

An overview of a *Siddha* poly herbal formulation *Vayu Keelaga Ilagam*

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ABSTRACT

Siddha medicines include 32 types of internal medicines and 32 types of external applications. Herbal drugs are given in the forms like *choornam* (powder), *ilagam*, *Mathirai* (tablets), *thylam* (oil) and mineral preparations in the form of *parpam* (white calcinated powder), *chendooram* (red in color) etc. The *siddha* formulation '*Vayu keelaga ilagam*' is a polyherbal formulation consists of nine herbal ingredients. According to *siddha* literature, the ingredients in this formulation have therapeutic effects on *vatha* diseases and this formulation itself indicated for *vatha* diseases especially *Uthira Vatha Suronitham*. The signs and symptoms said in *Uthira Vatha Suronitham* can be correlated with Rheumatoid arthritis in modern medical science. Analyzing various research articles, the ingredients of this formulation possesses Anti-inflammatory, Analgesic, Anti-oxidant, Anti-arthritis, Immuno Modulatory, Anti-Rheumatoid arthritis anti-osteoporotic activity which will improve the symptoms of illness as well as prevent the complications of disease. This review explainsthe phytoconstituents and pharmacologyof each ingredient of *Vayu keelaga ilagam* that has been mentioned in *Prana Rakshamirtha Sindhua* classical *siddha* literatue.

Key words

Vayu keelaga ilagam, *Uthira Vatha Suronitham*, Rheumatoid arthritis, *Siddha*, *ilagam*

INTRODUCTION

India also boasts of traditional system of medicine like *Ayurveda*, *Siddha*, *Unani* etc., The siddha system has been practiced mostly in South India, especially in Tamilnadu. The term Siddha is derived from '*Siddhi*', which means accomplished, achievement and attainment of perfection. This Siddha medicine had works were bestowed by the greatest *Siddhars*, after attaining spiritual knowledge through physical perfection and spiritual salvation. As per the Siddha literature *Vali*, *Azhal* and *Iyam* (i.e. *Vatham*, *Pitham* and *Kapham*) are the three humours, which are the life constitution of the body. i.e., *vali* for creation, *Azhal* for protection and *Iyam* for destruction of our body. The essential of Siddha medicine based on the five elements (Earth, Water, Fire, Air and Space) and three constitutions (*Vali*, *Azhal* and *Iyam*). Siddha drug classified into 2 types – Internal and external medicine, each type consist of 32 forms. Siddha drugs belong to herbal, mineral, metal or herbo-mineral and animal origin. *Ilagam* is one of herbal based internal medicine. Shelf life of *Ilagam* is 6 months. Siddha system of medicine has better answer for many of the refractory diseases, i.e. Diabetes mellitus, Cancer, Rheumatoid arthritis etc., while western medicine hardly cures. In the western system of medicine certain diseases can neither be prevented nor cured. Some of the traditional Siddha drugs may also have high effectiveness in certain ailments.

Yugi the *Siddhar* describes *Vali azhal keel vayu* as, it is a chronic disorder of the joints with palpable systemic involvement characterized by pain and swelling of the ankle, knee and smaller joints of the hand. Pain and tenderness present in minor joints, fever and loss of appetite. The signs and symptoms said in *Uthira Vatha Suronitham* can be correlated with Rheumatoid arthritis in modern medical science. Rheumatoid arthritis is a chronic, systemic inflammatory disorder that may affect many tissues and organs, but initially attacks the synovial joints. Although the cause of rheumatoid arthritis is unknown, autoimmunity plays a major role in chronicity and prognosis of the disease and it is considered a systemic autoimmune disease. It can be a disabling and painful condition, which leads to substantial loss of functioning and mobility if not adequately treated. In modern medical science the treatment for Rheumatoid arthritis includes Disease – modifying antirheumatic drugs (DMARDs), anti – inflammatory agents and analgesics.

Vayu keelaga ilagam is apoly herbal siddha formulation said in the siddha text "*Prana Rakshamirtha Sindhu*" especially in the treatment of *Uthira Vatha Suronitham* (Rheumatoid arthritis). The ingredient of this formulation includes *Parangipattai* (*Smilax china*.Linn), *VenKodivelivearpattai* (*Plumbago zeylanica*.Linn), *Sanganvearpattai* (*Azematetrantha*. Linn), *Seemaiamukkarakizhangu* (*Withania somnifera* .Linn), *Chukku* (*Zingiber officinale* .Linn) *Milagu* (*Pippernigram* .Linn), *Thippili* (*Piper longam* .Linn), *Elakkai* (*Elettaria cardamomum* .Linn),

Seeragam(*Cuminumcyminum* .Linn). These ingredients have therapeutic effect on *vali noigal* said in *Yugi vaidhya chinthamani*. Analyzing various research articles, the ingredients of this formulation possesses Anti-inflammatory, Analgesic, Anti-oxidant, Anti-arthritic, Immuno Modulatory, Anti-Rheumatoid arthritis anti-osteoporotic activity which will improve the symptoms of illness as well as prevent the complications of disease. This review paper deals with the herbs used as ingredients in this formulation with scientific data.

Table 1.Description of phytopharmacology of *VAYU KEELAGA ILAKAM*

S. NO	PLANTS NAME	BOTANICAL NAME &FAMILY	PART USED	PHYTOCHEMICAL S	ACTIVITIES
1.	<i>Parangi pattai</i> (China root)	<i>Smilax china</i> .Linn Liliaceae	Rhizome	Prosapogenin-A of Diosin,Dioscin,G racillin, Me-protogracellin, Me-protodioscin and 22 hydroxy –analog, Beta sitosterol glucoside, Smilaxin,Two Forustan and one spirostane glycosides Tannins,Carbohydrates and gums ¹ .	<ul style="list-style-type: none"> • Anti-inflammatory^{2,3} • Analgesic³ • Anti-oxidant^{4,5} • Anti-cancer⁶ • Hepatoprotective⁷ • Anti-diabetic⁸ • Anti-obesity⁹ • Anti-hyperuricaemic¹⁰ • Nephro protective¹⁰ • Alternative¹¹ • Anti-syphilitic¹¹ • Aphrodisiac¹¹ • Depurative¹¹
2.	<i>Kodiveliver Pattai</i> (Lead wort Ceylon lead wort)	<i>Plumbago zeylanica</i> .Linn Plumbaginaceae	Root bark	Plumbagin, 3-Chloroplumbagin, 2,3 biplumbagin, 6,6biplumbagin, Zeylinone,Iszeylinone, Chitranone, Droserone, Plumbagic acid,	<ul style="list-style-type: none"> • Anti-Inflammatory¹⁴ • Analgesic¹⁵ • Anti-arthritic¹⁶ • Anti –oxidant¹⁷ • Immuno modulatory^{18,19,20} • Hyperlipididemic²¹ • Anti-viral²²

				Plumbazeylanone, Glucose, Fructose, Enzymes as Protease and Invertase ^{12, 13} .	<ul style="list-style-type: none"> • Wound healing²³ • Anti-malarial²⁴ • Anti-carcinogenic²⁵ • Hepatoprotective²⁶ • Anti-periodic¹¹ • Diaphore¹¹
3.	<i>Sanganvear</i> (Beesting bush)	<i>Azema tetracantha.Lam</i> Salvadoraceae	Root	Azimine Ascarpaine Carpaine Indoleglucosinolate Alkalpides Flavonoides Tannins Glycosides,Lupeol, Glutinol and β sitisterol,Friedelin,Am ino acid ²⁷	<ul style="list-style-type: none"> • Anti-inflammatory^{28,29} • Analgesic²⁹ • Anti -arthritic²⁸ • Anti-pyretic²⁹ • Anti-oxidant and free radical scavenging activity³⁰ • Anti-nephrotoxic³¹ • Diuretic¹¹ • Stimulant¹¹ • Astringent¹¹ • Tonic¹¹ • Anti-periotic¹¹ • Expectorant¹¹
4.	<i>Amukkara</i> <i>Kizhangu</i> (<i>Seemai</i>) (Winter cherry)	<i>Withania somnifera.Duna</i> l Solanaceae	Rhizom e	Alkaloids(Isopellitarin e and Anferine,Ashwagandh ine, Cuscohygrine,Anahyg rine, Trophineetc...), Saponine(Sitoindoside VII and VIII),Steroidal lactone (Withanolides A Y,WithaferineA,Witha somniferineA,Withaso mniferols A-C,	<ul style="list-style-type: none"> • Anti-inflammatory³⁴ • Analgesic³⁵ • Anti-arthritic^{36,37} • Anti-oxidant^{38,39} • Immuno modulatory^{40,41,42,43} • Anti-cancer^{44,45} • Anti-stress^{46,47,48} • Cardio protective^{49,50} • Musculotrophic activity^{51,52} • Aphrodisiac⁵³

				Withasomnidienone, Withanoneetc) Root also contain rich Iron andWithaniol,Acylster ylglucosides,Starch,Re ducingsugar,Ducitol,A mino acids. ^{32,33}	
5.	<i>Chukku</i> Dried ginger	<i>Zingiber officinale</i> .Linn Zingiberaceae	Rhizom e	Non –volatile pungent; Zngerols, Shogaols, Paradols, Zingerone. Essential oils, Flavonoids, Glycoside, Saponins, Steroids, Terpenoids, Tannin, Carbohydrates, Protein, Alkaloids, Olieresin, Proteolytic enzymes and Waxes ⁵⁴ .	<ul style="list-style-type: none"> • Anti-inflammatory^{55,56} • Analgesic^{57,58} • Anti-oxidant^{59,60,61} • Immuno modulatory^{64,65} • Anti-arthritis^{62,63} • Anti-cancer⁶⁶ • Anti-diabetic⁶⁷ • Anti-microbial^{68,69} • Anti-noceptive⁷¹ • Anti-platelet aggregation Activity⁷² • Stimulant¹¹ • Stomachic¹¹ • Carminative¹¹
6.	<i>Milagu</i> Black pepper	<i>Piper nigram</i> .Linn Piperaceae	Dried unripe berries	Piperine Isopiperin Chavicine Isochavicine Pipene Piperamide Piperamine Amides,steroids, Ligans,Noeligans,terp enes and chalcones ⁷²	<ul style="list-style-type: none"> • Immuno modulatory⁷⁵ • Anti-oxidant⁷⁴ • Anti-inflammatory⁷³ • Analgesic⁷³ • Anti-arthritis⁷³ • Anti-diarrhoeal⁷⁶ • Hepatoprotective⁷⁷ • Anti-depressant⁷⁸ • Anti-cancer⁷⁹

					<ul style="list-style-type: none"> • Anti-septic¹¹ • Rubefacient¹¹ • Stimulant¹¹ • Resolvent¹¹ • Anti –vatha¹¹ • Anti –dote¹¹
7.	Thippili Indian long Pepper	<i>Piper longum</i> .Linn Piperaceae	Dried fruits	Piperine,Piper longumine,Piper longuminine,Methyl- 3,4,5 trimethoxycinnamate, piplatin,PiperlactumA &B, Piporadione,Starch,Pr otein,Alkaloids,Saponi n, Amygdalin and volatile Oil ^{80, 81} .	<ul style="list-style-type: none"> • Anti-inflammatory^{82,83} • Anti-Rheumatoid arthritic^{85,86} • Anti –Arthritic⁸⁴ • Immunomodulatory⁸⁷ • Anti-oxidant^{88,89} • Protective myocardial Activity⁹⁰ • Hepatoprotective⁹¹ • Anti-asthmatic⁹² • Anti –Diabetic⁹³ • Anti-hyperlipidemic⁹³ • Anti -Tumor⁹⁴ • Stimulant¹¹ • Carminative¹¹
8.	Elakkaai Lesser cardamomu m	<i>Elettaria cardamomum</i> . Linn zingiberaceae	Seeds	Terpineol, Terpinene Cineol, Limonene Sabinene, Bornneol Camphene, Geraneol D-limonene, Linalool Menthone, Citral Citronellal, Farnesol Myrcene, Heptane Alkaloids, Flavonoides , Saponins, Sterols and Tannins. ^{95, 96.}	<ul style="list-style-type: none"> • Anti- inflammatory^{97,98,99} • Analgesic¹⁰⁰ • Anti –spasmodic¹⁰⁰ • Anti –oxidant¹⁰¹ • Immuno modulatory^{102,103} • Insecticidal and Anthelmintic¹⁰⁴ • Laxative¹⁰⁵ • Diuretic Stimulant¹⁰⁶ • Carminative¹¹

					<ul style="list-style-type: none"> • Stomachic¹¹
9.	Seeragam White Cumin	<i>Cuminum cuminum</i> .Linn Apiaceae	Seeds	Cuminaldehyde,Limonene Eugenol, α, β pipene,1,8 Cineole α and β Cymene β and δ Terpinene Linalool,Protein Volatile oil Carbohydrates ¹⁰⁷	<ul style="list-style-type: none"> • Anti-inflammatory^{108,109} • Analgesic^{108,109,110} • Anti-oxidant^{111,112,113} • Immunomodulatory¹¹⁴ • Anti-estrogenic¹¹⁵ • Anti-diabetic^{110,116} • Anti-cancer¹¹⁷ • Anti-diabetic¹¹⁸ • Anti-Cancer¹¹⁹

1.SMILAX CHINA

Anti-inflammatory activity and analgesic activity

Raghu et al (2010) Ethyl acetate and methanolic extract of S.china had the significant dose dependent Anti- inflammatory and analgesic activity at higher concentration in acute carrageenan induced rat paw oedema model and Eddy's hot plate method respectively. *Inamullah et al (2008)* studied the lipoxygenase inhibition (IC₅₀:38 μ M) was due to the presence of Seiboldogenin in S.china. In this study significant inhibition (P<0.05) of carrageenan induced hind paw oedema was observed at the dose of 10 and 50 mg /kg.

Anti-oxidant activity

Chang et al (2013), the highest Anti-oxidant property was obtained from the ethyl acetate fraction of S.china correlated with high phenolic levels, especially catechin and Epicatechin.

2.PLUMBAGO ZEYLANICA

Anti-oxidant activity

Nile et al (2010), isolated new flavonoid 2-(2,4-Dihydroxyl phenyl)-3,6,8-trihydroxy chroman -4 one from the root of the P.zeylanica has Anti-oxidant activity in free radical scavenging and super oxide scavenging methods. *Zahin et al. (2009)*, evaluated in vitro Anti-oxidant activity methanolic extracts of P.zeylanica (root), A.calamus (rhizome), H.indicus(stem) and

H. antidyenterica (bark). According to FTC assay, the order of Anti-oxidant potential was found to be highest in P. zeylanica.

Immunomodulatory activity

Tsai et al (2008), detected the immune modulatory effects of seselin from P. zeylanica which significantly reduced the IL-2, IFN gene expression on phytohemagglutinin (PHA) stimulated cell proliferation in human Peripheral Blood Mononuclear Cells (PBMC). *Checker et al (2009)*, T-cells proliferation was inhibited by Plumbagin in response to polyclonal mitogen concanavalin A (Con A) by blocking the cell cycle progression. The immunosuppressive action of Plumbagin on cytokine levels were also studied *in vivo*. In this Plumbagin was completely inhibited Con A induced I KB alpha degradation and NF-KB activation. It also prevented graft versus host disease-induced mortality in mice.

Anti-inflammatory activity

Sheeja et al (2010) and *dang et al (2011)* analyzed two models of acute inflammation in *Phyllanthus emblica*, *Plumbago zeylanica* and *Cyperus rotundus*. The results showed that P. zeylanica reduced the carrageenan induced rat paw oedema, as well as it suppressed the activation of NF-Kappa B and tumour cells. Two groups of animals treated with P. zeylanica inhibited the acute inflammation 31.03% and 60.3% respectively at a dose of 300 and 500 mg/kg body weight.

Anti-arthritic activity

Poosarla and athota (2007) Ethyl acetate fraction of the root extract of P. zeylanica in its anti-suppressed collagen type II induced arthritis in DBA/I mice in a dose dependent manner. In addition the treatment with P. zeylanica stimulated con-A induced T-cell proliferation to normal level in arthritic mice.

3. AZEMA TETRACANTHA

Anti-arthritic activity

Sredharan et al (2008), the ethanolic extract of A. tetraantha possessed anti-arthritic activity in Freund's complete adjuvant (FCA) induced arthritis method. The Rheumatoid factor and C-reactive protein levels were decreased.

Anti-inflammatory, analgesic and antipyretic effect

Paulrayer et al (2011), in acute phase inflammation the maximum inhibition effect of Friedelin was found in carrageenan induced hind paw oedema and Croton oil induced ear oedema.

Friedelin also reduced the formation of granuloma tissues significantly. Significant analgesic effect was found acetic acid induced abdominal constriction response and formalin induced paw licking response. Significant anti-pyretic effect was found in yeast induced hyperthermia in rats.

4. WITHANIA SOMNIFERA

Anti-inflammatory activity

Gupta et al (2014), the root powder of *W.somnifera* (600mg/kg) significantly reduced the severity of the arthritis and improved the functional recovery of the motor activity and the radiological score in arthritic rats. Withaferin A and 3-b-hydroxy-2,3dihydrowithanolide F isolated from *W.somnifera* showed significant Anti-bacterial, Anti-inflammatory and immune modulatory activity.

Anti-arthritic activity

Paval et al (2009), the compound withaferin A was found to exhibit fairly potent Anti-arthritic & Anti-inflammatory activity. It was found to suppress the adjuvant-induced arthritic changes in rats without any toxic effects.

Anti –oxidant activity

Bhatayala et al (1997), administration of active principles of Siterosides VII-X and Withaferin A increased Superoxide dismutase (SOD), Catalase (CAT) and Glutathione peroxidase (GPX) activity in rat brain frontal cortex and striatum. The other active principle of Glyco-withanolides possess Anti – oxidant effect, Anti- inflammatory, Immunomodulatory, anti –ageing and cognition facilitated the effects produced by them in animals.

Immunomodulatory activity

Battacharya et al (1992), Withaferin A and Withanolide E exhibited specific immunosuppressive effect on human B and T Lymphocytes and in mice thrombocytes. Withanolide E had specific effects on T –Lymphocytes, whereas Withaferin A affected both B and T Lymphocytes.

5.ZINGIBER OFFICINALE

Anti-oxidant activity

Eleasu et.al (2012), studied the anti-oxidant potential in six varieties of Ginger. All the six varieties had strong anti-oxidant activities and possessed high quantities of Phenols, that could

produce the Anti-oxidant effect. *Masuda et al. (2004)* the compounds Gingerol, Shagoals, Gingerdiols, Gingerdiones and Dehydrogingerdiones isolated from the Dichloromethane extract of the Ginger rhizomes showed Anti-oxidant activity. In Vitro Ginger has been shown to exhibit Anti-oxidant effect. Gingerol produce HL-60cells from oxidative stress.

Immunomodulatory activity

Dugenci SK et al (2003) Nonspecific immunity was increased in rainbow trout eating a diet containing 1% of dried aqueous ginger extract for three weeks. *Pauri et al (2010)*, Mice fed with 50% ethanolic ginger extract (25 mg/kg) for seven days had higher haemagglutination antibody titer and plaque forming cell counts, consistent with improved humoral immunity. *Iqbal et al (2001)*, in an in Vitro study Ginger suppressed lymphocyte proliferation and it was mediated by decreased IL-2 and IL-10 production.

Analgesic activity

Suekawa et al (1987) the active principle of (6) Shogaol has inhibited acetic acid induced writhing in mice and to elevate the nociceptive threshold of the yeast inflamed paw. *Onogi et al (1992)* observed that (6) Shogaol inhibited the release of substance P by stimulating the primary afferents from their central terminal and hence shared this site of action with Capsaicin.

Anti-inflammatory activity

Junk et al (2009), the anti - inflammatory action was evaluated in Hexane fraction of dried ginger methanolic extract which suppressed the pro-inflammatory gene expression in LPS activated BV2 microglial cells. Gingerol and Shogaol exert inhibitory effect on biosynthesis of Prostaglandins and Leukotrienes by suppressing prostaglandin synthase or 5 lipoxygenase.

Anti-arthritic activity

Kattiyar et al (2016), Alcoholic and aqueous extract of *Z.officinale* possessed a significant anti-arthritic action against formaldehyde induced arthritis in a dose dependent manner i.e., at a dose of 100,200 and 400 mg/kg b.w respectively.

6. PIPER NIGRAM

Anti-inflammatory, anti-arthritic and analgesic activity

Bang et al (2012), the anti-inflammatory, analgesic, and anti-arthritic activities were found in piperine. The in vitro anti-inflammatory effect was evaluated on interleukin 1 β stimulated fibroblast-like synoviocytes obtained from rheumatoid arthritis and anti-arthritic including analgesic activities

were evaluated on carrageenan induced acute paw model of pain and arthritis in rats. Piperine treated groups significantly inhibited the synthesis of prostaglandin E2 at the concentrations of 10-100 µg/ml. Piperine treated groups significantly reduced the pain and arthritic symptoms in rats.

Anti-oxidant activity

Akbar et al (2014), the ethanolic extract of P.longum and P.nigram fruits exhibited good Anti-oxidant effect which might have prevent or reduce the process of different oxidative stress related diseases.

Immuno-modulatory activity

Sharma et al (2014), In vitro immune modulatory assay Piperine treated mouse splenocytes exhibited an increased secretion of Th-1 cytokines (IFN-γ and IL-2), increased macrophage activation and proliferation of T and B cell. Protective effect of piperine and rifampicin (1 mg/kg) combination against Mycobacterium tuberculosis was reported due to the immuno-modulatory effect of piperine.

7.PIPER LONGUM

Anti –inflammatory activity

Mamta et al (2012),Decoction of P.longam fruit showed a marked anti- inflammatory effect on carragenan induced rat oedema. The anti – inflammatory effect was due to the inhibitory effect of the piper extract and the phyto-component of piperine which inhibited prostaglandin and Leucotrienes COX-1. *Stoha et al (2001)*, The Chloroform extract of P. longum revealed larger amount of Phenol and had significant Anti – Inflammatory effect when compared to the extracts obtained from Hexane, Ethyl acetate and Ethanol, Hydro ethanol and aqueous extract.

Anti-arthritic activity

Sharma et al (1980), Aqueous extract of p.longum showed anti- arthritic effect on Complete Freuds Adjuvant (CFA) induced arthritis in rat. Aqueous extract of P.longum fruit at a dose of 400mg/kg and 200 mg/kg body weight significantly reduced the paw edema in rats.

Anti – oxidant activity

Stoha et al (2001), The Ethanolic extract of P.longum showed a good Anti- oxidant effect compared to aqueous extract in a dose dependent manner.

Protective myocadial activity

Mishra et al (2010), one of the main active components of Piper aldehyde in Piper longum had significant DPPH scavenging activity and exert protective effect in the myocardial narcotic rats.

Immunomodulatory activity

Manavalan et al (1979), Test such as Haemagglutination titer (HA), Macrophage Migration Index (MMI) and Phagocytic Index (PI) in mice have demonstrated the immune stimulatory action on P.longum fruits to be specific and non-specific. The immune-modulatory effect was higher at a lower dose of 225 mg/kg (lower dose) and it was marginally reduced when the dose was increased.

Anti-rheumatoid activity

Yende et al (2010), aqueous extract of P.longum with a dose of 200 & 400 mg/kg administered orally in Freund's Adjuvant induced arthritis rat. The swelling was reduced in the Diclofenac sodium (13.5 mg/kg) treated group (55% inhibition) and followed by P.longum 400 mg/kg (46.32% inhibition) treated group and finally P.longum 200 mg/kg (15.04%) treated group.

8.ELETTARIA CARDAMOMUM

Anti-inflammatory activity

Sermugapandian et al (2019), E.cardamom oil 0.175 mg/kg administered orally significantly reduced the paw edema in rats. It also reduced the pro-inflammatory cytokines level such as Tumour Necrosis Factor $\hat{I}\pm$, Interleukin (IL) 1 and IL 6 level in serum. In histopathological evaluation resulted that there is a marked reduction of congested blood vessels with no marked impression for inflammation.

Analgesic and anti-spasmodic activity

Pawar et al (2010), 233 μ L/kg of the oil extracted from E.cardamom seeds produced 50% protection against the writhing (Stretching syndrome) induced by intraperitoneal administration of a 0.02% solution benzoquinine in mice. *Al Zuhair et al, (1996)*, reported that the oil extracted from E.cardamom seeds had anti-spasmodic effect through muscarine receptor blockage.

Anti-oxidant activity

Beddows et al (2000), E.cardamom possesses anti-oxidant components of phenolic and flavonoids.

Immunomodulatory activity

Amin et al, (2010), Aqueous extract of *E. cardamomum* and black pepper enhanced the splenocyte proliferation significantly in a dose dependent synergetic fashion. Enzyme linked immune sorbent assay revealed that *E. cardamomum* and black pepper significantly enhanced and suppressed T-helper (Th) 1 cytokine and Th2 cytokine released by splenocytes.

9. CUMINUM CYMINUM

Analgesic and anti-inflammatory activity

Intra peritoneal injection of Cumin oil (0.1 ml/kg) in rats inhibited the carrageenan induced paw oedema compared with that of the standard drug Diclofenac sodium. *Sangeetha et al (2014)*, Aqueous and ethanolic extract of *cuminum cyminum* (200mg/kg and 500mg/kg) had significant effect of analgesic activity and anti-inflammatory activity than control group.

Analgesic activity

Purnima et al (2015), the analgesic activity was found in the methanolic extract of cumin seeds individually or with the combination of *Coriandrum sativum* seeds.

Anti-oxidant activity

Saini N Singh et al (2014), the aqueous extract of Cumin seeds indicated that less amount of Cumin was needed for scavenging and superoxide radicals'.

Immunomodulatory effect

Chauhan et al (2010), immuno modulatory effect was found in *C. cyminum* in normal and Cyclosporin –A-induced Immune suppressed animals. It significantly increased the T –cells (CD4&CD8) and Th I predominant immune response in a dose dependent manner. Modulation of T lymphocyte expression enhances the immune modulatory activity of *C. cyminum*. In stress induced immune-suppressed animals, the active compound of *C. cyminum* countered the depleted T lymphocytes and decreased the increased level of corticosterone.

Estrogenic /anti-osteoporotic activity

Shirke et al (2008), in their study, the phytoestrogen present in Cumin has an osteoporotic effect. The methanolic extract of cumin reduce the excretion of calcium in urine and augmentation of calcium content the animals receiving methanolic extract of cumin, significant reduction in urinary calcium excretion and augmentation of calcium content and also the mechanical strength of bones.

The bone and ash densities increased in animals and the microarchitecture also improved, without adverse effects such as body weight gain and the weight of atrophic uterus.

Conclusion

The herbal ingredients of this formulation has significant analgesic, anti-inflammatory, anti-arthritic, anti-pyretic actions as well as a good immune modulatory effects while searching experimental studies carried out by various researches. Furthermore this formulation should be subjected to preclinical evaluations to understand the safety and better effectiveness of the herbal medicine before prescribing to the patients.

REFERENCE

- 1) Sabari senthil B and Kalai selvan VK; A review on Pharmacological activities of *S.china* and *S.zeylanica*; *IJCPS*; 2017, Vol.8 (1).
- 2) Inamullah Khan, Mohammad Nisar, Farooq Ebad, Mohammad Saeed and Haroon Khan; Anti-inflammatory activities of Seiboldogenin from *S.china* .Linn; *Experimental and computational study; journal of Ethnopharmacology* ,2009;121(1);175-177.
- 3) S.Ragunatha Reddy, Poppa Rajani, Koteswara rao .Divi, YK Naidu, Sarath Chanthiran ,MP Kalyan Reddy; Anti –Inflammatory and Analgesic activity of *S.chinensis*; *RJPBCS*; 2010; Vol 1; 1(2); 1
- 4) Chang Ho Jeong, Hee Rokjeong, Ji Hyun Kwak, Jihye Kim; Phenolic composition and invitro anti-oxidant activity of *S.china* root ; *Journal of Food and Biochemistry*, 2013; 37(1).98-107.
- 5) Si eun Lee, Eun Miju and Jeong Hee Kim; Free radical scavenging activity and anti-oxidant fortifying activities of extract from *S.china* root; *Experimental and molecular medicine*, 2001; 33(4); 262-268.
- 6) Yuan Li Li , Guo Ping Gan , Hui Zhan Zhang, Hezhen Wu and Youn Ping Huang; A flavonoid glycoside isolated from *S.china* rhizome vitro anti-cancer effect of human cancer cell lines . *journal of Ethnopharmacology* .2007; 1139(1); 115-124.
- 7) Venkidesh R, Subhash C, Mundal, Dilipkumar Pal , Mohana lakshmi ; Hepatoprotective activity of *S.chinensis*.Linn in carbon tetrachloride induced hepatotoxicity in rats . *International Journal of Biological and pharmaceutical Research*; 2010; 1(2); 72-75.
- 8) Venkidesh R, Subash C, Mudal , Dilipkumar pal , Mohana lakshmi; Anti-diabetic activity of *S.chinenses*.Linn.in alloxon induced diabetic rats. *International Journal of Pharmacy and Pharmaceutical Science*, 2010, 2; 2(suppl 2); 52-54.
- 9) The anti-obesity effect of *S.china* extract *Korean Journal of Microbiology and Biotechnology* 2014.42(4); 354-360.

- 10) Lvyi Chen, Huafeng Yin, Zhou lan, Shuwei Ma; *Anti-hyperuricemic and nephroprotective effects of Smilax china L.* *Journal of Ethnopharmacology*, 2011; 135(2); 399-405.
- 11) Gunapadam mooligai vaguppu; Vaithya Rathinam Ka.Sa. Murugesu muthaliyar; Page No; 651, 383, 414, 29, 470, 760, 514, 65, 459.
- 12) Chen et al ., *Synthesis , characterization and preliminary cytotoxicity evaluation of five Lanthanide (III)-Plumbagin complexes;* *J of inorganic Biochem.*, 2011; 105; 308-316;
- 13) Mandavkar and Jalapur et al, *A comprehensive review on P.Zeylanica.* *Linn, AJPP Vol 5(25)*, 2011; 2738-2747.
- 14) checker R, Sharma D, Sandur SK, Khanam S, Poduval TB ; 2009; *Anti-inflammatory effect of Plumbagin are mediated by inhibition of NF-Kappa B activation in lymphocytes;* *Int .Imunopharmacol.*, 9(7-8); 949-958
- 15) Vineeth mittal, SK Sharma, Deepak Kaushik, Meenu khatri, Kusum Tomar; *Comparative study of Analgesic activity of Plumbago zeylanica Linn .callus and root extract in experimental animals;* *RJPBCS*; 1(4); 2010; 830.
- 16) Poosarla, Athoda RR ; 2007; *Alleviation of collagen induced arthritis by P.zeylanica in mice;* *Pharma., Bio.*, 45; 54-59.
- 17) Nile SH and Khobragade CN; 2010; *Anti-oxidant activity and Flavonoid derivatives of Plumbago zeylanica;* *J Nat Prod* , 3, 130-133.
- 18) Sakamoto S, Putalan W, Tsuchihashi R, Putalan W, Kinjo J, Tanaka H, Morimoto S; 2010; *Expression , purification and characterization of anti-Plumbagin single chain variable fragment antibody in Sf9 insect cells.* *Hybridoma Larchmt*, 29(6); 481-488.
- 19) Tsai WJ, Chenc YG, Wuc MH , Lina LC , Chuangd KA , Change SC ; 2008; *Seselin from P.zeylanica inhibit phytohemagglutinin (PHA) -stimulated cell proliferation in human peripheral blood mononuclear cells.* *J Endopharmacol.* 119; 67-73.
- 20) Checker R, Sharma D, Sandur SK, Khanam S, Poduval TB ; 2009; *Immunomodulatory effect of Plumbagin are mediated by inhibition of NF-Kappa B activation in lymphocytes;* *Int .Imunopharmacol.*, 9(7-8); 949-958.
- 21) Alpana R 1996 , *Effect of Plumbago zeylanica in hyperlipidaemic in Rabbits and its modification by Vit E;* *Indian Journal of Pharmacology* ; 28, 161-166.
- 22) Marian TG, Neubert R, Schmidt PC, Wutzler pand, Schmidtke M; *Anti-viral activity of some Ethiopian medicinal plants used for the treatment of dermatological disorders;* *Journal of Ethnopharmacology* 2006; 104(1-2); 182-187.
- 23) Reddy JS, Rao RP, Reddy MS (2002), *Wound healing effect of Heliotropium indicum, Plumbago zeylanica and Acalypha indica in rats;* *Journal of Ethnopharmacol.* 79; 249-251.

- 24) Simonsen HT, Nordskjold JB, Smitt UW, Nyman U, Palpu P, Joshi P, Varughese G; *In Vitro screening of Indian medicinal plants for Anti-plasmodial activity*; *J Ethnopharmacol* 2001;74;195-204.
- 25) Nguyen AT, Malonne H, Duez P, Fastre RV, Vanhaelen M; *Cytotoxic constituents from P.zeylanica* *Fitoterapia* 2004 ;July 75(5);500-504.
- 26) Kumar et al., *Hepatoprotective activity of aerial part of P.zeylanica against carbon tetrachloride induced Hepatotoxicity in rats* *JPPS*;2009;1;171-175.
- 27) T R Prashith kekuda, H L Ragaventhra; *Phytochemistry ,traditional uses and pharmacological activity of A.tetracatha –An updated review*; *International Journal of Green Pharmacy* ;2017;11(4);217.
- 28) Sridharan C , Jose MA , Rhadhakrishnan R; *Anti-inflammatory and Anti-arthritic activity of A.tetracantha , Whole plant in Wister rats* ; *IJPPS* 2008;40;S83.
- 29) Paulrayer Antonisomy, Veeramuthu Duraipandian and Savarimuthu Ignacimuthu. *Anti-inflammatory, Analgesic and Anti-pyretic effects on Friedelin isolated from A.tetracantha in mouse and rat models*. 2011.
- 30) Bennett RN mellon FA , Rosa EA , Perkins L ; *profiling glucosinolates, Flavonoides , Alkaloides and other secondary metabolites in tissues of A.tetracantha L*; *J Agric Food Chem* 2004;52;5856-62. al., 2004; *JAF*;52(52);5856-62
- 31) Manikandaselvi S, Ramya D, Ravikumar , Thinagarbabu R; *Evaluation of Anti-nephrotoxic potential of A.tetracantha .lam* ; *Int Jour Pharm Sci* 2012;4;566-8.
- 32) Ganzera M et al, *HPLC Analysis of Withanolides in W.somnifera*, *fitoterapia* 74(1-2); 68-76(2003).
- 33) Bilal ahmad et al; *Botanical, chemical and Pharmacological review of W.somnifera*; *Indian Journal of Drug and Diseases*; Vol 1(6), 2012 , 2278-2958.
- 34) Gupta A, Singh S ; *Evaluation of Anti-inflammatory effect of Withania somnifera root on collagen induced arthritis in rats*; *Pharm Biol*; 2014;52(3);308-320.
- 35) Amitabha Dey, Shyam sundar Dipl C Chatterjee, Vikas kumar; *Analgesic activity of Withania somnifera extract in stressed mice; Oriental pharmacology and experimental medicine* ;16(4);2016;0245-7.
- 36) Bector NP, Puri AS, Sharma D (1968) *long term effect of herbal drug W.somnifera on adjuvant induced arthritis in rats*, *Res* 56;1581-1583.
- 37) Jaijesh Paval, Srinivasan Keloth kaitheri, Bhagath potu, Sreejith Govindhan, Raju suresh kumar; *comparing the Anti-arthritic activities of plants Justicia gendarussa burum F and Withania somnifera*; *IJGP*; Vol 3; 4; 2009; 101.

- 38) Anonymous, *The Wealth India Vol X, (SP-N) publication and information directorate council Scientific and Industrial Research (CSIR), New Delhi (1982); 580-585.*
- 39) Battacharya S K, Satyan KS, Ghoshal; *Anti-oxidant activity of glycowithanolides from Withania somnifera; IJEP; 35(3); 1997; 297-99.*
- 40) Rasool M, Veralakshmi P. *Immuno modulatory role of W.somnifera root powder on experimental induced inflammation; An in Vivo and Vitro study; Vasculpharmacol .2006; 44(6); 406-410.*
- 41) Leemol Davis, Girija kuttan; *Immunomodulatory activity of Withania somnifera; Journal of Ethnopharmacology; 71; 2000; 193-200.*
- 42) Dugenic SK, Arda N, Candan A; *Some medical plants as immune stimulant for fish; Journal of Ethnopharmacology; 2003; 88(1); 99-106.*
- 43) Wilasrusmee C, Siddiqui J, Brush D; *In Vitro immunomodulatory effects of herbal products; American surgeon .2000; 68(10); 860-864.*
- 44) Prakash J, Gupta SK, Dindr AK, *Nutr Cancer 2002; 42; 91-95.*
- 45) Jeyaprakasam B, Zhang F, Seeram N, Nair M; *Life Science 2003, 74; 125-132.*
- 46) Battacharya S.K. *Evaluation of adoptogenic activity of some Indian medicinal plants; W.somnifera and O.sanctm with special reference to stress induced gastric ulcer in swiss albino rats. Proc. Int. Seminar on Traditional Med. Calcutta; 1992; 7-9.*
- 47) Khare CP ; *Indian Medicinal Plants –An illustrated Dictionary ; First Indian Reprint , Springer (India) Pvt. Limited , New Delhi; 2007; 717-18.*
- 48) Archana R, Namasivayam ; *Anti-stress effect of W.somnifera: Ethnopharmacol 1999; 64(1); 91-93.*
- 49) Andallu B, Radhika B; *Ind Jour of Experimental Biology; 19; 1981; 245-49.*
- 50) Andallu B, Radhika B; *Indian Journal of Experimental Biology; 1981, 19; 245-49.*
- 51) Anonymous . *The Wealth India , Vol X (SP-N) publication and information , CCIR , New delhi (1982); 580-85*
- 52) Anonymous *standardization of single drug of Unani medicine; Part3, 1st Edition; CCRUM; New Delhi 2007; 9-14.*
- 53) Kaspate, AR, Ziyaurrehman, TSaldanha, P More, : *To study on Aphrodisiac activity of Hydro alcoholic extract of W.somnifera dried roots in female wistar rats; Int Jour of Pharmaceutical Sci and Res 2015; 2820-36.*
- 54) IJyotsna Dhanik et al., *A review of Z.officinale; Journal of pharmacognocny and Phytochemistry; 2017; 6(3); 174-184.*
- 55) Srivastava K C, Mustafa T; *Ginger and Rheumatic heart disease .Med Hypothesis; 1989; 29(1); 25-28.*

- 56) Junk HW, Yoon CH, Park KM; Hexane fraction of *Z. rhizomacrudus* extract inhibit the production of nitric oxide and proinflammatory cytokines in LPS stimulated BV2 microglial cells; *Food chemistry and Toxicology*; 2009; 47(6); 1190-1197.
- 57) Suekawa M, Ishige A, Yussa K. Pharmacological studies on Ginger pharmacological action on pungent constituents, (6) Shogaols and (6) Gingerol; *Journal of Pharmacobiodyn*; 1987; 7; 13-18.
- 58) Ongi T, Minami M, Kuraishi Y, Satoh M: Capsaicin like effect of (6) Shagaol on substance P containing primary afferents of rats; a possible mechanism of its analgesic action. *Neuropharmacology*; 1992; 31(11); 1165-69.
- 59) Eleazu CO, Eleazu KC: Physico chemical properties and Anti-oxidative potential of 6 new varieties of Ginger (*Z. officinale*); *American Journal of Food Technology*; 2012; 7(2); 214-221.
- 60) Masuda T, Maekava T, Hidaka K; Chemical studies on Anti-oxidant mechanism of Curcumin. Analysis of oxidative coupling products from curcumin and linoleate. *J. of Agri and Food Chem*; 2001; 49(5); 2539-2547.
- 61) Wang CC, Chen LG, Lee LT and Yang LL; Effect of (6) Gingerol, an anti-oxidant from ginger, on inducing in human leukemic HL-60 cells, *in Vivo*; 2003; 17(6); 641-645.
- 62) Dr .Dev Prakash, Nishant Singh katiyar, Amrit pal singh, Anil kumar gangwar; Evaluation of Anti-arthritis potential of *Zingiber officinale* in experimental rats; *EJPMR*; 2016; 2(4); 305-8.
- 63) Funk JL, fyre JB, Ozarzo JN, Timmermann BN; Comparative effective of Two Gingerol containing *Z. officinale* on experimental Rheumatoid arthritis; *J Nat Prod*; 2009, 72; 403-407.
- 64) Dugenic SK, Arda N, Candan A; Some medical plants as immune stimulant for fish; *Journal of Ethnopharmacology*; 2003; 88(1); 99-106.
- 65) Puri A, Sahai R, Singh KL; Immuno stimulant activity of dry fruit and plant materials used in Indian Traditional Medicinal System for after child birth and invalids; *Journal of ethnopharmacology*; 2000; 71(1-2); 89-92.
- 66) Agarwal BB, Shishodia S; Molecular targets of dietary agents for prevention and therapy of Cancer; *Biochem Pharmacol* 5, 14; 71(10); 1397-1421.
- 67) Akhiani SP; Anti-diabetic activity of *Z. officinale* in streptozotocin induced type I Diabetic rats; *Jour of Pharmacol*, 2004 Jan, 56(1); 101-105.
- 68) Miri P, bae J and Lee DS; Anti-bacterial activity of (10) –gingerol and (12) gingerol isolated from ginger rhizome against peri odontal bacteria; *Phytotherapy Res*, 2008; 22; 1449-8.
- 69) Kamrul Islam, Asma Afroz, Rowsni, Md Murad Khan; Anti-microbial activity of ginger (*Z. officinal*) extract against food borne pathogenic bacteria; *International Journal of Science environment in Technology*, Vol .3, No 3, 2014, 867-871.

- 70) Ma J, Jin X, Yang L and Liu XL, : *Diaryl –heptanoides from the rhizomes of Zingiber officinale*, *Phytochemistry* 2004;65(8),1137-1143.
- 71) Verma SK, Singh J, Kamersra R and Bordia A; *Effect of Ginger in platelet aggregation in man;* *Indian Journal of Med Res.* 1993, 98; 240-242.
- 72) Zoheir A Damanhoury et al., *A review on therapeutic potential of P.nigrum ,the king of spices;* *Med Aromatic Plants* ;2014;3:161;
- 73) Bang JS, Oh da H, Choi HM, Sur BJ, Lim SJ, et al. (2009) *Anti-inflammatory and anti-arthritic effects of piperine in human interleukin 1beta-stimulated fibroblast-like synoviocytes and in rat arthritis models.* *Arthritis Res Ther* 11: R49. 23
- 74) Akbar et al., *Anti-oxidant activity of P.longum and P.nigrum fruits in Bangladesh /WJPS* 2014; 2(9) 931-941.
- 75) Sharma S, Kalia NP1, Suden P2, Chauhan PS2, Kumar M1, et al. (2014) *Protective efficacy of piperine against Mycobacterium tuberculosis. See comment in PubMed Commons below Tuberculosis (Edinb)* 94: 389-396.
- 76) Shamkuwar PB, Shahi SR, Jadhav ST (2012); *Evolution of Anti-diarrhoeal effect of black pepper;* *Asian Journal of Plant Science and Research* 2;48-53.
- 77) Nirwane AM Bapet AR (2012); *Effect of methanolic extract of Piper nigrum fruits in ethanol CC14 induced hepato toxicity in Wistar rats;* *Der pharmacia Lettre* 4; 195-802.
- 78) Mao Q, Huang Z, Zhong XM, Xianyf IP SP (2014); *Piperine reverses the effect of Corticosterone on behavior and hippocampal BDNF expression in mice.* 74;36-41.
- 79) Makhov P, Golovine K, canter D, Kutikov A, Simhon J (2012); *Co-administration of Piperine and docetaxel results in improved anti-tumour efficacy via inhibition of CYP3A4 activity,* 72; 661-667.
- 80) Dhanalakshmi et al., *Phytochemistry and pharmacology of P.longum-A systematic review;* *WJPPS* , Vol 6(1);2007
- 81) Chauhan khushbu, Solanki Rohinin, Pattel anal, Macwan carol; *Phytochemical and therapeutic potential of Piper longum .Linn;* *IJRAD*, 2011, 2(1), 157-161.
- 82) Chikkanna D, Dinesha Ramadas, Harsha R Karshyap Subhas Chandrappa Mundasada, Sandhosh Kumar ; *In Vitro Anti-Inflammatory activity of proteins isolated from pippali (Piper longum);* 2016; *RJLBPCS* 2(1); P.No;34.
- 83) Mumtha kumara, B K Ashok, B Ravishankar, Tarulata N Pandya, Rubinarayan Acharya; *Anti – inflammatory activity of two variety of Pippili (Piper longum.Linn);* *AYU*; 33(2); 2012; 307-310.
- 84) Sharma A and Singh R: *Screening of Anti –inflammatory activity of some indigenous drug of carrangeenan induced hind paw oedema in rats.* *Bull.Med.Res* 1980;2; 262.

- 85) Yende SR, Sannapuri VD, Vyawahare NS; Anti-Rheumatoid activity of aqueous extract of *P.longum* on Freund's adjuvant induced arthritis in Rat; *IJPSR* ;2010;I(9);129-133.
- 86) Subhash R, Yende , Vrushali D, Sannapuri , Niraj S ; Anti-Rheumatoid activity of Aqueous extract of *P.longum* on Freund's adjuvant induced arthritis in rats; *Int Jour of Pharm Science and Res* ;2010;8232 .1 (9-5);129-133.
- 87) Manavalan G et al, Chemical and some pharmacological studies on leaves of *Piper longum*. *Indian J pharm science* 1979;41:190.
- 88) Stoha JR , Xiaso PG , Bauer R (2001) constituents of Chinese piper spices and their inhibitory activity on prostaglandin & Leucotriens biosynthesis in vitro , *Journal of Ethnopharmacology* ,75;133-139.
- 89) Proity Nayeab Akbar, Ismet Ava Jahan; Anti-Oxidant activity of *P.longum* ad *P.nigrum* fruits grown in Bangladesh; *WPJS* 2014; 2(9); 931-941.
- 90) Mishra P (2010), Isolation, spectroscopic characterization and computational modeling of chemical constituents of *Piper longum* natural product . *International journal of Pharmaceutical science review and research* .2(2); 10-27.
- 91) Jagruthi A, Patel , Urvi S. Shah; Hepato protective activity of *P.longum* traditional milk extract carbon tetrachloride induced liver toxicity in Wistar albino rats; *Bol Latinoam caribe plant med* 8 (2);121-128;2009.
- 92) Dhirender Kaushik, Rubi rani, Pawan Kaushik, Disha Sacher and Jyoti yadav; In Vitro and In Vivo Anti-asthmatic studies of plant *Piper longum*. *Linn; International Journal of Pharmacology* ; Vol 8; Issue 3; 2012; 192-197.
- 93) Shanmugam manoharan, Simon sylvan, krishnamoorthi Vasudevan , Subramanian balakrishnan; Antihyperglycemic and Antilipidperoxidative effect of *P.longum* , dried fruits in Alloxan induced Diabetic Rats; *Journal of Biological Sciences*; ;2006; Vol 7; I(1); 161-168.
- 94) E.S. Sunila , G. Kuttan ; Immunomodulatory and Anti-tumor activity of *P.longum* Linn and Piperine ; *Journal of Ethnopharmacology* 90 (2004); 339-346.
- 95) Palatty A.S and Shivanna K.R. Pollination ecology of cardamom (*Elettaria cardamomum*) in the Western gats, India; *Journal of tropical Ecology*; 23(2007); 493-496.
- 96) Ravindran P.N, Shaylaja M, Babu K.N, False Cardamomum, 2002; *Medicinal and Aromatical plants industrial profiles*, 30(Cardamomum); 330-340.
- 97) Owoyele B V, Olaleye S B, Oke J M, Elegbe R A; ; Anti-inflammatory and Analgesic activity of *Nothospondias staudii* , *Nigerian Journal of Physiological Science*, 2004: 19(1-2); 102-106.
- 98) Radhi N, recta K.H, Madiratta P K, jain H, Cough C; 2003 ; Effect of oxytocin in formalin induced pain response in mice; *Indian Jour of Pharmacology*, 35; 128-136.

- 99) Nithya sermugapandian, Rubini R, martina V; Anti inflammatory activity of *Elettaria cardamomum* oil on Carrangeenan induced paw oedema using rats based on tumour necrosis factor α , Intereukin 6 and Interleukin 1 levels in serum; *AJPCR*; 2018; 11(2); 207-209.
- 100) Al.Zhhair H, l Sayesh B, Ameen HA, al Shoora H; Pharmacological studies of *Elettaria cardamomum* oil in animals; *Parmacologica research* 1996; 34; 79-82.
- 101) Amin F. Majdalawiesh and Ronald I Carr; Invitro investigations of the potential immunomodulatory and Anti-Cancer activity of black pepper (*Piper nigrum*) and *Cardamomum* (*Elettaria cardamomum*); *Journal of medicinal food*; Vol 13; 2; 2010; 1131.
- 102) Gurdip S, Kiran S, Marimuthu P, Isidorova vera 2008; Anti-oxidant and Anti-microbial activities of essential oil and varies oleoresins of *Elettaria cardamom* (seeds and pods); *Journal of the Science of Food and Agriculture*, 88(2); 280-289.
- 103) Nayar S, Nagar R, Gupta R; Antioxidant phenolics and flavonoids in common Indian foods; *J Assoc Physician India* ; 1998; 46(8); 708-710.
- 104) Kumar V.L, Shivkar Y.M, Wormicidal activity of latex of *Calotropis procera*; *Indian Journal of Pharmacology*; 2003; 35; 128-136.
- 105) Capasso F, Mascolo N, Autore G, Ramano V; Laxative and production of autocooids by rat colon; *J Pharm .Pharmacol* 13; 1986; 627-29.
- 106) Sripanid kulchai Bugorn , Wangpanch Varima, laupattarakasem Pisamai, Suwansakri jamsai, Jirakulsomchok Dusit; Diuretic effect of selected Thai , indigenous medicinal plants in Rats; *Journal of Ethnopharmacol*, 2001; 75; 185-190.
- 107) Rai N, Yadav S, Verma AK, Tiwari L and Sharma RK; A monographic profile on quality specifications for a herbal drug and spice of commerce – *Cuminum cyminum* Linn; *IJAHS* 2012; 1(1); 1-12.
- 108) Sangeetha P Bhat, Wassem Rizhvi , Anil kumar ; Effect of *C. cyminum* seeds extract on pain and inflammation; *Journal of Natural remedies*; Vol (14)(2) July 2014.
- 109) Bat SP, Rizvi W and Kumar A; Effect of *Cuminum cyminum* Linn seed extract on pain and inflammation; *Journal of Natural Remmedies*; 2014; 14(2); 186-192.
- 110) Purima N, Hossain N, Saha M; Anti-hyperglycemic and analgesic studies with methanol extract of mixture *C. cyminum* and *C. sativum* seeds; *J CPR*; 2015(7); 80-84.
- 111) Saini N Singh GK, Nagori BP; Spasmolytic potential of medicinal plants belonging to family *Umbelliferae*; *Int. Journal of Ris Ayurvedha*; 2014; 5; 74-83.
- 112) Allahghadri T, Rasooli I, Owlia P, Nadooshan MJ, Ghazanfari T, Teghizadesh M; Anti-microbial property , Anti-oxidant capacity and cytotoxicity of essential oil from Cumin produced in Iran *J Food Sci.* 2010; 75(2); H54-61.

- 113) Zahin M ,AqilF, Ahmad I ;*The invitro Anti-oxidant activity and total phenolic content of four Indian medicinal plants;IJPPS;1(2009);89-95.*
- 114) ChauhanPS ,SattiNK,Suri KA ; *Stimulatory effects of C.cuminum and flavonoid glycoside on cyclosporine A and restraint stress induced immune suppression in Swice albino mice .Chem Bio Interac ;2010;185;66-72.*
- 115) ShirkeSS,JadhavSR,JagtapAG,*Methanolic extract of C.cuminum inhibit overectomy induced bone loss in rats;Exp Bio Med;2008;233-1403*
- 116) Jagtap AG,Patil PB,*Anti-hyperglycemic activity and inhibition of advanced glycation and product formation by Cuminum cuminum in streptozotocin induced Diabetic rats;Food chemical Toxicol. 2010;48(8-9);2030-2036.*
- 117) Dhandapani S,Subramaniyan VR,Rajagopal S,Namashivayam N;*Hypolipidemic effect of Cuminum cuminum in Alloxon induced rats; Pharmacol Research 2002;46(3);251-255.*
- 118) Aruna K,Shivaramakrishnan VM;*Anticarcinogenic effect of some Indian plant products;Food and Chemical toxicology; 1992; 30(11); 953-956.*
- 119) Prana Rakshamirtha Sindhu, Thamarai noolagam, 2008
- 120) Yugi vaidhya chinthamani,2nd edition , Directorate of Indian medicine and Homeopathy, Chennai-106
- 121) K.S Murugesu mudhaliyar, Gunapadam part-1 mooligai vaguppu, 1st edition 9th reprint, Directorate of Indian medicine and Homeopathy, Chennai-106
- 122) K.N Kuppusamy mudhaliyar, Siddha Maruthuvam (Pothu) 1st edition 9th reprint, Directorate of Indian medicine and Homeopathy, Chennai-106