ABSTRACT
Herbs and herbal medicine have not been studied in the same way that prescription medicine for rheumatoid arthritis (RA) have. There is a tremendous disconnect between their widespread usage and peoples belief in their efficacy compared to what has been proven scientifically. Many herbs/their extracts have been used as anti-rheumatic agents by practitioners of alternate system of medicine (mainly Unani and Ayurvedha). Use of these herbal medicines is based on the anti-rheumatic phytoconstituents present in them. This article is a compilation of different phytoconstituents used as anti-rheumatic drugs or are drugs under investigation for the same purpose.

Key words: Rheumatoid arthritis, Unani and Ayurvedha.

ALKALOIDS
1. Tetrandrine: It is chemically a bis-benzylisoquinoline alkaloid which is a natural analogue of berbamine and is extracted from the tuberous roots of creeper *Stephania tetrandra* & *S. moore* (Menispermaceae). It is used for the treatment of rheumatic diseases and is also efficacious in silicosis associated with inhibition of collagen synthesis. It inhibits neutrophil and monocyte locomotion and lymphocyte transformation. Tetrandrine suppresses the release and activity of inflammatory cytokines, lipid mediators, histamine and has an inhibitory capacity on monocytes to produce tumor necrosis factor (TNF)-α. Tetrandrine is considered as a prototypic tool compound for the development of new class of anti-rheumatic agents [1, 2].
2. **Berbamine**: It is an isoquinoline alkaloid obtained from *Berberis vulgaris*. It is also found to have significant inhibitory activity on prostaglandin E$_2$ (PGE$_2$) generation, with stronger inhibitory effects on natural-killer cell population.\textsuperscript{[3]}

3. **Sinomenine** (SIN): This bioactive alkaloid derived from the Chinese medicinal plant, *Sinomenium acutum* (*Menispermaceae*) was investigated on collagen-induced arthritis (CIA) in mice at varying doses (s.c) for 55 days. The severity of arthritis was evaluated according to clinical score. The results showed that treatment with SIN was followed by decreases in the incidence and severity of CIA, anti-CII IgG and the antigen-specific splenocyte proliferation. Production of all isotypes of antibodies including anti-CII IgG$_{2a}$, IgG$_1$ and IgE as well as secretion of cytokines such as IFN-$\gamma$ (interferon gamma) and IL-5 were suppressed by SIN. In addition, SIN enhanced the secretion of TGF-$\beta$ (transforming growth factor beta) while it had no obvious effect on production of IL-10. These results suggest that the anti-arthritic effect of SIN may be related to the suppression of both Th1 and Th2 (T helper lymphocyte 1 & 2) immune responses. TGF-$\beta$ may at least in part contribute to the suppression of Th1 as well as Th2 immune responses.\textsuperscript{[4]}
4. **Stachydrine**: It is a crystalline alkaloid from *Capparis spinosa* L. (*Capparidaceae*) fruits. It has been used as anti-arthritic. The adjuvant arthritic rat model was developed to evaluate the anti-arthritic effects of different fractions of ethanol extract from *C. spinosa* L. The fraction eluted by ethanol-water (50:50, v/v) had the most significant anti-arthritic activity which contained stachydrine.[5]

![Stachydrine](image)

5. **Colchicine**: This alkaloid is present in corns and seeds of *crocus* like plants and is an established clinical agent for arthritic disease and leukocytoclastic vasculitis[6]. Best known for its preventive action against gout, it also reduces pain and swelling in degenerative and immunological inflammatory disease[7].

![Colchicine](image)

6. **Aconitine**: This alkaloid from the main root of *Aconitum carmichaeli* has marked suppressive effect on the swelling of rat's hind paw induced by injections of fresh egg protein, carrageenin, histamine and 5-HT, on the mouse’s ear oedema induced by bimethylphenyl, on the exudate and proliferation of granulation tissue of granuloma pouch induced by croton oil, on the leukocyte migration and on the contents of PGE in the exudate of the swelling hind
paw induced by injecting carrageenan. Aconitine has been found useful in inhibiting significantly such immune inflammations as reversible passive arthus reaction, rat's delayed skin hypersensitivity and adjuvant arthritis.\[8\]

\[8\]

![Aconitine](image)

**Aconitine**

7. **Bukittinggine:** This major alkaloid of *Sapium baccatum* Roxb. (*Euphorbiaceae*) exhibited a significant inhibitory effect in carrageenan-induced hind paw oedema and adjuvant-induced arthritis in rats. Its anti-inflammatory activity in both test models was comparable to that of acetyl salicylic acid. Bukittinggine also showed an inhibitory effect on the late proliferative phase of the inflammatory process in cotton pellet-induced granuloma formation in rats. In carrageenan-induced rat pleurisy, bukittinggine exhibited marked inhibitory activity on exudate formation, accumulation of leukocytes and on PGE$_2$-like activity in the exudate.\[9\]

\[9\]

![Bukittinggine](image)

**Bukittinggine**

8. **Spilanthol:** Isolated from *Spilanthes acmella* (*Paracress*), this alkaloid was studied for its anti-inflammatory activity on murine RAW 264.7 macrophage by down-regulating LPS-induced(lipopolysaccharide-induced) inflammatory model. The result suggested that spilanthol, attenuates the LPS-induced inflammatory responses in murine RAW 264.7 macrophages, partly due to the inactivation of nuclear factor kappa-light-chain-enhancer of activated B cells(NF-kappaB), which negatively regulates the production of proinflammatory mediators.\[10\]

\[10\]
9. **Diaboline**: This major alkaloid from *Strychnos potatorum* Linn was found responsible for the antiarthritic activity. The extract of *Strychnos potatorum* Linn., seed at dose of 200 mg/kg, p.o. showed reduction in the paw volume in Freund’s adjuvant induced arthritic rats\(^{[11,12]}\).

10. **Gentianaine**: Isolated from *Gentiana caucasa* (*Gentianaceae*) leaves, it has shown low anti-inflammatory activity in carrageenan-induced hind paw oedema\(^{[13]}\).

11. **Gentianadine**: This sesquiterpene alkaloid found in the aerial parts of *Gentiana turkestanorum*, *G. olgae*, and *G. olivieri* (*Gentianaceae*) has shown anti-inflammatory and muscle relaxant actions\(^{[13]}\).
12. **Gentianamine**: Isolated from leaves of *Gentiana olivieri* and *G. turkestanorum* (*Gentianaceae*), this alkaloid has shown anti-inflammatory activity in carrageenan-induced hind paw oedema [13].

![Gentianamine](image)

13. **Betonicine**: The piperidine alkaloid isolated from *Betonica officinalis*, *Marrubium vulgare*, *Stachys sylvatica* (*Labiatae*), *Achillea moschata*, and *A. millefolium* (*Compositae*) has been found to significantly inhibit carrageenan-induced hind paw oedema [14].

![Betonicine](image)

14. **Tylophorine**: Isolated from leaves of *Tylophora indica* (*Asclepiadaceae*), this alkaloid was shown to inhibit the primary and secondary responses of adjuvant-induced arthritis [15].

![Tylophorine](image)

15. **Tylophorine analog- DCB 3503**: Isolated from Chinese herb *Tylophora atrofolliculata*, it significantly suppresses the development and progression of collagen-induced arthritis (CIA). Moreover, it completely blocks the LPS-triggered acceleration of joint inflammation and destruction. Consistent with its effects in vivo, it significantly suppresses the synthesis of pro-inflammatory cytokines in inflamed joints as well as cytokine synthesis by macrophages examined ex vivo. DCB 3503 treatment also reduces the levels of inflammatory cytokines (IL-6, IL-12, and TNF) produced by bone marrow–derived dendritic cells in vitro. However, it shows no direct effect on T cell proliferation and B cell antibody response [16].
16. Trilobine and Isotrilobine: These two alkaloids from roots of *Cocculus trilobus* (*Menispermaceae*) showed inhibitory effect against cotton pellet and adjuvant arthritis in rats \[17\].

17. Hypaconitine: The betalain alkaloid from *Aconitum colliantum*, *A. carnichaeli*, and *A. Napellus* (*Ranunculaceae*) showed significant inhibitory activity against carragenan-induced oedema \[18\].

18. Piperine and piperidine (*Piper nigrum* Linn (*Piperaceae*): Black pepper increases the secretion of gastric juices and also the bio-availability of certain drugs. Piperine when administered orally at a dose level of 20 and 100 mg/kg/day for eight days caused decrease in the arthritic symptoms in carrageenan induced acute paw arthritis \[19, 20\].
19. Thalidasine: The bis-isoquinoline alkaloid obtained from the leaves of *Thalictrum dasycarpum* (*Ranunculaceae*) (reported for its effect on rheumatic swelling of joints and sprains) exhibited anti-inflammatory activity in carrageenan-induced hind paw oedema [21].

Thalidasine

20. Tinosporine, Tinosporidine, and Tinosporaside: These major alkaloids and other constituents as Cordifolide, diterpene glycoside Cordifol, Heptacosanol, Clerodane furano diterpene, Diterpenoid furanolactone, Columbin and β-sitosterol have been isolated from *Tinospora cordifolia* Linn. (*Menispermaceae*). The plant is used to improve the immune system and the body's resistance to infections. The bitter principle present shows antiperiodic, antispasmodic, anti-inflammatory and antipyretic properties. It is used in the treatment of rheumatoid arthritis. At the dose of 100 mg/kg it showed reduction of paw volume in collagen induced arthritic rats [22, 23].
FLAVONOIDS

21. Aromadendrin, Apigenin and Vitexin: Isolated from *Justicia gendarussa* linn (*Acanthaceae*) these are used to treat inflammation and rheumatoid arthritis in folk medicine. Its ethanolic extract showed significant anti-arthritic activity similar to that of aspirin against Freund’s adjuvant-induced and collagen-induced arthritic rat models \(^{24, 25, 26}\).

22. Baicalin, Baicalein and Wogonin: The flavonoids from leaves of *Scutellaria baicalensis* Georgi (*Labiatae*) have been screened in comparison with three standard anti-inflammatory agents viz phenylbutazone, indomethacin, and dexamethasone for activity in various experimental models of inflammation. All the test substances were found to inhibit an increase in vascular permeability in mice induced by acetic acid and reduce acute paw oedema in rats. They also suppressed the secondary lesion in developing adjuvant-induced arthritis in rats \(^{27}\).
23. Kolaflavanone: Isolated from the rind of *Garcinia kola* (*Guttiferae*), it inhibited primary and secondary responses of adjuvant induced arthritis in rats \(^{[28]}\).

24. Rutin, Quercetin (*Flavonols*) and Hesperidin (*Flavanone*): The anti-inflammatory activities of these flavonoids were investigated in rats using the Mizushima et al’s model of acute and chronic inflammation. Intra-peritoneal administration of rutin, quercetin and hesperidin, given at daily doses (80 mg/kg) inhibited both acute and chronic phases of inflammation. Rutin was the most active in the chronic phase. \(^{[29]}\)
25. **Epiafzelechin**: This flavonoid isolated from aerial parts of *Celastrus orbiculatus* (*Celastraceae*) is an inhibitor of cyclo-oxygenase (COX-1) activity of prostaglandin H₂ synthase. (-)-Epiafzelechin exhibited about 3-fold weaker inhibitory potency on the enzyme activity than indomethacin as a positive control. (-)-Epiafzelechin exhibited significant anti-inflammatory activity on carrageenan-induced mouse paw oedema, following (100mg/kg) dose administrated orally 1 h prior to carrageenan treatment.\(^\text{[30]}\)

26. **Chrysin, Oroxyline, Oroxylin-A, Scutellarin and Biochinin-A**: These flavinoids from *Oroxyllum indicum* are responsible for the anti-inflammatory, anti-arthritic, and anti-bacterial activities of this plant\(^\text{[31, 32]}\).
27. **3-O-methylviolanone**: Found in heartwood of *Dalbergia odorifera* T. Chen. (*Leguminosae*) this is a traditional Chinese medicine known as jiangxiang which has been used to treat blood disorders, ischemia, swelling, necrosis, and rheumatic pain. It has shown significant anti-inflammatory activity \(^{[33]}\).

![3-O-methylviolanone](image)

**GLYCOSIDES**

28. **Robinin**: The kaempferol glycoside isolated from *Robinia pseudacacia* leaves (*Leguminosae*) has shown inhibition of exudative and proliferative phases of the cotton pellet granuloma (50 mg/kg/day p.o. in 7 days) \(^{[34]}\). It is also used as an anti-inflammatory and anti-rheumatic agent in Spain’s folklore medicine.

![Robinin](image)

29. **Stephanoside E and Stemucronatoside K**: These steroidal glycosides from the roots and stems of *Stephanotis mucronata* (Blanco) Merr. (*Asclepiadaceae*) are used for the treatment of rheumatoid arthritis and rheumatic aches in Chinese folklore medicine \(^{[35]}\).

![Stemucronatoside K](image)
30. Xanthorhamnin: Isolated from the seeds of *Rhamnus infectoria* (*Rhamnaceae*), it has been patented as an anti-inflammatory agent and recommended for the treatment of rheumatoid arthritis and for use in ophthalmology [36].

![Xanthorhamnin](image)

**Xanthorhamnin**

31. Stereospermin, Stereospermiside and Stereostin: Isolated from *Stereospermum kunthianum* (*Bignoniaceae*), these are used to treat various ailments including inflammatory conditions (rheumatoid arthritis) and pain. A study using different models of inflammation, these flavinoids at dose levels of 20 mg/kg, (Stereostin, Stereospermin (p<0.0001) and Stereospermiside(p<0.05) ) significantly increased the carrageenan-induced pain threshold compared to the distilled water treated animals. Similarly, at the same doses the three compounds significantly (p<0.0001) inhibited both phases of the formalin-induced pain with a more pronounced effect on the second phase than in the first phase. [37]

![Stereostin](image)

![Stereospermin](image)

32. Benzoxazinoid: isolated from the roots of *Coix lachryma-jobi* L. (*Graminae.*) It is present in plants as glucoside. The roots of *C. lachryma-jobi* have been used in China for the treatment of rheumatism and neuralgia. [38]
33. **Harpagoside**: This iridoid glycoside from *Harpagophytum procumbens* has been used for thousands of years in Africa for the treatment of fever, rheumatoid arthritis, and skin conditions and is currently available as an alternative treatment for pain and osteoarthritis\[^{39}\]. Harpagoside has been shown to suppress lipopolysaccharide-induced inducible nitric oxide synthase and cyclooxygenase (COX)-2 expression through inhibition of nuclear factor-κB activation.\[^{40}\]

![Harpagoside](image)

34. **Salicin and Populin**: These phenolic glycosides from *Populus alba* have been used for polyarthritis and were part of *Unguentum populi*, an ointment used for gout and rheumatism.\[^{41}\]

![Salicin](image) ![Populin](image)

35. **Cimigoside** and **27-deoxyactein triterpene glycosides**: These are found in the roots and rhizomes of black cohosh (*Actaea racemosa* Linn. Family, *Ranunculaceae*). The roots and rhizomes are used in arthritis, dyspepsia, kidney problems, malaria, snake bite and as insect repellent. These are used to decreases the inflammation produced due to the arthritis. Other
chemical compounds extracted from the black cohosh, include acteina, salicylic acid, and an isoflavone- formononetine.\(^{[42, 43, 44]}\).

![Cimigoside](image1.png)  ![27-deoxyactein](image2.png)

![salicylic acid](image3.png)  ![formononetine](image4.png)

36. **Asperuloside** and **deacetyl asperuloside**: These two iridoid glycosides isolated from *Lasianthus acuminatissimus* Merr are used for treatment of rheumatoid arthritis. Other iridoid glucosidic dimmers present in the plant are nonglycosidic iridoid, paederoside, daphylloside, citraside A, benzyl 6-o-a-L-rhamnopyranosyl - b-D-glucopyranoside.\(^{[45]}\)

![Asperuloside](image5.png)  ![Paederoside](image6.png)

![Daphylloside](image7.png)
37. Chiisanoside and chiisanogenin: These triterpenoid glycosides found in the leaves and stem bark of *Acanthopanax chiisanensis* Nakai (*Araliaceae*) have been used as anti-rheumatic. To find the anti-inflammatory constituents of the herb leaves, phytochemical isolation procedures were performed by activity-guided fractionation in carrageenan- and Freund’s complete adjuvant (FCA) reagent-induced rat models. The anti-inflammatory effects of the two compounds were supported by the reduction of carrageenan-induced lipid peroxidation and hydroxy radical in serum \[^{46}\].

![Chiisanoside and chiisanogenin](image)

38. Anthraquinone, anthracene, cinnamic acid and anthranilic acid: The anthraquinone glycosides found in *Aloe Vera* plants are responsible for the activity. The anti-arthritic property of *aloe vera* is due to the anthraquinone compounds. these stimulate the immune system and are powerful antinflammatory agents. Topical application of aloe vera extract resulted in the reduction of inflammation and arthritis in adjuvant induced arthritis in Sprague Dawley rats \[^{47, 48, 49}\].

![Anthraquinone and anthracene](image)

![Cinnamic acid and anthranilic acid](image)
SAPONINS

39. Smilaxin, Prosapogenin A, Dioscin, Gracillin, Pseudoprotodioscin, Methygracillin and Methylprotodioscin: These saponins found in the extract of *Smilax sarsaparilla* L. and *Smilax china* L. are used in traditional Saudi Arabian medicine for rheumatism, arthritis, gout and other inflammatory diseases. *Smilax china* L. is used for the treatment of rheumatoid arthritis, gout and other inflammatory ailments.\[^{50}\].
40. **Momordin Ic (saponin) and oleanolic acid:** Isolated from *Kochia scoparia* fruits, these possess anti-rheumatoid activity. MeOH extract of *Kochia scoparia* was fractionated into CHCl3-(chloroform), EtOAc-(ethyl acetate) and BuOH (butyl alcohol) extracts and the last fraction were hydrolyzed by 3%-NaOH (MeOH-H2O) to compare the bioactivities on antinociceptive and anti-inflammatory effects. Silica gel column chromatography of BuOH fraction afforded a large amount of 3-O-beta-D-xylopyranosyl (1 ➔ beta-D-glucuronopyranosyl oleanolic acid (momordin lc) and that of acid hydrolysate of BuOH fraction gave 3-O-beta-D-glucuronopyranosyl oleanolic acid (momordin lb), its 6'-O-methyl ester and oleanolic acid. Silica gel column chromatography of alkaline hydrolysate afforded a large amount of momordin lc. MeOH extract and both EtOAc- and BuOH fractions were active in the rheumatoidal rat induced Freund's complete adjuvant reagent (FCA) whereas CHCl3 fraction was inactive. Momordin lc and oleanolic acid showed significant activities in the same assay but oleanolic acid 3-O-glucuronopyranoside showed no activity. These results suggest that momordin lc and its aglycone, oleanolic acid, could be active principles for rheumatoid arthritis. [51, 52].

![Momordin Ic](image1)

![oleanolic acid](image2)

41. **Echinocystic acid:** Isolated from leaves of *Baccharis trimera* (Asteraceae), it possesses activity capable of preventing various chemically induced oedemas in rats and abdominal writhing following acetic acid injection in mice [53]. This South American plant is used in traditional medicine, internally, for the treatment of rheumatism, hepatobiliary disorders, and diabetes.

![Echinocystic acid](image3)
42. Phytolaccoside B: This glucosidal saponin isolated from roots of *Phytolacca americana* L. (*Phytolaccaceae*) exhibited anti-rheumatic and anti-inflammatory actions \[^{54,55}\].

![Phytolaccoside B](image)

**TERPENOIDS AND STEROIDS**

43. Boswellic acid: In India, the oleo-gum resin of *Boswellia serrata* Roxb. Ex Coleb (*Burseraceae*) under trade name “Sallaki” is used for the treatment of rheumatism and nervous diseases. It has been established that anti-inflammatory and antiarthritic activities are due to the presence of boswellic acid and other related pentacyclic triterpene acids\[^{56}\].

![Boswellic acid](image)

44. Germacrene D, (Z)-β-farnesene, β-caryophyllene, α-pinene, δ-cadinene (sesquiterpenes): Found in plant *Teucrium Chamaedrys* (*Lamiaceae*), these are responsible for the biological activity of plant. The plant has been used as anti-inflammatory, Anti-rheumatic, digestive and diuretic.\[^{57,58}\]

![Germacrene D](image)  
![β-farnesene](image)  
![β-caryophyllene](image)
45. **Hydroxyachillin**: This sesquiterpene lactone from aerial parts of *Tanacetum microphyllum* (*Compositae*) is used in the Iberian peninsula since ancient times and in Spanish traditional medicine as an anti-inflammatory and anti-rheumatic agent, and for its beneficial effects on the digestive tract. A study was carried out to investigate the effects of hydroxyachillin on mouse ear oedema induced by PMA (phorbol myristate acetate). Hydroxyachillin significantly (p≤0.01) inhibited ear swelling in a dose-dependent manner, and was as effective as the reference drugs. The PMA-induced vascular permeability was significantly (p≤0.05) reduced by hydroxyachillin at the highest dose (3 mg/ear). Histologically, the signs of inflammation were greatly reduced in the hydroxyachillin-treated ear lesions. the data suggests that hydroxyachillin is an effective anti-inflammatory agent in this model, and that the inhibition of Protein kinase- C may be one of the mechanisms of hydroxyachillin's effect.[59]

46. **Mezerein, genkwadaphin, 1, 2-dehydrodaphnetoxin** and **daphnetin**: These diterpenoids from various species of *Daphne* (*Daphne tangutica, Daphne mezereum, Daphne laureola L and Daphne oleoides* Schreb) have been used traditionally for inflammatory complaints. These phytoconstituents were found to be responsible for anti-rheumatic activity.[60, 61].
47. **Bartogenic acid** (BA): This triterpene isolated from *Barringtonia racemosa* Linn (*Lecythidaceae*) is responsible for anti rheumatic activity of this plant. It has anti-microbial, anti-oxidant and anti-inflammatory activities, thus finds a use in rheumatoid arthritis. BA protected rats against the primary and secondary arthritic lesions, and haematological perturbations induced by Complete Freund’s Adjuvant (CFA)\(^{62, 63, 64}\).

48. **Mannitol, beta-amyrin** (triterpenoid), **beta-sitosterol, benzoic acid and benzoic ester of longanin, nycthanic acid**: From Night jasmine (*Nyctanthes arboristris*) Linn. (*Oleaceae*), these are used for the treatment of rheumatoid arthritis. Its leaves inhibited the acute inflammatory oedema produced by different phlogistic agents, viz. carrageenan, formalin, histamine, 5-hydroxytryptamine and hyaluronidase in the hindpaw of rats. Acute and chronic phases of formaldehyde induced arthritis were significantly inhibited. *Nyctanthes arboristris* Linn. Was also found to inhibit the inflammation produced by immunological methods, viz. Freund's adjuvant arthritis\(^{65}\).
COUMARINS

49. Osthol: Isolated from Cnidium monnieri, it has been reported to exhibit various biological activities. Study to demonstrate its anti-inflammatory activity showed that osthol inhibited TNF-α (Tumor necrosis factor alpha), NO and COX-2 expression in LPS (lipopolysaccharide)-stimulated macrophages, without reducing the expression of IL-6. Furthermore, the phosphorylation of p38-JNK1/2 (c-Jun N-terminal kinase1/2), PKC-α (protein kinase C) and PKC-ε induced by LPS was inhibited by osthol; however, the phosphorylation of ERK1/2 (extracellular signal regulated kinase 1/2) and PKC-δ was not reduced by osthol. Osthol also inhibited NF-κB activation and ROS release in LPS-stimulated macrophages. The results indicate that osthol is the major anti-inflammatory ingredient in Cnidium monnieri seed[^66].

![Osthol](image)

50. Chromones: The isomers of coumarin derivatives of benzopyran with a substituted keto group on the pyran ring, these are present in number of plants like 6,7-dimethoxy-2,3-dihydrochromone isolated from Sarcolobus globosus. Eucryphin (chromone rhamnoside) isolated from the bark of Eucryphia cordifolia and Chromone 3-[(2-(3, 5-dimethoxy phenyl)ethyl)1]-2-methyl from Erucaria microcarpa. Latter has been proved as a scavenger for DPPH (2,2-diphenyl-1-picrylhydrazyl) free radical. Free radicals have been proposed to induce cellular damage which may play a role in rheumatoid arthritis, inflammatory disorders as well as aging process[^67,68].

![Chromones](image)
XANTHONES

51. Dehydrocycloguandin: The xanthone derivative isolated from *Calophyllum brasiliense* and *C. inophyllum* leaves (*Guttiferae*) demonstrated anti-inflammatory activity on the exudative and proliferative phases of cotton pellet granuloma, formaldehyde-induced arthritis, and carrageenan oedema\(^{[69]}\).

![Dehydrocycloguandin](image)

52. Mangiferin and isomangiferin: These xanthone derivatives from the leaves and bark of *Mangifera indica* Linn. (*Anacardiaceae*) showed strong antioxidant effect. The methanolic extract of *Mangifera indica* possessed anti-inflammatory activity which is shown by the arthritic parameters like arthritic index, paw oedema and rheumatoid factor\(^{[70, 71, 72]}\).

![Mangiferin and Isomangiferin](image)

TANNINS

53. Chebulinic acid (ellagitannin): isolated from *Terminalia chebula* Retz., it is used in chronic ulcer, leucorrhoea and fungal infections of skin. It is also used as neuroprotective and antioxidant. Hydro-alcoholic extract of this plant showed anti-arthritic activity in formaldehyde or complete Freund's adjuvant induced arthritis. The anti-arthritic activity of *Terminalia chebula* Retz., is thought to be due to its modulatory effect on proinflammatory cytokine expression in the synovium\(^{[73, 74, 75]}\).
PEPTIDES, CATECHINS AND FATTY ACIDS

54. **Aurantiamide acetate** (dipeptide) and **1, 3-Dibenzyl Urea**: Isolated from roots of *Moringa oleifera*, these were found to be anti-inflammatory/ Anti-arthritic and analgesic. Aurantiamide acetate showed significant inhibition on TNF-α and IL-2 but not on IL-6. While 1, 3-dibenzyl Urea, showed significant analgesic activity in dose dependant manner and significant inhibition on IL-2. These results indicate that these compounds may be responsible for the anti-inflammatory/ antiarthritic and analgesic activity.\[76\]

55. **Epigallocatechin**: It is a catechin found in *Camellia sinensis* Linn. (*Theaceae*). Other constituents are caffeine and essential oils. The most important in Green Tea (-) epigallocatechin 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 be lower in serum in arthritic joints of green tea-fed mice \[77,78\].
Eicosapentenoic acid: An omega-3 fatty acid, found to be of great medicinal value because of its importance in curing coronary heart disease, asthma, high blood pressure and inflammatory disorders as rheumatoid arthritis. The components isolated from Heliotropium indicum have different medicinal values which compare very well with the traditional uses of the plant. For example, it also cures Rheumatoid Arthritis, menstrual problems and wound healing by preventing blood from clotting, reduces pain and swellings. This acid is sufficient to sterilize wounds and keep them off from other microbes which may not strive under harsh acidic medium.[79]

ORGANIC COMPOUNDS: Myristicin: It is a phenylpropene, a natural organic compound, found in various plants like nutmeg, parsley and dill. A study was carried out to find the anti-inflammatory effect of myristicin on double-stranded RNA (dsRNA)-stimulated macrophages. Myristicin did not reduce the cell viability of RAW 264.7 mouse macrophages at concentrations of up to 50μM. Myristicin significantly inhibited the production of calcium, nitric oxide (NO), interleukin (IL)-6, IL-10, interferon inducible protein-10, monocyte chemotactic protein (MCP)-1, MCP-3, granulocyte-macrophage colony-stimulating factor, macrophage inflammatory protein (MIP)-1α, MIP-1β, and leukemia inhibitory factor in dsRNA [polyinosinic-polycytidylic acid]-induced RAW 264.7 cells (P < 0.05). In conclusion, myristicin has anti-inflammatory properties related with its inhibition of NO, cytokines, chemokines, and growth factors in dsRNA-stimulated macrophages via the calcium pathway[80].

Eicosapentenoic acid
MISCELLANEOUS: *Uncaria tomentosa* (Rubiaceae) contains several alkaloids, steroids, terpenoids, flavonoids and tannins that are responsible for its medical effects. These are Ajmalicine, akuammigine, corynantheine, corynoxeine, iso-pteropodine, pteropodine, speciophylline, rhyn chophylline (alkaloids), campesterol, sitosterols, stigmasterol, strictosidines, daucosterol (anabolic steroid), chlorogenic acid, hirsuteine, hirsutine, loganic acid, lyaloside, mitraphylline, oleanolic acid, (terpenoids), rutin, procyanidins, cinchonain (flavonoids), catechin, epicatechin, palmitoleic acid (fatty acid) and quinovic acid, (glycosides). It is used as anti-inflammatory, anti-arthritic, anti-oxidant, anti-diabetic, and in chronic fatigue disease. Animal study of anti-inflammatory activity of cat’s claw extract showed its ability to reduced paw oedema in carrageenan induced inflammation rat model[81, 82, 83].
chlorogenic acid

cinchonain

corynantheine
corynoxeine

Daucosterol
epicatechin

hirsuteine
hirsutine

iso-pteropodine

loganic acid
Lyaloside

mitraphylline

palmitoleic acid

procyanidins

pteropodine

quinovic acid

rhynchophylline

rutin

sitosterols

speciophylline

stigmasterol
Table 1: Summarises various antirheumatic phytoconstituents and their plant sources.

<table>
<thead>
<tr>
<th>Sr. No.</th>
<th>Chemical Constituent</th>
<th>Plant Source</th>
<th>Reference</th>
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<tbody>
<tr>
<td><strong>ALKALOIDS</strong></td>
<td></td>
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</tr>
<tr>
<td>1.</td>
<td>Tetrandrine</td>
<td><em>Stephania tetrandra</em>&lt;br&gt;<em>Menispermaceae</em></td>
<td>Ferrante et al., 1990.&lt;br&gt;Teh BS et al., 1990.</td>
</tr>
<tr>
<td>4.</td>
<td>Stachydrine</td>
<td><em>Capparis spinosa L.</em>&lt;br&gt;<em>Capparidaceae</em></td>
<td>I. Feng X et al., 2011.</td>
</tr>
<tr>
<td>5.</td>
<td>Colchicine</td>
<td><em>corns and seeds of</em>&lt;br&gt;<em>crocus like plants</em></td>
<td>Saiš G et al., 1995.&lt;br&gt;Malkinson FD 1982.</td>
</tr>
<tr>
<td>8.</td>
<td>Spilanthol</td>
<td><em>Spilanthes acmella</em></td>
<td>Wu LC et al., 2008.</td>
</tr>
<tr>
<td></td>
<td>Compound</td>
<td>Source</td>
<td>Reference</td>
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<tr>
<td>14</td>
<td>Tylophorine analog, DCB 3503</td>
<td>Tylophora atrofolliculata</td>
<td>Xin You et al., 2006</td>
</tr>
<tr>
<td>15</td>
<td>Tylophorine</td>
<td>Tylophora indica Asclepiadaceae</td>
<td>Handa et al., 1992</td>
</tr>
<tr>
<td>16</td>
<td>Trilobine, Isotrilobine</td>
<td>Cocculus trilobus Menispermaceae</td>
<td>Johji et al., 1975</td>
</tr>
<tr>
<td>17</td>
<td>Hypaconitine</td>
<td>Aconitum colianthum, A. carniheli, and A. Napellus (Ranunculaceae).</td>
<td>Djerassi et al., 1994</td>
</tr>
<tr>
<td>18</td>
<td>piperine, piperidine</td>
<td>Piper nigrum Linn (Piperaceae)</td>
<td>Bang et al., 2009, Pradhan et al., 2009</td>
</tr>
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<td>19</td>
<td>Thalidasine</td>
<td>Thalictrum dasycarpum Ranunculaceae</td>
<td>Phillipson et al., 1985</td>
</tr>
<tr>
<td>20</td>
<td>tinosporine, tinosporide, tinosporaside,</td>
<td>Tinospora cordifolia Linn. (Menispermaceae)</td>
<td>Singh SS et al., 2003, Paval J et al., 2009</td>
</tr>
<tr>
<td>22</td>
<td>Baicalin, Baicalein Wogonin</td>
<td>Scutellaria baicalensis Labiatae</td>
<td>Kubo et al., 1984</td>
</tr>
<tr>
<td>23</td>
<td>Kolaflavanone</td>
<td>Garcinia kola Gutiferae.</td>
<td>Saini and Ghosal, 1984</td>
</tr>
<tr>
<td>24</td>
<td>Rutin, Quercetin (Flavonols)</td>
<td>Celastrus orbiculatus Celastraceae</td>
<td>Teresita Guardia et al., 2001</td>
</tr>
<tr>
<td>25</td>
<td>Epiafzelechin</td>
<td>Celastrus orbiculatus Celastraceae</td>
<td>Min et al., 1999</td>
</tr>
<tr>
<td>27</td>
<td>3-O-methylviolanone.</td>
<td>Dalbergia odorifera Leguminosae</td>
<td>Chan et al., 1998</td>
</tr>
<tr>
<td>28</td>
<td>Robinin</td>
<td>Robinia pseudacacia Borja Leguminosae</td>
<td>Cabor M 1979</td>
</tr>
<tr>
<td>29</td>
<td>stephanoside E, Stemucronatoside K</td>
<td>Stephanotis mucronata (Asclepiadaceae)</td>
<td>Xiao-yu Li et al., 2012</td>
</tr>
<tr>
<td>30</td>
<td>Xanthorhamnin</td>
<td>Rhamnus infectoria Rhamnaceae</td>
<td>Harbone and Mabry, 1975</td>
</tr>
</tbody>
</table>

**FLAVONOIDS**

- 21. aromadendrin, Apigenin, vitexin
- 22. Baicalin, Baicalein Wogonin
- 23. Kolaflavanone
- 24. Rutin, Quercetin (Flavonols) Hesperidin (Flavanone):
- 25. Epiafzelechin
- 26. chrysion, oroxyline, oroxylin-a, scutellarin baicalein, biochanin-a and ellagic acid
- 27. 3-O-methylviolanone.

**GLYCOSIDES**

- 28. Robinin
- 29. stephanoside E, Stemucronatoside K
- 30. Xanthorhamnin
| 34. | Salicin Populin | Populus alba | Hiller et.al, 2006. |

**SAPONINS**


**TERPENOIDS AND STEROIDS**

<table>
<thead>
<tr>
<th>No.</th>
<th>Compounds</th>
<th>Identification/Species</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>48.</td>
<td>mannitol, β-amyrin, β-sitosterol, benzoic acid and benzoic ester of longanin, nycthanic acid</td>
<td><em>Nyctanthes arbortristis</em> Linn. (Oleaceae)</td>
<td>Sandhar HK et al., 2011.</td>
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</table>

**COUMARINS**

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<th>No.</th>
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<th>Identification/Species</th>
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<tr>
<td>49.</td>
<td>Osthol</td>
<td><em>Cnidium monnieri</em></td>
<td>Pei-Chun Liao et al., 2010.</td>
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</table>

**XANTHONES**

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<th>No.</th>
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**TANNINS**

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<th>No.</th>
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**PEPTIDES, CATECHINS AND FATTY ACIDS**

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<tr>
<th>No.</th>
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<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>54.</td>
<td>Aurantiamide acetate, 1, 3-Dibenzyl Urea</td>
<td><em>Moringa oleifera</em></td>
<td>Koneni et al., 2009.</td>
</tr>
<tr>
<td>56.</td>
<td>Eicosapentenoic acid</td>
<td><em>Heliotropium indicum</em></td>
<td>Shoge et al., 2011.</td>
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</table>

**ORGANIC COMPOUND**

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<th>No.</th>
<th>Compounds</th>
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<tr>
<td>57.</td>
<td>Myristicin</td>
<td><em>Myristica fragrans</em> Houtt (Myristaceae)</td>
<td>Ji Young and Wansu 2011.</td>
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</tbody>
</table>

**MACELLINIOUS**
<table>
<thead>
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<th>Page</th>
<th>Content</th>
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</thead>
<tbody>
<tr>
<td>58.</td>
<td>Ajmalicine, akuammigine, corynantheine, corynoxeine, isopteropodine, pteropodine, speciophylline, rhynchophylline (alkaloids), campesterol, sitosterols, stigmasterol, strictosidines, daucosterol (anabolic steroid), chlorogenic acid, hirsuteine, hirsutine, loganic acid, lyaloside, mitraphylline, oleanolic acid, (terpenoids), rutin, procyanidins, cinchonain (flavonoids), catechin, epicatechin, palmitoleic acid (fatty acid) and quinovic acid, (glycosides).</td>
</tr>
<tr>
<td></td>
<td>Uncaria tomentosa (Rubiaceae)</td>
</tr>
</tbody>
</table>

**REFERENCES**


81. Cat's Claw, available from http://fastflustop.com/Cats Claw.html(as viewed on 14/2/12)