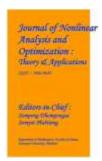
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# AN OVERVIEW ON MANAGEMENT OF OSTEOARTHRITIS USING HOMOEOPATHY AND A BRIEF EXPLANATION OF DR. HEINER FREI'S USE OF POLARITY ANALYSIS SOFTWARE TO ACHIEVE PRECISE HOMOEOPATHIC SIMILIMUM

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#### **ABSTRACT**

This review provides a comprehensive overview of the efficacy of homoeopathic medicines in treating Osteoarthritis (OA). Through a meticulous examination of available literature, the article explores the causes, signs, and conventional treatments of OA from the unique perspective of homoeopathy. Homoeopathic interventions, rooted in the principle of "like cures like," are scrutinized for their ability to alleviate joint pains associated with OA. The analysis reveals promising outcomes, indicating that homoeopathy holds the potential in reducing the discomfort caused by OA and contributing to the enhancement of Activities of Daily Living (ADL). By focusing on the holistic approach of homoeopathy, which considers individual constitutional factors, this review sheds light on the mechanism of action of homoeopathic remedies in managing OA symptoms. Notably, the examination emphasizes the role of homoeopathy in not only mitigating pain but also positively influencing overall joint function. The article underscores the importance of functional independence in OA management and suggests that homoeopathy may play a valuable role in improving ADL.

In conclusion, this review consolidates existing knowledge on the subject, providing valuable insights into the efficacy of homoeopathic medicines for OA treatment. While acknowledging the positive impact of homoeopathy on joint pains and ADL, it encourages further research to establish a more robust evidence base and facilitate the integration of homoeopathy into mainstream OA therapeutic strategies.

An attempt is made to understand Dr. Heiner Freis's Polarity analysis software and the different studies on its efficacy.

**KEYWORDS:** Osteoarthritis, Homoeopathy, Polarity Analysis Software, Homoeopathic Medicine. \*Corresponding Author Email: drpriyasheth14@gmail.com

### INTRODUCTION:

Osteoarthritis (OA) is a prevalent multifactorial joint disease that progresses over time and is characterized by functional disability and chronic pain. The burden of Osteoarthritis grows with age and obesity, accounting for nearly 4/5 cases of OA worldwide. The basic sign is degeneration of the articular ligament. characterized by diminished joint space, osteophytes, and different deformities that develop as the disease advances. The disease essentially influences the weight-bearing joints in our body. Homoeopathic prescriptions are truly significant in decreasing agony and side effects of osteoarthritis, with critical improvement noted utilizing the WOMAC Index. Osteoarthritis is the second most common rheumatological issue and is the most prevalent joint disease with a prevalence of 22% to 39% in India compared with other rheumatological diseases (Gout, Ankylosing Spondylitis, Psoriatic Arthritis, rheumatoid Arthritis, etc.) According to World Health Organization (WHO) 9.6% of men and 18.0% of women aged over 60 years have symptomatic osteoarthritis worldwide. 80% of

those with osteoarthritis have limitations in movement, and 25% cannot perform their major daily activities of life.<sup>4</sup>

### **Risk Factors:**

Age, sex, genetics, post-menopausal changes, obesity.

Other causes include macro trauma, recurrent microtrauma, and a Sedentary lifestyle.

# **Pathological Changes:**

The chondrocytes in the surface region of the articular cartilage expand, proliferate, and become disorganized; this is the first structural alteration in osteoarthritis. The matrix of the cartilage deteriorates through fibrillation and matrix fracture. The underlying cancellous bone thickens and becomes sclerotic. At the edges of the articular surface, osteophytes grow. In most joints with end-stage OA, tiny calcium phosphate and calcium pyrophosphate dehydrate crystals are visible. <sup>4</sup>

# Signs and symptoms of osteoarthritis:

Knee pain during rest, day or night, may be severe or mild. While the joint is moving, there may be a crackling sound. warmth over the joint restricted range of motion

## Diagnosis of osteoarthritis:

Swelling and tenderness during a physical examination along with restriction of motion. Research and laboratory tests: X-ray of the affected joint. Blood tests: To eliminate other potential reasons for joint discomforts, such as Rheumatoid Arthritis. Arthroscopy and Joint fluid analysis. By examining the patient's gait as soon as they walk into the room.

# **Knee Joint Inspection:**

Pay attention to any other swelling in or around the knee. Look for the disappearance of the usual hollows around the patella, an indication of swelling in the knee joint and suprapatellar pouch.<sup>4</sup>

**Palpation**: Instruct the patient to flex their knees while sitting on the edge of the examination table. Bony landmarks are easier to see and palpate in this posture because the muscles, tendons, and ligaments are more relaxed.

# The first step in preventing osteoarthritis:

Weight management, frequent exercise, and a dietary intake should be maintained. Eat healthy. Prevent injuries or have them treated. Osteoarthritis is most frequently caused by injury to the joint. No single diet has been proven to stop osteoarthritis. A lower risk of the disease or its severity has been linked to a number of nutrients. They consist of omega-3 fatty acids. While bad fats might worsen joint inflammation, these good fats reduce it. Fish oil and several plant/nut oils, such as walnut, canola, soybean, flaxseed/linseed, and olive, are excellent providers of omega-3 fatty acids. D vitamin: Numerous studies have revealed that vitamin D supplementation reduced knee pain.

## Osteoarthritis and Homoeopathy:

Based on Homoeopathic principles and the Homoeopathic classification of chronic conditions, osteoarthritis falls under chronic illness, as per Master Hahnemann, Aphorism 72 made specific notice of chronic diseases.

"They are diseases of such a nature that, with little, frequently invisible beginnings dynamically disrupt living things in their peculiar ways and can cause them to gradually shift from the healthy state, such that the Vital force, an automatic life force that is simply intended to maintain health opposed to them at the start and throughout their faulty development, inappropriate, ineffective resistance, but is unable to put them out on its own, thus must unable to do anything but watch them grow and become unnaturally more and more insane, eventually leading to the derangement. They are caused by infection with a chronic Miasm."

The main aim of conventional medicine for Osteoarthritis is pain control and reduction of the progression of joint damage to minimize disability and maximize the quality of life. Many therapeutic interventions are currently employed for the management of OA, including physiotherapy, antidepressant therapy, patient education, monthly telephone calls from lay personnel, and weight control. In addition, drug therapy includes non-opioid analgesics such as paracetamol, non-steroidal anti-inflammatory drugs (NSAIDs), topical analgesics, opioid analgesics, and intra-articular steroid injections. Such treatments may prove ineffective in some patients, and NSAIDs are potentially toxic

with serious adverse effects. Gastrointestinal complications are frequently reported, with 12000 hospitalizations and about 2000 deaths attributed to NSAID use in the UK every year. In severe cases of OA, joint replacement surgery, e.g. knee arthroplasty is recommended.<sup>5</sup>

This, however, carries risks, especially for senior people who frequently have co-morbid medical disorders. In the treatment of patients with OA, there seems to be a common demand for drugs with high efficacy and minimal toxicity. Patients who do not respond well to standard medical care and who are not candidates for surgery or refuse it specifically need these drugs. A growing number of these patients are turning to complementary or alternative therapies (CAM). Homoeopathy is one of the most widely used CAM therapies among patients with rheumatic disorders, and its use is both very prevalent and growing. In the USA, arthritis is the condition that CAM practitioners most frequently mention treating. The general population and medical community generally hold a strong and expanding belief in the efficacy of homoeopathy.  $\pm$  20 Arthritis and musculoskeletal disorders were the most often treated conditions in homoeopathic practises, according to a survey comparing them to primary care settings that did not offer homoeopathy. This review's objectives included locating and evaluating all randomised clinical trials (RCTs) that used homoeopathy to treat patients with osteoarthritis (OA), examining the outcomes of customised homoeopathic treatments, and contrasting homoeopathic combinations with NSAIDs.  $^6$ 

### **POLARITY ANALYSIS:**

Polarity Analysis A Path to Precise Prescription in Homoeopathy

In this article, an attempt is made to comprehend the value of Dr. Heiner Frei's Polarity Analysis (PA) as a method for enhancing the accuracy of homoeopathic prescriptions. In addition, the concept of contraindication developed by Boenninghausen, which served as the basis for PA, is being studied. To ensure that the PA analysis is used appropriately and carefully, the potential downsides of the method have also been listed.<sup>8</sup>

#### **Methods:**

This review summarises the articles showing the efficacy of Polarity analysis software. Kinds of literature were searched in web databases, PubMed, and ResearchGate with the following keywords-Polarity analysis software, B.T.P.B, Dr. Heiner Frei,

In our quest for the advancement of homeopathy, knowledge, rational methodologies, and improved outcomes have to evolve together. Polarity analysis (**PA**) was created for the rigorous scientific Swiss double-blind study with homoeopathic treatment of hyperactive kids, a study that showed a substantial difference between high-potency homoeopathic remedies and placebo. 7

The reliability of all the factors used to select a cure needed to be improved, which was a major obstacle in achieving this outcome. With a preamble based on Boenninghausen's Therapeutic Pocketbook (BTPB) and its still unmatched grading of symptoms, the polarity analysis technique has improved homoeopathic prescribing skillfully. The accuracy of prescriptions has significantly increased as a result of the application of these new techniques in the treatment of, acute and chronic illnesses and multimorbid diseases. To effectively communicate the fundamentals of polarity analysis, this text gives the reader a thorough, hands-on introduction to the working of this new technique. To demonstrate the wide range of issues encountered in clinical practice, we have included a plethora of case examples. They advise us to utilize one of the software tools available that is based on the updated version of Boenninghausen's Therapeutic Pocketbook to try to replicate the remedy selection procedure in these circumstances (PB).

Utilizing the Boenninghausen Working Group's repertoire programme (BOWG).

It's best to start treating your own patients with acute illnesses once you have mastered the new remedy determination concepts. You can begin dealing with chronic sickness if you have gained some experience in this area. After that, you can start working with the most difficult patients, hyperactive kids, and patients with multiple conditions

# Development of polarity analysis

1. Boenninghausen's contraindications:

The polarities are first mentioned in the preface to the revised edition of Boenninghausen's Pocket Book by Klaus-Henning Gypser. When choosing a remedy, Boenninghausen strived to match the patient's set of symptoms and especially the modalities (that is, the circumstances that aggravate or ameliorate the symptoms) as closely as possible to the genius of the remedy

The genius of a remedy includes the modalities, sensations, and clinical findings that have repeatedly appeared in the proving at various locations, and which can generally be healed. These are the actual characteristics of an individualistic remedy.

Polar symptoms are those symptoms that can have an opposite aspect, an "opposite pole" such as thirst /thirstlessness, cold aggravates / cold ameliorates, or desire for fresh air/dislike of fresh air.

Polar symptoms of the remedy in question should be matched at as high a grade as possible (3-5). If the opposite pole is listed for the remedy at a high grade (3-5) but the patient's symptom at a low grade (1-2), the genius of the remedy does not match the patient's symptom set. The remedy is therefore contraindicated.<sup>7</sup>

# Polarity Difference Click or tap here to enter text.

Boenninghausen's idea of contraindications was the basis for polarity analysis, a mathematical process that produces higher hit rates and more significant clinical improvements than had previously been observed with traditional homoeopathic techniques, which was first used in 2001 during the initial phase of the ADHD double-blind study. Polarity analysis determines the possibility of recovery by rating the polar symptoms of the selected treatments and determining the polarity difference.

This is determined for each remedy by adding the patient's polar symptoms in grades. The grades of the matching opposite polar symptoms are deducted from the resultant value. Assuming there are no contraindications, the cure correlates to the patient's typical symptoms more closely the higher the polarity difference computed in this way. The accuracy with which we can identify the right treatment undergoes a quantum leap when these discoveries regarding the polarity of symptoms are rigorously applied. Several prospective outcome studies have investigated the effects on the prescriptions' accuracy and the quality of the improvements.<sup>7</sup>

Because it is the only program that utilizes the updated version of Boenninghausen's PB, which includes his final thoughts on the grading of symptoms as well as several entries by him, we favour this software. It has the benefit of being extremely well-organized and simple to use. The positive results of polarity analysis demonstrate that it has a level of reliability that is currently unmatched.

The absence of contraindications and the magnitude of the polarity difference are the most crucial factors for the weighing of the repertorization results, followed by the thoroughness with which symptoms are covered and, finally, the correspondence determined during the Materia medica comparison.<sup>9</sup>

The completeness of the symptom covering has a substantially lower weight than polarity difference and contraindications when we obtain a large number of polar symptoms, as is typical for multimorbid situations. But this symptom coverage criterion becomes more

### **METHODS:**

**Identification of Articles:** Systematic literature searches were performed to identify all RCTs, individualised homeopathic medicines, comparison of homeopathic combinations with NSAIDS. Computer databases used were Medline, Full-text terms homeopathy, and the MeSH terms homeopathy, homeopathy, and alternative medicine were used. A manual search for additional trials was performed using the bibliographies of studies and reviews located through the computer database searches and scanning our own files.

**Inclusion /Exclusion:** There were no restrictions regarding the age, studies that were included are randomized control trials, and comparative studies of one homeopathic treatment measured against another active drug were included. There were no restrictions regarding the form or mode of application of the homeopathic treatment. RCTs with any type of objective and /or subjective parameters were considered.

Below is the table describing the articles used to study the effectiveness of homoeopathic treatment in the cases of osteoarthritis. Table 1.

 $\textbf{JNAO}\ Vol.\ 14,\ No.\ 2,\ No.01\ (2023)$  Table.1. The effectiveness of homoeopathic treatment in the cases of osteoarthritis.

S. N	Auth or	Joint locati	Samp le size	Design	Interventi on/ control	Treatm ent	Primary outcome	Main results
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	)			controlled,	capsules of	t	night pain	were
				crossover,	fenoprofen	regimen	(VAS), and	observed
				double-	(each		four p	between
				dummy	containing			Rhus
					300 mgs) or			toxicodend
					two			ron and
					capsules of			placebo
					placebo			treatment
					three times			phases.
					daily; Oral			Treatment
					administrat			with
					ion of five			fenoprofen
					drops of			produced
					Rhus			highly
					toxicodend			significant
					ron (6x:			pain relief
					1=1000			compared
					000			with both
					dilution) or			Rhus
					5 placebo			toxicodend
					drops three times daily.			ron and placebo
					Treatment			treatment
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					consisted of			phases
					(1) placebo			
					capsules			
					and placebo			
					drops (2)			
					fenoprofen			
					capsules			
					and placebo			
					drops or (3)			
					placebo			
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					and Rhus			
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	(2000			controlled	piroxicam		joint	the two

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					officinale			ic
					(comfrey),			treatment,
					Rhus			was found.
					toxicodend			No
					ron (poison			significant
					ivy), and			difference
					Ledurn			between
					palustre			groups was
					_			found for
					(marsh-tea)			
					to knee			the single-
					three times			joint
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3	Sheal	knee	65	Double-	Oral	30 days	Average pain	improvem
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					ron,			differences
					Causticum			observed
					and Lac			between
					Vaccinum)			homeopath
					and placebo			ic
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					times daily			and
					or a liquid			paracetam
					placebo and			ol.
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				parallel	intra-		measured by	for both
				arms	articular		patient	treatments.
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					injections		assessment at	Tolerance		
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					or five		treatment	for both		
					injections			treatments,		
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				performed	symptoms,		RAPID3 on	paired		
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of personality

#### **RESULTS:**

A Randomized controlled trial comparing topical piroxicam gel with homoeopathic gel in osteoarthritis of the knee: R.A Van Haselen and P.A.G.Fisher: The objective of this study is to compare the effectiveness and safety of a homoeopathic gel with an NSAID gel (piroxicam) for treating knee osteoarthritis. Out of 184 patients who were enrolled, 172 had endpoints for the primary outcome criteria. The NSAID gel was not as well tolerated or as effective as the homoeopathic gel. It is impossible to rule out the existence of a clinically significant difference between treatment groups. Patients with osteoarthritis may find the homoeopathic gel and basic analgesics to be helpful therapeutic option.<sup>10</sup>

Homoeopathic Management in Osteoarthritis Yogeshwari Gupta: In this article, the author summarized the literature available for osteoarthritis, including the classification of OA, clinical features, Differential diagnosis, and diagnosis along Homoeopathic remedies useful in the treatment of OA like Bryonia, Calcarea flour, causticum, Colchicum, Colocynth, Rhustox, OA Nosode, Formica rufa, Guaicum, veratrum alb, By lowering the symptoms and rate of joint degeneration, homoeopathic medications effectively treat OA and enhance the quality of life. 11

Study of the Significance of Individualization in Management of Osteoarthritis: The second most prevalent musculoskeletal condition worldwide is osteoarthritis. It is the most prevalent type of arthritis, primarily affecting older people. It is a major contributor to elderly people's pain and impairment. Analgesics and NSAIDs, which have adverse effects on the liver, kidney, gastrointestinal tract, and cardiovascular system and cause further suffering for the patient, are the mainstays of treatment. The disease is not treated by homoeopathy. It provides a patient with a long-lasting, safe, and effective cure. To put it simply, it individualizes. Homoeopathic medications are said to offer the best palliative, reparative, and genetic constitutional effects; as a result, homoeopathic medications taken infrequently increase overall health, behavioral changes, and pain tolerance, which lowers the risk of deformity and enhances the quality of life.<sup>12</sup>

An observational study on the effect of individualised homoeopathic medicine administered based on totality of symptoms vis-à-vis personality in cases of osteoarthritis knee: The observational study involved 60 osteoarthritis knee patients with a clinical diagnosis, 30 of which received homoeopathic treatment based on the whole range of symptoms, and 30 on the basis of personality. Computergenerated numbers were used for the randomization process. The 44-item Big-Five Inventory was used to evaluate the patients' personalities. A custom tool was created to translate trait components to homoeopathic repertory rubrics. Before and after therapy, the Routine Assessment of Patient Index Data 3 sheet scores for knee osteoarthritis on physical function, pain, and patient global estimate were compared. The paired difference mean of RAPID3 for the entire symptom-based and personality-based administrations was 4.06 and 1.92, respectively, with standard deviations of 3.91 and 3.29. When treating patients with osteoarthritis of the knee, homoeopathic medicine based on the totality of symptoms is proven to be more effective than homoeopathic medication that is customised based on personality.<sup>13</sup>

Homeopathic remedies for the treatment of osteoarthritis: a systematic review. Two trials comparing homeopathic complexes with conventional treatments reported pain reduction equivalent to those found with conventional medicine, with fewer adverse effects. Nahler et al's study was not doubleblind due to differences in viscosity and recommended frequency of applications. Due to its brief

length, small sample size, and simplistic symptomatic premise, Shipley et al.'s study of a single homoeopathic cure for a brief period in OA has received harsh criticism. In the treatment of moderate osteoarthritis of the knee, Van Haselen et al. found that homoeopathic gel SRL1 is at least as effective and well tolerated as NSAID piroxicam gel. There is strong evidence that SRL1 gel is at least as effective as piroxicam gel based on the sample size of 184 patients' ability to identify a difference in pain (VAS) between the two treatments. According to the study, only people who are currently taking oral NSAIDs for pain may benefit from applying piroxicam gel topically to treat their discomfort. Controlled trial of Homoeopathic treatment of osteoarthritis: In a double-blind, placebo-controlled crossover study to compare the homoeopathic remedy Rhus tox. 6X with fenoprofen in osteoarthritis of the hip and knee, fenoprofen was shown to have beneficial analgesic and anti-inflammatory effects which differed significantly from those of placebo. The effects of Rhus tox. 6X and placebo did not differ significantly. Patient preference was for fenoprofen. Side-effects were not severe but were seen more frequently with fenoprofen. Similar results were seen in all patients regardless of whether they had been referred to and assessed by a homoeopathic physician or a rheumatologist.

Effect of Homoeopathic treatment on Activity of Daily Living (ADL) in Knee Osteoarthritis: A prospective observational study: To study how individualised homoeopathic treatments can improve ADL by easing pain and stiffness and stopping the progression of the disease. Materials and Procedures A minimum of twelve months of follow-up was required for 131 consecutive patients with OA of the knee. Upon performing a clinical examination on the patients, two orthopaedic surgeons determined the disease's diagnosis. Individualised homoeopathic simillimum was prescribed by three qualified homoeopathic doctors, and patients' pain levels were assessed using the WOMAC Osteoarthritis Index LK3.1 (IK) survey form, which measures pain, stiffness, and ADL. For confirmation, the pain was also assessed using the numerical pain rating scale. As a result, customised homoeopathic medications supplied in accordance with the law of similia reduced the mean ADL from 35.85 to 19.08 (p-0.0001).<sup>13</sup>

### Different studies that used polarity analysis to reach similimum

H1N1 Influenza: A Prospective Outcome Study with Homeopathy and Polarity Analysis<sup>9</sup>. This study assesses the effectiveness of polarity analysis (PA) in the management of influenza in Switzerland during the pandemic of 2010–2011. The swine flu virus /H1N1 (2009) predominated this outbreak, accounting for 83% of all influenza cases.32 patients (62%) saw an improvement of 50% or more two days after taking the first treatment, eliminating the necessity for the second medication. After taking the second medicine, 13 patients (or 25%) showed this improvement, and as a result, were cured. In six individuals (11.5%), there was no response. They required a follow-up session because neither the first nor the second therapy was effective in curing them (figure 1). With the second remedy, one female patient saw complete improvement for 10 days before relapsing. She was also included in the group of patients (total: 13%) who had no reaction.<sup>9</sup>

Homeopathic Treatment Of Children With Attention Deficit Hyperactivity Disorder: A Randomised, Double-Blind, Placebo-Controlled Crossover Trial: More and more parents are using homoeopathy to calm down their hyperactive kids. A clinical observation study and a randomized, partially blinded experiment both found that homoeopathy is effective in treating patients with attention deficit hyperactivity disorder (ADHD). The purpose of this study was to gather empirical support for homeopathy's efficacy in treating ADHD. 83 kids between the ages of 6 and 16 who had ADHD according to the Diagnostic and Statistical Manual of Mental Disorders-IV criteria were enrolled in the study. They were given individually prescribed homoeopathic drugs prior to the randomized, double-blind placebo-controlled crossover research. The trial included 62 participants who saw a 50% improvement in their Conners Global Index (CGI). This eligibility criterion (CGI) was not met by thirteen patients. Verum was administered to arm A of the responders for six weeks, followed by a placebo for the same Number of weeks, while arm B received the opposite regimen. Parents reported the CGI at the start of the trial and following each crossover period, and patients completed neuropsychological testing. At the conclusion of each crossover period and again throughout long-term follow-up, the CGI rating was once again assessed. Cognitive abilities like impulsivity, divided

attention, and visual global perception had greatly improved undoped-labeled treatment at the start of the crossover phase (P 0.0001). CGI parent ratings were considerably lower in the crossover trial when verum was used (average 1.67 points vs. placebo; P = 0.0479). The improvement in the long-term CGI was 12 points (63%, P 0.0001).  $^{11,17}$ 

Polarity analysis a case study of a masked depression in duchenne muscular dystrophy: The case study demonstrates how difficult it is to use homoeopathy to treat a fatal disease like muscular dystrophy. However, it is possible to lessen or even eliminate the disease's adverse effects, making the patient's life more tolerable and, most likely, thereby lengthening that person's life expectancy. Although the primary complaints, in this case, were mental, the cure was chosen based on the physical symptoms. The polarity analysis-based treatment frequently discloses the psychodynamic origins of the patient's suffering. The term "holistic" here refers to the fact that we can infer conclusions about the mind from physical symptoms. <sup>19</sup>

Homeopathy in acute otitis media in children, treatment effect or spontaneous resolution: Antibiotic resistance is one of the issues with the traditional antibiotic therapy of acute otitis media (AOM). It has been demonstrated that homoeopathy is effective at treating AOM. Since AOM has a high rate of spontaneous remission, any therapy benefit must be proven through a trial that shows very quick symptom relief. The goal of this study was to determine how many children with AOM experience pain relief after 12 hours of starting homoeopathic treatment, negating the need for further treatment. In the paediatric office, 230 AOM patients received their first homoeopathic prescription on an individual basis. After six hours, if pain relief was still insufficient, a second (different) homoeopathic medication was administered.<sup>20</sup>

#### **CONCLUSION:**

From the above articles, it can be concluded that osteoarthritis can be managed with Homoeopathic treatment effectively along with some lifestyle modifications like regular exercise or yoga, properly balanced diet, maintaining fitness, reducing stressful life, avoiding sedentary life habits etc. Maintaining a healthy lifestyle is necessary. Constitutional treatment with homoeopathy, by considering the mental and physical generals gives good relief from the symptoms and can be managed with homoeopathy effectively. Some specific homoeopathic medicines can be thought of to reduce pain, pain, stiffness and improve activities of daily life of a person. Polarity analysis software is useful in improving the first prescription by selecting modalities that are highly reliable. Only a few studies were carried out using Polarity Analysis Software, still, more studies are needed to be carried out.

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# **CONFLICT OF INTEREST:**

The authors have no conflicts of interest to declare.

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