A bioavailable alternative to ordinary pterostilbene

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Pterostilbene is a powerful polyphenol and has beneficial properties as anti-aging ingredient through modulating the hallmarks of aging such as inflammation, oxidative damage, telomere attrition, and cell senescence [1]. It has been known to exhibit other health beneficial effects such as anti-atherosclerosis, anti-diabetic, anti-inflammatory, anti-obesity, antioxidant, cardioprotection, cognitive support, and neuroprotection as well [2]. An another well-known and structurally related pharmacological active polyphenol is resveratrol, but in various studies, pterostilbene was reported to be more bioavailable (80% compared with 20% in resveratrol) [1]. Pterostilbene has two methoxy (–OCH3) groups, which makes it more lipophilic and enhances its membrane permeability, bioavailability, and biological potency [1,2]. Caffeine is known for its positive effect on arousal and fatigue, perceptual processing, motor behavior, stress, learning and memory, and energy and performance in limited dose [3,4].

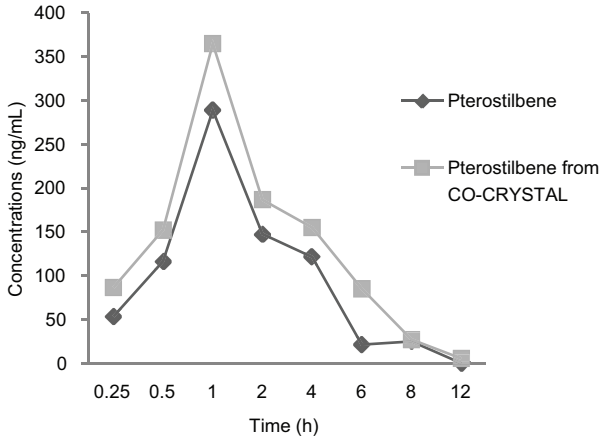
Laurus Labs introduced a combination of pterostilbene and caffeine as pterostilbene caffeine co-crystal (CO-CRYSTAL), a unique and patented ingredient that includes the benefits of both pterostilbene and caffeine. CO-CRYSTAL offers higher bioavailability and longer half-life and along with functional health benefits of pterostilbene, which include cognitive function, anti-oxidant activity, and heart health. Bioavailability and half-life of CO-CRYSTAL were tested in the pharmacokinetic study at Vimta Labs, a 'National Accreditation Board for Testing and Calibration Laboratories' accredited premier preclinical research facility in India. The objective of this study was to assess the comparative pharmacokinetic profile of pterostilbene and caffeine when administered alone as well as in a combined CO-CRYSTAL form in Sprague Dawley rats by the oral route.

In this study, rats were administered orally with pterostilbene at 15 mg/kg, caffeine at 11.29 mg/kg, or CO-CRYSTAL at a dose of 26.29 mg/kg (of which 15 mg/kg of pterostilbene and 11.29 mg/kg of caffeine) as a single dose through gavage. Following the dose administration, 250–300 μl of blood sample from each rat at 0 (before the dose), 0.25, 0.5, 1.0, 2.0, 4.0, 6.0, 8.0, 12.0, and 24.0 h after the dose was collected through retro-orbital plexus into prelabeled K_2EDTA-coated microcentrifuge tubes. The plasma from the blood samples was centrifuged and separated and was analyzed for test item levels by the liquid chromatography–mass spectrometry/mass spectrometry method. The mean plasma concentration versus time profile was used to calculate pharmacokinetic parameters using noncompartmental analysis tool WinNonlin Software V 6.2.1 (Pharsight Corporation USA, a Certara™ company). The protocol was approved by the Institutional Animal Ethics Committee of Vimta Labs, and all the ethical practices as laid down in the CPCSEA guidelines for animal care were followed during the conduct of the study.

The results suggest that peak plasma concentration (C_{max}) of pterostilbene in CO-CRYSTAL was 26% higher than pterostilbene alone. As shown in Fig. 1, the results validate that there were more pterostilbene from CO-CRYSTAL compared with pterostilbene alone over a 12-h period. The outcomes of the rat study ensure that CO-CRYSTAL has extended-release and sustained profile over pterostilbene alone. Caffeine also showed similar trends.

The area under the curve (AUC) is one of the most important parameters in pharmacokinetics as bioavailability generally refers to the fraction of

Figure 1



Peak plasma concentration of Pterostilbene.

Table 1 Comparative pharmacokinetic profile in Sprague Dawley male rats

Groups	$AUC_{(0-24)}$ (h*ng/ml)	$t_{1/2}$ (h)	Highlights
Pterostilbene in CO-CRYSTAL	1204.38	4	50% higher $AUC_{(0-24)}$
Pterostilbene alone	804.72	2	2 times longer half-life

AUC, area under the curve.

compound absorbed systemically, and this is often measured by quantifying the AUC. The mean extent of absorption (AUC_{0-24}) for pterostilbene in CO-CRYSTAL was increased by ~ 50%, as compared with pterostilbene alone (Table 1). Another factor, half-life, has important implications for dosing. If the half-life is too short, it may require more frequent dosing to maintain the desired exposures. The half-life of pterostilbene in CO-CRYSTAL was reported two times longer in comparison with pterostilbene alone (Table 1). Caffeine also showed similar trends.

The literature review revealed a study in healthy male adults (n = 12) where pterostilbene caffeine co-crystal delivered ~50% more total pterostilbene into the blood than pterostilbene alone and also showed no adverse events [5]. The results suggest that formulators have a choice to reduce the amount of pterostilbene needed in their formulations. This difference is also significant as pterostilbene acts as an anti-oxidant and is known to support heart health, cognitive function, healthy cellular ageing, and metabolism.

Pterostilbene is reported to exert anti-oxidant activity by scavenging reactive oxygen species, thus prevent oxidative stress and reactive oxygen species-induced cell damage [2]. It may stimulate the nuclear factor erythroid 2-related factor 2 (Nrf2)-mediated pathway and enhance the expression of several anti-oxidant enzymes, such as superoxide dismutase [6]. Pterostilbene is also known to inhibit inflammation by reducing the expression of different inflammatory mediators, such as cyclooxygenases, inducible nitric oxide synthase, interleukin-1β, nuclear factor κB, and tumor necrosis factor-α [2,6]. Co-crystalizing pterostilbene and caffeine modulates the bioavailability of the two components and provides a choice for a reduction in the amount of pterostilbene in different products without noticeably affecting the consumer experience.

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Conflicts of interest
There are no conflicts of interest.

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