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Should Probiotics be considered as Vitamin Supplements?

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Definition of Probiotics

The definition of probiotics that is widely accepted [1] describes probiotics as "living microorganisms that on ingestion in certain numbers exert health benefits beyond inherent basic nutrition". The important aspects of the definition of probiotics are that probiotics need to be a live microorganism, such as yeast or bacteria, and probiotics need to have a health benefit. Therefore, these microorganisms need to have undergone *in vitro* and experimental studies in order to be properly named a beneficial strain of probiotics, and to prove its health benefit and safety. An extensive body of evidence demonstrates that probiotics have a clinical use and can be recommended in the treatment of certain diseases, such as antibiotic induced diarrhoea, infectious diarrhoea of adults and children and prevention of atopic eczema and cow's milk allergy [2]. Naming the species is important are there are multiple microorganisms that can be classified under the general term "probiotics" yet each may have a different effect on metabolism. Thus, knowledge of which organism is used is crucial in designing experiments or making claims of function. As they become more popular and easily available, we need specific knowledge of function. New sequencing techniques that seem to evolve year by year are revealing more and more species of bacteria in the human body that previously we were unaware of.

Microbiome

The Microbiome is a heterogeneous system consisting of millions of microbes that share our body space, leading some to suggest it is a "newly discovered organ". It has been shown that the interaction between the microbiome and its host play a major role in immune modulation, as well as in several metabolic functions. Colonization of the gut starts before birth, and is dependent on known factors such as mode of delivery, type of feeding and gestational age. Disequilibrium between the beneficial and pathogenic bacteria of the gut will lead to alteration in the defence barrier mechanisms and in immune functions, and is associated with a number of acute and chronic conditions, such as sepsis, NEC, inflammatory bowel disease (IBD), type 2 diabetes, allergy and obesity. Supplemental bacteria have been demonstrated to modulate a variety of disorders in children and adults, including: inflammatory bowel diseases [3]; bowel cancer [4], ulcerative colitis [5]; irritable bowel syndrome [6], obesity [7], cholesterol levels [8] and diarrhea, secondary to oral antibiotics [9].

Microorganisms in the Gut and its Function

Bacteria in the lumen of the digestive system can be classified accordingly: (a) beneficial; (b) potentially pathogenic; and (c) pathogenic bacteria. Probiotics are within the pool of beneficial bacteria. Two of the most common beneficial bacteria are *Lactobacillus sp.* and *Bifidobacter sp*. With respect to the gastrointestinal environment, the beneficial microflora has three important functions: metabolic, trophic and protective [10]. For example, bacteria produce short-chain fatty acids and vitamins and participate in mucosal epithelial cell proliferation and differentiation.

Probiotics and Vitamin Production

Vitamins are essential micronutrients that are necessary for vital reactions in all living cells. We humans are incapable of synthesizing most vitamins in amounts required to meet our physiological needs, and so they consequently have to be obtained exogenously. One of the multiples benefits that probiotics have is the capacity to synthesize vitamins. We have known for some time that commensal bacteria produce vitamins, particularly B vitamins, and play a major role in meeting our needs for these essential nutrients. What we now have to consider with the advent of probiotics as a player in achieving optimal health is how much of a role do they play as vitamin supplements? This is uncharted territory and indeed, while we know vitamin K is produced by bacteria in the gut, recent evidence indicates vitamin D is as well [11]. *In vitro* and studies in humans have documented the capacity of some probiotic strains to synthesize vitamin K, folic Acid, vitamin B_2 and B_{12}. As we are able to identify more and more strains in the human microbiome, it may be only a matter of time until we identify new species that produce all the known vitamins, and may I daresay newly discovered vitamins as well!

To remind you: There are two different forms of vitamin K, *Phylloquinone* or vitamin K_1, present in all photosynthetic plants and *menaquinons,* or Vitamin K_2 which is primarily of bacterial origin [12]. It has been demonstrated *in vitro* that strains of *Lactobacillus* produce high levels of folate (about 100 µg/L). The same is possible with *bifidobacteria* strains, which may contribute to folate intake, due to the synthesis and secretion of folates in the human intestine by *bifidobacteria* [13]. It has been demonstrated in human and piglet that the quantity of folate produced in the intestine affects folate status [14]. The production of vitamin B_1 and B_2 by bacteria contributes to the total intake of vitamin B_1 and B_2 [15]. It was reported that *Lactobacillus reuteri* CRL1098 was able to produce B_{12} [16].

Although it is very clear that microbes can synthesize most likely all known vitamins, it is far from clear how much they can be a source of vitamins. Important issues are: a) the microbes might produce vitamins, but they might not be excreted, or might not survive the challenges of the other microflora, and therefore, be catabolized before they can be absorbed. b) This raises the second issue, absorption: most transporters for vitamins are in the duodenum and ileum, not in places where most of the microbes are found. Therefore, it needs to be established if the vitamins, even if produced in high amounts and not metabolized, are bioavailable. For example, the special case of Vitamin B_{12}, which needs intrinsic factor to be absorbed. The vitamin B_{12} which is produced in the colon will never be in touch with intrinsic factor, and will never get in touch with the receptors for intrinsic factors in the ileum.

Clearly residential bacteria and now probiotic supplements play a role in vitamin production and metabolism. How much of a role needs to be studied, particularly in vulnerable groups, such as newborn

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infants, premature infants, the elderly and those with chronic or acute illnesses. The use of vitamin-producing microorganisms may represent a more natural alternative to fortification using synthesised molecules, and may permit production of foods with elevated concentrations of vitamins that are less likely to cause undesirable side-effects.

In conclusion, the possibilities are endless. A whole new methodology for delivering vitamins to those in need may present itself in bacteria as a new carrier. Furthermore, once bacteria take up residence, they keep producing these essential microorganisms, until they are displaced. A nutrigenetic approach may yield huge benefits, if we can modify bacteria to produce vitamins in quantities that meet our needs. Instead of vitamin supplements, we can consider seeding the gut with our new vitamin producing microbes! We even have to change our definition of "vitamin" and "essential", if our needs are met by a healthy microbiome. At the very least those of us in vitamin assessment must now take into account the potential contributions of probiotics.

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