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Pre-meal high-performance inulin supplementation reduce post-prandial glycaemic response in healthy subjects: A repeated single-arm clinical trial

Hendy Wijaya [a, *], Yudy Tjahjono [a], Kuncoro Foe [a], Diga Albrian Setiadi [a], Elisabeth Kasih [a], Hevi Wihadmadyatami [b]

[a] Biomedical Laboratory, Faculty of Pharmacy, Widya Mandala Catholic University, Jl. Kalisari Selatan No.1, Kalisari, Mulyorejo, Surabaya, East Java, 60112, Indonesia
[b] Faculty of Veterinary Science, Gadjah Mada University, Jalan Fauna 2, Sleman, 55281, Yogyakarta, Indonesia

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ABSTRACT

Background and aims: High-performance (HP) inulin, a dietary fiber consists of more than 10 fructose polymers, have been shown to reduce post-prandial glycaemic response (PPGR) and could prevent the occurrence of Type-2 diabetes mellitus (T2DM). Currently, there are no data on whether pre-meal HP inulin supplementation could decrease PPGR.
Methods: 8 healthy adults consumed 20 g of formula that contain 60.2% inulin (w/w) dissolved in water. Blood glucose was measured in fasted participants and at 30–120 min after starting to eat a prepared meal. This test was repeated every week with different supplement formulas.
Conclusion: pre-meal HP Inulin formula supplementation could suppress the post-prandial glycaemic response.

1. Introduction

It is well known that post-prandial hyperglycemia increases the risk of Type-2 diabetes mellitus (T2DM) and cardiovascular diseases (CVD), even in the non-diabetic range [1], closely linked to higher fasting plasma glucose [2], and could induce T2DM and CVD by promoting inflammation [3], and endothelial dysfunction [4]. Post-prandial blood glucose measured 2 h after the oral administration of 75 g glucose is a better predictor of deaths from all causes and CVD than fasting blood glucose [5].

Daily intake of dietary fiber could reduce post-prandial glycaemic response to food [6] and significantly lower the risk of T2DM by inhibiting the digestion and absorption of carbohydrates and fats in the gastrointestinal tract, maintaining satiety, and reducing caloric intake [7]. The recommended consumption of dietary fiber is around 19–38 g per day [8]. However, the general consumption rate of dietary fiber is still low.

Inulin or inulin-type fructan (ITF) is a form of dietary fiber. High-performance inulin (HP-Inulin) is ITF which has a degree of polymerization ≥10. HP-Inulin has been shown to have positive effects on the glycaemic status of subjects, for example, reducing hemoglobin A1c (HbA1C), plasma insulin concentration, triglycerides concentration, and improving insulin sensitivity [9,10]. However, no data is available regarding the effect of pre-meal HP-inulin supplementation on post-prandial blood glucose (PPBG) and post-prandial glycaemic response (PPGR) in healthy subjects. This manuscript indicates the potential of HP-inulin as a food supplement, which may be beneficial to suppress the PPBG and PPGR in healthy subjects.

2. Materials and methods

2.1. Subjects

Eight (n = 8) healthy subjects were voluntarily recruited. Inclusion criteria were body mass index (BMI) of 18.5–25.0, normal diet, not pregnant, not under any medication, and not having any kind of diseases and acute infection.

* Corresponding author.
E-mail address: hendy_wijaya@ukwms.ac.id (H. Wijaya).

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2.2. Trial design, intervention, and supplementation

This experiment adapted a single-arm trial analysis (see Supplementary Fig. 1). For the first week, we measured the glycaemic response to the meal without any intervention and used those data as a baseline. Three days before the intervention, every subject was informed to maintain their normal diet, physical activities, enough sleep (6–8 h/day) and fasted 10–12 h before the intervention. For the intervention, we used the untreated control without supplementation (NS), HP-Inulin (IF), isomaltooligosaccharides/IMO (IM, this formulation is marketed as Fibercreme®), the combination of HP-inulin and IMO (MF), dextrose solution (DS), and vehicle-glucose (VO) in the form of powder (PT. Lautan Natural Krimerindo, Mojokerto, Indonesia; detailed composition: see Supplementary Table 1). The Supplement was given orally before a meal for five consecutive weeks in the above orders. All formulas were prepared in 100 ml total volume with 20% concentration (w/v), diluted with distilled water. IMO solution was chosen as a control because it could act as partially digestible dietary fiber [11]. In VO, glucose syrup was added as the caloric source (control for IF). The isocaloric-"ready meal" (Charoen Pokphand, Jakarta, Indonesia)was given after intervention.

2.3. Blood sampling, blood glucose, and glycaemic response (iAUC)

Peripheral vein whole blood samples were taken for analysis of glucose concentration using FreeStyle Optium glucose monitoring system (Abbot Laboratories, Chicago, Illinois, USA). Blood glucose was measured at 0, 30, 60, 90, and 120 min after intervention and meal. The first measurement at 0 represented the fasting plasma glucose (FPG). The PPGR was described as the incremental area under the curve (iAUC) of blood glucose, and carried out using a linear trapezoidal method as described in the literature [11].

2.4. Statistical analysis

The data were analyzed statistically using paired-samples T-Test methods. The data were presented graphically as the mean ± standard deviation (SD) with Graphpad Prism™ 5.0 (San Diego, USA). All results were interpreted as significant if $p < 0.05$.

3. Results

All subjects have completed the trial. Their characteristics are shown in Table 1. The pre-meal supplementation with high performance-Inulin (IF) suppresses the PPBG-concentration at a certain measurement point (Fig. 1). From 30 until 90 min, the mean blood glucose concentration (in mg/dL) in IF is significantly lower than in the DS ($p < 0,05$). At 30 min, blood glucose concentration in IF is lower than NS ($p = 0.056$). However, at 60 min, blood glucose concentrations in IF are significantly lower than NS ($p = 0.036$), though they are no longer significant at 90 and 120 min (p=0.244 and p=0.069, respectively). At 30 and 60 min, blood glucose concentration in IF is significantly lower than the VO (p=0.037 and $p = 0.030$, respectively). There is no statistical difference in blood glucose concentration after 120 min.

The pre-meal supplementation with IF decreased the glycaemic response. The glycaemic response (Fig. 2) in IF intervention is significantly lower than DS (p=0.001). However, IF is not significantly lower than NS, VO, IM, and MF (p=0.105, $p = 0.079$, p=0.211, and p=0.093, respectively).

Table 1
Baseline characteristics of trial subjects.[a].

Characteristics	Value ± SD
Age (years old)	27.38 ± 4.37
Sex	
Male	2
Female	6
Weight (kilograms)	59.50 ± 7.79
Height (centimeters)	161.00 ± 8.00
BMI (kilograms/m^2)[b]	22.90 ± 1.80
EER (Kcal)[c]	1950.73 ± 338.44

[a] Results are presented as means ± standard deviation.
[b] BMI: Body Mass Index.
[c] EER: Estimated Energy Requirements.: calculated based on the *Harris-Benedict* formula, with the physical activity level 1.0 (sedentary activity).

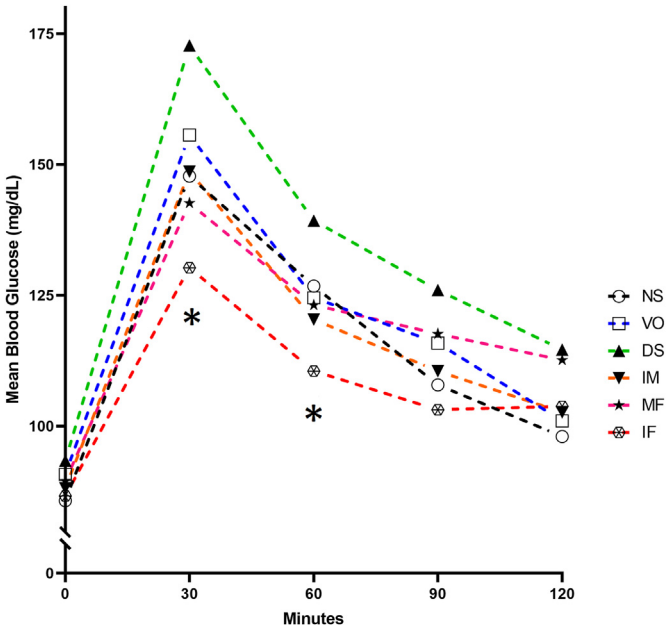

Fig. 1. Mean blood glucose concentration (mg/dL) was measured within 120 min after meal and supplementation for every intervention. NS = without supplementation; IF= HP-Inulin formulation; , IM = isomaltooligosaccharides(IMO)-formulations; MF = the combination of HP-inulin and IMO formula,DS = dextrose solution, VO = vehicle-glucose formulations *$p < 0.05$ IF vs DS and VO.

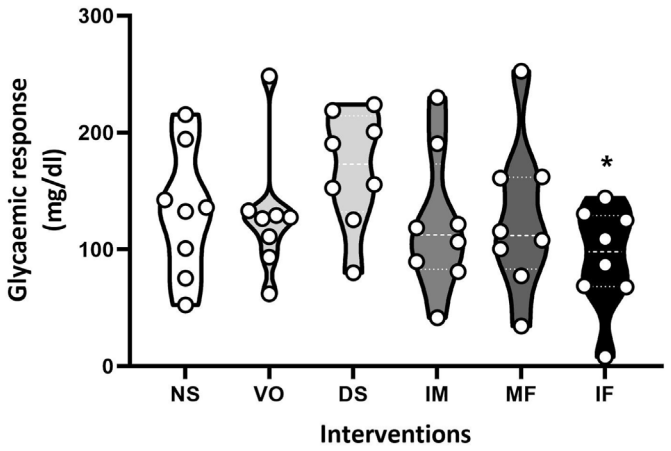

Fig. 2. Glycemic response for every intervention (iAUC). NS = without supplementation; IF= HP-Inulin formulation; , IM = isomaltooligosaccharides(IMO)-formulations; MF = the combination of HP-inulin and IMO formula,DS = dextrose solution, VO = vehicle-glucose formulations.*$p < 0.05$ vs DS as assessed by t-test. The graph represents the mean ± standard deviation.

4. Discussion

HP-inulin (IF) supplementation could suppress the increase of postprandial blood glucose and glycaemic response. This hypothesis has been proved by low PPBG (Fig. 1) and PPGR (Fig. 2). Interestingly, PPBG in IF intervention is lower than any other interventions, particularly in 60 min. Those results indicate that IF can suppress PPBG-absorption for at least 60 min after a meal.

The reported PPGR of trial subjects with IF-intervention is in accordance with the study using ITF extracted from chicory [12]. The PPGR-reduction resulted from HP-inulin supplementation is likely caused by the ability of HP-Inulin to decrease the gastric emptying time by affecting gut peptides [13]. This finding is in line with the previous study regarding ITF supplementation of up to 10 g per day [9]. Because IMO is partially digestible, the combination of HP-inulin and IMO has a lower effect in PPGR than HP-inulin alone [14]. However, further experiment to confirm this effect such as using acetaminophen as a marker of the gastric emptying time should be performed in the future studies [15].

In addition to the PPGR, HP-inulin has also been proven to have many other health benefits, for example, reducing low density lipoprotein-cholesterol, bodyweight, systolic and diastolic blood pressure [16]. Inulin can also alter the biodiversity of colonic microbiota and increase short-chain fatty acids production [17]. Inulin can enhance food taste and texture and providing a fat-like mouthfeel. Inulin can also reduce caloric intake through the action of satiety hormones such as glucagon-like peptide-1 (GLP-1), PYY, and ghrelin in several experiments [18–20]. The increase in the inulin-induced GLP-1 is also associated with the improvement in glucose homeostasis. However, the effects of inulin in this experiment in reducing post-prandial blood glucose is unlikely caused by the action of inulin on colonic cells to produce GLP-1, because the time interval between inulin administration and the glycaemic response measurements are too short. It needs a minimum of 4–6 h before any significant amount of inulin reaches the colon.

Even though we could demonstrate the role of IF in PPBG and PPGR, the empirical results reported herein should be considered in light of some limitations. The clinical impact of IF in metabolism should be investigated further by measuring several critical parameters such as insulin, GLP-1, PYY, and ghrelin. In addition, further studies such as the bigger dose and longer-term effects of pre-meal IF in the greater number of samples, and additional validation by using acetaminophen as a marker of gastric emptying are needed.

In summary, HP-inulin is beneficial as a pre-meal supplement to reduce the post-prandial blood glucose in healthy non-diabetic subjects. The dual benefits of inulin: better sensorial character, and a nutritious value, made HP-inulin an important fiber supplement to improve the glycaemic response in healthy subjects.

Ethics approval and clinical trial registration

This research was approved by the Health Research Ethics Committee of Widya Mandala Catholic University Surabaya (No.131/WM12/KEPK/DOSEN/T/2020) and registered on clinicaltrials.gov (reg no.NCT04994353).

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Author contributions

Methodology: Development of study design and study methodology: H.Wijaya. Investigation: Study conducting and data collection: H.Wijaya. Conceptualization: Design of the present exploratory study including research goals, aims, and analyses: H.Wijaya, Y Tjahjono, K Foe, D.A Setiadi, E Kasih, H Wihadmadyatami. Responsible for carrying out the statistical analyses: H.Wijaya, Y Tjahjono, D.A Setiadi and E Kasih. Writing - Review & Editing: Interpretation of the findings: H.Wijaya, Y Tjahjono, K Foe and H Wihadmadyatami. Writing - Original Draft: Writing of the initial draft: H.Wijaya and Y Tjahjono. Preparation including critical review and revision of the manuscript: H.Wijaya, Y Tjahjono, K Foe and H Wihadmadyatami. Responsibility: Responsible for the work including ensuring that the descriptions are accurate and agreed by all authors: H.Wijaya.

Declaration of competing interest

The author declare no conflict of interest.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.dsx.2021.102354.

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