

SEMESTER VII

DISCIPLINE SPECIFIC CORE COURSE-19

CREDIT DISTRIBUTION, ELIGIBILITY, AND PRE-REQUISITES OF THE COURSE

Course title & Code	Credits	Credit distribution of the course			Eligibility criteria	Pre-requisite of the course (if any)
		Lecture	Tutorial	Practical/ Practice		
ADVANCED INSTRUMENTAL METHODS 1	4	3	0	1	12 th Class: Physics, Chemistry, Mathematics	-

Course Objectives:

- To introduce the students to advanced techniques in molecular structure elucidation using instrumental methods.
- To provide theoretical and practical knowledge of Mass Spectrometry and Nuclear Magnetic Resonance Spectroscopy.
- To develop skills for interpreting spectral data and deducing the structure of unknown compounds using a combination of techniques.

Learning Outcomes:

By the end of this course, students will be able to learn:

- Interpret and analyze mass spectra to identify molecular weights and fragment patterns.
- Understand and apply 1D and 2D NMR techniques in structural elucidation.
- Integrate data from UV-Vis, IR, NMR, and MS to deduce complex molecular structures.
- Perform hands-on experiments using spectroscopy instrumentation and software tools for spectral interpretation.

SYLLABUS OF DSC- 19**THEORY COMPONENT****UNIT 1: Mass Spectrometry****(15 Hours)**

Basic principles: Instrumentation: Sample Inlet system,

Ionization techniques; (EI, CI, ESI, MALDI, API, FAB), Mass analysers: Quadrupole, Time-of-Flight (TOF), Magnetic Sector, Radius of ion, Orbitrap, FT-ICR. Positive fragment ions

peak, metastable peak, isotopic mass peaks, Recognition of M^+ Peak, singly, doubly and multiply charged ions. General fragmentation rules and fragmentation of different classes of compounds, factors governing general fragmentation processes, Mc Lafferty Rearrangement and Ortho effect, Nitrogen rule, Rule 13.

Applications: High-resolution mass spectrometry (HRMS), isotope patterns, exact mass, tandem MS (MS/MS). Use known compounds for spectrum-based analysis: **Acetophenone** (Analyze fragmentation and base peak formation), **n-Butylamine** (Use nitrogen rule and α -cleavage pathways), **Toluene** (Observe loss of CH_3 and formation of tropylium ion (m/z 91)), **Methionine (amino acid)**: Apply ESI and analyze isotope peaks for sulfur.

UNIT 2: Advanced NMR Spectroscopy (15 Hours)

^{13}C NMR Spectroscopy: Natural abundance, resolution and multiplicity of ^{13}C NMR, 1H decoupling, noise decoupling, broad band decoupling, Deuterium, fluorine coupling; NOE signal enhancement, off-resonance, DEPT (Distortionless Enhancement by Polarization Transfer): DEPT-45, DEPT-90, DEPT-135 (Identify CH_3 , CH_2 , CH , and quaternary carbons in ethylbenzene).

Two-Dimensional Nuclear Magnetic Resonance Spectroscopy (2D NMR): Basic introduction of 2D NMR, The spin-echo experiment, multi-pulse NMR, Homonuclear correlation experiments (COSY), Heteronuclear correlation (HETCOR, HMQC, HSQC), NOE experiments (NOESY, HOESY, ROESY), and INADEQUATE, Exchange Spectroscopy (ESXY)

Variable Temperature and Dynamic NMR: Study of conformational changes and fluxional behavior, Coalescence temperature and line shape analysis, Arrhenius/Eyring plots for rate constant determination, **VT NMR** of N,N-dimethylformamide (DMF): Observe restricted rotation of N- CH_3 groups at low temperatures, **Dynamic NMR** of cyclohexane: Detect chair inversion and estimate activation barrier.

Solid-State NMR (Basics Only), Magic Angle Spinning (MAS), Cross-Polarization (CP-MAS).

UNIT 3: Structure Elucidation (7 Hours)

Structure elucidation of complex organic compounds based on 1H -NMR, ^{13}C -NMR, 2D NMR, IR, UV, and MS spectral data: Functional group identification, fragment identification, connectivity, symmetry, diastereotopicity, shielding/deshielding effects, spin-spin coupling, exchangeable protons. Contour plot reading and identification of interactions.

UNIT 4: Quantitative NMR (8 Hours)

Quantitative NMR (qNMR): Principles of quantitation using NMR, proportionality of signal intensity and number of nuclei, factors affecting accuracy: relaxation time (T_1), pulse angle, acquisition time. Applications of qNMR: Purity determination, quantification of mixture, stability study, degradation/reaction/process monitoring, intermediate identification, etc,

Use of spectral databases (NIST, SDBS, ChemSpider), Introduction to software: MestReNova, Delta JEOL, ACD/NMR, Bruker TopSpin, ChemDraw for spectra simulation.

PRACTICAL COMPONENT**(30 Hours)**

1. Identify the possible fragment ions for the following classes of compounds (Provide the mass spectra and discuss the fragmentation processes)
 - a) Alkyl-substituted benzenes
 - b) Phenols
 - c) Aldehydes and ketones
 - d) Esters
 - e) Amines
 - f) Nitro compounds
 - g) Alkyl halides
2. Process the given FID files of NMR spectra using any NMR processing software, and identify the compound (Provide the molecular formula)
3. Record the NMR spectra of simple organic compounds, simulate the NMR spectra of same compounds using ACD/NMR, ChemDraw, MestReNova or any other software, and compare the results.
4. Elucidate the structure of organic compounds using UV-Vis, MS, IR, ^1H NMR and ^{13}C NMR (Provide the spectral data).
5. Interpret 2D NMR spectra of organic molecules (provide the spectra).
6. Estimate the percentage of purity or percentage of isomers using the given ^1H NMR spectrum.
7. Analyze ^{13}C CP-MAS data of polymers or crystalline drugs (Identify carbon environments and discuss applications)

RECOMMENDED/ESSENTIAL TEXTBOOKS AND REFERENCES**Theory:**

1. Pavia, D. L., Lampman, G. M., Kriz, G. S., & Vyvyan, J. R., Introduction to Spectroscopy (5th Edition) – Cengage Learning
2. Silverstein, R. M., Webster, F. X., & Kiemle, D. J., Spectrometric Identification of Organic Compounds (7th Edition) – Wiley
3. Williams, D. H., & Fleming, I., Spectroscopic Methods in Organic Chemistry (6th Edition) – McGraw Hill
4. Lambert, J. B., Shurvell, H. F., Lightner, D. A., & Cooks, R. G., Organic Structural Spectroscopy – Pearson
5. Claridge, T. D. W., High-Resolution NMR Techniques in Organic Chemistry – Elsevier

Practicals:

1. Pavia, D. L., Lampman, G. M., Kriz, G. S., Introduction to Organic Laboratory Techniques – Cengage
2. Instrumental manuals and user guides (Bruker, JEOL, Thermo, Agilent etc.)
3. Online Platforms:
 - Spectral Database for Organic Compounds (SDBS)
 - ChemSpider
 - NIST