

PROBIOTICS AND DEFINITIONS: A SHORT OVERVIEW

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SUMMARY

Probiotics receive increasing attention in the medical field. This is partly due to the recognition that microbial resistance to antibiotics presents a serious world-wide problem. In addition, fast growing insight into host-microbe interactions opened new routes in the development of rational alternatives in therapy and prevention of diseases as result of the complex procaryotic-eucaryotic evolutionary symphony. Consequently, long existing aspects of probiotics came into focus, and already provide exiting prospects. However, there is no consensus about an appropriate definition of the term probiotic. The International Study Group on New Antimicrobial Strategies (ISGNAS) proposed the distinction into medical, pharmaceutical, and alimentary probiotics. It is mandatory to accept clear-cut definitions and link these to accordingly differentiating regulations to foster probiotics in therapy and prevention, where suitable, and to optimise antibiotic measurements, where necessary.

The majority of recent publications refer to more or less the same sources concerning the definition of the term probiotic. It is attributed to *Lilly* and *Stillwell* to have coined the term first in 1965 (*Conway*, 1996a, 1996b, 1996c; *Fuller*, 1989, 1992; *Havenaar* and *Huis in't Veld*, 1992; *Ouwehand* et al., 1999). *Lilly* and *Stillwell* defined probiotic as "a substance produced by one microorganism stimulating the growth of another microorganism" and understood a probiotic as opposite to an antibiotic (*Lilly* and *Stillwell*, 1965). A totally different view was introduced by *Parker* (1974): "Organisms and substances which contribute to intestinal microbial balance". *Fuller* followed this line and defined in 1989 a probiotic as "a live microbial feed supplement which beneficially affects the host animal by improving its intestinal microbial balance" (*Fuller*, 1989). *Havenaar* and

Huis in't Veld broadened this scope 1992 and associated a probiotic with the description: "A viable mono- or mixed culture of microorganisms which, applied to animal or man, beneficially affects the host by improving the properties of the indigenous microflora" (*Havenaar* and *Huis in't Veld*, 1992). In 1996 *Conway* claimed: "Today it is generally agreed that a probiotic is a preparation of live microorganisms which, applied to man or animal, beneficially affects the host by improving the properties of the indigenous microbiota". The same year *Sanders* issued her view: "Probiotics, simply defined, are microbes consumed for a health effect. The term probiotic is used in food applications. The term biotherapeutic is used in clinical applications" (*Sanders*, 1996).

Today, numerous definitions of the term probiotic are existing (*Conway*,

1996a, 1996b, 1996c; Fuller, 1989, 1992; Hanson and Yolken, 1999; Havenaar and Huis in't Veld, 1992; Ouwehand et al., 1999; Tannock, 1999). Unfortunately, in contrast to Conway's claim that it is generally agreed that a probiotic is a preparation of live microorganisms which improve the indigenous microbiota, there is no consensus among the experts. In fact, the definition of the term probiotic is still controversial as experienced earlier (see Fuller et al., 1995).

Most of the proposed definitions for probiotics centre around the ingestion of viable microorganisms with the purpose to modulate the host's intestinal microflora, with the exception of Lilly's and Stillwell's connotation and concentration onto growth factors (Lilly and Stillwell, 1965). It is generally neglected that there are other compartments in man and animals colonised by symbiotic microbes such as the oral cavity, the skin or the vagina, for instance. Furthermore, despite noticing of immunological effects of probiotic microbes, an eventually most important mode of action, immunomodulation, is not explicitly part of any definitory concept. Additionally, non-viable microorganisms or microbial components are not considered. In fact, there are publications on effects of microbial preparations onto compartments other than the intestine (e.g., see Heidt et al., 1999), as well as there are studies on the effects of viable and non-viable microorganisms and microbial components (e.g. see: Ottendorfer and Zimmermann, 1997; Ouwehand et al., 1999; Panijel and Burkhard, 1993; Rusch et al., 2001). Finally, the term probiotic was not first introduced by Lilly and Stillwell in 1965.

In the electronic era scientific knowledge is confined to databases reaching back not too far. Since most scientists today rely upon databases, tracking of

older work or of publications in languages other than English is difficult or even impossible. Back to the roots. During one of the more recent Old Herborn University Seminars, Christoph Persin drew the attention of the author to an article written by Werner Kollath in an old German journal. Kollath was a renowned nutritionist (Koerber et al., 1999). He wrote in 1953: "High value food should supplement low value food. In order to make such food supplements palatable to people one may denote all organic and inorganic complexes as *probiotics* in contrast to harmful *antibiotics*. All these factors, probiotics, are common in vegetable food as vitamins, aromatic substances, enzymes or possibly other substances connected with vital processes in accordance with Santo and Rusch. This connotation links probiotics with food ingredients, however, includes yet another aspect indicated in the last words of the quotation. This aspect was cultivated further in a group of physicians engaged in natural medicine with whom Kollath was associated. Out of this group evolved a more focussed view of probiotics, as expressed by Vergin in 1954: "It is more important to perceive that *antibiotics* affect our autochthonous microorganisms living together with us in a biocoenosis or even in a symbiosis and thus deplete us of essential *probiotics*. Werner Kollath proposed the term *probiotics*. Consequently, *probiotics* are the opposite of *antibiotics*." The quoted "other substances connected with vital processes" as expressed by Kollath lead to the author's father, Hans Peter Rusch, who was convinced that physiological bacteria and their constituents delivered via vegetables are an important health factor. The lead is further continued to physicians joined in an *Association for Microbial Therapy* in the early fifties of the last century. This group was dedicated to explore therapy

with physiological microbes and pre-
sided by *Hans Kolb*, *Helmut Mommsen*,
and *Hans Peter Rusch*. Quotations
reveal a clear therapeutic approach in
connection with probiotics. "Antibiotic
therapy causes flora damage. In such
cases we administer cultures of symbi-
onts. In this way, deleterious effects of
antibiotics are prevented by *probiotic
therapy*" (*Kolb*, 1955). "Symbioflor
provides us with a biological antiseptic.
This kind of disinfection has the ad-
vantage of affecting pathogenic but not
physiological microorganisms, and in
addition enhances cellular functions.
Thus, *Mommsen* designates bacterio-
therapy in contrast to antibiotic therapy
as probiotic" (*Rusch sr.*, 1956).

Out of past and present it becomes
obvious that it is mandatory to distin-
guish different categories of probiotics.
This is due to the mode of action of
probiotics, the aims of administration of
probiotics and their mode of admini-
stration as well as claims in relation to

food and drug legal regulations. Conse-
quently, the International Study Group
on New Antimicrobial Strategies
(ISGNAS, see *Araneo et al.*, 1996 and
Rusch et al., 1996) developed a concept
for the detailed definition of probiotics
in three categories: 1. Medical probiotics
(drugs), 2. Pharmaceutical probiotics
(food supplements), and 3. Alimentary
probiotics (food) (ISGNAS 1998). A
medical probiotic is a microbial
preparation which contains live and/or
dead microorganisms including their
components and products determined to
be employed as a drug for therapeutic
purposes. A *pharmaceutical probiotic* is
a microbial preparation designed for
manufacture of food supplements. An
alimentary probiotic is a microbial
preparation designed for use in food
fermentation or food production. The
mode of action includes immunomodula-
tion, host microflora modulation, and
the modulation of metabolic processes.

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