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Research Article

A Comprehensive Review of Tamil Culinary Delight 'Rasam' As A Functional Food Against On Uterine Fibroids And Tumors

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ABSTRACT

Background: Uterine fibroids are benign tumors which affect the women in their reproductive age. Nowadays there are so many medicines and remedies available to reduce the size of the fibroids and symptoms. However, these drugs are expensive and associated with significant adverse effects. In this contemporary era, traditional practices from the Siddha system and Tamilian dietary habits have generated a global attention for their potential preventive and therapeutic efficacy against uterine fibroids and associated lifestyle disorders.

Objective: This paper speaks about the culinary ingredients which are used to prepare '*Rasam'* such as*Seeragam (cumin* Seeds*), Milagu (pepper), Poondu (garlic), Perungayam (asafoetida),Manjal(turmeric)* and *Thakali(tomato*) have an effect against uterine fibroid and anti-tumour activity.

Materials & Methods:A systematic search was performed on Siddha drugs with anti-uterine fibroid activity and anti-tumour activity using search engines including Pub-med and Google Scholar.

Results: This culinary preparation is taken as a preventive and healthy diet promoting method that maintains the homeostasis of Uterus in women of all age groups.

Conclusion: This review is based on the literature evidence, of six culinary ingredients, which are also used in Siddha System of Medicine. It provides useful information regarding the mechanism of the Siddha drugs in exerting anti-uterine fibroid activity and anti-tumour activity suggesting their potential use as a beneficial dietary choice for uterine fibroids.

Key words:*Rasam*, Uterine fibroid, anti-tumour activity, Siddha Medicine, culinary preparation.

Introduction:

Uterine fibroids (UF) are generally known as leiomyoma are benign tumours in the womb which affect the women nowadays in their reproductive age. It proliferates from the myometrial smooth muscle cells into discrete masses[1]. The common signs and symptoms of uterine fibroids include heavy menstrual bleeding, menstrual periods lasting more than a week, bleeding between periods, 'fullness' in the lower abdomen, with or without rectal or urinary problems due to compression, infertility, backache or lower abdominal pain, recurrent miscarriages and other associated complication. Depending on the location, size and number of the fibroids the women have mild to severe symptoms. The exact cause of uterine fibroids are still unclear; however, genetics, cytokines, growth factors, hormones such as estrogens and progesterone and/or their respective receptors, environmental and epigenetics, and the excessive synthesis of extracellular matrix, have

been associated with the pathogenesis of uterine fibroids[2] , and also microbiota were also associated with the development of Uterine fibroids[3].

UF needs hysterectomy for the definitive treatment, because the ongoing treatment for UF, only gives temporary or partial relief, but also produces serious side effects on the women. For this reason, they are moving to an alternative option for the remedy on UF.

In this modern era, abundant research was conducted in medicinal plants and its extracts for treating UF. Hence, we have focused a detailed literature search to provide a general overview of the medicinal plants that are used to prepare culinary preparation '*Rasam'* which is daily food practice among the Tamil peoples. The ingredients of *Rasam such as Seeragam (cumin* Seeds*), Milagu (pepper), Poondu (garlic), Perungayam (asa*foetida), *Manjal*(turmeric) and *Thakali*(tomato) the ingredients have the anti tumour activity and anti-uterine fibroid activity with their mechanism of action.

There are so many medicines and pharmacological products obtainable to reduce the fibroid size and mitigate the symptoms of the UF. However, these drugs are expensive and associated with significant adverse effects. In this contemporary life, our Siddha system and *Tamilian* dietary practices are emphasized to get global attention for their preventive and potential therapeutic efficacy of uterine fibroids and lifestyle disorders.

Methods:

For this review, well illustrious and globally accepted scientific databases, namely, PubMed, Google Scholar and ScienceDirect were searched systematically to gain relevant references, using the term 'uterine fibroid', 'anti-tumour activity', 'Siddha', 'medicinal plant', alone or paired with UF.

Purview of Tamil culinary practices:

Hysterectomy being the only definitive solution for UF. Hysterectomy is the surgical removal of the uterus and hence is not ideal for fertile women who intend to retain their uterus. In such a condition, myomectomy, UAE (Uterine artery embolization), or FUS (FocussedUltrasound) will be an alternative option for women who are not willing to do Hysterectomy. However, limitations of these surgical methods are based on their complications and cost.

In an economically booming country like India, the cost of surgical and pharmaceuticals is unaffordable for all middle class people. As a proper lifestyles and diets are already being practiced by *Tamilian* ancestors. They first found out different diets for survival and they gradually improved them. The traditional food habits of Tamilian are primarily a component of its culture. It has strongly suggested the role of diet in both preventive and therapeutic medicines. The therapeutic effect of food is a confirmed belief for many generations in Tamilnadu. Hence, people are searching related to such medical methods and traditional food styles. Siddha system of medicine is one such medical method. The Tamilian food culture and siddha system of medicine are interlinked with each other. So consumption of such traditional food which contains herbs is already practiced in siddha system of medicine. They provide excellent health promotion and prevention from diseases. In Tamilnadu most of the people take the traditional foods that possess bio-active components like spices and herbs. At present recommendations are warranted to support them. It is estimated that an adult in India consumes 80-200mg/day of curcumin, the bioactive component of turmeric, and 50g of garlic in a week. Based on the parameters this paper tries to determine the siddha culinary herbs which make '*Rasam*' act as a food supplement against Uterine Fibroids[4].

Table 1: Phytochemical and Pharmacological action of Rasam ingredients.

Culinary herbs	Tamil name/ Botanical name	Phytochemical:	Pharmacological action	Ref:
Cumin Seeds	*Seeragam/* Cuminum cyminum	alkaloid , coumarin, anthraquinone, flavonoid, glycoside, protein, resin, saponin, tannin and steroid.[5]	antimicrobial, insecticidal, anti-inflammatory, analgesic, antioxidant, anticancer, antidiabetic, antiplatelet aggregation, hypotensive, bronchodilatory, immunological, contraceptive, anti-amyloidogenic, anti-osteoporotic, aldose reductase , alpha-glucosidase and tyrosinase inhibitory effects, protective and central nervous effects.	5
Pepper	*Milagu* / Piper Nigrum	carbohydrates, proteins, calcium, magnesium, potassium, iron, vitamin C, tannins, flavonoids and carotenoids[6].	antihypertensive, antiplatelet, antioxidant, antitumor, anti-asthmatics, analgesic, anti-inflammatory, anti-diarrheal, antispasmodic, antidepressants, immunomodulatory, anticonvulsant, anti-thyroids, antibacterial, antifungal, hepato-protective, insecticidal and larvicidal activity .	6,7
Garlic	*Poondu/* Allium sativaum	alliin, allicin, ajoenes, vinyldithiins, and flavonoids such as quercetin[8]	antibacterial, antiviral, antifungal, antiprotozoal, antioxidant, anti-inflammatory, and anticancer	8
*Asa*foetida	*Perungayam* /Ferulaasafoetida	carbohydrates, protein, fat, minerals and fiber. The resin fraction contains ferulic acid and its esters, coumarins, sesquiterpene coumarins and other terpenoids. The gum includes glucose, galactose, 1-arabinose, rhamnose, glucuronic acid, polysaccharides and glycoproteins, and the	relaxant, neuroprotective, memory enhancing, digestive enzyme, antioxidant, antispasmodic, hypotensive, hepatoprotective, antimicrobial, anticarcinogenic, anticancer, anti cytotoxicity, antiobesity, anthelmintic and antagonistic effect.	9

		volatile fraction contains sulfur-containing compounds, monoterpenes and other volatile terpenoids[9].		
Turmeric	*Manjal* / **Curcuma longa**	Curcumin, demethoxy curcumin and bis-demetho-hydroxycurcumin[10]	anti-oxidant, anti-inflammatory, anti-carcinogenic, anti-mutagenic, anti-fungal, anti-viral and anti-cancer properties	10
Tomato	*Thakali*/ Solanum lycopersicum	minerals, vitamins, proteins, essential amino acids (Leucine, Threonine, Valine, Histidine, Lysine, Arginine), monounsaturated fatty acids (Linoleic and Linolenic Acids), Carotenoids (Lycopene and β-Carotenoids) Phytosterols (β-Sitosterol, Campesterol and Stigmasterol) and phenolic compounds (Quercetin, Kaempferol, Naringenin, Caffeic Acid and Lutein) annulene Caffeic acid, Catechin, Chlorogenic acid, Chrysin, Cinnamic acid, Epicatechin, Ferulic acid, Luteolin, Lycopene, P-coumaric acid, Phloretic acid, Resveratrol, Rutin, Sinapic acid, Vanillic acid.	anti-inflammatory, anticancer, and anti hyper lipidemic activity.	11,12

Table:2 - Anti-UF mechanism of *Rasam* ingredients.

This shows the summarized information regarding the mechanism of the ingredients of *Rasam* and in exerting anti-uterine fibroid activity.

Culinary herbs	**Tamil name/ Botanical name**	**Parts used**	**Pharmacological action in Siddha aspect** **	**Possible anti-UF/ antitumor mechanism**	**Ref:**
Cumin Seeds	*Seeragam*/ Cuminum cyminum	Seeds	Carminative, stimulant,Stomachic	↑Antioxidant activity ↑Caspase 3 ↑Caspase 9 ↑PARP cleavage ↑Bax, Bid, Bad, Apaf-1 ↑cytochrome c	18
Pepper	*Milagu* / Piper Nigrum	Dry fruit	Stimulant, rubefacient, Carminative, errhinesialogogue, antiperiodic	↑Caspase 3 ↑Caspase 9 ↓PCNA ↓BCL-2 ↓NFjB ↓AP-1 ↓ERK1 and ERK2	19, 21
Garlic	*Poondu*/ Allium sativaum	Bulb	stimulant, rubefacient, errhine, diuretic, antispasmodic,	↓ PCNA ↑ Caspase 3 ↓bFGF mediated angiogenesis ↓NF_kB ↓ERK1 and ERK2 ↓ECM ↓BCL-2 ↓CDK 1 ↑P53	26
*Asa*foetida	*Perungayam* /Ferulaasafoetida	oleo-gum resin	Antispasmodic, stimulant, rubefacient, emmenagogue, errhine, anthelmintic, expectorant, laxative, carminative, aphrodisiac.	↓ cyclin d1/E ↑P53 ↑TNF-α, ↑P21, ↑Cas3 genes	39, 36
Turmeric	Tamil name/ Botanical name	Rhizome	Tonic, deobstruent, carminative, stomachic, anodyne, antiseptic.	↑Antioxidant activity ↑PPARγ ↑Caspase 3 ↑Caspase 9 ↓ERK1 and ERK2 ↓ECM ↓NF_kB ↓BCL-2/BCL-XL	42,45,47
Tomato	*Seeragam*/ Cuminum cyminum	Fruit	---	↑Antioxidant activity ↑AMP ↑ERK1 and ERK2 ↑P53 ↑NF_kB	52, 55

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*Rasam*ingredient drugs with Anti-Uterine Fibroid Activity

1. *Cuminum cyminum L (Apiaceae) as a culinary herb for Uterine Fibroids:*

Cumin seeds have so many pharmacological activities.*Cuminum cyminum* contains: alkaloid , coumarin, anthraquinone, flavonoid, glycoside, protein, resin, saponin, tannin and steroid.According to earlier pharmacological research, *cuminum cyminum* has inhibitory effects on aldose reductase, alpha-glucosidase, tyrosinase, antimicrobial, insecticidal, anti-inflammatory, analgesic, antioxidant, anticancer, antidiabetic, antiplatelet aggregation, immunological, contraceptive, anti-amyloidogenic and anti-osteoporotic[5].

Cumin seed may have chemopreventive properties against cancer because of its capacity to modify the metabolism of carcinogens. Cumin's antioxidants, such as limonene, have potent anti-tumor effects.Additionally, recent studies have revealed that cumin may inhibit the growth of colon and breast cancer cells. A study in 2003, reported a strong correlation between diet and cancer[13]. For ages, cumin has been a part of the diet. It is a popular spice regularly used as a flavoring agent in a number of ethnic cousins. A study on cancer chemopreventive potentials of different doses of a cumin seed-mixed diet were evaluated against benzo(a)pyrene [B(a)P]-induced stomach tumorigenesis and 3-methylcholanthrene (MCA)-induced uterine cervix tumorigenesis. Results revealed significant inhibition of stomach tumor by cumin. Thus the study conveys the use of cumin as a helper in the therapy or the control of the cancer of Colon, ovary, liver and prostate. Cumin use in diet may reduce the risk of cancer[14].

In India, Seeds of Cyminum are extensively used in cooking which can be demonstrated as anti-carcinogenic agents[15].Thousands of years ago, it was recognized that the components of *cuminum cyminum* demonstrated anti-cancer properties, however this important traditional remedy has not yet undergone the proper scientific scrutiny. Further investigation should be highlighted back to this because it is harmless and acts as an anticancer agent[16].

The dietary supplements of cumin have prevented the occurrence of rat colon cancer induced by a colon-specific carcinogen and also decrease the activity of β-glucuronidase and mucinaseenzymes. In cumin-colon treated rats, the levels of cholesterol, cholesterol/phospholipids ratio and 3-methylglutaryl COA reductase activity were reduced. The other inhibition activities of dietary cumin in mice are benzopyrene-induced for stomach tumorigenesis, 3-methylcholanthrene induced uterine cervix tumorigenesis, and 3-methyl-4-dimethylaminoazobenzene induced hepatomas[17].

Retrospective review results indicate that cumin seed, its essential oil, ethanoic extract, and 1-(2-Ethyl, 6-Heptyl) Phenol (EHP), a biologically active compound that was previously extracted by benzene, have anti-cancer activity against six animal models and thirteen different cell lines, including OVCAR-5.

The probable mode of these anti-cancer activities in above cell line or animal models may be due to increased expression of Bax, Bid, Bad, Apaf-1, cytochrome c, caspase-9, -3 and PARP cleavage; inhibition of superoxide formation, lipid peroxidation, inducing increased detoxifying enzyme system glutathione S-transferase(GST) activity; modulatory effects on the hepatic levels of Cytochrome P- 450 (Cyt. P-450), Cytochrome b5 (Cyt. b5)[18].

2. *Piper nigrum (Liliaceae) as a culinary herb for Uterine Fibroids:*

Black pepper, called the 'King of spices' was used in cooking as well as medicine among Tamil people from ancient times. It has a lot of preventive and curative properties. Banerjee states that piperine which is the main constituent of black pepper acts against human leukemia cell line, K-562 cells. This cell line was significantly cytotoxically affected by the pure piperine (PIP) and black pepper (BP-M) methanolic extracts.The translation of Bax, caspase-3 and caspase-9 genes was found to be upregulated with subsequent downregulation of Bcl-2 gene and was further confirmed by the downregulated expression of proliferating cell nuclear antigen (PCNA).PIP's binding to PCNA and Bcl-2 was demonstrated by molecular docking experiments, which corroborated the in vitro results.When combined, these results indicate that black pepper and PIP have anticancer properties, suggesting that black pepper is a powerful nutraceutical that can slow the course of chronic myeloid leukemia[19].

Pushpa states that Piperine alone did not cause cytotoxicity or inhibition of cell proliferation. Howeverpiperine enhanced the cytotoxic and anti proliferative effect of paclitaxel(with polyoxyethylated castor oil) and doxorubicin when used in combination. Further, piperine in combination with drugs shown to induce P21 expression and reduce surviving expression[20].

*Aumeeruddy*showed that piperine inhibited proliferation and induced apoptosis via activation of caspase-3 and PARP cleavage.Blocked ERK1/2 signaling to reduce SREBP-1 and FAS expression. Also suppressed production of MMP-9 generated by EGF by blocking the activation of NF-jB and AP-1 through disruption of the p38, ERK1/2, MAPK, and Akt signaling pathways. This results in a reduction in migration[21].

3. *Allium sativum (Liliaceae) as a culinary herb for Uterine Fibroids:*

This is also used by Tamilian from ancient times. Garlic extracts corrected imbalances in estrogen metabolism linked to excess catechol estrogens and elevated inflammatory prostaglandins. They also acted to remove catabolic waste from the pelvic cavity and from uterine and ovarian tissues, which accelerated metabolism,

lymph drainage, and the sloughing-off of tissues. It also appears that garlic extracts stimulated the secretion of gonadotropins and ovarian hormones and inhibited proliferation of cancer cells. Because Garlic extracts activated the secretion of gonadotropins and ovarian hormones at the pituitary gland; promoted the exit of cells from the golgi phase of the cell cycle; enhanced the unliganded estrogen receptor's capacity to transduce growth impulses via alternative pathways, resulting in the death of fibroid cells. This combination may provide a means of treating fibroids in women for prolonged periods of time without requiring surgery or hormone replacement therapy. The results of this study may offer the possibility of treating women with fibroids for extended periods of time without the need for surgery or hormone add-back[22].

*Green*on his study states, that Garlic was used practically as a purifier and cleanser in the human system. Those who wait for pregnancy or have not started having children, chew raw garlic (coated with garden egg leaves) or take it in the form of prepared jell to cleanse the womb against fibroid[23].Direct anti-angiogenic drugs may help treat uterine fibroids, according to a recent study on anti-angiogenic medicines used in conjunction with conventional chemotherapy for the treatment of cancer[24,25]. Mousa Research has demonstrated the anti-angiogenesis properties of alliin, a component found in garlic. In the chick chorioallantoic membrane (CAM) model, the garlic-derived component allicin showed dose-dependent suppression of fibroblast growth factor-2 (FGF2)-induced human endothelial cell (EC) tube formation and angiogenesis. In the CAM model, allicin also showed strong suppression of vascular endothelial growth factor (VEGF)-induced angiogenesis[26].

Allium and its components have been linked to a number of health advantages, including anticancer, immunological stimulation, blood glucose regulation, radioprotection, improved memory loss, and protection against microbial, viral, and fungal infections. Dietary consumption of Allium vegetables may be inversely correlated with the risk of several cancer types, according to population-based case control studies. Organosulfur compounds (OSC), which are particularly effective in providing protection against cancer in animal models generated by a range of chemical carcinogens, are thought to be responsible for the anticarcinogenic action of Allium crops, including garlic.Recent research has demonstrated that several naturally occurring analogs of OSC can inhibit the growth of cancer cells both in culture and in vivo. Changes in the proliferation of cancer cells caused by OSC are often linked to disruptions in the cell cycle and the activation of G2/M phase arrest.In both cell culture and in vivo settings, it has been shown that the OSC can also cause apoptosis through the intrinsic pathway by changing the ratio of the Bcl-2 family of proteins. Additionally, garlic-derived OSC has been shown to have anti-angiogenic properties[27].

Tumor growth requires angiogenesis. Blood arteries provide nutrition and oxygen to cells. Without neovascularization, tumors cannot enlarge to a size of more than 1-2 mm. When neovascularization takes place, tumor growth may become unrestricted. Consequently, a good target for cancer chemoprevention is inhibiting angiogenesis. In the wound assay and the Matrigel chemoinvasion assay, respectively, AGE inhibited cell motility and invasion while increasing endothelial cell adherence to collagen and fibronectin. Reduced cell motility may be linked to stronger cell adherence to an extracellular matrix. Moreover, AGE strongly suppressed endothelial cell growth and tube formation. According to these findings, AGE may be able to stop the development of tumors by preventing angiogenesis by reducing endothelial cell motility, proliferation, and tube formation. Cancer cells cannot proliferate without angiogenesis; instead, they stay dormant[28].

Cell cycle dysregulation is one of the frequent processes in the formation of tumors. The degree of PCNA expression often corresponds well with the mitotic activity of neoplastic cells and tumor grade. PCNA is recognized as a marker of cell proliferation.Reduced PCNA activity was linked to the garlic derivative diallyl disulfide (DADS)-mediated suppression of breast cancer cell growth.In a mouse tumor xenograft model of oral cancer, s-allylcysteine (SAC), another product of garlic, decreased PCNA protein levels. This may be the result of AGE suppressing tumor-specific proliferation and it is well known that tumor cells which grow more quickly than normal mucosa cells possess extremely high levels of PCNA.These results indicate that the antitumor effect of AGE on the development of colonic tumors is correlated with suppression of the proliferative activity of dysplastic lesions[29].

Numerous organosulfur compounds (OSCs) produced from garlic have been shown to have an anti-carcinogenic impact in both animal models caused by a range of chemical carcinogens and in numerous cancer cell lines that have been cultivated, including those from the breast, colon, prostate, stomach, and lung cancers. Recent studies have revealed that certain OSCs can suppress the proliferation of cancer cells by regulating cell cycle progression such as the induction of G2/M phase arrest, due to activation of P53, and have also been shown to induce apoptosis via the intrinsic pathway by altering the ratio of the BCL-2 family of proteins both in cell culture and *in vivo* models. Caspase-3 is a critical executioner of apoptosis, and cleavage to its active form induces apoptosis. AGE promoted delayed cell cycle progression of 2–3 h at the G2/M phase compared with normal conditions, which was followed by the downregulation of cyclin B1 and cdk1 protein expression[30].These results suggest that AGE-mediated cell cycle delay at the G2/M checkpoint but not apoptosis induction is associated with a slight decrease in cyclin B1 and cdk1 protein levels. Delay of the cell cycle at the G2/M phase caused a decrease in the population of cells in the S phase, and was consistent with the suppressed PCNA labeling index of colon tumor tissue from the AGE-fed rats[31].

Human pancreatic, breast, prostate, and lung cancer cells, as well as colorectal carcinomas, have constitutively active NF-κB transcription factor, which creates an environment that is conducive to the growth of cancer cells. Furthermore, NF-κB is activated in human colon tumor lesions and adenomatous polyps[32]. NF-κB activation

involves its translocation from the cytoplasm to the nucleus, where it binds to target sequences to regulate gene expression. NF-κB is blocked by over-expression of the mutant form of its inhibitor, IκB, which reduces NF-κB translocation to the nucleus and decreases cell survival via downregulation of cyclin B1 expression[33]. In this manner, NF-κB regulates cell proliferation by controlling cyclin B1 expression levels. Pai *et al* showed that SAC included in AGE was able to inhibit the activation of NF-κB in a mouse xenograft tumor model [34].

4. Ferula asafoetida (Apiaceae) as a culinary herb for Uterine Fibroids:

Asafoetida also practiced in cooking, home remedy and medicinal preparation in Tamil nadu. *Ferulaassafoetida* commonly consumed as a healthy beverage has been demonstrated to posses a range of biological properties, such as anti-cancer, anti-oxidation, and anti-obesity effects. In treated mice, *asafoetida* effectively reduced both the tumor weight and volume. In female BALB/c mice, body weight dramatically increased compared to control. Apart from the antitumor effect, *asafoetida* decreased lung, liver and kidney metastasis and also increased areas of necrosis in the tumor tissue respectively[35].

FA(Ferulic acid) induced cell apoptosis and G0/G1 phase arrest in Hela and Caski cells through inducing the cell cycle-related protein expression such as p53 and p21, and reduced Cyclin D1 and Cyclin E levels[36]. Galbanic acid is a one of the ingredients of *Ferulaassafoetida* which has Anti-angiogenesis and Antiproliferative activity[37,38].

Ferulaasafoetida have the anti-cancer (alpha-pinene,alpha-terpineol, diallyl-disulfide, ferulic acid,isopimpinellin,luteolin, umbelliferone, vanillin), anti-inflammatory (alpha-pinene, beta-pinene, azulene, ferulic acid, isopimpinellin, luteolin,umbelliferone) antispasmodic (ferulic acid, azulene, valeric-acid, luteolin,umbelliferone) activity[39].*Ferulaasafoetida* have the anti-cancer activity[40,41].

5. Curcuma longa L (Zingiberaceae) as a culinary herb for Uterine Fibroids:

From ancient period *tamilian* food culture gave a primary place to *Curcuma longa*, known as *Manjal*in Tamilnaducommonly known as *turmeric*. Curcumin, a well-known component of turmeric, has been reported to prevent various diseases such as cancer, diabetes, obesity and reduction in tumour cell proliferation, decrease in blood cholesterol and suppression of thrombosis and myocardial infarction. Using Eker rat-derived uterine leiomyoma cell lines (ELT-3), an in vitro study demonstrated curcumin's capacity to function as a PPARγ ligand and suppress leiomyoma cell growth while promoting apoptosis[42].

Curcuma longa is also used in Siddha as an ingredient for the formulation *Rasaganthimezhugu*, and is indicated for the management of *Vippuruthi* in *pulippani Vaithiyam*-500. It reduce the symptoms and disappearance or reducing the size of fibroid[43]. Curcumin, essential oils, anthocyanins, and tannins are the components of *curcuma longa*. Drinks made from curcuma longa have fundamental analgesic and anti-inflammatory qualities,that have the ability to lessen dysmenorrhea pain. Curcumin in turmeric is phenolic compound that possesability as antioxidant. The antioxidant activity that is produced tends to increase with more and more concentrations of tamarind acid and sprouts added .The tamarind fruit has a natural active agent anthocyanin as an anti-inflammatory and antipyretic. Adding to this, the*Tamilian* food *Rasam* made by the basis of tamarind fruit juice. When heated, the antioxidant resistance of β-carotene can be increased by the combination of tamarind and spices. The antioxidants in turmeric can remain stable with the presence of tamarind. Antioxidants can stabilize hormones in the body, so menstrual pain is reduced[44].

Natural substances, such as curcumin, can reduce the oxidative stress and protect against inflammation in leiomyoma. Curcumin is one of the three major curcuminoids in turmeric plants (*Curcuma longa*). Numerous studies have highlighted its antioxidant, anti-inflammatory, anti-carcinogenic and immunoregulatory activity at the molecular level [9,10,11].Curcumin can prevent cancers, especially uterine myomas, from growing and forming by inhibiting anti-apoptotic proteins.

Feng et al. demonstrated in an animal model that *RhizomaCurcumae* (RC) and *RhizomaSparganii* (RS), used in traditional Chinese medicine, were effective in preventing and treating UFs in rats[12,13]. When RC and RS were combined, the expression of collagen, fibroblast activating protein, and transforming growth factor beta (TGF-β) was successfully reduced. At the same time, the expression levels of signaling factors (AKT, ERK, and MEK) in cell proliferation were also decreased[13]. Similar effects were observed by Yu et al andthey observed that important pathways like MAPK, PPAR, Notch, and TGF-β/Smad involved in UF cell proliferation and ECM formation were modulated by RC/RS herbs. Thus, curcumin can lessen oxidative stress and shield the body from inflammation [14].This activity is expressed through modulation of proinflammatory cytokines and signaling pathways, including before mentioned peroxisome proliferator-activated receptor gamma (PPAR-γ)[45].In conclusion, it seems that both thewomen who already have uterine myomas and those who are at risk of getting them should include turmeric in their diets[46].

*Malik et al.,*demonstrated, that curcumin inhibited uterine leiomyoma cell proliferation via regulation of the apoptotic pathway, and inhibited production of the ECM component fibronectin. Curcumin provides a novel direction for leiomyoma therapies. Induction of caspase-3 and caspase-9, as well as a decrease in ERK1, ERK2, and NF-κB p50 and p65 subunits, were all connected with leiomyoma cell inhibition[47].

6. Solanum lycopersicum(Solanaceae) as a culinary herb for Uterine Fibroids

Russo reported that Tomato has potential apoptotic and/or necrotic effects due to its carotenoids compound and acts against several types of cancer cell lines[48].
Fisetin (3,3′,4′,7-tetrahydroxyflavone) is a bioactive flavonol found in tomato. This compound exhibits a multiple bioactive role in chronic diseases, showing anti-inflammatory, antidiabetic, antioxidant, antitumorigenic, anti invasive, antiangiogenic, neuroprotective, and cardioprotective effects[49].
A tomato is a good source of potassium, folic acid, vitamin C, and carotenoids like lycopene. Its postulated cancer chemopreventive potential of lycopene[50]. In vitro and in vivo, lycopene suppresses angiogenesis at a concentration that ought to be attainable through diet[51].This activity has been related to the MMP-2/uPA system inhibition through VEGFR-2-mediated PI3K-Akt and ERK/p38 signaling pathways[52].
Aside from lycopene, cystine-knot mini proteins present in tomato fruit (TCMPs) are now being postulated as useful inhibitors of angiogenesis. These proteins, present in mature tomato fruits, display resistance to gastrointestinal proteolytic attack and resistance to industrial processing. Their antiangiogenic activities, demonstrated in vitro by the inhibition of endothelial tube formation and migration, as well as in vivo by using a zebrafish model, suggest that these proteins, along with lycopene and other antioxidants, may confer beneficial effects to tomato dietary intake [53,54].
It is expected from an ideal chemotherapeutic agent to target and exterminate tumor cells without showing cytotoxic effects on normal cells[18]. Fisetin, an excellent chemotherapeutic drug, has been demonstrated to have considerable anticancer action in a variety of cancer types in addition to its antioxidant activity. This is because it plays a crucial role in regulating critical signal pathways like AMP (5′-Adenosine monophosphate-activated protein) kinase, ERK (extracellular signal-regulated protein kinase) 1 and 2, p53 and nuclear factor kappa B (NFκB)[55].

Table 3: Common anti-Uterine Fibroid mechanism of Siddha culinary herbs.

Anti-UF mechanism	Cell cycle arrest	Caspase cascade activation	↓Extracellular matrix	↓PCNA expression	Hormone regulation	↑BAX/BCL-2 ratio
Culinary herbs	Lycopersicum Allium sativum asafoetida	Piper nigrum Lycopersicum Asafoetida Allium sativum	Lycopersicum Allium sativum	Piper nigrum Allium sativum Lycopersicum	Allium sativum	Asafoetida Piper nigrum Allium sativum

At present, although conventional pharmacological agents used foruterine fibroid continue to exhibit numerous drawbacks, it is stillconsidered the final choice of treatment for patients who prefer anon-invasive approach. Natural herbs which is used to make food, whichhave been widely reported in vitro and in vivo showed favourableoutcomes in the food supplement of uterine fibroid. It is important totake into consideration that many phyto constituents have a lowbioavailability when they are consumed orally as the body consideredthem xenobiotics, and, thus, may produce a significantly different result as that demonstrated from in vitro studies[56]. Therefore, before they are introduced and included in therapeutic guidelines for the treatment or prevention of uterine fibroids, more clinical research is required to ascertain their safety and efficacy in a well-designed clinical trial.
Among the culinary herbs reviewed, only *Curcuma longa*[57], and *Allium sativum*[22]have been investigated in clinical trials on their effect against UF.The rest of the herbs *Ferula asafoetida*[37], *Piper nigum*[20], *Cuminum cyminum*[14], and *Solanamlycopersicum*[52] have beeninvestigated in clinical trials on their effect against anti-tumoreffect. Among these, the clinical studies against *Curcuma longa* werelimited without the presence of a negative control group, and the clinicalstudies against Garlic (Allium sativum) with the presence of a negative control group. The other herbs were not directly proof of theirwork on UF. But all of these drugs had an effect againstangiogenesis. In addition, the culinary herbs may exert anti-UFactivity and anti-tumour activity via the same mechanism, as shown inTable 2&3. Thus, combining the different culinary herbs to promotesynergistic effect via the same or different pathway can be consideredand investigated. It is also possible for future studies toinvestigate the safety and efficacy of using Siddha culinarypreparation or traditional food preparation may allow the dose of thepharmacological agents to be reduced the size of UF, additionally reducing theadverse effects experienced by the patients.

Conclusion:

The use of culinary herbs by Tamils as a part of Siddha prophylactictreatment has been practiced since ancient times, and in this eraemphasis is being placed on forgotten or excluded foods such as*'Rasam'* needs the evaluating mechanism of action against UF. There areso many foods practiced among the people which have moreattraction without any nutrient value or minimal nutrient value alongwith so many health issues. Traditional foods plays a paramountimportance against UF. Even though pharmacological intervention and treatment are already ongoing in the management of UF, they are farbehind from achieving a balanced state and have brought the treatmentof UF to a rough path. In any disease, medicine alone doesn't play an important role, but also the food and drinks have thesignificant effect. Therefore, researchers have been investigatingvarious culinary preparations which are made by herbs that could be asupporting food for

UF. Still now UF remains a significant healthcondition for many women all over the world, the reformation of foodor use of traditional food of an effective, safe and less costlymanagement could greatly benefit the society. However a validatedtesting protocol is needed to standardize the active constituents inthe culinary herbs for use as a supportive food in anti-UF treatmentin ensuring a reproducible therapeutic effect.

CONFLICT OF INTEREST

Conflict of interest declared none.

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