

Scientific Validation on the Effect of *Siddha Sashtric* Formulations in Chemotherapy Induced Nausea and Vomiting - A Review

Vigneshwari S¹, Antony Duraichi R²

¹PG Scholar, Department of Gunapadam, ²Lecturer, Department of Gunapadam, Government Siddha Medical College, Palayamkottai, Tirunelveli, Tamil Nadu, India.

Corresponding Author: Vigneshwari S

ABSTRACT

Siddha system is one of the major Indian systems of medicine. Siddha sashtric formulations are used for the treatment and management of non communicable diseases like stroke, cancer, diabetes, chronic lung diseases etc. Of these, cancer is the second leading cause of death globally. CINV is a significant burden for patients undergoing anticancer therapy. Nausea and vomiting are rated as two of the most distressing symptoms by chemotherapy patients and have been shown to significantly and adversely affect quality of life and physical function during treatment (Carelle et al., 2002). Many siddha sashtric formulations are available for nausea and vomiting. All of the available information about Siddha anti emetic Formulations, their ingredients and chemical constituents were collected from the rich collection of ancient Siddha books held in the library, Government Siddha Medical College, Palayamkottai, Tirunelveli. Electronic searches also made. They also have the therapeutic actions like anticancer, antioxidant, anti inflammatory, chemo preventive, gastro protective etc. This review explains the scientific evidences for the effect of Siddha Sashtric formulations in the treatment and management of chemotherapy induced nausea and vomiting. This documentation provides the baseline information about the therapeutic importance of Siddha medicines in chemotherapy induced nausea and vomiting and it will be useful for further clinical trials.

Key Words: Siddha medicine, cancer, chemotherapy, CINV, nausea and vomiting.

INTRODUCTION

Globally about one in six deaths is due to cancer (who). There are many types of cancer treatment. Most people have a combination of treatments, such as surgery with chemotherapy and/or radiation therapy. But chemotherapy causes some side effects by damaging healthy cells. They include anaemia, hair loss, nausea and vomiting, appetite changes, constipation, diarrhea, mouth, tongue and throat problems, weight changes etc. Chemotherapy induced nausea and vomiting is a common side effect of many cancer treatments. Modern antiemetics are used to control chemotherapy-induced nausea and vomiting

but nausea and vomiting still affects up to 60% and 37% of patients undergoing chemotherapy respectively (Bloechi Daum et al., 2006).

Traditionally many Siddha Sashtric formulations have been used for centuries to treat gastrointestinal complaints. They have many therapeutic actions including digestive, stimulant, antioxidant, anti-inflammatory, chemo preventive, bio-enhancer, anti cancer, immuno modulatory, gastro protective, anti mutagenic, anti ulcer, anti secretory, anti tumerogenic, anti emetic, anti apoptotic, anti hyperglycemic, anti lipidemic, radio protective, hepato protective, anti microbial, anti bacterial,

carminative, cytotoxic, anaesthetic, anti cholinesterase activity. So I decided to review the scientific evidence for the effect of Siddha sashtric formulations in the treatment and management of chemotherapy-induced nausea and vomiting.

Information on antiemetic siddha therapeutic formulations was collected from ancient siddha books held in the library, Government siddha medical college, Palayamkottai, Tirunelveli. Electronic

searches also made. Information on the chemical constituents and therapeutic actions of the ingredients were collected. This study will be useful for researchers and give relief to the patients undergoing chemotherapy.

Therapeutic formulations used for nausea and vomiting are listed in the table 1. They are available in the forms of medicinal powder, lozenges, electuary, medicated ghee, syrup, distilled extracts.

Table 1: List of medicinal formulations used for nausea and vomiting

S.NO	MEDICINAL FORMULATIONS	PHARMACOLOGICAL FORM	INDICATIONS	REFERENCES
1	<i>Seeraga chooranam</i>	Medicinal powder	Vomiting, indigestion	<i>Siddha vaidhya thirattu</i>
2	<i>Inji chooranam - I</i>	Medicinal powder	Vomiting, indigestion	<i>Siddha vaidhya thirattu</i>
3	<i>Inji chooranam - II</i>	Medicinal powder	Abhorrence of food, vomiting	<i>Siddha vaidhya thirattu</i>
4	<i>Thaalisaathy vadagam</i>	Lozenges	Vomiting, indigestion	<i>Siddha vaidhya thirattu</i>
5	<i>Panja deebaakkini ilagam</i>	Electuary	Vomiting, flatulence, indigestion	<i>Siddha vaidhya thirattu</i>
6	<i>Inji ilagam</i>	Electuary	Abhorrence of food, vomiting, flatulence	<i>Siddha vaidhya thirattu</i>
7	<i>Puliyaarai nei</i>	Medicated ghee	Tastelessness, vomiting	<i>Siddha vaidhya thirattu</i>
8	<i>Maadhulai manapagu</i>	Syrup	Anaemia, tastelessness, vomiting	<i>Siddha vaidhya thirattu</i>
9	<i>Ealathy chooranam</i>	Medicinal powder	Heartburn , vomiting	<i>Marunthu sei iyalam kalaiyum</i>
10	<i>Kesari ilagam</i>	Electuary	Heartburn, tastelessness, nausea, vomiting	<i>Marunthu sei iyalam kalaiyum</i>
11	<i>Vilvathy ilagam</i>	Electuary	Loss of appetite, heartburn , vomiting	<i>Marunthu sei iyalam kalaiyum</i>
12	<i>Ooma theeneer</i>	Distilled extracts	Vomiting, apesia	<i>Marunthu sei iyalam kalaiyum</i>
13	<i>Paruththi vithai chooranam</i>	Medicinal powder	Vomiting	The siddha formulary of india part - II
14	<i>Inji manapagu</i>	Syrup	Vomiting, abhorrence of food	<i>Sikitcha rathna deebam</i>

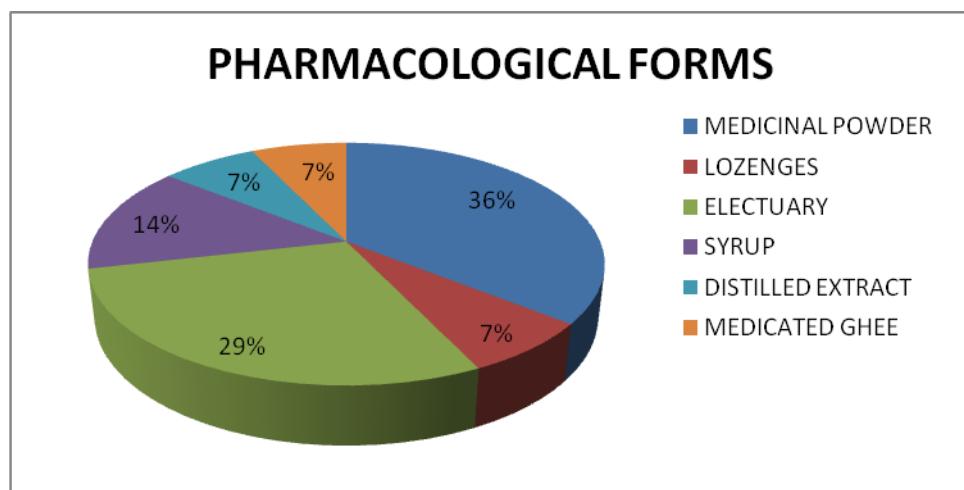


Figure 1: Pharmacological forms of Siddha Antiemetics

Main ingredients of 14 antiemetic therapeutic formulations are given in the

table 2. Phytopharmacology of these ingredients are given in the table 3.

Table 2: Main ingredients of antiemetic siddha therapeutic formulations

S.NO	MEDICINAL FORMULATIONS	MAIN INGREDIENTS
1	<i>Seeraga chooranam</i>	Cuminum cyminum, Citrus limon, Saccharum officinarum, Mukia maderaspatana, Phyllanthus emblica, Solanum trilobatum, Azadiracta indica, Leucas aspera.
2	<i>Inji chooranam – I</i>	Zingiber officinale, Cuminum cyminum.
3	<i>Inji chooranam – II</i>	Zingiber officinale - fresh and dried rhizome, Piper longum fruit & root, Piper nigrum, Elattaria cardamomum, Myristica fragrance pod & aril, Nardostachys jatamansi, Cuminum cyminum, Pimpinella anisum, Costus speciosus, Taxus buccata.
4	<i>Thaalisathy vadagam</i>	Taxus buccata, Piper longum fruit & root, Piper nigrum fruit & root, Zingiber officinale, Cinnamomum verum, Cinnamomum tamala, Mesua ferrea, Elattaria cardamomum, Vetiveria zizanoids, alpinia galanga.
5	<i>Panja deebaakkini ilagam</i>	Zingiber officinale, Piper nigrum, Piper longum, Elattaria cardamomum, Cuminum cyminum.
6	<i>Inji ilagam</i>	Zingiber officinale – fresh and dried rhizome, Solanum surattense, Tribulus terrestris, Raphanus sativus, Citrus limon, Piper nigrum, Piper longum, Elattaria cardamomum, Cuminum cyminum, Embelia ribs, Syzygium aromaticum, Taxus baccata.
7	<i>Puliyaarai nei</i>	Oxalis corniculata, Prosopis cineraria, Alternanthera sessilis, tender coconut water, Cuminum cyminum, Elattaria cardamomum, Glycyrrhiza glabra, Quercus infectoria, Myristica fragrans.
8	<i>Maadhulai manapagu</i>	Punica granatum.
9	<i>Ealathy chooranam</i>	Elattaria cardamomum, Zingiber officinale, Curcuma angustifolia, Taxus baccata, Mesua ferrea, Piper nigrum, Syzygium aromaticum.
10	<i>Kesari ilagam</i>	Coriandrum sativum, Piper nigrum, Piper longum, Myristica fragrans, Taxus baccata, Costus speciosus, Citrus limon.
11	<i>Vilvathy ilagam</i>	Aegle marmelos, Zingiber officinale, Piper longum, Piper longum, Elattaria cardamomum, Cinnamomum verum, Mesua ferrea, Syzygium aromaticum, Myristica fragrans, Taxus baccata.
12	<i>Ooma theeneer</i>	Carum copticum.
13	<i>Paruththi vithai chooranam</i>	Gossypium arboreum, Limonia acidissima, Oryza sativa, Piper longum, Carum copticum.
14	<i>Inji manapagu</i>	Zingiber officinale, Citrus limon.

Table 3: Phytopharmacology of Main Ingredients

S.NO	INGREDIENTS	PART USED	CHEMICAL CONSTITUENTS	THERAPEUTIC ACTIONS
1	Cuminum cyminum ^{1,2}	Seed	Cuminaldehyde, cuminol, cymene, cuminoide, cimonene, eugenol	➤ Digestive ➤ Stimulant ➤ Antioxidant ➤ Anti inflammatory ➤ Chemo preventive ➤ Bio enhancer activity
2	Citrus limon ³	Fruit	Coumarins, polyphenols, terpenes, citric acid	➤ Antioxidant ➤ Chemo preventive
3	Saccharum officinarum ⁹	Stem	Phytosterols, flavonoids, glycosides, phenolic acid, fatty acids	➤ Antioxidant
4	Mukia maderaspatana ⁴	Leaf	Phenolic compounds, saponarin, quercentin, phloroglucinol, flavonoids, steroids, tannin	➤ Immunomodulatory ➤ Antioxidant
5	Phyllanthus emblica ⁵	Unripe fruit	Emblicanin A & B, punigluconin, kaempferol, chebulinic acid, gallic acid	➤ Antioxidant ➤ Gastro protective ➤ Chemo preventive ➤ Anti inflammatory ➤ Anti – mutagenic effect
6	Solanum trilobatum ⁶	Leaf	Saponins, carbohydrates, phytosterols, tannins	➤ Antioxidant
7	Azadiracta indica ⁷	Bark	Azadiractin, nimbinin, nimbidol, isomeldenin, nimbin, nimbinene, nimocenol, margocin, nimbidin, nimban, nimboesterol, quercentin	➤ Anti ulcer ➤ Anti secretory ➤ Anti cancer ➤ Antioxidant ➤ Immunomodulatory
8	Leucas aspera ⁸	Leaf	Triterpene, diterpene, fatty acid ester, fatty acid amide	➤ Anti inflammatory ➤ Anti cancer ➤ Antioxidant
9	Zingiber officinale ¹⁰	Rhizome	Gingerol, paradol, shagoal, polyphenols, carotene, tannins, flavonoids,	➤ Anti inflammatory ➤ Anti tumorigenic ➤ Immunomodulatory ➤ Anti emetic ➤ Antioxidant ➤ Anti apoptotic ➤ Anti hyperglycaemic ➤ Anti lipidemic
10	Piper longum ¹¹	Fruit	Piperine, piperlongumine, sylvatin, sesamin, pipermonaline, piperundecalidine	➤ Carminative ➤ Immunomodulatory ➤ Antioxidant ➤ Anticancer ➤ Anti inflammatory ➤ Hepatoprotective ➤ Anti ulcer

Table 3: Continued...

11	Piper nigrum ¹²	Fruit	Piperine, piperidine, chavicine, piperetine, phenolic amino acids, feruperine	➤ Immunomodulatory ➤ Antioxidant ➤ Anticancer ➤ Anti inflammatory ➤ Hepatoprotective
12	Piper longum ¹³	Root	Piperine, piperlongumine, sylvatin, sesamin, pipermonaline, piperundecalidine	➤ Antibacterial ➤ Antidiabetic ➤ Anti hyperlipidemic
13	Elattaria cardamomum ¹⁴	Fruit	Cineole, limonene, terpinolene, myrcene, linalool, alpha terpinyl acetate	➤ Chemo preventive ➤ Immunomodulatory ➤ Anticancer
14	Zingiber officinale ¹⁰	Dried rhizome	Gingerol, paradol, shagoal, polyphenols, carotene, tannins, flavonoids,	➤ Anti inflammatory ➤ Anti tumorigenic ➤ Immunomodulatory ➤ Anti emetic ➤ Antioxidant ➤ Anti apoptotic ➤ Anti hyperglycaemic ➤ Anti lipidemic
15	Myristica fragrans ¹⁵	Pod	Myristicin, myristic acid, elemicin, safrole, trimyrishtin, myrcene	➤ Anti inflammatory ➤ Immunomodulatory ➤ Antioxidant ➤ Carminative ➤ Hepatoprotective ➤ Stimulant ➤ Radio protective
16	Nardostachys jatamansi ¹⁶	Root	β – eudesmol, elemol, β – sitosterol, algelicin, jatamansin	➤ Anti cancer ➤ Antioxidant ➤ Hepatoprotective
17	Costus speciosus ¹⁸	Root	Tigogenin, diosgenin, diosgenone, cycloartenol, octacosanoic acid	➤ Antioxidant ➤ Anti inflammatory ➤ Anti cancer ➤ Hepatoprotective ➤ Anti cholinesterase
18	Myristica fragrans ²⁰	Aril	Myristicin, myristic acid, elemicin, safrole, trimyrishtin, myrcene	➤ Anti inflammatory ➤ Immunomodulatory ➤ Antioxidant ➤ Radio protective
19	Taxus baccata ¹⁹	Leaf	Taxol, taxane, taxine, taxoids	➤ Anti cancer
20	Piper nigrum ¹²	Root	Piperine, piperone, pipertol, nerol, hexenol, α – terpinol, acetophenone	➤ Antioxidant ➤ Anticancer ➤ Anti inflammatory
21	Cinnamomum verum ²³	Bark	Eugenol, E- cinnamyl acetate, cinnamaldehyde, caryophyllene oxide	➤ Anti microbial ➤ Antioxidant ➤ Anticancer ➤ Anti inflammatory ➤ Anti diabetic
22	Cinnamomum tamala ²⁴	Leaf	Pinene, myrcene, camphene, p- cymene, limonene, eugenol, methyl eugenol	➤ Antioxidant ➤ Immuno suppressive ➤ Carminative ➤ Gastro protective
23	Mesua ferrea ²⁵	Flower	α – copaene, biflavonoids, rhusflavanone, mesuaferrone B	➤ Anti microbial ➤ Immuno modulator ➤ Antioxidant ➤ Anti inflammatory ➤ Hepato protective
24	Elattaria cardamomum ¹⁴	Seed	Cineole, limonene, terpinolene, myrcene, linalool, alpha terpinyl acetate	➤ Chemo preventive ➤ Immunomodulatory ➤ Anticancer
25	Vetiveria zizanioides ²⁶	Root	β – vetivenene, β –vetivone, α - vetivone, vetisenlinenol, β – vetispirene, khusimol	➤ Antioxidant ➤ Cytotoxic ➤ Anti tuberculosis
26	Alpinia galanga ²⁷	Rhizome	Alpinin, galangol, galangin, campheride, galanolactone	➤ Immuno stimulating activity ➤ Antioxidant ➤ Anti inflammatory ➤ Anticancer ➤ Anti ulcer ➤ Carminative ➤ Gastro protective
27	Solanum surrattense ²⁸	Leaf	Solasonine, campesterol, campeferol, diosgenin	➤ Hepatoprotective ➤ Antioxidant ➤ Anti apoptotic ➤ Anti bacterial

Table 3: Continued...

28	Tribulus terrestris ²⁹	Whole plant	Terrestrin C,D,E, kaempherol, tribulusterine, vanillin, furostanol	<ul style="list-style-type: none"> ➤ Antioxidant ➤ Immunomodulatory ➤ Anticancer ➤ Anti inflammatory ➤ Hepatoprotective ➤ Absorption enhancing activity
29	Raphanus sativus ³⁰	Root tuber	Glucosinolate, myrosinase, isothiocyanate	<ul style="list-style-type: none"> ➤ Chemo preventive ➤ Cytotoxic ➤ Anti microbial
30	Embelia ribes ³¹	Fruit	Embelin, embolic acid, embelinol, christembine, cinnamic acid, rapanon	<ul style="list-style-type: none"> ➤ Antioxidant ➤ Cardio protective
31	Syzygium aromaticum ²²	Bud	Myricetin, eugenol, eugenol acetate, limonin, ferulic aldehyde	<ul style="list-style-type: none"> ➤ Anti cancer ➤ Anaesthetic ➤ Antioxidant ➤ Anti inflammatory ➤ Anti microbial
32	Oxalis corniculata ³²	Leaf	Galacto – glycerolipid, isutiexin, volatile oil	<ul style="list-style-type: none"> ➤ Antioxidant ➤ Anti inflammatory ➤ Anti microbial ➤ Anti cancer ➤ Anti ulcer ➤ Hepato protective
33	Prosopis cineraria ³⁵	Leaf	Prosogerin A,B,C,D,E, apigenin,1 – arabinose, tryptamine	<ul style="list-style-type: none"> ➤ Anti cancer ➤ Antioxidant ➤ Anti inflammatory ➤ Anti microbial
34	Alternanthera sessilis ³³	Leaf	β – carotene, α – spirasterol, uronic acid, β – sitosterol, ricinoleic acid, myristic, palmitic, stearic, oleic and linoleic acids	<ul style="list-style-type: none"> ➤ Anti microbial ➤ Anti cancer ➤ Hepato protective
35	Tender coconut water ³⁴	-	Auxin, gibberellins	<ul style="list-style-type: none"> ➤ Hepato protective ➤ Antioxidant ➤ Anti inflammatory
36	Glycyrrhiza glabra ³⁷	Root	Glycyrrhizin, glabrin, liquortin, semilicoisoflavone, methoxyficiolinol	<ul style="list-style-type: none"> ➤ Anti inflammatory ➤ Anti ulcer ➤ Antioxidant ➤ Anti cancer ➤ Anti hepato toxic
37	Quercus infectoria ³⁶	Unripened fruit	Tannin, gallic acid, ellagic acid, pyrogallol, syringic acid, amentoflavone	<ul style="list-style-type: none"> ➤ Antioxidant ➤ Anti inflammatory ➤ Cytotoxic ➤ Anti leismanial
38	Punica granatum ²¹	Fruit	Punicalagin, oleanic acid, ellagitanins, gallotanic acid, anthocyanins, phenols, flavonoids	<ul style="list-style-type: none"> ➤ Chemo preventive ➤ Antioxidant ➤ Anti inflammatory ➤ Anti carcinogenic
39	Curcuma angustifolia ⁴¹	Root tuber	Curzerenone, camphor, germacrone	<ul style="list-style-type: none"> ➤ Antioxidant
40	Coriandrum sativum ³⁸	Seed	Linalool, decanoic acid, capric acid, nerol,cis – dihydrocarvone, decanal	<ul style="list-style-type: none"> ➤ Antioxidant ➤ Anti inflammatory ➤ Hepatoprotective
41	Aegle marmelos ⁴⁸	Root	Marmelosine, aeglemarmelosine, marmine, marmisine	<ul style="list-style-type: none"> ➤ Antioxidant ➤ Chemo preventive ➤ Anti inflammatory ➤ Anti cancer ➤ Ulcer healing activity
42	Carum copticum ³⁹	Seed	Paracymene, β – pinene, thymol, terpinolene, α – cymene, carracol	<ul style="list-style-type: none"> ➤ Antioxidant ➤ Carminative ➤ Hepatoprotective ➤ Anti inflammatory ➤ Anti emetic ➤ Anti mutagenic activity
43	Gossypium arboreum ⁴⁹	Seed	Gossypol, cyclopropenoid, linoleic acid, oleic acid, palmitic acid	<ul style="list-style-type: none"> ➤ Antioxidant ➤ Anti bacterial
44	Limonia acidissima ⁴⁰	Seed	Maemesin, marmin, feronia lactone, feronone, umbelliferone, dictammine, scroparone	<ul style="list-style-type: none"> ➤ Antioxidant ➤ Anti microbial
45	Oryza sativa ⁵⁰	Seed	Starch, glucose, fructose, galactose, glutamic acid, aspartic acid	<ul style="list-style-type: none"> ➤ Antioxidant
46	Foeniculum vulgare ¹⁷	Seed	Alpha pinene, beta myrcene, beta pinene, bitter fenchone, camphene, estragole, fenchone, limonene, p-cymen, safrole.	<ul style="list-style-type: none"> ➤ Antioxidant ➤ Anti inflammatory ➤ Anticancer ➤ Hepato protective ➤ Carminative ➤ Digestive

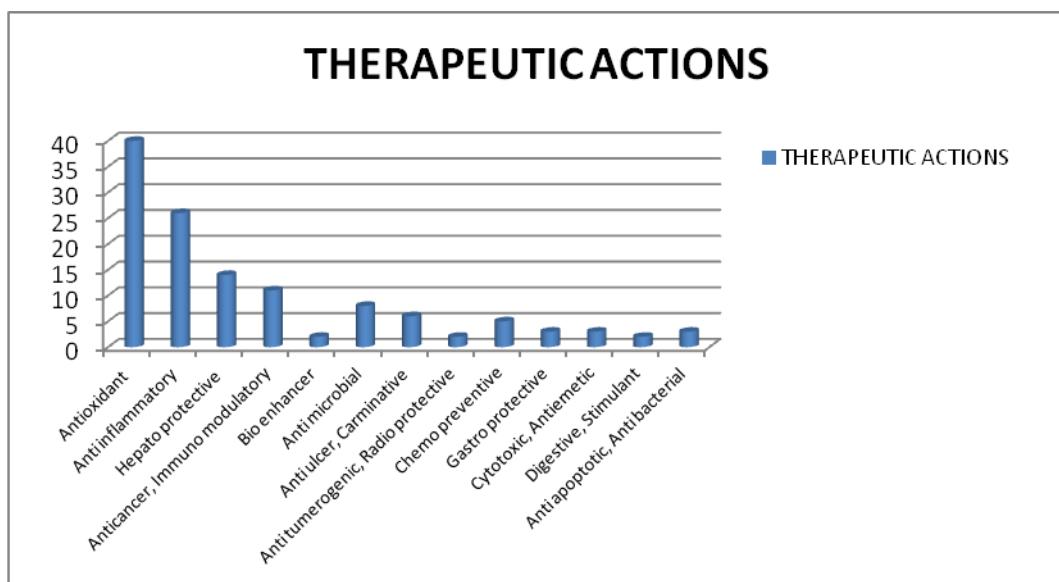


Figure 2: Therapeutic actions of Main ingredients

Totally 46 ingredients are reviewed. They have digestive (2), stimulant (2), antioxidant (40), anti-inflammatory (26), chemo preventive (5), bio-enhancer (2), anti cancer (11), immuno modulatory (11), gastro protective (3), anti mutagenic (1), anti ulcer (6), anti secretory (1), anti tumerogenic (2), anti emetic (3), anti apoptotic (3), anti hyperglycaemic (1), anti lipidemic (2), radio protective (2), hepato protective (14), anti microbial (8), anti bacterial (3), carminative (6), cytotoxic (3), anaesthetic (1), anti cholinesterase (1), cardio protective (1), anti tuberculosis (1), anti leishmanial (1) activities. So these formulations definitely cure and manage CINV and reduce the burden of patients undergoing chemotherapy.

CONCLUSION

Considering the therapeutic actions and chemical constituents of the ingredients in Siddha antiemetic therapeutic formulations, a need was felt to carry out further preclinical studies and clinical trials on these formulations. This will provide a sound foundation for continuous research in this area. This will be useful for the researchers and the patients undergoing chemotherapy.

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