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Review on Essential Oils and Ways to Use them for the Treatment of Arthritis

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In order to study the existing information about the positive uses of essential oils (EOs) in treating arthritis, this review gives an overview of how natural essential oils, which have various characteristics like natural occurrence, commending penetration ability and partitioning action into skin, are used in the treatment of arthritis, also which can help various drugs penetrate the skin more effectively for the same. While reviewing various scientific experiments, we found that various oils were used alone or in combination, in different ways/ methods on patients suffering from arthritis or on animals induced with arthritis (in-vivo study) & the results were quiet positive & effective in treating types of arthritis. As a result of our scientific literature survey, we found number of studies evaluating potential anti-arthritic activity of EOs and their major constituents has increased giving hope to an interesting new therapeutic applications of EOs in the future.

Keywords: Arthritis; Aromatherapy; Essential Oils; Research studies; Skin.

Skin is the largest organ of the human body having various abilities like to protect the body from heat, cold, micro-organisms, maintain the temperature of the body and as a sensory organ. When applying topically to the skin, a dosage form must be crossed between stratum corneum and allow it to penetrate into other layers of your skin. A good candidate for topical administration would be medicines with low solubility and shorter half-life. There are 3 possible routes through which an active ingredients can permeate the skin i.e. intercellular, intracellular and appendageal pathway[1].

Three main layers of skin are: [2]

A. Epidermis
B. Dermis
C. Hypodermis.

Epidermis is the top most layer of skin having a stratified, squamous, keratinizing epithelium. Major part are covered by the keratinocytes, which has the property as barrier of the skin. There are capillaries system of dermis under the epidermis which circulates blood across the whole body. Active ingredients enters into the blood stream, if it has the penetrating ability into the stratum corneum. A normal drug can pass through the layer by the process called passive diffusion.

Dermis is mainly composed of connective tissues and is the layer of skin that provides support to the epidermis. The junction between epidermis and dermis layer is known as dermal-epidermal junction which stops penetration of

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larger molecules. This layer can be sub-classified into papillary and reticular dermis. Dermis consists of oil glands, sweat glands, hair follicles & nerve endings.

Hypodermis refers to the layer of fat tissue that connects the dermis, aponeurosis and fasciae (the muscles). Subcutaneous adipose tissue is deeply integrated into the dermis via blood vessels and neural networks. It's a layer of loose connective tissue and the thickness varies according to the surface of the body.

Arthritis

Arthritis is a prevailing chronic health issue and a major contributor to disability. The Greek word "arthritis" is derived from the root words "arthron" and "ites" meaning "inflammation of joints". Arthritis is a long-term, inflammatory, systemic autoimmune disease that causes stiffness, swelling and pain in the joints[3]. Arthritis is the medical term for swelling or inflammation of the joints. It depicts various ailments that have an impact on connective tissues, joints, and surrounding tissues. Arthritis can be of different forms such as osteoarthritis (OA), rheumatoid arthritis (RA), psoriatic arthritis, gout and fibromyalgia but the 2 main types of arthritis are:

1). Osteoarthritis is the most common form of arthritis which is characterized by the loss of cartilage that supports the bones in your joints.

2). Rheumatoid arthritis caused when immune system attacks the joints, beginning with the lining of joints.

Signs & Symptoms: It involves the joint:

- Pain & Stiffness
- Swelling & Redness
- Decreased range of motion

An osteoarthritis is a degenerative disease that causes damage to the cartilage that supports the joints of the knee, hip, and other lower extremity joints. Women are at an increased risk of knee osteoarthritis (OA) by 47% compared to 40% for men, and this risk is expected to rise as the population ages and becomes more overweight.[3]. About 0.5–1% of the world's population suffers from rheumatoid arthritis (RA), which is 2-3 times more common in women than in men. The major symptoms of RA include pain, swelling & inflammation of joints, cartilage destruction thus causing irreversible disability[4]. The pathogenesis of RA is influenced by a series of factors including genetic, environmental and autoimmunity. All of these factors activate the immune system, causing antigen self-expression (stimulation of antigen specific T and B cells) and abnormal inflammatory cytokine production, resulting in synovitis and bone damage (destruction of cartilage and bone tissue in the subchondral area). Additional articular organs (skin and cardiovascular system) may also be involved[3]. In rheumatism, the inflammatory process is triggered by the release of pro-inflammatory cytokines like tumour necrosis factor (TNF-á) and interleukin (IL-1) and other cytokines in the synovial cavities. These cytokines increase vascular cell infiltration, hepatocytes produce more protein C, and osteoclast activity is increased by bone erosions. These defensive responses cause tissue damage that worsens over time, leading to joint injuries, functional disabilities and discomfort that lowers quality of life[5]. The aim in the treatment for patients suffering from rheumatoid arthritis is to eradicate symptoms, disease progression and improve the quality of life.

Various Medications are used in the Treatment of Arthritis like NSAIDs, DMARDs, Steroids, Immunosuppressive drugs & other Herbal treatments. NSAIDs (non-steroidal anti-inflammatory drugs) are one of the most popular and prescribed arthritis drugs. A NSAID is an inhibitor of COX (cyclooxygenase). The two forms of COX-inhibitors are known as COX-1 and COX-2. NSAIDs act on both forms of COX-1 acts on the maintenance of healthy tissue while COX-2 acts on the inflammation pathway. This research gave rise to a new class of NSAIDs called COX-2 selective inhibitors, examples include Diclofenac, Piroxicam, Indomethacin, Sulindac and Mefenamic acid while COX-2 inhibitors include Celecoxib, Rofecoxib and Valdecoxib etc., the drug therapy to modify the course of the disease or induced remission. It prevents the basic destruction process occurring in joints, thereby altering the course of disease and even inducing remission[6].

Numerous side effects, few of which may be serious, can be caused by regular use of NSAIDs. The most common adverse reactions are the development of ulcers in the stomach and duodenum, suppression of uterine contraction, hypersensitivity reactions, headaches, nausea and vomiting, digestive issues, heartburn, diarrhoea,

weight gain and respiratory issues. Excessive use of corticosteroids can result in suppression of the functions of the pituitary gland, hyperglycaemia and increased susceptibility to infections. The biological properties of many plants have long been known to treat inflammatory diseases in ethno medicine.

Essential oils, which are derived from plants, are commonly used as herbal remedies in traditional medicine and are often responsible for biological properties. These essential oils have been found to have various effects such as anti-inflammatory and anti-radical properties[7]. Many medicines are obtained from the plant source. Safety, affordability, effectiveness and ease of availability are the main advantages for plants when it comes to treating different diseases. In view of these advantages, traditional doctors are more likely to use herbs in their practice. In Indian traditional system of medicines, medicinal plants from Indian origin have been successfully used for treating various disease conditions such as chronic fever, cough & cold, malaria, arthritis, diabetes, diarrhoea, bronchial asthma, skin diseases, etc., also in treatment of cardiovascular, gastric, hepatic & immunological disorders[8].

Essential oils

In the 16th century, Paracelsus von Hohenheim, first coined the term 'Essential Oil' as the effective component of a drug in his book, 'Quinta essential'. Terpenes/terpenoids, aromatic and aliphatic molecules, which are referred to as low-molecular-weight fragrance chemicals, are the main components of essential oils. Essential oils and some of their constituents are used in a wide range of products today, including cosmetics, air fresheners, household cleaners, food and agriculture, and medicine. Additionally in aromatherapy as well as in other paramedical practices, essential oils are also used. Antioxidant activity is one of the areas in essential oil which have been researched the most. The reason behind it is, oxidation alters various biological components and leads to the cause of many diseases, such as cancer, Alzheimer, liver disease, arthritis, inflammation, diabetes, Parkinson's disease, etc.[9]. The essential oil therapy is an additional healing technique, which can be stated as the ancient art and science of combining naturally extracted oils so that they are able to improve health in all types of body, mind or spirit. Essential oil therapy is backed up by clinical studies, case studies, clinical audits, and patient reports. It helps build our physical and/or our emotional well-being, and helps to manage different symptoms like pain, anxiety, and depression[10]. The property of an EO can be of different types depending on the plant, species, botanical family, geographic location, cultivation, weather, season and method & duration of distillation. Essential oils from certain plants have been found to contain a bunch of different chemicals that can help protect you from things like inflammation, fungi, bacteria, viruses, and more. They can also help make you feel better, boost your immune system, and even help fight cancer. In addition to aromatherapy, they are also used topically or orally for a number of medical conditions including pain, arthritis, bruises, cuts, scars, fleas and so on[11]. Some studies researched about the role of essential oils in rheumatic diseases as a topical and inhalation application. So far, only three types of rheumatic disease have been treated with essential oil therapy: Fibromyalgia, Osteoarthritis and Rheumatoid Arthritis. After a massage, the essential oil increases the body's pain threshold through the release of endorphins. Other ways essential oils can help include increased vagal activity, serotonin levels, dilation of the superficial vessels, and blood flow. These mechanisms are important for rheumatic diseases because they are often associated with localized or diffused pain. Massage therapy with essential oil is commonly used to treat inflammatory diseases, such as arthritis and rheumatism. Today, aromatherapy is accepted globally and has become a science. It is a widely used, multi-disciplinary approach that can be used in conjunction with massage, acupuncture, physiotherapy as well as other traditional medical therapies[10].

Penetration enhancers[12]

In order to facilitate the absorption of drugs into the skin, penetration enhancing substances are employed that temporarily interfere with the skin barrier, narrow the lipid pathways between the coenocytes, modify drug delivery within the skin structure, or improve distribution into the skin. Properties of penetration enhancers are that they:

1. Should be non- allergenic, non-irritating and non-toxic.

2. Quick action and their effect's activity and duration should be determinable and repeatable.
3. It is not expected to bind to receptor sites and, as a result, has no pharmacological activity in the body.
4. It should allow therapeutic substances to enter the body while avoiding the loss of the body's endogenous material.
5. It should work well with both the excipients and the drugs. It should also work well for the formulation of various topical products.
6. They should be cosmetically acceptable while providing smooth feel.

Mechanism

Action of penetration enhancers is by following mechanisms:
1. Disruption of the stratum corneum lipids highly organized structure.
2. Interaction with intercellular protein.
3. Improved transport of drugs, co-enhancers and solvents into stratum corneum

Most of the essentials oils are excellent penetration enhancers, also which help other active ingredients to increase the penetration enhancing potential to the intended area in treating various ailments/diseases.

Various essential oils used in the treatment of arthritis

Peppermint oil[11]

(*Mentha piperita L.*)

Family

Lamiaceae.

It is combination of water mint and spearmint. The EO is obtained from the plant's flowers and leaves.

Composition

1,8-cineole, menthol, menthone, menthyl acetate, â-pinene, limonene, â-caryophyllene and flavonoids.

Uses

Used for various purposes such as neurological pain, digestive problems, allergies, oral health, arthritic pain, anti-fungal, skin care etc.

Palmarosa oil[11]

(*Cymbopogon martinii var. motia*)

Family

Poaceae.

This plant is native to India. Commonly known as Indian Geranium, ginger grass or rosha.

Composition

Palmarosa oil yields an essential oil rich in geraniol which is used in top-quality perfumes and cosmetics[13]. Linalool, geraniol, geranyl acetate, (E)-â-ocimene and (E,Z)-farnesol were the main phytoconstituents. In addition, whole herb oil was also found to contain higher levels of linalool and â-carophyllene as well as (E,Z)-farnesol. Inflorescence oil was found to be rich in (E)-ocimene and geranyl acetate, whereas oils from parts of leaf, were rich in geraniol.

Uses

Palmarosa EO has antioxidant, anti-inflammatory, antifungal, bactericidal and antiviral activities and is widely used in fever, arthritis and rheumatism, infectious diseases, digestive problems, wounds and nerve-related pain.

Lavender oil[11]

(Lavandula latifolia, L. angustifolia)

Family

Lamiaceae

Composition

The main constituents include linalool and linalyl acetate, along with trace amounts of terpinene-4-ol, lavandulol, and lavandulyl acetate. Various chemical constituents were found in the EO obtained from the dried flowers of Lavandula angustifolia (grown in Poland) having linalool, â-caryophyllene, geraniol, linalyl acetate and lavandulyl acetate[14]. Also linalool, á-terpineol, linalyl acetate, t-p3-ocimene, lavandulyl acetate, nerol, neryl acetate and â-caryophyllene was found[15].

Uses

Analgesic, antiseptic, antioxidative, anticonvulsant, antidepressant, anti-rheumatic, anti-inflammatory, antibacterial, deodorant, hypotensive, sedative, antiviral, etc.

Cinnamon oil[11]

Cinnamomum zeylanicum and Cinnamomum verum (both refer to the same tree).

Family

Lauraceae

Composition

Main constituents of oils from leaf and bark of cinnamon are cinnamaldehyde, eugenol, eugenol acetate and cinnamyl acetate. Through a study, EO of the bark of C. altissimum Kosterm consisted of highest of linalool, then methyl eugenol, limonene, á-terpineol, á-terpinene, ã-terpinene, terpinen-4-ol, and 1,8-cineol [16].

Uses

It helps to stimulate the digestive & immune systems, also relieves pain associated with rheumatism. It has a calming & invigorating effect on mind, thus improving cognitive function and memory. It also has many healing properties such as antioxidant, anti-inflammatory, anti-rheumatic, antifungal, astringent, antiviral, antibacterial, antispasmodic, carminative, immune-stimulating, etc.

Chamomile oil[11]

German chamomile (Matricaria chamomilla) & Roman chamomile (Chamaemelum nobile)

Family

Asteraceae.

German chamomile and the Roman chamomile are the two major types of species. Chamomile originates from Southern and Eastern part of Europe. Now it is also grown in India, Brazil & many European countries.

Composition

The main ingredients in this essential oil are the terpenoids á-bisabolol and their oxazulenes, which include chamazulene and acetylene compounds. It's made from chamomilla flowers grown in Germany. The other major bioactive ingredients are á-bisabolol, chamazulene or azulene, bisabolol oxides A and B, farnesene, flavonoids (apigenin, luteolin, patuletin, and quercetin), glycosides, hydroxycoumarines, coumarins (herniarin and umbelliferone), spiroether sesquiterpene lactones, terpenoids and mucilage[17].

Uses

It has antioxidant, anti-inflammatory, antispasmodic antiseptic, carminative & sedative properties. Therefore, it is being used for many conditions such as hay fever, rheumatic pain, skin diseases (eczema, chickenpox & psoriasis), menstrual disorders, neuralgia, sciatica, and etc[17-19]. It turns out that Chamomile oil has anti-inflammatory properties because it stops the release and build-up of COX-2, which is a type of enzyme that helps break down prostaglandins caused by LPS. It doesn't affect the body's ability to make COX-1[20].

Cannabis oil[11,21]

(*Cannabis sativum Linn.*)

Family

Urticaceae. This is a carpellate plant, native to Iran, Western and Central Asia, now widely cultivated throughout India.

Composition

The main chemical composition is volatile resin oil which contains canabene, canabene hydride, canabinon and canabine; including cannabinol, pseudo-cannabinol, cannabinin and some terpenes. Hemp oil's phytochemistry is intricate because it has constituents like á-pinene, CBD, â-myrcene, â-caryophyllene, CBD, limonene, humulene, linalool and terpinolene. The abuse of cannabis products has behavioural side effects, so the use of medical marijuana is still a contentious and divisive topic.

Uses

Cannabis/hemp/cannabidiol (CBD) oil is used in medicine from years. It has shown outstanding effects in treating pain, osteoarthritis, obesity, atopic dermatitis, hypertension, cancer, COPD, diabetes, etc. Seed oil is used in rheumatism.

Coriander oil[21]

(*Coriander sativum Linn.*)

Family

Umbelliferae. It is widely cultivated in India and is used for its seed, fruit and leaves.

Composition

The extract of its fruit contains volatile and essential compounds such as borneol, geraniol and linalool / coriandrol.

Uses

Oil is very useful for rheumatism in an emulsion form. Linoleic acid and cineole, which is one of the 11 components of coriander essential oil, have anti-rheumatic and anti-arthritic properties.

Curcuma (Turmeric) [21]

Turmeric oil (*Curcuma longa Linn.*) (CL)

Family

Scitaminaceae/ Zingiberaceae. CL is an annual plant commonly grown in Asian countries such as India and China.

Composition

ar-turmerone, á-turmerone and â-turmerone are three of the most important chemicals found in turmeric rhizome oil[22].

Uses

Turmeric essential oil has an anti-inflammatory and anti-arthritic activities. CL rhizome essential oil with streptococcal cell wall induced arthritis has shown to have anti-arthritic activity.

Celery oil[23]

(*Apium graveolens L.*)

Family

Apiaceae or Umbelliferae. This plant has been used for decades to treat various diseases due to its high therapeutic benefits and as a flavouring ingredient in many food products due to its high nutritional value.

Composition

Majority of essential oil is present in the leaves while little amount in seeds of celery. The main constituents of celery oil are 3-n-butyl phthalide, sedanenolide, sedanolide, and sedanonic anhydride. The essential oil consists of salience, sesquiterpenes, limonene and typical fragrance. It is rich in folic acid, sodium, potassium, fibers, â-carotene, magnesium, silica and chlorophyll. The scented volatile oils obtained from the leaves mainly consists of terpenes, phenol and anhydrides. Oils extracted from seeds are called as fixed oils and mainly composed of fatty acids which contains linoleic acid, linolenic acid, palmitic acid, oleic acid, stearic acid and petro selenic acid. Sesquiterpenes, alcohol (1–3%), and fatty acids are the main constituents of the essential oil found in celery leaves, stems, and seeds.

Uses

The celery leaf essential oil is used as a potential compound for natural immunotoxicities and has antioxidant properties. Seed oils in coumarins have muscle relaxant property and phthalide have anti-rheumatic activity. Its seed oil has successfully been used for rheumatoid arthritis.

Ginger oil[24]

(*Zingiber Officinale*)

Family

Zingiberaceae. Uses of Ginger is well known worldwide as a cooking spice, condiment and household herbal remedy.

Composition

Ginger oil contains major active ingredients such as sesquiterpenes: zingiberene, bisapolene and zingiberol.

Uses

The enzymes of the prostaglandin and leukotriene biosynthetic pathways i.e. cyclooxygenase (prostaglandin synthetase) and lipoxygenase, are both inhibited by ginger and its pungent components, making them dual inhibitors of arachidonic acid metabolism[25-27]. Traditional medicine of India, Ayurveda, has been using ginger since decades to stop excessive clotting (related to heart disease), regulate cholesterol and combat arthritis. Essential oil of ginger hindered chronic adjuvant arthritis in rats[28].

Tulsi oil[29]

(*Ocimum sanctum Linn.*)

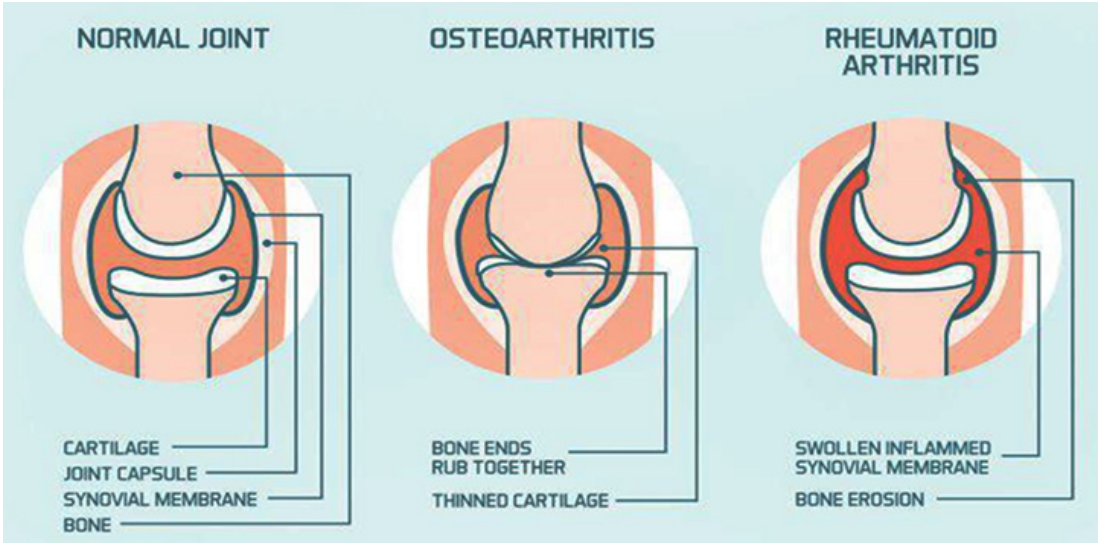

Fig. 1. Difference between Normal joint & joint with arthritic conditions
Source: https://www.mcjr.com/blog/whats-the-difference-between-osteoarthritis-and-rheumatoid-arthritis

Family

Lamiaceae

Ocimum sanctum L. and Ocimum basilicum are the species included in this family. Tulsi is considered sacred plant in India & is an important plant in Ayurveda.

Composition

The essential oil contains Carvacrol, methylchavicol, caryophyllene & limatol. Caryophyllene, camphene, pinenes, terpinene 4-decylaldehydes, selinene & nerol are some other constituents of the oil. Thymol and citral are two of its chemical constituents. Along with aromatic monoterpenes like camphor, the essential oil also contains aromatic monoterpenoids like limonene and (E) ociemene. Tulsi oil mostly contains 13-20 % of bisabolene, 9-33 % of eugenol, 3-19 % of methyl chavicol, 4-9 % of (E) bisabolene and 1.7-7 % of terpineol.

Uses

Tulsi oil has been demonstrated to be an effective anti-inflammatory agent in a variety of studies in rats exposed to Freund's adjuvant, formaldehyde, and turpentine oil. This oil has been shown to be effective in reducing arthritis and swelling associated with carrageenan-induced paw edema in rats. Furthermore, the inhibitory properties of Ocimum Sanctum fixed oil have been demonstrated to be effective in inhibiting the cyclooxygenases and lipoxygenases, thus allowing for the reduction of inflammation.

Table 1. Research studies done on essential oils using aromatherapy for treating arthritis found through literature survey

Essential oil used	Purpose/method of study used	Results/ Outcomes of the study	Reference
Lavender oil	A 5% blend of lavender, juniper, ylang-ylang and rosemary oils in ratios of 3:3:2:2 for 100 ml coconut carrier oil has been applied to this study. For 6 weeks, the participants were given a thirty minute massage three times a week.	Reflexology seemed to reduce pain and fatigue scores more effectively than aromatherapy massage for those with rheumatoid arthritis, according to the study. Researchers came to the conclusion that reflexology and aromatherapy massage will help RA patients feel less tired and in discomfort. Although more research is need to be done.	37
Eucalyptus oil	To research how inhaling eucalyptus oil after having a total knee replacement (TKR) surgery affects pain and inflammation. 52 participants were randomized, 25 to the eucalyptus oil and 27 to the almond oil (control) group. For about 30 minutes during the continuous passive movement (CPM), patients were exposed to eucalyptus or almond oil for 3 days in a row.	Participants who inhaled eucalyptus essential oil preparations at 30-minute intervals for three consecutive days reported less pain and lower blood pressure readings than those who inhaled an almond oil control. Thus, Eucalyptus oil inhalation was successful in lowering the patient's pain and blood pressure after TKR.	38
Lavender oil	A total of 90 patients (30 in each group) with knee osteoarthritis were randomly assigned to one of three treatment groups: intervention (Lavender essential oil aromatherapy massage), placebo (Almond oil massage), and control (No massage).	Lavender oil aromatherapy reduced arthritic pain in patients with knee osteoarthritis (n = 30 per group) when compared to a placebo. However more research need to be done to confirm the findings.	39
Orange oil & Ginger oil	To check the effectiveness of aromatic essential oil Ginger oil & Orange oil massage on elderly people with moderate to serious knee pain. Number of older people were taken for the double-blinded & placebo-controlled experimental study. The intervention group got 6 massage sessions over three weeks with ginger and orange oil. The control group didn't get any massage while the placebo group got the same massage intervention with olive oil.	The results of the study showed that while aroma massage therapy with ginger & orange was effective in the short-term in relieving moderate to severe pain, stiffness and daily functioning, it was not effective in improving quality of life and there were no reported side effects.	40

Table 2. Researches in topical formulations prepared using essential oils as permeation enhancers & for the anti-inflammatory activity

API used	Ingredients used in formulation	Study purpose	Results & outcomes from the study	Researchers
Etoricoxcib (NSAID)	HPMC K4M, Carbopol 940 , Carbopol 934, Span 80, Tween 80, Propylene glycol (PG), methyl paraben, Clove oil , Almond oil, Olive oil.	To develop an emulgel formulation using Etoricoxcib an NSAID, effective in treatment of Osteoarthritis, Rheumatoid Arthiritis, Acute Gouty Arthiritis, Spondylitis, etc.	Batch F8 (8% almond oil) showed better spreadability, better loading capacity, easy of application and good patient compliance & batch F12 (8% Olive oil) formulation showed good release when compared with other formulations	Usha A *et. al.*[41]
Capsaicin	HPMC K4M, HPMC K100M, Carbopol 930, Carbopol 974, Hydroxy ethyl, Propylene glycol, Span 80, Tween 80, Methyl paraben, Clove oil	To prepare emulgel using capsaicin, an analgesic as drug of choice. Emulgels are better drug delivery method for hydrophobic drugs to pass through the skin.	Formulations F1-F7 pass all assays with good results. Emulgel F1 (carbopol 974-1%) formulation demonstrated highest spreadability and can be utilized to produce rapid pharmacological action.	Navaneetha K *et. al.*[42]
Coriandrum sativum seeds oil	Carbopol 940, Carbopol 934, Span 20, Tween 20, Triethanolamine, Peppermint oil, liquid paraffin, methyl paraben, propyl paraben, Propylene glycol.	To prepare and formulate an emulgel with Coriandrum sativum seed oil for anti-inflammatory activity. Linalool, which makes up 60–70% of Coriandrum sativum seed oil, has anti-inflammatory properties.	In the in vitro studies, the F9 formulation showed maximum drug release in 7 hours i.e. (92.9 ± 1.1%). A test for paw edema induced by carrageenan showed that the emulgel has anti-inflammatory activity. Therefore, Coriandrum Sativum seeds oil emulgel demonstrated significant anti-inflammatory action.	Mohite *et.* al.[43]
Mefenamic Acid (NSAID)	Carbopol 940, Tween 20, Span 20, Liquid paraffin, Propylene Glycol, Methyl & Ethyl Paraben, Ethanol, Clove Oil, Mentha Oil	To prepare emulgel of Mefenamic acid using clove oil and mentha oil as penetration enhancers for analgesic and anti-inflammatory activity & Carbopol 940 as a gelling agent.	The *in-vitro* & *in-viv* studies revealed that the formulation F4 containing 10% clove oil gave maximum drug release than others in 240 min. Anti-inflammatory and analgesic activity was proved by Carrageenan induced paw edema and hot plate tests. The formulations F2 and F4 demonstrated similar analgesic and anti-inflammatory activity to commercially available diclofenac sodium gel.	R. Khullar *et. al.*[44]
Diclofenac Potassium (NSAID)	Carboxypolymethylene (CPM), Triethanolamine, Turpentine oil and	In order to demonstrate the long-term release of the model drug, the	Formulation containing 10% turpentine oil showed maximum flux through rabbit skin.	Hussain Abid *et. al.*[45]

	olive oil, Ethanol (96%)	researchers designed new gel formulations of Diclofenac Potassium. The essential oil of Turpentine and Olive oil as carrier oil was used as a penetration enhancer to test the permeation enhancement potential of Diclofenac potassium	Turpentine oil showed high potential to be used as natural penetration enhancer for formulation of hydrogels as compared to olive oil.	
Methotrexate	Carbopol 940, Eucalyptus, Peppermint oil and Olive oil, Triethanolamine (TEA)	They prepared Methotrexate Transdermal Gel using various oils to study & improve the transdermal permeability of Methotrexate using those oils as natural permeation enhancers.	The results showed that formulations were safe, non-irritant or not caused necrosis to rats' skin and stable till 60 days. In conclusion, transdermal MTX gel (peppermint oil 4% v/v) showed better permeation across semi-permeable membrane, resulting in a better permeation for stratum corneum.	Ashoor Jamal Ali *et. al.*[46]
Naproxen (NSAID)	Carbopol P940, propylene glycol, Ethyl alcohol & sandalwood oil	They formulated & evaluated topical gel of Naproxen containing sandalwood oil for the treatment of rheumatoid arthritis. Sandalwood oil was used to reduce inflammation and give soothing and cooling effect.	F3 formulation containing Carbopol P-940 (1%) & Sandalwood oil (0.6 ml) gave highest drug release.	Palak Joshi *et. al.*[47]
Diclofenac sodium (NSAID)	Carbopol, Propylene glycol, Triethanolamine, Geraniol, Menthol & Calendula oil	They prepared Diclofenac Sodium gel using Geraniol, Menthol & Calendula oil as penetration enhancers to check the permeation enhancement of Diclofenac Sodium.	Calendula oil was found to have a greater permeation-enhancing effect than geraniol and menthol, resulting in a nearly 20-fold increase in Diclofenac sodium permeability coefficient.	Bodhankar *et .al.*[48]

Anti-arthritic activity[30]

Rats with formaldehyde-induced arthritis were used to test the anti-arthritic activity of Ocimum sanctum L. fixed oil. It greatly decreased the diameter of the inflamed paw. Arthritic condition was improved in rats after 10 days of intraperitoneal administration of the fixed oil. The fixed oil inhibited carrageenan as well as inflammation-induced mediators (bradykinin, histamine, serotonin and PGE2) in inflammatory models. These data suggest anti-arthritis properties in inflammatory models (including adjuvant-induced and Turpentine- induced joint edema, rats).

Eucalyptus oil[31]

(*Eucalyptus globulus*)

Family

Myrtaceae.

One of the most widely used essential oils, with a wide range of biological properties, is obtained from eucalyptus leaves through steam distillation.

Table 3. Some well-known Marketed preparations containing essentials for relieving pain related to Arthritis

Product	Brand Name	Essentials oils used	Manufacturer
Balm	Iodex	Wintergreen oil, Turpentine Oil, Eucalyptus oil, Clove oil	GlaxoSmithKline (GSK)
Ointment	Dr. Ortho	Eucalyptus Oil, Turpentine Oil, Clove Oil, Ajwain Oil, Cinnamon Oil	Dr. Ortho Ayurvedic
Roll-on	Amrutanjan	Wintergreen Oil, Clove Oil	Amrutanjan Health Care Ltd
Spray	Relispray	Clove oil, Peppermint oil, Camphor oil, Eucalyptus oil, Turpentine oil, Wintergreen oil, Cinnamon oil	MidasCare Pharmaceuticals Pvt Ltd
Gel	Myolaxin-D	Menthol, Eucalyptus oil, Camphor oil	Geno Pharmaceuticals Ltd
Liniment	Rumalaya	Sesame Oil, Wintergreen Oil	Himalaya Drug Company
Cream	Arthorex	Eucalyptus oil, Turpentine oil, Katuvera (Red chilly) oil, Clove oilWintergreen oil	JMD Medico
Oil	Zandu Ortho Vedic Oil	Mahanarayan Oil, Mahamasha Oil, Vishgrabha Oil, Wintergreen Oil, Eucalyptus Oil, Clove Oil, Sarsapa (Mustard) Oil, Sesame Oil	Emami Ltd
Patch	Dr Ortho Pain Relief Patch	Peppermint Oil, Camphor Oil, Clove Oil, Capsicum Oil, Eucalyptus Oil, Wintergreen Oil	Dr Ortho Ayurvedic

There are other topical formulations also in the market intended & effective to alleviate the arthritic pain.

Composition

The main constituent of eucalyptus oil is eucalyptol [1,8-cineole]. 70–90% of eucalyptus oil is made up of eucalyptol, a monocyclic monoterpene ether, also á-pinene, á-phellandrene, p-cymene, cuminaldehyde, limonene, terpinen-4-ol and trans-pinocarveol are some of its minor constituents.

Uses

It has anti-inflammatory properties that help reduce pain and inflammation associated with Rheumatoid Arthritis. The oil has also been shown to have antioxidant properties in some studies.

Turpentine oil[31]

(*Pinus longifolia Roxb.)*

Family

Pinaceae

Turpentine oil is a cyclic aliphatic terpenoid. It is naturally occurring in wood and balsam/gum, as well as sulphate-based turpentine oil. It is mainly composed of monoterpene compounds, such as á-pinene and â-pinene. It is obtained from the wood, oleoresin, young twigs, cone trunks, and other Pinaceae species using the fractionation or steam distillation methods.

Composition

á-pinene and â-pinene are the major constituents of turpentine oil. Constituents like careen, camphene, dipentene, terpinolene, and are also present in small amounts.

Uses

In preparations like gel and matrix type transdermal patches where used as an additive for permeation, Turpentine oil increases the permeation of NSAIDs including diclofenac potassium, Ibuprofen or ketorolac tromethamine.

Rosemary oil[32]

(*Rosmarinus Officinalis Linn.*)

Family

Lamiaceae. Steam distillation of leaves and flowering tops is used to extract the oil.

Composition

This essential oil is mainly made up of 1,8-Cineole, á-pinene, borneol, bornyl acetates, camphenes and camphor. Monoterpenes like 1,8-cineole, bornel, camphene, limonene, myrcene, pinene and camphor are predominantly present in rosemary essential oil[33].

Uses

The oil can be used in arthritic pain, asthma, mental fatigue, memory loss & muscular pain.

Black Cumin Seed oil[34]

(*Nigella sativa L.*)

Family

Ranunculaceae

Composition

Thymoquinone, thymol, alpha-pinene, carvacrol, limonene, p-cymene, 4-terpineol, longifolene and t-anethole benzene. Seeds contain unsaturated fatty acids, including linoleic acid (LA), oleic acid (OA), palmitic acid, etc. Flavonoids, cardiac glycosides, saponins, vitamins (Thiamine, Niacin, Folic Acid) & some minerals (Calcium, Iron, Phosphorus, Copper & Zinc).

Uses

Seed oil from this plant is traditionally used to treat skin conditions, back pain, rheumatoid arthritis, and other inflammatory conditions. The anti-inflammatory properties of the oil have been demonstrated in a number of inflammatory models in experimental encephalomyelitis, colitis, peritonitis, arthritis and edema. These models work by inhibiting inflammatory mediators, prostaglandins and leukotriene.

Essential Oils used In Aromatherapy For Treating Arthritis

Aromatherapy came from the words "aroma" which means smell or fragrance and "therapy" synonym to treatment. Essential oils can be used in a variety of ways, like being absorbed through the skin, inhaled through the nose or throat, or ingested through the digestive system. In recent years, there's been a lot of interest in using essential oils to help improve health, which is known as aromatherapy or phytotherapy. Essential oils are made up of a variety of organic compounds. Their bioavailability and smell are determined by their chemical structure. Essential oils fall into a few categories based on their fragrance: citrus, floral, herbaceous, earthy, camphor, woody, spicy and minty. Olfactory aromatherapy can improve moods or otherwise help states of mind that have been negatively impacted by factors of life and the consequences of life-threatening conditions such as anxiety, depression and stress, along with physical conditions associated with immune system disorders such as digestive disorders, allergic conditions, arthritis, cancer and skin diseases[35]. Aromatherapy is a form of complementary therapy that utilizes essential oils as a key component in the treatment of a wide range of conditions. Essential oils, or volatile oils, are extracted from the plant's bark, fruit, flowers, leaves, stem, roots and more[36]. Aromatherapy can be classified into: [36]

1. Cosmetic aromatherapy
2. Medical aromatherapy
3. Olfactory aromatherapy
4. Massage aromatherapy
5. Psycho-aromatherapy

While Aromatherapy doesn't cure major diseases, it does help with relaxation, stress reduction, mood and wellness and improve the immune system, respiratory system and circulatory system[35].

Safety concerns while using essential oils[36]

Most essential oils are in general harmless and do not cause any undesirable effects. A few of them have been approved as food additives by the US Food and Drug Administration (US-FDA), which classifies them as generally recognized as safe (GRAS).

1. The most frequent side effects are eye, skin, and mucous membrane irritation and sensitization, especially when using oils that contain phenols and aldehydes.
2. Oxidation of monoterpenes is a more frequent cause for contact sensitivity, often due to incorrect storage conditions.
3. There have only been a few reports of allergy reactions, most of which are caused by topical application.
4. Essential oils should always be diluted with carrier oils before using it topically
5. Should be kept away from pets, small children & away from fire.

DISCUSSION AND CONCLUSION

While there are many Non-Steroidal Anti-Inflammatory Drugs (NSAIDs), Disease Modifying Anti-rheumatic Drugs (DMARD), steroids, and immunosuppressive medications available to treat or slow down the development of arthritis, they all have some side effects. We have been blessed by nature with an abundance of herbal plants that are widely used around the world as a source of medicine to treat and prevent various

illnesses[21]. EOs are use in the medicines & in various other ways to treat many diseases. Essential oils are plant's secondary metabolites used for aromatherapy and different traditional medicines with a variety of pharmacology properties, including an inhibitory effect on multiple models of inflammation[7]. Many *in-vitro*, pre-clinical and clinical trial studies have demonstrated that essential oils of aromatic and medicinal plants are effective in treating arthritis[4,49]. From various literature survey it was found that the natural oils has reported promising enhancement of drug permeation across skin when used as permeation enhancers. It is also to be noted that the efficacy of oil as penetration enhancer depends on their concentration as well as drug's physicochemical characteristics[1]. In order to protect and preserve the delicate balance of nature, essential oils should be taken into much greater consideration as natural and secure substitutes for synthetic alternatives[9]. The role of EOs in drug development has been well reported since ancient times, however, they are used directly as therapeutic agents due to their proven track record in traditional indigenous medicine systems like Ayurveda, Unani, Siddha, Homeopathy and in modern medicine. Additionally, EOs contain GRAS (Generally Recognized as Safe) bioactive compounds[50]. When we looked into different scientific studies, we found that different oils were used on people with arthritis or on animals induced with arthritis (*in-vivo* studies), the results were surprisingly positive and effective in treating different types of arthritis. However, further research is needed to validate the results and gain expertise in this field so that we can gain a better understanding of the biological properties of essential oils for use against various degenerative conditions without relying on synthetic chemicals. Hence from above review we conclude that there are many natural EOs that have anti-arthritic properties which must be researched deeply & used for our well-being.

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Conflict of Interest

There are no conflict of interest.

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