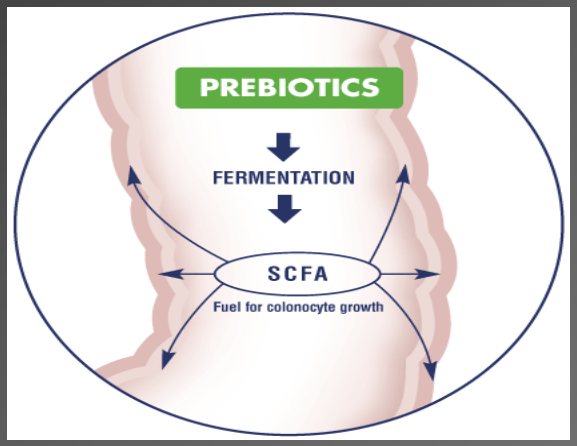
Short chain fatty acid (SCFA) exchange across the liver and gut

Implications for research on prebiotics



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Health claims

GEZONDHEID

Zo. 11 november 2007. Het laatste nieuws lees je het eerst op NU.nl

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Nederland massaal aan fruitdrankjes

Uitgegeven: 9 november 2007 15:23

Groente- en fruitdrankjes winnen aan populariteit: de verkoop ervan is in ons land enorm gestegen.

Dit jaar hebben Nederlanders zo'n 360 miljoen euro uitgegeven aan groente- en fruitdrankjes, zo schrijft dagblad De Pers. Dat is ongeveer 21 euro per Nederlander: 200 procent meer dan twee jaar geleden.

Het Voedingscentrum reageert met het advies om niet meer dan één portie groente of fruit per dag te vervangen door een sapje. Het gezondheidseffect van echte groenten en vruchten is volgens het centrum veel groter.

It's all about fibres!

Scientific literature

1: Mol Nutr Food Res. 2005 Jun;49(6):609-19.

Dietary fibres as "prebiotics": implications for colorectal cancer.

Lim CC, Ferguson LR, Tannock GW.

1: Lancet. 2003 May 3;361(9368):1496-501.

Dietary fibre in food and protection against colorectal cancer in the European Prospective Investigation into Cancer and Nutrition (EPIC): an observational study.

Bingham SA, Day NE, Luben R, Ferrari P, Slimani N, Norat T, Clavel-Chapelon F, Kesse E, Nieters A, Boeing H, Tjønneland A, Overvad K, Martinez C, Dorronsoro M, Gonzalez CA, Key TJ, Trichopoulou A, Naska A, Vineis P, Tumino R, Krogh V, Bueno-de-Mesquita HB, Peeters PH, Berglund G, Hallmans G, Lund E, Skeie G, Kaaks R, Riboli E; European Prospective Investigation into Cancer and Nutrition.

1: J Nutr. 2007 Nov;137(11):2580S-4S.

Overview of experimental data on reduction of colorectal cancer risk by inulin-type fructans.

Pool-Zobel BL, Sauer J.

1: Nutr Rev. 2007 Feb;65(2):51-62.

Influence of dietary fiber on inflammatory bowel disease and colon cancer: importance of fermentation pattern.

Rose DJ, DeMeo MT, Keshavarzian A, Hamaker BR.

Effects of SCFA

Clinical applications

Ulcerative colitis

Short bowel syndrome

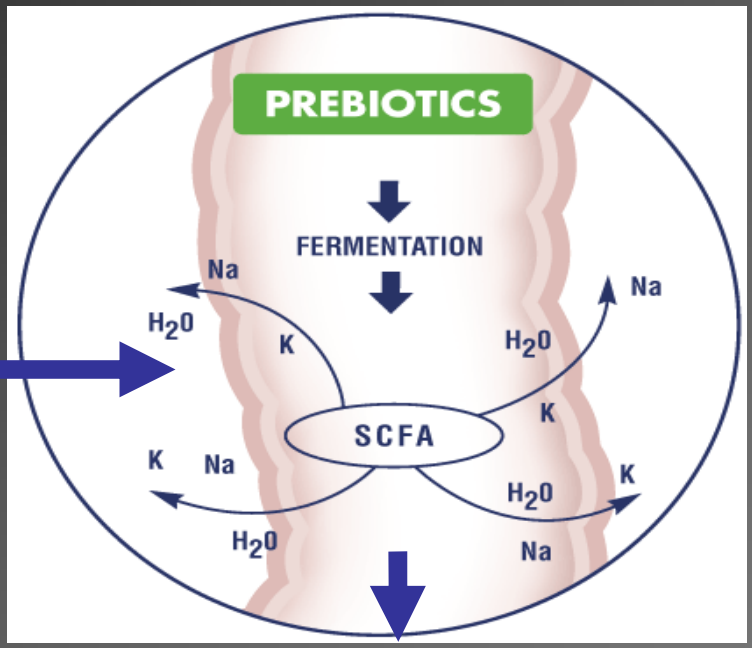
Diversion colitis

Colon carcinogenesis

Etc. etc.

Paradox

~70-90% metabolized directly

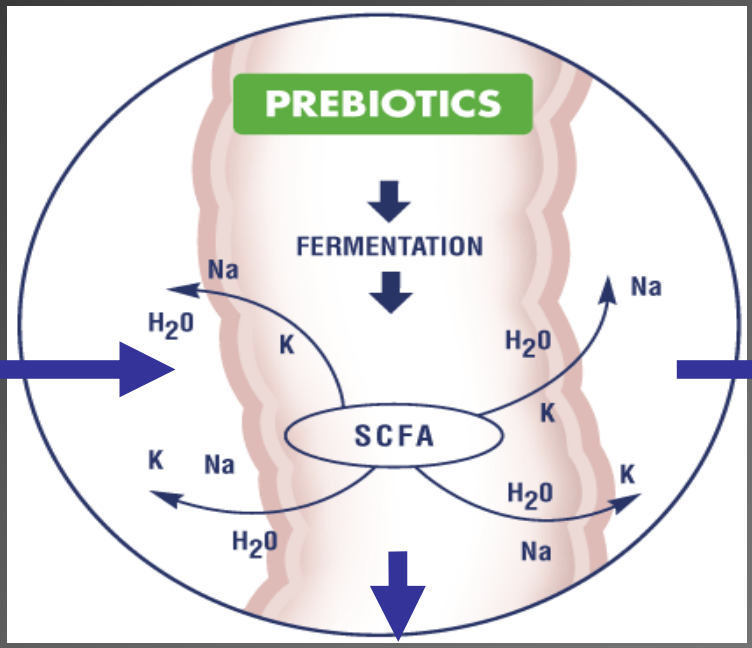


< 5% in faeces

Bergman, Physiological reviews, 1990

Paradox

~70-90% metabolized directly



Surplus:

Portal release

?

< 5% in faeces

High systemic SCFA concentrations are toxic!

Bergman, Physiological reviews, 1990

Aim

Clarify interorgan SCFA exchange across gut and liver in humans with normal liver function

Fermentation process

Colon

+ H_2O ⟶ SCFAs + CO_2 + gas + energy

Bacterial hydrolases

Anaerobic bacteria

Topping Phys Rev 2001

Fermentation process

Colon

+ H_2O ⟶ SCFAs + CO_2 + gas + energy

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Fermentation process

Colon

+ H_2O → SCFAs + CO_2 + gas + energy

Bacterial hydrolases

Anaerobic bacteria

6 Acetate : 2 Propionate : 1 Butyrate

Topping Phys Rev 2001

Materials & Methods

12 patients undergoing upper abdominal surgery

Fasted state

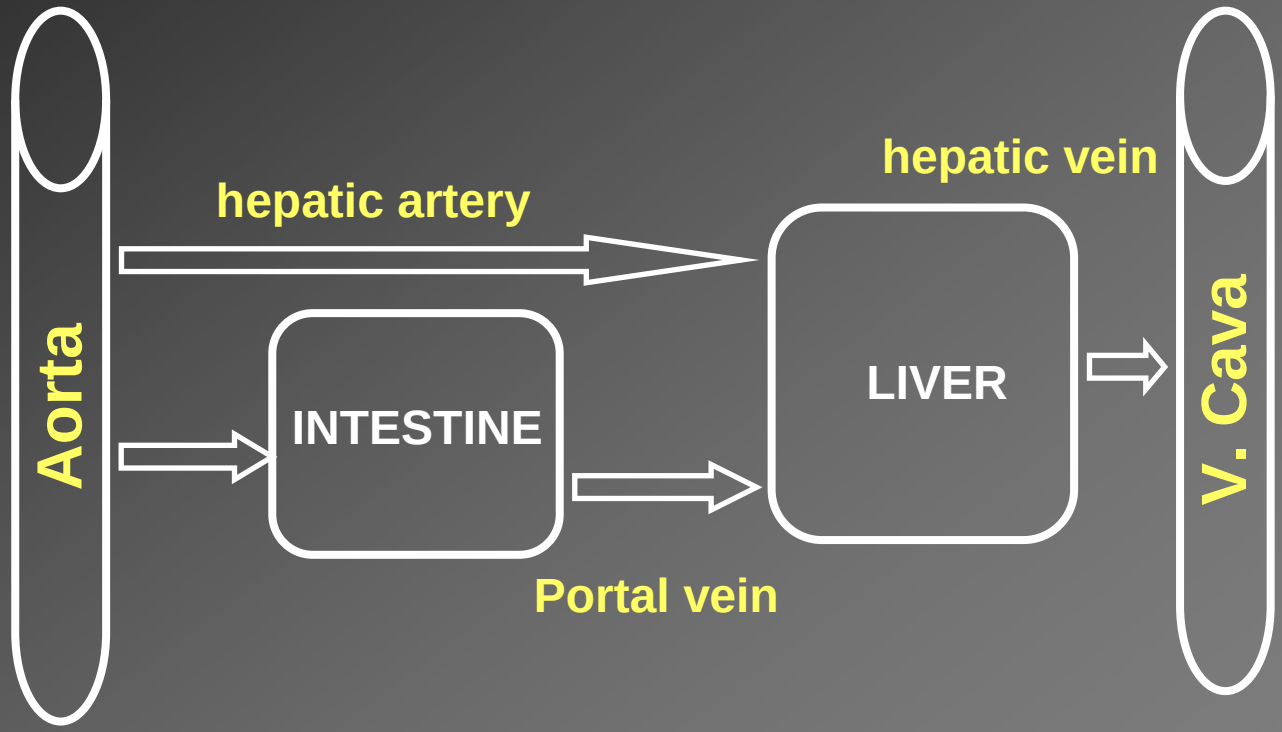
Blood sampling: radial artery, portal and hepatic vein

Blood flow measured with Duplex

Analyzing blood samples with LC-MS system

Materials & Methods

Flux = AV difference x plasma flow



Liver flux = splanchnicus flux – PDV flux

Results

Table 1. Patient Characteristics	
Parameter	**Median (range)**
Male/Female	9/3
Adenoca liver/ adenoca PDV/ benign	9/2/1
Age (years)	62.5 (51-76)
Weight (kg)	91.6 (63-134)
BMI (kg/cm^2)	29.6 (22.5-40.0)
AST	22.5 (6.6) U/L

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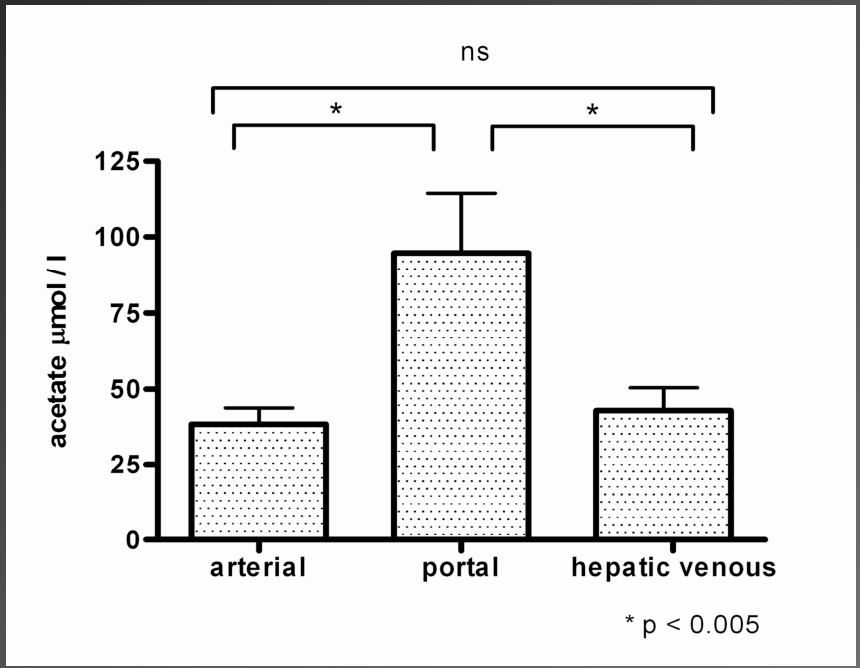
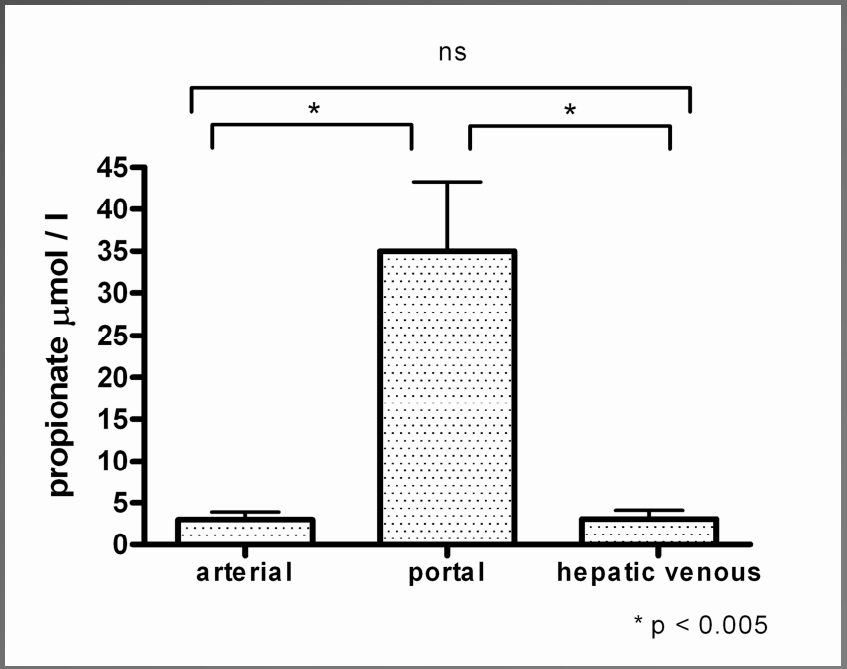

ns
*
*
125
100
75
50
25
0
acetate µmol / l
arterial
portal
hepatic venous
* p < 0.005


ns
*
*
45
40
35
30
25
20
15
10
5
0
propionate µmol / l
arterial
portal
hepatic venous
* p < 0.005

Results

Table 2 Organ Flux of Short Chain Fatty Acids			
	PDV (µmol/kg/h)	Liver (µmol/kg/h)	Splanchnic (µmol/kg/h)
Butyrate	1.3 (0.9) ◊	-1.3 (0.9) ◊	0◊
Acetate	12.3 (3.8)	-10.9 (3.6)	1.4 (1.2) ◊
Propionate	6.8 (1.9)	-6.8 (1.8)	0.0 (0.2) ◊
◊ indicates fluxes that are not significantly different from zero. ND: not detectable.			

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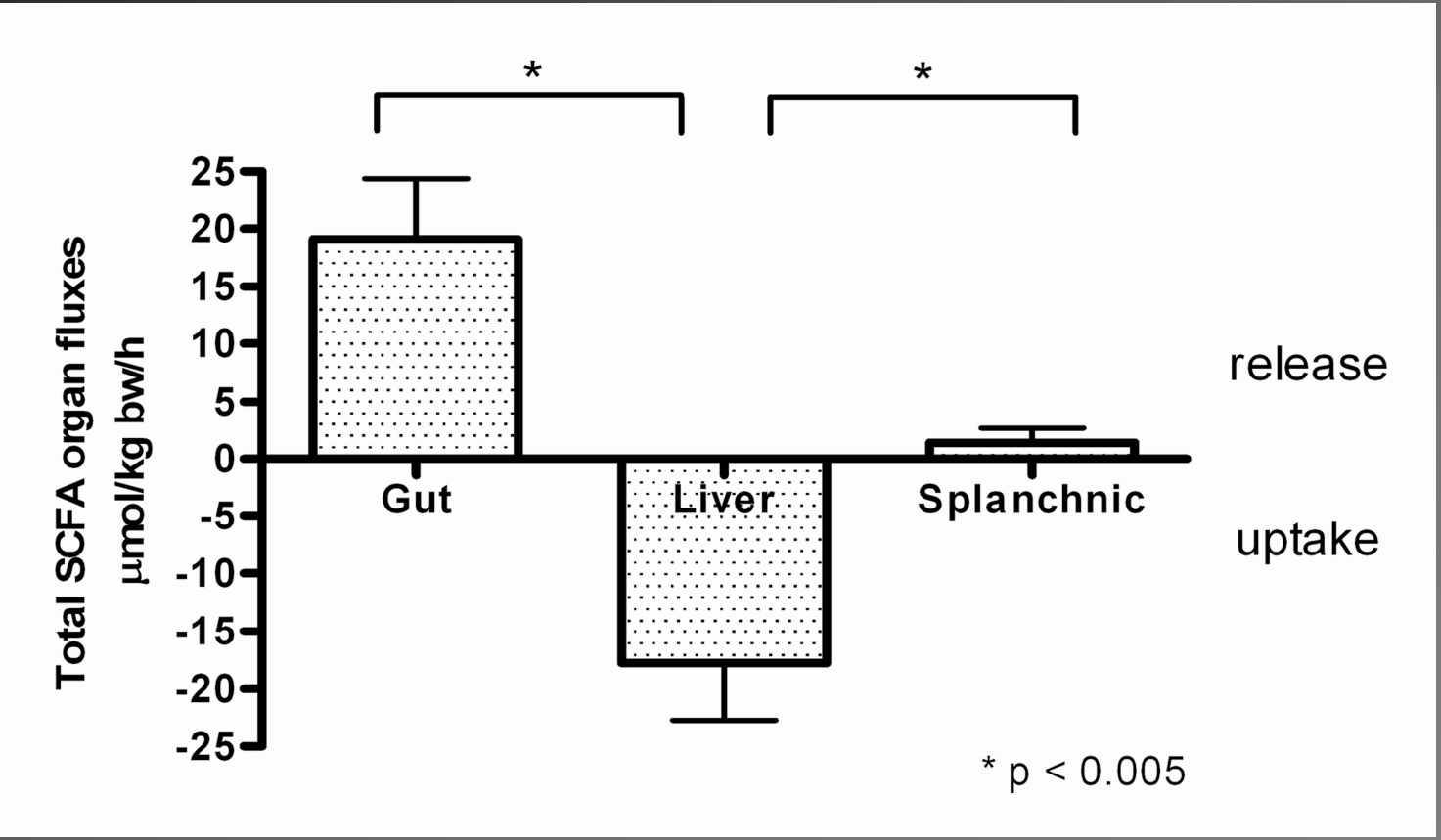
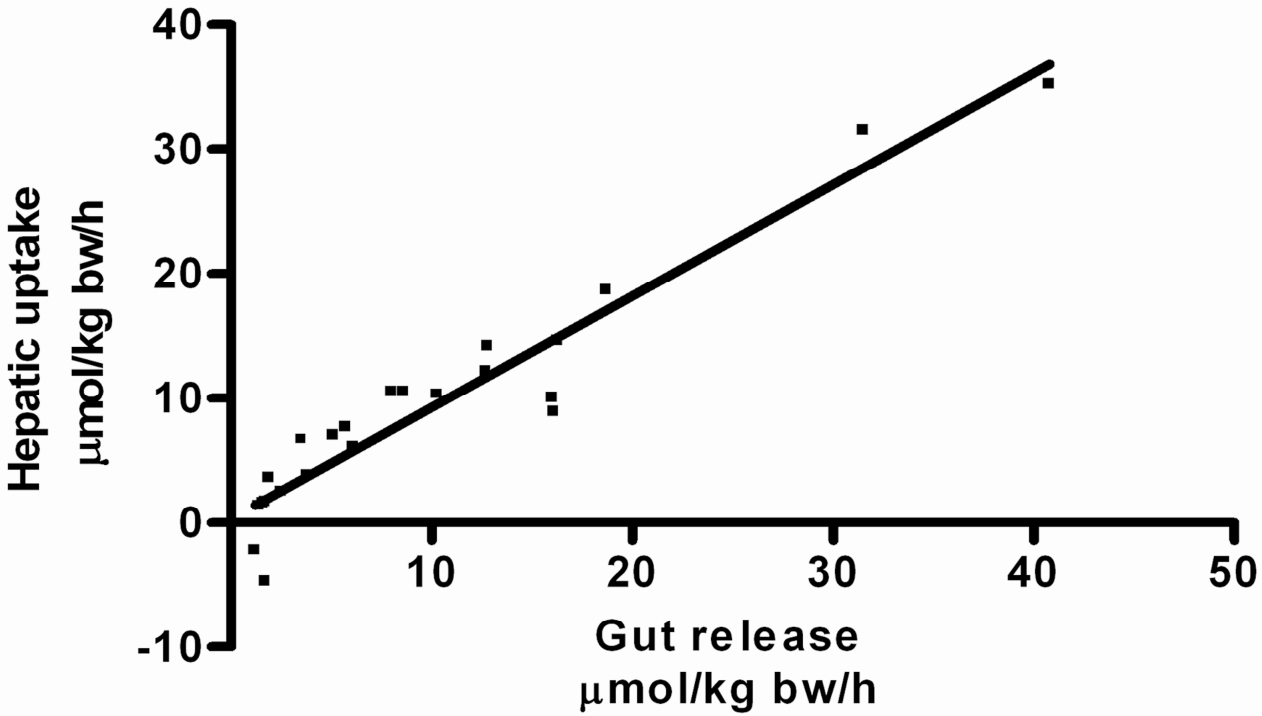

*
*
25
20
15
10
5
0
-5
-10
-15
-20
-25
Total SCFA organ fluxes
µmol/kg bw/h
Gut
Liver
Splanchnic
release
uptake
* p < 0.005

Results



$R^2 = 0.92$ **p< 0.0001**

Conclusion

✓ First in vivo study that quantifies SCFA exchange

✓ PDV flux balances liver flux for acetate, propionate and butyrate

✓Splanchnic flux equals zero for acetate, propionate and butyrate

➔ Intestinal release

➔ Efficient uptake by liver

Future perspectives

- ✓ SCFA metabolism in patients with:
  - ✓ liverfailure
  - ✓ ulcerative colitis
  - ✓ partial colectomy
- ✓ Intervention with butyrate enema and prebiotics

Questions