



A Novel Next-Generation Caffeine Alternative



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PUREENERGY™ - A Novel Next-Generation Caffeine Alternative

Introduction

PUREENERGY™ is an innovative patent-protected caffeine product that is a co-crystal of caffeine and pTeroPure® pterostilbene. *PUREENERGY* provides a novel next-generation healthy and functional caffeine solution that can provide consumers with a sustained energy boost over a significantly extended period of time while offering formulators the ability to reduce the amount of caffeine needed to produce expected results. As demonstrated in a recently completed human clinical study, *PUREENERGY* delivered almost 30% more caffeine into the blood over a longer period of time than caffeine taken by itself and it had a 25% extended half-life compared to caffeine alone. It also showed statistical significances at six hours for fatigue and concentration and a trend toward significances for energy, focus and concentration—caffeine did not.

PUREENERGY was developed as a high-quality caffeine alternative by ChromaDex® Inc., which holds the exclusive worldwide patent rights for the ingredient. ChromaDex is working with several clients to incorporate *PUREENERGY* into products with applications in energy, focus and concentration, weight management and sports nutrition. Specifically, *PUREENERGY* provides the energy market with a solution to address growing regulatory scrutiny and consumer expectations. Regulatory agencies and consumer groups are closely examining the caffeine content in energy beverages and products, and ChromaDex's *PUREENERGY* offers companies producing these products a caffeine solution that will satisfy present and future expectations while delivering the same product performance results for the consumer.

What is *PUREENERGY*?

PUREENERGY is a patent-protected, next-generation caffeine alternative that is a combination of caffeine and pTeroPure pterostilbene; it is a co-crystallization of approximately 43% caffeine and 57% pTeroPure, the only clinically studied 99% pure nature-identical all-trans pterostilbene with seven patents issued or pending. In this formulation, pterostilbene and caffeine are held together by hydrogen bonding to form a co-crystal.

Comprising more than 50% of the formulation, pterostilbene is an important compound in *PUREENERGY*. Pterostilbene is an analog of resveratrol found naturally in blueberries and grapes. Resveratrol is one of the compounds thought to contribute to the “French Paradox” associated with red wine consumption. Like resveratrol, it belongs to a class of compounds called stilbenoids, which are naturally produced by plants. The main difference between pterostilbene and resveratrol is structural, and the difference in structure causes pterostilbene to have a higher potential for cellular uptake (Lin 2009). Pterostilbene also has a much longer half-life in the blood than resveratrol, approximately 105 minutes versus 40 minutes (Remsberg 2008), and when administered orally, pterostilbene showed 80% bioavailability, higher than the 20% bioavailability of resveratrol (Kapetanovic 2011). In pTeroPure pterostilbene's first prospective, randomized, double-blind, placebo-controlled human clinical trial finalized in 2012 and conducted at the University of Mississippi School of Medicine it was shown that pterostilbene helps maintain healthy blood pressure in subjects with blood pressure that is already within normal ranges.

PUREENERGY is the first product available that bonds pterostilbene and caffeine as a co-crystal, and this co-crystallization enables numerous energy-related benefits over traditional caffeine.

What are the Benefits of *PUREENERGY*?

As demonstrated through both human and animal studies, *PUREENERGY* offers significant benefits in performance that enable it to serve as a healthy and functional alternative to traditional caffeine. Specifically, *PUREENERGY* offers more efficient delivery of caffeine into the blood; improved concentration, energy, alertness and focus levels compared to traditional caffeine; extended half-life compared to caffeine; and functional benefits stemming from pterostilbene.

In 2013, the first human clinical study on *PUREENERGY* was completed, and the results confirmed that *PUREENERGY* offers statistically significant energy-related benefits over traditional caffeine. The purpose of the study was to determine the safety, relative bioavailability and pharmacokinetics of *PUREENERGY* as compared to pTeroPure pterostilbene and caffeine alone. The study lasted approximately four weeks with subjects attending four test visits, receiving a different ingredient at each visit. At one test visit, subjects received pTeroPure, at one test visit caffeine, at one test visit *PUREENERGY* and at one test visit a placebo. The study was single blind cross over study, so subjects did not know the ingredient identity. There were no adverse events observed in the study.

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PUREENERGY is a potent ingredient that can deliver caffeine to the body much more efficiently than caffeine alone. The study results demonstrated that PUREENERGY delivers almost 30% more caffeine into the blood over a longer period of time than caffeine taken by itself, as measured by the area under the concentration versus time curve above the baseline concentration, and the difference in delivery levels is, statistically speaking, highly significant. The rate of absorption into the bloodstream, as measured by the time at which maximum caffeine concentration was observed, was also significantly slower with PUREENERGY than with caffeine alone, by about 30% (see Figure 1).

Additionally, in this study PUREENERGY provided a more sustained energy boost than caffeine alone. The study demonstrated that at six hours after ingestion, PUREENERGY showed significantly reduced fatigue and improved concentration levels compared to the baseline, whereas caffeine did not. For fatigue, there were statistically significant decreases in fatigue scores for PUREENERGY at two and six hours, whereas caffeine alone only recorded statistically significant decreases at 0.5 and one hours (see Figure 1a). For concentration, there were statistically significant increases in concentration scores for PUREENERGY at six hours, as compared to caffeine alone, which only had statistically significant increases for caffeine at 0.5 and three hours (see Figure 1b). Similarly, at six hours, PUREENERGY showed a trend toward significance for higher energy, alertness and focus levels compared to the baseline measurement, whereas caffeine did not.

Another factor potentially contributing to the energy boost benefits of PUREENERGY is the effect of co-crystallization of caffeine and pterostilbene on caffeine half-life. The study results demonstrated that PUREENERGY increased the half-life of caffeine elimination by 25% compared to caffeine alone. Finally, PUREENERGY delivers approximately 50% more total pterostilbene into the blood compared to pTeroPure alone, thus potentially enhancing any proven functional benefits of pterostilbene. Some benefits of pterostilbene include promoting heart health by helping to maintain blood pressure levels already within normal ranges; potential improvements in cognitive function; supporting a healthy metabolism; and supporting healthy cellular aging (see Figure 2).

These results further validate conclusions from a study conducted on rats, which demonstrated that over a 12-hour period, PUREENERGY provides a sustained release and an extended energy profile over caffeine alone. In the study, the time to peak plasma concentration for PUREENERGY was double the time to peak plasma concentration for caffeine alone, and the molecular half-life for PUREENERGY was extended by a factor of eight compared to caffeine alone (see Figure 3).

Taken in sum, these results suggest that PUREENERGY offers a rapid and sustained energy boost for at least six hours, offering significant improvements over caffeine, which traditionally offers an energy boost for approximately four to five hours. However, PUREENERGY enables a

Figure 1:

Caffeine During PK Sampling

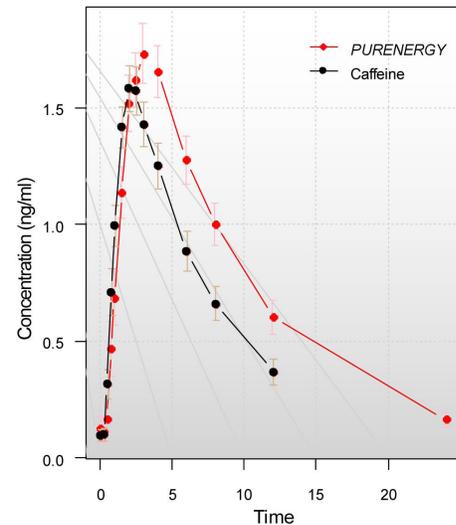


Figure 2:

Total Pterostilbene During PK Sampling

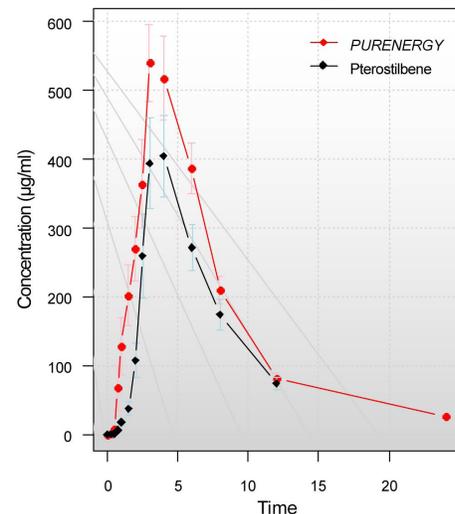
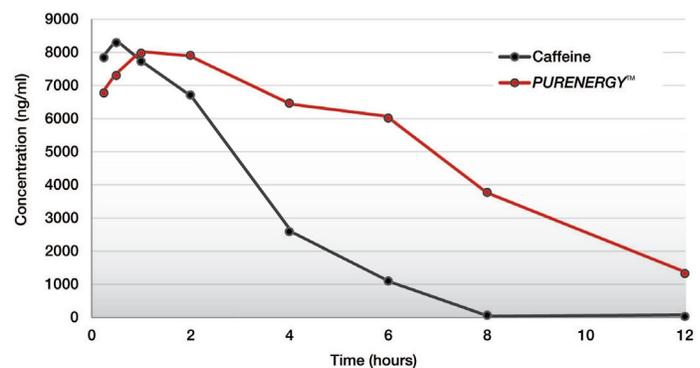


Figure 3:



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reduction in the amount of caffeine needed in a formulation to produce these tangible results, as shown by the ingredient's positive effect on fatigue, focus, concentration, energy and alertness. Due to the extended half-life and slower absorption rate, *PUREENERGY* also offers the potential for a more moderated and gradual finish, potentially preventing the "crash" associated with caffeine products.

A Novel, Next-Generation Healthy and Functional Caffeine Solution

Over the past year, highly caffeinated energy beverages and products have been coming under increased regulatory and consumer scrutiny due to the possible risks of consuming high amounts caffeine. The U.S. Food and Drug Administration (FDA) announced in May 2013 that, in response to a trend in which caffeine is being added to a growing number of products, it would investigate the safety of caffeine in food products. The FDA recommends a daily caffeine limit of 400 milligrams a day, which equates to approximately four to five mildly caffeinated cups of coffee per day, but an increasing number of caffeinated products contain caffeine levels close to this limit in only one or two servings (Peterson 2013). Additionally, there has been some concern about caffeine consumption among those under 18 years of age, as the effect of highly caffeinated products on minors is unclear. Therefore, consumer and governmental groups have advocated for increased regulation of caffeinated products.

PUREENERGY offers the energy market a solution to address these growing concerns and identify solutions to reduce the caffeine content of its products while delivering the same product performance that consumers have come to expect. As demonstrated through a human clinical study, this ingredient delivers more caffeine to the blood over a longer period of time, extending the half-life of caffeine beyond the expected four to five hours, thus reducing the amount of caffeine needed in a supplement or beverage to provide the same energy boost delivered by traditional caffeine.

As a result, *PUREENERGY* can be used as an alternative to traditional caffeine in a range of energy beverages and products, including for energy boost, all day energy, pre-workout, weight management, focus and concentration and endurance training applications.

Conclusion

PUREENERGY is a novel ingredient that offers a healthy, functional caffeine solution, and more importantly, it offers the same energy-related benefits as traditional caffeine while enabling a reduction in the amount of caffeine needed in a formulation to produce those results expected by consumers. Considering that the energy product industry is facing increasing scrutiny from a range of stakeholders, there is a need for ingredients that offer companies in that industry an opportunity to reduce caffeine content in their product formulations while still delivering the same performance results. *PUREENERGY*, the efficacy of which has been demonstrated in both animal and human clinical studies, can play an important role in helping those companies meet consumer and regulatory expectations.

To learn more about *PUREENERGY* go to www.chromadex.com or contact us at ingredients@chromadex.com.

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