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Do plant Nano-Vesicles (Exosomes) offer a novel approach to managing health disorders?

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Editorial

Plant nano-vesicles: Overview and biogenesis

Plant-derived exosome-like nano-vesicles (PELNVs), sometimes referred to as "plant exosomes," are phospholipid-bilayer structures with particle sizes of 10-1000 nm (1). To date, PELNVs have been isolated from the fruits, roots, leaves, grains, and whole tissues of certain plants (1,2). Plant nano-vesicles contain various substances, including lipids, nucleic acids, proteins, small RNAs, metabolites, antioxidants, and phytochemicals (Alkaloids, polyphenols, flavonoids, etc.) (1-7). Indeed, these bioactive substances are encapsulated within PELNVs (7). Plant vesicles perform various physiological functions, including facilitating cell-cell, cell-tissue, and environmental communication through the transfer of bioactive molecules; stimulating cellular responses to environmental stress; preserving tissue homeostasis; and exerting immunomodulatory effects (5,7). Recent studies have identified three main pathways involved in the biogenesis of PELNVs: 1) fusion of multivesicular bodies (MVBs) with the plasma membrane, 2) vacuolar release, and 3) the extracellular polymeric organelle or exo-positive organelle (EXPO) pathway. Additionally, it has been hypothesized that PELNVs are associated with autophagosomes (4,7). In general, PELNVs are formed intracellularly and subsequently released into the extracellular space in a manner similar to that of animal exosomes.

Therefore, can their potential applications in health disorders be effectively exploited?

To the best of our knowledge, PELNVs exert beneficial effects by regulating the biological pathogenesis of diseases and conditions such as inflammation (1), oxidative stress (3), gut dysbiosis (2,3), viral infections (4,6), skin infections and wounds (5), fibrosis, and cancer (7). As edible and naturally biocompatible materials, PELNVs have demonstrated a favorable safety profile in cellular and animal studies, with no significant toxicity in major organs (1). Consistent with the pharmacological effects of PELNVs, grapefruit-derived exosomes exhibited anti-colitic effects against dextran sodium sulfate (DSS)-induced colitis in mice through selective uptake by intestinal macrophages (2). Moreover, PELNVs derived from Robinia pseudoacacia flowers, Pueraria lobata roots, Folium Artemisiae, ginseng, and pomegranate ameliorated intestinal injury by reducing oxidative stress in various animal models (3). A recent study showed that broccoli nano-vesicles absorbed by the intestinal microbiota ameliorate gut microbial dysbiosis through the metabolic regulation of short-chain fatty acids and tryptophan. Likewise, garlic nano-vesicles act on the gut-brain axis to enhance insulin sensitivity in peripheral tissues, thereby restoring central nervous system health (4). Hence, they may balance gut microbial diversity and treat diseases directly or indirectly through this mechanism. This evidence indicates their mediating role in the gastrointestinal tract as regulators of intestinal macrophage homeostasis. PELNVs have also exhibited beneficial therapeutic effects on skin health and in cosmetic applications through various biological activities, including antioxidant, anti-inflammatory, and immunomodulatory effects (5-7). Collectively, these advantages suggest that PELNVs are promising candidates for the development of therapeutic applications.

Why has their application become a major research focus?

Although PELNVs exhibit physicochemical and functional similarities to animal exosomes, several differences exist between them (1,2). PELNVs provide higher yields, require shorter extraction times and cycles, are readily accessible, and provoke a weaker immune response (Immunogenicity). In contrast, animal exosomes must be obtained by culturing large numbers of cells, and their yield is low. In addition, animal exosomes may induce greater immunogenicity through their isoforms (2). Thus, PELNVs may overcome limitations associated with animal exosomes, such as low availability and high immunogenicity. Moreover, lysosomes readily recognize and degrade certain animal exosomes. The synthesis of liposomes and modification of exosomes may cause adverse effects, such as cellular stress, inflammation, and apoptosis. Conversely, PELNVs can achieve targeted delivery to specific tissues and minimize off-target effects through specific endocytic pathways. Therefore, they demonstrate favorable biocompatibility and lower cytotoxicity toward healthy tissues (2). Owing to their small dimensions, negative surface charge, long circulation time, similarity to cell membranes, and remarkable physicochemical stability across a wide range of pH values and temperatures, PELNVs have attracted considerable research interest (1,6). These strengths may even qualify them as endogenous carriers for delivery systems.

From the perspective of delivery systems, PELNVs have emerged as novel drug-delivery carriers owing to the aforementioned characteristics and their documented ability to traverse the blood-brain barrier without crossing the placental barrier, thereby improving safety (1,4). To date, researchers have used exosomes derived from several plants to encapsulate drugs, RNAs, or small molecules. Previous studies examining the delivery role of PELNVs derived from ginger, grapefruit, Carthamus tinctorius L., Citrus reticulata Blanco cv., broccoli, aloe vera, coniferous cherry, cauliflower, pomegranate, and red cabbage have demonstrated substantial improvements in the physicochemical and pharmacological effects of encapsulated substances while maintaining high safety (1,3,7). However, despite the numerous advantages attributed to them, comprehensive investigations of this new generation of drug carriers are required to address existing limitations, including pharmacokinetic properties, toxicity, and material-loading technology.

Taken together, although research on PELNVs is still in its infancy, current evidence indicates that they can serve as both therapeutic agents and drug carriers, making them a promising platform for future applications.

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