Advances in Medical Sciences 62 (2017) 302–306

Contents lists available at ScienceDirect

Advances in Medical Sciences

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

Original research article

Mulberry leaf extract decreases digestion and absorption of starch in healthy subjects—A randomized, placebo-controlled, crossover study

Jan Józefczuk[a], Klaudia Malikowska[b], Aleksandra Glapa[b], Barbara Stawińska-Witoszyńska[c], Jan Krzysztof Nowak[b], Joanna Bajerska[d], Aleksandra Lisowska[b], Jarosław Walkowiak[b,*]

[a] Pediatric Division, City Hospital, 39-360 Nowa Deba, Poland
[b] Department of Pediatric Gastroenterology and Metabolic Diseases, Poznan University of Medical Sciences, Poznan, Poland
[c] Department of Epidemiology, Chair of Social Medicine, Poznan University of Medical Sciences, Poznan, Poland
[d] Department of Human Nutrition and Hygiene, Poznan University of Life Sciences, Poznan, Poland

ARTICLE INFO

Article history:
Received 3 October 2016
Accepted 8 March 2017
Available online xxx

Keywords:
Breath test
Carbohydrate
Diabetes
Nutritional trial
Obesity

ABSTRACT

Purpose: Mulberry (*Morus alba L.*) leaf tea has recently received much attention as a dietary supplement due to the wide range of putative health benefits, such as antidiabetic effects. Nevertheless, data evaluating its influence on carbohydrate metabolism in humans are scarce. The present study aims to investigate the effect of mulberry leaf extract supplementation on starch digestion and absorption in humans.
Materials and methods: The study comprised of 25 healthy subjects, aged 19–27 years. In all subjects, a starch ^{13}C breath test was performed twice in a crossover and single blind design. Subjects were initially randomized to ingest naturally ^{13}C-abundant cornflakes (50 g cornflakes + 100 ml low fat milk) either with the mulberry leaf extract (36 mg of active component-1-deoxynojirimycin) or the placebo and each subject received the opposite preparation one week later.
Results: The cumulative percentage dose recovery was lower for the mulberry leaf extract test than for the placebo test (median [quartile distribution]: 13.9% [9.9–17.4] vs. 17.2% [13.3–20.6]; p = 0.015). A significant decrease was detectable from minute 120 after the ingestion.
Conclusions: A single dose of mulberry leaf extract taken with a test meal decreases starch digestion and absorption. These findings could possibly be translated into everyday practice for improvement of postprandial glycemic control.

1. Introduction

Obesity is considered an epidemic and may contribute to the pathophysiology of various disorders such as postprandial hyperglycemia, diabetes, glycosphingolipid storage diseases and diabetic cardiovascular complications [1,2]. Therefore much attention has been focused on the improvement of postprandial glycemic control [3]. Materials that delay or inhibit digestion or absorption of carbohydrates could be helpful in this respect [4,5]. Although the effectiveness of digestive enzymes inhibitors is undoubtable, many pharmaceutics of this group cause serious side effects, such as diarrhea or abdominal pain [6,7]. For this reason, the use of well-tolerated, natural dietary supplements could be considered as complementary and supportive treatment for obesity and associated carbohydrate-mediated disorders [8–10].

Mulberry leaf has recently received much interest as a herbal supplement due to the wide range of its biological activity, which includes antioxidant, neuroprotective, anti-inflammatory, and antimicrobial actions [11]. The worldwide known antidiabetic application of mulberry leaf extract has been ascertained to be the effect of a complex combination of various constituents, such as flavonoids, soluble dietary fiber, and iminosugars, that may act through alpha-glucosidase inhibition [12–14]. Mulberry leaves are rich in amino group-containing sugar analogs – termed iminosugars – in which the most abundant (accounting for 50%) iminosugar – 1-deoxynojirimycin (DNJ) – is believed to be the most bioactive agent [14–16]. Many studies show that mulberry preparations decrease glucose absorption in vivo [13,17–20]. In the

* Corresponding author at: Department of Pediatric Gastroenterology and Metabolic Diseases, Poznan University of Medical Sciences, Szpitalna Street 27/33, 60-572 Poznan, Poland.
E-mail address: jarwalk@ump.edu.pl (J. Walkowiak).

http://dx.doi.org/10.1016/j.advms.2017.03.002

few randomized controlled trials, postprandial glucose levels decreased after mulberry ingestion [13,21–24]. Nevertheless, data evaluating its influence on carbohydrate digestion and absorption in healthy humans is scarce. Zhong et al. examined the effect of a mixture of black, green and mulberry teas on breath hydrogen concentrations after a rice containing test meal comparing with placebo [23]. In the study by Mudra et al., the effect of mulberry leaf extract (MLE) on blood glucose and breath hydrogen response was measured after saccharose loading in type 2 diabetic patients and control subjects [24]. However, there are no data on the influence of mulberry on starch digestion.

In order to assess starch digestion and absorption we used a reliable method of non-invasive ^{13}C breath test [25]. In the present study, we used cornflakes abundant in starch as a test meal. Starch is digested to monosaccharides such as glucose, which in excess may contribute to elevated post-prandial hyperglycemia. During the test, the ^{13}C isotope naturally present in maize is digested in the small intestine then absorbed and metabolized in the liver and transported to lungs. Exhaled CO_2 is labelled with the ^{13}C isotope and measured as a cumulative percentage dose recovery values (CPDR).

Different studies have evaluated the various effects of mulberry leaf on humans. The primary outcome of this study is to measure the effect of mulberry leaf extract on carbohydrate digestion and absorption after a starch test meal. The ingredient of the extract responsible for the decrease in starch digestion and absorption is 1- deoxynojirimycin which has been shown to inhibit α-glucosidase activity in vitro and in animal studies [12–14]. In the present study, we aimed to assess the influence of MLE on starch digestion and absorption in healthy human subjects with the use of a non-invasive ^{13}C breath test.

2. Materials and methods

2.1. Study population

The study comprised of 25 healthy subjects (10 men and 15 women) (Table 1). Subjects were recruited from the Vocational Technical High School for Computer Science in Nakło nad Notecią, Poland over May 2013–May 2014.

As subjects were expected to ingest milk, those suffering from lactose malabsorption were excluded via a hydrogen-methane breath test. The eligibility criterion was age ≥18 years. Inclusion criteria were as follows: willingness to participate in the study (confirmed by informed written consent) and good health status defined as no physical complaints in the month preceding the study, no acute or chronic disease, no current pharmacotherapy, no past hospitalizations for gastroenterological indications, and good nutritional status (weight and height within normal reference values and BMI cut-off points within 18.50–24.99 kg/m^2). Exclusion criteria comprised of: celiac disease, exocrine pancreatic insufficiency [26,27] and other gastrointestinal diseases, medication that might affect digestion or absorption of carbohydrates, antibiotic therapy within the preceding month, and the use of mulberry preparations within the preceding month. Prior to the test, all subjects fasted for 12 h. The subjects were also informed not to eat any food naturally abundant in ^{13}C, such as products made of maize, cane sugar, pineapple, or kiwi fruit for 5 days preceding the examination. Fifty-one subjects were assessed for eligibility, of whom 26 were excluded (lactose intolerance n = 17; not meeting inclusion criteria n = 9) (Fig. 1). Eventually, 25 subjects were randomized and assigned to the first intervention: 13 subjects in the placebo arm and 12 in the MLE arm. One week later, 12 subjects received placebo and 13 subjects received MLE. No participants left the study or were excluded after the randomization had taken place.

The protocol of the study was conducted according to the Declaration of Helsinki and approved by the Bioethical Committee of Poznan University of Medical Sciences, Poland (decisions 605/12 and 752/13).

Table 1
Basic data of study subjects (n = 25).

Parameter	Median	1st–3rd quartile
Age [years]	24	19–27
Body weight [kg]	63.0	58.2–76.5
Height [cm]	170	165–182
[a]BMI [kg/m2]	22.0	20.1–23.2

[a] Body Mass Index (BMI).

2.2. Randomization and blinding

The protocol of starch ^{13}C breath test was applied as described previously [28]. The order of the tests (MLE/placebo test first) was determined according to the randomization list prepared by a qualified dietician. One week later, the second test was performed in a crossover manner: the subjects took the opposite preparation from that ingested initially. In this way, subjects served as self-controls to themselves. The trial was single-blinded. Only the qualified dietician was aware of the subject allocation. The allocation ratio was 1:1.

2.3. Intervention

After collection of baseline breath samples for $^{13}CO_2$ analysis, subjects took MLE or placebo and then ingested naturally ^{13}C -abundant cornflakes (50 g cornflakes + 100 ml low fat milk). The ingestion of the test meal took consistently less than 10 min. The use of cornflakes as a test meal proved to be useful in evaluating the digestibility of carbohydrates [25,28,29]. The total energy load

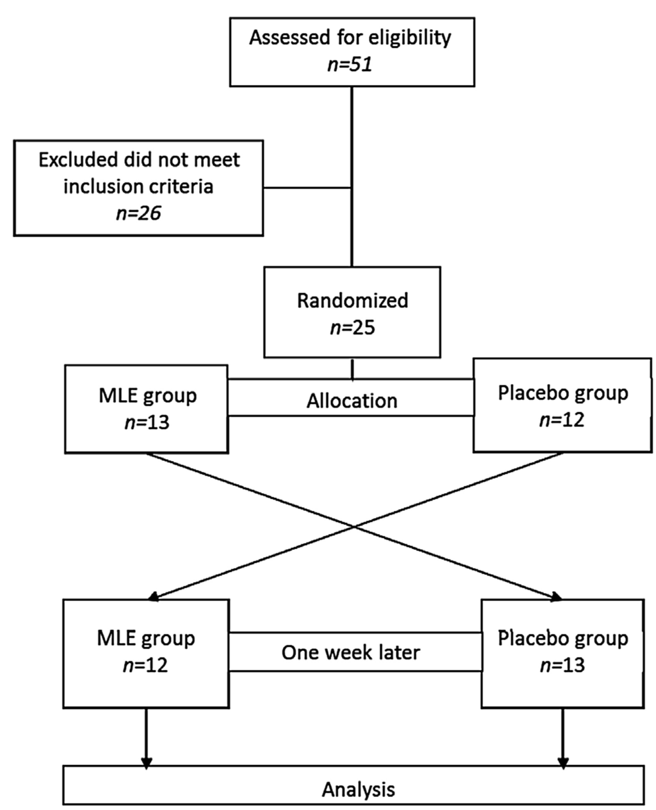

Fig. 1. The flowchart of the study.