

Effects of Curcumin on Breast Cancer



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October 18, 2018

Outline

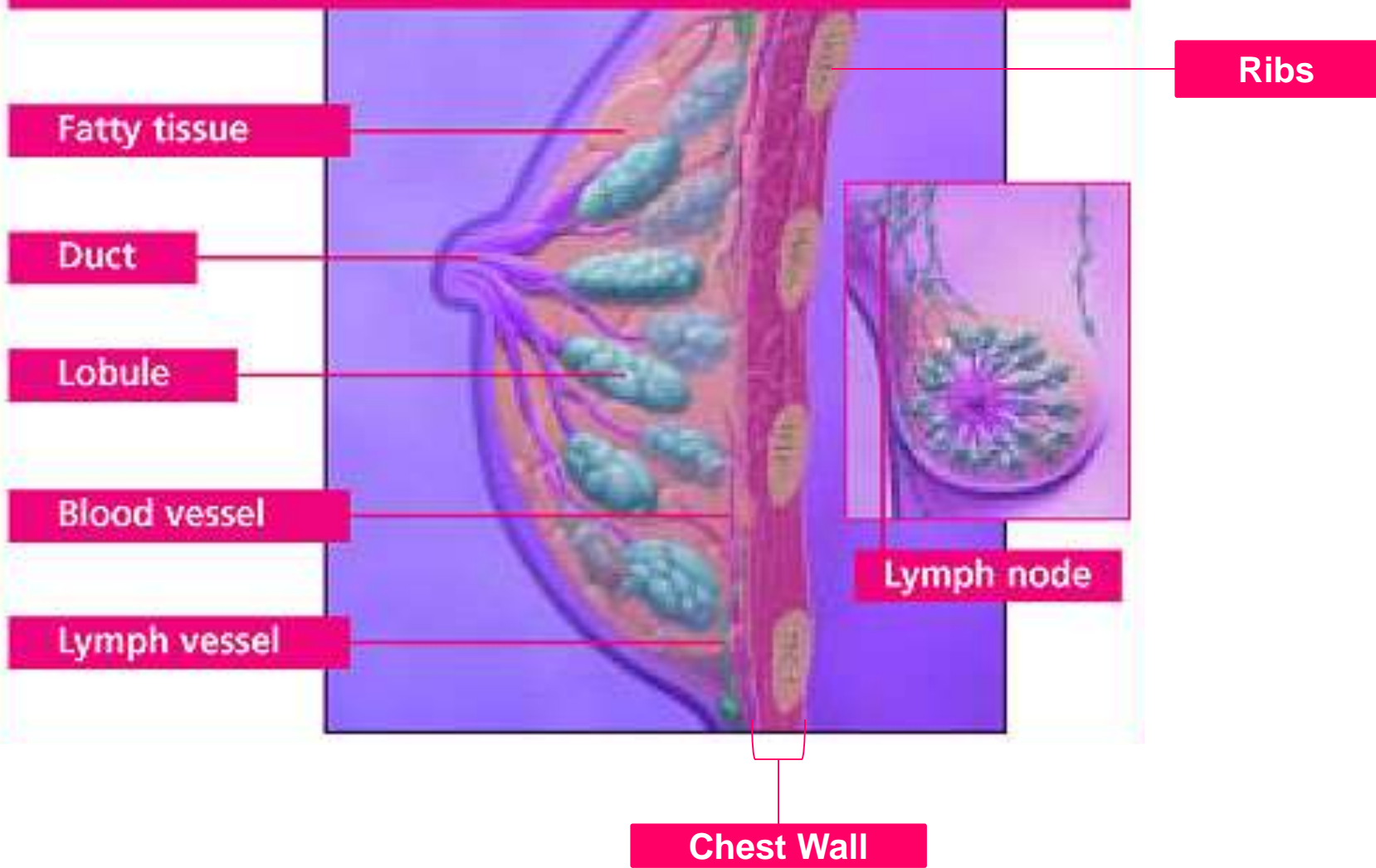
- Breast Cancer
- Turmeric/curcumin
- Effects of curcumin on breast cancer

Breast Cancer



- 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 (≥ 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

- 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 (≥ 2 mm) in the lymph nodes **OR** the tumor (≤ 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 ≥ 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

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

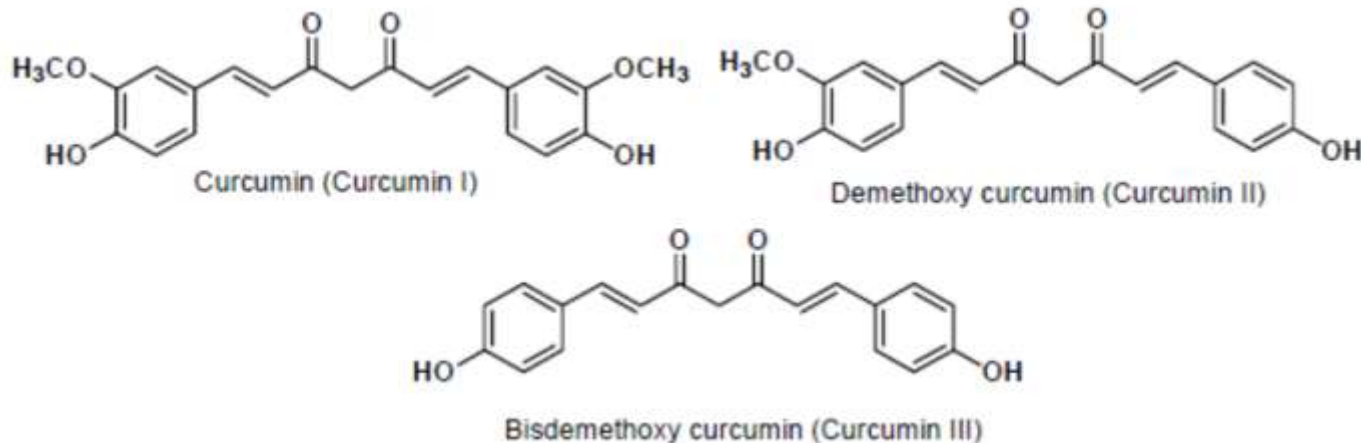
Turmeric (*Curcuma longa*)

- 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

- 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

- 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.

- 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.

- 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.

- 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.

- 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.

- Curcumin reduced HER2 and NF- κ 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

- 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

- 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

- 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

- 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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