Solid Lipid Nanoparticles for delivery of Dopamine and Grape Seed Extracts in differentiated SH-SY5Y neuronal cell model of Parkinson disease.

Rosanna Mallamaci [1], Debora Musarò [2], Stefano Castellani [3], Lorenzo Guerra [1], Giuseppe Fracchiolla [4], Rosa Angela Cardone [1], Adriana Trapani [4,] and Michele Maffia [5,]

[1] *Department of Biosciences, Biotechnologies and Environment, University of Bari "Aldo Moro", 70125 Bari, Italy; rosanna.mallamaci@uniba.it (R.M.); lorenzo.guerra1@uniba.it (L.G.); rosaangela.cardone@uniba.it (R.A.C.).*

[2] *Department of Biological and Environmental Science and Technology, University of Salento, Via Lecce-Monteroni, 73100 Lecce, Italy; debora.musaro@unisalento.it (D.M.).*

[3]*Department of Pharmacy-Drug Sciences, University of Bari "Aldo Moro", Via Orabona 4, 70125 Bari, Italy; giuseppe.fracchiolla@ uniba.it (G.F.); adriana.trapani@uniba.it (A.T.).*

[4] *Department of Precision and Regenerative Medicine and Ionian Area (DiMePRe-J), University of Bari "Aldo Moro", 70125 Bari, Italy; stefano.castellani@uniba.it (S.C.).*

[5] *Department of Experimental Medicine, University of Salento, Via Lecce-Monteroni, 73100 Lecce, Italy; michele.maffia@unisalento.it (M.M.).*

Parkinson's disease (PD) is a prevalent neurodegenerative disorder, primarily associated with dopaminergic neuron depletion in the Substantia Nigra. Current treatment focuses on compensating for Dopamine (DA) deficiency, but the blood-brain barrier (BBB) poses challenges for effective drug delivery. Using differentiated SH-SY5Y cells, we investigated the co-administration of DA and the antioxidant Grape Seed Extract (GSE) to study the cytobiocompability, the cytoprotection against the neurotoxin Rotenone, and their antioxidant effects. In this context, two Solid Lipid Nanoparticles (SLN) formulations, DA-co-GSE-SLNs, and GSE-ads-DA-SLNs, have been synthesized. Such SLNs showed mean particle size in the range of 187-297 nm, zeta potential values in the range -4.1-9.7 mV and DA association efficiency changed from 35 to 82%, according to the formulation examined. Herein, the results shown that DA/GSE-SLNs did not alter cell viability and have a cytoprotective effect against Rotenone-induced toxicity and oxidative stress. In addition, we have also evaluated, on Alpha-synuclein (aS) levels evaluation; SLNs have shown the potential to modulate the Rotenone-mediates aS levels increase.