International Journal of Health Technology and Innovation
An Official Journal of **Kalam Institute of Health Technology** | ISSN - **2583-8547**

RESEARCH ARTICLE

Radio Frequency (RF) Mediated Hyperthermia of Nickel Ferrites-A Potential Application of Cancer Therapy

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Received: 18th January, 2024; Revised: 09th February, 2024; Accepted: 20th March, 2024; Available Online: 05th April, 2024

ABSTRACT

We present an invitro study of the hyperthermia application of nanomaterials for the cancer treatment by Radiofrequency (RF). Nickel-ferrite nano materials are synthesized by using microwave hydrothermal method at different pH values under a lower temperature of 160°C for a short holding time of 30 minutes. RF source generator is being used that opeartes at 100 KHz and a temperature regulator monitors the temperature of the solution.The in-vivo experimemnt was conducted with the nanomaterials dispersed in the ferrofluid, and RF energy is appiled when the solution is being placed in a magnetic stirrer. The results shows that the temperature of the nanomaterials has increased beyond 40°C and went up to 45°C with the increase in frequency of the RF under the constant magnetic field of 100 Oe. As the strength of the magnetic field increases the Nanomaterials have shown rapid variation in their temperature Characteristics. The nickel-ferrites have shown linear temperature characteristics under the magnetic field of 100Oe with the RF frequency of 100 KHz. Hence the nickel-ferrites are most suitable for the Hyperthermia application of cancer treatment..The cancerous cells are destroyed by 'Active cell destruction' or they are swollen till the cells burst. The superconductivity property of nano particles and Radio Frequency coils used plays the major role in the treatment.

Keywords: Hyperthermia, Radio-Frequency ablation, Nanomaterials.

International Journal of Health Technology and Innovation (2024)

How to cite this article: Suman D, Raja VS, Mutta V. Radio Frequency (RF) mediated hyperthermia of nickel ferrites-A potential application of cancer therapy. International Journal of Health Technology and Innovation. 2024;3(1):40-43.

Doi: 10.60142/ijhti.v3i01.07

Source of support: Nil.

Conflict of interest: None

INTRODUCTION

Uncontrolled cell division that either invades or metastasizes into other tissues is the hallmark of the condition known as cancer. Using a technology called nuclear medicine, cancer is diagnosed by looking at how well tumor cells absorb radioactive particles injected into the body. Tumor cells produce greater radiation than normal cells due to their higher functional absorption of the radionuclide; this can be observed and recorded using a variety of advanced diagnostic tools, including as a gamma camera, scintillation counter, PET, and SPECT, among others. The World Health Organization (WHO) reports that between 1975 and 1977, the average five-year survival rate for cancer patients was 50%. The survival rate increased to 66% after advances in cancer research during the recent years (1996-2003). Despite this increase, statistics continue to indicate that cancer is a serious illness and one of the top causes of death globally. Chemotherapy and radiation therapy are the cancer treatment alternatives. Chemotherapy employs a number of anti-cancer medications known as "antineoplastics," which are distinguished by their capacity to target tumor cells, which proliferate and divide quickly. Despite the abundance of medications on the market, none of them are dependable in providing targeted treatment, meaning that they little impact normal cells. The other alternate strategy, known as radiotherapy, involves exposing the tumor site to high energy electromagnetic radiation, which damages the genetic material of the tumor cell. Regarding targeted treatment, radiation-induced disorders, and radiation exposure time, radiotherapy has its limitations. Radiation and chemotherapy can kill malignant cells, but they can have some very dangerous side effects that include fatigue, nausea, diarrhoea, and loss of fertility. Many researchers have proved that the cancerous cells are sensitive to thermal effect which could be an alternative tool to develop novel cancer treatments [2]. Hyperthermia uses

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thermal energy which is applied at the tumour site causes the cells to damage at the temperature range between 41-46°C. The thermal effect can be caused by using different procedures, such microwave, radiofrequency and ultrasound. The challenge lies in these methods is that these techniques are not very localized, hence with the advent of nanotechnology, hyperthermia treatment can be improved by employing Nanomaterials. The literature has shown that hyperthermia can be achieved through magnetic nanoparticles with the application of an oscillating magnetic field, known as magnetic fluid hyperthermia. With this motivation, here we are describing the synthesis and characterization of the nickel-ferrites and design of RF source generator for the hyperthermia unit.

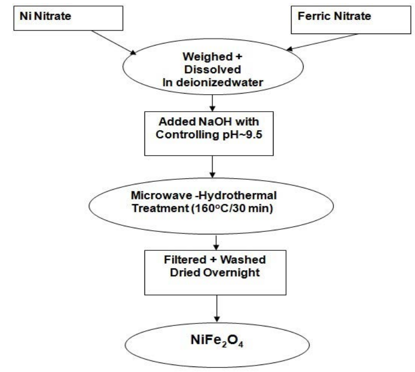
Synthesis and characterization of Nickel-ferrites

Though there have been many methods in chemical synthesis of Nano materials, hydrothermal method possesses many advantages for synthesis of nanocrystalline oxide materials and other metal powders [1]. In the present investigation, we have adapted modified version of hydrothermal method i.e. Microwave–Hydrothermal (M-H) method for the synthesis of nanoparticles of nickel ferrites. Nickel ferrite Nano-powders were synthesized at different pH values, using the microwave-hydrothermal method at a lower temperature of 160^{O}C for a short holding time of 30 minutes. Through careful manipulation of the thermodynamic factors (temperature, pressure, and composition), materials (chemical compounds) can be directly crystallized from aqueous solutions using a technique called hydrothermal synthesis [3]. The temperature and pressure ranges in which synthesis reactions can be conducted are 100 to 1000 OC or more, as well as 1 atmosphere to several thousand atmospheres. The majority of hydrothermal experiments are carried out below the supercritical temperature of water, which is 374 OC. Any other solvent or water can be used to conduct the reactions. The term “hydrothermal processes” refers to procedures that use water as a solvent. The synthesis procedure of Nickel-Ferrite by using Micro wave hydro thermal method is briefly shown in the flowchart-1.

The synthesized nickel-ferrites were characterized by using different techniques like XRD, TEM, and The Scherer equation was used to estimate the particle sizes of the produced powders, and the average particle size of the ferrites under investigation is between 10 and 15 nm. These ferrites nanoparticles had uniform size and a roughly spherical shape [4]. Similar to the XRD pattern, the selected area electron diffraction (SEAD) pattern is likewise sharply resolved at the reflections of (220), (311), (400), (422), (511), and (440). Saturation magnetization and coercively is also measured at room temperature under 5kOe using pulse width hysteresis loop tracer.

Design of RF Source Generator for RF Hyperthermia

The block diagram in Figure.1 shows the basic blocks of the RF source generator in which the A.C source of 230V is converted in to dc by using a rectifier arrangement achieved through diodes. In order to supply the coil with high frequency current, the DC source is later connected to a high frequency switching circuit. A high frequency magnetic field is created around



Flow chart 1: Synthesis of Nickel ferrites

a coil that is conducting high frequency current, according to Ampere’s Law. This is the main idea behind employing an RF oscillator which produces alternating magnetic fields induced by A.C currents which are passed through RF coil [5]. A dc-to-dc boost converter and a boost power factor corrector share the same power circuit. The huge input capacitor that is typically connected to the AC to DC conversion function has been transferred to the boost converter’s output. Instead, a diode bridge is placed ahead of the inductor to correct the AC input voltage.

Though the process is same, at high output powers it is creating lot of troubles. The first one being, low power factor and also distorted current waveform. This happens due to the rectifier and the associated filter. In order to overcome this problem, one has to use a boost rectifier, which improves the power factor nearly to unity and it also reduces the current harmonics. A microcontroller is employed in the block diagram to automate the functioning of the RF hyperthermia unit. The microcontroller is programmed in such a way that the Frequency of RF oscillation and amplitude of the waveforms can be set with the options in the monitor. If a conductive Object, (the container of a Magnetic Nano Particles) is introduced in the magnetic field, there induces a voltage as per the Faraday’s Law, hence the eddy currents are created on the skin depth of the container [6]. Hence this generates heat energy on the Magnetic Nano Particles. Figure.1 shows the block diagram of the process.

MINIMALLY INVASIVE METHOD

To regulate the tumor site’s temperature, we have created an RF source generator with a temperature feedback controller. The produced nanoparticles, known as nickel-ferrites, will be injected into the body together with a tracer element that has an affinity for the tumor site following the biocompatibility experiments. Through the use of an RF coil, which applies Faraday’s Law to create a voltage, the tumor location is exposed to radiofrequency energy. As a result, eddy currents are produced at the outer layer’s skin depth, producing heat energy that kills tumor cells on magnetic nanoparticles that are over room temperature and close to 41–45 degrees Celsius. A relay that is attached to the RF generator’s power supply and the thermocouple’s negative feedback mechanism

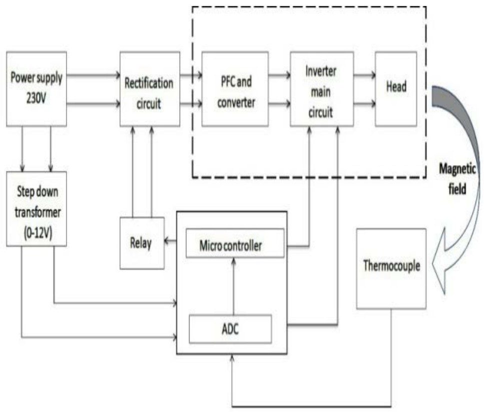


Figure 1: Block diagram of RF source generator for Hyperthermia treatment

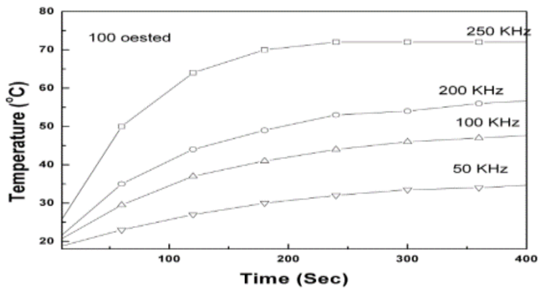


Figure 2: Temperature Vs RF energy Characteristics of Nickel-Ferrites at 100 Oe

allow for temperature control [7]. A biocompatible sheath-encased catheter is used to guide the thermocouple to the tumor site, where it measures the temperature of the tissue undergoing repair. A negative feedback control mechanism with a relay microcontroller arrangement is used to regulate the temperature, as illustrated in Figure 1.

RESULTS AND DISCUSSIONS

The nanoparticles of nickel ferrite used in the present investigation which are synthesized using microwave-hydrothermal method were successfully dispersed in water for the analysis of their heat generation at varying AC magnetic fields. The self-heating characteristics have been carried out at different frequencies at different magnetic fields. The temperature characteristics of the Nano ferrites with respect to the applied magnetic field are shown in the Figure.2, Figure.3.

It is clearly evident from the figures that the temperature of the Nanomaterials increases with the increase in frequency of the RF under the constant magnetic field of 100 Oe. As the strength of the magnetic field increases the Nanomaterials have shown rapid variation in their temperature Characteristics which is not viable for the application of hyperthermia. The nickel-ferrites have shown linear temperature characteristics under the magnetic field of 100Oe with the RF frequency of 100 KHz. Hence the nickel-ferrites are most suitable for the Hyperthermia application of cancer treatment. For the

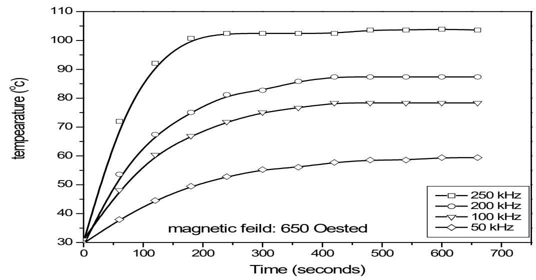


Figure 3: Temperature Vs RF energy Characteristics of Nickel-Ferrites at 650 Oe

purpose of applying RF hyperthermia in a minimally invasive manner, we have therefore built an RF source generator that is equipped with a temperature regulator. The cancerous cells are destroyed by 'Active cell destruction' or they are swollen till the cells burst.

The heat produced by this mechanism is primarily due to eddy currents generated in the nano particles which can be scaled as

$$SAR \ \alpha \ r^2.A^2.f^2 \quad \text{...Eq.1}$$

Where SAR from Eq.1 is the specific absorption rate of the tissue, r is radius of area treated, f is the RF frequency and A is the amplitude.

CONCLUSIONS

The main advantage of this mechanism is a more localized destruction of diseased tissue. Additionally, it minimizes the possible side effects such as systemic toxicity or infection and is minimally invasive. it was found that the magnetic field of 100Oe at a specific frequency of 100 kHz frequency is more suitable for the application in the RF-hyperthermia. Though the technique has many advantages it also has some limitations during in vivo applications in terms of the temperature regulation of the body tissue under repair, and thermocouple characteristics and the cooling system design of the RF coil. The major drawback of thermocouples has been their interaction with the electromagnetic fields employed in hyperthermia. Some alternatives like application of absorbing ferrite beads around the probe leads, measurement of temperature during power interruption have been proposed which can avoid this problem considerably, but these methods have to be further investigated to arrive at a more substantial solution. Extensive research on these fronts could help in improving the therapy so that the society gets benefitted.

ACKNOWLEDGEMENTS

This study is supported by the science and Engineering Research Board (SERB), Govt. of India under the Teacher Associateship for Research Excellence (TARE) scheme. Sanction order: TAR/2022/000114.

The authors would like to thank Director, Indian Institute of Chemical Technology (IICT) for providing the infrastructure support to implement the project.

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