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Development of novel drug delivery systems based on extracellular vesicles and cell membranes for cancer therapy

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INTRODUCTION & AIM

Nanoscale drug delivery systems represent a promising approach for improving efficiency and safety of chemotherapy.

Many synthetic nanocarriers may cause **toxicity** and **immune reactions**. In this study, we developed **hybrid nanoparticles** based on **extracellular vesicles** and **cell membranes**. Such nanoparticles may combine **high biocompatibility** of vesicles with membrane-derived biological functions and the ability to **cross biological barriers**.

METHOD

Human embryonic kidney **HEK293 cells** were used as a source of extracellular vesicles and cell membranes. Hybrid nanoparticles were prepared by **extrusion method**. To optimize particle size distribution, we tested different numbers of extrusion cycles (5, 10, 15, 20, and 25). **Doxorubicin** (DOX) **loading** was performed using two methods: a **pH-gradient** and an **ammonium sulfate gradient**. The resulted particles were analyzed by spectrophotometric and dynamic light scattering methods.

RESULTS & DISCUSSION

Table 1. Hydrodynamic diameter of particles prepared from extracellular vesicles (EV) and cell membranes (CM) depending on the number of extrusion cycles

№ sample	Ratio EV:CM	Number of extrusion cycles	Hydrodynamic diameter, nm	Polydispersity index
1	1:100	5	98 ± 13	0,31 ± 0,07
2		10	99 ± 9	0,29 ± 0,09
3		**15**	**110 ± 22**	**0,31 ± 0,1**
4		20	88 ± 1	0,28 ± 0,08
5		25	110 ± 24	0,33 ± 0,11

Using **15 extrusion cycles**, it was possible to obtain particles with an average diameter necessary for **effective drug delivery to tumor tissues.**

Table 2. Characteristics of hybrid particles obtained by various methods

Methods of DOX incorporation in hybrid nanoparticles / Characteristics	**pH-gradient**	$(NH_4)_2SO_4$
DOX, mkg/ml	**12 ± 1**	10 ± 3
Average hydrodynamic diameter, nm	**250 ± 190**	780 ± 360
Polydispersity index	**0,46 ± 0,06**	0,74 ± 0,15

The **pH gradient method** ensured the production of particles in the required range necessary for **effective delivery of DOX to the tumor**, and the DOX content was one of the highest.

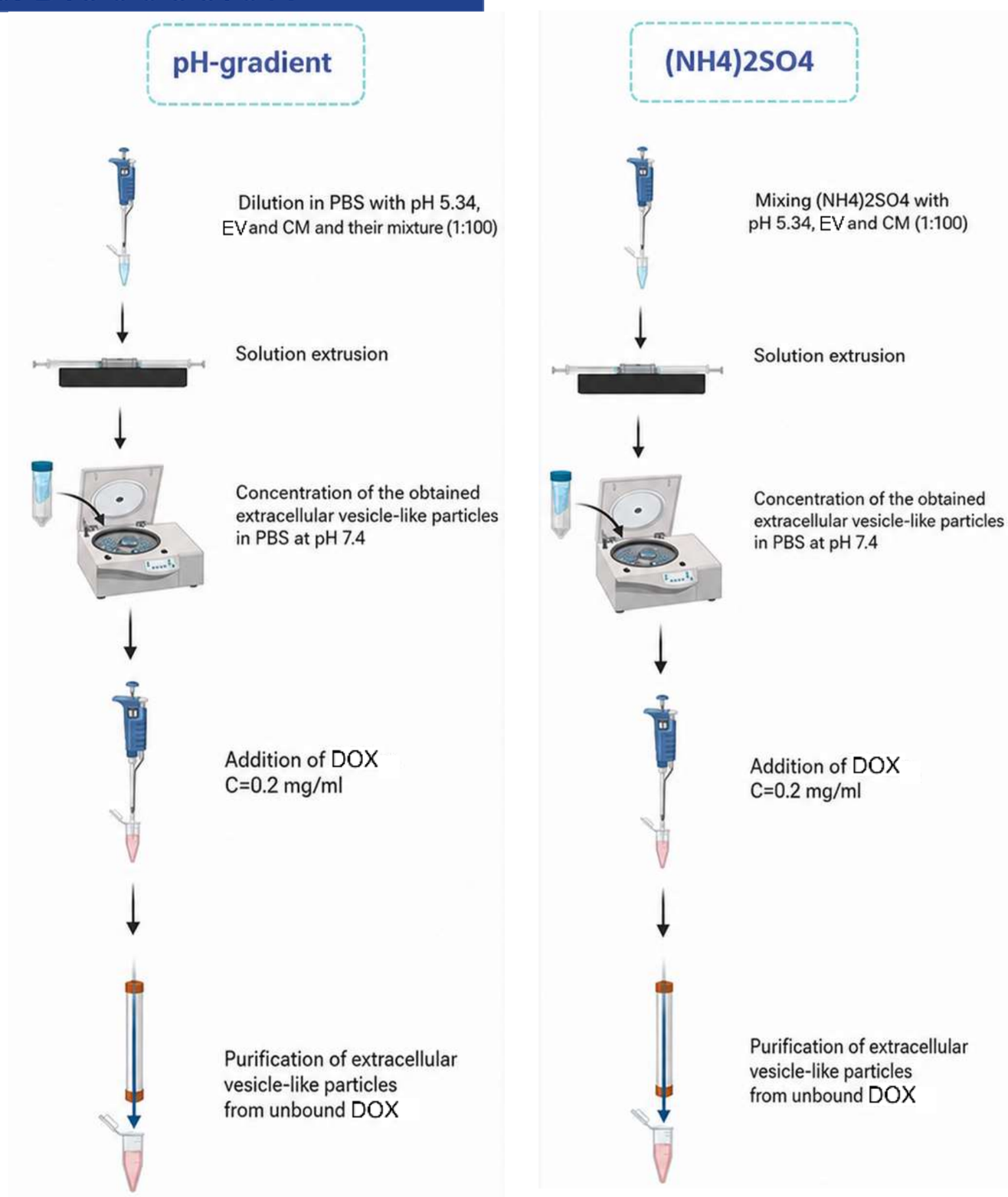

Fig 1. Schemes for DOX loading in hybrid particles

CONCLUSION

Overall, **the pH-gradient method** was more suitable for the preparation of **DOX-loaded hybrid nanoparticles** with improved tumor accumulation. The developed hybrid system represents a **biocompatible platform** for further *in vitro* studies **as a drug delivery approach for cancer therapy**.

FUTURE WORK/REFERENCES/ ACKNOWLEDGMENT

- Increasing the drug loading;
- Drug release and hemolysis study;
- Testing for cytotoxicity;
- Studying of particles accumulation in cells.

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