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Generation and characterization of zein nanoparticles conjugated with folate as a proposal for oral vaccine nanocarriers

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INTRODUCTION & AIM

Organic protein-based nanoparticles (NPs) are of particular interest in vaccinology due to their high affinity for biomolecules and being capable of maintaining sustained release of active compounds due to their hydrophobic nature. **Zein**, a prolamine derived from maize, is a great example of this type of protein. Zein surface charge is pH-dependent, so changes in pH can promote interactions with specific hydrophilic molecules.

On the other hand, the oral route of drug administration is one of the most desired due to its ease of ingestion and low manufacturing costs. To overcome limitations associated with this route, targeted drug delivery systems are sought. Conjugating **folic acid**, a low molecular weight molecule with high affinity for dendritic cell receptors, to zein NPs can generate an atractive antigen-carrier system prototype that can be used as a model for oral vaccines development.

This project aims to develop folate-conjugated zein nanoparticles as antigen carriers for oral vaccine prototypes, evaluate their antigen adsorption efficiency and evaluate their cytotoxicity.

METHODOLOGY

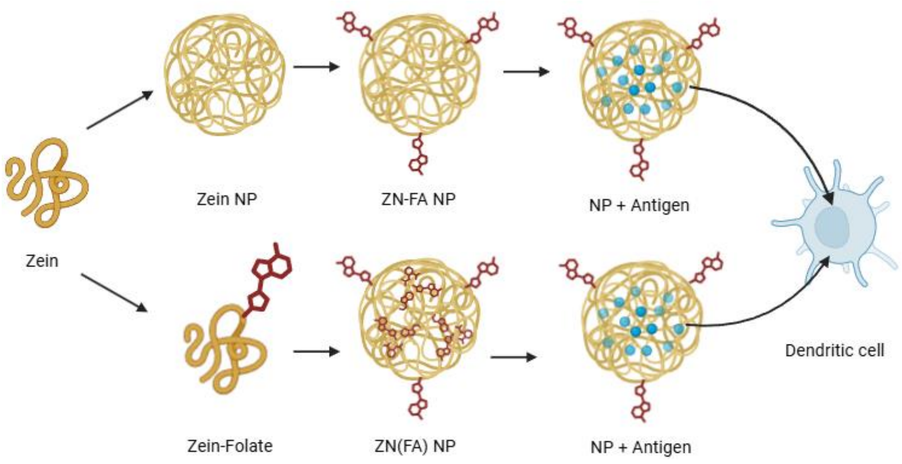

Fig 1. General overview of the zein nanoparticles synthesis pathway

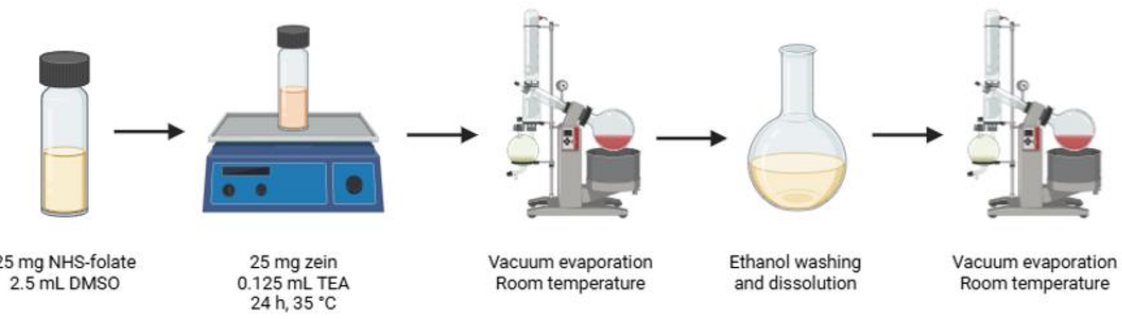

Fig 2. Synthesis of covalently bonded zein-folate or ZN(FA)

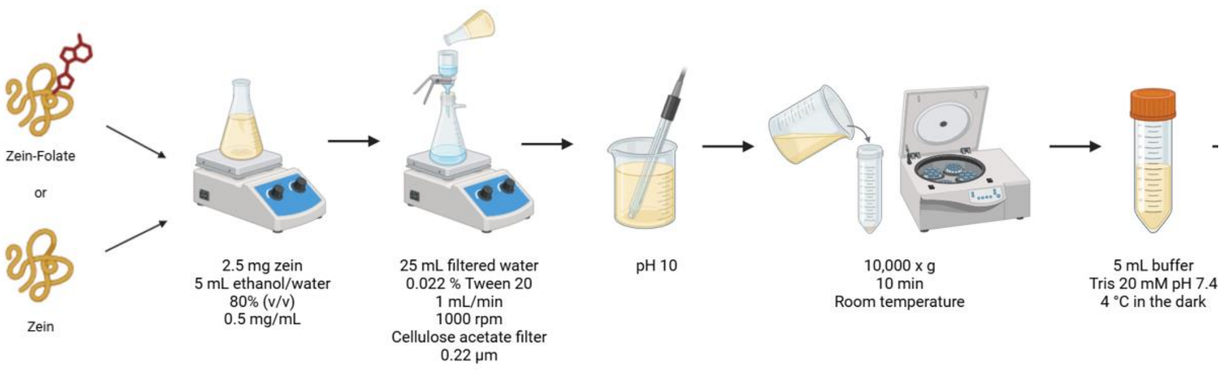

Fig 3. Synthesis of zein nanoparticles (ZN NPs) and zein-folate nanoparticles (ZN(FA) NPs)

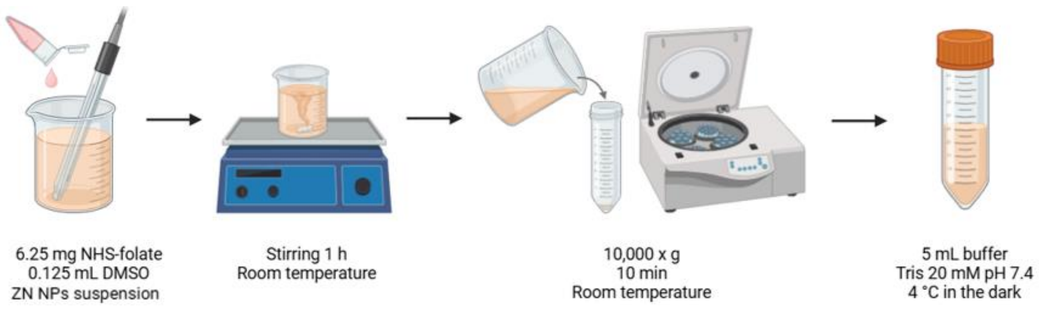

Fig 4. Synthesis of zein NPs with folate electrostatically bonded on their surface (ZN-FA NPs)

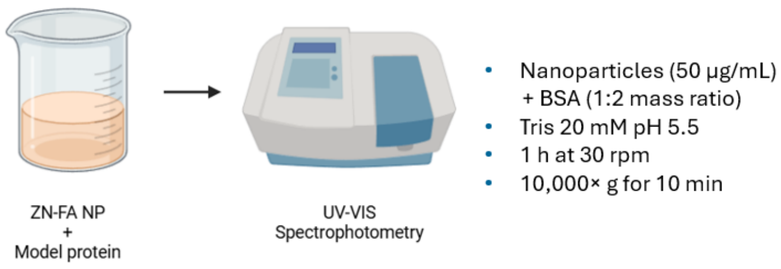

Fig 5. NPs and antigen adsorption process

RESULTS & DISCUSSION

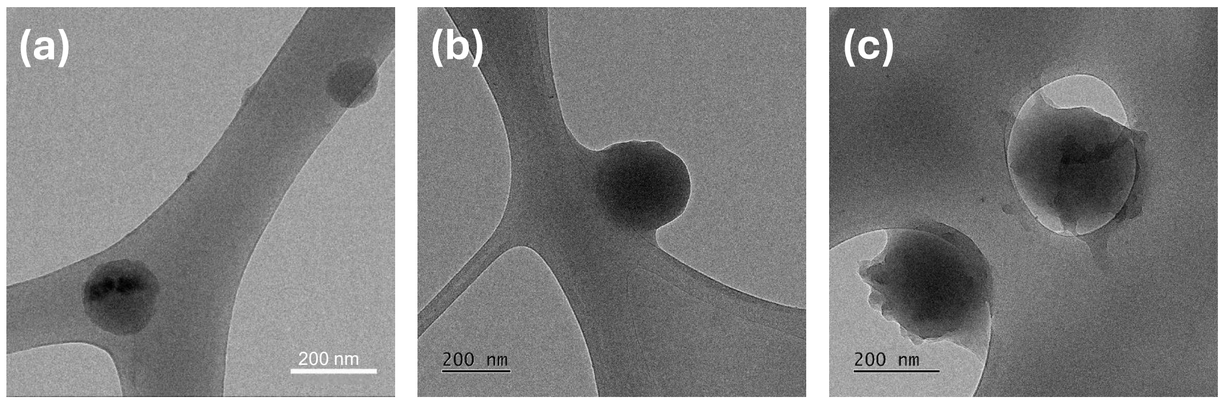

Fig 6. TEM micrograph of **(a)** ZN NPs, **(b)** ZN(FA) NPs, **(c)** ZN-FA NPs

Fig 7. FTIR spectra confirming the formation of a C-N covalent bond between folate and zein at 1108 cm^{-1}.

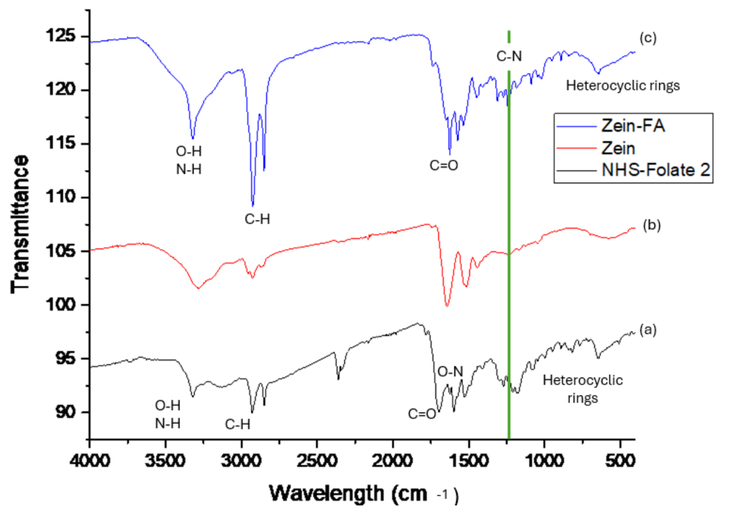

Table 1. Zein nanoparticles characterization. Data obtained from a DLS equipment.

	Particle size (nm)	PDI	Zeta Potential (mV)
Zein NPs	339.24 ± 29.32	0.31 ± 0.13	-14.58 ± 1.97
ZN(FA) NPs	455.77 ± 69.55	0.34 ± 0.16	-18.36 ± 2.54
ZN-FA NPs	366.42 ± 39.84	0.35 ± 0.06	-18.16 ± 4.00

Table 2. Adsorption data on zein nanoparticles obtained from a UV-VIS spectrophotometer.

	Adsorption efficiency (%)	BSA concentration per NP (mg BSA / mg NP)
Zein NPs	44.61 ± 9.69	0.892 ± 0.19
ZN(FA) NPs	41.00 ± 21.81	0.820 ± 0.43
ZN-FA NPs	45.44 ± 20.72	0.908 ± 0.41

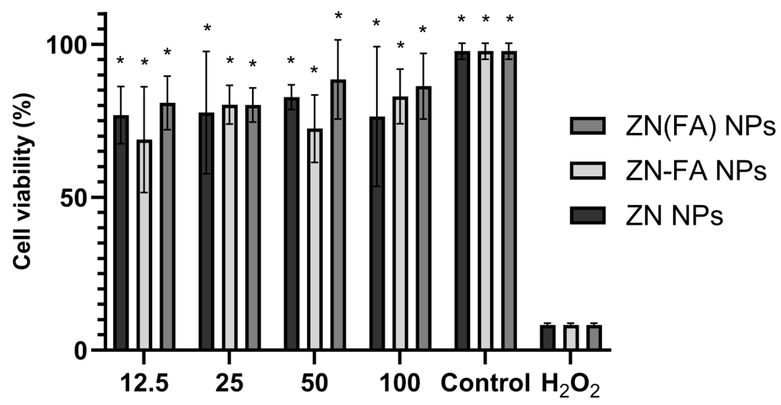

Fig 8. Cell viability in dendritic cells following treatment with different concentrations of NPs. The asterisks denote significant differences respect the cells treated with H_2O_2 ($p < 0.05$). Control cells were treated with the vehicle alone.

CONCLUSION

The proposed methodology allowed the successful incorporation of folate to zein nanoparticles using two methods: prior to NPs formation and after NPs formation. This incorporation was evidenced by FT-IR and UV-VIS analysis. BSA was absorbed onto the functionalized NPs, confirming the potential use of these NPs as antigen delivery systems. Preliminary data from the resazurin assay suggest that the three types of NPs are not cytotoxic.

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