TiO_2-free capsules

Market scenario in capsule development.

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Whitepaper Summary

US and Europe are the leaders in the healthcare market. Recently, Europe has banned the use of TiO_2 as a food additive, owing to its hazardous effects. Industries are looking for the best alternatives to TiO_2. What are they?

Titanium dioxide (TiO_2) is no longer permitted as a food additive in the EU, due to its toxicity.

TiO_2, also known as E171, is a popular whitening agent in a variety of food products, medications, and cosmetics for external use. It is used extensively as an opacifier to enhance the quality standards of medicinal and nutritional supplements, and its primary function is to enhance the appearance of food or consumables. According to the conclusions of a 2017 study by the National Institute of Agronomic Research, ingesting TiO_2 may be harmful. It was revealed that, as a metal oxide, it may react with cellular components of the body, increasing the risk of cancer and cellular damage.[1]

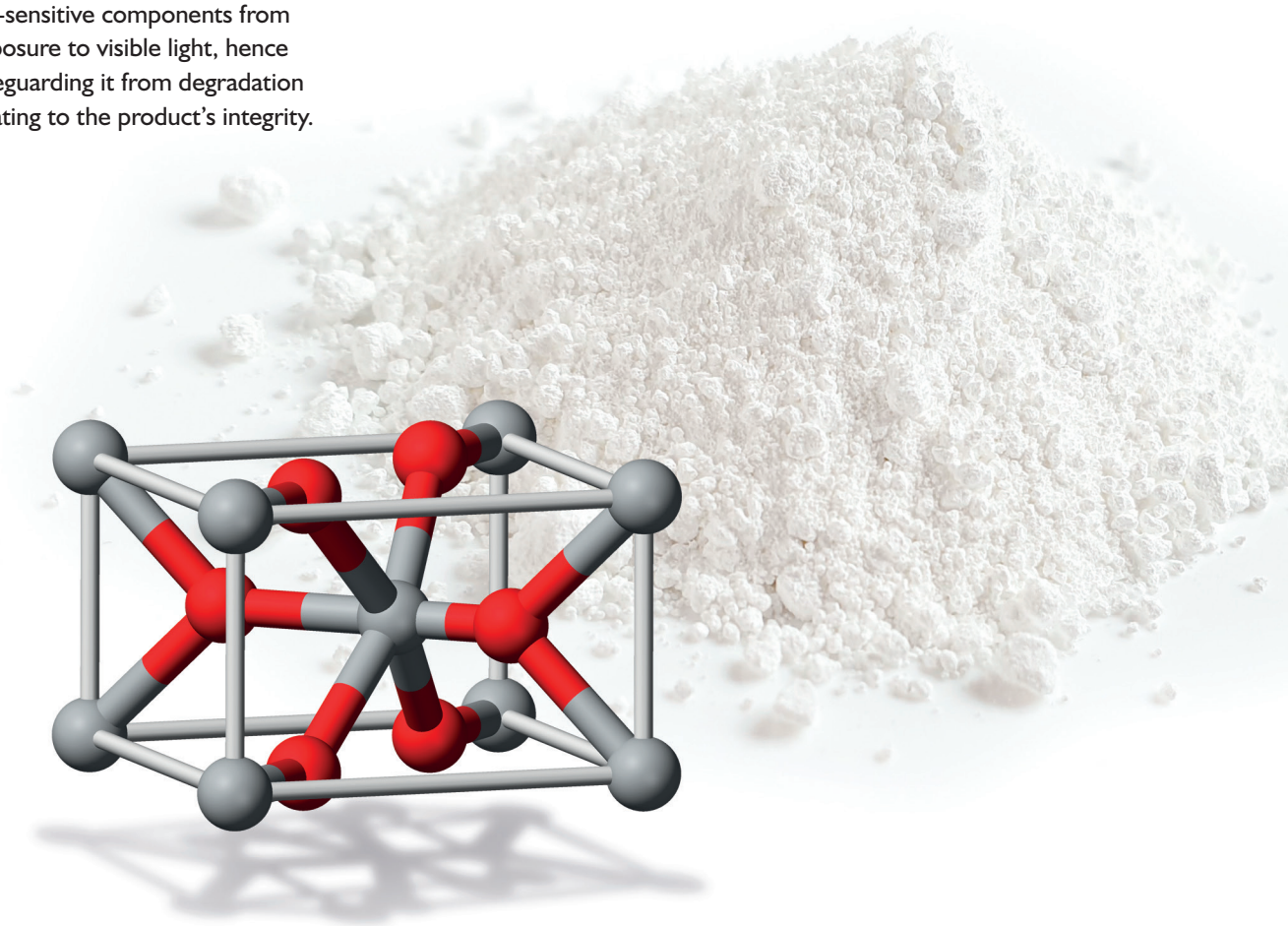
In May 2021, the European Food Safety Authority (EFSA) investigated the safety of TiO_2 as an additive, and declared it unsafe.[2] According to the reports, TiO_2 has properties that can lead to outcomes such as inflammation, neurotoxicity and cytotoxicity. In October 2021, the EFSA also claimed that TiO_2 may alter human genetic information. The European Medicines Agency (EMA) has recommended a regulatory framework to support the removal or replacement of TiO_2 in medicine, in order to maintain health and safety in food standards. It firmly prohibits the use of TiO_2 as an excipient in dietary supplements, despite other countries deeming it safe.

Regulatory authorities revoked permission for the use of TiO_2 in food additives in January 2022, yet have allowed TiO_2 to remain on the list of recognised additives – allowing it to be used as a colourant in medicinal products. The US FDA examined the EFSA studies and determined that TiO_2 had no significant effect on the human organ system in terms of organ toxicity, or reproductive and developmental toxicity. They have designated TiO_2 as 'generally recognised as safe' (GRAS) up to a weight limit of 1% for consumables. Yet, given the increased demand for clean-label products, the industrial sectors are keen to find a viable substitute for TiO_2. The nutraceutical and pharmaceutical industries are therefore seeking viable alternatives to these crucial solid excipients.

Titanium dioxide as an opacifier.

Titanium dioxide is used as a colouring element in a variety of ingestible and topically delivered drugs. It is present in many pharmaceutcial products, like pellets, capsules, and film-coated tablets. TiO_2 has the intrinsic property of scattering light due to its high refractivity index, enabling both the product differentiation and brand recognition. Even a small amount can have a huge impact on the product's appearance. It also offers a unique combination of qualities that protect against UV, light and heat degradation. It forms a protective layer that aids in protecting the product's safety, efficacy and quality over its shelf life. In addition, TiO_2 functions as a stabiliser for photosensitive formulations, by preventing UV-sensitive components from exposure to visible light, hence safeguarding it from degradation relating to the product's integrity.

A complete ban on TiO_2 in pharmaceutical formulations is still controversial and uncertain, yet there is currently no exact equivalent. Researchers are therefore seeking alternatives, as they will likely be required for all formulations. Meanwhile, much of the concern raised relates to the potential impact on products' appearance, such as opacity loss, and the light-resistance and film-coating capabilities of alternatives to TiO_2. The appropriate placement and management of such alternatives can ultimately improve the product's performance.



TiO_2-free capsules

Several studies have confirmed that a product's appearance influences customers' buying decisions. Titanium dioxide is a popular whitening agent, and a common component of empty capsules. It also offers a homogeneity that minimises batch-to-batch variation, and allows a unique appearance. Many pharmaceutical and nutraceutical companies use specific colours for their capsule branding, as this provides a prominent white appeal to the product.

But the real question is whether the absence of TiO_2 has any effect on the capsules themselves…

It seems not. The absence of TiO_2 appears to have no effect on overall capsule attributes, such as dissolution profile, strength, stability, shelf life, moisture humidity resistance, separation, or locking and filling capacity.

TiO_2 is currently being replaced by a variety of natural alternatives, including different carbonates, phosphates, starches, polyols and cellulose derivatives. These all gives capsules an opaque quality. Calcium carbonate, however, is considered as a great replacement among all. It is the next most promising ingredient in terms of protection against the external environment, and is a white mineral with bigger particles than TiO_2. Its refractive index deviates slightly from TiO_2, resulting in a minor decrease in whitening and opacity. When compared with TiO_2 capsules, it can attain semi-opacity, and protect contents from light by hiding the capsule's fill materials.

Another TiO_2 alternative is calcium sulphate, a low-cost opacifier. Compared with TiO_2, the amount of calcium sulphate required to produce the necessary level of whiteness is much lower.

Additionally, investigators are looking at novel alternatives, such as calcium hydrogen phosphates, magnesium carbonate, talc, zinc oxide, aluminium silicate and aluminium hydroxide.

Innovators are also exploring natural substances as colouring components for capsules. Natural colour produced by fruits, grains, vegetables, malt or other plant-based basic materials is already being used in capsule production. Vegetables are an excellent source of colour as they can survive extreme temperature, light, chemical and physical changes. Naturally coloured clean capsules are ideal for nutraceutical compositions, including dietary supplements.

As a capsule-shell manufacturer, ACG Capsules is ahead of the curve, offering excellent alternatives for a 'post-TiO_2' environment...

ACGcaps™ TSafe use the cleaner opacifier calcium carbonate, and are designed with consumers' preference for clean products in mind. Meanwhile, ACGcaps™ NTone are naturally coloured capsules that come in five different shades.

These capsule ranges provide an excellent opportunity for the development of clean-label products that facilitate a new aesthetic appeal and brand uniqueness. ACG also provides capsules that contain iron oxide as an alternative opaque colouring agent.

Considering the whole TiO_2-free scenario, this is the best way to capitalise on market trends and remain one step ahead of future regulations. Embracing these alternatives for product development not only supports future sustainability initiatives, but also helps to lead and stay ahead of clean-label trends in capsule development. Ultimately, the right capsule selection will protect market revenue in the Pharmaceutical and Nutraceutical industries.

Reference:

1. What You Need to Know about TiO_2-Free Capsules. Available online: https://www.dcatvci.org/

2. Ban on Titanium Dioxide (E171) on the EU Food Market: What Are the Consequences for Medicines?

Available online:
https://www.propharmagroup.com/thought-leadership/titanium-dioxide-e171-ban