Evaluation of Dietetic Product Innovations: The Relative Role of Preclinical and Clinical Studies

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There is great potential for nutritional interventions in early life to result in improved health outcomes. This is based on the large body of evidence of both experimental and epidemiological studies showing that good nutrition during pregnancy and early life may enhance neurodevelopmental outcomes, reduce the prevalence of allergies, improve body composition and may ultimately reduce the prevalence of chronic diseases. With such promise, the evaluation of nutritional interventions, which often take the form of specialized products or food innovations, is of paramount importance. The scope of this paper is to review the relative role of preclinical and clinical studies in the assessment of both safety and efficacy for new food innovations.

Role of Preclinical Studies

There is a vast range of preclinical studies that are relevant to the assessment of food innovations, and these extend from cellular studies to studies with experimental animals. There are many immortal cell lines available to screen bioactive molecules or fractions that are dietary components. Such assays can happen quickly, and it is possible to investigate or screen multiple bioactive compounds in specific cell types and gain insight into possible mechanisms of action. However, it is difficult to assess the relevance of such studies to women and children when the putative bioactive compounds are included as part of a dietary regimen. Such cellular studies provide an important first-pass evaluation to select bioactive molecules (for example, protein or lipid fractions) worthy of further investigation.

Animal models offer greater diversity and specificity of effect than is possible in cell studies, although they are more time consuming and resource intensive. Numerous models are available to assess
the effects of dietary components in situations relevant to the human target group. For example, the (rat) pup-in-a-cup model aligns well with the neural and gastrointestinal maturity of a very preterm infant. The intricacies and complexities of the model in many ways are not surprising as the rat pup requires some of the extra supports (thermoregulation) that would also be required in a neonatal intensive care unit. More commonly, however, animal models are based on genetic predisposition, such as Brown Norway rats, which are allergy prone, and offer a model of an allergy-sensitive human. Animal models are useful in identifying target outcomes for human trials. It is possible to harvest organs and so provide information about how nutrients or bioactive ingredients are acting. There are, however, some dangers in overextrapolation to humans as effects in animal models are not always translated to the human situation. For example, conjugated linolenic acid has a long history of improving growth and body composition in animal studies, and is widely used in the pig industry for this reason. However, human studies have consistently failed to demonstrate the positive effects observed in other animals.

One of the most important roles of animal studies is safety evaluation. Safety in experimental animals is commonly assessed using a toxicological approach, where the innovative ingredient is fed at concentrations well beyond what would normally be expected in typical dietary patterns. This allows the determination of tolerable safe levels and gives an indication of the safety buffer in relation to usual dietary intake.

**Role of Clinical Studies**

The ultimate evaluation of food innovations are through well-designed and appropriately powered clinical trials. Although often complex, time consuming and expensive, clinical trials provide the most robust and directly relevant answers regarding the efficacy and safety of new food or supplement innovations. It is for this reason that major randomized controlled trials are not generally undertaken without a body of congruent evidence from preclinical studies and other human biochemical or physiological studies that all point towards a safe and efficacious dietary intervention. As clinical trials are never designed to investigate harm, safety evaluation is traditionally through the monitoring of adverse events, while the key efficacy outcome generally forms the primary research question.