Toxicology Reports 4 (2017) 543–553

Contents lists available at ScienceDirect

Toxicology Reports

journal homepage: www.elsevier.com/locate/toxrep

Review

# A Review on the toxicology and dietetic role of bacterial cellulose

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ARTICLE INFO

*Keywords:*
Bacterial cellulose
Dietetic properties
Acute toxicity
Subchronic toxicity
Cytotoxicity
Genotoxicity
Mutagenicity
Reproductive toxicity
Embryotoxicity
Teratogenicity

ABSTRACT

Bacterial cellulose (BC) is a biopolymer synthesized by certain acetic acid bacteria strains. The safety of BC regarding its potential use in food applications is here reviewed. The acute, sub-acute and subchronic oral toxicity assays showed that consumption of BC had no adverse effects in rats. Several studies demonstrated that BC is not genotoxic, did not induce chromosomal aberrations in CHO cells under both non-activating and metabolic activating conditions, is inactive in the *in vitro* Rat Primary Hepatocyte Unscheduled DNA Synthesis Assay, had no reproductive toxicity in mice and exerted no embryotoxicity and teratogenicity effects in rats.

Several studies on the BC in biomedical applications further reinforces its safety: a primary eye and dermal irritation studies in the rabbit showed that BC was non-irritating. The inflammatory reaction to subcutaneously implanted BC has been evaluated in animal models and for different periods of time, demonstrating that BC is biocompatible and does not trigger a harsh inflammatory reaction.

Altogether, and considering its longstanding history of human consumption in Asian countries, as well as its utilization in biomedical devices, it may be concluded that BC is safe for applications in food technology.

## 1. Introduction

The determination of toxicants in foods/food substances has become increasingly important, to ensure that the benefits of the substances intended for use by humans, outweigh the risks from their use. Many countries have a well-established regulatory framework (and under constant revisions), to ensure the proper scientific evaluation of foods, food additives and ingredients, processing aids and food contacting substances, before their market approval. The toxicity tests that food operators are required to provide, for a pre-market approval of their products, depends on the type of substance, its intended use and on the regulations of a particular country. To this effect, several standard tests are available to evaluate different effects such as acute, sub-acute, subchronic and chronic toxicity, carcinogenicity, mutagenicity, reproductive and developmental toxicity, neurotoxicity, and several *in vitro* tests. Some products may require additional toxicity test such as irritancy and skin sensitization studies [1–7].

The safety of numerous kinds of plant cellulose and their derivative products has been extensively reviewed by national and international regulatory agencies such as the US Food and Drug Administration (FDA), The European Food Safety Authority (EFSA), the Joint FAO/WHO Expert Committee on Food Additives (JEFCA), the Select Committee on Generally Recognized as Safe (GRAS) Substances (SCOGS). The information provided below includes a comprehensive review on the toxicological data available for bacterial cellulose.

Bacterial cellulose (BC) is a pure cellulose exopolysaccharide produced by certain strains of acetic acid bacteria, such as those of the *Komagataeibacter* genus. The cellulose synthesized by these strains is identical to that of plants, regarding its molecular formula and polymeric structure. However, BC presents in general, a higher crystallinity. Also, BC is chemically pure, i.e. it is free of lignin, hemicelluloses and other biogenic compounds. Under static culture conditions, the synthetized BC, is presented as a gelatinous film consisting of a 3D nanofibrilar arrangement of pure cellulosic fibres (Fig. 1). These randomly assembled ribbon-shaped fibrils are less than 100 nm wide and composed of elementary nanofibrils, aggregated in bundles with lateral size of 7–8 nm; these fibrils have several micrometres in length [8–12]. The taxonomy of these bacteria [13], the BC biosynthesis [14] and potential applications in food [15–17], have been extensively reviewed.

## 2. Dietetic properties and human consumption

In Asian countries, BC is already produced at large scale and has a long history of use, being marketed under the trade name “nata de coco” [18–20]. Ever since its discovery in the eighteenth century, nata de coco gained widespread popularity in Asian countries, being first produced in large scale in the Philippines [21]. Philippines and Indonesia are the major producers and exporters of nata de coco products for human consumption. Thailand, Vietnam and Malaysia are also among the most representatives commercial producers (Phisalaphong

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http://dx.doi.org/10.1016/j.toxrep.2017.09.005
Received 5 May 2017; Received in revised form 4 September 2017; Accepted 24 September 2017
Available online 25 September 2017


**Fig. 1.** Scanning electron microscopy of cellulose pellicles and cells from G. xylinum IFO 13693, after 10 days of static culture. Reprinted from Chávez-Pacheco et al., 2005 with permission from John Wiley & Sons.

and Chiaoprakobkij 2013). Among non-traditional coconut export products in 2009, nata de coco was the second largest, earning US $6034 million from the sale of 6051 MT. The greatest market for nata de coco was Japan (77.8%) and the second largest market was the USA. From 2009–2011, the volume of nata exports from the Philippines has been within a calculated and steady average range of 6000 MT which corresponded to a market value of US$6 million [22,23]. These figures demonstrate the long-standing human consumption of nata de coco/bacterial cellulose. There are, to our knowledge, no reported cases of health related issues associated to the human consumption of BC or nata de coco, thus unequivocally supporting the claim on its safety. In fact, several studies demonstrate beneficial effects from the dietetic point of view, as observed bellow.

A study by Chau et al. [24] investigated and compared the hypolipidemic and hypocholesterolemic effects of plant cellulose and BC, specifically, the absorption and excretion of lipids and cholesterol in Golden Syrian hamsters' diets (Table 1). Three types of diets were prepared, the difference between them being the addition of bacterial cellulose on the "bacterial cellulose diet", plant cellulose on the "cellulose diet", and the "fibre-free diet" (a control diet, without fibre). All diets were supplemented with cholesterol (2.0 g/kg of diet) to induce the alimentary hypercholesterolemia in hamsters; also the insoluble fibre content was standardized to 50 g fibre/kg of diet in the diets containing fibre. For 30 days, food and drinking water were supplied *ad libitum*.

The results showed that the serum triglyceride concentrations in hamsters fed with BC and plant cellulose diets, were significantly reduced, by 55.5 and 46.6%, respectively, as compared to the fibre-free diet. No significant changes in the serum high-density lipoprotein (HDL) cholesterol concentration were observed among the three diet groups. However, significantly higher HDL/total cholesterol ratios were found for the plant cellulose and BC supplemented groups (0.60 and 0.65, respectively) versus the fibre-free group (0.50) suggesting the higher antiatherogenic potential of BC. Further, the administration of both types of cellulose to hamsters, effectively decreased the concentration of serum total cholesterol (by 17.4% with plant cellulose and by 27.9% with BC) and also decreased the serum low-density lipoprotein (LDL) cholesterol (plant cellulose: −41.9%; BC: −47.9%). The cation-exchange capacity of bacterial cellulose, 67.5 mequiv/Kg of fibre, was found to be 6-fold higher than that of plant cellulose. The higher cation-exchange capacity of BC was proposed to better entrap, destabilize and disintegrate a lipid emulsion, leading to a decrease in diffusion and absorption of cholesterol and lipids. By the end of the experiment, no significant variations in the mass of the hamsters' visceral organs including small intestine, cecal wall, colon plus rectum, liver and kidney, among the three types of diets, were observed. Chemical analysis of the hamsters' liver tissues revealed that the addition of BC to the diet was more effective in reducing the concentration of the liver total lipids (-10.3%) and liver cholesterol (-16.3%) than with plant cellulose (-6.5% and −11.8% respectively), as compared to the fibre-free diet. Analysis of the hamsters' faeces showed that, as compared to the "fibre-free diet" group, the group fed with plant cellulose and BC had an increase in the excretion of total lipids (plant cellulose: +44%; BC: +82%), cholesterol (plant cellulose: +36%; BC: +103%) and bile acids (plant cellulose: +159%; BC: +379%). Also, the faecal moisture content of hamsters fed with BC was higher than those fed the fibre-free and plant cellulose diets (+37% (BC) and +20% (plant cellulose)). With the addition of plant cellulose and BC to fibre-free diet, the faecal dry weight increased by +42% and +49%, respectively. No significant differences in the faecal dry weight were observed between the plant cellulose and BC groups. The results thus indicated that BC was able to incur a higher output of total lipids, cholesterol and bile acids in faeces than plant cellulose.

Okiyama et al. [25] studied the faecal excretion and transit time of BC in rats for up to 16 days (Table 1). Eight weeks old male Wistar rats were fed with a diet containing 5% of BC, or plant cellulose powder or guar gum. Feeding was provided twice a day and drinking water was supplied *ad libitum*.

Rats fed with BC-containing meals showed the greatest increase (+223%) in faecal weight. Addition of BC to the diet decreased the transit time by 50%, as compared to no fibre diet group. There were no differences on lipoprotein cholesterol levels in plasma (total cholesterol, HDL, and LDL fractions) between the dietary fibres group and fibre-free diet (control). The guar-meal gum group had significantly lower lipoprotein cholesterol levels, as compared to the dietary fibre groups. Both BC and guar decreased (-52%) neutral sterol excretion in faeces and increased (+106%) faecal bile acid excretion. The proportion of coprostanol to total neutral sterols in the cecum was not significantly different between rats fed with BC and those fed with the fibre-free diet.

Mesomya et al. [26] compared the serum triglyceride and the serum cholesterol lowering effect of five kinds of dietary fibre diet on weanling male Sprague-Dawley rats (Table 1). These diets had different fibre and nutrient proportions: diet 1 was had a total of 33% (m/m) dietary fibre from unpolished rice, mung bean, sweet corn and 22% BC; Diet 2 had 60% fibre from the same plant sources and 40% BC. Diets 3, 4 and 5 had 100% apple pectin, plant cellulose and casein respectively. Cholesterol content was of 13%, 11.4%, 14.2%, 14.1% and 13.5% mg/100 g in diets 1, 2, 3, 4 and 5, respectively. After four weeks of study, diet 2 gave the best lowering effect of serum triglyceride in rats, as compared with those fed with apple pectin (diet 3) and cellulose (diet 4), even though the total dietary fibre content in diet 2 (2.86%) was lower than that of apple pectin diet 3 (7.76%) and of plant cellulose diet 4 (10.39%). Diet 2 however, had no effect in lowering serum cholesterol levels.

Mesomya et al. [27] investigated the effects of the cereal and BC supplementation on the serum lipids of hyperlipidemic human subjects for a period of 24 weeks: 4 weeks without (as the control) and 20 weeks with supplementation (Table 1). The supplements (15 g) were given twice daily for these 20 weeks, and consisted of 40% (m/m) BC, 6% (m/m) unpolished rice, 36% (m/m) sweet corn and 18% (m/m) mung bean. After 20 weeks, the subjects who complied with the dietary assignment (≥90% of the time; 15 subjects) were classified as group A, and those with < 90% (7 subjects), as group B. During the first four weeks (control) the subjects showed no significant changes in serum lipid levels. Afterwards, Group A showed gradually decreasing levels of serum total triglyceride (TC). By week 16/20 under supplementation, the serum total cholesterol (TC) level decreased by 20%.

A summary of the above-mentioned studies is present in Table 1.