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# Review on magnetic nanoparticles for magnetic nanofluid hyperthermia application



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#### HIGHLIGHTS

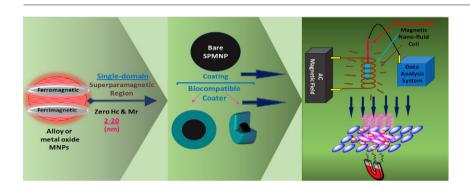
#### GRAPHICAL ABSTRACT

- The efficiency of magnetic nanofluid hyperthermia therapy as the induction heating power and temperature has been reviewed.
- Magnetic alloys and metal oxides are the promising nanoparticles for hyper-thermia therapy.
- Core-shell structure and remaining the Curie temperature below 45 °C are important to control the hyperthermia temperature.
- The roles of the features of the magnetic field on the efficiency of hyperthermia therapy have been investigated.

#### A R T I C L E I N F O

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#### ABSTRACT

Hyperthermia cancer atherapy designed by magnetic particles as heating nano-mediators has been greatly applied for in vitro purposes to make reliable and certain conditions for in vivo trials. This intracellular treatment has found higher efficiency as compared to conventional ones due to generating heat locally through superparamagnetic nanoparticles for inaccessible tumors with minimal damage to the healthy cells nearby. The main challenges of this novel cancer therapy are the enhancement of heating power of such nanoparticles and the control of the local tumoral temperature. Those hyperthermia factors basically derived from magnetic nanoparticles as well as magnetic field. Thereby, the efficiency of magnetic hyperthermia is principally dependent on the proper determination of their features. This study tried to provide a comprehensive evaluation on the magnetic hyperthermia therapy through the determination of magnetic nanoparticles such as surface chemistry, intrinsic and extrinsic magnetic properties. In addition, the features of the magnetic field that substantially play on induction heating power and hyperthermia temperature are reviewed.

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#### 1. Introduction

Nanoparticles (NPs) are ultrafine particles with at least one dimension in nanometer range (1 to 100). NPs present high surface-

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http://dx.doi.org/10.1016/j.matdes.2017.03.036 0264-1275/© 2017 Elsevier Ltd. All rights reserved. area-to-volume ratio and are thus extremely reactive, versatile, and strong as compared to the bulk ones. These features confer unbounded possibilities to improve the unique mechanical, optical, and magnetic properties of NPs. NPs are mainly classified into either organic group, including carbon nanotubes, liposomes, and fullerenes, or inorganic group, including quantum dots and magnetic nanoparticles (MNPs) [1–6]. MNPs have gained great popularity because of their capability to be functionalized at both cellular and molecular levels [7].

MNPs are inorganic and zero-dimensional materials with metalbased configuration. These NPs have gained increased importance because they can be easily manipulated using alternating current magnetic field (ACMF) and subsequently employed in various applications. Nanometer-sized MNPs exhibit intrinsic and unique properties, such as high saturation magnetization (Ms), biocompatibility, and less toxicity; in this regard, some breakthroughs have been conducted in various fields, such as industrial, environmental, analytical, and biomedical applications. In particular, MNPs have attracted attention for biomedical applications because these particles feature easy controllability, biological compatibility, physicochemical properties, and superior magnetic properties.

Biomedical applications depend on the properties of MNPs; such properties, in turn, are affected by the type of applied MNPs, synthesis methods, interaction among particles, particle size distribution, and particle size and shape of NPs. As such, a suitable synthesis method should be selected to attain specific performance (based on certain biomedical applications). Biomedical applications with MNPs are generally classified into in vitro (outside the body) and in vivo (inside the body). In vitro applications are mainly used in diagnostic processes, such as separation/selection, magnetic relaxometry, and magnetic resonance imaging (MRI). In vivo applications include diagnostic processes, such as nuclear magnetic resonance imaging, as well as therapeutic applications (e.g., drug delivery and magnetic hyperthermia) [8].

Hyperthermia is a therapeutic method for cancer treatment; the term "hyperthermia" is derived from two Greek words, "hyper" and "therme," meaning "rise" and "heat," respectively [9], because this condition is attributed to increasing body temperature. Busch [10] and Coley [11] observed that a sarcoma disappeared after a very high fever; this finding had been the reaction of immune systems toward a bacterial infection. Based on this study, cancer cells are considered vulnerable to high temperatures; the growth of these cells can be terminated at temperatures ranging from 41 °C to 46 °C or below 47 °C for at least 20 min to 60 min (varies in the literature) [12,13]. Although this technique has gained prospects and significant advances, it may also cause several discouragements and frustration because of undesirable effects, such as blister, burns, and pain, increased rapidly in healthy cells. Therefore, hyperthermia method is used locally, instead of exposing the whole body (WB) to high temperatures, to overcome adverse side effects and increase the treatment efficiency.

Hyperthermia method has not been very effective to cure serious cancers because of basic problems associated with local hyperthermia; such problems include heterogeneous temperature distribution in tumor mass and incapability to prevent overheating at the deepseated tumor region. Therefore, a novel method must be developed to deal with these critical issues. In this regard, scientists have proposed a nanotechnology that can provide a safe, easy, and effective treatment approach. The use of MNPs with high Ms indicates that heat will be produced to enhance the hyperthermia efficiency. Technically, MNPs can be injected locally or through the intravascular region within the vicinity of external ACMF. This procedure leads to focus-generated heat on the affected cells, and the process is called magnetic hyperthermia or magnetic nanofluid hyperthermia therapy (MNFHT). In this technique, magnetic fluids are used as stable colloidal suspensions of NPs in liquid media, such as water or hydrocarbon fluids [14].

MNFHT features broadened new advancements in cancer treatment through several studies and applications of varied MNPs with high magnetic properties in different media for in vitro and in vivo applications. Experimentally, cancer treatment through MNFHT was first performed in 1957 by Gilchrist et al. [15]; in this study, maghemite ( $\gamma$ -Fe<sub>2</sub>O<sub>3</sub>) NPs, with 20 nm to 100 nm particle size, were heated by 1.2 MHz ACMF at temperature ranging from 43 °C to 46 °C to cure carcinoma by destroying metastases in lymphatic nodes. The procedure has been well established for application of MNPs in hyperthermia therapy (HT) and has been used to treat various cancers over the past 50 years. To date, MNFHT has been applied to clinical phase trials for prostatic and esophagus cancers and brain and neck tumors as well as to research on other types of cancers under clinical prophase and animal-based experiment stages [16]. Therefore, MNFHT can be considered a novel alternative therapy with few side effects compared with conventional therapies, such as surgery, chemotherapy, and radiotherapy [17].

The proper functionality of MNPs for MNFHT depends on their intrinsic magnetic properties [Curie temperature (Tc) and Ms] as well as biophysical properties [nontoxicity, colloidal stability, biocompatibility, and specific absorption rate (SAR or specific loss power)] under physiological pH conditions. The surface chemistry of MNPs and their stabilization, which are proportional to those of MNFHT, are important to achieve the above properties appropriately. Surface chemistry plays an essential role in synthesis of MNPs to avoid agglomeration of bare MNPs. The surface chemistry of MNPs should be stabilized by coating them with different materials, such as polymeric, non-polymeric, organic, and inorganic surfactants [18]. These considerations can enhance the compatibility and circulation of MNPs in the blood as well as reduce the toxicity and risk of blood capillary obstruction.

Heat-generation in MNFHT is a main aspect that should be considered in synthesis of MNPs. High-heat generation is basically acquired for MNPs with high magnetization to achieve power for cancer cell destruction. Otherwise, MNPs are disabled to alleviate serious cancers. The generated heat by ACMF and its quantity from ACMF are measured using SAR, which is the amount of electromagnetic energy power absorbed per unit and mass. SAR is described as the ability to produce heat through magnetic connection between the magnetic field and moments of MNPs. SAR is ascribed to three heating mechanisms, namely, hysteresis loss, relaxation loss, and eddy currents. Different types of MNPs demonstrate varied heating mechanisms. The magnetic heat dissipations from such mechanisms are dependent on the intrinsic and extrinsic characteristics of MNPs; such characteristics include particle shape, particle size, and saturation temperature known as hyperthermia temperature (T<sub>H</sub>), as well as ACMF parameters, such as frequency and amplitude [19].

Over the past decades, various review articles have been published to determine the different features of MNPs, particularly their synthesis, functionalization, and magnetic properties, for biomedical applications. Many synthesized MNPs with varied characteristics and magnetizations for in vivo and in vitro MNFHT have been studied. The current review presents a comprehensive classification of different types of MNPs and their magnetism states applied for MNFHT. An informative explanation is provided regarding the intrinsic and extrinsic magnetic properties of MNPs and their effects on hyperthermia application. Recent advancements on the HT procedure through the decades and its features are also discussed. The highlight of this review is the investigation of the efficacy of MNPs characterizations and ACMF features attributed to the critical parameters of MNFHT. Finally, some recommendations related to the selection of characteristics for MNPs and the appropriate conditions are provided to achieve the highest efficiency for MNFHT application.

#### 2. Classification of MNPs for hyperthermia application

Throughout the years, various MNPs with different properties and morphological metallic structures have been applied for magnetic hyperthermia therapy. These MNPs are mainly classified into two categories on the basis of their structure; magnetic alloy nanoparticles (MANPs) and magnetic metal oxide nanoparticles (MMONPs). This section explains the main characterization and synthesis of the above NPs. The different types of MNPs discussed in this section are summarized in Table 1. Download English Version:

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