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**Bioavailability** is the extent to which a drug or any other substance is taken up by a specific tissue or organ after administration; the proportion of the dose of a drug that reaches the systemic circulation intact after administration by a route other than intravenous. The term holds its meaning for most of the drugs particularly the ones which fall under biopharmaceutical classification system (BCS) class IV.

Market driven information on natural products especially polyphenolic phytochemicals is widespread and has further fostered their use in daily life. In most countries there is no universal regulatory system that ensures the safety and activity of phytopharmaceuticals (Bhattaram et al., 2002). Nevertheless, in recent years, data on evaluation of the therapeutic and toxic activity of herbal medicinal products is becoming available. Further, the advancement in analytical technology tools, is presenting an ever-increasing list of putatively active constituents, and establishing the pharmacological basis for efficacy of these phytochemicals is a constant challenge. However, evidence-based proof of the efficacy of these agents is still frequently lacking. Latter being assigned to the fact that most of the polyphenols from phytopharmaceuticals have lower intrinsic activities or bioavailabilities as a result of poor absorption from the intestine, extensive metabolism following absorption, or a combination thereof (Greger, 2001). In general, the metabolites that are found in blood and target organs that result from digestive or hepatic enzymes may differ from the native substances in terms of biological activities. Therefore, extensive knowledge of the bioavailability of polyphenols is necessary if their health effects are to be clearly elucidated and pharmacologically enhanced (Williamson and Manach, 2005).

Most of the polyphenols present in food are in the form of esters, glycosides, or polymers, hence they are not absorbed in their natural form (Rapaka and Coates, 2006). During the course of absorption, polyphenols are conjugated in the small intestine, later in the liver, and possibly in the kidneys too. The conjugation of polyphenols is a metabolic detoxification process that restricts their potential toxic effects and facilitates their biliary and urinary elimination by increasing their hydrophilicity.
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Lack of bioavailability including low plasma concentration also makes it difficult to correlate in vitro and in vivo mechanisms of action of these agents. Therefore, poor bioavailability, low potency and lack of exclusive patent protection are major challenges associated with developing natural polyphenols into "conventional pharmaceuticals" (Manach et al., 2005).

In general, the body treats consumed polyphenols as xenobiotics, or foreign substances, similar to most pharmaceuticals and these are subjected to the same protective xenobiotic-metabolising and efflux mechanisms. This often results in major changes in biological activity and usually greatly increased rate of excretion from the body.

Presumably, if the polyphenol overcomes the defence mechanisms of the gut and the liver, it will enter the systemic circulation and be distributed by the bloodstream to the other major organs of the body and possible site(s) of action. It is assumed that the blood concentration is an acceptable index for the concentration or exposure at the site of action. It is apparent that there is a complex interplay between the physicochemical properties of polyphenols and the processes of metabolism and active transport that control the extent of exposure of the bioactive body site(s) to these compounds. From experience with pharmaceuticals, it would appear feasible to manipulate these processes to obtain an improvement in bioavailability and greater exposure at the site(s) of action, to produce appropriate health benefits from these polyphenols.

Polyphenols can pass with ease through the pores of the capillaries of organs such as the heart and lungs, but not the brain. The brain capillaries are surrounded with a protective cellular sheath of glial cells (the so-called blood brain barrier; BBB) resulting in permeability characteristics more closely resembling those of tightly bound tissue cell walls. To gain access to the brain, a polyphenol must be highly lipid-soluble, or subject to an active uptake by various transport processes. In addition, the BBB contains a number of ABC transporter efflux pumps, which are involved in reducing the penetration of xenobiotics into the brain with an aim to protect it from neurotoxins (Mizuni et al., 2003; Youdim et al., 2004).