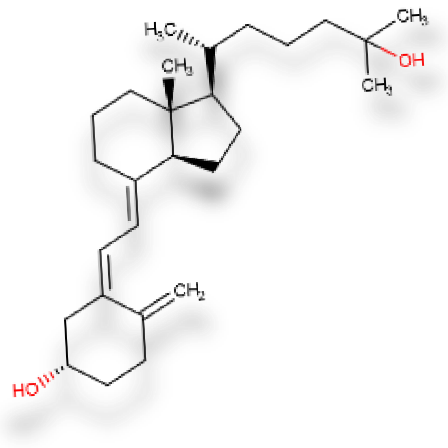
$25\text{-}OH\text{-}D_3$: An Indispensable Tool to Managing Antibiotic Free Feeding Programs for Commercial Broilers



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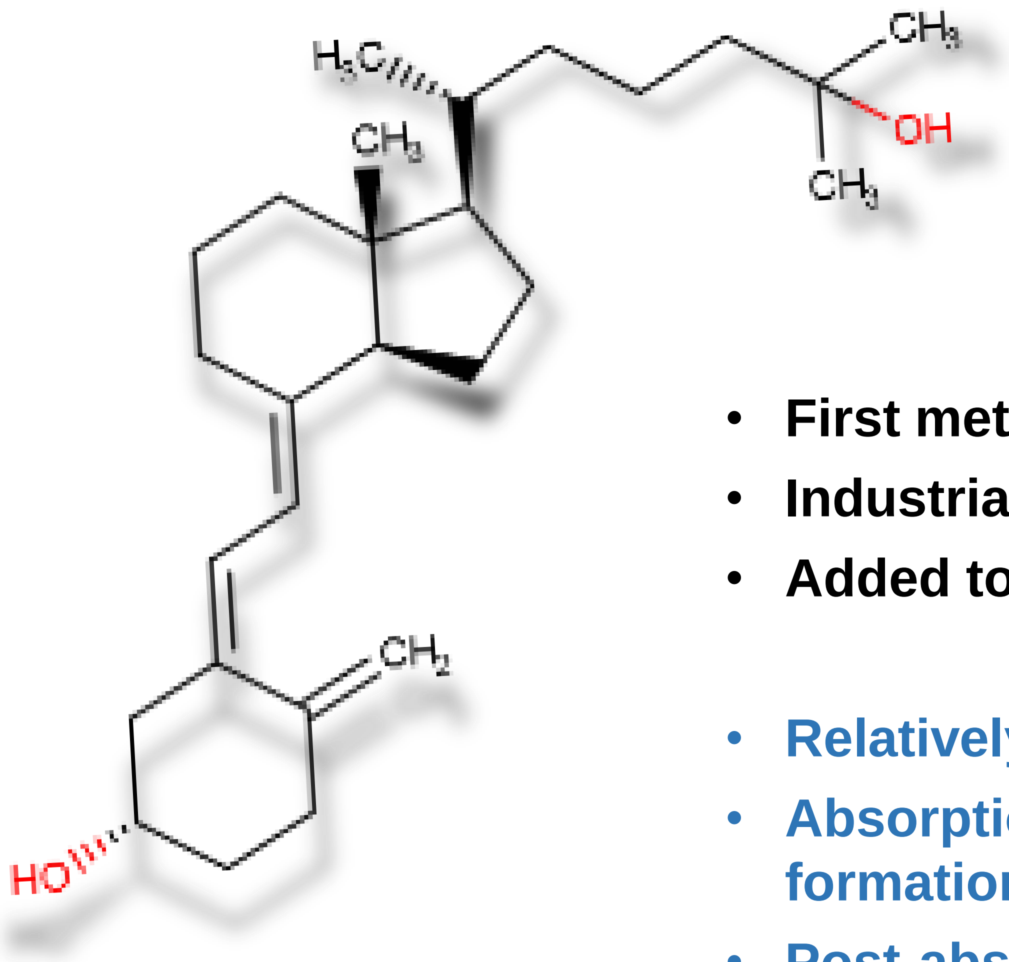
Road Map

- **What is 25-OH-D_3 and its biological effects?**
- **Experimental disease-challenged models**
    - ***E. maxima***
    - ***E. maxima* and *C. perfringens combined***
- **Treatment design and results**
- **Proposed mechanism of action of 25-OH-D_3**
- **Conclusion**

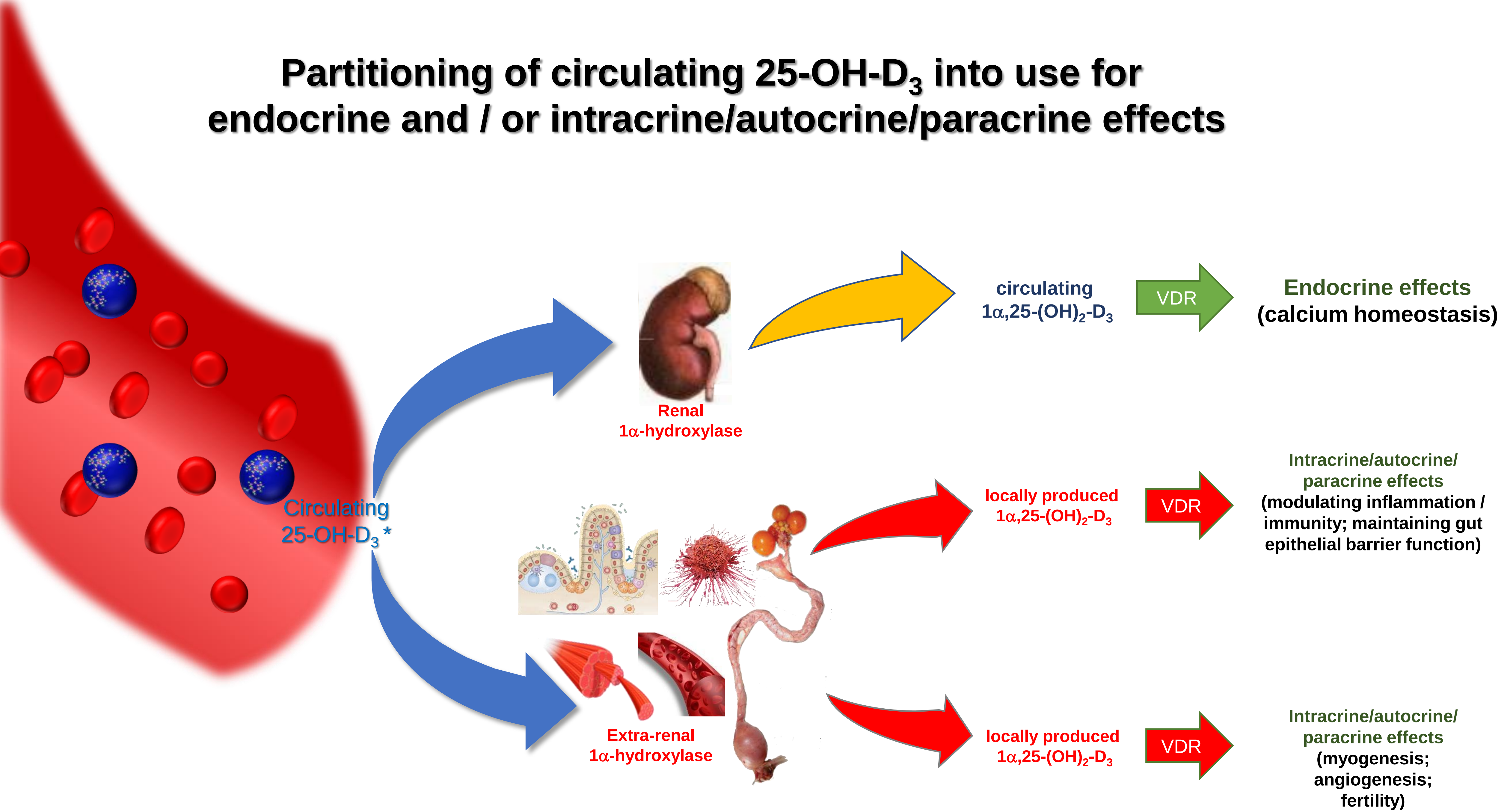


25-OH-D_3

- First metabolite of vitamin D_3 metabolism
- Industrially produced
- Added to animal diets as a regulatory approved feed additive

- Relatively more polar molecule
- Absorption less dependent on bile acids and micelle formation and less affected by intestinal insults
- Post-absorption, bypassing liver and entering circulation directly (circulating 25-OH-D_3)

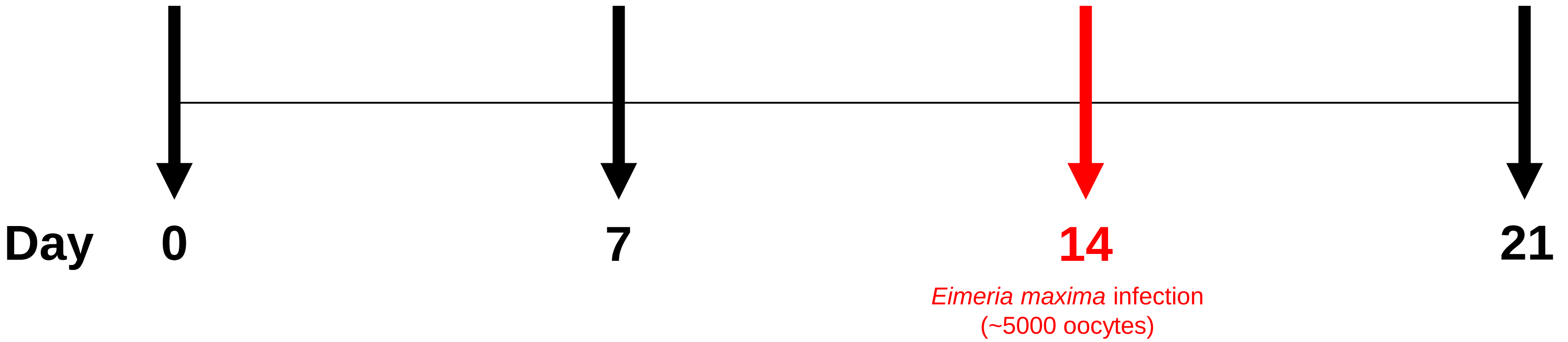
Partitioning of circulating 25-OH-D_3 into use for endocrine and / or intracrine/autocrine/paracrine effects



*Availability of circulating 25-OH-D_3 level is the first limiting factor!!!

Diseased-Challenged Models

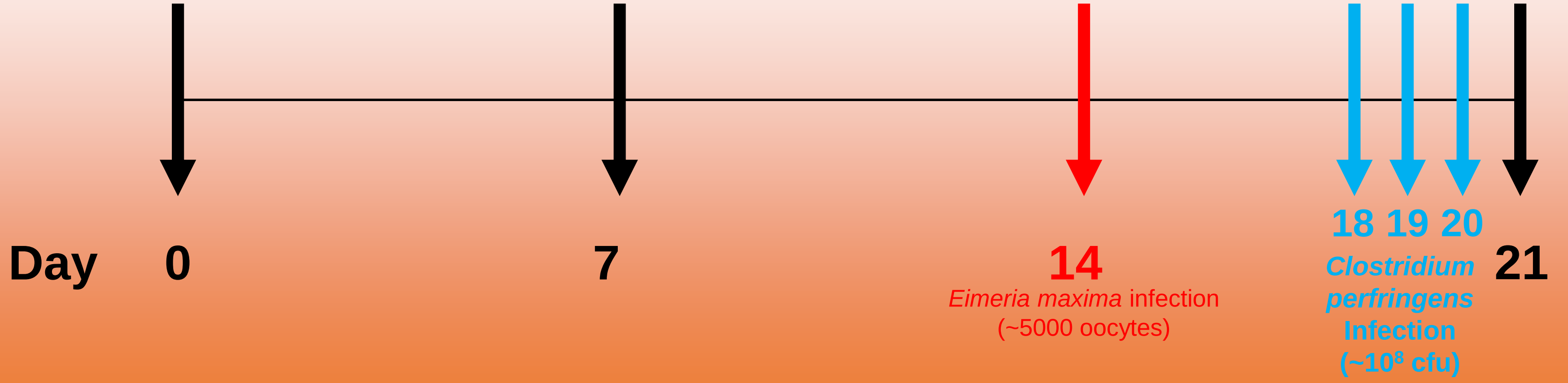
E. maxima-challenged model



Parameters

- Serum 25-OH-D_3 level
- Mortality-adjusted FCR
- Oocyst shedding counting

E. maxima-and-C. perfringens-challenged model

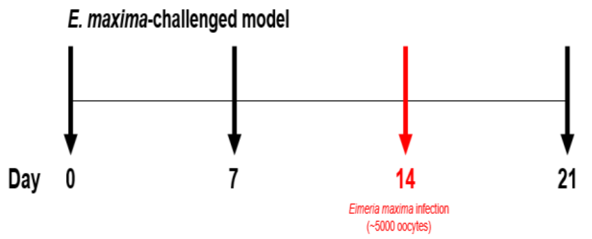


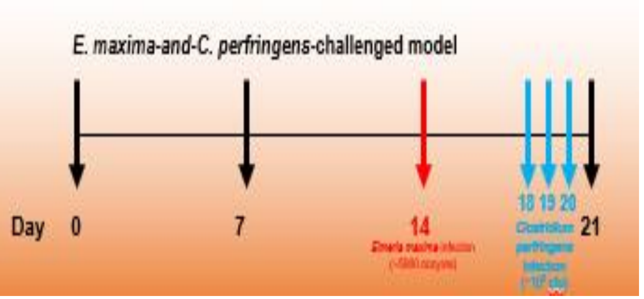
Parameters

- Serum 25-OH-D_3 level
- Mortality-adjusted FCR
- Anti-inflammatory cytokine gene expression (jejunum)

Treatment Design

Disease-challenged models





Treatment group	Treatment	*E. maxima*-challenged	*C. perfringens*-challenged	25-OH-D3 (mcg/kg diet)
C0	Positive Control	No	No	No
C1	Negative Control	Yes	No	No
C1-LD	Negative Control	Yes	No	34.5
C1-HD	Negative Control	Yes	No	69.0
CNE0	Positive Control	No	No	No
CNE1	Negative Control	Yes	Yes	No
CNE1-LD	Negative Control	Yes	Yes	34.5
CNE1-HD	Negative Control	Yes	Yes	69.0

- 512 Male Cobb 500 broilers
- 8 Treatments X 8 Replicates X 8 Birds per replicate
- Antibiotic-and-anticoccidial-free diets
- Petersime battery cages
- 21-day trial

Results: Serum 25-OH-D_3

Treatment group	Treatment	*E. maxima*-challenged	*C. perfringens*-challenged	25-OH-D_3 (mcg/kg diet)	Day 14 serum 25-OH-D_3 (ng/mL)	Day 21 serum 25-OH-D_3 (ng/mL)
C0	Positive Control	No	No	No	5.41^{b}	8.08^{b}
C1	Negative Control	Yes	No	No	5.81^{b}	2.09^{c}
C1-LD	Negative Control	Yes	No	34.5	25.06^{a}	13.26^{a}
C1-HD	Negative Control	Yes	No	69.0	26.48^{a}	13.79^{a}
CNE0	Positive Control	No	No	No	6.75^{c}	9.81^{a}
CNE1	Negative Control	Yes	Yes	No	6.89^{c}	1.55^{b}
CNE1-LD	Negative Control	Yes	Yes	34.5	25.51^{b}	8.78^{a}
CNE1-HD	Negative Control	Yes	Yes	69.0	31.08^{a}	11.25^{a}

- At Day 14 (i.e., before challenged), birds fed supplemental 25-OH-D_3 increased serum 25-OH-D_3 versus those fed without 25-OH-D_3.
- At Day 21 (i.e., post infection), serum 25-OH-D_3 was lowered in birds both fed with and without supplemental 25-OH-D_3.
- The magnitude of decrease in serum 25-OH-D3 was greater in the cocci-and NE-challenged birds than the cocci-challenged birds.
- Birds fed 69 mcg 25-OH-D_3 per kg diet maintained higher serum 25-OH-D_3 numerically than those fed 34.5 mcg 25-OH-D_3 per kg diet and those fed without 25-OH-D_3 at 7 days post infection.

Results: Mortality-adjusted feed conversion ratio

Treatment group	Treatment	*E. maxima*-challenged	*C. perfringens*-challenged	25-OH-D_3 (mcg/kg diet)	Day 21 mortality-adjusted FCR
C0	Positive Control	No	No	No	**1.616**
C1	Negative Control	Yes	No	No	**2.011**
C1-LD	Negative Control	Yes	No	34.5	**2.089**
C1-HD	Negative Control	Yes	No	69.0	**1.958**
CNE0	Positive Control	No	No	No	**1.598**
CNE1	Negative Control	Yes	Yes	No	**2.213**
CNE1-LD	Negative Control	Yes	Yes	34.5	**2.161**
CNE1-HD	Negative Control	Yes	Yes	69.0	**2.122**

- In *E. maxima*-challenged and combined *E. maxima*-and *C. perfringens*-challenged models, birds fed high level of supplemental 25-OH-D_3 had respectively 13 and 4 points advantage of mortality-adjusted FCR over those fed low level of supplemental 25-OH-D_3 and respectively 5 and 9 points over those fed without 25-OH-D_3 (i.e., negative control).

Results: E. maxima oocyst shedding

Treatment group	Treatment	*E. maxima*-challenged	*C. perfringens*-challenged	25-OH-D_3 (mcg/kg diet)	Day 21 *E. Maxima* oocyst shedding (oocysts per gram)
C0	Positive Control	No	No	No	**0[b]**
C1	Negative Control	Yes	No	No	**121,869[a]**
C1-LD	Negative Control	Yes	No	34.5	**150,725[a]**
C1-HD	Negative Control	Yes	No	69.0	**105,211[ab]**
CNE0	Positive Control	No	No	No	**Not determined**
CNE1	Negative Control	Yes	Yes	No	**Not determined**
CNE1-LD	Negative Control	Yes	Yes	34.5	**Not determined**
CNE1-HD	Negative Control	Yes	Yes	69.0	**Not determined**

- At Day 21 (i.e., 7 days post infection) under *E. maxima*-challenged conditions, oocyst shedding was significantly lower in birds fed 69 mcg 25-OH-D_3 per kg diet than those fed 34.5 mcg 25-OH-D_3 per kg diet and those fed without 25-OH-D_3.

Results: IL-10 gene expression in jejunum

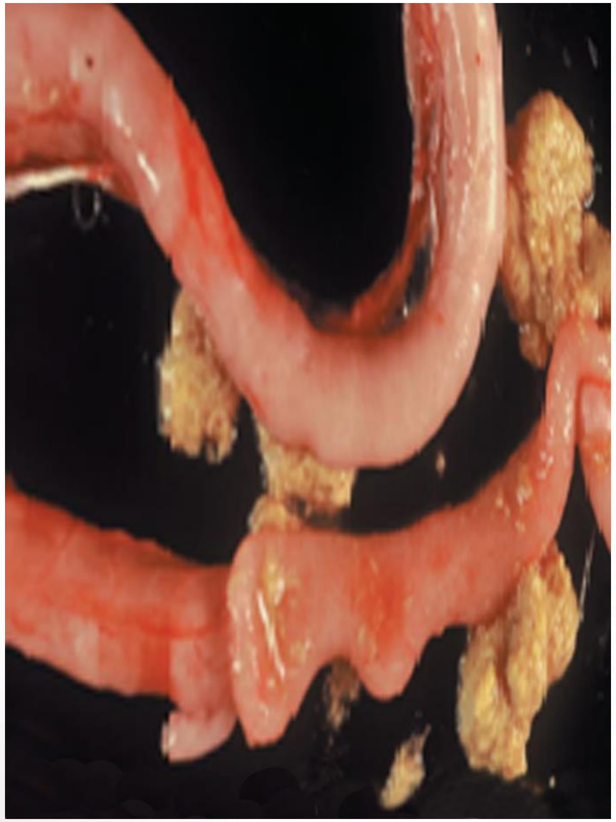
Treatment group	Treatment	*E. maxima*-challenged	*C. perfringens*-challenged	25-OH-D_3 (mcg/kg diet)	Gene expression of IL-10
C0	Positive Control	No	No	No	**Not determined**
C1	Negative Control	Yes	No	No	**Not determined**
C1-LD	Negative Control	Yes	No	34.5	**Not determined**
C1-HD	Negative Control	Yes	No	69.0	**Not determined**
CNE0	Positive Control	No	No	No	**24.081[b]**
CNE1	Negative Control	Yes	Yes	No	**22.509[b]**
CNE1-LD	Negative Control	Yes	Yes	34.5	**36.870[a]**
CNE1-HD	Negative Control	Yes	Yes	69.0	**40.195[a]**

- IL-10 is anti-inflammatory cytokine and as such possesses anti-inflammatory activity which downregulates inflammatory response.
- Birds fed supplemental 25-OH D_3 up-regulated the gene expression of IL-10 when compared to those fed without 25-OH-D_3 (i.e., negative control).

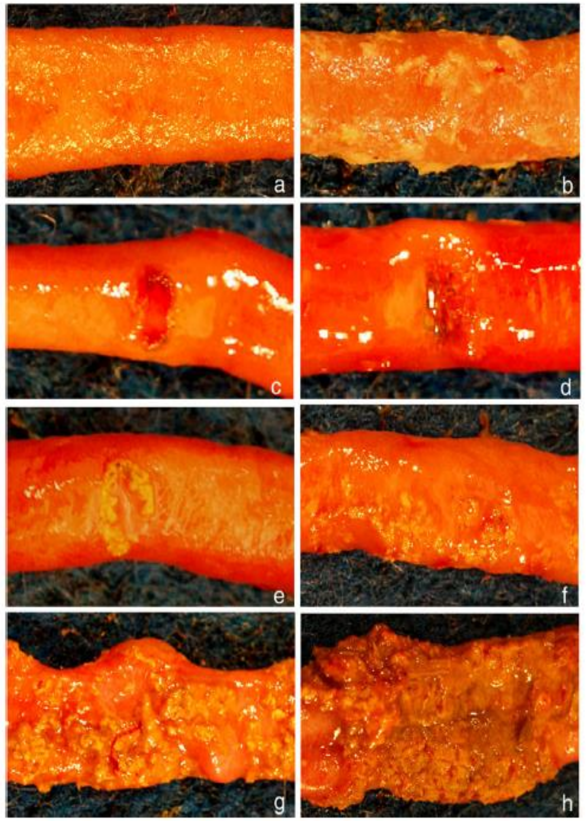
Coccidia . . . Does not come Alone

Coccidiosis goes hand-in-hand with other gut diseases because it damages the gut mucosa and allows bacteria to enter causing secondary infections

Intestinal mucosal inflammation



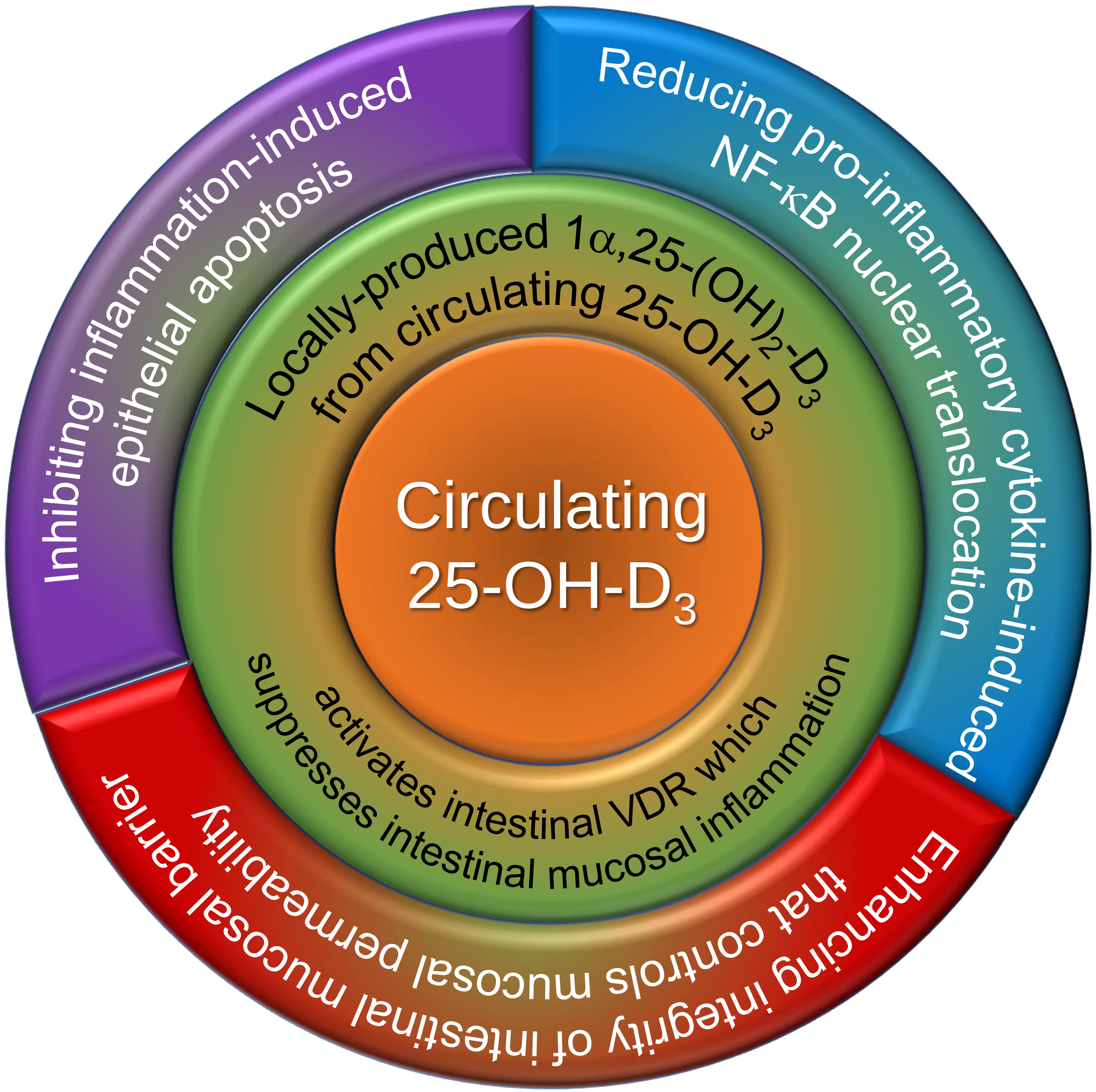
E. maxima lesions



Necrotic enteritis lesions

Shojadoost *et al. Veterinary Research* 2012, **43**:74

$25\text{-OH-}D_3$, mechanism of action ???



Conclusion

- 25-OH-D_3 partially alleviated detrimental consequences of coccidiosis and clostridiosis.

- Higher levels of supplemental 25-OH-D_3 might be beneficial to birds subject to challenged condition of coccidiosis and clostridiosis.

- 25-OH-D3 may be considered as an indispensable feed additive to managing antibiotic-and-anticoccidial-free feeding programs for commercial broilers.