Correlation between *in vitro* and *in vivo* data on food digestion. What can we predict with static and dynamic digestion models?

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Improving health properties of food by sharing our knowledge on the digestive process

International Network

Dr. Didier DUPONT, Senior Scientist, INRA, France
372 scientists - 140 institutes – 39 countries
Industry involvement

42 private companies are following INFOGEST
INFOGEST

Chair

Didier Dupont - France

Vice-chair

Alan Mackie - UK

In vitro/in vivo correlations

WG1

Didier Dupont

In vitro semi-dynamic model of digestion

WG2

Alan Mackie

Models for specific populations

WG3

Uri Lesmes

Digestive lipases and lipid digestion

WG4

Myriam Grundy

Digestive amylases and starch digestion

WG5

Nadja Siegert

In silico models of digestion

WG6

Choi-Hong Lai

The “Mind-the-Gap” group

Guy Vergeres

Frederic Carriere

Fred Warren

Steven Le Feunteun

www.cost-infogest.eu
In vitro gastro-intestinal digestion
Consensus INFOGEST protocol

**Oral phase**
Mix 1:1 with Simulated Salivary Fluid (SSF)
salivary amylase (75 U/mL)
2 min, pH 7

**Gastric Phase**
Mix 1:1 with Simulated Gastric Fluid (SGF)
Pepsin (2000 U/mL)
2h, pH 3

**Intestinal Phase**
Mix 1:1 with Simulated Intestinal Fluid (SIF)
Enzymes
  - Pancreatin (based on trypsin 100 U/mL) or
  - Pure enzymes
Bile (10mM)
2h, pH 7

Minekus et al. 2014
Food Funct. 5, 1113-24
Highly Cited Paper (1%)
The consensus model can be learned with videos on YouTube
The Conference has been created by Infogest and is now an event regularly followed by 200 scientists.
We are pleased to announce the next 6th International Conference on Food Digestion in Granada, Spain, 2-4 April 2019
Static *in vitro* digestion models
Static *in vitro* digestion models: pro’s & con’s

**Main Reasons:**
- Ethical
- Technical
- Financial

**Advantages:**
- Standardisation of the experimental conditions
- Good reproducibility and repeatability
- Easy sampling, possibility to follow kinetics

**Disadvantages:**
- Impossible to mimic the complexity of the GI tract in a test tube!!!

What can we predict with static digestion models?
Static *in vitro* digestion models can be useful to compare series of samples or understand molecular mechanisms.

Static *in vitro* digestion models can be relevant to estimate end-point values such as:

- Glycaemic index
- Some micronutrient bioavailability

Static *in vitro* digestion models are too simple to study more complex phenomena like kinetics of digestion, food structure evolution in the GI tract, bacteria survival...
Carbohydrate digestion

14 foods tested:
Lentils
Soya beans
Marrowfat peas
Kidney beans
Wholemeal bread
Instant mashed potato
White rice
Brown rice
White spaghetti
Wholemeal spaghetti
Sweet potato
Buckwheat
Millet
Porridge oats

In vitro model requiring fresh human saliva and human post-prandial jejunal juice (no gastric phase)

Jenkins et al, 1982. Diabetologia, 22, 450-455

21 foods tested:
Bakery products
Breakfast cereals
Pasta
Pulses
Starch vegetables

GGE = grams of glucose equivalents


Oro-gastrointestinal model with an in vivo oral phase and the combined use of amyloglucosidase and pancreatin
Comparing the peptidome obtained during Skim Milk Protein digestion

Egger et al. 2018 Food Res Int, submitted

The INFOGEST consensus protocol is relevant for protein digestion

What about for the other nutrients?

Future experiments in WG4 and WG5
Bioaccessibility/bioavailability of carotenoids

Correlation of bioaccessibility and bioavailability of various carotenoids (lycopene, beta-carotene, lutein), as presented by Reboul, et al. 2006 (black points) and Alminger, et al. 2012 (grey points)
Bioaccessibility/bioavailability of iron

In conclusion, for micronutrients:

Direction of bioavailability (higher, lower, equally well) appears to be generally predictable by in vitro digestion

But does mostly not predict the magnitude of bioavailability in humans

Transport, metabolism, colonic changes (especially for polyphenols), biodistribution and (renal) excretion affect bioavailability

Correlation of iron bioaccessibility (dialysis method) following in vitro digestion from various iron containing test meals and bioavailability (as estimated via erythrocyte incorporation) employing the same formulations. Empty black dots: Data from Walter et al. (2003). Black dots: Data from Aragon et al. (2012). Grey dots: Data from (Davidsson et al. 2002). Empty grey dots: (Sandberg 2005).
Dynamic *in vitro* digestion models
Mono-compartmental models

Dynamic Gastric Model (DGM)

Multi-compartmental models

Digestion Dynamique Gastro-Intestinale (DIDGI)

Engineered Stomach and small INtestinal (ESIN)

TNO Gastro-Intestinal ModelTIM

SIMulator of the GastroIntestinal tract (SIMGI)

Human Gastric Simulator (HGS)

Simulator of the Human Intestinal Microbial Ecosystem (SHIME)

Artificial Colon (ARCOL)
Can dynamic in vitro digestion systems mimic the physiological reality?


Submitted soon to Crit Rev Food Sci Nutr

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DGM - Simulation of grinding in the stomach

Comparison of the Mean Breaking Time of agar gel beads in low viscosity (LV) and high viscosity (HV) meals

- Increasing the viscosity of the meal reduces the survival time of the harder beads
- Good *in vitro / in vivo* correlation
HGS – Comparison of white rice gastric emptying and intragastric pH with growing pigs data
Cumulative gastric and ileal delivery of a meal expressed as a percentage of total intake: *in vivo* (human n=7) gastric (●) and ileal (O) delivery of yoghurt and gastric (■) and ileal (□) delivery of blue dextran in the model simulating the slow transit of yoghurt
TIMcarbo: prediction of human glycemic response curve by combining CHO digestion in tiny-TIM, rapid glucose/fructose analysis and in silico modelling.

Glycemic response: In vivo (dotted) vs. predicted (solid)

Bellmann et al., submitted for publication
SHIME® – *in vitro / in vivo production* of Short-Chain Fatty Acid during fermentation of various polysaccharide sources

- **Arabinogalactan**
- **Pectin**
- **Starch**
- **Xylan**

**Legend:**
- ■ In vivo
- □ Ascending colon
- ◊ Transverse colon
- △ Descending colon
DIDGI® - Validation of protein digestion in infant formula

**Infant Formula**

**In vitro**

N=3

**In vivo**

18 piglets

**Caseins**

- **Stomach**
- **Intestine**

**β-lactoglobulin**

- **Stomach**
- **Intestine**

Menard et al. 2014

Food Chem. 145, 1039-45
Conclusion

- Static *in vitro* digestion models are interesting for comparing large series of samples in the same conditions or understanding interaction between constituents.

- They could also be valuable for predicting end-point values (glycaemic index, micronutrient bioaccessibility...) but are not relevant for investigating dynamic events.

- Dynamic *in vitro* digestion models can perfectly mimic the physiological reality when parameters are available in the literature.

- But when a system has been validated for a specific food, does this means that it is relevant for all kind of foods? Can we define large categories of foods (liquids, gels, solids) and validate them?

- More validated *in vitro* dynamic digestion models are needed to simulate the digestion process of specific populations (infant, elderly...)

- An international consensus could be found on the parametering of *in vitro* dynamic systems.

↘️ Next objectives of the Infogest network
The next INFOGEST Workshop will be held on the 12-13 of April 2018 in Leeds UK connected to:

17th Food Colloids Conference : Application of Soft Matter Concepts

8th - 11th April 2018
The University of Leeds, UK

Food Colloids is a biennial conference in the field of physical chemistry of complex foods.