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Therapeutic Nanomedicine based Strategies for the Treatment of Atherosclerosis and Cancer

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Doctoral Thesis

**Therapeutic Nanomedicine based Strategies for the Treatment of
Atherosclerosis and Cancer**

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Doctoral Program

Course of Bio-Nano Science Fusion

Graduate School of Interdisciplinary New Science

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Summary of Doctoral Thesis

Primarily two thirds of worldwide deaths are caused due to cancer and cardiovascular diseases. The estimate cost involves 2.8 million dollars by the next year i.e. 2020. Activation of inflammatory pathways have been studied to be the major contributors to the cause of these diseases. Current therapies have proved to be ineffective with increased toxicities and systemic side effects. Nutraceuticals serves as an alternative in this scenario. However, due it to its low bioavailability and poor solubility they have reduced clinical efficacy. Nanotechnology arises here with selective targeting and delivery that improves the solubility and release of therapeutic drugs at the targeted sites. Here, we study the effect of nutraceuticals with a natural enhancers BioPerine that can improve the bioavailability and absorption of the nutraceuticals resulting in enhanced efficacy. The fabrication of phytonutrient based- hybrid polymeric nanoparticles (NPs) also aims at reversing multi- drug resisting breast cancers and comparing the effect with conventional chemotherapy drugs. The various changes in lifestyle including diet can cause the lipid accumulation leading to the development of atherosclerosis while, mutations within the body causes cancer. In order to overcome the defects of the current failing treatments, nutraceuticals from natural compounds has been found to be the best alternative. Due to the low bioavailability of nutraceuticals, we have introduced the incorporation of nanotechnology to increase its efficiency for a better approach in the treatment of the diseases.

Atherosclerosis characterized by the development of cholesterol-rich arterial plaques is a major cause of heart disease. The arterial plaques have highly upregulated inflammatory cytokines which are secreted by the macrophages that finally become cholesterol-laden foam cells. These

foam cells gradually lead to atheroma. In this work, we chose to incorporate curcumin and also increase its bioavailability by including Bioperine (derived from *Piper nigrum*) a natural enhancer inside a polymeric drug delivery system for targeting atherosclerotic plaque sites.

Despite continuous endeavor's and ground-breaking achievements in the pursuit of finding better cancer therapeutic avenues, drug resistance is still a menace to hold back. We fabricated phytonutrient based-hybrid polymeric nanoparticles (NPs) encapsulated with Resveratrol (RES) a polyphenolic compound found in grapes and bioperine which has been studied as a bioenhancer for different nutraceuticals in varied clinical purposes. Recent studies have accounted regarding the inhibitory activity of BioPerine against P-glycoprotein in multidrug resistant cancers. It has potent anti-oxidant, anti-cancerous and anti-inflammatory activities. However, BioPerine due to its low solubility and metabolic instability limits its clinical translation. We designed a hybrid poly-lactic acid (PLA) coated with chitosan and polyethylene glycol (PEG) nanoparticles encapsulating BioPerine and check its P-glycoprotein inhibition against MDA-MB 453 triple negative breast cancer cells. We will be carrying out a comparative analysis of our BioPerine-loaded PLA NPs with a commercially available P-glycoprotein inhibitor verapamil hydrochloride and analyse its inhibitory activity on drug resistant cancer cell lines. This study holds an intriguing premise for the development of phytonutrient-based NDDS in combination with traditional chemotherapies as a crucial approach to tackling MDR in cancers as a considerable further research avenue.

