

Seeds of change

EPIITALIS® offers a natural osteoarthritis treatment

- Osteoarthritis (OA) causes joint pain that can seriously affect people's quality of life.
- Unfortunately for people living with the condition, safe and effective therapies are limited.
- In a major step forward, researchers at Australian company Interpath have developed EPIITALIS®, a new OA treatment derived from a plant seed oil.
- In a three-month trial in patients with knee OA, the supplement was found to be safe and efficacious.
- The findings raise hopes that an alternative treatment to the current problematic standards of care will soon be available.

As we get older, our knees, hips, and even fingers can start to creak and ache. This joint pain may be due to osteoarthritis (OA) – a condition in which multiple tissues in the articulating joint undergo pathological changes that ultimately lead to pain and deterioration in joint function. One feature of the disease is the breakdown of cartilage (the smooth and lubricated surface where bones meet) and underlying bone in our joints. Without cartilage, pain-free and smooth joint movement is difficult and can greatly impact a person's quality of life. According to a review in the medical journal *The Lancet*, OA is the fourth leading cause of disability in the world⁶, with the World Health Organization estimating that OA affects 528 million people worldwide, but treatment options remain limited³.

Non-steroidal anti-inflammatory medications (NSAIDs) provide some pain relief, but do nothing to address the condition itself and carry significant risks – such as gastrointestinal bleeding, renal toxicity, and cardiovascular events – particularly when taken long-term and in old age.

Several potential therapeutic options, such as tanezumab, have failed at expensive late-stage clinical trials and many pharmaceutical companies have exited the OA research and development phase. Ultimately, many patients require invasive interventions such as injections into the joint or total joint-replacement surgery.

As such, new oral OA treatments that are safe and effective are urgently needed. Fortunately, one company is on the case – Interpath Pty Ltd.

EPIITALIS® – a plant seed oil treatment

Interpath, a family-owned research and development company based in Australia, creates clinically proven, naturally derived OA treatments. Interpath has already successfully treated OA in dogs, cats, and horses. Their signature animal product range 4CYTE™, containing their patented plant seed oil extract EPIITALIS®, is the largest-selling natural veterinary joint-health product range in

Australasia. Now the researchers want to answer another question: can the same treatment be successful in humans?

To find out, the team at Interpath's collaborators Vedic Life Sciences carried out a double-blind, randomised, placebo-controlled trial in humans. They presented the results at the Osteoarthritis Research Society International (OARSI) 2021 annual congress and published them in the journal *Inflammopharmacology*. More than 200 patients diagnosed with knee OA, aged between 40 and 65, participated in the trial. The participants were randomly chosen to take an encapsulated placebo oil, or encapsulated high dose (HD), medium dose (MD), or low doses (LD) of EPIITALIS® for 56 days. A validated clinical tool, in which patients were asked to rate their knee pain before, during, and at the end of the trial, was used as the primary outcome to evaluate the efficacy of the intervention. Several additional exploratory outcomes were also used to assess pain, function, and quality of life (QoL), with all changes in these endpoints demonstrating similar levels of EPIITALIS® efficacy at the end of the trial.

Efficacy on knee pain

The efficacy of EPIITALIS® for joint pain treatment was measured in several ways. The primary pain endpoint was measured using the visual analogue score (VAS), which required all patients to rate their pain on a scale of 1–100. At the end of the trial, all three doses of EPIITALIS® resulted in similar levels of pain reduction by approximately 50% (35 points), with the changes in each EPIITALIS® group being highly significantly different vs. the change in the placebo group of approximately 12.5% (10 points) (Figure 1). An exploratory clinical endpoint (WOMAC pain) also demonstrated similar

beneficial qualitative and quantitative changes in OA pain in each of the EPIITALIS® groups vs. the placebo group (Figure 2).

Pain reduction and more

In addition to pain, the WOMAC clinical tool was also used to assess knee function and stiffness. Similar levels of clinical benefit were

We show – using several measures – that EPIITALIS® decreases joint pain, improves joint function, and improves the patients' quality of life.

observed in both these exploratory outcomes as per the benefits to knee pain. The patients’ QoL was also investigated as an exploratory outcome using the SF-36 questionnaire – a clinically validated tool that assesses several domains of importance to QoL including physical, mental, emotional, and social functioning, plus general vitality and health. In each EPIITALIS® group, similar highly beneficial changes in each SF-36 domain were measured between the start of the study and the end. In contrast, only minimal change in each SF-36 domain was observed in the placebo group (Figure 3).

Dr Peter Mitchell, a research consultant at Interpath, explains, ‘The exploratory endpoints measuring pain, function, stiffness, and QoL all demonstrated similar qualitative and quantitative changes in the EPIITALIS® groups, as observed versus the primary VAS pain outcome.’

Notably, the safety profile of EPIITALIS® was also assessed at regular time points by measuring the patients’ heart, kidney, and liver function – all were within normal ranges throughout the trial. ‘Taken together, these results are very promising’, says Mitchell. He adds, ‘They begin to provide hope for a safe and efficacious solution for patients suffering from osteoarthritis.’

A cure for osteoarthritis?

Precisely what the active component in EPIITALIS® is and how it works at the molecular scale is still to be elucidated. However, there is significantly consistent evidence from both cell and animal studies to suggest that EPIITALIS® reduces the inflammatory response in osteoarthritic joints over time. This hypothesis is consistent with the gradual increase in efficacy seen in the current trial (Figure 5). In a recent 2021 equine trial, EPIITALIS® also demonstrated disease-modifying activity, substantially inhibiting changes in bone pathology (measured via X-ray), an activity consistent with EPIITALIS® treating the underlying structural disease pathology– a remarkable discovery². These findings for EPIITALIS® and its effectiveness contrast with existing nutraceutical products marketed for treating OA. In many cases, the human clinical evidence for the efficacy of nutraceutical supplements comes from either low quality and/or small trials that have not been adequately replicated. In contrast, in a robust, double-blind and placebo-controlled human trial, EPIITALIS® demonstrated remarkable improvements in pain and other symptoms associated with knee OA and was instrumental in significantly improving the QoL of patients with the condition.

Interpath is making significant progress in addressing an area of highly unmet medical need, providing hope for a safe, cost-effective, and efficacious treatment for a debilitating condition. In the future, EPIITALIS® may prove to be the treatment of choice for OA-related symptoms, while also providing meaningful improvements in QoL for patients with this degenerative condition. 2024 will bring further milestones with the launch of a new, unique OA supplement created by Interpath, Epijoint®, containing purified Epiitalis®. From March 2024, the product will be available for purchase via Chemist Warehouse pharmacies Australia-wide, with plans to launch into additional international geographies already in play.

Interpath is also continuing research to identify the mechanism of action of EPIITALIS®, the identity of active species in the oil, and the potential for disease-modifying activity.

Patients taking a daily dose of EPIITALIS® improved their knee pain by 50% compared to 12.5% knee pain improvement for those using placebo.

Figure 1: VAS score change, Baseline to Day 56 (mean change 95% confidence interval)

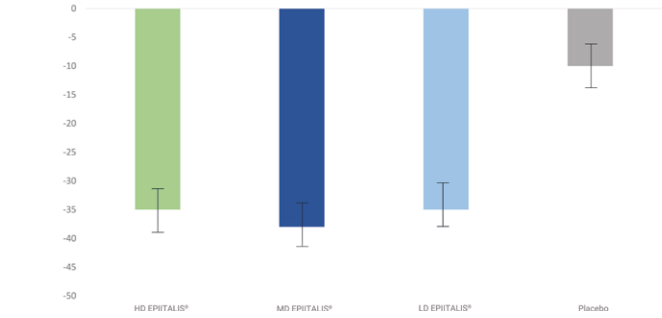


Figure 2: Total WOMAC score change (pain/stiffness/function), Baseline to Day 56 (mean change 95% confidence interval)

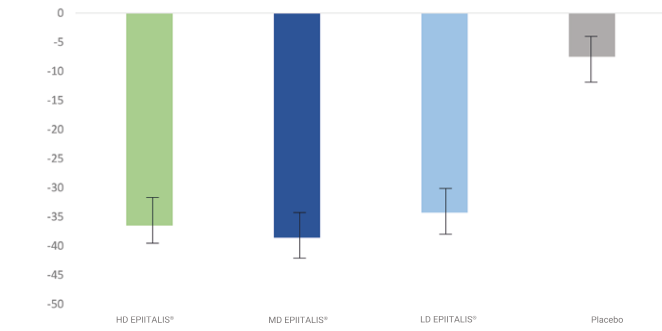


Figure 4: OMERACT-OARSi Responder Index, Day 56

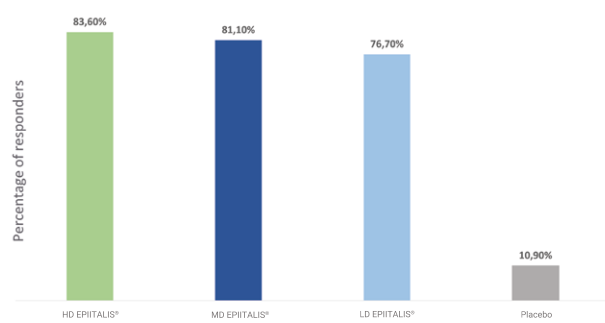
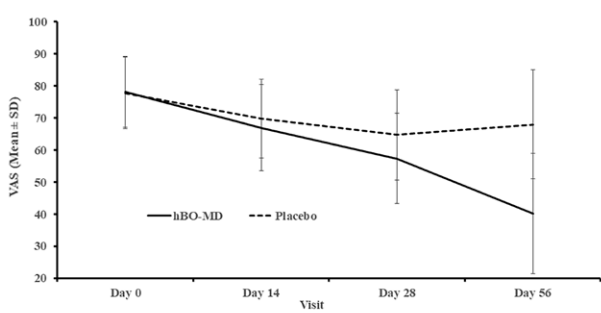


Figure 5: Kinetics for onset of clinical efficacy induced by EPIITALIS®



Personal response

What first made you consider that plant seed oils might have potential to reduce osteoarthritis pain?

Historically, conifers have been used for pain relief. Often the leaf and/or the stem are used, but we chose to assess the seed oil for the following reasons:

- Extracts of the leaf and/or stem can harbour toxins such as Thuja.
- Seeds are normally not toxic, so birds and other animals can eat them and spread them in their faeces.
- Natural product seed oils contain structurally diverse fatty acids (typically bound up as triglycerides), some of which possess unique bioactivities.
- The seed oil has a much higher oil concentration, and has differences in composition, compared to that extracted from leaves and stems.
- Fatty acids are generally bound into triglyceride molecules, requiring absorption and subsequent digestion (hydrolysis) to make them available to the body. These absorption and hydrolysis steps can be incomplete/inefficient. Interpath developed our own proprietary method to release the bioactive fatty acids from triglycerides and make these much more readily absorbable and bioavailable.

How did you determine the criteria for how people responded to the trial?

Criteria for defining responders to an OA intervention have previously been established and clinically validated by experts in the field (termed the ‘OMERACT-OARSi responder index’). Although the onset of clinical efficacy in the EPIITALIS® groups was relatively slow (weeks), by the end of the study (Day 56) each EPIITALIS® group contained approximately 80% responders, compared to only 10.9% in the placebo group (Figure 4).

What are the goals of your next human trial and other future work?



Osteoarthritis of the knee: the cartilage in the knee joint breaks down, enabling the bones to rub together.

We have several projects underway or planned:

- Human clinical trials in OA are long, expensive and, by necessity, need to focus on a specific type of OA – in our case knee OA. In the future we may perform human trials in other joint types eg, hip or hand, or in additional indications, such as rheumatoid arthritis, joint injury, etc.
- Determining the types of *in vitro* bioactivities in the seed oil and the identity of the responsible molecule(s); we are more than three years into this.
- Assessing gene expression and pathway changes stimulated by isolated active subfractions. This *in vitro* work is ongoing and is using all the major cell types represented in a human joint.
- Continuing our work in clinical veterinary populations with OA to assess the clinical efficacy of both EPIITALIS® and more purified fractions.

Can you tell us some more about your hypothesis on how EPIITALIS® works?

We believe EPIITALIS® works on different pathway(s) to common anti-inflammatories (eg, NSAIDs, COX-2 inhibitors, steroids). Although still extensively used to treat OA symptoms, NSAIDs and COX-2 inhibitors are associated with increased incidences of serious side effects – stomach ulcers, heart attack, and stroke. To date in both extensive veterinary use and in our human experience, we have not observed any of these types of side effects associated with EPIITALIS® use. We believe our extensive *in vitro* research programme will further elucidate the types of bioactivities, pathways, and molecules that may be contributing to the clinical efficacy of EPIITALIS®. We already have issued patents with claims relating to EPIITALIS® reducing inflammation and inducing cartilage cell proliferation – our ongoing work will build on the work in these patents.

Details



e: admin@interpath.global
w: www.interpath.global
(website not available in all countries due to regulatory requirements)

Funding

Interpath Pty Ltd

Collaborators

- Dan Bright
- Corina Bright
- Dr Peter G Mitchell
- Vedic Life Sciences

Bio

Interpath Pty Ltd is an Australian-based research and development company that has developed EPIITALIS®, a new treatment for human osteoarthritis.

Dan Bright and Corina Bright are founders and owners of Interpath and Managing Director and Director, respectively. Dr Peter G Mitchell is Interpath’s research consultant.

Further reading

1. Mitchell, PG, et al, (2022) [The Biota orientalis oil extract Epiitalis®, is efficacious at reducing the symptoms of knee osteoarthritis: a pilot, multi-site, dose-ranging, randomized, blinded, placebo-controlled trial. Inflammopharmacology, 30\(4\): 1323–1334.](#)
2. Seabaugh, KA, et al, (2022). [Examining the symptom-modifying and disease-modifying effects of the oral supplement Biota orientalis in the osteochondral fragment-exercise model of osteoarthritis. Front Vet Sci, 9, 858391.](#)
3. World Health Organization, (2022) Musculoskeletal Health, www.who.int/news-room/fact-sheets/detail/musculoskeletal-conditions [Accessed 08/12/2022]
4. Mitchell, PG, et al, (2021) [A multi-site, double-blind, dose-response, randomized, placebo-controlled study to assess the efficacy of Epiitalis on knee pain in patients suffering from knee osteoarthritis. Osteoarthritis Research Society International \(OARSi\) Annual Congress, 29\(1\), S288–S289.](#)
5. Hunter, DJ, Bierma-Zeinstra, S, (2019) [Osteoarthritis. The Lancet, 393\(10182\), 1745–1759.](#)