Microbiological Research 192 (2016) 159–171

Contents lists available at ScienceDirect

Microbiological Research

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

Review

Bifidobacteria—Insight into clinical outcomes and mechanisms of its probiotic action

Amrita Sarkar*, Santanu Mandal

School of Chemistry and Manchester Institute of Biotechnology, The University of Manchester, 131 Princess Street, Manchester M1 7DN, UK

ARTICLE INFO

Article history:
Received 23 February 2016
Received in revised form 12 June 2016
Accepted 7 July 2016
Available online 11 July 2016

Dedicated to Professor Sabine L. Flitsch.

Keywords:
Gut microbiome
Pathogen protection
Clinical application
Adverse effects
Immunomodulatory effect
Combinatorial therapy

ABSTRACT

The invasion of pathogens causes a disruption of the gut homeostasis. Innate immune responses and those triggered by endogenous microbiota form the first line of defence in our body. Pathogens often successfully overcome the resistances offered, calling for therapeutic intervention. Conventional strategy involving antibiotics might eradicate pathogens, but often leave the gut uncolonised and susceptible to recurrences. Probiotic supplements are useful alternatives. *Bifidobacterium* is one of widely studied probiotic genus, effective in restoring gut homeostasis. Mechanisms of probiotic action of bifidobacteria are several, often with strain-specificity. Analysis of streamlined literature reports reveal that although most studies report the probiotic aspect of bifidobacteria, sporadic documented contradictory results exist, challenging its therapeutic application and prompting studies to unambiguously establish the strain-associated probiotic activity and negate adverse effects prior to its clinical administration. Multi-strain/combinatorial therapy possibly relies on a combination of underlying operating mechanisms, each contributing towards enhanced probiotic efficacy, understanding which could help in developing customised formulations against targeted pathogens. Bifidogenic activity is also mediated by surface-associated structural components such as exopolysaccharides, lipoteichoic acids along with metabolites and bifidocins. This highlights scope for developing advanced structural therapeutic strategy which might be pivotal in replacing intact cell probiotics therapy.

Contents

* Corresponding author.
E-mail addresses: amrita08sarkar@gmail.com, amrita.sarkar@manchester.ac.uk (A. Sarkar).

http://dx.doi.org/10.1016/j.micres.2016.07.001
0944-5013/

1. Introduction

Increasing population of antibiotic resistant virulent pathogens has triggered the search of alternate means of pathogen combat. Photopharmacotherapy and probiotics in combination with prebiotics has become routes of major diversion from conventional use of antibiotics (Velema et al., 2014; Wang et al., 2013). They not only serve as green channels in reducing built-up of active antimicrobial elements in the environment but also lower drug resistivity in deadly pathogens. Since the acceptance by United Nations FAO and WHO in 2001 (Castellazzi et al., 2013), probiotics have found extensive applications. Healthy gut bacteria in humans are acquired during birth, which confer health promoting effects to the host. This neonatal microbial population gradually alters with age serving as a biomarker for health. Reduction in intestinal probiotic community often poses serious risks of pathogenic invasions and colonisation of gut epithelium, intake of probiotic supplements can be particularly useful.

Numerous bifidobacterial strains have found to be useful in treating different clinical conditions. Therefore it is likely that different strains operate through a combination of more than one pathway instead of a single mechanistic route. The present communication aims to provide the current perspective of the concepts evolving about the mechanisms of probiotic action of bifidobacteria in humans rather than a comprehensive literature summary. Understanding mechanisms could be helpful in identification of suitable probiotic strains for prevention and customised therapeutic treatment of infections with known pathogenesis and prognosis. Interestingly these apparently benign and mostly probiotic microorganisms have been reported to have adverse effects on human health. Although infrequent, but these reports emphasise on the need for in-depth study prior to developing probiotic formulation for clinical administration.

2. Clinical prospect of bifidobacteria

Bifidobacterial flora in neonatal gut is established within the first few days after delivery and constitutes upto almost 80% of the microfloral composition during infancy (Turroni et al., 2012). The gut flora established at birth and weaning, gradually alters with age, dietary, seasonal and geographical variations along with intake of probiotics along with other endogeneous and exogeneous factors (Balamurugan et al., 2008; Lagier et al., 2012; Davenport et al., 2014; Mitsuoka, 1990). Clinical study shows that usage of antibiotics on neonates not only causes a delay in developing a normal bifidobacterial intestinal flora, but also increases risk of colonisation by pathogenic bacteria such as Kleibsella, Enterobacteria, Citrobacter, Pseudomonas *etc.* (Hussey et al., 2011). The delayed and disturbed bifidobacterial colonisation during infancy increases the risks of childhood diseases and could also influence the health of the host in future (Marra et al., 2006; Alm et al., 2008; Bailey et al., 2014).

2.1. Beneficial effects

Breakdown of probiotic barrier against pathogens often leads to gastrointestinal problems such as gastroenteritis, enterocolitis, irritable bowel syndrome (IBS), diarrhoea and food allergies/intolerances (Bermudez-Brito et al., 2012; Guglielmetti et al., 2011; Groschwitz and Hogan, 2009). Bifidobacteria shows efficacy in alleviating related symptoms of constipation, abdominal pain, flatulence, bloating by rebalancing the gut flora and preventing abnormal bacterial fermentation of food residues (O'Mahony et al., 2005). Specific strains of *B. infantis* and *B. lactis* along with *Streptococcus thermophiles*, *L. acidophilus* and *L. rhamnosus* show efficacy in alleviating symptoms of acute gastroenteritis in infants (Erdogan et al., 2012; Vandenplas and Hert, 2011). Diarrhoea often follows antibiotic therapy or chemotherapy/radiotherapy in cancer patients (Fox et al., 2015; Demers et al., 2014). Administration of *B. lactis* BB12, B94, *B. longum* BB-536 and specific strains of *B. Bifidum* in combination with *L. rhamnosus* GG, *L. acidophilus* La-5, LAC-361 is reported to reduce episodes and symptoms of diarrhoea in infants and adults (Demers et al., 2014; Fox et al., 2015; İşlek et al., 2014; Dinleyici et al., 2013; El-Soud et al., 2015). The increasing trend of IBS among people (~15–20%) raises a major concern about the prevention and treatment strategies. Clinical study shows that administration of *B. bifidum* MIMBb75 strain as nutritional supplement could substantially relieve patients of IBS symptoms and promote a healthy life compared to those on placebo (Guglielmetti et al., 2011). *B. bifidum* KCTC12199BP, *B. lactis* KCTC 11904BP, W51, *B. longum* KCTC12200BP are some of the other strains exhibiting efficacy in IBS therapy (Rossi et al., 2015; Yoon et al., 2014). While *B. animalis* DN-173010 is particularly found to be helpful in improving faecal colonic transit time in people with long transit times (Picard et al., 2005). *In vitro* studies using human intestinal HT-29 cell lines also revealed the anti-inflammatory effects of *B. animalis* subsp. *lactis* PBS075 (Presti et al., 2015). Similar studies using human colonic microbiota model reveal that *B. longum* subsp. *infantis* NCIMB 702205 strain has the ability to reduce the gut-derived lipopolysaccharide which is related to chronic inflammatory and metabolic diseases (Rodes et al., 2013). Specific strains of *B. breve* and *B. lactis* along with *L. casei* have been reported to improve intestinal motility along with lowering of nosocomial sepsis and mortality in neonates and infants diagnosed with necrotising enterocolitis (Braga et al., 2011; Dilli et al., 2015). Bifidobacteria is also reported to exhibit probiotic effects against Crohn's disease, ulcerative colitis and pouchitis (Shen et al., 2014; Tamaki et al., 2016; Saez-Lara et al., 2015). Other health benefits include antagonistic effect on colorectal cancer and treatment of *Helicobacter pylori* infections (Khodadad et al., 2013; Chitapanarux et al., 2015; Chong, 2014; Yoon et al., 2014; Lee et al., 2008; Bindels et al., 2012). Particularly interesting study recently showed *B. bifidum* PRL2010 assisting in cholesterol assimilation through upregulation of genes encoding putative transporters and reductases (Zanotti et al., 2015). While double blinded, randomised, placebo controlled trial involving Japanese obese adults showed *Bifidobacterium animalis* ssp. *lactis* GCL2505 assisted reduction of visceral fat (Takahashi et al., 2016). Bifidobacteria not only improves lactose utilisation but also helps in stabilisation of gut mucosal barrier (Kailasapathy and Chin, 2000).

Atopic dermatitis/eczema is a chronic and pruritic skin disorder affecting infants and adults of all age group (Eichenfield et al., 2014; Wollenberg et al. 2016). Although its cause is not clearly understood, may arise due to immunological disorder related to IgE mediated reactions. The first line of treatment includes hydrational and anti-inflammatory topical medications (Wollenberg et al., 2016; Ring et al., 2012) with continuous search for alternative non-pharmacologic therapies. The first role of probiotic bifidobacteria in prevention and therapeutic intervention in such atopic diseases is well established, with *B. breve* LMG 23729, *B. longum* BB536, *B. lactis*