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# A STUDY ON BIOCHEMICAL AND ANTIOXIDANT STATUS IN KEELVAYU NIVARANA CHURUNAM ON CARRAGEENAN INDUCED INFLAMMATORY RATS

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## ABSTRACT

Inflammation is a part of the complex biological response of vascular tissues to harmful stimuli, such as pathogens, damaged cells or irritants. It is characterized by redness, swollen joints, joint pain, its stiffness and loss of joint function. The pathogenesis of many diseases and different pathological conditions, including inflammation, is associated with excess production of reactive oxygen species (ROS). Inflammation is currently treated by NSAIDs. Unfortunately these drugs cause increased risk of blood clot resulting in heart attacks and strokes. Therefore, the developments of potent anti-inflammatory drugs from the natural products are now under considerations. Natural products are rich source for discovery of new drugs because of their chemical diversity. A natural product from medicinal plants plays a major role to cure many diseases associated with inflammation. The conventional drug available in the market to treat inflammation produces various side-effects. Due to these side-effects, there is need for the search of newer drugs with less or no side-effects. In the present study to investigate the anti-inflammatory activity of Keelvayu Nivarana Churunam on carrageenan induced inflammatory rats. The present study aimed to investigate the effects of the Keelvayu Nivarana Churunam on carrageenan induced inflammation, as well as on the endogenous levels of cell enzyme and non-enzyme antioxidants in rat. Over all, the experimental studies suggest that Keelvayu Nivarana Churunam possess anti-inflammatory activity.

**Keywords:** Keelvayu Nivarana Churunam, Inflammation, Carageenan, cotton pellet granuloma

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## INTRODUCTION

Inflammation is a biological reaction caused by the disruption of the tissue homeostasis, occurring in response to the presence of a biological, chemical, or physical agent in the body (Medzhitov, 2008). Some of these agents may be pathogens (bacteria, fungi, and viruses), trauma (shock or burns), toxic compounds (pollutants), as well as reactions of the immune system (hypersensitivity) (Ashley, Weil, & Nelson, 2012).

The symptoms of inflammation are characterized by pain, heat, redness, swelling and loss of function that result from dilation of the blood vessels leading to an increased blood supply and from increased intracellular spaces resulting in the movement of leukocytes, protein and fluids into the inflamed regions (Medzhitov, 2008; Parham, 2000)**.** This is very necessary to understand the role of chemical mediators of inflammation. These mediators are the substances released as plasma proteins, or that come from cells like mast cells, platelets, neutrophils and monocytes/macrophages. They are triggered by allergic or chemical irritation, injury and infections. These mediators, depending on the duration of injury determine the severity of inflammation and are termed pro-inflammatory fundamental factors. These substances bind to specific target receptors on the cells and may increase vascular permeability, promote neutrophil chemotaxis, stimulate smooth muscle contraction, increase direct enzymatic activity, induce pain and/or mediate oxidative damage (Coleman, 2002).

Natural compounds are now gaining more pharmacological attention as many unexplored plant products are showing a wide range of activities like anti-inflammatory and anti-cancer (Raghav *et al.*, 2007). It is estimated that about 80% of the world's population primarily those of developing countries rely on plant-derived medicines for their healthcare needs. In many developed countries popular use of traditional/complementary and alternative medicine is also expanded due to great concern about the adverse effects of modern drugs (World Health Organization, 2002).

It is estimated that approximately one quarter of the best selling drugs worldwide were natural products or derived from natural products (Balunas and Kinghorn, 2005). Nearly 25% of all prescribed drugs are derived from plants with or without further modification (Raskin and Ripoll, 2004) and still several pharmacologically active plant-derived compounds remain unexplored (Raskin *et al.,* 2002). The anti-inflammatory activities of plants are due to the secondary metabolites. These bioactive compounds consist of polyphenols, flavonoids, alkaloids, terpenoids, steroids, carotenoids, coumarins and curcumins (Saeed *et al.*, 2010). The conventional drug available in the market to treat inflammation produces various side-effects. Due to these side-effects, there is need for the search of newer drugs with less or no side-effects. In the present study to investigate the anti-inflammatory activity of Keelvayu Nivarana Churunam on carrageenan induced inflammatory rats.

## MATERIALS AND METHODS

**Plant material and preparation of extracts**:

The barks of *Withania sonifera*, *Simlax china* and roots of *Hemidimus indicus* and *Alpenia officinanum* were purchased from Traditional Medicinal shop, Thanjavur, Tamil Nadu, India. Healthy roots and barks were washed several times with distilled water to remove the traces of impurities from the roots. Shade dried at room temperature for about 10 days and ground in to fine powder using mechanical grinder. The powder was extracted with ethanol. A semi solid extract was obtained after complete elimination of alcohol under reduced pressure. In treatment *Withania sonifera*, *Simlax china*, *Hemidimus indicus* and *Alpenia officinanum* taken in the ratio of 1:1:1:0.5.

**Experimental Design:**

**Anti-inflammatory activity**

Anti-inflammatory activity was evaluated using the carrageenan induced rat paw oedema according to the technique of Winter *et al*. (1962). After 12hrs fast rats were divided into four groups of six each. Each animal was marked for identification and regularly monitoring. Group II served as normal group. Group II served as control group received carrageenan only. Group II, animals received ethanol extract of Keelvayu Nivarana Churunam at a dose of 500 mg/kg orally. Group V was orally administered compound indomethacin (3 mg/Kg body weight) as a standard drug. The animals were pretreated with the extract half an hour before the administration of carrageenan. Acute inflammation was produced by the subplantar administration of 0.1 ml of 1% carrageenan in normal saline in the right paw of the control and experimental rats. The paw was marked with in at the level of lateral malleous and immersed in mercury up to the mark and measured by mercury volume displacement methods. The paw volume was measured ½, 1, 1½ and 2 hours after injection of carrageenan to each group. The difference between the readings was taken as the volume of oedema and the percentage of anti-inflammatory activity was calculated. (Winter *et al*. 1962; Ghosh, 2008).

$$\% \text{ of inhibition rate} = \frac{V_c - V_t}{V_c} \times 100$$

Where $V_c$ is the oedema value of the control group and $V_t$ is the oedema value of treated groups.

## RESULTS AND DISCUSSION

**Effect of Keelvayu Nivarana Churunam on Carrageenan induced inflammatory rats.**

The levels of MDA content, activity of GPx and Catalase in plasma of control and experimental rats represent in table 1. The levels of MDA were significantly (P <0.05) increased in inflammatory rats when compared to control rats, whereas their level was significantly increased by Keelvayu Nivarana Churunam treatment. The expression of GPx and catalase were significantly decline in inflammatory rats compared to control, whereas animals treated with Keelvayu Nivarana Churunam showed a normal expression of GPx and catalase (Fig. 1) in plasma The levels of protein, albumin and globulin content in plasma of control and experimental rats represent in table 1. The levels of protein, albumin and globulin were significantly (P <0.05) decreased in inflammatory rats when compared to control rats, whereas their level was significantly increased by Keelvayu Nivarana Churunam treatment (Fig. 1).

Oxygen free radicals (OFR) have been implicated as mediators of tissue damage in rheumatoid arthritis. The involvement of free radicals in various inflammatory conditions like synovitis and RA are well documented (Merry *et al*., 1989; Halliwell *et al*., 1988). There is evidence that the inflammatory cells such as neutrophils, lymphocytes and macrophages are present in synovial fluid and produce large amounts of superoxide and hydrogen peroxide radicals (Halley and Cheesemen, 1993). The increase in plasma and tissue lipid peroxide levels in the arthritic control rats indicate that, the tissues are subjected to increased oxidative stress. The increased level in plasma but decreased level in liver lipid peroxide content may be due to the increased removal of lipid peroxides from liver into blood in arthritic animals. It was also proposed that the suppression of liver lipid peroxidation in the adjuvant treated rats is caused by a damage of the ascorbic acid-$Fe^{2+}$ dependent mechanism, which is responsible for lipid peroxidation in the liver (Roback, 1978).

The results of the present study indicate that, Keelvayu Nivarana Churunam decreased the lipid peroxide content in plasma by interception of the formation or by scavenging the active oxygen species. The lipid peroxide level in the drug treated group was considerably increased; showing that the removal of lipid peroxide from liver to blood was reduced. Superoxide dismutase can convert superoxide anion radical to hydrogen peroxide (Free, 1980). Also, this increase in enzyme activity may be due to protection against the extracellular oxygen free radicals (Marklund *et al*., 1987).

In the present study, administration of Keelvayu Nivarana Churunam to inflammatory rats caused a significant increase in GPx level. Catalase cleaves the hydrogen peroxide into water and oxygen. Glutathione peroxidase is also a detoxifying enzyme, changing the peroxides to water (Lawrence and Burk, 1976). The decrease in catalase activities was observed in rats, which may be due to the degradation of the enzyme by free radicals during detoxification process (Karatas *et al*., 2003). It was also proposed that, increased accumulation of $H_2O_2$ causes inhibition of GPx and catalase (Rister and Banchner, 1976). Keelvayu Nivarana Churunam administration produced a significant (P<0.05) increase in their activity, which enables scavenging of the free radicals produced during arthritic condition. The increase in superoxide radical activity may cause increased dismutation of superoxide anion radicals into hydrogen peroxide, but the hydrogen peroxide could not have been detoxified by the decreased levels of GPX and catalase. Thus, the hydrogen peroxide may possibly be converted into reactive oxygen species, which may be involved in the increased lipid peroxidation in adjuvant induced arthritic rats. All these abnormal alterations that occurred were found to be significantly normalized by reducing the Keelvayu Nivarana Churunam activity and enhancing the GPx and catalase activities by treating the arthritic rats with Keelvayu Nivarana Churunam. The results of present study also correlate with such findings (Selvarani and Viji Stella Bai, 2015; Ekambaram *et al*., 2011).

The inflammatory rats causes changes in plasma protein concentrations that are manifested as an increase in the globulin fraction and decrease in the albumin fraction (Cawthorne *et al*., 1976). It was also postulated that during inflammation, the mediators released, histamine, bradykinin and prostaglandins increase the permeability of vascular tissues to albumin leading to reduction in its serum levels (Kohn and Barchet, 1976). Thus treatment with Keelvayu Nivarana Churunam could significantly increase protein level in inflammatory rats which indicates that Keelvayu Nivarana Churunam might have a suppressive action on the mediators of inflammation. The protein synthesis is decreased in inflammatory rat was reported by Sanmugapriya *et al*. (2010).

## CONCULSION

Supplementation of Keelvayu Nivarana Churunam extract to inflammatory rats restored the altered above said parameters. The antioxidant activity of Keelvayu Nivarana Churunam extract may be due to the phytochemical constituents such as flavonoids, alkaloid, saponin etc. present in it.

**Table.1: Biochemical and antioxidant status in experimental rats**

| Parameters | Groups | | | |
|---|---|---|---|---|
| | I | II | III | IV |
| **MDA (nmol of MDA formed/L)** | 8.12±0.56 | 12.06±0.84 | 7.60±0.53 | 7.78±0.54 |
| **GPx (U/ml)** | 8.10±0.56 | 6.88±0.48 | 8.62±0.60 | 8.70±0.60 |
| **Catalase (U/ml)** | 5.94± 0.41 | 4.11±0.28 | 6.40±0.44 | 6.30±0.44 |
| **Total protein (g/dl)** | 6.85±0.47 | 6.04±0.42 | 7.42±0.51 | 7.24±0.50 |
| **Albumin (gm/dl)** | 4.12±0.28 | 4.50±0.31 | 4.16±0.29 | 4.20±0.29 |
| **Globulin (gm/dl)** | 2.73±0.19 | 1.54±0.10 | 3.26±0.22 | 3.04±0.21 |

Values are expressed as Mean± SD for six rats

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