ISSN: 0975-833X

Available online at http://www.journalcra.com

International Journal of Current Research
Vol. 8, Issue, 09, pp.38561-38566, September, 2016

INTERNATIONAL JOURNAL OF CURRENT RESEARCH

RESEARCH ARTICLE

ANALGESIC AND ANTI-INFLAMMATORY ACTIVITY OF SIDDHA DRUG VILLAIVER KUDINEER CHURANAM

[1,*]Sugunthan, S., [2]Shailaja, R. and [3]Mohamed Musthafa

[1] National Institute of Siddha, Tambaram Sanatorium, Chennai, India
[2] Velumailu Siddha Medical College, Sriperumbudur, India
[3]Government Siddha Medical College, Arumbakkam Chennai

ARTICLE INFO

Article History:
Received 22nd June, 2016
Received in revised form
10th July, 2016
Accepted 09th August, 2016
Published online 30th September, 2016

Key words:
Villaiver kudineer,
Siddha medicine,
Analgesic and
Anti-inflammatory activity.

ABSTRACT

Musculoskeletal diseases are an increasing healthcare issue globally, being the second leading cause of disability. For these ailments anti inflammatory, analgesics and corticosteroids are the drugs of choice which often results in many adverse effects like hepatotoxicity, nephrotoxicity, immuno-suppression. Traditional herbal medicines are being in use since time immemorial for these ailments. Villaiver Kudineer (VVK) is a poly herbal formulation from the traditional Siddha literature. It is traditionally being advocated for ailments related with musculo skeletal system. Hence, an attempt had been ventured to study the anti inflammatory and analgesic activity of VVK in laboratory animals. The animals were divided into four groups containing five animals each for analgesic activity and anti-inflammatory activity. Analgesic activity was done in acetic acid induced writhing method and anti-inflammatory activity was done in Carrageenan induced rat paw oedema method. Administration of VVK at the dose of 100 mg/kg and 200 mg/kg b.w produced analgesic and anti-inflammatory activity. Both the experiments had shown dose dependent activity against their standards Diclofenac sodium and Indomethacin for analgesic and anti-inflammatory activity respectively.

Citation: Sugunthan, S., Shailaja, R. and Mohamed Musthafa, 2016. "Analgesic and anti-inflammatory activity of Siddha drug Villaiver Kudineer Churanam" *International Journal of Current Research*, 8, (09), 38561-38566.

INTRODUCTION

Musculoskeletal diseases are an increasing healthcare issue globally, being the second leading cause of disability (Barbe Mary, 2013). They are the most frequent health complaint by European, United States and Asian Pacific workers (Hauke *et al*., 2011). The incidence rate for musculoskeletal diseases among the working population in 2014 was 31.9 newly diagnosed MSDs per 10,000 full-time workers **(**Bureau of Laborstatistics, 2016). They are widespread in many occupations, including those with heavy biomechanical load like construction and factory work, and those with lighter loads like office work (Sprigg *et al*., 2007). For these ailments anti inflammatory, analgesics and corticosteroids are the drugs of choice. Prolonged use of higher doses of NSAIDs produce analgesic nephropathy, salt and water retention and many of these drugs produce hepatotoxicity and nephrotoxicity with chronic usage (Padmaja udhyakumar, 2013).

Corresponding author: Sugunthan,
National Institute of Siddha, Tambaram Sanatorium, Chennai, India.

Hence an alternative drug with less or no adverse effect is the need of the hour. Today herbal medicines are in great demand in the developed world for primary health care due their efficacy, safety and lesser side effects (Kamboj, 2000). Siddha Medical System is a Dravidian based medicine with its roots in Tamil language speaking regions. The sources of medicines are utilized from herbal, herbo-mineral, metal and animal kingdom. Of these, the medicines of plant origin are given prime importance and given first hand to treat diseases (Thiagarajan, 1998). It enlists sixty four kinds of medicine including thirty two kinds of internal medicines and thirty two kinds of external medicines. *Villaiver Kudineer (VVK)* is a poly herbal formulation from the traditional *Siddha Varmam* literature. It is traditionally being advocated for ailments related with musculo skeletal system and sleep disorders (James, 2010). Though it is in clinical use for many years, no scientific studies have been carried out on this drug till date. Hence an attempt had been taken to study the anti inflammatory and analgesic activity of the drug in laboratory animals.

MATERIALS AND METHODS

Polyherbal drug - *VillaiVer Kudineer* (VVK)

VVK is a Siddha polyherbal formulation from the Varmam literature Varma odivu murivu sara soothiram-1500 consists of 40 herbs namely Roots of *Aegle marmelos,* Roots of *Ficus racemosa,* Roots of *Trianthema decandra, Centella asiatica,* Roots of *Spermacoce hispida,* Roots of *Ricinus communis, Lippia nodiflora*, *Adathoda vasica, Solanum nigrum, Coleus aromaticus, Sida rhombifolia, Trichosanthes cucumerina, Mukia maderaspatana, Abrus precatorius, Aerva lanata, Scoparia dulcis, Solanum torvum, Cassia occidentalis, Roots of Cardiospermum halicacabum, Phyllanthus fraternus, Pergularia daemia, Alangium salvifolium, Cassytha filiformis, Roots of Strychnos nux-vomica, Picrorrhiza kurroa, Costus speciosus, Brassica nigra, Trachyspermum ammi, Roots of Piper nigrum, Cedrus deodara, Phyllanthus emblica, Terminalia chebula, Terminalia bellerica, Mesua ferrua, Crocus sativus, Foeniculum vulgare, Aquilaria agallocha, Acorus calamus.*

All the ingredients were procured from Country drug shop R.N Rajan & Co, Chennai. The identification and authentication was done at Department of Pharmacognosy, Siddha Central Research Institute, Chennai and the voucher specimen was retained in the Herbarium. The ingredients were open air dried under the shade pulverized into a coarse powder with a wooden pestle and stored in an air tight container as per the Siddha sasthric literature.

Animal

Healthy swiss albino rats of both sexes weighing 220–240 g were taken for the study. Animals were housed at CL Baid Metha College of Pharmacy, Chennai, under standard laboratory conditions in a ventilated room whose temperature was maintained at $22^0(\pm 3^0)$ and were fed with conventional laboratory diets with an unlimited supply of drinking water.

Experimental design for analgesic activity

Grouping of animals

Animals are randomly grouped as four groups with 5 animals in each group. The control group received 10ml/kg distilled water orally. The reference group received Diclofenac Na 25mg/kg (dissolved in distilled water) p.o. Groups 3 and 4 were orally pretreated with sample 100mg and 200mg/kg doses respectively.

Chemicals and drugs

Acetic acid (1%), carrageenan (1%), distilled water, standard drugs (Diclofenac sodium and Indomethacin) were used in this study. All the chemicals and drugs used were of analytical grade.

ANALGESIC ACTIVITY

VVK was evaluated for the analgesic activity using acetic acid induced writhing method in mice (Calvino *et al*., 1984) (Calvino *et al.,* 1984). The chemical agent used for pain induction was acetic acid and was administered intra-peritoneally to the experimental animals. The standard drug used was diclofenac sodium. The drugs for test group and other groups were administered orally 30 min before i.p. injection of 0.6 % v/v 1ml/kg glacial acetic acid. Animals were observed individually and the number of writhes (extension of hind limb as a result of contraction of abdominal muscle). The number or writhes immediately after the injection of acetic acid was counted for 30 min. The reduction in the number of writhes of treated groups was compared to that of the control and standard groups. The reduction in writhing is indication of analgesic property.

Anti Inflammatory Activity

Acute inflammation was assessed by measuring right hind paw of rats which is produced by injecting 0.1 ml of 1% v/v carrageenan into the sub plantar region of animals in all the groups, according to the method described by Winter *et al*. (1962)

Grouping of animals

Group-I: Animals (control) received vehicle 30 min prior to administration of carrageenan injection.

Group-II: Animals (the standard) were given p.o. aqueous solution of Indomethacin (5 mg/kg), 30 min prior to administration of carrageenan injection.

Group-III: Animals received 100mg/kg Villaiver kudineer churanam 30 min prior to administration of carrageenan injection.

Group-IV: Animals received 200mg/kg of Villaiver kudineer churanam 30 min prior to administration of carrageenan injection.

The right hind paw volume was measured using plethysmograph in all the groups, immediately after 1hr of injection, again at 2, 3, and 4^{th} hour after drug treatment. The mean volume was compared with control group.

Drug treatment

Test drug was administered one hour prior to the carrageenan injection and paw volume was measured before and after injection of carrageenan at a fixed interval of 0, 30, 60,120 and 180 mins. Indomethacin (5mg/kg) p.o was used as standard drug and administered as CMC suspension by oral route.

Paw volume measurement

The change in hind paw volume was measured using plethysmometer and expressed as mean paw volume of the rats. The change in paw volume was measured as the difference between the final and initial paw volume. The anti-inflammatory activity of Villaiver kudineer churanam was determined by carrageenan induced paw edema method. Paw edema was induced by 0.1ml of 1% carrageenan in

physiological saline into the sub planar tissue of left hind paw of each rat. Samples (100mg, 200mg/kg) were administered orally 30 mins prior to carrageenan.

RESULTS

The results of analgesic and anti-inflammatory activity are presented in Tables 1 & 2.

Table 1. Results of analgesic activity of VVK

Treatment	Dose	No. of writhing (mean ±S.E.M)	Inhibition (%)
Control (Saline)	10 ml/kg	31.17±0.40	-
Diclofenac Na	25 mg/kg	5.33±0.49	82.89
Villaiver kudineer churanam	100 mg/kg	17.83±0.300	42.79
Villaiver kudineer churanam	200 mg/kg	11.67±0.76	62.56

No. of writhes are expressed as mean依SEM. n=5,*: P<0.05 significant, **: P<0.01

Table 2. Results of Anti inflammatory activity of VVK

Group	Dose mg/kg	Mean Paw volume ±SEM(ml) & %inhibiton			
		1hr	2hr	3hr	4hr
Control	Vehicle	1.333±0.0160	1.333 ±0.0176	1.440±0.0081	1.530±0.0129
Indomethacin	5mg/kg	1.310±0.0173	1.255±0.0170	1.255±0.0206	1.285±0.1312
Villaiver kudineer churanam	100mg/kg	1.295±0.0221	1.285±0.0221	1.273±0.0047	1.250±0.0500
Villaiver kudineer churanam	200mg/kg	1.290±0.0129	1.255±0.0095	1.215±0.0095	1.030±0.005

Analgesic activity

Acetic acid induced writhing method

In the present study, the analgesic activity of polyherbal formulation of *Villaiver Kudineer* was studied. The test was executed with four groups of animals. The test group was given two different doses of VVK 100 mg/kg and 200 mg/kg body weight and one group was given standard drug Diclofenac Sodium 25 mg/kg and another served as control which received saline 10 ml/kg. The results portray the dose dependent activity of VVK. The standard group showed high rate of inhibition than test groups. Among the test group advocated groups VVK at the dose levels of 200 mg/kg had shown higher inhibition than the group which received100 mg/kg. The results suggest that VVK is a moderate analgesic when compared to Diclofenac sodium. The results (mean value) are assured as a good Analgesic response of trial drug

Anti-inflammatory activity

Carrageenan induced rat paw oedema method

By the observed results from table -2 percentage of inhibition of oedema induced by villaiver kudineer churanam with two different doses was compared with the positive control drug indomethacin (5mg/kg) p.o. The results (mean value) are assured as a good inflammatory response of trial drug.

DISCUSSION

Acute inflammation has three components. They are increased blood flow, structural changes in microvasculature that allows plasma protein and leucocytes and emigration of leucocytes from microcirculation and their accumulation in the focus of injury. Inflammation is fundamentally a protective response which aims to get rid the organism of both the initial cause of cell injury (e.g., microbes, toxins) and the effects of such injury, necrotic cells and tissues. However inflammation and repair may be potentially harmful, for instance inflammatory reactions underlie the life threatening hypersensitivity reactions to insect bite, drugs and toxins as well as diseases like rheumatoid arthritis, atherosclerosis, lung fibrosis (Robbins, 1992).

Inflammation is regarded as main cause in the development of many human diseases including neurological, intestinal, cardiovascular, dental and renal disorders (Lumeng and Saltiel, 2011; Kuek *et al*., 2006; Grivennikov *et al*., 2010; Jenny, 2012; Hoque *et al*., 2012; Marchant *et al*., 2012; Wyss-Coray, 2002). It is linked with ageing, diabetes, obesity, pancreatitis, ankylosing spondylitis and cancer. The strategies to succumb inflammation will help to reduce inflammation. Hence the current study was undertaken to evaluate analgesic, anti-inflammatory activity of VVK in Swiss albino rats. This formulation consisting of 40 constituents was described in at least three varmam literatures and claimed to have efficacy in correcting Enbu & narambu kayam (bone and nerve lesions). This is the basis of selection of hitherto unexplored and tried composition. This formulation was supposed to be given as Kudineer (decoction) for body pain, generalized tiredness, head ache. It is evident from the review of literature, that most of the ingredients indicated in the formulation regulate vatham and pittam. This may be a factor for eradicating the symptoms. For instance, roots of *Aegle marmelos, Trianthema decandra, Ricinus communis, Lippia nodiflora, Coleus aromaticus, Sida rhombifolia, Glycyrrhiza glabra, Solanum torvum, Cardiospermum halicacabum, Pergularia daemia, Alangium salvifolium, Picrorrhiza kurroa, Solanum giganteum, Mesua ferrea, Acorus calamus* pacifies air flow (*vatham)* (Murukaesa mudhaliar, 2002). *Aegle marmelos, Adathoda vasica, Trichosanthes cucumerina, Melothria maderaspatana, Solanum torvum, Phyllanthus fraternus, Cassytha filiformis, Strychnos nux-vomica, Phyllanthus emblica, Terminalia bellirica* reduces heat or bile (Pittam) (Murukaesa mudhaliar, 2002). *Trachyspermum ammi, Pergularia daemia, Cedrus deodara, Solanum giganteum, Phyllanthus emblica, Crocus sativus, Piper longum* regulates phlegm (Murukaesa mudhaliar, 2002) component of the body. Further, most of the constituents of this drug have scientifically proven pharmacological activities like anti inflammatory, analgesic activity (Jothy,

2011; Zulfiker, 2010; Geetha lakshmi, 2010; Mathew George, 2009; Kumar, 2011; Manpreet Rana, 2012; Forestieri *et al*., 1996; Murad ali khan, 2009; Yung jia ju, 2012; Ravi Kanth and Diwan, 1999; João, 1998; Lokesh and Nikajoo, 2009; Badrul alam et al., 2011; Mallikadevi, 2012; Khadse *et al*., 2013; Rajesh *et al*., 2011; Sonia Maria De Farias Freire, 1993; Ej Ndebia, 2007; Kanakam Vijayabhaskar et al, 2013; Adnan, 2011; Ming-Hsing Huang, 2011; Hepcy Kalarani1, 2012; Ram sahu, 2009; Wu yin, 2003; Siddhendu bhattacharjee, 2013; Shruti Srivastava, 2013; Apurba Sarker, 2012; Mohammad and Zarshenas,2014; Aravind manohar, 1990; Jaijoy, 2010; Md. Safkath Ibne Jami, 2014; Arif-ullah Khan, 2010; Manoj kumar chahar, 2012; Hosseinzadeh, 2002; Sangeeta, 2014; Trupti and Chitre, 2008; Rupali Singh, 2011; Veethanayaki geetha,2003). This shows that Siddhas formulation which were written before many centuries and indicated for particular diseases goes in hand with all scientific parameters of testing. In the current study, the anti inflammatory and analgesic activity of VVK has been established. Analgesia is defined as a state of reduced awareness to pain. Analgesics are substances which decreases pain sensation by increasing pain threshold to painful stimulant. Painful reactions in the experimental animals can be produced by applying various stimulants such as radiant heat or by means of thermal, chemical or physical methods. The analgesic activity was studied through acetic acid induced writhing method. The chemical agent acetic acid is known to stimulate the production of noxious substances within the peritoneum resulting in writhing response (Bartolini *et al*., 1987). It is a simple, rapid and reliable model and especially suitable to evaluate peripheral type of analgesic action of a drug (Shinde *et al*., 1999). Administration of VVK extract showed significant analgesic activity on peripheral nervous system revealed through suppression of acetic acid induced writhing. Inflammation is a tissue reaction to infection or irritation due to a foreign substance. There are several mechanisms involved in inflammatory reactions such as release of histamine, bradykinin or prostaglandin. In animals, inflammatory reaction is readily produced in the form of paw oedema by the help of Carrageenan, Formalin or Histamine Carrageenan produces inflammation and oedema. The carrageenan induced rat paw oedema method is a test of acute inflammation, while cotton pellet granuloma is a model of chronic inflammation (Ismail, 1997). The polyherbal formulation was found to be significantly inhibiting the carrageenan–induced paw oedema, a test which has a significant predictive value for anti-inflammatory agents acting by inhibiting mediators of inflammation (Mossa, 1995). Extracts of VVK significantly inhibited the oedematous response over time at all doses assayed. However its greatest inhibition was obtained 3 h after carrageenan injection and this was also observed with the reference drug indomethacin. The mechanism behind these activities is poorly understood. However Phytochemical screening revealed the presence of Flavanoids, proteins, amino acids, alkaloids, tannins, hydroquinone derivatives in methanolic and acetone extract. Terpenes were estimated in chloroform extract which may be responsible for the activity (Sugunthan, 2015).

Conclusion

The study elicits the analgesic and anti-inflammatory activity of poly herbal formulation Villaiver Kudineer. It indicates relatively high anti-inflammatory activity than analgesic activity. The reason for this may be because of free radical scavenging activity of the drug and the presence of phytochemicals like flavanoids and alkaloids which may involve in suppression of activation of pro-inflammatory cytokines including TNFα, IL-1β and IFNγ and activity of cyclooxygenase enzymes. Therefore further studies are needed to bring out the molecular mechanism of the drug.

REFERENCES

Adnan, J.M. *et al*. 2011. Anti-inflammatory, antinociceptive and antioxidant activities of ethanolic extract of *Solanum nigrum L*. fruits, *Iraqi National Journal of Chemistry*, volume 42,252.

AHM Zulfiker *et al*. In vivo analgesic activity of ethanolic extracts of two medicinal plants - *Scoparia dulcis* L. and *Ficus racemosa* Linn. eISSN: 09748369,2010.

Apurba Sarker, *et al*. 2012. Anti-inflammatory activity of medicinal plants native to Bangladesh-Brassica: A review Journal of Applied Pharmaceutical Science 02 (02); 2012: 07-10

Aravind manohar *et al*, Anti inflammatory activity of piperine, *Jap.J.Med.Bio.Sci.*43, 1990.

Arif-ullah Khan, Antisecretory and analgesic activities of *Terminalia bellerica,* African Journal of Biotechnology Vol. 9 (18), pp. 2717-2719, 3 May, 2010Available online at http://www.academicjournals.org/AJB ISSN 1684–5315,2010 *Academic Journals*

Badru alam *et al*. Antioxidant, Anti-inflammatory and Anti-pyretic Activities of *Trichosanthes dioica* Roxb. Fruits, *Journal of pharmacology and toxicology*, vol 6, pg 443-53

Barbe, Mary, F. Gallagher, Sean, Massicotte, Vicky S., Tytell, Michael, Popoff, Steven N., Barr-Gillespie, Ann, E. 2013. The interaction of force and repetition on musculoskeletal and neural tissue response and sensorimotor behaviour in a rat model of work related musculoskeletal disorders, BMC Musculoskeletal disorders. 14: 303

Bartolini, A., Galli, A., Ghelardini, C. *et al*. 1987. "Antinociception induced by systemic administration of local anaesthetics depends on a central cholinergic mechanism," *British Journal of Pharmacology*, vol. 92, no. 4, pp. 711–721, 1987.

Calvino, B., L. Villanueva and D. Le Bars, 1984. The Heterotopic Effects of Visceral Pain: Behavioural and Electrophysiological Approaches in the Rat, Pain, 20 261-271

Forestieri, A. M., Monforte, M. T., Ragusa, S. and Trovato, A. 1996. Anti inflammatory Analgesic and Antipyretic Activity in Rodents of Plant Extracts used in African Medicine, PHYTOTHERAPY RESEARCH, VOL. 10,100-106 *Lippia nodiflora*

Geetha lakshmi *et al*, *Trianthema decandra* L: A review on its phytochemical and pharmacological profile, Research gate, Jan-2010

Grivennikov, S. I., Greten, F. R. and Karin, M. 2010. "Immunity, inflammation, and cancer," *Cell*, vol. 140, no. 6, pp. 883–899, 2010.

Hauke, Angelika; Flintrop, Julia; Brun, Emmanuelle; Rugulies, Reiner July 1, 2011. 'The impact of work related psychosocial stressors on the onset of musculoskeletal disorders in specific body regions: A review and meta-

analysis of 54 longitudinal studies', Work & Stress. 25 (3): 243-256

Hepcy Kalarani1*et al*, Antidiabetic, Analgesic and Anti-Inflammatory activity of Aqueous extracts of Stem and Leaves of *Alangium salvifolium* and *Pavonia* zeylanica, International Journal of Drug Development & Research October-December 2012 | Vol. 4 | Issue 4 | ISSN 0975.

Hoque, R., Malik, A., Gorelick, F. and Mehal, W. 2012. "The sterile inflammatory response in acute pancreatitis," *Pancreas*, vol. 41, no. 3, pp. 353–357.

Hosseinzadeh, H. *et al*. 2002. Antinociceptive and anti-inflammatory effects of Crocus sativus L. stigma and petal extracts in mice, BMC pharmacology, - biomedcentral.com

Ismail *et al*., 1997.

Jaijoy K *et al*, Anti-inflammatory and analgesic activities of the water extract from the fruit of *Phyllanthus emblica* Linn, *International Journal of Applied Research in Natural Products* Vol. 3 (2), pp. 28-35, June-July 2010

James, T.K., Varma odi murivu sara soothiram – 1500, May 2010, Sekar pathipagam. Chennai, Pg no.607

Jenny, N. S. 2012. "Inflammation in aging: cause, effect, or both?" *Discovery Medicine*, vol. 13, no. 73, pp. 451–460.

João B. Calixto et al, A Review of the Plants of the Genus Phyllanthus: *Their Chemistry, Pharmacology, and Therapeutic Potential,* plants of the genus *phyllanthus.*

Jothy *et al*. 2011. Evaluation of the antiinflammatory activity of *Aegle marmelos* (Bilwa) root, *Indian J Pharmacol. Jul* Aug; 43(4): 393–397

Kamboj, V. P. 2000. Herbal Medicine, *Current Science*, Vol 78, no. 1. 10 Jan.

Kanakam Vijayabhaskar*et al*, analgesic and anti-inflammatory activities of the extract of *Cassia occidentalis* Linn animal model, IJPC

Khadse C.D.1*, Kakde R.B.2, Chandewar A.V. Anti-Inflammatory Activity Of Methanol Extract FractionsOf Abrus precatorius Leaves, *International Journal of PharmTech Research: IJPRIF ISSN*: 0974-4304,Vol.5, No.3, pp 1426-1433, July-Sept 2013.

Kuek, A., Hazleman, B. L., Gaston, J. H. and Ostor, A. J. K. 2006. "Successful treatment of refractory polyarticular juvenile idiopathic arthritiswith rituximab," *Rheumatology*, vol. 45,no. 11,pp. 1448–1449.

Kumar, G.V.S., Evaluation of anti inflammatory and analgesic activity of spermacoce hispida in experimental models,ijprd.com

Lokesh, T. Nikajoo, 2009. Analgesic activity of aqueous and alcohol root extracts of pergularia daemia (forsk.) Chiov , *International Journal of Pharmacy and Pharmaceutical Sciences*, Vol. 1, Suppl 1, Nov.-Dec.

Lumeng, C. N. and Saltiel, A. R. 2011. 'Inflammatory links between obesity and metabolic disease', *The Journal of Clinical Investigation*, Vol 121, no. 6, pp 2111-2117.

Mallikadevi, T. *et al*. 2012. *In vitro* and *in vivo* anti-inflammatory activity of whole plant methanolic extract of *Mukia maderaspatana* (l.) m.roem. *International Journal of Pharmacy and Pharmaceutical Sciences*, ISSN- 0975-1491 Vol 4, Suppl 5.

Manoj kumar chahar *et al*. 2012. Antinociceptive and anti inflammatory activity of mesuol isolated from *Mesua ferrea* l. Seed oil, *International journal of current pharmaceutical research*, Issn- 0975-7066 vol 4, issue 1, 2012

Manpreet Rana *et al*, Ricinus communis L. – A Review. *International Journal of PharmTech Research CODEN (USA): IJPRIF* ISSN: 0974-4304 Vol.4, No.4, pp 1706-1711, Oct-Dec 2012

Marchant, D. J., Boyd, J. H., Lin, D. C., Granville, D. J., Garmaroudi, F. S. and McManus, B. M. 2012. "Inflammation in myocardial diseases," *Circulation Research*, vol. 110, no. 1, pp. 126–144.

Mathew George *et al*. Anti-allergic, anti-pruritic, and anti-inflammatory activities of *Centella asiatica* extracts, George *et al., Afr. J. Trad. CAM* (2009) 6 (4): 554 – 559

Md. Safkath Ibne Jami, Evaluation of Analgesic and Anti-Inflammatory Activities on Ethanolic Extract of *Terminalia chebula* Fruits in Experimental Animal Models.

Ming-Hsing Huang *et al*. 2011. Antioxidant and anti-inflammatory properties of Cardiospermum halicacabum and its reference compounds ex vivo and in vivo, *Journal of Ethnopharmacology,* Volume 133, Issue 2, 27 January, Pages 743–750

Mohammad M. Zarshenas, An Overview on Ajwain (*Trachyspermum ammi*) Pharmacological Effects; Modern and Traditional, *Journal of natural remedies*.

Mossa *et al*., 1995.

Murad ali khan *et al*, Anti-inflammatory, analgesic and antipyretic activities of *Physalis minima* Linn, *Journal of Enzyme Inhibition and Medicinal Chemistry*, Vol 24,2009.

Murukaesa mudhaliar KS, Gunapadam part-1, 2002, Dept of Indian Medicine and Homeopathy, Chennai.

Ndebia, E.J. *et al*, *Analgesic And Anti-Inflammatory Properties Of Aqueous Extract From Leaves of Solanum torvum (Solanaceae), African Journal of Traditional, Complementary and Alternative Medicines*

Occupational injuries/Illnesses and Fatal injuries profiles, Bureau of Labor statistics, United States Department of Labor, 2014. Retrieved 25 March 2016

Padmaja udhyakumar, Medical Pharmacology,4th edition, CBS publishers & distributors, Pg.no.263, 254

Rajesh R, Padmaa M, *Aerva lanata* (Linn.) Juss. ex Schult. – An overview, ijnpr, March 2011

Ram sahu *et al*, Screening of Anti pyretic and analgesic potential of ethanol extract of *Cassytha filiformis*, Research gate.

Ravi Kanth, V. and Diwan, P. V. 1999. Analgesic, Antiinflammatory and Hypoglycaemic Activities of *Sida cordifolia, Phytother. Res.* 13, 75–77.

Robbins, Cotran, Kumar, Pathologic Basis of Disease, 5th edition, chapter 3, page no. 51y

Rupali Singh et al, Pharmacological Properties and Ayurvedic Value of Indian Buch Plant (*Acorus calamus*): A Short Review, *Advances in Biological Research* 5 (3): 145-154, 2011.

Sangeeta P. Bhat, Effect of Cuminum cyminum L. Seed Extracts on Pain and Inflammation, *Journal of natural remedies*.

Shinde, U.A *et al*, 1999. Studies on the anti-inflammatory and analgesic activity of Cedrus deodara (Roxb.) Loud. wood oil , *Journal of Ethnopharmacology*, Volume 65, Issue 1, 1 April 1999, Pages 21–27

Shinde, U.A., Phadke, A. S., Nair, A.M., Mungantiwar, A. A. Dikshit, V. J. and Saraf, M.N. 1999. "Studies on the anti-inflammatory and analgesic activity of *Cedrus deodara* (Roxb.) Loud. wood oil," Journal of Ethnopharmacology, vol. 65, no. 1, pp. 21–27.

Shruti Srivastava, P. *et al*, 2013. Antiinflammatory, Analgesic and Antipyretic Activities of Aerial Parts of Costus speciosus Koen, *Indian J Pharm Sci.,* Jan-Feb; 75(1): 83–88.

Siddhendu bhattacharjee *et al*. 2013. A review on medicinally important species of picrorhiza, ijprbs, volume 2(4): 1-16.

Sonia Maria De Farias Freire, Analgesic and antiinflammatory properties of Scoparia dulcis L. Extracts and glutinol in rodents, *Phytotherapy Research*, Volume 7, Issue 6, pages 408–414,November/December 1993

Sprigg C. A., Stride C. B., Wall T. D., Holman D. J., Smith P. R. 2007. "Work characteristics, musculoskeletal disorders, and the mediating role of psychological strain: A study of call center employees". *Journal of Applied Psychology*, 92 (5): 1456–1466.

Sugunthan, S. 2015. A comparative clinical study to evaluate the efficacy of *"Villaiver Kudineer"* (internal) and *"Varmam therapy"* (external) in the treatment of *"Cegana vatham*" (cervical spondylosis), The Tamil Nadu Dr. MGR Medical University, Chennai, Dissertation submitted in 2015.

Thiagarajan, R. 1998. Gunapadam part 2 & 3;7th edition, Chennai, Dept of Indian Medicine and Homoeopathy.

Trupti. Chitre *et al*, Analgesic and anti-inflammatory activity of heartwood of *Aquilaria agallocha* in laboratory animals, Pharmacologyonline, 1: 288-298

Veethanayaki geetha *et al*, Analgesic activity of piper longum, IJEB, VOL 41.pg 649-52

Winter, C.A., Risley, E.A., Nuss, W. 1962. Carrageenan induced edema in hind paw of rats as an assay for antiinflammatory drugs. *Proc Soc Exp Biol Med*., 111:544-547.

Wu yin *et al*. 2003. Analgesic and anti-inflammatory properties of brucine and brucine N-oxide extracted from seeds of Strychnos nux-vomica**,** *Journal of Ethnopharmacology,* Volume 88, Issues 2–3, October, Pages 205–214

Wyss-Coray, T. and Rogers, J. 2012. "Inflammation in Alzheimer disease-a brief review of the basic science and clinical literature," *Cold Spring Harbor Perspectives in Medicine*, vol. 2, no. 1,Article ID a006346.

Yung jia ju *et al*, Analgesic and Antiinflammatory Activities of the Aqueous Extract from Plectranthus amboinicus (Lour.) Spreng. BothIn Vitro and In Vivo, Evidence-Based Complementary and Alternative Medicine, Volume 2012 (2012), Article ID 508137, 11 pages

****