International Journal of Advances in Engineering and Management (IJAEM)
Volume 5, Issue 1 Jan. 2023, pp: 318-333 www.ijaem.net ISSN: 2395-5252

A Review: Herbal Ointment for Arthritis

Payal R. Shinde
Dr.Vedprakash Patil Pharmacy College, Aurangabad.

Date of Submission: 01-01-2023 Date of Acceptance: 10-01-2023

ABSTRACT:
Rheumatoid arthritis is a general inflammatory disorder touching about 1.3% of the grown-up census of the world. Over the last two decades, a significant development has been done in the thoughtfulness of RA pathophysiology, best outcomes, and successful treatment strategy, and the credit of the significance of diagnostic agents and treating RA near the beginning. Earlier than novel treatments were obtained, RA caused notable incapability and deaths. At present, it is customary that principal diagnostic agents and therapy are significant and helpful. Development in the treatment of RA made it likely to manipulate signs in inflammatory arthritis. The early hour diagnosis and treatment of RA can prevent or reduce the progression of joint erosion to about 90% of patients; by this means irreversible disability can be prevented. In advance and more effective treatment significantly improves the prognosis of RA. The advancement of novel instruments to assess disease activity and recognize remission has brought about innovative treatment strategies to inhibit RA ahead of joint damage forever. The pharmacological therapy consists of the nonsteroidal anti-inflammatory drug (NSAIDs), glucocorticoids (GC); disease-modifying antirheumatic drugs (DMARDs), biological drugs is of two types: 1) Monoclonal antibodies, 2) bisphosphonate agents. The price of a few treatments is considerable, but their use has come down with the advancement of biosimilars. A target-treatment strategy aims to decrease disease activity by around 50% in three months and achieve a reduction of disease succession in six months, with continuous therapy if needed, which can prevent RA-related disability. There is a restoration of attention in plant products because of the present belief that green medicine is safer and more trustworthy than expensive synthetic drugs. The outlook is towards the synchronized multidimensional research intended to correlate botanical and phytochemical activities to exact anti-arthritic activity is achieved.

KEYWORDS: herb; osteoarthritis; rheumatoid arthritis; pain; inflammation.

I. INTRODUCTION:

Arthritis is a common health issue that affects millions of people in the United States[(1)]. Patients suffering from arthritis struggle with severe joint pain and nearly half of all adults with arthritis experience persistent pain[(1,2).] More than 100 types of arthritis have been identified [(3)]. Two of the most common types are osteoarthritis and rheumatoid arthritis. Both osteoarthritis and rheumatoid arthritis impair joint structure and function but differ in symptoms, pathophysiology, and treatment.

Osteoarthritis, also known as degenerative joint disease, is the most common form of arthritis [(4)]. OA is a biomechanical and inflammatory disease influenced by several factors such as mechanical and oxidative stress, injury, age, obesity, and metabolic disease [(5)]. OA is characterized by joint cartilage degeneration, changes in the underlying bone, and synovitis [(6).] Pro-inflammatory and pro-catabolic mediators are found localized in synovial fluid and hydrolytic enzymes, such as matrix metalloproteinases (MMPs), are associated with cartilage degeneration. Extracellular matrix breakdown can trigger the accumulation of innate immune cells that lead to inflammation and tissue destruction [(7)]. Signalling pathways and responses, such as those involving nuclear factor kB (NF-kB) and mitogen-activated protein kinase (MAPK), have also been found to play a role [(5)].

Rheumatoid arthritis (RA) is a systemic condition involving immune dysregulation and inflammation, affecting multiple joints. Female gender, genetics, and smoking are risk factors for developing RA [(8)]. The presence of antibodies, or lack thereof, help classify RA into a seropositive or seronegative disease. Seronegative patients have more inflammation upon presentation, whereas seropositive patients have increased inflammation and joint damage over the course of the disease [8]. Extra-articular manifestations may be observed in seropositive cases or severe disease. Anti-citrullinated protein antibody (ACPA) perpetuates inflammation and is associated with bone erosions and pain [(9)]. The inflammatory nature of this

International Journal of Advances in Engineering and Management (IJAEM)
Volume 5, Issue 1 Jan. 2023, pp: 318-333 www.ijaem.net ISSN: 2395-5252

disease eventually leads to permanent deformity. Overall, RA patients face a high rate of disability, with approximately 60% unable to work by at least 10 years after disease onset [10]. Symptoms of RA include tender, warm, and swollen joints as well as stiffness in the morning and from inactivity [11].

Despite modern disease-state knowledge, providing effective treatment for OA and RA is challenging. The American College of Rheumatology/Arthritis Foundation recommends current treatment options [12,13]. According to these guidelines, recommendations for OA include oral and topical non-steroidal anti-inflammatory drugs (NSAIDs), oral analgesics, serotonin, and norepinephrine reuptake inhibitors, and intra-articular corticosteroids [12]. For early and established RA, traditional disease-modifying antirheumatic drug (DMARD) monotherapy, especially methotrexate (MTX), is strongly recommended for patients with low disease activity levels [13]The mechanism of action of current drugs for OA and RA treatment has been reviewed previously [14].

Current pharmacotherapy provides options for alleviating pain and symptoms of OA and RA. However, the side effects associated with these treatments may limit their use. NSAIDs may be associated with gastrointestinal, cardiovascular, and nephrotoxic effects and have been excluded for long-term treatment of arthritis [15,16]. Acetaminophen can induce hepatotoxicity [17]. Tramadol can alter the gastrointestinal and central nervous system [18]. Intra-articular corticosteroids may have questionable efficacy for OA treatment and may further damage joints and tissues [19]. Hyaluronic acid injections provide OA pain relief with reasonable safety but may be expensive [19]. Non-biologic DMARDs are highly efficacious in early RA with low disease activity level; however, treatment with these drugs increase the risk of gastrointestinal disturbance, hepatotoxicity, nephrotoxicity, and blood disorders [20]. Biologics are effective for moderate to severe RA, but have low tolerability and increase the risk of serious infection, cancer, and heart failure [21]. Finally, Janus kinase inhibitors to manage moderate to severe RA, carry a risk of infection and blood disorders [22].

Concerns regarding the safety and costs of conventional arthritis therapies have sparked interest in natural remedies. In addition, difficulty with chronic pain management in arthritis has led to the investigation of herbal therapies. Herbs may offer a complementary or alternative method for effective and safe treatment. In this review, we summarize current pharmacological therapy utilized for OA and RA and we provide recent findings regarding herbal arthritis management. Specifically, we set out to describe the mechanisms, safety, and efficacy (including pain and inflammatory outcomes) of select herbal medications used for OA and RA.

PATHOPHYSIOLOGY:

The core reason of RA is unidentified. Although viruses, bacteria, and fungi have extensively been assumed, but not been proved. It is thought that the propensity to grow RA may be hereditary [23,24] . RA is classified as an autoimmune disease, which occurs due to the overactivity of the immune structure by offending the body's own cells and tissues. In people with RA, the immune system stimulates unusual inflammation in the membrane that covers joints i.e., the synovial membrane. Inflammation of synovium; causes ache, swelling, and stiffness of joints. In harsh situations, inflammatory reactions damage the bone, joints and surrounding tissues within the joints, resulting in bigger damages [25]. Immune cells, called lymphocytes, are stimulated, and chemical messengers (cytokines, such as tumour necrosis factor/TNF, interleukin-1/IL-1, and interleukin-6/IL-6) are produced in the inflamed regions [26,27]. Synovial fibroblasts are major players in RA. They motivate a pro-inflammatory situation in the synovial membrane, cooperate with the immune system, and control the differentiation of monocytes to osteoclasts[27,28] .

Major genetic agents of RA are variations in Human Leukocyte Antigen (HLA), particularly the HLA-DRB1 gene. The amino acids synthesized by HLA assist the immunity to differentiate its own amino acids apart from foreign ones of viruses and bacteria[29,30].

Environmental agents also appear to take a prime role in causing RA. Smoking tobacco, contact with silica, and long-term periodontal disorders raise the threat of budding RA. Studies regarding gut organisms that can stimulate the beginning of RA in hereditarily vulnerable candidates [31,32] .

Risk Factors and Complications:

CDC reported that patients with an elevated threat of attacking RA can comprise individuals of age 60 years or above, female, overweight, smoking [32,33].

Diagnosis:

The diagnosis depends on the clinical presentation. The existence of rheumatoid factor and citrulline antibody (Abs). The occurrence of nodules and X-ray changes [33].

International Journal of Advances in Engineering and Management (IJAEM)
Volume 5, Issue 1 Jan. 2023, pp: 318-333 www.ijaem.net ISSN: 2395-5252

STAGES OF RHEUMATOID ARTHRITIS:

The stages of RA by the condition of cartilage, ligament, and joints are as follows.

Stage I: early RA: Negative effect on X-ray, whereas symptoms of joint thinning may be present.

Stage II:moderate progressive: X-ray confirmation of joint thinning surrounding a bone with or devoid of little joint erosion.

1. little cartilage destruction is probable.
2. Joint movement is restricted; the absence of bone deformities are seen.
3.Atrophy of surrounding soft tissue.
4.Damage of muscle adjacent to joints.

Stage III: severe progression:

1. X-ray examination of joints shows erosion .
2.Joints deformities with reversible stiffness joints.
3. Widespread soft tissue atrophy.

Stage IV: terminal progression:

1.X-ray observation of joint damage and osteoporosis surrounding the joints.
2. Joint deformities with irreversible stiffness of the joints (ankylosis).
3. Widespread soft tissue atrophy and abnormalities.

II. METHODS AND MATERIALS:

Inclusion and exclusion criteria

We sought to identify clinical trials of herbal preparations administered orally or topically for RA in which patients were randomly assigned to receive either herbal medicines or control treatments, i.e. placebo or active therapy. Additional inclusion criterion were that

(i) the dosage of the herbal was described

(ii) both baseline and endpoint clinical data were included, and

(iii) if the sample included patients with other forms of arthritis, results could be determined separately for the RA patients. Animal studies were excluded from the review, as were studies of semisynthetic plant-based drugs. One mixed herbal remedy (Phytodolor1) was excluded from this systematic review because it has recently been submitted to a separate review [(34)].

Search strategy

The general structure of the search strategy was 'arthritis (or synonyms) and herbal (or synonym)'. No methodological filter was applied and the search was not limited by language. We used the following keywords: 'arthritis', 'rheumatoid arthritis', 'reactive arthritis', 'adjuvant arthritis', 'infective arthritis', 'osteoarthritis', 'gouty arthritis', 'juvenile rheumatoid arthritis', 'psoriatic arthritis' and 'periarthritis'. The free-text search terms included '(arthritis)' and the combined terms '(hip, knee, joint, musculoskeletal-skeletal)' and '(pain, inflammation, movement, stiffness)'. Herbal keywords included 'medicine herbal', 'medicines herbal', 'herbal medicine', 'drugs Chinese herbal', 'plants medicinal', 'phytomedicine' and 'phytotherapy'; freetext search terms included 'herb*' and 'plant*'. Additionally, we searched the bibliographies of articles obtained for further trials.

Data extraction

Two raters (KLS and SAM) independently assessed whether the identified studies met the inclusion criteria and extracted information regarding the sample, treatment duration and dosage, adverse effects and results. In addition, both raters assessed the methodological quality using the Jadad scale[(35)] which assesses randomization, double-blinding and drop-outs. Where possible, we computed effect sizes (ESs) comparing treatment and control conditions for the change from baseline. Any differences between raters in extraction and rating were resolved through discussion.

Electronic databases including PubMed, Google Scholar, and ClinicalTrials.gov were searched using general keywords such as "herb", "arthritis", "pain", "inflammation" and "clinical trial". We also conducted our search by using specific herb names. We excluded clinical trials that tested formulations with 4 or more combined herbs. A total of 23 clinical trials including 9 herbs: Boswellia spp., Curcuma spp., Eremostachys laciniata, Eucommia ulmoides, Matricariachamomillia L., Paeonia lactiflora, Tripterygium wilfordii Hook F, Withaniasomnifera, and Zingiber officinale were reviewed.

HERBS USED IN ARTHRITIS:

1.Aloe:

Botanical Name: Aloe barbadensis
Other Name: Curacao aloe, Lily of the desert
Family: Liliaceae

Aloe barbadensis is cultivated in Europe and in many parts of India, including north-west Himalayan region. Aloe has been one of the most important plants used in folk medicine. Anthraquinone, anthracene, cinnamicacid and anthranilicacid are found in the aloe plants that are responsible for its activities. It has also antibacterial and antifungal properties, used as blood purifier, antiinflammatory, diuretic, uterine tonic,

International Journal of Advances in Engineering and Management (IJAEM)
Volume 5, Issue 1 Jan. 2023, pp: 318-333 www.ijaem.net ISSN: 2395-5252

spermatogenic, laxative, and purgative and fever reliever. Aloe stimulates the immune system and it is a powerful anti-inflammatory agent. Topical application of aloe extract result in the reduction of inflammation and arthritis in adjuvant induced arthritis in Sprague Dawley rats.[36-38].

2.Shallaki:
Botanical Name: Boswellia serrata Linn.
Other Name: Boswellia; Indian Frankincense
Family: Burseraceae

Boswellia serrata Linn. is a moderate to large branching tree found in India. In India it is found in Bihar, Madhya Pradesh and Gujarat. Strips of boswellia bark are peeled away; yielding gummy-oleo resins having inflammatory, anti-atherosclerotic and anti-arthritic activities. Extract of this gummy oleo resins have also been used as astringent[39].analgesic and sedative. It is also known to regain integrity of the vessel in the joints from damage or spasm. Extract of Boswellia serrate have natural anti-inflammatory activities at sites where chronic inflammation is present by switching off pro-inflammatory cytokines and mediators which initiates the process. Non steroidalanti inflammatory drugs can cause a breakdown of glycosaminoglycan synthesis which can accelerate the articular damage in arthritic conditions where as Boswellia serrata reduces the breakdown of glycosaminoglycan synthesis..

3.Ginger:
Botanical Name: Zingiber officinale
Other Name: Ginger root
Family: Zingiberaceae

Ginger is one of the most useful herbal supplements. It is native of South East Asia, but it is cultivated in Caribbean island, Africa, Australia, Mauritius, Taiwan and India. More than 30 % production is in India. Ginger consists of volatile oil, starch, fat, fiber, inorganic material, and residual matter. Ginger oil contains monoterpine, hydrocarbons, sesquiterpine hydrocarbons, oxygenated mono- and sesquiterpine. Ginger is used as an aromatic, a carminative, flavouringagent. It is used to treat nausea, vomiting, diarrhoea. It is also used as antioxidant, antiinflammatory, antiseptic, anticarcinogenic, antifungal, and anti-microbial. Ginger extract is one of the effective arthritis joint pain remedies recommended by physicians. Main constituents are sesquiterpenoids, with (-) zingiberene. Sesquiterpene Lactones are natural products responsible for anti-inflammatory activity[40,41].

4.Bastard guelder:
Botanical Name: PremnacorymbosaRottl.
Other Name: Buas Buas
Family: Verbenaceae

Premnacorymbosa Rottl., is a small size tree or long shrub. The plant is widely distributed throughout the India. All the parts of the plant are useful. The roots are astringent, bitter, acrid, sweet, thermogenic, anti inflammatory, alexeteric, cardiotonic, alternant, expectorant, depurative digestive, carminative, stomachic, laxative, febrifuge, antibacterial and tonic. The leaves are stomachic, carminative, galactogogue and they are useful in dyspepsia, colic flatulence, agalactia, cough, fever, rheumatalgia, neuralgia, hemorrhoids and tumors. Upon long term treatment with Premnacorymbosa ,it significantly suppressed the development of chronic arthritis induced by Complete Freund's Adjuvant.[42,43].

5.Night jasmine:
Botanical Name: Nyctanthesarbortristis Linn.
Other name: Coral Jasmine
Family: Oleaceae

Nyctanthesarbortristis is a shrub or a small tree It is used as laxative, diuretic, diaphoretic, used to experoundworm and threadworm in children's, to relieve cough, also used for the treatment of rheumatoid arthritis. The leaves of Nyctanthesarbortristis inhibited the acute inflammatory edema produced by different phlogistic agents, viz. carrageenin, formalin, histamine, 5-hydroxytryptamine and hyaluronidase in the hind paw of rats(Ref. needed). Acute and chronic phases of formaldehyde induced arthritis are significantly inhibited (Ref needed). Nyctanthesarbortristis Linn, also found to inhibit the inflammation produced by immunological methods, reund's adjuvant arthritis.[44,45].

6.Indian sarsaparilla:
Botanical Name: Hemidesmus indicus Linn.
Other name: Anantamul, Pseudosarsa
Family: Asclepiadaceae

Hemidusmus indicus Linn. is a species of plant that is found in South Asia. It contains coumarin, essential oil, starch, tannic acid, triterpenoid saponin. It is used in the treatment of rheumatoid arthritis, nephritic complaints, chronic skin disease, chronic ulcer, and blood purifier. The ethanolic extract of Hemidusmus indicus reducing the paw volume and paw thickness more than Diclofenac sodium.[46].

7.Aginbuti:
Botanical Name: Ammaniabaccifera Linn.

International Journal of Advances in Engineering and Management (IJAEM)
Volume 5, Issue 1 Jan. 2023, pp: 318-333 www.ijaem.net ISSN: 2395-5252

Other name: Acrid weed, Monarch red stem, Tooth cup
Family: Lythraceae

Ammaniabaccifera Linn. is a glabrous, erect branching herb, found as weed in rice-fields and marshy localities throughout India. It contains sterols, glycosides, alkaloids, triterpenoid and saponin. Plants have hypothermic, hypertensive, anti urolithiasis, antibacterial, seminal weakness, and fever, flatulence and CNS depressant activities. The aerial parts of Ammaniabaccifera Linn. posses significant anti-inflammatory and anti arthritic activity in rats (Ref. needed). Ethanolic extract inhibit of inflammation in Cotton pallet granuloma test and Adjuvant arthritis model.[47].

8.Chhota halkusa :
Botanical Name: Leucas aspera Linn.
Other name: Gophaa, Tumba, Dronapushpi
Family: Lamiaceae

Leucas aspera Linn. is a small erect, branched annual herb. It is distributed throughout India from the Himalayas down to Ceylon. The plant is used traditionally as an antipyretic and insecticide. Medicinally, it has been proven to possess various pharmacological activities like antifungal, antioxidant, antimicrobial, antinociceptive and cytotoxic activity. It contains triterpenoids, oleanolic acid, ursolic acid and b-sitosterol, nicotine, sterols, glucoside, diterpenes and phenolic compounds. Ethanolic extract of Leucas aspera Show anti rheumatoid arthritis effect in Complete Freund's adjuvant induce arthritis.[48,49].

9.Crocus:
Botanical Name: Crocus sativus Linn
Other Name: Saffron
Family: Iridaceae

Crocus sativus is used widely in tropical and sub tropical countries for a variety of purposes in both house hold and for medicinal purposes.the stigmas of the plant contains a varity of chemical constitutents like the crocetin, crocin and other flavanoids which make them suitable to posses diversified medicinal properties for treating various ailments countries like india saffron is been used in their traditional medicine from the pre-historicages. It is considered as a tonic for heart and nervous system and for smoothing menstruation and also posses anti rheumatic property.[50].

10. Camphor:
Botanical Name: Cinnamomum Camphora
Other Name: Camphor Tree, Gum Camphor, Camphor Laurel, French Camphor, Howood
Family Name: Lauraceae

Camphor is used as anti-bacterial, anti-fungal, analgesic, analeptic, anthelmintic, antispasmodic, aromatic, aphrodisiac, carminative, diaphoretic, sedative, stimulant, narcotic and tonic. It is used as nervine depressant in case of hysteria, epilepsy, chorea and convulsions. It acts as stimulant for cardiac, circulation and respiration. It is used to treat arthritis since olden days. Anti arthritic activity of the plant have been proved clinically.[51].

11.Mango:
Botanical Name: Mangifera indica Linn
Other Name: mamidi, manga
Family: Anacardiacea

Mangifera indica Linn., a species of mango. It is now cultivated throughout the tropical and subtropical world for commercial fruit production. Mangiferin is extracted from mango at high concentrations from the young leaves, bark and from old leaves. Mangiferin shows strong antioxidant effect. It has a number of pharmacological actions. The methanolic extract of Mangifera indica posses the anti inflammatory activity show in the arthritic parameter like arthritic index, paw edema and rheumatoid factor.[52].

12.Mint:
Botanical name: Mentha arvensis Linn
Other names: pudina, podina
Family: Lamiaceae

Anti inflammatory and anti arthritic activity of methanolic leaf extracts of Mentha arvensis Linn in arthritis induced male albino rats. It is estimated for assessing the anti inflammatory and Antiarthritic activity of methanolic extract of Mentha arvensis .their investigation conclude that the methanolic extract of Mentha arvensis posses a significant anti inflammatory and anti arthritic activity.[53].

13. Ashwagandha:
Botanical Name: Withaniasomnifera Linn.
Other Name: Winter cherry, withania root
Family: Solanaceae

Ashwagandha also known as Indian ginseng, is an important ancient plant. The roots of Ashwagandha have been employed in Indian traditional systems of medicine, Ayurveda and Unani. The pharmacological activity of the root is attributed to the alkaloids and steroidals lactones. Among the alkaloids, withanine, withanine, pseudowithanine, tropine, pseudo-tropine, somniferine, somnine are mainly present. Oral administration of Witheniasomnifera Linn. root

International Journal of Advances in Engineering and Management (IJAEM)
Volume 5, Issue 1 Jan. 2023, pp: 318-333 www.ijaem.net ISSN: 2395-5252

powder showed the anti arthritic effect in adjuvant induced arthritic rats.[54].

14. Turmeric:
Botanical name: Curcuma longa Linn.
Other Name: Turmeric root, Indian saffron Plant
Family: Zingiberaceae

Turmeric is cultivated for its rhizome in India, China, Shrilanka, Indonesia, Jamaica, and Peru. Turmeric contains volatile oil, resins, starch grains and yellow color substances known as curcuminoids. The chief component of curcuminoids is known as curcumin. Curcumin, a natural compound present in the rhizomes of plant Curcuma longa, demonstrated its anti inflammatory action. It is used in wound healing, hepatoprotection and neuroprotection etc. It has antimutagenic, antispasmodic, antimicrobial and anticancer activities. Daily ip administration of the low dose of purified curcuminoids (4 mg total curcuminoids/kg/d) inhibited joint inflammation in both the acute and chronic phases of arthritis.[55].

15. Black pepper:
Botanical Name: Piper nigrum Linn.
Other Name: Pepper
Family: Piperaceae

Black pepper is indigenous and cultivated in South India. It is also cultivated in Indonesia, Brazil, Malaysia and Shrilanka. India ranks first in the cultivation of this drug. Pepper contains an alkaloid piperine, volatile oil, pungent resins, piperidine and starch. It is used as a aromatic, stimulant, stomachic and carminative. It increases the secretion of gastric juices. It also increases the bioavailability of certain drugs. Piperine isolated from black pepper. Piperine administered orally at a dose of 20 and 100 mg/kg/day for eight days cause decrease in the arthritic symptoms in carrageenin induced acute paw arthritis.[56].

16.Cat's claw
Biological name: Uncaria tomentosa
Common Name: Hawk's claw, saventaro Plant
family: Rubiaceae

Cat's claw is a woody vine that grows in the tropical jungle of South and Central America, and it derived its name from its claw shaped thorns. It contains several alkaloids, tannins that are responsible for its medical effects. It contain phytochemicals like Ajmalicine, akuammigine, campesterol, catechin, chlorogenic acid, cinchonain, corynantheine, corynoxeine, daucosterol, epicatechin, harman, hirsuteine, hirsutine, iso-pteropodine, loganic acid, lyaloside, mitraphylline, oleanolic acid, palmitoleic acid, procyanidins, pteropodine quinovic acid glycosides, rhynchophylline, rutin, sitosterols, speciophylline, stigmasterol, strictosidines[57].It is used in the cancer, in HIV infection, anti-inflammatory, anti-oxidant [58,59], gastric ulcers, chron's disease, tumors, diabetes, chronic fatigue disease. It is also used as anti bacterial agent. Animal study of anti inflammatory activity of cat's claw extract showed the ability to reduced paw edema in carragenan induced inflammation rat model [60-62]

17.Milkweed
Biological Name: Calotropis Procera Linn.
Common name: Giant Swallow Wort
Family: Asclepiadaceae

Calotropis procera Linn., is a species of flowering plant in the dogbane family Apocynaceae, that is native to North Africa, Tropical Africa, Western Asia, South Asia, and Indochina. Different parts of this plant have been reported to exhibit anti inflammatory, analgesic, antioxidant and antifungal activity. The latex of this plant has potent antiinflammatory property in various animal models. The latex petroleum extract shows significant antimicrobial activity[63]. Both latex and its methanolic extract have been shown to inhibit the inflammatory cell influx and edema formation induced by various inflammagens. It also improves locomotor functions in experimentally induced monoarthritis in rats. In cotton pellet induced granuloma and carrageenan -induced paw edema model, roots of Calotropis Procera Linn., at doses of 180 mg/kg (methanol extract) and 200 mg/kg (other extracts), show anti-inflammatory activity[64-66].

18.Green tea
Biological Name: Camellia sinensis Linn.
Common Name: Green tea extract, Chinese tea
Family: Theaceae

Camellia sinensis Linn., is an evergreen shrub or small tree. Camellia sinensis Linn., is native to mainland China, South and Southeast Asia, now cultivated across the world in tropical and subtropical regions. The active constituents of Camellia sinensis Linn., are polyphenols (catechins and flavonols). Other constituents are caffeine and essential oils. The most important catechin in Green Tea is (-) epigallocatechin that is a potent antioxidant. The reduced collagen induced arthritis incidence and severity was reflected in a marked inhibition of the inflammatory mediators COX-2, IFNγ, and TNFα in arthritic joints of green tea-fed mice. Total immunoglobulin's (IgG) and type II collagen-specific IgG levels were found to

International Journal of Advances in Engineering and Management (IJAEM)
Volume 5, Issue 1 Jan. 2023, pp: 318-333 www.ijaem.net ISSN: 2395-5252

be lower in serum and arthritic joints of green tea-fed mice[67-69].

19.Ashok

Biological Name: Saracaasoca Roxb.
Common Name: Asok, Osaka
Family: Caesalpiniaceae

Saracaasoca Roxb., is found in the foothills of central and eastern Himalayas, in scattered locations of the northern plains of India. Preliminary phytochemical methanolic and ethanolic extracts indicate the presence Carbohydrates, tannin, flavonoid, saponin, glycosides, proteins and steroids [70]. It is used as spasmogenic, oxytoxic, uterotonic, anti-bacterial, antiimplantation, anti-tumour, anti-progestational, anti-estrogenic, anti-cancer and anti-rheumatoid arthritis. Methanol extract of SaracaasocaRoxb., reduced the paw thickness in adjuvant induced arthritic rats[71,72].

EVALUATION PARAMETER FOR HERBAL OINTMENT:

Visual Properties Inspection:
Colour, texture, and homogeneity were all evaluated as physical attributes of the finished compositions. The consistency of numerous compositions was assessed through visual observation

Sensitivity:
A small amount of the substance was applied to the forehead to test if it irritated it.

Colour Change:
The samples were kept for seven days so that colour changes could be seen.

Water washability:
A little amount of testing was applied on the hand for a few minutes to test washability, and then washed with tap water.

Consistency:
From a set length of 10 cm, the cone attached to the retaining rod was lowered until it landed in the centre of the SSD cream-filled measuring cylinder. The cone's distance travelled was measured after 10 seconds.

Viscosity measurements:
The viscosity (in cps) of the products was measured using a Brookfield viscometer (Brookfield, MA). The spindle was spun at a speed of 2.5 revolutions per minute. Before the analyses, the cream specimens were permitted to stay for 30 minutes at the specified temperature (25±1°C).

Extrudability:
The mass in grams required to extrude a 0.5-cm strip of the composition in 10 seconds was estimated. Herbal cream extrusion force has been reported.[73].

Spreadability:
One gram of the herbal combination was placed between two clear slides, and a weight of 500g was applied. After measuring the time it took to slip off the slides.

Skin irritation test:
Herbal creams with varying concentrations of herbal preparation were applied to the epidermis. The sample cream and the swab carrying it has adhered to thetreated area with adhesive strips. Then any erythema was detected and assessed according to the application site's state.[74,75].

Stability analysis:
Temperatures of 10°C, 30°C, and 45°C were used to keep the composition. For four weeks, the viscosity, pH, and appearance of the specimens were monitored [76,77]. Toxicity test: The toxicological tests were carried out for a total of 28 days.

TREATMENT:

Non-Pharmacological Treatment:
Rest: During a flare, the patient should rest. Swollen and acheful bones make signs worse.
Exercise: Upon remission, signs are gentle; patients must often exercise to improve health and reinforce the soft tissues surrounding the bones. The finest workout is that which does no tension on the bones, like swimming.
Diet: Subsequently, healthy food with lots of fruits and vegetables will improve the patient, allow feeling better, and maintaining a healthy weight [78,79] .

Pharmacological Treatment:
Nonsteroidal Anti-Inflammatory Drugs (NSAIDs): Chronic administration and high concentrations result in adverse effects like gastric upset, elevated BP, kidney damage, and liver injuries [80] .
Corticosteroids: They intend to decrease aches and inflammatory responses and can slow down bone injuries, although they may not heal RA. Corticosteroids are very useful in acute signs or short-term flares. Chronic therapy of corticosteroids causes severe side effects like being overweight [81] .
Disease-modifying Antirheumatic Drugs (DMARDs): DMARDs decrease the succession of RA and stop irreversible erosion of the joints and other soft tissues by intrusive overactivity of the immune system. It is largely successful in the near beginning stages. Adverse effects liver includes marrow and immune suppression.

International Journal of Advances in Engineering and Management (IJAEM)
Volume 5, Issue 1 Jan. 2023, pp: 318-333 www.ijaem.net ISSN: 2395-5252

Tumour Necrotic Factor Alpha Inhibitors (TNF-Alpha Inhibitors): TNF-alpha is an inflammation-causing agent. TNF-alpha blockers avoid inflammatory reactions. Blockers diminish ache, morning rigidity, and inflamed joints [81,82]. Probable adverse effects comprise elevated threat of infection, blood-related diseases, heart failure, demyelinating disorders.

Surgery: Surgery restores injured bones, corrects deformity, and decreases ache.

Arthroplasty: It is a complete bone replacement; surgeons take out injured structures and add a metallic or plastic prosthesis [83].

Tendon Renovate: If tendons have loosened or ruptured surrounding joints, surgery helps renovate them [84] .

Synovectomy: This process involves the elimination of the synovial membrane due to inflammation and ache.

Arthrodesis: The doctor can combine bones to reduce ache and to steady joints.

HERBAL THERAPY FOR ARTHRITIS:

Sr no.	Natural product	Source	Part used	Active principle	MOA and molecular pathways involved	Challenge and adverse effect
1	Boswellia Serrate Indian frankincensesalai/salaigugglu	The resin of Boswellis	Oleo gum resin from the trunck of the tree	Triterpenic acid that is b-boswellic acid 11 keto b-boswellic acid and acetyl 1-keto-b- b-boswellic acid Curcumin	Acts via 5-LOX inhibition	Stomach pain,nausea diarrhoea and allergic rashes reported
2	Turmeric Curcumin Curcuma Longs	Curcuma Long a Linn	Dried as well as fresh rhizome	Curcumin	It acts by inhibition of COX, 5-LOX and glutathione S-transferase	Higher dose long term administration causes nausea and diarrhea
3	Gamma limol (GLA)	Rapeseed canola oil soy beans walnuts and flex seedlinseed oil	Plant seed oil	O-mega 6 fatty acids	Dietary GLA it converted directly to DGLA increased levels of DGLA promote the synthesis of in-flammatory metabolites i.e, series	It is safe at the dose 2.8 g/day up to year besides it causes softening of tools belching and intestinal gas

International Journal of Advances in Engineering and Management (IJAEM)
Volume 5, Issue 1 Jan. 2023, pp: 318-333 www.ijaem.net ISSN: 2395-5252

					prostaglandins PGEI suppress chronic inflammation	
4	Ginger Zingiberoffici n ale	Zingiberoffici nails Linn	Rhizomes	It contains high proportions sesquiterpenes, predominantly zingiberene and gingerols	It inhibits PG and LTs biosynthesis via an inhibitory action on PG synthetase and 5-LOX, and addition to this also inhibits pro-inflammatory cytokines such as IL 1 TNF, and IL-8	It is safe, but some minor side effects such as heartburn diarrhoea, stomach discomfort, and skin irritation may take place
5	Thunder God vine	Tripterygui mwif ordii	Skinned root (extract)	Its major compositions are di-terpenoid triptolide	It interferes with the production of PGs cytotoxic T-cell proliferation and IL-2 too	GIT disturbances such as nausea, abdominal pain, indigestion flatulence, constipation, hair loss male infertility, and significant immune suppression
6	Celastrol	Tripterygui mwil for dii (lei gong teng thunder of god vine), which belongs to the Celast	Root and work	A yellow quinoidenor triterpene called Celastrol which is a pentacyclic triterpene	Celastrol has beneficial antiaarthritic effects by suppersion of proinflammatory cytokines mediated MMP-9 expression and lipopolysa	Diarrhoea headache nausea, and infertility, especially at high dose

International Journal of Advances in Engineering and Management (IJAEM)
Volume 5, Issue 1 Jan. 2023, pp: 318-333 www.ijaem.net ISSN: 2395-5252

		racea e famil y			chardies	
7	Thymoquinone (TQ)	TQ is obtain ed from the volati le oil of black the black caraw ay seed Nigell a sativa Ranu uncul aacea e famil y	Volatile oil of the black seed	TQ is a major bioactive it constituent of the volatile oil og black seed (54%)	It extracts antiarrhriti c action against carrageen an induced paw oedema in rats by inhinitingt he inflammat ory mediators	It is safe and may cause allergic rashes
8	Sinomenine	It is obtain ed from the root of Sino menin eActu m	Roots	Sinomenine is alkaoid	Sinomeni ne may inhibit proliferati on of synovial fibroblasts in arthritis	It produces abnormal immunosuppression
9	Paeoniflorin	It is obtain ed from the root of a Paeon ia	Roots	It is a major constituent of paeonialacfl ora	It extracts anti-arthritic action by inhibition of IL-6 and COX-2	Abdiminal upset and skin Rashes
10	Asiatocide and madecesso side	Two whole plants of cebtel laasia tica	whole pant	It contains large amounts of pentacyclic triterpenoid, including asiatico and madecassosi de	It provides productio n against joint destructio n in CIA mice	Skin allergy, burring sensations, headache nausea, extreme drowsiness and contact dermatitis

11	Epigallocate chin	It is obtained from oldenlandia Diffuss and fruits	Fruit	Epigallocate chin gallate also know as epigallocata chin 3-gaalateia an ester of epigallocata chin and gallic acid	It showed effective action against arthritis by TNF, an inhibition	It hampered iron absorption in a dos-dependent
12	Naringin	It is obtained from grapes and citrus fruits	Grapes and citrusfruit	Naringin is a flavanone-7-Oglycoside	It showed antiiarthritic action by suppression of MMP-9	Biiter and taste
13	Hesperidin	It is obtained from the fruit of citrus aurrations	Citrus fruits	Flavanone glycoside	It suppression the Tlymphocyte proliferation and IL-2 production in rats too	Limited bioavailability
14	Resveratrol	It is obtained from grapes and redn wine	Grapes red wine and berries	Resveratrol polyphenolic compounds	It mediated antiarthritic action by targeting NF-Kb and simultaneously decreases AGEsstimulated expression and prevent AGEs-mediated destruction of CLAAA	Poor oral bioavailability

III. CONCLUSIONS:

Current pharmacological therapy options recommended for OA and RA are associated with variable efficacy and safety, especially for the treatment of chronic pain and inflammation. Certain herbal medicines may be used as a complementary therapy to work with or reduce the need for pharmacological agents. Treatment with herbal medicines may also offer a safer alternative with equal or superior efficacy.

The anti-arthritic mechanisms of herbs include inhibition of pro-inflammatory and pro-catabolic mediators such as cytokines, PGE2, MMPs, ROS, apoptotic proteins via signalling pathways (NF-kB, RANKL, and PI3K/Akt). These activities may contribute to improvement in OA and RA joint pain, inflammation, swelling, structure, and function, with minimal adverse effects.

For future research, more trials are needed to determine the clinical safety and efficacy of herbal medicine in arthritis and other chronic pain conditions. Further studies on herbal chemical compounds and isolates may also help to provide more targeted therapy options. Lastly, the development of natural product formulations with ideal bioavailability and kinetics will be necessary for optimizing treatment.

REFERENCES:

[1]. Barbour, K.E.; Boring, M.; Helmick, C.G.; Murphy, L.; Qin, J. Prevalence of Severe Joint Pain Among Adults with Doctor-Diagnosed Arthritis—United States, 2002–2014. MMWR Morb. Mortal. Wkly. Rep. 2016, 65, 1052–1056. [CrossRef] [PubMed].

[2]. Kennedy, J.; Roll, J.M.; Schraudner, T.; Murphy, S.; McPherson, S. Prevalence of Persistent Pain in the U.S. Adult Population: New Data from the 2010 National Health Interview Survey. J. Pain 2014, 15, 979–984. [CrossRef].

[3]. CDC. Arthritis Types. Updated 20 February 2019. Available online: https://www.cdc.gov/arthritis/basics/types.html (accessed on 5 October 2020).

[4]. CDC. Osteoarthritis. Updated 20 February 2019. Available online: https://www.cdc.gov/arthritis/basics/osteoarthritis.htm (accessed on 5 October 2020).

[5]. Mobasheri, A.; Batt, M. An update on the pathophysiology of osteoarthritis. Ann. Phys. Rehabil. Med. 2016, 59, 333–339. [CrossRef] [PubMed].

[6]. Chen, Z.; Li, X.-P.; Li, Z.-J.; Xu, L.; Li, X.-M. Reduced hepatotoxicity by total glucosides of paeony in combination treatment with leflunomide and methotrexate for patients with active rheumatoid arthritis. Int. Immunopharmacol. 2013, 15, 474–47.

[7]. [CrossRef] [PubMed] 7. Mora, J.C.; Przkora, R.; Cruz-Almeida, Y. Knee osteoarthritis: Pathophysiology and current treatment modalities. J. Pain Res. 2018, 11, 2189–2196. [CrossRef].

[8]. Derksen, V.F.A.M.; Huizinga, T.W.J.; Van Der Woude, D. The role of autoantibodies in the pathophysiology of rheumatoid arthritis. Semin. Immunopathol. 2017, 39, 437–446. [CrossRef].

[9]. Ruffing, V.; Bingham, C. Rheumatoid arthritis signs and symptoms. Retrieved from Johns Hopkins Arthritis Center website. 2016. Available online: http://www.ggpodiatry.com (accessed on 5 October 2020).

[10]. Curtis, J.R.; Singh, J.A. Use of Biologics in Rheumatoid Arthritis: Current and Emerging Paradigms of Care. Clin. Ther. 2011, 33, 679–707. [CrossRef].

[11]. Sasane, P.; Saroj, U.R.; Joshi, R.K. Clinical evaluation of efficacy of Alambushadi Ghana Vati and Vaitarana Basti in the management of Amavata with special reference to rheumatoid arthritis. AYU (Int. Q. J. Res. Ayurveda) 2016, 37, 105–112. [CrossRef].

[12]. Kolasinski, S.L.; Neogi, T.; Hochberg, M.C.; Oatis, C.; Guyatt, G.; Block, J.; Callahan, L.; Copenhaver, C.; Dodge, C.; Felson, D. 2019 American College of Rheumatology/Arthritis Foundation Guideline for the Management of Osteoarthritis of the Hand, Hip, and Knee. Arthritis Rheumatol. 2020, 72, 220–233. [CrossRef].

[13]. Singh, J.A.; Saag, K.G.; Bridges, S.L., Jr.; Akl, E.A.; Bannuru, R.R.; Sullivan, M.C.; Vaysbrot, E.; McNaughton, C.; Osani, M.; Shmerling, R.H.; et al. 2015 American College of Rheumatology Guideline for the Treatment of Rheumatoid Arthritis. Arthritis Rheumatol. 2015, 68, 1–26. [CrossRef].

[14]. Grässel, S.; Muschter, D. Recent advances in the treatment of osteoarthritis. F1000Research 2020, 9, 325. [CrossRef] [PubMed].

[15]. Solomon, D.H.; Husni, M.E.; Wolski, K.E.; Wisniewski, L.M.; Borer, J.S.; Graham, D.Y.; Libby, P.; Lincoff, A.M.; Lüscher, T.F.; Menon, V.; et al. Differences in Safety of Nonsteroidal Antiinflammatory Drugs in Patients With Osteoarthritis and Patients With Rheumatoid Arthritis. Arthritis Rheumatol. 2018, 70, 537–546. [CrossRef].

[16]. Fowler, T.O.; Durham, C.O.; Planton, J.; Edlund, B.J. Use of nonsteroidal anti-inflammatory drugs in the older adult. J. Am. Assoc. Nurse Pr. 2014, 26, 414–423. [CrossRef] [PubMed].
[17]. Towheed, T.; Maxwell, L.; Judd, M.; Catton, M.; Hochberg, M.C.; Wells, G.A. Acetaminophen for osteoarthritis. Cochrane Database Syst. Rev. 2006, CD004257. [CrossRef].
[18]. Vazzana, M.; Andreani, T.; Fangueiro, J.; Faggio, C.; Silva, C.; Santini, A.; Garcia, M.; Silva, A.; Souto, E. Tramadol hydrochloride: Pharmacokinetics, pharmacodynamics, adverse side effects, co-administration of drugs and new drug delivery systems. Biomed. Pharmacother. 2015, 70, 234–238. [CrossRef] [PubMed].
[19]. Weick, J.W.; Bawa, H.S.; Dirschl, D.R. Hyaluronic Acid Injections for Treatment of Advanced Osteoarthritis of the Knee. JBJS 2016, 98, 1429–1435. [CrossRef].
[20]. Gilani, S.T.A.; Khan, D.A.; Khan, F.A.; Ahmed, M. Adverse effects of low dose methotrexate in rheumatoid arthritis patients. J. Coll. Phys. Surg. Pak. 2012, 22, 101–104.
[21]. Codreanu, C.; Damjanov, N. Safety of biologics in rheumatoid arthritis: Data from randomized controlled trials and registries. Biol. Targets Ther. 2015, 9, 1–6. [CrossRef] Medicines 2020, 7, 67 15 of 18.
[22]. Yamaoka, K. Janus kinase inhibitors for rheumatoid arthritis. Curr. Opin. Chem. Biol. 2016, 32, 29–33. [CrossRef].
[23]. Schuerwegh AJ, et al. Evidence for a functional role of IgEanticitrullinated protein antibodies in rheumatoid arthritis. Proc. Natl Acad. Sci. USA. 2010;107:2586–2591.
[24]. vanDongen H: Efficacy of methotrexate treatment in patients with probable rheumatoid arthritis: a double-blind, randomized, placebo-controlled trial. Arthritis Rheum 2007; 56: 1424–32.
[25]. Sellam J: B cell activation biomarkers as predictive factors for the response to rituximab in rheumatoid arthritis: a sixmonth, national, multicenter, open-label study. Arthritis Rheum 2011; 63: 933–38.
[26]. Seegobin SD: ACPA-positive and ACPA-negative rheumatoid arthritis differ in their requirements for combination DMARDs and corticosteroids: secondary analysis of a randomized controlled trial. Arthritis Res Ther 2014; 16: 13.
[27]. Mori M, Yamada R, Kobayashi K, Kawaida R and Yamamoto K: Ethnic differences in allele frequency of autoimmune-disease-associated SNPs. J Hum Genet 2005; 50: 264–66.
[28]. McCarthy C: Brief report: genetic variation of the alpha1 - antitrypsin gene is associated with increased autoantibody production in rheumatoid arthritis. Arthritis Rheumatol 2017; 69: 1576–79.
[29]. Castaneda-Delgado JE: Type I interferon gene response is increased in early and established rheumatoid arthritis and correlates with autoantibody production. Front Immunol 2017; 8: 285.
[30]. Svendsen AJ: On the origin of rheumatoid arthritis: the impact of environment and genes--a population based twin study. PLoS ONE 2013; 8:57304.
[31]. Hensvold AH: Environmental and genetic factors in the development of anticitrullinated protein antibodies (ACPAs) and ACPA-positive rheumatoid arthritis: an epidemiological investigation in twins. Ann Rheum Dis 2015; 74: 375–80.
[32]. Van der Woude D: Gene-environment interaction influences the reactivity of autoantibodies to citrullinated antigens in rheumatoid arthritis. Nat Genet 2010; 42: 814– 16.
[33]. Klareskog L: A new model for an etiology of rheumatoid arthritis: smoking may trigger HLA-DR (shared epitope)-restricted immune reactions to autoantigens modified by citrullination. Arthritis Rheum 2006; 54: 38–46.
[34]. Ernst E. The efficacy of Phytodolor1 for the treatment of musculoskeletal pain—a systematic review of randomized clinical trials. Natural Med J 1999;2:14–7.
[35]. Jadad A, Moore R, Carroll D et al. Assessing the quality of reports of randomized clinical trials: is blinding necessary? Control Clin Trials 1996;17:1–12
[36]. Davis RH, Agnew PS, Antiarthritic Activity of Anthraquinones found in aloe vera for podiatric medicine. Journal of the American Podiatric Medical Assoc 1986; 76(2): 1-8.
[37]. Joshph B and Raj SJ Pharmacognostic andpharmacology properties of Aloe vera. International journal of Pharmaceutical

Sciences Review and Research 2010; 4(2): 106-109.
[38]. Devis RH, Agnew PS, Shapiro E Anti arthritic activity of anthraquinones found in aloe for Podiatric Medicine. Journal of the American Podiatric Medical Assoc 1986; 76(2): 61-66.
[39]. Kumar AM, Ethnomedicinal plants as antiinflammatory and analgesic agents. Research Signpost, 2010; 267-293.
[40]. Rehman R, Akram M, Akhtar N, Jabeen Q, Saeed T, Shah SMA et al, Zingiber officinale Roscoe (pharmacological activity). Journal of Medicinal Plants Research 2011; 5(3): 344-348.
[41]. Zakeri Z, Izadi S, Bari Z, Soltani F, Narouie B, Rad MG Evaluating the effects of ginger extract on knee pain, stiffness and difficulty in patients with knee osteoarthritis. Journal of Medicinal Plants Research 2011; 5(15): 3375-3379
[42]. Rai S, Vaishnav A, Chandy A, Singh M and Singh MP Antipyretic activity of ethanolic extract of PremnacorymbosaRottl. Leaves (Verbenacea). Research journal of pharmacognosy and phytochemistry 2011; 3(6): 278.
[43]. Karthikeyan M, Deepa K Effect of ethanolic extract of Premnacorymbosa (Burm. f.) Rottl. &Willd. Leaves in complete Freund's adjuvant-induced arthritis in wistar albino rats. Journal of Basic and Clinical Physiology and Pharmacology, 2010; 21(1): 15-26.
[44]. Bhalerao AR, Desai SK, Serathia BR, Vartak KM, Antiarthritic studies on Nyctanthesarbortristis and Maharasnadighan. Scholars Research Library 2011; 3(4): 101-110.
[45]. Sandhar HK, kaur M, Kumar B, Prasher S, An update on Nyctanthesarbortristis Linn. International pharmaceuticasciencia 2011; 1(1): 77-86.
[46]. Mehta A, Sethiya NK, Mehta C, Anti-arthritis activity of roots of Hemidesmus indicus R.Br. (Anantmul) in rats. Asian Pac J Trop Med 2012; 5(2): 130-5.
[47]. Tripathy S, Pradhan D and Anjana M, Antiinflammatory and antiarthritic potential of Ammaniabaccifera Linn. International Journal of Pharma and Bio Sciences 2010; 1(3): 1-7.
[48]. Prajapati MS, Patel JB, Modi K, Shah MB Leucas aspera: A review. Pharmacognosy Review 2010; 4 (7): 85-87.
[49]. Kripa KG, Chamundeeswari D, Thanka J, Reddy C UM Effect of hydro alcoholic extract of aerial parts of Leucas aspera (Willd.) link on inflammatory markers in complete freund's adjuvant induced arthritic rats. International Journal of Green Pharmacy 2010; 4(4): 281-287.
[50]. Vijaya Bhargava K, Medicinal Uses and Pharmacological Properties of Crocus Sativus Linn, Inter Journal of Pharmacy and Pharmaceutical Sciences, 2011, 3(3), 22-26.
[51]. Cheeke PR, Anti-inflammatory and anti-arthritic effects of yucca schidigera: A review, journal of inflammation,3(6),1-7.
[52]. Garrido, González, Delporte, Backhouse, Quintero, Nunez-Selles AJ , Analgesic and anti-inflammatory effects of Mangifera indica L. extract (Vimang). Molecules 2001; 15(1): 18-21.
[53]. DhinekPrasath, Anti-inflammatory and antiarthritic activity of methanolic leaf extracts of Mentha arvensis Linn in arthritis induced male albino rats South Asian Journal of Biological Sciences, 2014; 4(1): 12-15.
[54]. Mirjalili MH, Moyano E, Bonfill M, Cusido RM and Palajon J, Steroidal Lactones from Witheniasomnefera, an ancient plant for noval medicines. Molecules 2009; 14: 2373-2393.
[55]. Funk JL, Oyarzo JN, Frye JB, Chen G, Lantz RC, Jolad SD et al Turmeric extracts containing curcuminoids prevents experimental rheumatoid arthritis. NIH Public Access 2006; 69(3): 351-355.
[56]. Bang JS, Oh DH, Choi HM, Sur BJ, Lim SJ, and Kim JY, Anti-inflammatory and anti-arthritic effect of piperine in human interleukin 1β-stimulated fibroblast like synoviocytes and in rat arthritis models. Arthritis Research and Therapy 2009; 11(20): 1-9.
[57]. Leslie Taylor Technical Data Report for Cat's claw, Preprinted from Herbal Secrets of the Rainforest.2nd ed, Published and copyrighted by Sage Press, Inc; 2002.
[58]. Sandoval M, Okuhama NN, Zhang XJ, Condezo LA, Lao J et al Anti-inflammatory and antioxidant activities of cat's claw (Uncaria tomentosa and Uncariaguianensis) are independent of their alkaloid content. Journal of Phytomedicine 2002; 9(4): 325-37.

[59]. "Anti-inflammatory activity of two different extracts of Uncaria tomentosa (Rubiaceae)". J. Ethnopharmacol 2002; 81(2): 271– 76.
[60]. Setty AR "Herbal medications commonly used in the practice of rheumatology: mechanisms of action, efficacy, and side effects." Semin. Arthritis Rheum 2005; 34(6): 773-84.
[61]. Jean Bruneton. Text book of Pharmacognosy, Phytochemistry of Medicinal Plants. 2nd ed. P. 299-301.
[62]. Cat's Claw, available from http://fastflustop.com/Cats Claw.html (as viewed on 14/2/12)
[63]. Raghavendra R and Mahadevan GD In vitro antimicrobial activity of various plant latex against resistant human pathogens. International Journal of Pharmacy and Pharmaceutical Sciences
[64]. Kumar VL and Roy S Calotropis procera latex extract affords protection against inflammation and oxidative stress in freund's complete adjuvant-induced monoarthritis in rats. Mediators of Inflammation 2007; 2007: 1-7. 2011; 3 (4): 70-72.
[65]. Mossa JS, Tariq M, Mohsin A, Ageel AM, Yahya AI, Said AI and Rafatullah S Pharmacological studies on aerial parts of Calotropis Procera. American Journal of Chinese Medicine 1991; XIX (3-4): 223-231.
[66]. Babu SAR, Karki SS Anti inflammatory activity of various extracts of roots of Calotropis procera against different inflammation models. International journal of pharmacy and pharmaceutical sciences 2011; 3(3): 191-194.
[67]. Ahmed S Green tea polyphenol epigallocatechin 3-gallate in arthritis: progress and promise. Arthritis research & therapy 2010; 12(2): 1-9.
[68]. Akroum S, Satta D, Lalaoui K Antimicrobial, Antioxidant, Cytotoxic Activities and Phytochemical Screening of Some Algerian Plants. European Journal of Scientific Research 2009; 31(2): 289-295.
[69]. Chopade VV, Phatak AA, Upaganlawar AB, Tankar AA Green tea (Camellia sinensis), Chemistry, traditional, medicinal uses and its pharmacological activities- A review. Pharmacognosy review 2008; 2(3): 157-162.
[70]. Mallikharjuna PB, Rajanna LN, Seetharamand YN, Sharanabasappa GK. Phytochemical Studies of StrychnospotatorumL.f.- A Medicinal Plant. E-Journal of Chemistry 2007; 4(4): 510-518.
[71]. Saha J, Mitra T, Gupta K, Mukherjee S Phytoconstituents and HPTLC analysis in SaracaAsocaRoxb., wilde. International Journal of Pharmacy and Pharmaceutical Sciences 2012. 4 Suppl 1:96-99.
[72]. Saravanan S, Babu NP, Pandikumar P, Ignacimuthu S Therapeutic effect of Saracaasoca (Roxb.) Wilde on lysosomal enzymes and collagen metabolism in adjuvant induced arthritis. Inflammopharmacology 2011; 19(6): 317-25.
[73]. Puvabanditsin P, Vongtongsri R. Efficacy of Aloe vera cream in prevention and treatment of sunburn and suntan. J Med Assoc Thai 2005;88(4):173- 6.
[74]. Lu et al., Lu QY, Zhang Y, Wang Y, Wang D, Lee RP, Gao K, Byrns R, Heber D. California Hass avocado: profiling of carotenoids, tocopherol, fatty acid, and fat content during maturation and from different growing areas. J Agric Food Chem. 2009; 57(21):10408-13.
[75]. Vogler BK, Ernst E. Aloe vera: A systematic review of its clinical effectiveness. British. J. Gen. Pract., 1999; 49: 823–828.
[76]. Ramachandra CT, Ramachandra P. Processing of Aloe Vera Leaf Gel: A Review. Amer. J. Agri. Biol. Sci. 2008; 3 (2): 502-510.
[77]. Chithra P, Sajithlal GB, Gowri F. Influence of Aloe vera on collagen characteristics in healing dermal wounds in rats. Molecular and Cellular Biochemistry, 1998; 181: 71–76.
[78]. Hu Y: Long-term dietary quality and risk of developing rheumatoid arthritis in women. Ann Rheum Dis 2017; 76: 1357–64.
[79]. Orellana C: Oral contraceptives, breastfeeding and the risk of developing rheumatoid arthritis: results from the Swedish EIRA study. Ann Rheum Dis 2017; 76: 1845–52.
[80]. Alpizar-Rodriguez D: Female hormonal factors and the development of anti-citrullinated protein antibodies in women at risk of rheumatoid arthritis. Rheumatology 2017; 56: 1579–85.

[81]. Van der Woude D: Epitope spreading of the anticitrullinated protein antibody response occurs before disease onset and is associated with the disease course of early arthritis. Ann Rheum Dis 2010; 69: 1554–61.
[82]. Krishnamurthy A: Identification of a novel chemokinedependent molecular mechanism underlying rheumatoid arthritis-associated autoantibody-mediated bone loss. Ann Rheum Dis 2016; 75: 721–29.
[83]. Wigerblad G: Autoantibodies to citrullinated proteins induce joint pain independent of inflammation via a chemokine-dependent mechanism. Ann Rheum Dis 2016; 75: 730–38.
[84]. Pianta A: Two rheumatoid arthritis-specific autoantigens correlate microbial immunity with autoimmune responses in joints. J Clin Invest 2017; 127: 2946–56.