Title: SALIVARY EXOSOMES MEDIATED DIAGNOSTIC SIGNATURES AND PHYTOTHERAPEUTICS FOR BREAST CANCER

ABSTRACT

Breast cancer ranks as the second most common cause of mortality among women. Timely detection and suitable treatment, accompanied by diligent monitoring, are crucial in minimizing the impact of this fatal disease. In the present study, we aimed to identify biomarkers that could assist in early and non-invasive breast cancer diagnosis. We isolated the exosomes from the saliva of HER-2-positive breast cancer patients with grade II ductal carcinoma and performed comparative proteomics using label-free LC-MS. Compared to the healthy control, we observed an increased diameter and number of exosomes in the patient cohort. Comparative proteomics identified 15.6% unique differential expressed proteins (DEPs) in the control group and 9.6% in the patient group. Most of the DEPs were found to be involved in the regulation of enzyme activity, binding with actin filament, regulation of various signalling pathways (VEGF and IL-17 signalling), and neutrophil extracellular trap formation. Among the DEPs, HSPB1, ANXA1, SERPINB3 and CSTB were upregulated; and FLNA, CAP1, and CST4 were downregulated. We further validated a few upregulated and downregulated proteins through western blotting. The obtained salivary biomarkers could be employed in the early diagnosis of HER2-positive breast cancer. Exosomes are extracellular vesicles released by cells that mediate intercellular communication by shuttling their cargo of biomolecules, including lipids, proteins, and nucleic acids. Besides having diagnostic roles, exosomes also play a role in cancer progression, angiogenesis, and metastasis. Inhibiting exosome release from cancer cells could be used as a therapeutic.

In conclusion, we identified salivary exosome proteins as potential biomarkers for early detection of HER2-positive breast cancer. We also found that the aqueous extract of Acorus calamus downregulated Rab27a and nSMase2 in breast cancer cells, leading to reduced exosome secretion compared to the control group.