

USDA Ongoing Research on The Impacts of Nutrition on Animal Health



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Current Research at USDA

- Quantify the impact of swine dietary regimens on nutrient metabolism and immune function of the G.I. tract and the whole animal.
- Multidisciplinary/collaborative approach.
 - Integration of physiological, molecular, and whole animal studies.

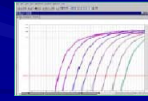
Physiological biomarkers



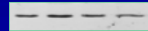
"Feed & weigh"



Gene expression analysis



Proteins

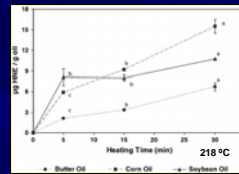


Oxidative Stress

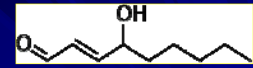


- Defined as imbalance between oxidants and AOX defense mechanisms.
- Altered inflammatory responses.
 - Promotes inflammation
 - Marker of inflammation.
- Increased cellular and tissue damage.
 - "Rancid" fats increase enterocyte turnover in swine and poultry (Dibner et al., 1996).
- Disease states in livestock.
 - Mulberry heart disease, white muscle disease.
 - Immune dysregulation in transition dairy cows (Sordillo et al., 2009).
 - Low longevity, companion animals.
- Relationship with feed efficiency.
 - Inverse relationship between markers of oxidative stress & g:f in poultry (Bottje and Carstens 2009).
- Impact of feeding byproducts?
 - DDGS
 - Fats – AV blends. Rancidity?
 - High amounts of PUFA in swine diets.
 - Relationships with dietary fiber?

Lipid aldehydes – 4-HNE

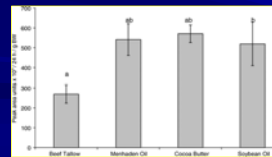


Han & Csallany, 2008



4-hydroxynonenal – 4-HNE

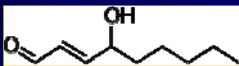
Produced by heating of oils, mainly 18:2. Can be absorbed from diet.



Csallany et al., 2005

Produced endogenously via peroxidation of PUFA both a marker and mediator or oxidative stress. Impacted by dietary fat type.

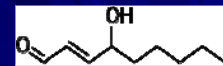
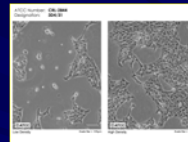
Biology of 4-HNE



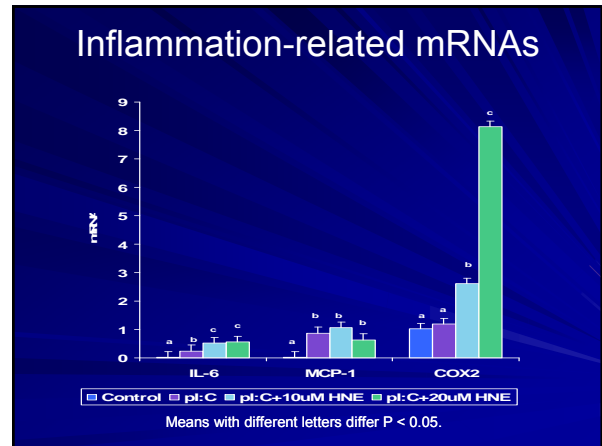
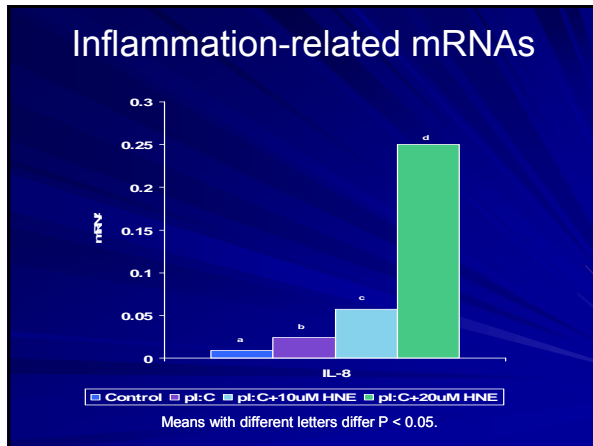
<http://www.hne-club.org/>

- Highly reactive molecule – binds proteins and nucleic acids.
 - Detoxified by glutathione.
- Associated with pathological states in humans.
 - Alzheimer's, diabetes, respiratory (COPD).
 - Alters expression of inflammatory genes.
- Can invoke arthritis.
 - Laminitis associated with ↑ 4-HNE (Yin et al., 2009).
 - Sow lameness?
- Impacts of oxidized fats on intestinal barrier function?

In Vitro Studies with 4-HNE



- Porcine 3D4/31 alveolar macrophages (MØ).
- Treated cells with various levels of 4-HNE.
 - 0, 10, or 20 µM 4-HNE for 1 h.
 - MØ were stimulated with poly I:C RNA – a TLR3 agonist used to mimic viral inflammation.
- Supernatant and cells harvested for cytokine secretion and mRNAs.
 - Cellular glutathione levels determined.



In Vitro Studies with 4-HNE

- 4-HNE augments expression of inflammatory mediators.
 - In short term incubations 4-HNE depleted cells of glutathione.
 - Demonstrates that oxidative stress can impact porcine response to viral challenges via 4-HNE.
- Ongoing studies to look at mechanisms and time course.
 - Glutathione regulation.
 - n-acetylcysteine and other compounds/nutrients ability to reverse 4-HNE induced hyperstimulation.

Future Directions

- National Pork Board Grant – “Evaluation of lipid source and oxidation level on digestible and metabolizable energy concentration, and the impact of lipid oxidation on intestinal barrier function.”
- Objectives:
 - Determine DE and ME content of 4 dietary fat sources ranging from 2 saturated animal fats: beef tallow, poultry fat; and 2 unsaturated oil sources: canola, corn oil.
 - Determine the impact of lipid oxidation on DE, ME and N retention.
 - Each fat source will be heated at 190°C for 6h.
 - Measure 4-HNE and other polar and non-polar aldehydes.
 - Other “quality” indicators: fatty acid profiles, PV, anisidine, etc.

Future Directions

- Objectives:
 - Determine the impact of dietary fat source and lipid oxidation on indicators of oxidative stress, inflammation and intestinal barrier function.
 - Serum and urinary TBARS, 4-HNE, and other aldehydes.
 - Urinary lactulose and mannitol will be determined as an indicator of intestinal permeability.
 - Serum endotoxin, acute phase proteins, and fecal IgA.
- Tissue collection and other analyses related to redox balance.

Questions?