Abstract
Markers of Dysmetabolism Revealed Using a Dietary Challenge and Dry Blood Spots in a Remotely Executed Clinical Trial †

Stephany Gonçalves Duarte 1, Tushar More 2, Carlos Mario Donado-Pestana 1,*, Rosa Maria Cerdeira Barros 1, Elias Da Silva Araújo 1, Karsten Hiller 2 and Jarlei Fiamoncini 1,*

1 School of Pharmaceutical Sciences, University of São Paulo, São Paulo 01221-000, Brazil; stephanyduart@usp.br (S.G.D.); donadopestana@usp.br (C.M.D.-P.); rmbarros@usp.br (R.M.C.B.); esacamelol@usp.br (E.D.S.A.)
2 Braunschweig Integrated Centre of Systems Biology, Technische Universität Braunschweig, 38106 Braunschweig, Germany; t.more@tu-braunschweig.de (T.M.); karsten.hiller@tu-braunschweig.de (K.H.)
* Correspondence: jarlei@usp.br

Abstract: Background and Objectives: The physiological changes that take place after the ingestion of a meal are largely controlled by insulin and can reflect changes in the response to this hormone. Different studies have reported metabolic differences among groups of subjects in the postprandial state, while failing at detecting differences in the fasted state. Dry blood spots (DBS) are a non-invasive tool for sampling and storing small volumes of biological fluids, useful in biomarker discovery studies or the analysis of responses to interventions. The aim of this study was to identify markers of dysregulated glucose postprandial metabolism in a clinical study conducted remotely, using DBS as a sampling strategy. Methods: 100 males and females (18–60 y.o., BMI: 18.5–34.9 kg/m²) went through a dietary challenge based on the intake of an energy-dense meal (75 g glucose, 60 g canola oil and 20 g casein) and blood sampling (as DBS) at 0, 30, 60, 90, 120 and 150 min. Capillary glycaemia was monitored using a portable glucometer. DBS samples were analyzed in an untargeted metabolomic platform using gas chromatography coupled to mass spectrometry. Results: The outcomes of the study confirm the viability of the remotely executed clinical study. Performing the dietary challenges at the homes of the study subjects did not interfere with the quality of the data collected. The subjects were sorted according to glucose AUC and divided into two groups. The blood levels of markers of insulin resistance such as branched-chain amino acids and tyrosine were increased in the subjects with the larger glucose AUC. The concentration of metabolites associated with glucose metabolism (monosaccharides, lactate and Krebs cycle metabolites) were also increased is the blood of individuals with higher AUC, in comparison to those with lower AUC values. Moreover, 30 other unidentified metabolites also displayed higher concentrations in the DBS collected from individuals with larger AUC of glucose, indicating a number of compounds with marker quality that remain to be identified. Discussion: This is the first clinical study that employed DBS as a sampling strategy during a dietary challenge and successfully described a metabolic signature of glucose metabolism dysregulation.

Keywords: metabolomics; GC-MS; DBS; metabolism; postprandial

Author Contributions: Conceptualization, J.F.; methodology, J.F., T.M., K.H. and E.D.S.A.; software, K.H.; formal analysis, T.M. and J.F.; investigation, S.G.D.; resources, J.F. and K.H.; data curation, T.M., J.F. and S.G.D.; writing—original draft preparation, C.M.D.-P. and R.M.C.B.; writing—review and editing, J.F.; supervision, J.F.; project administration, R.M.C.B., S.G.D. and E.D.S.A.; funding acquisition, J.F. and K.H. All authors have read and agreed to the published version of the manuscript.

Funding: This research was funded by FAPESP grant number 22-02941-6.
Institutional Review Board Statement: The study was conducted in accordance with the Declaration of Helsinki and approved by the Institutional Ethics Committee of The School of Pharmaceutical Sciences—USP (CAAE 15438019.7.0000.0067) on 29 April 2020.

Informed Consent Statement: Informed consent was obtained from all subjects involved in the study.

Data Availability Statement: The data presented in this study are available on request from the corresponding author.

Conflicts of Interest: The authors declare no conflict of interest.

Disclaimer/Publisher’s Note: The statements, opinions and data contained in all publications are solely those of the individual author(s) and contributor(s) and not of MDPI and/or the editor(s). MDPI and/or the editor(s) disclaim responsibility for any injury to people or property resulting from any ideas, methods, instructions or products referred to in the content.