

perluxan[®]

softgels

*A unique botanical supplement
for joint health**

*A proprietary hops extract
containing 150 mg alpha acids*



SOFT GEL
TECHNOLOGIES, INC.



Joint Discomfort: An American Affliction



In 2002, when the Centers for Disease Control assessed the number of people who suffer from occasional tenderness or limited mobility in their joints, the agency was surprised by its own results. Previously, the CDC had estimated that 46 million American adults were affected by

occasional joint discomfort. But the CDC's survey showed that in fact, this problem affects as many as 70 million U.S. adults — or an astonishing one in three.¹

The COX Problem

Understandably, many consumers reach for remedies that inhibit the cyclooxygenase or COX enzymes, which are responsible for discomfort. Unfortunately, these remedies are not typically selective; they inhibit both the COX-1 and COX-2 enzymes with varying intensity. So, while discomfort may be reduced by blocking the COX-2 enzyme, non-selective inhibition of COX-1, whose job is to protect the gastro-intestinal (GI) tract lining, can lead to GI-related adverse events.²

There are selective COX-2 inhibitors — substances that shut down COX-2 enzymes but not COX-1. Unfortunately, these have even more dangerous side effects. The problem is that they are too selective. By completely shutting down COX-2, these remedies are theorized to suppress production of cardio-protective enzymes, thus endangering the heart. ►

With the prevalence of joint discomfort and the risks presented by standard remedies, it's no surprise that sales of joint health supplements have soared. In fact, the joint health category has surpassed calcium to become the largest market of condition-specific dietary supplements, according to a recent *Packaged Facts* report.³

Glucosamine: Only Part of the Puzzle

Leading the joint supplement pack is glucosamine. As a component of cartilage, glucosamine may be able to support the renewal of cartilage and protect joint function. However, glucosamine does not work immediately to alleviate discomfort. In fact, it usually takes a minimum of eight weeks to feel an effect.



For Rapid Relief, Trust Perluxan Soft Gels

Derived from hops, Perluxan is a unique botanical agent clinically demonstrated to relieve joint discomfort *quickly*.^{*} The subject of multiple *in vitro*, *ex vivo* and human clinical trials, Perluxan:

- **Acts fast, relieving joint discomfort within two hours of ingestion***
- **Moderately inhibits COX-2 and mildly inhibits COX-1***
- **Is well-tolerated and does not cause GI distress**

Soft Gel Technologies is pleased to offer Perluxan in an off-the-shelf soft gel formulation.

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The Quest to Find a Plant-Derived Joint Health Agent

Perluxan is a proprietary supercritical hops extract standardized to contain a specific amount of alpha acids — the active constituents — and designed to be virtually free of phytoestrogenic and sleep-inducing compounds.

It was not developed by chance.

During the late 1990s, a handful of research companies began looking for natural ways to ease occasional joint discomfort. Hundreds of different botanicals were examined. Piles of scientific literature were reviewed. And at the end of this painstaking process, about 20 candidates were identified for further study.

All of the prospects — including highly regarded botanical agents such as curcumin and boswellia — were subjected to *in vitro* testing to determine their bioactivity potential.⁴ Of those, one ingredient was identified as having the highest chance of success: a hops extract standardized to contain high amounts of naturally occurring alpha acids: Perluxan.



Whole Blood Assay Reveals Surprising Results

The next step in evaluating Perluxan's efficacy was to conduct a Williams Harvey Modified Whole Blood Assay — considered the “gold standard” for evaluating a substance's COX activity and selectivity. There were three possible outcomes:

1. If Perluxan moderately inhibited both COX-1 and COX-2, then it could be assumed to cause GI problems.
2. If Perluxan shut down COX-2 completely without affecting COX-1, it could be assumed to increase the risk of cardiovascular events.
3. However, if Perluxan could *moderately* inhibit COX-2 while only *mildly* inhibiting COX-1, then the researchers would have a winner.

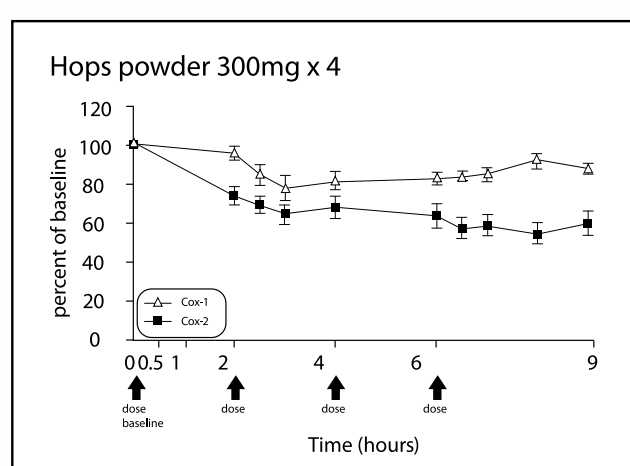
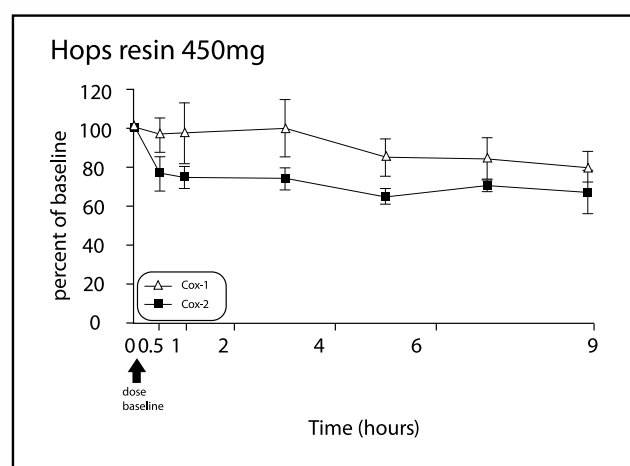
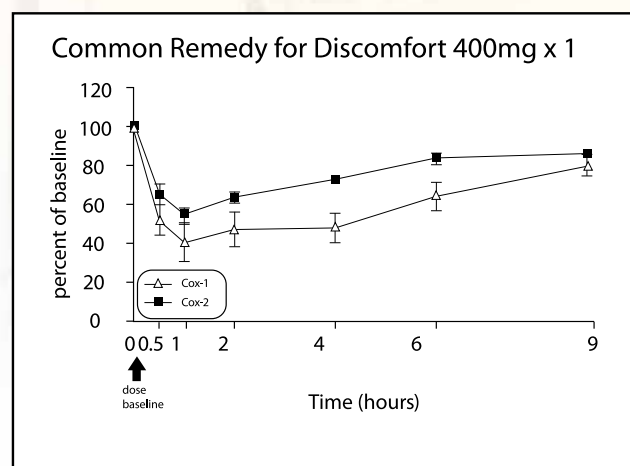
The results? **Perluxan achieved the perfect middle ground.** It inhibited COX-2 strongly enough to be able to alleviate discomfort, but not so strongly that it shut down the enzyme altogether.* And it only mildly inhibited COX-1, so GI toxicity was extremely unlikely.⁵

Having passed these initial hurdles, Perluxan was ready for the final test: human clinical trials.

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Hops Extract vs. Common Remedy for Discomfort in Cyclooxygenase Models



Perluxan Human Clinical Research

Study #1: A dietary supplement is a selective COX-2 inhibitor both *in vitro* and *ex vivo* in healthy human volunteers.*

A double-blind, randomized parallel design trial was conducted on 19 healthy subjects.⁶ The subjects received a single dose of a common pain remedy (400 mg), a soft gel containing hops resin (450 mg), or a capsule containing the hops resin converted to a powder form (300 mg 4x/day). Both supplements forms were standardized for hops alpha acids (150 mg). Levels of COX-1 and COX-2 were monitored at regular intervals over nine hours after the initial dose.

Results

The hops preparations were as effective as the conventional remedy at inhibiting COX-2, but had significant COX-1 sparing activity over a nine-hour period. Interestingly, the hops resin soft gel was only administered once, whereas the hops powder capsules were administered in four divided doses over a nine-hour period. The soft gel had a faster onset of action and gradually reduced excitatory enzymes over the period of the study.* This improved activity of the soft gel was probably the result of the natural state of the resin, solubilized in oil, as opposed to the conversion of resin-to-powder for capsules and tablets.

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Perluxan Human Clinical Research

Study #2: Efficacy of Oral Perluxan Intake: A Randomized, Double-Blind Study

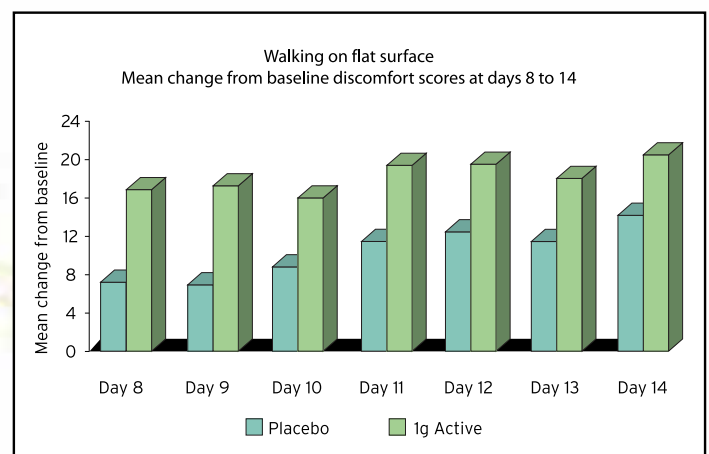
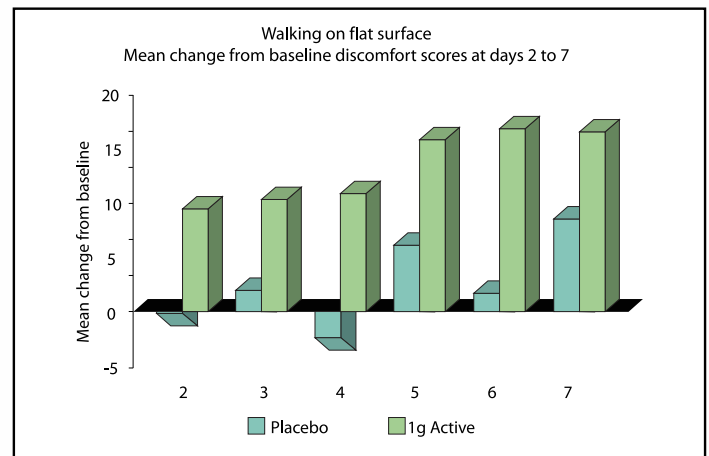
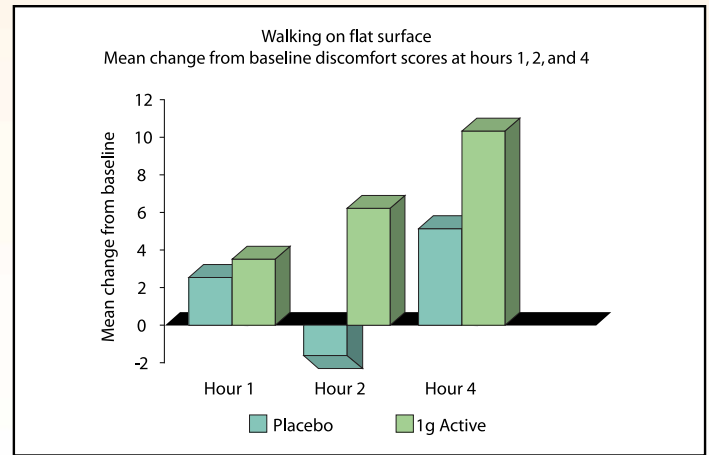
After successful *in vitro* and *ex vivo* trials, it was time to put Perluxan to the ultimate test: Would it benefit subjects with occasional knee discomfort?

A double-blind, placebo-controlled randomized trial evaluated the effects of 14 days of Perluxan oral supplementation.⁷ Thirty-six subjects completed a questionnaire to evaluate joint comfort levels at baseline. The time to perform a 20-meter walk on a flat surface was also recorded. Study participants were then assigned to take either Perluxan or a placebo.

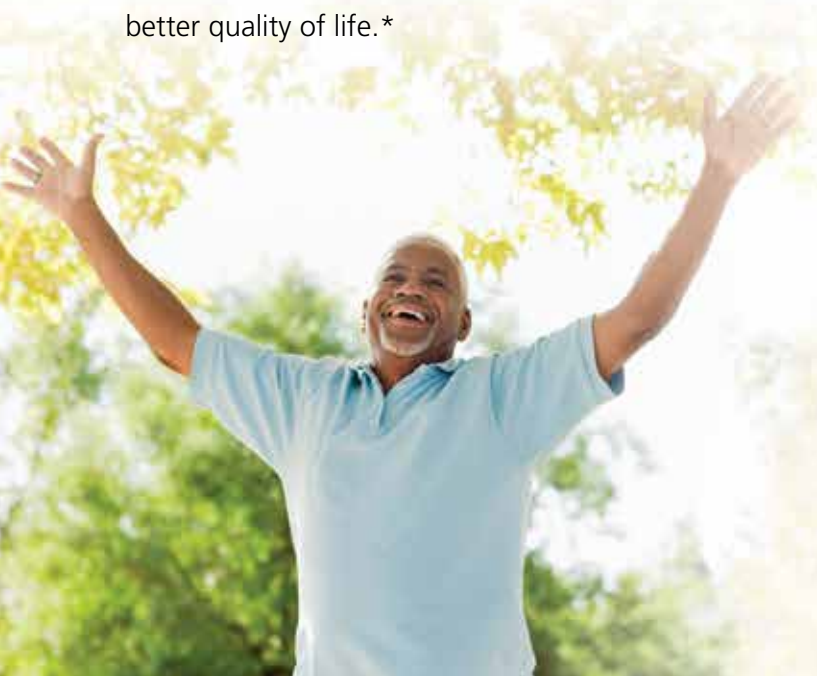
On day 15, the time to perform a 20-meter walk on a flat surface was again measured and improvements in joint function were assessed.

Results

- Perluxan intake showed fast-acting relief; significant improvement over placebo could be measured only two hours after ingestion of the first dose.*
- 1,000 mg per day of Perluxan significantly improved parameters of joint comfort, including relief while in bed, sitting, lying, and walking on a flat surface.*
- The researchers concluded that Perluxan provided relief in subjects with occasional knee discomfort, with the ultimate outcome of increased function and better quality of life.*



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Mechanism of Action

Discomfort is caused by the activation of COX enzymes. Without primarily inhibiting the COX-2 pathway, there can be no fast reduction in discomfort. *In vitro* and *ex vivo* studies reveal that Perluxan:

- Moderately inhibits COX-2, thus reducing excitatory enzymes without creating cardiovascular risk*
- Mildly inhibits COX-1, thus dramatically reducing the likelihood of GI adverse effects*

Bioavailability

In vitro testing, utilizing the CACO-2 cell monolayer assay, indicates that the permeability of the alpha acids contained in Perluxan is high. High permeability predicts good human oral bioavailability.

Safety

Perluxan's safety has been confirmed in a double-blind placebo-controlled human clinical trial. The comparison of pre- and post-supplementation blood work, as well as adverse side effect monitoring, showed that Perluxan was well-tolerated and led to no GI discomfort.

Additionally, studies in rats and dogs have demonstrated that hops alpha acids caused no changes in hematological examinations, blood chemistry, urine tests, or pathological examinations, and are non-toxic even in doses that far exceed the amount found in Perluxan. Hops alpha acids have also tested negative for mutagenicity (the ability to cause mutations) and genotoxicity (the ability to cause genetic damage).

Purity

Perluxan is made from hops that are grown in the United States, inspected by the USDA, and fully traceable to the farm where they are cultivated. The hops are extracted in an ISO-certified facility, using a supercritical extraction process that is free of chemical solvents. The finished product is subjected to heavy metal analysis and regularly screened for the presence of 73 different pesticides.



Patents

Perluxan is protected by U.S. patents — U.S. Patent #7,144,590B2, U.S. Patent #7,279,186, U.S. Patent #5,604,263, and U.S. Patent #5,679,716 — and patents pending.

Regulatory Status

- Supercritical hops extract is GRAS (generally regarded as safe) in the United States
- Perluxan has been approved by the Australian government and is listed on the Australian Register of Therapeutic Goods
- Perluxan has been approved for clinical research and use by the Korean Food Drug Authority

Delivery System

Soft Gel Technologies is pleased to offer Perluxan as an off-the-shelf formulation in a soft gelatin capsule. In addition to Perluxan hops resin, the soft gels contain peppermint and ginger oils to counteract any possible GI upset.

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Perluxan Soft Gels Highlights

Available exclusively from Soft Gel Technologies, Perluxan soft gels contain a proprietary hops resin extract standardized to alpha acids — key bioactive constituents — clinically demonstrated to have a fast-acting effect in subjects with mild, temporary joint discomfort.*

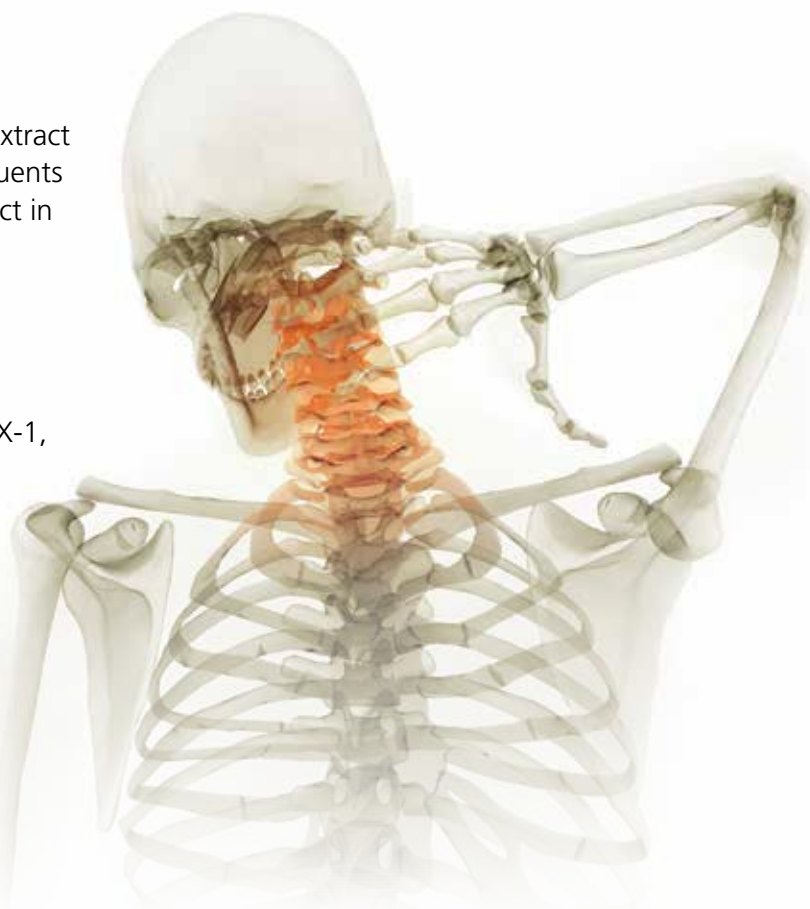
Research has shown that Perluxan:

- Moderately inhibits the enzyme COX-2, thus providing relief*
- Only mildly inhibits the GI-protective enzyme COX-1, thus avoiding GI distress*
- Significantly improves joint function and enhances quality of life*

Indications

- Joint discomfort
- Minor aches and pains

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References

- ¹ Centers for Disease Control. Oct. 24, 2002. <http://www.cdc.gov/media/pressrel/r021024.htm>
- ² Wolfe MM, et al. NEJM. 1999 Jun 17;340(24):1888-99.
- ³ Heller, Lorraine. New report breaks down US supplement market. Nutraingredients-usa.com. Aug. 21, 2008. <http://www.nutraingredients-usa.com/Consumer-Trends/New-report-breaks-down-US-supplement-market>
- ⁴ Lemay M, et al. Nutrilite Health Institute, Access Business Group LLC, Buena Park CA.
- ⁵ Lidbury, et al. The effects of AH88 on the activity of COX-1 and COX-2 using human whole blood and A549 cells. Pharmachem Laboratories, Kearny NJ.
- ⁶ Lemay M, et al. A dietary supplement is a selective COX-2 inhibitor both in vitro and ex vivo in healthy human volunteers. Nutrilite Health Institute, Access Business Group LLC, Buena Park CA.
- ⁷ Jager R, Purpura M. Efficacy of Oral Perluxan Intake: A Randomized, Double-Blind Study. Pharmachem Laboratories, Kearny, NJ.



Why Choose Perluxan?

- **Clinically tested.** In addition to multiple *in vitro* and *in vivo* studies, Perluxan is backed by several human clinical trials, including a 14-day double-blind oral supplementation study, which found Perluxan effective at relieving joint discomfort compared to placebo.*
- **Fast-acting.** The 14-day oral supplementation study found that Perluxan intake showed fast-acting relief: significant improvement over placebo could be measured only two hours after ingestion of the first dose.*
- **Active.** Perluxan has been shown to be more potent than several common remedies at inhibiting the excitatory enzyme COX-2.*
- **Selective.** Perluxan only mildly inhibits COX-1, the enzyme that protects the GI tract lining, so it does not cause GI distress.*
- **Bioavailable.** *In vitro* testing of Perluxan has predicted good human oral bioavailability.
- **Safe:** The 14-day oral supplementation study in humans found that Perluxan was well-tolerated and led to no GI discomfort, adding to hops' proven record of safety.
- **Pure.** Perluxan is free of solvents and is regularly tested for heavy metals and pesticides.

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