The 8th International Electronic Conference on Medicinal Chemistry (ECMC 2022)
01–30 NOVEMBER 2022 | ONLINE

MESOPOROSOUS SILICA NANOPARTICLES AS A DRUG DELIVERY SYSTEM AGAINST TRIPLE NEGATIVE BREAST CANCER

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pharmaceuticals MDPI

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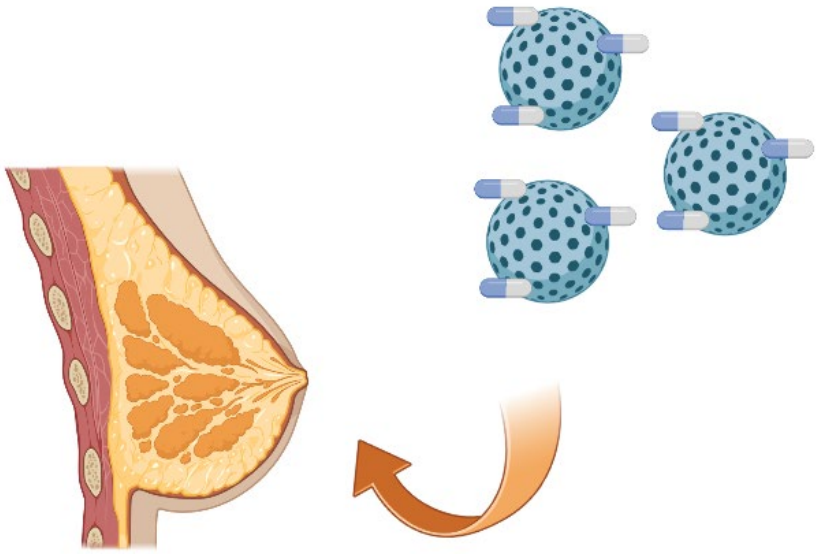
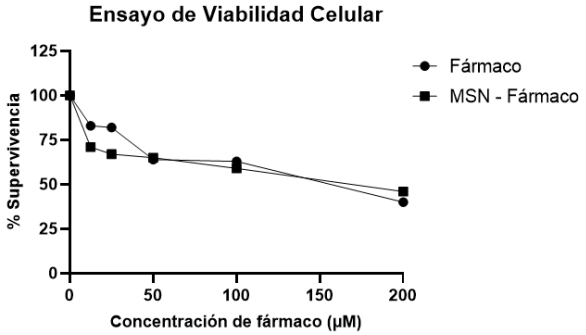
Graphical Abstract





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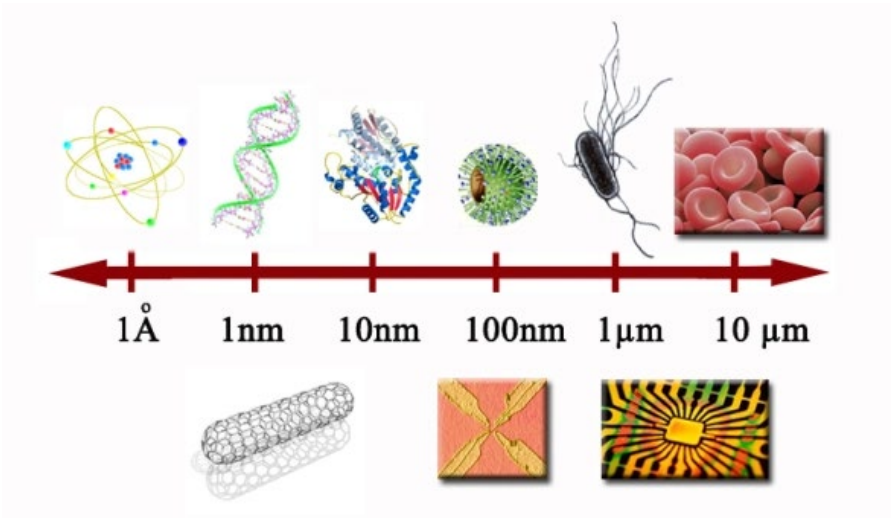
Abstract:

Mesoporous silica nanoparticles (MSNs) represent a novel platform for drug delivery systems, reducing the cytotoxicity of the drug and being able to be functionalized to increase its effectiveness. Its activity is currently being investigated in numerous diseases, among which cancer stands out. Cancer is the main malignant neoplasm in women and the second worldwide, with more than 2.2 million new cases diagnosed in 2020. Of these, 15% belong to the triple negative subtype (TNBC), defined by the absence of receptors for both hormones and the epidermal growth factor HER2, which makes it difficult to develop treatments. In this work, the antitumor effect of MSNs loaded with a proapoptotic drug against TNBC has been confirmed by cell viability techniques and apoptosis assays, confirming the mechanism of action.

Keywords: nanomedicine; controlled release; triple negative breast cancer; apoptosis

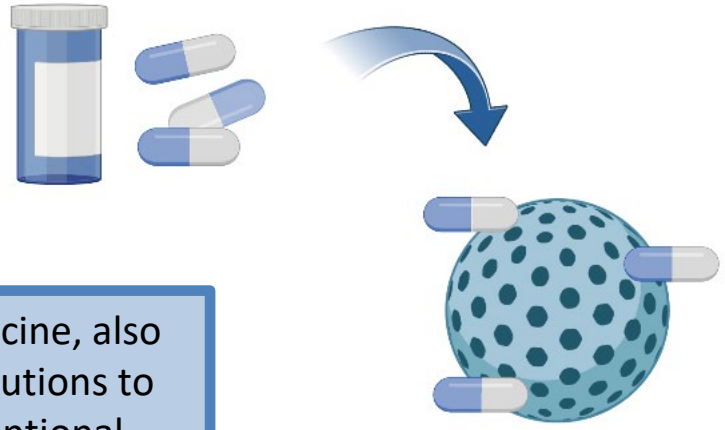
Introduction



Nanotechnology and nanomaterials have greatly advanced during the last 30 years due their potential in many different fields of research. In particular, in medicine and biomedicine, nanomaterials have shown unique physical-chemical characteristics that improve the pharmacokinetic parameters of conventional treatments.

One of the greatest potential applications in the use of nanomaterials in biomedical research is their use as drug delivery systems. The development of nanosystems allows improving the absorption and distribution of drugs for the treatment of bacterial infections or even the treatment of certain types of cancer by dosing antitumor drugs.

Introduction



The implementation of nanomaterials in medicine, also known as nanomedicine, is helping to find solutions to several important issues arising from conventional therapies or diagnostic tests and generating new effective, versatile, reliable, and cost-effective nanosystems, which are capable of overcoming most of the biophysical, biomedical, and biochemical obstacles of the human body and those due to different diseases, acting in most cases as drug-delivery platforms that safely transport therapeutic or imaging agents to their biological targets. Silica-based theragnostic materials can easily be obtained by the simple incorporation of a therapeutic agent, and this kind of systems are currently being developed with special interest in the fight against cancer.

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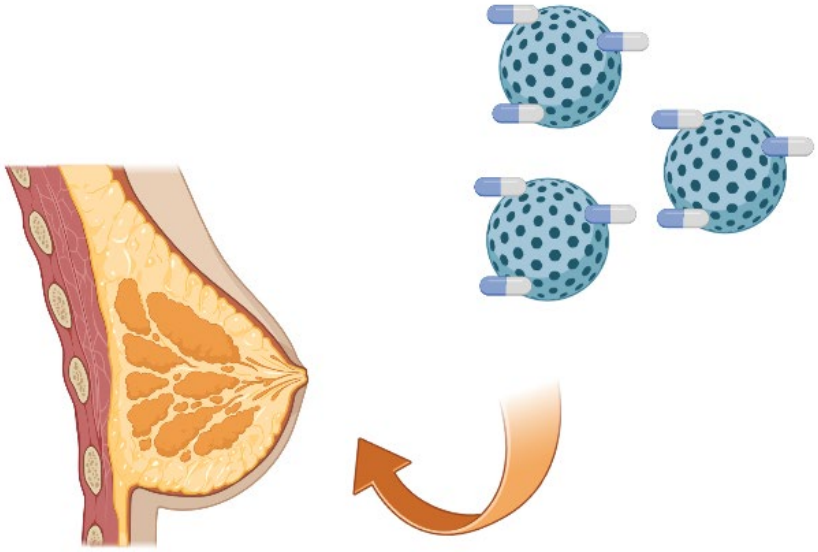
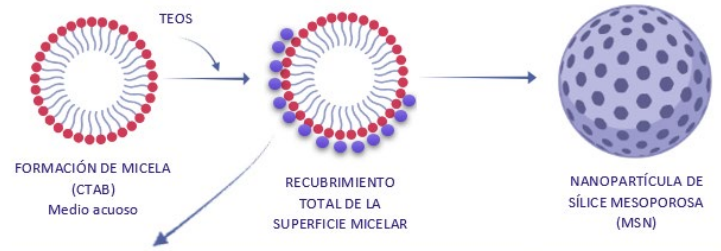
Introduction

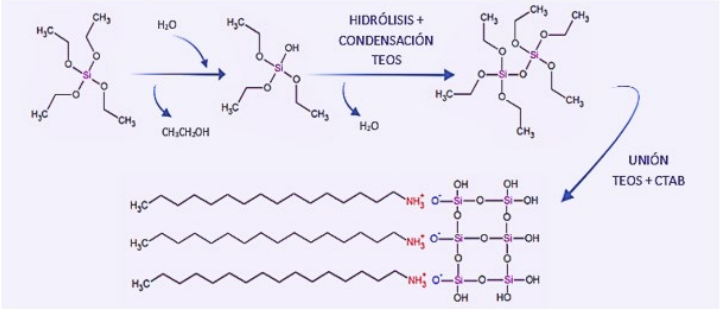
Breast cancer is characterized by great intratumoral heterogeneity and is clinically divided into: Luminal A, Luminal B, HER2 positive and triple negative breast cancer (TNBC). The TNBC subtype, treated in this study, is characterized by the absence of receptors, which means that it currently does not have a targeted treatment.



In recent decades, numerous compounds have been developed to treat TNBC. There are also PARP inhibitor drugs approved for use as monotherapies in BRCA-mutated TNBC, tested in phase III clinical trials. These drugs improve the prognosis of 50% of patients with BRCA-mutated TNBC, but there have also been cases of resistance.

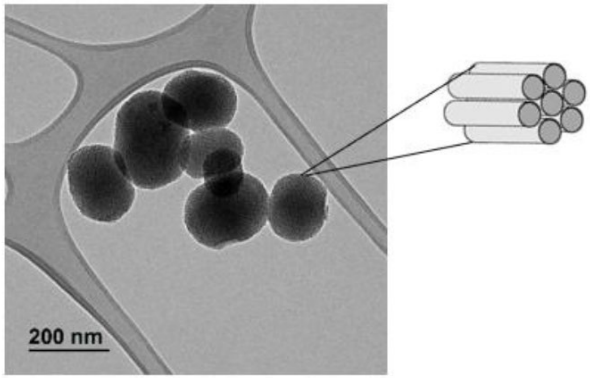
Results and discussion





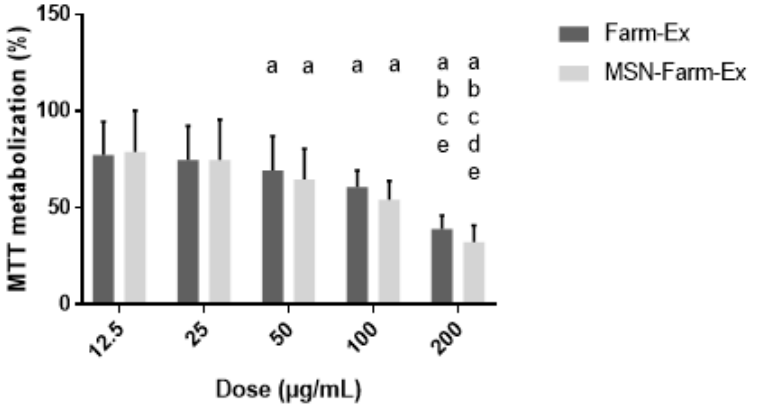
The synthesis of the starting material MSN was carried out starting with an aqueous solution of hexadecyltrimethylammonium bromide (CTAB, 1 g, 2.74 mmol), prepared in 480 mL of Milli-Q water. Subsequently, sodium hydroxide (2 M, 3.5 mL) was added to the solution and the temperature increased to 80°C. Afterwards, the silica precursor tetraethyl orthosilicate (TEOS, 5 mL, 22.4 mmol) was added dropwise under vigorous stirring and the mixture allowed to react for 2 additional hours. The resulting white precipitate was isolated by filtration and washed with abundant Milli-Q water and then with methanol and dried for 24 h at 80 °C in a stove. Finally, a calcination process at 500 °C was carried out for 24 h.

The drug was loaded into the silica nanoparticles after an incubation in EtOH for 24 hours.



Results and discussion

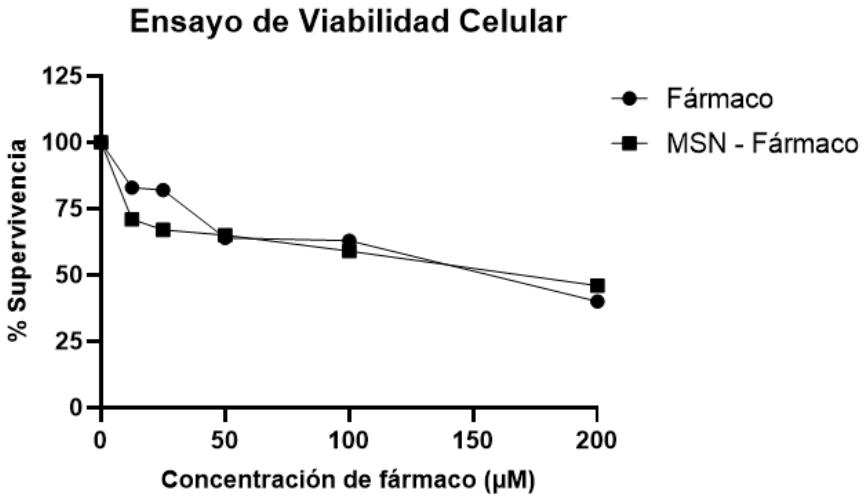
After spectroscopic characterization of the nanoparticles, we proceeded to compare their biological activity with the free drug carried on them. For this, cell viability assays were performed to determine the minimum amount necessary to inhibit 50% of the cell viability of the MDA-MB-321 tumor cells of the TNBC subtype. An antitumor activity of the MSNs were appreciated even at the lowest concentration evaluated (12.5 µM), this activity is dose-increasing.



Effect of 72 h exposition of Farm-Ex and MSN-Farm-Ex employing triple-negative breast tumoral cells (MDA-M-231). a vs untreated cells; b vs 12.5 µg/mL; c vs 25 µg/mL; d vs 50 µg/mL; e vs 100 µg/mL; n=3;$p<0.05$.

Results and discussion

Last, the IC_{50} value for both treatments was determined. Under the test conditions, the drug treatment showed an IC_{50} value of 127.3 µM, while for the treatment with the nanoparticles this value was reduced to a concentration of 112.4 µM.



Treatment	IC_{50} (µM)
Farm-EX	127.3
MSN-Farm-EX	112.4

Conclusions

The results demonstrate the great potential of these "drug delivery" systems in the development of targeted therapies for many types of cancer, as they can maintain or even increase the biological activity of the drugs they transport. This makes nanotechnology an interesting strategy to encapsulate and direct drugs, thus being able to create targeted therapies for different types of cancer that currently do not have an established therapy, as could be the case of TNBC.