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BREAST CANCER GUIDE – ENCOURAGING SELF-STUDY AMONG PATIENTS OF NON-MEDICAL SCIENTIFIC PROFESSIONALS, DO IT YOURSELF

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Abstract

Medical journals are seldom touched by the scientific professionals that worked in non-related field of study. However, using cancer journals to solve the health issues independently may be rare without relying on medical doctors and professionals that charge very high cost of medical consultation. For those patients potentially have been affected by breast diseases particularly related to cancer, then it is recommended to assist oneself by taking additional initiatives to understand more about the health problem by summarising the content of independent cancer
research as below, not only able assist the patient affected but also helping the cancer professionals to cure the breast diseases faster with proper care of diets.

The research paper is about the knowledge usually of interest among non-medical professionals about breast cancer, particularly in the aspects of food, nutrition, genetic, methodological research etc. The areas covered in the paper are usually based on randomised study about the cause, consequences and prevention of the breast disease. Possessing basic understanding about the knowledge described may be useful as additional therapeutic methods particularly via food that may be achievable by anybody with breast cancer care requirement.

RELATIONSHIPS BETWEEN REPRODUCTION SYSTEM AND BREAST CANCER [1]

Human reproductive system is believed to contribute risk to the occurrence of breast cancer. Those nuns with nulliparity had high prevalence of breast cancer, noted by scientist Bernardino Ramazzini 300 years ago where hormonal effects are believed to play roles. Long term use of oral contraceptives may increase the risk for premenopausal breast cancer.[2] Risk of breast cancer may also be increased by the conditions of late menopause and early menarche. Breast feeding for extended time may reduce the risk of breast cancer moderately.[3] Even men may develop breast cancer, but not limited to women only, that may suffer from 0.88% of the expected 180,300 new breast cancer cases.[4] Various epidemiologic studies depicted that the dietary factors, fertility duration, history of reproduction and lactation, that mediate the
cumulative exposure of breast tissue to progesterone and estrogen, may be the major factors leading to cases of breast cancer.[5]

ADENOCARCINOMA AND FIBROADENOMA OF THE BREAST

Treatment choice for breast adenocarcinoma may be radical mastectomy, now known as lumpectomy or removal of the carcinomatous lump, proceed with chemotherapy and irradiation, that is a quite effective curing method as a radical mastectomy. However, the mutilating surgical procedures may cause physical and psychological trauma to the patients when all tumor cells are attempted to be extirpated by removing the selected contents of the muscles underlying the breast and armpit. In contrast to less complicated situation of fibroadenoma, the extirpation of the mass could be easily removed from the breast when the lesion is encapsulated.[6] Experiments from mice also show that the hormone of progestins may be able to modulate the mammary cancer cell growth without progesterone receptor by interacting on the glucocorticoid receptor.[7] Generally glucocorticoids may be applied in the prevention of human breast cancer cells.[8] However, the actions of progesterone on cancer cells varied between human and rat samples, that may posses antiestrogen, antiandrogen and antiglucorticoid properties.

BREAST CANCER TREATMENT - HORMONAL THERAPY FOR POSTMENOPAUSAL WOMEN
Estrogen has been confirmed as a major source of hormone among women that induces the growth of tumor cells in breast. For postmenopausal women, estrogen production may be able to be suppressed by the aromatase inhibitors (AIs) when the peripheral tissues with aromatase activity is the main source of estrogen.[9] Alternative to hormonal therapy is by applying cytotoxic chemotherapy, that possesses more adverse events like myelosuppression, nausea and vomiting in spite of prophylactic antiemetics.[10] In the adjuvant endocrine therapy, aromatase inhibitors played an important role, with third generation aromatase inhibitors being able to prevent conversion of androgens to estrogen in peripheral tissues, leading to the significant estrogen deprivation among women, especially those with primary breast cancer.[11] However, there exist controversial on the best combination of hormone, regarding also the optimal aromatase inhibitor and best administrative sequence for letrozole, tamoxifen, anastrozole, arimidex etc that may prevent osteoporotic side effects, at the same time, increase survival rate and reduce relapse of the disease among the breast cancer patients.

GENERAL NUTRITIONAL SUPPLEMENT FOR BREAST CANCER PATIENTS [12]

Primary defense against all cancer accordingly may be obtained from the nutritional supplement like LM1, acidophilus fiber, conjugated linoleic acid, DEF, bromelain, DHA/EPA, repairase, bioenhanced CoQ10 and mitochondrial support. However, typical formulation of nutrient for hormonally insensitive tumors may be added with lactobacillus 8, lymphodran, indole-3-carbinol, tocopheryl succinate or vitamin E, genistein complex and activated B6 (P5P). Slightly different nutritional supplement may be provided for patients with hormonally sensitive tumour, by applying supplements like D glucaric acid, indole-3-carbinol, limonene, melatonin, linseed
meal, vitamin D and shiitake, with supplement like vitamin E or tocopheryl succinate, activated B6 (P5P) and lactobacillus 8 also suitable for all breast tumors.

RELATIONSHIPS BETWEEN BREAST CANCER AND DAILY FOOD CONSUMPTION

Hormonal activities has been confirmed as the major source of breast and many different human cancer occurrence, that may have been able to be affected by diet.[14] Diets may also be a part of cultural factors or lifestyle that varied the risk of breast cancer occurrence among different ethnic groups. Egg consumption may be inversely correlated with breast cancer mortality, but the reversed has been observed with intake of table fats, beef, protein, calories, milk and fat.[15] A link has also been found between consumption of animal fat and protein with breast cancer. More frequent consumption of sweet desserts, pork, beef and other red meat increased the relative risk of breast cancer significantly.[16] One case control study involving 77 controls and 77 breast cancer cases revealed that dairy products (except milk), fried foods, hard fat used for frying, white bread and fried potatoes were associated with breast cancer, with relative risks ranged from 1.6 to 2.6.

BEANS PRODUCTS AND BREAST CANCERS
Isoflavones are found in high concentrations in legume and soy, that may be able to inhibit tumorigenesis among the women affected by breast cancer.[17] Examples of soy and soy-based foods containing isoflavones are dry soybean, bean curd, green soybean, dried or pressed bean curd, soybean sprouts, fried bean curd, soybean milk, skin of soybean milk and fermented bean curd, with dietary intakes of isoflavones may be classified based on the consumption of total isoflavones, genistein, glycitein and daidzein. In natural, isoflavones occur as ring compounds in plants as a class of bioactive phytochemical.[18] It has also been proven in many breast cancer research that the isoflavones from beans mainly exert anticarcinogenic effects on hormone-related cancer.[19] Isoflavones of high intake may also act as partial estrogen antagonists or agonists because they have a chemical structure similar to that of 17-beta estradiol that may compete with estrogens for binding with estrogen receptors (ERs). However, some other studies showed also that the estrogenic activity may not involve in the inhibitory pathway of isoflavones, and other estrogen and p53-mediated pathways may combinatively involved in tumorigenesis of breast cancer. Animal experimentation using rats, however, suggested that daidzein and soy protein rather than genistein to be the active ingredients in soy beans that reduce the mammary tumors.[20] Chemopreventive effects of genistein against breast cancer has been inconsistent in experimentation even bean consumption is highly recommended.

TYPICAL HERBAL FORMULATION AND BENEFICIAL EFFECTS AGAINST BREAST CANCER [21]
Vegetables and fruits have been understood as good sources of food and natural medicines to cure various diseases but not limited to breast cancer where such consumption is based more on health rather than religious practises. They contain dietary lignans and indole-3 carbinol (I3C) that posses metabolic effects on estrogen elimination pathways. The metabolites from human body like the interconvertible estrone and estradiol, influence the risk for breast cancer and other estrogen-related cancers. The only metabolites that are weakly estrogenic or possibly anti-estrogenic are 2-hydroxy-estrone (2-OHE1) and 2-hydroxyestradiol (2-OHE2), also called C-2 hydroxylation metabolites for both, whereas others are carcinogenic like 16 alpha-hydroxyestrone (16 alpha-OHE1) an endogenous carcinogen that binds irreversibly with the estrogen receptor, and also mutagen semi-quinones formed by 4-hydroxyestradiol (4-OHE2) and 4-hydroxyestrone (4-OHE1).

TEA AND CANCER PREVENTION [24]

Tea is produced from the plant *Camellia sinensis*, where the plant product the tea leaves are not eaten but consumed as liquid when brewed with hot water. Similar form of natural therapeutic preparation may also be applied to certain plant material that posses anti-cancerous component, namely methanolic extracts that may be obtained from Rose Cactus or Rose Wax, with the scientific name of *Periskia bleo* from the familty of *Cactareae*. Other synonyms for the plant are *P. corrugata, P. cruenta, P. panamensis, Cactus bleo, Rhodocactus bleo or corrugatus.*[25] The antioxidant component of the herb with decorative flowering properties have been proven to retard the growth of tumour cells in breast cancer.[26] The Malay language of the *Periskia bleo*
is "jarum tujuh bilah", or "qixingzhen" in Chinese language, means the seven star needle signifying the thorns available from the therapeutic plant. Common tea leaves derived from the plant of *Camellia sinensis* have about one third of the dry weights as antioxidant polyphenols and the enzyme of polyphenol oxidase.[27] Similar to fresh fruits and vegetables, tea may also induce a number of metabolic enzymes of specific cytochromes P450s that possessed potent antioxidant activities. However, there exists literature that deny the effectiveness of tea in cancer treatment with empirical studies.[28]

FAT AND BREAST CANCER [29]

The observations of breast cancer occurrence established the fact that the environmental basis plays a great role in the fatal breast disease, with breast cancer incidence rates vary by five folds between the high risk countries like the Australia, Northern Europe, United States etc, and low risk countries such as Japan.[30] One of the factors of differences is fat consumption. In both animal and human experiments, it was discovered that the olive oil has protective effects against breast cancer.[31] High fat diets with coconut oil or olive oil do not promote tumorigenesis, perhaps due to a favorable omega-3 / omega-6 polyunsaturated fatty acids (PUFA) ratio in the unsaturated fat component in the diet. Example of dietary omega-3 PUFA, such as eicosapentaenoic acid (EPA, C20:5, omega-3), or conjugated linoleate retards mammary tumour development.[32] In contrast, linoleic acid, an omega-6 PUFA (omega-6 PUFA) present in corn and safflower oils may stimulate tumor cell growth.
BONE MINERAL DENSITY AND BREAST CANCER [33]

Adjuvant aromatase inhibitors (AIs) are associated with the estrogen deprivation that may reduce the risk of breast cancer especially among the post-menopausal women. Such treatment of utilizing adjuvant anastrozole for those breast cancer patients of early stage with hormone receptor (HR)-positive, possessing additional side effects of health risk like postmenopausal osteoporosis. The danger of losing bone mineral density (BMD) may be mitigated by applying oral bisphosphonate in addition to osteoclast inhibitors like risedronate and ibandronate.[34] Another type of aromatase inhibitor tamoxifen, a selective estrogen receptor (ER) modulator (SERM), been able to improve relapse-free and overall survival to reduce the contralateral breast cancer by adjuvant setting.[35] Vitamin D plus calcium supplement may be used as conventional nutrients to mitigate bone density loss.

GENES INVOLVED IN BREAST CANCER [36]

There are a very few important genes that are directly involved in chromosome breast cancer, namely BCRA genes available on human chromosome 17, although other genes may also be involved in some patients according to molecular genetic techniques. In BRCA1, there contains a zinc finger domain, that is located in D17S855 under the chromosomal region 17q21. The gene is of autosomal dominant that codes for a suppressor protein of 1863 amino acids.[37] The other gene is BRCA2, situated in the chromosome 13q12-13 under the region of 6-cM.[38] p53 genes
gene has putative roles in transcription, DNA replication and cell cycle control, by inhibiting also the oncogenes like ras and myc. When somatic alteration occurs by point mutations or deletions at p53, abnormal p53 genes accumulation prevent transcription regulation by blocking nucleus entrance when normal p53 genes allowed so. The p53 mutation could be inherited in Li-Fraumeni syndrome when chemical carcinogenesis may play important role in breast cancer.[39] All three genes abovementioned BRCA1, BRCA2 and p53 have tumor suppressor mechanism. However, another cancer causing gene HER-2/neu could not be inherited but acquired through refractoriness to chemotherapy. The gene is amplified and overexpressed up to 30% of all breast cancers, although the class I growth factor-receptor tyrosine kinase family gene has no direct relationships of human breast cancer development. Rare cases of male breast cancer are caused by the constitutional mutation in the androgen receptor gene on the X chromosome of male patient.[40] The effects of androgen receptor gene on females are not yet known. Li-Fraumeni or SBLA syndrome caused by p53 mutation could be related to soft tissue sarcoma (S), brain tumour (B), leukaemia and lung cancer (L) and adrenocortical tumors (A).

**SELECTION FOR THE TREATMENT OF BREAST CANCER**

In the treatment of metastatic breast cancer systematically, cytotoxic chemotherapy and endocrine manipulation are usually employed, in addition to immunotherapy that is currently investigational.[41] Although combination of the application of cytotoxic chemotherapy and endocrine manipulation may be thought to be more effective than single modality of treatment, it may create problems in the difficulties in determining which modality has conferred the actual
benefit to the patients. Certain medical literatures have shown that endocrine manipulation may interfere with the usage of chemotherapy successfully.[42] Since there is a lack of knowledge about cytokinetic and biochemical interactions in hormonal therapy and chemotherapy, the combinative usage of both forms of breast cancer treatment remains empirical with high levels of uncertainties.[43] Table: Hormonal Agents Used for Advanced Breast Cancer - Commercially available agents approved by the FDA of United States of America for the treatment of breast cancer.[44] Notation: A=agent, C=class, D=Dose and Schedule of Administration. A = Tamoxifen (Nolvadex), C = Antiestrogen,, D = 20mg once daily; A = Megestrol acetate (Megare), C = Progestin, D = 40 mg 4 times daily; A = Diethylstilbestrol, C = Estrogen, D = 5 mg 3 times daily; A = Fluoxymesterone (Halotestin), C = Androgen, D = 10-40 mg daily divided dose; A = Methyltestosterone, C = Androgen, D = 50-200 mg daily divided dose; A = Testolactone (Telac), C = Androgen, D = 250 mg 4 times daily; A = Letrozole (Femara), C = Selective aromatase inhibitor, D = 2.5 mg once daily; A = Anastrozole, C = Selective aromatase inhibitor, D = 1 mg once daily; A = Goserelin, C = GnRH agonist analogue, D = 3.6 mg once monthly.

CHEMOTHERAPY WITH ENDOCRINE MANIPULATION - EFFECTIVENESS

COMMENTS [45]

There were many experiments conducted about the application of endocrine manipulation and chemotherapy concurrently, further denying the effectiveness of combined usage of 2 breast cancer treatment methods. In reverse, such combination of breast cancer treatment has produced no significant differences in comparison to single treatment modality, wasting the money and
resources with potential negative psychological effects among the patients that may thought that more treatment may be more effective, that was in fact unproven. The pharmacological doses of some hormones may even further antagonize the effects of cytotoxic chemotherapy.[46] A good example and exceptional benefit of combined usage of endocrine manipulation and chemotherapy is involving tamoxifen oral doses for 10 days, then Premarin estrogen physiological dose for 4 days, finally with citrovorum factor rescue and 5-FU of sequential methotrexate. However, the irreplicability of this finding make the validity of the said successful combined treatment methodology questionable.[47]

MINOR FACTORS AND BREAST CANCER OCCURENCES [48]

Minor risk factors like benign breast diseases and prior treatment for cancer may increase the rate of breast cancer occurrences because of the increased incidence of delayed neoplasms when aggressive combined-modality therapy are applied especially among children and young adults.[49] Surprisingly emotional factors play no causative role towards breast cancer development according to some research studies.[50] However, overstressed patients may have high chances of susceptibility to various diseases caused by the lowered immunity of the body. Other common factor is age, with higher incidence of breast cancer occurred among women having advancing ages. This may be possibly due to the requirement for multiple hits of somatic mutations for the genes of breast cancer. Data of the following shows the risk of developing breast cancer with A denotes By Age (Year) and R denotes Risk (Data from National Cancer Institute, reported in Science 1993; 259:618). A = 25, R = 1/19608; A = 30, R = 1/2525; A = 35, R = 1 / 622; A = 40, R = 1/217; A = 45, R/93; A = 50, R =1/50; A = 55, R = 1/53; A = 60, R =
NEW METHOD FOR INDEPENDENT TREATMENT OF BREAST CANCER FOR NON-MEDICAL PROFESSIONALS

Complicated methodology that utilizes expensive instruments that require consistent maintenance and over-expensive drugs with high level of treatment uncertainties may not be suitable for those breast cancer patients from poor family background, limited medical budget and lacking of medical science knowledge about the suitable treatment that should be applied, suitable for the requirement of breast cancer patients with wide ranges of background. After being diagnosed with breast cancer, whether male or female, the concentration of estrogen receptors (ERs) and progesterone receptors (PRs) in tumour tissue should first be assessed. Endocrine manipulation is typically suitable for those patients with ER-positive tumour, also tends to be more useful among postmenopausal women patients of advanced age in comparison to premenopausal groups. In typical experimental data, there depicts hormone receptors and response to endocrine therapy with RS means Receptor Status, N means Number of Patients, RR means Response Rate (%), ER means estrogen receptor, PgR means progesterone receptor.[51] RS = ER-PgR-, N = 96, RR = 10; RS = ER-PgR+, N = 12, RR = 33; RS = ER+PgR-, N = 132, RR = 34; RS = ER+PgR+, N = 159, RR = 74. Oral consumption of hormonal formulation is easier to be administered than injections used in chemotherapy. Alternative method is immunotherapy where antibody to tumour-associated antigen may increase survival rate.[52]
Although there are existing treatment methods of breast cancer applying modern medical technology like hormonal manipulation and chemotherapy, the relapsing rate of the fatal disease is considered high with 40% among women affected by the metastatic disease, ranking the top of cancer-related death.[53]

Immune system in human body has been shown to be able to control the relapses of breast cancer via tumour surveillance or other protective mechanism, when only 15% of breast cancer recurrence observed among 40% of patients that did not go through surgical removal even with lymph node involvement among them.[54] This finding has also initiated the prospective new cancer treatment of breast via immunotherapy. Certain medical literature states the existences of cancer stem cell that could not be eradicated fully via traditional cancer therapies. This special transformed population of breast stem cell, that are believed to assist origination and maintenance of tumours, may involve in cancer establishment, progression and resistance to the current treatment. Removing breast cancer stem cells via immunotherapy targeting of tumour-associated antigen may be the potential treatment against the relapse of the disease.[55] Another aspect of immunotherapy is against the tumour-associated carbohydrate antigens among the patients affected by breast cancer by continuous research on glycosylation changes in tumour cells when the presence of these antigens are usually associated with poor prognosis, further reducing the survival rate of breast cancer patients.[56] There are efforts to immunize breast
cancer patients via patient-tailored and multi-targeting strategies but none of these vaccines for cancer have been effectively proven up to year 2010.

IMMUNOLOGIC FACTORS AND BREAST CANCER [57]

Age of a person is directly correlated to the occurrence of breast cancer. The possible role of immune function in cancer risk has also been related to age, which is also an important potential confounder. Changes of immune function at different ages causes the prevalence of breast cancer at older age as well.[58] Vitamin C, an antioxidant is able to neutralize free radicals that can cause DNA damage, besides serving as nutrient that improves the body's defence system. Unlike folate that is associated with reduced breast cancer, the role of Vitamin C in cancer protection, as other antioxidant like vitamin E, remain inconclusive.[59] At birth, the immune system of babies is mainly from the colostrums of breast milk containing immunoglobin with short half-life. As the age increases, naive lymphocytes capacity to generate new T cells, proliferative response of T cells, capacity to generate cytotoxic effector, antibody affinities are decreasing concurrently with the reduction of levels of antibodies produced, macrophage activities, functional activities of natural killer (NK) cells increases.[60] Such declining immune capability of aged may increase the chances of breast cancer occurrences.

MALE BREAST CANCER – A SUMMARY [61]
The breast cancer of men is recommended to manage in a way analogous to those breast cancer women, with concentration of estrogen and progesterone to be first assessed to determine the suitability of treatment with endocrine manipulation. Breast cancer in men is linked to germline mutations in $BRCA2$. Breast cancers of men is also related to family history with breast cancer, with less than 1.5% all malignant tumours of breast and 1% of all breast carcinomas in men. Klinefelter’s syndrome is one of the predisposing factors. Radiation exposure has also been understood to cause male breast cancer. Combined treatment with chemotherapy is usual.

**SAMPLE RESEARCH PROPOSAL FOR BREAST CANCER**

Title is "Immunotherapy Applying Vitamin E Analogue Against Breast Cancer Tumour Cells". The proposed project is about the application of immunotherapy in the treatment of breast cancer, as a special alternative to the conventional cancer treatment method applying chemotherapy and hormone therapy. Improved survival rate has also been observed when primary tumour is able to be removed by lymphoid infiltration. Antibodies produced by the breast cancer patients have also previously been shown to be able to kill tumour-associated antigens, further increasing the survival rate. At different stages of the development of breast cancer, circulating levels of a mammary tumour antigen has also been reported to vary. These observation may also show that the indirect causal effects of human body immune system to deal with breast cancer tumour. Although the development of vaccination and immunological treatment against the breast cancer has been continually, progressively and
gradually understood in order to kill the breast cancer carcinoma cells and other potentially derived antigens since year 1975 when such ideas are first developed, surprisingly the true role of immune system in the prevention and treatment of breast cancer has not been clearly and fully understood by many scientists for the last 35 years when the modern technology has been advanced to the sophisticated levels with much financial resources being allocated to deal with breast cancer, one of the most prominent death-causing reasons among women.[70] The main focus of the research proposed may involve (a) the search of various causal relationships of body immune system with breast cancer (b) the qualitative and quantitative analysis of body defence systems and the prevalence of breast cancers and other related or unrelated diseases due to immune system at subnormal levels (c) the looking forward to nutritional therapy and lifestyle adjustment methods of cheap and economic stages at the preliminary levels, in order to prove that the improvement of body defence systems may lower the risks of breast cancer occurrence at premenopausal and postmenopausal levels, as null hypothesis of the research.

Various forms of vitamin analogue, namely derived from vitamin D and vitamin E has been able to suppress tumour growth in breast. The proposed study may involve the consumption of alphatocopheryloxyacetic acid (alpha-TEA), a novel ether derivative of alpha-tocopherol, by breast cancer patients and healthy samples wherever applicable. The vitamin E alpha-tocopherol (alpha-TOH) analogs (VEA) consists of alpha-tocopheryl succinate (alpha-TOS) and alphatocopheryloxyacetic acid (alpha-TEA), are of interest in the proposed breast cancer studies due to their selective toxicity towards tumour cells.[71] Alpha-TEA structurally shares the phytyl tail and the chroman head with alpha-TOH, but differs from alpha-TOH in that the hydroxyl group at the number 6 carbon of the phenolic ring of the chroman head is replaced by an acetic
acid residue that is attached by a nonhydrolyzable ether bond which makes the oral administration of the alpha-TEA possible. Due to the cost factors of the research project the material and instrument applied to the project may also be simplified, namely applying cheaper conventional vitamin C and vitamin E in the treatment of breast cancer by observing the mechanism of changes of tumour growth where such results of conventional vitamin C and vitamin E treatment, usually used to improve the defence system of the consumer, has not been fully understood about the mechanism of immunity improvement potentially against the breast cancer diseases on experimentation of laboratories when the qualitative research on the relationships of vitamin C and vitamin E has been inconsistent in the breast cancer treatment.

Preliminary results: [72] The initial findings show that vitamin E analogue may be able to reduce the size of tumour growth. The proposed method should be simple scientifically proven well.

Experimental plan: Preparation of alpha-tocopheryloxyacetic acid: alpha-TEA, 2,5,7,8-tetramethyl-(2R-(4R,8R, 12-trimethyltridecyl) chroman-6-yloxy) acetic acid was synthesized or purchased as a ready-made reagent. To a suspension of NaH (4.39, 181 mM) in dry tetrahydrofuran (THF, 400 mL) under argon at 0 degree C was added a solution of (R,R,R)-alpha-tocopherol (59.9, 139 mM) in dry THF (200 mL), following the prescribed procedure. Tumour cells and cell culture, especially those with breast cancer was prepared, that was latter to be treated with the medium containing vitamin-E analogue as the focus of research, compared with conventional vitamin C and vitamin E control blank medium to observe the changes of breast cancer culture growth conditions added with different additives.
Depending on the availability of different sources of breast cancer cell and the funding to support the operations of experimentation, the methodology of research may be modified to observe the diversified breast cancer tumour cell growth on various mediums added with selected ingredients that are able to be consumed by human beings, at the same time, has been renown to be able to improve the immune system of the body of the consumer.

Specific aims of the project: The project objectives are to systematically design in vitro experiments, applying the economic vitamin mediums and the analogue with body immune system, enhancing the effects against breast cancer tumour growth, and also further prove the direct relationships of immunoglobulin efficiency in the disease prevention against the antigen of breast tumour cells that may have a variety of effects from different sources of breast carcinoma.

Ethical approval statement: There is no ethical approval requirement for the proposed project that adopt in-vitro technique rather than in-vivo using human or animal live organism.

BREAST CANCER: CHEMOTHERAPY AND BREAST CANCER

Breast cancer has caused increasing mortality among woman in the world but only a little progress has been achieved in enhancing survival rate even such malignant neoplasm prevails, with opinion divergence in its optimal primary treatment.[73] The survival time could not been enhanced by applying a short course of thio-TEPA used as an adjuvant following radical mastectomy in a large controlled study.[74] Similar effect observed in oophorectomy as an
adjuvant to mastectomy in pre-menopausal patients, however delay in the appearance of recurrence.[75]

EFFECTS OF ONE-CARBON METABOLISM NUTRIENT IN REDUCING BREAST CANCER RISKS

Low intakes of folate and vitamin B6 among woman could substantially increase the risk of postmenopause breast cancer, which is also associated with the MTHFR 677TT genotype.[76] The risk of occurrence of breast cancer may also vary by menopausal status and nutrient intake that interrupt or contribute to one carbon metabolism.[77] Lowest dietary folate intake with vitamin B6 group of breast cancer women has strong association with high numbers of variant T alleles in the cancer cells by applying VITamins And Lifestyle (VITAL) cohort with genotyping to the patients, where the effects of nutrients against breast cancer is highly significant as well.

EFFECTS OF NATURAL AND COMMON FOOD CONSUMPTION AGAINST CANCER

Various laboratory as well as epidemiological studies revealed strong correlation between diet and cancer whether breast-related or not.[78] Natural spices like ginger, hot chilli pepper etc has been described as possessing potential cancer chemopreventive activities.[79] Gingerol, as a major pungent principle found in ginger or Zingiber officinale Roscoe, able to attenuate 12-O-tetradecanoylphorbol-13-acetate (TPA)-induced turn or promotion in experimental Guiney pigs.
The beverages of green tea, black tea etc contains phytochemicals, especially from the plant *Camellia Sinensis*. Such chemicals could be chemopreventive.

**DIETARY MODIFICATION EFFORT AGAINST BREAST CANCER**

Dietary cancer like breast cancer can be promoted and initiated by fat, where cancer cell growth could be severely inhibited when the intake of cholesterol is limited dramatically. Those breast cancer patients having a shorter life span, if having a high serum cholesterol and high fat intake, in comparison to patients with low serum cholesterol with normal or low fat intake. Younger Japanese women that have adopted a more Western diet and culture, as American women, have more chances than the older generation of Japanese women, that are less obese, eat high-fiber, low fat diet with vitamins and minerals, to get cancer of breast with lower life span of survival.

**CHEMICALS IN CHEMOTHERAPY AGAINST BREAST CANCER**

Various targeted therapy of breast cancer, by maximizing the use of markers predictive response to chemo mainly, includes tumor recognition that overexpress c-erbB-2 (HER2/neu), may be very sensitive to anthracycline and trastuzumab (herceptin or an anti-HER 2 monoclonal antibody). Although chemotherapy was fairly compared to local surgery, castration and
radiotherapy, the application of doxorubicin (adriamycin)-cyclophosphamide (AC), cyclophosphamide-methotrexate-5-fluorouracil (CMF) etc became popular since 1960.\[85\] In the adjuvant treatment in operable breast cancer, the patients may experience nausea, with side effects of mucositis (18%), cystitis (28%), amenorrhea (54%), alopecia (55%) etc, with lower relapse rate among treated group (n=207, 5.3%) compared to control group (n=179, 24%).\[86\]

NEUROPEOTIDE RECEPTORS AND BREAST CANCER \[87\]

Neuropeptide, for example, bombesin/gastrin-releasing peptide (GRP), is a growth factor for some human breast cancer cells, where the mechanism of cell proliferative actions, by specific surface receptors binding, signaling events initiation of complex cascade, may lead to Swiss 3T3 cell division with DNA synthesis, small cell lung carcinoma (SCLC) autocrine growth etc.\[88\] Growth promoting factor of bombesin on breast cancer cells elicited where phenol ref free medium supplemented with heat-inactivated and dextran-coated charcoal-treated fetal bovine serum were cultured with cells to remove oestrogen.

Conflict of Interest Statement

There is no any financial and personal relationships with other people or organizations that could inappropriately influence the article. There is also no conflict of interest in employment, consultancies, stock ownership, honoraria, paid expert testimony, patent applications/registration, and grants or other funding related to this article.


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