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The search for a new paradigm to study micronutrient and phytochemical bioavailability: From reductionism to holism ☆

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ABSTRACT

The study of micronutrient and phytochemical (MaP, *i.e.,* non-energy nutrients) bioavailability has been mainly studied through a reductionist and pharmacological approach. This has led to associate one health effect to one MaP. However, human interventional studies have given conflicting and disappointing results about MaP supplementation. This is because the health effect is the result of the synergetic action of numerous MaPs supplied by foods and/or diets at nutritional doses. A food is not a drug. Therefore, there is a need for more holistic approach to study MaP bioavailability, then their health effect to achieve general recommendations. This paper aims to hypothesize for such a paradigm shift in this topic and to lay new foundations for research in MaP bioavailability.

Introduction

Why to study micronutrient and phytochemical (MaP, *i.e.*, non-energy nutrients) bioavailability? Indeed, first, there is an important issue that has not yet been answered: do differences in MaP bioavailability and release kinetics reflect significant differential health effects in humans, especially on a long term? To the best of our knowledge, today, one cannot precisely answer this question. The only studies are bioavailability and interventional studies generally led in healthy humans unraveling different absorption fractions or bioavailability percentages according to food sources with or without phytates or fibre [1–7]; but such differences were not related with health effects on a long term. Moreover, what about non-micronutrient phytochemicals? There are several hundreds phytochemicals (*e.g.* polyphenols and carotenoids), and it is not possible to study them individually.

The role of the food matrix is a second important issue: what is its role in MaP health effects? Results tend to show that MaP bioavailability cannot be considered separate from the food matrix [4,6,7] and its effect on the maintenance of human physiological functions, e.g. vitamin B12 and β-carotene are absorbed more efficiently in situation of body deficiency [8,9].

Third, each individual is unique; therefore, how can scientific results about MaP bioavailability be extrapolated into general recommendations for preventive nutrition?

These considerations open a real complexity where MaPs may occupy a negligible place. Indeed, behind the complexity, the variability of the matrix and the inherent variability of individuals present difficulties. Matrix, e.g., a plant-based product considered as a diversified source of MaPs, is highly dependent on variety, growing conditions and the processes used to transform it. Moreover, individuals are unique. An individual may belong to different categories based on age, gender, anthropometric parameters, and cultural or socio-economic criteria, among others. Using a biological background, genetic criteria – polymorphisms and epigenetics – can differentiate one individual from another, and under different environmental conditions, these genetic criteria can express differences within an individual.

Conversely, the maintenance of important biological functions in an equilibrated state, e.g., via preventive nutrition, is difficult to characterize and cannot be defined by the few biomarkers currently used. However, experience shows that it is always possible to conduct research in the plant MaP field in relation to the effect of a given MaP on a health biomarker. On the contrary, it seems almost impossible to design a research project considering the complexities described above and leading to applicable results that satisfy societal issues as well as questions arising from the agro-food industry and national and international agencies responsible for regulating food issues and populations' diets.

This paper aims to hypothesize and search for a paradigm shift in this topic that will lay new – and complementary – foundations for research in MaP bioavailability. Indeed, it appears that holistic approaches (e.g., using metabolomics and data mining, and/or

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