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OP Vzdělávání pro konkurenceschopnost
INVESTICE DO ROZVOJE VZDĚLÁVÁNÍ

Name: # LIPOSOMES AS DRUG CARRIERS AND THEIR CHARACTERIZATION USING DIFFERENT ANALYTICAL METHODS

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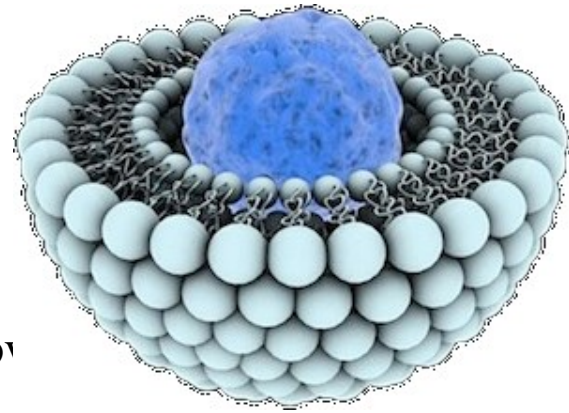
Název projektu: Partnerská síť centra excelentního bionanotechnologického výzkumu

NanoBioMetalNet

Liposomes



- Firstly described in 1964.
- Proposed as potential drug carriers immediately after disco
- Drugs carried by nanotransporters – not so toxic as drugs alone and the effect of drug is maintained; possibility of targeted delivery and better effect.
- Lipid bilayer often contains cholesterol.
- Cholesterol supports the stability of lipid bilayer and enables the control of permeability and solubility of liposome's membrane; it also gives liposomes a similarity to natural cell membranes.
- The release of drug from liposomes is usually based on the fusion with cell's membrane, but other options can be used, e.g. sonication.

Our aim

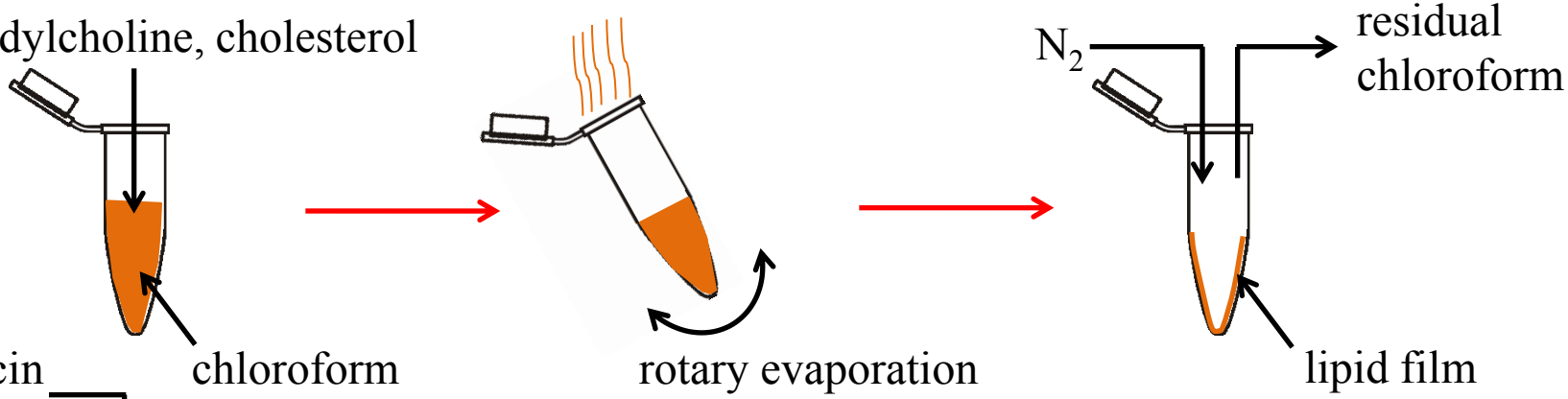
- Focus on different properties of synthesized liposomes, which differ in the content of cholesterol in the lipid bilayer.

- How are the electrochemical properties of liposomes affected by cholesterol and how is the toxicity of liposomal doxorubicin changed?

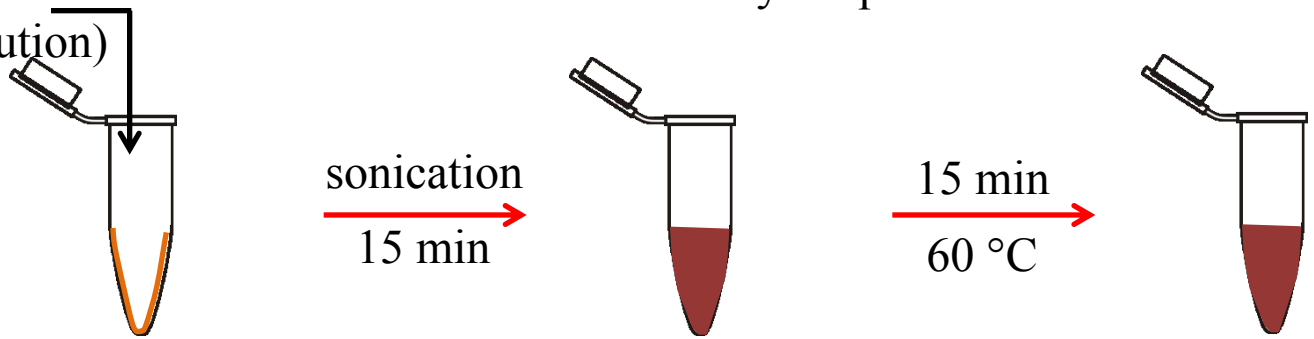
Our samples

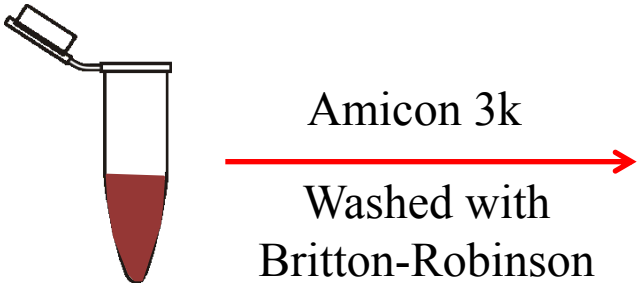
1,2-dioleoyl-sn-glycero-3-phospho-rac-(1-glycerol) sodium salt

phosphatidylcholine, cholesterol

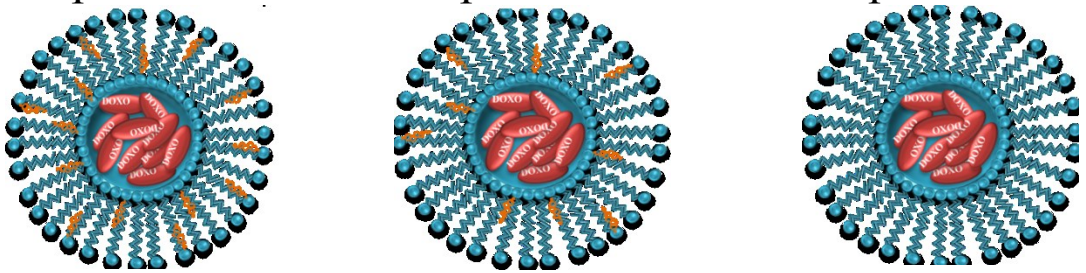


Doxorubicin (water solution)





Liposome 8 | Liposome 9 | Liposome 10



FIA-ED

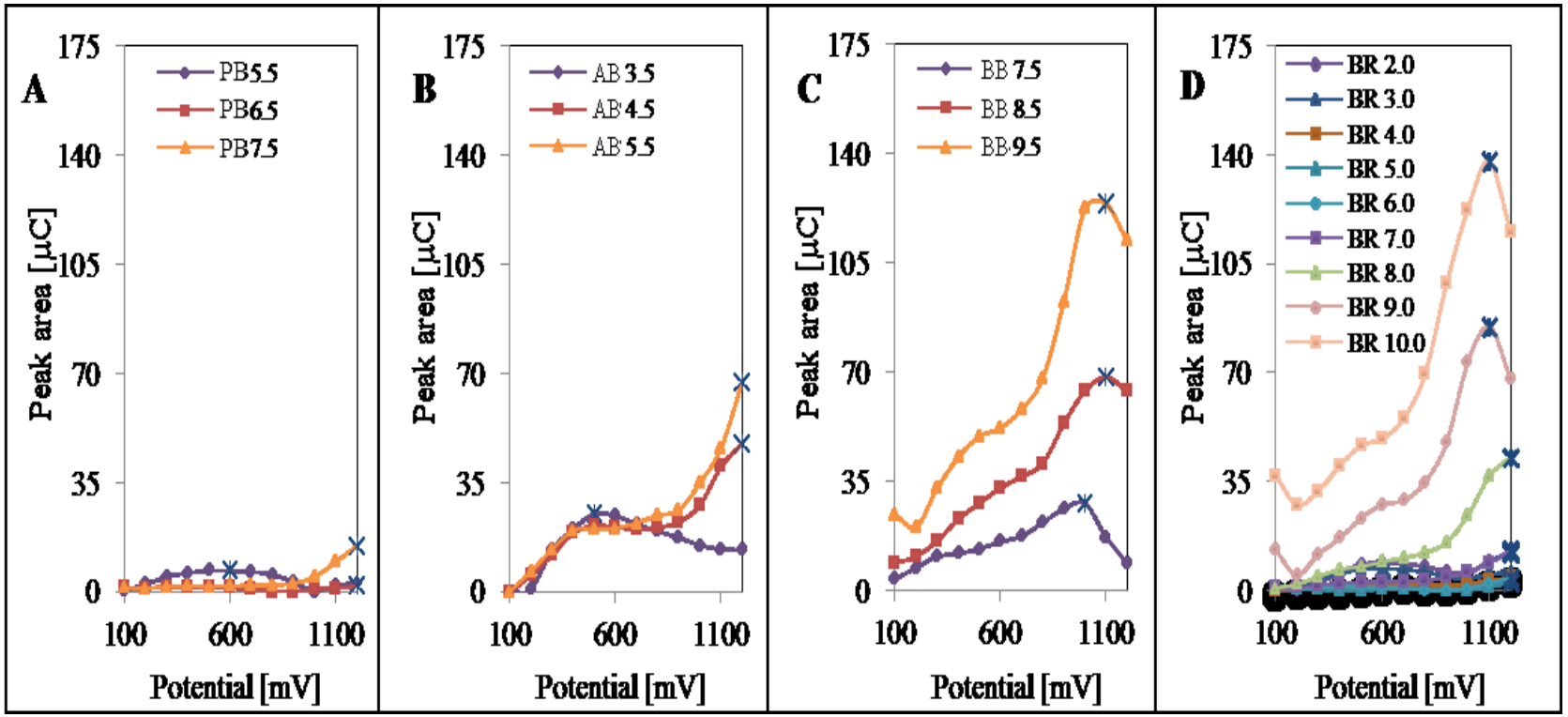
Detector

Chromatographic pump

Autosampler

Amperometric cell (glassy carbon working electrode)

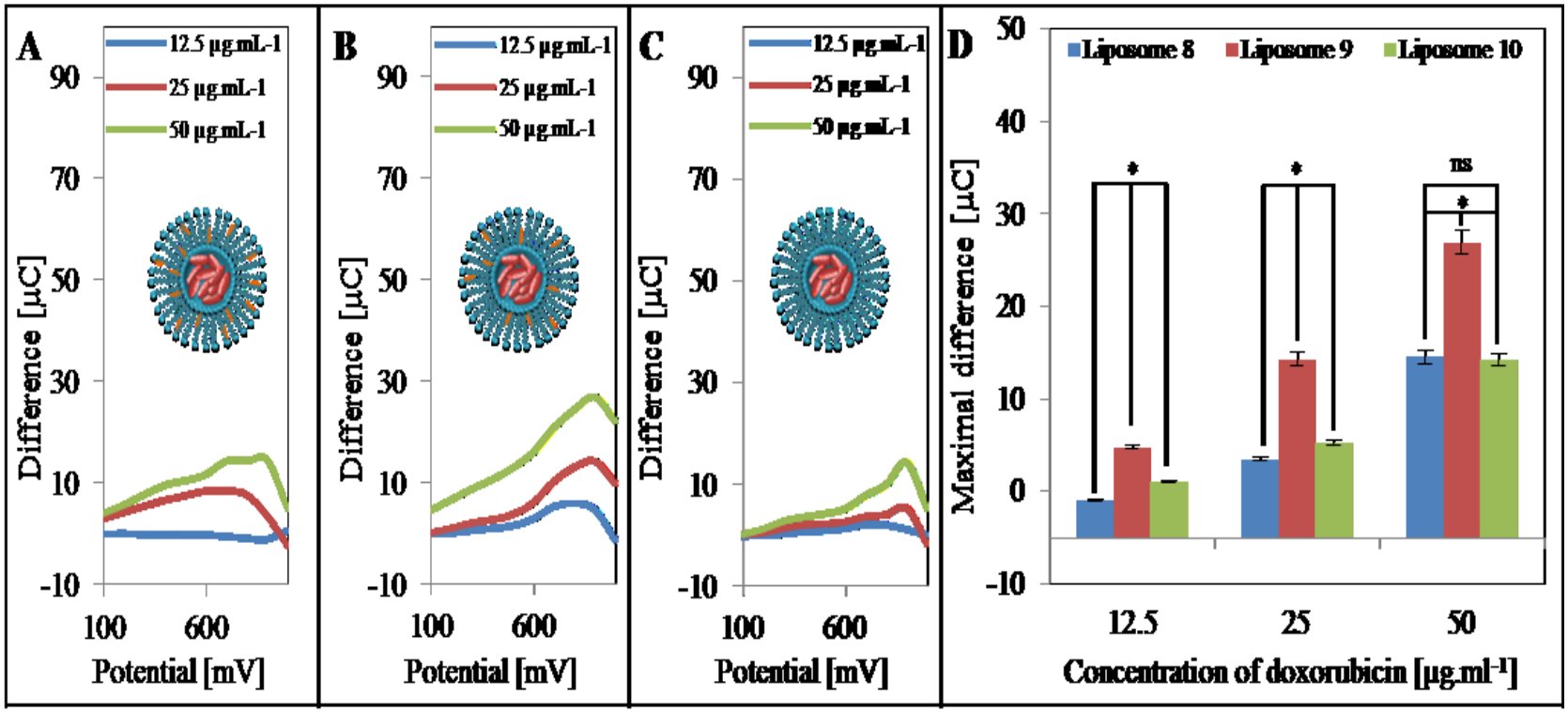
Optimization of FIA-ED conditions



Legend: Optimization with working solution of doxorubicin (50 µg.ml^{-1}). **(PB)** Phosphate buffer, **(AB)** acetate buffer, **(BB)** borate buffer and **(BR)** Britton-Robinson buffer.

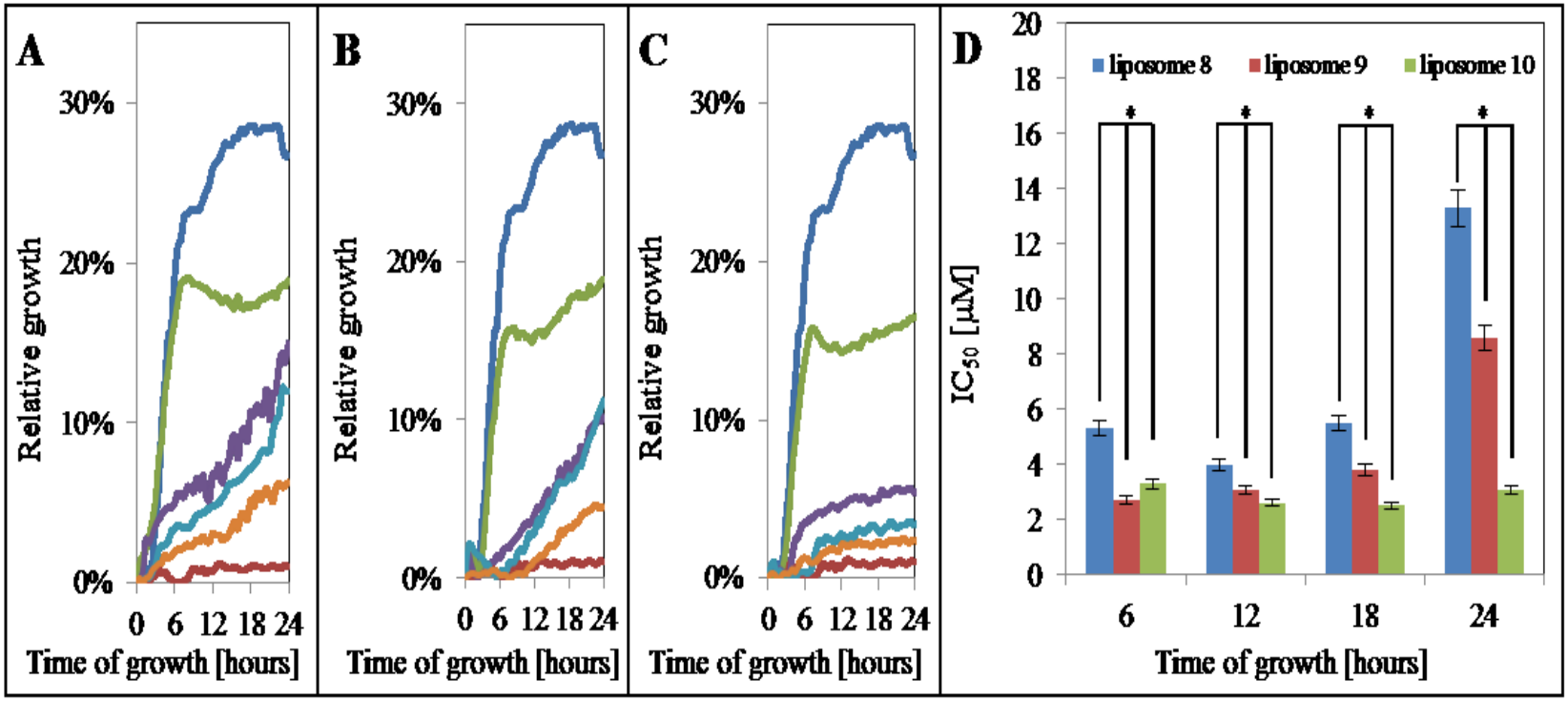
Best conditions: Britton-Robinson buffer at pH 10.0.

FIA-ED analysis with construction of differential HDVs



Legend: (**A**) Liposome 8, (**B**) liposome 9 and (**C**) liposome 10.

Growth curves and IC_{50} determination



Legend: (**A**) Liposome 8. (**B**) Liposome 9. (**C**) Liposome 10. (**D**) IC_{50} values (μM) for doxorubicin encapsulated in liposomes. Doxorubicin (100 $\mu g.ml^{-1}$, red curve) and *Staphylococcus aureus* (S.a.) (dark blue curve). Concentrations of doxorubicin in liposomes were 0 (olive green curve), 12.5 (purple curve), 25 (azure curve) and 50 (orange curve) $\mu g.ml^{-1}$ – it's 0, 23, 46 and 92 μM after conversion.

Conclusion

- New approach to compare the influence of different variants of liposomes on detection of carried doxorubicin was used – the electrochemical detection with construction of differential hydrodynamic voltammograms.

- Cholesterol influenced the electrochemical properties of liposomes in the way that it probably enhanced the electron transfer in phospholipid bilayer, but this enhancement has a limitation factor in concentration of cholesterol.

- The toxicity of liposomal doxorubicin is very dependent on the concentration of cholesterol in liposomes' bilayers. The IC_{50} values at 24 hours were increased even nearly four times when comparing liposome 8 (with the highest amount of cholesterol) to liposome 10 (without cholesterol).

Publication

KOMÍNKOVÁ, M., **GURÁŇ, R.**, ANGEL MERLOS RODIRGO, M., KOPEL, P., BLAŽKOVÁ, I., CHUDOBOVÁ, D., NEJDL, L., ZÍTKA, O., ADAM, V. and KIZEK, R. The effect of doxorubicin enclosure into different types of liposomes on its electrochemical and fluorescence behaviour. *International Journal of Molecular Sciences*. **2013**, in review process.

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TIKÁ V KAŽDÉ RODINĚ
LIGA PROTI RAKOVINĚ PRAHA

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Thank you for your attention!

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