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High-drug-loading Magnetic Nanoplatforms

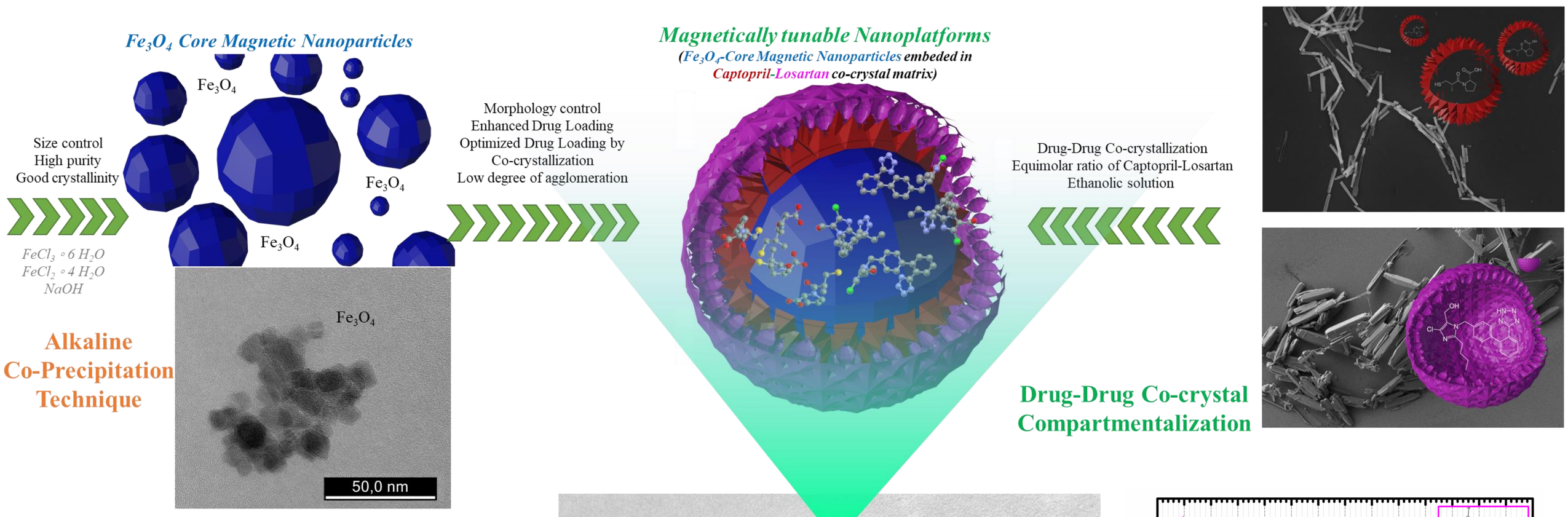
Anca Emanuela Minuti, Camelia-Mihaela Danceanu, Cristina Stavila, Horia Chiriac, Nicoleta Lupu, Daniel Gherca*, Adrian-Iulian Borhan, Dumitru-Daniel Herea, Luminita Labusca

National Institute of Research and Development for Technical Physics, 47 Mangeron Boulevard, Iasi 700050, Romania
**dgherca@phys-iasi.ro*

GOAL OF THE STUDY

Nanomedicine is regarded as one of the most promising applications of nanotechnology, as it would allow the development of tailored therapies, with a high level of selectivity and efficacy[1]. Most nanomedicines have low drug loading (few weights percent 10÷20%) and the clinical translation of such nanomedicines is challenging due to high production cost, issues in scale-up productions, irreproducible properties and toxic side-effects from the nanoparticles. To achieve a drug therapeutic window, very high particle concentration is required, but the very viscous solution of such high NP concentration leads to many difficulties[2] and it is critical to increase drug loading[3]. Therefore, high drug-loading nanoparticles would be ideal to achieve the high drug dose with a reduced amount of carrier material[4]. The present study aims to design, assemble and fabricate a new generation of multifunctional nanoplatforms for performing controlled drug loading for biomedical applications. The proposed tasks are made possible by combining two components within the nanoplatforms ***(i)*** Fe_3O_4 magnetic nanoparticles that allow high drug load and ***(ii)*** self-assembled drug-drug co-crystal (Captopril-Losartan potassium) attached to the surface of the magnetic particles in high weight (>30%) that allow selective delivery of the structure to target receptor.

METHODOLOGY OF THE INVESTIGATION



MAIN RESULTS FROM THE STUDY

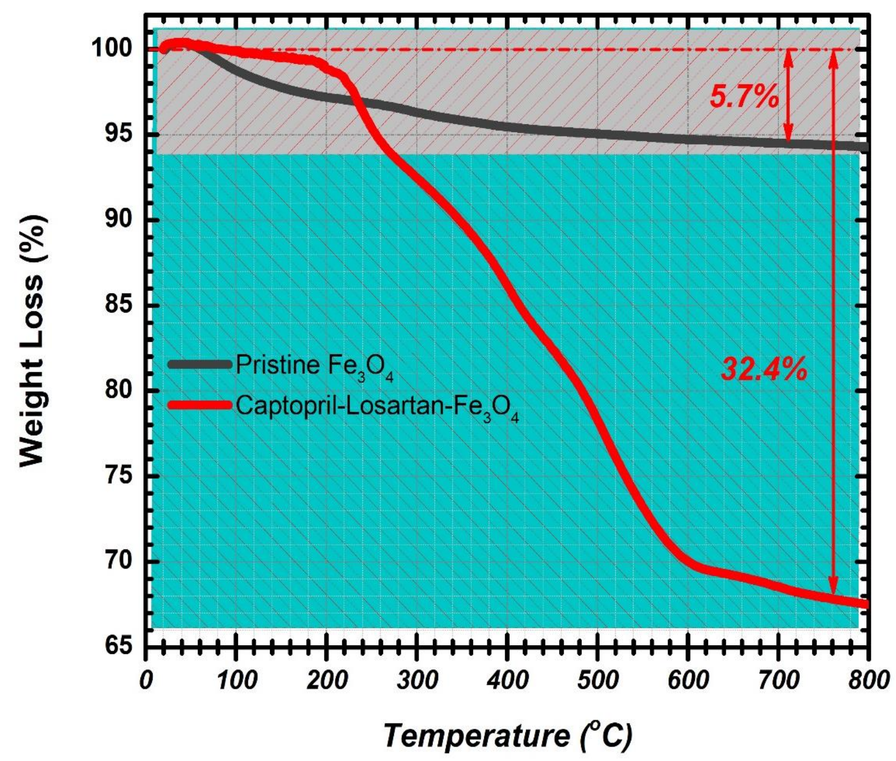


Figure 1. *TGA thermograms of pristine Fe_3O_4 magnetic nanoparticles and Captopril-Losartan co-crystal -Fe_3O_4 magnetic nanocomposite.*

The TG thermogram shows different decomposition steps in the temperature range 25–800 °C. For, pristine Fe_3O_4 nanoparticles, the weight loss of max. 5.7%, is observed between the temperatures range of 25–800 °C and is due to the evaporation of physically adsorbed water on the surface. For Captopril-Losartan co-crystal-Fe_3O_4 magnetic nanocomposite, it may be observed that in the temperature range of 90–250 °C no mass loss occurs, confirming a good thermal stability of the nanocomposite. The major thermal event which occurs in the temperature range 250-600°C a linear mass loss can be observed up to 32.4% which can be assigned to the decomposition process of the drug attached to the Fe_3O_4 nanoparticles. The TGA results confirmed that the embedded Fe_3O_4 nanoparticles with Captopril-Losartan co-crystal (wt. 32.4%) has been done successfully.

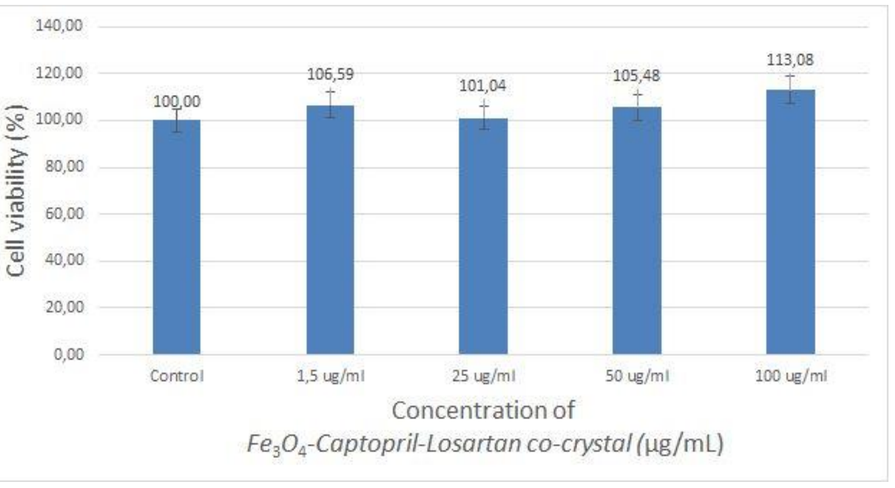


Figure 3. *Viability of fibroblasts cells incubated with Captopril-Losartan co-crystal -Fe_3O_4 magnetic nanocomposite as a function of concentration.*

Figure 2. *XRPD diffractograms of Losartan (black), Captopril (red), pristine Fe_3O_4 magnetic nanoparticles (blue) and Captopril-Losartan co-crystal -Fe_3O_4 magnetic nanocomposite (magneta)*

A mixture of Captopril-Losartan and Fe_3O_4 nanoparticles was the outcome from XRPD analysis of the powder obtained after loading process (magenta line). The diffractograms recorded from the powder XRD of sample show new peaks at 2θ position completely different from that of pure active pharmaceutical ingredients (black and red lines) indicating a new structure.

Cell viability tests were performed by MTT (5-dimethylthiazol-2-yl-2, 5-diphenyltetrazolium bromide - Vibrant ®TermoFisher Scientific) assay according to supplier's instructions. Absorbance was read at 570 nm. Cell viability (CV) as expressed by MTT optical density (OD) was calculated using the formula CV = 100 x (ODs-ODb) / (ODc-ODb), where ODs = OD of particle treated cells; ODb = OD of blank (media only); ODc = OD of untreated cells. The cytotoxicity of the Fe_3O_4-Captopril-Losartanco-crystal was evaluated indirectly by measuring the cell proliferation rate for concentrations of nanoplatforms in cell culture media ranging between 1.5-100 µg/mL on normal human dermal fibroblasts. No cytotoxic effect was observed, even at high concentration rates of 100 µg/mL.

CONCLUSION

"Post-loading" strategy to fabricate nanoplatforms was successfully applied in this work to achieve high drug-loading nanoparticles (*Fe_3O_4-Captopril-Losartan co-crystal with 32.4 wt.%*)
The results of the viability assay showed that Fe_3O_4 nanoparticles loaded with Captopril-Losartan potassium are not toxic to the normal cells tested.

KEY REFERENCES

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