The Influence of shear stress on nanomaterial's uptake by cancer cells

Samar Shurbaji[1], Hüseyin C. Yalçın[1] , Ahmed Elzatahry[2]

[1]Biomedical Research Center, Qatar University, PO Box 2713, Doha, QATAR
[2]Reseaarch and graduate studies office, Qatar University, PO Box 2713, Doha, QATAR

Background

Cancer is a growing global problem that is manifested by the uncontrolled division of abnormal cells in part of the body. Current cancer therapy such as chemotherapy and radiotherapy suffer from low efficacy and low specificity against tumors and are associated with severe side effects influencing non-cancer tissue. Photothermal therapy (PTT) has emerged as a highly efficient and highly selective treatment technique against tumors for cancer therapy. PTT depends on heat generation upon exposure of tumor cells to near-infrared radiation (NIR). For PTT therapy to be effective, PT agents needs to be internalized by cancer cells. Recently, MXene, a novel material that contains transition metal carbides, was reported as a suitable PT agent, due to the presence of the transition metal "Titanium" in MXene. Similar previous studies use static cultures to investigate internalization of NPs by cancer cells. However, in the body cancer cells are influenced by fluidic shear stress caused by blood flow in the vascular microenvironment and interstitial flows in the tumor microenvironment. Shear stress experienced by cells were shown to influence internalization of NPs for normal and for cancer cells.

Objectives

- To study the influence of shear stress on Mxene and MX/Au nanometals uptake and viability by MDA-231 breast cancer cells .
- To compare between Mxene and Mxene/Au in terms of uptake and killing efficiency.

Methodologies

1.Production of MXene and MXene\Au nanomaterials:

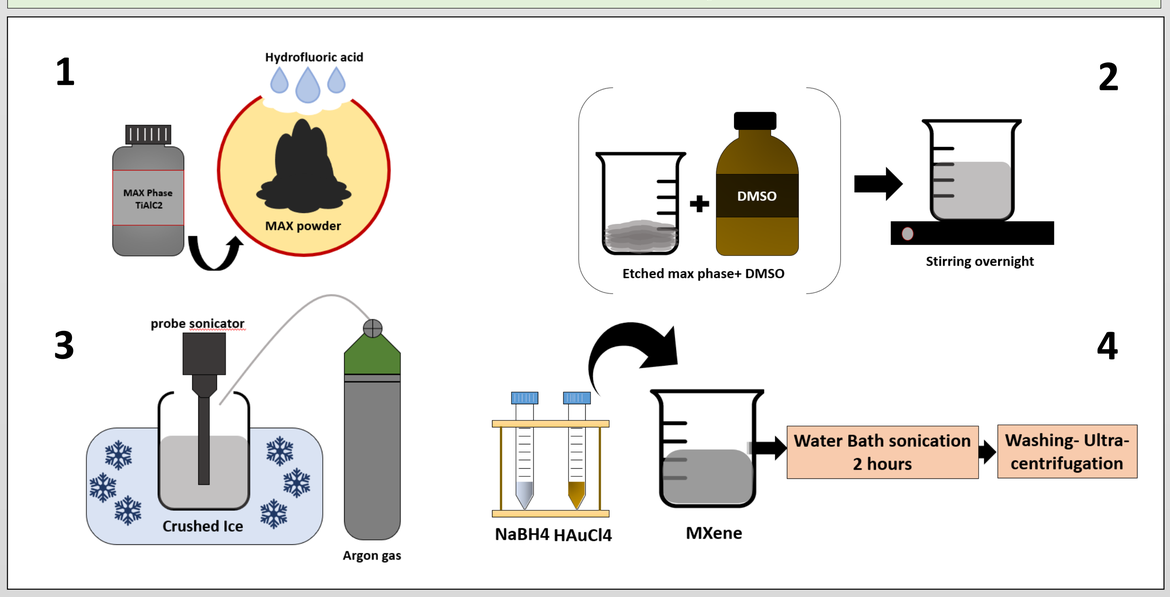

Figure 1: production of Mxene and Mxene/Au. Mxene is produced by chemical etching of MAX phase followed by delamination using DMSO , and sonication to produce single 2D sheets. whereas gold nanoparticles were deposited on Mxene sheets surface by reduction of AuCl4. These nanomaterials were characterized using SEM, TEM and XRD.

2.Inducing shear stress in static culture using Bioptech flow chamber

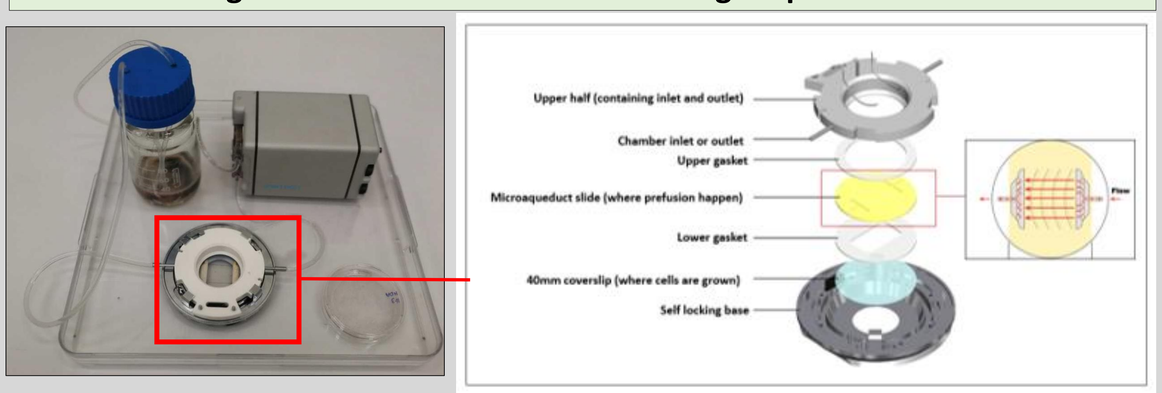

Figure2 : Breast cancer cells MAD-231 were grown in circular coverslips until confluence and assembled in a flow chamber. The flow chamber was connected to peristaltic pump at 0.1 dyn/cm2 shear rate. The shear rate was calculated using Hagen-Poiseuille equation assuming a Newtonian fluid that has steady and laminar flow. MXene at 100ug/ml concentration was diluted in cell media and allowed to flow in the chamber to induce shear for four hours.

3. Uptake assessment

Transmission electron microscopy (TEM)

Energy dispersive spectrometer EDS (Elemental analysis) was used also to have an idea about the uptake

4. Viability assessment

We irradiated the cells using an 808 nm laser at 1 and W/cm2 power density for 5,10 and 15 minutes. Following laser exposure, the viability rate was quantified by live/dead staining. *Live/dead stain stains the dead cells red, and the live cells green.

Different parameters were studied including:

- Effect of incubation time
- Effect of the presence of serum in cell media
- Effect of laser power density
- Effect of laser exposure duration
- Effect of MXene concentration
- Different chamber dimensions
- Effect of shear adaptation

Results and Discussion

SEM and TEM

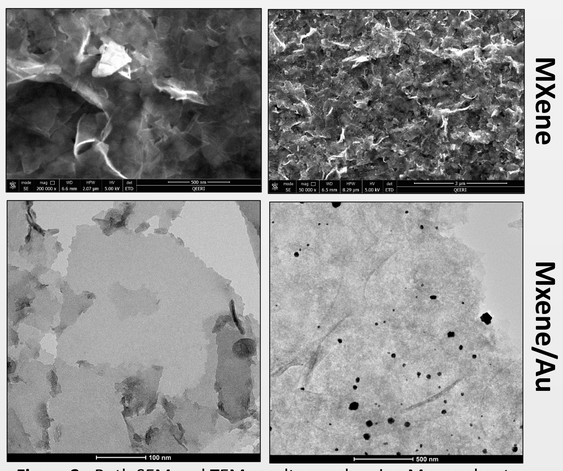

Figure 3 : Both SEM and TEM results are showing Mxene sheets with Au nanoparticles on top of the sheets

XRD

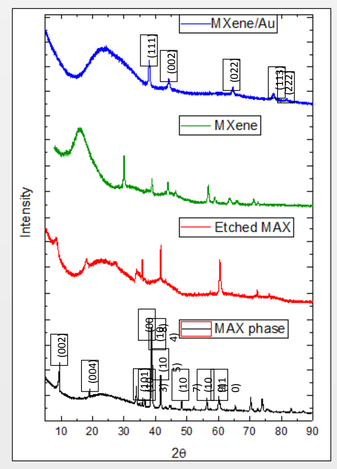

Figure 4: XRD peaks for MAX phase, etched MAX, MXene and MXene/ Au nanocomposite.

Thermal measurement

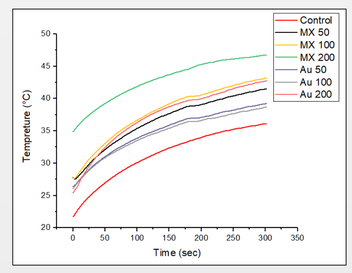

Figure 5: Different temperature measurements for MXene and MXene/Au at PD=1 W/Cm2

Nanomaterial's uptake assessment- TEM results

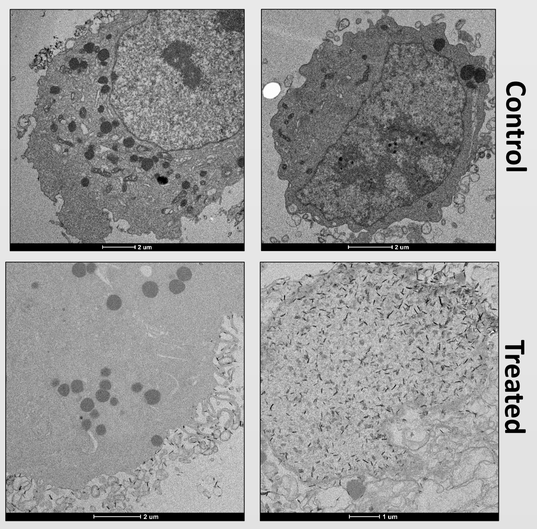

Figure 5: TEM images for control and treated cells.

Nanomaterial's uptake assessment- EDS results

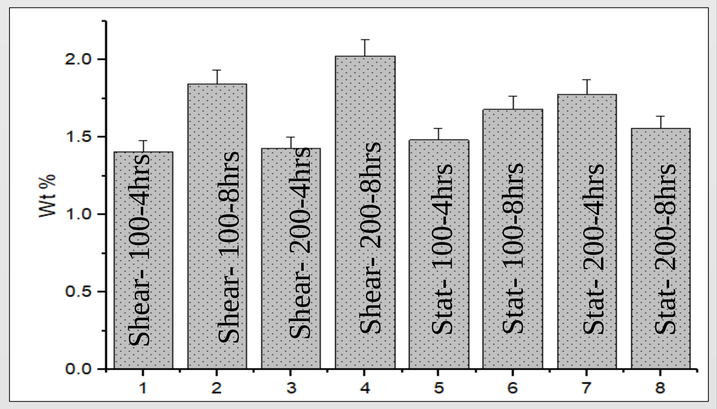

Figure 6: Bar chart represents wt% for Ti for 8 different cases, without significant difference between all groups.

Different factors that might affect viability results

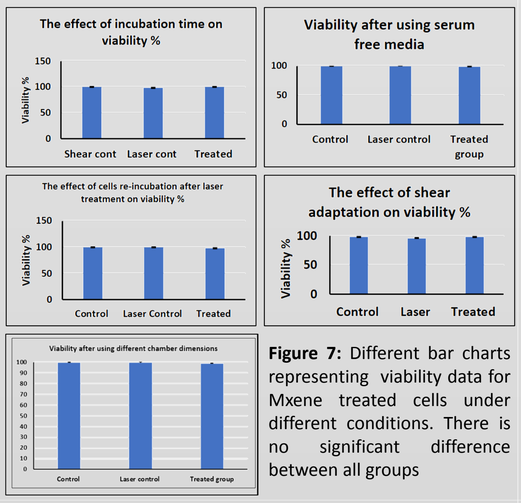

Figure 7: Different bar charts representing viability data for Mxene treated cells under different conditions. There is no significant difference between all groups

The effect of using different laser power densities& MXene concentration

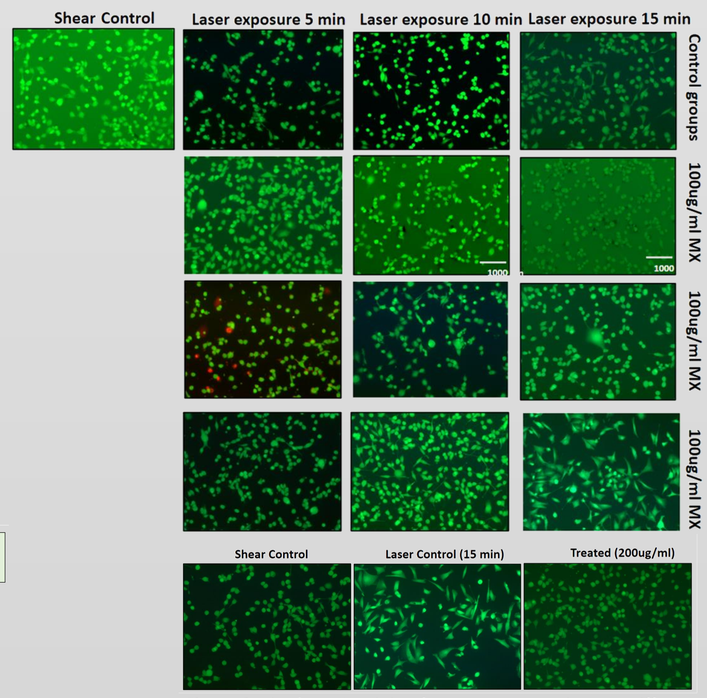

Figure 8: Live/ dead staining for cells treated with two different Mxene concentrations (100 and 200ug/ml) with three different power densities (1,3 and 5 W/Cm2).
**Green color represintes live cells*
**Red color represents dead cells*

Cytoskeleton staining

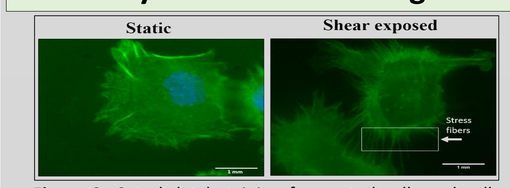

Figure 9: Cytoskeletal staining for control cells and cells exposed to shear stress. Representing stress fibers in the shear exposed group

Conclusions

MXene can be a good candidate for PTT for cancer treatment, but its cellular internalization should be enhanced. This can be achieved by coating the MXene surface and labeling the material with certain ligands that is cancer cell specific

Acknowledgments

This work was supported by Qatar University student grant :QUST-1-CAS-2019-37