Magnetic drug delivery of Xanthohumol to adipocytes using Ultrasmall Superparamagnetic Iron Oxide Nanoparticles.

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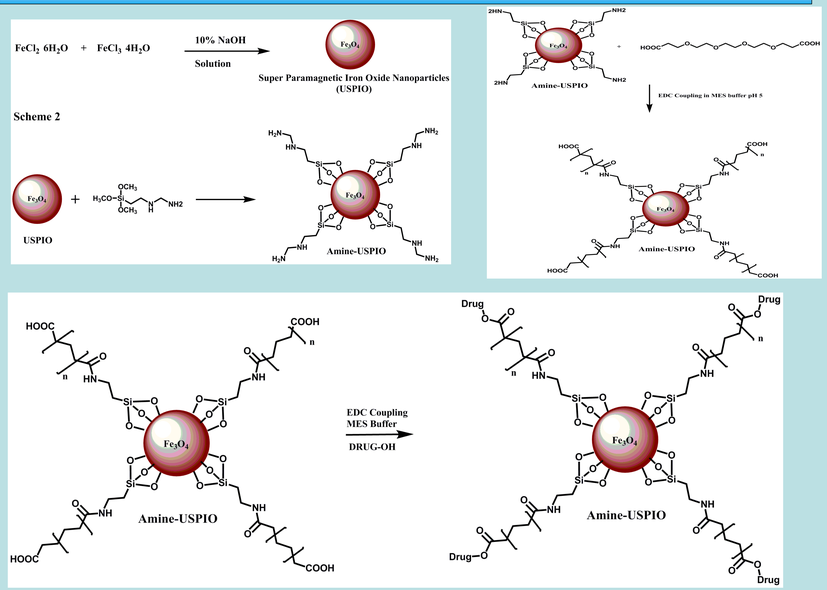
Introduction

According to the CDC's National Center for Health Statistics, more than one-third (36.5%) of U.S adults are obese. It is the main risk factor for type-2-diabetes, hypertension, dyslipidemia and atherosclerosis. Nutraceuticals such as Xanthohumol have shown potential to inhibit adipogeneis, however, their bioavailability has remained controversial. Hence there is a need to develop targeted therapy which will increase the concentration of Xanthohumol on adipose tissues. Currently, magnetic drug delivery has been used to develop targeted therapies where conventional therapies have proven to be less effective. Among various types of nanoparticles ultrasmall superparamagnetic iron oxide nanoparticles (USPIO) have found considerable attention in magnetic drug delivery as they are easy to synthesize, inert, and are biocompatible.

Materials and Methods

The synthesized USPIO-amine would be conjugated to XN via HOOC-PEG-COOH linker. The general reaction for the development of XN loaded superparamagnetic iron oxide nanoparticle is shown in scheme 1. The presence of USPIO, USPIO-amine, and USPIO-PEG was confirmed by FTIR and the XN loading capacity of USPIO-amine would be evaluated using HPLC.

Development of XN Loaded Iron Oxide nanoparticles



Scheme 1: Synthetic Scheme for the development of XN loaded nanoparticles.

Results

Ninhydrin Assay

The presence of amine functional groups on the surface of USPIO was quantified using ninhydrin Assay. The ninhydrin assay revealed that 1 mg of amine functionalized UPSIO had 22μg of amine groups. Xanthohumol was then conjugated to the surface of amine-USPIO using via a polyethylene glycol linker. The presence of amine and PEG on the surface of nanoparticles was confirmed via IR (Fig 2). The amount of Xanthohumol tagged onto the surface of nanoparticles will be quantified using HPLC. The particle size of the synthesized nanoparticles was evaluated using TEM. TEM confirm the presence of spherical morphology with average particle size of 20-25nm and the toxicity and therapeutic potency of Xanthohumol tagged to USPIO will be evaluated in vitro.

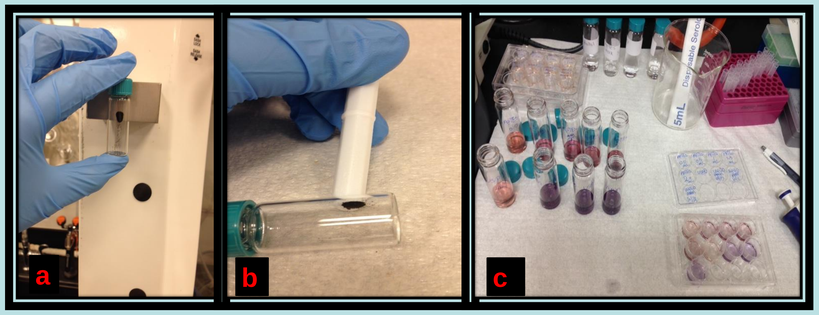


Figure 1:

IR Spectroscopy

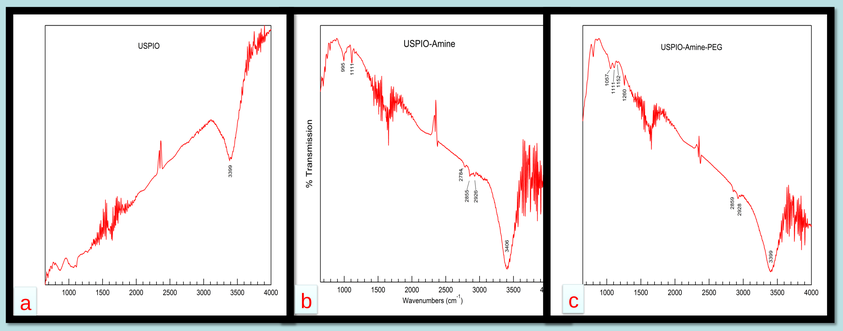


Figure 2: Presence of stretching and bending vibrational bands in the region of 2700 – 3000 cm^{-1} and 900-1300 cm^{-1}, respectively, confirm the presence of amine and PEG on the USPIO nanoparticle.

Transmission Electron Microscopy

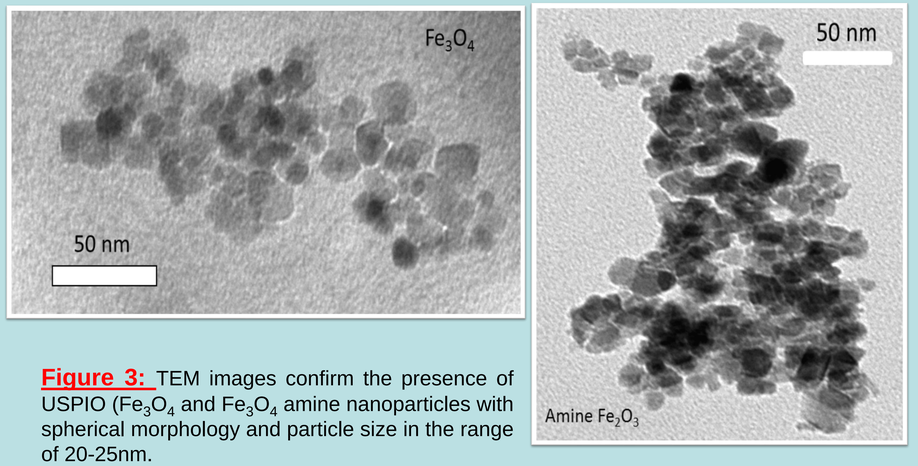


Figure 3: TEM images confirm the presence of USPIO (Fe_3O_4 and Fe_3O_4 amine nanoparticles with spherical morphology and particle size in the range of 20-25nm.

Summary and Conclusions

We have successfully loaded PEG on to the iron oxide nanoparticles. Presence of stretching and bending vibrational bands in the region of 2700 – 3000 cm^{-1} and 900-1300 cm^{-1}, respectively, confirm the presence of amine and PEG on the USPIO nanoparticle. The evaluation of Xanthohumol onto the surface of iron oxide nanoparticle is being characterized and via FTIR. The percentage loading on XN on nanoparticles will be quantified via HPLC. These XN loaded nanoparticles can be directed to any sites on the body under the influence of external magnetic field. This will improve the bioavailability of Xanthohumol as well as reduce systemic toxicity if any.

References

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