Absorption and Metabolism of Berry Polyphenols

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Polyphenols in berries

- Anthocyanins
  - up to 1000 mg/kg (aglycones)
- Flavonols
  - < 300 mg/kg, mainly quercetin glycosides
- Flavan-3-ols and proanthocyanidins
  - < 300 mg/kg, from 500 to 5000 mg/kg
- Phenolic acids
  - cinnamic acid derivatives < 400 mg/kg
  - benzoic acid derivatives < 200 mg/kg

Absorption

- Most of the polyphenols are absorbed in some extent after the hydrolysis of glycosides.
- Peak concentrations occur about 1- 2 hours after the supplementation, and half lives are usually few hours.
- Percentage absorption values are mainly based on urinary excretion of the parent compounds or their glucuronide conjugates.
- Percentage absorption would be higher if metabolites were taken into account.

Metabolism

- Most of the polyphenols are extensively metabolised after the absorption
- All polyphenols are conjugated with glucuronic acid (~80%) and sulphates (~20%) in human body, and the amount of aglycones is about 10% of the total in blood circulation.
- Polyphenols are methylated and dehydroxylated, and many of them also fragmented in colon.
- Metabolism of polyphenols is rarely taken into account when health effects are studied, although it is extensive in most of the cases.

Absorption and Metabolism of Anthocyanins

- Anthocyanins are studied mainly as a group of compounds
- Plasma concentrations about 0 - 100 nmol/L after the supplementations (Manach & al. Am. J. Clin. Nutr. 2005)
- Low variation in plasma concentrations and urinary excretion, although the supplemented doses vary from 3 to 1200 mg
- In maximum 5 % of the supplemented amount excreted in urine as such or glucuronides
- Fragmentation to phenolic acids by gut microflora in vitro

Absorption and Metabolism of Flavonols

- Only quercetin and its glycosides studied
- Plasma concentrations range from 100 to 7600 nmol/L although the supplemented doses vary only from 1.6 to 200 mg. Source and type of glycoside affects absorption. (Manach & al. Am. J. Clin. Nutr. 2005)
- Urinary excretion of quercetin is under 10 % of the dose
- Fragmentation to phenolic acids by gut microflora in vitro, products are 3,4-dihydroxy- and m-hydroxyphenylacetic acids.
- Methylation and dehydroxylation of quercetin occurs

Absorption and Metabolism of Flavan-3-ols

- Plasma concentrations range from 100 to 6900 nmol/L after the wide variety of doses from about 30 mg up to 2000 mg. (Manach & al. Am. J. Clin. Nutr. 2005)
- Urinary excretion is usually under 10% of the dose, but in a few studies almost 30%
- Fragmentation to valerolactones occur
- Proanthocyanidins are not absorbed as such

Absorption and Metabolism of Phenolic acids

- Mainly studied cholorogenic, caffeic and ferulic acid
- Plasma concentrations range from 6.6 to 505 nmol/L, and doses range from 1 mg to 900 mg. (Manach & al. Am. J. Clin. Nutr. 2005)
- Urinary excretion ranges from 0.3 to 25% of the dose.
- No studies on benzoic acid derivatives

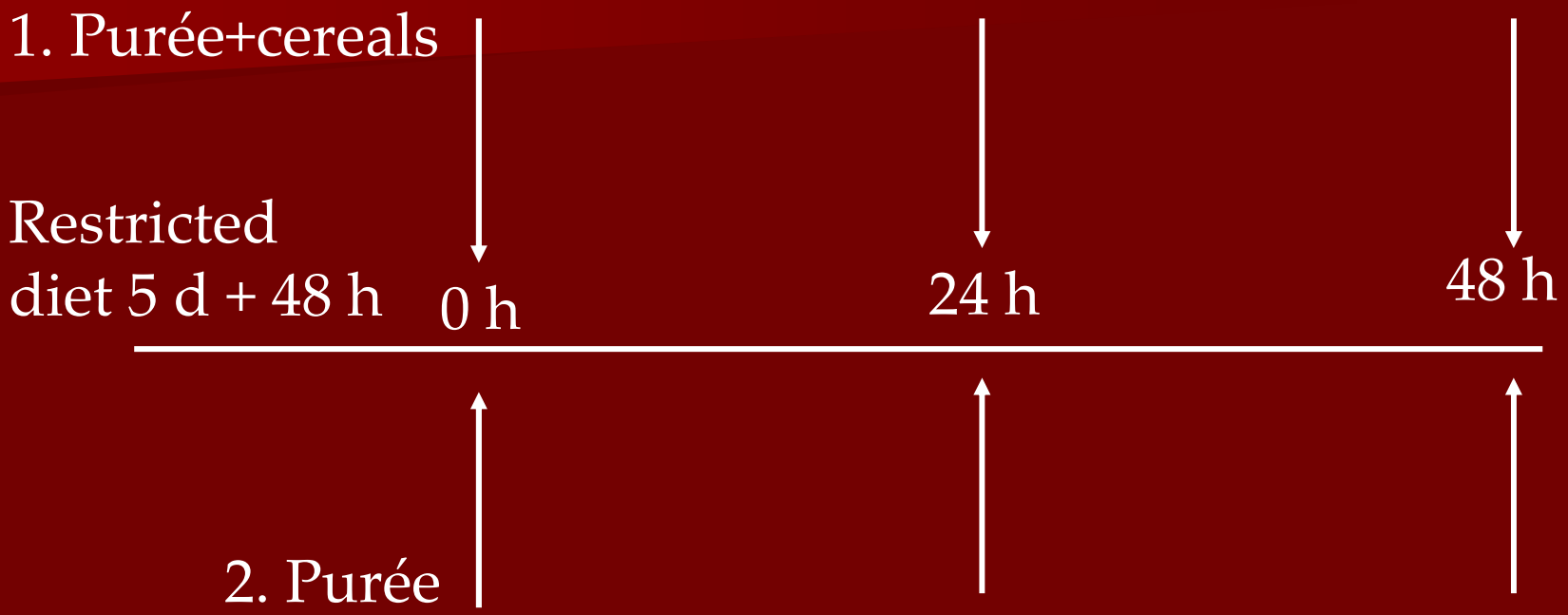
Absorption and Metabolism: summary

- Absorption of berry polyphenols occurs, but the amounts are not known.
- Sources and types of glycosides affect absorption.
- All polyphenols and their metabolites conjugate with glucuronic acid in human body.
- Fragmentation occurs in colon.

Berry studies at the Research Institute of Public Health

- Aim of these two trials was to study the absorption, metabolism and kinetics of phenolic compounds present in bilberries and lingonberries, and effects of oat cereals on the aforementioned parameters.

Berry studies: study design



Blood samples: 0, 0.5, 1.5, 3, 6, 8, 12, 24, 30, 36, 48 h

Urine samples: -24, 0-2, 2-4, 4-6, 6-8, 8-12, 12-24, 24-30, 30-36, 36-48 h

Berry studies: study meals

Polyphenols

- Anthocyanins 590 mg = 1113 µmol
- Flavonols 37 mg = 80 µmol
- Flavan-3-ols 54 mg = 140 µmol
- Phenolic acids 86 mg = 429 µmol

- TOTAL 767 mg equal to 1800 µmol

- Study meals contained 50 g of berry purée concentrated from bilberries and lingonberries (3:1) to supplement approximately 600 mg of anthocyanins.

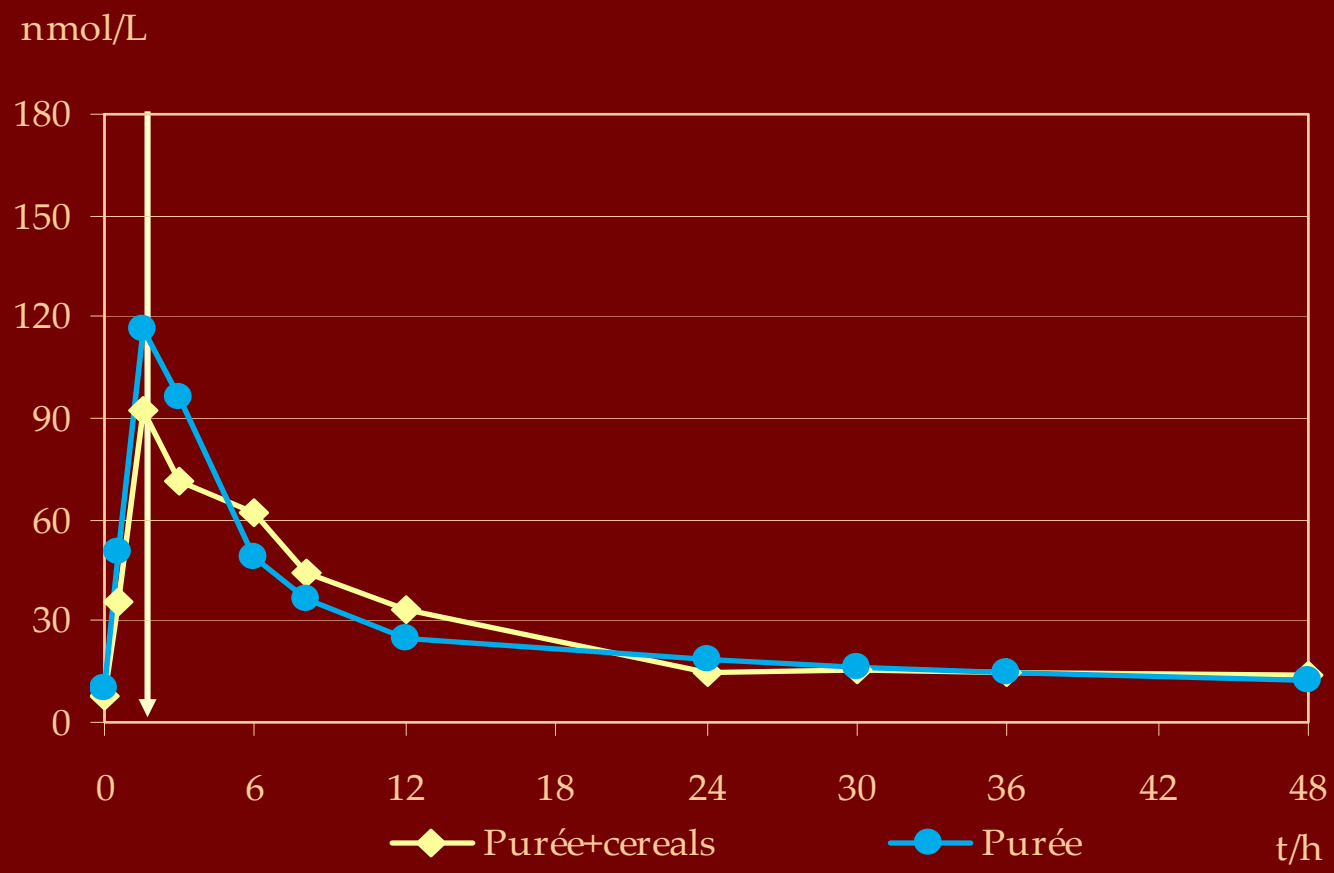
- The other meal included also 50 g of oat cereals, which contained mainly caffeic and ferulic acid (12 mg).

Anthocyanin results

- Maximum concentration of plasma anthocyanins was 150 nmol/L after the purée and oat cereals, and 138 nmol/L after the purée alone.
- Peak concentrations occurred 3 and 1.5 hours after the meals. Oat cereals postponed the peak, but no effect on the concentration was observed.
- Urine samples of one subject were analysed up to 8 hours after the meal. The excretion of anthocyanins was 0.3 % of the ingested amount.
- Anthocyanins were possibly fragmented to phenolic acids in some extent.

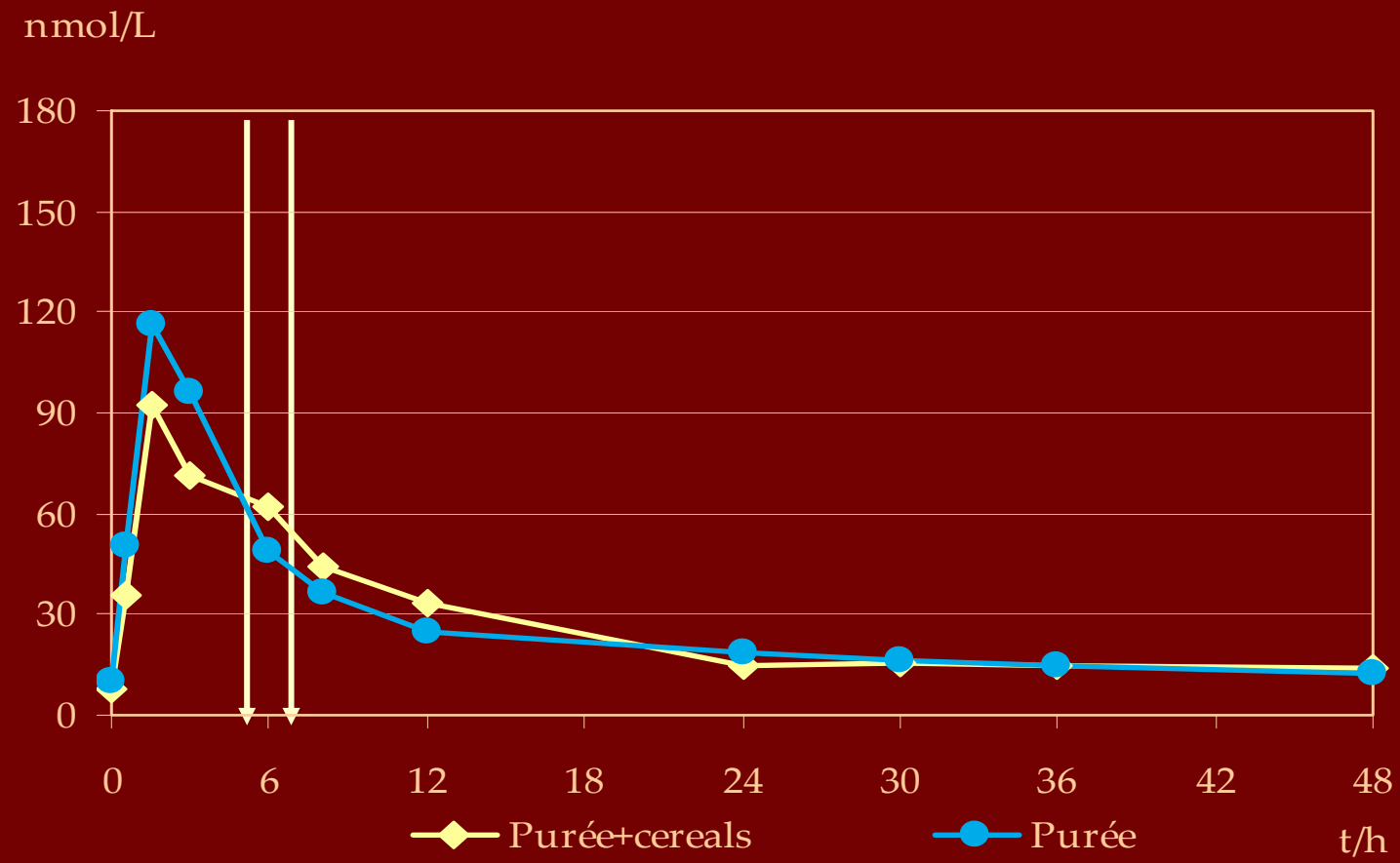
Flavonol results: plasma quercetin

- The maximum concentration was higher after the purée meal (120 vs. 90 nmol/L), but the peak was achieved in both trials in 1.5 hours.



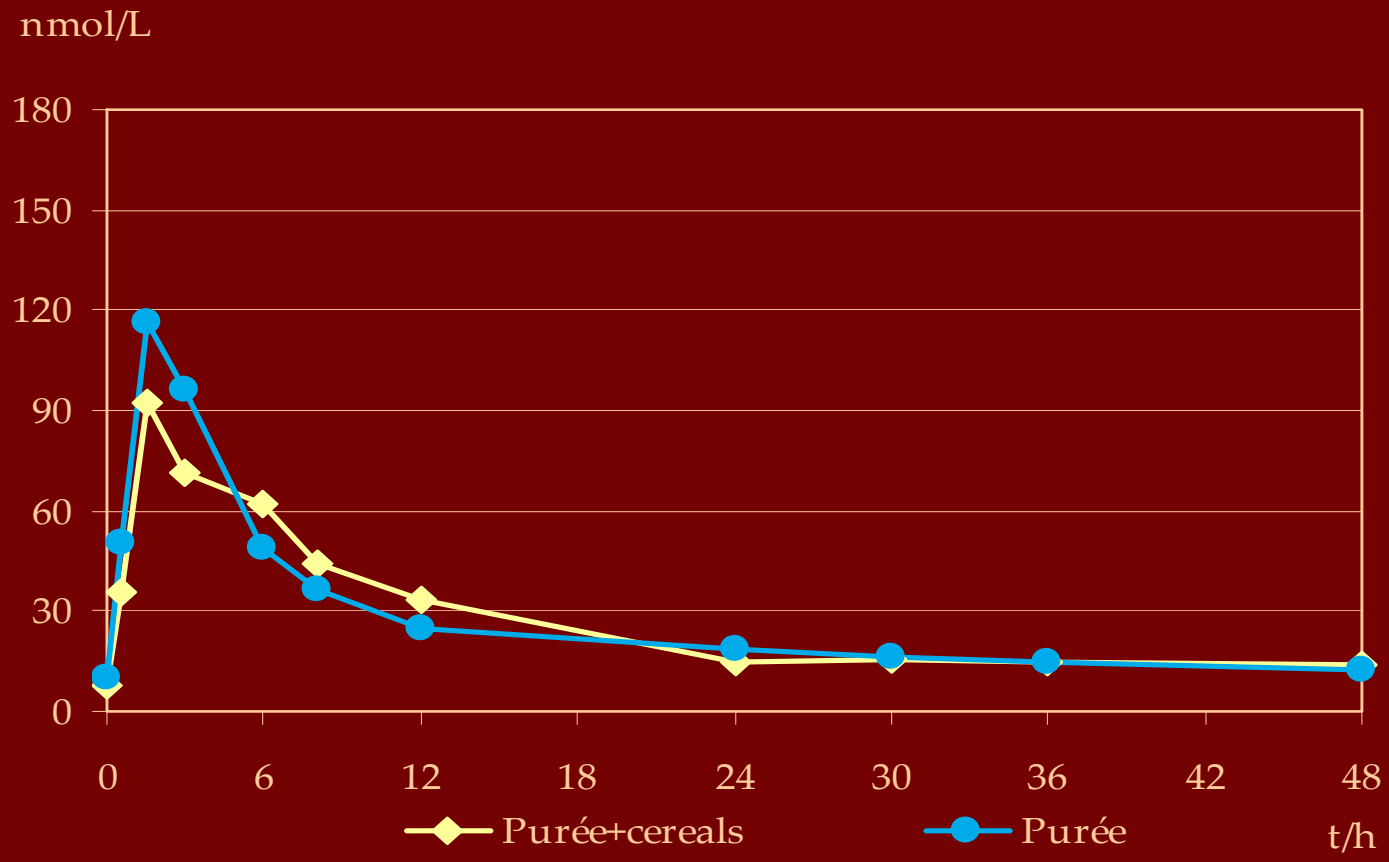
Flavonol results: plasma quercetin

- The half life was 4 hours after the purée + cereals, but only 2.7 hours after the purée alone. (Calculated values)



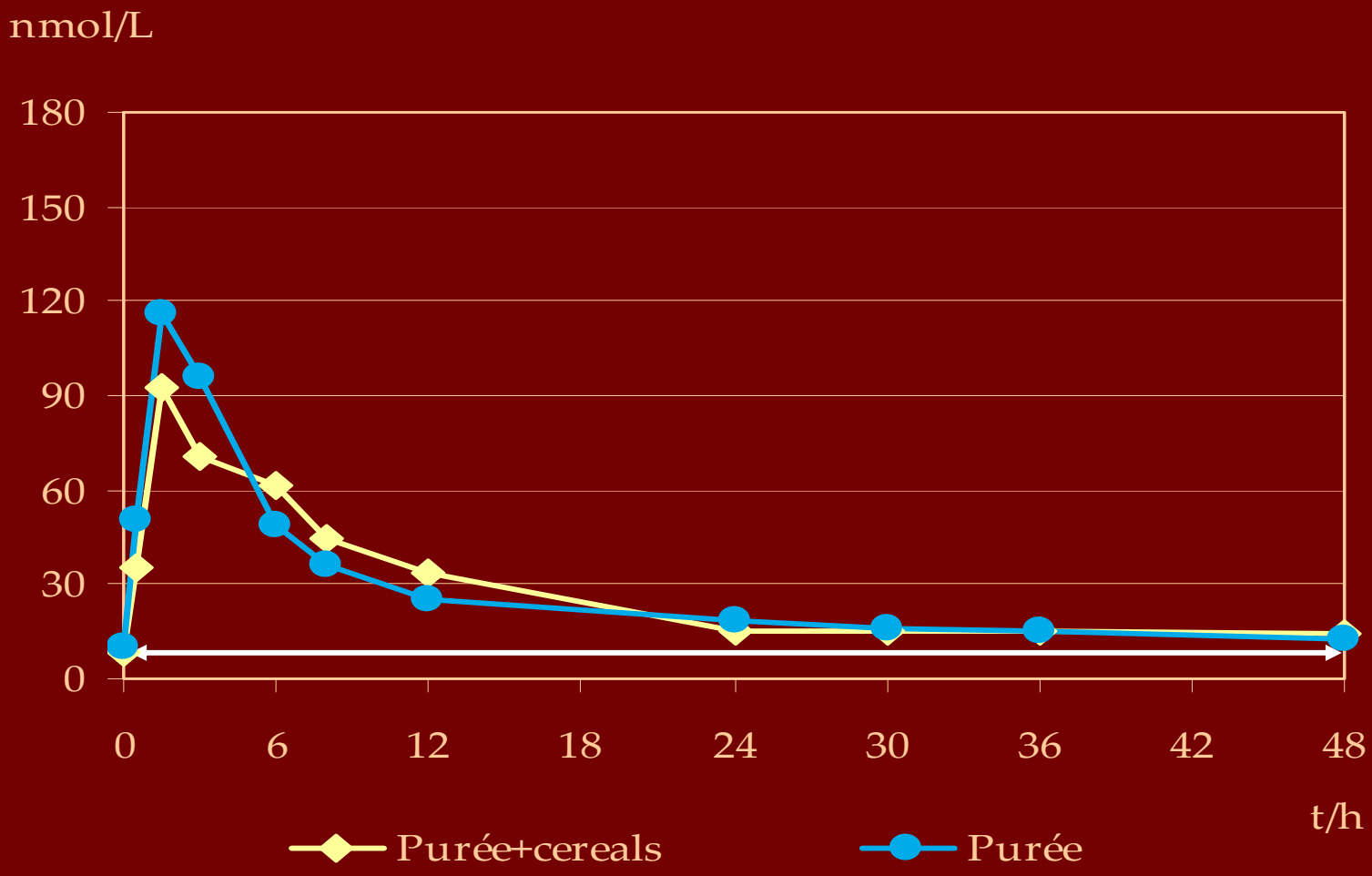
Flavonol results: plasma quercetin

- AUC values (1.3 µmol/L*h) were equal in both studies representing approximately 4.0 % of the ingested quercetin amount.



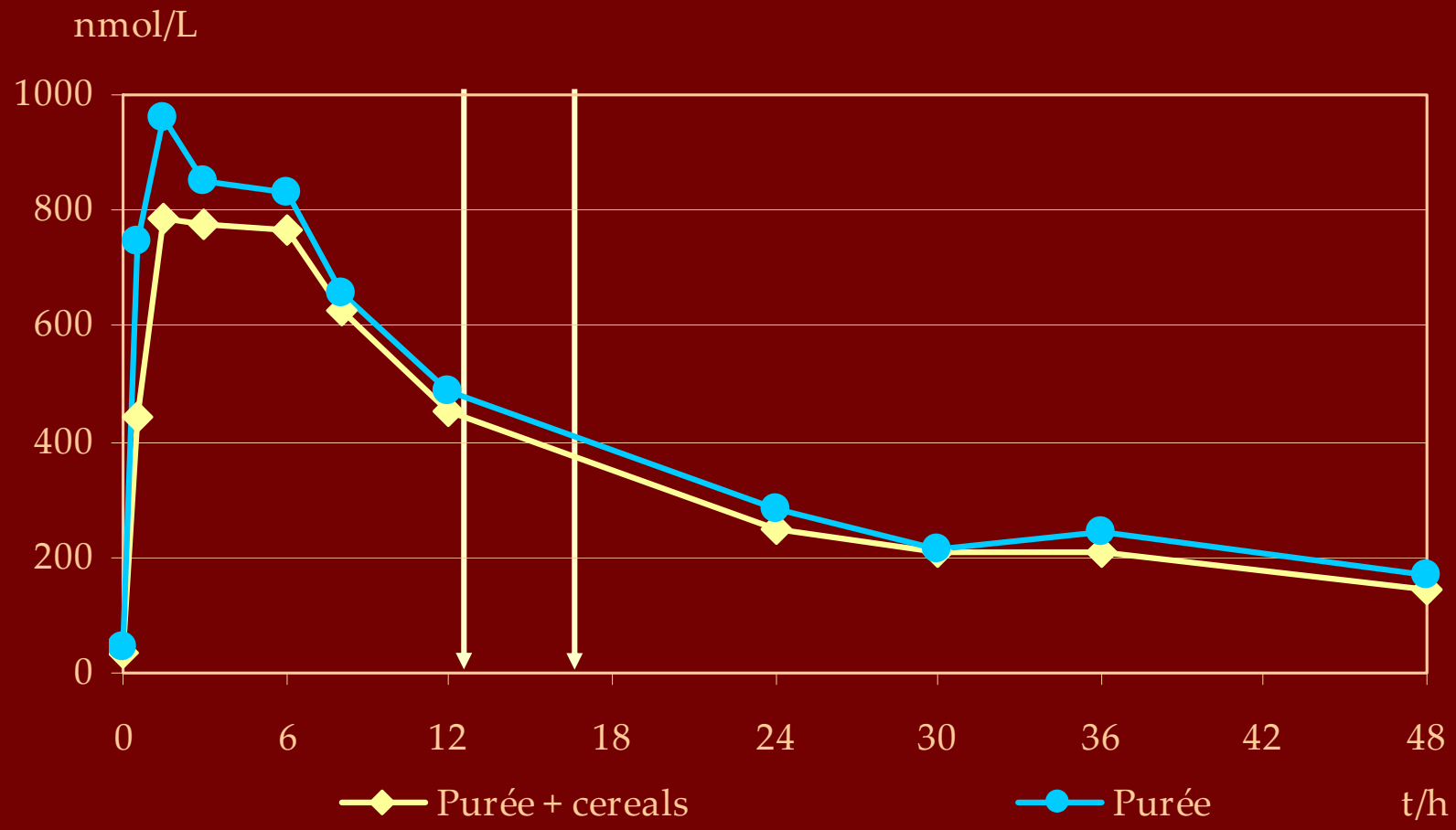
Flavonol results: plasma quercetin

- The maximum concentrations were 10 x higher in contrast to the baseline values, and still slightly above after 48 hours.



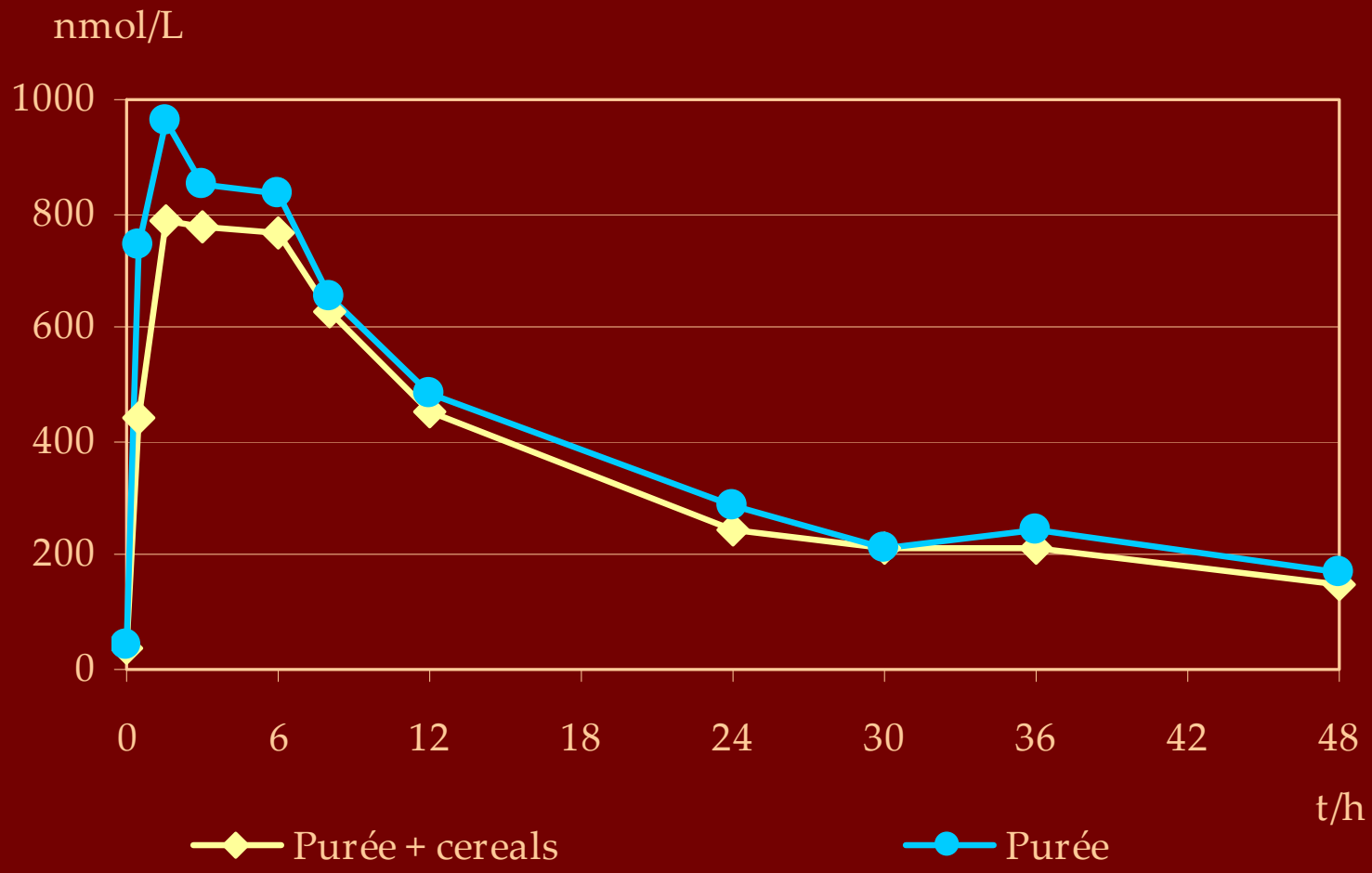
Phenolic acid results: plasma caffeic acid

- The maximum concentration of caffeic acid was higher after the purée meal (962 vs. 788 nmol/L), but the half life was shorter (14 vs. 17 hours, calculated values)



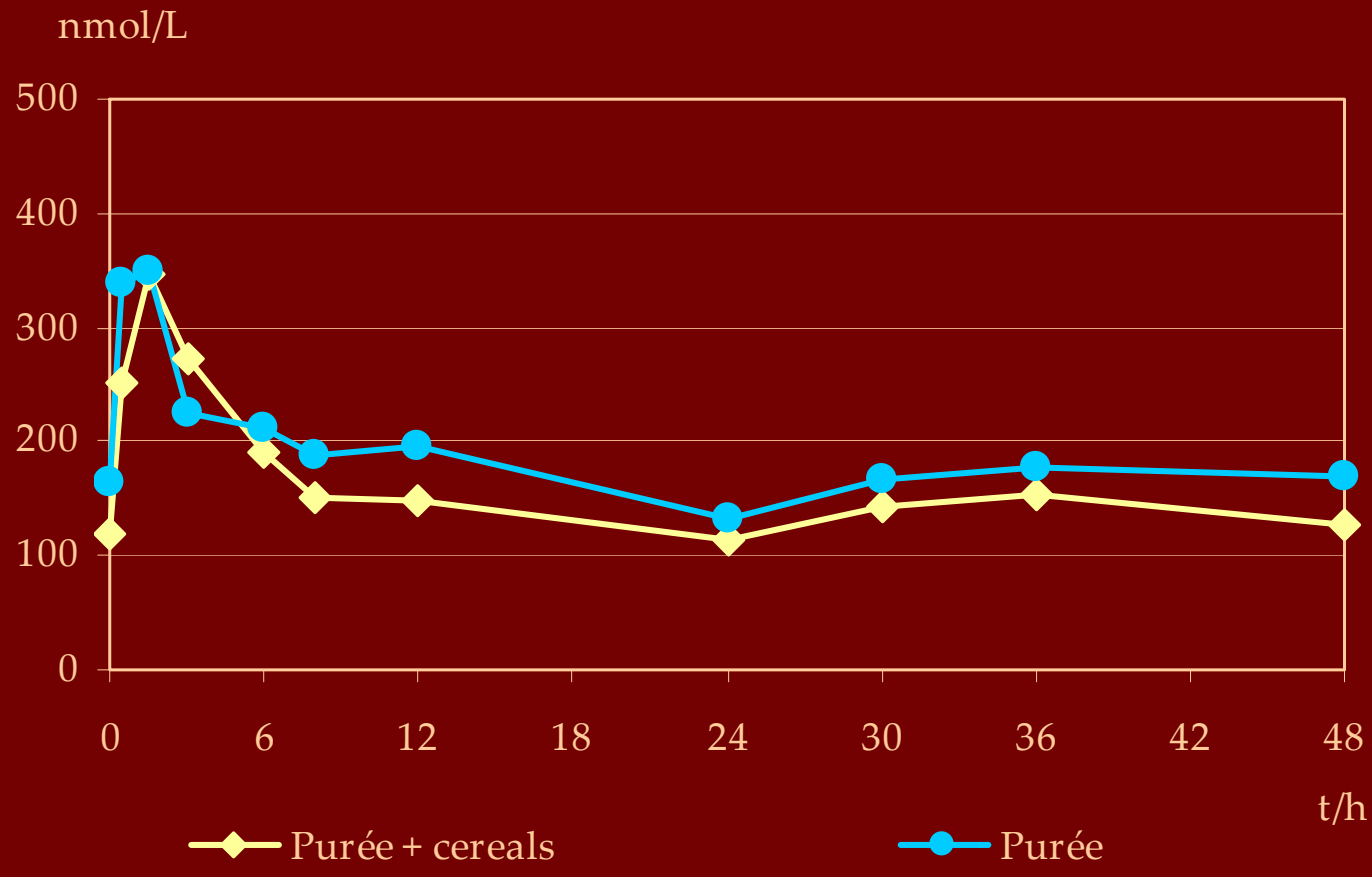
Phenolic acid results: plasma caffeic acid

- AUC values of caffeic acid were 16.8 and 18.7 µmol/L*h which were equal to 40 - 51% of the ingested amount.



Phenolic acid results: plasma ferulic acid

- AUC value of ferulic acid was 8.7 µmol/L*h after the purée and 7.4 µmol/L*h after the purée + cereals, although the ingested amount of ferulic acid was 70 % lower in the purée meal.



Phenolic acid results: urinary excretion

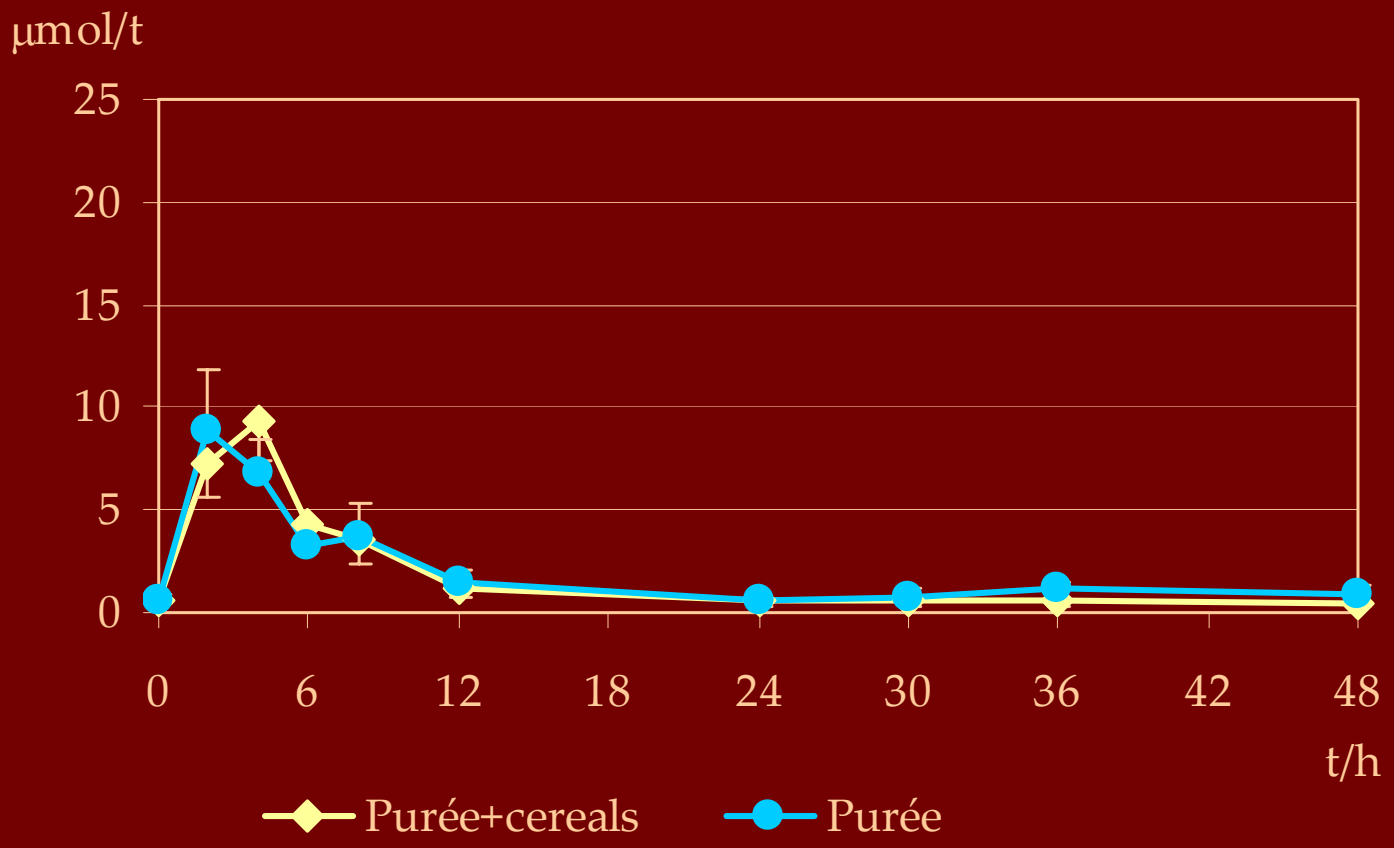
- 16 different phenolic acids were analysed
- Dietary phenolic acids:
  - caffeic, ferulic, isoferulic, p-coumaric, protocatechuic and syringic acid (gallic acid in selected samples)
- Metabolites:
  - 3,4-dihydroxyphenylpropionic acid
  - m-hydroxyphenylpropionic acid
  - dihydroferulic acid
  - dihydroisoferulic acid
  - 3,4-dihydroxyphenylacetic acid
  - m-hydroxyphenylacetic acid
  - homovanillic acid
  - vanillic acid
  - p-hydroxybenzoic acid
  - m-coumaric acid

Phenolic acid results: urinary excretion

- Total excretion of phenolic acids was 115 μmol/d during the preceding 24 hours prior to purée + cereals supplementation (190 μmol/d prior to purée meal).
- Total excretion of phenolic acids was about 320 μmol/d during the first 24 hours of follow-up in the both trials.
- Total excretion of phenolic acids was 150 μmol/d during the next day (24-48 h) of follow-up after the purée + cereals, but 240 μmol/d after the purée.
- Changes in the excretion after the purée supplementation were hidden because of high baseline excretion and continuous metabolism of diet derived compounds.

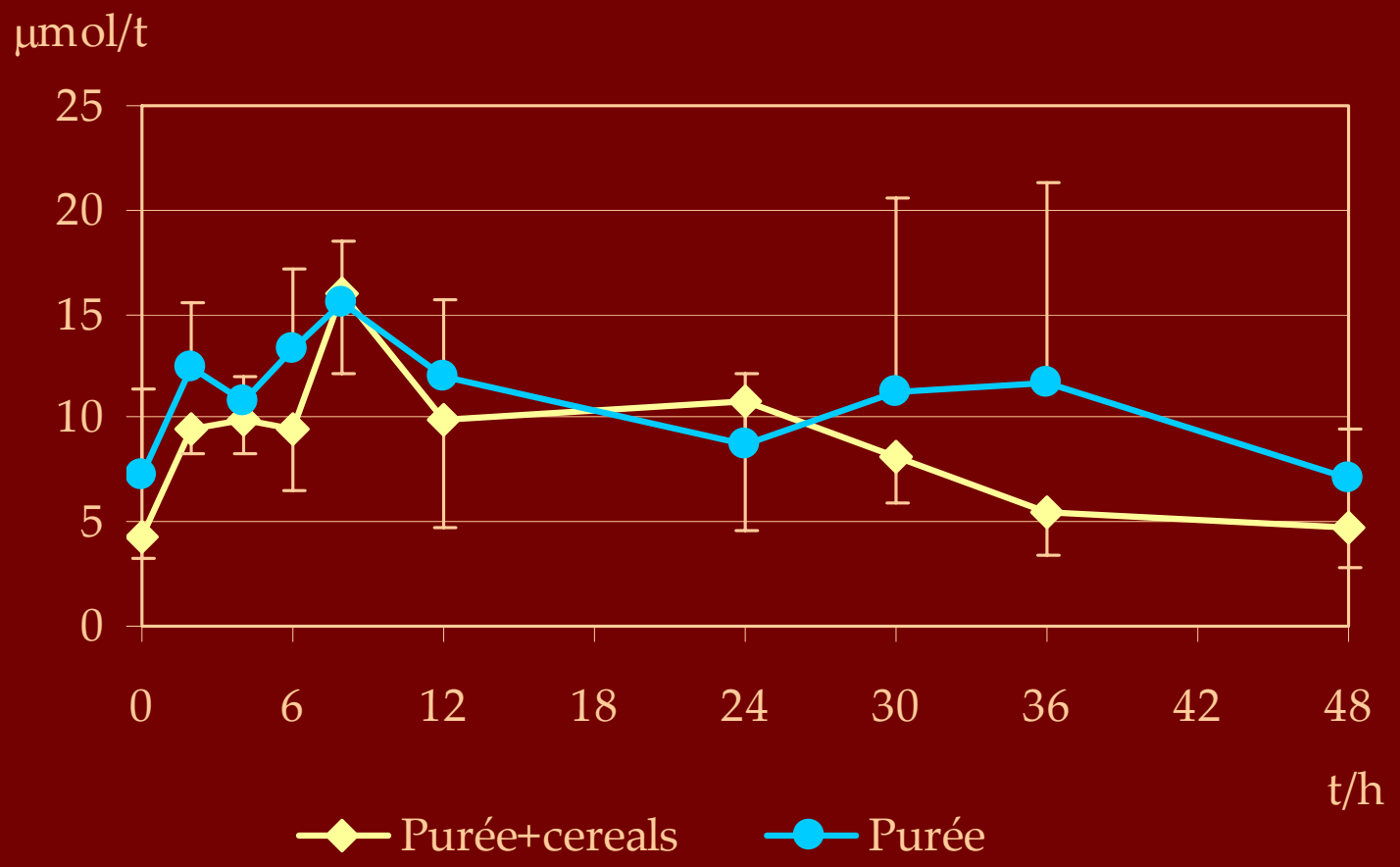
Urinary phenolic acids: dietary compounds

- Dietary phenolic acids presented 10% of the total excretion prior to, and their excretion was doubled after the supplementation. The peak was achieved in 2 - 4 hours.



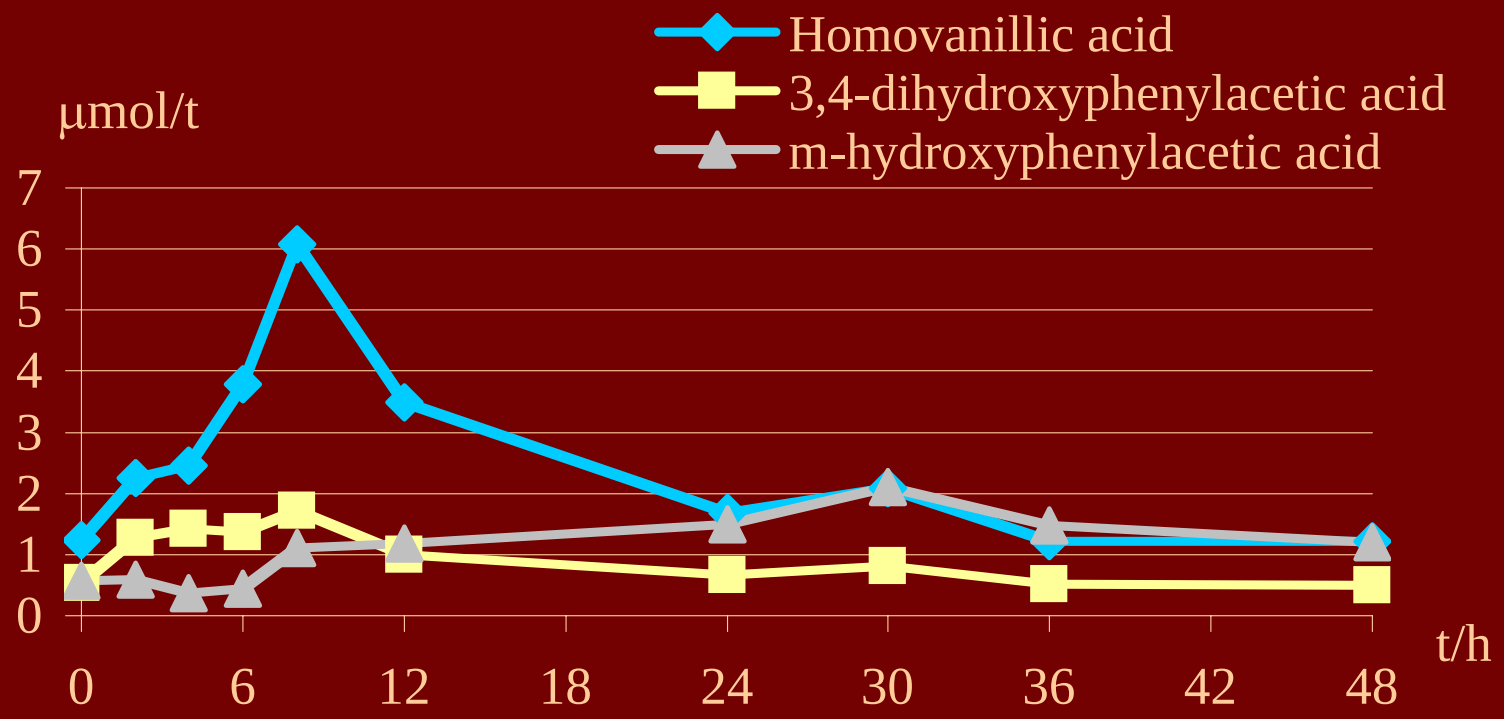
Urinary phenolic acids: metabolites

- Excretion of metabolites continued up to 48 hours.



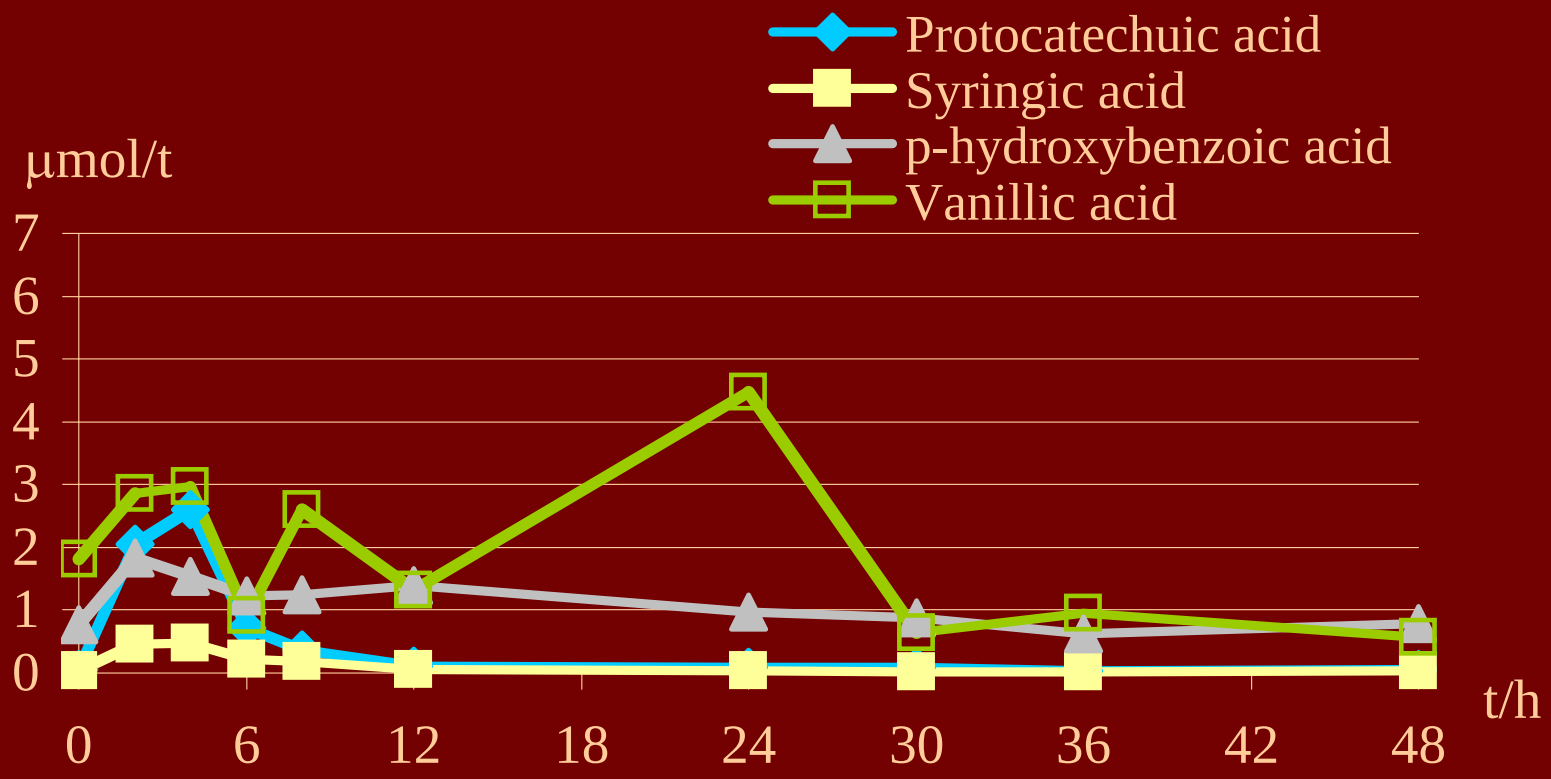
Urinary phenolic acids: metabolites

- Main metabolite during the first 12 hours was homovanillic acid



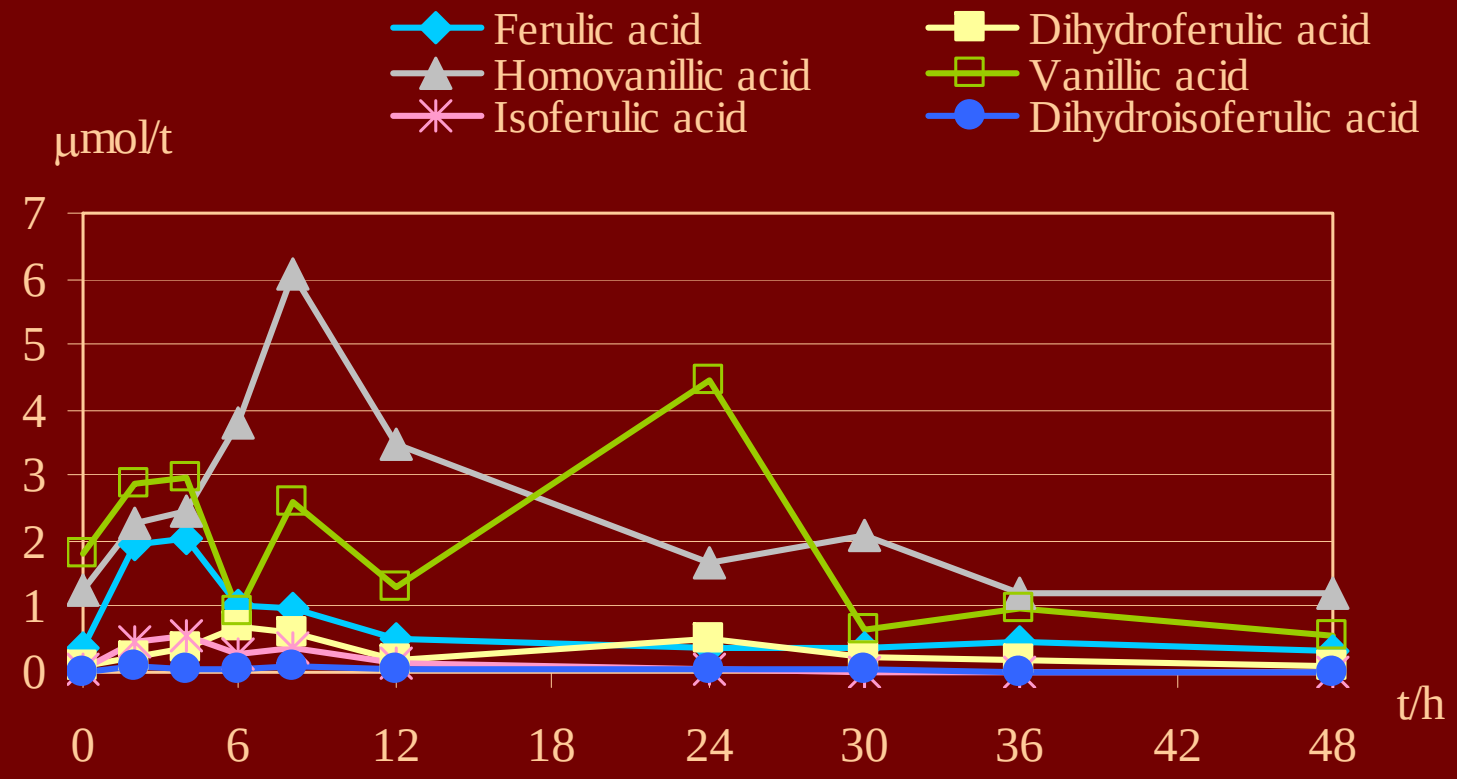
Urinary phenolic acids: metabolites

- Main metabolite during 18 - 28 hours was vanillic acid.



Urinary phenolic acids: metabolites

- Excretion of methylated phenolic acids.



Conclusions: anthocyanins

- Plasma concentrations and urinary excretion of anthocyanins were low as has been in previous studies as well.
- Urinary excretion of protocatechuic and syringic acid were so low that they were not major fragmentation products of purée anthocyanins. Also their kinetic behaviour indicated them to be dietary compounds.
- Gallic acid was not detected at all, but homovanillic and vanillic acid can be metabolites of anthocyanins.
- Kinetic behaviour of 3,4-dihydroxyphenylacetic acid indicated that it might be a metabolite of anthocyanins.

Conclusions: quercetin

- Quercetin concentrations were slightly low when compared to the other supplementation studies.
- Half lives were short in contrast to the other supplementation studies, but also the peak concentrations in our studies were low, which shorten the half life.
- During 24 - 36 hours urinary excretion of m-hydroxy- and 3,4-dihydroxyphenylacetic acid increased, which might indicate that they were fragmentation products of quercetin, or anthocyanins.

Conclusions: plasma phenolic acids

- The peak concentrations of caffeic and ferulic acid were high in contrast to the other supplementation studies, in particular when in our study the amount of supplemented phenolic acids in study meals was low.
- Half lives have not been presented in the other studies.
- AUC values for ferulic acid were equal, although the supplemented amount in the purée + cereals was 3 x higher than in purée.
- Ferulic acid might have been metabolised to homovanillic and vanillic acid after the purée + cereals, which would explain the similarity of ferulic acid AUC values.

Conclusions: urinary phenolic acids

- Dietary phenolic acids were mainly excreted during the first 6 hours.
- Excretion of metabolites continued up to 48 hours.
- Main metabolites were homovanillic and vanillic acid, which might partly have been produced from ferulic acid, but also from anthocyanins (in maximum 18 % of petunidin and malvidin).
- Anthocyanins and quercetin might have been fragmented to 3,4-dihydroxy- and m-hydroxyphenylacetic acid.

Conclusions

- Anthocyanins circulate in human body in very low concentrations, and possible evidence was obtained about the fragmentation in colon.
- Possible health effects of berry anthocyanins must be mediated with some still unknown metabolites.
- Continuous consumption of plant foods keeps the concentration of phenolic compounds high in the body.
- Conjugation and intensive metabolism must be taken into account when bioactivity of polyphenols is studied in vitro.

Thank you for your attention!

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