Protective cardiometabolic effects of milk polar lipids in postmenopausal women: potential role of sphingomyelin-cholesterol interactions in the gut

Vors C,[1,2] Joumard-Cubizolles L,[3] Lecomte M,[1] Meiller L,[2] Cheillan D,[1] Combe E,[1] Drai J,[1,2] Blond E,[1] Raynal K,[4] Gaborit P,[4] Joffre F,[5] Le Barz M,[1] Gesan-Guiziou G,[6] Cotte E,[7] Ouchchane L,[8] Vidal H,[1] Laville M,[1] Lambert-Porcheron S,[1,2] Malpuech-Brugère C,[3] Michalski MC[1,2]

[1] INRA UMR1397, INSERM U1060, Univ. Lyon-1, CarMeN laboratory, Pierre-Bénite, France; [2] CRNH Rhône-Alpes, Pierre-Bénite, France; [3] Université Clermont Auvergne, INRA, Unité de Nutrition Humaine, CRNH Auvergne, Clermont-Ferrand, France; [4]ACTALIA, Surgères, France; [5] ITERG, Pessac, France; [6] Science et Technologie du Lait et de l'Œuf (STLO), INRA, Agro Campus Ouest, Rennes, France; [7] Hospices Civils de Lyon, Chirurgie digestive, Pierre-Bénite, France; [8] Université Clermont Auvergne, UMR 6602 CNRS/UCA/SIGMA, Institut Pascal, Clermont-Ferrand, France.

Background

- Dietary synthetic emulsifiers alter drastically gut microbiota and promote inflammation and metabolic syndrome in rodent models.
- **Polar lipids (PL)** are **natural emulsifiers** widely used in food formulation, mainly from vegetal sources (soya).
- The **milk fat globule membrane** naturally contains PL, rich in **sphingomyelin (SM)**, which was shown in preclinical studies to reduce intestinal cholesterol absorption and improve lipid metabolism.
- Available **clinical studies** with milk PL were **rather inconclusive regarding their beneficial impact on human lipid metabolism**.

Objective: *To investigate whether milk PL impact human intestinal lipid absorption, metabolism, and associated markers of cardiometabolic health.*

Clinical trials

① Double-blind randomized controlled trial (VALOBAB-C) in overweight postmenopausal women at risk for CVD (IMC >25kg/m²; HDL-chol <1.6 mM) (n=58)

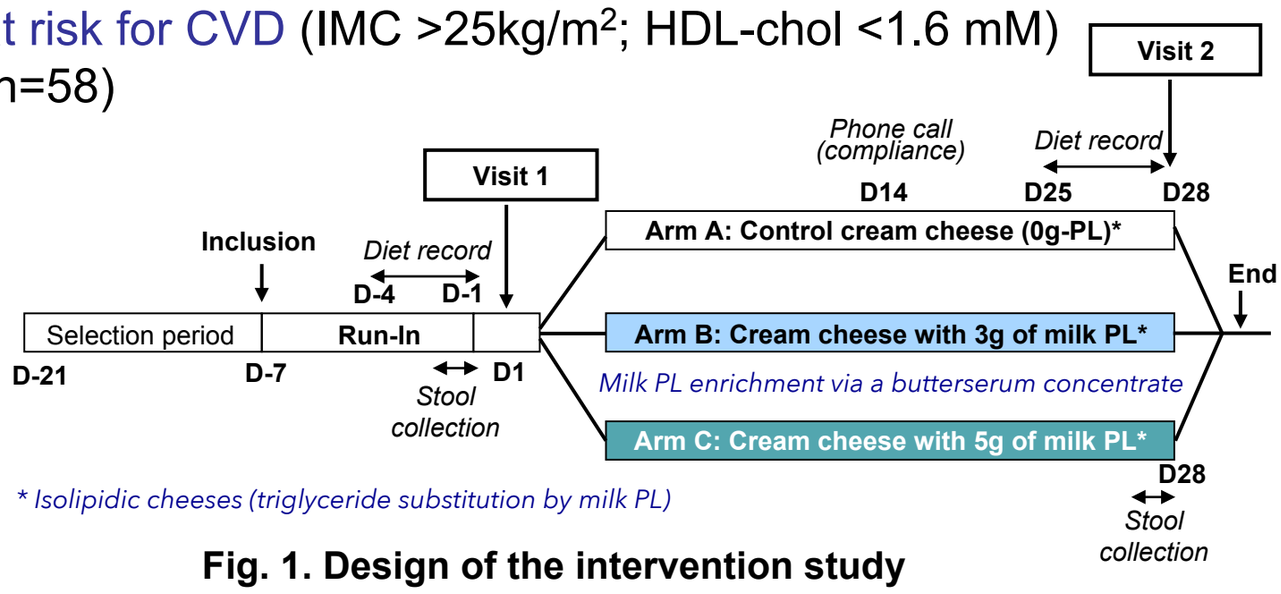


Fig. 1. Design of the intervention study

② Proof-of-concept mechanistic crossover study (VALOBAB-D) in ileostomized subjects:

8h-postprandial tests (n=4)

3 visits (crossover design): Ingestion of cream cheeses with 0-, 3- or 5g-PL + tracer

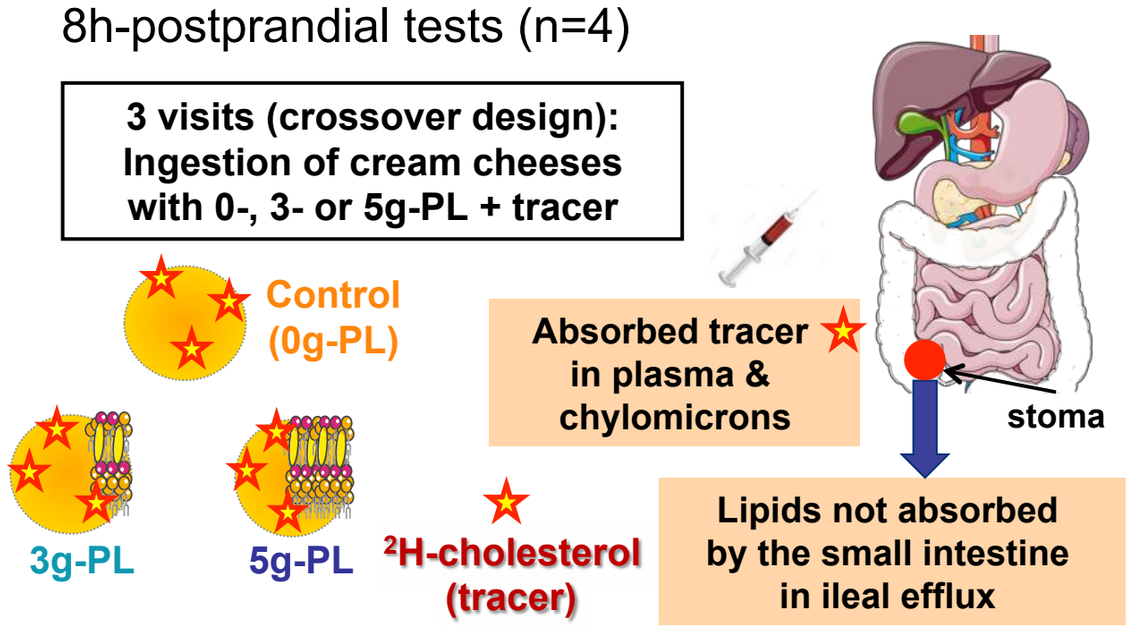
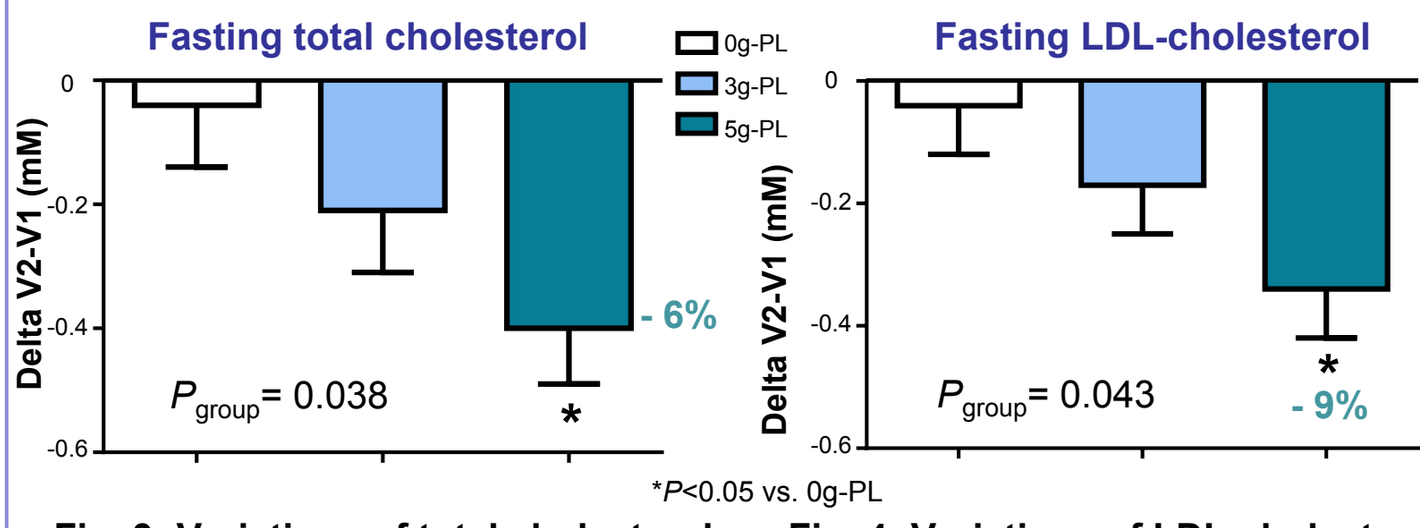


Fig. 2. Design of the postprandial study

Serum lipids: milk PL intervention effect



*P<0.05 vs. 0g-PL

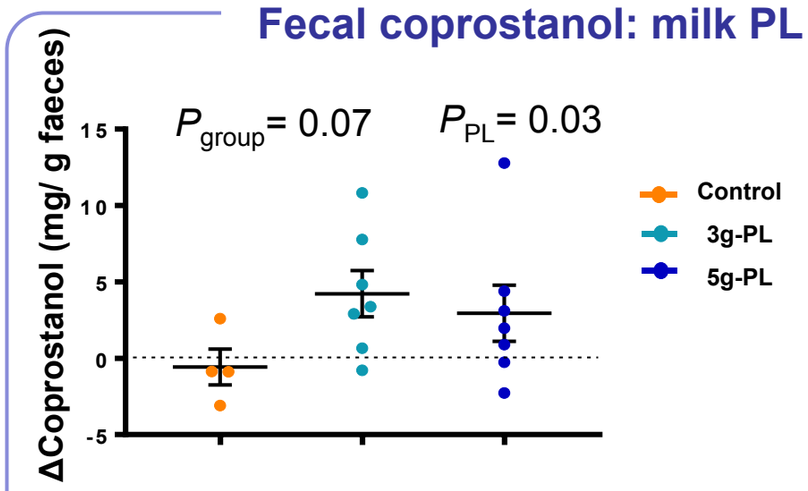
Fig. 3: Variations of total cholesterol

Fig. 4: Variations of LDL-cholesterol

Concomitant variations:
Triglycerides **- 15%**; ApoB/apoA1 **- 7%**; HDL-cholesterol **+ 5%**

Cholesterol fate in the gut? Decreased absorption? Conversion into non-absorbable coprostanol?

Fecal coprostanol: milk PL intervention effect



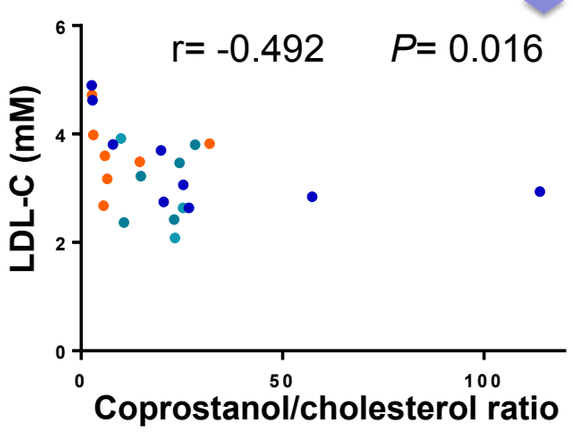


Fig. 5: Variations of fecal coprostanol

Fig. 6: Correlation between fecal coprostanol/ cholesterol ratio and serum LDL-C

²H-cholesterol in plasma and chylomicrons

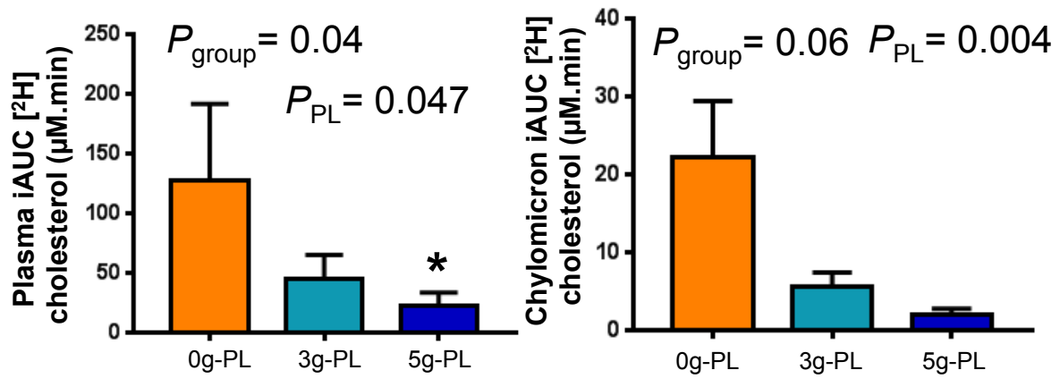


Fig. 7: Postprandial accumulation of ²H-cholesterol in plasma and chylomicrons of ileostomized subjects

Cholesterol and SM in ileal efflux

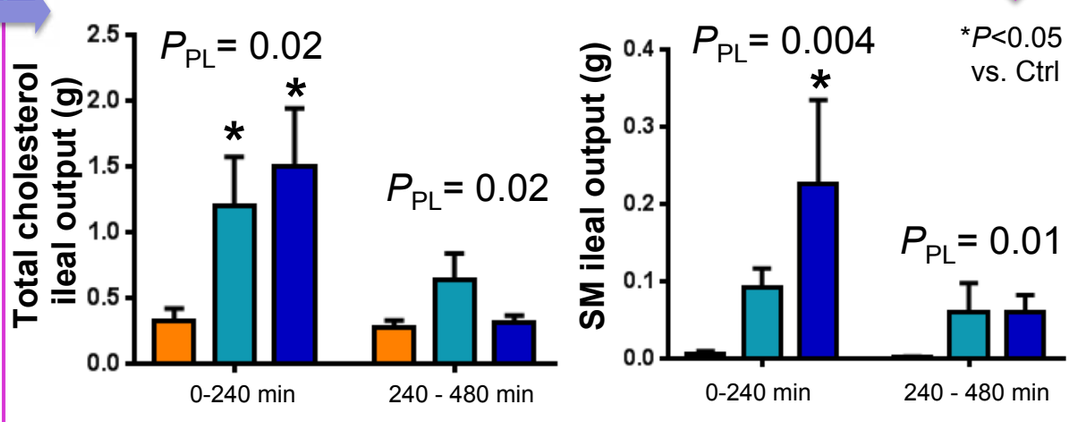


Fig. 8: Ileal excretion of cholesterol and sphingomyelin (SM)

Conclusion: Four-week supplementation with milk PL decreases significantly several lipid markers of CV risk.

Mechanisms of action for cholesterol lowering effects of milk PL in humans:

- ↗ **bacterial conversion of cholesterol to coprostanol**
- ↗ **co-excretion with unabsorbed milk SM**

➡ **Towards a larger use of milk PL as natural functional food ingredients**

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Contacts: cecile.vors@univ-lyon1.fr; marie-caroline.michalski@inra.fr

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