

APPLICATIONS OF NANOFLUIDICS IN DRUG DELIVERY SCIENCE AND TECHNOLOGY

Abstract

Clinical trials and some types of biomedical research have found a wide range of applications for suspensions of different nanoparticles or nanocomposites recently. The term “nanofluid” refers to these useful suspensions that let the nanoparticles spread and behave in uniform, stable environments. The benefits of nanofluids in various biological applications have been highlighted in a number of research works. Reviewed studies that provide a summary of the many biological uses of nanofluids, including diagnostic and therapeutic applications, are rare. Since nanosuspensions are nanofluids containing solid particles, they are the main topic of this review. Nanosuspension is the primary form of nanofluid and finds extensive use. Hence, this work provides succinct information regarding the main biological uses of nanofluids in drug delivery systems, imaging, and antibacterial activity. In order to target medication administration, diagnose hyperthermia, and make differential diagnoses, for instance, magnetic nanofluid systems are a valuable tool. To combat the resistance to antibiotics, nanofluids may also be employed as a possible antibacterial agent. Providing new and practical strategies for success in modern medicine might be a benefit of this study.

Keywords: Biological application, nanofluid, diagnosis, therapy, drug delivery, antibacterial activity.

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I. INTRODUCTION

Researchers have been creating unique gadgets since the nanofabrication industry first emerged, utilising the exact characteristics which may produce at such a little size. Particularly, movable objects fabricated within the nano scale using nanofabrication processes may make it possible to analyse, distinct, focus, control, and find biomolecules accompanied by more sensitivity, capacity, and convenience compared with better “classical” or traditional approaches. Furthermore, within the nanoscale, electrical fields may utilise for accelerate motion, concentrated biomolecules, and have an impact on transportation as well as separation of biological mixtures, unique DNA sequencing, influence molecular reactions and hybridizations, provide for innovative biomolecule detection techniques, and so on. Some fundamental nanoscale phenomena, such as entropy, sterics, electrostatics, electrostatics, and adsorption dynamics, as well as frequently the coupling of two or more of these phenomena, enable the realisation of these kinds of applications.^[1] Microfluidics research and the creation of related technologies, like the micro pump and micro valve, have been ongoing for more than 20 years.^[2] This field of study, which has its roots in university laboratories, has looked at how fluids behave between the micron and sub-micron sizes; discovered and characterised unusual natural behaviours that differ from the usually accepted behaviours and attributes of bulk fluids in mass. The kind of liquid used along with the average fluid molecule free route is the two factors that most significantly affect how fluids behave between the micron and sub-micron size gadgets. For instance, slip-free velocity model may still be used to analyse microscale liquid flow even while slip-free velocity near a channel barrier cannot be employed.^[3-7] Additionally, traditional Navier-Stokes modelling and analysis have shown to be quite successful for microscale liquid flow. Although viscous factors predominate the behaviour of liquids at this size, the normal bulk fluid viscosity is still true.^[8,9] These minute geometries, like microchannels and microtubes, can produce specific flow profiles and thermodynamic behaviours according to the liquid or gas kind of fluid. According to official definitions, nanofluidics is an analysis of fluid behaviour, stratagems, and power in apparatuses with a minimum of one dimension smaller beyond 100 nm. The use of nanofibers and nanoparticles in materials has enabled the achievement of unique features, and distinctive scale based fluid impacts including tiny gadgets provide evidence of fluid flow.^[10] Because its term was first introduced in 1995 as a counterpart to the field of microfluidics, that had only just gained scientific recognition approximately five years ago, nanofluidics is sometimes viewed as a young field of study.^[11] One can observe a collapse in continuous appropriateness as well as consequently traditional Navier-Stokes model in nanoscale fluidics.^[12,13] At this stage, the molecule size cannot be regarded as endlessly tiny in relation to stream (i.e., large parameters like viscosity and density begin to geometries variation).^[14,15] Fluids have particular physical behaviours due to this dimension’s constraints that are absent in bigger structures. New features of the fluid are present in some regions that are not seen during bulk flow, for instance enhanced the viscosity close to porous wall^[16] including the influence of thermodynamic features^[17,18]. Micro and nanofluidics is a subject of study that is becoming more popular since recently improvements to micro and nanofabrication. The layout and deployment of such devices have become significant due to the growth in the value of micro and nanofluidics research that has entered the business world. Fuel cells^[19], inkjet print heads^[20], and instruments for dissociation, investigation, and observation are all examples of products that use micro- and nanofluidics technology^[21-22]. Nanofluidic phenomena, however, have previously been investigated and employed in amazing detail for a century, in fields like dispersion sciences; barrier chemistry; both physical and colloidal chemistry; fluid dynamics; despite the fact that its term only first

emerged in the 1990s.^[23] The distinct scientific topic of nanofluidics did not emerge until micromachining techniques began to be applied in this area, and its emergence was entirely analogous to that of microfluidics. Thus, just as associated with disciplines among MEMS and NEMS, these disciplines are founded on the broad use of technical advancements achieved throughout 1960s and 1970s in the sector of microelectronics.^[24]

II. CHARACTERIZATION OF NANOFLUIDS

Compared to the basic fluid, nanofluids often exhibit improved thermal characteristics. The characteristics and thermal behaviour of nanofluids have been measured using a variety of methods in attempt to quantify this difference. Other features, like as shape, stability, both consistency and the dispersion of particle sizes are also very significant while evaluating the nanofluid's efficiency in addition to its thermal properties.^[25]

Transient plane source (TPS) theory is the foundation example of techniques used for gauge the thermal conductivity of nanofluids. The Fourier's Law of heat conduction is applied as the framework that the technique follows while detecting thermal conductivity, which uses the Transient plane source element as both a temperature sensor and a heat source. This innovative approach has various benefits, including quick and simple studies, significant variations in thermal conductivity (ranging from 0.02 to 200 W/mK), nothing more sample arrangement is required, as well as sample size variability.^[26, 27] Another technique used to gauge the heating capacity of sample nanofluids is the transient hot-wire (THW). As in approach, a continuous flow of current applied to wire, including the heat efficiency is determined by comparing the rate at which the wire's temperature changes over time.^[28, 29] To assess the thermal efficiency of a system conducting a method for transferring heat via nanofluid, the coefficient of convective heat transfer is also measured. Experimental measurements of the transmission of heat increase of nanofluid flow within vertical helically coiled tubes at thermal entrance area were made.^[30] Using an experimental setup, examined the laminar convective heat transfer of (Al₂O₃-Cu)/water nanofluid. This experimental setup included a test section, pump, cooling system, and fluid reservoir. The use of nanofluids increases the heat transfer coefficient in all of the documented scenarios.^[31] Sedimentation balance, pH, and zeta potential are all utilised in order to draw conclusions about the crucial aspect of nanofluid stability. However, zeta potential analysis is now the most often used technique to assess stability.^[32-34] Zeta potential has value since it may be utilised to determine the degree of stability of the colloidal dispersions. As a result, colloids having high zeta potentials, either positive or negative, are electrically stabilised, whereas colloids having low zeta potentials have a propensity to flocculate.^[35] Molecular shape and structure of nanofluids are revealed through their morphology. The usage of field-emitting scanning electron microscopy and transmission electron microscopy in many investigations to characterise the micro structural characteristics (size and shape) of nanoparticles such as ZnO, TiO₂, Al, Mg, Al₂O₃ and Au suspended in nanofluids.^[33, 36-39] The crystallite size and the phase composition of powders have both measured by the utilising of X-ray diffraction (XRD).^[40]

It is possible to specify the ideal formulation from family of nanofluids by measuring the size range of nanoparticles. Using by dynamic light scattering (DLS) method, it is possible to establish the particle size range of newly created alumina and TiO₂ nanofluids.^[37, 38, 41] A particle counter using electrophoretic light scattering (ELS) was used to measure the size distribution of silver and carbon black (CB) nanoparticles floating in nanofluids.^[42] An

electron diffractometer (ED) was utilised to establish the size range of gold nanoparticles.^[32] Al₂O₃ nanoparticles floating in the nanofluid have been characterised by their analysed using a particle size analyser attached to an X-ray disc centrifuge.^[26] Last but not least, the Scherrer equation was utilised to establish the average grain size of the hybrid Al₂O₃-Cu nanoparticles floating in a nanofluid.^[31]

III. APPLICATIONS IN DRUG DELIVERY

Several industrial uses, including delivery, gadgets, biological medicine, food production, and heat exchangers, nanofluids -emulsions or suspensions of nanoparticles in fluids allows utilised for the directly accelerate heat transmission.^[43] Since nanofluids are increasingly being used in nano biomedical technology, their physicochemical properties differ dramatically from those of their solid counterparts. Recent biomedical uses of nanofluids including medication transportation and antibacterial remedies.^[44] Nanofluid-based combination systems imaging, and diagnosis (such as medication administration imaging, high fever imaging), or multimodal imaging (such as optical and MR imaging and PET and MR imaging) are some examples.^[45] One of the best including safest usage of nanofluids must meet a few fundamental requirements. These requirements precisely describe the content, size-range, crystallinity, and form. Additional essential qualities include stability, non-agglomeration, and biocompatibility.^[46] The manufacture of nanomaterials, physical mixing, ultrasonic homogenization, surface engineering, usage of the surfactants including other chemical additives are some of the processes that may be considered in order to get a stable nanofluid.^[47] Additionally, it is necessary to take into account the legality and medical safety of these additives. The material, surface science, and colloid theory have been the main foci of investigations on nanofluids. Consequently, several aspects of nano-based systems have been improved. However, in practise, nanofluid applications in the biomedical field are far from straightforward and need for more research.^[48-50]

1. Uses for Drug Delivery: To release the medicine in a regulated manner at the intended spot is the intended use of a medication delivery mechanism. Drug release kinetics, polymers, pH and temperature sensitivity, nasal administration, and oral medication delivery were the main topics of the initial study into medication delivery techniques.^[51] The utilisation of nanomaterial in medication delivery systems is one of the topics that has drawn the interest of many academics in recent years. This practise is thought to have several advantages, including the ability to deliver drugs precisely to their target cells, the improvement of security and healing capabilities, a reduction in toxicity, as well as biocompatibility.^[52] In order to produce a nanofluid formulation for the medication administration, the mechanism needs properties for drug filling and discharge, a long shelf life, and biocompatibility.^[53] The charge of nanoparticles in fluid is one of the key factors in nanofluidic medicines. The inside borders of blood arteries are polarised adversely, and surface charge of the basic biological components found in blood is virtually negative. Thus, they oppose one another, preventing blood cells from accumulating in channels. Therefore, in order to prevent aggravation, the therapeutic particles often need to be negatively charged.^[54]

A key defence mechanism for macrophages against external invaders including bacteria and viruses is opsonization, a process carried out by the opsonin proteins. The bioavailability of medications in nano-colloidal form can reduce in the case of nano-drug delivery carriers, which is an issue. Numerous solutions have offered, and considerable

effort has put into overcoming these restrictions. The most popular technique is the adsorption of polyethylene glycol (PEG) on nanoparticles.^[55] Another component preventing opsonization of the nanoparticle is negatively charged albumin.^[56] During preclinical and clinical studies, a number of colloidal medication delivery systems of analgesic medication possesses acceptably effective performance.^[57, 58]

- 2. Magnetised Drug Delivery:** Magnetic nanoparticles are one of the many forms of nanoparticles that have attracted attention as medication carriers. This issue is brought on by the management, tiny size, as well as surface quality of magnetic nanoparticles, in order to direct the carrier to appropriate position by a magnetic field. Blood is used to make the primary fluid in the magnetic drug delivery, whereas the drug is transported by magnetic nanoparticles. The drug-filled magnetic nanoparticles are able to be supplied near to cancer, where tumour can soak up it, because of the potent and concentrated magnetic gradient. The negative effects of chemotherapy are lessened by employing this technique. This approach also has the benefit of allowing for the use of bigger anticancer medication dosages in the absence of endangering whole some supporting tissues.^[59-61]

By utilising magnetic nanoparticles, that includes putting a magnet next to tumour as well as providing the drug to tumour towards the blood vessels that are closest to the tumour, a notable example of efficient ways to treat cancer. These nanoparticles behaviour might be affected by the waves' peristaltic motion, generated in the asymmetrical, cone-like channel surfaces. Assessing the nanofluid flow which is impacted by this type of motion can help eradicate malignant tissues far more successfully.^[60] Remarkably common magnetic nanoparticle utilised in medical purposes for magnetic medication delivery is super paramagnetic iron oxide (SPIO). Numerous SPIO uses in cancer screening, diagnosis, and treatment have been discussed in recent publications.^[62] A research was also conducted on the green biological production of super paramagnetic magnetite Fe_3O_4 nanoparticles and their significance in biomedicine as targeted anticancer medication transportation systems. Additionally, certain cases of Fe_3O_4 -based nanoparticles being used as a cancer prevention medication carrier to treat various carcinoma cell lines with cancer prevention medications becomes documented in recent years.^[63] In addition, a recent study in 2018 found that multifunctional magnetic nanoparticles (Fe_3O_4) coupled among chlorin e6 and folic acid had increased photodynamic anticancer effects in the prostate as well as breast cancer cells.^[64] The iron oxide core of SPIOs is encased in a hydrophilic group-containing shell that promotes solubility. Fatty acids, organic polymers, or polysaccharides are frequently used as the shell.^[65] In a trial, the medication (curcumin) was placed inside a hollow made of modified cyclodextrin. One of the well-known cancer treatments is curcumin, however due to its poor solubility in water, it needs to be administered through a carrier in order to reach the intended tissue.^[66] A modified carrier that works well for hydrophilic medicines is cyclodextrin.^[67] The pH-sensitive medication delivery magnetic nanoparticles, which act as theragnostic nano-transporters and discharge the chemotherapy medication doxorubicin when cancer cells are acidic, were produced in an intriguing therapeutic dosage research. Magnetic resonance imaging (MRI) might be used to monitor the medication release kinetics of pH-sensitive medication delivery magnetic nanoparticles as well as pattern of nanoparticle accumulating within tumour cells to aid in the optimisation of medication dosage regimens.^[68] Therefore, the results of these insightful investigations might be applied to develop smart drug delivery systems that increase the efficacy of medications while lowering their negative effects.^[69]

- 3. Microelectromechanical Bio-Systems Utilisation:** Researchers looked at ways to transmit and control the flow while using micro fluidic technology. In order to distribute fluids with extreme accuracy, micro fluidic equipment frequently includes parts like pumps, valves, mixing devices, activating agents, filtration systems, or heat transfer devices. Nano-drug transport devices can be used, for example, to speed up the drug development process or to keep track of how target cells react to drug stimuli.^[59, 70,71-75] The nanoparticles are in an aqueous solution in this instance, and both the solvent temperature and particle concentration are preset. These micro channels are used to transfer the nanofluids to the living cells. The testing of pharmaceuticals and carrying out high-efficiency biological studies are only two examples of the various uses for this micro fluidic gadget.^[70-74] The solution or cleaning fluid is kept in a reservoir. By modifying their internal pressure or resistance, the little passage ways might alter volume of the fluid that enters experiment location. A homogeneous nanomedicine concentration upon little passageways output is key objective. The fluid-drug combination is given to cellular life at a certain degree that is optimal (37°C), thanks to the existence of an adequate heat flow from the bottom little passageways. Both the cleaning fluids and the nanofluid's velocities have an impact on how much heat is transferred. Additionally, the homogeneity of the drug's concentration is improved by the existence of this heat flux. The length of the channel, the size of the nanoparticles, Reynolds number associated with the nanofluid's origin, as well as primary little passageways are a few variables that, in general, have an impact on the consistency of nano-drug's content.^[76]
- 4. Nanocrystals and Nanoparticles:** Drug-nanoparticles without any additional joined molecules are known as nanocrystals. Suspension is a nanocrystal nanofluid. In water, or a different solvent is used stabilised with surfactant or stabiliser, of poorly soluble medication (in the majority of instances). Rapamycin, Aprepitant, Fenofibrate, and Megestrol are just a few of nanocrystal medications that are readily available on the market. The solubility enhancement, improved dissolving speed, excellent bioavailability, ease of use, and saturation solubility of nanocrystals are their key benefits.^[77] The finest ZnO nanoparticles as well as their pairings used for nanobiotechnology and nanomedicine. The correct state of the electrons in the nanoparticle's valence-shell (with big bundles) is what's causing this problem. The ZnO nanoparticles might be employed in the treatment of cancers like breast cancer owing to their biological characteristics (UV protection, antibacterial properties, and minimal toxicity).^[78] Studies have looked on cytotoxic properties of zinc oxide nanoparticles on hepatoma cells. Additionally, it was demonstrated that ZnO further harmed the cancer cells' rapid cell division.^[79-81] A study looked at the harmful impacts of two different forms of the ZnO nanoparticles on development of the MCF-7 cell ancestry in breast cancer. According to findings of study, the likelihood of breast cancer MCF-7 cellular lines dropped when ZnO NP concentrations were raised after 48 and 72 hours of treatment.^[80] By fusing both thyroid-stimulating hormone and thyroid-specific antibodies to multi-walled carbon nanotubes (CNTs), Dotan *et. al.*, created a nanofluid platform. With little cytotoxic impact on untargeted cells, the nanofluid in vitro specifically targeted and destroyed the papillary thyroid cancer cells.^[82]

IV. APPLICATIONS IN HEALTHCARE

1. Hyperthermia Method: Cancer can be treated with hyperthermia. The Greek terms for increase and heat, respectively, “hyper” and “thermia,” are the source of the English word “Hyperthermia.”^[83] According to research, heating in the (41 to 46) °C range at the least (20–60) mins stop cancer cells from multiplying.^[84, 85] The unequal heat distribution of the tumour mass including the in capable of stopping rooted tumours from overheating are two flaws in the hyperthermia method. So, in response to the requirement for a suitable solution to solve these issues, scientists have proposed magnetic nanoparticles. This technique, known as MNFHT (magnetic nanofluid hyperthermia treatment), allows for the uniform delivery of heat with the use of magnetic nanoparticles. Temperature control and thermal dispersion are both essential during this therapy strategy.^[86, 87]

The specific absorption rate, whose unit is W/kg, has been used to represent the distribution of energy.^[73] A large number of temperature monitors inserted within agarose gel were employed to determine that value, which demonstrates capacity of the magnetic nanoparticles to eliminate cancerous cells. In a research, mobility of the nanofluids through extracellular tissue was investigated by injecting them into an agarose gel.^[87] Agarose gel was utilised like a tissue analogue during *in-vitro* portion of this study.^[88] It was determined that in the event a gel's nanofluid dispersion was sphere-like, the study's objective of providing a mechanism for controlled tumour heating could be accomplished. The repeated injection technique has been suggested to create a consistent increase in tumour temperature in tumours with unique geometrical features.^[87] The findings show that nanoparticles' cubic shape exhibits greater specific absorption rate than their conical shape, sphere, rod, triangle, and polyhedron forms.^[88]

A few factors that impact the specific absorption rate measurements including temperature, rate of magnetic field changes, magnetic field intensity, size, and form of the nanoparticles.^[84,88] One of the crucial factors affecting magnetic nanoparticles' efficacy is their dimension. The ultra-paramagnetic (ultra-magnetic) modes of nanoparticles, improved specific absorption rate, increased heat distribution, and avoided agglomeration are a few advantages of their tiny size. Despite such advantages, they would perform worse if the nanoparticle size was smaller than typical (2–5 nm).^[88] Due to their ability to produce a substantial amount of heat and exhibit low-frequency fluctuation, super paramagnetic nanoparticles (10 to 40 nm in size) were found to be useful for therapeutic applications in 2005.^[89]

2. Hyperthermia of Magnetic Fluid: By utilising magnetic nanoparticles and an external magnetic field, magnetic fluid hyperthermia involves selectively heating the targeted tissue.^[52] Employing magnetic nanoparticles, in their 2008 study using laboratory mice used for experimentation, Salloum *et. al.*, looked at the degree of temperature rise within animal tissues following hyperthermia. The two most important variables in the investigation's discussion of magnetic hyperthermia were the pace of blood perfusion and the amount of nanofluid given to tissue.^[87]

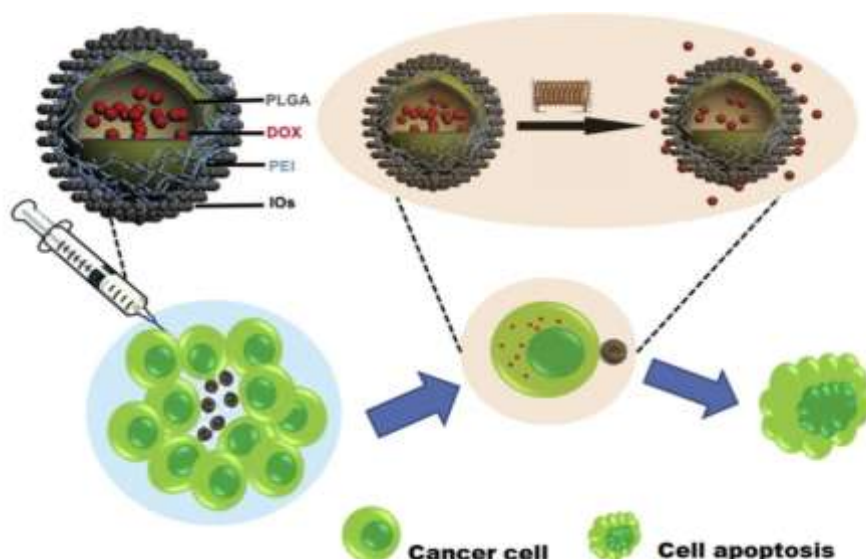


Figure 1: Illustration of the Magnetic PLGA Porous Microspheres ‘Responding to Change the Magnetic Field.’^[92]

Cancer cells may be treated with carbon nanotubes (CNTs) when a magnetic field is present. In the associated research studies, blood vessels that are near to the tumour are injected with nanoparticles. And a magnet is implanted there as well.^[90,91] In order to prevent the growth of breast cancer tumours, magnetic PLGA, or poly (lactic-co-glycolic acid), microspheres packed with doxorubicin are developed..^[92]

- 3. Nano-Cryosurgery:** Cryosurgery is one of the most effective techniques for totally removing and managing cancer cells. Liquid nitrogen and solid carbon dioxide are both also employed in this method. When the temperature is so low that ice crystals start to form, the target cell’s membrane may break because there is less liquid water available (dehydration).^[74,93] However, there are several drawbacks with using this procedure, such as incorrect freezing, that may cause damage to the tissues on the healthy side. To greater degree of freezing capability, highly-conductive nanoparticles are loaded with tumour tissue.^[73,74,93] A number of studies have looked at the toxicity of nanoparticles and how they affect healthy tissues. Al_2O_3 , Fe_3O_4 , and Au nanoparticles have been proven to be physiologically acceptable and have the potential to be widely employed in medical applications thanks to these findings.^[66,67,75,76] Additionally, it has been demonstrated that Au nanoparticles, out of all commonly used nanoparticle kinds, have the best freezing efficiency and can make the biggest ice balls. The presence of nanoparticles may influence the range as well as development of frozen crystals, which are created during the process of freezing, in addition to speeding up the freezing rate. The surrounding healthy tissues are not significantly harmed as a result of the eradication of unwanted malignant tissues caused by this feature.^[74] Distinct nanoparticle solution types and doses may have distinct impacts on the method of freezing and produce varying freezing efficiencies. Determining the best nanoparticles to use and adjusting the nanoparticle suspension dosage would therefore be critical concerns for next research projects.^[94]

4. **Treatment of Anaemia Using Magnetic Nanofluids:** Stability at fluid interface is one of the prerequisites for hiring is the ability to operate magnetic iron oxide nanoparticles for use in healthcare.^[81] Vazhnichaya *et. al.*, investigation from 2015 uncovered a sustained magnetic nanoparticle-nanofluid containing features that prevent anaemia. Both Mexidol (2-ethyl-6-methyl-3-hydroxy pyridine succinate) and PVP (polyvinyl pyrrolidone) were employed to preserve those nanoparticles. Then, after severe loss of blood, they assessed the objects using 109 male albino mice employed as test subjects under both suitable settings. The results of investigation show the nanofluid encouraged animals in good health to produce more red blood cells (RBCs), haemoglobin, including haematocrit. Recovery from severe anaemia-causing blood loss is aided by a nanofluid, which also increases the number of reticulocytes. In intact animals, this nanofluid increases erythropoiesis and turns on the regenerative blood loss causes an erythron response in anaemic patients.^[95]
5. **Ablation via Radio-Frequency:** The intended tissue becomes heated up substantially using radio waves with short wavelengths (350–500 kHz) during the medical process referred to as radio frequency ablation (RFA). In reality, this method involves inserting an ablation electrode through the tumour's tissue, where the waves that helps electrodes to generate raise the temperatures. The surrounding tissue, which is often tumour tissue, would subsequently be heated, resulting in tissue destruction. If enough heat were being supplied, the cancer tissue will disappear swiftly.^[96,97] In research, the radio frequency ablation approach accustomed to look at the applicability of iron nanoparticles (iron nanoparticles accompanied by carbon surfacing). The results of investigation show, the usage of nanofluid, thermal conductivity improved approximately 41%.^[97]

V. APPLICATIONS FOR DIAGNOSIS

1. **Imaging:** Utilising nanomaterials for magnetic resonance imaging (MRI) is among the most intriguing diagnostic medical uses of these technologies. The contrast and sensitivity of magnetic resonance imaging are enhanced when magnetised nanoparticles are used (Figure 2). Super paramagnetic nanoparticles are among the best solutions for enhancing contrast in magnetic resonance imaging. Iron oxides, gold, including gadolinium nanoparticles are some examples of potential components for such compounds.^[98] The super paramagnetic nanoparticles composed of a colloiddally stable polymeric framework containing an iron oxide centre. The centre may also comprise Fe and Mn combined. Both the European Medicines Agency (EMA) and the US Food and Drug Administration (FDA) have endorsed a number of injectable magnetic contrast agents. Magnetic resonance imaging typically employs gadolinium-based contrast materials.^[99] There are certain restrictions on the use of gadolinium because of toxicity worries, particularly in individuals with renal insufficiency.^[98]

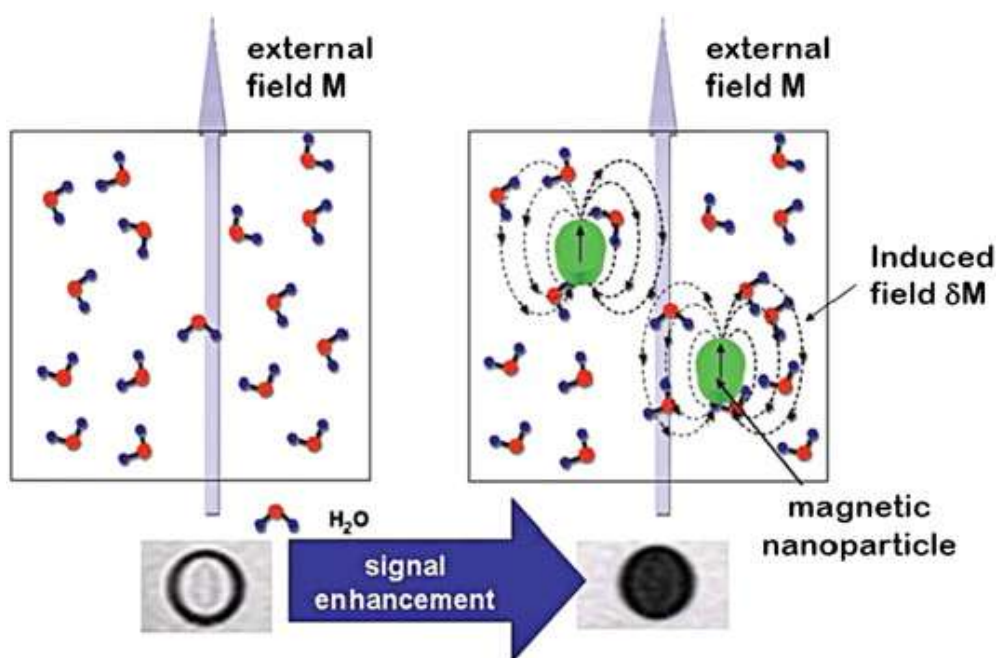


Figure 2: Magnetic Nanoparticles in the Water Produce a Magnetic Contrast Effect that Makes the Magnetic Resonance Picture Appear Darker.^[98]

The cellular fluids outside of cells (also referred to as intravenous contrast substances), the intravascular contrast agents (also referred to as blood pool contrast substances), and contrast materials used in magnetic resonance imaging may all be divided into three categories. The target-specific agents and the general agents. In addition to formulations created for intravenous injection, several magnetic resonance imaging contrast agents are given orally.^[100,101] Important and significant aspects are the contrast media's safety and toleration. The body's quality contrast agent needs to be totally and completely eliminated with no any side effects and must be physiologically and chemically inert.^[102,103] There are several of these contrast agents on the market, and they are often utilised.^[104,105] The concentration of agents at the target locations increases as a result of the focusing contrast agents. A greater concentration of contrast substances at the intended place is detected by the focused magnetic resonance imaging, which results in a precise diagnosis. On the target organ, focusing substances often bind with tissue-specific antibodies. The liver has been imaged using the overwhelming majority of contrast substances with a target.^[106] Both liposome-based targeted contrast agents and super paramagnetic iron oxide are offered for sale commercially.^[107] During the context, Fe₃O₄O-dextran nanoparticles (Fe₃O₄ having a dextran covering that is oxidised) have been utilised to create contrast in magnetic resonance imaging. These nanoparticles are highly stable, don't cause a lot of cytotoxicity, with great biocompatibility as well as having biological conjugation.^[108] Magnetic resonance imaging pictures of cancer cells provided with Fe₃O₄O-dextran nanoparticles (given antibody titers) at various amounts were shown by a study. The picture of cancerous cells darkened as the iron concentration rose from 0.75 mM to 1.15 mM, providing evidence that the presence of nanoparticles upgrade magnetic resonance imaging contrast. Furthermore, the pictures from NP5 to NP15 were darker creasing the central area of nanoparticles while maintaining the concentration. With and without antibodies were used to take the photos in two different ways. Additionally useful for magnetic hyperthermia, high-performance magnetic bio-

separation, and drug delivery approaches, these nanofluids can also be used in these fields.^[109]

- 2. Uses for Antibacterial Agents:** Every day, new disease strains with increased resistance appear as a result of overusing the conventional antibacterial agents. As a result, it appears that the creation of novel approaches to the management of diseases with a high level of resistance is required. The capacity to suspend both organic as well as inorganic various nanoparticles have demonstrated the characteristics that fight bacteria during the past few years.^[110]
- 3. Metal and Metal-oxide Nanofluids:** In the business, bacterial inhibitors are crucial for food packaging, medical uses, textile manufacturing, and water disinfection.^[111-113] Zinc oxide (ZnO), an example of numerous kinds of the metal-oxide nanoparticles, has a notable effective antimicrobial characteristics that work against different microbes.^[113,114] Among various nanofluids, zinc oxide nanofluids which are secure for human cells to survive the subject of most research.^[115] Numerous elements of zinc oxide hazards (the bacterial cell wall is damaged by these nanoparticles.) have been discovered according to morphological investigations on the zinc oxide-treated bacterial cell wall seen by SEM and FESEM. Reactive oxygen species are produced. The production of antibacterial ions, mostly Zn^{2+} , and reactive oxygen species are two further features of the zinc oxide toxicity.^[116] The stability of zinc oxide nanofluids has been increased by using dispersants such sodium silicate, sodium carbonate, or polyethylene glycol (PEG), as well as deflocculants.^[116,117] Furthermore, ZnO_2 and TiO_2 and SiO_2 nanoparticles both possess antimicrobial properties. When compared to TiO_2 and SiO_2 , Zinc Oxide has stronger antibacterial capabilities.^[113] Reactive oxygen species are generated and have a greater antibacterial action as a result of UV illumination. The three nanoparticles mentioned above are light responsive, and titanium di-oxide is currently utilised in the water purification techniques.^[118] Magnesium oxide and $Mg(OH)_2$ nanostructures have also received a lot of interest over the years because of their usage across the pharmaceutical sector.^[119] On *E. coli*, *B. phytofirmans*, several additional bacteria, $Mg(OH)_2$ nanoparticles have been shown to have a considerable antibacterial impact.^[120] When OH ions build up in cells of bacteria, the pH value rises to 10, that kills a bacteria. This is fundamentally different from how metal-based chemicals work in terms of their antibacterial properties. Additionally, magnesium oxide nanoparticle works well as a bactericidal agent against *Salmonella Stanley* and *E. coli*, two common food borne bacteria.^[121] It is possible that reactive oxygen species generation and oxidative stress are not necessary for the Magnesium oxide nanofluid to be harmful to *E. coli*. Therefore, they came up with a fresh hypothesis on cellular membrane deterioration unaffected by lipid peroxidation is a component of the magnesium oxide toxicity process.^[122]

A variety of gram-positive as well as gram-negative bacteria have shown to be resistant to copper and copper oxide nanoparticles' antibacterial properties.^[123-126] The size of nanoparticles and the temperature at which they were created both affect the antibacterial activity. More antibacterial activity is attained when the copper oxide nanoparticles are smaller. The bacterial cell wall may be traversed by the copper oxide nanoparticles.^[126] It is hypothesised that these nanoparticles attach to cellular enzymes and inhibit a cell's essential functions.^[124,127] The copper oxide nanoparticles do not significantly cause cytotoxicity in HeLa cell strains.^[124] Accordingly, it seems like copper nanoparticles unable to interact with eukaryotic cells through cytoplasmic

membrane. For millennia, people have used silver and its derivatives to treat burns, scalds, and to clean water. The usage of compounds based on silver has decreased as a result of the creation of new kinds of antibiotics. The use of silver nanoparticles as an antibacterial agent has gained significant interest in recent decades with the development of nanotechnology.^[128] Numerous studies have been done on the toxicity of silver due to its cytotoxicity, environmental toxicity, and potential negative impacts. Silver nanoparticles can induce toxicity in a wide variety of ways, but the main one is that they can interfere with mitochondrial function by altering how permeable the membrane around the mitochondria is. Aside from that, the creation of reactive oxygen species by silver nanoparticles causes inflammatory reactions.^[129] It appears improbable that resistant strains would arise given the wide variety of toxicity mechanisms that silver employs.^[130] Additionally, gold nanoparticles are recognised to be biologically compatible and substantially decreased cytotoxicity of nanostructured with a wide variety of applications. The creation of reactive oxygen species has no bearing on bactericidal activity of the gold nanoparticles. The bactericidal action of gold nanoparticles is often dependent on two mechanisms: suppression of the RNA bound to the ribosome and reduction of ATP generation with modifying cellular activity.^[131]

The aforementioned justifications point out that metallic nanoparticles have a few drawbacks in biomedical applications, like stability, biocompatibility challenges, including appropriate physical removal from human body. The solubility issues are crucial for metal as well as metallic oxide nanoparticles. The toxicity that has been noticed is related to the discharge of metal ions from dissolved nanoparticles. The type and structures of nanoparticles are strongly correlated with their biological properties. In order to boost their biocompatibility and minimise their toxic effects, it is important to take into account alterations to them, like surface alteration and artificially controlled size including form.

- 4. Blended Nanoparticles:** Other research combined zinc oxide and iron oxide to create combination magnetic nanoparticles with enhanced colloidal stability and adequate antibacterial properties. These nanoparticles effectiveness against bacteria was tested on the microorganisms *Escherichia coli* and *Staphylococcus aureus*.^[132,133] These investigations' findings suggested that the antibacterial capabilities of certain substances were inversely correlated with weight proportion of zinc and iron, meaning that it represents a proportion grew, the ability to combat bacteria also increased. The highest antibacterial action against *E. coli* was also seen for zinc oxide particles. *Staphylococcus aureus* was significantly inhibited from growing when zinc oxide as well as iron oxide were combined in a weight ratio greater than 1:1.^[133]

Researchers assessed the effects of a trimetallic aluminium, platinum, silver-based nanofluid on several bacterium varieties in 2018, including they found that it outperformed both of them. Bimetallic aluminium and platinum nanofluid and monometallic Au nanofluid are also examples of this.^[134]

A controlled release reagent for diverse substances has also been suggested for Fe₃O₄/oleic acid nanofluid.^[135] On *S. aureus* and *E. coli* cultures, it has been demonstrated the function of Fe₃O₄ or oleic acid in transporting cephalosporin antibiotics as well as antibacterial action of nanofluid.^[125]

VI. ADDITIONAL USES FOR NANOFUIDS

- 1. Wound Dressing using Nanofluids:** During therapy, it is usual for skin lesions to get too infected; as a result, using a good dressing is crucial and essential. In order to stop *Candida albicans* from colonising wounds and forming biofilms, Anghel *et.al.* (2013) looked at the usage of iron nanofluid in wound dressing. The dressing patches are composed of an active magnetic nanoparticle mixture, like iron oxide, and the desired nanoparticle surrounded by this nanofluid. The study's conclusion was that by combining the special qualities of iron oxide nanoparticles with *Satureja hortensis* oil, a novel product might be created that would inhibit the growth of biological films as well as fungi over a range of surfaces found on health care and scientific supplies.^[136]
- 2. Cryopreservation:** He and his collaborators (1999) created quartz micro-capillary approach to unique, very quick mammalian cells is vitrified. Their research's findings suggest that vitrification with a little number of internal cells cryoprotectants might be a practical as well as efficient method for cryo protection using mouse foetal stem cells. Commonly, hazardous cryoprotectants are used in excessively high concentrations in the traditional vitrification processes (typically greater than 4M). The cryoprotectant concentration in this probe, there was 2Ma similar concentration that is often employed in place of the standard slow-freezing procedures. Therefore, that procedure adding the benefits of quick cooling as well as conventional gradual chilling. With the survivability speed comparable with the control cells that are not frozen, this technique was used to vitrify mouse embryonic stem (ES) cells. The three distinct proteins among a transcription factor Oct-4, the outer membrane glycoprotein SSEA-1, including alkaline phosphatase, were expressed in pluripotent murine post-vitrification embryonic stem cells to confirm the maintenance of their undifferentiated characteristics.^[137]

VII. CONCLUSION AND FUTURE WORK

The investigation of fluid behaviour, exploitation including management at nanoscale sizes is known as nano-fluidics, and it is a relatively young but expanding area of study. As of now, technologies such as dynamic light scattering (DLS) technique, electrophoretic light scattering (ELS), electron diffractometer (ED), X-ray disc centrifuge (particle size analyser) are used for characterization of nanofluidic structures. One may include the use of nanofluids in medical and biological situations among the many different uses for these fluids. The use of nanosuspension nanofluids for drug administration, medical therapy, illness diagnostics, antibacterial cases, wound dressing, and cryopreservation is examined in this work. In order to facilitate future road maps for nanofluid applications in biomedical therapy and to create a suitable framework for these specific investigations, this study set out to: Antibacterial cases and diagnosis. A list of closing statements is made based on the study that has been done. Then, some recommendations are made for upcoming works.

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