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A META ANALYSIS OF CHEMOTHERAPY VERSUS PHYTOTHERAPY OF CANCER – AN OVERVIEW

Karnan P[1], Anbarasu A[2] , Ramalingam K[3] and R.Usha[4]

1. Associate professor, GRT College of Education, Tiruttani, TN-631209.
2. Assistant Professor, Vadaranyam College of Education, Tiruvallur, TN-631203
3. Mediclone Biotech Research centre, Chennai-48,
4. Former HOD Dept of Zoology, Presidency College, Chennai-5.

ABSTRACT

A meta-analysis of chemotherapy and phytotherapy reveals that some indigenous plants or herbs and their bioactive compounds like flavonoids, phenols, polyphenols, Triterpenoids, saponins, β-carotinoids etc could arrest the cancer cells growth, proliferation, cell viability and metastasis and bring apoptotic cell death in cancers. Their short-duration clinical manifestations of cancer cells death with no or little side effects by multifarious mechanisms antagonistic to the cancer survival, reveal their therapeutic efficacy in cancer treatment either as an alternative therapy or as an adjuvant complementary therapy to conventional cancer drugs and prove in their own right as potential formidable agents to fight cancer which is causing worldwide six million cases of incidence every year with attendant mortality also equally in millions. Chemotherapy brings alongside considerable cancer cell destruction, an array of traumatic manifestations in the form of fatigue, sleeplessness, loss of appetite, hair loss, depression, nausea, memory loss etc. Over and above these other harmful effects such as secondary cancers due to recurrence, drug resistance, immunological disorders, cardiac disorders, haematologic problems and harmful effects of on nephric, neurologic, gastro-intestinal system and psychological problems are inadvertent in allopathic chemotherapy. Green synthesized nanoparticles will give the following oncological advantages viz. Prolonged circulation period in the blood stream.Bioavailability to the target cancer tissue.Enhanced permeability and accumulation and retention of herbal phyto molecules.Sustained release of these molecules inside the cancer cells etc. and collective and synergistic effects.These bioactive compounds / substances are more invasive in the cancer tissues than in the normal counterparts and represent a promising strategy and molecular level effectors without aggravating the cells of the tumour / cancer. The above aggravation often occurs in the case of invasive surgery either as a preoperative or post-operative option during the selection of chemotherapy regimens and / or option in clinical settings.

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Corresponding Author *:* Karnan P *:*

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INTRODUCTION

Chemotherapy refers to the cytotoxic drugs that directly kill the cancer cells in their primary site. The neoadjuvant chemotherapy also called preoperative chemotherapy refers to the use of four main classes of drugs given in various combinations, with a view to reducing the metastatic risk and also the surgery. Clinical trials and outcomes have revealed that the cure rate did not show marked improvement when chemotherapy was carried out earlier as compared to using the same after surgery in the case breast cancers. (Ramalingam et al., 2019) The strategy of chemotherapy also differs in treating early breast cancer as opposed to metastatic breast cancer.

The first category of drugs employed for adjuvant treatment is the alkylating types which bind directly to the DNA of the cancer cells and prevent their replication e.g cyclophosphamide.

The second category of drugs which also inhibit DNA duplication is the anthracyclines, derived from fungi. E.g Adriamycin / Doxorubil and Elcone / epirubicin.

The third most commonly used class the taxanes, drugs made from yew tree, to stop cancer cell division by disrupting the microtubules system and their assemblage e.g Paclitaxel and Docetaxel.

The antimetabolites drugs viz., Methotrexate and Fluouracil constituting the fourth category arrest the enzyme necessary for the synthesis of new DNA.

Different chemotherapy drugs act on different phases of the cancer cell cycle specifically viz., S phase specific M phase specific and cycle Non phase specific in order to achieve the goal of stopping the cancer cells growth and proliferation / multiplication. (Ramalingam et al., 2019)

The treatment of chemotherapy throws several queries, with reference to the patient status and the drug of choice. As for cancer, though cancer cells are said to be a homogenous and monoclonal population in nature, in reality it is not so. Even a single cancer cell or cell group is different in their manifestations of cell cycle stages, expression of tumour surface specific receptors,in their protein growth factors. The above kaleidoscopic epigenetic expression of cancer cells / cell groups makes the individual different from others suffering the same. (Ramalingam 2019)

When cancer cells are in stage 1&2 without lymph node involvement chemotherapy seems to be a promising strategy. However when their receptor markers show difference again the choice of treatment becomes diverse. For instance when ER,PR and Her2 hormone receptors are positive, hormonal therapy becomes unwarranted and chemotherapy becomes the only option to address the potential of spreading breast cancer (Wardley 2006; Goss et al 2007). Again the epigenetic expressions of these receptors which are subjected to genetic recombinations, and the permutation combination of their positive expression and negative expression make the cancer cells too diversified. As a result we may expect eight different types of gene cum receptor signatures.

A cancer cell differs from a normal cell in a variety of ways, both in its structural and functional attributes. Structural diversifications (Brachet and Mirsky 1961) include

i) The complex variability of glycocalyx of its cell membrane.
ii) The compositional variation in the constituents of glycocalyx.
iii) Loss of typical morphology and acquisition of pleomorphic structure.
iv) Variation in the surface receptors some of them resembling the normal cells while others being tumours specific and yet others being anew

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v) Structural modifications in such internal cytoplasmic organellae as mitochondria endoplasmic reticulum, nucleus etc.,

The functional modifications include.

i) Primarily the genetic variations brought by the cumulative mutations in specific gene segments which control and / or regulate the cellular metabolism in normal counter parts.

ii) Over expression of certain genes.

iii) Down regulation of certain genes

iv) Synthesis of growth factors of proteinaceious nature

v) Epigenetic expression of certain novel proteins or enzymes which are involved in their non- step cell division and proliferation.

vi) Development of genetically programmed Anti-apoptotic pathways.

vii) Involvement of specific transcription factors which modulate and operate the synthesis of onco proteins and receptor proteins, and several other intricate mechanisms to enable the cancer cells survival, multiplication, growth invasion and metastasis to distant organs, as cites formation etc.,

Target therapy:

The scope of chemotherapy involves the discovery of cytotoxic drugs which reach the primary site of tumours through systemic route to destroy the cancer cells. Varied categories of such cytotoxic drugs are currently in vogue to effect the target oriented mass cell kills at the tumours (primary) site. However the multitude of side effects currently, warrants the discovery of novel and improvised real magic bullet drugs which could destroy the cancer cells without the side effects. Until such new class of chemotherapeutic agents to be developed which could overcome all chemotherapeautic drawbacks, the current usage of treatment continue to be in vogue in clinical settings. In this context, it is of interest to bring to the attention that several phytochemical compounds / molecules and supplementary nutrients were able to bring the cytotoxic death of cancer cells by their manifold and / or their multi hit functions. It also envisages that herbal and natural products are safer as compared to chemodrugs since these products bring their anticancer activity without much side effects as revealed by animal model and cell line studies and also by trials with human subjects.

The various phytochemical constituents include sterols, glycosides saponins, carbohydrates, alkaloids, flavonoids, Tannins, Terpenes, Triterpenoids, polyphenols etc (Ramalingam et al 2019). These plant medicines constitute the modern pharmacopoeia. Alongside these plant based substances, the nutritional suppliments iz., the antioxidant vitamins and minerals could revive and reinstate the immunopotency of the patient and make him immune competent to ward off cancer cells through his cellular armamentaria (CMI) like the NK cells, Mac cells, Tcells, CTLs, Dendritic cells and their revival of activity.

A perusal of literature revealed the multifacious mechanisms of the above mentioned anti cancer functionalities by the herbal products.

The oil components derived from *Anemopsis californica* revealed antiproliferative activity against various cancer cell lines VIZ., Hela cells , human colon cancer cells, breast cancer cells. The water extract and chloroform extract of *Alangium salvifolium* revealed that its alkaloid, Phenolic compounds, flavonoids, terpenoids and glycosides demonstrated anti-cancer activity by altering the

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signal transduction pathways of cancer cells which promote their and by leading to their growth; stimulating apoptosis in cell lines and also enhanced in vitro, the human peripheral blood lymphocyte and T- cell proliferation. Catherine et al (2010); Laizuman et al (2012).
The semi- synthetic triterpenoid isolated from the stem bark of a tropical tree.

Amoornin inhibited the cancer cells growth, the cell viability, induced apoptosis, and cell cycle in G2 + M phase, and also inhibited the telomerase activity in cell lines and in mice models (Rabi et al 2002). The root extract of *Arnebia nobilis* blocked the cell cycle in G1 phase, decreased the bcl2 expression at transcriptional level and also enhanced the pro apoptotic caspace-3 activity. (Bibi et al 2012)

The organic extracts of *Aegle Marmelos* demonstrated the apoptosis of epithelial cancer cells through activation of tumors necrosis factor- α (TNF- α) and also induced the apoptosis at G1 phase of cell cycle (Lampronti et al., 2003 and Jagetia et al., 2005). The heated extract of garlic *Allium sativum* demonstrated the cyto toxicity against cancer cells via a postulated apoptosis mechanism involving activation of mitochondrial dependent caspase cascade. The molecular mechanism of anticancer activity, involved cell signaling pathways such as nuclear transcription factor kappa B (NFVB) and mutagen activated protein kinesis (MAPK) (36-39). The garlic cloves containing steroidal saponins and organic selenium compounds viz. r- glutanyl S-methyl seleno cysteine and another derivative S-allyl mercapto cysteine arrest the cancer cells in their G2- M Phase and induce apoptosis through JNK1and Caspase-3 signaling pathways (Thomson et al., 2003 and Shukla et al 2007).

The chloroform and ethanol extracts of the whole plant *Cuscuta reflxa* down regulated the TNF-α and COX-2, bloked NFKB-binding to its motifs and induced apoptosis in cancer cells. It also up regulated the pro-apoptotic factors and P53 and concurrently down regulated the Anti-apoptotic Bcl-2 factors (Chatterjee et al., 2011 and Suresh et al., 2011). The aqueous extract of Cinnamon bark (*Cinnamomum zeylanicum*) demonstrated its anti-cancer effect through increase in intracellular calcium signaling, loss of mitochondrial membrane potential, down-regulation of MMP-2 expression. In addition, the extract brought the apoptosis by the following changes viz., (Gomez et al., 2010)

Changes in nuclear morphology, DNA fragmentation, rapid loss of mitochondrial trans membrane potential , ROS production, release of mitochondrial cytochrome-c into the cytosol, induction of procaspase-9 and procaspase-3 etc (Koppikar et al., 2010). The polyphenols of present in the extract of *Emblica officinalis* were observed to induce apoptosis in Daltons lymphoma Ascites (DLA) and Ce Ha carcinoma cell lines. It was also found to increase the Fas gene expression a critical gene to enable the apoptotic pathway in cancer cells. Pyrogallol a catechin compound in E.offinalis showed anti-proliferative effect on some human cancer cell lines (Yang et al., 2009; Poojari et al., 2010 and Baliga et al.,2011)

The extract of the stem, leaves and roots of *Liriodendron tulipifera* demostrated their anti proliferative effect by arresting G2/M phases in human Colomic tumour cells (HT-29) (Moon et al., 2007 and Wang et al., 2012). The common *Nelumbo nucifera* and its leaf extract and seed pod and seed extract showed diverse mechanisms of growth inhibition of cancer cell lines of mouse, human and fibroblast cells. (Yanga et al., 2011)

The extract of the leaves of *Euphorbia hylonoma* induced the cancer cell cycle arrestin G1 phase in addition to its antioxidant fraction (Guo et al 2011). Recently Ramalingam etal (2019) have also cited the ameliorative effect of

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the N.nucifara on brain cells and the dementia in rat models. Its constituents include the main polyphenols such as gallic acid, Rutin, Quarcetin and an isoquninoline alkaloid (S) arme pavine. The compounds were found to arrest the cancer cells cell cycle phases G0/G1and G1 and bring the tumour cell death by apoptosis.

Amoung the terpenoid, phenolic and alkaloid derivatives of plant extract, Triterpenoids revealed the highest anti-proliferative activity than others. Studies on cell lines have also revealed that several plant derived compounds like saponins, and other steroids could arrest the cell growth in cancers, cell viability, and bring programmed cell death via mitochondrial dysfunctions.

The above literature on the effects of some medicinal plants revealed that their bioactive compounds could provide the basis for the derivation of novel anti-cancer medicines possessing enhanced cytotoxic action alongside reduction in side effects. In chemotherapy though the quality of overall survival years has been prolonged, The quality of life is more important and vital for a cancer patient than quantity of his survival period and its prolongation with chemotherapeutic side effects. Chemotherapy bring alongside considerable cancer cell destruction, an array of traumatic manifestations in the form of fatigue, sleeplessness, loss of appetite, hair loss, depression, nausea, memory loss etc. Over and above these other harmful effects such as secondary cancers due to recurrence, drug resistance immunological disorders, cardiac disorders haematologic problems and harmful effects of on nephric, neurologic, gastro intestinal system and psychological problems are in advertent in allopathic chemotherapy. (Lange 2016) The herbal constituents have demonstrated their innumerable potentials to cure cancer. These may also be employed through metallic nanoparticles. Such green synthesized nanoparticles will give the following oncological advantages viz.,

- Prolonged circulation period in the blood stream.
- Bioavailability to the target cancer tissue.
- Enhanced permeability and accumulation and retention of herbal phyto molecules.
- Sustained release of these molecules inside the cancer cells etc. and collective and synergistic effects.

These bioactive compounds / substances are more invasive in the cancer tissues than in the normal counterparts and represent a promising strategy and molecular level effectors without aggravating the cells of the tumour / cancer. The above aggravation often occurs in the case of invasive surgery either as a preoperative or post operative option during the selection of chemotherapy regimens and / or option in clinical settings.

Thus the findings of phytochemical effects on cancer cells envisage their impact over the main cancer cell cycle phases which are breached and the division potential of a cancer cell becomes ultimately uncontrolled which are otherwise regulated by the check points i.e by the gene products or sub set of gene products in normal and developing cells making the sequence of cell cycle phases a continuum with time limits and stops their uncontrolled proliferation and also destroy the mutated cells by apoptosis. However these normal regulations are all circumvented or superceded by the cancer cells through their anti apoptotic mechanisms and pathways to enable their barn burning expedition.

Reference:

1. Baliga M S, Dsouza J J and Amia (2011) Emblica officinalis a wonder berry in the treatement and prevention

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of cancer. Eur. J Cancer. Pre. 20(3): 225-239.

2. Bibi Y., Nisa S., Zia M., Waheed A., Ahmed S., Chaudhary M.F., (2012). Adenocacinoma Cell line (MCF-7) and phytochemical analysis Pak.J. Pharm Sci . 25 (1): 183-7.

3. Brachet J, Mirsky A E, (1961). Cells and their components parts. Academic press, NewYork. Xiv+916pp.

4. Catherine N., Seth G.L., Lowery. J., Guerra .L., Slambrouck. S.V Win F.A. in vitro anticancer activity of *Anemopsis California* Oncol. Lett. 2010. 1(14): 711-15.

5. Chan LL, Sherine G, Irfan A, Saujanya GL, Atiya A et al., (2011) Cytotoxicity effects of Amoora rohituka and chittagonga on Breast and Pancreatic cancer cells. Evid Based Complement Alternat Med. Article ID 860605. 8 pages.

6. Chatterjee D, Sahu R K, Jha A K and J. Dwivedi. (2011) Evaluation of Anti tumour Activity of Cuscuta Reflexa Roxb (Cuscutaceael) Against Ehrich Ascites Carcinoma in Swiss Albino Mice. Trop J Pharm Res. 10(4): 447-54.

7. Gomez- Flores R., Martinez H.H., Gurra P.T., Gurra R.T., Licea R.Q., Enriqueta C.M., Padilla C.R., (2010). Anti tumour and immunomodulating potential of *Coriandrum sativum, Piper nigrum* and *Cinnamomum zeylamicum* . J. Natl.Prod. 3:54-63.

8. Goss P.E., Ingle J.N., Martino S (2007). Efficacy of letrozole extended therapy according to estrogen receptors and progesterone receptor status of the primary tumour: National Cancer Institute of Cascade Clinical Trial groups MA:17. J.Clin. Qrcol. 25(15): 2006-2011.

9. Guo Z, Xu Y, Han L, Bo X, Huang C and Ni L. Antioxidant and cytotoxic activity of the acetone extracts of root of Euphoria hylonoma and its ellagic acid derivaties. J. Med. Plant. Res. 5(23):5584-9.

10. Hughes K S, Schnaper L A, Berry D et al (2004) Lumpectomy plus tamoxiten with or without irradiation in women 70 years of age or older with early breast cancer. N. Engl. J. Med. (2004) 351(10):951-977.

11. Jagetia G.C., Venkatesh P., Baliga M.S.,(2005). *Aegle marmelos (L)* correa inhibits the transplanted Ehrlich Ascites Carcinoma in Mice Biol. Pharm. Bull. 28(1): 58-64.

12. Koppikar SJ, Choudhari AS, Suryavashi SA, Kumari S, Chattopadhyay S and R. Kaul-Ghanekar. (2010) Aqueous Cinnamon Extract (ACE-c) from the bark of *Cinnamomum cassia* apoptosis in human cervical cancer cell line (SiHa) through loss of mitochondrial membrance potential. BMC Cancer. 10(1):210.

13. Laizuman N., Ronok Z., AShik M., Saiful I., Anamul H., Abdul F., Mele. J. (2012). Antioxidant and anti tumour activity of Chloroform extract of *Alangium salvifoluium* flowers. Phytopharmacol. 2(1): 123-34.

14. Lampronti ID, Martello N, Bianchi M, Borgatti et al., 2003. In vitro antiproliferative effects on human tumor cell lines of extracts from the Bangladeshi medicinal plant *Aegle marmelos* Correa. Phytomedicine.10(4):300-8.

15. Lange, Maxine A, Papadakis, Mcphee SJ (2016).Current medical diagnosis & Treatment. McGraw Hill education.

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Impact Factor Indexed Journal

Online ISSN: 2277–1077
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International Journal of Research in Education and Communication Technology

A Blind Peer Reviewed and Open Access Journal

Publications Under UGC of India Care and SCOPUS Norms / Volume: 05 Issue No: 17 March-May 2021/64-71 pp

16. Mc Donald ER and EL Dciry W S. (2000) Cell cycle control as a basis for cancer drug denelopment. Int. J. Oncol. 16:871-86.
17. Poojari R Gupta S, Maru G, Khade B, Bhagwat S. (2010). Hepatoprotective effects of Embelin on N-Nitrosodiethylamine and Carbon Tetrachloride induced Preneoplasia and toxicity inRat Liver. Asian Pac J Cancer Prev. 11(4): 1015-20.
18. Rabi T., Karunagaran D., Nair MK., Bhattathiri V.N., (2002). Cytotoxic activity of amooranin and its derivatives. Phytother. Res. 16(51):84-6.
19. Ramalingam K, Indira D, Ambika S and Mathiyalagan A. (2011). Research impetus towards bimolecular medicine development .An Overview. J.Biochem.Tech.
20. Ramalingam K, Indira D, Ambika S and Mathiyalagan A. (2013). Research impetus towards bimolecular medicine development .An Review. Journal of Microbiology and Antimicrobials. 3(7),pp. 160-173.
21. Ramalingam K (2015). Essential fatty acids- A Biomarker and prognostic factor for Breast cancer induction. International Journal of Pune and Applied Biosceience.
22. Ramalingam K,(2015).Gene signatures and gene function profiles in cancer manifestation-A review. International Journal of Recent Scientific Research. 6(3):3254-3258.
23. Ramalingam K (2015). Primary cancer cell metastasis and secondary Niches: Novel cures From Metabolic for Strategic therapy. Journal of Cytology Histology, 6:329.
24. Ramalingam K, Indira Alias Muthu Meena , Karthik R (2016). Cytomorphology of gastro-intestinal cancers of south Indian Cohort- case studies report. Acta Biomedica Scientia. 3(2): 103-109.
25. Ramalingam K Trojan Horse Immuno therapy using Biomolecules- A novel strategy in cancer cure. Proceedings-Current Trends in Bioscience and Biotechnology – Regional Symposium.
26. Ramalingam K, Anbarasu A, Karnan P, Ruvanthika PN (2019) Immunosuppression-A precedent degree or an aftermath of cancer: A research Note. IJRAR: 6(2):729-737.
27. Ramalingam K, Anbarasu A, Karnan P. (2019. Anticancer chemotherapy drugs-Magic bullets or tragic bullets: A search for real Magic Bullet in near sight Oncology clinics & Research, 1(2): 38-43.
28. Ramalingam K, Anbarasu A, Paulraj K, Karnan P, Kanagavalli S(2019). Lepidomic Therapy to Cancer. A Novel Drug designing strategy- A Research Note Journal of Cancer Science & Treatment. 1(2): 42-46.
29. Ramalingam K, Mathiazhagan A, Kaliappan Gopal (2019). Strategic Approach in Metastatic Cancer Therapy: Phytochemical Nutrient Ajuvants- A Mini Review: Journal of clinical Trials & Research 2 (1): 59-62.
30. Shokney and Tsangris (2008). The Johus Hopkins Breast cancer Handbook for Health care professionals. Jones and Bartlett. Publishers Massachsettss.
31. Shukla Y. Kalra N. (2007). Cancer chemoprevention with garlic and its constituents Cancer.Lett. 247(2):167-181.

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International Journal of Research in Education and Communication Technology

A Blind Peer Reviewed and Open Access Journal

Publications Under UGC of India Care and SCOPUS Norms / Volume: 05 Issue No: 17 March-May 2021/64-71 pp

32. Suresh V. Sruthi V. Padmaja B. Asha VV. (2011). In vitro anti-inflammatory and anticancer activities of *Cuscuta reflexa* Roxb. J Ethnopharmacol. 134(3): 872-7.

33. Thamson M., Ali M., (2003). Garlic *(Alium Sativum)* a review of its potential use as an anti cancer agent. Curr. Cancer Drug. Targets. 3(1): 67-81.

34. Wang L, Xu G E, Liu XX, Chang AX, Xu MK, Ghimrey AK, Pico JP, Cho DH. Invitro antioxidant properties and induced G2 / M arrest in HT-29 cells of dichloromethene fraction from *Linodendron tulipfera*. J. Med. Plants. Res: 6(3):424-33.

35. Wardley A.M (2006). Emerging data on optimars adjuvant endocrine therapy breast International Group Trial 1-98 / M.A.17. Clin Breast Cancer 6(Suppl-12) %-45-550.

36. Yang C J, Wang C S, Huang H W, Chia Y C, Wang P H, Wang C F and Huang M S (2009) Pyrogallol induces G2 M arrest in Human lung cancer cells and inhibits Human growth in an animal model. Lung Cancer: 66(2): 162-168.

37. Yanga MY, Changa YC, Chanb KC, Leec YJ, Wanga CJ (2011). Flavonoid-enriched extracts from *Nelumbo nucifera* leaves inhibits proliferation of breast cancer in vitro and in vivo .Euro J Integr Med. 3(3):e153-63.