Fight Cancer with Phyto –Medicine with Siddha system of medicine

Dr. P.T. Kalaichelvan & Dr. Akila Kalaichelvan[1]

Introduction

It would be sacrilegious to confine such an elaborate and divine medical science having several dimensions and levels to it like Siddha Vaidyam within the framework of a puny definition. However, for the sake of brevity Siddha Vaidyam can be defined as a comprehensive and scientific system of medicine which accurately diagnose all types of human ailments by gauging the pulses of dasa nadis (ten principal nerves) and curing the diseases by administering a wide range of elixir like medicines prepared out of medicinal plants, herbs and other ingredients. Neetumarunnukal-medicines prepared from navalohas (nine metals) like mercury, gold, silver, copper etc. and 64 types of poisonous substances (64 pashanas) - give extra curing edge to Siddha system. Panchabhoota and Thridosha theories had been first pro- pounded by ancient Siddhars. Fully developed Marma Sasthra (science of vulnerable points) is one of the unique features of Siddha Vaidyam. Siddha system believes that every individual is unique. Hence Siddha practitioners always try to treat the patient, not the disease. Most of the modem time medical systems like Ayurveda, Unani, aturopathy, Magnetic Therapy and even Allopathy owe a great deal to Siddha Vaiydam (Siddha Vaidyam is popularly known as the Thai Vaidyam - the Mother Science).

Siddha system classifies diseases - stages of diseases to be exact - into three categories. According to Siddha scriptures around 80% of human ailments fall into the first category, saddhayam. Saddhyam category diseases are the ones, which can easily be cured within a short span of time. One mandalam (41 days) is the usual duration of the treatment for saddhyam category of diseases.

Those diseases,which are difficult to cure, but curable fall into klishta saddhyam category. Around 17% of the diseases belong to this group. One to three years is required to cure klishta saddhyam category of diseases. Three per cent diseases fall into the third category, assadhyam. It is impossible to cure assadhyam category of diseases. But Siddha treatment will certainly improve the condition of patients affected with assaddhyam group of diseases.

Most of the diseases which are incurable ones to other medical sciences are only either saddhyam or klishta saddhyam diseases to Siddha Vaidyam. If Siddha medicines are consumed for diseases like uterine growths, gynaec disorders, piles, tonsillitis, bladder and kidney stone, gangrene, goiter etc surgeries can be avoided. Siddha medicines are highly effective for heart blocks too.

---

[1] Dr. P.T. Kalaichelvan Centre for Advanced Studies in Botany, University of Madras, Guindy Campus, Chennai - 600 025, TN, India ptkalai2003@yahoo.com and Dr. Akila Kalaichelvan Director, Sculpture Institute India SII, Mylapore, Chennai - 600 004, TN, India. akilakalai@gmail.com , akilakalai@yahoo.com

When things become complex, only the tough system can deliver on par with expectations. Asthma, psoriasis, hypertension, rheumatic diseases like arthritis, spondylitis etc., diabetes, cancer, gynecology disorders - popular medical sciences, including modern medicine may wilt and turn ineffective before some of the so called incurable and grave diseases like cancer. By administering appropriate *neettu marunnu* in less than homeopathic dose, a seasoned Siddha practitioner may salvage people from even the clutches of killer diseases like cancer.

The Cancer continues to be one of the major causes of death worldwide next to heart diseases and only modest progress has been made in reducing the morbidity and mortality of this disease [1] According to a report of World Health Organization, more than 80% of world's populations depend on traditional medicine for their primary health care needs [2 3]. Altogether, there are 200 forms of cancer (affecting virtually every type of cell in the human body) Unlike ordinary cells; cancer cells have lost their ability to stop dividing. They are Immortal-they proliferate without limit until they choke off normal bodily function and kill the victims. [4]

Cancers may be caused in one of three ways, namely incorrect diet, genetic predisposition, and via the environment. As many as 95% of all cancers are caused by life style and may take as long as 20– 30 years to develop. Current estimates from the American Cancer Society and from the International Union Against Cancer indicate that 12 million cases of cancer were diagnosed last year, with 7 million deaths worldwide; these numbers are expected to double by 2030 (27 million cases with 17 million deaths). [2] Plants have a long history of use in the treatment of cancer and it is significant that over 60% of currently used anti-cancer agents are come from natural sources [5]

Scientists are now on the threshold of a complete understanding of how cancer develops at the molecular level is the main; "*the mystery of cancer has been solved*". Cancer has now been revealed to be a genetic disease, and the precise sequence of four to six mutations necessary to create a cancer cell for many common cancers is now known. Not only have the main genes involved been identified: scientists also know the basic molecular steps through which a normal cell suddenly becomes cancerous. [4] Naturally occurring drugs that are part of the war against cancer include vinca alkaloids (vincristine, vinblastine, vindesine, vinorelbine), taxanes (paclitaxel, docetaxel), podophyllotoxin and its derivative (etoposide, teniposide), camptothecin and its derivatives (topothecan, irinothecan), anthracyclines (doxorubicin, daunorubicin, epirubicin, idarubicin) and others. In fact, half of all anti-cancer drugs approved internationally were either natural products or their derivatives and were developed on the basis of knowledge gained from small molecules or macromolecules that exist in nature [6,7]

Nature is an attractive source of new therapeutic candidate compounds as a tremendous chemical diversity is found in millions of species of plants, animals, marine organisms and microorganisms as potential anti-cancer agent [8, 9] Scientists are now on the threshold of a complete understanding of how cancer develops at the molecular level in the main; *the mystery of cancer has been solved*. Cancer has now been revealed to be a genetic disease, and the precise sequence of four to six

mutations necessary to create a cancer cell for many common cancers is now known. Not only have the main genes involved been identified: scientists also know the basic molecular steps through which a normal cell suddenly becomes cancerous. [4]

Medicine is being thrust into its third stage by the Bio-molecular revolution.

During the first stage of medicine, Shamans and mystics painfully scoured the plant kingdom for thousands of years looking for herbs that might scare dreaded spirits away, at times stumbling upon valuable remedies that are used even today. Some of our common drugs have their origin during this primitive but important stage. But for every herb that was, by trial and error, found to be effective against certain ailments, there were thousands more which did not work, some of which even injured the patients. For example a country doctor who became one of the founders of the famed Mayo clinic in Rochester, Minnesota, recorded with rare candor that most of his potions were worthless, but there were two things in his black bag which were guaranteed to work every time: morphine and his saw which were used in amputations.

Beside this there is numerous agents identified from fruits and vegetables can be used in anticancer therapy. The agents include curcumin (turmeric), resveratrol (red grapes, peanuts and berries), genistein (soybean), diallyl sulfide (allium), S-allyl cysteine (allium), allicin (garlic), lycopene (tomato), capsaicin (red chilli), diosgenin (fenugreek), 6-gingerol (ginger), ellagic acid (pomegranate), ursolic acid (apple, pears, prunes), silymarin (milk thistle), anethol (anise, camphor, and fennel), catechins (green tea), eugenol (cloves), indole-3-carbinol (cruciferous vegetables), limonene (citrus fruits), beta carotene (carrots), and dietary fiber. In this review active principle derived from natural products are offering a great opportunity to evaluate not only totally new chemical classes of anticancer agents, but also novel lead compound and potentially relevant mechanisms of action.

Dietary source of anti-cancer agents:

Natural dietary agents including fruits, vegetables, and spices have drawn a great deal of attention from both the scientific community and the general public owing to their demonstrated ability to suppress cancers. Recent studies suggest that the consumption of food rich in fruits, vegetables and spices have a lower incidence of cancers (stomach, esophagus, lung, oral cavity and pharynx, endometrium, pancreas and colon) [10-12].

Dietary agents consist of a wide variety of biologically active components that are responsible for the anti-cancer effects like curcumin, genistein, resveratrol, diallyl sulfide, S-allyl cysteine, allicin, lycopene, capsaicin, diosgenin, gingerol, ellagic acid, ursolic acid, silymarin, anethol, catechins, eugenol, isoeugenol, dithiolthiones, isothiocyanates, indole-3-carbinol, isoflavones, saponins, phytosterols, inositol hexaphosphate, Vitamin C, D-limonene, lutein, folic acid, beta carotene, selenium, Vitamin E and flavonoids (Table 3). Many of which have been used in traditional medicines for thousands of years. These dietary agents are believed to suppress the inflammatory processes that lead to transformation, hyper proliferation, and initiation of

carcinogenesis. Their inhibitory influences may ultimately suppress the final steps of carcinogenesis i.e. angiogenesis and metastasis [13].

Some of the Dietary sourcesas anti- cancer agents with their Botanical Name, Source, Compound and Reference viz: Carica papaya,Family- Caricaceae, Berries β-Cryptoxanthin[14] Glycyrrhiza glabra; Glycyrrhiza radix; Glycyrrhiza uralensis, Family-Leguminosae ,Licorice root,Glycyrrhizin [15] Cannabis sativa, Family- Cannabiaceae, Hemp, Cannabinol, [16] Rosmarinus officinalis, Family- Lamiaceae, Rosemary, Carnosol, [17] Pueraria lobata radix, Family- Fabaceae, Genistein [18]Glycine max, Family- Fabaceae, Soybeans, Genistein, [19] Prunus armeniaca, Family- Rosaceae, Apricots, Carotenoids, [20] Zingiber officinale, Family- Zingiberaceae, Tuber, Gingerol, [21]

Lycopersicon esculentum, Family- Solanaceae, Tomato, Lycopene, Lutein, Kaempferol [22] Piper nigrum; Piper longum, Family- Piperaceae, Black pepper, Purpurogallin; Piperine, [23] Ocimum sanctum, Family-Lamiaceae, Basil, Ursolic acid [24] Betula alba, Family- Betulaceae, Birch tree Betulinic acid [25] Crocus sativus, Family- Iridaceae, Saffron, Carotenoids, [26] Silymarin marianum, Family- Asteraceae, Milk thistle, Silymarin [27]

Capsaicum annum; Capsaicum frutens, Family- Solanaceae, Red chilli, Capsaicinoids, Capsaicin [28] Camellia sinensis, Family- Theacea, Green and black teas, Catechin and theaflavins [29] Vitis vinifera, Family- Vitaceae, Grapes, Resveratrol [30] Daucus carota sativus, Family- Apiaceae/umbelliferae, Carrot,β-Carotene, [31] Tabebuia avellanedae, Family- Bignoniaceae, Lapacha tree, Lapachone [32] Citrus aurantium, Family- Rutaceae, Orange, Hesperidin, [33] Prunus dulcis, Family- Rosaceae, Almond, Morin [34,35] Aloe arborescens, Family- Asclphodelaceae, Aloe vera, Emodin [36] Opium poppy, Family- Paparveraceae, Poppy, Morphine and its analogues [37] Curcurbita moschata, Family-Cucurbitaceae, Pumpkin β-Carotene [38]Azadirachata indica, Family- Meliaceae, Neem Polyphenolics, Polyphenolics [39].

Sulfur mustard was synthesized in 1854. By the late 1880s it was recognized that sulfur mustard could cause blistering of the skin, eye irritation possibly leading to blindness, and severe lung injury if inhaled. In 1917 during World War I, sulfur mustard was first used as a chemical weapon. By 1919 it was realized that exposure to sulfur mustard also produced very serious systemic toxicities. Among other effects, it caused leukopenia (decreased white blood cells) and damage to bone marrow and lymphoid tissue. During the interval between World War I and World War II there was extensive research into the biological and chemical effects of nitrogen mustards (chemical analogs of sulfur mustard) and similar chemical-warfare compounds.

The toxicity of nitrogen mustard on lymphoid tissue caused researchers to study the effect of nitrogen mustard on lymphomas in mice. In the early 1940s nitrogen mustard *mechlorethamine* was discovered to be effective in the treatment of human lymphomas. The efficacy of this treatment led to the widespread realization that chemotherapy for cancer could be effective. In turn, this realization led to extensive research, discovery, and development of other cancer chemotherapeutic agents. *Phyto*-medicine obtained from herbal sources are in great demand in the developed

world as they are able to cure many infectious diseases.

These plant-based drugs provide outstanding contribution to modern therapeutics. The natural medicine are attracting renewed attention from both practical and scientific view points, but the mode of action of folk herbal medicines and related products from nature is even more complex than mechanistic clarification of a single bioactive factor. They have proved their efficacy for primary health care because of their safety and lesser side effects. They also offer therapeutics for age-related disorders like memory loss, osteoporosis, immune disorders, etc. The new- found popularity is due to their almost miraculous success with cases, which were given up as hopeless by the allopathic doctors as their side-effect free treatment.

In the second stage of medicine, which began after World War II, the mass distribution of vaccines and antibiotics temporarily vanquished whole classes of disease. Abigial salyers and Dixie whit, authors of Bacterial pathogenesis, write:" one of the main reasons for the elevation of Physicians to their current status as respected professionals was that antibiotic actually enabled them to cure disease for which in the past they had only been able to provide ameliorative (and largely ineffective) therapy"

Fortunately now we are entering the third stage of medicine "Molecular medicine" perhaps the most exciting and profound of all. For the first time in history, each level of pathogenesis, protein for protein, Molecule for molecule even atom for atom, is now being revealed like a general eagerly reading the map of the enemy's defenses, scientist today can read a germ's complete genome and identify the molecular weak spots in it's armor. In-spite of the Human Genome project and cancer genome project and various drugs being in the market still cancer is felt dreaded at this juncture the In Phyto-medicine too A variety of approaches are being employed to identify chemical compounds that may be developed and marketed. The current state of the chemical and biological sciences required for pharmaceutical development dictates that 5,000–10,000 chemical compounds must undergo laboratory screening for each new drug approved for use in humans. Of the 5,000–10,000 compounds that are screened, approximately 250 will enter preclinical testing, and 5 will enter clinical testing. The overall process from discovery to marketing of a drug can take 10 to 15 years. This section describes some of the processes used by the industry to discover and develop new drugs.

Natural products have been a prime source for the treatment of many forms of cancer, many of which are consumed daily with the diet. They provide significant protection against various cancers and many other diseases. The antioxidant medicinal plants and their products prevent from the cancer and other diseases by protecting cells from damage. Thus, consuming a diet rich in antioxidant fruits, vegetables, herbs etc. will provide health-protective effects. Microbes and marine organisms also have been offering the great role in the prevention and treatment of cancer. All the natural products discussed in this review exhibit anticancer activities. Natural products offer a great opportunity to evaluate not only totally new chemical classes of anticancer agents, but also novel and potentially relevant mechanisms of action.

To conclude Cancer is a combination of 200 different forms and nearly 100-diiferent diseases any number of methodologies, diagnosis, treatment, and types of treatment is essential at any era of time and it is definite that the future medicine will turn back towards Siddha Phyto-medicine. The integration of phyto-medicine into the health system will be developed in such a way to bring harmony between the traditional and modern system of health care with minimum threat to each other.

References

1. Hail Jr N. Mitochondria: a novel target for the chemoprevention of cancer. Apoptosis. 2005;10:687–705.

2. Farnsworth NR. Ethnobotany and the Search for New Drugs, Wiley Willett WC. Diet and health: what should we eat. Science. 1994;264(5158):532–7.

3. Duraipandiyan V, Ayyanar M, Ignacimuthu S. Antimicrobial activity of some ethno- medicinal plants used by Paliyar tribe from Tamil Nadu, India. BMC Comp Alter Med. 2006;6:35-41.

4. Michio Kaku: Visions a book on How Science will Revolutionize the 21st Centuary year 1997

5. Cragg GM, Kingston DGI, Newman DJ. Anticancer Agents from Natural Products. Taylor & Francis Group, Boca Raton, FL. Brunner-Routledge Psychology Press; 2005.

6. Cragg GM, Newman D J, Weiss RB. Coral reefs, forests, and thermal vents: the worldwide exploration of nature for novel antitumor agents. Semin Oncol. 1997; 24:156-163.

7. Newman DJ, Cragg GM. Natural products as sources of new drugs over the last 25 years. J Nat Prod. 2007;70:461–477.

8. Butler MS. Natural products to drugs: natural product derived compounds in clinical trials. Nat Prod Rep. 2005;22:162–195.

9. Bailly C. Ready for a comeback of natural products in oncology. Biochem Pharmacol. 2009;77:1447–1457.

10. Block G, Patterson B, Subar A. Fruit, vegetables, and cancer prevention: a review of the epidemiological evidence. Nutr Cancer. 1992;18(1):1–29.

11. Steinmetz KA, Potter JD. V egetables, fruit, and cancer prevention: a review. J Am Diet Assoc. 1996;96(10):1027–39.

12. Reddy L, Odhav B, Bhoola KD. Natural products for cancer prevention: a global perspective. Pharmacol Ther. 2003;99(1):1– 13.

13. Aggarwal BB, Shishodia S. Molecular targets of dietary agents for prevention and therapy of cancer. Biochem Pharmacol. 2006;71:1397–1421.

14. Hoyoku N, Michiaki M, Harukuni T, et al. Cancer prevention by carotenoids. Arch Biochem Biophys. 2009;483:(2):165-168.

15. Wan X, Luo M, Li X, et al. Hepatoprotective and anti-hepatocarcinogenic effects of glycyrrhizin and matrine. Chem Biol Interact. 2009;181:(1)15-19.

16. Caihua L, Michael DMc, Carmen M, et al. A Population-Based Case-Control Study of Marijuana Use and Head and Neck Squamous Cell Carcinoma. Cancer Prev Res. 2009;2(8):759-768.

17. Shiu-Chen H, Chi-Tang H, Shoei-Yn L, et al. Carnosol inhibits the invasion of B16/F10 mouse melanoma cells by suppressing metalloproteinase-9 through down-regulating nuclear factor-kappa B and c-Jun. Biochem Pharmacol. 2005;69(2):221-232.

18. Li M, Zhang Z, Hill DL, et al. Genistein, a dietary isoflavone, down-regulates the MDM2 oncogene at both transcriptional and posttranslational levels. Cancer Res. 2005;65(18):8200–8.

19. Ruiz D, Egea J, Tomas-Barberan FA, et al. Carotenoids from new apricot (Prunus armeniaca L.) varieties and their relationship with flesh and skin color. J Agric Food Chem. 2005;53:6368-74.

20. Kim GY, Kim JH, Ahn SC, et al. Lycopene suppresses the lipopolysaccharide-induced phenotypic and functional maturation of murine dendritic cells through inhibition of mitogen-activated protein kinases and nuclear factor-kappaB. Immunology. 2004;113(2):203–11.

21. Sunila ES, Kuttan G. Immunomodulatory and antitumor activity of Piper longum Linn. and piperine. J Ethnopharmacol. 2004;90:(2- 3):339-346.

22. Shishodia S, Majumdar S, Banerjee S, et al. Ursolic acid inhibits nuclear factor-kappaB activation induced by carcinogenic agents through suppression of IkappaBalpha kinase and p65 phosphorylation: correlation with downregulation of cyclooxygenase 2, matrix metalloproteinase 9, and cyclin D1. Cancer Res. 2003;63(15):4375–83.

23. Takada Y, Aggarwal BB. Betulinic acid suppresses carcinogen-induced NF-kappa B activation through inhibition of I kappa B alpha kinase and p65 phosphorylation: abrogation of cyclooxygenase-2 and matrix metalloprotease-9. J Immunol. 2003;171(6):3278–86.

24. Cheng YH., Shen TF, Pang VF, et al. Effects of aflatoxin and carotenoids on growth performance and immune response in mule ducklings. Comp Biochem Physiol Toxicol Pharmacol. 1999;128:19– 26.

25. Abdullaev FI. Cancer chemopreventive and tumoricidal properties of saffron (Crocus sativus L.). Exp Biol Med. 2002;227:20-5.

26. Kohno H, Marda M, Honjo S. Prevention of colonic preneoplastic lesions by the beta- cryptoxanthine and hesperidine rich powder prepared from Citrus Unshiu Marc. Juice in male F344 rats. J Toxicol Pathol. 1999;12:209-215.

27. Han SS, Keum YS, Seo HJ, et al. Capsaicin suppresses phorbol ester-induced activation of NF-kappaB/Rel and AP-1 transcription factors in mouse epidermis. Cancer Lett. 2001;164(2):119–26.

28. Yang F, Oz HS, Barve S, et al. The green tea polyphenol (-)-epigallocatechin-3-gallate blocks nuclear factor-kappa B activation by inhibiting I kappa B kinase activity in the intestinal epithelial cell line IEC-6. Mol Pharmacol. 2001;60(3):528–33.

29. Manna SK, Mukhopadhyay A, Aggarwal BB. Resveratrol suppresses TNF-induced activation of nuclear transcription factors NF-kappa B, activator protein-1, and apoptosis: potential role of reactive oxygen intermediates and lipid peroxidation. J Immunol. 2000;164(12):6509–19.

30. Cheng YH, Shen TF, Pang VF, et al. Effects of aflatoxin and carotenoids on growth performance and immune response in mule ducklings. Comp Biochem Physiol Toxicol Pharmacol. 1999;128:19– 26. 152. Berkarda B, Koyuncu H, Soybir GT, et al.

31. Inhibitory effect of hesperidin on tumor initiation and promotion in mouse skin. Res Exp Med. 1998;198:93-99.

32. Laughton MJ, Evans PJ, Moroney MA, et al. Inhibition of mammalian 5-lipoxygenase and cyclooxygenase by flavonoids and phenolic dietary additives. Relationship to antioxidant activity and to iron ionreducing ability. Biochem Pharmacol. 1991;42(9):1673–81.

33. Soliman KF, Mazzio EA. In vitro attenuation of nitric oxide production in C6 astrocyte cell culture by various dietary compounds. Proc Soc Exp Biol Med. 1998;218(4):390–7.

34. Kumar A, Dhawan S, Aggarwal BB. Emodin(3-methyl-1,6,8-trihydroxyanthraquinone) inhibits TNF-induced NFkappaB activation, IkappaB degradation, and expression of cell surface adhesion proteins in human vascular endothelial cells. Oncogene. 1998;17(7):913– 8.

35. Geng Z, Rong Y, Lau BH. S-Allyl cysteine inhibits activation of nuclear factor kappa B in human T cells. Free Radic Biol Med. 1997;23(2):345–50.

36. Sueoka N, Sueoka E, Okabe S, et al. Anti- cancer effects of morphine through inhibition of tumour necrosis factor-a release and mRNA expression. Carcinogenesis. 1996;17(11):2337-2341.

37. Kune GA, Bannerman S, Field B, et al. Diet, smoking, serum beta-carotene and vitamin A in male nonmelanocytic skin cancer patients and controls. Nutr Cancer. 1992;18(3):237.

38. Gogate SS. Cytotoxicity of neem leaf extract: an antitumor. Natl Med J India. 1991;9:297.

39. Cadenas ME, Sandfrison A, Cutler NS, et al. Signal transduction cascades as targets for therapeutic intervention by natural products. Trends Biotechnol. 1998;16:427-433.