Editorial Note on Absolute Bioavailability

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Absolute bioavailability compares the bioavailability of the active drug in systemic circulation following non-intravenous administration (i.e. after oral, buccal, ocular, nasal, rectal, transdermal, subcutaneous, or sublingual administration), with the bioavailability of the same drug following intravenous administration. It is the fraction of the drug absorbed through non-intravenous administration compared with the corresponding intravenous administration of the same drug. The comparison must be dose normalized (e.g., account for different doses or varying weights of the subjects); consequently, the amount absorbed is corrected by dividing the corresponding dose administered.

In pharmacology, in order to determine absolute bioavailability of a drug, a pharmacokinetic study must be done to obtain a plasma drug concentration time plot for the drug after both intravenous (and extravascular (non-intravenous, i.e., oral) administration. The absolute bioavailability is the dose-corrected area under curve (AUC) non-intravenous divided by AUC intravenous. The formula for calculating the absolute bioavailability of a drug administered orally is given below:

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\text{Absolute Bioavailability} = \frac{\text{AUC non-intravenous}}{\text{AUC intravenous}}
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Therefore, a drug given by the intravenous route will have an absolute bioavailability of 100% whereas drugs given by other routes usually have an absolute bioavailability of less than one. If we compare the two different dosage forms having same active ingredients and compare the two drug bioavailability is called comparative bioavailability.

Although knowing the true extent of systemic absorption (referred to as absolute bioavailability) is clearly useful, in practice it is not determined as frequently as one may think. The reason for this is that its assessment requires an intravenous reference; that is, a route of administration that guarantees all of the administered drug reaches systemic circulation. Such studies come at considerable cost, not least of which is the necessity to conduct preclinical toxicity tests to ensure adequate safety, as well as potential problems due to solubility limitations. These limitations may be overcome, however, by administering a very low dose (typically a few micrograms) of an isotopically labelled drug concomitantly with a therapeutic non-isotopically labelled oral dose (the isotopically-labelled intravenous dose is sufficiently low so as not to perturb the systemic drug concentrations achieved from the non-labelled oral dose). The intravenous and oral concentrations can then be deconvoluted by virtue of their different isotopic constitution, and can thus be used to determine the oral and intravenous pharmacokinetics from the same dose administration. This technique eliminates pharmacokinetic issues with non-equivalent clearance as well as enabling the intravenous dose to be administered with a minimum of toxicology and formulation. The technique was first applied using stable-isotopes such as C and mass-spectrometry to distinguish the isotopes by mass difference. More recently labelled drugs are administered intravenously and accelerator mass spectrometry (AMS) used to measure the isotopically labelled drug along with mass spectrometry for the unlabelled drug.

There is no regulatory requirement to define the intravenous pharmacokinetics or absolute bioavailability however regulatory authorities do sometimes ask for absolute bioavailability information of the extravascular route in cases in which the bioavailability is apparently low or variable and there is a proven relationship between the pharmacodynamics and the pharmacokinetics at therapeutic doses. In all such cases, to conduct an absolute bioavailability study requires that the drug be given intravenously.

Intravenous administration of a developmental drug can provide valuable information on the fundamental pharmacokinetic parameters of volume of distribution and clearance.