International Journal for Multidisciplinary Research (IJFMR)

E-ISSN: 2582-2160 ● Website: www.ijfmr.com ● Email: editor@ijfmr.com

Nuclear Magnetic Resonance Spectroscopy: Instrumentation: A Comprehensive Review

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ABSTRACT:

One of the most important analytical methods to emerge in recent decades is nuclear magnetic resonance (NMR) spectroscopy. NMR has been used to study a wide range of biological and nonbiological applications, from a single cell to organs and tissues. numerous parts of this technology are still being studied, and there are still numerous NMR functions that need to be better understood and acknowledged. Thus, the goal of this review is to give a broad overview of the fundamental ideas, varieties, and benefits and drawbacks of NMR spectroscopy. Furthermore, an understanding of the present applications of NMR in dentistry and medicine as well as the continuous advancements in NMR spectroscopy for potential future uses have been covered.

INSTRUMENTATION: How NMR Spectroscopy determines the physical and chemical properties of atoms (or) molecules An analytical chemistry technique used in quality control and research to determine the quality,purity & molecular structure of a material.

KEYWORDS: Nuclear magnetic resonance, Metabolism, Multiple sclerosis, Spectroscopy, Magnetic resonance imaging, Magnetic controller

INTRODUCTION:

In the medical area, electromagnetic spectra are frequently used to identify anomalies and fractures as well as to monitor healing tissues. However, this valuable diagnostic tool has the risk of subjecting patients to excessive radiation exposure. Even though X-rays are quick and painless, prolonged exposure to their radiation can have negative consequences, such as damaging cells. In recent years, a number of highly effective analytical methods have been created that can provide accurate results with little risk of harming bodily structures. In the 1940s, nuclear magnetic resonance (NMR) was initially identified.

The NMR is a commonly used technique in physics and chemistry that makes use of the magnetic properties of certain atomic nuclei. This technique is primarily useful in dentistry to investigate the structure of amorphous glasses and dental cements, the interaction of bioactive glasses with oral tissues, the identification of salivary metabolites for disease detection, and the comprehension of periodontal diseases through the analysis of gingival crevicular fluid biomarkers. is frequently employed to examine the fluoride of the tooth structure's apatite surfaces.

Thus, the goal of this review is to give a broad overview of the fundamental ideas of NMR, the various varieties of this technology, and the benefits and drawbacks of NMR spectroscopy. A discussion of the ongoing advancements in NMR spectroscopy for potential future applications is also included, along with an overview of the existing medical applications of NMR.

Principle of NMR

Let's look at the spining top's motion to comprehend the nmr concept.A circle perpendicular to the earth's field will be traced by the spinning top's axis when it is slightly dispersed.Precession is the term for such motion.

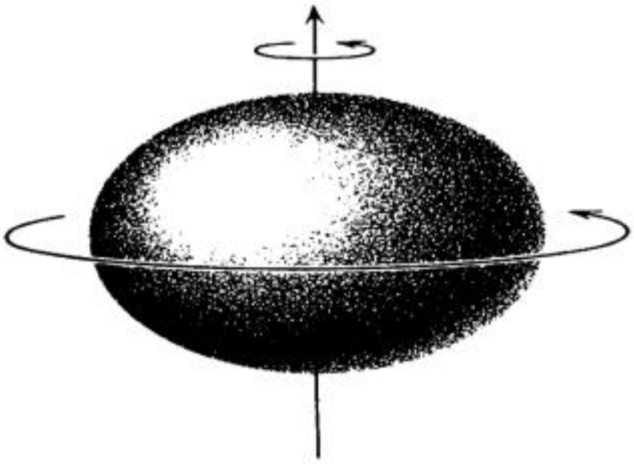


Fig 1 .Spinning charge on proton generates magnetic dipole

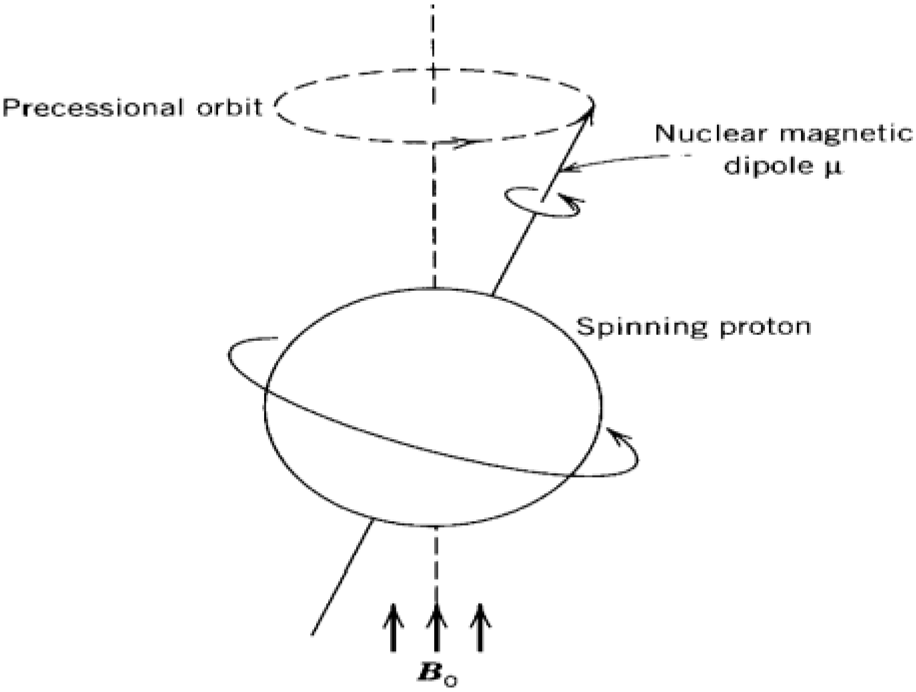


Fig 2 . Classical representation of a proton preccessing in a magnetic field of magnitude Bo in analogy with a preccessing spinning top .

INSTRUMENTATION:

The NMR Spectrophotometre consist of following components

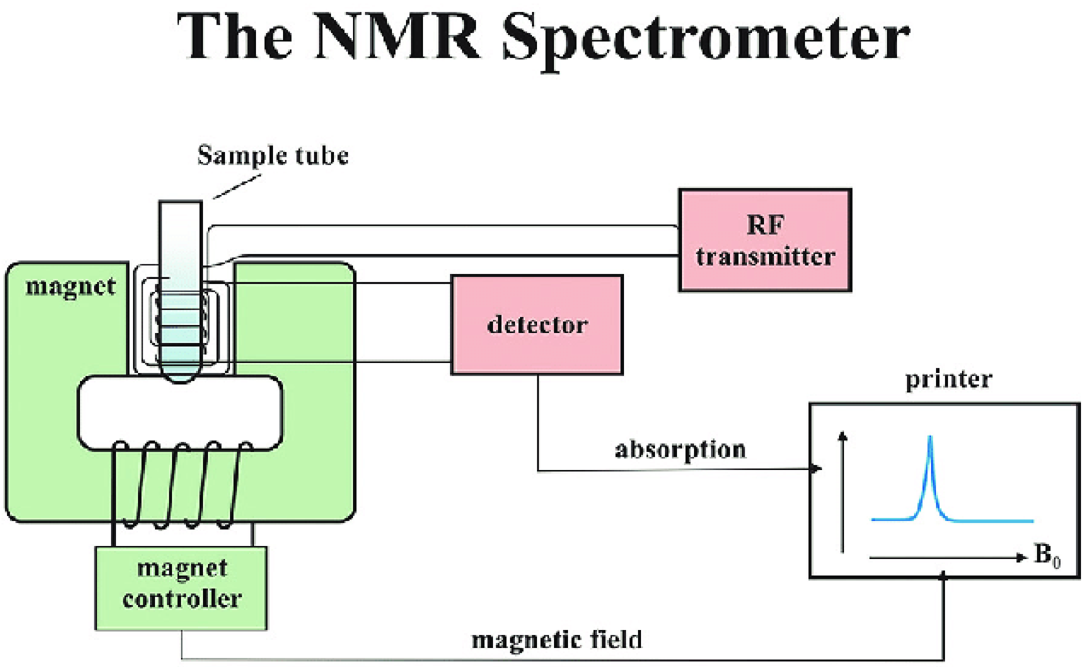
- Sample holder
- Permenant magnet
- Magnetic coil
- Radio frequency generator
- Radio frequency receiver

- Read out system

Basic Mechanism of Action of NMR:

The fundamental idea behind NMR is that each substance's nucleus, which has its own unique magnetic field, can provide information about its structure and chemical makeup. A magnetic field and a specialized detector are used in the basic NMR spectrometer's analysis to evaluate the changes. Electrically charged nuclei migrate from a lower energy level (E1) to a higher energy level (E2) in response to the strength of the external magnetic field. The difference between E2 and E1 is represented by the symbol ΔE, which depends on the nuclear field moment's size and the magnetic field's power.Eight electromagnetic radiation rhythm causes the nuclei to shift to a higher energy level (E1/E2) in order to obtain the NMR signal with a frequency (v).

The nuclei relax and achieve thermal equilibrium when this electromagnetic radiation is ceased. The computer records this energy release from the nuclei as spectra, which are unique to each nucleus and correspond to the energy levels between the two states (E2/E1).



Basic mechanism of instrumentation:

The sample (under research) is exposed to an RF pulse by the NMR spectrometer, as shown in the figure. The sample is exposed to a strong magnetic field during the experiment, and the spin's time response following the pulse application is recorded. The equipment's ability to function depends on the magnet and probe. Analysis requires a strong magnetic field, and the greatest commercially available magnetic field is 17.55 T, which is typically used in high-resolution studies. Between 4.7 and 9.4 T can be produced by standard equipment. Superconducting solenoids based on Nb3Sn or NbTi multi-filament wires are typically used to make magnets, and they are more frequently placed in liquid helium. However, in order to produce even larger magnetic fields—which are essential for nanoscience and nanotechnology research—new and superior materials are needed.

In addition, the magnetic field needs to be uniform. A high magnetic field improves both resolution (by increasing the chemical shift dispersion) and sensitivity (by increasing the Boltzmann factor). Higher magnetic fields, however, have a negative impact on powder linewidths when line broadening is solely determined by chemical shift anisotropy, even while they lessen second-order quadrupole effects. The measurement of receptivity (Rx) establishes how easily distinct nuclei can be seen.

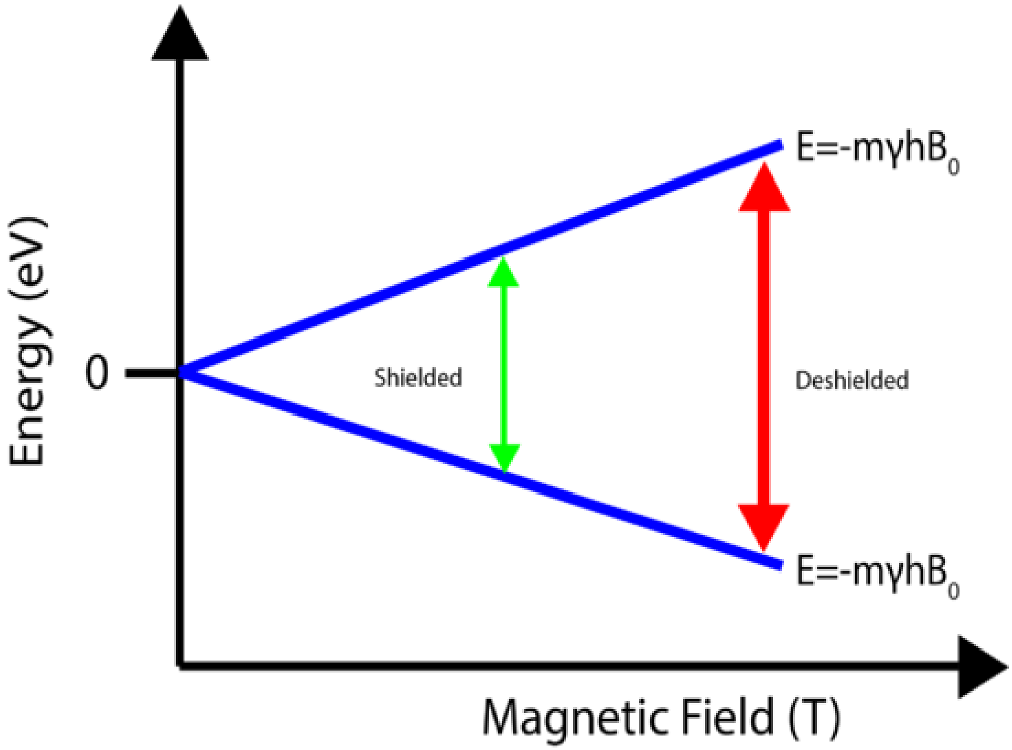
$$Rx = \gamma x \; 3CxIx(Ix + 1)$$

Here Cx stands for the nucleus's inherent abundance. The RF transmitter should generate brief (μs) and powerful (about 1 kW) pulses while dealing with solids. The impact of these pulses on a spin-1/2 nucleus is modeled using the Bloch vector model in a spinning reference frame. When a Tp pulse is administered precisely at resonance, it produces a resultant field that is orthogonal to B0 in the rotating frame of reference. This causes the magnetization to rotate coherently, tilting it away from B0 by an angle θp in the transverse (xy) direction.

$$\theta p = \gamma B1$$

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.

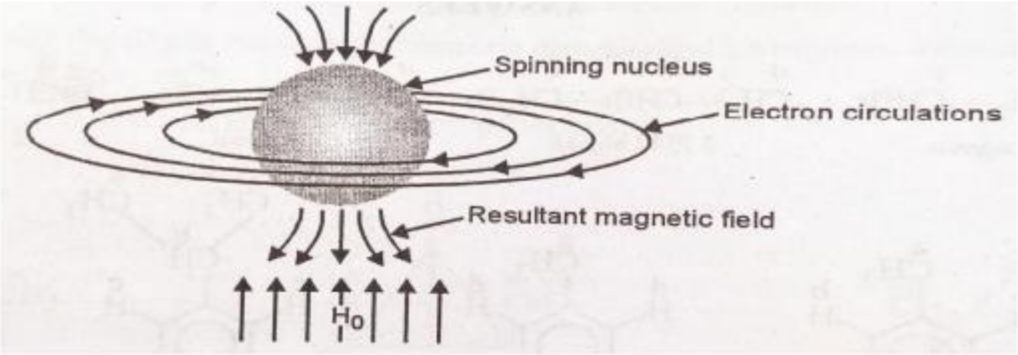


Chemical Shift:

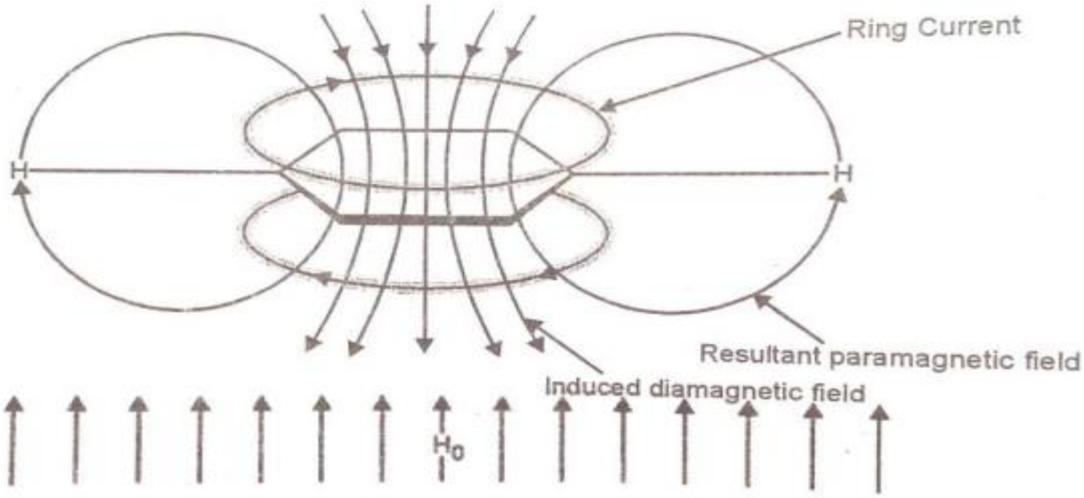
A magnetic field is produced in and around the nucleus by the motion of the electrons. The direction of this generated magnetic field differs from that of the external magnetic field. Any alteration in the magnetic field results in a corresponding alteration in the NMR spectra. The nature of the nucleus and the motion of the electrons in the atoms and molecules around it govern this sum of the shift. We refer to this phenomena as "chemical shift (CS)." To measure CS 9 and identify and distinguish magnetically inequivalent nuclei in a molecule, a reference chemical is required.

Positionof signals—shielding and deshielding :

The applied magnetic field causes the electrons around the protons to circulate when a molecule is placed in a magnetic field to obtain its PMR spectrum. The induced magnetic field is a secondary magnetic field created by this electron circulation.The applied magnetic field may be strengthened or opposed by this induced magnetic field.For instance, the movement of electrons in sigma-bonds around protons creates an induced field that is opposite to the magnetic field that is applied.



On the other hand, circulation of electrons particularly the π-electrons generates an induced field which may either oppose or reinforce the applied field acting upon a proton depending upon its location in the induced field. For example, circulation of π-electrons in benzene derivatives produces an induced field which reinforces the applied field.



The proton is considered to be protected when the induced field opposes the applied field, reducing the actual acting on it. The shielded proton is considered to be protected by decreasing the absorption signal it produces.The applied field must be slightly raised to achieve the same effective field strength at which absorption takes place in order to obtain an absorption signal from the shielded proton.Consequently, sheiklding causes the absorption to go up field.Conversely, the proton is said to be desheilded when the induced field strengthens the applied field and the actual field operating on it increases.

Spin–Spin Coupling:

Because of the difference in the direction of their magnetic fields, nearby nuclei cause an incident known as spin–spin coupling (SS). NMR signals may split as a result of this direction, which could be either in the direction of or against the magnetic field. Depending on the particular nuclei with characteristic distance and relative potency, this magnetic field direction may either enhance or weaken the NMR signals, which can split into two or more components.

TYPES OF NUCLEAR MAGNETIC RESONANCE SPECTROSCOPY:

Solid in a solid state. The main technique frequently used in a solid-state NMR is magic angle spinning (MAS). This magic angle makes the resolution of the sample more precise by making the broader lines of the NMR narrower, resulting in narrower signals giving isotropic values and spinning sidebands to identify the CS of the nuclei for structural determination of solid materials.

1.Phosphorus Nuclear Magnetic Resonance:

In the solid-state NMR, phosphorus is one of the isotopes used to study the molecules and structures of different samples. Compound classes of phosphorus were identified which included orthophosphate diesters, polyphosphate, phosphonates, orthophosphate monoesters, and orthophosphates.

2. Proton Nuclear Magnetic Resonance:

Proton is the initial and the most frequent atom to be used in NMR spectroscopy. It is also called hydrogenNMR (1 H-NMR) that provides information about the different varieties of hydrogen present in the molecule and also gives information about its adjacent surroundings. 13 1 H-NMR spectrum of main materials shows small CS range for usual compound is being studied. This CS ranges from +14 to –14 ppm and a broad difference in extent of coupling constant was observed.

3. icon Magic Angle Spinning Nuclear Magnetic Resonance:

Silicon is an essential element, and its Si isotope, which is used in Si-NMR, has 4.70% natural occurrence with the half spin nucleus. It is another spectroscopic technique used to investigate the structures of organic compounds. Its value of the magnetic moment is a little low causing a low resonance frequency. The predominance of Si-NMR shifts is present in a range from +50 to –200 ppm.

4. Fluorine Magic angle Spinning Nuclear Magnetic Resonance:

Isotopes of fluoride are naturally present in very less quantities except for the F isotope is the only constant isotope of fluorine found in large quantities. Due to its good nuclear qualities and a great quantity, it is used in F MAS NMR technique. F-NMR technique is very rapid when compared with 1 H-NMR technique, and without a doubt, 19 F nucleus is one of the most amenable NMR nuclei. Fluorine has a spin of half-nucleus. Its nucleus in molecules is usually encircled by nine electrons, and its binding energy is 147,801 keV. The sensitivity of F-NMR spectroscopy to its CS (to study the fine details of the local surrounding) is much high for fluorine, thus making it very reactive to NMR measurements with an extremely broad CS range. Yesinowski and Mobley verified the capacity of this NMR to differentiate between fluorapatite, fluorohydroxyapatite, and calcium fluoride in massive phase and also on hydroxyapatite surfaces. F-NMR can identify fluoride even in minimal concentrations starting from 0.1%. F-NMR technique has also been used to study the metabolism of drugs containing fluoride.

5. Carbon Nuclear Magnetic Resonance Spectroscopy:

This technique is a significant tool to recognize carbon atoms in any organic material. It also gives detailed information regarding the chemical structure of the organic compound being studied. 13 C is an isotope ofcarbon which has a spin quantum number of ½ and is only 1.1% naturally present, and this isotope can be detected by 13 C-NMR. 13 C-NMR is less responsive to carbon in view of the fact that the main isotope of carbon is 12 C, which is not magnetically active; therefore, it cannot be detected through this technique. The intensities of the signals in carbon-NMR are not usually comparative to the number of corresponding 13 C atoms. They are strongly reliant on the numerals of adjacent spins. Magnets utilized in C-NMR is less responsive to carbon in view of the fact that the main isotope of carbon is 12 C, which is not magnetically active; therefore, it cannot be detected through this technique. The intensities of the signals in carbon-NMR are not usually comparative to the number of corresponding 13 C atoms. They are strongly reliant on the numerals of adjacent spins. Magnets utilized in C-NMR have a usual diameter of 10 mm and its usual range of CS is much larger compared with proton NMR. 13 C-NMR can be used to find out the composition of different molecules and is also used in the drug industry to verify drug purity.

6. Aluminum Magic Angle Spinning Nuclear Magnetic Resonance:

Aluminum MAS-NMR has a natural abundance of 100%, and it has a 5/2 nuclear spin. The nucleus of aluminum is very responsive giving wide lines over the broad range of CS. The main application of this NMR is to identify the existence of aluminum and to observe the probable structural changes of the different varieties of aluminum. In a previous study, Al-NMR has been used to observe alteration of Al (IV) into Al (VI) in the setting glass carbomer cement.

ADVANTAGES OF NMR SPECTROSCOPY:

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. The fact that both spectrum and imaging can be obtained without destroying the sample is noticeably the greatest advantage of NMR as in in vivo studies.

Lack of Ionizing Radiation: Another major advantage of NMR is its lack of ionizing radiation. Many techniques are being used in vivo studies involving ionizing radiations. NMR has made it possible to avoid the exposure from radiation, which could be harmful to both the researcher and the subject. NMR utilizes isotopes which are stable such as carbon-13 to measure metabolic fluxes instead of radioactive compounds. NMR not only minimizes the exposure to observer and subject from the harmful rays but also eliminates the need to dispose of the radioactive tissues and other materials that might be contaminated during the study. 1 Thus, the application of NMR can ensure the safety of the employees as well as reduce experimental cost due to the removal of discarded radioactive substances.

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. With NMR, a single study can be performed with the same basic technique in both humans and animals, which is important to increase the translation of information. 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: Over the period, NMR has played a major responsibility in determining the mechanisms and chemical connections at a molecular level. This technique has helped to obtain information regarding the mminute 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, which could be calculated for the extended period of times with NMR. It utilizes the pseudo wave function to get information about large compound structures. NMR has the capability to assist studies of biochemical processes conducted in vivo, which is not efficiently achieved with other imaging techniques. Lee et al proposed that NMR is a better uality technique as compared with X-ray diffraction in determining the archaeological bone structure.

DISADVANTAGES:

Presence of High Magnetic Field Surroundings Is Essential: An unavoidable outcome when performing the NMR technique is the requirement to perform in a surrounding which has a high magnetic field. The presence of the magnetic field can affect the proper functioning of monitors and computer-controlled devices. If any sharp objects such as a scalpel, scissors, or stapler are present in the NMR magnetic field area, it can get attracted to the magnet field which can cause severe injuries to the workers. Nowadays, monitoring devices used in the magnetic field area are being designed to function properly under the magnetic field. Furthermore, instruments being used in NMR studies are made nonferromagnetic to reduce the problems encountered with high magnetic field surroundings.

NMR system cannot be purchased by a single investigator or for single research because of its high cost.

The greatest disadvantage of NMR spectroscopy and imaging compared with other modalities is the intrinsic insensitivity of the methods. The signal that can be generated in the NMR experiment is small and, for practical purposes, most strongly coupled with the concentration of the nuclei in the sample.

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

APPLICATIONS OF NMR:

CT scan images of the cranium are restricted by artifacts, but this limitation does not occur with NMR. In the field of medicine, NMR gives the benefit of identifying pediatric tumors, hematomas, and other pathologies. Since multiple sclerosis is a very tricky disease to identify, NMR has become the prime diagnostic device for multiple sclerosis. 15 NMR has particular use for certain body areas such as brain where it produces very detailed and definite images showing delineation between gray and white matter, whereas some tissues such as bone, having low water percentage cannot emit strong signals to create images for NMR. Moreover, NMR is apparently victorious in identifying breast cancer at an early stage. According to a radiologist at Cleveland, a mammogram cannot differentiate between small cancer and a spot, when there are multiple cysts in the breast; however, with NMR, this distinction is possible. NMR technique also gives good images of fatty tissues, and a large quantity of fat creates wonderful images. In addition, the diagnosis of vascular diseases is promising with the NMR as it enables the detailed structural analysis of the surfaces of blood vessels and their abnormalities.

By studying the peaks of nuclear magnetic resonance spectra, chemists can determine the structure of many compounds. It can be a very selective technique, distinguishing among many atoms within a molecule or collection of molecules of the same type but which differ only in terms of their local chemical environment. NMR spectroscopy is used to unambiguously identify known and novel compounds, and as such, is usually required by scientific journals for identity confirmation of synthesized new compounds.Nuclear magnetic resonance is extremely useful for analyzing samples non-destructively.

Radio-frequency magnetic fields easily penetrate many types of matter and anything that is not highly conductive or including RNA and DNA, or proteins, can be studied using nuclear magnetic resonance for weeks or months before using destructive biochemical experiments. This also makes nuclear magnetic resonance a good choice for analyzing dangerous samples.

In dentistry, the aim of treatment is to preserve natural tissue and reconstruct the loss tissue with the help of biomaterials. These dental biomaterials are studied by many characterizing machines such as mechanical tester, physical testing, rheological testing, and biocompatibility testing. For that, NMR spectroscopy is a miracle machine to understand in-depth chemical reaction of materials ingredients and their effect with natural tissues. Extensive research on gas ionomer cement (GIC), resin composites, dental bone cements, and periodontal membranes materials has been conducted using the NMR spectroscopy. Prosser et al used NMR spectroscopy and reported the role of tartaric acid in the setting reaction of GIC, was “The fluid cement pastes have shown that tartaric acid reacts more readily than the polyacid with the glass, and hence suppresses the premature gelation of the cement.” A novel antimicrobial polymeric dental restorative material was experimentally synthesized to see the biocompatibility, strength, and remineralization property by NMR (1 H- and 13 C-NMR) spectroscopy. The advancements of proteomics in dentistry have brought a revolution in the management of oral diseases and analysis of molecular changes during the reconstruction or rehabilitation of oral tissues (soft and hard) with dental materials. To observe the orthodontically induced external apical root resorption biomarkers, Zhou et al studied the 1 H-NMR-based metabolomics and detected the inflammatory metabolites from saliva samples. This study brings an importance of NMR spectroscopy in the field of clinical dentistry and dental early diagnosis.

A rapid and quantitative 1H nuclear magnetic resonance (NMR) method was developed to analyse histamine in cheeses. The procedure is simple because the acid extract is analyzed directly, without any need for further filtration, derivatization, or other manipulation. The NMR method was successfully applied to different types of cheese, ranging from soft to hard .

The application of 1H nuclear magnetic resonance (NMR) spectroscopy to the measurement of conjugated linoleic acid (CLA) content in the lipid fraction of dairy products is both a novel and inviting alternative to traditional methods such as gas chromatography (GC), which can require time-consuming sample derivatization. 1H NMR analysis approach has potential application in the dairy industry as a screening technique for total CLA concentrations in large numbers of cheese samples and in the screening of CLA content in other dairy products.

Solid-state 31P nuclear magnetic resonance (NMR) to determine the different states of phosphates in cheeses was used. Sixteen semi-hard cheeses of various compositions were studied, and three fractions of phosphates (P) were distinguished according to their mobility: (1) mobile soluble P (ca. 10 % of total P), (2) mobile insoluble P (70 %) and (3) immobile insoluble P (20 %). In accordance with chemical composition and buffering capacities of the cheeses, these fractions could represent respectively (1) soluble inorganic P,(2) inorganic colloidal calcium P and phosphorylated serine residues (Pser) involved in a loose structure and (3) Pser involved in a tight environment.It was thus demonstrated that solid-state NMR is an appropriate method to observe the distribution of phosphates in cheese matrix and their evolution during cheese-making .

One-dimensional 31P NMR and two-dimensional (2D) 31P,1H COSY NMR spectroscopy was used for the determination of the phospholipids which comprise an important important lipid class in food because of their technological use as emulsifiers and their nutritional value. The total phospholipids content in cheese fat and fish oil ranged from 0.3 to 0.4% and from 5 to 12%, respectively. Minor phospholipids were identified in forms of phosphatidic acid, lysophosphatidic acid, and phosphatidylglycerol .

Discrimination between apple juices produced from different varieties has been achieved by applying principal components analysis (PCA) and linear discriminant analysis to 1H NMR spectra of the juices by Belton et al. Under optimum conditions a 100% success rate was achieved. Examination of the principal component loadings showed that the levels of malic acid and sucrose were two important chemical variables, but variations in the composition of the minor constituents were also found to make a significant contribution to the discrimination .

Green teas from different countries was collected and analyzed by 1H NMR. It was proposed to establish if the teas could be discriminated according to the country of origin or with respect to quality. After an extensive assignment of spectra, NMR spectroscopy has been shown to provide a wealth of information about the main metabolites of the teas studied. Tea components were determined for discrimination of teas.

Application of 1H NMR was used quality control and authenticity of instant coffee by Charlton et al. The presence of inherent differences between coffees produced by different manufacturers, and even between those produced by the same manufacturer, by identifying 5-(hydroxymethyl)-2-furaldehyde as a marker compound using the structural characteristics were determined by NMR Another study, 31P NMR was used to determine the amount of mono- and diglycerides in virgin olive oils. It was found that quantification of other constituents of olive oils bearing functional groups with labile protons could be extended by quantitative 31P NMR spectroscopy .

NMR can be used for foodomics because of ease of quantification and identification, short time and low costs needed for analysis and high number of metabolites that can be measured through a single-pass. Because of highest sensitivity of NMR focus on hydrogen is prefered for foodomics studies .

The molecular fatty components of Pecorino Sardo Protected Designation of Origin (PS PDO) cheese were characterized through an exhaustive investigation of the 1 H- and 13C-NMR spectra of the extracted lipids. Several fatty acids (FA), such as long chain saturated, oleic, linoleic, linolenic, butyric, capric, caprylic, caproic, trans vaccenic, conjugated linoleic acid (cis9, trans11–18:2), and caproleic (9–10:1) were unambiguously detected. The positional isomery of some acyl groups in the glycerol backbone of triacylglycerols (TAG) was assessed. The NMR signals belonging to 1,3 diacylglycerols (DAG), and free fatty acids (FFA) were analysed as a measure of lipolytic processes on cheese. 1H-NMR resonances of saturated aldehydes and hydroperoxides were detected .

1Studies has shown that characterization of geographical origin could be done by using NMR spectroscopy. NMR technique was used for characterisation of the geographical origin of buffalo milk and mozzarella cheese by means of analytical and spectroscopic determinations. Isotopic ratios (13C/12C and 15N/14N) and other variables were affected by the specific area of origin of milk samples while NMR data, together with isotopic ratios, were useful for the discrimination of mozzarella samples .

CONCLUSION:

Considering the potential advantages of the NMR technique, it can be concluded with authority that it has become a preferred choice of technique for any diagnosis, treatment planning, and maintenance of treatment and also to see the behavior of foreign materials interaction with the human body. NMR is still a growing technology, and it is being anticipated that few discoveries are now just around the corner.

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