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Fabrication, characterization of PLGA loaded nano-particle of umbelliferone exhibited the antihypertensive and Vasorelaxant effect on rats via endothelium-dependent and endothelium-independent pathways

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Objectives: Hypertension disease is considered one of the most serve causes for and consequences of vascular disease, ischemic heart disease, diabetes, atherosclerosis, non-alcoholic steatohepatitis and heart failure. Hypotension is considered as the 2nd leading risk factor for the global burden of disease. Umbelliferone isolated from the *agale marmelos* and having antihypertension and vasorelaxation effect, but the molecular mechanism for antihypertensive effect not explored. The aim of the current study to comfort the vasorelaxant and antihypertensive effect of PLGA loaded nano-formulation of umbelliferone (UF) on blood pressure and vascular tension in rats and explore the underlying mechanism.

Methods: Nanoparticle formulation for umbelliferone (UF-PLGA) formulated via using the ultrasonication technique and Box-Behnken design was used for the determination of influential formulation parameters to obtain the acquire quality range desired nano-size compound. For the vasorelaxant effect of UF-PLGA was investigated on thoracic aortic rings. For the molecular mechanism, the effect of UF-PLGA-NPs was scrutinized in the presence of blockers and antagonists on aorta isolated from the rats.

Results: UF-PLGA-NPs showed the average particle size 182 nm along with the poly-dispersity index 0.21 zeta potential <20 mV, drug loading capacity >93.2% and drug release (96%) after the 48h. UF showed the vasorelaxation effect on the aortic rings pre-incubated with the KCL. Pre-treatment of aortic rings with atropine, 9-(tetrahydro-2-furanyl)-9H-purine-6-amine, propranolol, indomethacin, 4-aminopyridine followed by addition of Phe before UF did not persuade the UF induced relaxation. In contrast, the vasorelaxant potential of UF was significantly suppressed via K+ channel blocker, NO synthase inhibitor and guanylyl cyclase inhibitor. Therefore, UF reduced the contractions in the absence of extracellular Ca2+. Moreover, UF reduced the systolic blood pressure with our alteration of heart rate in the experimental rats.

Conclusions: Based on the result, we can conclude that umbelliferone exhibited the vasorelaxant and hypertensive effect via endothelium-dependent and endothelium-independent pathways.