# Vitamin D and Metabolites in Poultry

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Vitamin D is a term encompassing several closely related molecules including vitamin $D_3$, 25-OH $D_3$, 1,25-$OH_2D_3$, 24,25-$OH_2D_3$, and numerous other metabolites with widely varying activity and safety profiles. It is a required nutrient for poultry that can be supplied either through the diet or by UV irradiation of the skin. In modern poultry production, birds are typically raised in controlled, indoor environments so that exposure to UV radiation is limited, thus eliminating this second route and making feed or water supplementation necessary. The two most common forms of vitamin D fed to chickens are $D_3$ and 25-OH $D_3$ due to the efficacy and safety of these two molecules.

Vitamin D functions through activation of the vitamin D receptor (VDR), which regulates or modulates gene expression within the target cell. 1,25-$OH_2D_3$ is the most active metabolite as it has the highest binding affinity for the VDR. Before affecting target organs, though, vitamin $D_3$ must first be metabolically activated to this final metabolite. Step one is hydroxylation of $D_3$ to 25-$OHD_3$, which is a partially regulated process occurring in the liver (Bhattacharyya, 1974, Tucker, 1973). Alternatively 25-$OHD_3$ (HyD®) is available as a feed ingredient or water supplement to bypass this step and promote adequate levels of this metabolite. 25-$OHD_3$ is the main circulating form of vitamin D and blood levels of this metabolite are generally considered the best indicator of vitamin D status in poultry (Soares, 1995).

The second step in vitamin D activation is hydroxylation of 25-$OHD_3$ to 1,25-$OH_2D_3$, which occurs in response to metabolic needs and is very tightly regulated as high serum calcium is toxic. The primary source of 1-alpha hydroxylase enzyme is located in the kidney and is activated by parathyroid hormone (PTH) in response to low blood calcium levels, which stimulates production of this enzyme. 1,25-$OH_2D_3$ produced in the kidney then acts on cells in the intestine, bones and kidney to activate the mechanisms necessary to raise blood calcium levels. It is also available to numerous other tissues such as immune cells, pancreas, heart, eye, brain, thyroid, and muscle with the VDR present, many of which have no role in calcium metabolism. In addition to the kidney, 1-alpha hydroxylase enzyme is also present in other tissue types in chickens, including muscle and immune tissues (Shanmugasundaram and Selvaraj, 2012). This indicates a high likelihood of autocrine functions of vitamin D at the tissue level independent of systemically circulating and tightly regulated 1,25-$OH_2D_3$ produced by the kidney.

### 25-$OHD_3$ versus Vitamin $D_3$ Supplementation

The biological activity of vitamin $D_3$ is dependent on adequate circulating levels of 25-$OHD_3$. When fed at equivalent levels, 25-$OHD_3$ supplementation consistently generates significantly higher serum 25-$OHD_3$ concentrations than $D_3$ only supplementation (Saunder-Blades and Korver, 2004, Vignale, 2013). The primary reason for this is efficiency of absorption and the lack of dependence on the liver for bioconversion of $D_3$ to 25-$OHD_3$. In broiler chicks, the absorption of 25-$OHD_3$ was reported to be more efficient (83%) than that for vitamin $D_3$ (66%). Significant differences in net excretion of vitamin D metabolites in vitamin $D_3$ fed chickens (20%) and 25-$OHD_3$ fed chickens (7%) was also described (Bar et al., 1980).

The differences in absorption are most evident during the first 2-3 weeks of the bird's life, which coincides with the most critical period of skeletal development, and during periods of malabsorption. The pancreas, which secretes lipase to aid in fat digestion, does not completely develop for 2-3 weeks, which may be a significant reason for the poor $D_3$ absorption during this period as vitamin $D_3$ absorption is dependent on fat absorption, which requires lipase and bile salts (Jin et al., 1998, Carew et al., 1972, Sell et al., 1986). 25-OH $D_3$ absorption occurs independently of fat absorption therefore absorption is not limited during the first 2-3 weeks. It's also possible the 25-hydroxylase enzyme activity in the liver is also not fully functional during this period.

During periods of malabsorption, fat absorption is compromised and thus vitamin $D_3$ absorption is also compromised. In experimentally induced malabsorption syndrome (MAS), 25-$OHD_3$ levels in chicks infected at day one were far less compromised at 6 and 8 days post-infection in the 25-OHD3 fed group (69 ug/kg dose) than in the equivalently dosed $D_3$ (2760 IU/kg) only group. In fact, 25-OH $D_3$ levels were below detectable levels in the latter group, meaning they'd be extremely vulnerable to the development of vitamin D deficiency related skeletal development issues such as rickets (Rebel and Weber, 2009).

**Role of Vitamin D in Poultry**

The main classically recognized biologic function of vitamin D is maintenance of calcium and phosphorus blood levels within a range that will support normal mineralization of bone as well as other cellular functions requiring these molecules. A deficiency of vitamin D results in skeletal mineralization disorders such as rickets, tibial dyschondroplasia, and deformities in growing birds and shell quality and osteoporosis in laying birds. A growing body of work, though, suggests the benefits of vitamin D supplementation go beyond this preventative role and research moving forward will therefore increasingly focus on exploring levels needed to achieve the maximum benefits of supplementation rather than determining the levels needed to avoid severe deficiency. A few of the several known or proposed roles for vitamin D beyond basic calcium and phosphorus homeostasis and skeletal development include:

- Regulation of cell growth and differentiation (Brown et al., 1999)
- Immune modulation (Hewison, 2010, Baeke et al., 2010, Mireles, 1999, Huff, 2000)
- Muscle growth and strength (Cannell et al., 2009, Starkey, 2013, Vignale, 2013)
- Insulin regulation (Alvarez, 2009)

The ability for vitamin D to fulfill all of its many roles is in the end dependent on the bird's ability to effectively absorb and utilize this critical nutrient to maintain adequate 25-OH $D_3$ stores. Due to its efficient absorption and lack of requirement for bioconversion, 25-OH $D_3$ is an excellent choice to safely and consistently achieve this goal.

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