NEUROPROTECTIVE EFFECT OF PLANT DERIVED NANOVESICLES IN ISCHEMIA MODEL

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Neurological complications are one of the main causes of morbidity and mortality during cardiac surgery characterized by acute ischemic brain lesions, ischemic stroke and inflammation [1]. Existing prevention of ischemic damage (artificial oxygenation and cooling) are insufficient to prevent the damage. Extracellular vesicles (EVs) are nanosized double membraned particles containing cell metabolites, microRNAs, proteins and other substances found in the cells. They are involved in intracellular communication and can pass through blood-brain barrier. Although there is plenty of research done on mammalian EVs, plant derived extracellular vesicles (PDVs) are more scalable and sustainable in comparison [2]. PDVs also exert anti-inflammatory, anti-oxidant, anti-fungal and antimicrobial activity. They contain bioactive metabolites and microRNAs capable of cross-kingdom regulation of gene expression [3]. Unique biological cargo and permeability makes PDVs a good tool for medical applications and might be used during and after cardiac surgery to reduce cerebral damage caused by ischemia.

The aim of this research was to test the neuroprotective effects of PDVs in ischemic model on mixed neuron-glial cell cultures. For this study nanovesicles from Rosa Damascena rose buds, cranberries, blueberries, guelder rose and nettle were isolated by using Exoplant-Lo kit (Exolitus). Nanosight 300 was used to determine size and concentration of nanovesicles (nanotracking analysis NTA). RNA concentration was determined using Trizol reagent. Protein concentration determined using Bradford method. Primary mixed neuron-glial cell culture was obtained from 5-7 days old Wistar rats. Cells were pretreated with PDVs for 24 hours and then transferred into hypoxic conditions (CO_2 5%, O_2 2%, N_2, 95%) for 48h. Percentage of live cells was evaluated with fluorescence microscopy using live/dead fluorescent dyes.

Results indicated that size of obtained nanovesicles was in a range of 50 - 250 nm depending on source plant. PDVs contained significant concentrations of RNA and proteins complying with data found in literature. A range of nanovesicles derived from Rosa Damascena rose buds ($1*10^{10}$ – $1*10^{7}$ particles/ml) had neuroprotective effects on mixed neuronal-glial cell cultures in an ischemic model, while other PDVs had no or toxic effects at higher doses.

In summary, PDVs from Rosa Damascena rose buds prevented cell death in neuronal-glial cells during hypoxia, showing a potential use during cardiac surgeries in order to prevent neurological damage. Also the differences between plant source can highly impact effects of PDVs, as some plant PDVs can have adverse effects depending on concentration.

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