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Management of Fibroid Uterus with a Traditional *Siddha* Formulation – A Review

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ABSTRACT

Among the traditional systems of medicine, *Siddha* medicine finds a significant place in the health care system of South India, Sri Lanka and Malaysia. *Siddha* system of medicine assures cure in certain disease conditions that are found to be complicated to treat by contemporary medical systems. Fibroid uterus, which is a pressing concern for many Indian women, can be well managed with *Siddha* regime according to various traditional literatures whereas contemporary solution provides mostly surgical intervention. Fibroids are benign growth present in about 30 % of women over the age of 30. Literary review reveals that a classical *Siddha* formulation - *Rasaganthi Mezhugu* mentioned in *Siddha* literature *Pulippani Vaithiyam- 500*, is indicated for the management of *Vippuruthi*. The treatment aims at relieving the symptoms and disappearance or reducing the size of fibroid. To prove the efficacy of *Rasaganthi Mezhugu*, this review has been done and it includes published articles on clinical trials and pharmacological studies on *Rasaganthi Mezhugu* and some of the herbal ingredients in *Rasaganthi Mezhugu*. A review on the herbal ingredients used in *Rasaganthi Mezhugu* reveals their anti tumour, anticancer, antioxidant and immuno - modulatory properties. This review on ingredients of *Rasaganthi Mezhugu* reveals the authenticity of traditional formulations and proves the synergistic effect of its ingredients.

KEY WORDS: Herbal ingredients, Fibroid uterus, *Rasaganthi Mezhugu*, *Siddha* Medicine

INTRODUCTION

Among the Traditional systems of medicine, *Siddha* Medicine finds a significant place in the health care system of South India, Sri Lanka and Malaysia. *Siddha* system of medicine assures cure in certain disease conditions that are found to be complicated to treat by contemporary medical systems. Fibroid uterus, which is a pressing concern for many Indian women, can be well managed with *Siddha* regime according to various traditional literatures whereas contemporary solution provides mostly surgical intervention. The clinical features of fibroid uterus are well correlated to those of *Karppa Vippuruthi* as described by the great *Siddhar Yugi*, in his text *Vaidya Chinthamani*¹. In *Siddha* clinical practice, this entity is commonly known as *Karuppai Sathai Kattigal*.

Uterine fibroid is defined as a benign tumour derived from smooth muscle tissue or a lump of muscle tissue that grows in the wall of the uterus in some women. Fibroids are benign growth present in about 30 % of women over the age of 30². There may be a single fibroid or multiple fibroids of varying size. The symptoms like abdominal distention, lower abdominal pain, weight loss, proliferation of uterine tissue with blood clots which gives a mass like structure and produce symptoms similar to rolling of foetus during pregnancy, constipation, headache and ulceration of the uterus occur in *Karppa Vippuruthi* which resemble those of fibroid uterus.

Literary review reveals that a classical *Siddha* formulation - *Rasaganthi Mezhu* (RGM) mentioned in *Siddha* literature *Pulippani Vaithiyam*- 500, is indicated for the management of *Vippuruthi*³.

Vippuruthi may be described as tumour characterized by the formation of connective tissue connecting the epithelial cells⁴. To be more specific, *Vippuruthi* pertaining to uterus is known as *Karppa Vippuruthi*. In allopathy medicine hormonal therapy is the only choice and apart from that surgery is the ultimate remedy for the removal of fibroid⁵. Myomectomy removes only the fibroids and leaves the healthy areas of the uterus intact that too if the fibroid is small and single⁶. As a last resort, hysterectomy is done when the fibroid is big in size and multiple⁷. But *Rasaganthi Mezhu*, a traditional compound formulation consisting of 48 ingredients of herbal, metal, mineral and animal origin is indicated in treating such fibroids⁸. In order to avoid the surgical risks and to improve the patients' Quality of Life (QoL) and to reduce the cost of the treatment, the classical preparation *Rasaganthi Mezhu*, has been selected and it is in practice for many centuries. To prove the efficacy of *Rasaganthi Mezhu* this review has been done and it includes published articles on clinical trials and pharmacological studies on *Rasaganthi Mezhu* and some of the herbal ingredients in *Rasaganthi Mezhu*.

BACKGROUND

Fibroid is derived from smooth muscle cells which rest either from vessel wall or uterine musculature, common during child bearing years (30 - 45 years). Fibroids are also called myomas, leiomyomas and fibromas². The cause of the fibroid is not exactly known. Fibroid is rarely found before puberty and they generally cease to grow after menopause. Women who are overweight or obese for their height or if their menarche began before the age of ten

are at greater risk and women who have given birth are at lower risk. Once a fibroid starts growing it seems to be linked to the hormone estrogen. The hormone progesterone may also promote fibroid growth². On the basis of the fact that uterine leiomyomas develop only after menarche and markedly shrink under hypoenestrogenic conditions such as late menopause, it is presumed that their growth depends on estrogens². The physiological effects of estrogen are mediated by estrogen receptors (ERs). Among them, ER- α is more highly expressed in uterine leiomyomas than in normal myometrium suggesting a possible link between uterine leiomyomas and ER- α expression level⁹. Uterine fibroid growths are classified by the location in which they are found in the uterus. Myometrial fibroids are found along the wall of the uterus⁵. Sub mucosal fibroids develop under the interior surface of the uterus. Sub serosal fibroids grow on the outside wall of the uterus. Pedunculated fibroids are generally seen growing outside of the uterus². The majority of the women with fibroids do not have symptoms. The symptoms depend on how large a fibroid is, its location and whether it is bleeding or pressing on an internal organ. The symptoms are low back pain, dysmenorrhoea, excessive menstrual bleeding and pelvic pain, feeling full in the lower abdomen, frequent urination, pain during sex, infertility etc. Uterine fibroid can be more significantly detected through Trans-vaginal ultrasound technology¹⁰. Apart from myomectomy and hysterectomy, recently a non surgical option of uterine artery embolization (UAE) is available. In this procedure, the blood supply to the uterus and fibroids are cut off making the fibroid to shrink¹¹.

Magnetic resonance guided focused ultrasound surgery is the newest treatment for fibroid in women wishing to pursue pregnancy in future¹².

Though above said many modern solutions available for the management of fibroids, it's really a question of affordability and accessibility for a common Indian woman. It's really need of the hour to explore the possibility of traditional claims in this arena. *Rasaganthi Mezhugu*, a herbo mineral formulation is one such common cost effective *Siddha* medicare for *Karppa Vippuruthi*.

Since the above mentioned treatments are expensive compared to the use of traditional medicines like *Rasaganthi Mezhugu*, it is highly essential to explore and validate more traditional formulations.

RATIONALE BEHIND SELECTING RASAGANTHI MEZHUGU

Rasaganthi Mezhugu is a traditional drug indicated for various ailments. In clinical practice, many practitioners have successfully observed the shrinkage of fibroid after the administration of *Rasaganthi Mezhugu*. *Rasaganthi Mezhugu* (RGM) is included in "The *Siddha* Formulary of India", Part-I (English), 1992, which is enlisted under Drugs and Cosmetics Act, 1940¹³.

Many works had been done with *Rasaganthi Mezhugu*, for various ailments, biochemically, pharmacologically and clinically. The bio-safety of the *Rasaganthi Mezhugu*, were established in various research works in different centers. Based on the possible therapeutic efficacies, *Siddha* text references, experiences from many traditional *Siddha* practitioners' made a three-drug *Siddha* regimen (RAN - *Rasaganthi mezhugu*,

Amukkara chooramam and Nellikkai lehyam) which has been approved by the Government of India for treatment of HIV in conjunction with allopathic treatments during the major quest for the management of pandemic¹⁴ *Rasaganthi Mezhugu* is the chief constituent of that RAN therapy (*Rasaganthi mezhugu, Amukkara mathirai, Nellikkai ilakam*) and was proved effective in many HIV patients in the Government Hospital for Thoracic Medicine (GHTM), *Tambaram* Sanatorium, Chennai, Tamilnadu¹⁵. A recently published paper entitled “Toxicity Studies of Siddha Medicine– *Rasaganthi Mezhugu*” reveals that administration of RGM for one year in HIV patients, and the authors found RGM didn't alter the hematological and serum parameters and also in the Hepatic and Renal function parameters¹⁶.

In Animal studies of *Rasaganthi Mezhugu*, the authors inferred that *Rasaganthi Mezhugu* has not produced any significant organ or hematologic toxicity. In the acute and chronic toxicity studies, the *Rasaganthi Mezhugu* did not produce any mortality or adverse reaction in rats¹⁷. All parameters obtained from the blood and serum was in normal range indicating that *Rasaganthi Mezhugu* did not show any noticeable toxic changes. Another publication reveals the possible potential of *Rasaganthi Mezhugu* as alternative medicine for prostatic cancer and also a sensitizing agent in the context of radiation therapy for prostate cancer as a complementary medicine¹⁷.

Rasaganthi Mezhugu is a compound formulation of 48 ingredients of herbal, metal, mineral and animal origin. All the ingredients are subjected to specific standard operating procedure (SOP) of detoxification. Likewise the toxicities of

metals, minerals are nullified by the active principles of the herbs. Curcumin pre-treatment has shown a protective effect against intoxication of mercury¹⁶. An observable regression on the severity such as haemorrhage, hepatocyte degeneration and tubular degeneration of kidney was observed in mercury - treated mice supplement with different doses of lycopene¹⁶. These appreciable observations, signifies *Siddha* preparations, having metals and minerals with several herbs in its process and as ingredients might have reduced the toxicity or even nullify.

This study brings up scientific evidence for the efficacy of RGM against the HPV-mediated cervical cancer cells and, if the toxic heavy metals are the limitation in its use, RGM would be a suitable candidate as evidence-based complementary and alternative medicine for HPV-positive cervical cancers¹⁸.

Rasaganthi Mezhugu presents a strong case for synergism as well as additivism of the multiplicity of compounds from the 38 herbs, most of which have been scientifically proven as associated with one or more aspects of interference with cancer. A review on the herbal ingredients used in *Rasaganthi Mezhugu* reveals their anti tumour, anticancer, antioxidant, detoxification and immunomodulatory properties. Specifically, the following medicinal plants possess one or more of these property / properties.

REVIEW OF SINGLE DRUGS OF RASAGANTHI MEZHUGU

To understand the efficacy, the herbal ingredients of *Rasaganthi Mezhugu* are reviewed for their pharmacological activities and therapeutic uses related

effects. Review of *Siddha* literatures and published articles on the herbal drugs used in *Rasaganthi Mezhugu* was done using the database of Science Direct website, Pubmed and tabulated in Table No.1.

Ginger may act as an anti-cancer and anti-inflammatory agent by inactivating NF kappa B through the suppression of the pro-inflammatory TNF-alpha²⁰. *Trachyspermum ammi* showed good antihelminthic activity against Indian earth worm²¹. The study states that the active constituent was found to be Curcumin which showed cytotoxicity to lymphocytes and Dalton's lymphoma cells at a concentration of 4 µg/ml. Initial experiments indicated that turmeric extract and curcumin reduced the development of animal tumours²².

Administration of alcoholic extract of *Piper longum* (10 mg / dose/animal) as well as piperine (1.14 mg/dose/animal) could inhibit the solid tumour development in mice induced with DLA cells and increase the life span of mice bearing Ehrlich ascites carcinoma tumour to 37.3 and 58.8% respectively, in Balb/c mice²³. The study reveals that two new diarylheptanoids (1,2), together with two known analogs (3,4) were isolated from the rhizomes of *Alpinia officinarum*. Compound 4 showed moderate cytotoxicity against human tumor cell lines. Hep g2, MCF-7 and SF-268 with no significant effect were found for compounds 1-3²⁴. The study concludes that *Saussurea lappa* petroleum ether extract (SLP) and *Saussurea lappa* alcohol extract (SLA) possesses anxiolytic activity. SLA appears to be active as compared to diazepam²⁵.

The study indicates that the aqueous extract of *Celastrus paniculatus* seed has cognitive enhancing properties and antioxidant effect might be involved²⁶. *Fennel* seed methanol extract (FSME) exhibited an anti tumour effect by modulating lipid peroxidation and augmenting the antioxidant defense system in EAC bearing mice with or without exposure to radiation²⁷. The study revealed vital information about the poly-pharmacological anti-tumor mode-of action of essential oils in *cardamom*²⁸.

Supplementation with *Cuminum cyminum* to diabetic rats significantly reduced the fatty changes and inflammatory cell infiltrates²⁹. The present review is an attempt to highlight the bioenhancing ability of piperine when it is given along with various drugs and nutrients³⁰.

Myristica seed extracts feeding also prevented the accumulation of cholesterol, phospholipids and triglycerides in liver, heart and aorta and dissolved atheromatous plaques of aorta by 70.9-76.5%. Faecal excretion of cholesterol and phospholipids were significantly increased in seed extracts fed rabbits³¹. Topical application of 100 mg/kg body weight of the active fraction (AF) of *Psoralea corylifolia* seeds inhibited the growth and delayed the onset of papilloma formation in mice, initiated with 7, 12-dimethyl benz(a) anthracene and promoted using croton oil³².

Methanol extract of galls of *Quercus infectoria* was found to possess antibacterial property against *Enterococcus faecalis*³³.

The study aimed to evaluate the anxiolytic activity of embelin that was isolated from *Embelia ribes*. On the basis of result, embelin showed its anxiolytic effect in

dose-dependent manner³⁴. In the isolated rabbit jejunum preparation the crude extract of *Acorus calamus* (Ac.Cr), which tested positive for the presence of alkaloid, saponins and tannins, caused inhibition of spontaneous and high K⁺ (80 mm)-induced contractions, with respective EC₅₀ values of 0.42 ± 0.06 and 0.13 ± 0.04 mg/mL (mean ± SEM; n = 6–8), thus showing spasmolytic activity, mediated possibly through calcium channel blockade (CCB)³⁵. Cytotoxic, antioxidant and antibacterial activities of these compounds have been evaluated by MTT, DPPH, agar disc diffusion and agar dilution assays respectively. These new compounds showed high cytotoxic effect against K562, jurkat and T₄₇Dcell lines³⁶.

The results suggest that the ethyl acetate and Methanol extracts of *Smilax chinensis* L. possesses analgesic and anti-inflammatory activities³⁷. SA-3C isolated from the kernel of *Semicarpus anacardium* is cytotoxic with tumor cell lines with IC₅₀ values lower than doxorubicin and even multidrug resistant tumor cell lines were equally sensitive to SA-3C. SA-3C isolated from the kernel of *Semicarpus anacardium* and it can be developed as an important anti cancer therapy³⁸

The results showed that all tested extracts and pure compounds of *Terminalia chebula* exhibited antioxidant activity at different magnitudes of potency³⁹. It is evident that *Nigella sativa* provides an important source of antioxidants⁴⁰. The study suggest that the ethanol extract of *Nigella sativa* seeds can generate antioxidants possess antitumour activity and ameliorate and prolong the lifespan of mice bearing EAT⁴¹. It was found that *V. anthelmintica* seeds possess antihelminthic activity against nematodes⁴².

The alcohol extract (50,100 and 200 mg / kg, P.O) of *Clerodendron serratum* produced a significant antinociceptive, anti-inflammatory and anti pyretic activities in animal models⁴³. Docetaxel, a semisynthetic analog of paclitaxel, made from the needles of the European Yew, *Taxus baccata*, is a potentially important chemotherapeutic agent for the treatment of cancer. Results show Docetaxel is a very active drug against breast cancer⁴⁴. Histopathological studies of the liver of different groups also support the protective effects exhibited by the methanol extract of grape pomace (*Vitis vinefera*) by restoring the normal hepatic architecture⁴⁵.

To screen the anti tumour effects of the four alkaloids: brucine, Strychnine, brucine N-oxide and isostrychnine from the seed of *Strychnos nux-vomica*. This paper indicates that the major alkaloids present in the seeds of *Strychnos nux-vomica* are effective against HepG2 cells proliferation, among which brucine proceed HepG2 cells death via apoptosis, probably through the participation of caspase -3 and cyclo - oxygenase-2⁴⁶. The diuretic effect was comparable with that of the standard drug Furosemide. The increase of cations in the urine on treatment with *Strychnos potatorum* seed extract (SPSE) was dose-dependent. This effect supports the use of the *Strychnos potatorum* seeds as a diuretic in folk remedies⁴⁷.

Assimilation of the quantitative foci data together with the findings of the modulation of tumor promoting markers give ample evidence to the anti-tumor promoting potential of *A. longifolia* seeds against chemically induced hepatocarcinogenesis in Wistar rats⁴⁸. An ethanol extract of *Asteracantha longifolia*

effectively restored the hematological parameters, serum iron and serum protein and normalized the microcytic, anisocytosis and hypochromic RBC's⁴⁹.

Sesamol is the main anti-oxidative constituent contained mainly in the processed sesame seed oil which has not been explored scientifically for its wound healing activity⁵⁰. The present results demonstrate *D. biflorus* seeds as a potential source of natural anti oxidant⁵¹. The coconut extract gave a dose dependent reduction in the haemolysis induced by distilled water. This suggests that the extract at low doses has potential anti inflammatory and anti ulcerogenic effects⁵².

The Methanol extract of the leaves of *Acalypha fruticosa* was evaluated for its anti tumour activity against Ehrlich's Ascites carcinoma (Eac) bearing swiss albino mice. The result indicates that the MEAF exhibited significant anti oxidant and anti tumour activity⁵³. The aim of the present study was to evaluate the anti oxidant, free radical scavenging and liver protective effects of friedelin isolated from *Azima tetraacantha* Lam.⁵⁴.

Withania somnifera has been used to stabilize mood in patients with behavioral disturbances and this investigations support the use of *Withania somnifera* as a mood stabilizer in clinical conditions of anxiety and depression⁵⁵. *Withania somnifera* is a known immunomodulator in indigenous medicine and the current experimental work deals with the immunomodulatory studies in the extract of *Withania somnifera* root powder against benzo (a) pyrene induced lung cancer in male Swiss albino mice⁵⁶. The anti-stressor properties of *Withania somnifera*

have been investigated and the results indicate that the drug treated animals show better stress tolerance⁵⁷. The ethanolic extract of tuber of *C.epigaeus* was given at different doses, such as 200 and 400 mg/kg body weight for each group and the studies were compared with a standard drug indomethacin (10 mg/kg body weight). Ethanol extract inhibited significant anti inflammatory activity⁵⁸. Plumbagin exerted anticancer activity on NSCLC cells by modulating the pro-survival and pro-apoptotic signaling that causes induction of apoptosis⁵⁹.

DISCUSSION

The various above inferences strongly warrant about the possible efficacy of *Rasaganthi Mezhugu* in fibroid uterus. The specialty and peculiarity of *Siddha* regime is synergy. Multiple modulators working towards multiple targets are the bottom line of *Siddha* therapeutics. The various presumptions achieved in various studies both as single ingredients and as *Rasaganthi Mezhugu*, certainly show a ray of hope for the regime for fibroid. The anti inflammatory, anti tumor, anti oxidant, anxiolytic and analgesic actions of various ingredients' and biosafety results of *Rasaganthi Mezhugu* in chronic studies adding up the probability towards the rationality. Fibroid uterus needs such regime only. The study not only indicate the definite probability of *Rasaganthi Mezhugu* but also open up many pathways for developing new regime of molecules for many other ailments, having similar or nearby path physiologies.

CONCLUSION

Rasaganthi Mezhugu though a widely used *Siddha* formulation, remains to be dubious among researchers regarding its safety in

human population. The basis of selective ingredients in a traditional formulation is still debatable. Though Mercury and other inorganic drugs are used in *Rasaganthi Mezhugu*, its extensive usage in practice and earlier peer reviewed researches proves its safety. Moreover the drugs of plant origin used in *Rasaganthi Mezhugu* are found to be scientifically proven for their efficacy in treating tumors, both benign and malignant. Still, the safety and efficacy studies of *Rasaganthi Mezhugu*, in large number of patients are much needed to substantiate the traditional claim. *Siddha* system of medicine, one of the oldest traditional systems, contains numerous collections of herbal / herbo-mineral formulations. These formulations are found to be time tested but require proof for its rationality in this contemporary world. This review is an attempt with scientific and analytical eyes on ingredients of *Rasaganthi Mezhugu*, reveals the strong possibility of its action against fibroid uterus with the synergistic effect of its ingredients. A detailed dispassionate clinical study and standardization of *Rasaganthi Mezhugu*, are certainly needed to go beyond.

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Table 1: Comparison of traditional and evidence based pharmacological activities of medicinal raw drugs used in RGM

Sl. No	Name of the Ingredient	Part used	Chemical constituents	Pharmacological action and therapeutic uses: Siddha	Pharmacological action (Evidence based)
1.	<i>Cukku</i> – <i>Zingiber officinale</i> Rosc.	Rhizome	Curcumin, Gingerol, Zingerone, 6 gingesulphonic acid etc	Stimulant ¹⁹ Carminative ¹⁹	Anti cancer ²⁰ Anti- inflammatory ²⁰
2.	<i>Ōmam</i> - <i>Trachyspermum ammi</i> L. Sprague	Fruit	Camphene, Carvacrol,	Carminative ¹⁹	Anthelmintic ²¹
3.	<i>Mañcal</i> – <i>Curcuma longa</i> L.	Rhizome	Curcumin, Desmethoxy- curcumin, Dihydrocurcumin B turmerone, ukonan A,B,C&D phytosterols	Carminative ¹⁹ Stimulant ¹⁹	Antitumor ²²
4.	<i>Tippili</i> – <i>Piper longum</i> L.	Fruit	Piper longumine, Longuminine, n-hepatadecane, Zingiberene, Piperine, Sesamin, Piperonaline, Sylvatin	Stimulant ¹⁹ Carminative ¹⁹ Diuretic ¹⁹	Antitumor ²³
5.	<i>Arattai</i> - <i>Alpinia officinarum</i> Hance	Rhizome	Galangin	Febrifuge ¹⁹	Anti inflammatory ²⁴
6.	<i>Kōstam</i> - <i>Saussurea costus</i> (Falc.) Lipsch.	Root	Alantolactone, Costunolide, Kushtin, Saussureal choleamine, Inulin	Stimulant ¹⁹	Anxiolytic ²⁵
7.	<i>Vāluluvai</i> – <i>Celastrus paniculatus</i> Willd.	Seed	Celapagine, Celastrol, Paniculatin, 5- stigmasten-3-β-ol	Stimulant ¹⁹ Alterative ¹⁹	Antioxidant ²⁶

8.	<i>Cōmpu - Foeniculum vulgare</i> Mill.	Fruit	Vit.C, Anisaldehyde, Foeniculin, stigmasterol	Carminative ¹⁹	Antitumor ²⁷
9.	<i>Ēlam - Elettaria cardamomum (L.) Maton</i>	Seed	Pinene, Geraniol, Terpine, Humulene	Stimulant ¹⁹ Carminative ¹⁹	Antitumor ²⁸
10.	<i>Cīrakam- Cuminum cyminum</i> L.	Fruit	Cuminaldehyde, cumin, β-Pinene, Glycosides of luteolin and apigenin	Carminative ¹⁹ Stimulant ¹⁹ Astringent ¹⁹	Anti inflammatory ²⁹
11.	<i>Mīlaku- Piper nigrum</i> L.	Fruit	Pipericide, Guineensine, Pellitorine, Piperonal, Piperin	Carminative ¹⁹ Stimulant ¹⁹ Resolvant ¹⁹ Antivata ²⁰	Bioavailability enhancer ³⁰
12.	<i>Cātikkāi – Myristica fragrans</i> Houtt.	Kernel	Eugenol, Geraniol, Myristicin, Trymyristin etc	Stimulant ¹⁹ Carminative ¹⁹ Tonic ¹⁹ Aromatic ¹⁹	Hypo cholestrolemia ³¹
13.	<i>Kārbōkarici- Psoralea corylifolia</i> L.	Fruit	Psoralen , Imperatorin, Angelicin, Bavachinine	Laxative ¹⁹ Stimulant ¹⁹	Antitumor ³²
14.	<i>Mācikkāi – Quercus infectoria</i> Oliv.	Gall	Ellagic acid, Pentadigalloyl- glucose	Astringent ¹⁹ Styptic ¹⁹ Tonic ¹⁹	Anti bacterial ³³
15.	<i>Vāiviṭaṅkam- Embelia ribes</i> L.	Fruit	Embelin, Quercitol, Embelic acid, Vilangin	Stimulant ¹⁹ Carminative ¹⁹	Anxiolytic ³⁴
16.	<i>Vacampu – Acorus calamus</i> L.	Rhizome	Asarone, Calamenol, Eugenol, Acordin, Asarylladehyde	Stimulant ¹⁹ Carminative ¹⁹ Disinfective ¹⁹ Germicide ¹⁹	Antispasmodic ³⁵
17.	<i>Ilavaṅkam – Syzygium aromaticum</i> Merr.	Flower bud	Caryophyllene oxide, Eugenol, Acetophenone, β- caryophyllene, Eugenine	Anti spasmodic ¹⁹ Carminative ¹⁹	Cytotoxic ³⁶

18.	<i>Paraṅkicakkai- Smilax china L.</i>	Root	Sarsaponin, Parallin, β-sitosterol, Daucosterol	Alterative ¹⁹ Depurative ¹⁹	Analgesic ³⁷ Anti inflammatory ³⁷
19.	<i>Cērāṅkoṭṭai- Semicarpus anacardium L.f</i>	Fruit	Bhilawanol, Anacordoside, Anacardic acid, Carpuflavanone	Alterative ¹⁹	Cytotoxic ³⁸ Anti cancer ³⁸
20.	<i>Kaṭukkāi – Terminalia chebula Retz</i>	Fruit	Anthroquinone, Chebulic acid, Chebulagic acid, Terachebin etc	Balances Trithodam ¹⁹	Antioxidant ³⁹
21.	<i>Karuṅcīrakam- Nigella sativa L.</i>	Seed	Psoralen, Imperatorin, Angelicin, Bavachinine	Emmenagogue, Diuretic ¹⁹	Anti oxidant ⁴⁰ Anti tumor ⁴¹
22.	<i>Kāṭṭu cīrakam- Vernonia anthelmintica Willd</i>	Fruit	Avenasterol, Vernosterol	Diuretic ¹⁹ Alterative ¹⁹	Anthelmintic ⁴²
23.	<i>Cīrutēkku – ClerodendrumSe rratum (L.) Moon</i>	Root	Serratagenic acid, Phylosterol, Scutellarein	Stimulant ¹⁹ Sedative ¹⁹	Antinociceptive ⁴³ Anti inflammatory ⁴³ Antipyretic ⁴³
24.	<i>Tāḷicapatiri – Taxus baccata L.</i>	Leaves	Taxine, Taxinine, Ephedrine, Taxicatin	Carminative ¹⁹ Tonic ¹⁹	Anticancer ⁴⁴
25.	<i>Tirāṭcai – Vitis vinifera L.</i>	Dried Fruit	Dulphinidin, Cyanidin, Ergosterol	Laxative ¹⁹ Coolant ¹⁹ Demulcent ¹⁹	Hepatoprotective ⁴⁵
26.	<i>Eṭṭi – Strychnos nux vomica L.</i>	Seed	Loganine,4 and 15 OH, Strychinine , Brucine	Antiseptic ¹⁹ Carminative ¹⁹ Purgative ¹⁹ Stimulant ¹⁹ Tonic ¹⁹ , Diuretic ¹⁹	Anti tumor ⁴⁶
27.	<i>Tērraṅ – Strychnos potatorum L.f.</i>	Seed	Diaboline, Brucine, Strychnine, Loganine, β-sitosterol	Alterative ¹⁹ Demulcent ¹⁹	Diuretic ⁴⁷

28.	<i>Nīrmuḷḷi vittu- Asteracantha longifolia</i>	Seed	Sterols, asterol I,II,III,IV, Asteracanthicine	Diuretic ¹⁹	Antitumour ⁴⁸ Haematinic ⁴⁹
29.	<i>Eḷ – Sesamum indicum L.</i>	Seed	Natural lipids, Sesomolin, Sesamolete	Stimulant ¹⁹ Diuretic ¹⁹	Antioxidant ⁵⁰
30.	<i>Kōḷḷu – Dolichos biflorus L.</i>	Seed	Urease, Streptogenin, β-Sitosterol, Psoralidin, Phyto- haemagglutinins, Genistein	Astringent ¹⁹ Diuretic ¹⁹ Tonic ¹⁹	Antioxidant ⁵¹
31.	<i>Tēnkāi – Cocos nucifera L.</i>	Endosperm	Lauric acid, Myristic acid, Phytosterol, Squalene	Coolant ¹⁹ Nutrient ¹⁹	Anti inflammatory ⁵² Antiulcerogenic ⁵²
32.	<i>Ciṇṇi vēr – Acalypha fruticosa Forssk.</i>	Root		Appetizer ¹⁹ Alterative ¹⁹ Attenuant ¹⁹	Antitumour ⁵³
33.	<i>Caṅkaṇ vēr – Azima tetracantha Lam.</i>	Root	Quercetin, Isorhamnetin, Azimine, Azcarpine, Carpaine	Diuretic ¹⁹ Stimulant ¹⁹ Astringent ¹⁹ Tonic ¹⁹	Antioxidant ⁵⁴
34.	<i>Amukkarā vēr- Withania somnifera (L.) Dunal</i>	Tuberous Root	Withasomine, Withanolide, Withaniol, Sominiferone, Withancine	Diuretic ¹⁹ Alterative ¹⁹ Tonic ¹⁹ Sedative ¹⁹ Hypnotic ¹⁹	Mood stabilizer ⁵⁵ Immuno- modulator ⁵⁶ Anti stressor ⁵⁷
35.	<i>Ākāśakarutaṇ Kiḷaṅku – Corallocarpus epigaeus</i>	Tuberous root	Bryonin	Alterative ¹⁹ Tonic ¹⁹	Anti inflammatory ⁵⁸
36.	<i>Citramōlam vērpaṭṭai – Plumbago indica L.</i>	Root bark	Plumbagin, Plumbagic acid, Plumbazeylanone	Antiperiodic ¹⁹ Diaphoretic ¹⁹	Anti cancer ⁵⁹