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Static *in vitro* digestion model adapted ➤ to the general older adult population: an INFOGEST international consensus

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“Ageing leads to changes in the functionality of the digestive tract”

But the impact of ageing on digestion, and absorption of nutrients
is still unclear



1. Exhaustive literature review

Oro-gastrointestinal tract physiological parameters

Healthy older adults ≤ 65 y.

In vivo data



2. Consensus static *in vitro* digestion model

Adaptation of the INFOGEST 2.0 digestion method

Brodkorb et al. *INFOGEST static in vitro simulation of gastrointestinal food digestion*. Nat Protoc 14, 991–1014 (2019)

EAT4AGE consortium & International workshop

WP 3: *In vitro* digestibility and nutrient bioaccessibility of age-tailored food products





Oral phase

Similar to
young adults

Ionic composition of saliva

Very poorly documented, data available only for at-rest saliva

Salivary amylase activity

Data are scarce, and not easy to compare when determined with different assays

pH

1 study measured a slight increase (up to pH 8), 3 others no significant differences

Food/saliva ratio

2 robust studies about insalivation rates for different food matrices



Ratio of 1 : 1 (weight of SSF or saliva added : dry weight of food) is more physiologically relevant

Food bolus particle size

Adapt their oral processing (increased number of chewing cycles) to reach same particles size

Need for a robust, simple, reproducible protocol to grind the food

Duration

Longer only for older adults equipped with a denture



Oral phase

Young adults ¹⁸⁺

Older adults ⁶⁵⁺

SSF composition	See Brodkorb et al., (2019)	Same
Food:SSF dilution	1:1	1:1 (volume or according to DM)
pH	7.0	7.0
Duration	2 min	2 min
Chewing protocol	See Brodkorb et al., (2019)	Meat mincer, then add SSF or saliva
Amylase	75 U ml ⁻¹ (using the DNS assay)	Same



Manual, 5 cm mincing disk,
0,5 cm mesh size, one pass



Gastric phase

Ionic composition of gastric secretions

No information, research extended to animal models

Different from
young adults

Gastric enzymes activities

Marked lack of knowledge in the postprandial state in older adult populations

Pepsin: reduced by 40% (basal & pentagastrin-stimulated pepsin output, n = 22)

Feldman et al. *Effects of ageing and gastritis on gastric acid and pepsin secretion in humans: a prospective study.* Gastroenterology, 110 (4), 1043-1052 (1996)

Gastric lipase: decline with age of activity (gastric mucosal biopsies, n = 22)

Moreau et al. *Human gastric lipase: variations induced by gastrointestinal hormones and by pathology.* Scand. J. Gastroenterol. 23 (9), 1044-1048 (1988)

pH

Gastric pH curve in fasted and fed conditions followed w/ the Heidelberg capsule technique (n=79, ±71 y.), significant increase in gastric pH with age. **Russel et al.** *Upper Gastrointestinal pH in 79 healthy, elderly, north American men and women.* Pharm. Research, 10 (2) (1993)

In static model: consider the pH at gastric emptying half-time ($t_{1/2}$)

Bolus/gastric secretions ratio

No specific data were found, following curve from *Russel et al.*: 50/50 dilution is calculated at $t_{1/2}$

Duration

Still controversial, but several studies have shown that gastric emptying slows down with age: increases by 34 - 46%

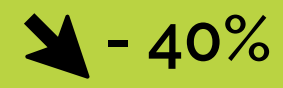


Gastric phase

Young adults ^(18⁺)

Older adults ^(65⁺)

SGF composition	See Brodkorb et al., (2019)	Same
Bolus:SGF dilution	1:1	1:1
pH	3.0	3.7
Duration	2 h	3 h
Pepsin	2000 U ml ⁻¹	1200 U ml ⁻¹
Gastric lipase	60 U ml ⁻¹	36 U ml ⁻¹





Intestinal phase

Ionic composition of intestinal secretions

No precise information, but 1 study shows an increase in Ca concentration with age: $[Ca^{2+}] = 0.01 \times \text{age} + 0.35$

Laugier et al. *Changes in pancreatic exocrine secretion with age: pancreatic exocrine secretion does decrease in the elderly*, Digestion, 50(3-4), 202-211 (1991)

Pancreatic enzymes activities

Some studies showed no difference, but general trends indicate a decrease in activity/output of enzymes of 13 to 35%

Pancreatic amylase: More data are available compared to the other pancreatic enzymes

Trypsin: Two studies showed opposite results

Chymotrypsin: No dif. or decrease in chymotrypsin output with ageing

Pancreatic lipase: Reported results highly controversial

Bile salts content

Limited data, decrease in bile acid synthesis

Different from young adults

Chyme/intestinal secretions ratio

Extremely difficult to assess, if we consider pancreatic exocrine secretions data are controversial: some saw a reduced volume of secretions, others no significant changes (n = 1615).

Dreiling et al. *The effect of age on human exocrine pancreatic secretion*. The Mount Sinai journal of Medicine, 52(5) (1985)

Duration

Not often monitored, if we consider whole gut transit time: no significant change in a recent study (n=111).

Nandhra et al. *Normative values for region-specific colonic and gastrointestinal transit times [...] Neurogastroenterology & Motility*, 32(2) (2020)



Intestinal phase

New model

Young adults ^(18⁺)

Older adults ^(65⁺)

SIF composition	See Brodkorb et al., (2019)	Same, except for [Ca ²⁺] = 1 mM	➔
Chyme:SIF dilution	1:1	1:1	
pH	7.0	7.0	
Duration	2 h	2 h	
Pancreatin	100 U ml ⁻¹ trypsin	80 U ml ⁻¹ trypsin	➔ - 20%
Bile salts	10 mM	6,7 mM	➔ - 33%

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Static *in vitro* digestion model adapted to the general older adult population: an INFOGEST international consensus

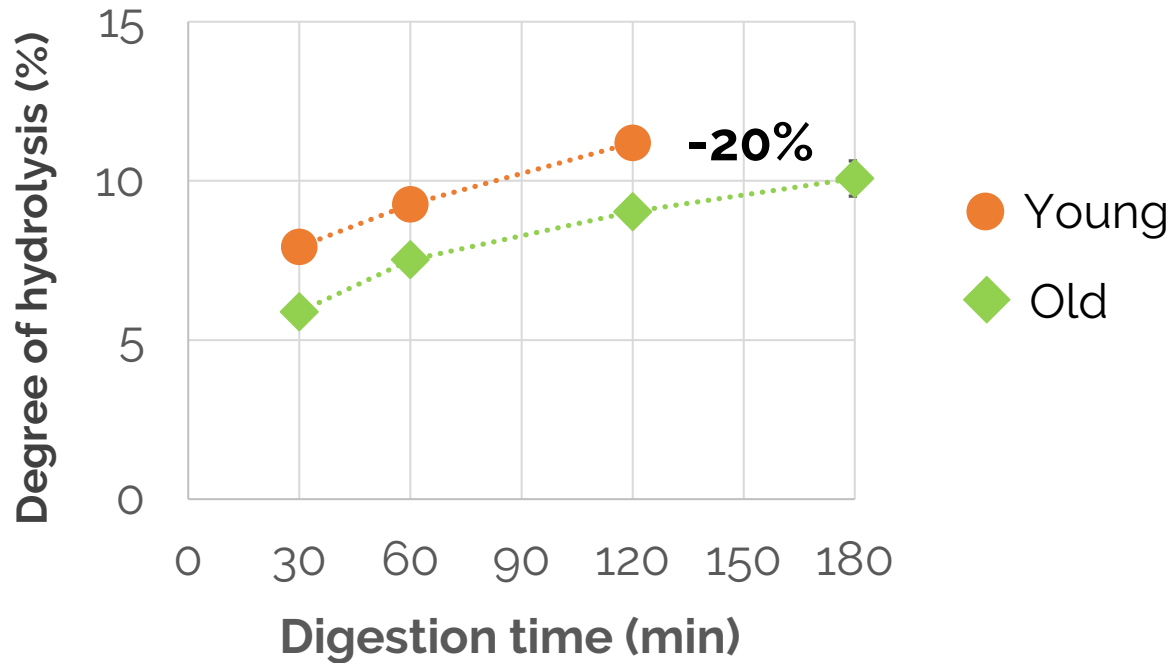
O. Menard,^{†a} U. Lesmes,^{†b} C. S. Shani-Levi,^b A. Araiza Calahorra,^c A. Lavoisier,^a M. Morzel,^a A. Rieder,^d G. Feron,^{e,f} S. Nebbia,^a L. Mashiah,^b A. Andres,^g G. Bornhorst,^{†h} F. Carrière,^{†i} L. Egger,^{†j} S. Gwala,^k A. Heredia,^l B. Kirkhus,^d A. Macierzanka,^{†m} R. Portman,^{†n} I. Recio,^{†o} V. Santé-Lhoutellier,^{†p} C. Tournier,^{†q} A. Sarkar,^{†r} A. Brodkorb,^s A. Mackie,^{†t} and D. Dupont,^{†u}



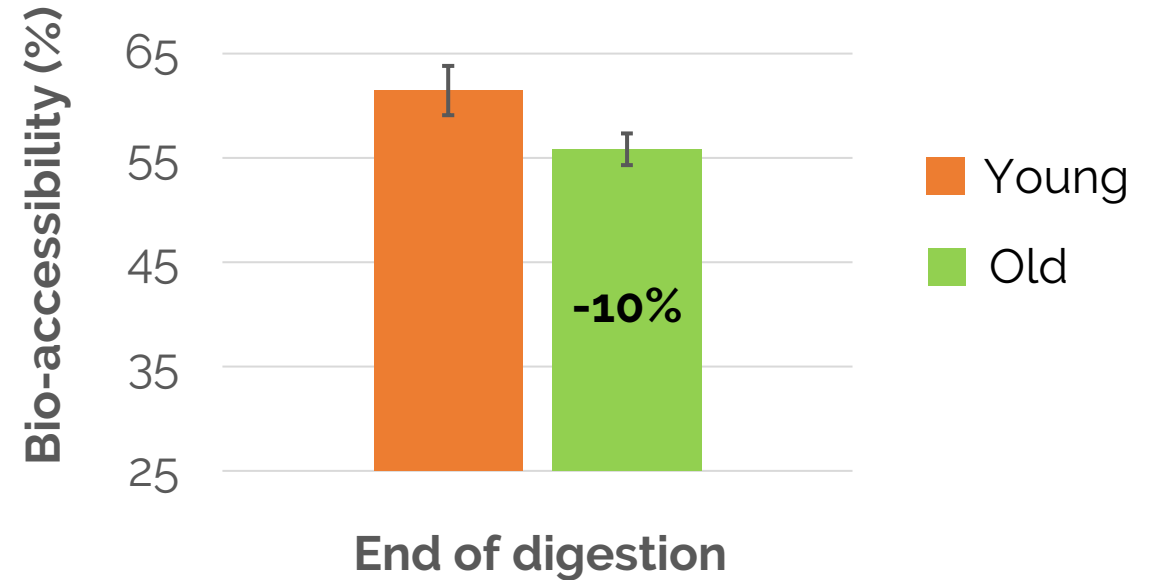
High-protein dairy products digestion

Skyr = commercial fermented dairy product containing mainly caseins (10% w/w)

Protein hydrolysis, gastric phase



Leucine release, intestinal phase



No difference in DH at the end of the digestion: **75-85%** in both conditions

Does age have an impact on food digestion?

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In vitro digestion of two protein-rich dairy products in the ageing gastrointestinal tract†

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Anaïs Lavoisier, ¹ Martine Morzel, Séverine Chevalier, Gwénaële Henry, Julien Jardin, Marielle Harel-Oger, Gilles Garric and Didier Dupont ¹

Yes, but

different scenarios depending on the composition & structure of the dairy products studied



8th International Conference on FOOD DIGESTION | INRAE | L'INSTITUT agro Rennes Angers | Qualiment | STLO

In vitro digestion of protein-rich dairy products adapted to the specific needs of older adults

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Introduction

- For older adults (> 65 y) insufficient energy and protein intake can lead to sarcopenia, characterized by the loss of muscle mass, strength, and function.
- To avoid this condition, healthy older adults need to consume nutrient-dense foods and increase the amount of high-quality proteins in their diet (at least 1g protein/kg body weight/day).
- Milk proteins are interesting to promote muscle health, and particularly whey proteins which are rich in leucine.
- Ageing leads to changes in the functionality of the digestive tract but the impact of ageing on the intake, digestion, and absorption of nutrients is still unclear.

Objective

Investigate the impact of age on the digestion (proteolysis & lipolysis) of high-protein cream cheese samples in different static *in vitro* conditions.

Materials & Methods

High-protein cream cheese

- 24% w/w of proteins, and 20% w/w of lipids
- WP-20 = formulated with a ratio of whey proteins (WP) to caseins (CAS) of 20 to 80% (- milk)
- WP-80 = formulated with a ratio WP-CAS of 80 to 20

Static in vitro digestion

Onli phase	Young adults	Older adults
pH	3.0	3.7
Duration	2 h	3 h
Pepsin	2000 U ml ⁻¹	3200 U ml ⁻¹
Gastric lipase	60 U ml ⁻¹	35 U ml ⁻¹
Intestinal phase		
ICa ²⁺	0.6 mM	1 mM
pH	7.0	7.0
Duration	2 h	2 h
Pancreatin	100 U ml ⁻¹	80 U ml ⁻¹
Bile salts	10 mM	6.7 mM

Results

Degree of protein hydrolysis (DH-P)

Degree of lipid hydrolysis (DH-L)

Conclusions

- Age had a significant impact on the digestion of high-protein cream cheese samples, however this effect depended on the ratio of caseins to WP in the product.
- At the end of the digestion, the hydrolysis of proteins was reduced in both samples in digestive conditions relevant to the physiology of older adults, but lipid hydrolysis was higher in the WP-rich sample (WP-80) than in the casein-rich sample (WP-20).
- Essential to carefully consider the composition, the structure, and the digestibility of dairy products to meet the specific needs of the older adult population.

For further information, please see also: Lavoisier, A. et al. *Food & Funct.*, 2023, 14, 9377-9399

Other applications

Fermented lentils and quinoa, whole and flours

Sánchez-García et al. *Protein digestibility and ACE inhibitory activity of fermented flours in older adults and standard gastrointestinal simulation*. FRI, 180, 114080 (2024)

Sánchez-García et al. *In vitro digestion assessment (standard vs. Older adult model) on antioxidant properties and mineral bioaccessibility of fermented dried lentils and quinoa*. Molecules, 28(21), 7298 (2023)

Cooked lentils

Duijsens et al. *From static to semi-dynamic in vitro digestion conditions relevant for the older population: starch and protein digestion of cooked lentils*. Food Funct., 15, 591-607 (2024)

Semi-dynamic & dynamic models



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8th International Conference on **FOOD DIGESTION**

Age-optimized digestion of two high protein dairy products: Gastric *in vitro* semi-dynamic digestion model of adult vs older adults

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Introduction

Nutrition & exercise contribute to healthy aging¹.

Adequate protein 25-30g/meal + Formulation of high protein food²

Age related GIT changes³

- Rational design of food targeted for older adults need to take G.I.T changes into account.
- In the older adult, the gastric phase has several significant differences.
- In vitro* gastric semi-dynamic digestion can provide insight into these changes.

Objectives

- To apply a physiologically relevant model to the older adult population.
- To establish differences in protein deconstruction due to application of an older adult parameters under semi-dynamic gastric conditions.

Key message

We show the importance of applying physiologically relevant parameters for the digestion of food targeted towards older adults.

Under *in vitro* semi-dynamic gastric conditions:

- proteolysis of both high protein yoghurt is slower for older adults.
- Proteins of 10 - 30 kDa in the whey based yoghurt are partially resistant to gastric digestion.
- Particle size is nevertheless reduced in the whey based yoghurt.

Point towards the need of a standardised semi-dynamic protocol.

Methods

Test food

- Casein based yoghurt (CBY)
- Commercial Skyr & dulce de leche base.
- Whey based yoghurt⁴ (WBV)
- In house (INRAE) yoghurt (80:20 whey to casein proteins combined with a WPI enriched caramel like base (Teagasc).

	CBY	WBV
Protein (%)	12.3	12.7
Carbohydrates (%)	11.1	12.4
Fat (%)	1.8	1.7
Calories/g	1.11	1.4

In vitro gastric semi-dynamic digestion

- 1 gastric emptying (GE) points
- Gastric half-time decreased by a factor of 1.5 for the older adult⁵.
- Pepsin concentration: adult 4000 U/ml, older adult 2400 U/ml

Analysis

- Particle size distribution (PSD) at gastric emptying points
- Confocal laser microscopy with Fast green and Nile red for staining protein and lipids, respectively.
- Size exclusion chromatography

Results & Discussion

Casein based yoghurt | **Whey based yoghurt**

CLSM and PSD show a progressive deconstruction of protein aggregates at gastric emptying.

SEC-HPLC reveals distinct pepsinolysis profiles between the adult and older adult models and with respect to the type of yoghurt.

Proteins of 10 - 30 kDa in the whey based yoghurt are resistant to gastric digestion. Attributed protein resistant fractions:

- larger proteins and peptic fractions are consistently more abundant in the older adult digests compared to that of the adult.

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EA4TAGIS project has received funding from the Irish Department of Agriculture and Marine (DAM) under the umbrella of the European Joint Programming Initiative 'A Healthy Diet for a Healthy Life' (JPI HDHL) and of the ERAC-NET on Food EFA (H2020-GIA-N° 696292) of the EU Horizon 2020 Research and Innovation Programme.

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Thank you



EAT4age
Palatable, nutritious and digestible foods for prevention
of undernutrition in active aging



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Bioactivity and Nutrition (BN) team