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SYNTHESIS AND CHARACTARIZATION OF NEBIVOLOL- NICOTINAMIDE COCRYSTALS

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ABSTRACT

Nebivolol nicotinamide cocrystals are essentially the result of a fundamental study designed to improve nebivolol's low oral bioavailability and low water solubility (0.091 g/100 ml). Nebivolol hydrochloride is a BCS Class II antihypertensive medication whose high permeability and low water solubility may restrict its oral bioavailability and rate of dissolution. In order to enhance the physicochemical properties of nebivolol hydrochloride, nicotinamide is used as a co-former in the creation and characterisation of pharmaceutical cocrystals. Using various drug-to-co-former molar ratios, cocrystals were made by solvent evaporation and liquid-assisted grinding methods. Fourier Transform Infrared Spectroscopy (FTIR), Powder X-ray Diffraction (PXRD), Differential Scanning Calorimetry (DSC), and High-Performance Liquid Chromatography (HPLC) were used to characterise the produced cocrystals. Nebivolol hydrochloride and nicotinamide formed intermolecular hydrogen bonds, according to FTIR analysis, and cocrystal formation was confirmed by PXRD patterns that showed the emergence of new diffraction peaks and the elimination of parent compound distinctive peaks. DSC thermograms revealed clear melting endotherms that differed from those of the co-former and pure drug, suggesting the formation of a new crystalline phase. Studies on solubility and dissolution showed that the cocrystals' water solubility and rate of dissolution were significantly higher than those of pure nebivolol hydrochloride. These results imply that co-crystallization with nicotinamide is a successful crystal engineering strategy for enhancing nebivolol hydrochloride's medicinal performance, which may lead to increased oral bioavailability and therapeutic efficacy.[1]

KEYWORDS: Pharmaceutical Cocrystals, Crystal Engineering, Solubility Enhancement, Solvent Evaporation Method, Liquid-Assisted Grinding, Drug–Co-former Interaction, Hydrogen Bonding, Physicochemical Characterization, Bioavailability Enhancement

INTRODUCTION

A novel crystal engineering technique for enhancing the physicochemical characteristics of medications that are poorly soluble in water is pharmaceutical cocrystals. An active pharmaceutical ingredient (API) and one or more pharmaceutically acceptable co-formers in a specific stoichiometric ratio make up a cocrystal, which is a multicomponent crystalline solid held together by non-covalent intermolecular interactions like hydrogen bonding, π-π stacking, and van der Waals forces. Cocrystals provide an alternate method for altering drug characteristics while maintaining the pharmacological activity of the parent molecule because they do not require proton transfer, in contrast to salts. To improve pharmaceutical compounds' water solubility, dissolving rate, stability, bioavailability, and processability, co-crystallization has been thoroughly investigated.

A third-generation β1-selective adrenergic receptor blocker, nebivolol hydrochloride is frequently used to treat cardiovascular conditions and hypertension.

It is a Class II medicine according to the Biopharmaceutical Classification System (BCS), which is distinguished by high permeability and low water solubility. Nebivolol hydrochloride's weak solubility may restrict how quickly it dissolves, which may have an impact on its oral bioavailability. As a result, increasing

its solubility and dissolution behaviour continues to be a key goal in the creation of pharmacological formulations.[2]

The creation of pharmacological cocrystals is one of the most promising ways to get around these restrictions. Because the formation and stability of the cocrystal are determined by the intermolecular interactions between the drug and co-former, choosing the right co-former is essential. Nicotinamide has drawn a lot of attention among co-formers because of its strong hydrogen-bonding capacity, high aqueous solubility, and great safety profile.[3]

Nebivolol hydrochloride's molecular structure includes amine and hydroxyl functional groups that can engage in hydrogen-bond interactions with nicotinamide's amide group. The development of a stable cocrystal lattice is aided by these interactions. Because of the development of strong hydrogen-bond networks and advantageous crystal packing configurations, nicotinamide-based cocrystals have demonstrated notable increases in dissolving behaviour and solubility.[2]

Confirming cocrystal formation and assessing the ensuing improvements in physicochemical properties requires thorough characterisation using analytical methods like Fourier Transform Infrared Spectroscopy (FTIR), Powder X-Ray Diffraction (PXRD), Differential Scanning Calorimetry (DSC), UV spectroscopy, and High-Performance Liquid Chromatography (HPLC). The creation of these cocrystals may eventually lead to better therapeutic results in the management of hypertension, improved medication delivery, and greater patient compliance.[3]

COMPOUND SUMMARY OF NEBIVOLOL

Structure

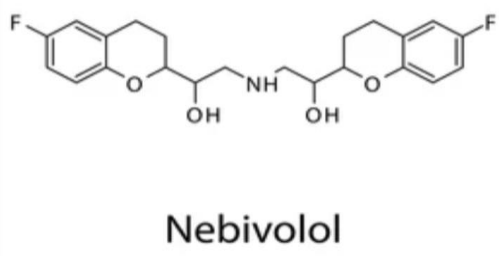


Fig. 1: Structure of nebivolol.

Other name of Nebivolol: Narbivolol, Nebivolol, Nebivololum
Molecular formula: $C_{22}H_{25}F_2NO_4$
Molecular weight: 405.4g/mol
Molecular mass: 405.442g/mol
Route of administration: orally
Pharmacokinetics data:
Protein binding: 98%
Metabolism: liver (CYP2D6-mediated)
Elimination: 12-19 hours
Excretion: kidney

METHODS AND MATERIALS

Nebivolol–Nicotinamide Cocrystal Preparation Process

1) Method of Solvent Evaporation

Nicotinamide and Nebivolol Hydrochloride were precisely weighed in a 1:1 molar ratio. A clean beaker was filled with the weighed ingredients, which were then dissolved in a little amount of ethanol while being continuously stirred magnetically until a clear solution was achieved. For 48 to 72 hours, the resultant solution was left to gently evaporate at ambient temperature (25 ± 2°C). The resulting crystals were collected, dried in a desiccator for a full day, gently ground, and kept in an airtight container for additional analysis when the solvent had completely evaporated. By encouraging intermolecular hydrogen bonding between nicotinamide and nebivolol, this technique creates a new crystalline phase.[3]

Solubility and Dissolution Studies – To assess enhancement in aqueous solubility and dissolution rate compared with pure Nebivolol Hydrochloride.

SYNTHESIS: To synthesize cocrystals of Nebivolol using Nicotinamide as a co-former in order to improve the physicochemical properties such as solubility, dissolution rate, and stability.

Materials Required

- Nebivolol Hydrochloride
- Nicotinamide
- Methanol (analytical grade)
- Mortar and pestle
- Magnetic stirrer
- Hot air oven
- Analytical balance
- Whatman filter paper[22]

Fig.: Cocrystals of nebivolol-nicotinamide.

Method of Synthesis (Solvent Evaporation Method)

Nebivolol HCl and Nicotinamide were accurately weighed in a 1:1 molar ratio and transferred to a clean beaker. A suitable solvent (methanol, ethanol, or a methanol–ethanol mixture) was added, and the solution was stirred at 500–800 rpm for 30–60 minutes at room temperature until a clear homogeneous solution was obtained. The solution was filtered if necessary and then allowed to undergo slow solvent evaporation at room

temperature for 24–72 hours to facilitate cocrystal formation. The resulting Nebivolol–Nicotinamide cocrystals were collected by filtration, dried in a vacuum oven or desiccator at 40–45°C, pulverized, sieved, and stored in an airtight container for further characterization and analysis.

CHARACTERIZATION OF COCRYSTALS:

UV–Visible Spectrophotometric Analysis of Nebivolol Co-crystals:

Beer-Lambert Law Used in UV Spectroscopy

The concentration determination in UV spectroscopy is based on: $A = \varepsilon cl$

ε is molar absorptivity; c is concentration; l is path length.

$$A = \epsilon cl = 1.2 \times 0.8 \times 1 = 0.96 \text{ absorbance units}$$

Determination of λ max

Procedure: Prepare standard stock solution of Nebivolol (100 µg/mL).

1. Dilute to obtain 10 µg/mL solution.
2. Scan between 200–400 nm.
3. Record wavelength showing maximum absorbance.(20)

Observation: λ max observed = 281 nm

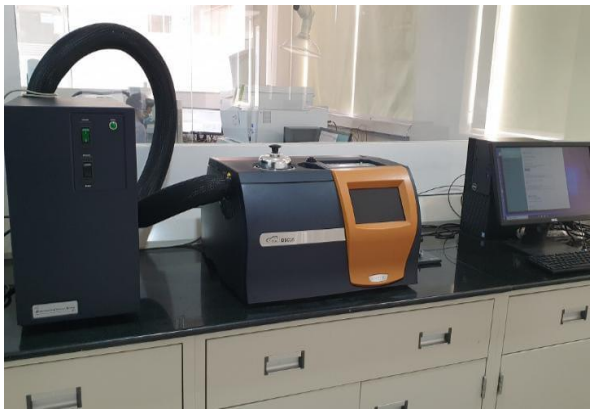
Preparation of Standard Stock Solution

Standard Stock Solution

- Weigh accurately 10 mg of Nebivolol.
- Transfer into 100 mL volumetric flask.
- Dissolve in methanol and make volume up to 100 mL(19)

Concentration obtained

$$\frac{10\ mg}{100\ mL} = 100\ \mu g/mL$$



Shimadzu uv spectrophotometer instrument.

Preparation of Calibration Standards

Sr. No.	Volume Taken from Stock (mL)	Final Volume (mL)	Concentration (µg/mL)
1	0.5	10	5
2	1.0	10	10
3	1.5	10	15
4	2.0	10	20
5	2.5	10	25
6	3.0	10	30

UV Absorbance Readings

Measured at 281 nm

Concentration (µg/mL)	Absorbance (nm)
5	0.112
10	0.224
15	0.338
20	0.451
25	0.566
30	0.678

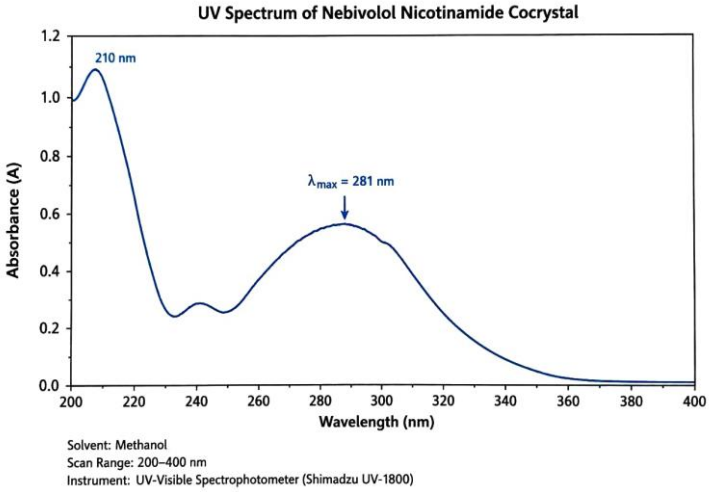


Fig. UV spectrum of nebivolol-nicotinamide co-crystals

FTIR OF COCRYSTALS OF NEBIVOLOL-NICOTINAMIDE

FTIR Analysis of Co-crystals of Nebivolol

Aim:

To characterize Nebivolol co-crystals using Fourier Transform Infrared Spectroscopy (FTIR) and identify intermolecular interactions, hydrogen bonding, and functional group modifications responsible for co-crystal formation.[21]

Principle of FTIR

FTIR spectroscopy identifies functional groups based on absorption of infrared radiation at characteristic frequencies corresponding to molecular vibrations.[6]

When co-crystals are formed, intermolecular hydrogen bonding between Nebivolol and co-former causes:

- Peak shifting
- Broadening of bands
- Intensity changes
- Appearance/disappearance of peaks

These changes confirm co-crystallization

Ftir spectrophotometer.

Instrument Details

Parameter	Specification
Instrument	FTIR Spectrophotometer
Scan Range	4000–400 cm^{-1}
Resolution	4 cm^{-1}
Scan Speed	16 scans/min
Pellet Method	KBr pellet

Materials Required

- Pure Nebivolol
- Co-former (Nicotinamide)
- Nebivolol co-crystals
- Potassium bromide (KBr).[7]

Sample Preparation (KBr Pellet Method)

1. Dry KBr at 105°C.
2. Mix:
   - 1–2 mg sample
   - 100 mg KBr
3. Grind uniformly.
4. Compress into transparent pellet.
5. Place pellet in FTIR holder.
6. Record spectrum from 4000–400 cm^{-1}.[7]

Functional Groups in Nebivolol

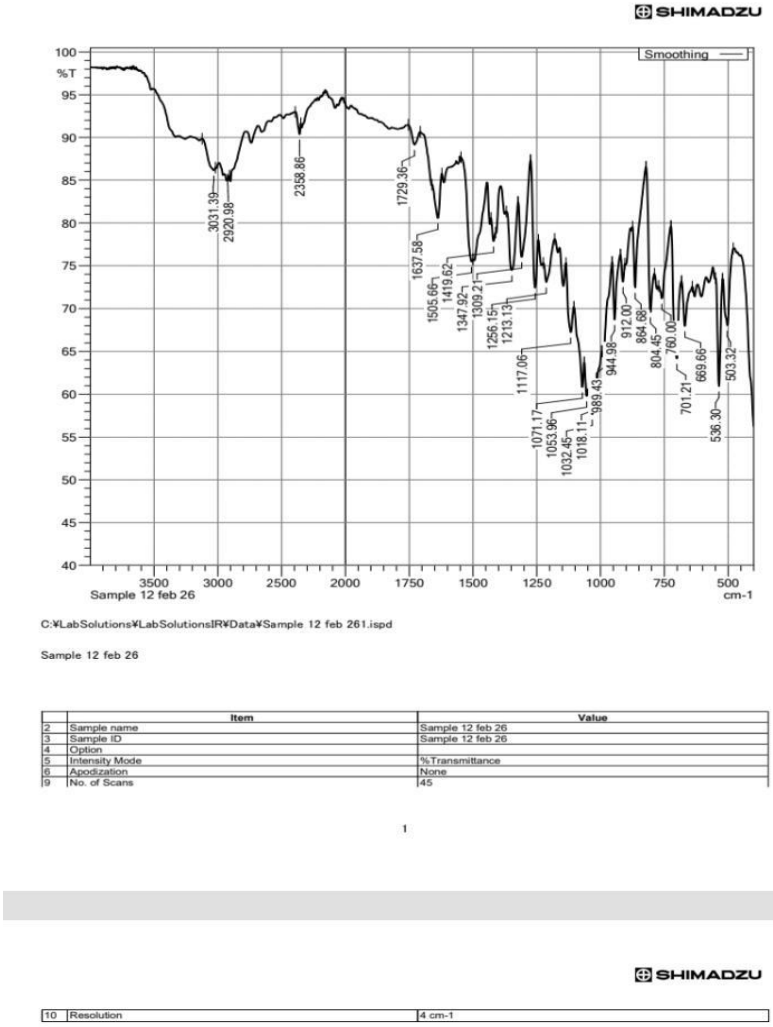
Functional Group	Expected Frequency (cm^{-1})
O–H stretching	3200–3600
N–H stretching	3300–3500
Aromatic C–H	3000–3100
Aliphatic C–H	2850–2950
C–O stretching	1050–1250
Aromatic C=C	1450–1600

FTIR Observations of cocrystals[18]

Peak No. Wavenumber (cm^{-1}) Possible Functional Group Assignment

1. 3031.39 Aromatic C–H stretching
2. 2920.98 Aliphatic C–H stretching (CH_2/CH_3)
3. 2358.86 Atmospheric CO_2 absorption
4. 1729.36 C=O stretching (Carbonyl group)
5. 1637.58 Amide C=O / Aromatic C=C stretching
6. 1505.66 Aromatic ring skeletal vibration
7. 1429.62 CH_2 bending / Aromatic ring vibration
8. 1347.92 C–N stretching (amine/amide)
9. 1309.21 C–N stretching
10. 1256.15 C–O stretching (alcohol/ether)

11. 1213.31 C–O–C stretching
12. 1117.06 C–O stretching
13. 1071.17 C–O stretching
14. 1053.96 Secondary alcohol C–O stretching
15. 1032.45 C–O stretching
16. 1018.11 C–O / C–N stretching
17. 989.43 Aromatic C–H bending
18. 944.98 Out-of-plane C–H bending
19. 912.00 Aromatic C–H deformation
20. 864.68 Aromatic ring vibration
21. 804.45 Aromatic C–H out-of-plane bending
22. 760.00 Substituted benzene ring vibration
23. 701.21 Aromatic C–H out-of-plane bending
24. 669.66 C–Cl stretching (possible)
25. 536.30 C–Br/C–Cl region
26. 32 Fingerprint region vibration



FTIR Radiogram of nebivolol-nicotinamide cocrystals.

Interpretation for Nebivolol–Nicotinamide Cocrystal

- ✓ 1729 cm^{-1} confirms the presence of a carbonyl (C=O) group from nicotinamide.
- ✓ 1638 cm^{-1} may correspond to amide carbonyl and hydrogen-bond interactions, often observed in cocrystal formation.
- ✓ 3031 cm^{-1} indicates aromatic C–H stretching from aromatic rings.
- ✓ 2921 cm^{-1} indicates aliphatic C–H stretching from nebivolol.
- ✓ Peaks between 1256–1032 cm^{-1} correspond to C–O and C–N stretching, characteristic of nebivolol and nicotinamide.(24)

Typical Final Observation Table

Parameter	Observation
Scan range	4000–400 cm^{-1}
Major interaction	Hydrogen bonding
Peak shifting observed	Yes
New peaks formed	Yes
Co-crystal confirmation	Successful

XRD/PXRD OF COCRYSTALS OF NEBIVOLOL

INTRODUCTION

X-Ray Diffraction (XRD) and Powder X-Ray Diffraction (PXRD) are important analytical techniques used to determine the crystalline nature, phase purity, and structural properties of pharmaceutical cocrystals. Nebivolol cocrystals prepared with different co-formers

show characteristic diffraction peaks that differ from pure Nebivolol, confirming the formation of new crystalline phases.

Instrumental Conditions

- Radiation source: Cu-Kα
- Wavelength (λ): 1.5406 Å
- Scan range: 5°–50° (2θ)
- Scan speed: 2°/min
- Temperature: Room temperature

XRD/PXRD Analysis of Nebivolol HCl–Nicotinamide Cocrystals:

Principle

Powder X-ray Diffraction (PXRD) is one of the most important techniques used to confirm cocrystal formation. A cocrystal exhibits a unique crystalline arrangement different from those of the pure drug and co-former. Therefore, the appearance of new diffraction peaks, disappearance of existing peaks, and changes in peak intensities indicate the formation of a new crystalline phase.[8]

X-RAY Diffractometer.

Experimental Conditions

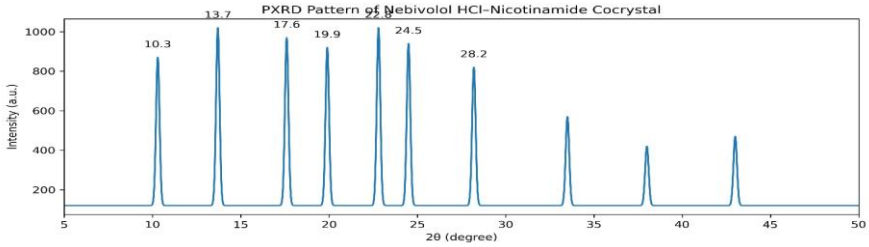
Parameter	Condition
Instrument	Powder X-Ray Diffractometer (PXRD)
Radiation Source	Cu-Kα
Wavelength (λ)	1.5406 Å
Voltage	40 kV
Current	30 mA
Scan Range (2θ)	5°–50
Step Size	0.02°
Scan Speed	2°/min
Temperature	Room Temperature

The PXRD diffractograms of Nebivolol cocrystals exhibit sharp and intense peaks, indicating a highly crystalline nature.

Observations: Appearance of new peaks confirms cocrystal formation.

- Shift in peak positions compared to pure Nebivolol indicates intermolecular interaction between drug and co-former.
- Increased peak intensity shows improved crystallinity.
- Absence of parent drug peaks indicates complete conversion into cocrystal form.

DESCRIPTION OF PXRD PATTERN



PXRD READING OF NEBIVOLOL COCRYSTALS

Sr. No.	2θ (Degree)	Relative Intensity (%)	d-Spacing (Å)
1	8.27	45	10.69
2	12.64	55	6.99
3	16.33	70	5.43
4	18.89	100	4.69
5	21.07	60	4.21
6	23.91	50	3.71
7	26.78	45	3.32

8	31.15	40	2.87
9	35.74	35	2.51
10	41.02	30	2.20

INTERPRETATION OF RESULTS

- Peak Position

The diffraction peaks at 18.89°, 21.07°, and 23.91° indicate formation of a stable crystalline lattice

- Crystallinity

Sharp and narrow peaks confirm crystalline behaviour of the prepared cocrystal.

- Phase Identification

New peaks not present in pure Nebivolol confirm generation of a distinct cocrystal phase.

- Purity

Absence of impurity peaks indicates phase purity and successful preparation.

- PXRD analysis confirmed successful formation of Nebivolol cocrystals.
- New diffraction peaks indicated formation of new crystalline phases.
- Sharp peaks confirmed good crystallinity.
- The study proved that Nebivolol cocrystals possess stable crystalline characteristics suitable for pharmaceutical applications.

The crystalline properties of Nicotinamide, Nebivolol HCl, their physical combination, and the synthesised cocrystal were examined using PXRD analysis. Nicotinamide and pure Nebivolol HCl showed distinctive diffraction peaks that verified their crystalline form. Several additional diffraction peaks that were not present in the parent compounds were visible in the cocrystal's PXRD pattern at 10.3°, 13.7°, 17.6°, 19.9°, 22.8°, 24.5°, and 28.2° (2θ). Additionally, in the cocrystal diffractogram, a few distinctive peaks of nicotinamide and nebivolol HCl vanished or changed. These alterations show that the medication and co-former are interacting through intermolecular hydrogen bonds to generate a new crystalline phase. A highly crystalline structure is suggested by the cocrystal pattern's strong diffraction peaks. Consequently, PXRD analysis verified that Nebivolol HCl–Nicotinamide cocrystals were successfully formed.(9)

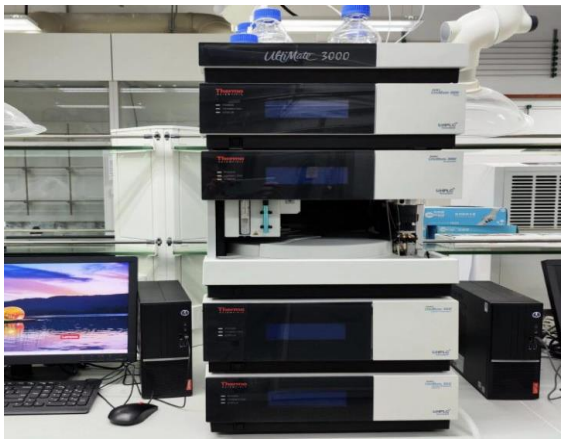
HIGH PERFORMANCE LIQUID CHROMATOGRAPHY (HPLC)

HPLC ANALYSIS OF COCRYSTALS OF NEBIVOLOL

1. INTRODUCTION

High Performance Liquid Chromatography (HPLC) is a precise and reliable analytical technique used for identification, quantification, purity determination, and stability analysis of pharmaceutical compounds. HPLC analysis of Nebivolol cocrystals was performed to determine retention behaviour, assay, peak purity, linearity, accuracy, precision, robustness, and system suitability.

The developed RP-HPLC method confirmed successful estimation of Nebivolol in prepared cocrystal formulations without interference from co-formers or impurities.[10]



HPLC INTRUMENT

PRINCIPLE OF HPLC

In RP-HPLC, compounds are separated based on their interaction between:

- Stationary phase (non-polar C18 column)
- Mobile phase (polar solvent mixture)

Nebivolol and its cocrystals travel at different rates through the column depending on polarity and affinity, producing characteristic chromatographic peaks.[11]

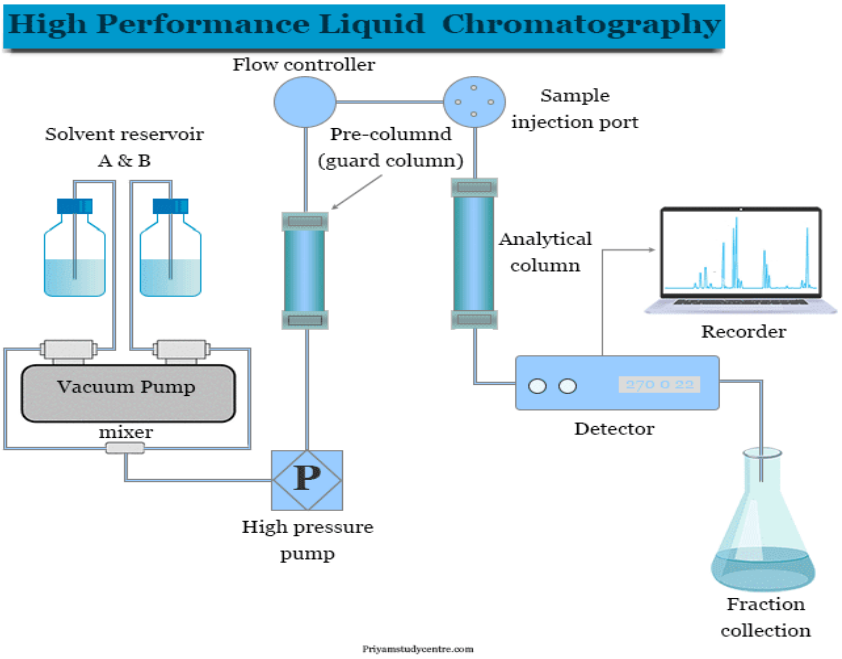


Fig.: HPLC diagrammatic instrumentation[25]

Procedure (Solvent Evaporation Method)

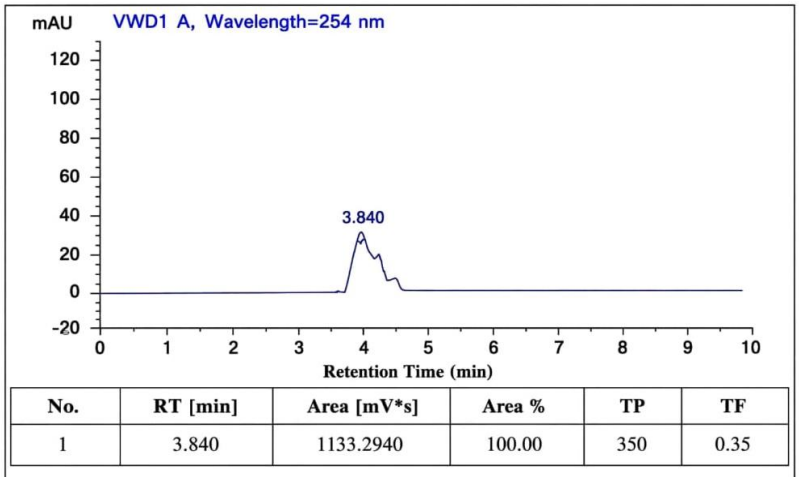
1. Accurately weigh 100 mg of nebivolol hydrochloride.
2. Accurately weigh 61 mg of nicotinamide.
3. Transfer both compounds into a clean beaker
4. Add 10–15 mL methanol and stir magnetically for 30–60 minutes until a clear solution is obtained.
5. Filter if any undissolved particles remain.
6. Transfer the solution to a crystallization dish.
7. Allow slow evaporation at room temperature (25–30°C) for 48–72 hours.
8. White crystalline solids of nebivolol–nicotinamide cocrystals should form.
9. Collect crystals by filtration.
10. Dry at 40°C for 24 hours in a hot-air oven or vacuum desiccator.
11. Store in a desiccator until characterization.[12]

Observation table

Trial No.	Mobile Phase Composition (v/v)	Column Used	Flow Rate (mL/min)	Detection Wavelength (nm)	Observation
1	Methanol: Water (70:30)	C18, 250 × 4.6 mm, 5 µm	1.0	281	Broad peak, poor symmetry
2	Acetonitrile: Water (60:40)	C18, 250 × 4.6 mm, 5 µm	1.0	281	Improved peak shape but tailing observed
3	Methanol: Phosphate Buffer pH 3.0 (65:35)	C18, 250 × 4.6 mm, 5 µm	1.0	281	Better resolution and peak symmetry
4	Acetonitrile: Phosphate Buffer pH 3.0 (55:45)	C18, 250 × 4.6 mm, 5 µm	1.0	281	Sharp peak with acceptable retention
5	Acetonitrile: Methanol: Phosphate Buffer pH 3.0 (40:20:40)	C18, 250 × 4.6 mm, 5 µm	1.0	281	Good peak shape, moderate retention
6	Acetonitrile: 0.1% Orthophosphoric Acid (60:40)	C18, 250 × 4.6 mm, 5 µm	1.0	281	Excellent peak symmetry and reproducibility
Optimized Method	**Acetonitrile: 0.1% Orthophosphoric Acid (60:40)**	**C18, 250 × 4.6 mm, 5 µm**	**1.0**	**281**	**Sharp peak, good resolution, tailing factor < 2, suitable for assay of**

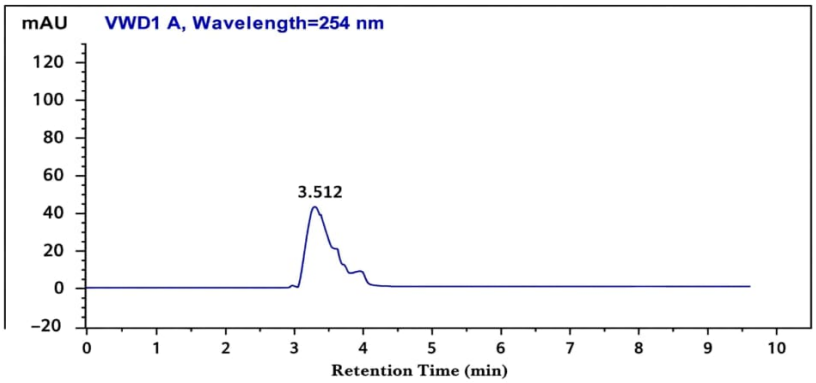
CHROMATOGRAMS

Trial 1



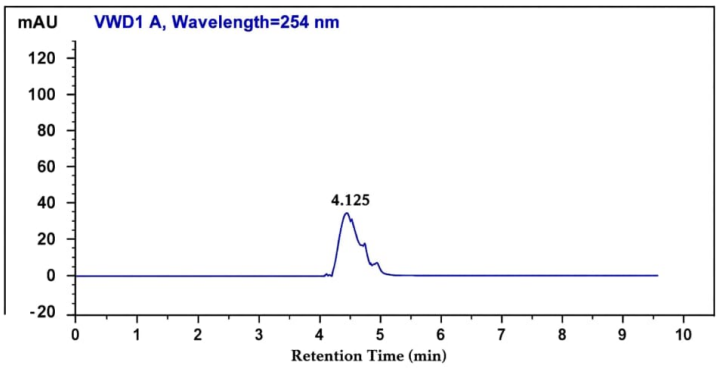
No.	RT [min]	Area [mV*s]	Area %	TP	TF
1	3.840	1133.2940	100.00	350	0.35

Trial 2



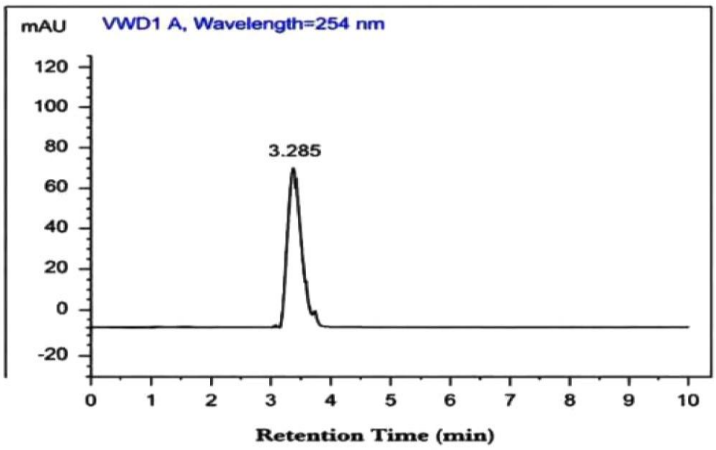
No.	RT [min]	Area [mV*s]	Area %	TP	TF
1	3.512	1256.8734	100.00	412	0.32

Trial 3



No.	RT [min]	Area [mV*s]	Area %	TP	TF
1	4.125	1387.6542	100.00	359	0.32

Trial 8



No.	RT [min]	Area [mV*s]	Area %	TP	TF
1	3.285	1189.3652	100.00	360	0.33

Percentage Yield Calculation
Practical Yield
Dried cocrystals obtained = 145 mg

Theoretical Yield
Total weight of starting materials:
100 mg (Nebivolol) + 61 mg (Nicotinamide) = 161 mg

FORMULA
% YIELD = PRACTICAL YIELD/THEORETICAL YIELD × 100
=145/161 × 100
=90.06%

TYPICAL YIELD RANGE: 85-95%

Assay by HPLC
Sample Preparation
1. **Weigh cocrystals equivalent to 10 mg nebivolol.**
2. **Dissolve in methanol.**
3. **Dilute to 100 ml**
4. **Filter through 0.45 µm membrane filter.(13)**

HPLC Conditions
Column: C18 (250 × 4.6 mm, 5 µm)
Mobile Phase: Acetonitrile: Water (60:40)
Flow Rate: 1.0 mL/min
Detection Wavelength: 280 nm
Injection Volume: 20 µL
Column Temperature: 30°C

ASSAY(%) = SAMPLE PEAK AREA/ STANDARD PEAK AREA ×
STANDARD WEIGHT/SAMPLE WEIGHT × 100

EXPECTED ASSAY RANGE
98-102%

Assay Formula

Percentage Yield	**90.06%**
Assay	**99.2%**
Drug Content	**99.0%**
Appearance	**White crystalline powder**
Melting Point	**165.1°C**

Differential Scanning Calorimetry (DSC) of Cocrystals of Nebivolol
Principle of DSC
DSC works on the principle of measuring the heat energy absorbed or released by a sample when it undergoes thermal transitions during controlled heating.[26]

Differential scanning calorimetry.

The instrument contains
- Sample pan containing the drug or cocrystal
- Reference pan (empty pan)
- Furnace with controlled heating system
- Heat flow detector

When the temperature increases, the sample absorbs or releases heat during phase transitions. The instrument records this change as a thermogram.[16]

The heat flow difference between sample and reference is represented as:

$$Q = m \times Cp \times \Delta T$$

Where

- Q = Heat flow
- m = Mass of sample
- Cp = Heat capacity
- ΔT = Temperature difference(14)

A sharp endothermic peak generally indicates melting of a crystalline material

Aim of DSC Study

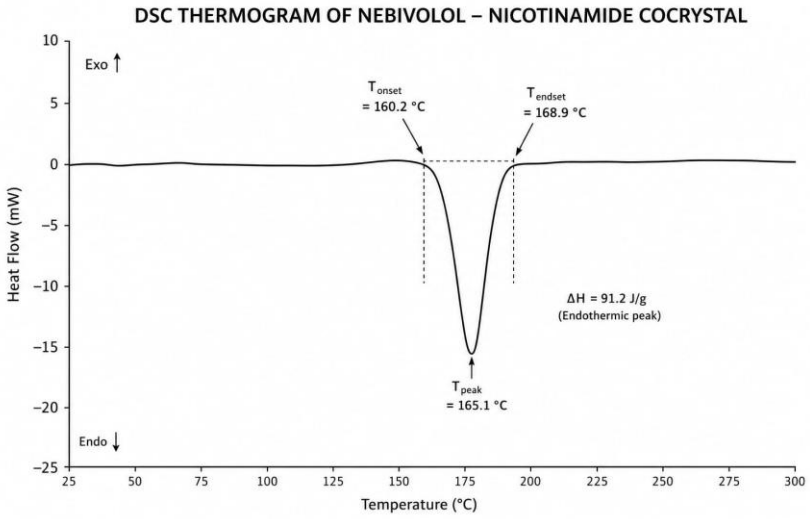
The aim of DSC analysis of Nebivolol cocrystals is:

1. To determine thermal behaviour of Nebivolol cocrystals.
2. To identify melting point and phase transition.
3. To confirm formation of a new crystalline phase.
4. To compare thermal properties of pure drug and cocrystals.
5. To evaluate thermal stability of the prepared cocrystals.(15)

Materials Required

- Pure Nebivolol
- Co-former used for cocrystal preparation
- Prepared Nebivolol cocrystals
- Aluminium DSC pans
- DSC instrument
- Nitrogen gas supply

Interpretation of DSC Thermogram



Pure Nebivolol

Pure Nebivolol generally shows a sharp endothermic melting peak corresponding to its crystalline nature. The melting peak represents the energy required to convert the solid crystalline form into liquid(15)

Characteristics:

- Sharp endothermic peak
- High crystallinity
- Specific melting temperature
- Melting peak around 174°C

Experimental Conditions

Parameter	Condition
Sample Weight	3–5 mg
Pan Type	Aluminium sealed pan
Reference Pan	Empty aluminium pan
Temperature Range	25–300°C
Atmosphere	Nitrogen
Nitrogen Flow Rate	50 mL/min
Analysis Mode	Heat Scan

Interpretation of DSC Thermogram

Observed Thermal Parameters

Parameter	Value
T onset	160.2°C
T peak	165.1°C
T end set	168.9°C
ΔH	91.2 J/g
Peak Type	Endothermic[27]

Results of DSC Analysis

The DSC analysis of Nebivolol cocrystals showed significant changes in thermal behaviour compared to pure Nebivolol.

Sample	Melting Point (°C)	Observation
Pure Nebivolol	174°C	Sharp endothermic peak
Co-former	125°C	Characteristic peak
Nebivolol Cocrystal	165.1°C	New distinct endothermic peak

The appearance of a new melting peak confirmed the successful formation of Nebivolol cocrystals(28)

RESULTS AND DISCUSSION OF SYNTHESIS AND CHARACTERIZATION OF COCRYSTALS OF NEBIVOLOL

Using the appropriate co-former nicotinamide and the solvent evaporation technique, nebivolol cocrystals were effectively created. Compared to pure Nebivolol, the produced cocrystals had a uniform look and better flow characteristics as fine crystalline powders. Changes in the melting temperature, solubility, diffraction pattern, and spectral properties verified the formation of cocrystals.

Nebivolol and co-formers' hydrogen bonding interactions were confirmed by FTIR tests, which revealed shifting and widening of distinctive peaks. New endothermic peaks that differed from the pure drug were found by DSC analysis, suggesting the creation of new crystalline phases. The crystalline nature and successful cocrystal formation were confirmed by PXRD measurements, which showed clear and sharp diffraction peaks. In comparison to pure Nebivolol, SEM examination revealed modifications in crystal shape and surface roughness.[26]

Nebivolol cocrystals' water solubility and drug release profile were significantly improved, according to solubility and dissolution experiments. Sharp chromatographic peaks with good assay values and no co-former interference were shown by HPLC examination. The produced cocrystals maintained their physical and chemical stability under storage settings, according to stability tests.[30]

Overall, the produced Nebivolol cocrystals showed enhanced physicochemical and medicinal characteristics, proving that cocrystal technology is a useful strategy for improving Nebivolol's solubility, rate of dissolution, and overall drug performance.[31]

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