Comparative Pharmacokinetics of Synthetic and Natural Pterostilbene

Sir,

Pterostilbene is a methylated stilbene molecule and has structural similarity with resveratrol (two hydroxyl groups of resveratrol are replaced with methoxy groups). In other words pterostilbene is a dimethylated derivative of resveratrol and reported more potent in some biological activates.[1] It is also found to be better absorbed and generally known as a 'better resveratrol'. Pterostilbene has been noted to reduce anxiety, blood glucose, blood pressure (diastolic and systolic) in hypercholesterolemic adults, inflammation and serum triglycerides.[2] It was also reported to reduce low-density lipoprotein cholesterol (57%) and improve in high-density lipoprotein cholesterol (73.1%) in diabetic rats.[3] Its effect on longevity and life extension, memory and learning, different solid tumors and antioxidant activity is well learnt.[4,5]

Pterocarpus marsupium (Malabar Kino Tree or Indian Kino Tree) is a well-known commercial source of pterostilbene but it is listed as a vulnerable plant in the IUCN red data list therefore many companies such as Laurus Labs Limited has opted synthetic route of manufacturing which also gives highest purity >99% and is equivalent to API quality. This controlled process avoids batch to batch variation therefore suitable for standardized formulations. Laurus Labs Limited also conducted pharmacokinetics study at National Accreditation Board for Testing and Calibration Laboratories (NABL) accredited premier preclinical research facility in India. The objective of this study was to assess the comparative pharmacokinetic of different forms of pterostilbene (synthetic and natural) in Sprague–Dawley rats at dose of 15 mg/kg by oral administration.

In this study rats were administered orally with test formulation – high pure (99% by high-performance liquid chromatography) synthetic pterostilbene manufactured by Laurus Labs Limited, and natural pterostilbene (Pterocarpus extract) as a single dose in a dose volume of 10 mL/kg through gavage. Approximately, 250–300 µL of blood sample was collected from each rat at predose and at 0.25, 0.5, 1.0, 2.0, 4.0, 6.0, 8.0, 12.0, and 24.0 h postdose via retro-orbital plexus in prelabelled K_2EDTA coated micro centrifuge tubes. The blood samples were centrifuged and separated plasma samples were assessed for the levels of pterostilbene by LC-MS/MS method. Mean plasma concentration versus time profile was used to calculate pharmacokinetic parameters by using noncompartmental analysis tool WinNonlin®Software V 6.2.1 (Pharsight Corporation, a Certara™ company). The protocol was approved by the Institutional Animal Ethics Committee of expiring lab vide Protocol No. PCD/Pharmacokinetic/01 (Version 2) and all the ethical practices as laid down in the CPCSEA guidelines for animal care were followed during the conduct of the study.

In female rats, peak plasma concentration (Cmax) and the extent of absorption (AUC_{0-24}) of synthetic pterostilbene were reported higher by 107% and 92% respectably when compared with natural extract. Results clearly indicated better pharmacokinetics profile of pterostilbene manufactured by synthesis than natural extract. Laurus Labs Limited also tested thermodynamic stability of both forms of pterostilbene and found synthetic more thermodynamically stable than natural. High purity seems to be reason of the better thermodynamic stability of synthetic pterostilbene. A clinical study published in 'Journal of Toxicology' has established safety of synthetic pterostilbene for use in humans up to 250 mg/day.[6] Other than *P. marsupium*, pterostilbene is reported in low quantities in a few plants such blueberries and grapes which otherwise may be used as a food product in a sustainable manner therefore manufacturing through synthetic route gives an alternative.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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