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LAY ABSTRACT

The estimated daily dietary intake of flavonoids, polyphenolic compounds, and related biofactors in the United States is in the range of one to three grams per day (e.g. originating from cereals, tubers, roots, nuts, methods vegetables, and fruits, and beverage components: cocoa, cola, coffee, wine, tea, and bacterial fermentation products). These “other” nutrients are commonly referred as the flavonoids or bioflavonoids, although such terms used generically often include other broad classes of compounds. About 4000 compounds have now been identified (mostly from plants and fermentation) that seem to have certain health benefits. Early clues to the health benefits of flavonoids evolved from studies of the "French paradox.”, i.e. that the French eat high fat diets and generally have higher cholesterol levels and blood pressures than do Americans; yet, are 1.5-2.5 times less likely than Americans to die of coronary heart disease. Now, there is considerable body of growing clinical and descriptive literature that given compounds in wine (also tea and chocolate) elicit effects such as vasodilatation (can affect blood pressure), blood clotting (thrombi formation- important to stroke and initiation of heart attacks), and possibly energy flux. However, there are fewer well-articulated reports focused on mechanisms of action, paticularly given the number of claims that are made regard various so-called, non-nutrient factors in foods. Most often the health effects are articulated in global terms (e.g. the food or component seems to have anti-oxidant properties) or are defined in the context of some arbitarially selected and operational clinincal measurement.

The real challenge lies not defining what these benefits are, but developing the approaches that provide mechanistic insight. As a model, we will address the mechanism of action of pyrroloquinoline quinone (PQQ). PQQ was discovered in 1979 and is found in virtually all foods. Because PQQ-deprived mice display abnormalities associated with compromised early development (based on our previous work), PQQ has been described as a new vitamin (e.g. <http://www.brain.riken.go.jp/labs/mdmd/pqq/index-e.html>). Further, PQQ has been linked with an enzyme important to the degradation of the amino acid lysine as a cofactor; however, we have questioned this possibility. Rather, we hypothesize that the action of compounds, such as PQQ, are more complex and interact directly with cell signaling pathways that are linked to cell organization and the genesis of specific organelles, such as the mitochondria. Using lysine as an example, lysine is catabolized in mitochondria and its catabolism is directly dependent on mitochondrial amount, rather than a defect in a given enzymatic, PQQ-requiring, step. Accordingly, we would hypothesize that the effects of PQQ and other similar compounds act in metabolic homeostatic pathways important to cellular organelle function and regulation of formation.