

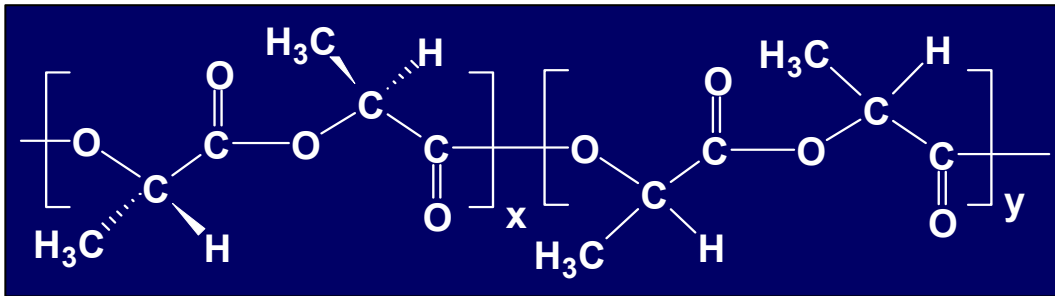
Laboratory of Bioactive Polymers

QUATERNIZED CHITOSAN-BASED ELECTROSPUN NANOFIBROUS MATERIALS WITH ANTITUMOR ACTIVITY

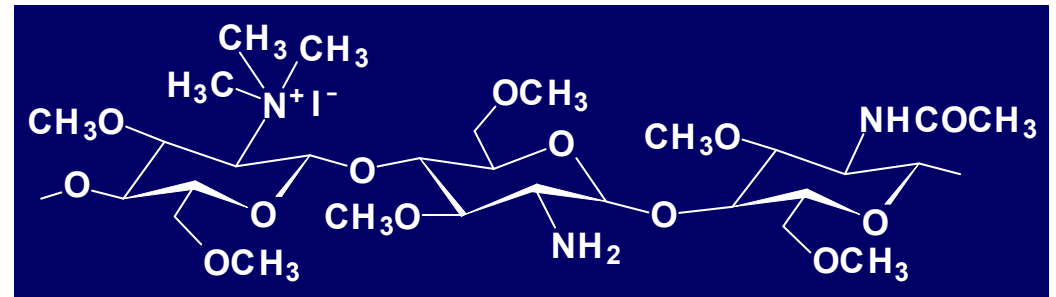
M. Ignatova, N. Manolova, R. Toshkova,
E. Gardeva, L. Yossifova, M. Alexandrov,
I. Rashkov

ELECTROSPUN NANOFIBROUS MATERIALS WITH ANTITUMOR ACTIVITY

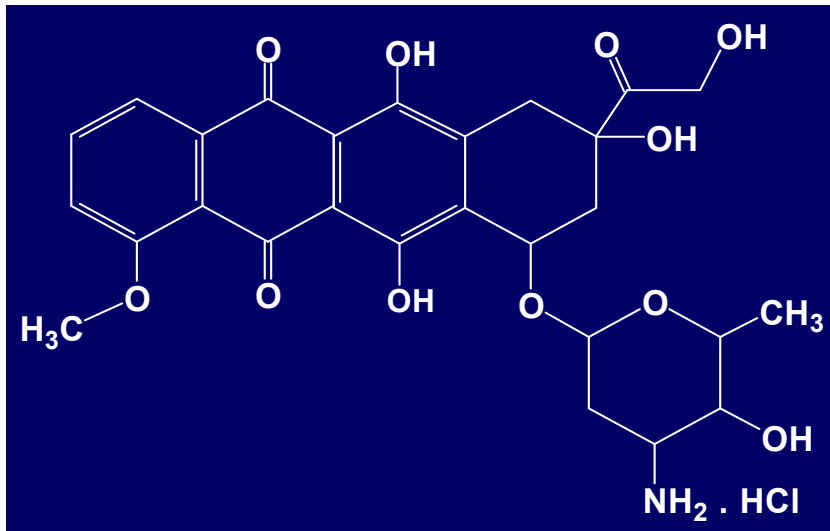
Poly(L-lactide-co-D,L-lactide) (coPLA)



Quaternized chitosan derivatives (QCh)



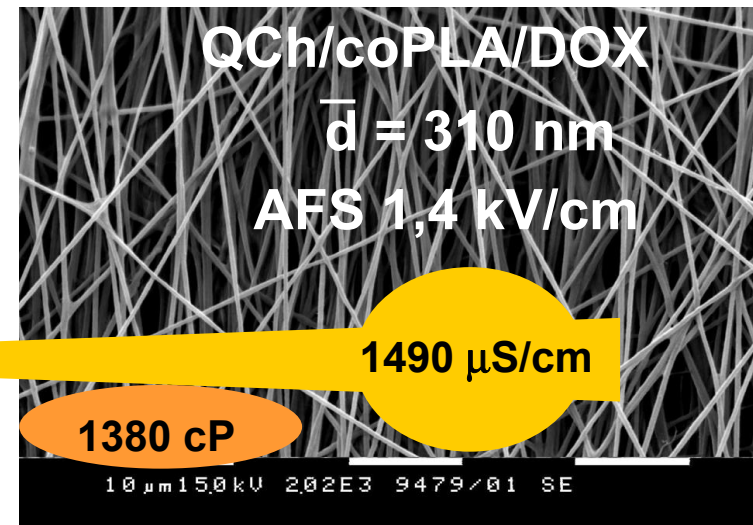
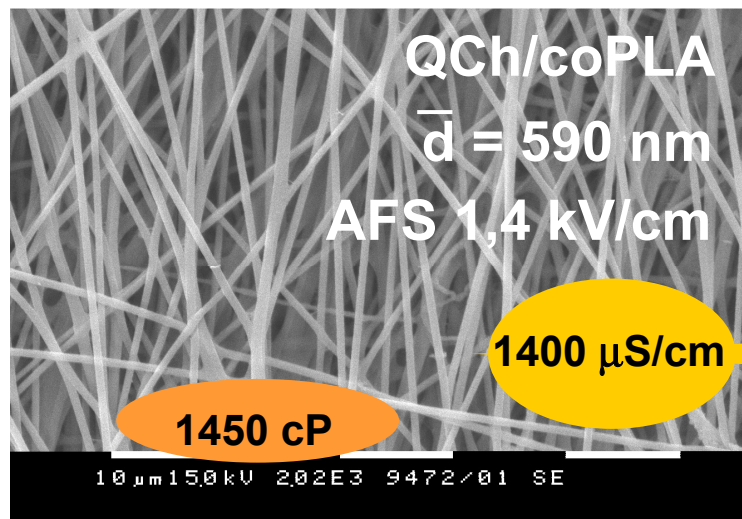
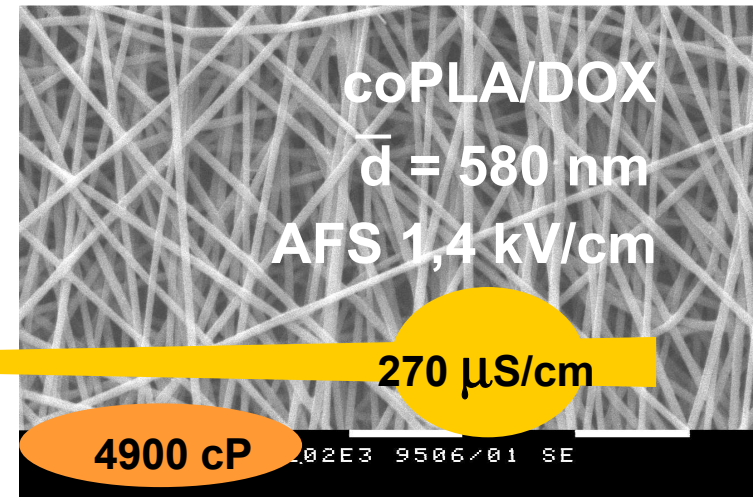
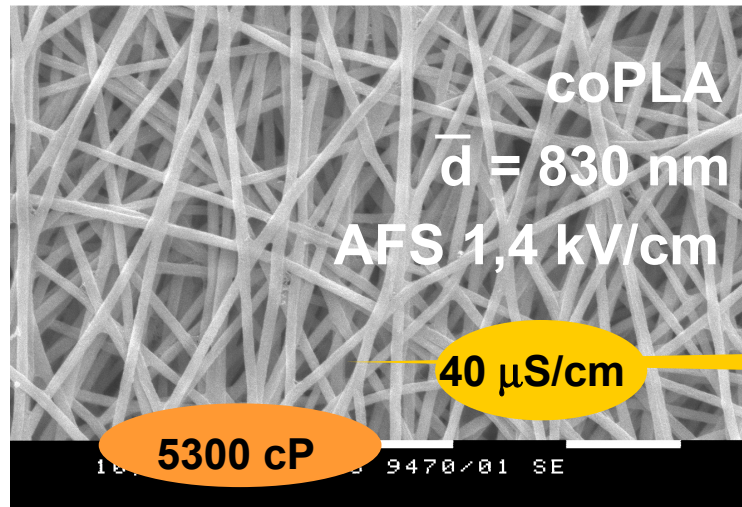
Doxorubicin hydrochloride (DOX)



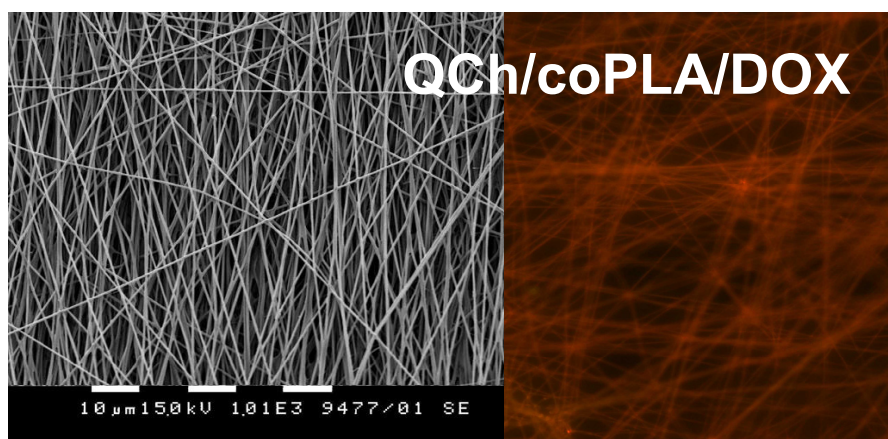
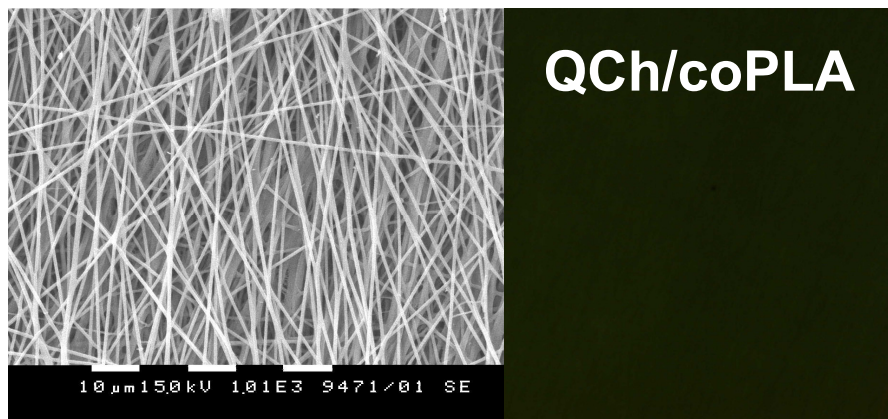
Electrospinning advantages:

- ❖ Fabrication of fibrous materials for variety of applications;
- ❖ Electrospun mats possessing unique properties:
 - high surface-to-volume ratio,
 - high porosity,
 - nano-scale diameter

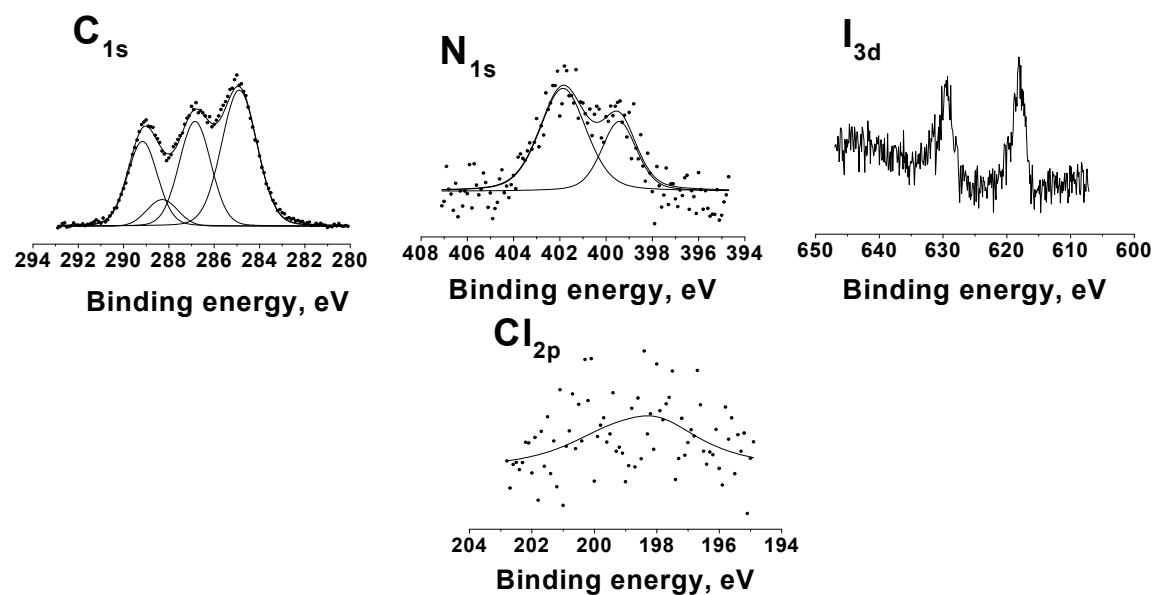
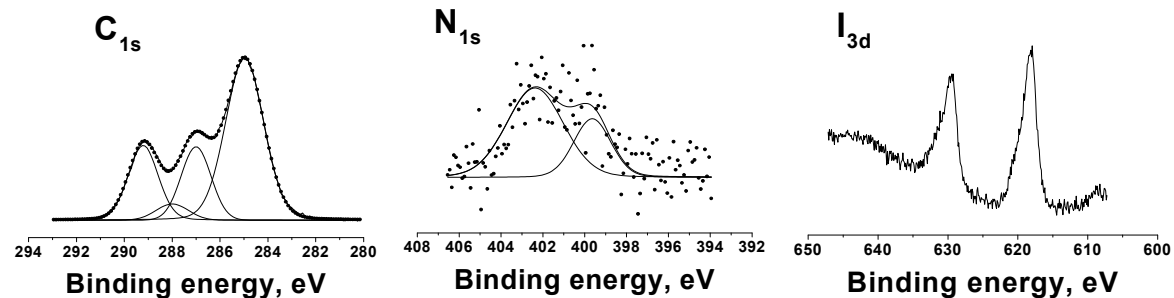
Novel hybrid nanofibrous materials with antitumor activity



Novel hybrid nanofibrous materials with antitumor activity

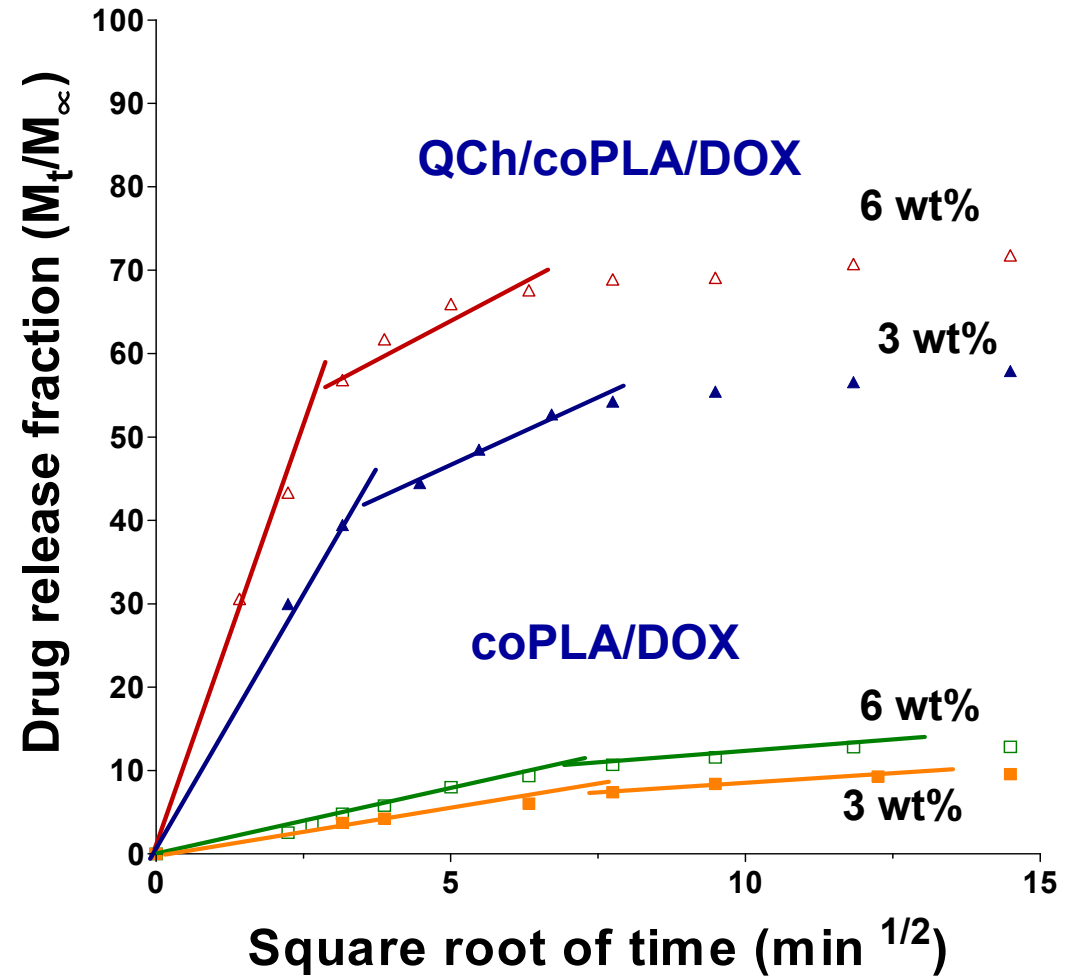
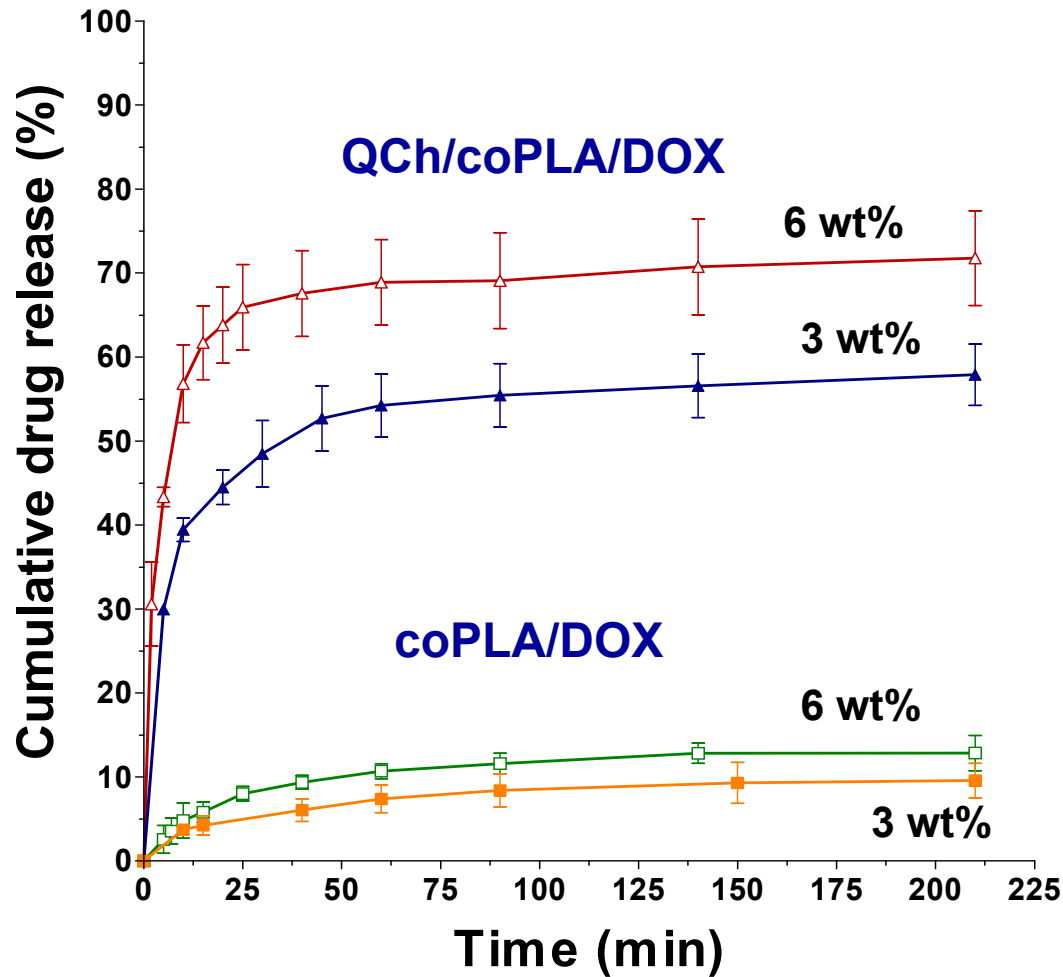


XPS analysis

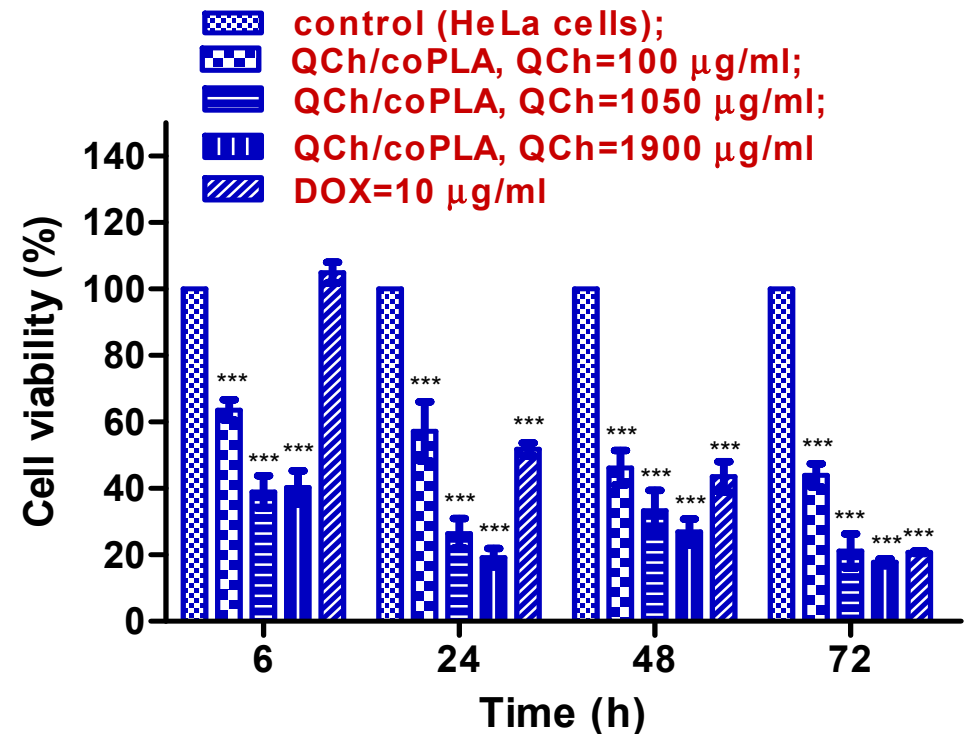
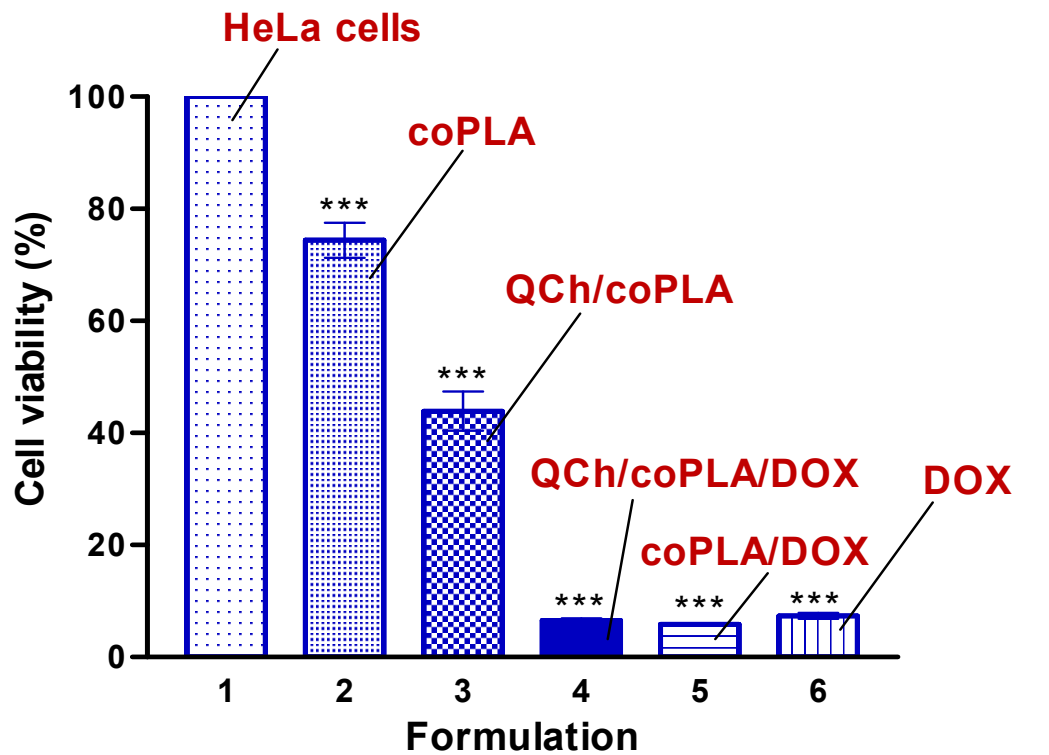


Novel hybrid nanofibrous materials with antitumor activity

The release profiles of DOX from the DOX-containing electrospun mats

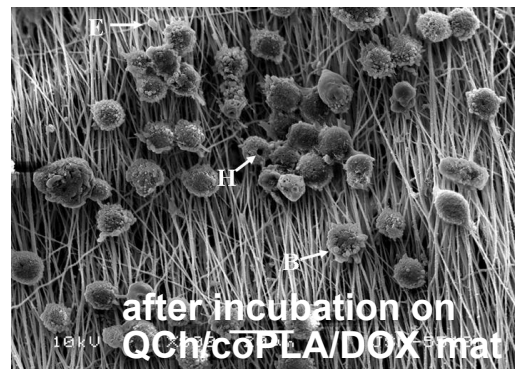
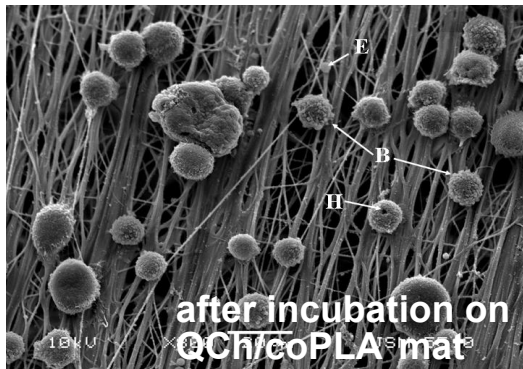
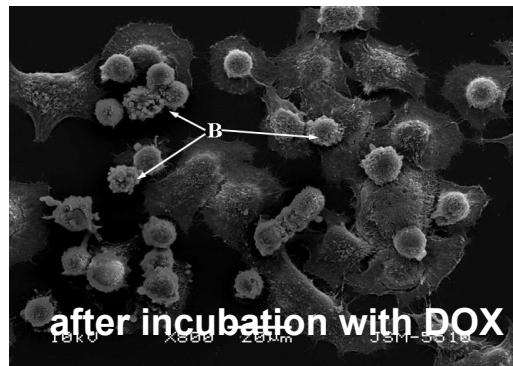
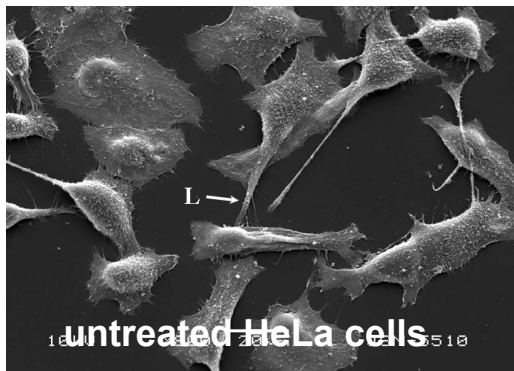


In vitro antitumor activity of the novel hybrid nanofibrous materials against human cervical cancer cells HeLa

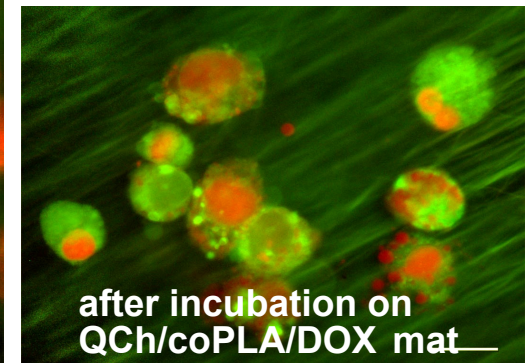
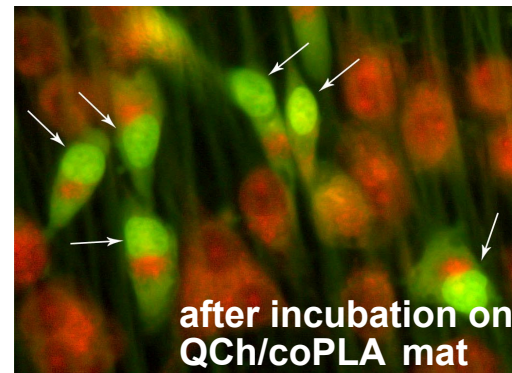
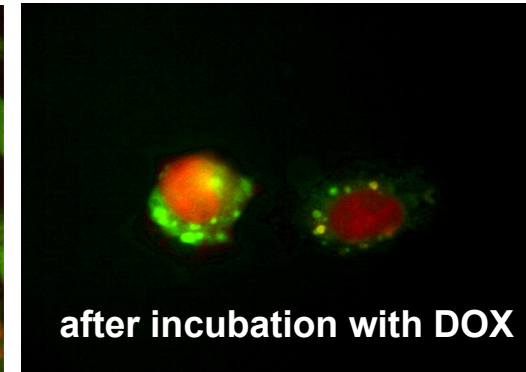
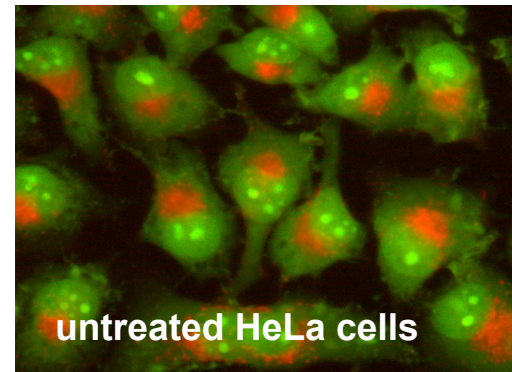


Novel hybrid nanofibrous materials with antitumor activity

SEM micrographs of surface ultrastructural characteristics of HeLa cells after 6 h incubation with pristine and DOX-containing electrospun mats

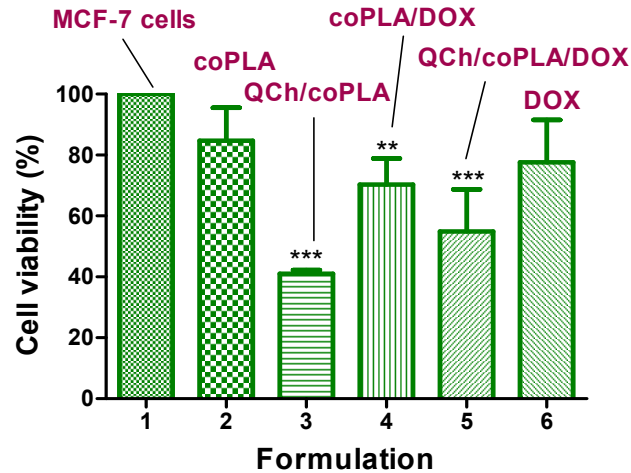


Fluorescent micrograph of AO and PI double-stained human cervical cancer cells lines HeLa incubated on pristine and DOX-containing mats for 24 h

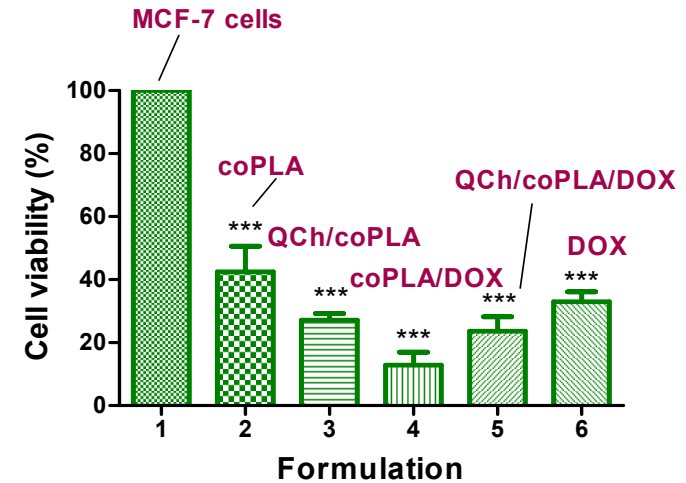


In vitro antitumor activity of the novel hybrid nanofibrous materials against MCF-7 human breast tumor cells

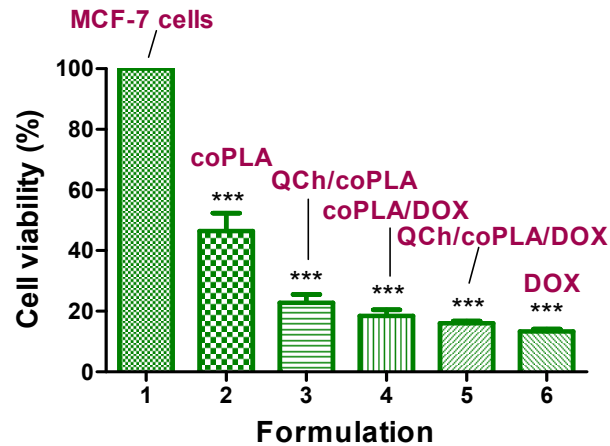
6h incubation



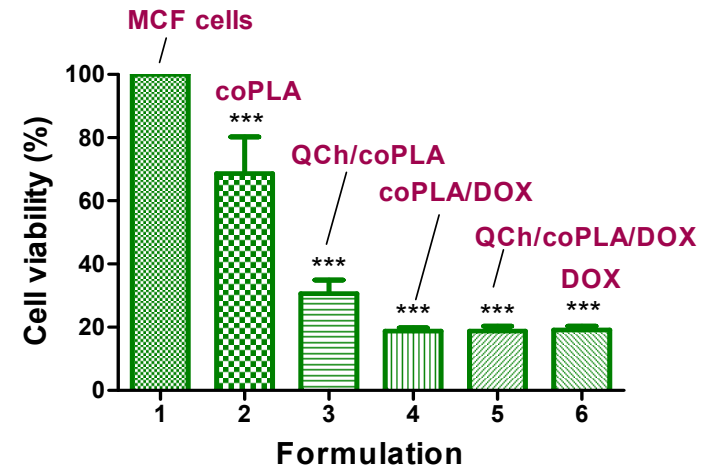
24h incubation



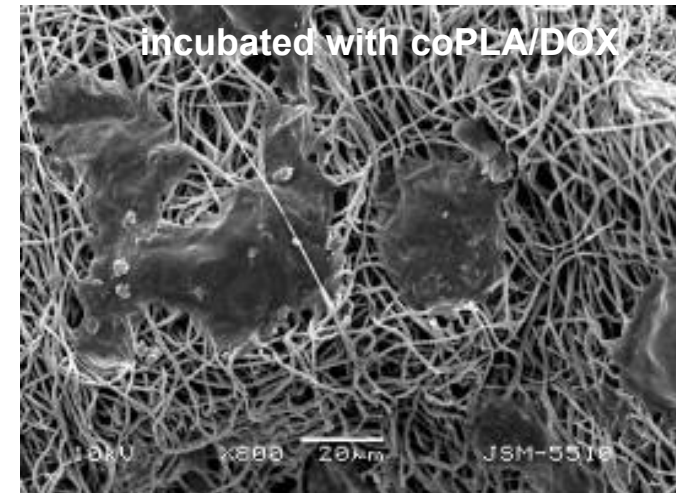
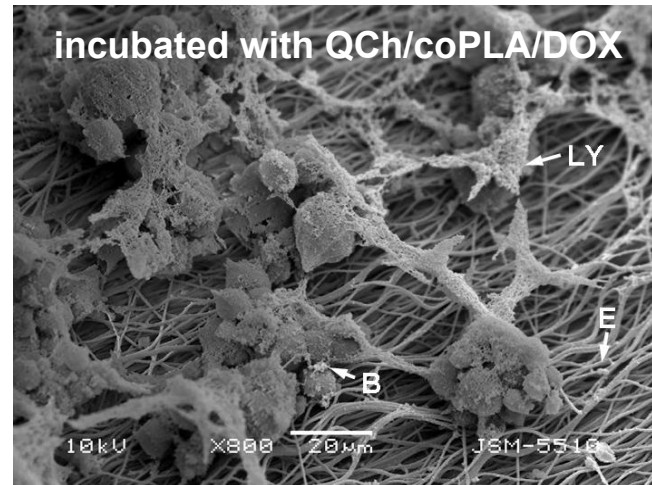
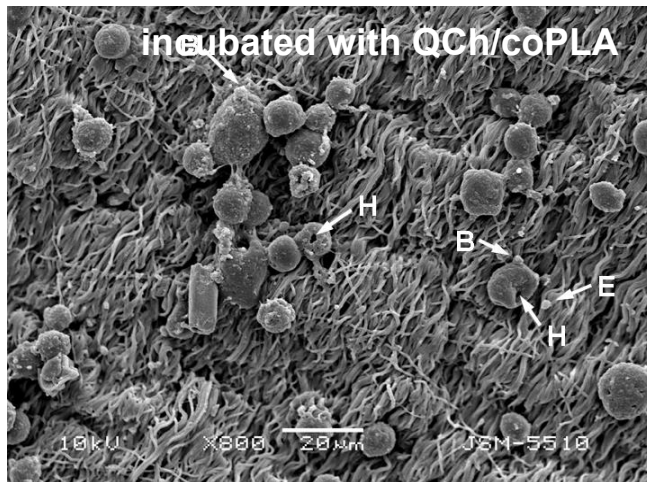
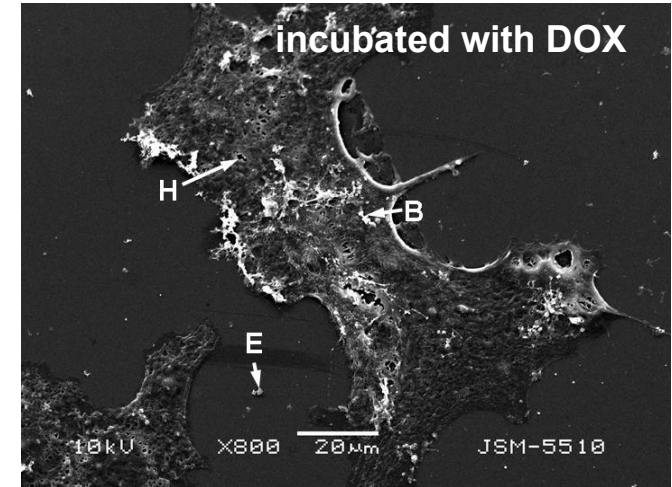
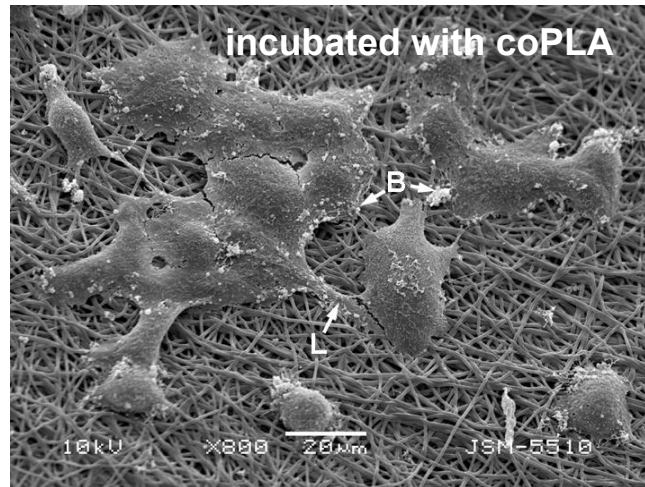
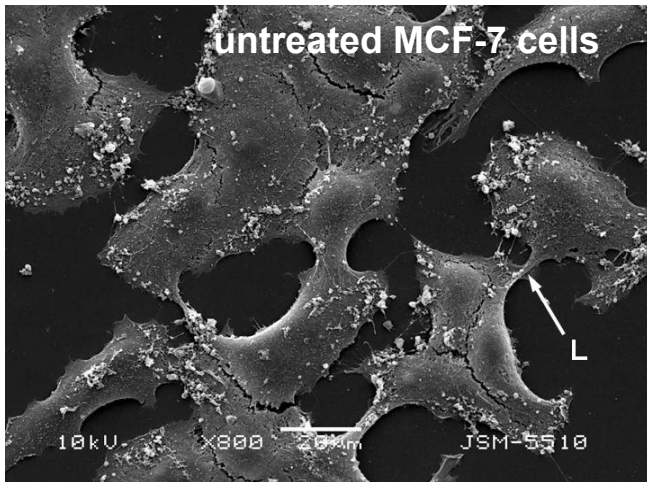
48h incubation



72h incubation

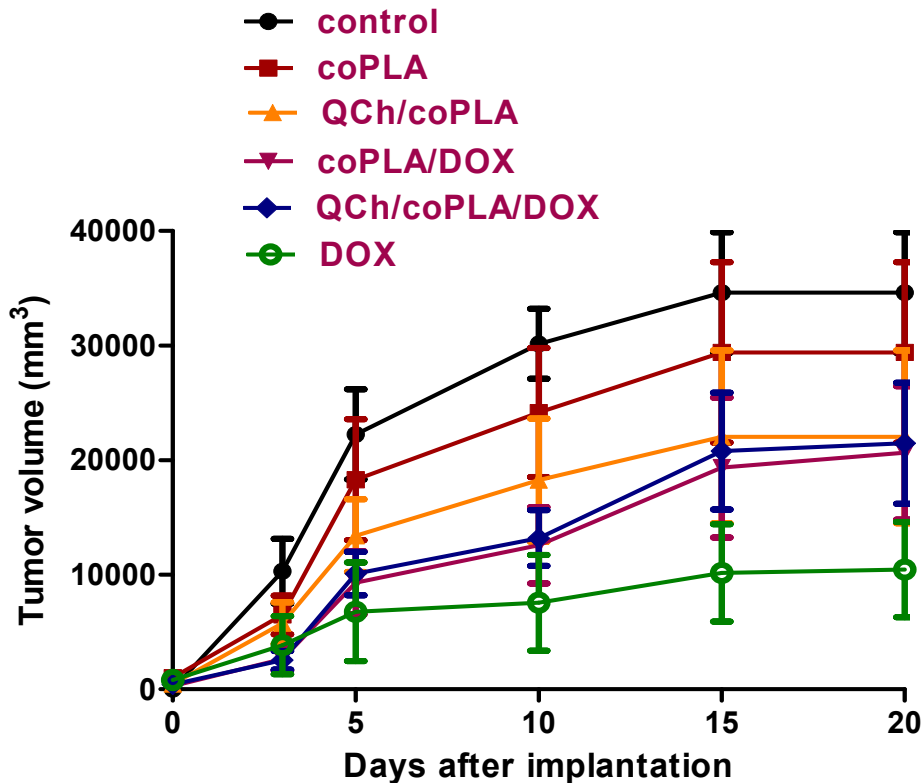


SEM micrographs of surface ultrastructural characteristics of MCF-7 cells after 24 h incubation with pristine and DOX-containing electrospun mats

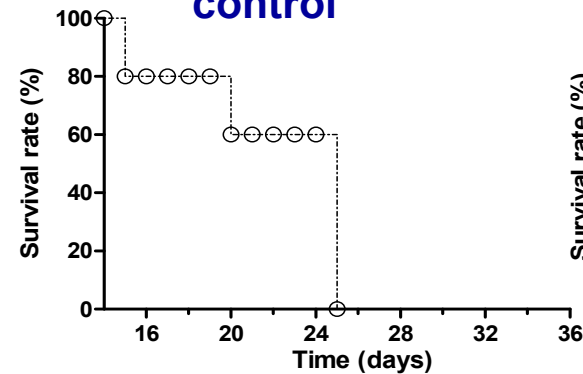


Antitumor activity of quaternized chitosan/doxorubicin containing nanofibrous implants against Graffi myeloid tumor

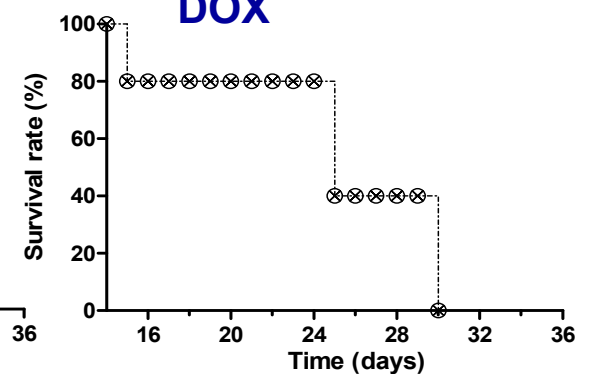
Tumor volume changes and survival rates of experimental and control hamsters bearing Graffi myeloid tumor after intratumoral insertion of nanofibrous implants



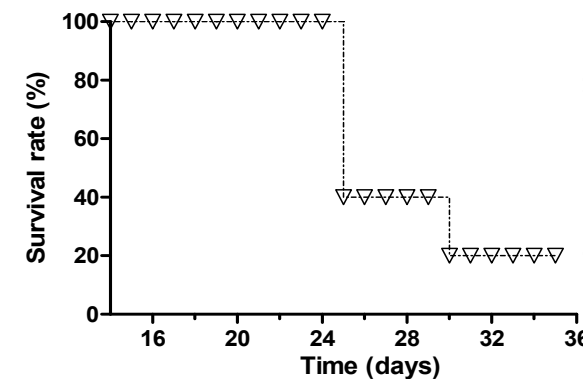
control



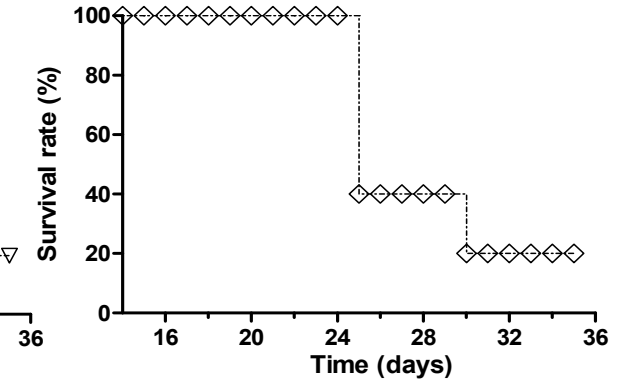
DOX



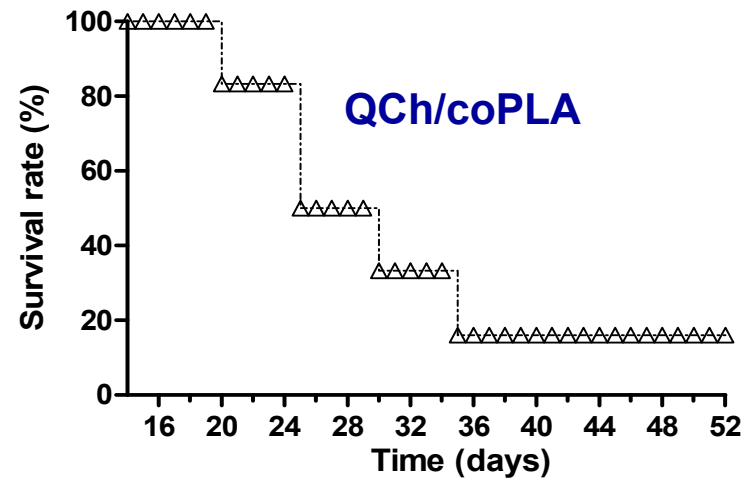
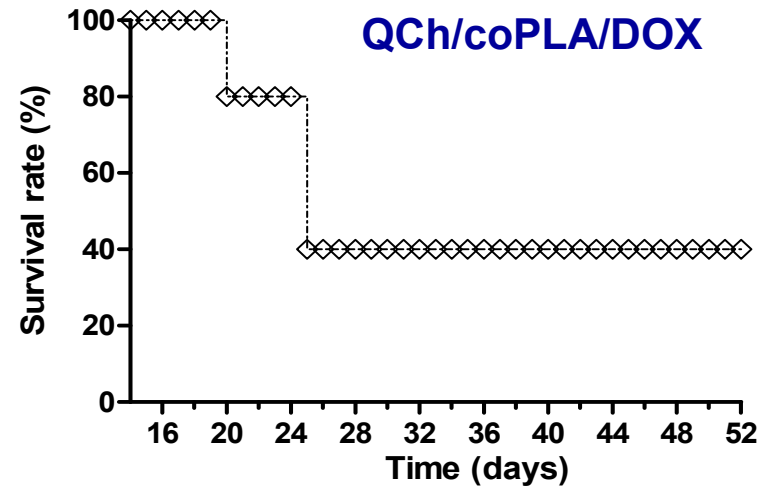
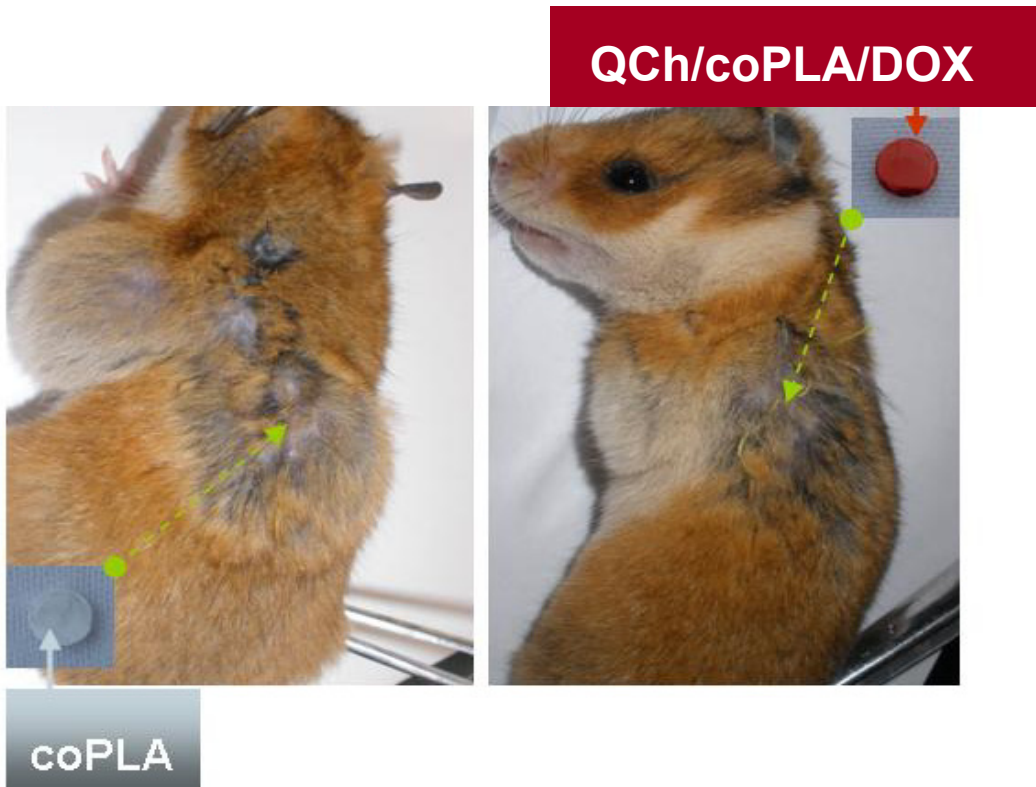
coPLA/DOX



QCh/coPLA/DOX



Antitumor activity of quaternized chitosan/doxorubicin containing nanofibrous implants against Graffi myeloid tumor





CONCLUSIONS

Nanofibers containing antitumor drug DOX have been easily prepared in one-step method by electrospinning of mixed DOX/coPLA and DOX/QCh/coPLA solutions in common solvent.

MTT cell viability studies revealed that DOX-containing coPLA and QCh/coPLA fibers exhibited high cytotoxicity against HeLa and MCF-7 cancer cells. Moreover, QCh/coPLA mats showed a great inhibition effect on HeLa and MCF-7 cells which is concentration- and time-dependent.

SEM and fluorescence microscopic observations confirmed that the antitumor effect of QCh-based and DOX-containing fibrous mats were mainly due to induction of apoptosis in the studied cancer cells.

The local application of the nanofibrous implants containing both QCh and DOX in the tumor tissue showed high antitumor efficacy *in vivo* and was better tolerated as compared to free DOX.

Therefore, the studied nanofibrous materials are potential candidates for antitumor drug delivery and for local chemotherapy of cervical tumor and breast tumor formations.

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Acknowledgement

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Thank you for your attention!

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