Delacon
performing nature

Phytogenic ingredients in the spotlight:

Turmeric – the “golden” bullet in human and animal nutrition?

During the last years, **the ginger look-a-like herb called turmeric** made its entry into supermarkets worldwide. A clear sign that the popularity of turmeric is steadily rising - among consumers. It was already known by the scientific community much longer.

No surprise, when looking at the **numerous benefits shown in scientific articles and studies**: Ranging from preventing chronic diseases to improving the antioxidant capacity of the body, only to name some of them.

As phytogenius minds, we always want to look under the surface and go deeper into the phytogenic universe. Therefore, we have **evaluated turmeric’s potential usage in human as well as animal nutrition**. How? By going through numerous studies and doing own research. Let’s see want we have been discovered.

AFTER READING THIS ARTICLE YOU WILL KNOW ...

- **What turmeric is**
- **Why it is known to the public**
- **What the active compounds of turmeric are**
- **What the mode of action (MoA) of these active compounds is**
- **What the beneficial effects for humans and animals are**

Delacon
performing nature

Turmeric in portrait

Turmeric (also known by its Latin name *Curcuma longa*) is a flowering plant whose rhizomes look quite similar to ginger roots from the outside but are intensively yellow colored in the inside. This similarity can be explained since both plants belong to the same family of Zingiberaceae.

Following the roots of turmeric, our journey leads us 2,500 years back in time to South-East-Asia, more specifically: to India and China. Being **first cultivated as a natural dye and kitchen herb**, it soon became an essential **ingredient in the Traditional Indian Medicine (Ayurveda) and the Traditional Chinese Medicine (TCM).**

In Europe and the US, turmeric is widely known as the main ingredient of curry where it adds a bitter and pungent taste. But more important than its taste is its strong dying capability, giving food and beverages a bright yellow-orange color. This is the reason why turmeric is also called the Indian saffron. Therefore, it is also used as a **dying agent in cosmetics and in fabrics.** When traditional eastern medicine approaches became popular in European and US countries, the potential healing properties of turmeric were put into focus of public interest as well. In this regard, especially the **use as supplement in human and animal nutrition** has seen a rising demand. However, turmeric gets more and more popular around the globe, the world largest consumer, producer and exporter is still India.

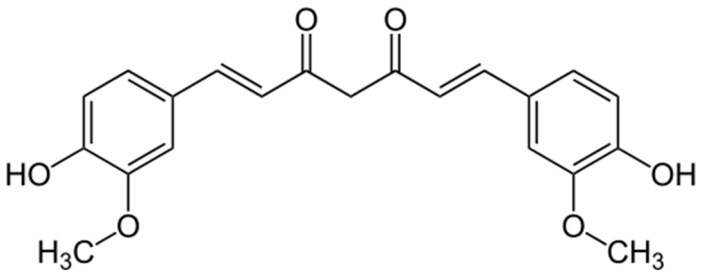
Figure 1: Turmeric plants as they flower

Getting a better understanding of the various effects of turmeric, it needs a closer look at the chemical structure and the mode of action. Curious what impressive details will be further unveiled?

Delacon
performing nature

Active ingredients in turmeric

Curcuminoids and essential oil components are the main active constituents of *Curcuma longa*.[1] The first group mainly comprises the phenolic compounds curcumin, demethoxycurcumin and bisdemethoxycurcumin. Turmeric essential oil consists mainly of ar-Turmerone, α-Turmerone and further constituents like Zingiberone, Atlantone and β-Turmerone, all belonging to the class of monocyclic sesquiterpenes.[2]



Curcumin is generally the most important substance in turmeric products. It is responsible for the typical yellow color and has been registered as food additive for gold-orange coloring with the E number 100.[3] Curcumin is also considered the most important compound of *Curcuma longa* regarding to its biological activity. Therefore, most research on detailed modes of action turmeric exerts in biological systems focuses on the effects of curcumin.

GOOD TO KNOW

- **Turmeric is best known for use of its ground rhizomes as spice and dying agent.**
- **Different extraction processes are used to obtain products enriched in active components of Curcuma longa. Turmeric oleoresins are deep brownish-orange viscous oily fluids, pasty semi-solids or hard amorphous solids that are insoluble in water and containing 37-55 % curcuminoids and up to 25 % volatile oil.[4]**
- **Extraction of the volatile compartments yields an orange-yellow liquid that does not contain curcuminoids. Instead, mainly monocyclic sesquiterpenes constitute most active components.**

Mode of action: Beneficial effects for humans and animals?

Numerous studies describe beneficial effects of turmeric on physiological processes in humans and animals. However, when having a closer look at those studies, some benefits need to be relativized. First, most studies demonstrating these effects are performed *in vitro* with cell cultures rather than whole animals or humans. And second, the majority of studies showing efficacy were not carried out by using the whole herb, but instead using turmeric's main active compound curcumin in a purified form. Now the question occurs: Are the beneficial properties of turmeric just of academic relevance restricted to specific circumstances or will it provide advantages beyond laboratory environments?

Turmeric actively influences the physiology

An extensive review of the generated data would overstress the scope of this article. Therefore, two examples for the role of curcumin in anti-inflammatory and antioxidant processes will be given in detail, while other effects of curcumin especially *in vivo* will be summarized in brief separately.

Inflammation can be triggered by a wide range of factors such as foreign substances, infections, and tissue damage. Cells in the body need to be capable to adapt to the respective stressors. **Curcumin was shown especially in cell culture studies to be able to inhibit multiple pro-inflammatory pathways**[5] indirectly by influencing genes and proteins involved in the normal cellular response to such stressors. One of the most important key factors in these processes is the "Nuclear factor kappa-light-chain-enhancer of activated B cells", in short NF-κB. This protein complex is found in almost all animal cell types and is involved in cellular responses to stimuli such as stress, cytokines, free radicals, heavy metals, ultraviolet irradiation, oxidized LDL, and bacterial or viral antigens. Beside cell culture studies, it was also shown for example in mice that anti-inflammatory effects of curcumin are, at least partly, mediated by its effects on NF-κB, resulting in protective effects against an experimentally induced inflammation.[6]

In contrast to the wide range of different factors leading to inflammation, oxidative stress is usually a result of a disequilibrium between the appearance of mainly reactive oxygen species in a biological system and its ability to detoxify these. Consequently, all parts of a cell can be damaged, including membranes, enzymes and DNA, leading to a loss of function. A master regulator to control expression of anti-oxidant proteins that protect against oxidative damage triggered by injury and inflammation is the Nuclear factor (erythroid-derived 2)-like 2, abbreviated to Nrf2.[7] **Curcumin has been shown to induce**

Nrf2, supporting production of the cells own anti-oxidative enzymes.[8] Additionally, to indirect effects via interaction with genes and proteins, **curcumin also has direct anti-oxidative properties.**[9] It is capable of directly scavenge reactive oxygen species and protect cellular structures from their damaging effects. Therefore, it acts both directly and indirectly to support biological systems against oxidative stress.

Situation of turmerics' effects regarding health *in vivo*

Beside its anti-inflammatory and anti-oxidant effects, **curcumin has been suggested as a potential natural health product against a variety of other problems**[10] provided a review, summarizing **antibacterial, antiviral and antifungal activity** of curcumin in different experimental assays, based **mainly on *in vitro* approaches** and rodent models. Curcumin is also discussed to be a **potent immunomodulatory agent**. For example, it was capable to improve the humoral immune response in laying hens, especially regarding the primary antibody responses[11]. **Anticancer properties** have been demonstrated for example in the *in vivo* ovarian carcinoma models SKOV3ip1 and HeyA8 in athymic mice, with curcumin being able to decrease tumor growth[12]. Regarding the role of curcumin and turmeric and their interaction with chemotherapy in gastrointestinal malignancies, several human studies have been conducted and were reviewed by Bar-Sela et al. [13]. According to their conclusion, treatment with curcumin is safe and provides enough positive clues of curcumin as chemo-preventive agent to justify phase III trials on specific gastrointestinal carcinomas.

The **antidiabetic** efficacy of curcumin was tested in a range of different models, but similarly to other topics, mainly *in vitro* using cell cultures or with rats and mice. In the rodent studies, application of curcumin resulted often in reduced blood glucose levels and beneficial response in other type-2 diabetes-mellitus related parameters such as insulin resistance, body and liver weight[14]. There are also indications that curcumin **could positively affect major problems of diabetes**, including insulin resistance, hyperglycemia, hyperlipidemia, islet apoptosis and necrosis in humans[15]. The authors of that study however, state that **more studies in humans are necessary to confirm the beneficial effects of curcumin on diabetes**. There has been also research on a disorder often associated with type-2 diabetes, the **nonalcoholic fatty liver disease** (NAFLD). Curcumin extract seems to be a promising candidate for reduction of certain parameters (alanine transaminase, and aspartate transaminase), while the **role for turmeric is less clear for treatment of NAFLD**[16].

Despite promising potential to the above described health disorders, there seem to be **fields of usage without any useful efficacy of curcumin**. For example, Mazzanti and Di Giacomo[17] came to a devastating conclusion when reviewing five clinical studies on the role of curcumin (they also reviewed resveratrol, another much praised plant compound) in the management of **cognitive disorders:** "The results of published trials are disappointing and

do not allow to draw conclusions about the **therapeutic or neuroprotective potential** of curcumin and resveratrol."

Given the sheer amount of publications concerning turmeric, it is basically impossible for researchers to keep up with the state-of-the-art in this research area. An attempt to summarize all knowledge on human *in vivo* and clinical studies was done by Nelson et al.[18] Analyzing more than 120 clinical studies related to different health topics, the authors concluded that no double-blinded, placebo controlled clinical trial of curcumin has been successful. Their explanation for this conclusion is based on the fact, that "no form of curcumin, or its closely related analogues, appears to possess the properties required for a good drug candidate (chemical stability, high water solubility potent and selective target activity, high bioavailability, broad tissue distribution, stable metabolism, and low toxicity)".

What about the performance of livestock animals?

In contrast to the detailed effects on inflammatory and oxidative processes observed *in vitro* with pure curcumin, *in vivo* studies using turmeric rhizomes and its preparations show inconsistent results on health-related parameters. Therefore, it is important to carefully review studies in livestock animals to evaluate potential growth performance enhancing effects. Studies cited in Table 1 show effects of dietary supplementation with turmeric rhizome powder on growth performance in broiler chickens. The results reveal inconsistent effects on growth performance, although similar concentrations have been used in these studies. However, there seems to be at least some consistency on improving feed efficiency in poultry. In post-weaning piglets, two studies with dietary inclusion of turmeric rhizome powder[19] or curcumin[20] showed no effects on growth performance. Based on the small sample size of these studies, it can be concluded that *in vivo* effects on growth performance in poultry and pigs are not consistent. It may be speculated, that several interacting topics are responsible for this discrepancy between *in vivo* and *in vitro* observations. *In vivo*, mostly ground rhizomes of turmeric are used as food or feed supplement, were active substances need to make the passage through the intestinal tract. From there, they need to be absorbed into the bloodstream and transported through the body for **systematic effects**. However, the bioavailability of curcumin is poor and the **low uptake through the intestinal tract** may be one of the main issues, why **inconsistent effects are observed in animals and humans**. In addition, ground rhizomes as natural product **vary in their composition** depending for example on harvest time, environmental conditions and variety. **Similar quantities of turmeric powder might therefore differ significantly in their content of active substances**. In contrast, most *in vitro* experiments use cell cultures and the pure active compounds, especially curcumin, will be applied directly on these. Therefore, the issues of varying concentrations of actives and

transportation to the site of interest are no issue *in vitro*. These circumstances may be an explanation for **the difference between *in vivo* and *in vitro* observation.**

Table 1. Effects of turmeric powder supplementation on growth performance in broiler chickens*

Trial setup	Trial duration [days]	Dosage in feed [g/kg]	Results	Reference
60-day old Cobb broiler; 10 birds/pen; 3 pens/treatment	35	0; 5	After 35 days no effects on BW gain or feed intake, FCR improved with turmeric supplementation	Abou-Elkhair et al., 2014[21]
112-day old Ross 308 broiler; 14 birds/pen; 2 pens/treatment	42	0; 2; 4; 6	After 42 days BW and BW gain (day 42) were higher for 2 g/kg and 4 g/kg turmeric powder compared to the control. Feed conversion ratio was improved with 4 g/kg compared to the control.	Al-Mashhadani, 2015[22]
120 day old Vencobb broiler; 10 birds/pen; 3 pens/treatment	42	0; 1; 2	After 42 days no effects on BW	Mehala and Moorthy, 2008[23]
120 day old Hubbard broiler; 10 birds/pen; 4 pens/treatment	35	0; 5; 10; 15	10 g/kg and 15 g/kg increased BW gain and improved FCR compared to control and 5 g/kg. In addition, 5 g/kg improved FCR compared to the control	Arslan et al., 2017[24]
120 day old Ross 308 broiler; 10 birds/pen; 4 pens/treatment	42	0; 2.5; 7.5	After 42 days no effect on weight gain and but improved FCR at 2.5 g/kg turmeric powder	Naderi et al., 2014[25]

*Only results for treatment groups containing turmeric and unsupplemented control groups are shown. BW: body weight; FCR: feed conversion ratio

Delacon
performing nature

Achieving satisfying results needs a deeper understanding and more research

To explain and overcome the inconsistency and discrepancy in studies on turmeric, **two aspects need to be emphasized.** First, when evaluating *in vitro* studies using curcumin is its high potential **to interfere with the used assays** (see green box). Because of this issue, generation of **misleading data could trick unprepared researchers into misinterpreting the results** of their investigations.[18] And second, the already mentioned **poor bioavailability**. In most instances, application of curcumin preparations will be enough to induce effects in cell cultures. But the main active compounds may simply not be able to reach cells and tissues in whole animals and humans outside the digestive tract. Using the isolated curcumin *in vivo* might reduce this problem to some degree, helping to explain the more positive results of curcumin compared to whole turmeric.

Therefore, an important topic for further turmeric related studies is improvement of the curcumin bioavailability. Due to importance of this, several solutions are suggested and tested already. One famous method to achieve this goal is the **addition of piperine from black pepper** to turmeric formulations, as this substance was shown to increase curcumin bioavailability in humans.[26] Further support might come from more technological solutions**. Formulation of curcumin nanoparticles and microencapsulation techniques** are utilized to enhance its bioavailability and may proof to be key to emulate *in vitro* observed effects *in vivo*. One example in this regards might be the use of phytosomal curcumin, as reviewed by Mirzaei et al. [27]. With this complex of curcumin with phosphatidylcholine it was shown *in vivo*, that bioavailability was improved in mouse and human studies.

GOOD TO KNOW

To understand the effect of substances, different experimental approaches are required. Depending on the questions to solve, studies are performed for example:

- ***in vivo* (whole, living organisms),**
- ***ex vivo* (tissue from an organism in an external environment),**
- ***in vitro* (studies are performed with micro-organisms, cells, or biological molecules outside their normal biological context), and**
- ***in silico* (via computer simulation).**

An important premise is the knowledge about possible problems for the chosen method. In this regard, curcumin is an example for a PAIN (pan-assay interference compound). Due to its very strong dying properties, it often interferes with measurements based on optical density, color or fluorescence, possibly falsifying the results. Experimental approaches therefore need to be chosen accordingly to avoid such possible problems to gather reliable data.

Delacon
performing nature

What did we learn?

Looking at the literature *Curcuma longa* is basically reported to have biological activity for virtually any health-related parameter. Without doubt, the **sum of turmeric's active ingredients proofed to be effective in *in vitro* models** with regards to their anti-inflammatory, anti-oxidative and other properties. However, ***in vivo* models and clinical studies show inconsistent and much less obvious effects** on health-related parameters and livestock growth performance. Authors from all sorts of studies regarding turmeric agree, that this discrepancy between *in vitro* and *in vivo* is most likely cause by the poor bioavailability of turmeric's active compounds such as curcumin. Therefore, the key aspect for successful utilization of turmeric as food or feed supplement needs to be further looked at in detail will be a better understanding of how to increase bioavailability. This knowledge will enable to unlock the full potential of this interesting plant and to transfer its impressive *in vitro* effects to animals and humans.

Delacon
performing nature

References

1 Jurenka, J.S., Anti-inflammatory Properties of Curcumin, a Major Constituent of Curcuma longa: A Review of Preclinical and Clinical Research. Alternative Medicine Review Volume 14, Number 2. 2009.

2 Ravindran, P.N., Nirmal Babu, K., Sivaraman, K. Turmeric: The Genus Curcuma. ISBN-13: 978-0-8493-7034-2. CRC Press. March 2017.

3 EFSA Pansel on Food Additives and Nutrient Sources added to Food (ANS); Scientific Opinion on the re-evaluation of curcumin (E 100) as a food additive. EFSA Journal 2010; 8(9):1679. doi:10.2903/j.efsa.2010.1679.

4 Li, S., Yuan, W., Deng, G., Wang, P., Yang, P., and Aggarwal, B. Chemical composition and product quality control of turmeric (Curcuma longa L.). Pharmaceutical Crops. 2011. Faculty Publications. Paper 1. 2: 28-54.

5 Aggarwal, B.B., Harikumar, B.K., Potential Therapeutic Effects of Curcumin, the Anti-inflammatory Agent, Against Neurodegenerative, Cardiovascular, Pulmonary, Metabolic, Autoimmune and Neoplastic Diseases. Int J Biochem Cell Biol. 2009 ; 41(1): 40–59. doi:10.1016/j.biocel.2008.06.010.

6 Zhong W. et al. Curcumin alleviates lipopolysaccharide induced sepsis and liver failure by suppression of oxidative stress-related inflammation via PI3K/AKT and NF-kB related signaling. Biomedicine & Pharmacotherapy 83 (2016) 302–313.

7 Kansanen, E., Kuosmanen, S.M., Leinonen, H., Levonen, A.L. The Keap1-Nrf2 pathway: Mechanisms of activation and dysregulation in cancer. Redox Biology 1 (2013) 45-49.

8 Soetikno V. et al. Curcumin alleviates oxidative stress, inflammation, and renal fibrosis in remnant kidney through the Nrf2–keap1 pathway. Mol. Nutr. Food Res. 2013, 57, 1649–1659.

9 Singh, G., Kapoor, I.P., Singh, P., de Heluani, C.S., de Lampasona, M.P., Catalan, C.A. 2010. Comparative study of chemical composition and antioxidant activity of fresh and dry rhizomes of turmeric (Curcuma longa Linn.). Food Chem Toxicol. 48 (4):1026-1031.

10 Moghadamtousi, S.Z. et. al. A Review on Antibacterial, Antiviral, and Antifungal Activity of Curcumin. BioMed Research International. Volume 2014

11 X. Zhou, A.S. Mueller, L. Jungbauer, J.D. van der Klis (2017). Der Einfluss von Chlorella und Curcumin auf Leistung und humorale Immunantwort bei Legehennen. In: A. Zeyner, H. Kluth, M. Bulang, M. Bochnia und M. Bachmann (Editors), Conference Proceedings of the 14. Tagung Schweine- und Geflügelernährung, 21.- 23. November 2017, Lutherstadt Wittenberg. Page 223-225. ISBN: 9783868298918

12 Lin, Y. G. et al. Curcumin Inhibits Tumor Growth and Angiogenesis in Ovarian Carcinoma by Targeting the Nuclear Factor-KB Pathway. Clin Cancer Res 2017; 13(11). 3423-3430.

13 Bar-Sela, G. et al. Curcumin as an Anti-Cancer Agent: Review of the Gap Between Basic and Clinical Applications. Current Medicinal Chemistry, 2010, Vol. 17, No. 1.

14 Wojcik, M. et al. Molecular Mechanisms Underlying Curcumin-Mediated Therapeutic Effects in Type 2 Diabetes and Cancer. Oxidative Medicine and Cellular Longevity. Volume 18.

15 Zhang, D. et al. Curcumin and Diabetes: A Systematic Review. Evidence-Based Complementary and Alternative Medicine. Volume 2013.

16 White, C. M., Lee, J. The impact of turmeric or its curcumin extract on nonalcoholic fatty liver disease: a systematic review of clinical trials. Pharmacy Practice 2019 Jan-Mar;17(1):1350.

17 Mazzanti, G., Di Giacomo, S. Curcumin and Resveratrol in the Management of Cognitive Disorders: What Is the Clinical Evidence? Molecules 2016, 21, 1243.

18 Nelson, K.M., Dahlin, J.L., Bisson, J., Graham, J., Pauli, G.F., Walters, M.A. The Essential Medicinal Chemistry of Curcumin. J. Med. Chem. 2017, 60, 1620−1637.

19 Maneewam, C., Yamauchi, KE., Mekbungwan, A., Maneewan, B., Siri, S. Effect of tumeric (Currucuma longa Linnaeus) on growth performance, nutrient digestibility, hematological values, and intestinal histology in nursery pigs. Journal of Swine Health and Production - September and October 2012.

20 Ilsley, S.E., Miller, H.M., Kamel, C., Effects of dietary quillaja saponin and curcumin on the performance and immune status of weaned piglets. J. Anim. Sci. 2005. 83:82–88.

21 Abou-Elkhair, R., Ahmed, H.A., Selim, S., 2014. Effects of Black Pepper (Piper Nigrum), Turmeric Powder (Curcuma Longa) and Coriander Seeds (Coriandrum Sativum) and Their Combinations as Feed Additives on Growth Performance, Carcass Traits, Some Blood Parameters and Humoral Immune Response of Broiler Chickens. Asian Australas. J. Anim. Sci. 27:847-854.

22 Al-Mashhadani, H.E., Effect of different levels of tumeric (Curcuma longa) supplementation on broiler performance, carcass characteristic and bacterial count. Egypt. Poult. Sci. Vol (35) (I): (25 -39) (2015).

23 Moorthy, M., Mehala, C. Effect of Aloe vera and Curcuma longa (Tumeric) on Carcass Characteristics and Biologocal Parameters of Broilers. Asian Network for Scientific Information, 2008.

24 Arslan, M., ul Haq, A., Ashraf, M., Iqbal, J., Mund, M.D., Effect of Turmeric (Curcuma longa) Supplementation on Growth Performance, Immune Response, Carcass Characteristics and Cholesterol Profile in Broilers. Veterinaria, Vol. 66, No. 1, 2017.

25 Naderi, M., Akbari, MR., Asadi-Khoshoei, E., Khaksar, K., Khajali, F. Effects of Dietary Inclusion of Turmeric (Curcuma longa) and Cinnamon (Cinnamomum verum) Powders on Performance, Organs Relative Weight and Some Immune System Parameters in Broiler Chickens. Poultry Science Journal 2014, 2 (2): 153-163.

26 Prasad, S., Tyagi, A.K., Aggarwal, B.B. Recent Developments in Delivery, Bioavailability, Absorption and Metabolism of Curcumin: the Golden Pigment from Golden Spice. Cancer Res Treat. 2014;46(1):2-18.

27 Mirzaei H. et al. Phytosomal curcumin: A review of pharmacokinetic, experimental and clinical studies. Biomedicine & Pharmacotherapy 85 (2017) 102–112.