Toxicology 278 (2010) 268–276

Contents lists available at ScienceDirect

Toxicology

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

Review

Bacterial metabolic 'toxins': A new mechanism for lactose and food intolerance, and irritable bowel syndrome

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ARTICLE INFO

Article history:
Received 26 March 2010
Received in revised form 18 August 2010
Accepted 5 September 2010
Available online 18 September 2010

Keywords:
Bacteria
Toxin
Lactose
Irritable bowel syndrome
Calcium

ABSTRACT

Lactose and food intolerance cause a wide range of gut and systemic symptoms, including gas, gut pain, diarrhoea or constipation, severe headaches, severe fatigue, loss of cognitive functions such as concentration, memory and reasoning, muscle and joint pain, heart palpitations, and a variety of allergies (Matthews and Campbell, 2000; Matthews et al., 2005; Waud et al., 2008). These can be explained by the production of toxic metabolites from gut bacteria, as a result of anaerobic digestion of carbohydrates and other foods, not absorbed in the small intestine. These metabolites include alcohols, diols such as butan 2,3 diol, ketones, acids, and aldehydes such as methylglyoxal (Campbell et al., 2005, 2009). These 'toxins' induce calcium signals in bacteria and affect their growth, thereby acting to modify the balance of microflora in the gut (Campbell et al., 2004, 2007a,b). These bacterial 'toxins' also affect signalling mechanisms in cells around the body, thereby explaining the wide range of symptoms in people with food intolerance. This new mechanism also explains the most common referral to gastroenterologists, irritable bowel syndrome (IBS), and the illness that afflicted Charles Darwin for 50 years (Campbell and Matthews, 2005a,b). We propose it will lead to a new understanding of the molecular mechanism of type 2 diabetes and some cancers.

Contents

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doi:10.1016/j.tox.2010.09.001

1. Lactose and food intolerance

Lactose and food intolerance, and irritable bowel syndrome, cause a wide range of gut and systemic symptoms. These include: gas, gut pain, bloating, borborygmi, diarrhoea or constipation, headache, severe fatigue, cognitive dysfunction, muscle and joint pain, heart palpitations, various allergies such as eczema and urticaria, increased micturition, and infertility (Matthews and Campbell, 2000; Campbell and Matthews, 2005a,b; Matthews et al., 2005; Waud et al., 2008; Campbell et al., 2005, 2009). We propose that these symptoms are caused by hydrogen and methane gas and toxins, produced by bacteria in the large intestine when they metabolise carbohydrates not digested fully in the small intestine (Campbell et al., 2005, 2009). These carbohydrates include lactose, sucrose, fructose, and starch from rice, potatoes, pasta, and flour. In order to digest carbohydrates such as lactose, sucrose and starch, these must first be degraded to monosaccharides, which can then be absorbed. There are thus two major causes of lack of full digestion of carbohydrates in the small intestine – deficiency in the enzyme degrading the carbohydrate to monosaccharides, or deficiency in the transporter enabling monosaccharides to be absorbed into the blood.

All mammals, apart from white Northern Europeans and a few races such as the Bedouins, start to lose the enzyme lactase-phlorizin hydrolase (lactase for short) after weaning. Thus some two thirds of the world's adult population, about 4000 million people, cannot digest lactose properly. Everyone can digest some lactose, unless they have the very rare disorder of congenital lactase deficiency. But those with a low lactase have threshold, which if crossed results in gut and systemic symptoms. Lactase is unique in having two active sites within the same polypeptide chain, and thus has two enzyme commission numbers (EC 3.2.1 62 and 108). One site cleaves lactose into its two constituent sugars – galactose and glucose (Fig. 1), while the other, discovered because it cleaves the diabetogenic compound phlorizin from apple bark, cleaves cerebrosides, providing essential sphingosine for tissues such as the brain. This is why we have to retain some to the enzyme after weaning. Dairying is only 6000–8000 years old (Campbell and Matthews, 2005b; Campbell et al., 2005, 2009). So, in evolutionary terms, since lactose is only found in significant quantities in mammalian milk, there would otherwise be no need to retain lactase after weaning. Thus, in order to digest cerebrosides, we all need some lactase, even if our diet contains no lactose. After cleavage of lactose by lactase, the galactose and glucose are absorbed through the sodium dependent glucose transporter, SGLUT1. This is distinct from GLUT5, responsible for absorbing fructose in fruits or formed from cleavage of sucrose (Fig. 1) by sucrase. Moreover, glucose and galactose uptake through SGLUT1 is inhibited by certain non-metabolisable tri- and tetra-saccharides, such as raffinose and stachyose (Fig. 1). These are found in many root vegetables, pulses and beans, including soya, and are the reason why large consumption of these during a meal causes gas.

2. The bacterial metabolic toxin hypothesis

Carbohydrates not digested and absorbed in the small intestine reach the large intestine, where there are over one hundred times as many bacterial cells than cells in the rest of the body, approximately 1 kg in weight, representing over 1000 species (Qin et al., 2010). There is little oxygen here. Thus, in order to make ATP via

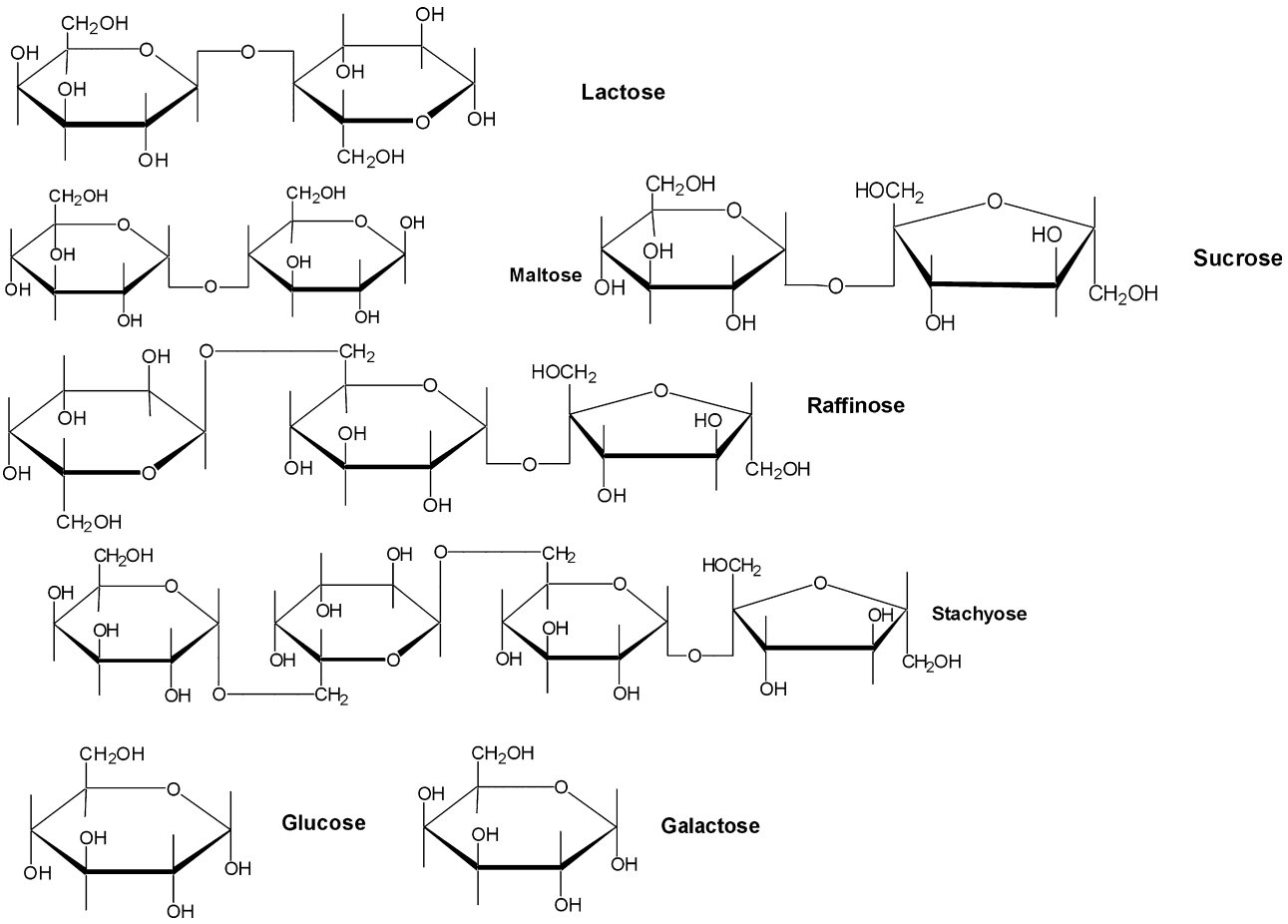

Fig. 1. The sugars.