Development the injectable in situ formulation of glucosamine-labeled liposomal cisplatin for chemoradiotherapy

Lu-Yi Yu[1], Chang-Ting Ke, Pei-Wei Shueng[2]*, Chun-Liang Lo[1]*
[1]Department of Biomedical Engineering, National Yang Ming Chiao Tung University, Taipei, Taiwan 112, ROC
[2]Division of Radiation Oncology, Far Eastern Memorial Hospital, New Taipei City, Taiwan 220, ROC
*cllo@nycu.edu.tw; * shuengsir@gmail.com

Abstract

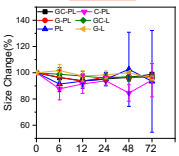
Precision therapy is playing an increasingly vital role in the treatment of oral cancer. Among the latest approaches, combining targeted nanomedicine with chemoradiotherapy has demonstrated strong potential to enhance treatment efficacy and minimize side effects, paving the way for new clinical strategies. In this study, we developed a glucosamine-functionalized liposomal nanocarrier capable of targeting cancer cells and delivering cisplatin and ceramide specifically to mitochondria. This liposomal formulation was combined with a high molecular weight polysaccharide solution and administered via intratumoral injection to achieve synergistic chemoradiotherapeutic effects. Characterization of the liposomes revealed an optimal particle size, high stability, and efficient drug encapsulation. In vitro assays demonstrated superior cytotoxicity against human oral squamous carcinoma (SAS) and mouse oral cancer (MOC1) cells compared to free drugs. Co-treatment with radiation further enhanced radiosensitivity. Mechanistic studies showed that the treatment induced mitochondrial dysfunction, increased reactive oxygen species (ROS) production, and triggered apoptosis in cancer cells. In vivo, the combined therapy significantly suppressed tumor growth and recurrence while mitigating immune evasion.

Results & Discussions

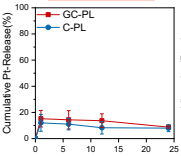
Characterization of the liposomes

	Size (nm)	PDI	Zeta (mV)	Ceramide		cisplatin	
				EE(%)	DL(%)	EE(%)	DL(%)
GC-PL	168.57	0.10	-11.73	91.48±2.32	4.16	21.03±0.39	7.99
C-PL	176.80	0.15	-0.62	99.22±0.70	4.51	31.98±1.06	11.79
PL	159.67	0.12	0.08	-	-	43.87±9.51	16.67
G-PL	159.37	0.17	-8.35	-	-	32.30±0.05	12.27
GCL	159.80	0.14	-10.74	99.57±0.48	6.22	-	-

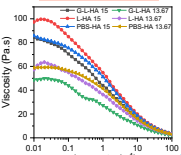
Stability



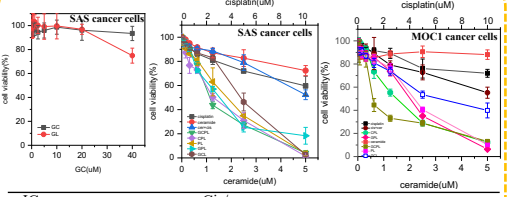
Drug leakage



Viscosity of gel

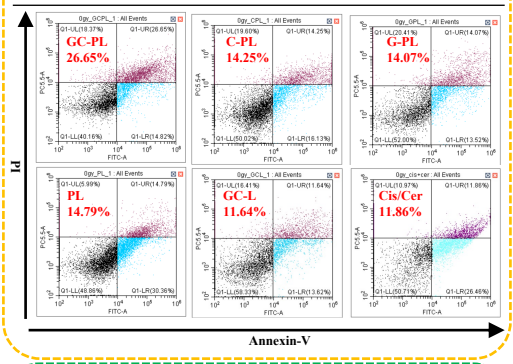


Cytotoxicity

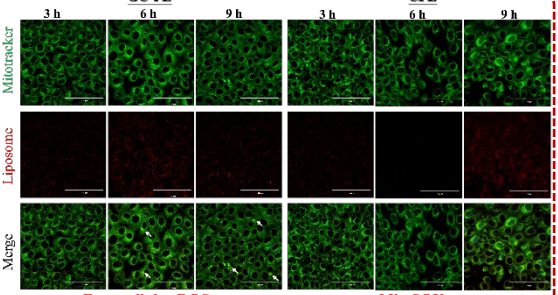


IC_{50} (SAS)	Cis	Cer	Cis/ Cer	GC-PL	C-PL	PL	G-PL	GC-L
Cis	19.36	-	9.91	1.96	2.74	4.07	3.12	-
Cer	-	9.36	5.06	0.98	1.37	-	-	2.01

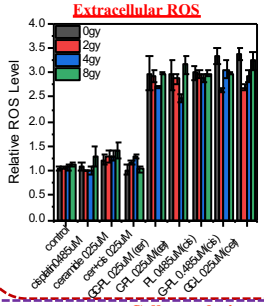
IC_{50} (MOC1)	GC-PL	C-PL	PL	G-PL	GC-L
Cis	2.13	4.09	7.21	6.63	-
Cer	1.06	2.04	-	-	4.45



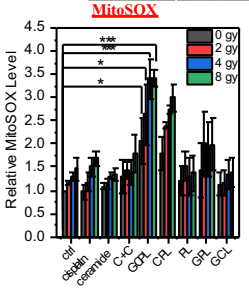
Mitochondria Targeting



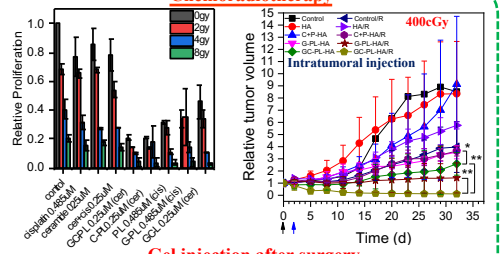
Extracellular ROS



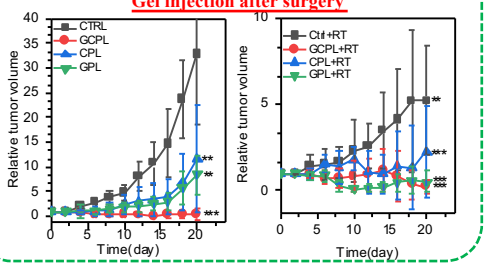
MitoSOX



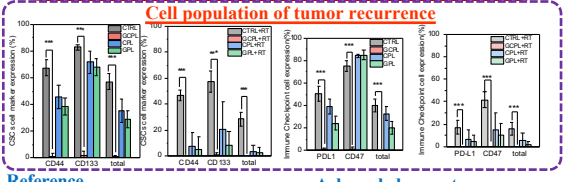
Chemoradiotherapy



Gel injection after surgery



Cell population of tumor recurrence



Reference

1. ACS Nano. 2020, 14(11), 15158–15175.
2. J. Pharm. Pharm. Sci. 2017, 121, 32, 17505–17513.
3. FASEB J. 2005, 19(12), 1657–1667.

Acknowledgements

The authors would like to thank the National Science and Technology Council, Taiwan (NSTC 113-2124-M-A49-006 and 110-2314-B-418 -007).