

A REVIEW ON MOST POTENT HERBAL DRUGS USED IN ARTHRITIS

Aishwarya S. Patil*, S. V. Pimpale and B. S. Wakure

Department of Pharmaceutics, VDF School of Pharmacy, Latur, MH, 413512. India.

Received date: 04 October 2022

Revised date: 24 October 2022

Accepted date: 14 November 2022

*Corresponding Author: Aishwarya S. Patil

Department of Pharmaceutics, VDF School of Pharmacy, Latur, MH, 413512. India.

ABSTRACT

Background: India is very traditional country and we are lucky to have treasure house of traditional medicine. now a days ayurvedic medicine has been a boon in the treatment of many disastrous disease. Rheumatoid arthritis is one of the autoimmune disorder which is due to faulty metabolism of body and stress. it becomes chronic inflammatory disorder which result in severe pain. allopathic medicine can reduce pain but the root cause remain untreated. Main body-in this paper we study on combination of most potent herbal drugs like ashwagandha, safed musli, mahayogiraj guggul and maharasandi kwath that have clinically proven anti-inflammatory, analgesic and anti arthritic activities when used alone. now a days such kind of inflammatory disorders increases day by day due to change in lifestyle. inflammation in any part of the body result either due to physical injury or due to internal faulty metabolism of the body. faulty metabolism of the body may be due to improper diet irregular food timings, anger, stress. As per Ayurveda, faulty metabolism of body produces Aam (toxins or Reactive Oxygen Species). These Aam or Reactive Oxygen Species (ROS) are highly unstable compounds and are key signaling molecules that play an important role in the progression of inflammatory disorders. As per Ayurveda ROS leads to imbalance in the three main pillars of the body that is vata-pitta-kapha. Under normal conditions, ROS levels are controlled by the body's complex antioxidant defense system and there is an equilibrium between ROS formation and degradation. Overproduction of ROS and/or inadequate antioxidant defense disturbs this equilibrium in favor of ROS upsurge that results in oxidative stress. A deficiency in the body's natural antioxidant defense mechanisms has been implicated as the etiological or pathological factor in several clinical disorders. Short conclusion- The accessible logical information support the end that ashwagandha, safed musli, mahayogiraj guggul, maharasandi kwath are genuinely powerful regenerative tonic (Rasayana of Ayurveda), because of its different pharmacological activities like enemy of stress, neuroprotective, antitumor, ligament pain relieving, calming and so on.

KEYWORDS: Rheumatoid arthritis, safed musli, ashwagandha, mahayogiraj guggul, green tea.

BACKGROUND

Plants have generally been assuming a significant part as expected wellspring of medications. Regular medications now and again can make genuine unfriendly impacts. Home grown medications have been widely utilized in evolved nations as they are regular and generally protected. The standard fundamental the utilization of more than one plant/plant item in these details is that they might create synergistic and additionally added substance impacts, or one might kill the harmful impact of another, which is generally restorative in the given setting.^[1] As indicated by World Health Organization, International guidelines connecting with human wellbeing expect that all new drug medications and plant items are tried for their security before their utilization in

human workers and patients. Natural plan are believed to be more protected and solid method for treating infection. A polyherbal against joint definition contains powders of Withania somnifera, mahayogiraj guggul, Safed musli, and maharasandi kwath that have clinically been demonstrated viable calming, pain relieving and hostile to ligament exercises when utilized alone. Ashwagandha is an unmistakable spice in Indian Ayurvedic medication and has turned into a famous enhancement because of its medical advantages. Restricted proof recommends that Ashwagandha lessens glucose levels through its impacts on insulin emission and responsiveness. It might assist with decreasing misery. The medication is accounted for with hostile to inflammatory, anti arthritic, cardioprotective, antistress. It has been displayed to increment bulk, diminish muscle

to fat ratio, and increment strength in men. It might assist with lessening the gamble of coronary illness by diminishing cholesterol and fatty substance levels. It enhancements might further develop mind capacity, memory and the capacity to perform undertakings. Despite the fact that Ashwagandha is ok for a great many people, explicit people shouldn't utilize it except if approved by their medical services supplier. Irritation in any piece of the body results either because of actual injury or because of inner broken digestion of the body. Defective digestion of the body might start from ill-advised diet, unpredictable food timings, outrage, stress. According to Ayurveda, defective digestion of body produces Aam (poisons or Reactive Oxygen Species). These Aam or Reactive Oxygen Speices (ROS) are exceptionally unsteady mixtures and are key flagging atoms that assume a significant part in the movement of incendiary problems. According to Ayurveda ROS prompts irregularity in the three primary mainstays of the body that is vata-pitta-kapha. Under ordinary circumstances, ROS levels are constrained by the body's mind boggling cancer prevention agent safeguard framework and there is a balance between ROS arrangement and debasement. Overproduction of ROS and additionally lacking cancer prevention agent safeguard upsets this balance for ROS upsurge that outcomes in oxidative pressure. A lack in the body's regular cancer prevention agent protection instruments has been ensnared as the etiological or obsessive component in a few clinical disorders.^[2] The medication is accounted for with hostile to inflammatory, anti arthritic, cardioprotective, antistress. It has been displayed to increment bulk, diminish muscle to fat ratio, and increment strength in men. It might assist with lessening the gamble of coronary illness by diminishing cholesterol and fatty substance levels. It enhancements might further develop mind capacity, memory and the capacity to perform undertakings. Despite the fact that Ashwagandha is ok for a great many people, explicit people shouldn't utilize it except if approved by their medical services supplier. Irritation in any piece of the body results either because of actual injury or because of inner broken digestion of the body. Defective digestion of the body might start from ill-advised diet, unpredictable food timings, outrage, stress. According to Ayurveda, defective digestion of body produces Aam (poisons or Reactive Oxygen Species). These Aam or Reactive Oxygen Speices (ROS) are exceptionally unsteady mixtures and are key flagging atoms that assume a significant part in the movement of incendiary problems. According to Ayurveda ROS prompts irregularity in the three primary mainstays of the body that is vata-pitta-kapha. Under ordinary circumstances, ROS levels are constrained by the body's mind boggling cancer prevention agent safeguard framework and there is a balance between ROS arrangement and debasement. Overproduction of ROS and additionally lacking cancer prevention agent safeguard upsets this balance for ROS upsurge that outcomes in oxidative pressure. A lack in the body's regular cancer prevention agent protection

instruments has been ensnared as the etiological or obsessive component in a few clinical.^[2] These arbiters come from plasma proteins or cells including mast cells, platelets, neutrophils and monocytes. They are host proteins. Synthetic go betweens tie to explicit receptors vascular penetrability, neutrophil, chemotaxins, animate smooth muscle compression, have direct enzymatic action, prompt agony or protein denaturation and intervene oxidative harm, making the protein lose its sub-atomic adaptation and capacities or become denatured.^[3-6] It is therefore concluded that, intensifies which can forestall these progressions and hinder thermally or heat instigated protein denaturation, have possible remedial worth as mitigating agents.^[5] The World Health Organization (WHO) has assessed that 80% of the world occupants used customary medication for their essential medical services needs and most of this treatment requires the utilization of natural concentrates and their dynamic parts. Different restorative plant bioactive concentrates and their recognized/segregated dynamic constituents have shown an assortment of therapeutic pharmacological properties against different intense and ongoing infections/disorders.^[7-9] Currently, the effect of oxidative pressure and its related variables has turned into a significant issue of human health.^[10] When the body is under a great deal of pressure, brings about protein denaturation and the development of ROS (e.g., hydroxyl extremists, superoxide anion revolutionaries, and hydrogen peroxide) is amplified.^[11] Endogenous enzymatic and non-enzymatic cancer prevention agent substance can't deal with the overburden of ROS and lead to uneven characters of the interaction, cell damage,¹¹ and wellbeing problems.^[12] Rheumatoid joint inflammation (RA) is an ongoing illness of obscure reason A provocative sickness of the synovium, it brings about torment, firmness, expanding, distortion and, in the end, loss of capacity in the joints. Since there is right now no known fix or method for forestalling RA, the American College of Rheumatology suggests the earliest conceivable determination and therapy with illness altering against rheumatic specialists to restrict the level of irreversible joint harm.^[13] It is a constant, balanced, fiery immune system illness that at first influences little joints, advancing to bigger joints, and in the end the skin, eyes, heart, kidneys, and lungs Often, the bone and ligament of joints are obliterated, and ligaments and tendons debilitate.^[14] This harm to the joints causes disfigurements and bone disintegration, typically extremely agonizing for a patient. Normal side effects of RA incorporate morning solidness of the impacted joints for > 30 min, weariness, fever, weight reduction, joints that are delicate, enlarged and warm, and rheumatoid knobs under the skin. The beginning of this sickness is for the most part from the age of 35 to 60 years, with abatement and intensification. It can likewise distress small kids even before the age of 16 years, alluded to as It can likewise beset little youngsters even before the age of 16 years, alluded to as adolescent RA (JRA), which is like RA with the exception of that rheumatoid variable isn't influences

adolescent RA (JRA), which is like RA aside from that rheumatoid element isn't found.^[15,16,17,18] In the West, the commonness of RA is accepted to be 1-2%.^[18,19] and 1% around the world.^[20] Clinically, the conclusion of RA can be separated from osteoarthritis (OA) as regions in RA are the proximal interphalangeal (PIP) and metacarpophalangeal (MP) joints; OA ordinarily influences the distal interphalangeal (DIP) joint. OA is the most widely recognized sort of joint inflammation and is brought about by mileage instead of an immune system condition. It no affects the lungs, heart, or insusceptible framework. Furthermore, OA regularly influences just a single side of the body, rather than the balanced idea of RA. Another separating factor is that RA patients experience the ill effects of industrious morning solidness for something like ≥ 1 h. Patients with OA might have morning solidness, yet this normally resolves or diminishes inside 20-30 min.^[21,22] The objectives of treatment for RA are to lessen joint aggravation and torment, boost joint capacity, and forestall joint annihilation and distortion. Treatment regimens comprise of mixes of drugs, weight-bearing activity, teaching patients about the infection, and rest. Medicines are by and large altered to a patient's requirements and rely upon their general wellbeing. This incorporates factors, for example, sickness movement, the joints in question, age, in general wellbeing, occupation, consistence, and instruction about the illness.^[23] This survey momentarily feature the work of art and current treatment choices accessible to address the distress/difficulties of RA. A thorough audit was as of late distributed by Smolen et al.^[24]

Main text

Features of rheumatoid arthritis

Warm, enlarged joints

Balanced example of impacted joints

Weariness, periodic fevers, loss of energy.

Joint aggravation frequently influencing the wrist and finger joints.

Joint aggravation in some cases influencing the joints in the neck, shoulders, elbows, hips, knees, lower legs and feet.^[25]

List of most potent herbal drugs used in arthritis

Ashwagandha (*Withania somnifera*)

Ashwagandha (*Withania somnifera*, fam. Solanaceae) is generally known as "Indian Winter cherry" or "Indian Ginseng". a significant conventional utilization of the spice is in "adjusting life force", practice It is one of the main spice of Ayurveda (the customary arrangement of medication in India) utilized for centuries as a Rasayana for its wide going medical advantages. Rasayana is portrayed as a natural or metallic planning that advances an energetic condition of physical and psychological wellness and grows bliss. These sorts of cures are given to little youngsters as tonics, and are additionally taken by the moderately aged and older to increment life span. Among the ayurvedic Rasayana spices, Ashwagandha holds the most noticeable spot. It is known as "Sattvic

Kapha Rasayana" Herb.^[26] The majority of the Rasayana spices are adaptogen/hostile to stretch specialists. Ashwagandha is normally accessible as a churna, a fine sieved powder that can be blended in with water, ghee (explained margarine) or honey. It upgrades the capacity of the mind and sensory system and works on the memory. It works on the capacity of the regenerative framework advancing a solid sexual and conceptive equilibrium. Being a strong adaptogen, it upgrades the body's versatility to push. Ashwagandha works on the body's protection against infection by further developing the cell-interceded insusceptibility. It additionally has strong cancer prevention agent properties that help safeguard against cell harm brought about by free revolutionaries.

Chemical Composition

The biologically active chemical constituents of *Withania somnifera* (WS) include alkaloids (isopelletierine, anaferine, cuseohygrine, anahygrine, etc.), steroidal lactones (withanolides, withaferins) and saponins.^[27] Sitoindosides and acylsterylglucosides in Ashwagandha are anti-stress agents. Active principles of Ashwagandha, for instance the sitoindosides VII–X and Withaferin-A, have been shown to have significant anti-stress activity against acute models of experimental stress.^[28] Many of its constituents support immunomodulatory actions.^[29] The aerial parts of *Withania somnifera* yielded 5-dehydroxy withanolide-R and withasomniferin-A.^[30]

Anti-arthritis effect

Ashwagandha is a pain relieving that mitigates sensory system from torment reaction.^[31] The strong enemy of joint properties.^[32,33] of Ashwagandha are presently broadly acknowledged and recorded; it is moreover observed to be successful as antipyretic as well as pain relieving too. Ashwagandha (1000 mg/kg/oral) created huge pain relieving movement for a rodent encountering heat absense of pain initiated by hot plate strategy. The pinnacle pain relieving impact of Ashwagandha was recorded as 78.03 percent at second hour of organization. The inclusion of agony arbiters; prostaglandin and 5-hydroxytryptamine in pain relieving action of Ashwagandha was contemplated by pretreatment with paracetamol (100 mg/kg, ip) and cyproheptadine (10 mg/kg, ip). The pain relieving movement of Ashwagandha was potentiated altogether by cyproheptadine, in any case, paracetamol neglected to display any tremendous change in its action, recommending the contribution of serotonin, however not prostaglandins in the pain relieving action of Ashwagandha.^[34]

Mahayogiraj guggul (oleoresin of *Commiphora wightii*)

Mahayogiraj Guggulu is a compound Ayurvedic definition including powders of local trimmings took care of with guggulu (oleoresin of *Commiphora wightii*). In Ayurveda, Mahayogiraj Guggulu is exhibited in a

collection Vataroga with different adjuvants.^[35] and is usually used in organization of rheumatoid joint agony (Aamavata). Relieving development of Mahayogaraj Guggulu is represented in preclinical examinations (36,37).Mahayograj Guggul (YG) is a poly-local specifying generally used by Ayurvedic experts to treat red hot conditions, similar to affliction, osteoarthritis, cervical and lumbar spondylosis .It contains Sunthi (*Zingiber officinale*), Pippali (*Piper longum* Pippalimula (*Piper longum* Linn), Chavya (*Piper retrofractum*), Chitraka (*Plumbago zeylanica* Linn), Hingabharta (Bioss), Ajamoda (*Trachyspermum ammi* (L) Sprague), Sarshapa (*Brassica campestris* Linn.), Swetajiraka (*Cuminum cyminum* Linn.), Krishna jiraka (*Carumcarvi* Linn.), Nirgundi (Linn.), Indrayava (*Halarrhena antidysenterica* Roxb.exFlem.Wall), Patha (*Cissmpelos pareira* Linn. Hirsute (DC) Forman), Vidanga (*Embelia ribes*), Gajapippali (*Scindapsis officinalis* Schott.), Katuka (*Picrorhiza kurroa* Royle ex Benth.), Ativisa (*Aconitum heterophyllum* Wall.),Bharangi (*Clerodendrum serratum* Linn.) Moon.), Vacha (*Acorus calamus* Linn.), Murva tenacissima Roxb. Moon), Haritaki (*Terminalia chebula* Bibhitaki (*Terminalia bellirica* Gaertn. Roxb.), Amalaki (*emblica* Linn.) in an equivalent extent alongside Guggul (*Commiphora wightii*). Guggul, which is included an amount comparable to the all out amount of the multitude of spices, establishes a significant piece of the definition.

Safed musli (*Chlorophytum borivilianum*)

Joint irritation has a high inescapability and addresses the model of a resistant framework combustible joint disease inciting moderate decimation of articular plans, particularly tendon and bone.^[38] Delicate to genuine desolation is connected with combustible condition and joint agony. The present open treatment of combustible issues generally use nonsteroidal relieving drugs (NSAIDs) and corticosteroids. Regardless of the way that usage of current meds for bothering has a facilitating sway, it is at this point forbidden on account of its not kidding side effects.^[39,40] Several typical things and their deduced definitions have been used in helpful applications for blazing issues and related illnesses.^[41] various regular recovering flavors and their parts have restorative worth and can be used to thwart, ease up or fix a couple of human contaminations.^[42] The Indian customary arrangement of medication 'Ayurveda' uses in excess of 1000 restorative plants, from which helpful specialists were determined and experimentally demonstrated for their viability and wellbeing boundaries. *Chlorophytum borivilianum* Sant. and Fern. (Liliaceae) known as 'Safed Musli' is a customary spice with arranged Ayurvedic importance. It has helpful application in Ayurvedic arrangement of medicine.^[43] *C. borivilianum* is a potential spice generally utilized in India and China to treat joint inflammation, oligospermia, diabetes and dysuria. In ayurvedic writing it is commended as a 'Divya Aushad' (edified medication) with unmatched restorative properties. In 'Raja Ballabh Nighantu' it is suggested as rejuvenator and

is useful in neurological (vatic) messes.^[44] It have antiviral, anticancer, immunomodulatory, antistress, sexual enhancer, antimicrobial.^[45] improvement in male sex health.^[46] anthelmintic.^[47] and hepatoprotective activity.^[48] Among every one of the types of *Chlorophytum* present in India, *C. borivilianum* produces the most extreme root tuber alongside the most noteworthy saponin content.^[49] Roots of these species contain saponins.^[50] around 2% to 4%,^[48,51] which incorporate borivilianosides A-D.^[52] borivilinoside E-H.^[55] chlorophytoside-I.^[54] furostanol and spirostanol saponins.^[50] Our starter research on rough saponins of *C. borivilianum* demonstrated calming activity.^[55] Present review was expected to additional fractionation of saponins and assessment of the mitigating hostile to joint and pain relieving movement of these parts.

Green tea (*Camellia sinensis*)

A result of the dried leaves of *Camellia sinensis*, is the most generally consumed drink on the planet with no known genuine incidental effects.^[56-59] The polyphenolic compounds segregated from green tea (PGT) are wealthy in cell reinforcements that have mitigating properties.^[56-59] The fundamental polyphenolic compounds with a flavonoid structure in PGT incorporate epicatechin (EC), epigallocatechin (EGC), EC-3-O-gallate (ECG), and EGC-3-O-gallate (EGCG).^[56-58] In this review in light of the rodent adjuvant-prompted joint pain (AA) model of human RA, we tried whether PGT can manage the cost of security against joint inflammation and furthermore inspected the impact of PGT on antigen-explicit insusceptible reaction associated with the sickness cycle. AA can be instigated in the innate Lewis rodents (RT.11) by subcutaneous (s.c.) vaccination with heat-killed *Mycobacterium tuberculosis* H37Ra (Mtb).^[60,61] and AA has a few clinical and histological similitudes with RA. The T cells coordinated against the 65-kD mycobacterial heat shock protein (Bhsp 65) have been conjoined in the pathogenesis of both AA.^[61-64] and RA.^[65,66] Antibodies additionally assume a part in the pathogenesis of immune system joint pain.^[67,68] The AA model has been utilized broadly for assessment of the antiarthritic action of new mixtures of engineered or regular beginning. In this review, we tried the T cell and neutralizer reaction to Bhsp65 in PGT-took care of Lewis rodents contrasted and water-took care of (control) Lewis rodents. For T cell reaction, we tried 2 proinflammatory cytokines [interleukin (IL)- 17 and interferon-g (IFNg)].^[69-71] and 2 calming/immunosuppressive cytokines (IL-4 and IL-10).^[72]

DISCUSSION

The discoveries from this study recommend that safes musli,ashwagandha,mahayogiraj guggul,maharasnadi kwath have intense antiarthritic properties. rheumatoid arthiritis is one of the immune system issue which is because of broken digestion of body and stess.it becomes ongoing provocative issue which bring about extreme agony. allopathic medication can lessen torment yet the underlying driver stay untreated. in this paper we study

on mix of most strong natural medications having clinically demonstrated antiinflammatory, analgesic and hostile to ligament exercises when utilized alone. now every days such sort of incendiary problems increments step by step because of progress in way of life. To keep away from additional complexities and results of allopathic medication we should go through natural medication. additionally to stay away from unevenness of bodies principle support points that is vata, kapha, pitta because of receptive oxygen species we should accept normal medication which assume part as antioxidant.

CONCLUSION

These home grown cures are consequently altogether regular and will decrease the aggravation and irritation in the joints. The accessible logical information support the end that ashwagandha, safed musli, mahayogiraj guggul, maharasnadi kwath are genuinely powerful regenerative tonic (Rasayana of Ayurveda), because of its different pharmacological activities like enemy of stress, neuroprotective, antitumor, against ligament, pain relieving what's more, calming and so on. It is helpful for various sorts of sicknesses like Parkinson, dementia, cognitive decline, stress initiated infections, malignoma and others. ashwagandha is utilized as a family cure by Indians, who think about it as the best tonic for elderly individuals and kids, and as love potion by youngsters.

Abbreviations

- ROS** -Reactive oxygen species
WHO -world health organisation
RA -rheumatoid arthritis
PIP -proximal interphalangeal
DIP -distal interphalangeal
OA -osteoarthritis
MP -metaphalangeal
NSAID - non steroidal anti inflammatory drug

REFERENCES

- Li XK, Motwani M, Tong W, Bornmann W, Schwartz GK, Huanglian A. Chinese herbal extract, inhibits cell growth by suppressing the expression of cyclin B1 and inhibiting CDC2 kinase activity in human cancer cells. *Molecular Pharmacology*, 2000; 58(6): 1287–93.
- Schmid-Schonbein GW. Analysis of inflammation. *Annu ReBiomed Eng*, 2006; 8: 93-151.
- Kandikattu K, Bharath RKP, Venu PR, Sunil KK, Singh R. Evaluation of anti-inflammatory activity of *Canthium parviflorum* by in-vitro method. *Indian J Res Pharm Biotech*, 2013; 1(5): 729-30.
- Dharsana JN, Mathew SM. Preliminary screening of antiinflammatory and antioxidant activity of *Morinda umbellata*. *Int J Pharm Life Sci.*, 2014; 5(8): 3774-79.
- Anyasor GN, Funmilayo O, Odutola O, Olugbenga A, Oboutor EM. Evaluation of *Costus afer* Ker Gawl. In vitro antiinflammatory activity and its chemical constituents identified using gas chromatography-mass spectrometry analysis. *J Coastal Life Med*, 2015; 3(2): 132-8.
- Sridevi G, Sembulingam K, Muhammed I, Srividya S, Prema S. Evaluation of in- vitro anti-inflammatory activity of *Pergularia daemia*. *World J Pharm Res.*, 2015; 4(6): 1100-8.
- Chatterjee P, Chandra S, Dev P, Bhattacharya S. Evaluation of anti-inflammatory effects of green tea and black tea: comparative *in vitro* study. *J Adv Pharm Technol Res.*, 2012; 3(2): 136-8.
- Tatti PN, Anitha S, Shashidhara S, Deepak M, Bidari S. Evaluation of *in-vitro* anti-denaturation activity of isolated compound of *Butea monosperma* Bark. *Pharma Sci Monit*, 2012; 3(4): 2314-20.
- Dar SA, Yousuf AR, Ganai FA, Sharma P, Kumar N, Singh R. Bioassay guided isolation and identification of antiinflammatory and anti-microbial compounds from *Urta dioica*.
- Krishnaiah D, Sarbatly R, Nithyanandam R. A review of the antioxidant potential of medicinal plant species. *Food Bioprod Processing*, 2011; 89(3): 217-33.
- Gerber M, Ruault MC, Hercberg S, Riboli E, Scalbert A, SiesMH. Food and cancer: state of the art about the protective effect of fruits and vegetables. *Bull du Cancer*, 2002; 89(3): 293-312.
- Bhatia S, Shukla R, Madhu SV, Gambhir JK, Prabhu KM. Antioxidant status, lipid peroxidation and nitricoxide end products in patients of type 2 diabetes mellitus with nephropathy. *Clin Biochem*, 2003; 36(7): 557-62.
- American College of Rheumatology. Ad Hoc Committee on Clinical Guidelines. Guidelines for the management of rheumatoid arthritis. *Arthritis Rheum*, 1996; 39: 713–22.
- Lee JE, Kim IJ, Cho MS, Lee J. A Case of Rheumatoid Vasculitis Involving Hepatic Artery in Early Rheumatoid Arthritis. *J Korean Med Sci.*, 2017 Jul; 32((7)): 1207–10.
- Fox CQ, Ahmed SS. *Physician Assistant's Clinical Review Cards*. Philadelphia: F. A. Davis Company, 2002; 138–139.
- McInnes IB, Schett G. The pathogenesis of rheumatoid arthritis. *N Engl J Med.*, 2011 Dec; 365(23): 2205–19.
- Chaudhari K, Rizvi S, Syed BA. Rheumatoid arthritis: current and future trends. *Nat Rev Drug Discov*, 2016 May; 15((5)): 305–6.
- Picerno V, Ferro F, Adinolfi A, Valentini E, Tani C, Alunno A. One year in review: the pathogenesis of rheumatoid arthritis. *Clin Exp Rheumatol*, 2015 Jul-Aug; 33(4): 551–8.
- Alamanos Y, Voulgari PV, Drosos AA. Incidence and prevalence of rheumatoid arthritis, based on the 1987 American College of Rheumatology criteria: a systematic review. *Semin Arthritis Rheum*, 2006 Dec; 36(3): 182–8.
- Chopra A, Abdel-Nasser A. Epidemiology of rheumatic musculoskeletal disorders in the

- developing world. *Best Pract Res Clin Rheumatol*, 2008 Aug; 22(4): 583–604.
21. McGonagle D, Hermann KG, Tan AL. Differentiation between osteoarthritis and psoriatic arthritis: implications for pathogenesis and treatment in the biologic therapy era. *Rheumatology (Oxford)*, 2015 Jan; 54(1): 29–38.
 22. Piyarulli D, Koolae RM. A 22-Year-Old Female With Joint Pain. In: Piyarulli D, Koolae RM, editors. *Medicine Morning Report: Beyond the Pearls*. Cambridge: Elsevier, 2016; 65–77.
 23. Staheli LT. Lower extremity management. In: Staheli LT, Hall JG, Jaffe KM, Paholke DO, editors. *Arthrogyrosis: A Text Atlas*. Cambridge: Cambridge University Press, 1998; 55–73.
 24. Smolen JS, Aletaha D, Barton A, Burmester GR, Emery P, Firestein GS, et al. Rheumatoid arthritis. *Nat Rev Dis Primers*, 2018 Feb; 4: 18001.
 25. Anonymous a, Handout on Health: Rheumatoid Arthritis, 2013.
 26. Changhadi Govardhan Sharma – Ashwagandharishta – Rastantra Sar Evam Sidhyaprayog Sangrah – Krishna–Gopal Ayurveda Bhawan (Dharmarth Trust), Nagpur, 1938; 743-744.
 27. Mishra, L.C., Singh, B.B., Dagenais, S. Scientific basis for the therapeutic use of *Withania somnifera*. (Ashwagandha): A review. *Alternative Medicine Reviews*, 2000; 5: 334-46.
 28. Bhattacharya, S.K., Goel, R.K., Kaur, R., Ghosal, S. Anti - stress activity of Sitoindosides VII and VIII. New Acylsterylglucosides from *Withania somnifera*. *Phytother. Res.*, 1987; 1: 32-37.
 29. Ghosal S., Srivastava R.S., Bhattacharya S.K., Upadhyay S.N., Jaiswal A.K., Chattopadhyay U. Immunomodulatory and CNS effects of sitoindosides IX and X, two new glycowithanolides form *Withania somnifera*. *Phytother. Res.*, 1989; 2: 201– 206.
 30. Atta-ur-Rahman, Samina-Abbas, Dur-e-Shahwar, Jamal, S.A., Choudhary, M.I. and Abbas. S. New withanolides from *Withania* spp. *Journal of Natural Products*, 1991; 56: 1000–1006.
 31. Twaij, H.A.A., Elisha, E.E. and Khalid, R.M., Analgesic studies on some Iraq medicinal plants; *International Journal of Crude Research*, 1989; 27: 109–112.
 32. Singh, N., Singh, S.P., Nath, C., Kohli, R.P. and Bhargava, K.P. Anti-stress plants as anti-rheumatic agents, 5th Sepal Congress of Rheumatology, Bangkok, 1984; 37.
 33. Singh, N. A pharmaco-clinical evaluation of some Ayurvedic crude plant drugs as anti-stress agents and their usefulness in some stress diseases of man. *Ann. Nat. Acad. Ind. Med.*, 1986; 2(1): 14-26.
 34. Mazen, E.S., Pavelescu, M., Grigorescu, E. Contributions to the Pharmacodynamic Study of roots of *Withania somnifera* Dun Species Of Pakistani origin. Testing of Analgesic Activity of Dichloromethanic and Methanolic Extract from *Withania-Somnifera* Roots; *Revista Medico-Chirurgicala Societatii de Medici si Naturalisti din Iasi*, 1990; 94(3-4): 603-605.
 35. Basisht, G.K.; Singh, R.H. and Chandola, H. Management of rheumatoid arthritis (Aamavata) using symbiohealth healthcare system. *Ayu.*, 2012; 33(4): 466-474.
 36. Bagul, M.S.; Srinivasa, H.; Kanaki, N.S. and Rajani, M. Antiinflammatory activity of two Ayurvedic formulations containing Guggul. *Indian J. Pharmacol.*, 2005; 37(6): 399-400.
 37. Lavekar, G.S.; Ravishankar, B.; Gaidhani, S.; Shukla, V.J.; Ashok, B.K. and Padhi, M.M. Mahayograj guggulu: Heavy metal estimation and safety studies, *Int. J. Ayurveda Res.*, 2010; 1(3): 150-158.
 38. Strietholt S, Maurer B, Peters MA, Pap T, Gay S. Review: Epigenetic modifications in rheumatoid arthritis. *Arthritis Res Ther*, 2008; 10: 219-225.
 39. Laar MV, Pergolizzi JV, Mellinghoff HU, Merchante IM, Nalamachu S, O'Brien J, Perrot S, Raffa RB. Pain Treatment in Arthritis-Related Pain: Beyond NSAIDs. *Open Rheumatol J*, 2012; 6: 320-330.
 40. Muluye RA, Bian Y, Alemu PN. Anti-inflammatory and Antimicrobial Effects of Heat clearing Chinese Herbs: A Current Review. *J Tradit Complement Med*, 2014; 4: 93-98.
 41. Hussein SZ, Yusoff KM, Makpol S, Yusof YA. Gelam honey inhibits the production of proinflammatory mediators NO, PGE2, TNF- α , and IL-6 in carrageenan-induced acute paw edema in rats. *Evid Based Complement Alternat Med*, 2012; 1-13.
 42. Kumar GP, Kumar R, Chaurasia OP, Singh SB. Current status and potential prospects of medicinal plant sector in trans-Himalayan Ladakh. *J Med Plant Res*, 2011; 5(14): 2929.
 43. Purohit SD, Dave A, Kukda G. Micropropagation of safed musli (*Chlorophytum borivilianum*), a rare Indian medicinal herb. *Plant Cell Tissue Organ Cult*, 1994; 39: 93–96.
 44. Singh A, Chauhan HS. Safed musli (*Chlorophytum borivilianum*) distribution, biodiversity and cultivation. *J Med, Arom Plant Sci*, 2003; 25: 712-719.
 45. Deore SL, Khadabadi SS. Screening of antistress properties of *Chlorophytum borivilianum*. *Pharmacologyonline*, 2009; 1: 320–328.
 46. Rath SK, Panja AK. Clinical evaluation of root tubers of Shweta Musali (*Chlorophytum borivilianum* L.) and its effect on semen and testosterone. *Ayu*, 2013; 34(3): 273–275.
 47. Panda SK, Das D, Tripathy NK. Anti-inflammatory potential of *Chlorophytum borivilianum* Sant. & Fern. root tubers. *J Global Trends Pharm Sci*, 2011; 2(2): 242- 251.
 48. Sharma SK, Kumar M. Hepatoprotective effect of *Chlorophytum borivilianum* root extract against arsenic intoxication. *Pharmacologyonline*, 2011; 3: 1021–1032.

49. Attele AS, Wu JA, Yuan CS. Ginseng pharmacology: Multiple constituents and multiple actions. *Biochem Pharmacol*, 1999; 58(11): 1685–1693.
50. Marais W, Reilly J. *Chlorophytum* and its related genera (Liliaceae). *Kew Bulletin*, 1978; 32: 653–663.
51. Thakur M, Chshuhsn NS, Bhargava S, Dixit VK. A comparative study on aphrodisiac activity of some Ayurvedic herbs in male albino rats. *Arch Sex Behav*, 2009; 38(6): 1009–1015.
52. Acharya D, Mitaine-Offer AC, Kaushik N, Miyamoto T, Paululat T, Lacaille-Dubois MA. Furostanetype steroidal saponins from the roots of *Chlorophytum borivilium*. *Helv Chim Acta*, 2008; 91: 2262–2269.
53. Acharya D, Mitaine-Offer AC, Kaushik N, Miyamoto T, Paululat T, Mirjolet JF, Duchamp O, Lacaille-Dubois MA. Cytotoxic spirostane-type saponins from the roots of *Chlorophytum borivilium*. *J Nat Prod*, 2009; 72(1): 177–181.
54. Singh D, Pokhriyal B, Joshi YM, Kadam V. Phytopharmacological aspects of *Chlorophytum borivilium* (safed musli): A review. *Int J Res Pharm Chem*, 2012; 2(3): 853–859.
55. Lande AA, Ambavade SD, Swami US, Adkar PP, Ambavade PD, Waghmare AB. Saponins isolated from roots of *Chlorophytum borivilium* reduce acute and chronic inflammation and histone deacetylase. *J Integr Med*, 2015; 13(1): 25–33.
56. Katiyar SK, Mukhtar H. Tea consumption and cancer. *World Rev Nutr Diet.*, 1996; 79: 154–84.
57. Graham HN. Green tea composition, consumption, and polyphenol chemistry. *Prev Med*, 1992; 21: 334–50.
58. McKenna DJ, Hughes K, Jones K. Green tea monograph. *Altern Ther Health Med*, 2000; 6: 61–8, 70–2, 4 passim.
59. Arab L, Il'yasova D. The epidemiology of tea consumption and colorectal cancer incidence. *J Nutr*, 2003; 133: S3310–8.
60. Pearson CM, Wood FD. Studies of polyarthritis and other lesions induced in rats by injection of mycobacterial adjuvant. I. General clinical and pathologic characteristics and some modifying factors. *Arthritis Rheum*, 1959; 2: 440–59.
61. Moudgil KD, Chang TT, Eradat H, Chen AM, Gupta RS, Brahn E, Sercarz EE. Diversification of T cell responses to carboxy-terminal determinants within the 65-kD heat-shock protein is involved in regulation of autoimmune arthritis. *J Exp Med*, 1997; 185: 1307–16.
62. Anderton SM, van der Zee R, Prakken B, Noordzij A, van Eden W. Activation of T cells recognizing self 60-kD heat shock protein can protect against experimental arthritis. *J Exp Med*, 1995; 181: 943–52.
63. Quintana FJ, Carmi P, Mor F, Cohen IR. DNA fragments of the human 60-kDa heat shock protein (HSP60) vaccinate against adjuvant arthritis: identification of a regulatory HSP60 peptide. *J Immunol*, 2003; 171: 3533–41.
64. Ulmansky R, Cohen CJ, Szafer F, Moallem E, Fridlender ZG, Kashi Y, Naparstek Y. Resistance to adjuvant arthritis is due to protective antibodies against heat shock protein surface epitopes and the induction of IL-10 secretion. *J Immunol*, 1998; 168: 6463–9.
65. Gaston JS, Life PF, Jenner PJ, Colston MJ, Bacon PA. (1990) Recognition of a mycobacteria-specific epitope in the 65-kD heat-shock protein by synovial fluid-derived T cell clones. *J Exp Med*. 2002; 171: 831–41.
66. Danieli MG, Markovits D, Gabrielli A, Corvetta A, Giorgi PL, van der Zee R, van Embden JD, Danieli G, Cohen IR. Juvenile rheumatoid arthritis patients manifest immune reactivity to the mycobacterial 65-kDa heat shock protein, to its 180–188 peptide, and to a partially homologous peptide of the proteoglycan link protein. *Clin Immunol Immunopathol*, 1992; 64: 121–8.
67. Monach PA, Benoist C, Mathis D. The role of antibodies in mouse models of rheumatoid arthritis, and relevance to human disease. *Adv Immunol*, 2004; 82: 217–48.
68. Taneja V, Behrens M, Mangalam A, Griffiths MM, Luthra HS, David CS. New humanized HLA-DR4-transgenic mice that mimic the sex bias of rheumatoid arthritis. *Arthritis Rheum*, 2007; 56: 69–78.
69. Chabaud M, Fossiez F, Taupin JL, Miossec P. Enhancing effect of IL-17 on IL-1-induced IL-6 and leukemia inhibitory factor production by rheumatoid arthritis synoviocytes and its regulation by Th2 cytokines. *J Immunol*, 1998; 161: 409–14.
70. McKenzie BS, Kastelein RA, Cua DJ. Understanding the IL-23-IL-17 immune pathway. *Trends Immunol*, 2006; 27: 17–23.
71. Nakae S, Saijo S, Horai R, Sudo K, Mori S, Iwakura Y. IL-17 production from activated T cells is required for the spontaneous development of destructive arthritis in mice deficient in IL-1 receptor antagonist. *Proc Natl Acad Sci USA*, 2003; 100: 5986–90.
72. Sundstedt A, O'Neill EJ, Nicolson KS, Wraith DC. Role for IL-10 in suppression mediated by peptide-induced regulatory T cells in vivo. *J Immunol*, 2003; 170: 1240–8.
73. Siemoneit U., Koeberle A., Rossi A., Dehm F., Verhoff M., Reckel S., Maier T.J., Jauch J., Northoff H., Bernhard F., et al. Inhibition of microsomal prostaglandin E2 synthase-1 as a molecular basis for the anti-inflammatory actions of boswellic acids from frankincense. *Br. J. Pharm.* 2010; 162: 147–162. doi: 10.1111/j.1476-5381.2010.01020.x
74. Safayhi H., Mack T., Sabieraj J., Anazodo M.I., Subramanian L.R., Ammon H.P. Boswellic acids: Novel, specific, nonredox inhibitors of 5-lipoxygenase. *J. Pharm. Exp. Ther.* 1992; 261: 1143–1146.

75. Majeed M., Majeed S., Narayanan N.K., Nagabhushanam K. A pilot, randomized, double-blind, placebo-controlled trial to assess the safety and efficacy of a novel *Boswellia serrata* extract in the management of osteoarthritis of the knee. *Phytother. Res.*, 2019; 33: 1457–1468. doi: 10.1002/ptr.6338.
76. Majeed M., Vaidyanathan P., Natarajan S., Majeed S., Vuppala K.K. Effect of Boswellin® Super on knee pain in Japanese adults: A randomized, double-blind, placebo-controlled trial. *Eur. J. Biomed*, 2016; 3: 293–298.
77. Shep D., Khanwelkar C., Gade P., Karad S. Efficacy and safety of combination of curcuminoid complex and diclofenac versus diclofenac in knee osteoarthritis. *Medicine*, 2020.