

Polymer-gated magnetic mesoporous silica nanocarriers for pH- and temperature-tunable resveratrol release

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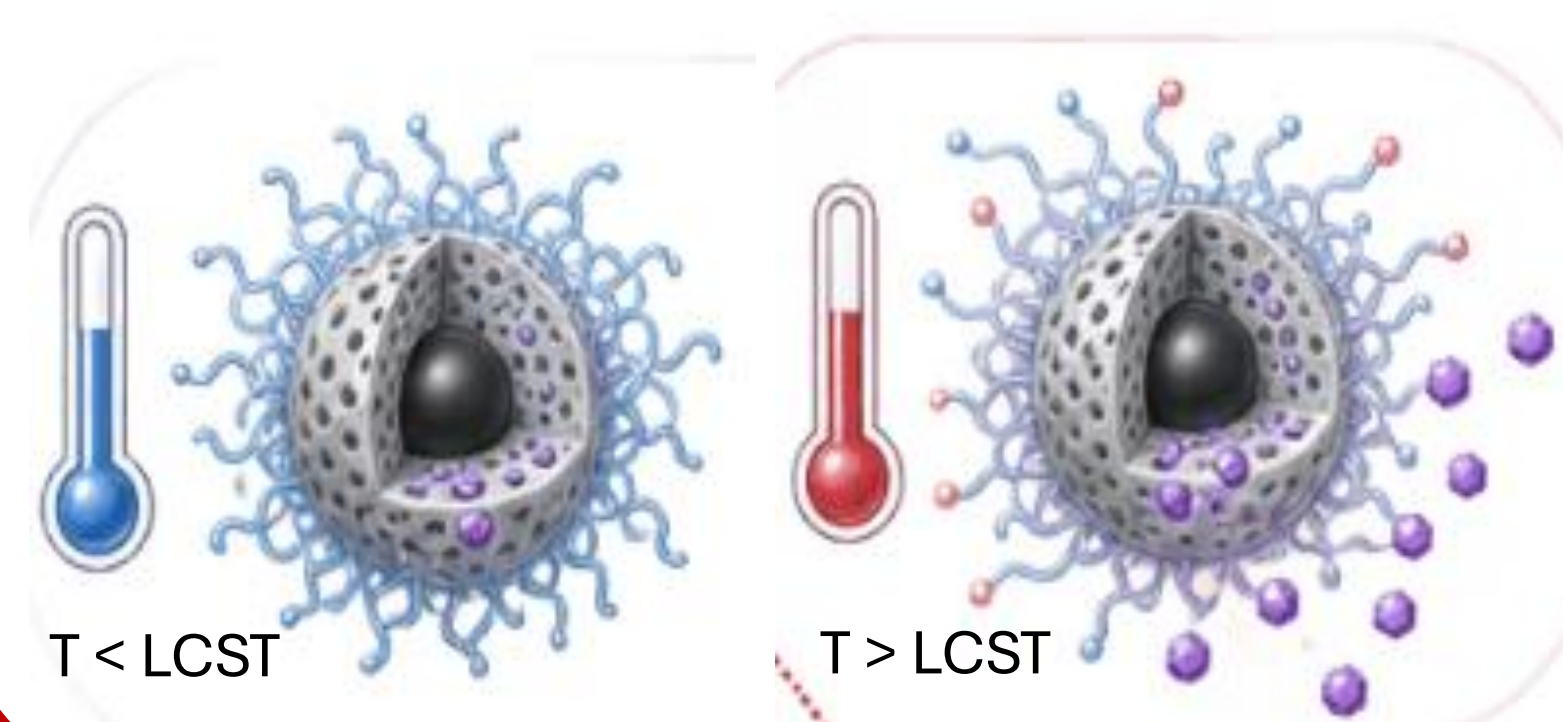
1 Introduction

In recent decades, **stimuli-responsive systems** have gained increasing attention in the field of targeted drug delivery [1].

Functionalized **magnetic nanoparticles (MMS NPs)** can enable selective drug release toward tumor tissues by exploiting the distinctive features of the tumor microenvironment, such as increased temperature and decreased pH.

2 Aim

Synthesis and characterization of a dual stimuli-responsive system able to release loaded drugs in the tumor microenvironment.



In this study, **resveratrol (RV)** was selected as a model molecule due to its well-known antioxidant and anticancer properties, but its therapeutic application is limited by poor solubility and low bioavailability [2].

3 Methods and Results

The nanoparticles were synthesized by a **multi-step procedure** involving the preparation of magnetite (Fe₃O₄) nanoparticles, the formation of a mesoporous silica shell, and subsequent surface polymer functionalization (Fig.1).

MMS NPs were functionalized with:

- **Thermoresponsive polymer:** poly(N-isopropylacrylamide) (PNIPAM) [3] characterized by a Lower Critical Solution Temperature (LCST). Above the LCST, the polymer undergoes a conformational transition that enables controlled pore opening
- methacrylic acid (MAA) reduce the transition temperature and **conferred pH sensitivity** [4].

Different samples were prepared varying the amount of MMA added (MMS-P0, MMS-P20 and MMS-P40).

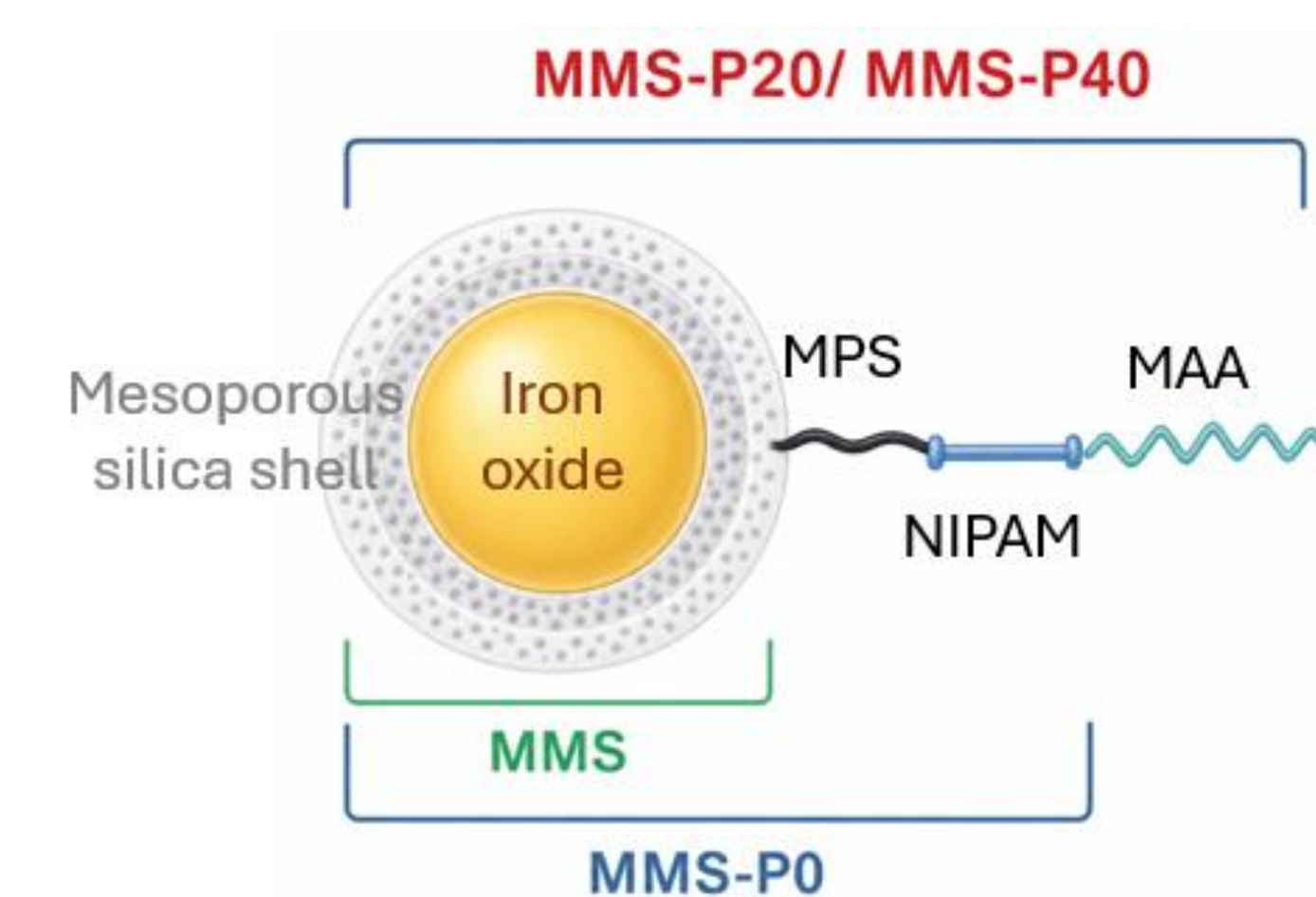


Figure 1 Representation of the MMS NPs

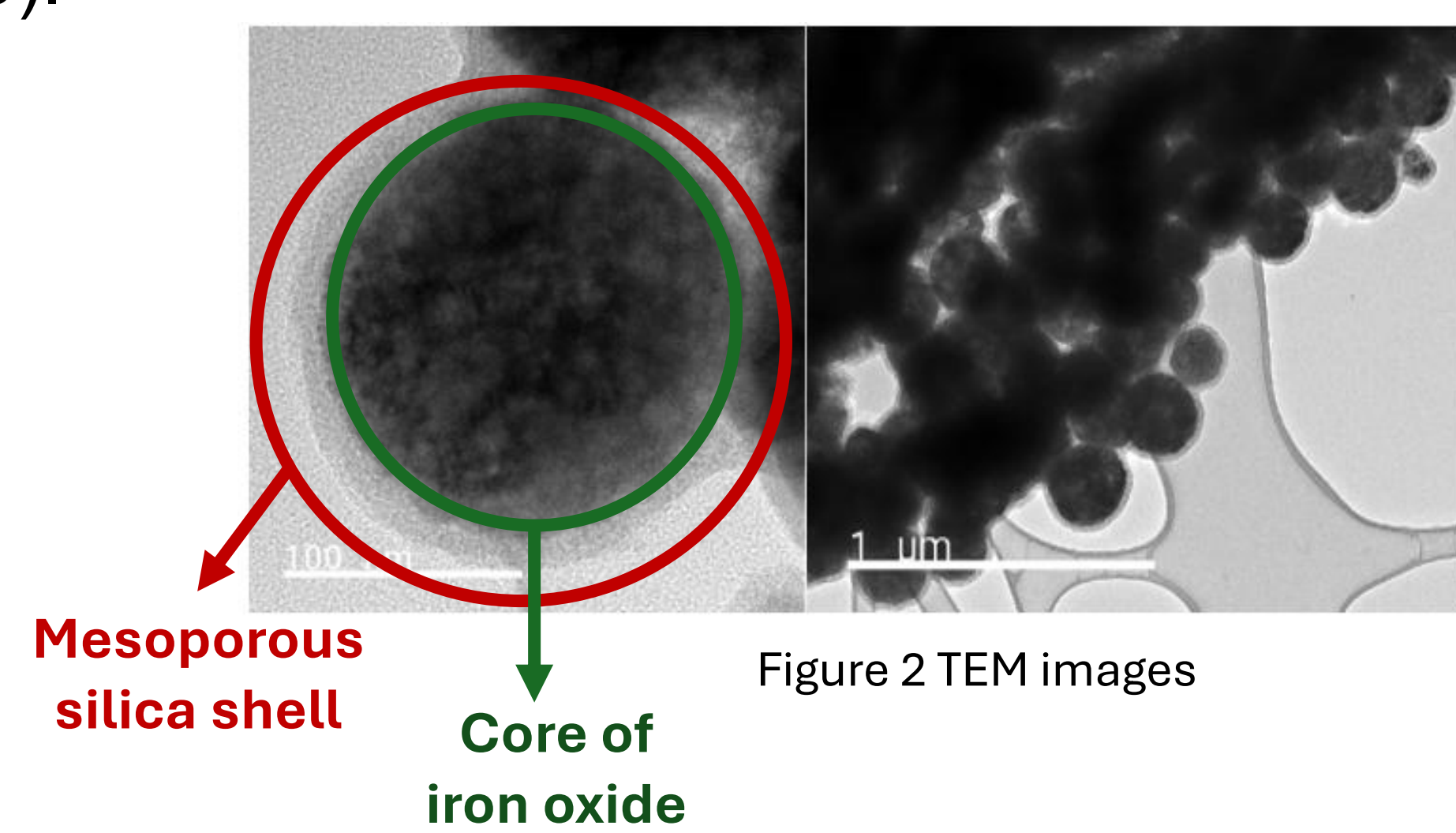


Figure 2 TEM images

The nanoparticles were characterized to ensure the formation and the surface polymerization with the **TEM images** (Fig. 2) and confirmed with the **FTIR** (Fig. 3).

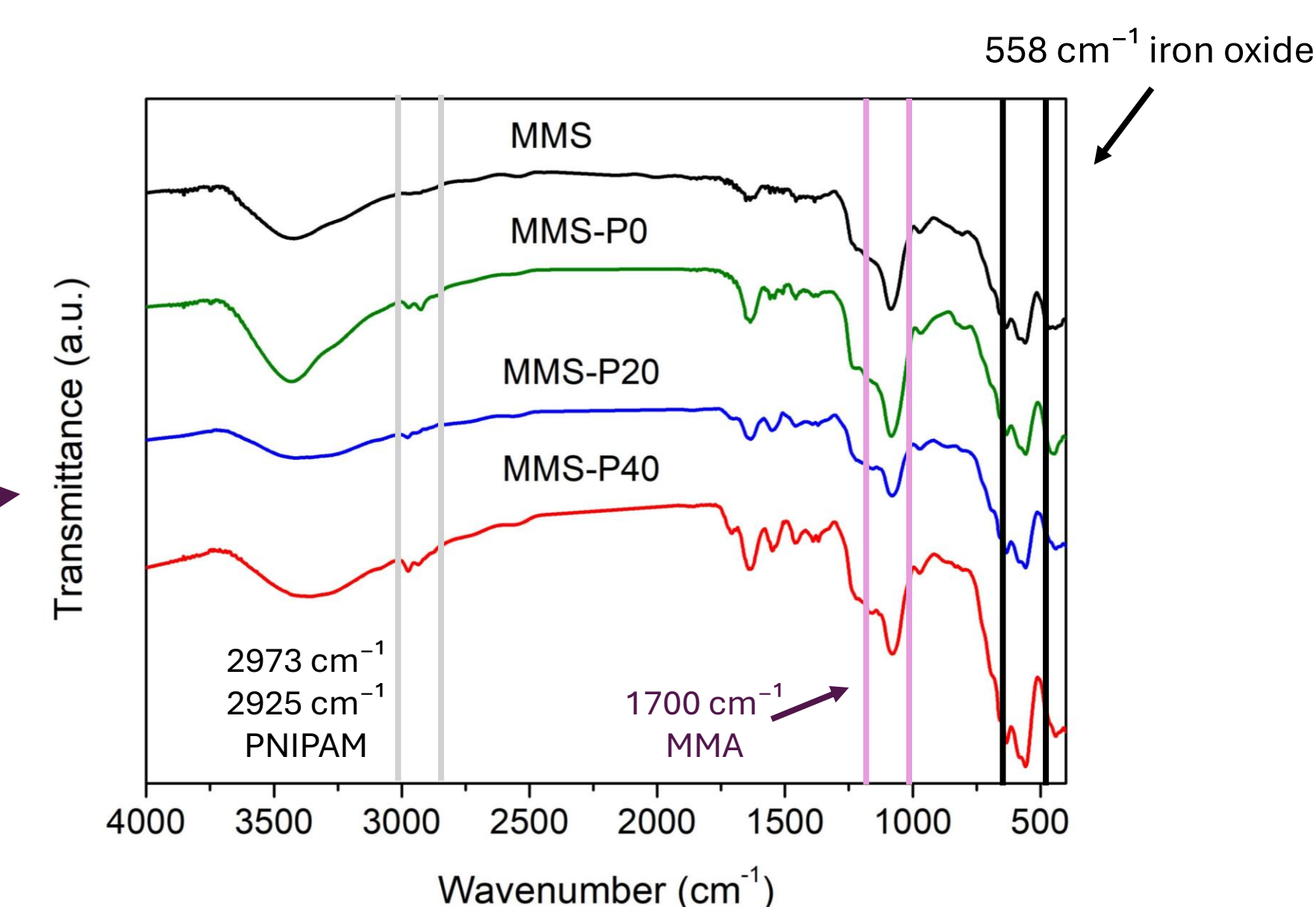


Figure 3 FTIR spectra of MMS NPs

DSC analysis demonstrated an increase in the LCST for each sample that is increased proportionally with the amount of thermopolymer added (Table 1).

Sample	LCST (°C)
MMS-P0	41
MMS-P20	45
MMS-P40	50

Table 1: LCST value of MMS-NPs

The antioxidant activity of RV-loaded MMS NPs was evaluated after storage, demonstrating preservation of the antioxidant properties and confirming the stability of the loaded formulation after 30 days.

Cytotoxicity assays demonstrated no toxicity effects in peripheral blood mononuclear cells (PBMCs) after 24, 48, and 72 h of incubation with blank MMS-NPs.

The **RV release tests**, performed at pH 7,4 and 5 and at two temperature 25 °C and 50 °C, confirmed the thermo- and pH- sensibility of the system (Fig. 4).

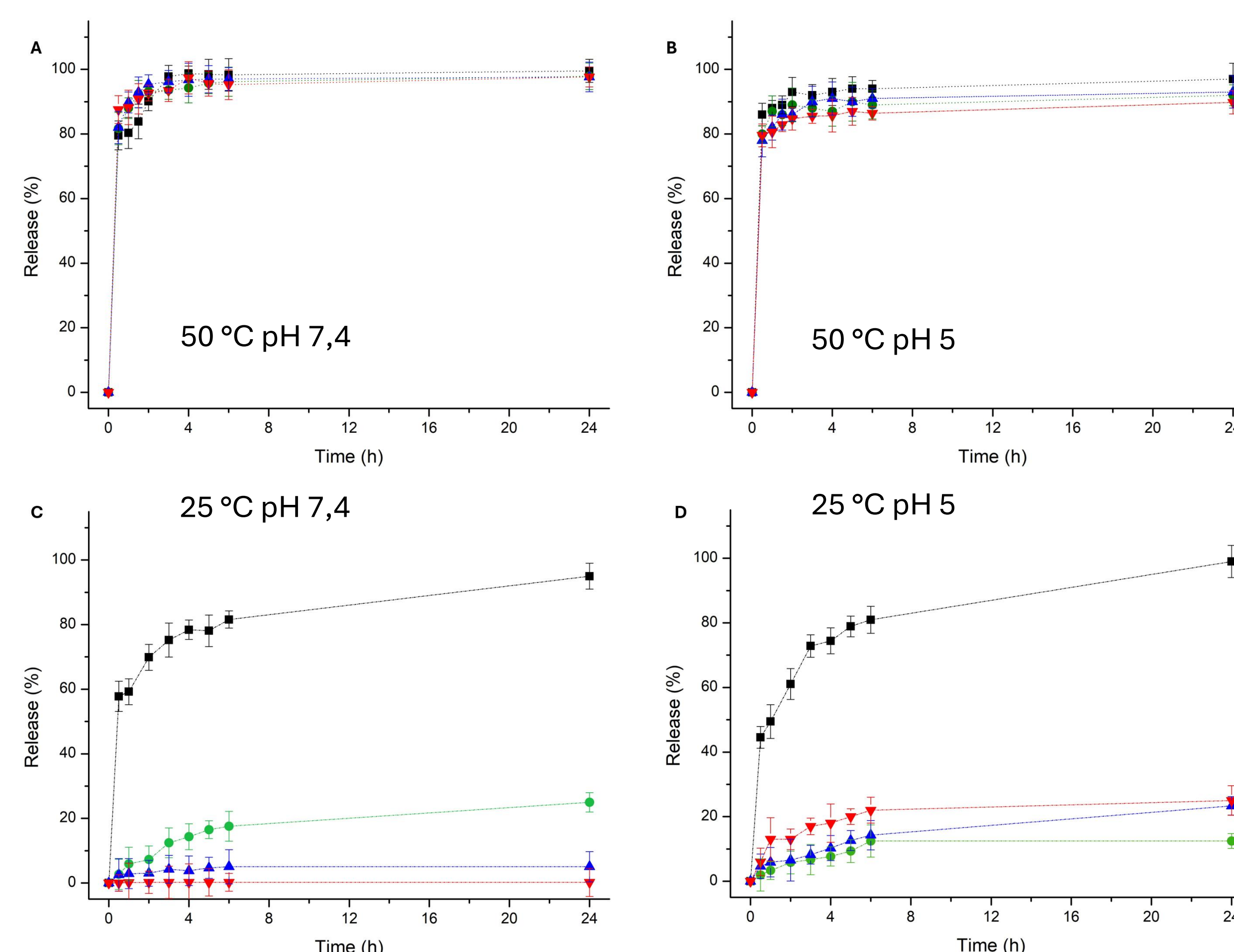


Figure 4: RV release from MMS NPs

4 Conclusion and future perspective

- Successful synthesis of a dual temperature- and pH-responsive nanosystem
- Efficient RV loading and preservation of its bioactivity
- Good biocompatibility
- Further *in vitro* investigations modulating the temperature

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