ORTHOLORD TABLETS: A Blend of Natural Ingredients Provides Nutritional Support for Joint Health

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ABSTRACT

Osteoarthritis is a chronic degenerative disorder that currently represents one of the main causes of disability within the elderly population and an important presenting complaint overall. Osteoarthritis is the most common form of arthritis, affecting millions of people worldwide. It occurs when the protective cartilage that cushions the ends of your bones wears down over time. Osteoarthritis (OA) is caused by aging joints, injury, and obesity. Aim of the study was to determine the clinical efficacy and safety of glucosamine phosphate and to evaluate the chemically related methylsulfonylmethane (MSM), collagen peptide, Hyaluronic acid, Curcuma, Boswellia serrata, piperin, in the treatment of OA to determine their efficacy and safety profile. in the management of vitamin c osteoarthritis. Studies were included if they met the following criteria, studies about primary hip and or knee OA patients with clinical and or radiologic diagnosis, studies of glucosamine, chondroitin, (MSM), collagen peptide, Hyaluronic acid, Curcuma, Boswellia serrata, piperin, or the two in combination against placebo, extractable data reporting the pain, function, stiffness, and the adverse events (AEs) of patients. A (vital signs, physical examination, pregnancy test, previous medical history, chest X-ray, electrocardiogram, urine examination, serology, haematological and biochemical parameters) The exclusion criteria were as follows, treatment methods described unclearly, studies of non-randomized or uncontrolled trials, interventions combined with non-steroidal anti-inflammatory drugs, studies or data reported repeatedly, and trial arms with sub-therapeutic doses. For each study, patients' characteristics including mean age, sex, mean duration of symptom, BMI, duration of follow-up, type of outcome (pain, function, stiffness, and AEs), trial design, trial size, details of intervention, treatment duration, and results were individually extracted. Data of intention-to-treat analysis was employed whenever possible. The primary outcomes of this were pain intensity, function improvement. Out of 68 patients with osteoarthritis diagnosis admitted to emergency department in our center, age range was from 21 to 75 years. About 45% of patients were female, and 55% were male. Severe Joint stiffness and Tenderness were the most prevalent manifestations that were present in patients. Glucosamine showed effect on stiffness outcome relieving pain and improving physical function. The data from the more rigorous MSM trials provide positive evidence in the treatment of mild to moderate OA of the knee. Chondroitin sulfate (CS) is recommended as a therapeutic intervention in the multimodal approach of osteoarthritis (OA) management. Hyaluronic acid is a potential bright spot for helping lower the side effects. Vitamin C might protect against the development of osteoarthritis, rheumatoid arthritis, and inflammatory polyarthritis, according to some studies. A powerful antioxidant, it fights molecules that trigger inflammation. It reduces pain and improves physical functioning significantly in OA patients; and it is safe for human consumption. It may exert its beneficial effects by controlling inflammatory responses through reducing proinflammatory modulators, and it may improve joint health by reducing the enzymatic degradation of cartilage in OA patients.

Keywords: Curcuma, Turmeric, Osteoarthritis, Dietary Supplements, Cartilage, Chondrocyte, Curcuma, Inflammation, Joint, Pain.

NUTRITIONAL FACTS Serving Size: 1 Tablet	Serving Per Container 90 Tabs
COMPOSITION	MG
Glucosamine Sulphate	1000
Methyl Sulphonyl Methane	800
Chondroitin Sulphate Sodium	500
Collagen Peptide	50
Hyaluronic Acid	5
Curcuminoid	50
Piperin	5
Vitamin C	100
Boswellia Serata	50

INTRODUCTION

Osteoarthritis (OA) is the most common chronic (long-lasting) joint condition. Osteoarthritis is the most common form of arthritis, affecting millions of people worldwide. It occurs when the protective cartilage that cushions the ends of your bones wears down over time. Osteoarthritis (OA) is caused by aging joints, injury, and obesity. A joint is where two bones come together. The ends of these bones are covered with protective tissue called cartilage. With OA, this cartilage breaks down, causing the bones within the joint to rub together. Some people call it degenerative joint disease or “wear and tear” arthritis. Osteoarthritis (OA) is the most common form of frequently in the hands, hips, and knees. These changes usually develop slowly and get worse over time. OA occurs most often in older people, although it can occur in adults

of any age. OA is also called degenerative joint disease, degenerative arthritis, and wear-and-tear arthritis. A

leading cause of disability, OA affects more than 30 million men and women in the United States. OA can cause pain, stiffness, and swelling. In some cases it also causes reduced function and disability; some people are no longer able to do daily tasks or work.

Causes

OA is caused by joint damage. This damage can accumulate over time, which is why age is one of the main causes of the joint damage leading to osteoarthritis. Osteoarthritis occurs when the cartilage that cushions the ends of bones in your joints gradually deteriorates. Cartilage is a firm, slippery tissue that enables nearly frictionless joint motion. Eventually, if the cartilage wears down completely, bone will rub on bone.

The older you are, the more wear and tear you've had on your joints. Other causes of joint damage include past injury, such as:

- ✎ Torn Cartilage
- ✎ Dislocated Joints
- ✎ Ligament Injuries

They also include joint malformation, obesity, and poor posture. Certain risk factors, such as family history and gender, increase your risk of osteoarthritis. But besides the breakdown of cartilage, osteoarthritis affects the entire joint. It causes changes in the bone and deterioration of the connective tissues that hold the joint together and attach muscle to bone. It also causes inflammation of the joint lining.

Symptoms

- ✎ Stiffness
- ✎ Inflammation
- ✎ Tenderness (discomfort when pressing on the area with your fingers)

Osteoarthritis symptoms develop slowly and worsen over time. Signs and symptoms of osteoarthritis include:

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- **Pain:** Affected joints might hurt during or after movement.
- **Stiffness:** Joint stiffness might be most noticeable upon awakening or after being inactive.
- **Tenderness:** Your joint might feel tender when you apply light pressure to or near it.
- **Loss of flexibility:** You might not be able to move your joint through its full range of motion.
- **Grating sensation:** You might feel a grating sensation when you use the joint, and you might hear popping or crackling.
- **Bone spurs:** These extra bits of bone, which feel like hard lumps, can form around the affected joint.
- **Swelling:** This might be caused by soft tissue inflammation around the joint.

Osteoarthritis of the Hip

The hip joint shown on the left side of the image is normal, but the hip joint shown on the right side of the image shows deterioration of cartilage and the formation of bone spurs due to osteoarthritis.

Stages

OA is a progressive condition with five stages, from 0 to 4. The first stage (0) represents a normal joint. Stage 4 represents severe OA. Not everyone who has OA will progress all the way to stage 4. The condition often stabilizes long before reaching this stage.

Stage 1 – Minor

This is the least severe stage of OA. Patients in stage 1 will develop minor wear-and-tear in their joints, but typically feel little to no pain in the affected area. If you have no history of OA, a doctor will most likely leave your symptoms untreated, but they may advise you take supplements or change up your exercise routine.

Stage 2 – Mild

This is when X-rays will start to show more noticeable bone spur growths (growths that often develop where bones meet each other in the joint). The affected area will start to feel stiff after long, sedentary periods, and will become uncomfortable. Your doctor might suggest a stricter workout routine or a fitted brace to wear.

Stage 3 – Moderate

In stage 3, the cartilage in the affected area starts to erode and narrow the gap between bone and joint. The joint becomes inflamed and starts causing discomfort during normal daily activity. Some treatments include over the counter pain medications, prescription pain relievers, and in severe cases, hyaluronic injections.

Stage 4 – Severe

This is the most severe stage of OA, which means it is also the most painful. At this point, the cartilage is almost completely gone, leading to an inflammatory response from the joint. The bone spurs that developed in the earlier stages have now multiplied, often causing excruciating pain. There are various treatment options that generally include bone realignment surgery and knee/hip replacement.

A. Risk Factors

Factors that can increase your risk of osteoarthritis include:

- ✎ **Older age:** The risk of osteoarthritis increases with age.
- ✎ **Sex:** Women are more likely to develop osteoarthritis, though it isn't clear why.
- ✎ **Obesity:** Carrying extra body weight contributes to osteoarthritis in several ways, and the more you weigh the greater your risk. Increased weight adds stress to weight-bearing joints, such as your hips and knees. Also, fat tissue produces proteins that can cause harmful inflammation in and around your joints.
- ✎ **Joint injuries:** Injuries, such as those that occur when playing sports or from an accident, can increase the risk of osteoarthritis. Even injuries that occurred many years ago and seemingly healed can increase your risk of osteoarthritis.
- ✎ **Repeated stress on the joint:** If your job or a sport you play places repetitive stress on a joint, that joint might eventually develop osteoarthritis.
- ✎ **Genetics:** Some people inherit a tendency to develop osteoarthritis.
- ✎ **Bone deformities:** Some people are born with malformed joints or defective cartilage.
- ✎ **Certain metabolic diseases:** These include diabetes and a condition in which your body has too much iron (hemochromatosis).

B. Complications

Osteoarthritis is a degenerative disease that worsens over time, often resulting in chronic pain. Joint pain and stiffness can become severe enough to make daily tasks difficult. Depression and sleep disturbances can result from the pain and disability of osteoarthritis.

Diagnosis

During the physical exam, your doctor will check your affected joint for tenderness, swelling and flexibility.

Imaging tests

To get pictures of the affected joint, your doctor might recommend:

- **X-rays:** Cartilage doesn't show up on X-ray images, but cartilage loss is revealed by a narrowing of the space between the bones in your joint. An X-ray can also show bone spurs around a joint.
- **Magnetic resonance imaging (MRI):** An MRI uses radio waves and a strong magnetic field to produce detailed images of bone and soft tissues, including cartilage. An MRI isn't commonly needed to diagnose osteoarthritis but can help provide more information in complex cases.

Lab Tests

Analyzing your blood or joint fluid can help confirm the diagnosis.

- **Blood tests:** Although there's no blood test for osteoarthritis, certain tests can help rule out other causes of joint pain, such as rheumatoid arthritis.
- **Joint fluid analysis:** Your doctor might use a needle to draw fluid from an affected joint. The fluid is then tested for inflammation and to determine whether your pain is caused by gout or an infection rather than osteoarthritis.

Treatment

Osteoarthritis can't be reversed, but treatments can reduce pain and help you move better.

Medications

Medications that can help relieve osteoarthritis symptoms, primarily pain, include:

- ✓ **ACETAMINOPHEN:** Acetaminophen has been shown to help some people with osteoarthritis who have mild to moderate pain. Taking more than the recommended dose of acetaminophen can cause liver damage.
- ✓ **NONSTEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDs):** Over-the-counter NSAIDs, such as ibuprofen and naproxen sodium, taken at the recommended doses, typically relieve osteoarthritis pain. Stronger NSAIDs are available by prescription. NSAIDs can cause stomach upset, cardiovascular problems, bleeding problems, and liver and kidney damage. NSAIDs as gels, applied to the skin over the affected joint, have fewer side effects and may relieve pain just as well.
- ✓ **DULOXETINE:** Normally used as an antidepressant, this medication is also approved to treat chronic pain, including osteoarthritis pain. Also approved to treat chronic pain, including osteoarthritis pain.

Therapy

- ✓ **Physical therapy:** A physical therapist can show you exercises to strengthen the muscles around your joint, increase your flexibility and reduce pain. Regular gentle exercise that you do on your own, such as swimming or walking, can be equally effective.
- ✓ **Occupational therapy:** An occupational therapist can help you discover ways to do everyday tasks without putting extra stress on your already painful joint. For instance, a toothbrush with a large grip could make brushing your teeth easier if you have osteoarthritis in your hands. A bench in your shower could help relieve the pain of standing if you have knee osteoarthritis.

Lifestyle and Home Remedies

Exercising and losing weight if you're overweight are important ways to lessen the joint pain and stiffness of osteoarthritis.

- **EXERCISE:** Low-impact exercise can increase your endurance and strengthen the muscles around your joint, making your joint more stable. Try walking, bicycling or water aerobics. If you feel new joint pain, stop.

- **LOSE WEIGHT:** Carrying extra weight increases the stress on your weight-bearing joints, such as your knees and your hips. Even minor weight loss can relieve some pressure and reduce your pain. Talk to a dietitian about healthy ways to lose weight.
- **MOVEMENT THERAPIES:** Many people use these therapies to reduce stress in their lives, and research suggests that tai chi and yoga might reduce osteoarthritis pain and improve movement.
- **HEAT AND COLD:** Both heat and cold can relieve pain and swelling in your joint. Heat, especially moist heat, can help muscles relax and ease pain. Cold can relieve muscle aches after exercise and decrease muscle spasms.
- **CAPSAICIN:** Topical capsaicin, a chili pepper extract, applied to your skin over an arthritic joint might help some people. You might have to apply it three to four times a day for several weeks before you see a benefit. Some people can't tolerate the irritation. Wash your hands well after applying capsaicin cream.
- **BRACES OR SHOE INSERTS:** Shoe inserts or other devices might help reduce pain when you stand or walk. These devices can support your joint to help take pressure off it.
- **ASSISTIVE DEVICES:** Assistive devices can help relieve stress on your joints. A cane takes weight off your knee or hip as you walk. Hold the cane in the hand opposite the leg that hurts.
- **ACUPUNCTURE:** Some studies indicate that acupuncture can relieve pain and improve function in people who have knee osteoarthritis. During acupuncture, hair-thin needles are inserted into your skin at precise spots on your body.
- **OMEGA-3 FATTY ACIDS:** Omega-3s, found in fatty fish and fish oil supplements, might help relieve pain and improve function.

Aims and Objectives

Aim

Aim of the study was to determine the clinical efficacy and safety of glucosamine phosphate, methylsulfonylmethane (MSM), Vitamin C, Curcuma, in the management of osteoarthritis

Objectives

To evaluate the Clinical Efficacy and Safety of Glucosamine, Hyaluronic acid, Collagen Peptides, boswellia serata in the management Osteoarthritis

Literature Review

Jean-Yves Reginster, et al., (2012): Over the last 20 years, several studies have investigated the ability of glucosamine sulfate to improve the symptoms (pain and function) and to delay the structural progression of osteoarthritis. There is now a large, convergent body of evidence that glucosamine sulfate, given at a daily oral dose of 1,500 mg, is able to significantly reduce the symptoms of osteoarthritis in the lower limbs. This dose of glucosamine sulfate has also been shown, in two independent studies, to prevent the joint space narrowing

observed at the femorotibial compartment in patients with mild-to-moderate knee osteoarthritis. This effect also translated into a 50 % reduction in the incidence of osteoarthritis-related surgery of the lower limbs during a 5-year period following the withdrawal of the treatment. Some discrepancies have been described between the results of studies performed with a patent-protected formulation of glucosamine sulfate distributed as a drug and those having used glucosamine preparations purchased from global suppliers, packaged, and sold over-the-counter as nutritional supplements.

Zhu X, et al., (2018): To assess the symptomatic effectiveness and safety of oral symptomatic slow-acting drugs (SYSADOAs) on the treatment of knee and/or hip osteoarthritis, such as chondroitin, glucosamine, and combination treatment with chondroitin plus glucosamine. We searched electronic database including PubMed, Embase, Cochrane Library, and the reference lists of relevant articles published from inception to May 22, 2018. An updated meta-analysis was performed to assess the effectiveness of these slow-acting drugs for osteoarthritis. Twenty-six articles describing 30 trials met our inclusion criteria and were included in the meta-analysis. The estimates between chondroitin and placebo showed that chondroitin could alleviate pain symptoms and improve function. Compared with placebo, glucosamine proved significant effect only on stiffness improvement. However, the combination therapy did not have enough evidence to be superior to placebo. Additionally, there was no significant difference in the incidence of AEs and discontinuations of AEs when compared with placebo. Given the effectiveness of these symptomatic slow-acting drugs, oral chondroitin is more effective than placebo on relieving pain and improving physical function. Glucosamine showed effect on stiffness outcome. Regarding on the limited number of combination therapy, further studies need to investigate the accurate effectiveness. This information accompanied with the tolerability and economic costs of included treatments would be conducive to making decisions for clinicians.

Juan Salazar, et al., (2014): Osteoarthritis is a chronic degenerative disorder that currently represents one of the main causes of disability within the elderly population and an important presenting complaint overall. The pathophysiologic basis of osteoarthritis entails a complex group of interactions among biochemical and mechanical factors that have been better characterized in light of a recent spike in research on the subject. This has led to an ongoing search for ideal therapeutic management schemes for these patients, where glucosamine is one of the most frequently used alternatives worldwide due to their chondroprotective properties and their long-term effects. Its use in the treatment of osteoarthritis is well established; yet despite being considered effective by many research groups, controversy surrounds their true effectiveness. This situation stems from several methodological aspects which hinder appropriate data analysis and comparison in this context, particularly regarding objectives and target variables. Similar difficulties surround the assessment of the potential ability of glucosamine formulations to alter glucose metabolism. Nevertheless, evidence supporting diabetogenesis by glucosamine remains scarce in humans, and to date, this association should be considered only a theoretical possibility.

S. Brien., et al, (2008): Conventional treatment of osteoarthritis (OA) with non-steroidal anti-inflammatory drugs is associated with serious gastrointestinal side effects and in view of the recent withdrawal of some cyclo-oxygenase-2 inhibitors, identifying safer alternative treatment options is needed. The objective of this

systematic review is to evaluate the existing evidence from randomised controlled trials of two chemically related nutritional supplements, dimethyl sulfoxide (DMSO) and methylsulfonylmethane (MSM) in the treatment of OA to determine their efficacy and safety profile. Methods: The electronic databases [Cochrane Library, Medline, Embase, Amed, Cinahl and NeLH (1950 to November 2007)] were searched. The search strategy combined terms: osteoarthritis, degenerative joint disorder, dimethyl sulfoxide, DMSO, methylsulfonylmethane, MSM, clinical trial; double-blind, single blind, RCT, placebo, randomized, comparative study, evaluation study, control. Inclusion and exclusion criteria were applied. Data were extracted and quality was assessed using the JADAD scale. Results: Six studies were included [evaluating a total of 681 patients with OA of the knee for DMSO (N ¼ 297 on active treatment); 168 patients for MSM (N ¼ 52 on active treatment)]. Two of the four DMSO trials, and both MSM trials reported significant improvement in pain outcomes in the treatment group compared to comparator treatments, however, methodological issues and concerns over optimal dosage and treatment period, were highlighted. Conclusion: No definitive conclusion can currently be drawn for either supplement.

Sudha Vidyasagar., et al, (2004): Osteoarthritis is progressive degenerative disease resulting in significant affection of joints. Nonsteroidal anti-inflammatory drugs (NSAIDS) are widely used in this condition but are associated with significant side effects; hence the aim of this study was to evaluate the efficacy and tolerability of nutritional supplements such as Glucosamine, Chondroitin sulphate and methyl sulfonyl methane in osteoarthritis as an alternative approach for this condition. Patients & Methods. Thirty-seven patients from medicine and orthopedic out patient departments were assessed for severity of osteoarthritis based on visual analog scale, Lequesnes index, goniometry, and radiography and enrolled into the open label study. All patients received cartivit (Glucosamine, Chondroitin sulphate and MSM) two tablets thrice a day for twelve weeks and were reassessed for changes in above parameters every four weeks.

The tolerability was also assessed during the monthly visits. Results. Out of 32 patients who completed study, there was significant improvement in pain and Lequesnes index at four, eight and twelve weeks ($p < 0.05$). There was gradual improvement in joint mobility over twelve weeks. There was no improvement in radiological changes in twelve weeks study period. Patients tolerated the study medication well and there was no abnormality observed in the various biochemical markers during the study. Conclusions. Glucosamine, chondroitin sulphate and methyl sulfonyl methane combination was useful in decreasing pain, improving functional ability and improving joint mobility and was well tolerated in patients with osteoarthritis.

Suresh Kumar, et al, (2014): Recent studies show that enzymatically hydrolysed collagen, the collagen peptide, is absorbed and distributed to joint tissues and has analgesic and anti-inflammatory properties. A double-blind, placebo-controlled, randomised trial with collagen peptides isolated from pork skin (PCP) and bovine bone (BCP) sources was carried out to study the effectiveness of orally supplemented collagen peptide to control the progression of osteoarthritis in patients diagnosed with knee osteoarthritis.

Improvement in treatment was assessed with reduction in Western Ontario McMaster Universities (WOMAC), visual analogue scale (VAS) and quality of life (QOL) scores from baseline to 13 weeks (Visit 7). Safety and tolerability were also evaluated. There was significant reduction from baseline to Visit 7 in the primary end points

of WOMAC and VAS scores and in the secondary end point of QOL score in subjects with PCP and BCP groups, while in subjects with placebo group the end point indices remained unaltered. Furthermore, all the score levels of WOMAC, VAS and QOL decreased significantly ($P < 0.01$) in the study group compared to placebo group in Visit 7. The study demonstrated that collagen peptides are potential therapeutic agents as nutritional supplements for the management of osteoarthritis and maintenance of joint health.

Kimberly Perkins, et al, (2017): The objective of this review is to identify, summarize, and evaluate clinical trials to determine the efficacy of curcuma in the treatment of osteoarthritis. A literature search for interventional studies assessing efficacy of curcuma was performed, resulting in 8 clinical trials. Studies have investigated the effect of curcuma on pain, stiffness, and functionality in patients with knee osteoarthritis. Curcuma-containing products consistently demonstrated statistically significant improvement in osteoarthritis-related endpoints compared with placebo, with one exception.

When compared with active control, curcuma-containing products were similar to nonsteroidal anti-inflammatory drugs, and potentially to glucosamine. While statistical significant differences in outcomes were reported in a majority of studies, the small magnitude of effect and presence of major study limitations hinder application of these results. Further rigorous studies are needed prior to recommending curcuma as an effective alternative therapy for knee osteoarthritis.

Drug Profile

Glucosamine Sulphate

Glucosamine sulfate is a naturally occurring chemical found in the human body. It is in the fluid around joints. Glucosamine also exists in other places in nature. For example, glucosamine sulfate used in dietary supplements is often obtained from the shells of shellfish. Glucosamine sulfate used in dietary supplements does not always come from natural sources. It can also be made in a laboratory. Glucosamine is commonly used as a treatment for osteoarthritis, although its acceptance as a medical therapy varies. It is an amino sugar and precursor of glycosylated proteins and lipids. Since glucosamine is a precursor for glycosaminoglycans, and glycosaminoglycans are a major component of joint cartilage, supplemental glucosamine may help to rebuild cartilage and treat arthritis.

Structure

Weight: 456.42

Chemical Formula: $C_{12}H_{28}N_2O_{14}S$

Side Effects

Side effects of taking glucosamine are reported to be mild and infrequent, but they can include:

- ✎ Stomach upsets
- ✎ Constipation
- ✎ Diarrhea
- ✎ Headaches
- ✎ Rashes

Pharmacodynamics

Osteoarthritis is characterized by the progressive degeneration of cartilage glycosaminoglycans. The formation of glucosamine is the rate limiting step in glycosaminoglycans synthesis thus the addition is glucosamine, would in theory provide a building block towards the synthesis of glycosaminoglycans and thus slow down the progression of osteoarthritis. Thus far however, the results have not been conclusive

How Does it Work?

Glucosamine sulfate is a chemical found in the human body. It is used by the body to produce a variety of other chemicals that are involved in building tendons, ligaments, cartilage, and the thick fluid that surrounds joints. Joints are cushioned by the fluid and cartilage that surround them. In some people with osteoarthritis, the cartilage breaks down and becomes thin. This results in more joint friction, pain, and stiffness.

Mechanism of Action

Glucosamine is a precursor of glycosylated proteins and lipids. Oral glucosamine is commonly used for the treatment of osteoarthritis. Since glucosamine is a precursor for glycosaminoglycans, and glycosaminoglycans are a major component of joint cartilage, supplemental glucosamine may help to rebuild cartilage and treat arthritis. Its use as a therapy for osteoarthritis appears safe, but there is conflicting evidence as to its effectiveness with more recent studies showing limited to no clinical benefit of use.

Glucosamine is not FDA approved for use in humans. Since glucosamine is classified as a dietary supplement, safety and formulation are solely the responsibility of the manufacturer; evidence of safety and efficacy is not required as long as it is not advertised as a treatment for a medical condition.

Pharmacokinetics

Absorption

When taken orally, glucosamine sulfate is absorbed readily into the system and can be traced to cartilage as soon as four hours after consumption. Additionally, in some laboratory tests, the glucosamine supplement demonstrated a protective effect on the cartilage as well.

Half Life: Glucosamine elimination half-life was only tentatively estimated to average 15 h.

Metabolism

A significant fraction of orally administered glucosamine undergoes first-pass metabolism in the liver. Blood levels achieved after oral glucosamine are only 20% those achieved with intravenous glucosamine.

Elimination

In humans, 90% of orally administered glucosamine is absorbed from the small intestine. After metabolism in liver, the metabolites of glucosamine are excreted mainly in urine along with the unchanged glucosamine, with a small amount eliminated in the faeces.

Methylsulfonylmethane (MSM)

Methylsulfonylmethane (MSM) is an organosulfur compound. It is also known by several other names including methyl sulfone and dimethyl sulfone (DMSO₂).

Use

MSM is commonly used for osteoarthritis, but may also benefit in alleviating GI upset, musculoskeletal pain, and allergies, boosting the immune system, and fighting microbial infections. MSM is widely used in the alternative medicine field and by people looking for a natural way to relieve joint pain, reduce inflammation and boost immunity.

Mechanism of Action

It also inhibits the breakdown of cartilage, a flexible tissue that protects the ends of your bones in joints. MSM improved symptoms of pain and physical function during the short intervention without major adverse events. The benefits and safety of MSM in managing OA. The data from the more rigorous MSM trials provide positive evidence in the treatment of mild to moderate OA of the knee.

Chondroitin Sulfate Sodium

Chondroitin sulfate is a chemical that is normally found in cartilage around joints in the body. Chondroitin sulfate is usually manufactured from animal sources, such as shark and cow cartilage. Chondroitin sulfate is used for osteoarthritis and cataracts.

Chondroitin sulfate is a glycosaminoglycan considered as a symptomatic slow-acting drug for osteoarthritis. It is suggested a pain relief and increased joint.

Use

Chondroitin is used in dietary supplements as an alternative medicine to treat osteoarthritis and also approved and regulated as a symptomatic slow-acting drug for this disease (SYSADOA). It is commonly sold together with glucosamine.

Chondroitin, along with commonly used glucosamine, should not be used to treat people who have symptomatic osteoarthritis of the knee as evidence shows that these treatments fail to provide relief for that condition.

Mechanism of Action

The anti-inflammatory effect of chondroitin sulfate is thought to be caused by the inhibition of the synthesis of inflammatory intermediates such as the inhibition of nitric oxide synthase, COX-2, microsomal prostaglandin synthase 1 and prostaglandin E2.

Chondroitin sulfate (CS) is recommended as a therapeutic intervention in the multimodal approach of osteoarthritis (OA) management. CS has been studied extensively to describe its pharmacology (pharmacokinetic, in vitro and in vivo effects) and its clinical efficacy. Clinical evidence is in favour of a slow-acting effect on symptoms in moderate knee OA

Collagen Peptide

Collagen Peptides is the hydrolyzed form of Collagen. After hydrolysis, the product loses its gelling ability and makes it soluble in cold water. Collagen Peptides is also known as 'Collagen hydrolysate'. Collagen peptides are a versatile source of protein and an important element of healthy nutrition. Their nutritional and physiological properties promote the health of bones and joints, and contribute to beautiful skin.

The study clearly demonstrates are effective supplements for the improvement in overall physical problems associated with OA and thereby help to improve the quality of life. It is hypothesised that the supplementation of collagen peptide regulates chondrocyte differentiation and stimulates synthesis of proteoglycans, resulting in the initiation of repair processes in cartilage tissue.

Hyaluronic Acid

Description

Hyaluronic acid (HA) is an anionic, nonsulfated glycosaminoglycan distributed widely throughout connective, epithelial, and neural tissues. It is unique among glycosaminoglycans in that it is nonsulfated, forms in the plasma membrane instead of the Golgi, and can be very large, with its molecular weight often reaching the millions. One of the chief components of the extracellular matrix, hyaluronic acid contributes significantly to cell proliferation and migration, and may also be involved in the progression of some malignant tumors.

Mechanism of Action

Hyaluronic acid works by acting as a cushion and lubricant in the joints and other tissues. In addition, it might affect the way the body responds to injury. Hyaluronic acid is a polysaccharide which is distributed widely in the extracellular matrix of connective tissue in man.

It forms a viscoelastic solution in water which makes it suitable for aqueous and vitreous humor in ophthalmic surgery. It is suggested to provide mechanical protection for ocular tissues and cell layers due to its high viscosity.

Uses

Hyaluronic acid is well known for its skin benefits, especially alleviating dry skin, reducing the appearance of fine lines and wrinkles and speeding up wound healing. It can also help relieve joint pain in people with osteoarthritis.

Hyaluronic acid is a potential bright spot for helping lower the side effects. Its effectiveness is due to the many methods of actions it deploys, including lubrication, anti-inflammatory and chondroprotective effects.

Curcuminoid

These compounds are natural phenols and produce a pronounced yellow color. . They have poor solubility in water at acidic and physiological pH, and also hydrolyze rapidly in alkaline solutions. Therefore, curcumin derivatives are synthesized to increase their solubility and hence bioavailability.

MOA

Curcumin blocks the formation of reactive-oxygen species, possesses anti-inflammatory properties as a result of inhibition of cyclooxygenases (COX) and other enzymes involved in inflammation; and disrupts cell signal transduction by various mechanisms including inhibition of protein kinase C.

Uses

Use of curcumin as a folk remedy continues today. As part of the ancient Indian medical system, Ayurveda, a poultice of turmeric paste is used to treat common eye infections, and to dress wounds, treat bites, burns, acne and various skin diseases.

Turmeric and especially its most active compound curcumin have many scientifically-proven health benefits, such as the potential to prevent heart disease, Alzheimer's and cancer. It's a potent anti-inflammatory and antioxidant and may also help improve symptoms of depression and arthritis.

Vitamin C

A six carbon compound related to glucose. It is found naturally in citrus fruits and many vegetables. Ascorbic acid is an essential nutrient in human diets, and necessary to maintain connective tissue and bone.

Its biologically active form, vitamin C, functions as a reducing agent and coenzyme in several metabolic pathways. Vitamin C is considered an antioxidant.

Mechanism of Action

In humans, an exogenous source of ascorbic acid is required for collagen formation and tissue repair by acting as a cofactor in the posttranslational formation of 4-hydroxyproline in -Xaa-Pro-Gly- sequences in collagens and other proteins. Ascorbic acid is reversibly oxidized to dehydroascorbic acid in the body. These two forms of the vitamin are believed to be important in oxidation-reduction reactions.

The vitamin is involved in tyrosine metabolism, conversion of folic acid to folinic acid, carbohydrate metabolism, synthesis of lipids and proteins, iron metabolism, resistance to infections, and cellular respiration.

Vitamin C also protects an important protein in your bones and joints. vitamin C deficit can negatively influence collagen production and inflammation control, as well as oxidative reactions, while its carefully construed administration is found to yield multiple potential pain-reducing benefits.

Vitamin C reduces the oxidative stress and inflammatory response of muscles in the context of postoperative care.

Boswellia Serata

Boswellia serrata is a plant that produces Indian frankincense. It is also known as Indian oli-banum, Salai guggul, and Sallaki in Sanskrit.

Uses

Boswellia, also known as Indian frankincense, is an herbal extract taken from the *Boswellia serrata* tree. Resin made from *boswellia* extract has been used for centuries in Asian and African folk medicine. It's believed to treat chronic inflammatory illnesses as well as a number of other health conditions.

This study provides important information about the efficacy and safety of in the treatment of OA, which may be useful in promoting as a promising alternative therapeutic strategy that may be used as a nutritional supplement against OA.

Piperin

It is an alkaloid isolated from the plant *Piper nigrum*. It has a role as a NF-kappaB inhibitor, a plant metabolite, a food component and a human blood serum metabolite. It is a member of benzodioxoles, a N-acylpiperidine, a piperidine alkaloid and a tertiary carboxamide.

It derives from an (E,E)-piperic acid. Aside from its use as a magnifier for other dietary supplements, piperine can also benefit the body on its own, and also it increases the bioavailability of nutritional supplements.

Mechanism of Action

Piperine has long been known as an anti-inflammatory agent. It also works as a pain reliever by blocking the expression of a gene that causes arthritis pain. It reduces the amount of pain the body feels, making things like arthritis and other injuries easier to withstand. Piperazine blocks the response of the worm muscle to acetylcholine, presumably by causing hyperpolarization of nerve endings, resulting in flaccid paralysis of the worm.

Uses

Piperine is a major alkaloid found in black pepper (*piper nigrum*), and the alkaloid is used as an herbal product for its purported anti-inflammatory, antioxidant, and antitumor properties. Curcumin, a demonstrates potential as a treatment agent for osteoarthritis, a disease with an underlying inflammatory cause. Its efficacy in reducing pain, physical function, and quality of life among osteoarthritic patients has been demonstrated in many clinical trials. The effects of curcumin on osteoarthritis can be attributed to its ability to prevent apoptosis of chondrocytes due to inflammation predominantly, and oxidative stress to a lesser extent.

Materials and Methods

Studies were included if they met the following criteria, studies about primary hip and or knee OA patients with clinical and or radiologic diagnosis, studies covering at least two of the following oral treatments, glucosamine, chondroitin, or the two in combination against placebo, extractable data reporting the pain, function, stiffness, and the adverse events (AEs) of patients. The exclusion criteria were as follows, treatment methods described

unclearly, studies of non-randomized or uncontrolled trials, interventions combined with non-steroidal anti-inflammatory drugs, studies or data reported repeatedly, and trial arms with sub-therapeutic doses. For each study, patients' characteristics including mean age, sex, mean duration of symptom, BMI, duration of follow-up, type of outcome (pain, function, stiffness, and AEs), trial design, trial size, details of intervention, treatment duration, and results were individually extracted. Data of intention-to-treat analysis was employed whenever possible. The primary outcomes of this were pain intensity, function improvement. The standard mean difference (SMD) was used to calculate. Data Sources were MEDLINE, EMBASE, Cochrane, Web of Science, Scopus databases were all searched.

A total of 68 patients were entered into the study. Patients suffering from osteoarthritis were eligible for the study. A prospectively designed study protocol defined the objectives of the study. A full medical history was taken, general examination performed and informed consent obtained before admission to the study. Patients were reviewed and blood pressure measured. Studies were screened by research analysts to exclude animal studies, non-qualifying languages, and nonrandomized clinical trials. Patients were eligible if they satisfied the following criteria: age ≥ 25 years, osteoarthritis,

Statistical Analysis

Variable	Number	Percentage
Sex		
Male	9	13.2%
Female	4	5.8%
BMI	7	10.2%
SBP(mmHg)	8	11.7%
DBP(mmHg)	5	7.3%
H/oHypertension	9	13.2%
Alcohol/Drug abuse	6	8.8%
Smoking	8	11.7%
Physical activity	5	7.3%
Hypertension	7	10.2%

Table 1: Demographic Characteristic

Continuous variables are expressed as the mean $\pm$ s.d. Frequency tables were generated for categorical or qualitative variables and data are presented as the n (%). Paired t-tests, and $P < 0.05$ was considered statistically significant. Chi square test for categorical variables. Frequency tables were generated for categorical or qualitative variables and data are presented as the n (%).

Results

Table 1

Out of 68 patients with osteoarthritis diagnosis admitted to emergency department in our center, age range was from 21 to 75 years. About 45% of patients were female, and 55% were male. Severe Joint stiffness and

Tenderness were the most prevalent manifestations that were present in patients. Table 1 shows male and female patient enrolled for the study, see example as below.

Graph 1: Demographic Characteristic

Table 2

Table 2: Clinical parameter of osteoarthritis patients

Variables	No. Patients
Joint pain	12
Lower back pain	10
Neck pain	9
Tenderness	7
Loss of flexibility	6
Bone spurs	8
Swelling	5
Inflammation	7
Crackles	4

Graph 2: Clinical parameter

Discussions

Osteoarthritis is a chronic degenerative disorder that currently represents one of the main causes of disability within the elderly population and an important presenting complaint overall. The pathophysiologic basis of osteoarthritis entails a complex group of interactions among biochemical and mechanical factors that have been

better characterized in light of a recent spike in research on the subject. Glucosamine showed effect on stiffness outcome. Regarding on the limited number of combination therapy, further studies need to investigate the accurate effectiveness. This information accompanied with the tolerability and economic costs of included treatments would be conducive to making decisions for clinicians. Osteoarthritis is a leading cause of disability and source of societal cost in older adults. With an ageing and increasingly obese population, this syndrome is becoming even more prevalent than in previous decades. In recent years, we have gained important insights into the cause and pathogenesis of pain in osteoarthritis. The diagnosis of osteoarthritis is clinically based despite the widespread overuse of imaging methods. Management should be tailored to the presenting individual and focus on core treatments, including self-management and education, exercise, and weight loss as relevant. Surgery should be reserved for those that have not responded appropriately to less invasive methods. Prevention and disease modification are areas being targeted by various research endeavours, which have indicated great potential thus far. This narrative Seminar provides an update on the pathogenesis, diagnosis, management, and future research on osteoarthritis for a clinical audience. The study demonstrated that collagen peptides are potential therapeutic agents as nutritional supplements for the management of osteoarthritis and maintenance of joint health. evaluate clinical trials to determine the efficacy of curcuma in the treatment of osteoarthritis.

A literature search for interventional studies assessing efficacy of curcuma was performed, resulting in 8 clinical trials. Studies have investigated the effect of curcuma on pain, stiffness, and functionality in patients with knee osteoarthritis. Curcuma-containing products consistently demonstrated statistically significant improvement in osteoarthritis-related endpoints compared with placebo, with one exception. In accordance with our results, GS has shown positive effects on symptomatic and structural outcomes of knee OA. Glucosamine showed effect on stiffness outcome relieving pain and improving physical function. In the aspect of safety, glucosamine sulphate are well tolerated. This information accompanied with the tolerability and economic costs of included treatments would be conducive to making decisions for clinicians. MSM (3 g twice a day) improved symptoms of pain and physical function during the short intervention without major adverse events. The benefits and safety of MSM in managing OA.

The data from the more rigorous MSM trials provide positive evidence in the treatment of mild to moderate OA of the knee. Hyaluronic acid is a potential bright spot for helping lower the side effects. Its effectiveness is due to the many methods of actions it deploys, including lubrication, anti-inflammatory and chondroprotective effects. curcuma formulations for treatment of osteoporosis have found similar efficacy compared to NSAIDs, and potentially to glucosamine; however, they also contain significant limitations that call into question validity of the results While statistical significant differences in outcomes were reported in a majority of studies, the small magnitude of effect and presence of major study limitations hinder application of these results. Vitamin C might protect against the development of osteoarthritis, rheumatoid arthritis, and inflammatory polyarthritis, according to some studies. A powerful antioxidant, it fights molecules that trigger inflammation. Vitamin C also protects an important protein in your bones and joints. vitamin C deficit can negatively influence collagen production and inflammation control, as well as oxidative reactions, while its carefully construed administration is found to yield multiple potential pain-reducing benefits.

CONCLUSION

In conclusion, in accordance with our results, GS has shown positive effects on symptomatic and structural outcomes of knee OA. Glucosamine showed effect on stiffness outcome relieving pain and improving physical function. MSM improved symptoms of pain and physical function during the short intervention without major adverse events. The benefits and safety of MSM in managing OA. Chondroitin sulfate (CS) is recommended as a therapeutic intervention in the multimodal approach of osteoarthritis (OA) management. CS has been studied extensively to describe its pharmacology (pharmacokinetic, in vitro and in vivo effects) and its clinical efficacy. Hyaluronic acid is a potential bright spot for helping lower the side effects. Its effectiveness is due to the many methods of actions it deploys, including lubrication, anti-inflammatory and chondroprotective effects. curcuma formulations for treatment of osteoporosis have found similar efficacy compared to NSAIDs, and potentially to glucosamine. Vitamin C might protect against the development of osteoarthritis, rheumatoid arthritis, and inflammatory polyarthritis, according to some studies. A powerful antioxidant, it fights molecules that trigger inflammation. Vitamin C also protects an important protein in your bones and joints. Boswellia serata reduces pain and improves physical functioning significantly in OA patients; and it is safe for human consumption. It may exert its beneficial effects by controlling inflammatory responses and it may improve joint health by reducing the enzymatic degradation of cartilage in OA patients.

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