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Anti Inflammatory Activity Of Amukkura Choornam On Carrageenan Induced Paw Oedema Model In Albino Wistarrats

Dinesh.P[1*], Dinesh.S.V[2], Nandhakumar N[3], Parthiban S[4], Krishnakumar P[5], Rathinavel[6]

[1]*Assistant Professor, Department Of Pharmaceutics, K.S.Rangasamy College Of Pharmacy, Tiruchencode, Tamil Nadu, INDIA.The Tamilnadu Dr.MGR Medical University, Chennai.*
[2]*QC Executive, Somerest Therapeutics Private Limited.*
[3]*Assistant Professor, Department of Pharmacology, K.S.Rangasamy College of Pharmacy, Tiruchengode, Tamil Nadu, India.*
[4,5]*Assistant Professor, Department of Pharmacology, K.S.Rangasamy College of Pharmacy, Tiruchengode, Tamil Nadu, India.*
[6]*Principal and Professor, Department of Pharmaceutical Chemistry, K.S.Rangasamy College of Pharmacy, Tiruchengode, Tamil Nadu, India*

ABSTRACT

Infammation is a complex biological response to harmful stimuli and is implicated in numerous acute and chronic disorders. Traditional Siddha medicine offers several herbal formulations with potential anti-inflammatory properties. Amukkara Choornam, a classical Siddha polyherbal formulation primarily containing Withania somnifera is traditionally used for inflammatory conditions.

Keywords: Infammation.

INTRODUCTION

The term “medicinal plant” include various types of plants used in herbalism ("herbology" or "herbal medicine"). It is the use of plants for medicinal purposes, and the study of such uses.Siddha medicine is one of the most ancient medical systems of India. Siddha is the mother medicine of ancient Tamils/Dravidians of peninsular South India. The word Siddha means established truth. The persons who were associated with establishing such a Siddha school of thought were known as Siddhars.According to the Siddha medicine system, diet and lifestyle play a major role in health and in curing diseases. This concept of the Siddha medicine is termed as pathiyam and apathiyam, which is essentially a rule based system with a list of “do’s and don’ts”.

When the normal equilibrium of the three humors – Vaadham, Pittham and Kapam – is disturbed, disease is caused. The factors assumed to affect this equilibrium are environment, climatic conditions, diet, physical activities, and stress. Under normal conditions, the ratio between Vaadham, Pittham, and Kapam are 4:2:1, respectively.

The relative unawareness and ignorance of Siddha in the West is due to various causes. First, most of the Siddha literature is still in Tamil. Second, when Western scholars like Max Muller were provided with translated versions of Sanskrit literature, including that of Ayurveda, no such effort seems to have been taken to introduce Tamil works to Western scholars. Thousands of Siddha literature still remains in the form of palm leaf manuscripts. Of late, Siddha is slowly gaining recognition in the world of complementary/alternative medicine. [1,2]

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INFLAMMATION

Inflammation is a local response of living mammalian tissues to injury. It is a body defense reaction in order to eliminate or limit the spread of injurious agent. There are various components to an inflammatory reaction that can contribute to the associated symptoms and tissue injury. Edema, leukocyte infiltration, and granuloma formation represent such components of inflammation.

Inflammation is the body's response against invading pathogens, which is typically characterized by redness, swelling, pain, and heat. Several reports have provided evidence that inflammation is involved in the pathogenesis of many diseases including aging, cancer,cardiovascular dysfunction, and other life-threatening and debilitating disorders.

When inflammation happens, chemicals from the body's white blood cells enter the blood or tissues to protect body from invaders. This raises the blood flow to the area of injury or infection. It can cause redness and warmth. Some of the chemicals cause fluid to leak into your tissues, resulting in swelling. This protective process may trigger nerves and cause pain. Higher numbers of white blood cells and the things they make inside your joints cause irritation, swelling of the joint lining, and loss of cartilage (cushions at the end of bones) over time.

Acute inflammation is a process that involved the overproduction of free radicals, activation of a complex enzymes, and release of several inflammatory and pro-inflammatory mediators. The carrageenan-induced paw edema is a well-known acute model of inflammation that is widely used for screening novel anti-inflammatory compounds. Carrageenan injection into the subplanar surface of rat paw induced a biphasic edema.

Inflammation may be a part of the complicated natural reaction of vascular tissues to volatile stimuli which incorporates pathogens, damaged cells, or irritants. it's the woodland all surrender cease hand over end cease results of concerted participation of a huge sort of vasoactive, chemotactic and proliferative factors at specific levels and there are numerous desires for anti inflammatory action. It's one among the primary and most vital responses of the immune tool after contamination. Inflammation, a important evil, furthermore mentioned as a sided sword, may be a protective attempt from the organism to get rid of the injurious stimuli and to impress the restoration method furthermore. Thus, the modern -day-day destruction of the tissue may moreover intransigent, the survival of the organism. Chronic infection moreover can motive ailments, which includes pollinosis, atherosclerosis, and atrophic arthritis, etc. The classic signs and symptoms of infection have prolonged been recognized; the tissues grow to be red, swollen, tender, or painful, there could also be nearby warmth and therefore the patient could also be febrile. However, at an equivalent time because the contamination device goes away and continues to simmer in our frame for a protracted period and starts offevolved to become detrimental, it's called persistent inflammation. Inflammation could also be categorized specifically as Chronic and Acute inflammatory. [1,3]

TYPES OF INFLAMMATION

ACUTE INFLAMMATION

CHRONIC INFLAMMATION

Acute Inflammation

Acute inflammation is typically caused by injuries, like a sprained ankle, or by illnesses, like bacterial infections and common viruses. The acute inflammation process happens quickly and can be severe. If you've ever broken a bone or cut yourself, you've seen inflammation in action.

Common signs of inflammation following an injury include:

- Redness
- Pain and tenderness
- Swelling, bumps, or puffiness
- Warmth at the injury site
- Bruising
- Stiffness

- Loss of mobility

Depending on the cause and severity of the wound, acute inflammation can last anywhere from a few days to a few months.

Sometimes acute inflammation is localized to one area and sometimes it is systemic, as with a viral infection. When your body identifies a harmful invader, such as a bacteria or virus, it initiates a whole-body immune response to fight it off.

White blood cells trigger the release of several inflammatory chemicals. This type of acute inflammation causes you to feel sick and exhausted, as your body puts all of its energy toward fighting off infection.

Symptoms of this type of inflammation include:

- Fever
- Nausea
- Lethargy
- Sleepiness
- Irritability
- Runny nose
- Sore throat
- Stuffy nose
- Headache

Signs and symptoms may be present for a few days or weeks, or possibly longer in more serious causes.

Some acute infections are caused by more localized inflammation. Like most conditions caused by inflammation, they tend to end in "itis."

Examples include:

- Acute bronchitis
- Tonsillitis
- Acute appendicitis
- Sinusitis
- Infective meningitis
- Chronic Inflammation

Chronic, long-term inflammation can last for years or even an entire lifetime. It often begins when there is no injury or illness present, and it lasts far longer than it should.

Scientists don't know why chronic inflammation happens, as it doesn't seem to serve a purpose like acute inflammation. But they do know that over time it can cause major changes to the body's tissues, organs, and cells.

Research has found an association between chronic inflammation and a wide variety of serious conditions. Keep in mind that there is a major difference between two things being *associated* and one thing *causing* another.

Chronic inflammation is one of several contributing factors in disease onset and progression. So far, the strongest link between chronic inflammation and disease has been seen in type 2 diabetes and heart disease.

Other conditions associated with chronic inflammation include:

- High blood pressure
- High cholesterol
- Kidney disease
- Various types of cancer
- Depression
- Neurodegenerative disorders
- Autoimmune disorders

Chronic inflammation often progresses quietly, with few independent symptoms. Despite its subtlety, chronic inflammation represents a major threat to the

health and longevity of a large population of individuals.

Researchers have identified several common causes of chronic systemic inflammation, many of which are closely associated with modern living and aging.

Causes of chronic inflammation include:

Physical inactivity: An anti-inflammatory chemical process occurs in the bloodstream when your muscles are in motion. People who don't meet the minimum activity recommendations for optimal health (about half of all American adults) have an increased risk of age-related diseases.

Obesity: Fat tissue, especially visceral fat (a deep layer of fat around the abdominal organs), actually produces pro-inflammatory chemicals.

Diet: Diets high in saturated fat, trans fat, and refined sugar are associated with increased inflammation, especially in overweight people.

Smoking: Smoking cigarettes lowers the production of anti-inflammatory molecules and increases inflammation.

Low sex hormones: Sex hormones like estrogen and testosterone suppress inflammation. Lower levels of these hormones, common in advanced age, increase the risk of inflammatory diseases.

Stress: Psychological stress is associated with increased inflammation.

Sleep disorders: People with irregular sleep schedules have more markers of inflammation than people who get a regular eight hours a night.

Age: Research shows that chronic inflammation gets worse as we age. [4]

TREATMENT

Treatment for inflammatory disease aims to reduce inflammation through out the body to prevent serious complication.

Acute Inflammation

For general inflammation, your healthcare provider may recommend:

Nonsteroidal anti-inflammatory drugs (NSAIDs): NSAIDs are usually the first-line treatment for short-term pain and inflammation. Most of these medications are available over-the-counter, including aspirin, ibuprofen, and naproxen. Your healthcare provider can also prescribe prescription-strength NSAIDs for certain inflammatory conditions.

Corticosteroids: This is a type of steroid commonly used to treat swelling and inflammation. Corticosteroids are available in pill form and as injections. These drugs are only prescribed for short periods, since they are known to cause serious side effects.

Topical medications: Topicals, including analgesics and steroids, can help with acute and chronic pain and inflammation of the skin and joints without the side effects of oral treatments. They are also helpful for managing long-term inflammation when they contain an NSAID, such as diclofenac or ibuprofen.

Chronic Inflammation

In addition to treating joint pain and inflammation, medications for inflammatory diseases can help to prevent or minimize disease progression. Medications may include:

Disease-modifying anti-rheumatic drugs (DMARDs), including Rheumatrex (methotrexate),Azulfidine (sulfasalazine), and Arava (leflunomide)

Biological drugs, such as Enbrel (etanercept), Humira (adalimumab), and Orencia (abatacept)

Anti-malarial drugs, such as hydroxychloroquine Statins

Diabetes medications

Because many medications used to treat inflammatory diseases can cause harsh side effects, it is important to see your healthcare provider regularly.[1]

MATERIALAND METHODS

Experimental Animals

Animals Male albino rats of Wistar strain approximately weighing 180-220 were used in this study. The animals were housed in spacious polypropylene cages bedded with rice husk. The animal room was well ventilated and maintained under standard experimental conditions (Temperature 27±2 °C and 12 hours light / dark cycle) throughout the experimental period. All the animals were fed with standard pellet diet and water ad libitum. They were acclimatization to the environment for 1 week prior to experimental use. [5]

DRUG: AMUKKARA CHOORNAM

Amukkara choornam (AC) is a popular polyherbal siddha formulation, composed of herbs and spices, used for gastric ulcer, spleen enlargement, leucorrhea, hiccup, anemia, tuberculosis, and kappa diseases. But there is no scientific evidence for its antiulcer activity. The presence of ulcer protective plant materials in this formulation has been investigated. Documented reports suggest that eugenol, piperine, trans-caryophyllene, and aferine A are marker components of AC having antiulcer activity through various mechanisms. Several chromatographic methods have been reported for the quantification of these bioactive principles in various crude drugs either as single or multicomponent analyses. However, there is no evidence for simultaneous estimation of these active compounds in any crude drug or any polyherbal formulation. There is evidence concerning the participation of reactive oxygen species in the etiology and pathophysiology of human diseases such as neurodegenerative disorders, inflammation, viral infections, autoimmune pathologies, and digestive system disorders gastrointestinal inflammation and gastric ulcer). A great number of spices and aromatic herbs contain chemical compounds exhibiting antioxidant properties. These properties are attributed to a variety of active phytochemicals including vitamins, carotenoids, terpenoids, alkaloids, flavonoids, lignans, simple phenols, and phenolic acids. The present study thus aimed to standardize the AC chemically for the content of anti-inflammatory activity.

INGREDIENTS OF AMUKKURA CHOORANAM

Nattu Amukkara Kizhangu – Ashwagandha – Withania Somnifera-25.2%

Chukku – Sonth (ginger) – Zingiber Officinale-12.6%

Thippili – Pippali (Long Pepper) – Piper Longum -6.3%

Milagu – Kali Mirch (Black Pepper) – Piper Nigrum -3.15%

Elam – Elaichi (Cardamom) – Elettaria Cardamomum 1.57%

Sirunagapoo – Dalchini (Cinnamon) – Cinnamomum Verum-0.79%

Kirambu – Laung (Clove) – Syzygium Aromaticum-0.39%

Sakkarai – Khand (Sugar) – Saccharum Officinarum-50%

Reference: AGATHIYAR VAIDHYA RATHTHINA CHURUKKAM

DOSAGE AND ADMINISTRATION

The general dosage of Amukkara Choornam is as follows.

Children -500 to 1000 mg,

Adults -1 to 2 grams

Maximum Possible Dosage:

6 grams Per Day (in divided doses)

Twice a day with appropriate adjuvant

Best Time to Take: Before Meal or After Meal

Adjuvants: Milk, Honey & Ghee

Calculation of Dose for animal study is by using the FDA Guideliness

ANTI INFLAMMATORY ACTIVITY

Carrageenan induced rat paw oedema

Anti-inflammatory activity was evaluated using the carrageenan induced rat paW oedema according to the technique of Winter et al., (1962). After 12 hrs fast rats were divided into five groups of six each. Each animal was marked for identification and regularly monitoring. Group I served as control group received Carrageenan only. Group II and III animals received Amukkura chooranam at a dose of 100 and 200 mg/kg orally. Group IV was dexamethasone (3 mg/Kg body weight) as a standard drug administered intraperitonealy. The animals were pretreated with the extract half an hour before the administration of carrageenan.

Acute inflammation was produced by the sub plantar 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 1, 2 and 3 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.

Percentage inhibition = $Vc - Vt\ /Vc \times 100$

Where Vc is the increased paw volume of disease control group and Vt is the increased paw volume of treated group.[6]

RESULTS AND DISCUSSION

Increase in paw volume

SN.	CARRAGENAN	DEXAMETHASONE	100mg Of amukkura choornam)	200mgOf (amukkura choornam)
1	0.73	0.125	0.334	0.222
2	0.64	0.132	0.324	0.234
3	0.63	0.134	0.329	0.229
4	0.72	0.122	0.319	0.226
5	0.68	0.129	0.345	0.232
6	0.66	0.128	0.368	0.231

Percentage inhibition of paw volume

SN.	CARRAGENAN	DEXAMETHASONE	100mg Of (amukkura choornam)	200mg Of (amukkura choornam)
1	0	82.8	54.2	69.5
2	0	79.3	49.3	63.4
3	0	78.7	47.7	63.6
4	0	88.0	55.6	68.6
5	0	81.0	49.2	65.8
6	0	80.6	44.2	65
Average		81.6	50.08	66.01

Carrageenan induced inflammation is a biphasic phenomenon and is a useful model to detect oral actions of anti inflammatory agents. In the present study, the effect of amukkura choornam in

carrageenan induced paw oedema was investigated. The rat's foot pad becomes oedemateous after injection of carrageenan. Administration of amukkura choornam reduces the paw oedema to inflammatory rats at a dose of 100 mg and 200 mg/kg of body weight. The dose dependent decrease of paw oedema was observed and the reference drug dexamethasone (3 mg/kgbody weight) exhibited significant decrease in paw volume was compared with the treated groups.Among the two doses, the 200mg/kg (body weight) of amukkura choornam possess potential anti-inflammatory activity at 3rd hour of carrageenan administration and it was nearest to the standard.Inflammation has been identified as a reaction of living tissues to damage and it is known to include a complex variety of enzyme activation, mediator release, and extravasations of fluid, cell migration, tissue breakdown and repair [5]. The most extensively utilized primary test to display novel anti-inflammatory agents calculate the capability of a compound to decrease local oedema induced in the right paw by injection of an irritant agent [6]. Carrageenan-induced paw oedema in rats is a classical model of acute inflammation and commonly used in screening of drugs [9]. Growth of oedema in the paw of the rats after injection of carrageenan is a biphasic event. The early phase (1-2 h) of the carrageenan model is thought to be mostly mediated by histamine, serotonin and improved synthesis of prostaglandin in the injured tissue surroundings. The late phase (3-4 h) has been demonstrated to be sustained by prostaglandin release and mediated by bradykinins, leukotrienes, polymorphonuclear cells and prostaglandins produced by tissue macrophages. Cyclooxygenase plays a significant role in conversion of arachidonic acid into prostaglandins in the later inflammation phase in the carrageenan-induced oedema model which enzyme is considered to be a recognized target for a number of NSAIDs like aspirin.

The anti-inflammatory activity of amukkura choornam against carrageenan-induced paw oedema in rat revealed time and dose-dependent inhibition. The results showed that the amukkura choornam at the dose of 100 mg/kg exhibit 50.08% reduction in the paw volume and 66.01% reduction in paw volume at 66.01%. The standard drug dexamethasone exhibits the reduction in volume up to 81.6% at the dose of 3mg/kg.

CONCLUSION

The present study on amukkura choornam has significant anti- inflammatory properties and it justifies the traditional use of this amukkura choornam in the treatment of inflammation. This suggests that amukkura choornam can be potentially used as a source of natural anti-inflammatory agent.

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