

Box-Behnken Design of Thermo-Responsive Nano-Liposomes Loaded with Platinum (IV) Anticancer Complex: Evaluation of Cytotoxicity and Apoptotic Pathways in Triple Negative Breast Cancer Cells

Nada K. Sedky¹ Maria Braoudaki², Noha Khalil Mahdy³, Kenzy Amin⁴, Iten M. Fawzy⁵, Eleni K. Efthimiadou⁶, Rana A. Youness^{7,8}, Sherif Ashraf Fahmy^{9*}

¹Department of Biochemistry, School of Life and Medical Sciences, University of Hertfordshire Hosted by Global Academic Foundation, R5 New Garden City, New Administrative Capital, Cairo, Egypt.

²Department of Clinical, Pharmaceutical, and Biological Science, School of Life and Medical Sciences, University of Hertfordshire, Hatfield AL10 9AB, UK

³Department of Pharmaceutics and Industrial Pharmacy, Faculty of Pharmacy, Cairo University, Kasr El-Aini Street, 11562 Cairo, Egypt.

⁴Department of Biochemistry, School of Life and Medical Sciences, University of Hertfordshire Hosted by Global Academic Foundation, R5 New Garden City, New Administrative Capital, Cairo, Egypt.

⁵Department of Pharmaceutical Chemistry, Faculty of Pharmacy, Future University in Egypt, 11835 Cairo, Egypt.

⁶Inorganic Chemistry Laboratory, Department of Chemistry, National and Kapodistrian University of Athens, Panepistimiopolis, Zografou 157 71, Greece.

⁷Biology and Biochemistry Department, Faculty of Biotechnology, German International University (GIU), New Administrative Capital, Cairo, Egypt

⁸Department of Biology and Biochemistry, School of Life and Medical Sciences, University of Hertfordshire Hosted by Global Academic Foundation, R5 New Garden City, New Administrative Capital, Cairo, Egypt.

⁹Department of Chemistry, School of Life and Medical Sciences, University of Hertfordshire Hosted by Global Academic Foundation, R5 New Garden City, New Capital, Cairo 11835, Egypt.

***Correspondance: S.A.F.; Phone: +201222613344; Email: sheriffahmy@aucegypt.edu**

Table S1. Average particle size, polydispersity index, zeta potential, and entrapment efficiency for the Asp/TLs prepared formulae

Formula	Particle Size (nm)	Polydispersity Index	Zeta Potential (mV)	Entrapment Efficiency (%)
F1	180.2	0.29	-7.84	61.67
F2	140.1	0.25	-21.67	84.2473
F3	137.6	0.23	-28.07	89.6
F4	131.233	0.245	-23.03	84.9075
F5	136.6	0.255	-30.98	82.9
F6	120.67	0.14	-20.12	82.6
F7	185	0.28	-5.98	62.98
F8	118.9	0.13	-18.7	78.8851
F9	185	0.289	-8.24	60.43
F10	119.67	0.135	-22.98	79.89
F11	135.7	0.249	-32.98	83.78
F12	158.3	0.248	-23.01	83.78
F13	123	0.132	-21.67	78.4741
F14	136.78	0.255	-31.78	83.78
F15	135.01	0.256	-34.45	84.0706
F16	120	0.27	-25.58	82.284
F17	175	0.301	-6.78	63.98

Table S2. Composition of the 3³ BBD for the prepared Asp/TLs NPs.

	Factor 1	Factor 2	Factor 3
Formula	Cholesterol:2DPPC	DSPE-PEG2000:2DPPC	lipid:1Drug
F1	1.5	0.26	5
F2	1	0.39	20
F3	1	0.26	12.5
F4	1	0.39	5
F5	1	0.26	12.5
F6	0.5	0.39	12.5
F7	1.5	0.26	20
F8	0.5	0.26	5
F9	1.5	0.39	12.5
F10	0.5	0.13	12.5
F11	1	0.26	12.5
F12	1	0.13	20
F13	0.5	0.26	20
F14	1	0.26	12.5
F15	1	0.26	12.5
F16	1	0.13	5
F17	1.5	0.13	12.5