



The Effect of *Morinda citrifolia* on health and performance of neonates

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Botanical Immunomodulators

➤ Metastasis Inhibitors



Tomato
(Lycopene)



Ginger (6-
Gingerol)



Tumeric
(Curcumin)

➤ Antioxidant Activity



Red Grapes
(Resveratrol)



Blueberries



Green tea

➤ Antibacterial Activity



Clove



Oregano



Rosmarinus
Officinalis
Rosemary

➤ Anti-Inflammatory Activity



Capsicum Baccatum
Peruvian hot pepper



Cinnamon



Pomegranate
(Ellagic Acid)

➤ Analgesic Effects



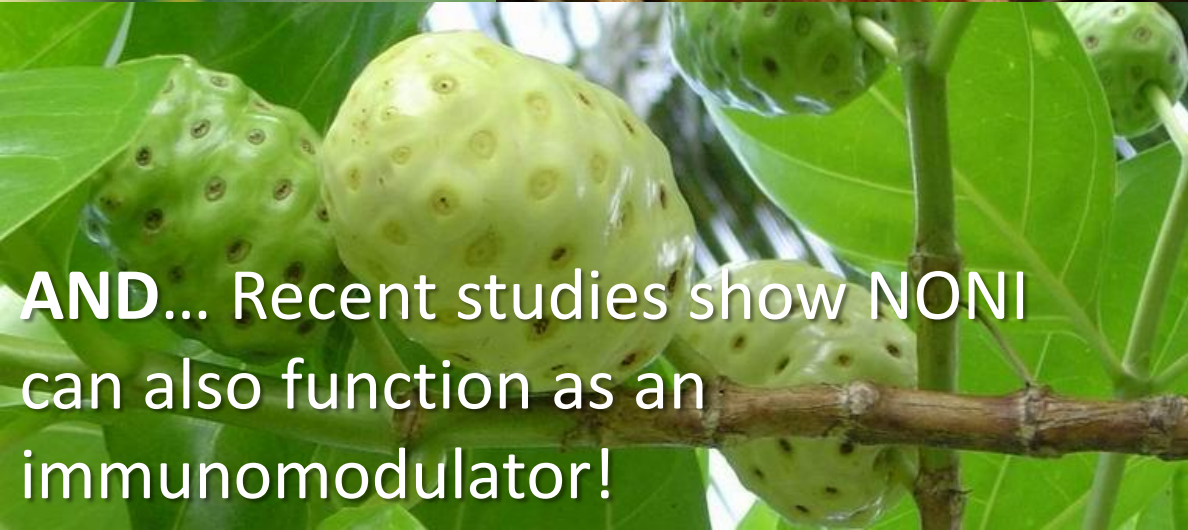
Red Chili
(Capsaicin)

Morinda citrifolia (NONI)



- Noni

- Indian mulberry, great morinda, cheezefruit, mouse's pineapple, yellow root, jumbie breadfruit, hog apple, pain killer,, nono,
- It is a large evergreen shrub or small tree to 6 m or more in height and 13 cm or more in stem
- The white tubular flowers are grouped in globose heads



AND... Recent studies show NONI can also function as an immunomodulator!



Enhanced Bactericidal Activity against *Escherichia coli* in Calves Fed *Morinda citrifolia* (Noni) Puree

M. Schäfer, P. Sharp, V.J. Brooks, J. Xu, J. Cai, N.S. Keuler, S.F. Peek, R.G. Godbee, R.D. Schultz, and B.J. Darien

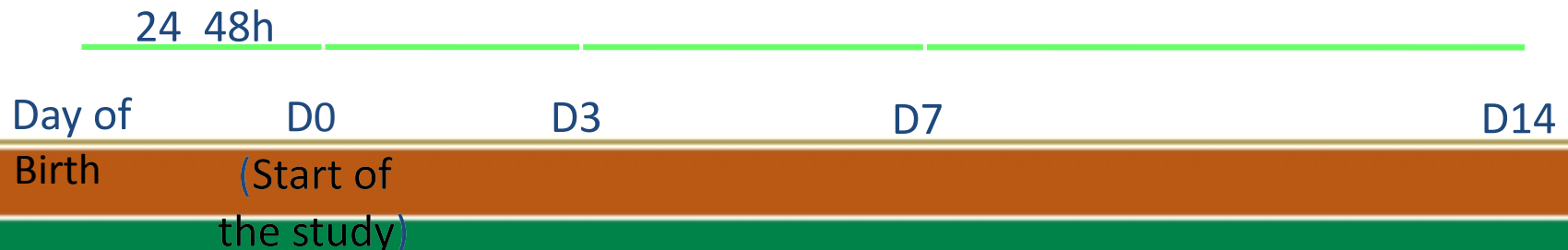
- Hypothesis: Neonatal calves fed noni puree would demonstrate whole blood phagocytic capacity in Gram-negative and Gram-positive in vitro assays



Increased Health
& Well-being

Study Protocol

- 2 groups (n = 9 in each)
 - Calf pairs
 - Control & Noni supplemented calves
- Inclusion criteria
 - Normal physical examination and $\text{IgG} \geq 1200 \text{ mg/dl}$
- Noni puree per calf = 1 oz/day p.o., BID
- Day 0 blood samples 36-48 hours of age before the first feeding of puree (day 0) & d's 3, 7, and 14



Study Methods

- Grp 1 control calves; Grp 2 received 30mL of noni puree q12h in milk replacer
- Daily health scores recorded
- Bactericidal assays determined % killing of *E. coli* and *S. epidermidis*.

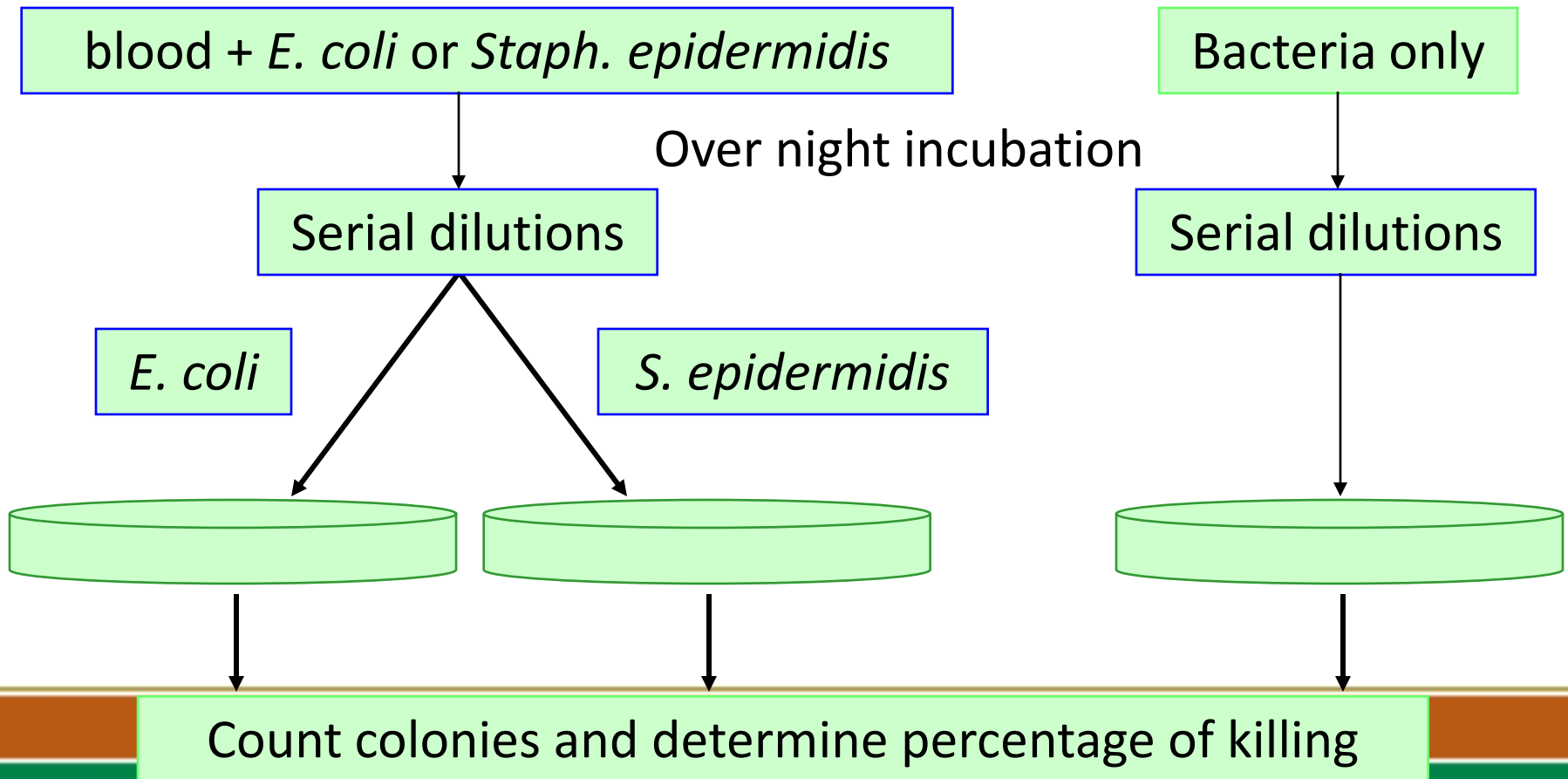
Table 1. Calf health scoring criteria

Score	Temperature	Cough	Nasal Discharge	Eyes or Ears	Fecal Score
0	37.8–38.3 °C	None	Normal serous discharge	Normal	Normal
1	38.3–38.8 °C	Induce single cough	Small amount of unilateral, cloudy discharge	Small amount of ocular discharge	Semiformed, pasty
2	38.9–39.4 °C	Induced repeated cough or occasional spontaneous cough	Bilateral, cloudy, or excessive mucus discharge	Moderate amount of discharge from both eyes or slight ear drop	Loose but enough consistency to stay on bedding
3	≥ 39.4 °C	Repeated spontaneous coughing	Copious, bilateral, mucopurulent nasal discharge	Head tilt or both ears dropped	Watery, sifts through bedding

Bactericidal Assay



- Estimate the ability of whole blood from control and noni puree Tx calves to engulf and kill Gram – and + bacteria



Bactericidal Assay

Formula used:

$$\frac{\text{Bacterial control cfu/ ml} - \text{Sample cfu/ ml}}{\text{Bacterial control cfu/ ml}} \times 100 = \text{Percent bacteria killed}$$

Example:

Bacterial control: 200 colonies

Sample: 100 colonies

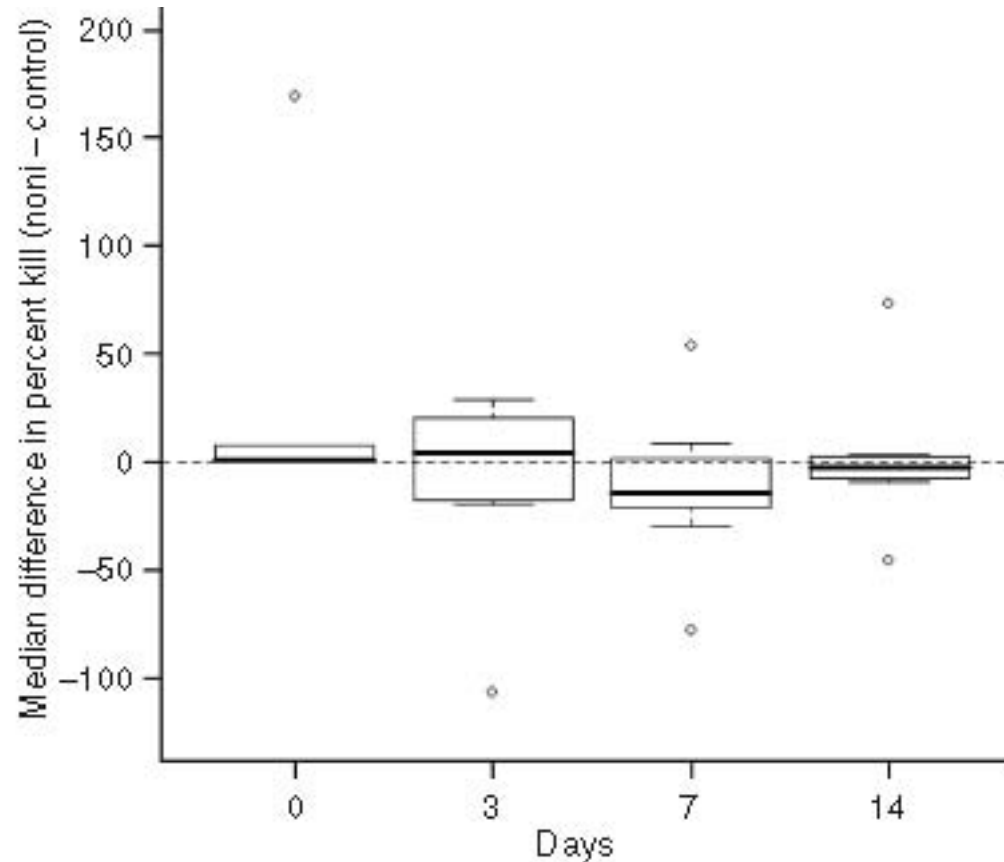
$$\frac{200 - 100}{200} \times 100 = 50 \% \text{ bacteria killed}$$



Difference: Noni % kill – control % kill

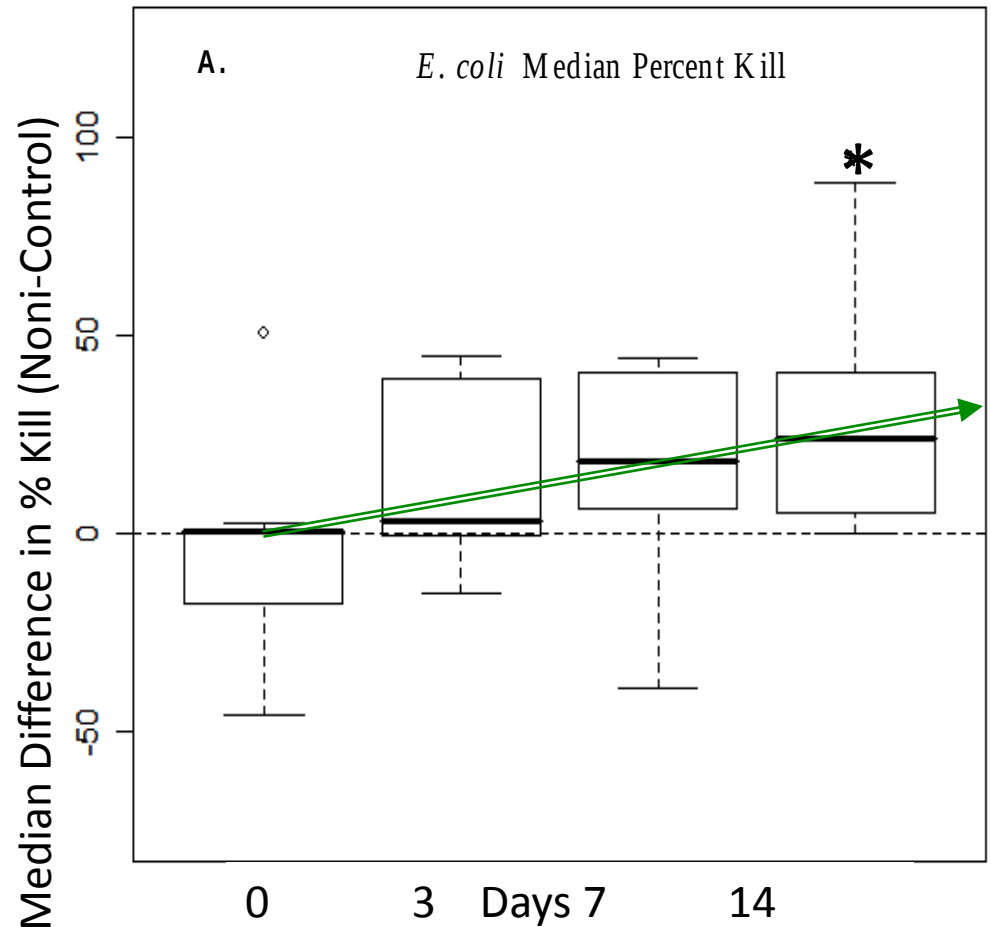
Results: Calf Health & Gram +

- No calves were removed from the study because of health reasons
- There were no differences between the groups for *S. epidermidis* bactericidal activity at any of the time points or between time points



Results: *E. coli*

- Significantly more bacterial killing on day 14 of *E. Coli* compared to control ($p = 0.0215$).
- *E. coli* bacterial killing between noni puree supplemented calves and control calves increased over time. ($p = 0.0534$).



Conclusions

- Given the role of polysaccharides as immunomodulators, noni puree potentially may stimulate the acquired innate immune response by modulating colostrum cells, neonatal mononuclear cells
 - General mitogenic effect on select pattern-recognition receptor activation
- Subsequent trials was warranted to investigate a modulating effect on naïve T cell activation.



CD4⁺ and CD8⁺T Cell Response In Neonatal Calves Fed *Morinda* *Citrifolia* (Noni)

V.J. Brooks^{1*}, R.G. Godbee², S.F. Peek¹, B.J.
Darien¹

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²University of Nevada, Reno

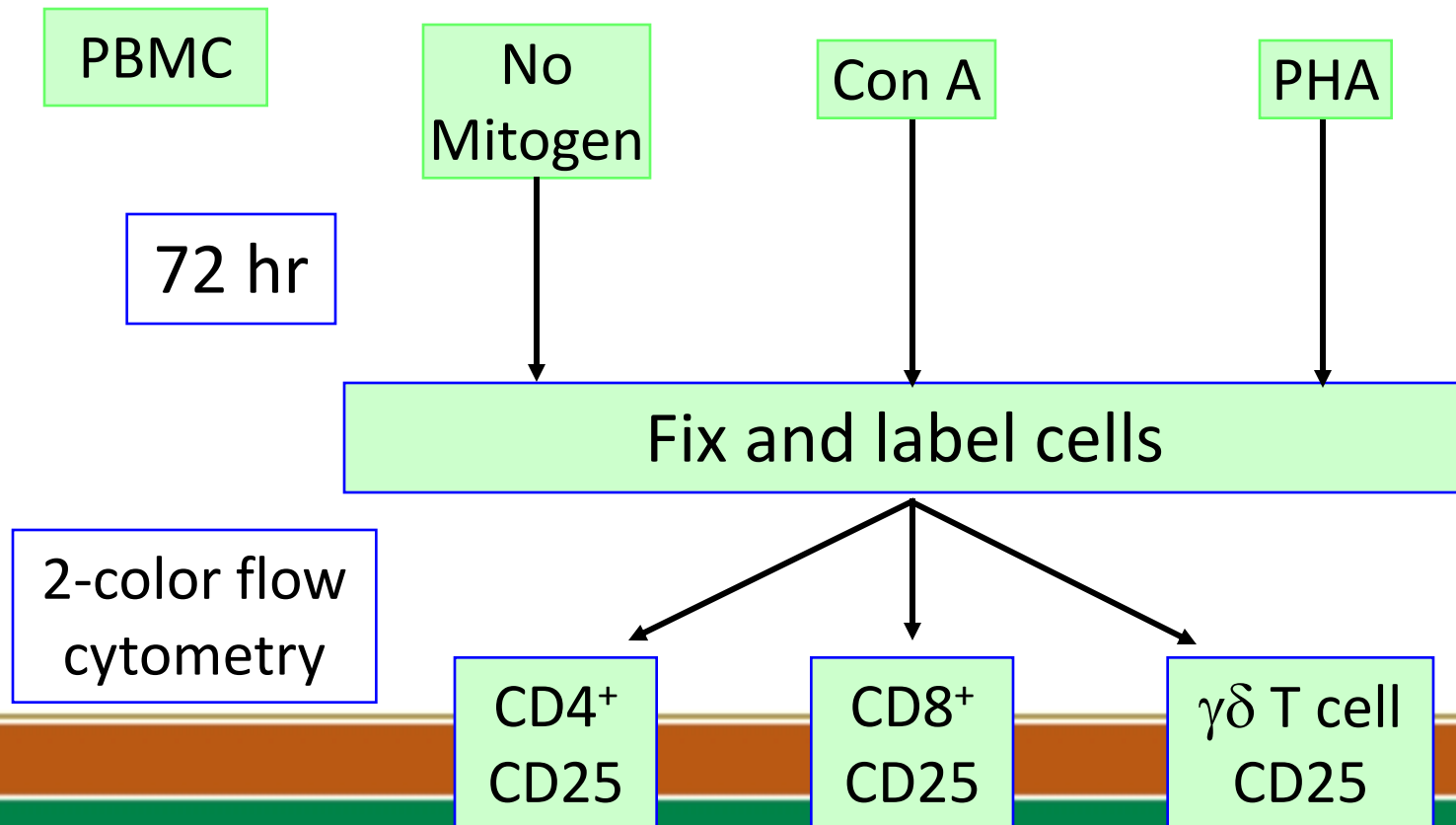
Hypothesis

- Colostral leukocytes & cytokines play a role in enhancing neonatal immunity
- Colostral IL-1, TNF- α , IFN- γ , play a role in enhancing neonate immunity by up-regulation of IL-2r on PBMC
- Ho #1: That supplementation of Noni pure would enhance T cell expression of CD25
- Ho #2: Noni induces cytokine expression in colostral leukocytes

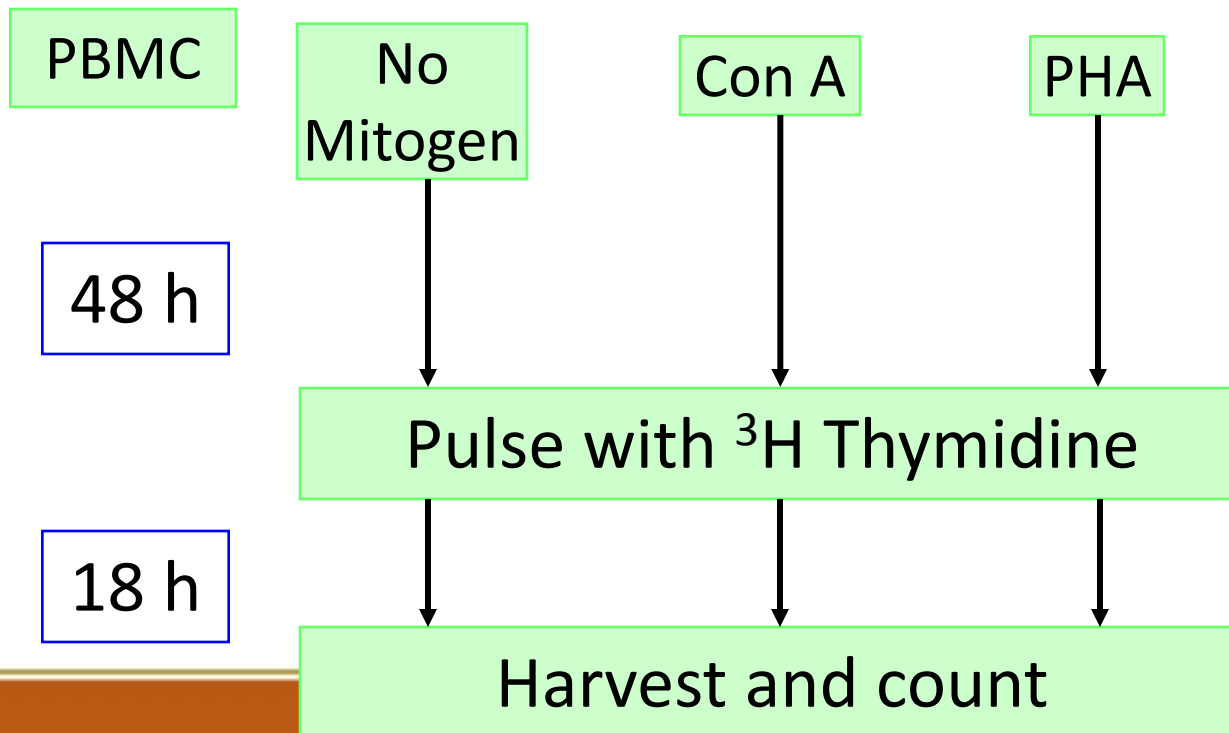
Protocol

- 2 groups (n = 10 in each)
 - Calf pairs
 - Control & noni supplemented calves
 - Daily calf health score evaluations
- Noni puree per calf = 30 mL po, q12h for 14 days
- Day 0, 3, 7 and 14 samples
- T cell activation and proliferation

- Objective **Lymphocyte Activation Assay**
 - Evaluate IL-2 receptor (CD25) expression as index of lymphocyte activation

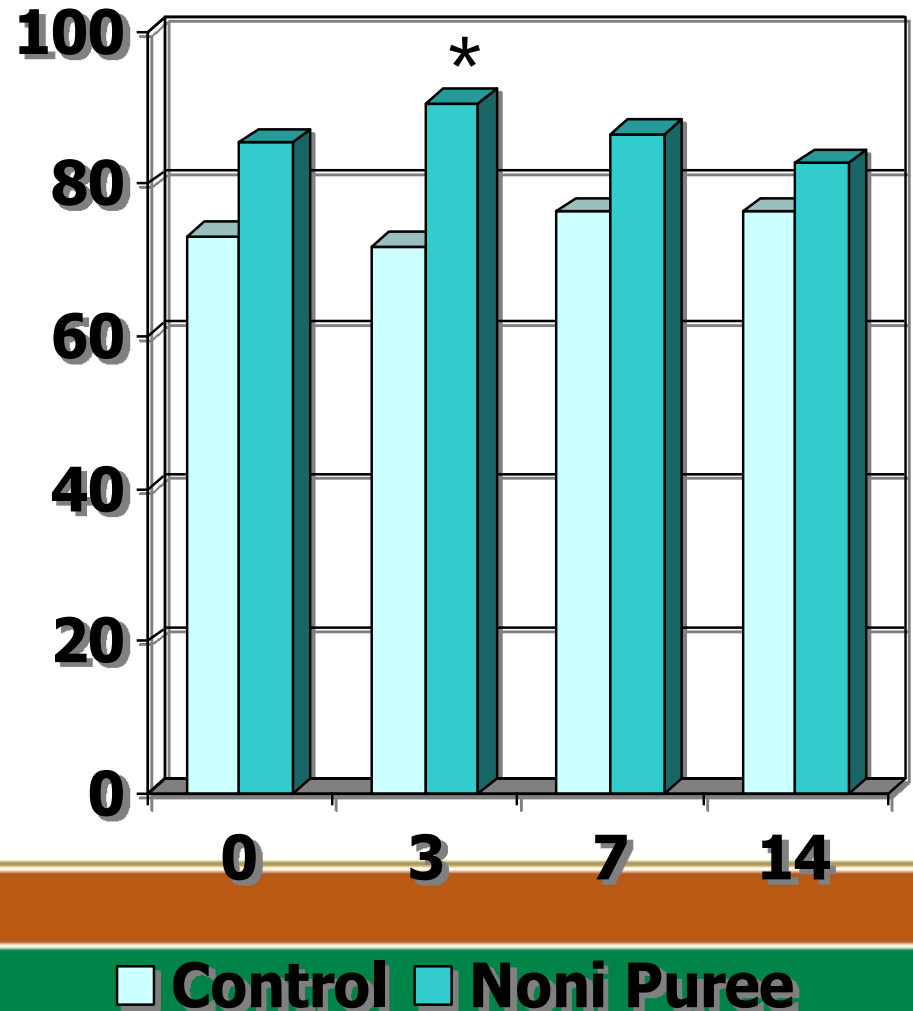


- Objective **Lymphocyte Blastogenesis Assay**
 - Measure lymphocyte proliferation in response to mitogen stimulation



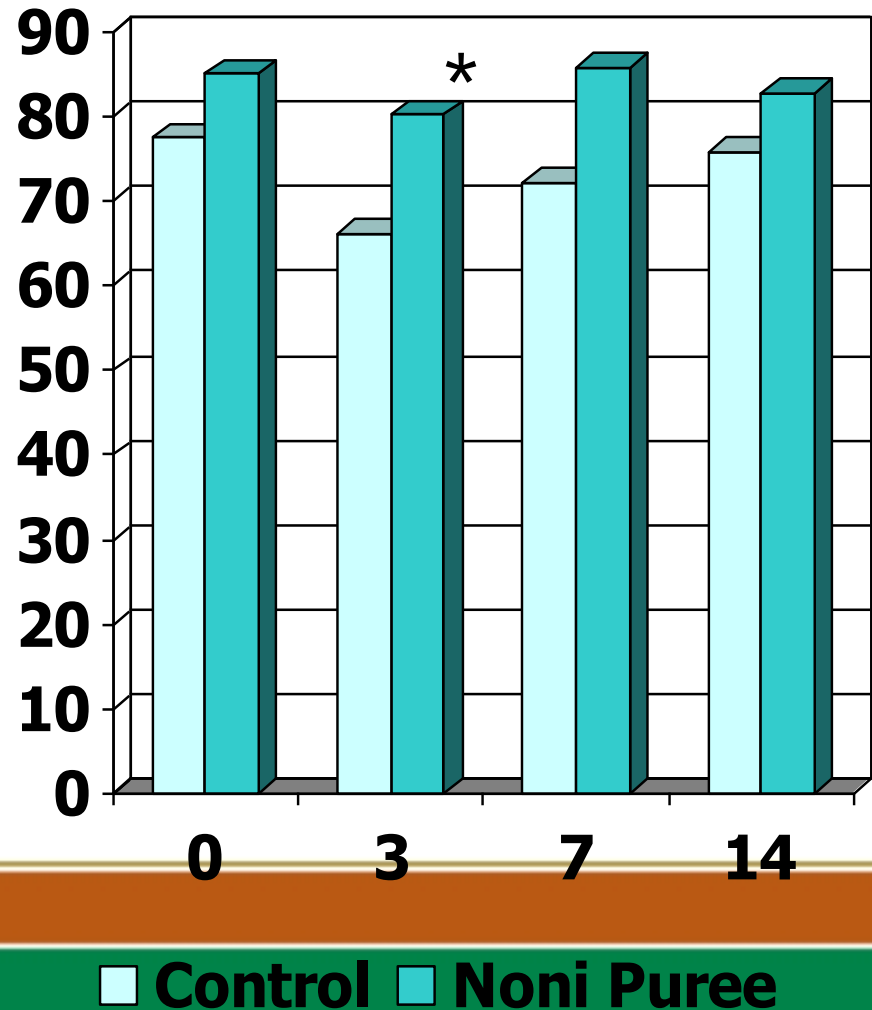
CD4⁺T Cell Activation in Neonatal Calves Fed (Noni) puree

- Significant increase in % activation (CD25r) of CD4⁺ T cells on day 3 after ConA stimulation



CD8⁺ T Cell Activation in Neonatal Calves Fed (Noni) puree

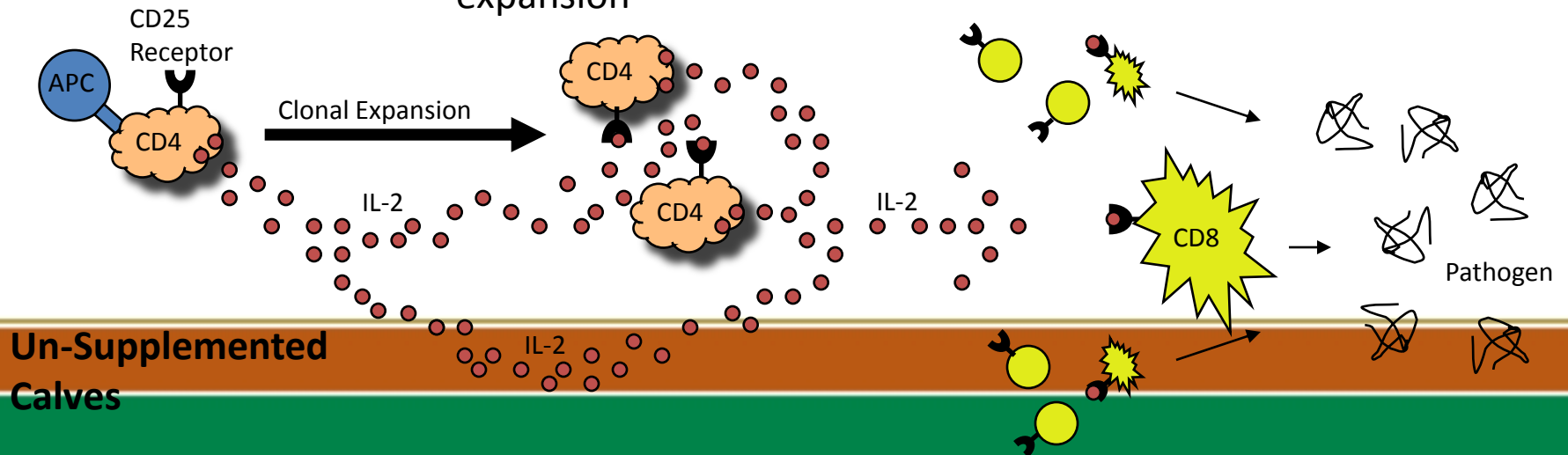
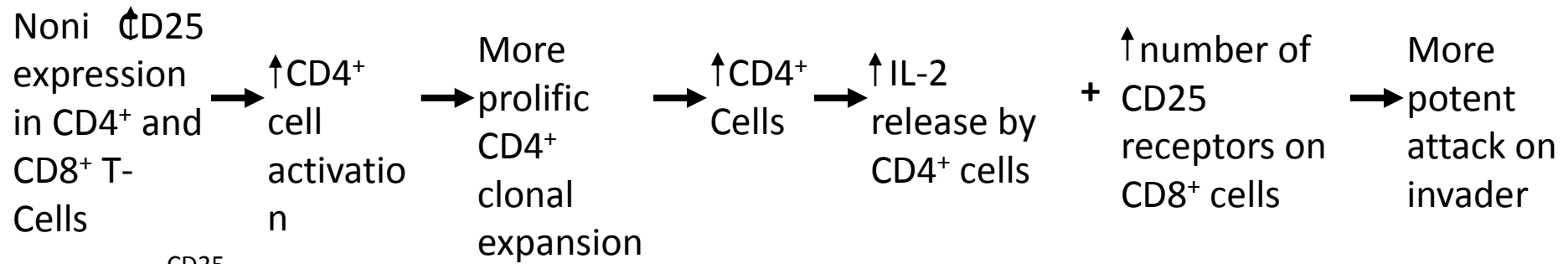
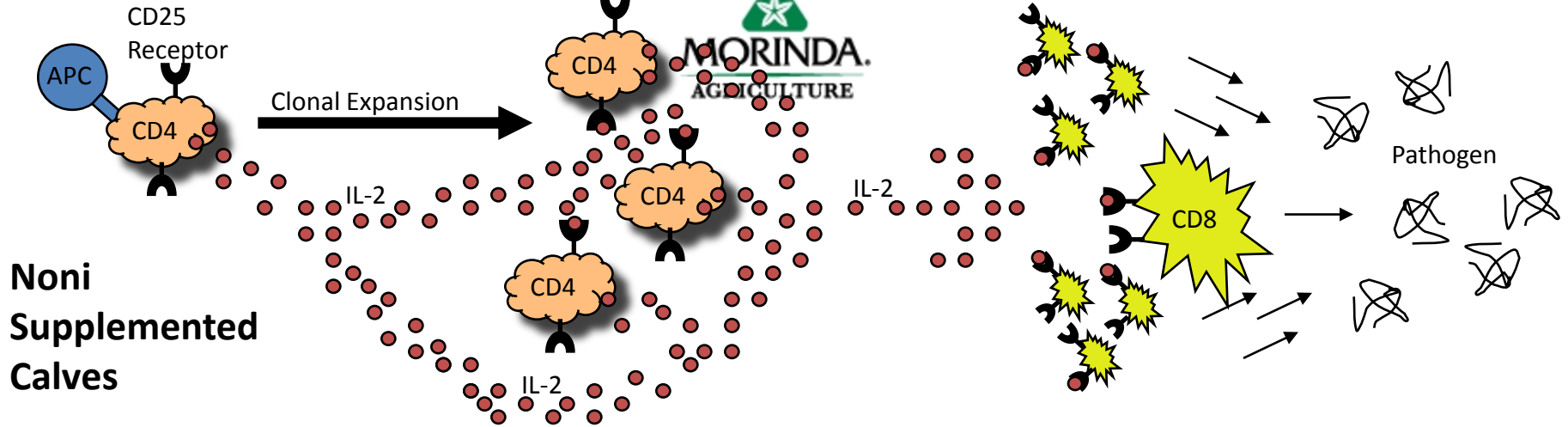
- Significant increase in % activation of CD8⁺ T cells on day After ConA stimulation
- Significant effect over time for CD8⁺ T cells



Results

- No significant differences
 - Activation of $\gamma\delta$ TCR⁺ cells
 - PHA activation response
 - Proliferation
- Increase in CD25 % expression on day 3
 - CD4⁺ T cells
 - CD8⁺ T cells
- Significant effect over time for CD8⁺ T cells

Mode of Action: Noni Immune Modulating Effect





A Clinical Trial Evaluating Morinda**Max**TM Calf[®] Immune-supplement on Health and Performance of Pre-weaned, Holstein, Heifer Calves.

V.J. Brooks^{1*}, R.G. Godbee²,
S.F. Peek¹, B.J. Darien¹

¹University of Wisconsin, Madison

²University of Nevada, Reno

Central Hypothesis

- Neonatal calves fed noni puree would be healthier and consequently wean earlier and increase profitability of the producer



Increased
Health
And
Well-being



Clinical Trial

- Large scale calf-raising farm in Central Wisconsin
- Endemic Salmonellosis
- Morinda**Max**[™] Nutritional Support for Calves was fed in a controlled blinded study



Clinical Trial

- 226 calves enrolled
 - Total Protein ≥ 5.0 g/dL
 - IgG ≥ 1200 mg/dL
 - Birth weight 70-120 lbs
 - Alive ≥ 48 hrs
 - 10 calves dropped
- Trial A (n=106) followed by Trial B (n=110)
- Calves fed 0, 15 (A) or 30 (B) mL of MorindaMax po, q12h for 21 days



Outputs

- Daily health scores
- Weaning age
- Average daily gain
- Medical treatments
- Economic impacts



Scoring example



Calf Health



Scoring Criteria

Combined Respiratory Score

Score	Temperature	Cough	Nasal Discharge	Eyes or ears	Fecal Score
0	100-100.9° F (37.8-38.3° C)	None	Normal serous discharge	Normal	Normal
1	101-101.9° F (38.3-38.8° C)	Induce single cough	Small amount of unilateral, cloudy discharge	Small amount of ocular discharge	Semi-formed, pasty
2	102-102.9° F (38.9-39.4° C)	Induced repeated cough or occasional spontaneous cough	Bilateral, cloudy or excessive mucus discharge	Moderate ocular discharge for both eyes or slight ear drop	Loose but enough consistency to stay on bedding
3	≥ 103° F (≥ 39.4° C)	Repeated spontaneous coughing	Copious, bilateral, mucopurulent nasal discharge	Head tilt or both ears dropped	Watery, sifts through bedding

Treatment protocol



Health Score	Treatment	Cost*
Fecal = 2	Electrolytes	\$0.03
Fecal = 3	Electrolytes (2x)	\$0.06
Fecal = 2 + blood	Electrolytes + Gentamicin	\$0.03 + 0.26
Fecal = 3 + blood	Electrolytes (2x) + Gentamicin	\$0.06 + 0.26
Total respiratory score of ≥ 5	1st Ceftiofur	\$3.20
	2nd Tulathromycin	\$7.56
	3rd Trimethoprim Sulfa	\$1.40
Temperature $\geq 39.4^{\circ}\text{C}$ ($\geq 103^{\circ}\text{F}$)	Flunixin meglumine	\$0.50

Incidence of Disease:

Fecal score ≥ 2

Total respiratory score of ≥ 5

Temperature $\geq 39.4^{\circ}\text{C}$

* Cost of treatment per calf per day

Economic Analysis

- Cost figures were attained from the *Economic Costs and Labor Efficiencies Associated with Raising Dairy Herd Replacements on Wisconsin Dairy Farms and Custom Heifer Raising Operations* report (2007) as analyzed by the Intuitive Cost of Production Analysis (ICPA) computer model.

Figures are based on:

- Weaning ages (days)
- Disease incidences derived from health scores
- Treatment costs



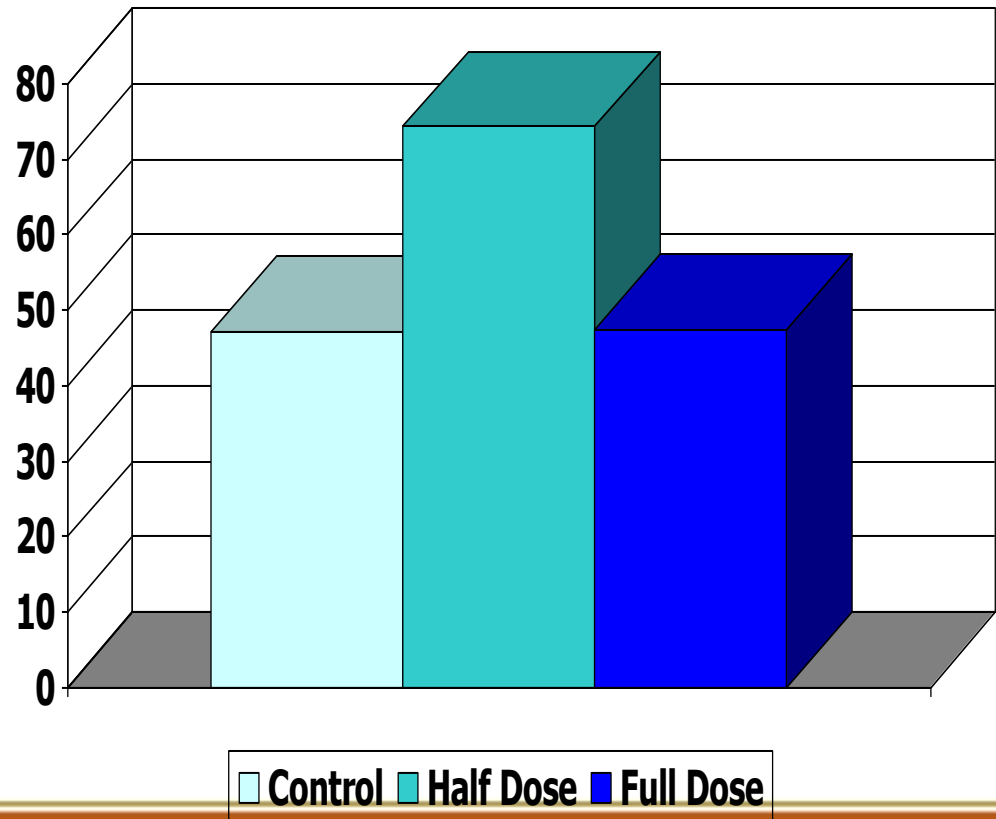
Economic Costs and Labor Efficiencies Associated with
Raising Dairy Herd Replacements
on Wisconsin Dairy Farms and Custom Heifer Raising
Operations

2007

Results: Trial A

- Significantly more calves weaned by 6 weeks of age that had received noni puree
- $p = 0.0385$
- Approx. 30% more

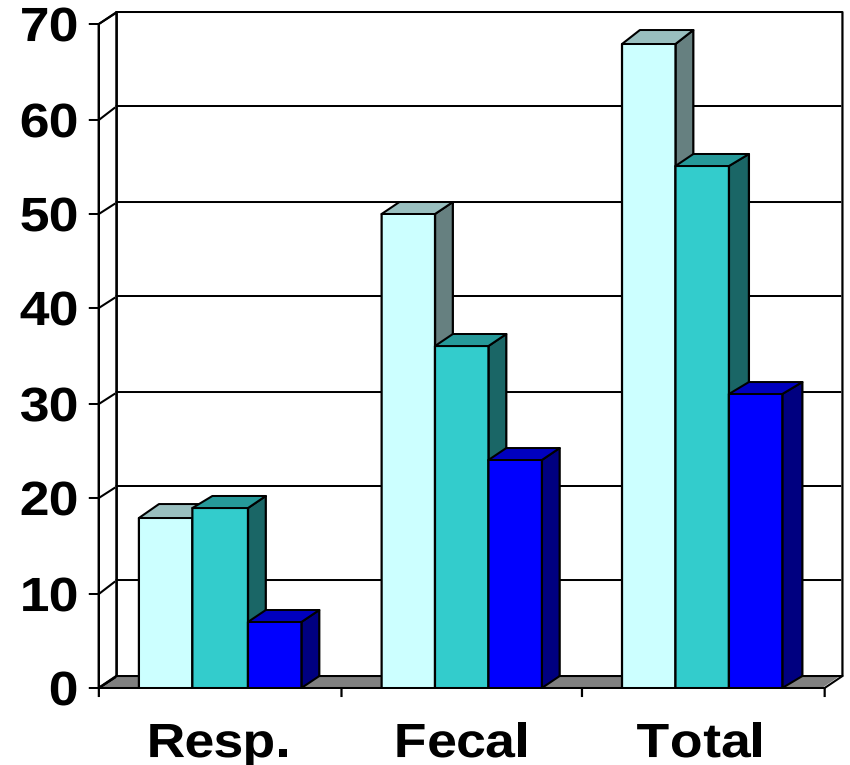
Percent weaned by 6 weeks of age



Results of Trial B

- Significantly fewer respiratory, fecal and total treatments
- In control calves:
 - 2.5X Respiratory
 - 2X Fecal
 - 2.2X Resp + Fecal scores

Number of medical treatments



Control Half Dose Full Dose

Summary

- Trial A
 - 30% increase in calves weaned by 6 weeks of age
 - Monetary savings of \$13.56 per calf
- Trial B
 - Significantly fewer respiratory, fecal and total treatments
 - Monetary savings of \$8.19 per calf

Summary of Calf Studies

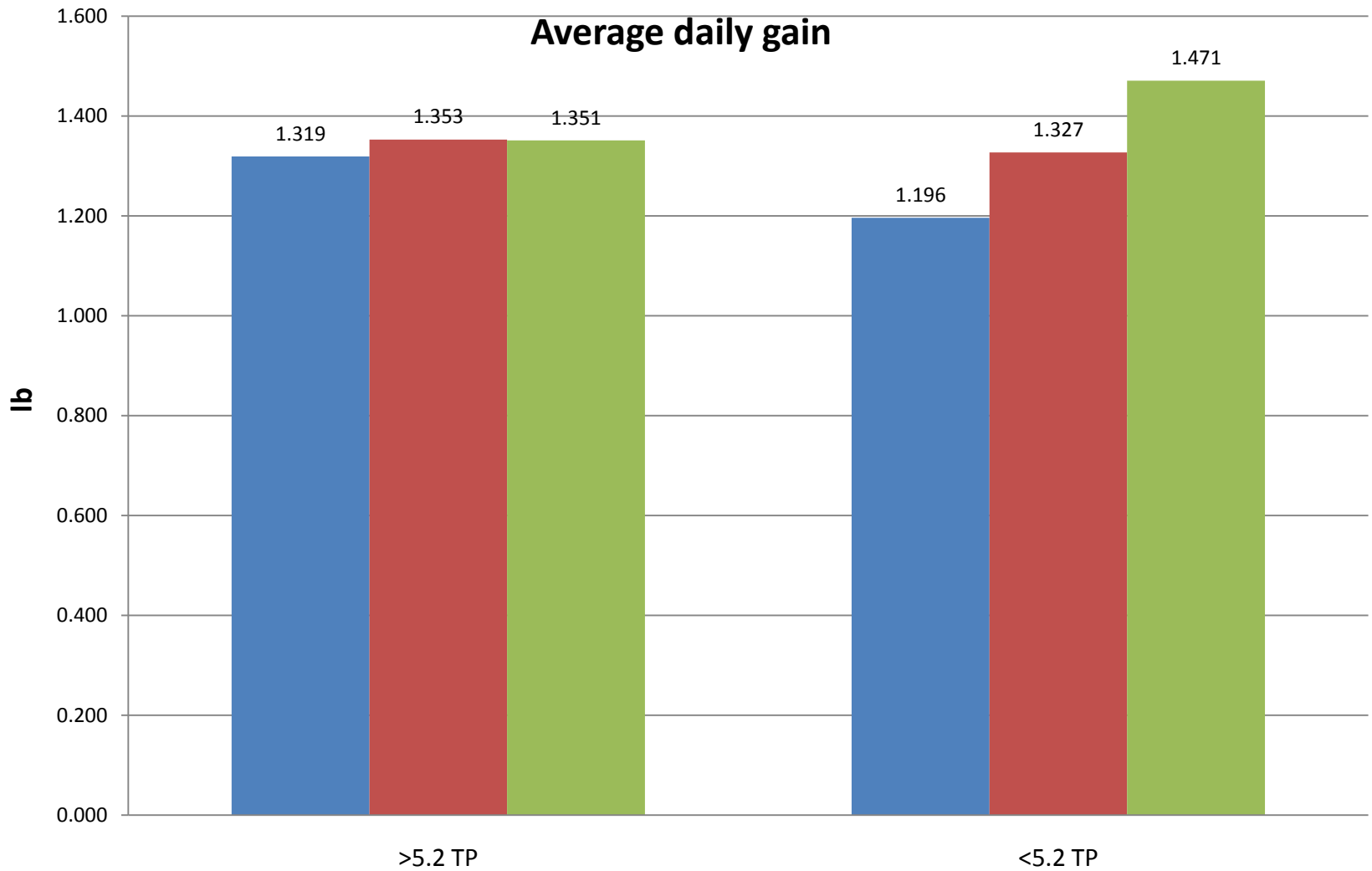
- Significant E. coli phagocytosis on day 14 compared to control
- E. coli bacterial killing increased over time
- Significant increase in % activation of CD4+ T cells on day 3
- Significant increase in % activation of CD8+ T cells on day 3
- Significant effect over time for CD8+ T cells

Summary of Findings

- Significantly more calves weaned by 6 weeks of age that had received 30 mL noni puree a day
($p = 0.0385$).
 - Monetary savings of \$13.56 per calf
- Significantly fewer respiratory, fecal and total treatments
 - Monetary savings of \$8.19 per cal

Effect of MorindaMax on performance of calves with APT or FPT (field trial)

- 180 calves divided into 6 treatment groups.
 - TP > 5.2 Adequate Passive Transfer
 - control
 - 15ml po BID 10d
 - 30ml po BID 10d
 - TP < 5.2 Failure Passive Transfer
 - control
 - 15ml po BID 10d
 - 30ml po BID 10d



■ control ■ 0.5oz BID ■ 1.0 oz BID



Summary

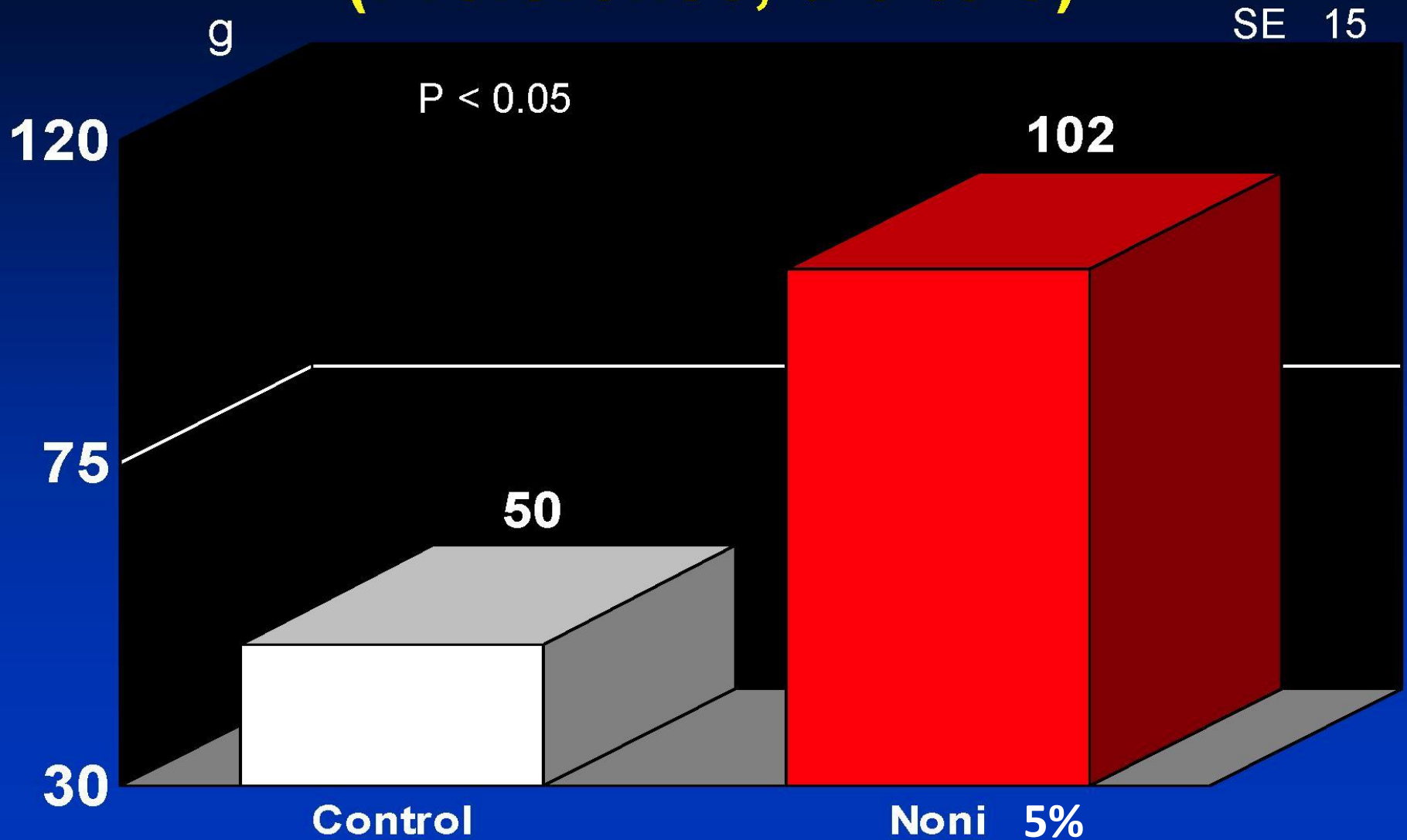
- Small improvement (2.6%) in average daily gain using MorindaMax BID for 10d in calves with APT.
- Feeding 30ml BID MorindaMax for 10d in calves with FPT resulted in a 23% increase in average daily gain.
- Feeding 15ml BID MorindaMax for 10d in calves with FPT resulted in a 11% increase in average daily gain.

Animal Research - Piglets

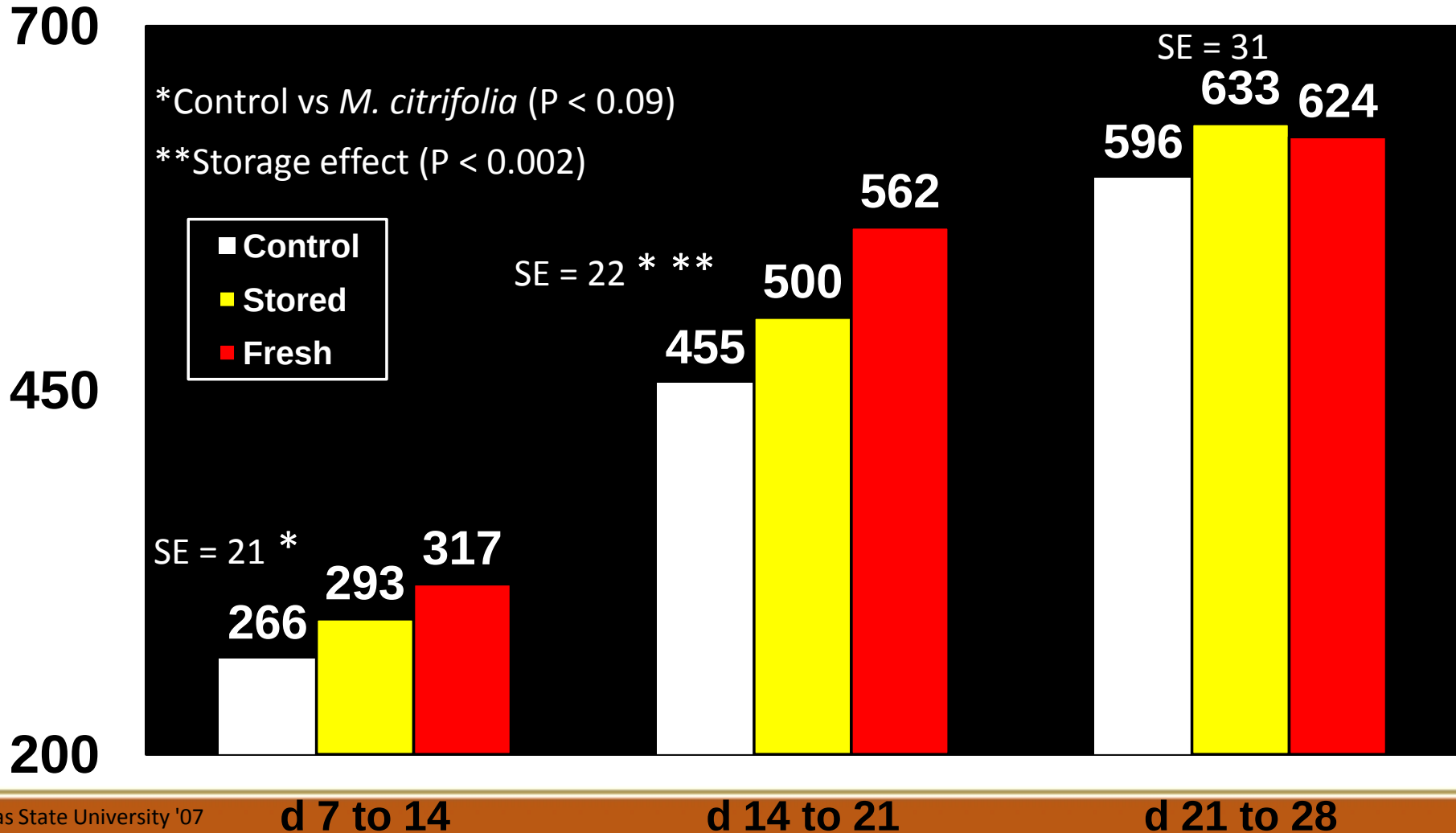
- Improved gains early in nursery phase.
- Carry-over effect after receiving MorindaMax Nutritional Support for Piglets.
- Improved Gain:Feed.
- Improved average daily gain.

Noni & ADFI

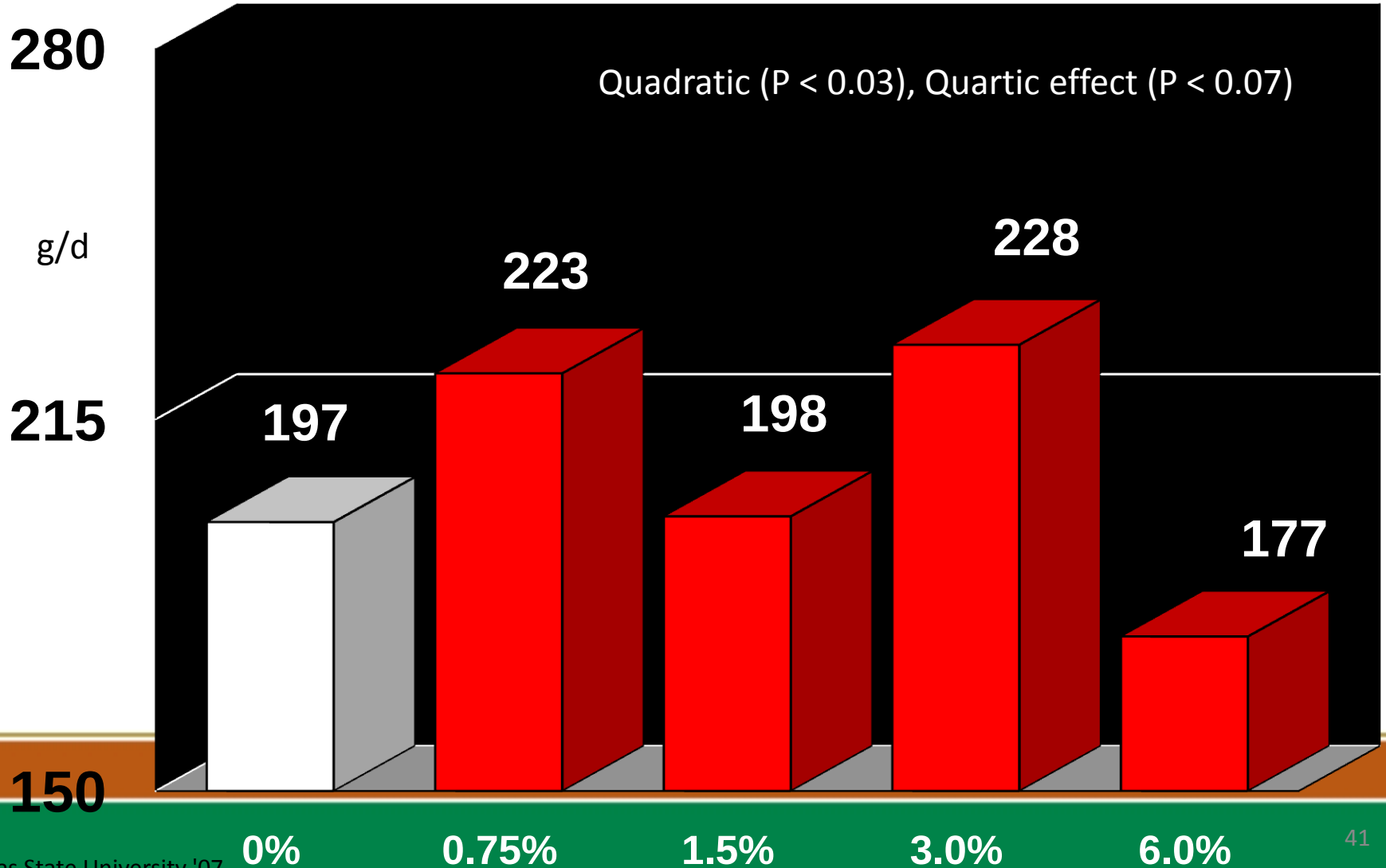
(Preference, d 0 to 5)



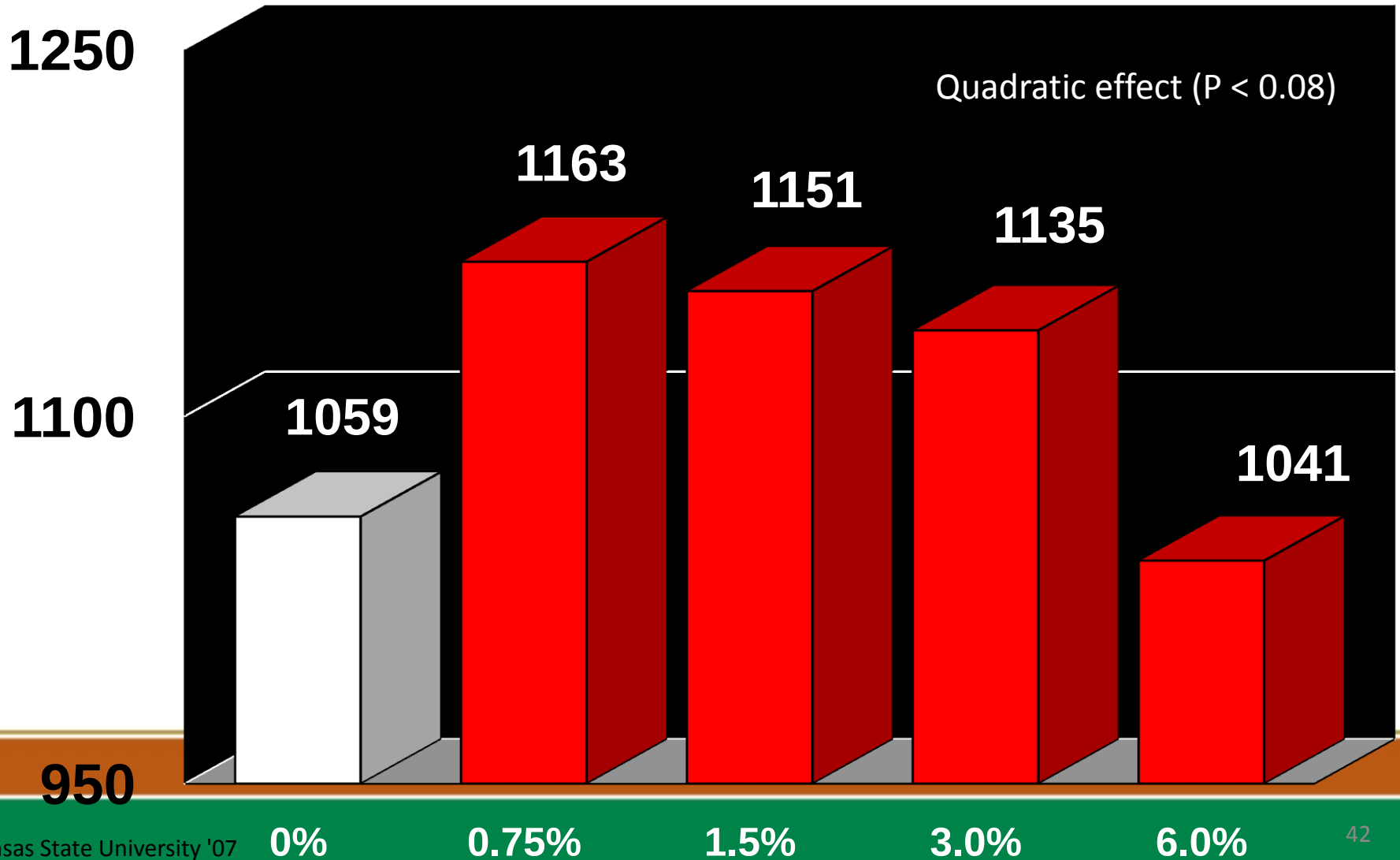
Prolonged Storage & ADFI



M. citrifolia Concentration & ADG(d 0 to 7)



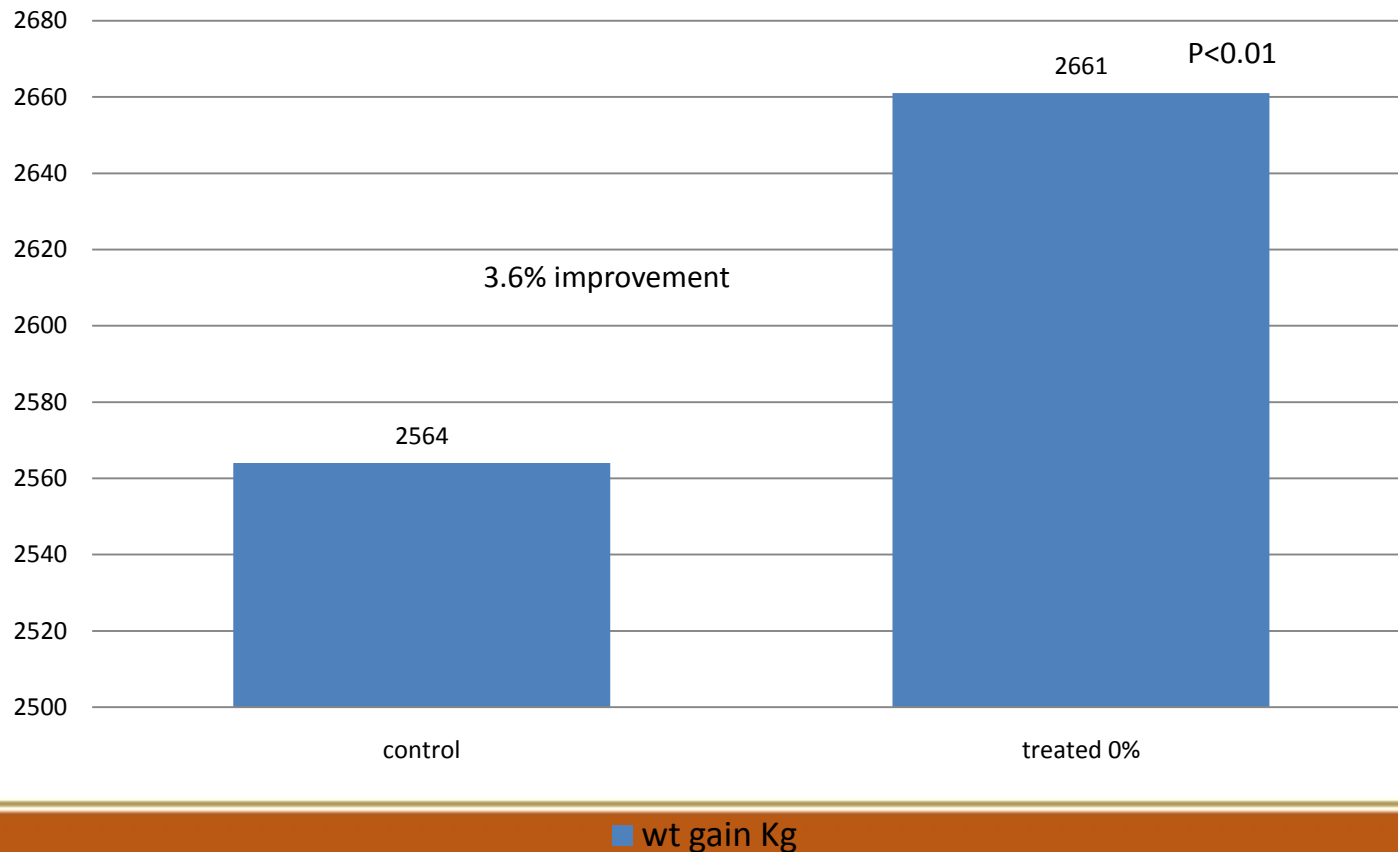
M. citrifolia Concentration & G:F (d 0 to 7)



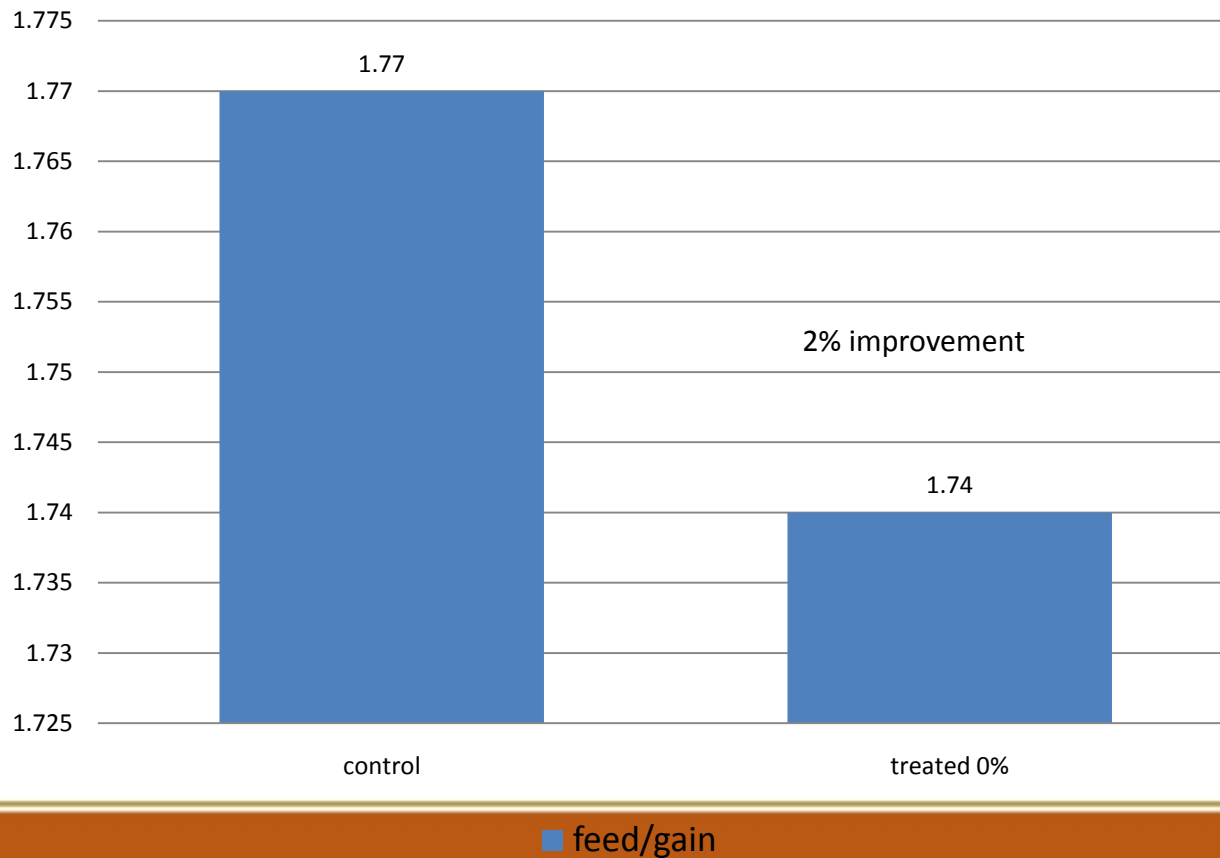
Animal Research - Broilers

- Improved average daily gain.
- Improved Gain:Feed.
- Improved total weight gain.

Effect of *M. citrifolia* on Broiler Chick Performance 1-42 Days of Age



Effect of *M. citrifolia* on Broiler Chick Performance 1-42 Days of Age



Thank You

