

## Electro-Turmeric (Curcumin)-Therapy for Effective Cancer Cure

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Turmeric is a naturally occurring polyphenolic phytochemical, which is hydrophobic and exhibits a number of therapeutic effects needed for our wellness, including antiseptic, anti-inflammatory, antioxidant, chemopreventive and chemotherapeutic properties. It has been used over six thousand years in Indian (daily) cooking and Ayurvedic (life of science) medicine. Curcumin, the yellow pigment is a major component of the spice turmeric, isolated from the rhizome of the turmeric plant, *Curcuma longa*. Curcumin is an inhibitor of cyclooxygenase-2 (COX-2) activity in the treatment of inflammation and cancer. *In vitro*, *in vivo* and human studies have identified curcumin as an anti-inflammatory and chemopreventive agent responsible for inhibiting a variety of anti-inflammatory molecules, such as phospholipase, lipoxygenase, cyclooxygenase 1, leukotrienes, thromboxanes, prostaglandins, nitric oxide, collagenase, elastase, hyaluronidase, monocyte chemoattractant protein-1 (MCP-1), interferon-inducible protein, tumor necrosis factor (TNF), and interleukin-12, all molecules associated with inflammation.

Chemically, curcumin is a bis-R, -unsaturated -ketone (commonly called diferuloylmethane), which exhibits keto-enol tautomerism having a predominant keto form in acidic and neutral solutions and stable enol form in alkaline medium. Commercial curcumin contains approximately 77% diferuloylmethane, 17% demethoxycurcumin, and 6% bisdemethoxycurcumin. It inhibits production of the free radicals  $H_2O_2$  and NO by macrophages and astrocytes *in vitro*. In experimental autoimmune encephalomyelitis (EAE), curcumin inhibits lymphocyte proliferation, decreases IL-17 production by TH17 cells, and down regulates the expression of Toll-like receptors 4 and 9.

The low incidence of gastrointestinal mucosal cancers is attributed to the dietary turmeric consumption in certain populations, based on the extensive epidemiological evidences. A number of experimental studies on human cancer cell lines derived from many solid tumors, such as colorectal, lung, breast, pancreatic and prostate carcinoma have indicated that there is cell cycle arrest and/or apoptosis caused by curcumin. It is also reported that there is increased blood-barrier integrity in animal models of hemorrhagic stroke due to curcumin. It could also be used for neural applications. Its pharmacological safety and efficacy makes it a promising agent for both prevention and treatment of a wide spectrum of human diseases. For example, UCLA researchers have also reported that curcumin can help prevent and treat head and neck cancers by blocking the protein that promotes tumor growth. Since the same protein is also responsible for causing joint inflammation, arthritis risk could be reduced using curcumin. It is also antitoxic, economical and has no or the least side effects. The several millions of cancer deaths worldwide each year warrants additional/alternative therapies for cancer and curcumin-based therapy is a welcome boon towards this.

In spite of its efficacy and safety, curcumin has not yet been established as a therapeutic agent. One major drawback is its reduced bioavailability and rapid metabolism. In order to circumvent these, it is possible to use electrical pulses to locally regionally upload turmeric as recently studied in our lab for MCF-7, human breast cancer cells and HL-60, human leukemia cells. In addition, nanoparticle encapsulated turmeric is also reported to enhance the uptake. For

example, "Curcumin-loaded magnetic nanoparticles for breast cancer therapeutics and imaging applications" reports the application of next generation technique using magnetic nanoparticles (MNP) with theragnostic (both therapeutic and diagnostic) applications to enhance the uptake of curcumin and there are similar other studies using encapsulated curcumin. These nanoparticles could also be uploaded using electrical pulses of appropriate magnitude and duration.

Curcumin is also studied for cervical cancer treatments. Its effect on Triple Negative Breast Cancer (TNBC), the most deadly of all types of breast cancers that kills many African American and African women (including younger women, in their 20s, 30s, and 40s, <50 years) is timely and nanoparticle-encapsulated curcumin could be effectively uploaded using electrical pulses. Results of studies undertaken to elucidate possible molecular mechanisms using curcumin on TNBC cells have indicated that they inhibit the proliferation of TNBC cells. Thus electro-turmeric-therapy is worth studying to save the pain, agony, suffering and cost for the socio-economically challenged breast cancer patients in India, Ghana and elsewhere.

Considering the immediate, short term, and long term impacts, including cardiac problems and reduced cognition of chemotherapy, the most commonly used therapy for TNBC, there is an urgent need for alternate, less toxic drugs. Cognitive deficits following breast cancer diagnosis and subsequent chemotherapy could be long lasting for 20 years or more has been reported using cyclophosphamide, methotrexate and fluorouracil (CMF). On neuropsychological tests, breast cancer survivors treated with CMF more than 20 years ago performed worse, on average than random population controls. Turmeric with no such side effects could be a boon to the TNBC and breast cancer patients' long term.

Although the incidence rate is lower, the mortality rate is the highest of all races for African American and African patients due to both aggressive TNBC tumors and poor socio-economic conditions. It is estimated that by 2020, 70% of all breast cancer cases worldwide will be in developing low and middle income countries, where the resources and facilities might be scarce. For a woman with breast cancer in the industrialized countries, many new diagnosis and treatments options are available, but not so everywhere. Also, while the disease may cross the borders freely, the cultural understanding doesn't. While it is a world of pink ribbons and *Live Strong* bracelets in one part, in other

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parts of the globe, it might not be a topic of discussion. In addition, late stage cancers are more prevalent in low and middle income countries, due to both lack of awareness and resources. Thus, there is a critical need for alternate techniques.

Towards this end, we could use electrochemotherapy using

curcumin, as it is efficient, economical (out-patient-based), physical (electrical pulse-mediated, applicable to all histological types of tumors), minimally invasive and medically proven. Curcumin is a drug with the most effective, anti-inflammatory, antiseptic, chemopreventive and chemotherapeutic polyphenol phytochemical with fewer side effects, if any, targeting this health care disparity.