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Nutrient essentiality revisited

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A B S T R A C T

With increased understanding of the complex roles nutrients play within metabolic pathways, the purpose of this contribution is to explore the rationale for expanding the definitions and criteria for nutrient essentiality. A further objective was to develop three case study scenarios to probe issues surrounding the definition of essentiality using dietary fibre, plant sterols and polyphenols. Current definitions and criteria for "essentiality" were reviewed through an environmental scan of the scientific literature. Additionally, international regulatory bodies were asked whether the terms "nutrient" and/or "essential nutrient" are regulated in their respective jurisdictions. Regulatory bodies including the EFSA, the US FDA, HC and FSANZ were found not to currently possess regulated definitions for the term "essential nutrient". Case studies examining fibre, plant sterols and polyphenols served as a means of presenting evidence for expanding the list of functional food constituents regarded as meeting criteria for essentiality. For each example, certain instances applied where these case study bioactives met criteria of essentiality. Thus, in order to reflect advances in current science, a series of non-classical compounds known to have bioactivity should be considered for their potential essentiality under certain situations.

Contents

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1. Introduction

From a clinical perspective, evidence for nutrient essentiality dates as far back as the 1670s when a British physician, Sydenham, reported observations that a tonic of iron filings produced improved clinical responses in anaemic patients (Harper, 1993). However, it was not until 1906 that essentiality for life, and of a specific organic molecule, was established when Willcock and Hopkins showed that a supplement of the amino acid tryptophan prolonged survival in mice given a tryptophan-deficient diet (Harper, 1993). By 1950, some 35 nutrients, including various essential fatty acids, amino acids, vitamins and minerals, had been identified as essential (Harper, 1999). For the most part, single nutrients were chemical compounds with a definable chemical structure, which may occur in clusters. In general terms, a nutrient was deemed essential when its removal caused a state of metabolic and/or clinical hypofunction, which could be normalized when that nutrient was added back in the diet. More recently, it could be argued that the notion of essentiality has been broadened. A new definition is one which goes beyond the level needed for minimal support for normal growth, development and maintenance of health to affording a level of protection against chronic degenerative diseases, if consumed beyond this minimal requirement. Therefore, the objective of this paper is to review current definitions and criteria for nutrient essentiality, and to present three case studies with a supportive rationale for why some functional food constituents should be re-evaluated in terms of their essentiality for specific populations and/or physiological conditions.

2. Methods

An environmental scan of the literature was conducted January 2013 using combinations of the terms "criteria", "definition"; and "essential nutrient", "nutrient essentiality", "conditionally essential nutrient" within the search engines PubMed and Google Scholar. No limits on the year of publication or language were used. Three contemporary nutrition textbooks were also consulted (Erdman, Macdonald, & Zeisel, 2012; Shils, Olson, Shike, & Ross, 1999; Whitney & Rolfes, 2002). Hand searching within the reference lists of textbooks and articles identified from the environmental scan was also conducted to locate further definitions and identify criteria for the aforementioned terms.

Additionally, inquiries were forwarded to international regulatory bodies including, the European Food Safety Authority (EFSA), the U.S. Food and Drug Administration (US FDA), Health Canada (HC), and Food Standards Australia New Zealand (FSANZ), as well as international organizations including the Institute of Medicine (IOM) and the Australian Government's National Health and Medical Research Council (NHMRC), asking whether the terms "nutrient" and/or "essential nutrient" are regulated in their respective jurisdictions.

Three case studies were also developed for the functional food constituents fibre, plant sterols, and polyphenols, components not currently considered as essential nutrients but possessing desirable health effects. A draft report was then reviewed and discussed by a group of international nutritional science experts.

3. Results

Based on current definitions, a "nutrient" is first and foremost considered a component of food useful to an organism for its growth, or functioning. More pragmatically, a nutrient is one for which a 'Nutrient Reference Value' (NRV) exists, the NRV provides a level to meet requirements for health (Codex Alimentarius Commission, 1985). Nutrients tend to belong to one of six broad categories: minerals, water, carbohydrates, lipids, proteins and vitamins; and they provide energy or structural materials and regulating agents to support growth, maintenance and repair of the body's tissues as well as being needed for growth, development, and maintenance of a healthy life. A deficit of a nutrient will cause characteristic biochemical or physiological changes to occur. The intake of certain nutrients at a particular level may reduce the risk of some diseases (Codex Alimentarius Commission, 1991; European Commission, 2006; Whitney & Rolfes 2002).

"Non-nutrients" tend to be defined as food constituents which do not fit in the six aforementioned categories, but contribute in a general manner to body functioning. This category can include phytochemicals, pigments and additives (Whitney & Rolfes, 2002) and generally speaking do not possess defined NRVs. The European Commission (EC) Regulation (No. 1924/2006) defines "other substance", in the context of health claims, as any substance other than a nutrient which has a nutritional or physiological effect (European Commission, 2006).

Regulatory bodies including the EFSA, the US FDA, HC and FSANZ do not currently report formal definitions for the term "essential nutrient" and generally refer to standard

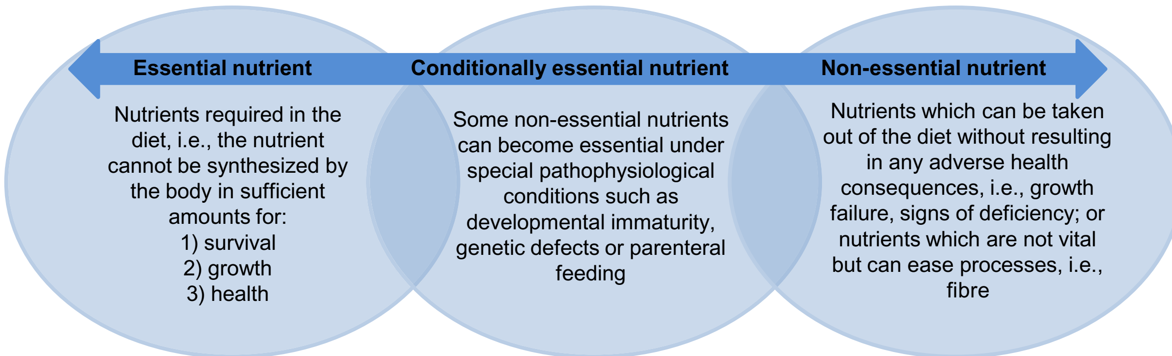

Fig. 1 – The continuum of nutrient essentiality.

definitions found in appropriate textbooks. Definitions for the concept and categorization of "essential nutrient", "non-essential nutrient", and "conditionally essential nutrient" collated from various documents and textbook sources can be represented as a continuum (Fig. 1) (Codex Alimentarius Commission, 1991; Harper, 1999; Whitney & Rolfes, 2002).

Other terms have been proposed to describe food constituents which may not be considered "essential" in the traditional sense, yet provide additional health benefits. These terms include "lifespan essential" in reference to polyphenols (Williamson & Holst, 2008); "physiological modulators", originally proposed for antioxidant vitamins, but also applicable to many other food constituents (Olson, 1996); and "desirable" (Steele, 1993). While the description and concept for these food constituents differ across sources, they all refer to the potential of chronic degenerative disease risk reduction. The appearance of these proposed terms in the literature suggests that there is an opportunity to review the working definitions of nutrients and of essentiality in light of advances in science. The following three case studies serve as a means of presenting a rationale for expanding the definitions and criteria for nutrient essentiality.

4. Case studies

4.1. *Case study # 1: fibre*

Dietary fibre has been defined by Codex as: ". . .carbohydrate polymers with ten or more monomeric units, which are not hydrolysed by the endogenous enzymes in the small intestine of humans and belong to the following categories: Edible carbohydrate polymers naturally occurring in the food as consumed; carbohydrate polymers which have been obtained from food raw material by physical, enzymatic or chemical means and which have been shown to have a physiological effect of benefit to health as demonstrated by generally accepted scientific evidence to competent authorities; synthetic carbohydrates polymers which have been shown to have a physiological effect of benefit to health as demonstrated by generally accepted scientific evidence to competent authorities" (Codex Alimentarius Commission, 2008).

While debate exists over whether fibre is indeed a nutrient (Marlett, 1993), the EC Regulation (No. 1924/2006) considers fibre to be a nutrient in relation to health claims (European Commission, 2006). Fibre is generally addressed in dietary guidelines and recommendations but it is not considered essential for growth, development or survival; however, we propose that certain fibres could be considered essential for specific populations or uses, as fibre has been linked to a large number of health benefits. In fact health claims for various fibres, such as beta-glucans, arabinoxylan, wheat bran, psyllium and resistant starch, have been approved in relation to promotion of regularity/laxation, reduction of blood cholesterol, and reduction of post-prandial glycaemic responses in various jurisdictions including the European Union (EU), the United States (US), Canada and Australia/New Zealand (Table 1). Specific populations which could benefit from classifying certain fibres as essential include those with high blood cholesterol, or those who could benefit from reduction of post-prandial glycaemic responses. As such, the term essential deserves additional consideration in the context of varying physiological circumstances.

From another perspective, the sub-group of fibres considered to be prebiotics could be considered essential as food for gastrointestinal microbiota, which are themselves a vital component of normal human physiology. Prebiotics have been defined as "a selectively fermented ingredient that results in specific changes, in the composition and/or activity of the gastrointestinal microbiota, thus conferring benefit(s) upon host health" (Gibson et al., 2011). The composition and activity of gastrointestinal microbiota are of interest since perturbed gastrointestinal microbiota balance has been increasingly associated with various disease states including, celiac disease, colon cancer, Type I and II diabetes, inflammatory bowel disease, irritable bowel syndrome, antibiotic-associated diarrhea, necrotizing enterocolitis and obesity (Binns, 2013).

In summary, fibre could be considered nominally essential in at least two different scenarios: 1) for specific subpopulations with certain conditions such as high cholesterol who could benefit from the cholesterol-lowering properties of specific fibres such as beta-glucans, and 2) in the form of prebiotics as food for gastrointestinal microbiota.

4.2. *Case study # 2: plant sterols*

Plant sterols (PS) possess chemical structures and biological functions similar to cholesterol but are found in plants

Table 1 – Summary of approved fibre-related health claims in the European Union, the United States, Canada and Australia/New Zealand.

Food or food constituent	Health relationship
Alpha-cyclodextrin	• Reduction of post-prandial glycaemic responses (European Commission, 2013)
Arabinoxylan produced from wheat endosperm	• Reduction of post-prandial glycaemic responses (European Commission, 2012)
Barley and oat beta-glucan	• Reduction of blood cholesterol (European Commission, 2011a, 2011b; Food Standards Australia New Zealand, 2013b; Health Canada, 2010a, 2012) • Reduction of dietary and biliary cholesterol absorption (Food Standards Australia New Zealand, 2013b) • Reduction of post-prandial glycaemic responses (European Commission, 2012) • Maintenance of normal blood cholesterol concentrations (European Commission, 2012) • Potential reduction in risk of coronary heart disease (Electronic Code of Federal Regulations, 2008)
Barley grain fibre	• Increase in faecal bulk (European Commission, 2012)
Coarse wheat bran	• Promotion of laxation/regularity (Canadian Food Inspection Agency, 2014)
Dietary fibre	• Contribution to regular laxation (Food Standards Australia New Zealand, 2013b)
Fibre-containing grain products, fruits, and vegetables	• Potential reduction in risk of some cancers (Electronic Code of Federal Regulations, 1993a)
Fruits, vegetables, and grain products that contain fibre, particularly soluble fibre	• Potential reduction in risk of coronary heart disease (Electronic Code of Federal Regulations, 1993b)
Glucomannan (konjac mannan)	• Reduction of body weight (European Commission, 2012) • Maintenance of normal blood cholesterol concentrations (European Commission, 2012)
Guar gum	• Maintenance of normal blood cholesterol concentrations (European Commission, 2012)
Hydroxypropyl methylcellulose	• Reduction of post-prandial glycaemic responses (European Commission, 2012) • Maintenance of normal blood cholesterol concentrations (European Commission, 2012)
Lactulose	• Acceleration of intestinal transit (European Commission, 2012)
Oat grain fibre	• Increase in faecal bulk (European Commission, 2012)
Pectins	• Reduction of post-prandial glycaemic responses (European Commission, 2012) • Maintenance of normal blood cholesterol concentrations (European Commission, 2012)
Psyllium	• Promotion of laxation/regularity (Canadian Food Inspection Agency, 2014) • Reduction of blood cholesterol (Health Canada, 2011) • Potential reduction in risk of coronary heart disease (Electronic Code of Federal Regulations, 2008)
Resistant starch	• Reduction of post-prandial glycaemic responses (European Commission, 2012)
Rye fibre	• Changes in bowel function (European Commission, 2012)
Wheat bran fibre	• Reduction in intestinal transit time (European Commission, 2012) • Increase in faecal bulk (European Commission, 2012)

(Berger, Jones, & Abumweis, 2004). Dietary sources of PS include vegetable oils, nuts, seeds, and grains (Berger, Jones, & Abumweis, 2004). The cholesterol-lowering effect of PS is well established and health claims for this food–health relationship have been approved in various jurisdictions around the world including the EU, the US, Canada and Australia/New Zealand (Table 2). An intake of 1–2 g PS/day is required to produce an inhibitory action on cholesterol absorption and results in a decrease in circulating low-density lipoprotein cholesterol (LDL-C) concentrations of 10–15%; however, current dietary intakes remain less than 300 mg/day (Jones & Varady, 2008). Based on this rationale, Jones and Varady previously suggested that PS be defined

Table 2 – Summary of approved health claims related to plant sterols and plant stanols in the European Union, the United States, Canada and Australia/New Zealand.

- Contribution to the maintenance of normal blood cholesterol levels (European Commission, 2012)
- Reduction of dietary and biliary cholesterol absorption (Food Standards Australia New Zealand, 2013b)
- Reduction of blood cholesterol (European Commission, 2009, 2010a, 2010b; Food Standards Australia New Zealand, 2013b; Health Canada, 2010b)
- Potential reduction in risk of coronary heart disease (Electronic Code of Federal Regulations, 2005)

as essential under physiological situations where body cholesterol pools are high (Jones & Varady, 2008). In those situations, PS are required to prevent the over-absorption of biliary and dietary cholesterol, thus protecting against vascular disease and optimizing health through that action (Jones & Varady, 2008). As such, the absence of PS results in distorted cholesterol metabolism through hyper-absorption, meaning that these compounds can be deemed essential.

It has been estimated that our ancestors in the Miocene era may have consumed approximately 1 g of PS daily (Jenkins et al., 2003), while as mentioned above current intakes of PS are less than 300 mg/day. At 1 g of PS per day, cholesterol absorption is suppressed at higher amounts; accordingly, disinhibition would result in hyper-absorption of cholesterol and thus increased risk of cardiovascular disease. In light of this information, it could be suggested that current North American diets are deficient in PS, thus providing further rationale for considering PS an essential nutrient, particularly for those genetically predisposed to hyper-absorption of cholesterol.

4.3. *Case study # 3: polyphenols*

Polyphenols are antioxidants which possess phenolic rings and are widely found in plant foods (Williamson & Holst, 2008). The potential human health benefits in relation to polyphenols have been of particular interest in the past 10–15 years; much research has been conducted on the effect of polyphenols and gut microbiota, and on risk factors for cardiovascular disease, obesity and diabetes (Tomás-Barberán & Andrés-Lacueva, 2012). Based on in vitro evidence health benefits for polyphenols exist, and thus a potential essential role; however, the purported health claims for the effect of polyphenols in vivo require further investigation. To date, the EU has only approved one health claim related to polyphenols, specifically, olive oil polyphenols contributing to the protection of blood lipids from oxidative stress (European Commission, 2012). Health claims for polyphenols have not yet been approved in the US, Canada or Australia/New Zealand. A consideration in evaluation of polyphenols in relation to human health is whether direct antioxidant effects exist in humans. For example, an ISLI Europe Functional Foods Expert Group investigated the antioxidant effect of polyphenols for cardiovascular health in humans (Hollman et al., 2011). This ILSI Expert Group found that retrospective studies showed differences in biomarkers of lipid peroxidation (F2-isoprostanes and oxidized LDL-C), and measures of total antioxidant capacity between cardiovascular disease patients and healthy controls; however, a causal relationship could not be found between these same biomarkers and cardiovascular health in prospective studies (Hollman et al., 2011). This group concluded that a direct antioxidant effect of polyphenols in vivo was unlikely since their levels in the systemic circulation and tissues are lower compared to those of other antioxidants, and extensive metabolism after consumption results in a lowered antioxidant activity (Hollman et al., 2011). On these bases, it would appear further data are required before polyphenols could be deemed as essential.

4.4. *Case studies summary*

While fibre and PS may not be considered essential in the traditional sense, i.e., for growth, development or survival, the argument presented here suggests that these dietary constituents could be considered essential for specific populations and/or physiological conditions. In the case of polyphenolic compounds, data are currently less compelling in suggesting that these compounds be defined as essential. Further research with specific individual phenolic constituents, together with reasonable physiological doses are required in order to ascertain whether any essentiality exists for molecules falling into this category. These examples broaden our lens through which the working definitions of essential nutrients might be placed in a wider perspective.

A consideration in investigating the essentiality of a food constituent is what type of evidence is required to establish essentiality. Based on the above case studies, approved health claims could be a source for identifying functional food constituents with established health benefits; if this is the case, evidentiary requirements for food health claims could also be used to establish essentiality for those bioactives within our food systems. Guidance for food health claim submissions from the EU (EFSA Panel on Dietetic Products, Nutrition and Allergies, 2011), the US (U.S. Food and Drug Administration, 2009), Canada (Health Canada, 2009), and Australia/New Zealand (Food Standards Australia New Zealand, 2013a) all emphasize the use of human studies, and while animal and/or in vitro studies can be submitted for a food health claim dossier, these studies can generally only be considered as supportive evidence due to scientific uncertainties in the extrapolation of data from non-human studies to humans. In terms of the types of human evidence required in the evaluation of health claims, both observational and interventional studies can be useful in the context of the totality of evidence; however, only prospective studies should be included in food health claim submissions, since retrospective studies cannot be used to establish a causal relationship. As a case in point, the polyphenol case study above showed that the ILSI Expert Group found changes in markers of lipid peroxidation in retrospective studies, while the same was not found for prospective studies (Hollman et al., 2011). In summary, in determining the type of evidence required for establishing essentiality of functional food constituents, human data from prospective studies need to be considered.

5. Conclusion

In nutritional science, the terms “nutrient” and “essential” possess specific meanings and applications, both involving the translation of scientific knowledge to policy and practice. While nutrients are food components, their pragmatic definition has been associated with a sense of essentiality. In the past, recognition that a nutrient plays an essential role has been linked to its ability to prevent a specific deficiency disease or whether it can be synthesized by the human body. This review has argued that the definition of essential nutrients needs to be expanded to reflect advances in scientific knowledge. A broader appreciation of functional food components means that additional dietary constituents could be considered essential nutrients. The essentiality of a nutrient can thus be assessed with a wider view to why it is essential or what it is essential for. Case studies presented in this paper provide a rationale for expanding definitions and criteria for nutrient essentiality. Furthermore, the arguments presented in this paper for fibre, PS and polyphenols to be considered as essential opens the door for further scientific investigation into the potential essentiality of many additional functional food components, some of which have been referred to as "bioactives" – "essential and non-essential compounds such as vitamins or polyphenols that occur in nature, are part of the food chain, and can be shown to have an effect on human health" (Biesalski et al., 2009).

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