Effects of administration of vitamin D3 delivered by liposomes to dairy cows during transition period

Fiorenzo Piccioli-Cappelli[1], Matteo Mezzetti[1], Alessandro Vercesi[1], Sophie Scemama de Gial-luly[1], Lorenzo Bosio[2], Dante Greco[2], **Erminio Trevisi[1,3]**

[1]*Department of Animal Science, Nutrition and Food – DiANA, Università Cattolica del Sacro Cuore, Piacenza, Italy*

[2]*Farmer spa, Porto Mantovano, Mantova, Italy*

[3]*Romeo and Enrica Invernizzi Research Center for Sustainable Dairy Production of the Università Cattolica del Sacro Cuore (CREI), 29122 Piacenza, Italy*

INTRODUCTION

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- In high-yielding dairy cows, during the transition period (TP) the metabolism undergoes drastic changes

  ☹ often inducing a poor calcium homeostasis after calving.

- vitamin D3 (vD3) is a key metabolite for Ca
  - absorption from gut
  - mobilization from skeletal bones

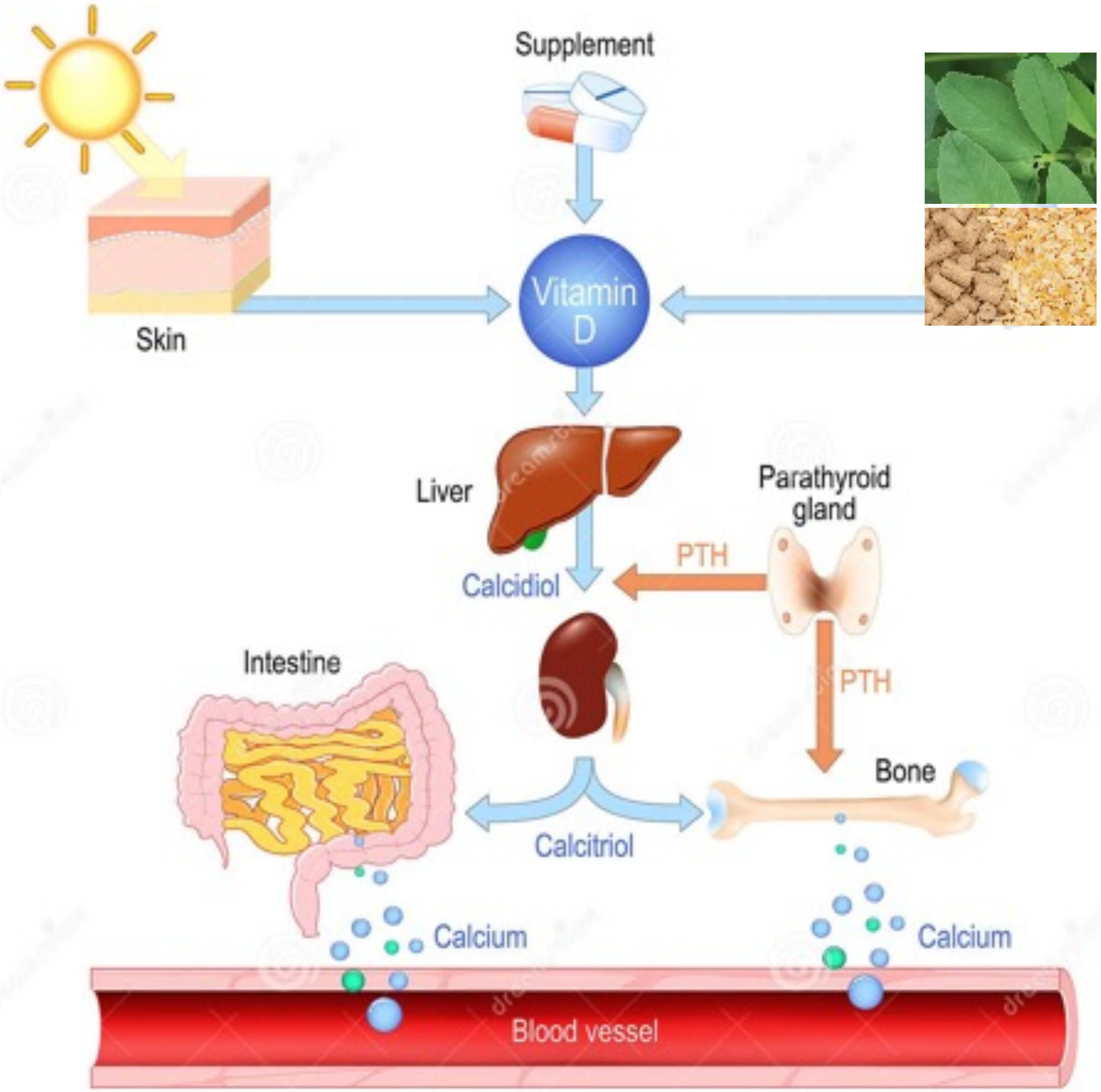
- Moreover, vD3 has been observed to exert hormonal activity (paracrine) on immune system cells,
  - increasing phagocytosis
  - enhancing secretion of H_2O_2
  - promoting differentiation of some immune cells
  - with a role in the restraint of inflammatory phenomena

INTRODUCTION: vD3

The vD3 precursors are absorbed in the gut (D2 or D3) or synthesized in the skin and need to be hydroxylated in the liver (calcidiol) and in the kidney (calcitriol)

During TP cows face

- ✓ low dry matter intake
- ✓ often impaired metabolism of liver



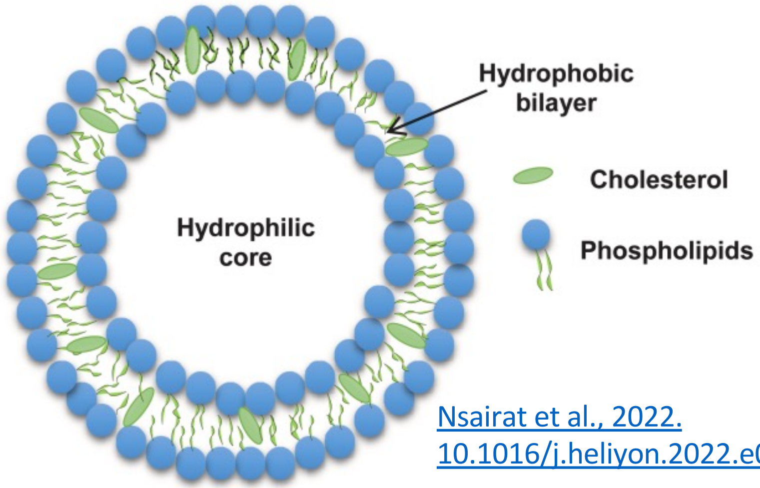
INTRODUCTION: liposome

Nano-liposome has been proposed as a potential carrier for vD3 for ruminants

vD3-nano liposome: verified their "resistance" in the rumen. More than 65% of vD3 is not degraded after 24 h in artificial rumen (Gallo, not published)

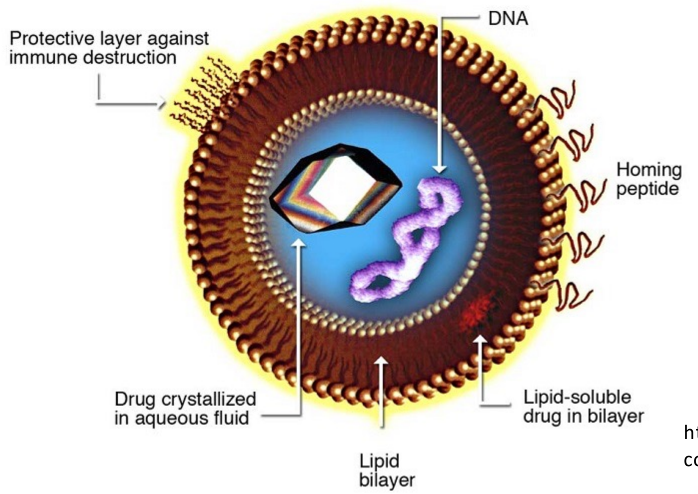
The permanence of nano-liposome in the rumen is likely much lower than 24 h

Liposome: Firstly described from Bangham A.D. (Babraham Institute), 1961



Nsairat et al., 2022. 10.1016/j.heliyon.2022.e09394

Liposome for Drug Delivery



https://www.biochempeg.com/article/122.html

OBJECTIVE

To evaluate the efficacy of administering a supplement containing liposomes loaded with vitamin D3 during the peripartum period of dairy cows on: efficiency of vitamin D3 absorption calcium metabolism immuno-metabolic status Milk production and composition

Production technology

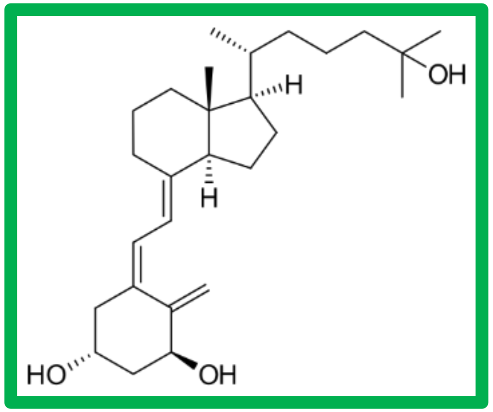
liposomes loaded with vit. D3 through the patented SMF (microfluidic-like) continuous production technique. Patent: PCT [2] WO2019159210

Product test features :

- Encapsulation efficiency > 95%

- Average particle size > 210 < 280 nm

- Suspension stability : potential Z < -25



MATERIAL & METHODS

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26 dairy cows were randomly divided in 2 homogeneous group

CTR: 13 cows received dry and lactation diets added with vitamin-mineral mix apporting **40,000 UI/d of vD3 as a spray-dried traditional supplement**

D3LP: 13 cows received dry and lactation diets with same vitamin-mineral **but** without vD3 from -21 to 28 days from calving. **40,000 UI/d of vD3 was delivered by nano-liposome (Lipobox® Farmer S.p.A.)**

Nutritional characteristic of diets

TMR	DM	Crude Protein	Fat	Starch	NDF	ADF	ADL	Ash	Ca	P	Mg	K	Na
	%	% DM	% DM	% DM	% DM	% DM	% DM	% DM	% DM	% DM	% DM	% DM	% DM
dry	48.7	12.6	2.19	18.6	47.2	31.3	4.2	7.85	0.9	0.35	0.25	1.35	0.28
lactation	47.0	15.17	2.68	30.0	33.0	17.6	2.31	6.30	0.80	0.35	0.28	1.27	0.48

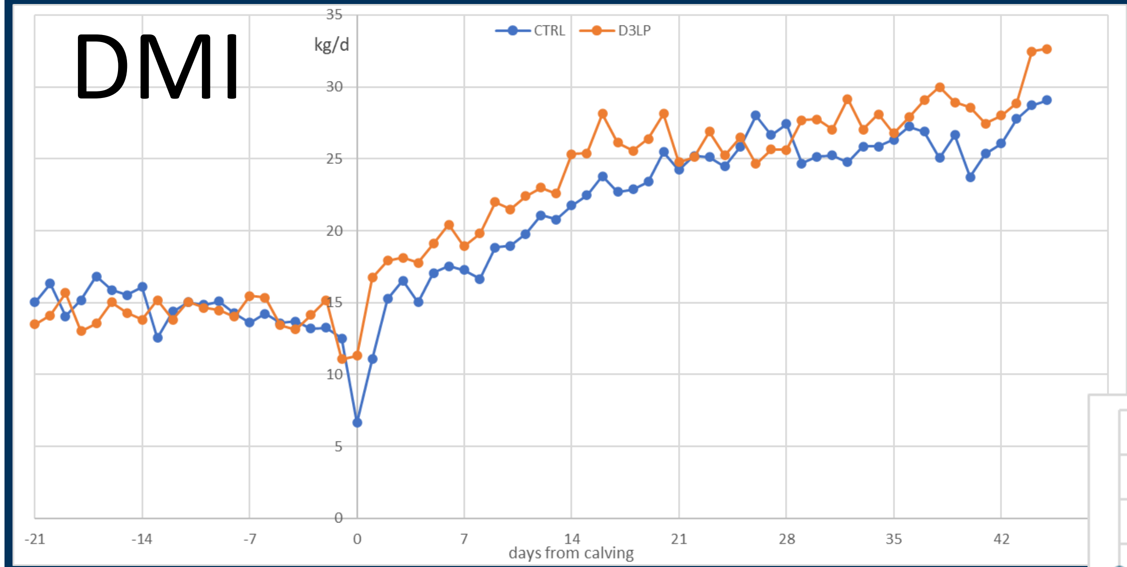
MATERIAL & METHODS

Dairy cows have been checked :

- daily for
  - health status
  - feed intake, rumination time
  - milk yield and its composition (after calving)
- at -21, -7, 1, 3, 14, 28 days from calving (DFC) for:
  - rectal temperature
  - BCS
  - blood sampling (immunometabolic profile)
  - after calving milk (composition & SCC content)

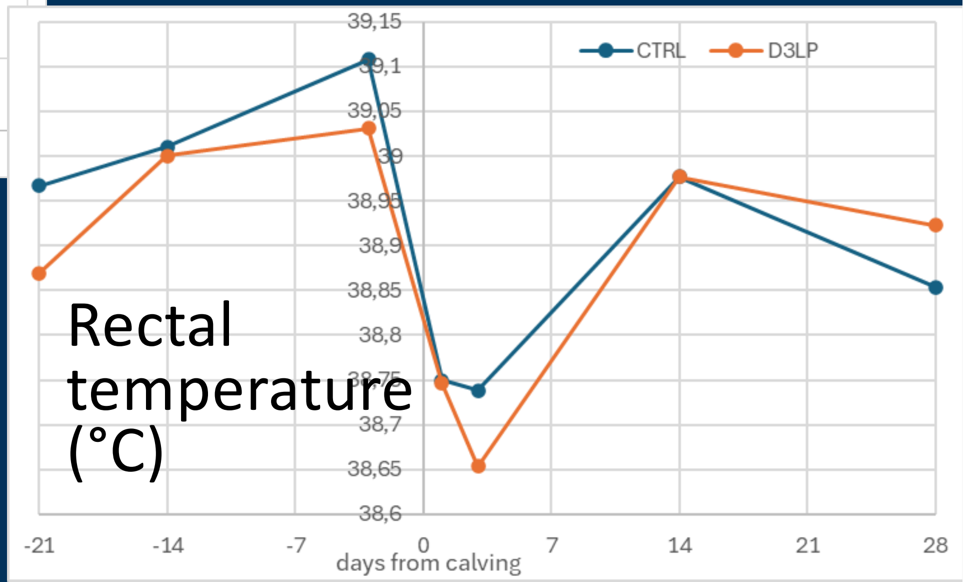
Statistical analysis: mixed model with the random effect of cow, period (dry or lactation), treatment and their interaction.

RESULTS
dry matter intake
rectal temperature



after calving D3LP had higher DMI during 28 days of supplementation with liposome: 22,7 vs 20,9 kg/d P=0,0926

Rectal temperature tends to be lower in D3LP, particularly after calving (P= 0.06 at 3 DFC)



RESULTS: blood level: no difference for energy and protein metabolism

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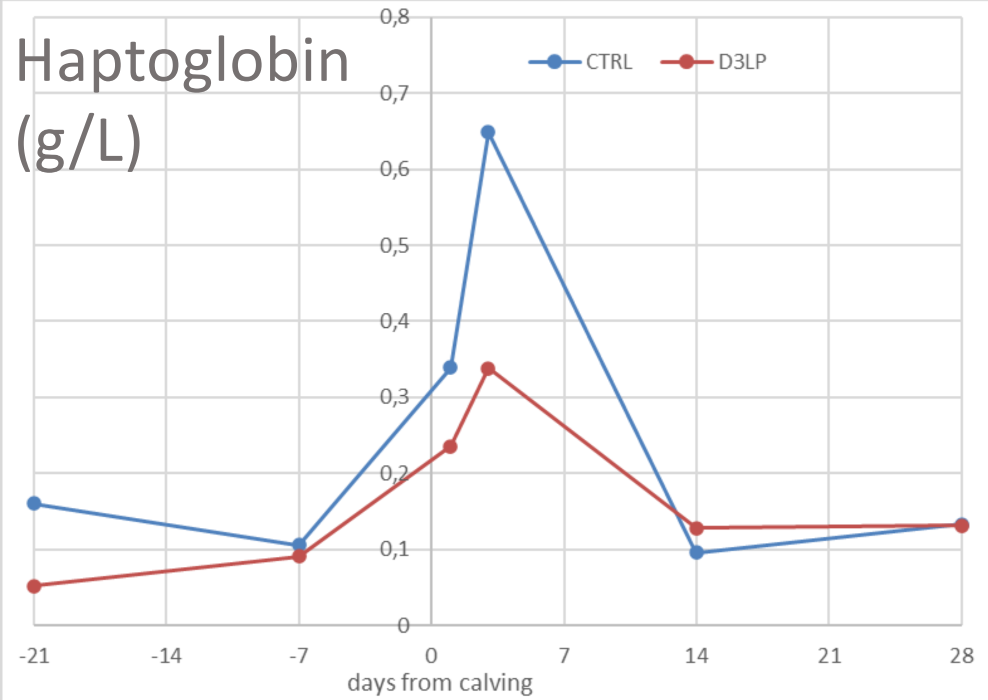
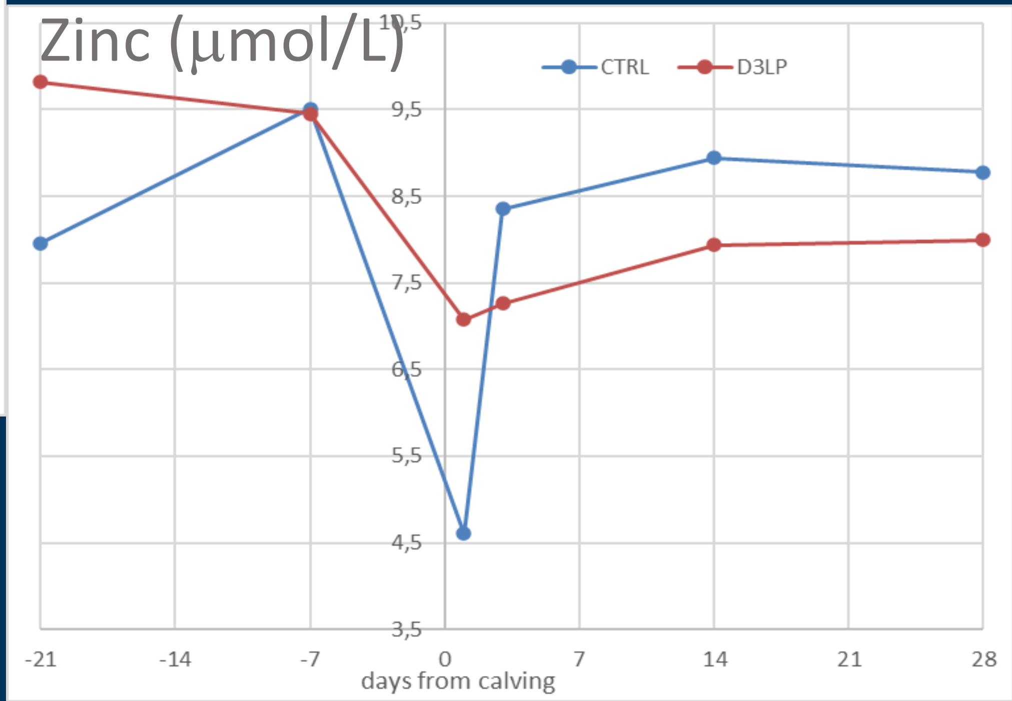
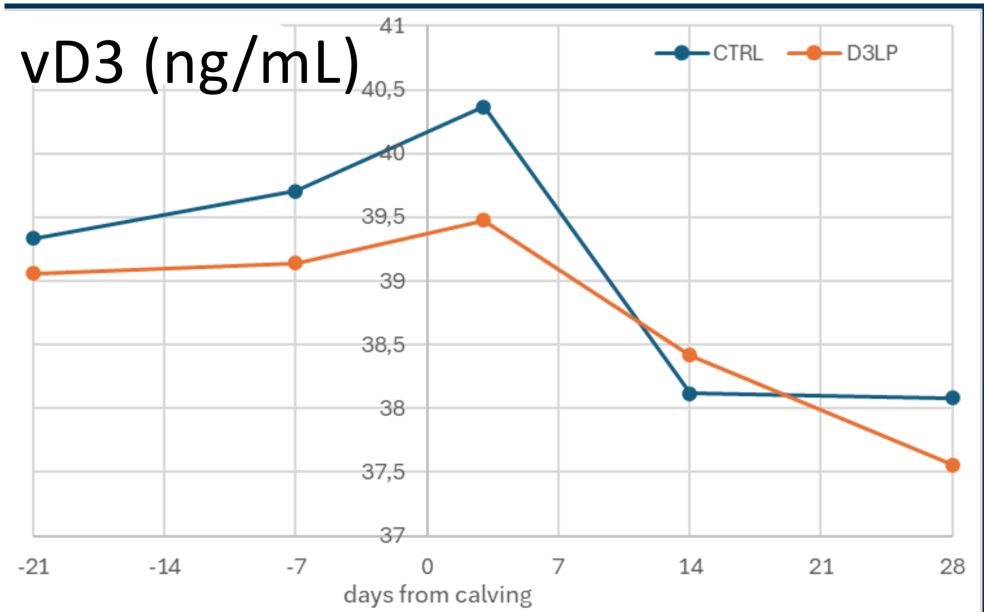


Cows of D3LP had less acute inflammation after calving: haptoglobin resulted lower at 3 DFC (P=0.009)



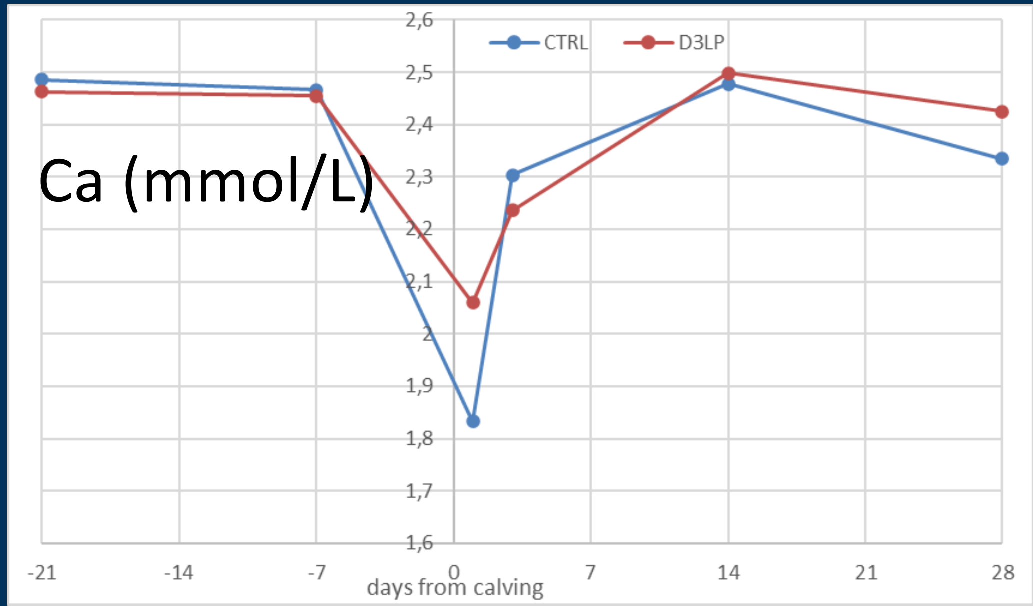
The lower acute inflammation is confirmed by lower drop of zinc after calving (P=0.0025 at 1 DFC)

RESULTS: plasma vitamin D plasma Ca



Delivering vitamin D3 with liposome do not affect its blood content

The day after calving cows receiving vitD3 delivered with liposome had higher blood Ca (2.06 vs 1.84 mmol/L, P=0.0189)



RESULTS: plasma P & ALP

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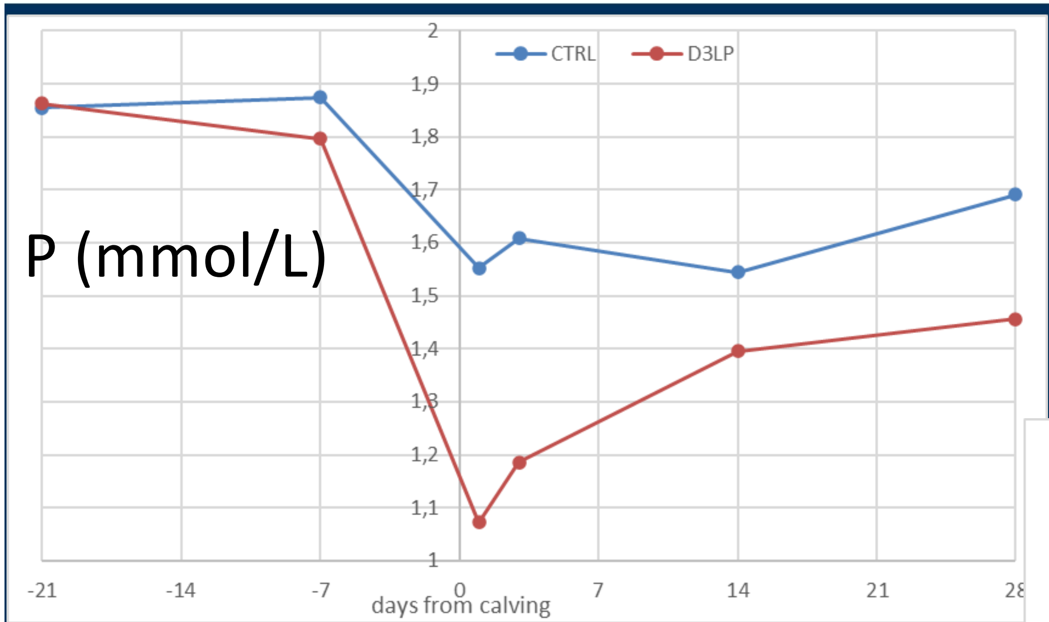
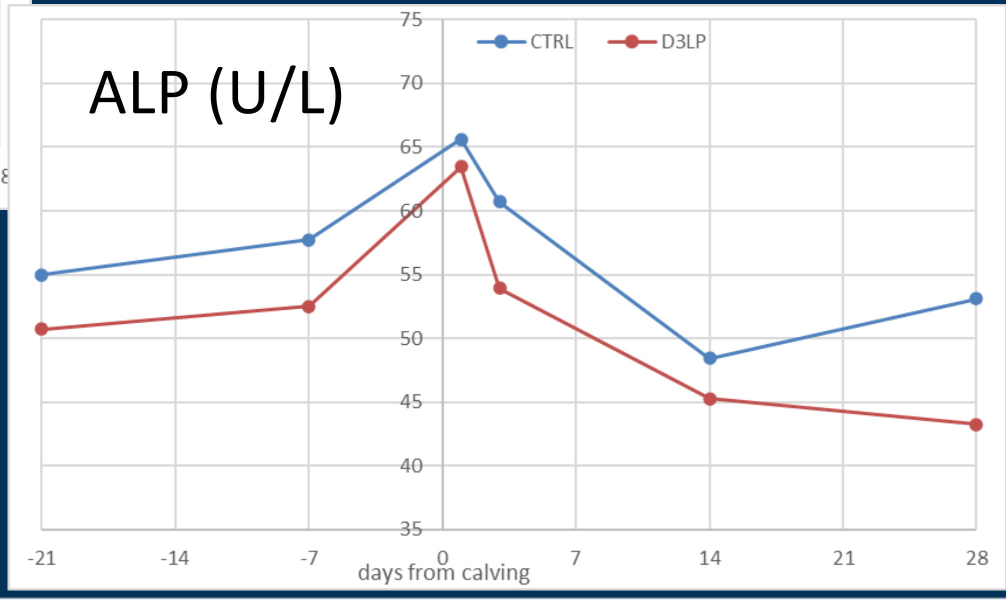


Plasma P was markedly lower after calving in in cows of D3LP group vs CTR. It seems that Ca was highly adsorbed from gut or kidney in D3LP, thus the mobilization from bone reduced (and P level in plasma)

Concentrations and pattern during transition period of ALP (alkaline phosphatase) were not affected by different delivering of vitamin D3



RESULTS: MILK YIELD

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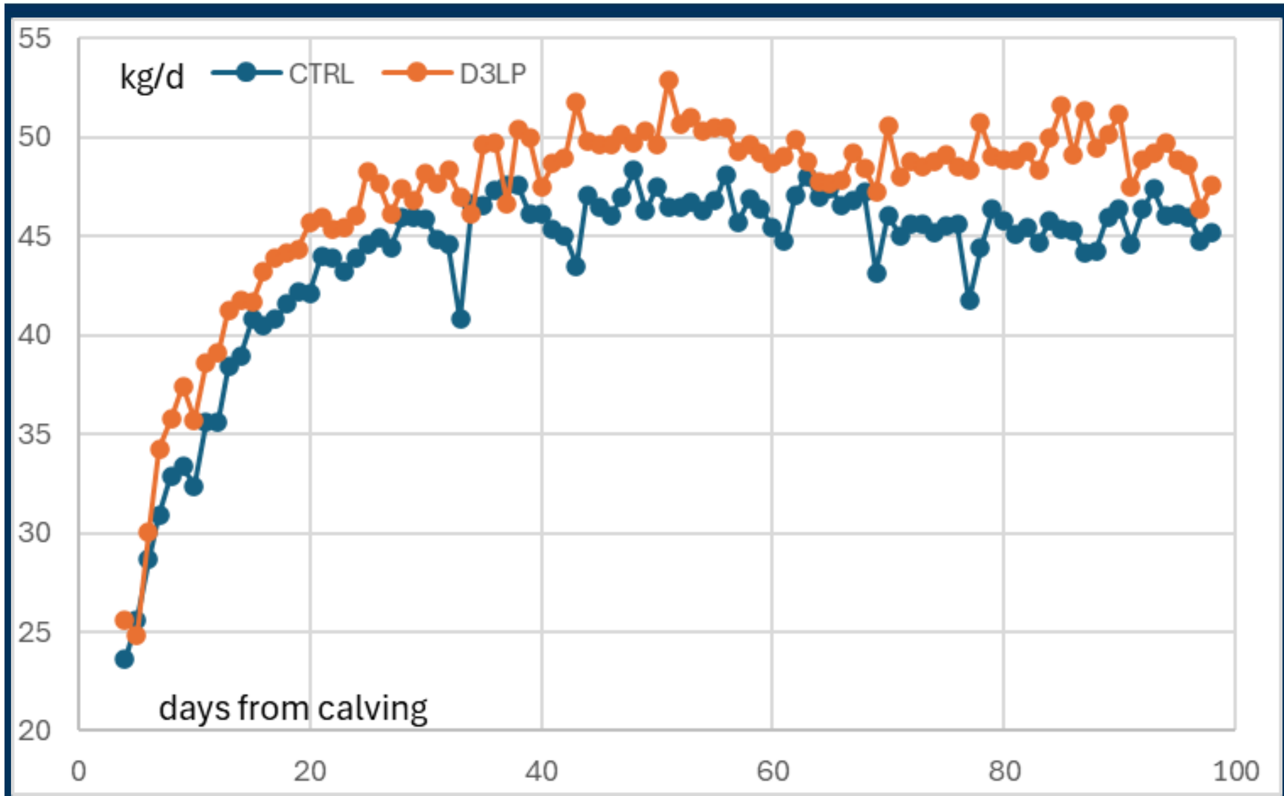

Average milk yield in first 90 DIM resulted consistently higher in D3LP cows (47.7 vs 45.5 kg/d, but not different statistically P=0.2842)

No differences were observed for milk composition and somatic cells content

CONCLUSIONS

Delivering vitD3 by liposome during transition period in dairy cows did not affect vitamin D3 content in blood.

Nevertheless, vitamin D3 delivered with liposome improved the metabolism of dairy cows in the transition period:

- ✓ regulating better the Ca metabolism
- ✓ reducing bone mobilization
- ✓ reducing inflammation after calving

Hypothesis: a higher absorption of vD3 or a better distribution of vD3 in the body using D3LP

D3LP cows seems more resilient at challenges of transition period, allowing better:

- DMI
- milk yield

CONCLUSIONS

This is the first experiment that use liposome as carrier of liposoluble vitamins and require further confirmation about the overall effects on dairy cows

The liposome transfer of vitamins (and perhaps nutrients) sin ruminants (animals) seems more efficient that traditional carriers/methods and this open new possibility for the precision feeding to meet the immune metabolic requirements