Liposomal murrayafoline a modified with chitosan-folic acid conjugate

<u>K.I. Dubatouka</u>¹, E.V. Koroleva¹, R.A.Oparenko², T.T. Quoc³ ¹Institute of Chemistry of New Materials NASB, Minsk, Belarus, e-mail: <u>*d_katerina@tut.by*</u>

²Belarusian State Technological University, Minsk, Belarus,

³Institute of Natural Products Chemistry, Vietnam Academy of Science and Technology, Hanoi, Vietnam

Murrayafoline A (MuA), isolated from Murraya koenigii in Vietnam, is a carbazole derivative that shows biological activity as cytotoxic agent [1, 2]. Liposomal form of MuA (L-MuA) modified with chitosan-folic acid conjugate [3] (Ch-FA) can be used to reduce the drug toxicity, improve its bioavailability and create the drug delivery system.

Liposomes were prepared from the mixtures of egg phosphatidylcholine (PC), cholesterol (Ch) and MuA (16:4:1 wt.) in chloroform using combination of the thin film hydration and sonication methods. Surface modification of negatively charged liposomes (-42.2 mV) by positively charged chitosan-folic acid conjugate (27.3 mV) was performed by mixing liposomes with polymer solution up to final Ch-FA concentrations of 0.05-2.00 %. The mean diameter (d) and ζ -potential, measured using dynamic light scattering, were in the range from ~ 148 to 361 nm and from -42.20 to -23.8 mV for different formulations respectively (Table).

Table.	Characteristics of L-MuA,
--------	---------------------------

Formulations	d, nm	ζ, mV
L-MuA	148±21	-42.2±1.6
L-MuA/Ch-FA0.05%	289±43	-38.1±2.2
L-MuA/Ch-FA0.5%	298±45	20.6±1.7
L-MuA/Ch-FA2%	361±60	23.8±0.6
Ch-FA	300±44	27.3±0.7

ζ-potential of unmodified liposomes was negative owing to negatively charged phosphate groups of phospholipids. Čpotential of Ch-FA-modified liposomes shifted to positive with increasing Ch-FA concentration. Due to the process of the surface modification the mean diameter of L-MuA/Ch-FA was higher than

for L-MuA and increased for formulations containing 0.05 - 2.00 % of conjugate. Thus, it was obtained and characterized liposomal Murrayafoline A modified with chitosan-folic acid conjugate that can be used in biomedicine.

Acknowledgment

This research was funded by VAST under grant number QTBY01.03 / 20-21 and BRFFR, grant №20V-001.

References

- [1] L. Anh et al. J. of Sci. Techn. (2016) 54: 2C
- [2] M. Itoigawa et al. J. Nat. Prod. (2000) 63
- [3] M. É. Lozovskaya, V.I. Kulikovskaya et al. Pharm. Chem. J. (2018) 52: 2