



Review Article

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SIDDHA HERBS AND MEDICINES FOR THE TREATMENT OF BREAST CANCER WITH EMPHASIS ON CELL LINE ACTIVITY: A REVIEW

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ABSTRACT

Breast cancer is the most common cancer in women worldwide. It causes major morbidity and mortality. Current treatment options for breast carcinoma include surgery, chemotherapy, radiotherapy and hormone therapy. The main challenge lies in treating the disease with fewer side effects and patient compliance as the above-mentioned therapies cause general as well as local complications. Siddha literature has many herbal, metallic and mineral preparations to treat breast cancer which can be used as an adjunct for treating breast cancer. For this review, the literature on diagnosis and treatment for breast cancer was collected from multiple sources like Siddha classical texts, traditional books, Siddha cyclopaedic medical dictionary. The main objective of this paper is to evaluate, document and discuss the important Siddha herbal, herbo-mineral and external medicines with Botanical name, Tamil name, Pharmacological activity and cell line model used in treatment of breast carcinoma.

Keywords: Breast cancer, Herbs, Medicines, Siddha, Alternative medicine

INTRODUCTION

In 2018, cancer ranked as the second leading cause of death worldwide, resulting in an estimated 9.6 million deaths, or one in six reported deaths. The types of cancer vary between genders, with lung, prostate, colorectal, stomach, and liver cancers being the most common among men. Among women, breast, colorectal, lung, cervical, and thyroid cancers are the prevailing types.¹In India, breast cancer accounts for 13.5% of all cancer cases and 10.6% of all deaths. There is an increasing trend of incidence from the past three decades and in all states. This indicates a need for robust screening and good therapeutic care. There is a vital role for Siddha medicines in the treatment of breast cancer and mitigating the side effects of other medications. This review briefly describes the historical aspects, various Siddha herbal, herbo-mineral formulations in the treatment of breast cancer with emphasis on mechanism of action and cell line activity.

REVIEW OF LITERATURE

Breast carcinoma is mentioned in an ancient Tamil Sangam literature "Silapathikaram" written in 5-6th century. The description mentions about the protagonist Kannagi with a painful breast swelling possibly describing inflammatory carcinoma of breast.²The other names mentioned in Siddha classical text "Siddhar Aruvaimaruthuvam" are Nagirkatti, Marbukatti, Sthanavippruthi and Marbusilanthe.³ While according to textbook by T.V. Sambavasilvappillai, breast cancer is used interchangeably as Arpudham Mulaiputtru- Cancer Breast, Mulaikatti-Mammary abscess, Mulaikattu- A carbuncle or ulcer on the breast, Mulaikiranthe, Marbusilanthe, Mulaisilanthe- Abscess or ulcer of the breast, Mulaithabitham-

Mulaithabam, Mulaivithruthi- Abscess in the breast of women, Nakir putru - breast tumour, Markazhalai- Tumour in the breast as adenoma, fibroma affecting the girls between 20 and 30 years. Sthanavazhali- Mammary sarcoma, Sthanavazharchi- Mammary inflammation or irritation⁴.

Modern Aspect

Worldwide, breast carcinoma is the most prevalent cancer among women and is a significant health concern. Incidence rates vary globally, with higher rates in developed countries. The development of breast carcinoma is multifactorial, involving genetic, hormonal, and environmental factors. Hormonal influences, especially oestrogen, play a crucial role in the pathogenesis. Genetic alteration, such as *BRCA1* and *BRCA2* deletion, are associated with an increased risk of breast cancer. Other risk factors include age, family history, hormonal replacement therapy, and certain lifestyle factors.⁵

Molecular Types: Breast carcinomas can be classified into several molecular subtypes based on the expression of hormone receptors such as Estrogen receptor (ER) and Progesterone receptor (PgR) and HER2/neu status.

1. Luminal A - ER positive, PgR +/- HER2-negative, Ki67 <14%
2. Luminal B - ER positive, PgR +/- HER2- +/-, Ki67 >14%
3. HER2-enriched - ER, PgR - Negative, HER2-positive.
4. Triple-negative - ER, PgR - Negative, HER2-negative.⁶

Prognosis varies based on factors such as tumour size, grade, lymph node involvement, and molecular subtype. Generally, early detection and treatment lead to better outcomes. Luminal A tumours often have a more favourable prognosis compared to

other subtypes. Triple-negative and HER2-positive subtypes may have a more aggressive course, but targeted therapies have improved outcomes in HER2-positive cases. Prognostic markers, such as Ki-67 and gene expression profiles, help predict the likelihood of recurrence and guide treatment decisions. In summary, breast carcinoma is a complex disease with diverse risk factors, molecular subtypes, and prognostic factors. Advances in understanding its pathogenesis and molecular characteristics have contributed to personalized treatment strategies, improving outcomes for many patients. Early detection through screening remains crucial for successful management.⁷

Herbal Siddha Medicines – General Overview

Various herbs, including *Allium sativum* (garlic), *Citrullus colocynthis* (bitter apple), *Crocus sativus* (saffron), *Curcuma longa* (turmeric), *Glycyrrhiza glabra* (liquorice), *Lepidium sativum* (cress), *Nigella sativa* (black seed), *Taxus baccata* (European yew), *Trigonella foenum-graecum* (fenugreek), *Vinca rosea* (periwinkle), and *Zingiber officinale* (ginger), are believed to possess anticancer properties. The compounds found in these herbs include alkaloids, phenols, and monoterpenes.

Some specific indicators, such as vinblastine, vincristine, curcumin, and Taxol, are recognized for their potential anticancer effects. These compounds exhibit various mechanisms of action, such as antioxidant properties, prevention of DNA damage, cell cycle arrest (particularly at the G2/M phase), induction of apoptosis (programmed cell death), and inhibition of angiogenesis in tumour cells.⁸ There is a growing trend of interest in natural alternatives to conventional medical treatments, especially among patients with chronic life-threatening diseases like cancer. Many individuals choose to combine herbal remedies with conventional therapies in the hope of enhancing the effectiveness of conventional medicine.⁹ Even though enormous varieties of medicinal plants available in the nature, but some plants have biochemical constituents to treat Marbaga putru (Breast cancer) and it also proved scientifically by its pharmacological activities and cell line activities such as MCF-7 – Michigan Cancer Foundation-7 and MDA-MB-231 – MD Anderson. This review discusses individual plants with the its pharmacological and cell line activities (**Table 1**), Siddha medicines in its various formulations described in classic literature and publications (**Table 2**).

Table 1: Siddha Medicinal Plants used in Marbaga Putru (Breast Cancer)

| Botanical name | Biochemical constituents | Pharmacological activities | Experimental model | Cell line Activity |
|---------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------|--------------------------|-----------------------------------------------------------------------------------------------------|
| <i>Aegle marmelos</i> (Vilvam) | Aegelenine, Aegeline, marmelosin, skimmianine, marmarin, marmesin, auraptin, xanthotoxin, scopoletin and psoralen, dimethoxycoumarin, tembamide ¹⁰ | Anti-cancer, Anti-microbial, Anti-oxidant and Hepatoprotective activities ¹¹ . | Human cell line | MCF-7, MDA-MB-231 breast cancer cell-line ¹² |
| <i>Allium sativum</i> (Poondu) | Allin, Allicin, Ajoenes, Vinylthiins and flavonoids such as quercetin ¹³ . | Hypocholesterolaemic, Antiplatelet aggregation activity, Anti-cancer ¹⁴ | Human cell line | MCF-7 ¹⁵ |
| <i>Catharanthus roseus</i> (Nithiyakalyani) | Vinblastine, Vincristine, Vinorelbine, Vinflunine, catharanthine and vindoline | Anti-cancer | Human cell line | MCF-7 Breast cancer cells ¹⁶ |
| <i>Centella asiatica</i> (Vallarai) | Sesquiterpenes and monoterpenoid including α -humulene, germacrene-D, and myrcene as the major constituents. Oxygenated sesquiterpenes (e.g. humulene epoxide, caryophyllene oxide, oxygenated monoterpenes ¹⁷ | Cytotoxic, Anti-cancer, Anti-inflammatory activities ^{18,19} . | Mice and human cell line | Breast cancer cell MCF-7 ²⁰ . |
| <i>Citrullus colocynthis</i> (Kumutikai) | Glucosides–isovitexin, isosaponarin, isoorientin, and the two cucurbitacin glucosides 2-glucopyranosyl-cucurbitacin L and glucopyranosyl cucurbitacin ²¹ | Anti-oxidant and Anti-cancer activities ²² . | Human cell line | (MCF-7) Breast cancer cell line ²³ . |
| <i>Coccus nucifera</i> (Thengu) | Vitamin B, nicotinic acid pantothenic acid, biotin, riboflavin, folic acid, lupeol methylether, skimmiiwallin, and isoskimmiiwallin ²⁴ . | Anti-tumour, Anti-inflammatory and Anti-oxidant effects ²⁵ . | Mice and Human cell line | MCF-7 human breast cancer cell & 4T1 Breast cancer line ²⁶ . |
| <i>Curcuma longa</i> (Manjal) | Curcumin ²⁷ | Anti-cancer, activity ²⁸ . | Human cell line | MCF-7 Breast cancer cell line ²⁹ |
| <i>Glycyrrhiza glabra</i> (Athimaduram) | Isoflavones, glabridin and hispaglabridins A and B, glabridin and glabrene ³⁰ . | Anti-oxidant and Anti-proliferative activities ³¹ . | Human cell line | MCF-7 cells (Human Breast cancer) than the other two extracts of <i>G. glabra</i> ³² |
| <i>Mimosa pudica</i> (Thottarsinugi) | Mimosine, nor-epinephrine, d-pinitol (3-mono-methyl ether of inositol), and b-sitosterol ³³ | Anti-cancer activity ³⁴ . | Human cell line | MCF-7 and Human breast cancer cell line ³⁵ |
| <i>Nigella sativa</i> (Karunseeragam) | Thymoquinone (TQ), Dithymoquinone (DTQ), Thymohydroquinone (THQ) and Thymol ³⁶ | Anti-cancer, Analgesic, Anti-microbial, Anti-inflammatory ³⁷ . | Human cell line | MCF-7 breast cancer cell line, MDA-MB-231 triple-negative breast cancer cells ^{38,39,40} . |
| <i>Plumbago zeylanica</i> (Kodiveli) | Plumbagin ⁴¹ | Anti-cancer, Anti-inflammatory and Anti-oxidant activities ⁴² . | Human cell line | MCF-7 ⁴³ |

| | | | | |
|---------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------|--------------------------|----------------------------------------------------------------------------------------------------------------|
| <i>Punica granatum</i> (Maadhulai) | Ellagic acid, gallagic acid, punicalagin, punicalin and anthocyanins such as cyanidin, delphinidin and pelargonidin ⁴⁴ | Anti-oxidant, anti-inflammatory and anti-oncogenic activity ⁴⁵ . | Human cell line | MCF-7 & MDA-MB-231 ^{46,47} |
| <i>Semecarpus anacardium</i> (Serankottai) | Anacardoside, semecarpetin, nallaflavanone, jeediflavanone, semecarpufflavanone, galluflavanone, anacardufflavone, mono-olefin I, diolefin II, bhilawanol-A, bhilawanol-B, amentoflavone tetrahydroamentoflavon esemecarpol, anacardic acid, biflavanone B ⁴⁸ . | Anti-cancer, Anti-inflammatory, Anti-oxidant and Anti-microbial activities ⁴⁹ . | Human inhibitory effect | Semecarpus nut extract for inhibitory effect on human breast cancer cells (T47D) ⁵⁰ |
| <i>Smilax china</i> (Parangipattai) | Rutin, kaempferol, and kaempferitrin ⁵¹ | Anti-cancer, antioxidant and antimicrobial activity ⁵² | Human cell line | MDA-MB-231 human breast cancer cells ⁵³ |
| <i>Tabernaemontana divaricate</i> (Nandhiyavattai) | Phytol, Stigmasterol | Anti-oxidant, Anti-microbial, Anti-cancer and Anti-inflammatory | Human cell line | Human Breast Cancer Cell Line-MCF-7 ⁵⁴ |
| <i>Terminalia chebula</i> (Kadukai) | Galic acid, punicalagin, chebulagic acid, neochebulinic acid, chebulanin, ellagic acid, chebulinic acid, corilagin, casuarinin, 3,4,6-tri-o-glloyl-D-glucose, casuarinin, 3,4,6-tri-o-glloyl-D-glucose, terchebulin ⁵⁵ . | Anti-cancer activity ⁵⁶ | Human cell line and Mice | Human (MCF-7) and mouse (S115) ⁵⁷ |
| <i>Trachyspermum ammi</i> (Omam) | γ -terpinene, ρ -cymene and thymol ⁵⁸ | Anti-inflammatory, antiplatelet-aggregatory, anti-microbial ⁵⁹ | Human cell line | MCF-7 ⁶⁰ |
| <i>Vitex negundo</i> (Notchi) | Limonene, 1,8-cineole, citral, cinnamic aldehyde, eugenol, terpinen-4-o, sabinene and viridiflorol ⁶¹ | Anti-cancer, Anti-microbial, Anti-inflammatory activities ⁶² . | Human cell line | Strong inhibition against the MCF-7 cell lines and weak inhibition against the Vero cell lines ⁶³ . |
| <i>Withania somnifera</i> (Amukkura) | Withalongolide A, Withanolide D and its triacetate derivatives have been found to possess anti-carcinogenic activities ^{64,65} | Anti-cancer, Anti-inflammatory ⁶⁶ . | Human cell line, Mice | MDA-MB-231 human breast cancer cell xenograft ⁶⁷ |
| <i>Zingiber officinale</i> (Inji) | Gingerol, paradol and shogoal ⁶⁸ | Anti-oxidant, anti-inflammatory anti-cancer | Balb/C mice | MDA-MB231 ⁶⁹ |

Cell line: MCF-7 –Michigan Cancer Foundation-7; MDA-MB-231 – MD Anderson⁷⁰**Table 2: Siddha Medicines (Herbs/ Minerals/Metals) to treat Marbaga Putru (Breast Cancer) according to Siddha Classical Literature**

| Herbo-mineral | Route of administration | Dosage | Adjuvant | Indication |
|---------------------------------------------------|--------------------------------|------------------|---------------------------------------------------------------|----------------------------------------------------------|
| Naaga chenduram ⁷¹ | Internal | 4.2g | Chitramoolaverpattai / Honey | Mulai putru (Breast Cancer) |
| Nandhi mezhugu ⁷² | Internal | 500mg | Palm jaggary | Marbaga putru (Breast Cancer) |
| Kandhaga chooranam ⁷³ | Internal | 4.2g | Butter/ghee/honey/Parangipattai Ilagam/Vaadhaam Parupu Ilagam | Maar silanthi (Mammary Abscess) |
| Rasagandhi mezhugu ⁷⁴ | Internal | 800mg | Palm jaggary | Maar silanthi (Mammary Abscess) |
| Putru pathangam ⁷³ | Internal | 30-60 mg | Cow milk | Marbu putrugal (Breast Cancer) |
| Kudori thylam ⁷³ | Internal | 4.1g | Karpogaris chooranam | Kongai putru (Breast Cancer) |
| Rasa parpam ⁷⁷ | Internal | 5.1g | Thalaga parpam | All types of cancer |
| <i>Semecarpus anacardium</i> lehyam ⁷⁵ | Internal | 3g ⁷⁵ | - | Marbaga putru (Breast Cancer) |
| Agasthiyar kuzhambu ⁷⁴ | External application | | Required quantity | Mulai silanthi (Abscess or ulcer of the breast) |
| Kowsigar kuzhambu ⁷⁴ | External in vapour form | | Required quantity | Marbani, marbu silanthi, (Adenoma, Cancer of the breast) |
| Pacchai sorvai ⁷⁸ | External application via cloth | | Required quantity | Marbu pilavai (Cancerous carbuncle of the chest) |

DISCUSSION

Traditional systems of medicine, including Siddha medicine, often incorporate a range of herbal, polyherbal, herbomineral and herbometallic formulations for managing various health conditions, including breast cancer (marbagaputru). These formulations are often based on a combination of plants, minerals, metals and other natural substances. They are believed to have synergistic effects that contribute to their potential therapeutic

benefits. Herbs, minerals, metals and natural ingredients used in these formulations may have anti-cancer properties. Additionally, some formulations might offer pleiotropic effects, meaning they could have multiple beneficial impacts on various systems in the body. There are several herbo-mineral formulations that are traditionally used as potential anti-cancer medications. These formulations often combine herbal ingredients with minerals and metals to create a holistic approach to healing. It is important to note that while these formulations have been used for centuries

and might have potential benefits, their efficacy and safety should be evaluated through scientific research and under the guidance of qualified healthcare professionals.

CONCLUSION

Siddha literature has provided a wealth of natural medication understanding the nuances of holistic approach. These medicines and different formulations have been used to treat Breast Cancer (Marbaga Putru), reducing the complication and mitigating comorbidities like with minimal side effects. The above-mentioned medicines have been studied and proved scientifically in cell studies and pharmacological studies. This review comprehensively illustrates the various breast cancer drugs, formulations available in siddha literature with its emphasis on mechanism of action.

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