CASE STUDY: **Effects of Proteolytic Enzymes on Degenerative Joint Disease of the Knee**

ABSTRACT

Plant extracts with a high content of proteolytic enzymes have been used for a long time in traditional medicine. One of the many enzymes with beneficial and medicinal properties is bromelain. Bromelain is a complex combination of multiple endopeptidases of thiol and other compounds derived from the pineapple fruit, stem and/or root. Fruit bromelain and stem bromelain are produced completely distinctly and comprise unique compounds of enzymes. Due to the efficacy of oral administration in the body, as a safe phytotherapeutic medication, bromelain was commonly suited for patients due to lack of compromise in its peptidase efficacy and the absence of undesired side effects. Various in vivo and in vitro studies have shown that they are anti-edematous, anti-inflammatory, anti-cancerous, anti-thrombotic, fibrinolytic, and facilitate the death of apoptotic cells. The pharmacological properties of bromelain are, in part, related to its arachidonate cascade modulation, inhibition of platelet aggregation, interference with malignant cell growth, anti-inflammatory action, fibrinolytic activity, skin debridement properties, and reduction of the severe effects of SARS-Cov-2. Due to these pharmacological properties bromelain has been used as an adjunct in conditions such as degenerative joint disease and osteoarthritis. Knee Osteoarthritis (OA), also known as degenerative joint disease, is typically the result of wear and tear and progressive loss of articular cartilage. It is most common in elderly people and can be divided into two types: primary and secondary. Primary osteoarthritis is articular degeneration without any apparent underlying cause. Secondary osteoarthritis is the consequence of either an abnormal concentration of force across the joint as with post-traumatic causes or abnormal articular cartilage, such as rheumatoid arthritis. Osteoarthritis is a painful, chronic joint disorder that primarily affects the knees, hands, hips, and spine. The intensity of the symptoms varies for each individual and usually progress slowly. Taking into consideration the evidence in the scientific literature regarding proteolytic enzymes such as bromelain and their anti-inflammatory properties we put them to clinical practice on a patient with osteoarthritis of the knee.

INTRODUCTION

The knee is the largest synovial joint in humans. It is composed by osseous structures (distal femur, proximal tibia, and patella), cartilage (meniscus and hyaline cartilage), ligaments, and a synovial membrane. The latter oversees the production of the synovial fluid, which provides lubrication and nutrients to the avascular cartilage. Unfortunately, given the high use and stress of this joint, it is a frequent site for painful conditions including OA. It was believed that OA was exclusively a degenerative disease of the cartilage; however, latest

evidence has proven that OA is a multifactorial entity, involving multiple causative factors like trauma, mechanical forces, inflammation, biochemical reactions, and metabolic derangements. It is also known that the cartilaginous tissue is not the only one involved. Given its lack of vasculature and innervation, the cartilage by itself is not capable of producing inflammation or pain at least on early stages of the disease. Hence, the source of pain is mainly derived from changes to the non-cartilaginous components of the joint like the joint capsule, synovium, subchondral bone, ligaments, and peri-articular muscles. As the disease advances, these structures are affected and changes including bone remodeling, osteophyte formation, weakening of periarticular muscles, laxity of ligaments, and synovial effusion can become evident. In OA, the synovial fluid has been found to contain multiple inflammatory mediators including plasma proteins (C-reactive protein, proposed as a marker for development and progression of OA), prostaglandins (PGE2), leukotrienes (LKB4), cytokines (TNF, IL1β, IL6, IL15, IL17, IL18, IL21), growth factors (TGFβ, FGFs, VEGF, NGF), nitric oxide, and complement components. Locally, all these components can induce matrix metalloproteinases and other hydrolytic enzymes (including cyclooxygenase 2 and prostaglandin E) resulting in cartilage breakdown secondary to proteoglycan and collagen destruction. As allopathic medicine is unable to halt this progression, conventional medical treatment is aimed at decreasing pain and improving function using NSAIDS, other analgesics, steroidal joint injections and, as a last resort, joint replacement. Because the high incidence of adverse events, especially gastrointestinal, associated with both non-selective and COX-2-selective NSAID use is high, effective but safer alternative treatments would be of benefit to osteoarthritis sufferers.

Transformation Enzyme Corporation has utilized various blends of mycelial and plant derived proteolytic enzymes for natural anti-inflammatory support for over 30 years. One of the many enzymes with beneficial and medicinal properties is bromelain. Due to the efficacy of oral administration in the body, as a safe phytotherapeutic medication bromelain was commonly suited for patients due to lack of compromise in its peptidase efficacy and the absence of undesired side effects. Various in vivo and in vitro studies have shown that they are anti-edematous, anti-inflammatory, anti-cancerous, anti-thrombotic, fibrinolytic, and facilitate the death of apoptotic cells. The pharmacological properties of bromelain are, in part, related to its arachidonate cascade modulation, inhibition of platelet aggregation, interference with malignant cell growth, anti-inflammatory action, fibrinolytic activity, skin debridement properties, and reduction of the severe effects of SARS-Cov-2. Due to these pharmacological properties bromelain has been used as an adjunct in Transformation's clinical protocols for conditions such as degenerative joint disease and osteoarthritis. While we are well aware of the power of protease, one of the challenges when it comes to therapeutic dosing is tolerance.

Until now, we have primarily used the product in capsule form with dosing varying from 6 capsules a day up to 20 depending on need, the severity of the disease, and tolerance. However, we believe dosing at this amount is merely scratching the surface when it comes to effectively reducing inflammation and supporting homeostasis. As the goal of taking 60 capsules a day is unrealistic and has low compliance, we wanted to observe how much protease could be tolerated using a powder blend to “mega dose.” A powder is ideal for those with advanced disease states since it allows a better opportunity to use efficacious doses. Unlike capsules, a powder blend does not have a minimum or maximum space capacity which would allow us to therapeutically dose without having issues with compliance.

The purpose of this case study was to determine if Transformation's Professional Protocol™ Protease powder blend could be tolerated and work as a more natural and safe alternative to traditional treatments for pain, inflammation, and slowing down the degenerative components of OA. The subject of the current case study was placed on the protease powder for 6 months to evaluate the effectiveness of protease supplementation on a male participant who trains CrossFit® 4 to 5 times a week and has been diagnosed with degenerative joint disease of the right knee since 2017.

CASE STUDY

In this present case study, we have a 49-year-old male patient with severe osteoarthritis of the right knee who is a dedicated CrossFit® athlete and trains up to 5 times a week using heavy weight on all gym movements ranging from 100 to 300 lbs to include squatting, cleaning, snatching, overhead lifting, etc. The patient walks with a limp and has limited ROM in all planes. He had been dealing with right knee pain for over 8 years and underwent knee arthroscopy in 2016.

5/2021 through 6/2021: The patient received four Orthovisc® 30mg/2mL injections which contained Hyaluronan. This innovative knee injection is made from Hyaluronan, a natural and non-animal substance found in high amounts in joint tissues and the fluid that fills the joints that acts as a lubricant and shock absorber in the joint, helping it function correctly. This treatment reduces bone friction and alleviates pain and stiffness in knee osteoarthritis. Injecting Orthovisc® into the knee joint enhances joint function by restoring synovial fluid's natural shock absorbing properties and improving mobility.

5/2023: The patient returned to his orthopedic doctor with pain and tenderness of the lateral patellar facet, the lateral joint line, and the medial joint line with flexion at 135 degrees and extension at -5 degrees. He had mild knee effusion, pain at extreme limits of range, positive McMurray's and Apley's comprehension tests, crepitus, and symptoms of locking, pulling, inability to straighten knee, and increased pain with planting/twisting. The patient was given an MRI for suspicion of meniscal tear but showed severe degeneration, multiple osteophyte formation, chondrosis, cartilage thinning and fissuring, subchondral edema, and moderate joint effusion.

> MRI OF RIGHT KNEE, 5/3/2023
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> Findings:
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> Intercondylar notch: The posterior cruciate ligament appears intact. Mucoid degeneration of the ACL. Osteophytes project into the notch and mildly encroach on the cruciate ligaments. Mild degenerative insertional change.
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> Collateral ligaments: The medial and lateral collateral ligaments are intact.
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> Medial compartment: Mild intrasubstance signal fraying in the medial meniscus. No large tear or parameniscal cyst. There are small to moderate osteophytes. The joint space appears mildly narrowed. There is mostly grade 1 to 2 chondrosis in the tibial plateau with cartilage thinning and grade 2 fissuring. There is cartilage thinning and fissuring with mostly grade 2 chondrosis in the weightbearing femoral condyle. A few scattered tiny grade 3 and 4 cartilage fissures are also seen in the weightbearing femoral condyle. A focal area of cartilage delamination is suggested in the posterior non weightbearing femoral condyle measuring roughly 8 by 11mm, seen on series 5, image 19 and image 18 with mild subchondral edema. Focal extension to the articular surface is not seen.
>
> Lateral compartment: Mild intrasubstance degeneration and fraying in the lateral meniscus. No large tear. Small to moderate osteophytes. No significant narrowing of the joint space. Mostly grade 1 chondrosis in the tibial plateau with fraying and shallow fissuring. There is a focal area of grade 4 cartilage fissuring/delamination roughly measuring 4X4mm in the medial weightbearing tibial plateau. Focal grade 3 and 4 cartilage fissuring also in the weightbearing femoral condyle, roughly 4X6mm. Grade 1 to 2 chondrosis suggested elsewhere in the femoral condyle. The iliotibial band, biceps femoris, and popliteus tendons are unremarkable.
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> Patellofemoral compartment: Mild extensor tendinosis. Low grade interstitial tearing. The retinacula appear intact. Mild lateral patellar tilt. No significant subluxation. Tibial tubercle to trochlear groove measurement is approximately normal. No significant patella alta. Small osteophytes. There are multiple grade 2 to 3 cartilage

fissures in the patella and trochlea with irregularity of the articular cartilage. A few tiny grade 4 cartilage fissure also suspected in the trochlea and patella. This is superimposed on background of grade 1 to 2 chondrosis. There is mild scarring in the Hoffa's fat, presumably from prior surgery. Please correlate with prior surgical history. Minimal edema in Hoffa's fat, nonspecific.

Other findings: No acute contusion or fracture. There is mild degenerative subchondral edema. Moderate joint effusion. Mild subcutaneous edema. Tiny Baker's cyst.

Impression:

1. Mild intrasubstance degeneration and fraying in the menisci. No large tear.

2. There is mucoid degeneration of the anterior cruciate ligament. Osteophytes mildly encroach on the cruciate ligaments. No acute sprain.

3. There are degenerative changes/chondromalacia in all 3 compartments with small to moderate osteophytes as detailed above. Focal area of cartilage delamination in the posterior non weightbearing medial femoral condyle without definitive articular surface extension roughly measuring 8X11mm with mild subchondral edema. Small area of grade 3 to 4 chondrosis elsewhere.

4. No acute contusion or fracture. Mild subcutaneous edema. Moderate joint effusion.

5/9/2023: The patient received a cortisone injection with a mixture of 20mg Kenalog® and 2mL 0.25% Sensorcaine®.

5/12/2023 The patient presented with decreased pain and was referred to physical therapy to improve ROM and gait without success so was given another round of Visco-supplementation.

5/2023 through 7/2023: The patient was given three injections with TriVisc® 10mg/mL at 2.5mL and was released with recommendations to take Naproxen 500mg in the morning and at night. Throughout all this knee discomfort the patient never stopped exercising, continued with heavy lifting, and pushed through the pain.

PROTOCOL

Assuring optimal protein digestion and proper blood flow is necessary for effective nutrient delivery, a healthy immune response, and the body's natural detoxification processes. Optimal circulation is dependent upon the presence of effective systemic proteolytic enzymes. Bromelain is a group of soothing plant enzymes which are known to help promote improved protein digestion and healthy elimination as well as overall cardiovascular, muscular, urinary, and immune system health, and Transformation's Professional Protocol™ Protease powder includes over 355,000 HUT units of protease activity from peptidases and bromelain in every 492 mg dose supporting healthy blood circulation, improved lymph circulation, and optimal immune health. The endo/exo peptidases are known to break the inner/terminal bonds of amino acid chains for more efficient hydrolysis of proteins and improved circulation to encourage delivery of oxygen and nutrients to the cell for health and vitality, removal of metabolic wastes from the cell, and transport of immune cells throughout the body to help maintain a healthy internal environment. The highly active systemic enzymes in this formula have a wide range of pH stability (3.0 pH – 10.0 pH) which is essential for maximum benefit.

The patient started with 5 grams three times a day of Transformation's Professional Protocol™ Protease powder for 5 days and then pushed up to 10 grams three times a day for approximately 6 months. Our objectives were to improve inflammation, edema, and pain as well as halt/slow the knee joint degeneration. We did not expect to reverse the OA findings due to the fact that there was a great deal of degeneration in the

cartilage, synovium, and many osteophytes present. The patient also did not want to stop his CrossFit® routine and continued heavy weightbearing exercises throughout the study which is not beneficial for his clinical status.

8/17/2023: The patient started the protocol and was at ROM flexion 130 degrees and extension 15 degrees with pain (normal 135 degrees flexion to 0 degrees extension). The week of the 21st went to his normal bi-weekly Chiro/rehab treatment for preventative maintenance. Upon the doctor starting light stretching he felt a release in the bottom of his knee to where his leg fully extended for a significant amount of time. This had not happened before starting the powder. While he was still not fully extended, he did notice seeing that it was becoming far easy to be extended while stretching and by simply slowing the leg to fully relaxed in a straight leg position with minimal down force.

9/27/2023: Nothing new but continued flexibility when comes to stretching and rehab treatment. According to the patient, knee felt stronger than previous few months before use and did not flare up with issues at all since starting the powder.

10/15/2023: Walked about 26.5 miles over 5 days while on vacation with no issues. This was not possible before starting the protocol. While he still had some discomfort the following mornings, simple stretching relieved the discomfort. Also, regular treatment by rehab doctor was going well where the doctor was able to compress knee down to 0 degrees with very little pain.

11/7/2023: Patient to continue 30 grams a day and add 1 capsule of Transformation's Professional Protocol™ Joint Health twice a day. This Transformation Enzyme Corporation formula is a unique blend of enzymes and NEM® brand eggshell membrane to supply nourishment for joint mobility and support healthy production of cartilage and connective tissues. Each capsule contains 500mg eggshell membrane which has been shown to be nearly five times more clinically effective than glucosamine and chondroitin.

1/26/2024: ROM flexion 139 degrees and extension 19 degrees. This was the end of the study and wanted to get a followup MRI to see any positive changes.

2/9/2024: Patient reports “I hate to say it but coming off the powder, my knee has been more problematic”. We started another 2 rounds of 30 grams a day of the powder and 1 cap of Joint Health twice a day before getting a second MRI on 4/11/2024.

> MRI OF RIGHT KNEE COMPARISON, READ 4/11/2024
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> Comparison is made to a prior right knee MRI performed at Alliance MRI on 5/3/2023.
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> *[Note: The word “stable” is used by the radiologist to point out that the findings have not progressively gotten worse from the previous MRI findings.]*
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> 1. Again, seen is severe mucoid degeneration of the ACL without a tear. There is mildly increased bone marrow edema adjacent to the tibial attachment of the distal ACL. Also again, seen is mild degeneration of the PCL without a tear.
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> 2. Again, seen is slight intrasubstance degeneration in the posterior horn of the medial meniscus. There is no meniscal tear.
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> 3. Fairly stable mild to moderate chondromalacia along the central and posterior weightbearing portions of the medial femoral condyle as well as a small chondral fissure along the posterior weightbearing portion of the medial femoral condyle. There has been interval development of focal subchondral bone marrow edema in the medial aspect of the medial tibial plateau with suspected overlying chondromalacia. There is stable mild to moderate marginal osteophytosis of the medial compartment.

4. Fairly stable overall mild chondromalacia along the lateral femoral condyle and lateral tibial plateau as well as focally moderate chondromalacia along the central to posterior weightbearing portion of the lateral femoral condyle. There is also stable mild to moderate marginal osteophytosis of the lateral compartment.

5. Stable mild to moderate chondromalacia along the patella and trochlear groove. The previously seen mild subchondral bone marrow edema in the lateral trochlear groove has resolved. There is also stable mild marginal osteophytosis of the patellofemoral compartment.

6. Stable minor patellar tendinosis without a tear.

7. Mildly decreased now moderate joint effusion. There may be some loose chondral bodies located posterior to the posterior lateral femoral condyle on axial PD FS.

DISCUSSION

Bromelain is considered to be a high-value enzyme in the therapeutics field as it is an effective treatment for inflammation and osteoarthritis. As a natural and nontoxic compound, bromelain can be used as an alternative to multiple chemical ingredients and artificially manufactured medicines. Bromelain in pineapple is a type of enzyme known as a protease, which breaks other proteins apart by cutting the chains of amino acids. Bromelain selectively prevents proinflammatory prostaglandins' biosynthesis obviously via indirect intervention. The sensitivity of the pineapple protease has been shown to be similar to the endogenous protease plasmin. Their anti-inflammatory properties include transcription factors being inhibited and proinflammatory mediators subsequently decreased. Bromelain also prevents cyclooxygenase and modulates prostaglandins, thromboxane, inflammation, coagulation, and bradykinin hydrolysis. These beneficial health properties of bromelain are what we consider to be the key in supporting conditions such as OA since in OA the synovial fluid has been found to contain multiple inflammatory mediators including plasma proteins (C-reactive protein, proposed as a marker for development and progression of OA), prostaglandins (PGE2), leukotrienes (LKB4), cytokines (TNF, IL1β, IL6, IL15, IL17, IL18, IL21), growth factors (TGFβ, FGFs, VEGF, NGF), nitric oxide, and complement components. Locally, all these components can induce matrix metalloproteinases and other hydrolytic enzymes (including cyclooxygenase 2 and prostaglandin E) resulting in cartilage breakdown secondary to proteoglycan and collagen destruction.

CONCLUSION

Here we have a 49-year-old male patient with severe OA of the right knee who is a dedicated CrossFit ® athlete and trains up to 5 times a week using heavy weight on all gym movements ranging from 100 to 300lbs to include squatting, cleaning, snatching, and overhead lifting among other high intensity movements. The patient was given adjunct support with 30 grams of Transformation's Professional Protocol™ Protease powder blend and 2 capsules of Transformation's Professional Protocol™ Joint Health product daily along with his chiropractic rehabilitative care in order to improve symptoms of OA. All end points of reducing pain, inflammation, and slowing down the degenerative components of OA were met as the patient reported significant differences while on the protocol in terms of mobility and tolerating heavy exercise with minimal discomfort. The patient's followup MRI also showed improvement in terms of the previously seen mild subchondral bone marrow edema in the lateral trochlear groove which had completely resolved. Even with this patient's intense exercise regimen with heavy weightbearing movements, according to the radiologist the MRI findings remained stable, e.g., the findings have not progressively gotten worse from the previous MRI findings. According to the MRI

comparison there is fairly stable mild to moderate chondromalacia along the central and posterior weightbearing portions of the medial femoral condyle; stable mild to moderate marginal osteophytosis of the medial compartment; fairly stable overall mild chondromalacia along the lateral femoral condyle and lateral tibial plateau; stable mild to moderate marginal osteophytosis of the lateral compartment; stable mild to moderate chondromalacia along the patella and trochlear groove; and stable mild marginal osteophytosis of the patellofemoral compartment and stable minor patellar tendinosis. It is important to understand that while proteolytic enzymes will not reverse OA, they will improve quality of life and reduce inflammation and symptoms enough to be able to perform activities of daily living without the side effects of steroids, pain meds, or NSAIDS.

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APPENDIX

Maintenance Protocol

- Transformation Professional Protocol™ Protease powder: 10 grams 3xday
- Transformation Professional Protocol™ Joint Health: 1 capsule 2xday

Protease vs Rx and OTC

Category	RX/OTC Names	Purpose	Active Ingredient	Inactive Ingredients	Side Effects
Systemic Enzyme Supplement	**Transformation Professional Protocol™ Protease**	**Works synergistically with endogenous protease to support healthy immune function, healthy inflammation response, and healthy circulation**	**355,000 HUT protease 600,000 PU bromelain 1 capsule = 638 mg**	**9.6 mg calcium citrate (0.015% DV)**	**None known**
Systemic Enzyme Supplement	Wobenzyme PS®	For individuals wishing to support healthy joint, immune, and circulatory function	1350 FIP bromelain 300 mg rutin 4320 FIP trypsin (from animal)	microcrystalline cellulose, calcium phosphate, hydroxypropyl cellulose, vegetable stearate, vegetable-based pH resistant enteric coating, silica, natural vanilla flavor and purified water	None known
Steroids, corticosteroid, glucocorticoid	Prednisone® (cortisone, hydrocortisone)	To suppress inflammation and the immune system for treatment of rheumatoid arthritis, lupus, asthma, allergies, etc	Prednisone - 2.5mg, 5mg, 10mg, 20mg, 50mg	lactose monohydrate, magnesium stearate, microcrystalline cellulose, pregelatinized starch and sodium starch glycolate – in addition, the 1 mg, 2.5 mg, and 5 mg tablets also contain stearic acid – Prednisone Oral Solution contains alcohol, citric acid, disodium edetate, fructose, hydrochloric acid, maltol, peppermint oil, polysorbate 80, propylene glycol, saccharin sodium, sodium benzoate, vanilla flavor, and water	elevated pressure in the eyes (glaucoma); fluid retention, causing swelling in lower legs; increased blood pressure; mood swings; weight gain, with fat deposits in abdomen, face, and back of neck; longer term: clouding of the lens in one or both eyes (cataracts); high blood sugar, which can trigger or worsen diabetes; increased risk of infections; thinning bones (osteoporosis) and fractures; suppressed adrenal gland hormone production; thin skin, easy bruising, and slower wound healing
NSAIDS / Aspirin	Pepcid AC®, Zantac®, Naproxen (Aleve®), Celecoxib (Celebrex® "COX-2 inhibitor")	Relieve pain and reduce inflammation and fever	Aspirin (acetylsalicylic acid Ibuprophen) Naproxen - sodium 220 mg	Aspirin: carnauba wax, corn starch, hypromellose, powdered cellulose, triacetin; Ibuprophen: carnauba wax, colloidal silicon dioxide, croscarmellose sodium, hypromellose, lactose, magnesium stearate, microcrystalline cellulose, propylene glycol, titanium dioxide; Naproxen: FD&C Blue #2, croscarmellose sodium, macrogol, magnesium stearate, polyvinyl alcohol, povidone, pregelatinized starch, talc, titanium dioxide; Celebrex: croscarmellose sodium, edible inks, gelatin, lactose monohydrate, magnesium stearate, povidone, sodium lauryl sulfate	stomach problems like bleeding, ulcer and stomach upset; high blood pressure; fluid retention (causing swelling, such as around the lower legs, feet, ankles and hands); kidney problems; heart problems; black, bloody, or tarry stools; coughing up blood or vomit that looks like coffee grounds; severe nausea, vomiting, or stomach pain; fever lasting longer than 3 days; rashes
Analgesics	Tylenol®	Pain and fever reducer	Acetaminophen	Caplets: cellulose, corn starch, hypromellose, magnesium stearate, polyethylene glycol, sodium starch glycolate; Tablets: carnauba wax, cellulose, corn starch, FD&C red no. 40, FD&C yellow no. 6, hypromellose, iron oxide black, polyethylene glycol, polysorbate 80, povidone, sodium starch glycolate, stearic acid, sucralose, titanium dioxide	liver damage due to large doses, chronic use, or concomitant use with alcohol or other drugs that also damage the liver; chronic alcohol use may also increase the risk of stomach bleeding
Blood thinners	Plavix®, Coumadin®	Anticoagulant used to prevent heart attacks, strokes, and blood clots in veins and arteries	Warfarin	Tablets: Lactose, starch, magnesium stearate; may also contain FD&C Blue No. 1 Aluminum Lake, FD&C Blue No. 2 Aluminum Lake, FD&C Yellow No. 6 Aluminum Lake, D&C Red No. 6 Barium Lake, D&C Yellow No. 10 Aluminum Lake, and/or FD&C Red No. 40 Aluminum Lake; for intravenous use: Sodium phosphate, dibasic, heptahydrate; Sodium phosphate, monobasic, monohydrate; Sodium chloride; Mannitol	nausea, vomiting, mild stomach pain; bloating, gas; altered sense of taste

Joint Health vs Rx and OTC

Category	RX/OTC Names	Purpose	Active Ingredient	Inactive Ingredients	Side Effects
NEM® with Systemic Enzymes	**Transformation Professional Protocol™ Joint Health**	**NEM® eggshell membrane is a whole food source supplying nutritional building blocks for healthy joints with enzymes for delivery and absorption***	**68,750 HUT protease 250 FIP lipase 500 mg NEM® (glucosamine, chondroitin, dermatan, keratan sulfate, hyaluronic acid, glycosaminoglycans, collagen)**	**Beet root fiber, cellulose, water**	**None known**
Glucosamine	Standard Process Glucosamine Synergy®	Boswellia serrata combined with vitamins, minerals, and glucosamine to help maintain healthy joint function	1 mg Manganese 500 mg Glucosamine Sulfate (from Crab Shells) 60 mg Boswellia serrata extract Proprietary Blend - includes multiple (9) bovine glandular extracts and various herbal nutrients including yeast, wheat, and soy	Gelatin, calcium stearate, manganese glycerophosphate, water, colors, arabic gum, starch, sucrose (beets)	None known
Steroids, corticosteroid, glucocorticoid	Prednisone® (cortisone, hydrocortisone)	To suppress inflammation and the immune system for treatment of rheumatoid arthritis, lupus, asthma, allergies, etc	Prednisone® - 2.5mg, 5mg, 10mg, 20mg, 50mg	Lactose monohydrate, magnesium stearate, microcrystalline cellulose, pregelatinized starch and sodium starch glycolate; Prednisone® tablets also contain stearic acid; Prednisone® Oral Solution contains alcohol, citric acid, disodium edetate, fructose, hydrochloric acid, maltol, peppermint oil, polysorbate 80, propylene glycol, saccharin sodium, sodium benzoate, vanilla flavor, water	elevated pressure in the eyes (glaucoma); fluid retention, causing swelling in lower legs; increased blood pressure; mood swings; weight gain, with fat deposits in abdomen, face, and back of neck; longer term: clouding of the lens in one or both eyes (cataracts); high blood sugar, which can trigger or worsen diabetes; increased risk of infections; thinning bones (osteoporosis) and fractures; suppressed adrenal gland hormone production; thin skin, easy bruising, and slower wound healing
NSAIDS / Aspirin	Naproxen (Aleve®), Celecoxib (Celebrex® "COX-2 inhibitor")	Relieve pain and reduce inflammation and fever	Aspirin (acetylsalicylic acid Ibuprophen) Naproxen - sodium 220 mg	Aspirin: carnauba wax, corn starch, hypromellose, powdered cellulose, triacetin; Ibuprophen: carnauba wax, colloidal silicon dioxide, croscarmellose sodium, hypromellose, lactose, magnesium stearate, microcrystalline cellulose, propylene glycol, titanium dioxide; Naproxen: FD&C Blue #2, croscarmellose sodium, macrogol, magnesium stearate, polyvinyl alcohol, povidone, pregelatinized starch, talc, titanium dioxide; Celebrex: croscarmellose sodium, edible inks, gelatin, lactose monohydrate, magnesium stearate, povidone, sodium lauryl sulfate	stomach problems like bleeding, ulcer and stomach upset; high blood pressure; fluid retention (causing swelling, such as around the lower legs, feet, ankles and hands); kidney problems; heart problems; black, bloody, or tarry stools; coughing up blood or vomit that looks like coffee grounds; severe nausea, vomiting, or stomach pain; fever lasting longer than 3 days; rashes
Analgesics	Tylenol®	Pain and fever reducer	Acetaminophen	Caplets: cellulose, corn starch, hypromellose, magnesium stearate, polyethylene glycol, sodium starch glycolate; Tablets: carnauba wax, cellulose, corn starch, FD&C red no. 40, FD&C yellow no. 6, hypromellose, iron oxide black, polyethylene glycol, polysorbate 80, povidone, sodium starch glycolate, stearic acid, sucralose, titanium dioxide	liver damage due to large doses, chronic use, or concomitant use with alcohol or other drugs that also damage the liver; chronic alcohol use may also increase the risk of stomach bleeding
Blood thinners	Plavix®, Coumadin®	Anticoagulant used to prevent heart attacks, strokes, and blood clots in veins and arteries	Warfarin	Tablets: Lactose, starch, magnesium stearate; may also contain FD&C Blue No. 1 Aluminum Lake, FD&C Blue No. 2 Aluminum Lake, FD&C Yellow No. 6 Aluminum Lake, D&C Red No. 6 Barium Lake, D&C Yellow No. 10 Aluminum Lake, and/or FD&C Red No. 40 Aluminum Lake; for intravenous use: Sodium phosphate, dibasic, heptahydrate; Sodium phosphate, monobasic, monohydrate; Sodium chloride; Mannitol	nausea, vomiting, mild stomach pain; bloating, gas; altered sense of taste