAS Number : 26839-77-0
Batch Number : GS-TIO-02501M1
Mol.Wt : 316.4 : 116.1
Mol. For : C₁₃H₂₄N₄O₃S : C₄H₄O₄



Timolol Maleate Ph. Eur. Impurity A ; Timolol EP Impurity A ; Timolol USP Related Compound A ; (+)-Timolol Maleate; d-Timolol Maleate ; (R)-(+)-Timolol Maleate ; (2R)-1-[(1,1-Dimethyl ethyl)amino]-3-[[4-(morpholin-4-yl)-1,2,5-thiadiazol-3-yl]oxy]propan-2-ol Maleate ; (R)-1-(tert-Butylamino)-3-(4-morpholino-1,2,5-thiadiazol-3-yloxy)propan-2-ol, (Z)-2-butenedioate ; (R)-1-(tert-Butylamino)-3-(4-morpholino-1,2,5-thiadiazol-3-yloxy)propan-2-ol maleate ; **26839-76-9** (Free Base); **26839-77-0** ; Chiral Standards, Pharmaceutical Standards, Intermediates, Fine Chemicals

m/z	fragments
317.39 (+ve mode)	[M+1]

The molecular mass of **Timolol Maleate Ph. Eur. Impurity A** (316.4) has been confirmed with fragments appears [M+1] 317.39 in positive mode. The signals of the mass spectrum and their interpretation are consistent with the structural formula.

Checked by

Approved by

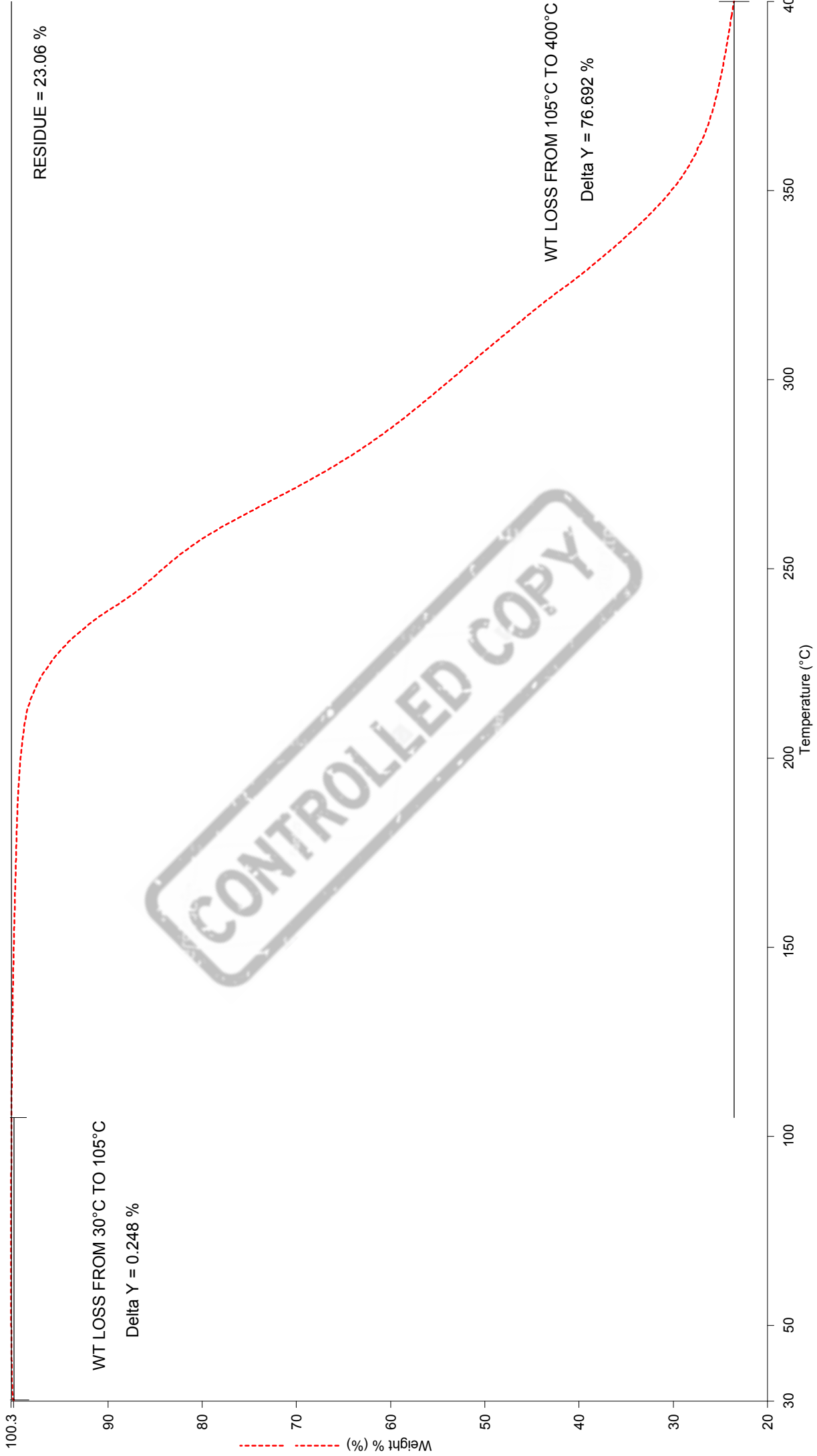
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Operator ID: GS-TIO-02501M1

Sample ID: GS-TIO-02501M1

Sample Weight: 9.540 mg

Comment: GS-TIO-02501M1



10-02-2025 14:53:30

- 1) Hold for 1.0 min at 30.00°C
- 2) Heat from 30.00°C to 415.00°C at 30.00°C/min
- 3) Hold for 1.0 min at 415.00°C

Final Results: (Timolol Maleate Ph. Eur. Impurity A)

1. Chromatographic purity : **97.46%** (HPLC (As per Ph. Eur. Method (0572)))

2. Assay : Results

Method 1: The assay “as is” is assessed by 100% method (mass balance) and is equivalent to the assay based on the not anhydrous and not dried substance respectively.

The calculation of the 100% method follows the formula:

$$(100 \% - \text{volatile contents} (\%)) * \text{Purity} (\%)/100\% = \text{Assay} (\%)$$

$$(100 - 0.248) * 97.46/100 = 99.752 * 0.9746 = 97.21 \%$$

Volatile contents are considered as absolute contributions and purity is considered as relative contribution. Inorganic residues are excluded by additional tests. **97.21 %**

Method 2: Value verifying technique - 100% method 100% method (mass balance) with chromatographic purity by HPLC **97.46 %** (As per Ph. Eur. Method (0572))

3. LOD (Loss on Drying) : Limit 2.0%; Observed Value by TGA **0.248 %**

4. Release Date : **24.02.2025**

5. Place : Salem, Tamilnadu.