



## International Journal of Pharmacology and Clinical Research (IJPCR)

IJPCR | Volume 3 | Issue 2 | July - Dec - 2019  
www.ijpcr.net

Review article

Clinical research

ISSN: 2521-2206

### A review of rheumatoid arthritis

**Dr. Challa Pradeep Kumar\*, Ravali Marati, B. Suhasini**

*Department of Pharmacology, Vaageswari College of Pharmacy, Karimnagar, India, 505001.*

**\*Address for correspondence: Ravali Marati**

**E-mail: ravalimarati@gmail.com**

#### ABSTRACT

Rheumatoid arthritis is a chronic inflammatory and systemic auto immune disease affecting people for the most part between the ages of 20-25 yrs with accidental course. About 1% of the worlds population is afflicted by rheumatoid arthritis and is 2-3 times more common in women than men. The rheumatoid arthritis due to the presence of pro inflammatory markers, cytokines and leukotrienes. The primary inflammatory markers are IL-1, TNF- $\alpha$ , IL-6, IL-15, IL-16, IL-17, IL-18, IFN- $\gamma$ , and the granulocyte macrophage colony stimulating factor, chemokines such as IL-8, macrophage inflammatory protein-1 and monocyte chemo attractant protein-1. IL-1, TNF- $\alpha$ , IL-6, B cells therapy all these blockade are therapeutic target for its treatment. estimate the anti arthritic activity of the plants are used in different animal models to induced arthritis. Medicinal plants have been used as major sources of pure of human diseases since time immemorial. Now a days most of the people depends on traditional medicines of the plants. The medicinal plants derived medicines for the first time of primary health care because of least or no side effects.

**Keywords:** Rheumatoid arthritis, Cytokines, Medicinal plants.

#### INTRODUCTION

Arthritis, generally inflammation of joints is occurring in all age groups it is a one of the oldest known diseases. In India, more than about 20% of total population is suffering from arthritis. RA is a chronic, systemic inflammatory disease for the most part affecting the joints & periarticular tissue. RA still remains a difficult disease being capable of producing severe crippling deformities, functional disabilities, cartilage destruction it commonly leads to major disability, caused by macrophages including reactive on species, ecosanoids such as prostaglandins, leukotrienes & cytokines. The

regulation of these mediators secreted by macrophages & other Immune cells. The modulations of arachidonic acid metabolism by inhibiting enzymes like COX & LOX are the potential target for chronic inflammatory conditions. Pro inflammatory cytokines such as TNF- $\alpha$ , IL- $\beta$ &IL-6 are important mediators of the disease continuation. The arthritis usually begins in the small joints of the hands & the feet, dispersion later to the larger joints, the inflamed joint lining or synovial extends & then erodes the articular cartilage & bone, causing joint deformity & progressive physical disability. Extra articular

5 features include nodules, pericarditis, pulmonary fibrosis, peripheral neuropathy & amyloidosis.

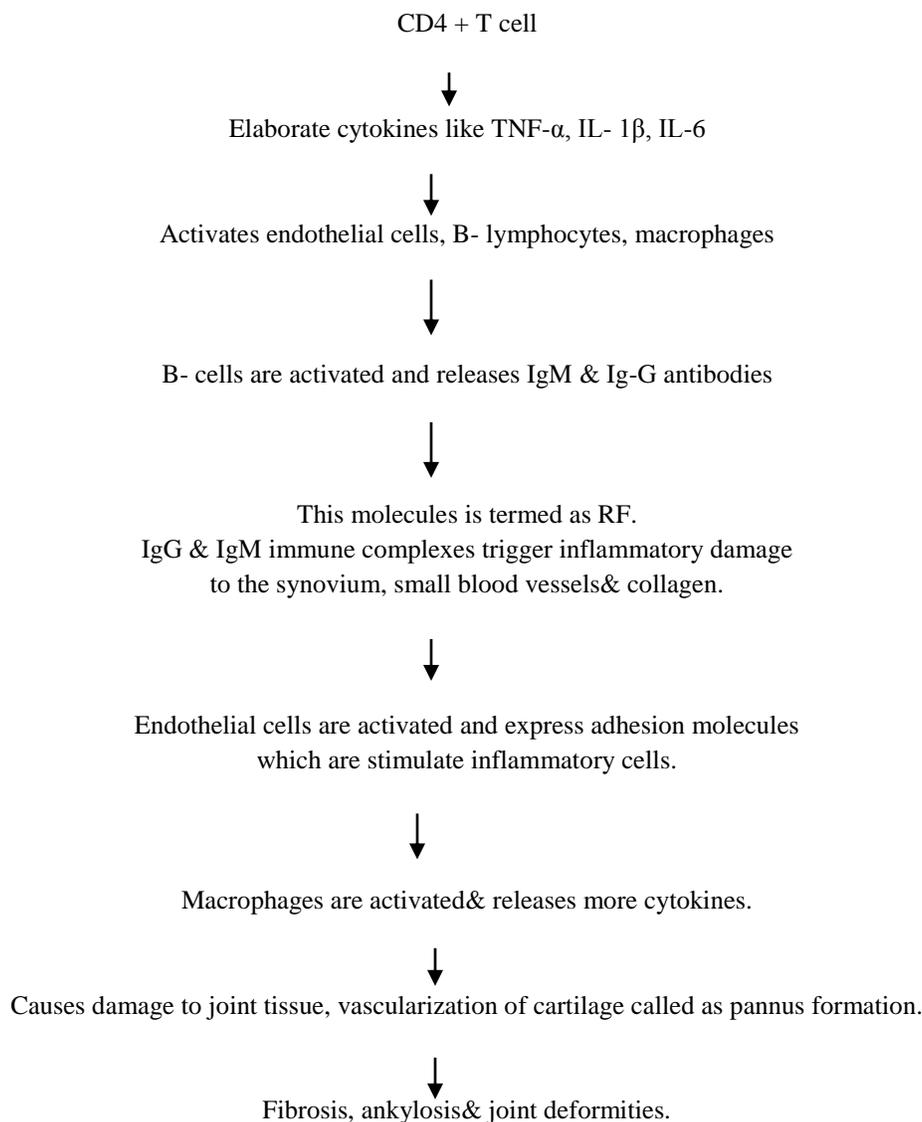
### Epidemiology

About 1% of the world's population is afflicted by RA, women 3 times more often than men. Represents 1 of the most prevalent chronic health problems & is a leading cause of disability, in 2002 U.S adults 43 million affected by arthritis, in 2020 expected to reach 60 million. It is upto 3 times more

common in smokes than non-smokers, particularly in men heavy smokers & those drank people, modest amounts of alcohol regularly were 4 times less likely to get RA than those who never drank.

### Pathogenesis of RA

In response to antigenic exposure in a genetically predisposed individual (HLA-DR), CD4+Tcell are activated.



### DIAGNOSIS

#### Blood tests

Routine viral screening by serologic testing does not significantly facilitate the diagnosis of RA in patients with early RA, nor is it helpful as a

potential identifier of disease. progression. potentially useful laboratory studies in suspected RA fall into 3 categories – markers of inflammation, heamatologic parameters & immunologic parameters are include the following: ESR (Erythrocyte sedimentation rate)

CRP (C-Reactive protein)

Complete blood count

RF assay

Antinuclear antibody (ANA) assay

- Anti-cyclic citrullinated peptide (Anti-CCP) & Anti mutated citrullinated vimentin (anti-MCV) assays (currently used in the 2010 American college of Rheumatology (ACR) / (European league against Rheumatism (EULAR). classification criteria, micro RNA.

### Hematological parameters

CBC – A CBC will test various levels of cells & chemicals present in blood, including the red & white blood cells, platelets, markers of liver & kidney function & uric acid. Patients with RA often have an abnormal CBC, with anemia (Decreased red blood cells or HB) & Thrombocytopenia (Decreased platelets).

Immunologic parameters:

Autoantibodies (RF, ANA, ACPA, AFA), mi RNA.

RF: It is an Ig M antibody directed against the FC (crystallisable fraction) fragment of IgG,i,e; present in approximately 60-80% of patients with RA over the course of their disease but in less than 40% of patients with early RA, 3%-5% of healthy adults have serum RF: this increases to 10-30% in the elderly. RF is more recognized as a biomarker for RA than anti-CCP, having been adopted as one of the ACR, classification criteria, for RA in 1987. The European clinical standing committee for International clinical studies including Therapeutics (ESCISIT) notes that it is one of several prognostic markers used to recognize patients with constant or erosive disease but does not optional RF as a diagnostic marker of RA. Most likely at least in part due to its limited specificity. RF is also common in other auto immune diseases, infectious diseases & malignancies, making it a relatively nonspecific marker of RA. Although ANAS are present in approximately 40% of patients with RA, test results for antibodies to most nuclear antigen subsets are negative.

### Herbal Therapy for the Treatment of Arthritis

Herbal medicines are used for the treatment of various ailments ancient times & in the mankind the herbal drugs are used is not an amplification. Herbal medicines are synthesized from the

therapeutic experience of cohort of practicing physicians of very old system of medicine for more than hundreds of years. Nowadays, investigator shows a great curiosity in those medicinal agents that are resulting from plants because the currently available drugs are either have certain side effects or highly expensive. The herbal plants which are widely distributed all over the world as a source of therapeutic agents for the prevention & cure of various diseases. According to WHO, World's 80% population uses herbal medicines for their primary health care needs. The medicinally important parts of these herbal plants are chemical constituents that produce a desired physiological action on the body. Since very old time India uses herbal medicines in the formally alternatives systems of health such as Ayurveda, Unani & Sidha, Homeopathy & Naturopathy. In, India, there are more than 2500 plants species which are currently used as herbal medicaments, for than 3000 years the herbal medicines are used either directly as folk medication or indirectly in the preparation of recent pharmaceuticals. Thus, from the knowledge of traditional plants one might be able to discover the new effective & cheaper drugs. In this review article, we have tried to cover all the ayurvedic strategies that are followed for the treatment of RA without any possible side effects. The future treatment of RA should provide more effective relief.

*Surender singh et al* Reported that anti-arthritis activity of poly herbal formulation of Majoon suranjan.in arthritis induced albino wistar rats. MS (450mg & 900,1800mg/kg, b.w) were tested for its anti arthritic activity by formaldehyde & complete freund's adjuvant induced arthritis. The results suggest that the anti-arthritis activity of MS was due to the interplay between its anti-inflammatory & disease modifying activities, thus supporting its use in traditional medicine for the treatment of RA. *Kore K.J et al* Reported that anti-arthritis activity of Hydro alcoholic leaf extract of Lawsonia innermis linn in adjuvant induced rats, To evaluate the Biochemical parameters such as HB, ESR. The results of the current investigation concluded, hydroalcoholic extract of Lawsonia innermis possess a significant anti-arthritis activity against adjuvant induced arthritis & formaldehyde induced arthritis model & justifying its therapeutic role in arthritic condition. The observed anti arthritic activity may

be due to the presence of phytoconstituents such as alkaloid & flavonoids. *PokhrajGuha et al* Reported that the analyses of human & rat clinical parameters in rheumatoid arthritis the use of crude Aloe Vera gel in disease Amelioration. To evaluated the anti arthritic roles of raw Aloe Vera gel & it's effects in rat model where arthritis was induced by using freundscomplete adjuvant. 3 essential conclusive statements were derived from the study. Firstly, the 6 clinical parameters that we have selected for the study namely, RA factor, CRP, ASO, ESR, Ceruloplasmin& serum creatinine were all essential for the different diagnosis of RA during its early& later stages, RA factor being the most sensitive of all parameters. Secondly this study has supported the use of the rat as a model for designing therapeutic strategies against. Lastly as evident from our study, Aloe Vera gel extracts can be beneficial for the reduction of inflammatory edema& also for the reduction of Ceruloplasmin in RA condition in rat model. However, further investigations are necessary for more refined therapeutic usage of aloe Vera for the treatment of RA in human. *Manjushachoudhary et al* The anti arthritic activity reported that Barleriapronitis Linn. leaves extract in arthritis induced rats. The extract of Barleriapronitis were tested for various preliminary phyto constitutes & were screened for anti arthritic activities using freunds complete adjuvant arthritis & formaldehyde induced arthritis in albino wister rats. The results conclude that arthritis assessment, paw volume, body weight, motor incoordination, nociceptive threshold in freunds complete adjuvant induced arthritis. The present investigation of plant extract protects synovial membrane by improving the health status through haematinic parameters and exhibits promising anti arthritic activity. *ArtiBhujade et al* The activity of anti arthritis reported that *Cissusquadrangularis* against adjuvant induced arthritis in albino wister rats. The anti arthritic activity of active fraction of *Cissusquadrangularis* obtained from acetone extract of *Cissusquadrangularis* has been reported by employing complete adjuvant arthritis. Rat paw edema was induced by carragenan, the alternated pharmacological parameters, biochemical parameters were determined. The results had indicated that AFCQ possesses a significant anti arthritic activity against freunds complete adjuvant

induced arthritis. Results were analyzed through histopathology& radiography. *Madhavi G. Patel et al* The anti arthritic activity of classical Ayurvedic formulation of alcoholic extract of Vatariguggulu in albino wister rats. Reported that the extract was administered to the rats by oral gavages in different doses. Joint swelling was measured in formaldehyde induced arthritis. To determine the various physical, biochemical, radiography parameters in CFA induced arthritis. *Divyamanipolireddy et al* Reported that the arthritic activity of ethanolic extract of *Sidacardifolia*. This *Sidacardifolia* Linn tested on rats showed potent anti oxidant & anti inflammatory activity. The observed results of anti arthritic activity may be due to the presence of phyto constitutes such as glycosides, flavonoids, saponins, alkaloids, Tannins, carbohydrates. *Vijayalaxmi A et al* The anti arthritic and the anti inflammatory activities are reported that Beta caryophyllene against freunds complete adjuvant induced arthritis in albino wister rats. To measure the arthritis assessment, paw volume, radiological examination was performed. To examine the histopathology, biochemical parameters like anti oxidant, total protein, lipid peroxidation, serum nitrates, SGOT, SGPT. The results are Beta caryophyllene significantly decreased in the arthritis which was evident with arthritis index, paw volume as well as the maintenance of biochemical parameters. Th3 histopathology and radiological examinations are also revealed the control in inflammation with Beta caryophyllene. *Madan Singh et al* The current study is aimed to evaluate the leaf extract of *Manilkarazapota* of anti arthritic activity by using in vitro inhibition of membrane stabilisation and protein denaturation model. The standard drug is acetyl salicylic acid. The results are revealed that the 2 different concentrations of ethanolic leaf extract of *Manilkarazapota* possessed significant anti arthritic activity compared to acetyl salicylic acid is the standard drug and the test plant extract shows the dose dependent activity. *Sumitra Singh et al* Reported that the study was planned to the in vitro bark extract of anti arthritic activity of *Acacia auriculiformis* A cunn. The ethyl acetate, ethanol, aq. Extracts of this plant were subjected to phytochemical constitutes screening. Denaturation was induced by incubating the extracts with bovine serum albumin under controlled experimental

conditions. The protein denaturation and membrane stabilisation were calculated by determination of their absorbance. The results showed that the plant extracts showed anti arthritic activity in a concentration dependent manner and the activity was increased on increasing the concentration of extracts. Ethanol extract was found to be more effective than the other extracts. In this study the phytoconstitutes are phenol, Tannins, flavonoids present in the plant. The recent study reveals that the stem bark software *Acacia auriculiformis* possesses anti arthritic activity. *Dr.Devprakash et al* To evaluate the activity of anti arthritic potential of *Zingiberofficinale* in rats. The alcoholic and aqueous extract of the *Zingiberofficinale* were tested for its anti arthritic activity by formaldehyde induced arthritis. Evaluation of the phytoconstitutes screening revealed the presence of alkaloids, flavonoids, Tannins, terpenoids, phlobotannins in both extracts. In both extracts the LD50 studies up to the maximum of 2000mg/kg dose level no mortality was observed. Their investigation concluded that both extracts of *Zingiberofficinale* possesses a significant anti arthritic activity. *Yong Chen et al* Reported that the arthritic activity of ethanolic extract of *Claoxylonindicum* on freunds complete adjuvant induced arthritis in albino wister rats. The results also found that there was a significant reduction level of expression of interleukin- 1B, TNF- alpha in the serum samples of freunds complete adjuvant rats. To determine the paw volume, severity of arthritis score, radiological examinations. In this the inflammatory responses in the joints of adjuvant induced arthritis suggested by the modulatory effects on paw swelling, hyperplasia, of lymphatic tissues and synovial membrane. The results are suggested that CIE possessed substantial anti arthritic activity due to immuno depression and regulation of cytokines, CIE may be a potential candidate for the treatment of RA. *MNL Aishwarya et al* Reported that anti arthritic activity of *Murraya exotica* against formaldehyde induced arthritis in rats. Evaluation of haematological, biochemical, radiographic examination of joints. The results demonstrated significant anti arthritic activity of *M.ecotica* at the doses (200&400 mg/kg, b.w, p.o) by ameliorating the changes in physical, haematological, biochemical parameters as compared to arthritic control evidenced by the radiographical

examinations of joints. *Madhavi G. Patel et al* Proved that the effects of ethanol extract an ayurvedic preparation (*pathyadya churna*) on arthritis in rats. Results indicate that the extract of *pathyadya churna* treatment reduced paw swelling in arthritis caused by both formaldehyde and CFA. In CFA treated rats, a significant decrease was seen in haemoglobin, red blood cell count. There also significant elevations in white blood cell count, ESR, total cholesterol, low density lipoproteins. Treatment with PCE significantly reversed all the haematological, radiographic changes in dose dependent manner. *Himanshu Sharma et al* Shows that the evaluation of anti arthritic activity of *Cinnamomum cassia* bark extract in experimental rats. The results indicates measure the joint diameter, ankle diameter, MDA levels. Also measured paw volume, serum TNF- $\alpha$ , IL-1 $\beta$ , histopathology. CCHE treatment significantly reduced MDA levels and joint swelling in a concentration dependent manner in rats with formaldehyde induced arthritis, in which GSH levels ere elevated. In rats CFA induced arthritis the CCHE treatment significantly reduced joint swelling, as well as TNF- $\alpha$ , IL-1 $\beta$  levels. *Chioma A Anosike et al* Shows the results of Membrane stabilization as a mechanism of the anti inflammatory activity of methanol extract of garden egg (*Solanum aethiopicum*). The methanol extracts of garden egg significantly and dose dependently reduced the acetic acid induced vascular permeability and agar induced leukocyte mobilization in rats. Te results show that methanol extract of *Solnum aethiopicum* has anti inflammatory properties and can reduce inflammatory injury and tissue damage.

## CONCLUSION

Arthritis is the chronic auto immune inflammatory disorders, primary cause of disability in western& developing countries. The presently available synthetic drugs in the market are not only reasonable management but also connected with adverse effects. The synthetic drugs includes NSAIDS, DMARDS like cyclophosphamide, intramuscular gold, sulfasalazine, methotrexate had the side effects of stomach ulcers, GIT bleeding, kidney, liver damage, hypertension. A large number of plants described this review clearly

established the importance of herbal plants in treatment of rheumatoid arthritis. The information discussed in this analysis might be moderately useful in obtaining monographs on plants & recommendations on their use. In this assessment,

we mainly deal with the security profile, pathogenesis, toxicity studies of plant extracts. The plant extracts & poly herbal formulations would be served as an exchange therapy for the treatment of arthritis with minor side effects.

## REFERENCES

- [1]. Patwardhan S.K., Bodas K.S., Gundewar S.S. Coping with arthritis using safer herbal options. *Int. J. Pharm. Sci.* 2(1), 2010, 2-11.
- [2]. Shin HY, Jeong – tang inhibits the stem cell factor-induced migration and inflammatory cytokines secretion in mast cells. *J. Ethnopharmacology* 85, 2003, 157-161.
- [3]. Kore KJ, Shete RV., Anti Arthritic activity of Hydro alcoholic extract of Lawsonia innermis against adjuvant arthritis. *Int.j.drugdev&res*; 3(4), 2011, 217-224.
- [4]. Rathore B., Mahdi A.A., Paul B.N., Saxena P.N., Das S.K. Indian herbal medicines: possible potent therapeutic agents for rheumatoid arthritis. *J Clin. Biochem. Nutri.* 41(1), 2007, 12-17.
- [5]. Deborah S., Colin M., Bruce P. The global burden of rheumatoid arthritis in the year 2000. *Global Burden of Disease 2000.* (Draft 15-08-06)
- [6]. Majithia V., Geraci S.A. Rheumatoid arthritis: diagnosis and management. *Am. J. Med* 2007; 120(11):936-939. doi:10.1016/j.amjmed.. 2007, 04-005.
- [7]. Siddiqui M.A., Amir A., Vats P., BRani K., Malik S.A., Arya A., Kapoor N., Kumar H. Arthritis database: A composite web interface for anti arthritic plants. *J. Med. Plant. Res.* 5(12), 2011, 2457-2461.
- [8]. Maxwell J., Gowers I., Moore D., Wilson A. Alcohol consumption is inversely associated with risk and severity of rheumatoid arthritis. *Rheumat. (Oxford, England).* 49, 2010, 2140-2146.
- [9]. Iain B. McInnes, Georg Schett. The pathogenesis of rheumatoid arthritis *N Engl J Med.* 365, 2011, 2205-19.
- [10]. Joseph T Dipiro *Pharmacotherapy: A pathophysiological approach.* 7, 2008.
- [11]. Emanuel Rubin, Gorstein, Raphael Rubin, Schwarting, Strayer. *Rubin's pathology clinicopathologic foundation of medicine Rheumatoid arthritis* 4, 2005.
- [12]. Varache, S., Narbonne, V, and Jouse-Joulin, S. Is routine viral screening useful in patients with recent onset polyarthritis of a duration of at least 6 weeks? Results from a nationwide longitudinal prospective cohort study. *Arthritis care Res (Hoboken).* 63(11), 2011, 1565-70.
- [13]. Venables, P.J.W. and Maini, R.N. Clinical features of rheumatoid arthritis. In: O'Dell JR, Romain PR, eds. *Up to date.* Wolters Kluwer Health. Accessed at: 2013.
- [14]. Nijenhuis, S., Zendman, A.J.W., Vossenaar, E.R., Pruijn, G.J.M. and Van venrooij, W.J. *Clin chem.*, 350, 2004, 17.
- [15]. 5. Arnett, F.C., Edworthy, S.M. and Bloch, D.A. *Arthritis Rheumat.* 31, 1988, 315.
- [16]. Combe, B., Landewe, R. and LUKAS, c. *Eular recommendations for the management of early arthritis: Report of a task force of the European standing committee for international clinical studies including therapeutics (escisit)* *Ann Rheum Dis.* 66, 2007, 34-45.
- [17]. Aletaha, D., Neogi, T., Silman, A.J., Funovits, J., Felson, D.T. and Bingham, C.O. 3<sup>rd</sup>. *Rheumatoid arthritis classification criteria: an American college of Rheumatology/European League Against Rheumatism collaborative initiative.* *Arthritis Rheum.* 62(9), 2010, 2569-2581.
- [18]. Tandon V, Gupta RK. *Histomorphological changes induced by Vitex negundo in albino rats.* *Indian J Pharmacol.* 36, 2004, 176-7.
- [19]. Vispute S, Khopade A, *Glycyrrhiza glabra* Linn. – *KlitK: A review.* *Int J Pharm Bio Sci.* 2, 2011, 42-51.
- [20]. Badami S, Moorkoth S, Suresh B. *C aespalinia sappan* a medicinal and dye yielding plant. *Nat Prod Rad.* 3, 2004, 75-82.
- [21]. Kalaria P, Gheewala P, Chakraborty M, Kamath J. *A phytopharmacological review of Alstonia scholaris: A panoramic herbal medicine.* *IJRAP.* 3, 2012, 367-371.

- [22]. Sudha K, Mathanghi SK. Traditional underutilized green leafy vegetables and its curative properties. Int J Pharm. 2, 2012, 786-93.
- [23]. Singh V, Patel H, Suvagiya V, Singh K. Some traditionally used anti arthritic herbs a review. Int Res J Pharm. 2, 2011, 43-5.
- [24]. Kiran DD, Rohilla A, Rohilla S, Khan MU. Phyllanthus amarus: An ample therapeutic potential herb. Int J Res Ayur Pharm. 2, 2011, 1096-9.
- [25]. Thirumal M, Vadivelan R, Kishore G, Brahmaji VS. Aristolochia bracteolata: An overview on pharmacognostical, phytochemical and pharmacological properties. Earth J. 1, 2012, 66-78.
- [26]. Kalita S, Kumar G, Karthik L, Rao BV. A review on medicinal properties of Lantana camara Linn. Res J Pharm Technol. 5, 2012, 711-5.
- [27]. Kasper DL, Fauci AS, Longo DL, Braunwald E, Hausman SL, Jameson JL. II. United States of America: Mc-Graw Hill Companies; 16, 2005. Harrison's principle of internal medicine.
- [28]. Surender singh, anti arthritic activity of Majoon Suranjan (a polyherbal Unani formulation) in rat. The Indian Journal of Medical Research. 2011, 384-388.
- [29]. Kore K.J\*. Anti arthritic activity of Hydroalcoholic extract of Lawsonia Innermis. International Journal of Drug Development & Research. 2011, ISSN 0975-9344.
- [30]. Pokhraj Guha analyses of Human and Rat clinical Parameters in Rheumatoid arthritis Raise the possibility of use of crude Aloe vera gel in disease Amelioration 2014.
- [31]. Manjusha choudhary anti arthritic activity of Barleria prionitis Linn. Leaves in acute and chronic models in Sprague Dawely rats. Institute of pharmaceutical sciences, pharmaceutical Chemistry.(ELSEVIER). 52, 2014, 199-209.
- [32]. Arti Bhujade In vivo studies on antiarthritic activity of Cissus quadrangularis against Adjuvant induced arthritis. J of Clinical and cellular immunology 2015.
- [33]. Madhavi G. Patel, anti arthritic activity of a classical Ayurvedic formulation Vatari Guggulu in rats. J of Traditional and complementary medicine 2015.
- [34]. Divya Mani Polireddy, evaluation of anti arthritic activity of ethanolic extract of Sida cardifolia. International Journal of Scientific and Technology Research ISSN 2277-8616. 2015.
- [35]. Vijayalaxmi A, Anti arthritic and anti inflammatory activity of Beta Caryophyllene against freund's complete adjuvant induced arthritis in wister rats, J. of Bone Reports & Recommendations 2015. ISSN 2469-6684.
- [36]. Madan singh ,In vitro anti arthritic activity of Manilkara zapota Linn J. of Pharmacognosy 2011.
- [37]. Sumitra singh\*, Evaluation of in vitro anti arthritic activity of Acacia auriculiformis A. Cunn. EX. Benth. Stem bark. J of pharmacy and pharmaceutical sciences 2016.
- [38]. Dr. Dev prakash, Evaluation of anti arthritic potential of Zingiber officinale in experimental rats. J of Pharmaceutical and medical research. 3(4), 2016, 305-308.
- [39]. Yong Chen anti arthritic activity of ethanol extract of Claoxylon indicum on freunds complete adjuvant induced arthritis in mice. BMC Complementary and Alternative Medicine 17, 2017, 11.
- [40]. MNL Aishwarya anti arthritic activity of Murraya exotica against formaldehyde induced arthritis in wister rats. J of Pharmaceutical, Biological and Chemical Sciences 2018.
- [41]. Madhavi G. Patel effect of ethanol extract of an ayurvedic preparation (Pathyadya churna 0 on arthritis in rats. Department of Pharmacognosy, 2018. IP: 117, 211, 126, 183.
- [42]. Himanshu Sharma, evaluation of the anti arthritic activity of Cinnamomum cassia bark extract in experimental models. Department of Pharmacology 2018.
- [43]. Chioma A Anosike, Membrane stabilization as a mechanism of the anti inflammatory activity of methanol extract of garden egg ( Solanum aethiopicum). J of Pharmaceutical sciences 2012.