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# Natural Sources of Plasmalogens

Dawn Scott, Andrew MacKenzie and Reece Whitby

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# Introduction

What are Plasmalogens ?

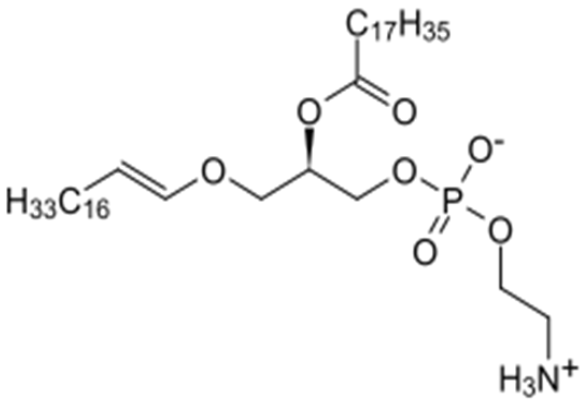
Potential health benefits

Survey of natural sources

Stability

Methods of enrichment

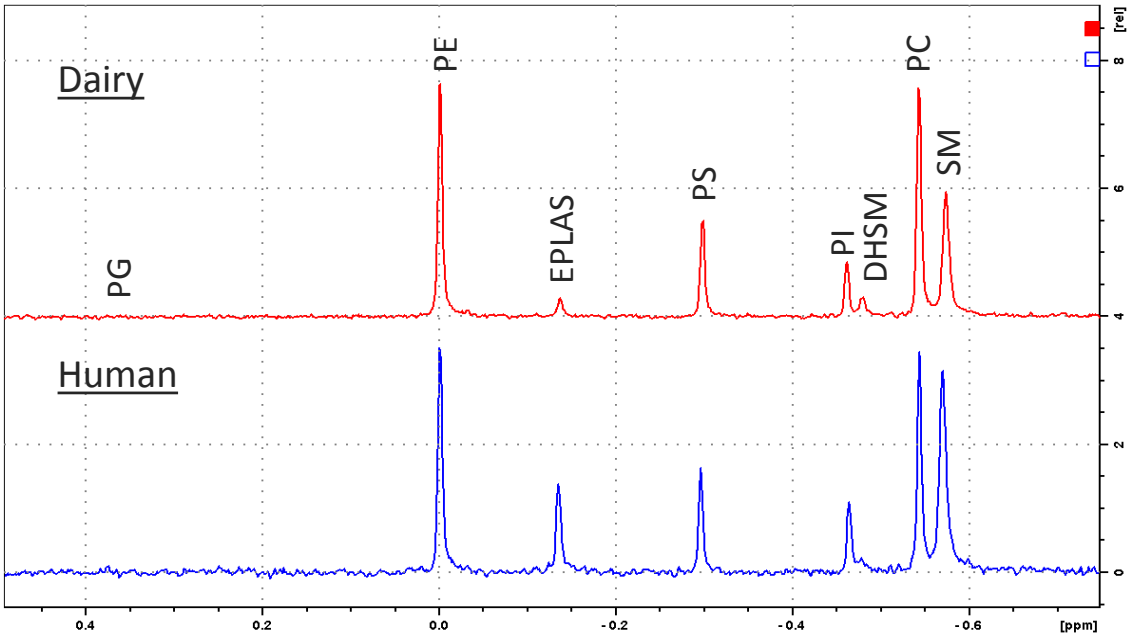
# Plasmalogens




- Lipid
- Phospholipid with a fatty acid at the sn-2 position, and a long chain vinyl ether at the sn-1 position of the glycerol
- Most commonly ethanolamine plasmalogen (EPLAS) and choline plasmalogen (CPLAS)

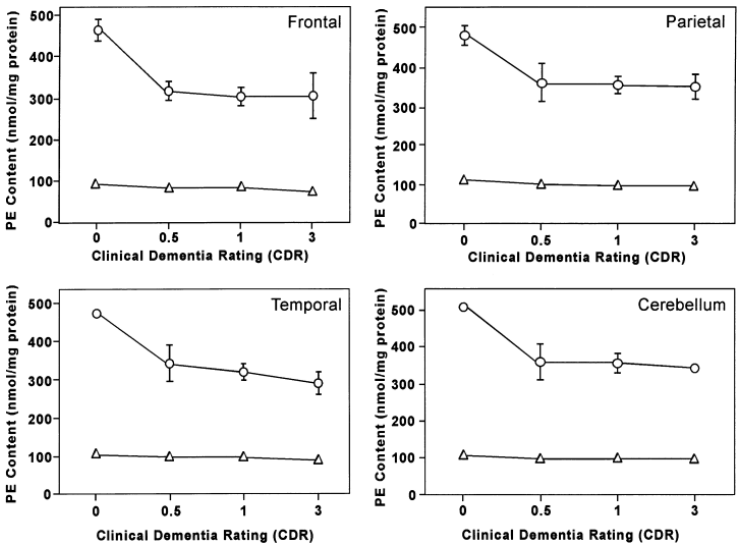
# Relevance - Milk

- Plasmalogen content is significantly higher in human milk (>30% of total PE) than in cow milk (<8% of total PE)
- Humanising Infant formula



# Plasmalogens and Disease

- Plasmalogen content is greatly reduced in the brain of Alzheimer's patients, also people with Down syndrome, Parkinson's disease, Niemann Pick Type C and Zellweger syndrome.
- "a dramatic decrease of up to 40 mol% in plasmalogen content of white matter in early AD stages." Braverman and Moser (2012).




Braverman, N.E. and Moser , A.B., Functions of plasmalogen lipids in health and disease. *Biochimica et Biophysica Acta* **1822**, 1442-1452 (2012)
Han, H., Holtzman, D.M and McKeel, D.W.Jr, Plasmalogen deficiency in early Alzheimer's disease subjects and in animal models: characterisation using electrospray ionization mass spectrometry. *Journal of Neurochemistry* **77,** 1168-1180 (2001)


# Plasmalogen Supplements

There are products on the market which claim to lessen the effects of different types of dementia.

## Most amazing improvement seen by the research team!

"This Lewy body dementia patient was initially expressionless, she became more responsive after consuming Scallop-derived PLASMALOGEN for 2 weeks. The hallucinations that she used to experience have also disappeared."

2 weeks

1 mg/day


https://lifestreamgroup.com/neuroregain

# $^{31}$P NMR Analysis

NMR = Nuclear Magnetic Resonance

Non-destructive method

i.e. sample can easily be recovered

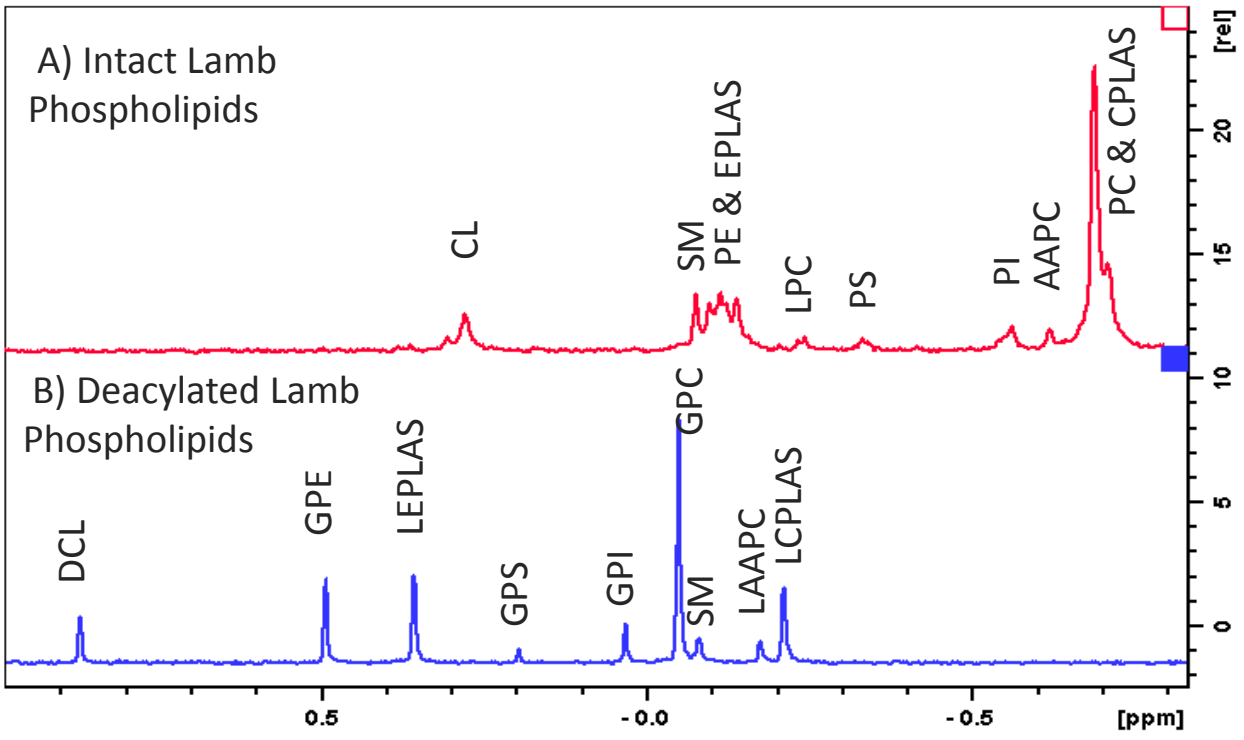
Only phosphorus is observed

- Non-phosphorus containing molecules (e.g. triglycerides, glycolipids) are not seen
- Crude mixtures (e.g. some milk powders) can be analysed without any extraction required
- Chemical shift (peak position) is determined by the environment surrounding the P atom.

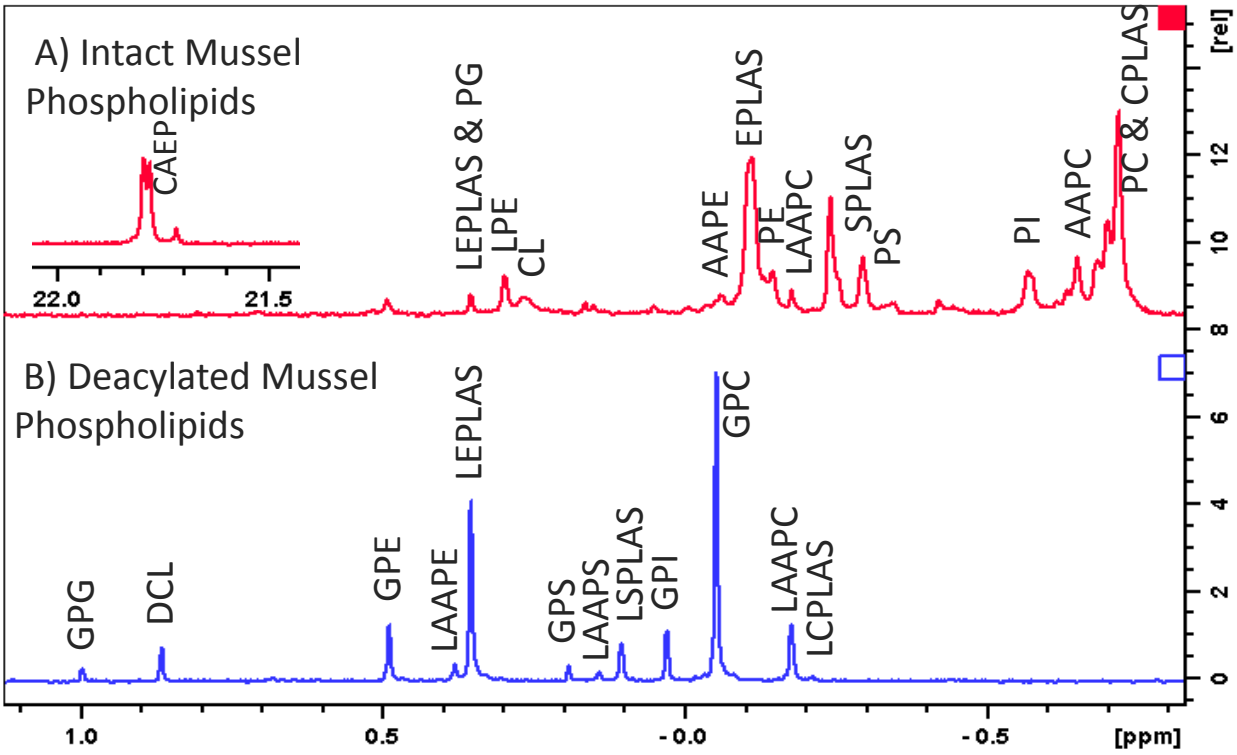
Method is Quantitative

- Individual lipid standards are not required for calibration
- MW needs to be known (can be calculated from fatty acid profiles, or MS data)

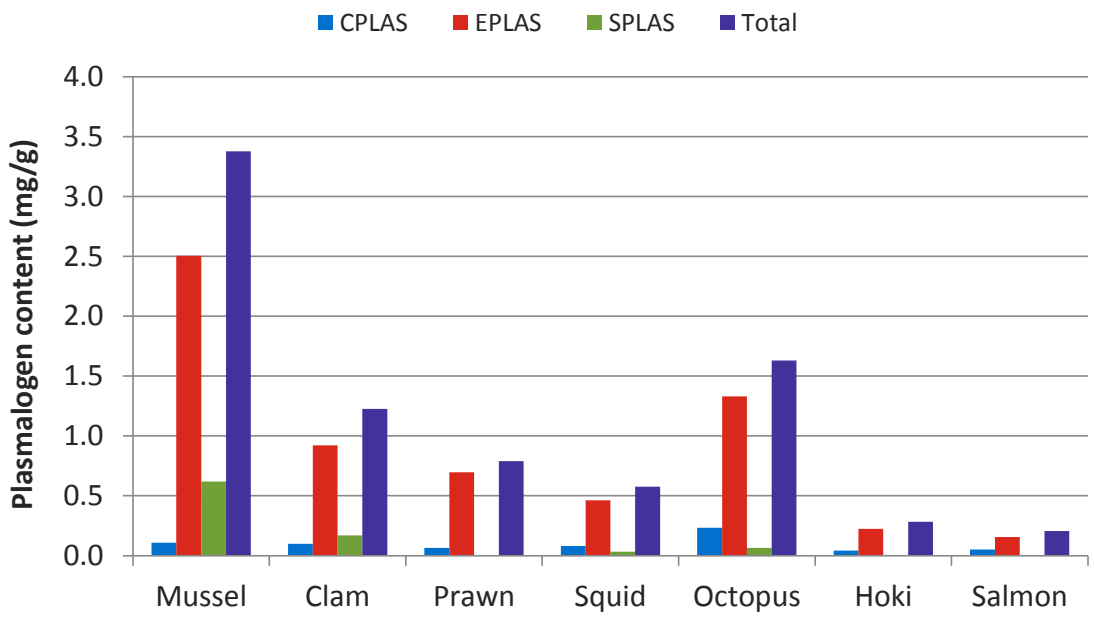
# $^{31}$P NMR Analysis – Lamb steak



# $^{31}$P NMR Analysis – Mussel



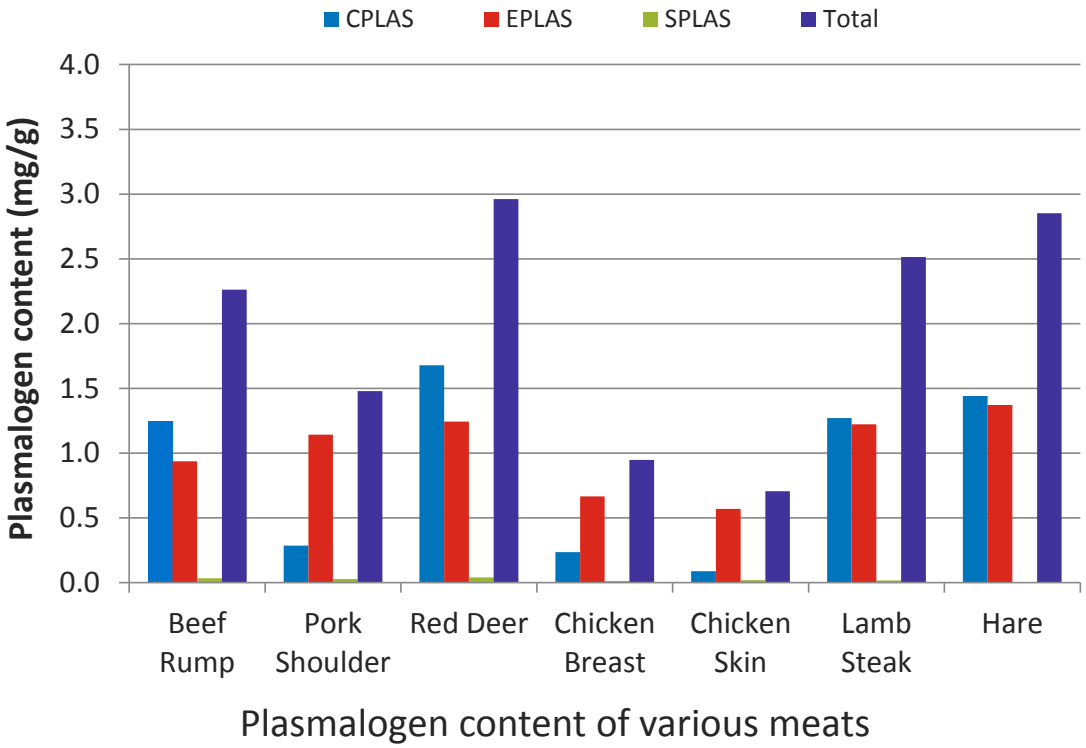
# Food Sources - Seafood




Plasmalogen content of various seafoods

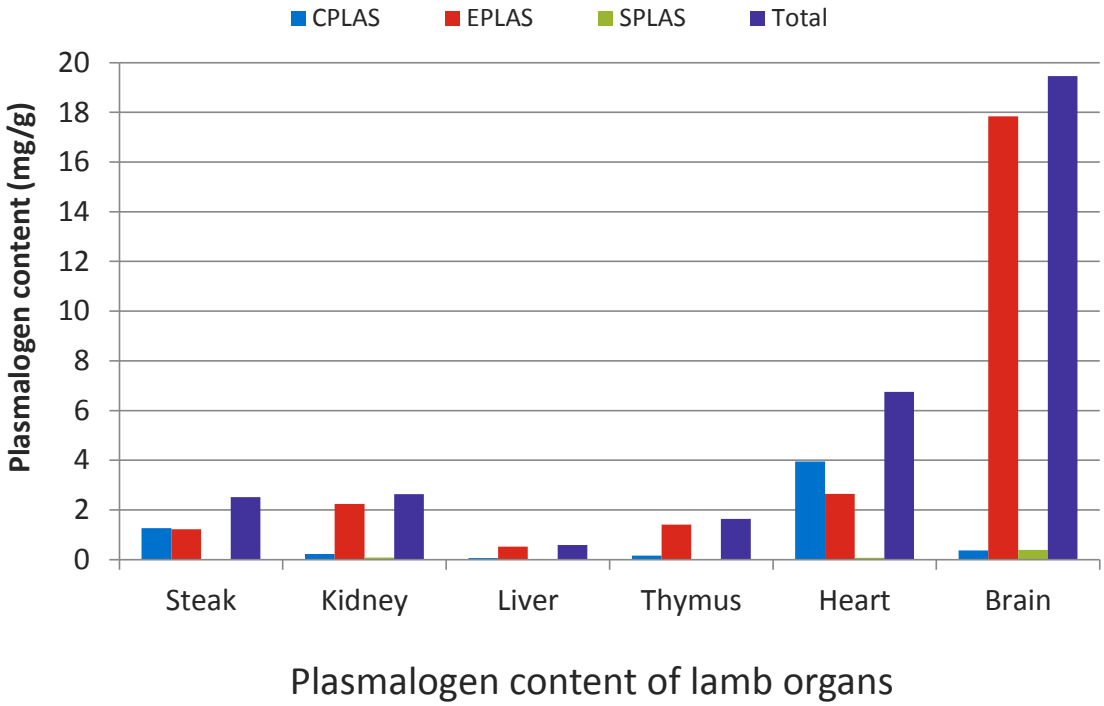
(Mussel, clam, prawn, squid and octopus were a precooked and frozen packaged mixture. Other samples were fresh)

# Food Sources - Meat



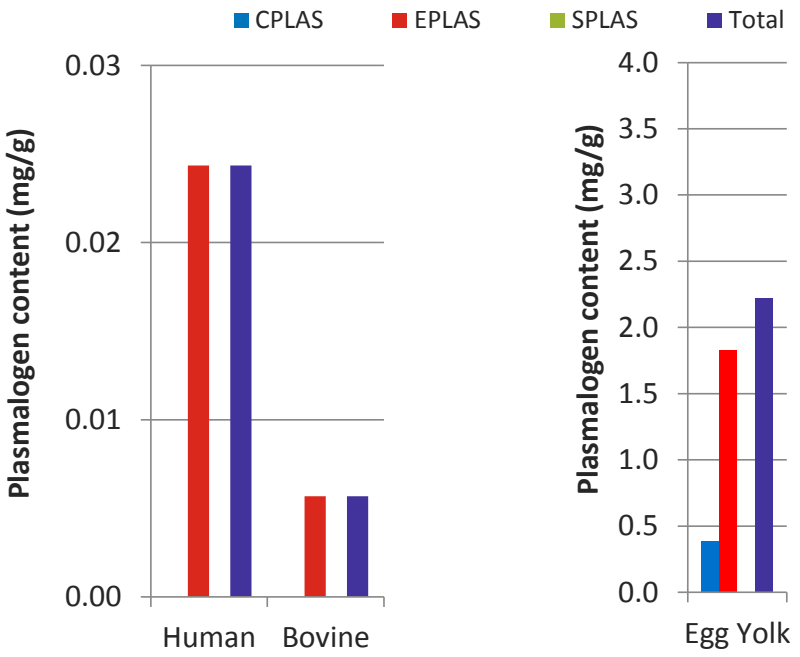

Plasmalogen content of various meats

# Food Sources – Lamb organs




Plasmalogen content of lamb organs

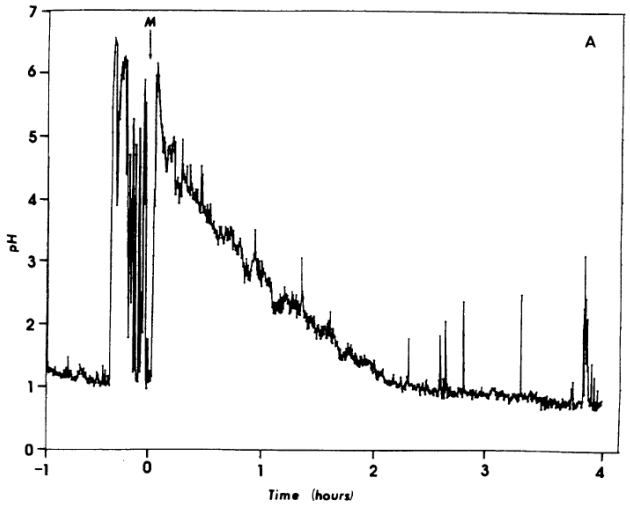
# Food Sources – Milk and Egg




Plasmalogen content of milk and egg

# Does stomach acid destroy plasmalogens?

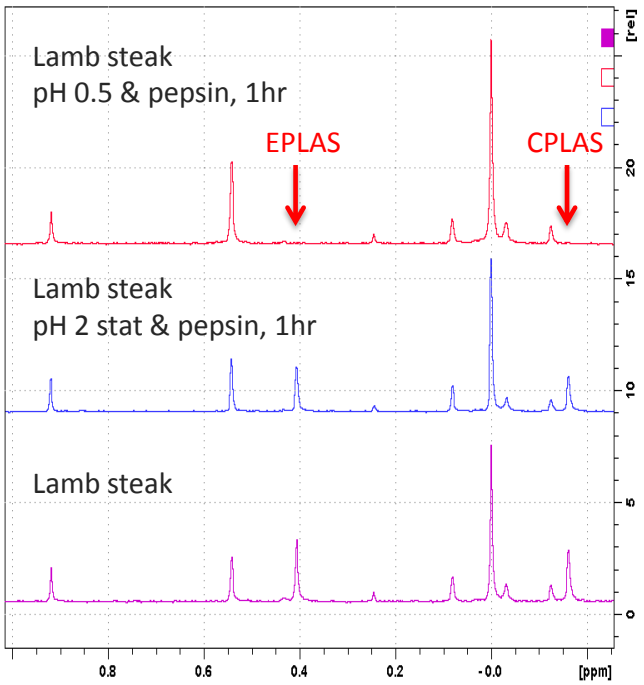
- The ether bond in plasmalogens is very unstable in acidic conditions.
- The vinyl ether group is cleaved to form a fatty aldehyde
- Can plasmalogens survive stomach acid?  (gastric juice pH <1.5)

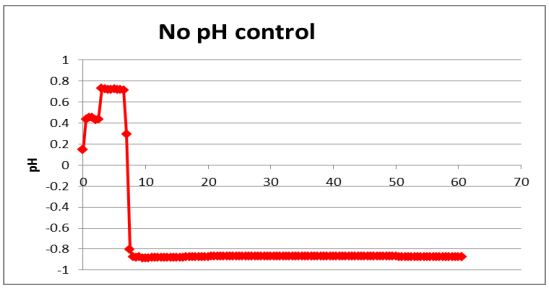


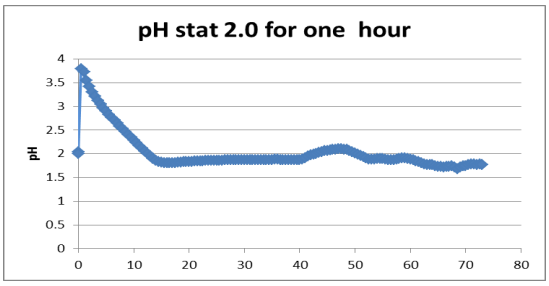

Typical pH profile in gastric phase after eating a meal. Dressman, et. al. (1990)

Dressman, J.B., Berardi, R.R., Dermentzoglou, L.C., Russell, R.L., Schmaltz, S.P., Barnett, J.L. and Jarvenpaa, K.M., Upper Gastrointestinal (GI) pH in Young, Healthy Men and Woman. *Pharmaceutical Research* **7**, 756-761 (1990)

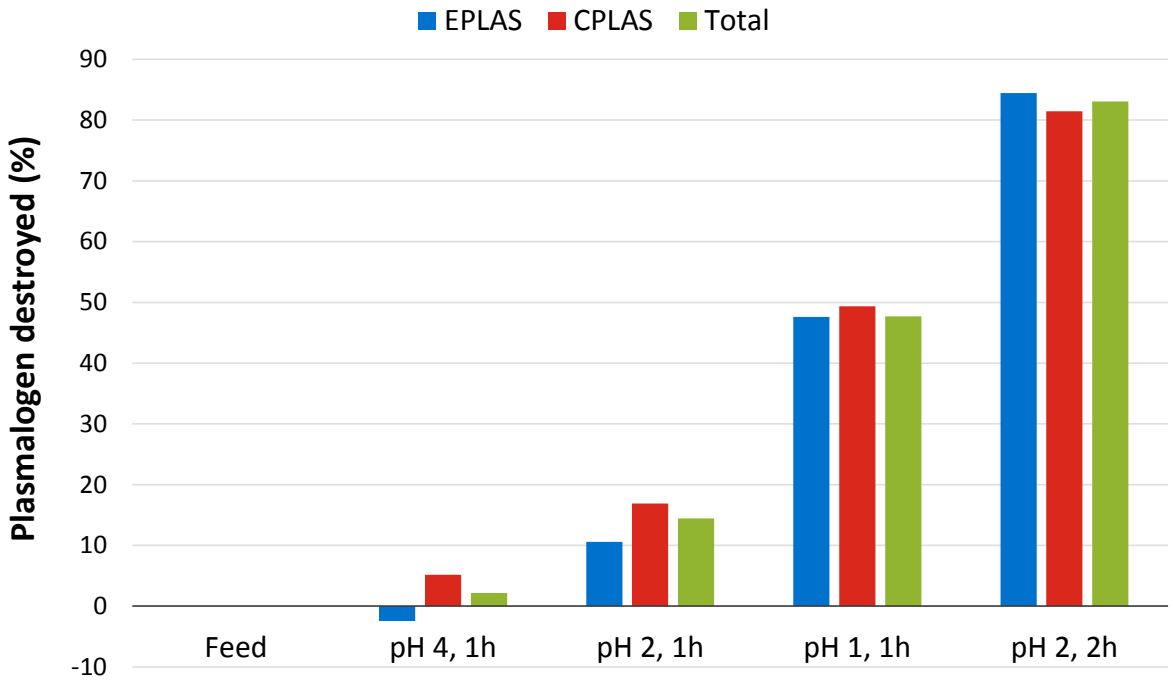
# Acidic Digestion



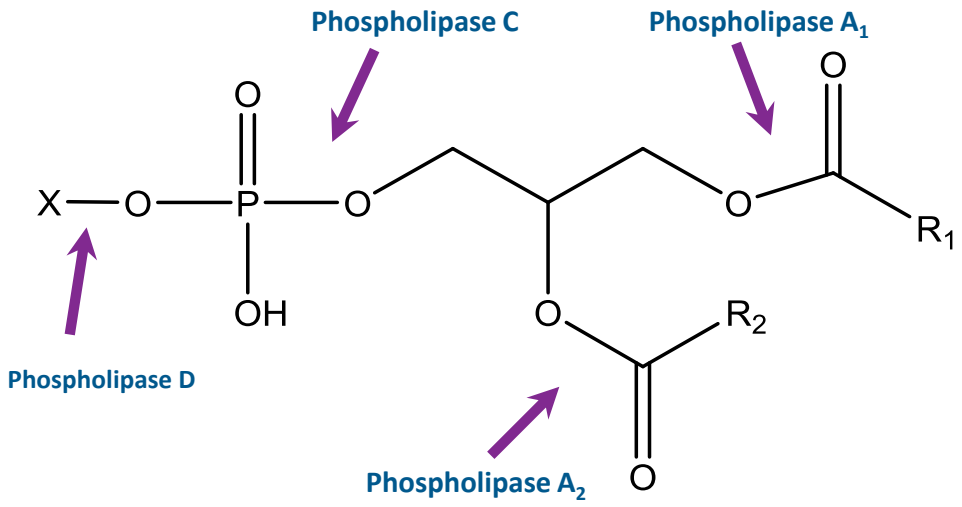



# Acidic digestion – Effect of pH and time

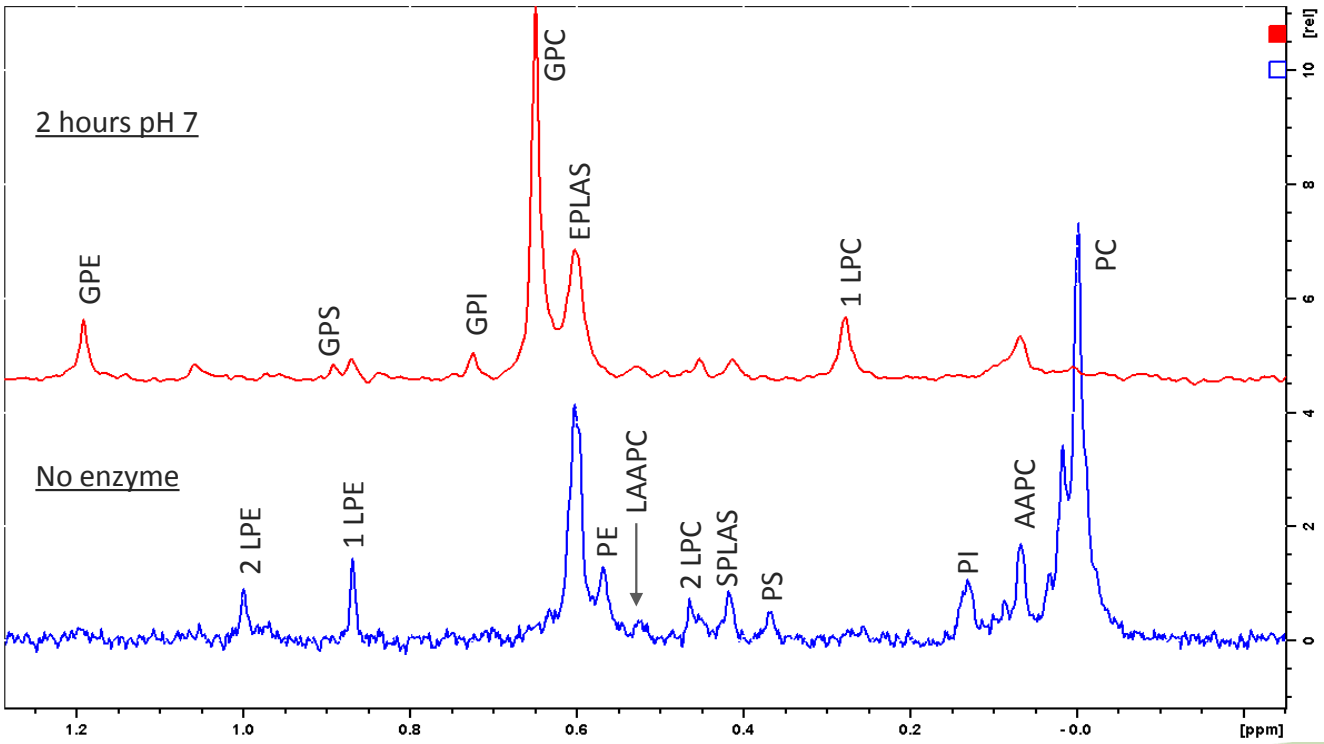


# Phospholipases mode of action




**X =H, choline, ethanolamine, inositol, serine, etc.**

# Enrichment using $PLA_1$ - Mussel



# Summary

- Plasmalogens are already being sold in Japan and Singapore as a health supplement especially aimed at AD.
- Levels of plasmalogen consumed in a normal diet are well above the supplement levels and appear to survive short exposure to stomach acid.
- Mussel is a rich source of plasmalogen with high levels of EPLAS (and SPLAS).
- Mussel powder is already produced and processed in NZ. The residual powder from that processing contains the phospholipids and therefore the plasmalogens.
- Further work needs to be done to better mimic stomach conditions.
- Enzyme modification can be used to enrich or prepare desirable compounds.