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ANTI-INFLAMMATORY ACTIVITY OF KIRANTHY OIL ACUTE MODEL – CARRAGEENIN INDUCED RAT PAW ODEMA

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ABSTRACT: *Kiranthy* is a common disorder affecting children is defined as an inflammation of the infantile skin, affecting the scalp and body. The available treatment of siddha have certain limitation, due to poor efficacies of compliance. The *Kiranthy* oil of Siddha drug is being used effectively to treat this disorder, but so far no scientific clinical trial had been done. Thus the researcher aimed to identify the anti- kiranthy activity of Kiranthy oil. This study was an observational, descriptive clinical trial. This is conducted as per the ethical clearance was approved by Ethical Review Committee Faculty of Medicine, University of Jaffna. The Anti- inflammatory activity of Kiranthy oil was performed by using the rat paw odema method. The oedema on the rat paw was induced with carrageenin (0.1ml of 1% suspension in 0.9% saline). The anti- inflammatory activity of kiranthy oil was carried out in wister albino rats. Ibuprofen was taken as the standard drug for the comparison of anti- inflammatory activity of the oil.. The oil was applied by spreading it on cotton wool and placing the wool with adhesive tape on the paw to which the carrageenin suspension was injected. Group III received Ibuprofen 100mg / kg and group IV served as solvent control (1%). After 30 minutes of drug administration, solution of 1% carrageenin was injected at a dose of 0.1 ml to the lateral malleolous of sub planter region of right hind paw of the rat. In the left paw same dose of normal saline was injected. The volume displacement of mercury was measured in both the paws (immersed up to the pre determined mark) before and after administration of carrageenin. The volume of paw was measured by using mercury plethysmograph. The measurement of paw volume was carried out at time intervals of 1hr, 2hr, 3hr, 4hr and 5hr. The percentage inhibition of the inflammation of Carrageenin is Induced artificial rat paw oedema was significantly ($P<0.01$) reduced by Ibuprofen. The oil exhibited peak oedema suppressant activity at the second hour of carrageenin injection like of Ibuprofen. The "Kiranthy oil" which was applied externally showed maximum significant ($P<0.01$) edema inhibitory activity.

Keywords: Kiranthy oil, Anti- inflammatory activity, carrageenin, Sri Lanka.

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1.INTRODUCTION

Kiranthy is a common disorder in child means an inflammation of the infantile skin affecting the scalp and body [1] .Balavagadam is the text book dealing with child care in Siddha system. It is the branch of medicine dealing with the pediatric diseases that are described symptomatically under common headings like *Karuvilthondrumnoigal* (Disease in utero), *Mantham* (Gastro intestinal disorders), *Kanam* (Respiratory disorders), Karappan (Skin Disorders) and are categorized according to the age of the infants[2]. The Siddha literature also deals with the traditional management through Siddha System of Medicine through strong basic principles and cultural background. The *senkiranthy "Pillai piranthaudanazuthu , Piragumidaruthanaikatti*" which means the cry of the neonate after birth following an apnoeic stage which can be correlated with the onset of apnoea followed by initial cry that favours the diagnosis of primary apnoea[3,35]. The second line "*Piragum idaruthankatti"* means the sudden cessation of voice or strider due to closure of glottis[4]. The third line "*Mella poonaikuralpondru*" logically equates the cry of the newborn as " Cat like cry" which is clearly stated in modern Pediatrics literature as weak cry or cat like cry of the new born due to esophageal atresia or tracho-oesophageal fistula which is said to be one of the causes of birth asphyxia[3], the fourth line "*Vidaamaneerm malam vayiroothy*"clearly states retention of urine and feces which may occur due to renal injury causing reduction in urine output and injury to GIT causing necrotizing entero-colitis to abdominal distension[4,35]. The fifth line "*Thulli kai kaalsivaeri*" describes the exaggerated movement followed by pink extremities. The reason behind this description may be due to the fact that an asphyxiated fetus behave like a strangulated individual and makes desperate exaggerated fetal movements [3,35]. This may also denote the vasomotor instability and peripheral circulatory sluggishness can be exposed by deep redness or purple lucidity in a crying infant. This discoloration may darken preceding a vigorous cry causing harmless acro-cyanosis of hands and feet[5]. The Subcutaneous fat necrosis which occurs following perinatal asphyxia causes hardened, erythematous lesions in arms and thighs sparing chest and abdomen. These lesions slowly soften in 6-8 weeks and completely regress after several months [4]. The line "*Summa Kidakumthanil"* states the lethargic state of infant in a crystal clear colloquial manner that is used in Tamil language. On comparing these lines with modern literature on birth asphyxia it found that the exaggerated fetal movements will intern followed by reduced or absent

physical movements terminally [3,35]. The final lines of *Senkiranthy* poem cautions the physicians as "*Kallam anna senkiranthy Thanaaikandukolle*" which stresses to suspect *senkiranthy* followed by all the above symptoms. Specialized neonatal care and follow up indicated for babies who establish effective breathing at 5 minutes [3]. The first line of *Karunkiranthy "Muzhangaa zhuthumulaiunna"* which means strong and vigorous cry followed by refusal to feeding that is described in modern pediatric text as excessive crying followed by lethargy and no effort in sucking and swallowing with pooling of secretions in oral cavity[3,35]. The next line *" Moorchaiyary mudal vethumbum*" means irritability, Jitteriness, fever that occurs in hypoxic ischemia. It is stated in the text book of neonatal care that high temperatures during usual care following hypoxic- ischemia were associated with increased risk of adverse outcome [6]. The third and fourth lines " *Kozhuganthirava vaivaratchi Kondeyatharam karuperum"* denotes inability to open the eyes and dehydrated lips with bluish discoloration. In severe stage of asphyxia changes in pupil of eyes, conjugate eye movement, reduced or absent of oculo-cephalic reflex and central cyanosis denoting central cyanosis [3]. The fifth line "*Azhungi alarum kuralkammum*" connote vigorous cry followed by inability to cry which is a silent feature denoting apnoeic attacks of HIE. This symptoms is followed by the line "*Athigama agavayiroothum*" that represents the distension of abdomen to greater extent due to oliguria, necrotizing enterocolitis, paralytic ileus and stasis. That are common gastro intestinal abnormalities which can cause excessive distension of abdomen [3]. The seventh line "*Puzhungum valikkum karunkiranthy*" means severe apnoeic stage with convulsions. It has to be noted here that Seizures can affect 50% of affected infants in HIE mostly within 6-12 hours after birth [3]. The last line *"Pollathenavum pugandranarey*" signifies that is a severe form of asphyxia as the persistence of neurologic abnormalities beyond seven days and usually associated with poor neuro motor outcome [3].According to modern literature birth asphyxia is caused due to prenatal antecedents like genetic factors, teratogenic agents and adverse early influences. The Siddha literature also lays emphasis on *Kiranthy* as *Karuvil thondrum noikal* which means prenatal cause. Birth asphyxia is associated with reduction in oxygen tension and accumulation of carbon-dioxide and fall in blood PH. This results in acidosis due to anaerobic utilization of glucose, production of lactic acid and accumulation of carbon-dioxide. These biochemical changes cause increase in pulmonary atrial pressure due to constriction of pulmonary arteriole resulting in reduced left heart and right to left shunt occurs. All of these physio chemical changes perpetuate asphyxia resulting in clinical, pathological, biochemical and metabolic changes. That affects many organ and systems like central nervous system, cardiovascular system, pulmonary, renal, adrenal, gastro intestinal tract, Skin and haemopoetic systems. The lines Healthy term infants have an outstanding ability to adapt to sudden episodes of reduced oxygen supply during labour. But situations that exceed fetal capacity sometimes can cause severe hypoxic episodes. The way in which an asphyxiated baby is managed at birth, determine the immediate morbidity and quality of life among survivors. Modern pediatric

literature states that about 25% with severe asphyxia are likely to develop Hypoxic ischemic encephalopathy (HIE) which cerebral ischemia resulting in multi organ dysfunction. This may dominate the clinical picture including seizures, hypotonia, poor feeding and a low level of consciousness, that usually lasts from 7-14 days with high risk of mortality [7]. Upon analyzing the ancient Siddha literature from the *Balavagadam* text, *Senkiranthy* refers to resolvable form of birth asphyxia. Moreover it is also said in Siddha literature that apart from few internal medicine kiranthy can be manageable by procedures like *Semmullikeerai* bath and Mukootu oil bath that can promote head cooling [4]. Several research works have also shown hypothermia to be a promising remedy for the management of hypoxic – ischemia. This age old procedure also lies in parallel with recent experimental modes of decreasing cerebral injury which involves selective head cooling cerebral hypothermia [8]. Moreover it is explicit that *Senkiranth*y (Birth asphyxia) is turn followed by *karunkiranthy* (HIE) which is described in the last line as " *pollathu*" which denotes the severity of illness. Recent research reveals that HIE followed by peri-natal asphyxia may result in long term neurologic squeals and mortality [9]. Hence from the above Interpretation of features of kiranthy it can be revealed that all the sign and symptoms of *Senkiranthy and Karunkiranthy*. That is mention in age old Siddha literature of Tamil culture correlates with that of modern pediatric complications of birth asphyxia and Hypoxic ischemic encephalopathy respectively. In Siddha system available treatment options have certain limitation, either due to poor efficacies or due to compliance issues. *Kiranthy* oil is being used effectively to treat this disorder but so far no scientific clinical trial had been done. Thus the researcher aimed to evaluate anti- kiranthy activity of *Kiranthy* oil. But this *Kiranthi* Oil is still in use. This is already observed by researcher and did clinical trial. Furthermore, these drugs are unable to prevent recurrence, which is common troublesome clinical problem. *"Kiranthy* Oil" is a polyhedral formulation indicated for *Kiranthy.* This oil contains 30 herbs [10].

Table 1: Ingredients of Kiranthy oil: [11].

S.No	Botanical Name	Measurements
1	*Zingibero fficinalis*	10g
2	*Piper nigrrum*	10g
3	*Costus speciosus*	10g
4	*curcuma longa*	10g
5	*Terminalia chebula*	10g
6	*Cuminum cyminum*	10g
7	*Nigella sativa*	10g
8	*Elattaria cardamonum*	10g
9	*Pongamiaglabra*	10g
10	*Mystrus caryophyllus*	10g
11	*Acorus calamus*	10g
12	*Glycyrrhiza glabra*	10g
13	*Santalum album,*	10g
14	*Coscinium fenestratum*	10g
15	*Carum copticum*	10g
16	*Quercus infectoria*	10g
17	*Myristica officinalis*	10g
18	*Eugenia caryophyllus*	10g
19	*Anethum graveolens*	10g
20	*Helicter esisora*	10g
21	*Areca catechu*	10g
22	*Alpinia galang*	10g
23	*Aquilaria agallocha*	10g
24	*Aquilaria agallocha*	10g
25	*Peucedanum graveolens*	10g
26	*Oldenlandia umbellate*	10g
27	*Premnato mentosa*	10g
28	*Hibiscus rosasinensis (Flowers)*	100
29	*Allium cepa*	250g
30	*Gingly oil*	1500ml

All are non-toxic herbs. The best quality of above ingredients were cleaned and purified initially with water. The ingredients were dried in shadow of sunlight. It is then powdered which is finally made into a oil consistency. The oil is filled and packed in air tight bottles. All are non-toxic herbs. The present study is to evaluate the Anti- inflammatory activity of "Kiranthy Oil"

2. MATERIALS AND METHODS

Experimental animals Colony inbred animal's strains of wistar rats of either sex weighing 200 - 250 g and swiss albino mice of either sex (18-25 g).Guinea pigs weighing 0.5 – 1.0 kg, either sex were used for the pharmacological and toxicological studies. The animals were kept under standard conditions 12:12 (day/night cycles) at 220 C room temperature, in polypropylene cages. The animals were fed on standard pellet diet (Hindustan Lever Pvt Ltd., Bangalore) and tap water ad libitum. The animals were housed for one week in polypropylene cages prior to the experiments to acclimatize to laboratory conditions.Anti-inflammatory studies Anti inflammatory activity Anti inflammatory activity was evaluated in both acute and chronic models of inflammation. Acute model a Carrageenin induced hind paw edema. The carrageenin assay procedure was carried out according to the method of Wintar. Oedema was induced by injecting 0.1 ml of 1% solution of carrageenin in saline into the plantar aponeurosis of the left hind paw of the rats. The extracts, reference drug and the control vehicle (distilled water) were administered 60 min prior to the injection of the carrageenin. The volumes of oedema of the injected and contra lateral paws were measured at +1, 3 and 5 hrs after induction of inflammation using a plethysmometer Bhatt and percentage of anti-inflammatory activity was calculated.

Experimental procedure

The following experimental procedure was followed to evaluate the repeated oral toxicity study of the Anti- inflammatory activity of *Kiranthy*oil was performed by using the rat paw odema method. The oedema in the rat paw was induced with carrageenin (0.1ml of 1% suspension in 0.9% saline). The anti- inflammatory activity of kiranthy oil was carried out in wister albino rats weighing 170-240 gms. Ibuprofen was taken as the standard drug for the comparison of anti- inflammatory activity of the oil. The animals were divided into four groups each consisting of 6 animals. Group I received kiranthy oil Emulsion 3 ml / kg (3ml) of oil in 1% carboxy methyl cellulose orally. Group II received the oil externally. The oil was applied by spreading it on cotton wool and placing the wool with adhesive tape on the paw to which the carrageenin suspension was injected. Group III received Ibuprofen 100mg / kg and group IV served as solvent control (1%). After 30 minutes of drug administration, solution of 1% carrageenin was injected at a dose of 0.1 ml to the lateral malleolous of sub planter region of right hind paw of the rat. To the left paw same dose of normal saline was injected. The volume displacement of mercury was measured in both, the paws (immersed up to the pre determined mark) before and after administration of carrageenin. The volume of paw was measured by using mercury plethysmograph. The measurement of paw volume was carried out at

time intervals of 1hr, 2hr, 3hr, 4hr and 5hr. the percentage inhibition of the inflammation was calculated and the data were tabulated.

Table 2: Anti- Inflammatory Activity of *Kiranthy* oil. Acute Model –Carragennin induced Rat Paw oedema

Group	Drug in Mg/Kg	1hr	2hr	3 hr	4hr	5hr
1	Kiranthy oil (3ml/mg)	0.30 +/- 0.01	0.35 +/0.02	0.43 +/0.03	0.52 +/0.03	0.61 +/0.03
2	Kiranthy oil(external)	0.21 +/- 0.01	0.29 +/0.02	0.39 +/0.01	0.50 +/0.01	0.54 +/0.02
3	Ibuprofen (100mg/kg)	0.32 +/- 0.02	0.34 +/0.02	0.42 +/0.03	0.50 +/0.04	0.55 +/0.03
4	Solvent Control	0.43 +/- 0.01	0.68 +/0.04	0.73 +/0.02	0.75 +/0.03	0.77 +/0.22

Significant reduction compared to control = Ibuprofen (P<0.01)

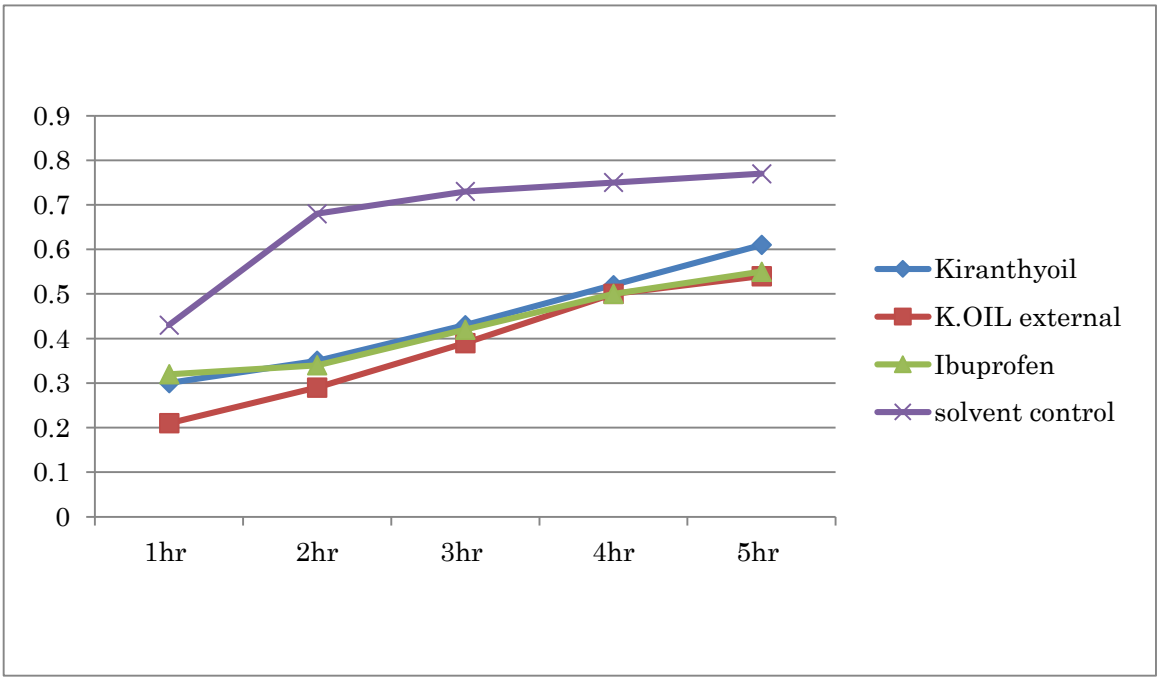

Fig 1: Graph showing the mean increase in paw volume

3. RESULTS AND DISCUSSION

"*Kiranthy* Oil" is a polyhedral formulation indicated for Kiranthy. This oil contains 30 herbs. Some herbs contain some active principles are anti-inflammatory, Immuno-modulator, Anti-tussive, Expectorant ect. Kim et al[12]reported that oral administration of piperine in different proportion to mice suppressed and reduced the infiltration of eosinophil, hyper responsiveness and inflammation due the suppression of the production of histamine, interleukin- 5, immunoglobulin E and interleukin-4[13]. The in vitro anti-inflammatory activities were evaluated on interleukin 1β stimulated fibroblast like synoviocytes obtained from rheumatoid arthritis, while antiarthritic

including analgesic activities was evaluated on carrageen an induced acute paw model of pain and arthritis in rats. In vitro immune modulatory activity of piperine was evaluated to enhance the efficacy of rifampicin in a murine model of Mycobacterium tuberculosis infection [14]. Mouse splenocytes were used to evaluate in-vitro immune modulation of piperine for 124 cytokine production, macrophage activation and lymphocyte proliferation. Piperine treated mouse splenocytes demonstrated an increase in the secretion of T-1 cytokines (IFN-γ and IL-2), increased macrophage activation and proliferation of T and B cell. Protective efficacy of piperine and rifampicin (1 mg/kg) combination against Mycobacterium tuberculosis was reported due to immune modulatory activity. Aqueous extract of *Terminalia chebula* (*T. chebula)* produced an increase in humeral antibody titre and delayed type hypersensitivity in mice. *T. chebula* found effective against the progression of advanced glycation end products-induced endothelia cell dysfunction [15]. Crude extract of *T. chebula* stimulated cell mediated immune response in experimental amoebic liver abscess in golden hamsters. The formulation showed highest cure rate of 73% at 800 mg/kg body weight in hepatic amoebiasis. In immune-modulation studies, humeral immunity was improved where T cell counts remained unaffected in the animals, but cell-mediated immune response was stimulated. Aqueous extract of dried fruit of T. chebula showed anti-inflammatory activity by inhibiting inducible nitric oxide synthesis[16]. Chebulagic acid extracted from tender fruit of T. Chebula significantly suppressed the onset and progression of collagen induced arthritis in mice. T. chebula in a polyherbal formulation (Aller-7) exhibited antiinflammatory effect against arthritis in rats[17]. Ethanolic extracts- Study confirms the immune modulatory activity of ripe T. Chebula fruits as evidenced. By increase in the concentration of antioxidant enzymes, GSH, T and B cells, the proliferation of which play important roles in immunity[18]. This phenomenon also enhances the concentration of melatonin in Pineal gland as well as the levels of cytokines. Gallic acid and chebulagic acid were isolated from the extract of a herbal medicine, kasha (*myrobalans:* the fruit of *Terminalia chebula*) as active principles that blocked the cytotoxic t lymphocyte (ctl)-mediated cytotoxicity[19]. *T. chebula*, ingredient of a polyherbal formulation (Aller-7), showed potent in vitro ant allergic activity [20]. Hydro-ethanol extract of T. chebula exhibit anti-histamine and anti-spasmodic in guinea pig ileum[21].Oral administration of an aqueous extract of fruit significantly suppressed histamine release from rat peritoneal mast cells 117 and also significantly increased production of tumour necrosis factor (TNF) by anti-dinitrophenyl IgE[22].The oral treatment of cumin stimulated the T cells (CD4 and CD8) T1 cytokines‟ expression in normal and cyclosporine, An induced immune suppressed animal [23].. Cumin also depleted T lymphocytes, decreased the elevated corticosterone levels and size of adrenal glands and increased the weight of thymus and spleen in stress induced immune suppressed mice [24]. The health modulating effects and immune modulatory properties of Cuminum were evaluated using flowcytometry and ELISA in normal and immunesuppressed animals [25]. Cuminum stimulated the T cells and Th1 cytokines expression in

normal animals. Swiss albino mice subjected to Cyclosporine. A induced immune suppression were dosed orally with *Cuminum cyminum* (25, 50, 100 and 200 mg/kg) on consecutive days. The results showed that administration significantly increased T cells (CD4 and CD8) count and Th1 predominant immune response in a dose dependent manner, suggesting immune modulatory activity through modulation of T lymphocytes expression[26]. In restraint stress induced immune suppressed animals, *Cuminum cyminum* countered the depleted T lymphocytes, decreased the elevated corticosterone levels and size of adrenal glands and increased the weight of thymus and spleen [27]. In vitro various essential oils, including cinnamon bark oil, used in the treatment of rheumatism and inflammation as well as some of their main constituents and phenolic compounds known for their irritant and pungent properties were screened for activity as inhibitors of prostaglandin bio synthesis. A combination of a prostaglandin synthesizing cyclo- oxygenase system from sheep seminal vesicles and an HPLC separation technique 136 for the metabolites of arachidonic acid was used as test system [27]. Cinnamon bark oil showed inhibitory cyclo-oxygenase activity. The active compound is probably eugenol (Wagner et al., 1986). In vivo dry ethanolic extract of *Cinnamomum zeylanicum* administered orally to rats at 400 mg/kg body weight showed an anti-inflammatory effect against chronic inflammation induced by cotton pellet granuloma indicating an anti-proliferative effect [28].The study concluded beneficial effect of eugenol administrated at 5 and 10 mg/kg per B.W. against lipopolysaccharide (LPS) induced acute lung injured (ALI) mice, for this purpose 0.5 mg/kg LPS was intra-tracheal infused[29]. Examination of lung tissues and broncho alveolar lavage fluid (BALF) suggested anti-inflammatory effect due to reduced production of pro-inflammatory cytokines. Additionally, in vitro studies revealed that clove oil polyphenol inhibits nuclear factor-kB (NFkB) activation in lipo poly saccharides initiated macrophages induced by inactivated cyclooxygenase activity (COX-2) and tumor necrosis factor (TNFa). Cyclooxygenase activity is prompted by LPS, cytokines and growth factors. During pulmonary inflammation in mouse, elevated TNF-a and neutropils were significantly reduced by eugenol at a dose of 160 mg /kg per body weight. It also protected against chemically induced dysfunction of macrophages and balanced the pro-inflammatory mediators. Mahapatra et al. investigated the in vitro protective effect of eugenol (1–20 μg/ml) against nicotine-induced (10 mm nicotine) cellular damage in mice peritoneal macrophages by analysing the radical generation, lipid, protein, DNA damage and endogenous anti-oxidant status. The results indicated that eugenol could be used as modulator of nicotine induced cellular damage and immuno-modulatory drug against nicotine toxicity[30]. The anti-inflammatory activity of *Myristica fragrans* was evaluated in carrageenin-induced edema in rats and acetic acid induced vascular permeability in mice. It was observed that the anti-inflammatory effect was approximately the same as that of Indomethacin.[31]. The results propose that myristicin present in mace is responsible for anti-inflammatory action.The anti-inflammatory property of myristicin might be due to inhibition of chemokines, cytokines, nitrous oxide and growth

factors in double stranded RNA (dsRNA) stimulated macrophages via the calcium pathway.[31]. The methanol extract from seeds of *Myristica fragrans* used for the treatment of inflammatory diseases also had inhibitory effects on nitric oxide (NO) production. Kim et al [12]. Investigated the effect of a hot water extract (DER app. 14:1) of clove to the immediate hypersensitivity in rats. The extract inhibited the compound 48/80-induced systemic anaphylaxis in rats with an IC50 of 31.25 mg/kg when administered intra-peritoneally. The extract also inhibited the local immunoglobulin-E mediated passive cutaneous anaphylactic reaction (IC50 = 17.78 mg/kg, i.v., IC50 = 19.81 mg/kg, p.o.). The extract also inhibited dose-dependently the induced histamine release from rat peritoneal mast cells. Clove essential oil increased the total white blood cell count and enhanced the delayed-type hyper sensitivity response in mice. Moreover, it restored cellular and humeral immune responses in cyclo phosphamide immune-suppressed mice in a dose-dependent manner. The immune stimulatory activity found in mice treated with clove essential oil is due to improvement in humeral and cell mediated immune response mechanisms [32].Kim et al [12]. induced asthma in Balb/c mice by ovalbumin sensitization. Piperine (4.5 and 2.25 mg/kg) was orally administered 5 times a week for 8 weeks and it was found that piperine- treated groups had suppressed eosinophil infiltration, allergic airway inflammation and airway hyper responsiveness and these occurred by suppression of the production of interleukin-4, interleukin-5, immunoglobulin E and histamine. Recent study documented the ability of a hexane fraction of dried ginger methanolic extract to suppress pro-inflammatory gene expression in LPS activated BV2 microglial cells, thus displaying anti neuro inflammatory activity. Gingerol and structurally related pungent principles of ginger including shogaol exert inhibitory effects on biosynthesis of prostaglandins and leukotrienes through suppression of prostaglandin synthesis or 5lipoxygenase. Several reports have addressed the anti-inflammatory effects of whole ginger extract on the production of NO/iNOS, PGE2/COX-2, TNF-a, IL-1b, and macrophage chemo-attractant protein-1 (MCP- 1) in murine macrophages, such as RAW264.7 cells and J774.1 cells, as well as human monocytes, U937 cells. The proposed mechanism behind 6shogaol inhibition of NO evolution in stimulated macrophages involves down regulation of inflammatory iNOS and COX-2 gene expression by inhibition of the activation of NF-jB, because NF-jB plays a critical role in the coordination of the expressions of pro-inflammatory enzymes. For the human being, the consumption of fresh ginger demonstrated promising results for the decrease of arthritis-induced. These results show that ginger could be used as anti-inflammatory agent and thus as anti-pain[33]. The beneficial effects of ginger in treating coughs, colds and flu is probably linked to immune-boosting properties of the plant.Few studies have examined the potential immune-modulatory activity of ginger. Non-specific immunity was increased in rainbow trout eating a diet containing 1% of a dried aqueous ginger extract for three weeks.Mice fed a 50% ethanolic ginger extract (25 mg/kg) for seven days had higher haemagglutination antibody titre and plaque-forming cell counts, consistent with improved humeral immunity. One in vitro study found

that ginger suppressed lymphocyte proliferation; this was mediated by decreases in IL-2 and IL- 10 production [34].The *Nigeella sativa*seeds are acrid, bitter, thermogenic aromatic, carminative, diuretic, emmunogogue, anodyne, antibacterial, anti - inflammatory, deodorant, appetizing, digestive, anthelmintic, constipating, sudorific, febrifuge, stimulant, galactagogue and expectorant. Child care in Siddha system. It is the branch of medicine dealing with the pediatric diseases that are *Karuvil thondrum noigal*. *Kiranthy* (Disease in utero), *Mantham* (Gastro intestinal disorders), *Kanam* (Respiratory disorders), Karappan (Skin Disorders) and are categorized according to the age of the infants. The Siddha literature also deals with the traditional management through Siddha system of Medicine through strong basic principles and cultural background. Upon analyzing the ancient Siddha literature from the *Balavagadam* text, *Senkiranthy* refers to resolvable form of birth asphyxia. Moreover it is explicit that *Senkiranthy (*Birth asphyxia) is turn followed by karunkiranthy (Hypoxic ischemic encephalopathy -(HIE).Currently available treatment options have certain limitation, either due to poor efficacies or due to compliance issues. *Kiranthy* oil is being used effectively to treat these disorders.

4. CONCLUSION

Carrageenin Induced artificial rat paw oedema was significantly ($P<0.01$) reduced by Ibuprofen. The" Kiranthy oil"exhibited peak edema suppressant activity at the second hour of carrageenin injection like of Ibuprofen. The oil which was applied externally showed maximum significant ($P<0.01$) of edema Inhibitory activity.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

The ethical guidelines of Medical Faculty University of Jaffna. The study protocol, case report forms, regulatory clearance documents, product related information and informed consent form (Tamil) were submitted to the Ethical Review Committee and approved by the same..

CONSENT FOR PUBLICATION

Not applicable.

AVAILABILITY OF DATA AND MATERIALS

The author confirms that the data supporting the findings of this research are available within the article.

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CONFLICT OF INTEREST

The authors have no conflict of interest.

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