Clinically supported efficacy reviews

50-72% Symptom Relief in Trial Responders◆

Randomized, Double-Blind, Placebo-Controlled Trial

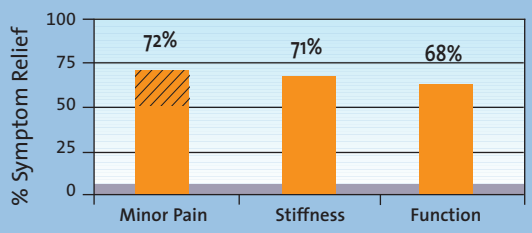

Figure 1. Symptom scores for 26 subjects during a randomized, double-blind, placebo-controlled trial. A greater decrease in symptoms was observed for subjects taking Kaprex as compared to the placebo. Placebo response was 50%.◆[1]

50% Reduction in Joint Discomfort◆

Open Label Observational Trial

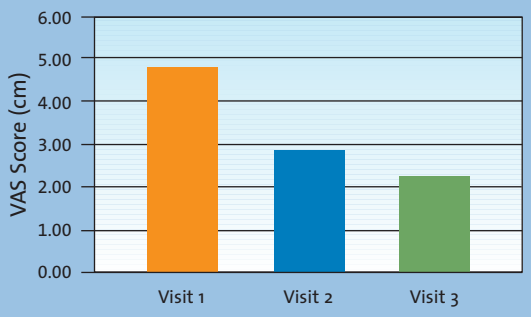

Figure 2. Visual Analog Scale score for 28 subjects completing an 8-week observational trial. A 50% decrease in joint discomfort was observed after 8 weeks on Kaprex, with the majority of the decrease occurring within the first 4 weeks.◆[2]

Kaprex®

GI-Friendly Joint Relief◆

Kaprex is a premium quality nutritional supplement featuring a proprietary blend of reduced iso-alpha acids (RIAA), rosemary extract, and oleanolic acid to provide potent, natural joint relief with an extraordinarily high level of predicted safety.◆

Kaprex advantages:

- Effective joint relief supported by numerous clinical investigations◆
- A high level of predicted safety. Extensive in vitro and human clinical experience suggest a high level of predicted safety on:
  - Gastrointestinal (GI) tract lining◆
  - Blood pressure◆*
  - Platelet function and blood coagulation◆
  - Kidney and liver function◆*
- Effective dose in as little as one tablet three times a day

**over a 6-8 week trial period*

A safer approach to effective joint relief.◆

Metagenics®
Genetic Potential Through Nutrition

For more information on efficacy and predicted safety visit us at **www.metagenics.com/kaprex**

Kaprex: Scientifically Engineered and Cli

EFFECTIVE, ALL-NATURAL JOINT RELIEF

Your patients can now experience powerful, all-natural joint relief—supported by human clinical trials and backed by cutting edge research and development.◆

Engineered for efficacy, bioavailability, and safety

Kaprex was developed in accordance with our exclusive ExpresSyn® Process, making it one of the most extensively researched natural alternatives for natural joint relief. A groundbreaking innovation in the development of natural alternatives, the ExpresSyn Process combines cell proteomic research, safety evaluations, human ex vivo research, and human clinical research to support efficacy, bioavailability, and a high level of predicted safety.◆

Clinically supported effectiveness

The effectiveness of Kaprex is supported by a legacy of research spanning from product development to human clinical trials, including clinical case studies, human ex vivo research, and taste and tolerance and observational clinical trials. And most recently:

- Preliminary results from a randomized, double-blind, placebo-controlled trial showed Kaprex to provide more joint relief than a placebo and at a level equivalent to published results for the top-selling formulas.◆[1] (See Figures 1, 3.)
- An open label, 8-week observational trial showed a statistically significant decrease in joint discomfort of 50% using the Visual Analog Scale (VAS), following supplementation with Kaprex.◆ (See Figure 2.)
  - ▷ A decreasing trend of C-reactive protein (CRP) was also observed in those subjects who presented with elevated CRP.◆
- Human ex vivo analysis indicates decreased prostaglandin E2 (PGE2) production that sustains for over 6 hours.◆

Kaprex outperforms leading competitors

Compared to leading competitive joint relief formulas, Kaprex appears to have greater inhibition of PGE2 production. In fact, at equal weights, Kaprex had 2.5 to 421 times greater activity than competitive formulas![3] (See Figure 4.)

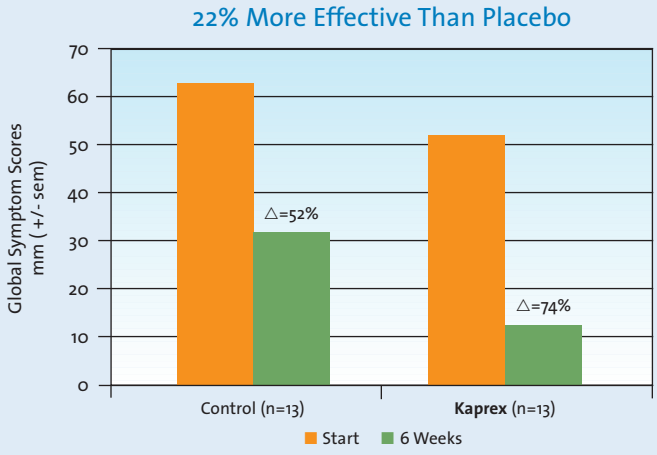

Figure 3. Global symptom scores decreased for subjects taking Kaprex from 52.3 ± 5.4 mm to 13.7± 9.3 mm. A placebo group showed less decrease in global symptom scores, from 63.6 ± 4.9 mm to 30.8 ± 4.8 mm.◆

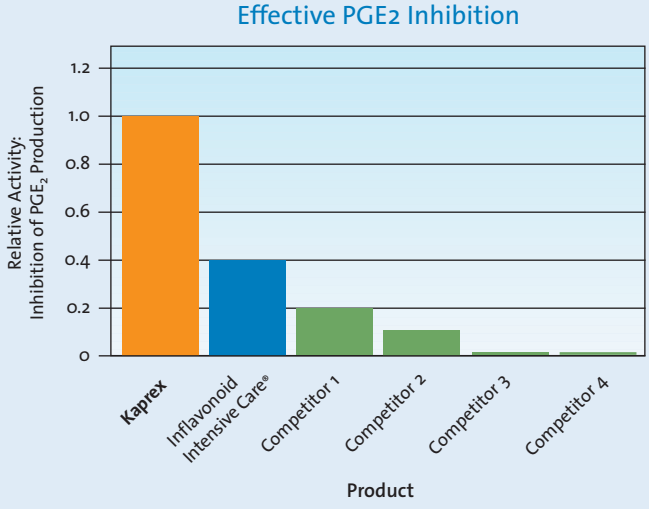

Figure 4. At equivalent weights, Kaprex showed much greater inhibition of PGE2 production than top competitors.◆

cally Tested

A SAFER APPROACH

In vitro data suggests that Kaprex works by selectively modifying the formation of enzymes associated with minor pain in target tissues (e.g., joint)—not by blocking the activities of those enzymes that are necessary for cellular health and maintenance in non-target tissues (e.g., GI).◆

No observed effect on blood pressure

The cyclooxygenase enzymes are known to be important in the maintenance of healthy blood pressure through their abilities to promote vasoconstriction and vasodilation. However, clinical trials have found an effect on blood pressure elevation (which averages about 5 mm Hg) after leading joint relief product use, and this increase is often seen within 6 weeks.◆

During clinical trials, Kaprex was found to have no impact on systolic or diastolic blood pressure for hypertensive and non-hypertensive patients during the trial period.◆[4] (See Figure 5.)

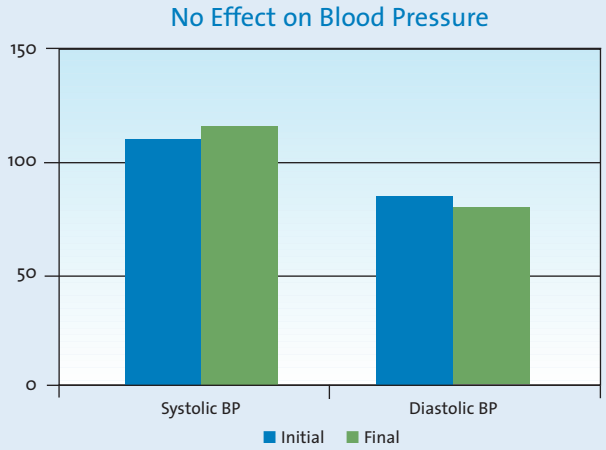

Figure 5. Absence of an effect on blood pressure in 50 subjects over 6 to 8 weeks.

No observed effect on platelet function, blood coagulation

Several botanical and therapeutic agents have been reported to have adverse effects on platelet function; therefore, evaluating the effect of Kaprex on platelet function and blood coagulation is an essential step in assessing clinical safety.

In a clinical trial, Kaprex was shown to have no direct affect on blood coagulation and did not influence platelet function during the trial period.◆[5] (See Figure 6.)

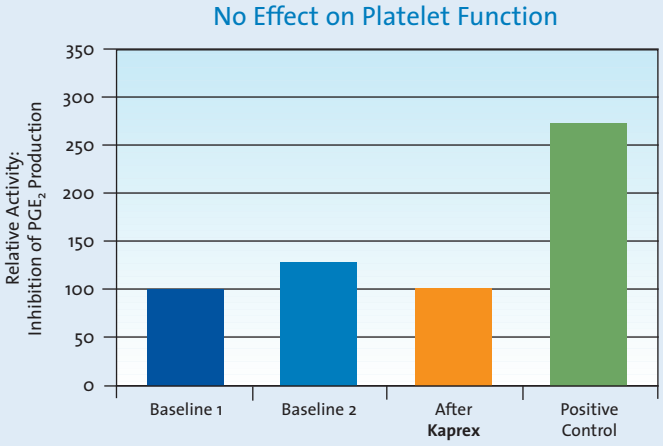

Figure 6. Assessment of platelet function using the platelet plug assay in 6 healthy subjects. The average closure time is shown; no significant difference was seen between Kaprex and baseline.

No observed effect on kidney, liver function

The cyclooxygenase enzymes are found in the kidneys and contribute to managing healthy renal flow.

In two clinical trials, kidney function markers remained well within the reference range after intervention with Kaprex during the trial periods. Electrolytes also remained within established reference range limits. Similar results were obtained for liver function markers, complete blood counts, and other chemistry values.◆

Thousands of people have experienced the benefits of Kaprex...
with *no reported serious* adverse effects.

Kaprex®

High level of predicted GI safety

It is important that product ingredients are active in specific target tissues (e.g., joint) while exhibiting minimal activity in non-target tissues (e.g., GI). This allows for effectiveness with reduced risk of adverse effects.

Using rigorous, published protein and gene expression technologies, we have performed a variety of tests which demonstrate that Kaprex has a high level of predicted GI safety due to minimal activity in these non-target tissues.◆[6]

- Proteomic research demonstrates that Kaprex inhibits PGE2 production in target cells but does not inhibit PGE2 production in GI cells where it is required for cellular maintenance and health.◆[7]
- A randomized crossover study to assess the effects of Kaprex on levels of fecal calprotectin (a marker for gastrointestinal inflammation) suggests that Kaprex produces little or no GI inflammation as compared to a leading competitor.◆[8]

Gastrotoxicity Comparison

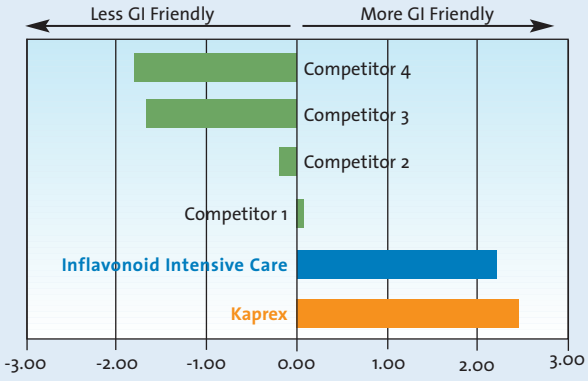

Figure 7. This graph shows the GI toxicity index of various products at an equivalent dose. Decreased PGE2 production in GI cells is equated with GI toxicity. The numbers on this graph represent a comparison of inhibition of PGE2 production in GI cells over that in target (macrophage) cells. A more positive ratio relates to lower toxicity.

For more information on Kaprex safety, visit us at www.metagenics.com/kaprex

Kaprex features a proprietary blend of:

- **Luduxin™† (Hops Extract)**
  Recent scientific data suggests that components of hops (*Humulus lupulus*)—primarily RIAA—may inhibit the formation of prostaglandins (e.g., PGE2) via upstream modulation of gene expression to help relieve minor pain.◆[8,10]
- **Rosemary Extract**
  Research suggests that rosemary (*Rosmarinus officinalis*) down-regulates the activation of transcription factors that result in perpetuation of the eicosanoid cascade.[10,11] Two components of rosemary—carnosol and carnosic acid—account for the majority of the antioxidant activity of rosemary leaves.◆
- **Oleanolic Acid**
  Research indicates that oleanolic acid may support joint health by interfering with the activation of enzymes involved in eicosanoid (e.g., PGE2) synthesis.◆[9,10]

Form: 30 and 90 Tablet Bottles

Recommendations: One tablet three times daily.

Caution: Kaprex has not been tested in pregnant or breastfeeding women; therefore, it cannot be recommended for use in these patients.

† Luduxin™ consists of reduced iso-alpha-acids from hops extract (*Humulus lupulus*) and magnesium salt produced via a proprietary process.

Patent pending.

◆ These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

ExpresSyn®

Kaprex was developed using Metagenics' exclusive ExpresSyn Process, making Kaprex one of the most extensively researched natural approaches for natural joint relief.◆ The ExpresSyn Process takes natural formula development to a new level through cellular research, safety evaluations, human ex vivo and clinical research, and competitive analysis.

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