Novel Highly Effective Formulation for the Oral Treatment of Hyperphosphatemia: Nanocrystalline Maghemite

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ABSTRACT SUMMARY
Nanocrystalline maghemite was synthesized and characterized as a candidate for a novel oral phosphate binder for the treatment of hyperphosphatemia. The physicochemical properties of the synthesized nanocrystalline maghemite were characterized by transmission electron microscopy (TEM), X-ray diffraction (XRD) and Mössbauer spectroscopy. The phosphate binding capacity and iron release was determined by performing multiple in vitro studies across a physiological pH range to simulate the gastrointestinal passage. The in vitro results revealed a high phosphate binding capacity combined with minor iron release over a wide pH range.

INTRODUCTION
One main reason for hyperphosphatemia is the loss of phosphorus balance due to renal excretion failure. Studies among patients with end stage renal disease (ESRD) have shown a connection between dysregulated phosphate homeostasis and increased mortality and morbidity [1]. The majority of patients with ESRD require treatment with oral phosphate adsorbers to bind phosphate found in the ingested food [2]. Currently available oral phosphate adsorbers fail to reduce serum phosphate to the recommended level in a large number of patients with hyperphosphatemia. Our research group developed the concept of phosphate binding nanocrystalline maghemite for the oral treatment of hyperphosphatemia.

EXPERIMENTAL METHODS
Maghemite (γ-Fe₂O₃) nanoparticles were obtained by dissolving FeCl₂ and FeCl₃ in a D-mannose solution followed by precipitating in a sodium hydroxide solution according to patent DE102011112898A1. The product was termed C-PAM-10. TEM, XRD, and Mössbauer spectroscopy at 300 K and at 5.4 K were performed to characterize the physicochemical properties of the synthesized maghemite nanoparticles. Multiple in vitro studies at pH values ranging from 1.2 to 8 were performed to determine the phosphate binding capacity of C-PAM-10.

RESULTS AND DISCUSSION
First TEM images revealed crystallite core sizes at around 2-5 nm. XRD and Mössbauer spectroscopy at 300 K characterized C-PAM-10 as an iron oxide (Figure 1 and 2). Mössbauer spectroscopy at 5.4 K identified the iron oxide as maghemit (Figure 3).

![Figure 1: XRD diagram](image1)

![Figure 2: Mössbauer spectrum (300 K)](image2)
Further in vitro studies were performed with a reduced amount of C-PAM-10 (0.028 M iron concentration) to determine the phosphate binding capacity in excess phosphate. Phosphate adsorption was lowest at pH 1.2 (774 mg ± 14 mg PO₄³⁻/g Fe), increased rapidly at pH 2.5 (1219 mg ± 11 mg PO₄³⁻/g Fe), and peaked at pH 7.5 (1430 mg ± 17 mg PO₄³⁻/g Fe) (Figure 6).

CONCLUSION

This newly developed nanocrystalline maghemite based product has a high phosphate-adsorbing capacity combined with minor release of iron ions over the gastrointestinal pH range. These properties make C-PAM-10 a promising candidate as an efficient oral phosphate binder.

REFERENCES


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