More on probiotics

To the Editor: We hereby wish to correct some information communicated about the product Lactéol Forte (capsule and sachet) in the recently published article entitled 'An evaluation of nine probiotics available in South Africa, August 2003'.[1]

Elliott and Teversham[1] tested nine products classified as probiotics, to obtain the bacterial content per gram for the indicated organisms and to determine the organisms present in the products. Among the probiotic products, Lactéol Forte (capsule and sachets) marketed in South Africa by Mirren Pty Ltd was studied in order to check the label information through taxonomic characterisation of recoverable bacterial strains.

Lactéol Forte is sold as a food supplement in South Africa, but is not a probiotic. Our product does not, indeed, answer to the definition given by the joint FAO/WHO Expert Consultation on the Evaluation of Health and Nutritional Properties of probiotics in food. From this definition, probiotic products should contain live lactic acid bacteria which, when consumed in adequate amounts as part of food, confer a health benefit on the host. Lactéol Forte capsules and sachets are sold as dietary supplements to be used as part of a prescribed diet to assist in the normalisation of intestinal microbiological imbalances.

We would like to point out that apart from South Africa, our product is registered in France and in over 40 countries around the world as a medicine used in the treatment of gastro-intestinal diseases such as acute infectious diarrhoea. The marketing authorisations obtained in those countries are supported by pharmacological and clinical studies.[2-13] Owing to its pharmaceutical status, our product gives every guarantee in terms of efficacy and safety. The quality of Lactéol Forte is controlled during all the industrial processes according to the French and European pharmaceutical regulations.

The specific characteristic of our product is that it consists of heat-killed LB bacteria (Lactéol strain) and fermented culture medium. The heat-killed LB bacteria from Lactobacillus genus are traditionally classified as a Lactobacillus acidophilus based on its biochemical characteristics. The Lactéol strain is derived from original bacteria isolated in 1907 by Pierre Boucard. A private reference deposit was made to the French Pasteur Institute. The LB bacteria and fermented culture medium are treated at 110°C for 60 minutes before freeze-drying. As opposed to probiotics, the absence of viable bacteria is a criterion of quality and safety. The heating of the microbial bodies in fact ensures the stability of the high concentration of bacteria (10 billion germs per sachet and 5 billion germs per capsule) for its shelf life and a high level of safety (no risk of translocation). This stabilisation by heating is possible as the pharmacological properties of the Lactéol LB strain are heat stable.

The microbial quality of each Lactéol Forte batch is controlled in accordance with our registration file and the European Pharmacopoeia. The other advantage of heat treatment is to enhance the shelf life of our product in terms of bacterial concentration in the finished product. The concentration is determined by counting of bacterial bodies using microscopy.

Clinical efficacy of Lactéol Forte

Lactéol Forte is widely used in the prevention and treatment of gastro-intestinal disturbances of bacterial and viral origin. Several clinical studies[10-13] have proved its effectiveness in reducing the duration of diarrhoea and stool frequency in children and adults.

Pharmacological data

In vitro and animal pharmacological study expert reports demonstrate four types of mechanisms: (i) direct bacteriostatic activity due to chemical substances contained in L. acidophilus LB; (ii) stimulation of growth of the defensive acidogenic flora; (iii) nonspecific immunostimulation of mucosa; and (iv) inhibition of adhesion to and invasion of human intestinal cells by enterovirulent micro-organisms

As mentioned, the Lactéol LB strain retains its pharmacological properties when it is stabilised by heating.[3]

We agree with the statement in the conclusion of the article that 'Certain health benefits of probiotics are strain specific'. Strain definition of products should, indeed, be linked to efficacy, eliminating the current extrapolation of data by some manufacturers. Lactéol Forte is a specific product, containing L. acidophilus (strain LB) and fermented culture medium. The heat-killed bacteria ensure the stability of the product, while the pharmacological properties are not altered. Therefore Lactéol Forte cannot be compared with the probiotic products mentioned in the article.

Elliott and Teversham[1] discredited the quality and efficacy of our product by subjecting it to evaluation methods that are not applicable or appropriate. We would appreciate either a correction from the authors or confirmation of their results by additional analysis performed on Lactéol Forte taking into account the specific nature of our pharmaceutical product.

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To the Editor: I wish to comment on the paper by Elliot and Teversham.[1]

As the marketing aspects of the paper and their repercussions have been extensively covered in the South African media, I shall concentrate on the scientific aspects only. In particular, I would like to point out a number of fundamental flaws and shortcomings of the paper that render the conclusions presented highly questionable.

1. Methodology used in the evaluation

1.1 Determination of viable counts of probiotic bacteria

While determining the viable counts of probiotic bacteria, particularly of bifidobacteria, which are strictly anaerobic micro-organisms, it is essential to use:

1.1.1 Special anaerobic diluents;

1.1.2 Anaerobic hoods in which the sampling of products, preparation of dilutions and plating should take place;

1.1.3 Media plates with reducing compounds;

1.1.4 Special anaerobic incubators, with a strictly regulated composition of gases, the ratios of which should be specified.

These conditions, the diluents, and the equipment listed above were not specified, described or even mentioned in the above paper. The statement in the paper that the plates were incubated 'under anaerobic and microaerophilic conditions' is inadequate. The conditions should have been specified quantitatively. The difference in the oxygen concentration between the 'anaerobic and micro-aerophilic conditions' was crucial in this study.

The conditions under which the samples were removed from the original containers, suspended, diluted and plated were also of utmost importance, as even very low concentrations of residual oxygen present during these procedures would lead to the depletion of bifidobacteria.

It should be stressed, however, that low concentrations of oxygen would not significantly affect the growth of Lactobacillus reuteri and other lactobacilli, which being micro-aerophilic can multiply in the presence of oxygen at low concentrations.

1.2 Problems with the counts in which no growth of micro-organisms was detected

No information is given concerning the lowest dilutions from which the triplicate aliquots were withdrawn to be plated on the selective media. This aspect is of particular importance to the products in which '0' viable count was reported. Unless the lowest dilution from which the aliquots were plated is specified and unless it represents the undiluted suspension, such a statement is incorrect and misleading. Before a conclusion that no living bacteria were detected can be justified, it should be clearly stated how many undiluted samples were tested.

1.3. Culture media

1.3.1 The modified Columbia agar is a blood-containing medium used for the cultivation of Brucella, Campylobacter, Helicobacter, Corynebacterium, Streptococcus, Staphylococcus, Gardnerella, etc. and is used in many different modifications.[2] Therefore, a detailed description of its preparation is required and should have been included in the paper. This medium is not generally used for the enumeration of bifidobacteria.[2,3]

The cultivation of bifidobacteria on this rather unusual medium could have caused a lower recovery of these bacteria, leading to false conclusions.

1.3.2 Culture media for the identification of Enterococcus faecium and Saccharomyces cerevisiae are not mentioned at all in the article. As reliance on the identification of micro-organisms based only and entirely on the electrophoretic patterns of the DNA is not generally accepted, other criteria should have been employed.

1.4 DNA determinations

Not a single proof of the electrophoretic analysis of the DNA originating from the investigated probiotic bacteria is presented. Likewise, no proof of the DNA analysis of the control strains is provided. For an example of how such a study should be presented, please see Bevilacqua et al.[4]

As the conclusions of the authors relating to the species of the probiotic bacterial strains investigated (and of the reported yeast as well as enterococcal 'infections') rely only and entirely on the DNA analysis, it was imperative to submit some kind of proof. The information that the reference strains originate

from the database kept at the University of Ghent without providing their designations (Culture Collection Numbers) is inadequate.

In addition, the extraction of DNA from lyophilised cultures instead of using freshly harvested cultures is not generally accepted.

2. Lack of statistical data

Basic statistical data, an essential part of any study of this nature, are not included in the paper. The missing data are:

2.1 The number of samples of each product tested as well as the number of capsules, tablets or sachets analysed for each product are not mentioned. It is essential to know whether the results reported and the conclusions drawn were based on just a single sample and a single analysis or on a greater number of samples. For a reliable enumeration, 5 and not 3 aliquots are customarily plated from each dilution on 'surface plates' or suspended in liquid agar media for 'poured plates'.

2.2 Data defining standard error and/or standard deviation. It is difficult to accept that the viable counts for all the analysed samples for each individual product were identical. Statistical data reflecting the reliability and accuracy of any biological determination cannot be omitted in a scientific publication.

In addition, such elementary information as a batch number of each product included in the study is missing.

3. Lack of controls

No control probiotic bacterial strains verifying the suitability of the media chosen for the evaluation are reported. In view of the unconventional medium used for the recovery and enumeration of Bifidobacterium, it was imperative to use a control laboratory strain of Bifidobacterium and confirm the viable count obtained.

Similarly, controls confirming the reliability of the DNA extraction method and of the determination of the electrophoretic DNA patterns were not described. As these determinations constituted the only taxonomic criterion used, this omission is significant.

4. Current classification and identification of bifidobacteria and lactobacilli

Since the publication of Leblond-Bourgey et al. in 1996[5] it has been known that Bifidobacterium longum and B. infantis are clustered together into cluster No. 6. In view of the fact that the SAMJ evaluation under discussion was based on genetic analysis, it is not surprising that the electrophoretic patterns of the DNA originating from B. longum and B. infantis were close or identical. Both names are currently used in the scientific literature, both are correct and both can be used on product labels.

In the light of the above, the conclusion in the paper regarding the 'mislabelling' of Combiforte product is incorrect.

For a reliable classification of bifidobacteria and lactobacilli, the use of a number of independent methods, the electrophoretic patterns being one of them, is recommended.[4] In view of the purpose of this publication, more than one test should have been included as 'the taxonomic significance of phenotypic characterisation of bifidobacteria cannot be neglected' (a recommendation in Bevilacqua et al.[4] p. 184).

5. Suitability of the DGGE method

The authors' conclusion: 'We believe that the DGGE [denaturing gradient gel electrophoresis] method provides a suitable standard for organism identification together with standardised quantification' is not substantiated. It is not based on the data presented as no comparison with other methods of identification was provided in the paper.

6. Contaminating micro-organisms

The authors reported the recovery of Saccharomyces cerevisae from Lactovita capsules and Enterococcus faecium from Culturelle sachets. However, they omitted to state from which dilution or at which concentration the contaminating micro-organisms were isolated (in other words, how many colonies were detected). As it is possible that a tested sample can be contaminated during sampling, weighing or other manipulations, their detection could have been purely accidental. The authors of the article do not provide any information regarding the degree of sterility during those procedures.

In view of the above, the statement relating to the presence of contaminating organisms (in the case of Lactovita the only recovered micro-organism) in these products should be disregarded as being unsubstantiated.

My concluding remarks

The paper makes an overall impression of being hurriedly prepared, with flaws and omissions that cast serious doubt on the results reported and conclusions drawn. Some of the basic prerequisites for a scientific paper of this nature, such as the inclusion of controls, presentation of statistical data and a detailed description of the methods used, are missing. In an evaluation of this nature the lack of batch numbers of the products tested is unacceptable.

In view of these very basic flaws and shortcomings of the paper, as discussed above, it is my opinion that:

1. The paper should not have been accepted for publication in a scientific journal.

2. The conclusions presented in the paper are unsubstantiated.

Taking into consideration the nature and purpose of this publication, I would like to invite specialists in the field of anaerobic bacteria and probiotic bacteria to evaluate my remarks. Should they confirm my comments and conclusions, I would like to suggest that:

1. The SAMJ should officially revoke the findings and conclusions presented in the paper.

2. In view of the far-reaching consequences of the conclusions published in the paper, the SAMJ should offer a public apology to the parties affected, to be disseminated in the media.

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See also editorial (p. 272), the front-page editorial (p. 227) and Editor's Choice (p. 229) The authors of the original article have been offered the opportunity to respond, but were unable to meet the deadline for this issue. — Ed.

Knowing what you can take — the ins and outs of drug-free sport

To the Editor: Last year Elana Meyer was suspended after winning a 10 km road race when the caffeine level in her blood was higher than the acceptable level. Yet in 2004 caffeine has been removed from the list of banned substances! Clearly the field of drugs in sports is changing very rapidly.

For this reason the Discovery Health UCT/MRC Research Unit of Exercise Science and Sports Medicine, in conjunction with the Institute for Drug Free Sport, have put together an informative workshop, which will serve to update everyone on the current list of banned substances and procedures. The workshop will include an overview of drugs in sport, a talk on the latest issues and controversies on drugs in sport, and a presentation on some facts and fallacies related to nutritional aids that supposedly enhance sporting performance.

The speakers include Dr Shuaib Manjra, Director of the South African Institute of Drug Free Sport, who will give an overview of the different classes of banned substances and procedures and explain the protocol for drug testing. Dr Ryan Kohler will discuss the controversies in drug testing and drugs in sport, and a registered dietician, Amanda Claassen, will discuss an evidence-based approach to nutritional sporting performance enhancers.

The workshop, sponsored by the Institute for Drug Free Sport and supported by the SA Sports Medicine Association (SASMA), will take place on 10 May 18h30 in the auditorium of the Sports Science Institute of South Africa. To reserve your place, please phone Pinky Bobo on (021) 650-4561. There will be a R20 donation to the Ziphelele Mbambo Memorial fund, but SASMA members and students can attend for free on presentation of their registration cards.

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Fee for service

To the Editor: Is it not interesting how the unaffordability-of-medical-care debate in the press is led by big business players and not by the patients or the doctors?

The villains of the piece are always the doctors and fee for service.

Is it not strange that in every other field of human endeavour fee for service works, but not in medicine! Could it be that the real problem lies with the third party payer? When I see a patient and charge R100 he gives the third party R120 to pay me — surely if we settled on R110 we would both be happier? Why do we need the intermediary?

The real beneficiaries in a managed care option are the third parties and their shareholders. For both the patient and the doctor the options become more and more restrictive. Is this not why the medical aid industry runs down fee for service and promotes managed care?.

Necessities such as food, clothing and housing are provided by private for profit markets. Or maybe food should also be regulated by a manager with a list of what you may or may not purchase. Food is certainly even more essential than medical care, and certainly has a much bigger effect on the health of the nation.

State interference in the market can only cause more problems, as I see with the minimum benefits that must be covered, some medical aids are only going to cover the benefit 100% if it is provided by a preferred provider! Hello! Who is the preferred provider? Why, the state hospital. What an easy way out for the medical aid industry!

Surely the best managers of the patients' affairs are the