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An integrated Caco-2TC7cells/biosensors device for the real time monitoring of intestinal glucose and polyphenols absorption and hypoglycemic effect of phytochemicals

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Abstract

An integrated device, for real-time monitoring of glucose and phenols absorption, that consists of a sensors/biosensors system (SB) and a Caco-2TC7 human intestinal cell culture, is shown here. The SB was made of a glucose oxidase-based biosensor, a sentinel platinum sensor, a laccase/tyrosinase-based biosensor and a sentinel carbon sensor located in the basolateral compartment (BC) of a cell culture plate. This system was able to monitor the glucose absorption and the hypoglycemic effect induced by different polyphenols and could be proposed to provide an effective strategy to manage postprandial hyperglycemia with natural compounds.

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Keywords: Postprandial hyperglycemia, enzyme biosensors, Caco-2TC7cells, glucose, polyphenols

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1. Introduction

Natural foods-based diets, rich in bioactive compounds, such as polyphenols, are attractive strategies to limit the glucose intestinal absorption and a potential tool of glycemic control mainly for type 2 diabetes mellitus (T2DM). Blueberry and pomegranate are important source of phenols [1,2] with potential hypoglycemic effect [3,4]. In order to deepen their *in vitro* hypoglycemic effects, a safe (without radiolabeled compound) diagnostic device, based on glucose oxidase (GOx) biosensors (SB1), laccase/tyrosinase (Lac/Tyr) biosensors (SB2) and Caco-2TC7 cells, was used for the real-time monitoring of glucose and polyphenols intestinal absorption.

2. Materials and methods

2.1. Fruit samples

The juices of pomegranate fruits (*Punica granatum* L.) *cv* Wonderful and blueberry fruits (*Vaccinum corimbosum* L.) *cv* Brigitta blue with glucose concentrations of 54 mM and 28 mM respectively, were used in this work.

2.2. Biosensors' design

A Corning® 6-wells cell culture plate was modified to be integrated with two potentiostats (fig 1A) connected with two sensor/biosensor systems (SBs): SB1 for glucose [5] and SB2 for polyphenols detection [6]. The BCs were all filled with 3mL of PBS, then inserts, constituting the apical compartments (ACs), containing the differentiated Caco-2TC7 cells [7], were gently added in each well (fig 1B). Glucose (1 mM) was added in AC in absence and in presence either of the inhibitors phloridzin (0.6 mM) and phloretin-2 O-xyloglucoside (0.2mM), or blueberry or pomegranate juices. The limit of detection (LOD), were 0.85 ± 0.07 µM and 1.59 ± 0.09 µM for GOx-based biosensors and Lac/Tyr-based biosensors respectively.

3. Results

After addition of glucose, a peak of about 40 µM was recorded at 20 min and then the transport from AC to BC continued with gradually decreasing fluctuations (fig. $1C_1$). The inhibitors negatively affected the glucose transport all along the 2 hrs, almost totally reducing its absorption. The glucose bioavailability was 5.1% but, in the presence of inhibitors, decreased of about 10 times. Phloretin and phloridzin were minimally transported in the BL compartment during the first 60 min then the signal progressively decreased (fig $1C_2$). With pomegranate juice, a higher amount of glucose was transported through the Caco-2TC7 monolayer in the BC (8‰) respect to the blueberry juice (1.7‰) (fig. $1D_1$). An increasing in polyphenols absorption was recorded by SB2 during the first 50 min for blueberry and pomegranate, then a constant decreasing occurred, reaching LOD at the end of the experiment. A higher amount of polyphenols was recorded for pomegranate juice in the BC (fig. $1D_2$). The hypoglycemic effect of both juices, recorded by SB1, were in agreement with previous studies [3,8,4,9]. With the present device we propose an original approach, in support of drug therapy, for a better management or prevention of T2DM. This approach can be easily extended to studies on different diseases by using different cellular models and/or different biosensor systems.

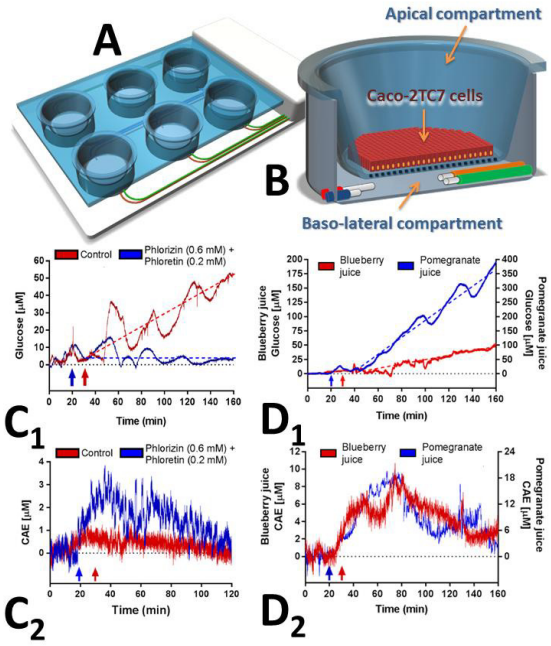

Fig. 1. (A) Schematic drawing of the diagnostic device: the case, including the two potentiostats, is integrated with the cell culture plate; (B) Apical and basolateral compartments with cells and sensor/biosensor systems; (C) Kinetics of glucose transport, in absence and in presence of glucose transport inhibitors, trough the Caco-2TC7 cells monolayer (C_1) and kinetics of phloridzin and phloretin transport through the Caco-2TC7 cells monolayer in the presence of 1 mM glucose (C_2); (D) Kinetics of glucose (D1) transport in the presence of blueberry and pomegranate juice and kinetics of blueberry's and pomegranate's polyphenols transport through the Caco-2TC7 cells monolayer (D2).

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