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An Overview Of Nuclear Magnetic Resonance Spectroscopy

Abhay M. Jagne, Riya V. Bhoyar, Devendra S. Borkar, Rani T. Bhagat, Tulsidas P. Nimbekar

Shri Laxmanrao Mankar Institute of Pharmacy Amgaon

Corresponding Author: Abhay M. Jagne

ABSTRACT:

Nuclear magnetic resonance (NMR) spectroscopy has emerged as a powerful analytical tool over the past few decades, with a wide range of applications in both biological and non-biological systems, from individual cells to organs and tissues. Despite its significance, various aspects of NMR spectroscopy remain under investigation, and a deeper understanding of its functions is still evolving. This review aims to provide a comprehensive overview of the fundamental principles, types, and advantages and disadvantages of NMR spectroscopy. Furthermore, it delves into the current applications of NMR in medicine and dentistry, as well as ongoing developments in the field, paving the way for future applications.

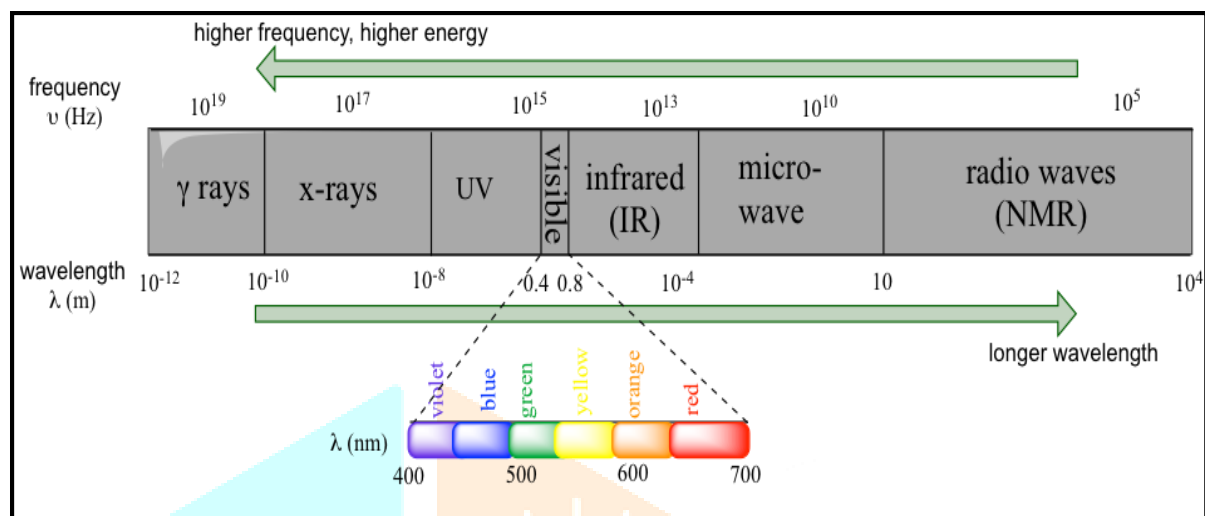
KEYWORDS: Magnetic Field, Chemical Shift, Sweep generator, Nuclear spin.

INTRODUCTION:

Spectroscopy: When white light is given to the surface of an atom, molecule, or other object, spectrum is seen from it which is called spectroscopy. The utilization of electromagnetic spectra in medical and dental diagnostics has revolutionized the detection of fractures and tissue abnormalities. Nevertheless, the associated radiation exposure poses potential health risks, including cellular damage. Fortunately, emerging technologies have yielded innovative.

Electromagnetic radiation (EMR):

It is the form of radiant energy which exhibit both wave and particle properties. Wave property of radiation source include phenomenon of reflection, refraction, interference.



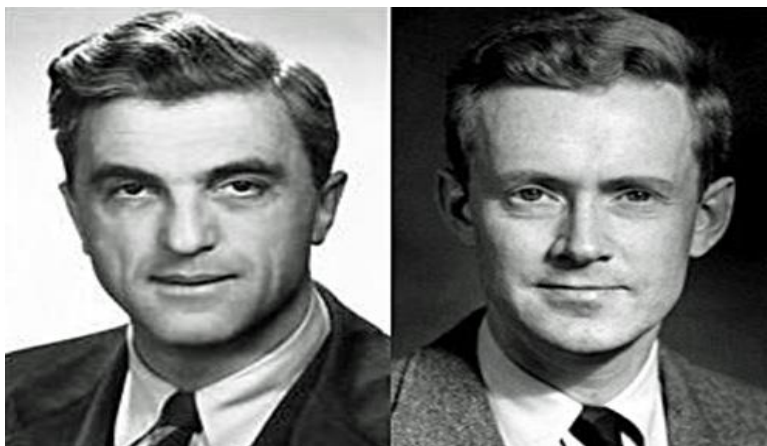
HISTORY OF NMR SPECTROSCOPY:

Nuclear Magnetic Resonance (NMR) spectroscopy has a rich history that spans over eight decades. The concept of NMR was first introduced in the 1930s, and since then, it has evolved into a powerful analytical tool used in various fields, including chemistry, biology, medicine, and materials science.

✓ Early Beginnings (1930s-1940s)

Nuclear Spin and Magnetic Moment (1930s): The discovery of nuclear spin and magnetic moment by physicists like Werner Heisenberg, Niels Bohr, and Isidor Rabi laid the foundation for NMR spectroscopy.

First NMR Experiments (1940s): Felix Bloch and Edward Purcell independently demonstrated the phenomenon of nuclear magnetic resonance in 1946. They were awarded the Nobel Prize in Physics in 1952 for their work.



Edward Purcell

Felix Bloch

✓ Development of NMR Spectroscopy (1950s-1960s)

First NMR Spectrometer (1952): The first NMR spectrometer was built by Varian Associates, founded by Russell Varian. High-Resolution NMR (1950s): The development of high-resolution NMR spectroscopy by scientists like Richard Ernst and Raymond Damadian enabled the analysis of molecular structure.

✓ Advancements and Expansion (1970s-1980s)

Pulse Fourier Transform (PFT) NMR (1970s): Introduced by Richard Ernst, PFT NMR revolutionized the field by allowing for faster data acquisition and improved spectral resolution. Two-Dimensional (2D) NMR (1980s): Developed by scientists like Richard Ernst and Ad Bax, 2D NMR enabled the analysis of complex molecular structures and interactions.

Solid-State NMR (1980s): This technique, developed by scientists like Charles Slichter and John Waugh, allowed for the study of solid materials, expanding the scope of NMR spectroscopy beyond liquids. Modern Era (1990s-Present)

High-Field NMR (1990s): The development of high-field magnets has enabled higher resolution and sensitivity in NMR spectra. Cryogenic Probe Technology (2000s): The introduction of cryogenic probes has improved sensitivity and reduced noise in NMR spectra. NMR Imaging and Microscopy (2000s): NMR has been applied to imaging and microscopy, enabling the study of biological systems and materials at the molecular level.

Nuclear Magnetic Resonance (NMR):

NMR is a spectroscopy technique which is based on the transition of Electromagnetic radiations in a radio frequency region 4 to 900 MHz by nuclei of atoms in the presence of magnetic field. In this radio frequency radiations are used to induce transitions between different nuclear spin states of samples in a magnetic field. When proton (hydrogen) is studied then it is called as Proton Magnetic Resonance (PMR). When other nuclei like ^{13}C , ^9F , ^{35}Cl etc. are studied then it is called as NMR. Nuclear Magnetic Resonance (NMR) spectroscopy, initially discovered in the 1940s, exploits the magnetic properties of specific atomic nuclei, revolutionizing research in physics and chemistry.

The discovery first came about when it was noticed that magnetic nuclei, such as ^1H and ^{31}P (hydrogen: proton and Phosphorus 31) were able to absorb radio frequency energy when placed in a magnetic field of a strength that was specific to the nucleus. Upon absorption, the nuclei begin to resonate and different atoms within a molecule resonated at different frequencies. This observation allowed a detailed analysis of the structure of a molecule. Since then, NMR has been applied to solids, liquids and gasses, kinetic and structural studies, resulting in 6 Nobel prizes being awarded in the field of NMR.

Types of NMR spectroscopy

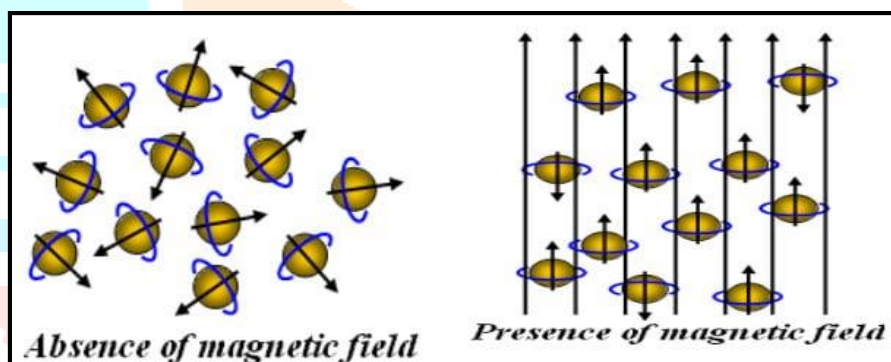
- ✓ ^1H is used to determine the type and number of atoms in an atom.
- ✓ ^{13}C NMR Used to determine the types of carbon atoms in an atom

PRINCIPLE OF NMR:

The structural and chemical composition of different substances can be determined by their nuclei, which possess unique magnetic fields. A basic NMR spectrometer utilizes a magnetic field and a special detector to analyze these nuclei and assess the resulting changes. The strength of the external magnetic field induces electrically charged nuclei to transition from a lower energy level (E_1) to a higher energy level (E_2). The energy difference between these two states, denoted as ΔE , is dependent on both the power of the magnetic field and the size of the nuclear field moment. The electromagnetic radiation rhythm generates the NMR signal with a frequency (ν), prompting the nuclei to transition to a higher energy level (E_1/E_2). When this electromagnetic radiation is ceased, the nuclei relax and attain thermal equilibrium. The subsequent release of energy from the nuclei is recorded in the form of spectra on the computer. These spectra are distinct for each nucleus and directly correspond to the energy levels between the two states (E_2/E_1).

Magnetic Field Strength:

NMR requires a magnetic field that is both strong and uniform. The magnetic field strength is measured in Tesla or MHz. The NMR requires a reference nucleus to represent the strength of the magnetic field.



Chemical Shift:

The movement of the electrons creates a magnetic field in and around the nucleus. This magnetic field created is different in the direction as compared with the outer magnetic field. Any change in the magnetic field causes a similar change in the spectrum of the NMR. This sum of the shift is controlled by nature of the nucleus and nature of the motion of electrons in its surrounding atoms and molecules. This phenomenon is called “chemical shift (CS).” A reference compound is needed to measure CS and to determine and differentiate magnetically inequivalent nuclei present in a molecule.

Spin Spin coupling:

When nuclei are in close proximity, they exhibit an effect known as spin-spin coupling (SS), which arises from the difference in their magnetic field orientations. The magnetic field direction of these nuclei can either align with or oppose the external magnetic field, resulting in the splitting of NMR signals. The strength or weakness of these signals, which can split into two or more components, depends on the specific nuclei involved and their characteristic distance and relative potency.

Nuclear Spin

The protons and neutrons of an atom exhibit spin. In some materials, the protons and neutrons exhibit paired spin such as carbon ^{12}C , oxygen ^{16}O , and sulfur ^{32}S , and in these cases, they cancel each other causing the nucleus not to spin. In some materials, the number of protons and neutrons in an atom are unpaired such as proton ^1H , phosphorus ^{31}P , and fluoride ^{19}F .

Spin relaxation:

Spin relaxation refers to the process by which energy levels return to a state of stability. This occurs when resonance signals are lost over time after the resonance frequency is released. There are two primary relaxation mechanisms that enable nuclear spins to return to stability: spin-lattice relaxation and spin-spin relaxation. The time it takes for a specific nucleus to regain thermal stability is represented by T_1 . Various factors, including:

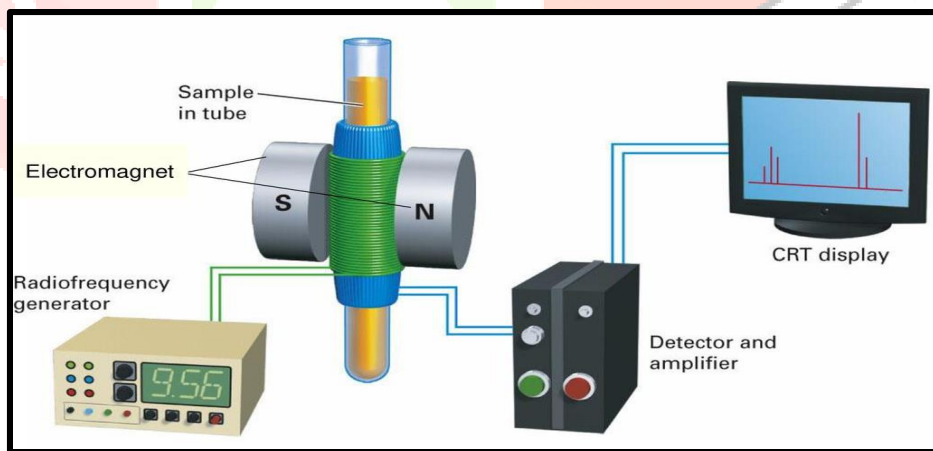
- Structure
- Molecular mass
- Temperature
- Solution properties

can influence this process. Spin-spin (SS) relaxation, on the other hand, occurs when energy is lost from nuclei, resulting in a loss of signals. This lost energy is transferred to nearby spin-active nuclei. The half-life of this process is denoted by the spin-spin relaxation time (T_2).

INSTRUMENTATION:

Nuclear magnetic resonance spectrophotometer consists of:

- 1) Sample holder
- 2) Sample probe
- 3) Permanent magnet
- 4) Magnetic coil
- 5) Sweep generator
- 6) Radio frequency generator
- 7) Radio frequency receiver
- 8) Amplifier
- 9) Readout device



Sample Holder:

Usually the dimension of sample holder is 8.5cm in length and 0.3 mm in diameter. Glass tubes are generally used as sample holder as these are more economic. The following ideal characteristics are there in the sample holder.

- It should be sturdy.
- It should be practical.
- It should be cheap.
- It should be transparent to radio frequency radiations.
- It should be chemically inert.

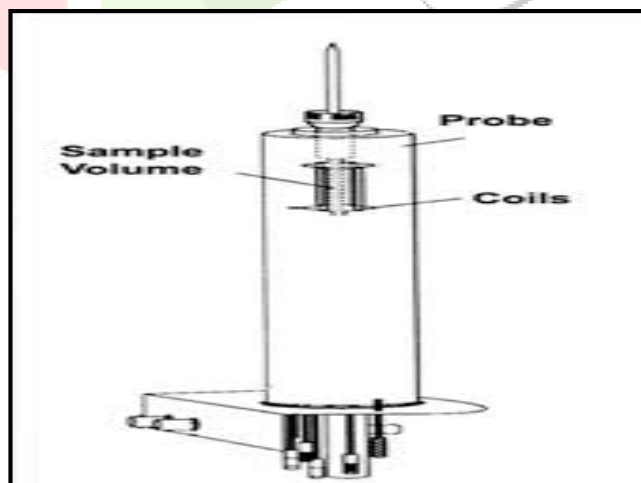
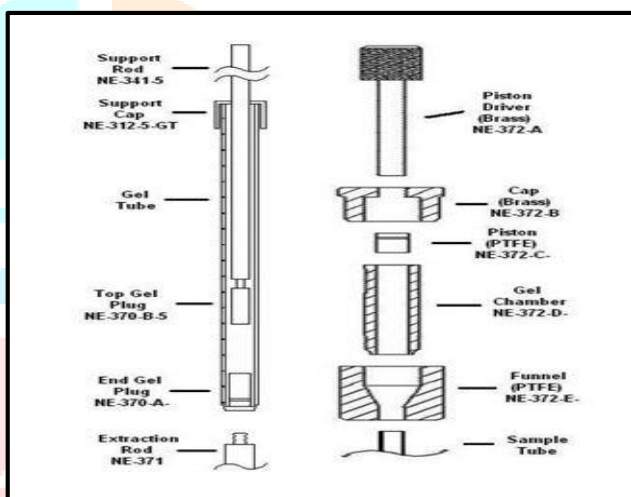
NMR solvent: Usually solvents without protons (aprotic) that interfere with the sample spectra with at least 10% solubility are preferred. The most frequently used NMR solvents for polar compounds are hexadeutero dimethyl sulfoxide (DMSO-d₆) and tetra deutero methanol (CD₃OD). For the analysis of relatively non polar compounds, solvents such as deuterated acetone, deuterated chloroform (CDCl₃), carbon tetrachloride (CCl₄).

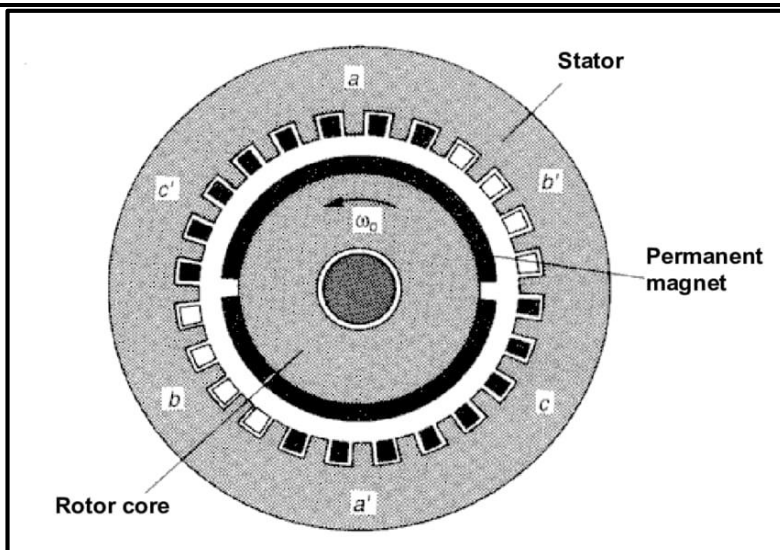
Sampleprobe:

It holds the sample tube in a magnetic field and rotates it along its axis, resulting in sharper lines with better resolution due to decrease in the effects of in homogeneities in the magnetic field. The probe may be either a single coil or system of coils depending upon the type of instrument.

PermanentMagnet:

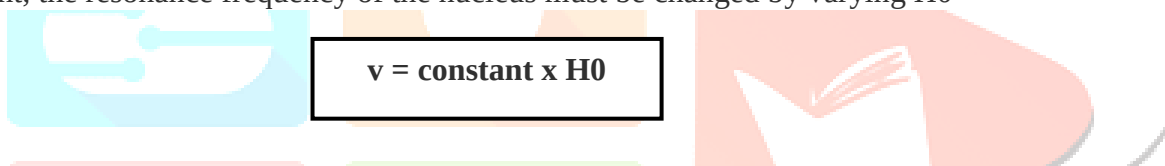
Permanent magnet or electromagnet has the important feature that it should give homogeneous magnetic field, i.e., the strength and direction of the magnetic field should not change from point to point. As the field strength is proportional to the chemical shifts, it must not be less than 20,000 gauss.





Magnetic Coils:

It is employed for the production of NMR spectra. It is achieved by passing direct current either through the coils that are wound around the magnetic pole or through a pair of Helmholtz coils located on either side of the sample probe. The relationship between the resonance frequency of the nucleus and the strength of magnetic field (H_0) is expressed as: From that equation, frequency is directly proportional to strength of magnetic field (H_0). If H_0 is kept constant, the precession frequency is fixed. If radiofrequency is kept constant, the resonance frequency of the nucleus must be changed by varying H_0 .



Sweep Generator:

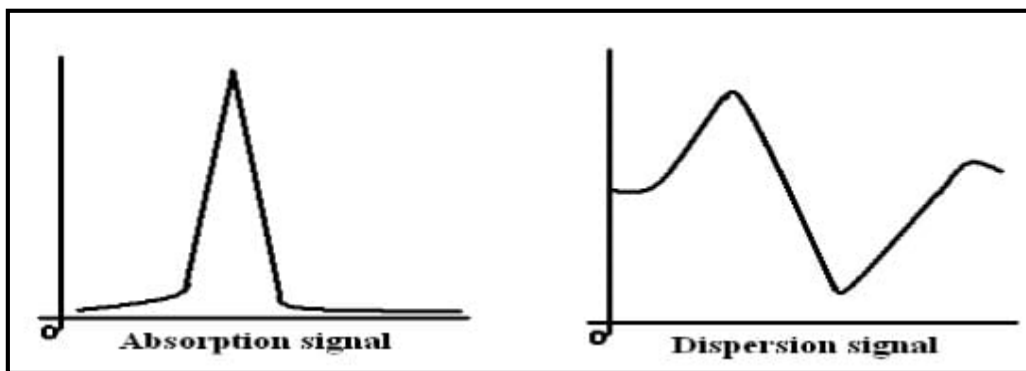
If precession frequency is equal to applied frequency radiations, this results in nucleus to resonate. Sweep generator method, is used to vary the magnetic field and it is easier, than the variation of radio frequency.

Radio Frequency Generator:

Radio Frequency Generator is also known as Radio Frequency Transmitter. In order to generate radio frequency radiation, radio frequency oscillator is used which irradiates the sample molecules. Due to applied radiofrequency, an energy difference occurs and the nuclei moves from ground state to excited state. The coil surrounding the sample results in resonance signals.

Radiofrequency Receiver:

When the radio frequency radiation is passed through the magnetized sample two phenomena namely absorption and dispersion may occur. The observation of either absorption or dispersion will enable the resonance frequency to be determined.



For the detection of resonance signal following methods are used:

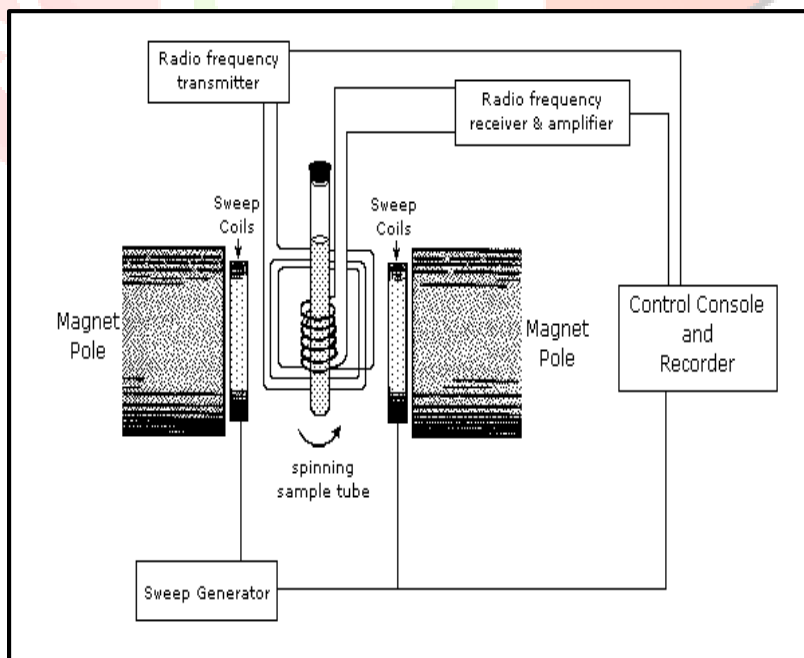
- a) Radio Frequency Bridge is employed under single coil instruments. It allows absorption and dispersion signals to appear as an output of EMF across the bridge. Signals can be recorded mechanically.
- b) This method employs a separate receiver coil which is sometimes called as crossed coil or nuclear induction method. In this the transmitter and receiver coils are arranged perpendicular to each other and to the direction of the magnetic field.

Amplifier:

The absorption signal received from radio frequency receiver is extremely weak. Therefore, it requires considerable amplification before it is fed to a chart recorder in which amplifier is used for amplification of weak signals.

Read Out:

The NMR spectra obtained from instruments are directly recorded via a computer or even mechanically.

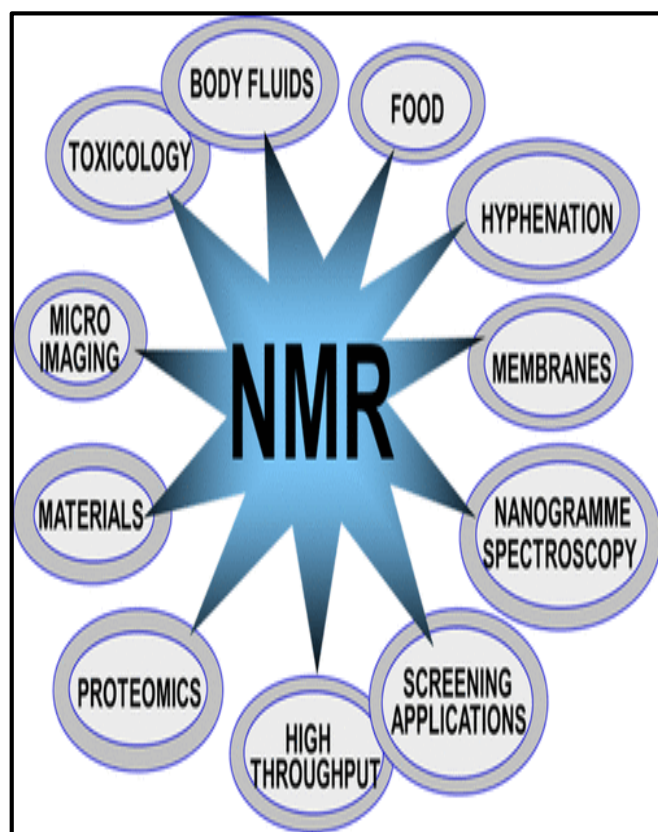


APPLICATION:Medical Applications:

1. Diagnostic Imaging (MRI)
2. Cancer Research
3. Neurological Disorders
4. Cardiovascular Disease Diagnosis
5. Metabolic Disorder Identification

Food and Beverage Applications:

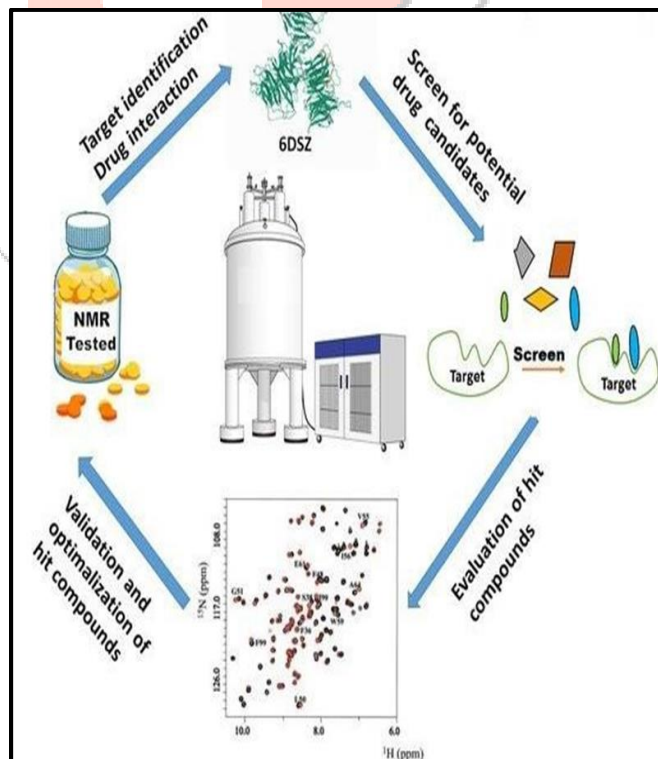
1. Food Authenticity Verification
2. Quality Control (e.g., wine, olive oil)
3. Contaminant Detection (e.g., pesticides)
4. Nutrient Analysis

Pharmaceutical Applications:

1. Drug Discovery and Development
2. Structure Elucidation of Molecules
3. Quality Control and Authentication
4. Impurity Identification
5. Drug Metabolism Studies

Biological Applications:

1. Protein Structure and Function Analysis
2. Gene Expression Studies
3. Metabolic Pathway Analysis
4. Microbial Identification



ADVANTAGES:

- ✓ **Noninvasiveness:** The fundamental quality of NMR is its noninvasiveness. Due to NMR, the studies of biological cells and tissues are now possible without damaging the sample.
- ✓ **Lack of Ionizing Radiation:** Another major advantage of NMR is its lack of ionizing radiation. NMR has made it possible to avoid the exposure from radiation, which could be harmful to both the researcher and the subject.
- ✓ **Adjustability:** Extensive variety of processes can be investigated through NMR due to the flexibility of the particular technique that can be applied. This technique not only gives information about the physiology of the tissues, but it also gives great images of those tissues. The computed tomography (CT) scan technique can only provide the imaging but not the metabolic or anatomic details, whereas NMR spectroscopy has the capability of acquiring a wide variety of information.
- ✓ **Detailed Structural Analysis:**
This technique has helped to obtain information regarding the minute details about the physical and chemical characteristics of structures. NMR can also analyze the parameters of CS, and it can give details on the local bonding environment around a particular atom.

DISADVANTAGES:

- ✓ This is good for more accurate determination of the structure, but not for the availability of higher molecular weight.
- ✓ The resolving power of NMR is less than some other type of experiments (ex. X-RAY CRYSTALLOGRAPHY) since the information got from the same material is much complex.
- ✓ Unfortunately we are just able to determine degree of probability of being of protein segment in the confirmation.
- ✓ The cost of the experimental implementation is increasing with the higher strength & the complexity of determination.
- ✓ NMR experiment is small and, for practical purposes, most strongly coupled with the Concentration of the nuclei in the sample.
- ✓ Expensive instrument.
- ✓ Relatively new technique.

CONCLUSION:

NMR spectroscopy is still very much in its infancy in environmental research. However, considering molecular interactions, associations, and dynamics fundamentally define environmental reactivity, and that NMR provides unrivalled molecular information in whole samples in their native state, it is clear it has a profound role to play in the field. Future considerations include the following.

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