PREVENTION OF EXTRAVASATION BY THE LOCAL APPLICATION OF HYBRID AEROGEL MICROPARTICLES AS DRUG DELIVERY SYSTEMS FOR CERVICAL CANCER CHEMOTHERAPY

6ER-017

UNIVERSITY of DEBRECEN

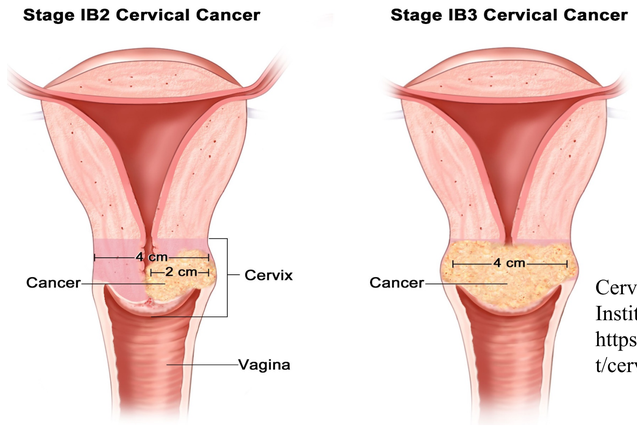
J. C. Egu[1], K. Moldován[1], P. Herman[1], I. Fábián[1], F. Fenyvesi[2], J. Kalmár[1]

chinonsojohnegu@gmail.com

1 Department of Inorganic and Analytical Chemistry, University of Debrecen, Debrecen 4032, Hungary
2 Department of Pharmaceutical Technology, University of Debrecen, Debrecen 4032, Hungary

INTRODUCTION

- Cervical cancer is the fourth most common cancer in women.
- 90% of the disease is caused by HPV.



Cervical cancer stage I. National Cancer Institute. https://www.cancer.gov/types/cervical/patient/cervical-treatment-pdq

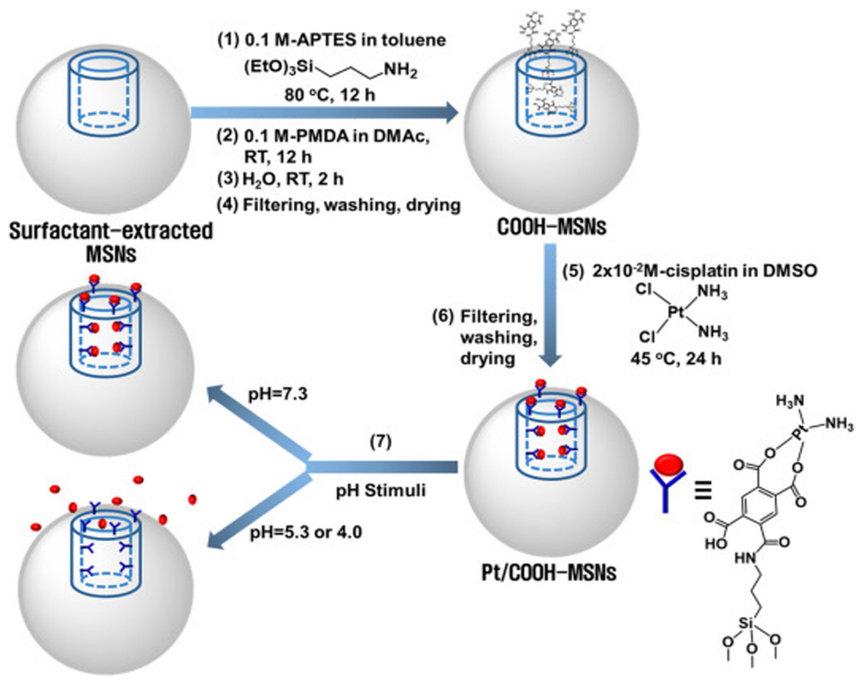
- In 2018, 570 000 women were diagnosed with the disease worldwide and about 311 000 women died from the disease (WHO, 2018).
- Cisplatin is the standard chemotherapeutic agent, usually in combination, for treating cervical cancer.
- Usually given IV over hours, patients might develop tissue necrosis due to the incidence of extravasation. This can be prevented by local administration of the drug using hybrid aerogel microparticles as therapeutic systems.

AIM AND OBJECTIVES

- Improve chemotherapy approach by developing a model that locally delivers Cisplatin to the tumour tissues of the cervix, colon, rectum. The developed aerogel microparticles should be biodegradable, biocompatible and mucoadhesive, and is capable to be delivered intravaginally and intrarectally (in suitable formulations) and releases Cisplatin in a modified, controlled-release manner.

MATERIALS AND METHODS

➢ **Synthesis:** The hybrid aerogels was synthesized by sol-gel method. 1.17g of gelatin was dissolved in 16ml of DMSO and 5.4ml of water under continuous stirring at 80^{O}C and then a mix of 16ml DMSO, 3ml TMOS and 1ml APTMS is added and stirred overnight. DMSO is then gradually replaced with Acetone for a period of 2 weeks after which a solution of 2.18g PMDA dissolved in 100ml DMAC was added. After 1 week, a solution of 100mg Cisplatin dissolved in 100ml DMSO was added to the alcogel and kept in the dark for 2 weeks to allow for Cisplatin incorporation. The particles were degassed and dried under supercritical CO_2.



Park, S. S., Jung, M. H., Lee, Y. S., Bae, J. H., Kim, S. H., & Ha, C. S. (2019). Functionalised mesoporous silica nanoparticles with excellent cytotoxicity against various cancer cells for pH-responsive and controlled drug delivery. Materials & Design, 184, 108187.

➢ **Porosimetry:** The aerogel specific surface area (as) was determined by the BET method. The pore size and pore volume was determined from the N2 adsorption isotherm using the BJH method, using the Quantachrome NovaWin 200e instrument. The measurement tube was washed with Argon. 32.3mg of Aerogels was used for the measurement, for 24 hours at 50OC

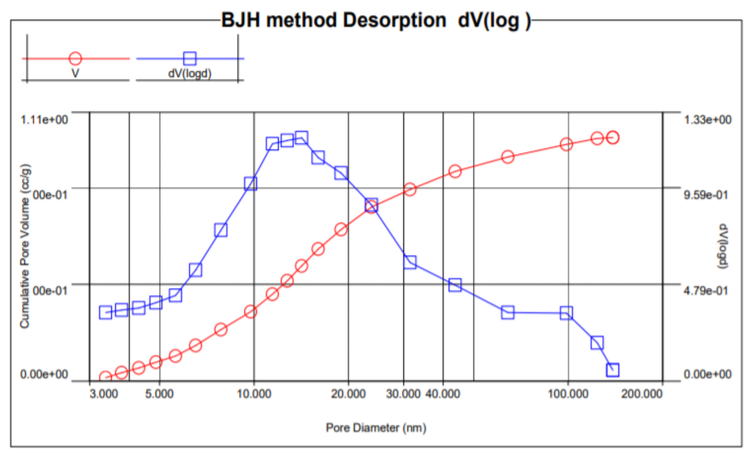
➢ **Morphology:** The morphology of the aerogels was imaged by Scanning Electron Microscope (SEM) which also showed the aerogel micropores and its skeletal framework.

➢ **Cytotoxicity:** Cytotoxicity studies was carried out on HeLa cells *in Vitro*. The particles were incubated with the cells over a period of 72h

ACKNOWLEDGMENT

The project was financially supported by the National Research, Development and Innovation Office, Hungarian Science Foundation (OTKA: FK_17-124571). Conference participation was financed by Debreceni Egyetem Tehetséggondozó Program (DETEP).

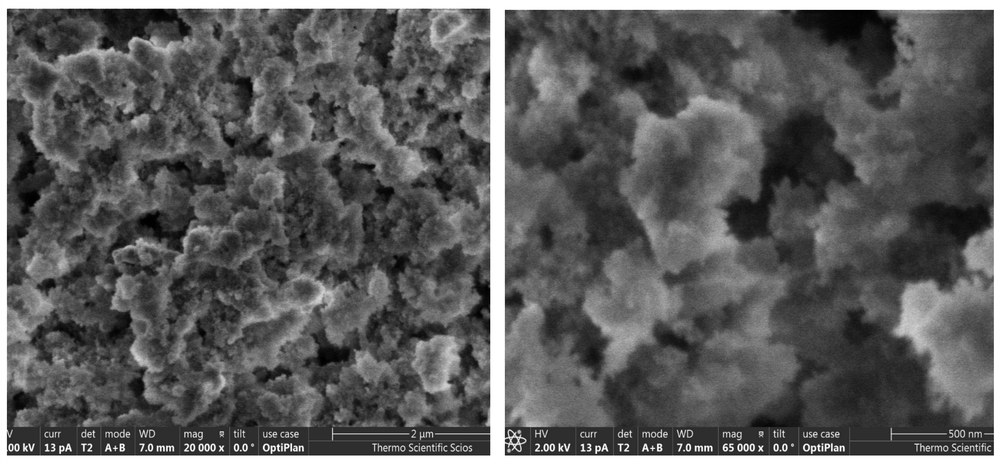
RESULT



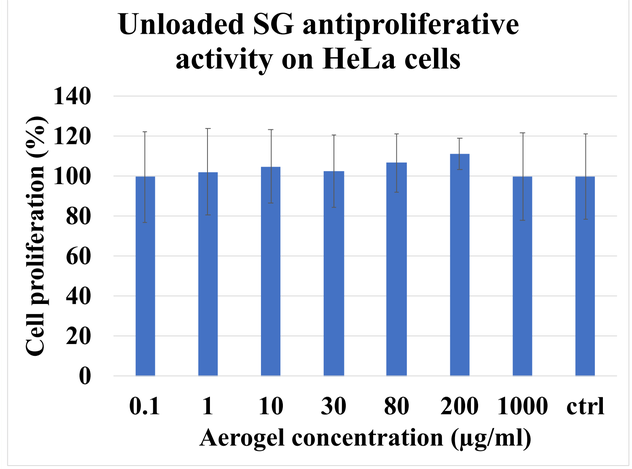
BJH desorption summary

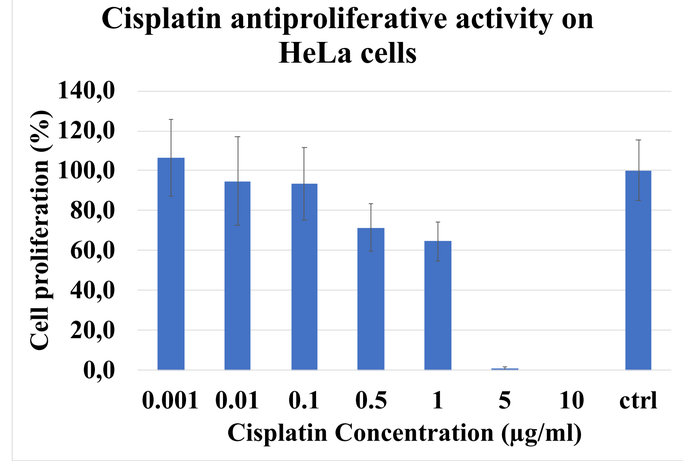
Surface Area =	316.173 m^2/g
Pore Volume =	1.007 cc/g
Pore Diameter Dv(d) =	11.446 nm

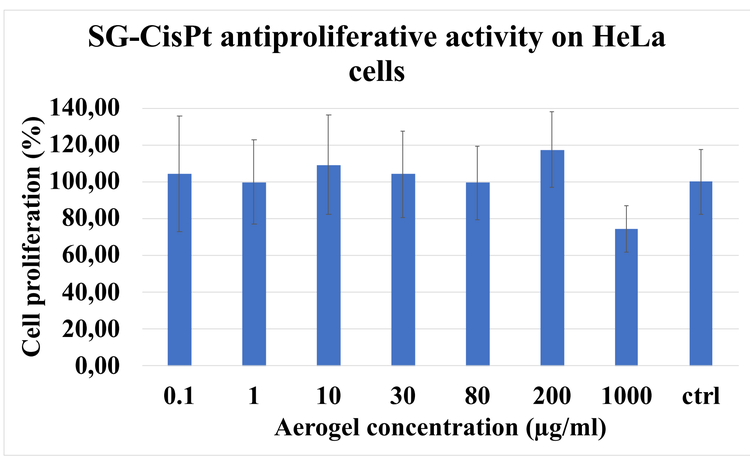
Structural parameters of Silica-gelatin aerogels estimated by the BET and the BJH methods from N_2 adsorption-desorption porosimetry data.



SEM images of the Silica gelatin aerogels







Unloaded aerogels, pure cisplatin, and cisplatin-loaded aerogels tested against HeLa cells *In Vitro.*

DISCUSSION AND CONCLUSION

➢ These novel aerogel microparticles are mesoporous having micro- and macropores. The pores and the loaded drug is accessible for extracellular liquid. 15-40µm particles SG-Cpt.

➢ Cisplatin content is 10-15mg/g.

➢ The pristine aerogel particles are biocompatible with the cells (95-120% viability).

➢ There is a significant difference in the antiproliferative effect observed at the highest concentration of SGCpt when compared to the control (t-test; $p < 0.01$). The highest concentration has approximately equivalent effect to the 0.5ug/ml free dose of cisplatin.

➢ The future goal is to formulate the system into suppositories which can be self administered.

REFERENCE

- Veres, P., Király, G., Nagy, G., Lázár, I., Fábián, I., & Kalmár, J. (2017). Biocompatible silica-gelatin hybrid aerogels covalently labelled with fluorescein. *Journal of Non-Crystalline Solids*, *473*, 17-25.
- Park, S. S., Jung, M. H., Lee, Y. S., Bae, J. H., Kim, S. H., & Ha, C. S. (2019). Functionalised mesoporous silica nanoparticles with excellent cytotoxicity against various cancer cells for pH-responsive and controlled drug delivery. *Materials & Design*, *184*, 108187.