Calcium Release Technologies (CaRT)

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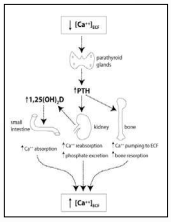
Notes:

PowerPoint Slides on next page

Calcium Response Technologies (CaRT)

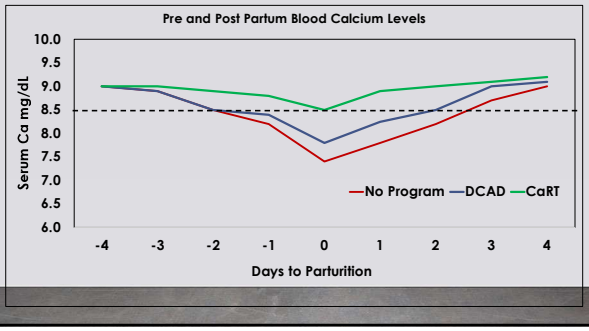
New Innovations to Prevent Hypocalcemia in Dairy Cattle



Patrick C Hoffman, Professor Emeritus, University of Wisconsin-Madison

1

Calcium Response Technology (CaRT)



2

Ca Response Technologies

- Dietary Ca Restriction
- Dietary P Restriction
- Zeolite A

- 5-HTP
- Solanum glaucophyllum

- Difructose Anhydride
- Calcidiol 25 (OH) Vit D_3

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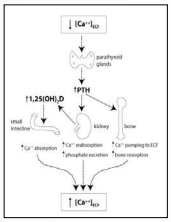
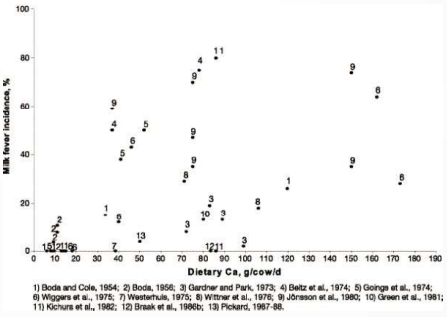
Calcium Restriction

•T Thilsing-Hansen, et al., 2002





1) Boda and Cole, 1954; 2) Boda, 1956; 3) Gardner and Park, 1973; 4) Beitz et al., 1974; 5) Goings et al., 1974; 6) Wiggers et al., 1975; 7) Westerhuis, 1975; 8) Wittmer et al., 1976; 9) Jörsson et al., 1980; 10) Green et al., 1981; 11) Kichura et al., 1982; 12) Braak et al., 1986b; 13) Pickard, 1987-88.

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Phosphorus Restriction

- 30 prefresh dairy cows
- Fed 0.16 or 0.30 % P
- Controlled feed offerings
- Fed for 28 d prior to calving
- Measurements
  - Blood Ca, P
  - PTH
  - 1-25 (OH_2) Vit D_3
  - Bone mobilization (CrossLaps-CTX)

J. Dairy Sci. 105:746–760
https://doi.org/10.3168/jds.2021-20726

Effects of restricted dietary phosphorus supply to dry cows on periparturient calcium status

S. Wächter,[1] I. Cohrs,[2] L. Golbeck,[1] M. R. Wilkens,[1]* and W. Grünberg[1]†

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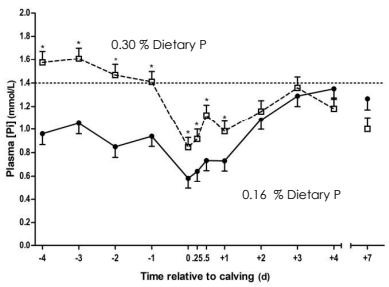
Wachter et.al., JDS-2022

Plasma P



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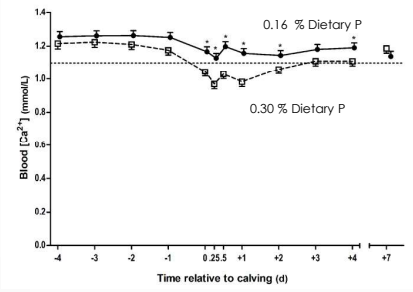
Wachter et.al., JDS-2022

Plasma Ca



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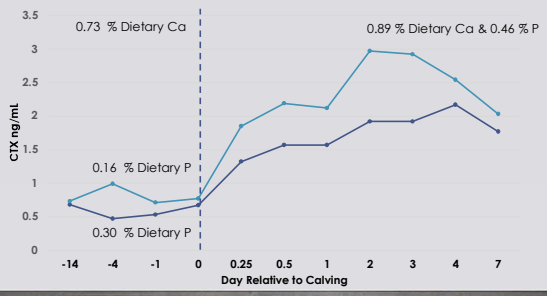
Bone Mobilization CrossLaps (CTX)



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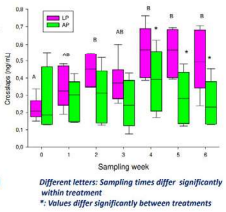
Grunberg et al., 2019

Results

CrossLaps ®

- Significant increases after 2 weeks of P-depletion
- Significantly higher concentrations in LP compared to AP from the 4. week of P-deprivation

➔ Indication for increased bone resorptive activity with P-deprivation



Different letters: Sampling times differ significantly within treatment
**: Values differ significantly between treatments*

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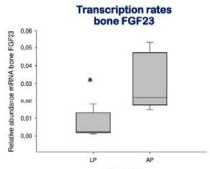
Grunberg et al., 2019

Results

Bone FGF23

- Relative abundance of mRNA of FGF23 in bone is markedly decreased after 6 weeks of dietary P-deprivation



**: Values differ significantly between treatments*

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Wachter et.al., JDS-2022 (Summary)
Feeding 0.16 % P vs 0.30 % P to prefresh cows……

- **Decreased blood P**
- **Increased blood Ca**
- **Increased bone mobilization**
- **PTH did not directly explain differences in bone mobilization**
- **1-25 (OH_2)D_3 status appeared to be under the influence of P homeostasis precalving and Ca homeostasis postcalving??**
- **Authors speculated that P homeostasis was under the control of FGF23 (not measured) as opposed to PTH**

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FGF23 Fibroblast Growth Factor

- Produced in bones cells
- Identified in the early 2000s
- Is a bone derived hormone
- Suppresses phosphate reabsorption (kidney)
- Modulates kidney Na and P transport
- Suppresses enzymes that activate 1-25 (OH_2)D_3
- Increases when blood P is high
- Decreases when blood P is low

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Zeolite A

- Synthetic Zeolite
- Heavily studied sodium aluminium silicate
  - High ion exchange capacity
- Commercially Available to Feed to Dairy Cows
  - To reduce milk fever
  - To reduce subclinical hypocalcemia
- Introduced as a Ca Binder
  - New research = binding of recycling P
- Fed 14-21 d prefresh

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Zeolite A - Kerwin et.al., JDS-2022


J. Dairy Sci. 102
https://doi.org/10.3168/jds.2019-16272
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Effects of feeding synthetic zeolite A during the prepartum period on serum mineral concentration, oxidant status, and performance of multiparous Holstein cows

A. L. Kerwin,[1] C. M. Ryan,[1] D. M. Lenz,[1] M. Jakobsen,[2] P. Theilgaard,[2] D. M. Barbano,[1] and T. R. Overton[1]*
[1]Department of Animal Science, Cornell University, Ithaca, NY 14853
[2]Vitelco Inc., Lucknow, ON, Canada N0G 2H0
[3]Vitelco, Graasten, Denmark 6300

- 55 prefresh Holstein dairy cows

Fed 0.38 % P or 0.38 % P + Zeolite A

Ad lib feed offerings

Fed for 21 d prior to calving

Measurements

- Blood Ca, P
- Clinical Milk Fever
- Sub-clinical hypocalcemia
- Milk Production
- Colostrum Quality

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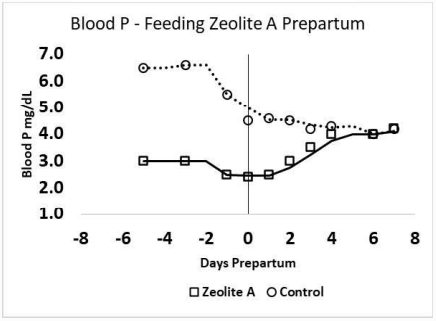
Kerwin et al., 2019



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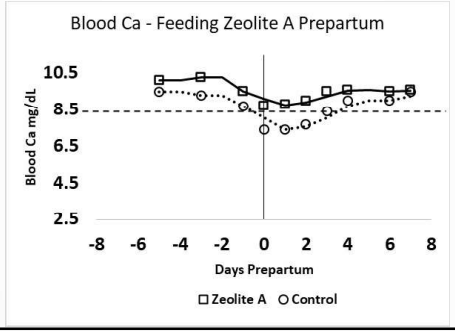
Kerwin et al., 2019



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Review of Zeolite A Feeding Trials

Reference	Treatments	Dietary Ca % DM		Dietary P % DM		Blood Ca Response % of Control	Blood P Response % of Control	Clinical Milk Fever % of Control
		Zeolite	Control	Zeolite	Control	Zeolite vs Control	Zeolite vs Control	Zeolite vs Control
Thilsing-Hansen et al., 2001	Zeolite vs Control	0.64	0.45	0.64	0.45	+ 27 %	NR	- 33 %
Kerwin et al., 2019	Zeolite vs Control	0.65	0.68	0.38	0.39	+ 22 %	- 50 %	0%
Frizzarini et al., 2022	Zeolite vs DCAD	NR	NR	NR	NR	+11 %	-47%	NR
	Zeolite vs Control	NR	NR	NR	NR	+17 %	-49%	NR
Crookenden et al., 2020	Zeolite vs Control	NR	NR	NR	NR	+ 13 %	-73 %	NR
Pallesen et al., 2007	Zeolite vs Control	0.61	0.69	0.61	0.69	+ 33%	- 10 %	- 75 %
	Zeolite vs Control	0.61	0.33	0.61	0.69	+ 57 %	- 72 %	-100 %
Grabherr et al., 2008	Zeolite vs Control	0.42	0.38	0.42	0.38	+ 11 %	- 22 %	NR
Saraiva de Oliveira, 2021	Zeolite vs DCAD	0.57	2.53	0.36	0.43	+ 13 %	- 45 %	-51%
Thilsing-Hansen et a., 2002	Zeolite vs Control	0.60	0.60	0.30	0.30	+12 %	- 36 %	0%
Khachouf et al., 2019	Zeolite vs Control	2.79	2.79	0.80	0.80	+ 8 %	0%	NR

NR = not reported

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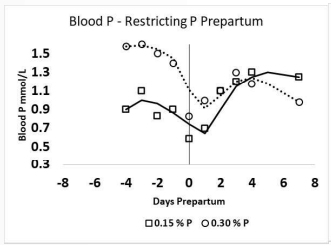
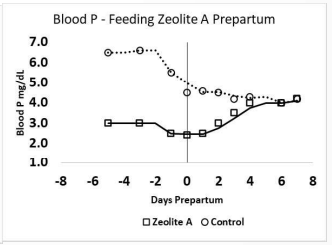
Feeding Zeolite A to Prefresh Cows Mimics Dietary P Restriction





A – Wachter et al., 2022

B – Kerwin et al., 2019

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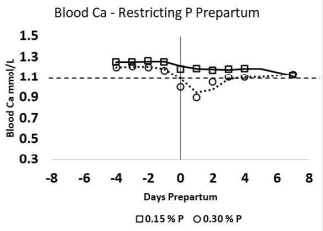
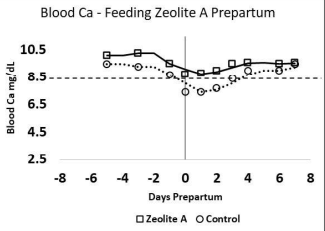
Feeding Zeolite A to Prefresh Cows Mimics Dietary P Restriction





A – Wachter et al., 2022

B – Kerwin et al., 2019

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Feeding Zeolite A to Prefresh Dairy Cows to Prevent Milk Fever and Hypocalcemia

- Research observations
  - Decreased milk fever and hypocalcemia
  - Lower blood P observed
  - Greater blood Ca consistently observed
  - Decreased urinary P and Ca excretion
  - Increases 1-25 (OH2) Vit D but Not PTH?
  - Decreases Salivary P
  - Increases Undigested Fecal Ortho PO4
  - Results are nearly identical to dietary P restriction experiments
  - **Feeding Zeolite A appears to reduce milk fever and hypocalcemia by binding P thereby inducing a dietary P restriction**

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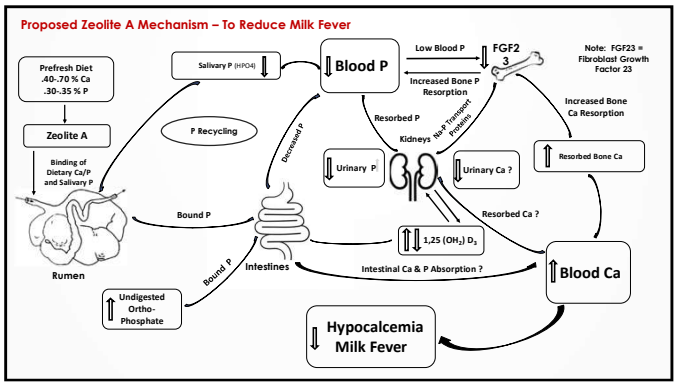
Proposed Zeolite A Mechanism – To Reduce Milk Fever
Prefresh Diet .40-.70 % Ca .30-.35 % P
Zeolite A
Binding of Dietary Ca/P and Salivary P
Salivary P (HPO4)
Blood P
Low Blood P
FGF2 3
Note: FGF23 = Fibroblast Growth Factor 23
Increased Bone P Resorption
Increased Bone Ca Resorption
P Recycling
Decreased P
Resorbed P
Kidneys
No-P Transport Proteins
Urinary P
Urinary Ca ?
Resorbed Bone Ca
Bound P
Resorbed Ca ?
1,25 (OH2) D3
Rumen
Intestines
Intestinal Ca & P Absorption ?
Blood Ca
Undigested Ortho-Phosphate
Bound P
Hypocalcemia Milk Fever

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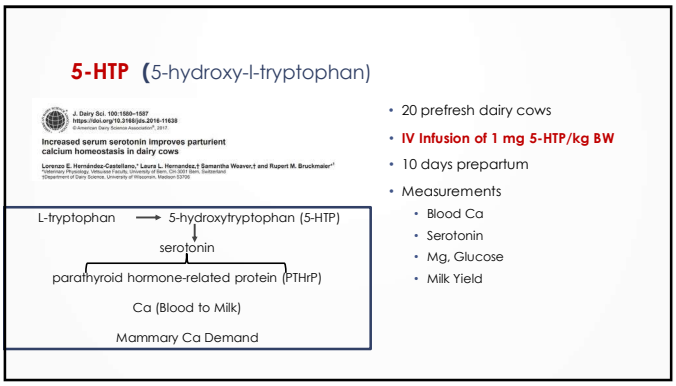
5-HTP (5-hydroxy-l-tryptophan)
J. Dairy Sci. 100:1580–1587
https://doi.org/10.3168/jds.2016-11638
Increased serum serotonin improves parturient calcium homeostasis in dairy cows
L-tryptophan → 5-hydroxytryptophan (5-HTP)
serotonin
parathyroid hormone-related protein (PTHrP)
Ca (Blood to Milk)
Mammary Ca Demand
20 prefresh dairy cows
IV Infusion of 1 mg 5-HTP/kg BW
10 days prepartum
Measurements
Blood Ca
Serotonin
Mg, Glucose
Milk Yield

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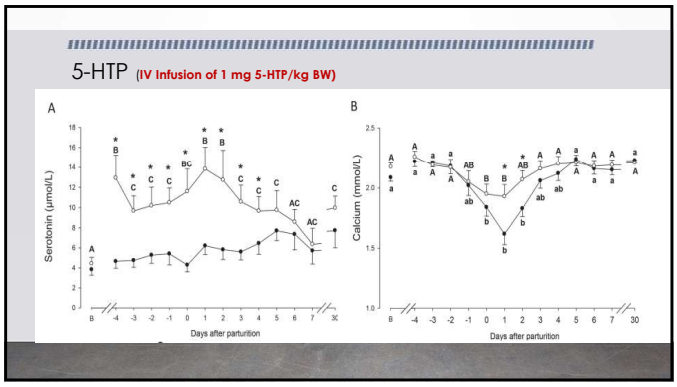
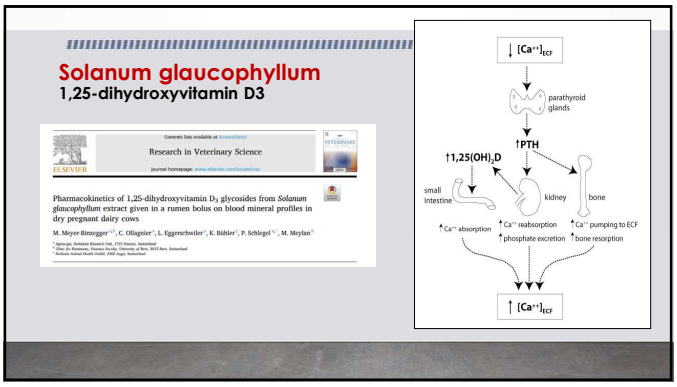

5-HTP (IV Infusion of 1 mg 5-HTP/kg BW)
A
B
Serotonin (µmol/L)
Calcium (mmol/L)
Days after parturition
Days after parturition

23


Solanum glaucophyllum
1,25-dihydroxyvitamin D3
Research in Veterinary Science
Pharmacokinetics of 1,25-dihydroxyvitamin D3 glycosides from Solanum glaucophyllum extract given in a rumen bolus on blood mineral profiles in dry pregnant dairy cows
↓ [Ca++]ECF
parathyroid glands
↑PTH
↑1,25(OH)2D
small intestine
kidney
bone
↑ [Ca++]ECF

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Solanum glaucophyllum – Meyer-Binzegger et al., 2022
- Bolus to Dry Cows
- When to give the bolus?

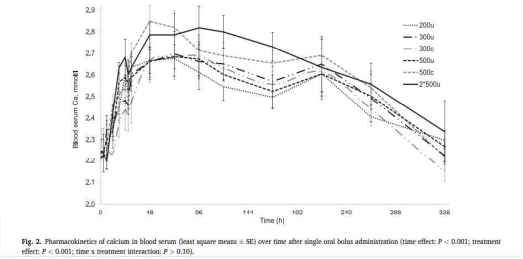

Fig. 2. Pharmacokinetics of calcium in blood serum (least square means ± SE) over time after single oral bolus administration (time effect: $P < 0.001$; treatment effect: $P < 0.001$; time x treatment interaction: $P > 0.10$).

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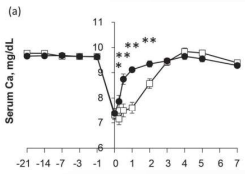
- Difructose Anhydride

J. Dairy Sci. 98:8686–8697
http://dx.doi.org/10.3168/jds.2015-9576
© American Dairy Science Association®, 2015.

Supplementation with difructose anhydride III promotes passive calcium absorption in the small intestine immediately after calving in dairy cows

M. Teramura,*† S. Wynn,* M. Reshalaitihan,‡ W. Kyuno,† T. Sato,† M. Ohtani,† C. Kawashima,‡ and M. Hanoda§

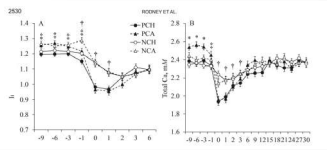


- Calcidiol 25 (OH) Vit D_3

J. Dairy Sci. 101:2519–2543
https://doi.org/10.3168/jds.2017-13737
© American Dairy Science Association®, 2018.

Effects of prepartum dietary cation-anion difference and source of vitamin D in dairy cows: Vitamin D, mineral, and bone metabolism

R. M. Rodney,*† N. Martinez,‡ E. Block,§ L. L. Hernandez,# P. Celi,|| C. D. Nelson,‡ J. E. P. Santos,‡¶ and I. J. Lean*†



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Ca Response Technologies - Summary

Technology	CaRT	On-Farm Reality
Dietary Ca Restriction	Yes	Infeasible
Dietary P Restriction	Yes	Difficult to formulate diets low enough in P
Zeolite A	Yes	Commercially available. Induces dietary P restriction – bone mobilization of Ca/P.
5-HTP	Yes	Commercial application in development
Solanum glaucophyllum	Yes	Commercial applications emerging
Difructose Anhydride	No	Increases Ca absorption post-partum
Calcidiol 25 (OH) Vit D_3	No	Improves Vit D status which has other benefits

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