EPIDEMIOLOGY AND HERBAL TREATMENT OF OSTEOARTHRITIS

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ABSTRACT Increase in prevalence of osteoarthritis has encouraged the researchers to find out novel, more efficacious drugs from plant sources. This study is a review of medicinal plants with anti-osteoarthritic effects in clinical trial and *in vitro/ in vivo* studies. Medicinal plants and herbal formulation/ products with anti-osteoarthritic effect are described. The plants and herbal products exerted anti-osteoarthritic effect by different mechanisms. The investigated plants contain the compounds that are able to contribute effectively to treat osteoarthritis. Therefore, the plants extract and herbal products discussed in this review article could open a way to conduct further clinical trials on large scales and greatly help researchers and pharmacists to develop new anti-osteoarthritic drugs.

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INTRODUCTION

Osteoarthritis is a common, inflammatory, skeletal, progressive, chronic and degenerative disorder (1). Protective cartilages on the endsof bones become worn, osteophytes form at the periphery of the joint surface and loose bodies may result (Fig. 1). Most common affected joints are knees and back (2-3). Manifestations of osteoarthritis include disability, swelling and painin moving the joints (4). Disease progression can be slowed by proper treatment (Fig. 2). Despite ongoing physiotherapy and the widespread use of nonsteroidal anti-inflammatory drugs (NSAIDs), this illness is of apprehension because it affects the mobility of persons and life quality. Now there is bigger attention in non-synthetic, natural remedies obtained from plants to well acceptability and decreased adverse drug reactions (ADRs) (5-7). Plants have anti-arthritic activities (Table 1). Various medicinal plants have been proved as anti-arthritic agent in clinical trials (Table 2). In this review, we have reviewed literature regarding approved efficacy of plants in osteoarthritis.

Millions of people are affected with osteoarthritis. Its more prevalent in male than female before ageof 45 and is more common in female than male after menopause. Its prevalence is increasing in United States and current 26 million peopleare affected with osteoarthritis in United State. Prevalence of osteoarthritis of distal inter-phalangeal joints was 75% in women between 60-70 years of age in United State. Prevalence of hand osteoarthritis in people above 40-50 years of age was 2.2% in Teheran that increased to 22.5% in people above 70 years of age. Study conducted by Dutch institute of public health indicated that prevalence of knee osteoarthritis is 15.6% in male and 30.5% in female. Prevalence is more in obese than normal weight persons. Prevalence of arthritis in Canadian adults was 13.4% and 17.6% in 1994 and 2002 respectively. Prevalence of arthritis was 16.9%, 14.2% and 14.7% in Ontario, Alberta and British Columbia. Prevalence of arthritis and rheumatism was 13.0%, 15.0%, 24%, 23.8% and 56.0% in the Medicinal plants having potential to treat arthritis Medicinal plants have been traditionally used to control pain and improve dysfunction in osteoarthritis (Fig.3). In developing countries, most of people rely on herbal medicine (8-10). Herbal medicines are

prescribed worldwide for the management of osteoarthritis since ancient times (11). Herbs and plants always have been prescribed in the management of different diseases including gouty arthritis and other associated musculoskeletal disorders ***Zingiber officinale*** (Zingiberaceae).

This spice is a proven in nausea remedy (13). It can come in handy for the nausea associated with altitude sickness or provoked by drivingon winding mountain roads (14). It is taken in various forms as a tea, tincture, capsules, raw or crystallized. It contains hexacosanoic acid 2,3-dihydroxypropyl ester, glycol monopalmitate, isovanillin, beta sitosterol palmitate, 1-(omega-ferulyloxyceratyl) glycerols, 6-shogaol, steroids, adenine, diterpenes, p-hydroxybenzaldehyde, gingerol analogue, maleimide-5-oxime and diarylheptanoids (15-17). It is anti-inflammatory, xanthine oxidase inhibitor, digestive, cyclo-oxygenase 2 inhibitor and antiarthritic (18). It is used in indigestion, inflammation, gouty arthritis and rheumatoid arthritis (19). Shimoda et al (2010) reported the anti-inflammatory effects of *Zingiber officinale* extract. This anti-inflammatory activity validates its efficacy in osteoarthritis (20).

A study was conducted to investigate the efficacy of *Zingiber officinale* extract as a substitute to NSAIDs and as a supplement medicine in the symptomatic management of osteoarthritis. The improvement of symptoms, defined as reduction in the mean change, was superior in the *Zingiber officinale* extract and ibuprofen groups thanthe placebo group. *Zingiber officinale* extractand ibuprofen were superior to placebo in the symptomatic treatment of osteoarthritis, while there was no significant difference between the *Zingiber officinale* extract and ibuprofen groupsin a test for multiple comparisons (21).

Punica granatum (Lythraceae).

Chemical constituents include punicalagin, tannins and anthocyanins (22). It is used in pain, inflammation, arthritis, obesity, alzheimer's disease, male infertility, infant brain ischemia, bacterial infections, erectile dysfunction, dental carries, diabetes mellitus, cardiovascular disorders and cancer (23). Pharmacological activities are anticancer, diuretic, anti-angiogenesis, anti-mutagenic, astringent, antioxidant and anti-inflammatory (24). Pomegranate juice reduced proteoglycan loss and cartilage damage in mouse model with osteoarthritis (25).

Artemisia herba-alba **Asso** (Asteraceae)

Whole plant is prescribed for management of numerous disorders (26). It contains piperitone, carvone, cis-thujone, chrsanthenone and camphor (27). It contains trans-pinocarveol, camphor, borneol, alpha thujune, beta thujune, trans-sabinyl acetate, 1-8 cineole, chrysanthenone, cirsilineoland hispidulin (28). It is used in diabetes mellitus, osteoarthritis, nervous disorders, pyrexia, syphilis, scabies, neuralgia, diarrhea, bronchitis, cough, cold and fungal infection. It is anti-inflammatory, antioxidant, hypoglycemic, antileishmania and smooth muscle relaxant (29). Arshad et al (2012) reported the ethno medicinal use of this plant in arthritis (30).

Harpagophytum procumbens (Pedaliaceae)

This plant is used to treat various ailments (31). This plant contain iridoids that possess anti-inflammatory effect. Chantre et al (2000) reported the potential of *Harpagophytum procumbens* in comparison with diacerhein in management of osteoarthritis in randomized clinical stud. This was a comparative study, in which efficacy of herbal product (Harpadol) was investigated in comparison with diacerhein. Six capsules of herbal medicine were given to patient daily. Each capsule contains 435 mg of powdered material. Diacerhein was given at dose of 100 mg/day. The duration of treatment was four months. Total no of patients with osteoarthritis was 122. Pain was significantly reduced in both management clusters. Efficacy of both drugs was comparable. After completion of trial duration, Harpadol treated patients were taking significantly less NSAIDs and analgesic drugs. Fewer side effects occurred in harpadol group than control group. 8.1% patients were suffered from diarrhea and 26.7% were in control group. This research indicated that test drug is equal in effect and better in safety to control group (32).

Dalbergia sissoo Roxb (Fabaceae)

Parts used are roots and wood. Active principles are isoflavones, flavonols and lignan glucoside (33). It is used in arthritis, boils, eruption of skin, leprosy, vomiting and inflammation (34). It is astringent, anti-inflammatory, anti-arthritic and gastroprotective (35). Dixit et al (2010) reported the ingredients from leaves of *Dalbergia sissoo* possessing estrogenic effect. Ethanol extract of this plant contains various constituents that have osteogenic effect in primary calvarial osteoblast cultures. Some compounds of this plant increased alkaline phosphatase activity. Osteogenic activityis evident from mineralization (36).

Commiphora mukul (Burseraceae)

It is used in hemorrhoids (37). It is laxative, antiseptic, anti-catarrhal, expectorant, carminative, astringent, antimicrobial, anti-inflammatory, demulcent, hepatoprotective and anti-diabetic (38). Singh et al (2003) reported the effectivenessof *Commiphora mukul* for osteoarthritis of the knee. *Commiphora mukul* has been investigatedfor its efficacy to treat osteoarthritis. Preclinical and clinical data shows that *Comminphora mukul* is effective in osteoarthritis. In a clinical trial, thirty male and female patients were selected for study. *Commiphora mukul* was administered to patients at dose of 500 mg in form of capsule. There was significant improvement in mobility and functions of joints when taken for 1 month continuously. Treatment was continued to improve at the 2-month marker and follow-up. *Commiphora mukul* was effective in participants during the trial. During the trial, no significant adverse effects were reported. This study showed that *Commiphora mukul* is safe and effective alternative to treat osteoarthritis (39).

Curcuma longa **(**Zingiberaceae).

It is used in rheumatism. It contains curcumin, bisdemethoxycurcumin, demethoxycurcumin, zingiberone, tumerone, atlantone, resins, protein and sugars (40). It is used in acute coronary syndrome, psoriasis, vitiligo, arthritis, cardiovascular disorders, tumor, gastric ulcer, peptic ulcer, diabetes mellitus, ulcerative proctitis, gastric inflammation, crohn's disease, diabetic nephropathy, ulcerative colitis, lupus nephritis, irritable bowel disease, acquired immune deficiency syndrome, tropical pancreatitis, atherosclerosis, idiopathic orbital inflammatory pseudotumor, diabetic microangiopathy, oral lichen planus, β-thalassemia, chronic bacterial prostatitis, biliary dyskinesia and cholecystitis (41). It is anti-inflammatory, antioxidant and anti-cancer (42). Cucumin containing formulation exhibited anti-inflammatory activity in patients with osteoarthritis (43).

Boswellia serrata **(**Burseraceae)

Chemical constituents are pentacyclic triterpene acids and beta-boswellic acid (44). It is used in asthma, inflammation, cancer and osteoarthritis(45). Pharmacological activities are anticancer, antioxidant, anti-asthmatic and anti-inflammatory (46). *Boswellia serrata* is prescribed in the treatment of osteoarthritis (47). Kimmatkar et al (2003) reported the efficacy of *Boswellia serrata* extract in management of knee osteoarthritis.In a clinical trial, 56 patients were randomized into two groups. 500 mg capsule of *Boswellia serrata* was administered to first group in three divided doses. Capsules were administered with lukewarm water. Total patients were 29 in first group. 23 patients were in 2nd group and capsule was administered with Luke water. In 2nd group, *Boswellia serrata* ointment was applied on joints. This treatment was given for 2 month duration. There was symptomatic improvement in both groups. Improvement in first group was with promising results (48).

Phyllanthus emblica **(**Euphorbiaceae)

Fruit of this plant is used in osteoarthritis (49). Chemical constituents include minerals, amino acids, emblicol, curcuminoids, phyllembelic acid, tannins and phenolic compounds (50). It is used in inflammation, jaundice, diarrhea and cancer (51). Pharmacological activities include antioxidant, gastroprotective, hepatoprotective, antiulcerogenic, antibacterial, hypolipidemic and anticancer (52). Sumantran et al (2008) reported the chondroprotective activity of *Phyllanthus emblica* in patients with osteoarthritis. Aqueous

extract of *Phyllanthus emblica* was investigated for its chondroprotective activity. In *In vitro* study, hyaluronidase and collagenase type
2 activities were inhibited by use of aqueous extract of *Phyllanthus emblica*. This data shows that *Phyllanthus emblica* extract can be used as chondroprotective agent in the treatment of osteoarthritis (53).

CONCLUSION

The current review reveals the anti-osteoarthritis efficacies of commonly used medicinal plants in Unani system of medicine. Since natural medicines are worldwide prescribed and the bio-active constituents isolated from these herbs may function as bio-marker in different natural formulations. Present review also supports the use of these herbal preparations that are used to prevent or control the inflammatory conditions.

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Table 1: Plants investigated for their anti-arthritic activity in animal model

S. No	Plant Name	Origin of plant	Use of plant	Use in which part of the World	Animal studies	Reference
1	*Punica granatum*	Iran, India and Pakistam	Antioxidant and anti-inflammatory.	Asia, Iran, Africa, India and Europe	Mouse model	(25)
2	*Semecarpus anacardium*	India	Anti-inflammatory, antiarthritic	India	Freund's adjuvant induced arthritis	(54)
3	*Withania somnifera*	Europe and Africa	Anti-inflammatory, antiarthritic	Pakistan and India	Carrageenan induced paw edema	(54)
4	*Vitex negunda*	Bhutan, Bangladesh, Afghanistan	Antiinflammatory, antiarthritic	Pakistan and India	Freuds adjuvant induced arthritis	(55)
5	*Ricinus communis*	Northeastern Africa and Middle East	Contraceptive andantiarthritic	Malta, Pakistan and India	Freund's adjuvant induced arthritis	(54)
6	*Clematis vitalba*	England	Antimicrobial, Antiarthritic	Italy, Turkey	Carrageenan induced paw edema	(56)
7	*Harpagophytum procumbens*	Africa	Analgesic, Antiarthritic	United Kingdom, Scotland	Freund's adjuvant induced arthritis	(57)
8	*Acanthopanax chiisanensis*	South Asia	Antiinflammatory, Antiarthritic	Korea, Japan	Freund's adjuvant induced arthritis	(58)
9	*Cissampelos pareira*	Nepal	Anticancer, Antiarthritic	India, Bangladesh	Freuds adjuvant induced arthritis	(59)
10	*Ulmus davidiana*	Japan, Siberia, Mongolia, and Korea	Anti-inflammatory, Antiarthritic	Korea	Collagen induced arthritis	(60)

11	*Sclerocarya birrea*	Africa	Antibacterial, Antiarthritic	Africa, Zimbabwe	Carrageenan induced paw edema	(61)
12	*Boswellia carteri*	Africa, Yemen andOman	Anticancer, Antiarthritic	Egypt, Japan	Adjuvant induced arthritis	(62)
13	*Hippocratea excels*	México and Central America	Gastropective, Antiarthritic	Mexico, Japan	Adjuvant induced arthritis	(63)
14	*Bridelia ferruginea*	South Asia andAfrica	Antiinflammatory, Antiarthritic	Nigeria and Germany	Adjuvant induced arthritis	(64)
15	*Kalopanax pictus*	China, Korea andJapan	Antiinflammatory, Antiarthritic	Korea	Freund's adjuvant induced arthritis	(65)
16	*Dorstenia barteri*	Cameroun andNigeria	Antiinflammatory, Antiarthritic	Nigeria, France	Carrageenan induced paw edema	(66)
17	*Tetrapleura tetraptera*	Western Africa	Antiinflammatory, Antiarthritic	South Africa, Nigeria	Egg albumin induced paw edema	(67)

Table 2: Clinical trials conducted for investigation of plants and herbal products in patients with arthritis

S. No	Plant Name/Formulation	Use of plant	No of patients	References
1	*Curcuma domestica*	Antioxidant, anti-inflammatory	52	(68)
2	*Boswellia serrata*	Analgesic, antiarthritic and anti-inflammatory	15	(47)
3	*Zingiber officinale*	Antiinflammatory and analgesic	40	(21)
4	*Elaeagnus angustifolia*	Wound healer, muscle relaxant, antiinflamamatory	97	(69-70)
5	*Nerium oleander*	Anti-inflammatory	18	(71)
6	*Harpagophytum procumbens*	Anti-inflammatory	89	(72)
7	Stinging nettle	Anti-inflammatory	27	(73)
8	Willow bark	Anti-inflammatory	78	(74)
9	Articulin-F	Anti-inflammatory	42	(75)
10	Avocado/soybean unsaponifiables	Anti-inflammatory	164	(76)
11	Capsaicin	Anti-inflammatory	133	(77)
12	Eazmov	Anti-inflammatory	60	(78)
13	Gitadyl	Anti-inflammatory	35	(79)
14	Reumalex	Anti-inflammatory	82	(80)

Fig 1: Molecular mechanism underlying pathophysiology of osteoarthritis

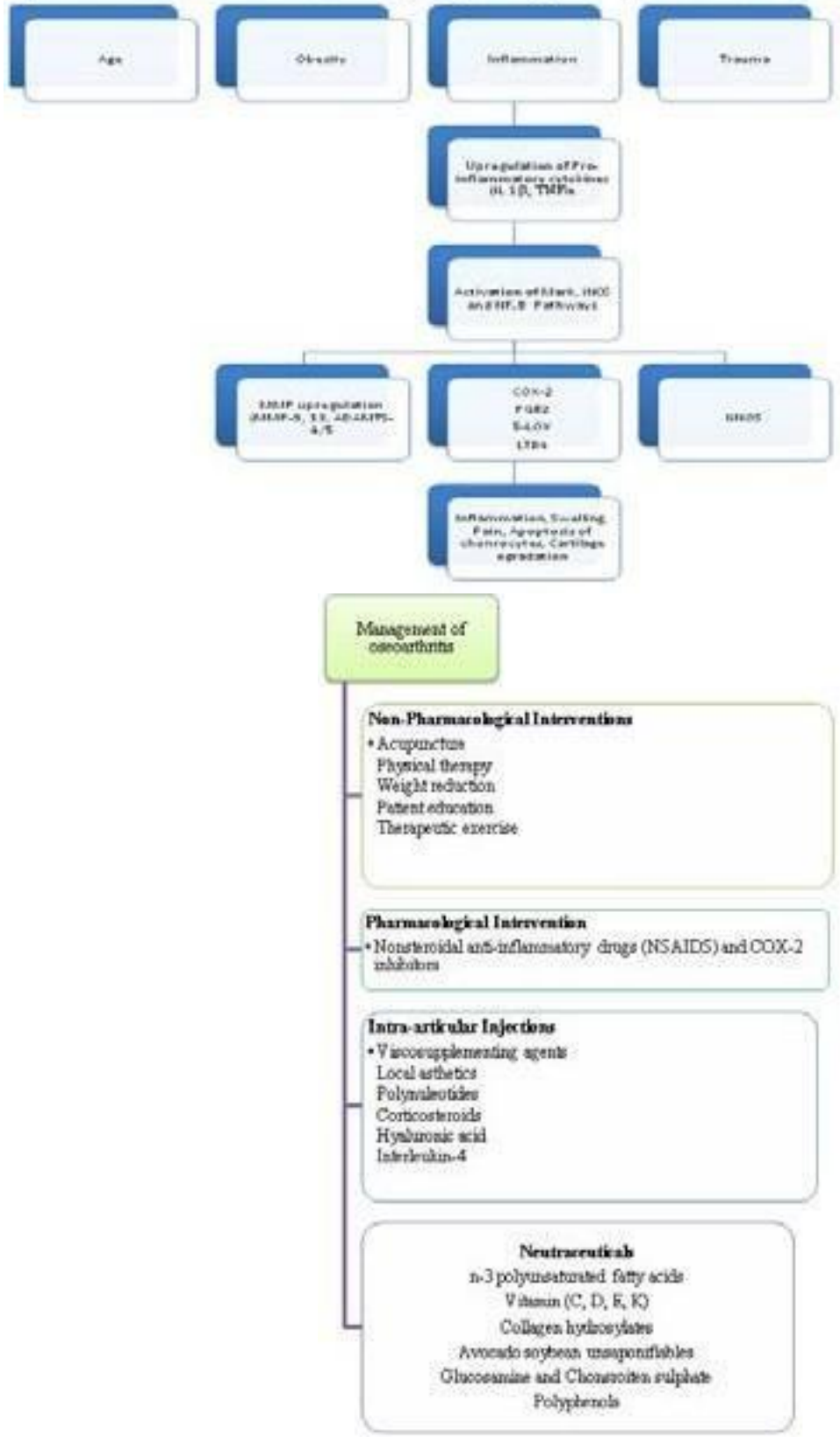

Fig 3: Medicinal plants having potential to treat ostearthritis