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# Self-heating evaluation of superparamagnetic MnFe<sub>2</sub>O<sub>4</sub> nanoparticles for magnetic fluid hyperthermia application towards cancer treatment

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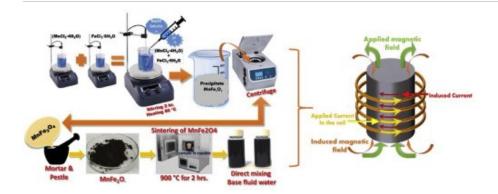
#### **Abstract**

In the vision of hyperthermia application, high quality superparamagnetic MnFe<sub>2</sub>O<sub>4</sub> <u>nanoparticles</u> (NPs) were synthesized *via* low cost and environment-friendly co-precipitation method. Thermogravimetric and <u>differential thermal analysis</u> studies confirmed the ferritization temperature at 900°C. The formation of crystals with a single-phase cubic spinel structure with the Fd3*m* space group has been confirmed by <u>XRD</u> analysis. SEM-EDX result reveals that the spherical nature of grains with some agglomeration and <u>elemental analysis</u> helps to calculate the atomic percentage of each detected element. An average particle size (~25 nm) was determined by TEM analysis. VSM analysis shows that saturation magnetization (Ms) increases with decreasing temperature in the range 54.18–59.67emu/g at room temperature (300K) to low temperature (5K), respectively, which displays temperature change affects the saturation magnetization and coercivity. FC-ZFC measurements indicated a blocking temperature of NPs around 97.17K. The induction heating study was performed on MnFe<sub>2</sub>O<sub>4</sub> magnetic NPs at 4kA/m AC magnetic field amplitude and 280kHz frequency for application in magnetic hyperthermia. The result demonstrates that the heating ability of MnFe<sub>2</sub>O<sub>4</sub> magnetic NPs can be achieved hyperthermia temperature (42°C) at small content of 0.4g/mL within 260sec-time duration, which confirms that

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the prepared material can be used as a heating agent in magnetic hyperthermic treatment. The <u>specific absorption rate</u> (SAR) was found at 217.62W/g, the obtained result is superior to the previous reports. The obtained results show that the newly synthesized superparamagnetic NPs can act as a promising candidate for hyperthermia therapy due to its high heat-generating capability at lower concentrations with less time period.

# Graphical abstract



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#### Introduction

Nanotechnology concerned with developing electric devices and materials into the size range from 1 to 100nm [1]. The nanoparticles (NPs) signifies a high degree of the surface to volume ratio. Therefore, they are highly reactive, flexible, and vigorous as compared to the bulk materials [2,3]. In particular, magnetic NPs have some special properties like simple controllability, high saturation magnetization (Ms), biocompatibility, biological adaptability, low toxicity, excellent physicochemical and magnetic properties. Due to this, they have drawn concentration to various fields such as manufacturing, ecological, diagnostic as well as biomedical applications [4,5]. Thus, all these unique properties of magnetic NPs depend upon synthesis techniques, size of the particle and its distribution. The combination of components such as the size of the grain, preparation method, oxygen parameter, time of breeding, cation distribution, Fe<sup>3+</sup> to Fe<sup>2+</sup> ion ratio, cooling conditions and sintering temperature determines the electrical as well as magnetic properties of polycrystalline material. The ferrites are magnetic ceramics, which attracts the medical diagnostics and information storage applications due to their good magnetic and electric properties [6]. For biomedical applications, materials should possess some important properties such as, high saturation magnetization with adjustable Curie temperature, huge chemical stability, high electric resistivity, low eddy current, low toxicity, which was observed in ferrite NPs.

Nowadays, researchers show their more attention in advanced synthesis techniques like hydrothermal, sol-gel auto combustion, chemical co-precipitation, and micro-emulsion to improve their properties as compared to the bulk [[7], [8], [9]]. These advanced synthesis techniques improve the uniformity of size and structure of the crystals, which was useful for protein separation, magnetic targeting, drug deliverance, hyperthermia and imaging (MRI) [10]. The hyperthermia application needs fine particles and the literature survey reveals that the chemical co-precipitation scheme can act as the best process for the synthesis of ultrafine NPs [4,11].

Hyperthermia is one of the therapeutic methods to treat cancer by generating suitable heat in the body [4]. Hyperthermia is originated from 'hyper' and 'therm', which means 'rise' and 'heat', respectively. It recognizes an increase in body temperature [12]. According to the National Cancer Institute of America, hyperthermia defined as "therapeutic hyperthermia is a type of treatment that involves the high temperature of body tissues to destroy the cancerous cells by the effect of radiation and certain anticancer drugs" [13]. Different approaches have been used to induce hyperthermia in the tumour region, but it causes side effects in healthy tissues too [14]. Magnetic hyperthermia has drawn attention to the potential of reducing clinical side effects and eliminating cancerous tumours [15]. Under the exterior guest field, magnetic NP's generate the heat to kill the cancer cells. The magnetic NPs surrounding the external ACMF can be injected *via* local or intravascular regions, which causes heat concentrated on the infected cells [3]. Generally, the optimum range of temperature is 42–46°C for this process [16].

In the present work, we have chosen the manganese ferrite NPs as they have low toxicity, high stability, easily synthesized and tunable magnetic properties [17]. Ibrahim Sharifi et al. studied Ferrite-based magnetic nanofluids used in hyperthermia applications and they mentioned pure metal (Fe, Co, Ni) nanoparticles are not relevant for biomedical applications due to the highest saturation magnetization, highly toxic and extremely sensitive to oxidation without a further appropriate surface treatment [18]. The MnFe<sub>2</sub>O<sub>4</sub> has a lower effective magnetic anisotropy and higher SLP [19]. Moreover, for self-controlled hyperthermia treatment, the well-adjusted therapeutic temperature of Mn-ferrites can potentially act as smart implants revealed by Antonoise et al [20]. Self-regulated hyperthermia plays an important role if a manganese ferrite is adjusted to the therapeutic temperature exactly [9,21]. They can be effortlessly changed by an exterior magnetic field and thus, they have gained increasing importance in various biomedical applications.

# Section snippets

#### Materials and methods

All the chemicals used in this study were analytical grade chemicals obtained from Merck, India

and used without further purification. Manganese chloridetetrahydrate ( $MnCl_2\cdot 4H_2O$ ) and ferric chloridehexahydrate ( $FeCl_3\cdot 6H_2O$ ) were used as a precursor, whereas, sodium hydroxide (NaOH) was used to maintain pH for the synthesis of  $MnFe_2O_4NPs$ . The molar ratio of 1:2  $MnCl_2\cdot 4H_2O$  and  $FeCl_3\cdot 6H_2O$  have been dissolved in pure water. After this, NaOH is also dissolved in the solution for controlling the pH...

#### Thermal analysis

Fig. 2. Shows the TG-DTA curve for the total calcinations process of pure  $MnFe_2O_4NPs$ . After three main TG steps the complete procedure has appeared at  $900^{\circ}C$ . In the TG-DTA experiment, under  $N_2$  atmosphere magnetic NPs were heated to  $1100^{\circ}C$  and changes in a weight loss of organic material were recorded. The result shows the first 1.16% weight loss occurred at the temperature range of  $200-300^{\circ}C$  and was attributed to the removal of solvents. In the next step, 0.88% weight loss arises mainly for...

#### **Conclusions**

We have successfully synthesized superparamagnetic MnFe<sub>2</sub>O<sub>4</sub> NPs by chemical co-precipitation method with an average crystallite size of 20nm. The sample was sintered at 900°C after studied by TG-DTA, which shows 3.18% as total weight loss and confirms the ferritization process. The confirmation of the spinel phase of manganese ferrite NPs without any other secondary phase formation with well-crystallized products was confirmed by XRD and EDX analysis. The spherical morphology and agglomeration ...

# Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper....

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