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Ph.D. DISSERTATION DEFENSE

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Title:	Dopamine based nano-formulations for drug delivery system with drug repurposing in cancer chemotherapy
Chairperson:	Dr. Junfeng Liang, Department of Chemistry and Chemical Biology, Schaefer School of Engineering & Science
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ABSTRACT

Cancer is a leading cause of death worldwide and chemotherapy is the principal modality for cancer treatment. Drug resistance in cancer poses a significant obstacle, undermining the effectiveness of treatment. Additionally, there is a high risk of severe side effects associated with those agents. Furthermore, the low efficiency of drug delivery restricts its ability to reach the target sites in sufficient concentrations. Addressing these limitations is crucial to improving the therapeutic outcomes of anticancer drugs and enhancing its clinical utility in chemotherapy.

Drug repurposing is an investigation of researching new therapeutic purposes with existing drugs. Orlistat, an FDA approved drug for obesity management, was shown to be a potent inhibitor for the thioesterase domain of FAS. Anticancer therapy was investigated through the inhibition of FAS activity. However, orlistat exerts an anticancer effect with high drug concentration due to its high hydrophobicity and low systemic uptake. The performance of other anticancer agents such as camptothecin (CPT) was limited due to the same reasons. Dopamine is an important neurotransmitter. It attracted broad attentions due to its multifunctional groups which endow its gift for the nano-formulation application. Moreover, dopamine is the major sources of ROS. The oxidation of dopamine triggers the damage of mitochondria and apoptotic cell death with the generation of ROS.

More importantly, except for the pharmacological actions of orlistat and dopamine respectively, we also revealed a synergistic effect between orlistat and dopamine in cancer treatment. Therefore, we developed various nanomaterials for anticancer drug delivery applications through self-polymerization and other assembly methods based on dopamine and through drug repurposing.