



"Cancer Perspectives And Recent Advances In Anti-Cancer Drug Research: A Review In The Lens Of Siddha Medicine"

Subathra.T^{1*}, Shanmugapriya.P², Ramamurthy.M³, Gomathi.R⁴, Priyadarshini.S⁴

¹*Research Scholar, Dept. of Nanju Maruthuvam, National Institute of Siddha Affiliated to The Tamil Nadu Dr. M.G.R. Medical University, Chennai. Mail Id: drsuba.bsms@gmail.com

²Associate Professor, Dept. of Nanju Maruthuvam, National Institute of Siddha Affiliated to The Tamil Nadu Dr. M.G.R. Medical University, Chennai.

³Associate Professor, Dept. of Noi Naadal, National Institute of Siddha Affiliated to The Tamil Nadu Dr. M.G.R. Medical University, Chennai.

⁴Medical Officer, National Institute of Siddha Affiliated to The Tamil Nadu Dr. M.G.R. Medical University, Chennai.

***Corresponding Author:** - Subathra.T

*Research Scholar, Dept. of Nanju Maruthuvam, National Institute of Siddha Affiliated to The Tamil Nadu Dr. M.G.R. Medical University, Chennai. Mail Id: drsuba.bsms@gmail.com

Abstract

Introduction: Cancer is a global health challenge, demanding innovative approaches for prevention, diagnosis, and treatment. Despite ongoing research efforts, finding a definitive cure for cancer remains a formidable challenge. In response to these challenges, the concept of integrative oncology has gained prominence, aiming to combine conventional treatments with evidence-based complementary therapies.

Objective: This review explores the integration of Siddha medicine, an ancient South Indian system, with modern oncology to offer holistic cancer care. Siddha perspectives on cancer, its classifications, etiopathogenesis, diagnostic methodologies, and treatment modalities are thoroughly analysed in comparison with modern approach. Recent research on Siddha medicines demonstrating anti-cancer potential is also being reviewed through a systematic literature analysis.

Methodology: Analyses of various Siddha texts is done to know the terminologies and categories of cancer. Siddha's etiopathogenesis, diagnostic methodologies and Siddha treatment modalities are discussed, emphasizing the balance of humours. Recent research on Siddha medicines for cancer treatment is compiled through a systematic literature review.

Discussion: The manuscript decodes Siddha's conceptual framework underlying cancer hallmarks, aligning *Vatham*, *Pitham*, and *Kabam* with the eight hallmark capabilities. Siddha diagnostic methodologies, including pulse reading and urine examination, are compared with modern techniques. Siddha treatment modalities, rooted in herbal formulations, are presented. A comprehensive compilation of Siddha drugs with anti-cancer potential is provided, supported by in-vitro, in-vivo, and clinical studies.

Conclusion: The multifaceted nature of cancer necessitates a comprehensive approach, and Siddha medicine provides unique insights. While Siddha may

<p>CC License CC-BY-NC-SA 4.0</p>	<p>not directly align with modern diagnostics, its holistic principles contribute valuably to cancer discussions. Integrating Siddha into mainstream oncology requires scientific rigor, with further research and clinical trials to validate safety and efficacy. The fusion of Siddha wisdom with modern oncology holds promise for a more holistic and patient-centric cancer care approach.</p> <p>Keywords: <i>Puttru Noi, Cancer, Siddha, Literature Review, Basic Principles</i></p>
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INTRODUCTION:

Cancer encompasses a diverse range of diseases that can impact any bodily organ, marked by unregulated cell proliferation, posing a substantial challenge to global health. Synonymous expressions for cancer include "malignant tumors" and "neoplasms"[1]. Globally, cancer stands as the second most prevalent cause of death, with an estimated 19.3 million new cases and nearly 10.0 million deaths recorded in 2020. The incidence of new cases is on the rise, particularly in low- and middle-income nations. In India, the year 2020 witnessed 1,324,413 new cancer cases, evenly distributed between females (678,383) and males (646,030), underscoring the substantial impact of this disease. [2]

The global impact of cancer is on the rise, placing significant physical, emotional, and financial burdens on individuals, families, communities, and healthcare systems. Due to its complex nature, addressing cancer requires a thorough comprehension of its biology and the development of innovative strategies for prevention, diagnosis, and treatment. Key characteristics of cancer include uncontrolled cell replication, an inability to heed growth signals leading to cell division arrest, sustained angiogenesis, resistance to apoptosis, and the capability to infiltrate surrounding tissues. [3] Healthcare systems in low- and middle-income countries are often ill-equipped to handle the increasing burden of cancer, and a significant portion of cancer patients worldwide lacks timely access to high-quality diagnosis and treatment.

Beside mortality, the impacts of cancer also include morbidity and decreased quality of life. Standard cancer care is expensive and often requires specialized healthcare assets, which may be lacking in resource-limited countries. The financial burden of cancer can also be enormous, as it affects, not only the patients, but as well as their families, communities and society at large. [4] While the conventional cancer treatments like surgery, chemotherapy and radiation, have made substantial advancement in the treatment and management of most cancers [5], many cancers patients yet seek complementary and alternative medicine options to support their conventional cancer therapy [6,7].

Despite ongoing research efforts, finding a definitive cure for cancer remains a formidable challenge. The complexities of cancer, including heterogeneity and adaptability, underscore the need for continuous exploration of novel therapeutic targets. In response to these challenges, the concept of integrative oncology has gained prominence, aiming to combine conventional treatments with evidence-based complementary therapies. Traditional systems of medicine, deeply rooted in cultural and historical contexts, play a vital role in integrative approaches to cancer care [8].

The importance of incorporating complementary and alternative medicine treatments lies in their ability to diminish toxicity, improve the management of cancer-related symptoms, enhance the immune system, and potentially exert a direct anticancer effect [9]. Siddha, an ancient system of medicine originating from South India, provides unique insights into holistic approaches for cancer symptom management. Rooted in ancient knowledge and practices, Siddha medicine emphasizes balancing the body's vital forces to promote overall well-being. As we explore the integration of Siddha with modern oncology, a nuanced and comprehensive approach to cancer management unfolds.

CANCER –A SIDDHA PERSPECTIVE:

In Siddha Medicine, a direct correlation to modern cancer diagnosis may not be established. However, by examining the signs and symptoms, it is possible to correlate it with certain diseases described in Siddha texts that exhibit similar features. Various terms are used in different texts to describe diseases that manifest symptoms similar to those observed in cancer. Siddha literatures such as *Yugi Vaidhya Chindaamani, Noi Villakkam, Dhanvandhiri Vaidhyam - I, Pararaasasekaram, Siddhar Aruvai Maruththuvam, Anubava Vaidhya Deva Rahasyam* and *Dhanvanthri – I* discussed about cancer like diseases with different terminologies. Those terms mentioned in various Siddha texts are listed as *Vippurudhi, Dhurmanankisam, Puttru Noi, Kazhalai, Kiranthi pun, Katti, Raajapilavai, Maamisamakotharam, Sathaiadaippu, and Silandhi*. [10]

CANCER - SIDDHA SYSTEM OF DISEASE CLASSIFICATION:

According to the Siddha System of Medicine, classifications of “*Puttru Noi*” can be categorized based on the types of humours, tissue origin, organs and functional disorders. As mentioned above, various terms were used to indicate cancer and also classified into various types in different texts.

Vippuruthi is classified into 7 types (*Kuvalai vippuruthi, Karppa vippuruthi, Chanthu vippuruthi, Vadha vippuruthi, Pittha vippuruthi, Saethuma vippuruthi* and *Odu vippuruthi*) in “*Yugimunivar Vaithya Chinthamani Perunool 800*” and 6 types (*ChathaiVippuruthi, Odu Vippuruthi, Madu Vippuruthi, Enbu Vippuruthi, Rana Vippuruthi* and *Puttru Vippuruthi*) in “*Pathinen Siddhar Aruli Seitha Aathma Ratshamirtham Ennum Vaidhya Saara Sangiragam*”. [11]

As per “*Siddhar Aruvai Maruthuvam*”, *Pilavai* is sub-classified into 5 types of *Sevi Pilavai* and 10 types of *Kabaala Pilavai*. “*Kiranthi*” is classified into 9 types (*Vali, Azhal, Iyya, Sathai, Kozhuppu, Kuruthi, Enbu, Narambu* and *Pun Kiranthe*). Some of the Siddha literature like “*Agasthiyar Ranavaithyam*”, “*Nagamuni Nayanavithi*”, “*Agasthiyar Nayanavithi*” describes cancers as *Naakku puttru* (Tongue cancer), *Sevi puttru* (Ear Cancer), *Vaai puttru* (Mouth cancer), *Kann puttru* or *Nayana puttru* (Eye Cancer). [11]

According to the T.V. Sambasivampillai dictionary, *Kazhalai* is classified into different types, including *Manarkazhalai, Ninakazhalai, Athimaamisakazhalai, Enbukazhalai, Rathakazhalai, Silanthikazhalai, Naarkazhalai, Narambukazhalai, Murunthukazhalai, Parukazhalai, Vishakazhalai, Ninaneerkazhalai, Rathakudakazhalai, Kaalankazhalai, Oodukazhalai, Pinineerpaikazhalai, Poorvakazhalai, Suthakazhalai, Salikazhalai, Posivukazhalai, Karuvikazhalai, Mulaimugakazhalai, Andakazhalai* and *Vidhaisadhaikazhalai*. [12]

DECODING SIDDHA ETIOPATHOGENESIS OF CANCER:

The term “*Puttru*” originally describes a small hillock thrown by animals made of soil. [13] However, due to its similarity to the growth pattern observed in cancer, the same term is used to denote the disease. This use of metaphorical language is not uncommon, where a term describing a physical structure is borrowed to convey a resemblance or characteristic in another context, such as in the case of cancer growth.

According to the basic principles of Siddha medicine, the onset of any disease is associated with the imbalance or derangement of the three humors, namely *vatham, pitham*, and *kabam*, in the body. Diseases arise when these humors are in a state of disproportion. *Vatham* can be related to anabolic growth phase. *Pitham* is responsible for various metabolic functions and *kabam* can be related to catabolic phase of morbidity. These three humors will be present in each and every cell in particular proportion. In this particular diseased condition, *Pitham* tends to decrease which spontaneously increases the *Kabam*. The excessive increase in *Kabam* leads to increase in *Vatham*. This results in the uncontrolled growth of tumor. [14]

The hallmarks of cancer [15] serve as a fundamental framework for making sense of the intricate nature of neoplastic diseases. This conceptualization encompasses eight biological capabilities, which cancer cells acquire throughout the extended stages of tumor development and malignant progression. The basic principles by which these eight hallmark events happening is explained with the Siddha concepts [16] in Figure - 1.

Figure-1: Conceptual Framework Explaining the Siddha Fundamental Principles Underlying the Eight Hallmarks of Cancer



The Siddha textbook "*Yugi Vaithiya Chinthamani*" suggests that the occurrence of "*Puttru Noi*" is attributed to the shift in people's lifestyles from a natural setting to the modern machine-driven life. Other contributing factors include excessive engagement in sexual activities, adherence to moral norms and human values, unhealthy eating habits, abnormal behavioural patterns of parents, emotions such as anger, unchecked desires, and fear. Additionally, the disease is believed to be influenced by the karmic effects of individuals. [17]

SIDDHA DIAGNOSTIC METHODOLOGIES FOR CANCER:

At the forefront of cancer management is the crucial initial step of early detection, significantly impacting the survival rates of patients. In the current era of scientific progress, cancer diagnosis is rapidly evolving, propelled by continuous advancements in our understanding of the disease and technological breakthroughs. The diagnostic process now encompasses physical examinations to detect abnormalities and a series of laboratory investigations, including the identification of cancer markers. Moreover, diagnostic tools such as Ultrasonography (USG), Magnetic Resonance Imaging (MRI), Computed Tomography (CT) scans, Positron Emission Tomography (PET) scans, along with histo-pathological examination, are employed to pinpoint and confirm the diagnosis, elucidating the various stages of the cancer. [18]

The diagnostic methodology in Siddha medicine relies on an Eight-fold examination encompassing *Naadi* (Pulse reading), *Sparisam* (Palpation), *Na thaervu* (Tongue inspection), *Niram thaervu* (Observation of skin complexion), *Mozhi thaervu* (Analysis of speech), *Vizhi Thaervu* (Examination of eye), *Malam thaervu* (Observation of stool) and *Neer thaervu* (Observation of urine). [16] On the experience of various Siddha physicians and documentation studies, it was evident that the majority of patients with confirmed diagnosis shows *Kabavatham* and *Vathakabam* in *Naadi* observation. It also stands in line with the pathogenesis of cancer, i.e., increased *Kabam* and *Vatham*. In the regard of urine examination, sesame oil is instilled on the surface of urine samples to observe the spreading pattern of oil indicating the predominant *thiridosham*. Rathiga.C., et.al., documented that among 40 patients, *Kabam* and *Vatham* predominant was found in 62.5% and 37.5% respectively. In addition to these methodologies, *Manikadainool* (Wrist circumetric parameter), Astrological parameters like *Maruthuva Jothidam*, *Prasannam*, *Pancha patchi* also practiced in Siddha system for diagnosis of cancer. [19]

SIDDHA TREATMENT MODALITIES FOR CANCER:

In the Siddha system of medicine, drug selection is based on taste potential to balance suppressed or vitiated humours. For the management of cancer, the decreased *Pitham* and increased *Vatham* and *Kabam* need to be balanced through appropriate medicines. To address decreased *Pitham*, bitter (*Kaippu*), sweet (*Inippu*), and astringent (*Thuvarpu*) tastes are employed. Increased *Vatham* is alleviated by sweet (*Inippu*), sour (*Pulippu*), and salty (*Uppu*) tastes. Elevated *Kapham* is mitigated with bitter (*Kaippu*), pungent (*Karppu*), and astringent (*Thuvarpu*) tastes. [14,16]

The ancient Siddhars have recommended various formulations for the management of cancer including single drugs, *Chooranam*, *Parpam*, *Chendhooram*, *Pathangam*, Medicated oils (*Thylam*), syrups (*Manapagu*), decoctions (*Kudineer*), etc. The formulations are derived from the knowledge and experiences passed down through ancient Siddha texts written in Tamil. The Siddha system of medicine, with its roots in Tamil Nadu, emphasizes the use of these herbal and mineral-based formulations to restore balance in the body's humors and promote health.

RECENT RESEARCH ON SIDDHA MEDICINES IN CANCER TREATMENT:

Numerous Siddha medications have been traditionally employed in the clinical treatment of cancer over several decades. Despite their legacy of use, it is imperative to substantiate their efficacy through rigorous scientific experiments to promote the global acceptance of the Siddha system of Medicine. Table-2 presents documented Siddha formulations that have demonstrated anti-cancer potential through in-vitro, in-vivo, and selected clinical case studies. The data presented in this list were gathered from Google Scholar using the search terms 'Siddha' and 'Cancer.' A thorough screening of approximately 300 articles was conducted to ensure relevance, resulting in the compilation below.

Table-2: Comprehensive Compilation of Siddha Drugs with proven Anti-cancer potential from in-vitro, in-vivo and clinical studies

S.No.	Medicine Name	Type of Cancer	Study Design	Reference
1.	<i>Maha Vallathy Leghiyam</i>	Oral Cancer	In-vitro (KB cell line); In-vivo (Wistar rat model)	20, 21

2.	<i>Neeradi Muthu Vallathy Leghiyam</i>	Oral Cancer	In-vitro (KB cell line)	20
3.	<i>Semecarpus Leghiyam / Serankottai Leghiyam</i>	Breast cancer	In-vitro (MCF-7 & MDA-231)	22
4.	<i>Rasagenthi Mezhugu</i>	Cervical cancer; Breast cancer; Colorectal carcinoma	In-vitro (ME-180; SiHa; COLO205; MDA-MB-231; HCT 116)	23, 24
5.	<i>Neeradimuthu Vallathi Mezhugu</i>	Cervical cancer, Skin Cancer	In-vitro (HeLa cells); In-Vivo (Swiss Albino mice model)	25, 26
6.	<i>Bhramasthiram</i>	Oral cancer, Cervical cancer	In-Vitro (KB cells, HeLa cell, SiHa cells)	27
7.	<i>Nandhi Mezhugu</i>	Cervical cancer, Ovarian Cancer	In-Vitro (HeLa cells & PA-1 cells)	28, 29
8.	<i>Narasimha leghiyam</i>	Breast cancer	In vitro (EAC cells)	30
9.	<i>Rasagenthi Lehyam</i>	Prostate cancer	In-vitro (PC-3 cells)	31
10.	<i>Nandhi Mezhugu Rasagandhi Mezhugu Amukkara Chooranam Kukil Parpam Thiripala Chooranam (Gargle) Seeraga Thylam (Oil bath) Kungiliya Vennai (External application)</i>	Buccal cancer	Observational clinical study (Case Report)	32
11.	<i>Kodiveli Chooranam</i>	Colorectal Cancer	In-vitro (HT-29 cells)	33
12.	<i>Panchamuga Chendhuram</i>	Breast Cancer	In-vitro (MCF-7 cells)	34
13.	<i>Veerarasa Padhangam</i>	Breast Cancer	In-vitro (MCF-7 cells)	34
14.	<i>Sathakuppai Chooranam</i>	Cervical Cancer	In-vitro (HeLa)	35
15.	<i>SoothaVennai Parpam</i>	Breast Cancer	Observational clinical study (Case Report)	36
14.	<i>Thayiriya Vendhan Chendhuram</i>	Breast Cancer	In-vitro (MCF-7)	37
15.	<i>Gandhaga Poora Parpam</i>	Cervical Cancer	In-Vitro (HeLa & SiHa cell line)	38
16.	<i>Naaga Chendhuram</i>	Breast cancer	In vitro (MCF-7 & MDA-MB 231 cell lines)	39
17.	<i>Ashta Bairava Chendhuram</i>	Oral Cancer; Osteosarcoma	In-Vitro (KB cells, OSCC & HOS cells)	40
18.	<i>Rasa Parpam</i>	Cervical cancer	In-vitro (HeLa cell line)	41
19.	<i>Kandha Rasa Villai</i>	Cervical cancer	In-vitro (HeLa, SiHa & C33A cell lines)	42
20.	<i>Kaalamega Narayana Chendhooram</i>	Oral Cancer	In-vitro (KB & OSCC cell lines)	43
21.	<i>Rasagandhi Mezhugu, Senkottai Nei, Amukkara Chooranam, Kukil parpam, Nilavembu Kudineer, Nellikaai Lehiyam & Madhulai Manapagu</i>	Tongue Cancer	Observational clinical study (Case Report)	44
22.	<i>Padikara Parpam</i>	Leukemia	In-vitro (THP-1 cells)	45
23.	<i>Thambira Chendhuram</i>	Oral Cancer	In-vitro (KB Cells)	46

24.	<i>Adaikamani Thailam</i>	Breast Cancer	In-vitro (MCF-7 cells)	47
25.	<i>Namachivaya Chendhuram</i>	Cervical Cancer	In-Vitro (HeLa & SiHa cells)	48
26.	Aya Thambira Chendhuram	Breast Cancer	In-Vitro (MCF-7 cells)	49
27.	<i>Karumsurathi Thailam</i>	Breast Cancer	In-Vitro (MCF-7 cells)	50
28.	<i>Chithiramoola Kuligai</i>	Cervical Cancer	In-Vitro (HeLa cells)	51
29.	<i>Vallarai Nei</i>	Cervical Cancer	In-Vitro (HeLa Cells)	52
30.	<i>Rasa Karpoora Kuligai</i>	Cervical cancer	In-Vitro (HeLa cells)	53
31.	<i>Vithu Rasa Mezhu</i>	Cervical cancer	In-Vitro (HeLa cells)	54
32.	<i>Vembu Karpam</i>	Lung cancer, Breast cancer	In-Vitro (A549 & MCF-7 cells)	55
33.	<i>Navamani Chendhuram</i>	Ovarian Cancer	In-Vitro (PA-1 cells)	56
34.	<i>Linga Chendhuram</i>	Cervical Cancer	In-vitro (HeLa cells)	57
35.	<i>Guru Pathangam</i>	Cancers of Lymphatic system	In-Vivo (Swiss Albino Mice model)	58
36.	<i>Pancha Pashana Chendhuram</i>	Cervical cancer	In-vitro (HeLa cells)	59
37.	<i>Semecarpus Ghee / Senkottai Nei</i>	Cervical Cancer	In-Vitro (SiHa Cells)	60
38.	<i>Kabasura Kudineer</i>	Lung cancer	In-Vitro (A549 cells)	61
39.	<i>Kalpaamrutha</i>	Hepatocellular carcinoma	In-Vivo (Male wistar Rat model)	62

In addition to the above list of drugs, *Pooranachandirodayam*, *Poora Mathirai* and *Rathinagara Rasa Mezhu* were also subjected to in-vitro studies for cancer types like colon cancer, cervical cancer, etc.

CONCLUSION:

The multifaceted nature of cancer requires a comprehensive approach to care, and the traditional Siddha system of medicine offers unique insights into holistic cancer management. While Siddha may not align directly with modern diagnostics, its understanding of imbalances and lifestyle factors contributes to cancer discussions. As we navigate the intricate landscape of cancer research, the integration of Siddha medicine into mainstream oncology opens avenues for novel therapeutic strategies. However, it is imperative to approach this integration with scientific rigor, conducting further research, clinical trials, and standardization processes to ensure the safety, efficacy, and reproducibility of Siddha interventions. The fusion of Siddha wisdom with modern oncology may lead to a more holistic and patient-centric approach to cancer prevention, diagnosis, and treatment.

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