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New HPLC method to support Withaferin-A PK study

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In recent years, interest in Withaferin-A (the active component of Ashwagandha root extract) has been growing. It has been shown to have a range of therapeutic properties, including anti-inflammatory, hypolipidemic, antitumor, radiosensitizing, anti-angiogenesis, immunosuppressive and antioxidant effects. It has also shown antiproliferative activity against a number of different cancer cell lines. However, to date, there was no bioanalytical method suitable for the determination of plasma levels of the compound and so no pharmacokinetic data was available. A paper in *Bioanalysis* by researchers in the Clinical Pharmacology department at the Advanced Centre for Treatment, Research and Education in Cancer (ACTREC),Tata Memorial Centre (India), addresses this gap and provides a simple HPLC method for studying the pharmacokinetics of Withaferin-A in human plasma.

Lead author Vikram Gota explained that they overcame several difficulties in developing the method: “We observed interference with the Withaferin-A peak in the initial runs. We found it extremely difficult to resolve the two peaks with our initial chromatographic conditions. Therefore we resorted to a gradient method and after quite a few trials we succeeded in separating the two peaks.” The sample preparation method was a simple acetonitrile-based protein precipitation method. It proved quite difficult to get adequate recovery of the analyte, but through experimentation Gota and colleagues deduced that recovery was best with a sample:acetonitrile ratio of 1:2.

The method is now going to be utilized in a phase I clinical trial of Ashwagandha extract in patients suffering from high grade osteosarcoma. Study enrollment is complete and the pharmacokinetic samples will be analyzed shortly using the developed method.

As Dr Gota enthused, “We are in a position to conduct pharmacokinetic assessment of withaferin-A. We can now study the bioavailability of withaferin-A from different routes of administration. Since withaferin-A has several potential clinical utility, pharmacokinetic studies will aid in the development of optimal formulations for specific indications, depending on desired plasma levels, exposure, release characteristics and so on.”

The department of Clinical Pharmacology at the ACTREC is a young department comprising of two scientists and a scientific assistant. It was established in July 2008. Dr Gota’s group primarily works on drug development, with the main research areas being Phase I clinical trials and clinical

pharmacokinetic studies. Safety and pharmacokinetic studies of Curcumin and Ashwagandha extracts have been undertaken under the phase I drug development programme. ACTREC is also part of several multicentric pharma sponsored phase I clinical trials. The group is also interested in studying the pharmacokinetics of anticancer drugs, especially those with high interpatient variability, to understand the disposition of these drugs in their population which would help to develop pharmacokinetically guided dosing strategies.

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Sources: Pilot Study of Curcumin Formulation and Ashwagandha Extract in Advanced Osteosarcoma (OSCAT) ClinicalTrials.gov Identifier: NCT00689195; Patial P, GotaV. Rapid and sensitive method for determination of withaferin-A in human plasma by HPLC. *Bioanalysis* 3(3), 285–289 (2011).