FACULTY OF VETERINARY MEDICINE
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EFFECT OF ORAL ALEURONE SUPPLEMENTATION ON GLUCOSE AND INSULIN DYNAMICS AND FECAL MICROBIOME OF HORSES IN TRAINING

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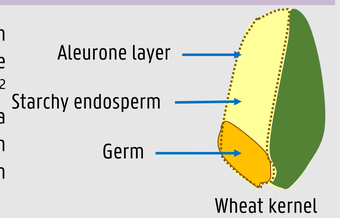
1. Introduction

Aleurone is known to positively modulate glucose and insulin dynamics in pigs and mice and is deemed to be responsible for the positive health effects of whole grain products.[1,2] Aleurone resides in the outer layer of the bran fraction of a wheat kernel. In the past our research group has reported on a dose-response trial of oral aleurone supplementation on glucose and insulin dynamics in untrained horses.[3]

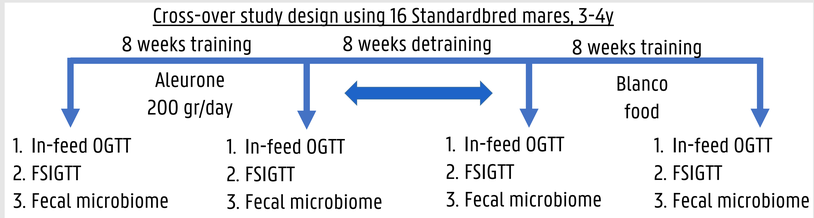


2. Aims of the study

To study the effect of oral aleurone supplementation on top of training in healthy horses, focusing on:

- Glucose and insulin dynamics
- Shifts in fecal microbiome composition
- The correlation between fecal microbiome and glucose and insulin dynamics

3. Materials & methods

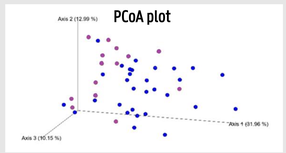


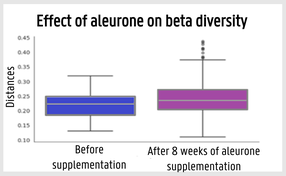
An in-feed oral glucose tolerance test (OGTT) and a frequently sampled intravenous glucose tolerance test (FSIGTT) were performed on set time points. The following parameters were monitored:

1. In-feed OGTT: $Maximum_{insulin}$, $AUC_{insulin}$, Time to $peak_{insulin}$, $Maximum_{glucose}$, $AUC_{glucose}$, Time to $peak_{insulin}$
2. FSIGTT: Minimal model analysis MINMOD Millenium version 6.02; Sg= Glucose effectiveness; AIRg Acute Insulin Response to glucose; SI=Insulin Sensitivity; DI= Disposition index
3. Fecal microbiome: PCR amplification of the V3-V4 region of the 16s rRNA genes. Enrichment of bacterial metabolic pathways was predicted by running PICRUST using the MetaCyc data.

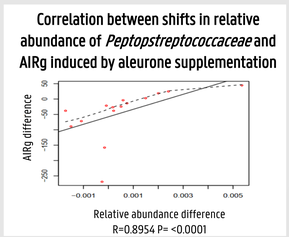
4. Results

1. **In-feed OGTT:**
   An effect of training was found on:
   - $Maximum_{insulin}$ was significantly lower (P=0.005)
   - Time to $peak_{insulin}$ was significantly higher (P=0.030)
   - $AUC_{insulin}$ was significantly lower after training (P=0.001)
2. **FSIGTT:** Aleurone had a significant effect on:
   a) Decreased **AIRg** (P=0.030)
   b) Increased **Sg** (P=0.021)
3. **Fecal microbiome:** Aleurone had a significant effect on:
   a) Diversity: Aleurone increased **beta diversity** (Weighted UniFrac Distance P=0.008; Bray-Curtis Distance P=0.03)
   b) Differentially abundant features:
   Aleurone decreased the abundancy of the genus of ***Desulfovibrio*** (logFC -4.536 FDR=0.002)
   c) Relative pathway abundancy (PICRUST):
   Aleurone induced changes in relative pathway abundancy: increased bacterial aromatic biogenic amine degradation (logFC 1,574 P=0.048)
4. **Correlations between FSIGTT parameters and relative abundance changes in the fecal microbiome:** Aleurone had a significant effect on:
   a) AIRg: Two of the *Firmicutes Clostridia Clostridialis* families, namely the *Peptostreptococcaceae* (r=0.895 P=<0.0001) and the *Lachnospiraceae* genus *Marvinbryantia* (r=0.732 P=0.002) show a strong and significant positive correlation with the changes in AIRg caused by aleurone.
   b) Sg: A strong negative correlation was found between differences in glucose effectiveness (Sg) induced by aleurone supplementation and the relative abundance of the bacterial family *Moraxellaceae*. (r=-0.735 P=0.002).





Beta diversity levels, PCoA plot based on 16S rRNA amplicon weighted UniFrac distances and boxplots showing 16s rRNA beta diversity. Before (blue) and after 8 weeks of training with aleurone (purple).

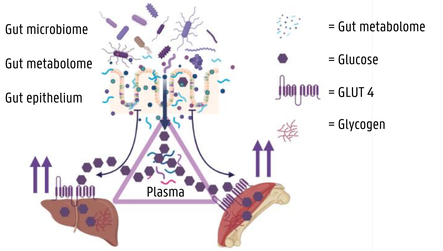


Spearman correlation between AIRg changes caused by aleurone and microbial abundancy changes at the family level.

5. Conclusions

- Training has a positive effect on insulin dynamics in the in-feed OGTT.
- Aleurone has an additional beneficial effect on glucose and insulin dynamics on top of training in healthy horses.
  → This is attributable to increased tissue glucose uptake capacity.
  → Moreover this is correlated to shifts in the fecal microbiome .
- Aleurone increases the beta diversity of the fecal microbiome in trained horses.

Aleurone supplementation in combination with training increased glucose-driven peripheral tissue uptake of glucose and this correlated to shifts in the fecal microbiome



The Gut-Muscle axis: Aleurone supplementation changed the gut muscle axis by inducing shifts in the gut microbiome composition and the accompanying predicted gut metabolome, which correlated to increased peripheral tissue uptake of glucose (Sg) and decreased the Acute Insulin Response to glucose (AIRg).

6. References

1. Graf D et al., (2019) Specific wheat fractions influence hepatic fat metabolism in diet-induced obese mice. *Nutrients* 11(10) doi:10.3390/nu11102348.
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Ethical animal research: All methods were approved by the Ethics Committee from Ghent University (approval#EC2016/40)

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