

Research Article

SOUTH INDIAN FOODS HIDDEN TREASURES: EXPLORING THE ANTICANCER ACTIVITY OF PONGAL FOOD INGREDIENTS

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Abstract

Pongal, a popular dish in South India, is made from ingredients like rice, Mung beans, black pepper, cumin, ginger, ghee, and curry leaves, which are rich in bioactive compounds with potential anticancer properties. Mung beans contain polyphenols and flavonoids that have antioxidant and anti-inflammatory effects, helping to prevent cellular damage linked to cancer. Black pepper's piperine enhances the effectiveness of other anticancer agents and inhibits tumor growth. Cumin and ginger help detoxify carcinogens and induce cancer cell death, while curry leaves protect against oxidative stress due to their high alkaloid and flavonoid content. This abstract highlights Pongal as more than a staple food, focusing on its ingredients as potential cancer prevention agents. Scientific exploration of these natural components may lead to innovative food-based strategies in cancer prevention and management.

Keywords: Foods, Pongal

INTRODUCTION

Cancer is one of the common lethal diseases which are caused by uncontrollable growth of cells. It is the second leading cause of mortality and every year and the death rates are probably to increase over 11 million by 2030 [1].The International Agency for Research on Cancer (IARC) and the American Cancer Society (ACS) collaborated to produce the report Global Cancer Statistics 2020, which revealed that approximately 17 million individuals worldwide were impacted by cancer in 2020, encompassing 36 different types of cancer across 185 different countries [2]. Numerous factors contribute to the development of cancer, including genetic mutations, infections, inflammatory conditions, poor dietary habits, radiation exposure, stress at work, and/or toxin ingestion [3, 4]. According to Siddha medicine, "food is medicine and medicine is food," emphasizing the healing power of our daily diet. South Indian cuisine, especially dishes like Pongal, is a perfect example of this wisdom. Made from rice, moong dal, pepper, cumin, ghee, and ginger, Pongal is rich in antioxidants, phytonutrients, and anti-inflammatory agents. These ingredients help in detoxifying the body, boosting immunity, balancing hormones, and fighting free radicals. Thus, Pongal is not just a traditional dish, but a therapeutic meal rooted in our ancient healing science.

Key factors of cancers

Breast cancer, ovarian, and cervical cancer.

Breast cancer: Breast cancer is currently one of the most prevalently diagnosed cancers and the 5th cause of cancer-related deaths with an estimated number of 2.3 million new cases worldwide according to the GLOBOCAN 2020 data [5].

Breast cancer develops and occurs as a result of several internal and external factors. Poor lifestyle choices, environmental factors, and social-psychological factors are all linked to its occurrence. It has been demonstrated that 5% to 10% of breast cancers can be attributed to genetic mutations and family history, and 20% to 30% of breast cancers can be attributed to factors that may be modifiable [6].

Ovarian cancer: Ovarian cancer is one of the most common malignant tumors of the reproductive organs and has the highest mortality rate among all gynecological malignancies [7]. At diagnosis, ~70% of patients present with advanced disease and most are resistant to platinum-based chemotherapy, resulting in a low five-year survival rate. Many factors including diet, inflammation, family history, age, and reproductive factors are involved in determining the risk of ovarian cancer [8].

Cervical cancer: Cervical cancer is the third most common cancer in women worldwide. Currently, >85% of cervical cancer deaths occur in low and middle-income countries [9]. Tragically, cervical cancer is the leading cause of cancer deaths in women of the developing world. Human papillomavirus is the main aetiological factor in the process of carcinogenesis [10].

Treatment for cancer

Cancer cells generally have a faster division rate than normal cells, making them more susceptible to chemotherapeutic agents. Generally, these drugs can be classified into five categories according to their biochemical properties: alkylating agents (for example, cisplatin), antimetabolites (5-fluoroacil), antitumor antibiotics (doxorubicin), topoisomerase inhibitors (topotecan), and tubulin-binding drugs (paclitaxel) [11] [12]. Despite the effectiveness of chemotherapeutic drugs, they can

also cause adverse reactions in normal cells, including nausea, vomiting, mucositis, alopecia, neuropathy, alopecia, and myelosuppression [13]. Furthermore, they have been found to be associated with multidrug resistance (MDR), an undesirable phenomenon responsible for more than 90% of the deaths of cancer patients undergoing chemotherapy. The heterogeneous nature of cancer has limited the efficacy of conventional therapies such as radiation and standard chemotherapy in treating and preventing it, as they are likely to kill both normal and cancerous cells in the process, resulting in serious hematological toxicities and damage to the tissues involved [14]. A growing number of patients acquire or develop multiple drug resistance, making chemotherapy a treatment with limited therapeutic benefits. A number of anticancer drugs have also been associated with significant side effects, including cardiotoxicity caused by doxorubicin, ototoxicity caused by cisplatin, and cognitive impairment caused by 5fluorouracil. The adverse effects of chemotherapy on patients, such as kidney damage, gastrointestinal problems, hair loss, and fatigue, compromise adherence to treatment. A negative perception of treatment is also a result of these factors [15].

Nutrition in the prevention of cancer:

The proverb "let food be your medicine," attributed to Hippocrates, the father of medicine, serves as the foundation for the use of nutraceuticals. Nutraceuticals can be regarded as any non-toxic dietary substances with added health advantages in addition to the fundamental nutritional value found in foods. Stephen DeFelice first used the term "nutraceutical" in 1989. It is the combination of two terms: "pharmaceutical" (a medicinal drug) and "nutrient," which refer to a nutritious food item. These are non-specific biological therapies that have the potential to prevent and regulate malignant processes while also enhancing overall well-being. Phytochemicals comprise the majority of the well-known nutraceuticals. Despite the lengthy history of using nutraceuticals for therapeutic purposes, scientific proof of their potential benefits has only recently come to light [16] [17]. Indian and Chinese medicine have been utilising plant and animal-derived items with anticancer capabilities since ancient times. The following plant polyphenols have been found to have proteasome-inhibitory activity: Genistein, luteolin, apigenin, chrysin, quercetin, curcumin, and tannic acid. They are discovered to have a noteworthy impact on a wide range of malignancies by conquering chemoresistance to various chemotherapeutic medications [18] [19] [20]. Despite the remarkable chemo preventive and chemo sensitizing effects of all the aforementioned nutraceuticals, their low bioavailability and short half-lives within the body pose significant challenges to their clinical application. Their failure in a therapeutic setting is also largely due to low serum levels, poor tissue absorption and distribution, a short half-life, and quick metabolism and elimination. In order to improve the therapeutic efficacy, much research is done to increase the bioavailability of these substances by integrating chemical changes, such as nanoencapsulation, glucuronidation, polymerization, etc. By lowering the drug's ideal dosage and reducing the expense and adverse effects of chemotherapy, the appropriate use of nontoxic nutraceuticals can improve the effectiveness of chemotherapeutic medications [21].

Need for natural alternatives of chemotherapeutic drugs:

Natural anticancer substances have the ability to destroy malignant or altered cells without endangering healthy cells.

Because of their low toxicity and few side effects, natural substances with anticancer benefits are being used more often in adjuvant therapy and cancer treatment [22]. A healthy diet is crucial for preserving one's health, and 5–10% of cancer cases are thought to be caused by poor eating habits. Natural products have been observed to influence multiple oncogenic signaling pathways simultaneously by modulating the activity or expression of their molecular targets. Various natural products affect multiple pathways, including apoptotic cell death, cell proliferation, migration/invasion, angiogenesis, and metastasis. Natural products are capable of generating intracellular signals that trigger events that lead to the death of cancer cells. Natural substances can have advantageous effects because they typically have fewer side effects than pharmaceuticals [23].

Research into the anticancer properties of food is essential for several reasons

Influence of diet on cancer risk

Diet plays a significant role in the development and progression of cancer. Certain foods contain bioactive compounds that may help reduce the risk of cancer or inhibit tumor growth. For example, cruciferous vegetables like broccoli contain sulforaphane, which has shown promise in reducing the size and number of cancer cells in laboratory studies. Similarly, foods rich in antioxidants, such as berries and green tea, may help combat oxidative stress, a contributor to cancer development. Natural food ingredients commonly consumed in the Asian diet, which carries relatively low toxicity have been proposed as one of the finest chemopreventive strategies to combat cancer [24].

Functional foods and their benefits

Functional foods are those that provide health benefits beyond basic nutrition. They may help maintain health and reduce disease risk, including cancer. Compounds like lycopene from tomatoes and allicin from garlic have been linked to lower cancer risks through mechanisms that involve apoptosis modulation and reduction of oxidative damage. However, more research is needed to understand their full potential in human health [25].

Need for comprehensive research

Despite promising findings, much of the existing research relies on animal and test-tube studies. There is a critical need for human clinical trials to validate these effects and determine effective dietary strategies for cancer prevention. Current evidence suggests that a varied diet rich in whole foods can lower cancer risk, but specific recommendations require further investigation [26].

Holistic approach to cancer prevention

Understanding the role of diet in cancer prevention is part of a broader strategy that includes lifestyle factors such as physical activity and weight management. A balanced diet can help maintain a healthy weight, which is crucial since obesity is a known risk factor for several types of cancer. Thus, integrating anticancer research into dietary guidelines can enhance public health strategies aimed at reducing cancer incidence. Cancer chemoprevention has been defined as the use of pharmacologic or natural agents to reverse, suppress, delay or prevent the incident and progression of carcinogenesis [27]. Herbs have been identified as an important source of novel bioactive compounds for medicine development including cancer chemotherapeutic drugs. Lower incident of breast and colon cancer in Asia especially India has been correlated with the diet and natural food ingredients while increasing of breast cancer incident has been correlated with the change of life style including consumption of Western high calorie-dense diet [16]. Human epidemiological studies, including both cohort and case-control studies of all cancer sites, supported by experimental observations from animal studies, suggest that cancer risk may be modified by changes in dietary habits or by consumption of naturally occurring antimutagens and anticarcinogens with food, including flavouring agents [27]. The major food items of India include rice and wheat, different dairy products like milk, cream and yogurt and plenty of fruits and vegetables. Besides these, there are several kinds of herbs and spices as ingredients of food that add flavouring and taste to the pyramid of Indian food cuisine. Combination chemoprevention, whereby one achieves significant synergism of two or more agents to obtain a desired preventive effect, while minimizing the toxic side effects of the individual components, represents an important challenge in this field. It is likely that the future practical development of chemopreventive regimens will rely on the use of this principle [19]. In this review, we describe Pongal, a nutritive breakfast of South Indians, on its chemopreventive effects in female cancers. We further analyse each component of Pongal and elaborate on the anticancer properties of those components.

Cumins

Cuminum cyminum, commonly known as cumin, has garnered attention for its potential anticancer properties. Various studies have explored its effects against different cancer cell lines and in animal models, highlighting its cytotoxic activity and chemopreventive potential. It is an important spice in Indian cooking. In a rodent study of cervical cancer, adding cumin to the diet has significant reduction of cancer incidence by 27.27% on a diet of 5% cumin seeds and incidence reduced even more further to 12.5% on a diet of 7.5% cumin seeds. The study further adds that cumins strengethened the antioxidant system by the elevation of superoxide dismutase and catalase whereas the production of lipid peroxides to be reduced [28]. Another study revealed that cumin powder and ethanolic extracts significantly reduced the tumor incidence and tumor volme in breast cancer induced rats. In addition, cumin powder diet altered the expression levels of CYP1A1, Era and CYPB1 [29]. Silver nanoparticles of the cumin extract were synthesized, and the results show lethal effects of AgNPs on MCF-7 breast cancer cells [30]. Mesoporous silica nanoparticle of cuminaldehyde, a compound found in cumins have been synthesized and this drug-nanoconjugate had induced apoptosis and cell cycle arrest in MCF-7 cells. In vivo studies have further analysed that cuminaldehyde mediated effective tumor growth reduction without any systemic toxicity [31].

Curry leaves

Murraya koenigii leaves have a slightly pungent, bitter and feebly acidulous taste and these characteristics are retained even after drying. Fresh and dried curry leaves are extensively used in South Indian culinary practices for seasoning and flavouring dishes. M. koenigii is more popular due to its large spectrum of medicinal properties. The major chemical constituents of the plant reported are carbazole alkaloids, coumarins and flavonoids. Methanolic extract of M. koenigii leaves possess anti-inflammatory and immunomodulatory activity. Mahanine, a carbazole alkaloid purified from M. koenigii leaves has apoptotic effects in human leukemia cells [32]. A study investigated the hydro-methanolic extracts of curry leaves in breast cancer cell lines and showed a significant cell cycle arrest and induction of apoptosis. Proteosome inhibition is an attractive approach in anticancer studies and M. koenigii extracts were known to induce proteosome and angiogenesis inhibition along with induction of apoptosis in a xenograft tumor model. The leaf extract also contains potent flavonoids such as apigenin, quercetin, rutin and kaempferol and these compounds are well studied for their anticancer efficacy [33]. Another study on 4T1 breast cancer cells reported that MK could reduce tumor size and prevent lung metastasis. In addition, MK could also attenuate inflammatory cytokines and inhibit immunostimulatory effect [34]. A study on the effect of MK extracts on cervical cancer also demonstrated potent cytotoxic activity of HeLa cancer cells [35]. A natural dietary compound of M. koenigii called Koenimbin, has been studied for its cancer preventive properties and a study has reported that koenimbine induced apoptosis in MCF-7 cells and a G0 cell cycle arrest [36].

Ghee

Cow ghee, prepared traditionally, is regarded beneficial in therapy and for health promotion. Ghee contains butyrate, a short-chain fatty acid known for its anti-inflammatory effects. Research indicates that butyrate can reduce inflammation in various tissues. DMBA induced breast cancer when fed with diet containing cow ghee, it was found that ghee could increase pro-apoptotic genes and reduce anti-apoptotic proteins which demonstrates the protective effect of ghee in mammary carcinogenesis [37].

Mung bean

Mung beans have been studied in Indian medicine for its therapeutic effect against a number of diseases. Mung bean extracts have shown anti-inflammatory and anti-cancer effects in MCF-7 breast cancer cells. In addition, aqueous extracts of mung beans have been studied as a radio-sensitizer for breast and ovarian cancer cells [38] [39].

PIPER NIGRUM (Pepper)

Cervical cancer:

Authors demonstrated that in paclitaxel-resistant cervical cancer cells, piperine enhanced cell apoptosis by reducing the expression of Mcl-1 and phospho Akt. In addition, the study also reports that six alkaloids derived from Piper nigrum also downregulated the expression of Mcl-1 and sensitized the cells to paclitaxel [40]. Another study reveals that piperine modulates tumor progression via attenuating the expression of Cox-2 in cervical cancer [41]. Yet another study on cervical cancer reported that piperine enhances mitomycin C treatment via altering dose dependent cell proliferation and decreasing phospho-STAT3 which was replicated in mice xenograft models [42]. Piperine has also been known to induce apoptosis and attenuates the growth of HeLa cells with an increase in

ROS generation. Growth inhibition of piperine was found to be associated with G2/M phase arrest and cell death. Piperine can also inhibit cervical cancer progression via regulating Th17 cell activation by modulating the NLRP3/IL-1 β axis.

Breast cancer:

Dietarly effect of piperine was studied by oral administration of the compound in rodents and was found that piperine arrested breast tumor growth. Ethanolic extracts of Piper nigrum suppressed Rac1 and RhoA expression in breast cancer and the extracts stimulated growth inhibition via G1 arrest, and attenuated cell migration through downregulating MMP2, MMP9, VEGFA and ICAMP1 gene expression. Piperine has been studied for its growth inhibitory effect in breast cancer, including triple negative breast cancer (TNBC). Piperine also inhibited Akt activation in breast cancer cells. It also acts as a radiosensitizer and caused mitochondrial apoptosis of TNBC cells [43]. Intratumoral administration of piperine has been associated with growth inhibition of TNBC xenografts [44]. Piperine has been studied for its potentiation to overcome multi-drug resistance in MCF-7 cells by inhibiting the transcription of ABC transporter genes [45]. Another study shows that piperine promoted anticancer effects by inhibiting ERK1/2, p38 MAPK and Akt signaling. Studies have also elaborated that piperine reduced mammosphere formation and inhibited breast stem cell renewal by arresting Wnt signaling. Piperine has also altered human glyoxalase-1 in MCF-7 breast cancer cells [46].

Several studies have illustrated the combinatorial benefits of piperine. A study employed synergistic combination of cisplatin with piperine induced heightened apoptosis. Piperine has beed noted to work in combination with other compounds as well in potentiating anticancer effect. In a study with hesperidin, piperine and bee venom, the combination of all three drugs had arrested G2/M phase of cell cycle in MCF7 and T47 D cells [47]. Another study utilised the synergistic combination of curcumin along with piperine loaded nanoparticles had significant cytotoxic effect on MCF-7 cells [48]. In addition, piperine along with Pentagamavunon-1 induced mitotic catastrophe and increased the number of senescent cells [49]. A recent study reported that piperine enhanced radiotherapy through modulation of ER-beta and ER-alpha and has studied to regulate NHEJ and DDR pathways [50]. Another combination of piperine with sorafenib cause a dose dependent cell death of MDA-MB-321 cells. Tamoxifen had also been studied in combination with piperine and has been reported to reduce the expression of Pglycoprotein in MCF-7 cells [44]. Piperine in combination with diclofenac and D-limonene has shown to increase ROS and induced cell cycle arrest and apoptosis [51]. Another recent study reports that combined effect of curcumin and piperine along with sorafenib enhanced the suppression of MCF-7 cell survival and this combination resulted in the decrease of vimentin, Notch, Smad4, Wnt10b and Snail1 genes [52]. Nanoparticle studies have also shown that piperine loaded PEG-PLGA with paclitaxel showed a significant reduction in the doses that were required for MCF-7 cells [53]. Piperine loaded nanoparticles have been found to arrest TNBC cell growth and induced apoptosis. Piperine loaded electrospun nanofibers have also been developed and studied in 4T1 tumor bearing mice [54]. Another recent study reported that piperine loaded nanoparticles exhibited exceptional cytotoxic effects that the naïve drug. A recent study of developing piperineloaded nanoemulsion revealed sustained release of piperine which can preserve the cytotoxic activity of piperine [55].

Ovarian cancer:

Piperine has shown to sensitize ovarian cancer cells to PAC and TOP and observed an increase in PTPRK expression [56]. Authors also added that piperine could control cancer cell migration. JNK/p38 MAPK pathway has been altered in ovarian cancer and supplementing piperine has decreased phosphorylation of the key proteins in p38 pathway and induced apoptosis on A2780 cells. A study on SKOV-3 cells established the synergistic effect of piperine and paclitaxel to induce apoptotic cell death and a G1 cell cycle arrest [57].

Ginger

Zingiber officinale (ginger), is an ancient herb used to treat a number of ailments and it has enormous antibacterial, antifungal and antioxidant properties. Ginger has been traditionally used in Indian medicine in the treatment of several cancers due to its anti-inflammatory properties. Potent phenolic compounds present in ginger includes gingerol, paradol and shogaol, and these have also been studied for their anticancer potential.

Endometrial cancer:

Authors have reported terpenoids steam distilled extract of ginger as potent inhibitor of tumor proliferation in endometrial cancer cells.

Cervical cancer:

In a study by Rastogi et al., the treatment of 50 µM 6-gingerol dramatically suppressed the development and proliferation of cervical cancer cells, both in vitro on Hela cells and in vivo on mice. These results imply that the apoptosis caused by 6gingerol in these cells is of the p53-dependent apoptosis type. 6-gingerol limits the action of proteosomes in cervical cancer cells by increasing the formation of reactive oxygen species and causing oxidative stress, according to Rastogi's study. The study's findings also demonstrate that 6-gingerol plays a key role in HPV-induced cervical cancer cells by reactivating p53 and apoptosis through proteasomal inhibition, whereas the cells' support mechanism is the promotion of ROS generation. The study also discovered that when 6-gingerol and cisplatin were administered together, as opposed to separately, the Ki67 cell proliferation marker in cervical cancer cells was considerably decreased in vivo. Additionally, apoptotic TUNEL production is more likely to occur in these cells. Thus, it may be concluded that the anti-cell proliferation action of cisplatin is supported when ginger is combined with it because it increases oxidative stress, DNA damage, and cell death in cervical cancer cells. Following treatment with 10-gingerol, morphological analysis of cervical cancer cells reveals that the combination decreases the number of cells, causes the cells to change from their normal state, and causes the cells to lose their connections with other cells. Additionally, apoptotic structures are seen, and many vacuoles are seen in the cytoplasm of these cells following 10-gingerol administration. All of these results demonstrate that by altering the morphology and structure of cervical cancer cells, this combination eradicates them.

Ingredient	Cancer Type	Key Mechanism	Affected Pathway
Cumin	Cervical, Breast	Induces apoptosis, reduces tumor incidence	SOD, Catalase, CYP1A1, ERα
Curry Leaves	Breast, Cervical	Cell cycle arrest, apoptosis, proteasome inhibition	Wnt, Angiogenesis Inhibition
Ghee	Breast	Upregulates pro-apoptotic genes, reduces COX-2	PPAR-γ, COX-2, Apoptosis
Mung Bean	Breast, Ovarian	Anti-inflammatory, radiosensitizer	ROS, Inflammation Pathways
Piperine	Cervical, Breast, Ovarian	Enhances chemo-sensitivity, apoptosis, inhibits migration	STAT3, MAPK, Akt, NLRP3/IL-1β
Gingerol	Cervical, Breast	Induces p53-dependent apoptosis, proteasome inhibition	ROS, Caspase Cascade, DR3/DR5

Table 1. Displays the key mechanisms mediated by the phytochemicals of Pongal

The expression levels of apoptotic proteins (DR3 and DR5) are markedly elevated by gingerol. Apoptotic markers like caspases 3, 8, and 9 are activated and cause the caspases to cascade when the expression of these proteins rises. 10gingerol can be useful in the treatment of cervical cancer because it causes apoptosis in cervical cells by initiating these cascades. 10-gingrol lowers the amount of phosphorylation of the mTOR pathway and inactivates it via increasing AMPK activation. Therefore, 10-gingerol causes cervical cancer cells to die by preventing cell division. According to reports, ginger extract greatly reduces the activation of NF- κ B in the CaOV3 and SKOV3 ovarian cancer cell lines. Additionally, 6-shogaol has been shown by Ling et al. to decrease NF- κ B transcriptional activity in MDA-MB-231 breast cancer cells.

Limitations

Amidst all the benefactory role of Pongal, the usage of Pongal is limited by the high calorie content and the hyperglycemic effect of the food. This could be overcome by addition of millets or foods that contain complex carbohydrates. Pongal also lacks fiber and this also can be compensated by consuming along with sambar (Indian broth) filled with vegetables.

Conclusion

This present review provides a clearer understanding how an Indian cuisine can a potential chemo preventive strategy against female cancers. This study also elaborates the effect of phytoconstituents present in each component of Pongal, and it illustrates the anticancer research carried out on each component so far. All these components when put as a complete meal, can be an effective strategy to protect against all these cancers. These components could act synergistically and have the ability to regulate the dysregulated signals of the cancer signaling cascades. Thus, we suggest that these kinds of nutritional and chemopreventive foods can be studied further and bioactive compounds derived from these phytochemicals could be developed as novel anticancer agents.

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