Plant-Derived NanoVesicles: the natural carriers for Drug Delivery

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INTRODUCTION

Plant-derived nanovesicles (PDNVs) are nanosized vesicles with a lipid-enriched membrane and containing different natural bioactive compounds, including vitamins, antioxidants, proteins, nucleic acids and other metabolites. All these bio-compounds have shown to maintain their biological activities when the Nanovesicles are uploaded into target cells. PDNVs are turning out to represent the perfect vectors for drug delivery inasmuch as (i) their lipid membranes protect bioactives from external agents; (ii) PDNVs efficiently transfer their cargo into recipient cells through membrane-to-membrane fusion; (iii) they are tolerated by the receiving organism, being contained in the foods currently consumed by human beings; (iv) they are scalable, thus suitable for industrial applications; and (v) they are non-toxic, as they are obtained from organic agriculture-derived fruits and vegetables**.**

FIGURE 1

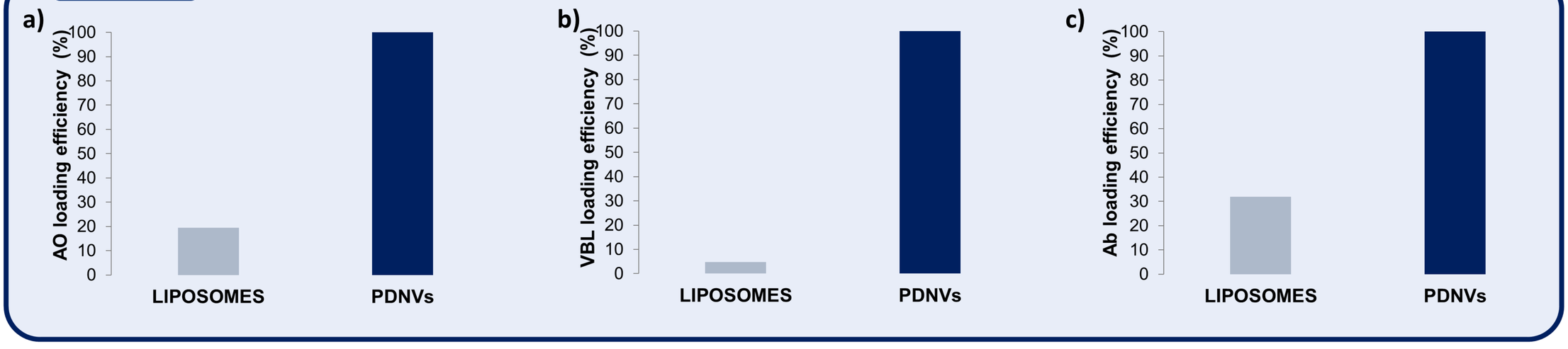

FIGURE 2

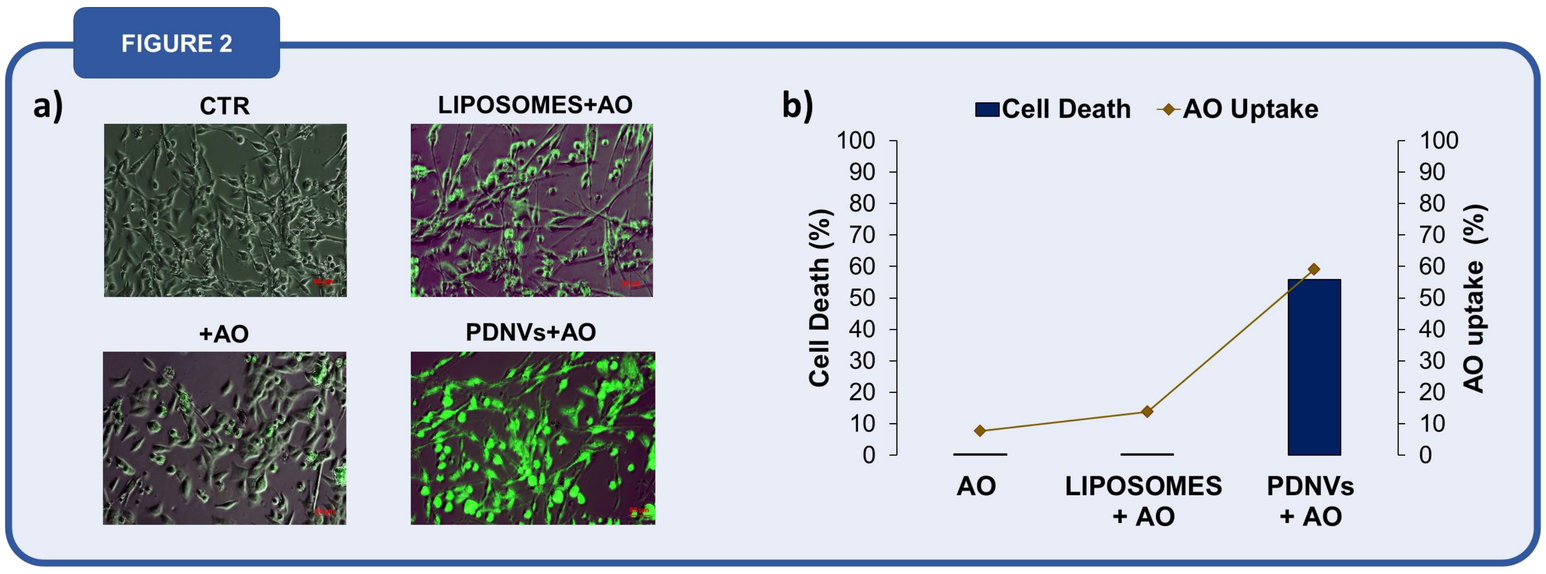

Figure 1 Drug delivery efficiency.
The same amount of plant-derived nanovesicles and commercial liposomes were electroporated with either (a) Acridine Orange (AO), or (b) Vinblastine BODIPY (VBL) or (c) AlexaFluor-488 Antibody (Ab). Mean fluorescence intensities were acquired through a Fluorescent Microplate Reader.

Figure 2. Evaluation of PDNVs+AO *in vitro*.
(a) Me30966 cells were treated with 0,1 µg/ml of free AO and AO loaded in PDNVs and liposomes. Images were acquired by Inverted Fluorescence Microscope.
(b) Me30966 cells were treated with 0,1 µg/ml of free AO and AO loaded in PDNVs and liposomes to evaluate cytotoxic effect correlated to cellular uptake.

FIGURE 3

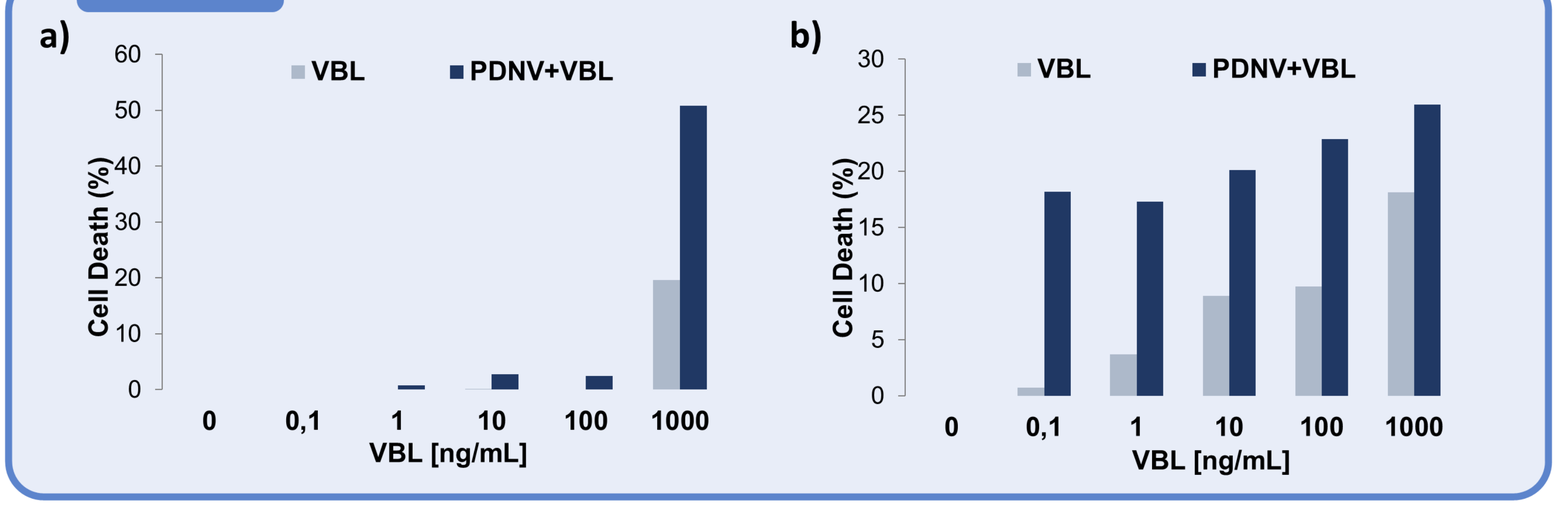

Figure 3. Cytotoxic effect of PDNV+VBL *in vitro*.
(a) Leukemic cells (CEM) sensitive to Vinblastine treated with free VBL and PDNV-VBL
(b) VBL-resistant cells (CEM/VBL100) treated with free VBL and PDNV+VBL. CEM/VBL100 cells overexpress P-glycoprotein (or multidrug resistance protein (MDR1), that prevents cellular uptake of VBL . CEM/VBL100 are resistant to vinblastine up to 100 ng/mL.

CONCLUSIONS

Our data demonstrated that PDNVs can be loaded with different compounds (AO, VBL and antibody) using trains of biphasic pulses, with higher drug efficiency loading compared to commercial liposomes. Moreover PDNVs loaded with AO can transfer their content in recipient cells more efficiently than liposomes, causing a more potent cytotoxic effect in human tumor cells. Loaded PDNVs also exert a more powerful anti-tumor effect than the free molecule, also triggering a reverse of multidrug resistance in human leukemic cells. These data support the potential medical application of plant-derived nanovesicles in drug delivery. Moreover, due to their high antioxidant content plant-derived nanovesicles can well implement the drug effectiveness.

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