Licochalcone A is an excellent candidate for preventing luminal and non-luminal breast cancers
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BACKGROUND
- Proven breast cancer prevention drugs have side effects that are not acceptable to 85% of women at high risk for breast cancer.1 There is no drug for preventing ER- cancer.
- Prevention strategies with optimal efficacy, less toxicity, and greater acceptance are needed.
- Natural products are ideal candidates2 if demonstrated to shift the breast microenvironment to a tumor preventive milieu with lower toxicity.
- Licochalcone A (LicA) from licorice inhibits aromatase activity and has antioxidant potential.3,4,5

OBJECTIVES
1. Does LicA reprogram metabolism and antioxidant pathways in high-risk human breast tissue?
2. Does LicA retard cell proliferation and reduce tumor growth in vivo?
3. Pharmacokinetics: is LicA orally bioavailable?

METHODS
- Microstructures were prepared from contralateral unaffected breast tissue of two cohorts of 6 postmenopausal women with unilateral breast cancer.
- They were treated with DMSO and LicA (5 uM) for 24 h, prior to RNA extraction and total RNA sequencing.
- Differentially expressed genes (DEGs) were identified. Gene ontology (GO) pathway analysis identified pathways with combined enrichment scores >4 and FDR<0.05. DEGs were analyzed with computational metabolic analysis.
- Live cell imaging/proliferation was analyzed in DCIS.COM/ER+ PR+, DCIS.COM, MCF-7, MCF-7aro, HCC1937, HCC-3153, and MDA-MB-231 treated with DMSO and LicA for 24 h.
- Western blot was performed on MCF-7 and MDA-MB-231 cells treated with LicA (10 uM) for 24 h.
- Xenografts in female athymic nude mice were created using luminal or triple negative breast cancer cells. LicA was administered for 28 days at the dose of 80 mg/kg.day and rate of tumor growth was evaluated.
- Oral bioavailability in plasma, liver, and mammary tissue of BALB/c female mice was studied using LicA at a dose of 100 mg/kg.

RESULTS

Breast Microstructures treated with LicA
- In high-risk women’s breast microstructures
- In ER+ and ER- pre-malignant and malignant breast cells
- In mouse models of luminal and TNBC

Licochalcone A (LicA): good candidate for preventing breast cancer

Upregulated
- NRF2 Pathway P value: 7.537e-11
- Ferroptosis P value: 2.952e-5
- NRF2 transcriptional activation P value: 6.380e-4

Downregulated
- Pentose phosphate pathway P value: 5.625e-4
- Cholesterol metabolism P value: 5.800e-5
- PI3K-Akt signalling P value: 2.363e-4
- Neovascularization process P value: 8.347e-12

REFERENCES

Supported by the Postdoctoral Fellowships: American Cancer Society, RHCCCL Translational Bridge, NCIC-CONSORT-T32, H Foundation Award, Department of Surgery Seed Funding, and by Bramsen-Hamill Fdn, Licochalcone A (LicA) from licorice inhibits aromatase activity and has antioxidant potential.3,4,5

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LicA lowers SREBP1 protein expression

LicA retards proliferation in ER+ and ER- breast cells

LicA reduces the growth of mammary tumors