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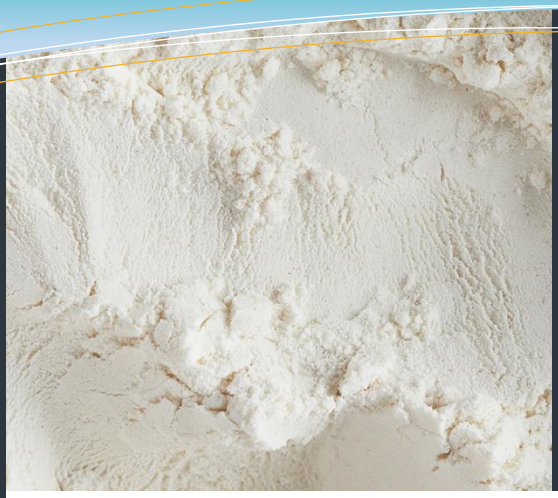
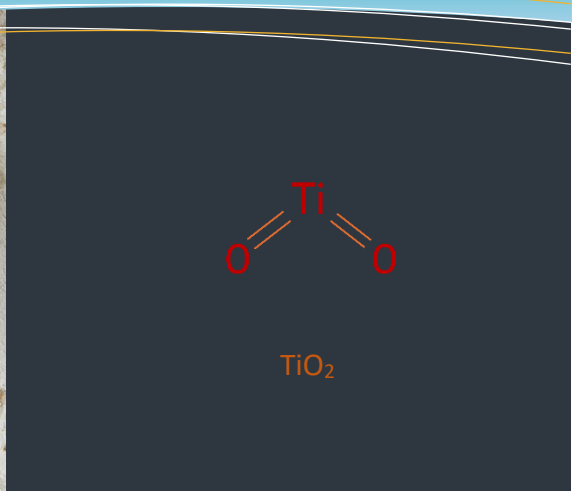
GERMAN SOCIETY OF
TOXICOLOGY

Poison of the month





Titanium Dioxide (TiO_2)

Titanium dioxide is an inorganic pigment that occurs in various crystalline forms, primarily in the rutile and anatase modifications. These forms differ in their crystal structure, physical properties, and stability.

Nanotechnology

Nanotechnology, the intentional scaling of materials to sizes ranging from 1-100 nm, emerged between the 1960s and 1980s as an interdisciplinary field of research. Scientists discovered that materials at the nanoscale exhibit unique physical and chemical properties that differ significantly from those of larger particles. Nanotechnology enables the manipulation of material structures and compositions at the nanoscale to create materials with specific optical, magnetic, or mechanical properties.

Nanotechnology combines chemistry, physics, biology, materials science, and engineering. It is applied in fields such as medicine, electronics, environmental technology, and food technology.

Evaluation (TiO_2)

Since E171 consists of a mixture of particles, of which some are nanoscale, the EFSA safety assessment of E171 has included studies conducted both with E171 itself and with other TiO_2 nanoparticles with the aim to better assess potential risks.

Thereby, EFSA took into account that in E171, less than 50 % of the particles are smaller than 100 nm. This proportion could possibly contribute to nanomaterial properties of E171. However, studies using pure TiO_2 nanoparticles <30 nm were considered only partially relevant, as this particle size is rare in E171.

Additionally, E171 can form larger agglomerates that behave differently, further complicating the assessment.

Titanium Dioxide (TiO_2) in the Food Industry: Divergent Safety Assessments and the E171 Controversy

Since the 1960s, titanium dioxide (TiO_2) has been used as a whitening agent and colorant in the food industry. Known as E171, it was widely applied in the EU in products such as candies, baked goods, dairy products, and chewing gum. TiO_2 has excellent whitening properties and high chemical stability, which make foods visually more appealing by giving them a uniform white or opaque color. From the beginning of its use, E171 consisted of particles of various sizes, with a certain proportion being under 100 nanometers (nm), which qualifies them as nanoparticles. Advances in nanomaterial analysis revealed that E171 often contains a significant proportion of nanoparticle, which put attention on E171's safety assessment.

In 2021, the European Food Safety Authority (EFSA) published an updated safety assessment of E171, stating that TiO_2 particles are generally poorly absorbed by the body and possess low bioavailability (less than 1%). However, the authority could not conclusively determine whether these particles could accumulate in the body due to their long half-life time. EFSA cited individual rodent studies in which particles were found in the intestinal lumen and accumulated in different organs like liver and spleen, though in very low concentrations. This may be indicative for a possible distribution within the body. Furthermore, concerns were raised regarding genotoxic properties, as TiO_2 particles caused DNA strand breaks and chromosome damage in some studies. In the assessment EFSA discusses that multiple mechanisms of action might be occurring simultaneously, though their relative contributions remain unclear. Together, uncertainties remained whether a threshold mechanism could be assumed, which is necessary for the establishment of a tolerable daily intake (TDI). Based on these conclusions, the EU banned the use of E171

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in foods in 2022.

In contrast to the EU, other international authorities still consider E171 safe. The U.S. Food and Drug Administration (FDA) and the Joint FAO/WHO Expert Committee on Food Additives (JECFA) re-evaluated the safety of E171 in 2023. Based on toxicological and biochemical data, both concluded that E171 poses no health risk when used in approved quantities of up to 1 % in food. Additionally, the genotoxicity studies referenced in the EFSA assessment were critically reviewed, as the FDA noted that many of these tests were conducted on TiO_2 test particles not representative of food additives. Moreover, no evidence of possible carcinogenic properties was found in studies by the U.S. National Toxicology Program (NTP).

In 2024, the Committee on Toxicity (COT) in the United Kingdom also published a comprehensive assessment of the potential health risks of E171. The experts analyzed various toxicological endpoints, including genotoxicity, immunotoxicity, and neurotoxicity, and found no reliable evidence of harmful effects from TiO_2 in food. The COT emphasized that even for high consumers, the intake level in foods does not exceed the established Health-Based Guidance Value (HBGV) of 10 mg per kilogram of body weight per day. Health risks are therefore considered unlikely, although a minimal excess over the HBGV might occur with extremely high consumption.

Other international regulatory agencies, such as Health Canada and Food Standards Australia New Zealand (FSANZ), neither share the EU's assessment and continue to allow the use of TiO_2 in food.

In the EU, however, E171 remains banned. The EU is relying on additional studies to resolve remaining uncertainties before a potential reregistration.

By Ute Haßmann

Safety Assessment of Nanoparticles

To assess the safety of a food ingredient or chemical, it is crucial to precisely characterize the substance and understand the mechanisms and concentrations at which adverse effects occur. This enables the establishment of a threshold level, known as the tolerable daily intake (TDI), considered safe.

Starting in the 2000s, comprehensive studies were conducted on the potential health risks of nanoparticles. It was found that nanoparticles, due to their small size, can penetrate human cells and tissues, which may have harmful effects on cells and organs.

Growing understanding of their mobility within the body and potential toxicity highlighted the need for regulation. Meanwhile various guidelines and regulations exist for all areas in which nanoparticles are used to ensure their safety. Food additives like E171, for instance, are regulated in the EU by the EU Regulation no. 1333/2008.

In the EU, TiO_2 nanoparticles are sill allowed an can be used in various applications, including cosmetics, medical devices, paints, coatings, plastics, papers, textiles, and environmental technology. In cosmetics, such as sunscreens, they are approved as UV filters, and nanoparticles must be labeled as such. For medical devices, strict safety requirements must be met, especially if the particles are in direct contact with the body.

However, discussions about a potential ban on TiO_2 nanoparticles are increasing in these fields in the EU as well. This is why TiO_2 applications are currently under close monitoring.

Literature and links:

- Safety assessment of titanium dioxide (E171) as a food additive
- EFSA Re-Assessment of Titanium Dioxide (E 171) , 2021 | Committee on Toxicity
- Regulation (EU) No 1169/2011
- Food-grade TiO2 impairs intestinal and systemic immune homeostasis, initiates preneoplastic lesions and promotes aberrant crypt development in the rat colon – PubMed
- https://www.fda.gov/industry/color-additives/titanium-dioxide-color-additive-foods
- Executive Summary - Statement on the safety of Titanium Dioxide (E171) as a Food Additive | Committee on Toxicity
- Picture of Olivie Strauss, unsplash+