A histological study for the evaluation of potential harmful effects of orally ingested iron oxide nanoparticles in mice

Potential harmful effects of iron oxide nanoparticles

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Abstract

Aim: The aim of this study is to search for the possible adverse effects of orally ingested iron oxide nanoparticles on the liver, kidney, and skeletal muscle of BALB/c mice.

Materials and Methods: Iron oxide nanoparticles were prepared with the co-precipitation method and characterized using Scanning electron microscope (SEM) and Energy-dispersive spectroscopy (EDS). BALB/c mice were chosen as an experimental animal model. Twenty-four mice were classified into four groups with six mice in each group. Group 1 was named control group. The second, third, and fourth groups were experimental groups which were given iron oxide nanoparticles daily in concentrations of 125, 250, and 500 mg/kg bodyweight for 21 days via oral ingestion. One day after the last feed of nanoparticles, the tissue specimen from the liver, kidney, and skeletal muscle were taken and processed for histopathological evaluation to study the evidence of any toxic effects of iron oxide nanoparticles on these organs.

Results: The histopathological assessment of the liver, kidney and skeletal muscle tissue of the three experimental groups revealed no evidence of necrosis, inflammation, or any degenerative changes in comparison to the control group samples.

Discussion: Oral ingestion of spherical shaped iron oxide nanoparticles (average diameter 50nm) is safe and there was no histological evidence of any toxic effects on the liver, kidney, and skeletal muscle of BALB/c mice in concentrations up to 500 mg/kg body weight for 21 days. These findings are in accordance with some studies but certain studies reported the toxic effects of iron oxide nanoparticles. This means that the size, shape, and route of exposure to iron oxide nanoparticles can affect their extent of toxicities.

Keywords
Iron oxide; Nanoparticles; Toxic effects; Histopathology

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Introduction
In the present era, nanotechnology is an emerging important tool in many fields such as biomedical, health care, food and agriculture, environmental control and protection, energy, construction, automobile industry, textile industry, electronic, defense and aerospace. The nanoparticles are classified into different categories on the basis of their characteristics, sizes, and shapes such as carbon-based nanoparticles, metal nanoparticles, ceramic nanoparticles, semiconductor nanoparticles, polymeric nanoparticles, lipid-based nanoparticles [1].

The different types of metal nanoparticles such as silver, gold, iron, copper, cadmium, and platinum are being employed for various uses in the medicine (for diagnostic and therapeutic purposes) and in other sectors such as fruit preservation and water quality monitoring [2]. The unique characteristics such as superparamagnetism, large surface area, and less difficult separation methodology of the iron oxide nanoparticles make these nanoparticles more attractive for consideration of its application [3].

After aluminium, iron is the next most abundant metal present in the crust of the earth but despite the abundance of iron, a huge number of people from all over the world suffer from iron deficiency anemia. Anemia is quite common in children and pregnant women [4-7]. Optimum availability of oxygen is vital for the normal functioning of living cells while in case of iron deficiency anemia, the oxygen-carrying capacity of the erythrocytes reduces and has a negative impact on the cellular functions.

The use of iron oxide nanoparticles revealed positive results for the management of iron deficiency anemia [8]. With the rising trend in the use of metal nanoparticles like iron oxide, it would be very important to evaluate the possibility of adverse effects of these nanoparticles. The assessment of the impact of different doses and sizes of nanoparticles on the living tissue is very vital. The aim of the present research project is to find out any histopathological evidence regarding the toxic effects of iron oxide nanoparticles on the liver, kidney, and muscle tissue of mice.

Material and Methods
Synthesis and Characterization of FeO NPs
For the purpose of making average and uniform nanoparticles, a co-precipitation method was utilized, in which a 1:2 ratio of ferrous and ferric chloride were mixed together in 50 ml of de-ionized water. In this prepared mixture, an 8.5 M sodium hydroxide solution was added very slowly till the pH of the solution reached 11. The obtained mixture was washed many times using distilled water and was later on dried using an oven at 100 °C [9]. These particles were characterized using a Scanning electron microscope (SEM) and Energy-dispersive spectroscopy (EDS).

Characterization of synthesized iron oxide nanoparticles:
Synthesized FeO nanoparticles were subjected to SEM to evaluate the structure and size of the particles. It was seen that these iron particles were of spherical shape and had an average diameter of 50 nm (figure1A). From EDS analysis it was observed that the synthesized particles constituted of an adequate amount of iron and oxygen while trace quantities of sodium and chloride were also present (Figure 1B).

Histopathological evaluation:
Microscopic examination of liver from all experimental groups of mice revealed intact architecture of the liver without any evidence of hepatocyte ballooning degeneration, necrosis, apoptosis, inflammation, or fibrosis. The slides made from kidney tissue of mice of all experimental groups revealed no histopathological evidence of any toxic effects on glomeruli, tubules, interstitium, and blood vessels. There is no evidence of any morphological abnormality in the muscle tissue specimens of all experimental groups.

Discussion
Nano-science is a rapidly developing field of science with promising results for the prosperity and well-being of humanity. Many substances are being used for the synthesis of nanoparticles and these nanoparticles are being evaluated for the potential beneficial effects. The studies reported positive results regarding the use of nanoparticles for the treatment of bacterial and viral infections [10-12]. The potential use of nanoparticles in the diagnostics and the therapeutics is being extensively studied, particularly the utilization of nanoparticles for the efficient delivery of drug to the targeted site without much exposure of normal cells to the toxic medicinal product [13]. The use of iron oxide nanoparticles based nanocarriers of anticancer drugs revealed less toxic effects of drugs on the normal cells [14, 15]. In the near future,
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The size and shape of iron oxide nanoparticles can modulate their toxic effects. As compared to sphere-shaped, the rod-shaped iron oxide nanoparticles revealed more toxicity [24]. It would be important to carry out more studies for the identification of toxic effects of iron oxide nanoparticles on various tissues with different concentrations, nanoparticle sizes, and routes of administrations.

Figure 1. A: Scanning electron microscopy (SEM) imaging for the synthesised FeO NPs. SEM shows that these iron particles were of spherical shape and had an average diameter of 50 nm. B: Energy-dispersive spectroscopy (EDS) spectrum of synthesised FeO NPs. EDS shows that the synthesised particles constituted of adequate amount of iron and oxygen and trace quantities of sodium and chloride were also seen. The use of nanoparticles for diagnosis as well as therapeutics is expected to rise. In this situation, the possibility of toxic effects associated with these nanoparticles may need to be studied extensively.

Oral ingestion, inhalation, and skin are the common portals of entry of nanoparticles in the human being. After absorption in the blood, these nanoparticles may accumulate in the liver and hepatocyte may be at more risk to bear the toxic effects of nanoparticles [16]. After degradation, the waste products are removed from the blood by the filtration process of the renal tissue. The kidney plays a vital role in the elimination of nanoparticles from the body [17]. After the liver, the renal tissue may also be exposed to the toxic effects of the nanoparticles. In our study, the three groups of mice were exposed to 250 mg/kg, 250 mg/kg and 500 mg/kg body weight when administered orally.

Conclusion

The spherical shaped iron oxide nanoparticles with an average diameter of 50 nm are relatively safer in the dosage of 125 mg/kg, 250 mg/kg and 500 mg/kg body weight when administered orally.

References


