



Bacterial NanoCellulose: what future?

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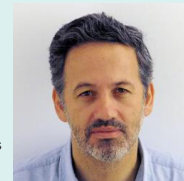
Acetic acid bacteria
 Bacterial nanocellulose
 BNC-based products
Komagataeibacter xylinus

Summary

Acetic acid bacteria (AAB) have been used in various fermentation processes. Of several AAB, the bacterial nanocellulose (BNC) producers, notably *Komagataeibacter xylinus*, appears as an interesting species, in large part because of their ability in the secretion of cellulose as nano/microfibrils. In fact, BNC is characterized by a native nanofibrillar structure, which may outperform the currently used celluloses in the food industry as a promising novel hydrocolloid additive. During the last couple of years, a number of companies worldwide have introduced some BNC-based products to the market. The main aim of this editorial is to underline the BNC potentials.

Author's Biosketch

Miguel Gama (Ph.D.) is an Associate Professor with Habilitation at Minho University, where he develops his Academic career since 1992. His current research interests include (i) bacterial nanocellulose production and its applications in food technology and the biomedical field, (ii) development of self-assembled nanogels made of polysaccharides, (iii) the production and characterization of the biomaterials, the development of drug delivery systems for antimicrobial peptides and low molecular weight hydrophobic drugs. Prof. Gama is currently Vice-Director of the Centre of Biological Engineering (2016-ongoing), has been Director of the Biomedical Engineering Integrated Master of Minho University (MIEBIOM) (2006-2008; 2012-2014) and Coordinator of the Clinical Engineering branch of the MIEBIOM (2006-2012). Regarding International activities he is Associate Editor of *BiolImpacts*, has been invited scientist, Programa CAPES Ciência sem Fronteiras, UFRN, Brasil, 2013-2015. On September 13, 2017 Prof. Gama was presented with the TUMS Distinguished Visiting Professor Title for the duration of 2017-2020 by Dean of School of Pharmacy.



Acetic acid bacteria (AAB) have a long history of application in several fermentation processes. Their exploitation gradually emerged in biotechnological utilizations, particularly in the biosynthesis of beneficial chemicals and processes for manufacturing of several fermented food products. Taxonomic studies, from the traditional to polyphasic approaches, have gradually allowed an appropriate classification of several AAB into distinct genera and species. For instance, the bacterial nanocellulose (BNC) producers, notably *Komagataeibacter xylinus*, exemplifies them.¹ These bacteria secrete cellulose as nano/microfibrils from a row of synthetic sites, along the longitudinal axis of the cell, which then merge to form larger cellulose ribbons. Under static culture conditions, these ribbons and associated cells, form a 3D-nanofibrillar floating pellicle that allows the non-motile, strictly aerobic bacteria to grow in the top oxygen-rich interface of the growth medium. Under agitated and/or aerated conditions, BNC is obtained in the form of fleeces with variable size. Compared to other sources, BNC is characterized by a

native nanofibrillar structure, higher purity (as is deprived of non-cellulosic material) and a higher tensile strength. Also, it shows high moldability *in situ*, high water holding capacity and high crystallinity. The unique properties of BNC and, because of these, its wide range of potential applications, have been widely reported in the literature.²⁻⁴

Commercial exploitation of BNC has its roots in the Philippines, from as early as 1819, from an accidental discovery in Laguna, in which pineapple peels exploited in bleaching the pina cloth, was used as a culture medium for the growth and cellulose production from AAB. After several fermentation trials under static culture, Nata de Coco (BNC) cottage industry has grown to become a successful traditional fermented food business in several countries of the Pacific region.⁵⁻¹¹

It has been demonstrated that BNC may outperform the currently used celluloses in the food industry as a promising novel hydrocolloid additive. Potential utilizations of BNC in food technology are pourable and spoonable dressings, sauces, and gravies; frostings and icings; sour cream and cultured dairy products; whipped



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toppings and aerated desserts, and frozen dairy products. Its use is specifically recommended in some special issues are required, including low use levels, lack of flavor interactions, foam stabilization, and stability over wide pH range, temperature, and freeze-thaw conditions. The utilization of BNC along with other agents (e.g., sucrose and carboxymethyl-cellulose) can ameliorate the dispersion of the product. Further, it is a low-calorie additive, thickener, stabilizer, texture modifier, and hence can be exploited in pasty condiments and in ice cream.¹²⁻¹⁵ Strong competition with colloidal MCC and other commercially available and well-established hydrocolloids in the food industry, makes the viability of such developments further uncertain.¹⁶ Furthermore, the exploitation of nata de coco products seems not to have been fully done, and there seems to be room for its usage, as a novel food, in sophisticated molecular gastronomy products.

Indeed, the technical and dietetic properties of BNC are indisputable. However, and despite some historical efforts, BNC still has not been made available commercially as a bulk product (especially in Western countries); nor and consequently has it been translated to actual products as a novel food additive or ingredient. In the 1990s, several Japanese companies such as Ajinomoto, Shimazu Construction, Nikki, Mitsubishi Paper, Nikkiso and Nakamori Vinegar and national governmental organizations such as Japan Key Technology Centre, a joint organization under Ministry of International Trade and Industry (MITI) and the Ministry of Post and Telecommunications have collaborated to set up interdisciplinary research programs on the commercial production of microbial cellulose.¹⁷ Nevertheless, because of the lack of efficient fermentation systems, the commercial production of BC was never achieved. Another example of the tentative large-scale production and commercialization of BC, is seen by the joint effort of two American companies, namely the Cetus Corporation (Emeryville, California) and Weyerhaeuser Company (Tacoma, Washington), by using a deep tank fermentation technique.^{18,19} With this technology, a commercial product, called Cellulon™ (a mixture of BC and sucrose), was aimed at different applications, including human food. By mid-nineties, NutraSweet Kelco Company (USA) purchased the microbial cellulose business from Weyerhaeuser and launched the BC product as PrimaCel™ (BC combined with sucrose and carboxymethyl cellulose), also aimed at food applications.^{20,21} These products, however, never reached to full commercial scale, presumably due to the high capital and production costs involvement.

As with many food businesses, Nata de Coco trade is characterized by high production volumes and low profit margins. On the other end of the spectra, associated with high-value-added niche markets, medical applications of BNC mostly include its use as wound dressings, with few examples of commercial products having been on the market, resulting from the exploitation of biotechnological fermentation BNC process. The first

efforts to commercialize BC on a large scale, initiated by Johnson & Johnson in the early 80s. This company made extensive research on the medical application of BC as a wound care dressing^{22,23} and developed a highly purified membrane for the replacement of the dura mater (by Depuis Synthes: <https://www.depuysynthes.com/>). However, such commercial products do not involve large-scale fermentation systems. By 1996, the company's patents were subsequently licensed exclusive worldwide rights to Xylos Corporation (Langhorne, USA), a company responsible for manufacturing of the XCell® family of BC-based wound care products. Xylos commercialized their products in 2000-2003,²⁴ but the business was also sold to Lohmann and Rauscher, in 2012. In the same line, BioFill Produtos Bioetecnológicos (Curitiba, PR Brazil) produced a range of products based on BC, including Biofill® and Bioprocess®, also for using in the therapy of burns, skin wounds and ulcers as temporary artificial skin; Gengiflex® was aimed at the treatment of periodontal disease. This company is no longer active. Examples of other spinoff companies active in the biomedical field include JenaCell, Polymet Jena and FZMB, all in Germany. In biomedicine, BNC can precisely be highly competitive in the use for tissues replacement and reconstruction. Apart from tensile strength and the simplicity of use, it offers properties like high water holding capacity, biocompatibility and internal structure mimicking the extracellular matrix, which make this biopolymer quite attractive as a potential tissue-engineered implant; further, due to the hydrophilic nature of BNC, water is abundantly kept within the nanofibril network and the material behaves as a hydrogel. Biocompatibility of BNC has already been investigated plentifully, with very good results each time. The first described medical application of BNC concerned the healing of skin wounds. Owing to its hydrophilic properties, BNC was discovered to be an excellent hydrogel for dressings production. However, only in 2006, Polish scientists from Lodz University of Technology published the first results of BNC membranes application in clinical treatment of second and third degree burns. The investigations showed that BNC membranes could significantly facilitate the process of scar formation by the removal of necrotic debris and improved the development of granulation tissue. As a result, it could accelerate the entire process of re-epithelialization, in comparison to traditional treatment methods. At the same time BNC dressings offered a substantial decrease in daily wound care needs and patients pain relief in comparison with control procedures.

This technology was recently bought by a Polish company – BOWIL Biotech Ltd., that has already started the production of BNC wound dressings and BNC-based cosmetic products (facial and eye masks) under the general name of CELMAT®. The extraordinary properties of BNC hydrogel applied for wounds healing and for internal tissues restoration, gave rise to the new area of BNC's medical use, acting naturally as an entry gate into

the domain of drug delivery systems.

Much effort has been devoted to designing an economical process for the production of BNC, through optimizing both the upstream and downstream processes. These efforts include the evaluation of several culture media compositions, fermentation systems, genetic engineering and post-production modification processes. However, still the scientific literature propagates the idea that the technological production of BNC is extremely expensive. Indeed, and as observed above, from the rise and fall of several BC production companies, insofar, biotechnological processes are highly capital-intensive as compared with traditional BNC fermentation methods. Coupled to the usually low BNC yields, the high capital investment and high operating costs associated, present a strong economic constraint to the commercialization of BNC at a “low” cost (as compared to nata de coco). Still, and due to the unique properties of BNC and the almost-reachable market potential, large efforts take place to enhance BNC from a food to a new generation of nature-based sophisticated materials. During the last couple of years, several young companies worldwide started to bring such BNC-based products to the market. The key question remains to be answered: will the modern BNC industry remain restricted to high-value niche markets? The next few years should witness major progresses in the area and provide an answer to this question.

Ethical approval

There is none to be declared.

Competing interests

No competing interests to be disclosed.

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