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REVIEW ARTICLE

Vibrating Sample Magnetometer and Its Application In Characterisation Of Magnetic Property Of The Anti Cancer Drug Magnetic Microspheres

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Abstract
The measurement of magnetic moment in magnetic materials is a widespread area of research in both academic and industrial frontier. The magnetic target drug delivery system has various applications in the field of cancer treatment. And its value depends on whether the system possesses super paramagnetic, biocompatibility, effectiveness of drugs and otherwise. A sample is placed inside a uniform magnetic to magnetize the sample. The sample is then physically vibrated sinusoidally, typically through the use of a piezoelectric material. The vibrating sample magnetometer (VSM) measures the magnetization of a small sample of magnetic material placed in an external magnetizing field by converting the dipole field of the sample into an ac electrical signal.

Keywords: Vibrating sample magnetometer, cancer drug, magnetization, magnetic microspheres

INTRODUCTION:-

Magnetism, is the oldest technology and a magical science. It was first recorded around 600 BC by the Greeks studying ferrite rocks (lodestone). The earliest mention of a magnetic compass used for navigation is from a Chinese text dated 1040–1044 A.D., but it may have been invented there much earlier. Magnetism is a sub-atomic phenomenon and is mainly caused due to the polarization of electric clouds, or magnetic dipoles of certain materials with unpaired electrons. Due to this imbalance, the atom gains a net angular momentum, and a magnetic field perpendicular to the rotation of spin of the excess charge is caused. The magnitude of this magnetic or spin moment is dependent on the species of atom. This spin-spin interactions classified materials into different magnetic classes. When atoms are brought in proximity to each other there is a chance of an electron jumping from one atom to another, known as the Heisenberg exchange. This interaction can indirectly couple the spin moments of the atoms, causing the spin moments to align parallel or antiparallel. In most materials the spin moments are small and aligned randomly, causing to paramagnetism. In some materials, specifically transition metals such as nickel, cobalt, and iron, the spin moments are large, and align in parallel or ferromagnetically. This causes a net spontaneous magnetic moment in the material.

The Vibrating Sample Magnetometer is a sensitive and versatile instrument for study of magnetic moments in different magnetic materials as a function of magnetic field and temperature. Its use to measure magnetization is based on the Faraday's laws of electromagnetic induction. (1)

The Vibrating sample Magnetometer was first designed by Simon Foner, in 1959 at the Lincoln laboratories. All the VSM work, involves the measurement of voltage induced in a stationary coil, otherwise called as detection coils, due to the harmonic vibration of the sample in a uniform magnetic field.(2)

VSM Application:

Magnetic Measurement:

The vibrating-sample magnetometer has been in use for routine magnetic measurements as a function of temperature and field of ferromagnetic, ferrimagnetic, anti ferromagnetic, paramagnetic, and diamagnetic materials. (2)

Magnetic field Measurement:

The magnetometer may be used as a field measuring device by using a paramagnetic sample. If the susceptibility is not too large and is field independent, the proportionality constant, accounting for the particular coil geometry and the susceptibility, is obtained by calibration with the nickel standard above magnetic saturation, or by an independent field measurement. (2)

Working Principle:

A vibrating sample magnetometer (VSM) operates on Faraday's Law of Induction, which informs that a changing magnetic field will produce an electric field. This electric field can be measured and provide us information

about the changing magnetic field. A VSM is used to measure the magnetic behavior of magnetic materials. The sample to be studied is kept in a constant magnetic field. If the sample IS magnetic, this constant magnetic field will magnetize the sample by aligning the magnetic domains, or the individual magnetic spins, with the field. The stronger the constant field, the larger the magnetization will be. The magnetic dipole moment of the sample will create a magnetic field around the sample, sometimes called the magnetic stray field. As the sample is moved up and down. this magnetic stray field is changing as a function of time and can be sensed by a set of pick-up coils. The alternating magnetic field will cause an electric current in the pick-up coils according to Faraday's Law of Induction. This current will be proportional to the magnetization of the sample. The greater the magnetization, the greater the induced current. The induction current is amplified by a transimpedance amplifier and lock-in amplifier. The various components are hooked up to a computer interface. Using controlling and monitoring software, the system can tell us how much the sample is magnetized and how its magnetization depends on the strength of the constant magnetic field.
The output is a hysteresis curve, which shows the relationship between the induced magnetic flux density and the magnetizing force and gives important information about the magnetic saturation, the remanence, the coercivity and the level of residual magnetism left in the material.[18]

The vibrating sample magnetometer operates on the principle that when a sample material is placed in a uniform magnetic field, a dipole moment proportional to the product of the sample susceptibility times the applied field is induced in the sample. A sample also undergoing sinusoidal motion induces an electrical signal in a set of stationary pick-up coils. This signal is proportional to the magnetic moment, vibration amplitude, and vibration frequency.

The material under study is contained in a sample holder, which is centered in the region between the pole pieces of an electromagnet. A vertical sample rod connects the sample holder with a transducer assembly located above the magnet, which supports the transducer assembly with sturdy, adjustable support rods. The transducer then converts a sinusoidal AC drive signal, provided by a circuit located in the console, into a sinusoidal vertical vibration of the sample rod, and the sample thus undergoes a sinusoidal motion in a uniform magnetic field. Coils mounted on the pole pieces of the magnet pick up the signal resulting from the sample motion. This AC signal at the vibration frequency is proportional to the magnitude of the moment induced in the sample, vibration amplitude and frequency. A servo system maintains constancy in the drive amplitude and frequency so that the output accurately tracks the moment level without degradation due to variations in the amplitude and frequency of vibration.The samples can be characterized by weight or volume.[20]

Vibrating Sample Magnetometer Parts [3]

Water cooled electromagnet and power supply

The water cooled electromagnet, along with the power supply, generate the constant magnetic field used to magnetize the sample.

Vibration exciter and sample holder (with angle indicator)

The sample holder rod is attached to the vibration exciter, and the end of it hangs down in between the pole pieces. The exciter moves the sample up and down at a set frequency, typically 85Hz. The sample rod can be rotated to achieve the desired orientation of the sample to the constant magnetic field. There are also three knobs for controlling the x,y, and z positions of the sample.

Sensor coils

The sample produces an alternating current in these coils at the same frequency as the vibration of the sample. The signal generated contains the information about the magnetization of the sample.

Amplifier

The amplifier does just that - amplifies the signal created by the sensor coils.

Control chassis

This controls the 85Hz oscillation of the exciter.

Lock in amplifier

This amplifier is tuned to pick up only signals at the vibrating frequency. This eliminates noise from the environment, such as from the overhead lights or hovering spacecraft nearby (unless the noise happens to be an 85Hz signal).

Meter

This is used to measure something important.

Computer Interface

The software makes data collection easier by automating the control of the various components during data collection. The data can be graphed and plotted on the printer.

Magnetic property characterization of Anticancer drug product using Vibrating sample magnetometer:

WuShiZuo, PengJin Hua, LiFengSheng in their Ph.D thesis tiled Preparation and Characterization of Fluorescent

Magnetic Target Drug Delivery Systems prepared Magnetic tetracycline microspheres by combining ultrasonic emulsion polymerization with ultrafine grinding technology. Superfine technology took average particle size of tetracycline powder down to about1μm so as to make the drug powder easier to dissolve in magnetic fluid solution, which was useful for the distribution of tetracycline drug particles in the emulsion reaction system. Based on the characterization results of transmission electron microscopy (TEM), vibration sample magnetometer, bacterial inhibition experiments and other tests, it could be found that the structure of microspheres were not break down when the drug was coated and the magnetic tetracycline microspheres had obvious drug activity compared to the control groups. To expand applications of ultrasonic emulsion polymerization method, hydrophilic fluorouracil was chosen as the coated drug. Hydrophobic fluorouracil microparticles were made by using a wet ball mil land and adding the stearic acid as a modifier, which can easily dispersed in magnetic fluid. Rhodamine B isothiocyanate was modified onto the surface of microspheres after loading the drug and successfully obtained fluorescent magnetic anticancer microspheres. Through vibrating sample magnetometer (VSM) and fluorescence analysis, they did characteristic study of the fluorescent magnetic anticancer microspheres and proved that they had good super paramagnetic and fluorescent light-emitting properties. [4]

Sundar et al fabricated etoposide loaded magnetic polymeric microparticles and characterized magnetic property of magnetic microspheres by using vibrating sample magnetometer. A typical characteristic of super paramagnetic material with no detected remainance or coacervity at room temperature in the study indicated that the single domain magnetic Fe3O4 nanoparticles remained in the prepared magnetic microspheres. [5]

Yun-Kai Lv et al prepared doxycycline imprinted magnetic microspheres by inversion emulsion suspension polymerization for magnetic dispersion extraction of tetracyclines from milk samples and characterized the magnetism property using Vibrating sample magnetometer. [6]

Abolfazl Akbarzadeh et al prepared doxorubicin-loaded Fe_3O_4 magnetic nanoparticles modified with biocompatible copolymers and performed characterization studies. They conducted magnetism test to study the magnetic properties of the nanoparticles by vibrating sample magnetometry at room temperature. The saturation magnetization was found to be 17.5 emu/g for doxorubicin-loaded Fe_3O_4 magnetic nanoparticles modified with PLGA-PEG copolymers, ie, less than for the pure Fe_3O_4 nanoparticles (70.9emu/g).This difference suggests that a large amount of polymer encapsulated the Fe_3O_4 nanoparticles and doxorubicin. With the large saturation magnetization, the doxorubicin-loaded Fe_3O_4 magnetic nanoparticles modified with PLGA-PEG copolymers could be separated from the reaction medium rapidly and easily in a magnetic field. In addition, there was no hysteresis in the magnetization, with both remanence and coercivity being zero, suggesting that these magnetic nanoparticles are super paramagnetic.[7]

Soodabeh davaran et al. Synthesised hydrogel nanocomposites containing magnetic nanoparticles for study. Magnetic nanoparticles (Fe_3O_4) with an average size 10 nm were prepared. At second approach, thermo and pH-sensitive poly (N-isopropylacrylamide -co-methacrylic acid-co-vinyl pyrrolidone) (NIPAAm-MAAVP) were prepared. Swelling behavior of co-polymer was studied in buffer solutions with different pH values (pH=5.8, pH=7.4) at 37°C. Magnetic iron oxide nanoparticles (Fe_3O_4) and doxorubicin were incorporated into co-polymer and drug loading was studied. The magnetic properties of the nanoparticles were analyzed by vibrating sample magnetometry at room temperature From hysteresis loop curve the saturation magnetization was found to be 18 emu/g for doxorubicin-loaded NIPAAm-MAA-VP magnetic nanocomposite, less than for the pure Fe_3O_4 nanoparticles (65emu/g). This difference suggests that a large amount of polymer encapsulated the Fe_3O_4 nanoparticles and doxorubicin. With the large saturation magnetization, the doxorubicin- loaded NIPAAm-MAAVP magnetic nanoparticles could be separated from the reaction medium rapidly and easily in a magnetic field. In addition, there was no hysteresis in the magnetization, with both remanence and coercivity being zero, suggesting that these magnetic nanoparticles are superparamagnetic. [8]

Hereba et al studied the effect of magnetic microspheres on the blood to lead optimization of the use of these microspheres. Five groups of normal blood samples were incubated with 10 mg magnetic chitosan microspheres then each group was compared to control group samples. Magnetism test was carried out using Vibratory sample Magnetometer .The hysteresis loop of the microspheres, in which the internal area of the hysteresis loop represents the capability of magnetic energy storage of magnetic materials was developed. For the prepared microspheres, the saturation magnetization was 6.205 electromagnetic unit/gram/division (emu/g/division), coercivity was 76.05 Oersted (Oe), and retentivity was 1.099 emu/g. In which the maximum field was 5000 Oe. [9]

Zhou et al .In their work magnetite (Fe_3O_4) nanoparticles with an average size 10 nm modified by sodium oleate

were prepared by the modified controlled chemical coprecipitation method, which can be well dispersed in water and linked well with protein molecules because of the presence of —COOH on their surface. Then magnetic poly(lactic acid) (PLA) and poly(lactic-co-glycolic acid) (PLGA) microspheres containing interferon alpha-2b (IFN-a-2b) were prepared by the modified water-in-oil-in-water solvent evaporation procedure. Including vibrating-sample magnetometer (VSM) analysis to study magnetic properties of the magnetic microspheres other characterization study were carried out..The magnetic properties of the resultant Fe3O4 nanoparticles were measured by a vibrating sample magnetometer (VSM, Quantum Design) at room temperature. A certain amount of microspheres were placed in the magnetometer. The magnetic properties were then determined by applying an increasing magnetic field over the sample, and the results were used to calculate the magnetism of the microspheres, which were characterized by weight. [10]

Yang et al prepared hollow poly(N,N0-methylenebisacrylamide-co-methacrylic acid) (P(MBAAm-co-MAA)) microspheres by the selective removal of poly(methacrylic acid) (PMAA) core from the corresponding PMAA/P(MBAAm-co-MAA) core-shell microspheres, which were synthesized via a two-stage distillation precipitation polymerization. The magnetic Fe_3O_4 nanoparticles onto the surface of hollow P(MBAAm-co-MAA) microspheres via partial oxidation of ferrous salt during the chemical deposition in the presence of potassium nitrate as oxidant with the aid of hexamethylene tetramine and the magnetic hollow microspheres were further functionalized with folic acid (FA) via the chemical linkage with amino groups of 3-aminopropyl triethoxysilane (APS)-modified P(MBAAm-co-MAA)Fe_3O_4 microspheres to afford the magnetite and tumor dual-targeting hollow microspheres. The resultant dual-targeting hollow polymer microspheres with pH-sensitivity were characterized by transmission electron microscopy (TEM), dynamic light scattering (DLS), Fourier transform infrared-spectrometer (FT-IR), UV Vis absorption spectroscopy, and vibrating sample magnetometer (VSM). [11]

Zhang et al used alginate-chitosan (Alg-CS) hydrogel beads for developing an oral water-soluble drug delivery system, occupying pH-sensitive property and superparamagnetic. Matrine as a model drug was loaded in Alg-CS hydrogel beads to study the release character of the delivery system. The amount of matrine released from the beads was relatively low in pH 2.5 over 8 h (34.90%), but nearly all of the initial drug content was released in simulated intestinal fluid (SIF, pH 6.8) within 8 h. The results demonstrated that Alg-CS hydrogel beads possess unique pH-dependent swelling behaviors. In addition, the magnetic beads were characterized by Fourier transform infrared spectroscopy, scanning electron microscope, X-ray diffractometry and vibrating-sample magnetometry. Magnetometer measurements data suggested that Alg-CS beads also had superparamagnetic property as well as fast magnetic response. It can be expected that the beads can deliver and release encapsulated anticancer agent at the tumor by the weak magnetic field, and hence could be potential candidates as an orally administered drug delivery system. [12]

R Turcu et al. obtained Magneto responsive microgels with high saturation magnetization values by a strategy based on the miniemulsion method using high colloidal stability organic carrier ferrofluid as primary material. Hydrophobic nanoparticles Fe_3O_4/oleic acid are densely packed into well-defined spherical nanoparticle clusters coated with polymers with sizes in the range 40–350 nm. Investigated Physical– chemical characteristics of magnetic microgels by TEM, SAXS, XPS and VSM measurements with the focus on the structure–properties relationship. Results showed that MTO-loaded microgels are promising structures for application in magnetic drug targeting. The static magnetization of the samples was measured by means of vibrating sample magnetometry at room temperature using an ADE Technologies VSM 880 magnetometer. The magnetic measurements were performed on dried samples of NPC stabilized with SDS and on the microgels obtained by polymer coating of NPC. For all the samples the magnetization at room temperature does not show any hysteresis loop, being consistent with a super paramagnetic behavior, as expected for oleic acid-coated magnetite nanoparticles of small sizes (less than 10 nm) from the ferrofluid used as primary material. Moreover, this fact indicates that the magnetite nanoparticles are still well separated in NPC and the magnetic dipole-dipole interactions between them are negligible. High saturation magnetization values were obtained for the nanoparticle clusters, M_S=64 A m^2 /kg and also for the magnetic microgels, M_S=53 A m^2 /kg for M-pNIPA and M_S=43 A m^2 /kg for M-pNIPA-pAAc, which are somewhat lower than the values measured for NPC, due to the influence of polymer coating. [13]

A. Rodzinski et al used magnetoelectric nanoparticles (MENs) to control drug delivery and release. The physics is due to electric-field interactions (i) between MENs and a drug and (ii) between drug-loaded MENs and cells. MENs distinguish cancer cells from normal cells through the membrane's electric properties; cancer cells have a significantly smaller threshold field to induce electroporation. In vitro and in vivo studies (nude mice with SKOV-3 xenografts) showed that (i) drug (paclitaxel

(PTX)) could be attached to MENs (30-nm $CoFe_2O_4$@$BaTiO_3$ nanostructures) through surface functionalization to avoid its premature release, (ii) drug-loaded MENs could be delivered into cancer cells via application of a d.c. field (~100Oe), and (iii) the drug could be released off MENs on demand via application of an a.c. field (~50Oe, 100Hz). MENs and control ferromagnetic and polymer nanoparticles conjugated with HER2-neu antibodies, all loaded with PTX were weekly administrated intravenously. Only the mice treated with PTX-loaded MENs (15/200μg) in a field for three months were completely cured, as confirmed through infrared imaging and post-euthanasia histology studies via energy-dispersive spectroscopy and immunohistochemistry. A room-temperature Lakeshore vibrating sample magnetometer (VSM) with a 3-T magnetic field sweep was used to measure key magnetic properties of nanoparticles under study including the magnetization saturation and the magnetic coercivity. Vibrating sample magnetometry (VSM) hysteresis loops curve obtained for 30-nm MENs and 30-nm CoFe2O4 ferromagnetic nanoparticles (FNs). FNs were used as control nanoparticles with a relatively strong saturation magnetization (40 times higher than that for MENs (~1 emu/g)) but displayed no ME effect. This difference between MENs and the control FNs helps understand the different roles of electric and magnetic fields in the studied delivery mechanism. [14]

B Saif et al. Morin (MR) is an anticancer drug present in fruits and Chinese herbs. Fe_3O_4 magnetic nanoparticles (MNPs) coated on 3-aminopropyl triethoxysilane (APTES) were synthesized (MNPs-APTES) as carriers for MR. The characterization of drug delivery system was confirmed by Fourier Transform Infrared (FTIR), Transmission Electron Microscope (TEM), X-Ray Diffraction (XRD), dynamic light scattering (DLS), and vibrating sample magnetometer (VSM). The magnetic properties were investigated with vibrating sample magnetometer (VSM, Lakeshore). The S-shape of MNPs-APTES exhibited zero coercivity and permanence indicating its superparamagnetism with a saturation magnetization (Ms) value 41.5 emu/g, which can be ascribed to the existence of APTES on surface of MNPs. Therefore, This MNPs-APTES having magnetic response could be carry drugs to targeted locations under an external magnetic field. The determined magnetic separation time is about 15 s. [15]

Wu et al. reported the synthesis of a hybrid nanocomposite material composed of Ru(bpy)-doped silica core–shell NPs and Pas (organic chromphore)–DTPA (chelate), through an water in-oil micro emulsion method. The magnetic characteristics of the synthesized NPs were studied by using a vibrating sample magnetometer (VSM). The saturation magnetization values of silica-coated and silica-free NPs were found to be 5.3 emu/g and 8.4 emu/g, respectively, whereas that of ferrofluid magnetic NPs were found to be 65 emu/g. [16]

Subbarayan Shanmugavel et al reported Synthesize of polystyrene nanoparticle by using Pickering emulsion Polymerization method without using surfactant. Designing of a magnetic nano core /shell assembly by using polystyrene nanoparticles as templates in which chitosan polymer as shell material and a hydrophilic anticancer drug (Methotrexate and Melphalan) are loaded into the core. Surface coating of the designed core/shell assembly with polyelectrolyte (sodium alginate). Step by step characterization in the experiment to conform the chemical reactions involved in each step. Magnetic property was evaluated by vibrating sample magnetometer which gives a hysteresis loop with magnetization value 50emu/g indicates that the super paramagnetic nature of the formulation. [17]

Márquez et al reported Hollow magnetite microspheres synthesis by a simple process through a template-free hydrothermal approach. Hollow microspheres were surface modified by coating with a silica nanolayer. Pristine and modified hollow microparticles were characterized by field-emission electron microscopy, transmission electron microscopy, X-ray diffraction, X-ray photoelectron spectroscopy, FT-IR and Raman spectroscopy, and VSM magnetometry. The variation in magnetization and coercivity of the hollow magnetite samples was determined by using a Lake Shore-7400 vibrating sample magnetometer (VSM) (Lake Shore Cryotronics Inc, Westerville, OH, USA) at room-temperature. The magnetic properties of the synthesized materials were also investigated by VSM magnetometry under room temperature conditions. The corresponding hysteresis loops in the -30 + 30 kOe range. The saturation magnetization (Ms) values were 69.6 emu g^{-1} (hollow magnetite) and 13.7 emu g^{-1} (SiO2hollow magnetite). The observed saturation of the magnetization profiles and the lack of coercivity and remanence were expected for ferrimagnetic magnetite particles. The difference in Ms observed when hollow spheres are coated by silica can be attributed to the non-magnetic contribution of diamagnetic silica onto the magnetite surface. However, specific interactions between the silica surface layer and the magnetite nanoparticles forming the hollow structure could not be ruled out at present. More detailed investigations concerning this deleterious effect of silica on the magnetization of the hollow structures are currently in progress. The absence of coercivity in the hollow magnetite structures could also suggest a super paramagnetic behavior that could be ascribed to the fact that magnetite microspheres are built by

many small nanoparticles. [19]

Sedighe Arabi et al prepared a modified amphiphilic polymer with targeting susceptibility to reduce side effects to normal cells. Polyethyleneimine (PEI) as a polycationic polymer reacted with sebacoyl chloride to make a new amphiphilic polymer and folic acid as a targeting agent to reduce cytotoxicity of polymer and increase specific entrance of nanoparticles to cancerous cells. Curcumin was loaded on (PEI-SbFA-MNPs) and the release behavior was studied. The VSM was applied to measure the magnetic properties of nanoparticles. The nanoparticles display saturation magnetization equal to 57.09 and 51.4 for Fe_3O_4 and modified PEI-Fe_3O_4 emu/g. Saturation magnetization amount of FA-PEISb-MNPs has a lower amount than the Fe_3O_4 that it is attributed to the modified polymer on the surface of nanoparticles. Paramagnetic behavior can prevent the aggregation of particles and make them suitable for use in the pharmaceutical field.[21]

Conclusion:

Seen in the broader historical perspective, it is the intimate connection between discovery and practical use which causes most of the magic of magnetism, and it is certainly illustrative for the magic of science in general.In recent years, the preparation of multi-functional magnetic target drug delivery system has become a new hotspot of cancer treatment to achieve its excellent magnetic response, drug activity and targeted tracing, etc

Vibrating Sample Magnetometry (VSM) is a measurement technique to determine the magnetic moment of a sample with very high precision and to characterize ferromagnetic samples.

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