

# Effects of Curcumin on Breast Cancer



Young Ju, Ph.D.

Human Nutrition, Foods and Exercise

Virginia Tech

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# Outline

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- Breast Cancer
- Turmeric/curcumin
- Effects of curcumin on breast cancer

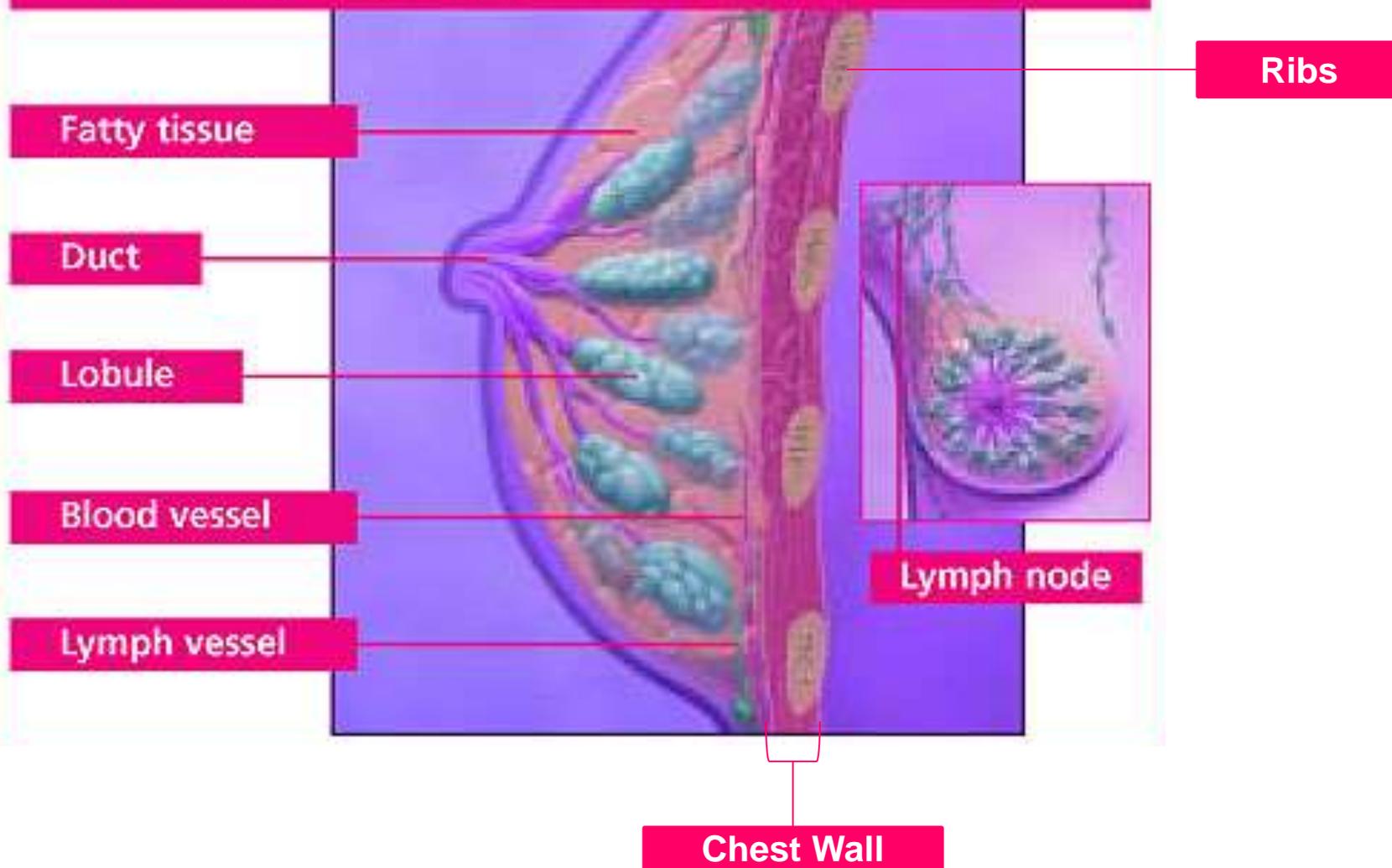
# Breast Cancer

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- BC is the second leading cause of cancer death in the US.
- A US woman's lifetime risk of invasive BC is about 1 in 8. A US man's lifetime risk of BC is about 1 in 1,000.
- Over 85% BC cases occur in women with no family history of the disease. ~5-10% of BC can be linked to inherited gene mutations.
- Approximately 77 % of BC cases occur in postmenopausal women ( $\geq 50$ -yr), however, BC is the most common form of cancer diagnosed in women of all ages.

## Parts of the breast



# Subtypes of Invasive Breast Cancer

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- Endocrine sensitive (or hormone sensitive)
  - Estrogen Receptor alpha – positive (ER+) and/or Progesterone Receptor - positive (PR+)
  - Hormone therapy
- Human Epithelial growth factor Receptor 2 – positive (HER2+)
  - Targeted therapy
- Triple-negative
  - ER-, PR-, and HER2-
  - Chemotherapy, radiation and other targeted therapy

## Early stages

### Stage 0

Cancer cells are present in either the lining of the lobules or the ducts. But cancer cells have not spread to the nearby fatty tissue.



### Stage I

**IA:** the tumor measures up to 2 cm **AND** the cancer has not spread outside the breast; no lymph nodes are involved.

**IB:** No tumor in the breast; small groups of cancer cells (0.2-2 mm) in the lymph nodes, **OR** A tumor in the breast (<2 cm); small groups of cancer cells (0.2-2 mm) in the lymph nodes.



### Stage II

**IIA:** no tumor in the breast, but cancer cells ( $\geq 2$  mm) in the lymph nodes **OR** the tumor ( $\leq 2$  cm) spread to the lymph nodes **OR** the tumor (2-5 cm) not spread to the lymph nodes

**IIB:** the tumor (2-5 cm); small groups of BC cells (0.2-2 mm) in the lymph nodes **OR** the tumor (2-5 cm); spread to 1-3 lymph nodes **OR** the tumor ( $> 5$  cm) not spread to the lymph nodes.



## Late stages



### **Stage III**

**IIIA:** no tumor in the breast; cancer is found in 4-9 lymph nodes **OR** the tumor (>5 cm); small groups of breast cancer cells (0.2-2 mm) in the lymph nodes **OR** the tumor (>5 cm); cancer has spread to 1-3 lymph nodes

**IIIB:** the tumor (any size) spread to the chest wall and/or skin of the breast **AND** the tumor spread to up to 9 lymph nodes

**IIIC:** the tumor (any size) spread to the chest wall and/or the skin of the breast **AND** the tumor spread to  $\geq 10$  lymph nodes



### **Stage IV (Advanced or Metastatic)**

Cancer has spread from the breast and lymph nodes to other parts of the body, such as the bone, liver, lungs, or brain, is known as metastatic cancer.

# Treatment Options

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- Surgery
  - Mastectomy
  - Lumpectomy
- Chemotherapy
- Radiation therapy
- Hormone therapy and/or Targeted therapy

# Turmeric (*Curcuma longa*)

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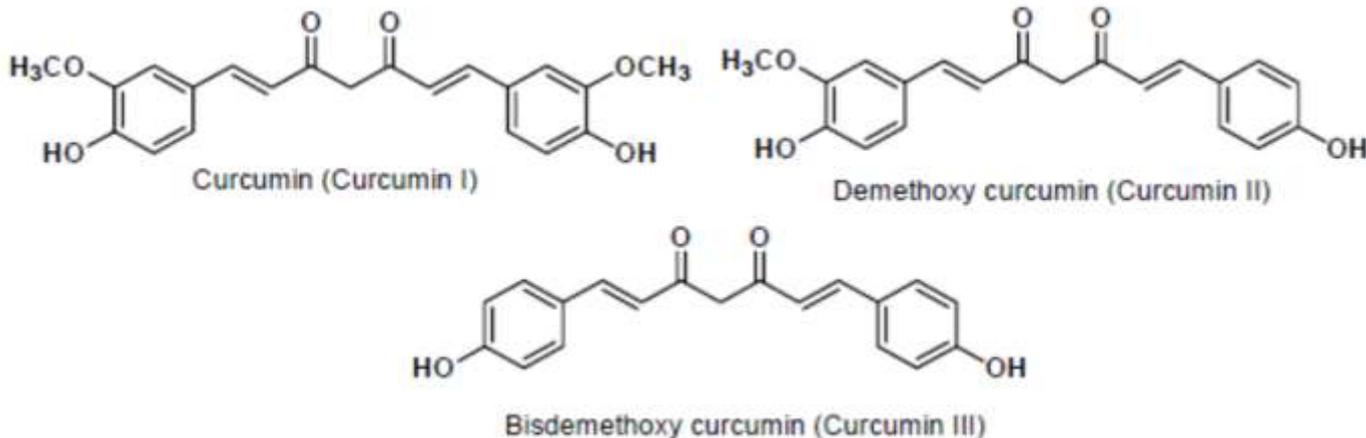
- Turmeric is widely used in food as a dietary spice and in traditional medicine as a remedy for different diseases.
- Turmeric contains 2% - 9% curcuminoids



# Curcuminoids

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- Three major curcuminoids
  - Curcumin (~77%)
  - Demethoxycurcumin (<20%)
  - Bisdemethoxycurcumin (<5%)



- Many studies have proved the various curcuminoids work synergistically and certain combinations of curcuminoids produce more biological action than any curcuminoid used alone.

# Turmeric/Curcumin

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- 1 Tablespoon of turmeric = ~7 g (~350 mg curcumin)
- 1 serving of curcumin supplement contains 500 mg - 1000 mg curcumin

# Turmeric/Curcumin in the U.S.

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- US: Turmeric is Generally Recognized As Safe (GRAS) (USFDA 2013)
  - **Acceptable Daily Intake level** for curcumin:  
0.1–3 mg/kg body weight (8-240 mg/80 kg adult)
    - Cut root: 1.5 – 3 g/day
    - Dried, powdered root: 1 - 3 g/day
    - Curcuminoids powder: 400 - 600 mg, upto 3 times/day
    - Liquid extract (1:1): 30 - 90 drops/day
    - Tincture (1:2): 15 - 30 drops, upto 4 times/day

<https://www.fda.gov/downloads/Food/IngredientsPackagingLabeling/GRAS/NoticeInventory/UCM549247.pdf>

# Anti-breast cancer activities



**↓ Proliferation**

**↑ Apoptosis**

**↓ Angiogenesis/Metastasis**

**↓ Inflammation**

**↓ Oxidative stress**

**↑ Chemo-/Radiation-sensitization**

# Curcumin inhibited the growth of breast cancer cells.

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- Curcumin alone, and in combination with chemotherapeutic agents, inhibit the growth of human breast cancer (ER+, ER-, HER2+, invasive, and triple negative) cells. (Calaf et al., 2018; Cine et al., 2013; Jian et al., 2013; Zhan et al., 2014; Kang et al., 2009; Quispe-Soto et al., 2016; Sun et al., 2012; Zhong et al., 2017)
  - ↓ Cancer cell proliferation
  - ↑ Cancer cell apoptosis
  - ↓ Oxidative stress

# Curcumin inhibited the growth of breast cancer cells.

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- Curcumin in combination with paclitaxel increased antitumor efficacy compared to curcumin or paclitaxel alone in ER+ human BC (MCF-7) cells and in the mice implanted with cancer cells (Zhan et al., 2014).
  - ↓ cancer cell viability, migration, normal cell apoptosis, EGFR signaling, and tumor growth
- Curcumin decreased tumor size, angiogenesis, and inflammation in the mice implanted with ER- human BC (MDA-MB-231) cells (Chen et al., 2017; Ferreira et al., 2015).

# Curcumin reduced breast cancer associated metastases and angiogenesis.

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- Review (Rohanizadeh et al., 2016)
  - Curcumin reduced breast cancer-associated bone metastases and vascularization.
- Phase I Clinical Trial (Bayet-Robert et al., 2010)
  - Curcumin (6 g/day) in combination with docetaxel chemotherapy was more effective to inhibit tumors in advanced and metastatic breast cancer patients (n=14) compared to monotherapy.

# Curcumin improved chemosensitivity.

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- Curcumin reduced HER2 and NF- $\kappa$ B expressions in doxorubicin-resistant breast cancer cells (Meiyanto et al., 2014).
- Curcumin (Zhou et al., 2017) and in combination with paclitaxel (Quispe-Soto and Calaf, 2016) reduced chemoresistance by increasing apoptosis in breast cancer cells.

# Curcumin reduced radiation-induced dermatitis

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- A randomized, double-blind, placebo-controlled clinical trial (Ryan et al., 2013)
  - 6 g curcumin capsules during radiotherapy in breast cancer patients with radiation dermatitis (n=30)
  - Curcumin administration reduced radiation dermatitis severity and moist desquamation but not redness and pain.

# Curcumin did not reduce radiation-induced dermatitis

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- A multi-site, randomized, double-blinded, placebo-controlled clinical trial (Wolf et al., 2018)
  - 6 g of curcumin during radiotherapy until 1 week post-radiation therapy in breast cancer patients with radiation dermatitis (n=686)
  - Curcumin administration did not reduce radiation dermatitis severity.



# Potential Adverse Effects

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- Curcumin is generally considered safe.
- High doses of curcumin (>6 g/day) may increase the chances of
  - Upset stomach, sour taste, gastrointestinal disturbances, nausea, diarrhea, loose stool ....

# Summary

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- Anti-breast cancer activities of curcumin have been demonstrated in cell studies and animal studies.
- Only few clinical trials showed benefits on specific cancer markers.
- Other clinical trials showed that curcumin can be used in combination chemotherapy or radiation therapy to reduce side effects of these therapies.
- Not observed any severe side effects.
- Bioavailability, safety and side effects need to be carefully evaluated.

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