

Metabolism after lung absorption in comparison to oral route. A key to interpret results of lung deposition studies based on PK

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As opposed to oral intake, drugs by inhalation do not pass hepatic metabolism first; their metabolic profile is quite peculiar, and more similar to transdermal or parenteral administration. Inhaler administration does not always allow optimal delivery at lung level, then drugs are partially absorbed in the gastro-enteric tract (mouth and/or lower segments). Hence, final PK and therapeutic results can be a complex mix of absorption routes. During development of new inhaler devices or drugs it is quite interesting to understand the mechanism of absorption in order to optimize the device performances and therapeutic results. In the present study 2 widely used steroids (budesonide, fluticasone propionate) and 2 beta agonist (formoterol, salmeterol) were administered by inhalation or orally or by mouth washing, and plasmatic PK profiles, including relevant metabolites, were determined (HPLC-MS/MS) to clarify peculiar pharmacokinetic aspects of each dosing route. The same experiments, were also performed with active charcoal blockade, to verify how this approach permits to measure specifically lung deposition. As expected, metabolism of all drugs was maximal after oral absorption, and minimal upon inhalation. So far, metabolic profiling proved to be a useful tool to understand absorption sites for new devices; charcoal blockade proved effective to selectively evaluate lung absorption even if some aspects, like enterohepatic recirculation inhibition, may complicate the results.

Biography

Dr. L. Silvestro graduated in Medicine in Turin (Italy) in 1984 and specialized in Pharmacology in 1988. From 1989 he is applying HPLC-MS in quantitation of bioanalytical samples as well as identification of drug metabolites. In 1996 he has co-founded 3S-Pharmacological Consultation & Research GmbH, a consultation company and CRO, in Germany and is still actively involved in the development of innovative analytical methods. From 1998 the company has expanded the activity in East Europe (Romania, Moldavia) creating an analytical laboratory in Romania (Bucharest). In his scientific activity he has contributed to more than 50 articles in international scientific journals.