USING LIGHT MICROSCOPE TO FIND STABLE CRYSTAL STRUCTURES

A matter of form

An active substance that forms fine needles or tiny cubes is an absolute highlight for researchers. To manufacture a drug or plant protection agent, scientists need to know what its stable crystalline form looks like, as many substances only display the desired properties in this state. Bayer researchers therefore structure promising active substances into a suitable crystalline shape right at an early phase of development in order to obtain crystals with optimum properties, such as the best possible solubility.

Be it a pharmaceutical drug or plant protection ingredient, three factors always count: the right time, the right place and the right dose. "A substance must be released in a controlled manner and made available to an organism at the required concentration," explains Dr. Britta Olenik, a chemist in Global Chemical & Pharmaceutical Development at Bayer HealthCare. For an active substance to reach its full potential, it has to be accompanied by an entire chemical package of additives.

"To be administered effectively, it is very important for an active substance to be available in a stable crystalline form," Olenik says. Take carbon atoms for instance. They can arrange themselves in a graphite or diamond lattice, with each structure leading to different properties. "Similarly, active substances for drugs or plant protection agents can crystallize in different solid shapes," the chemist explains. This has an effect on the substance's properties, for example its solubility or bioavailability.

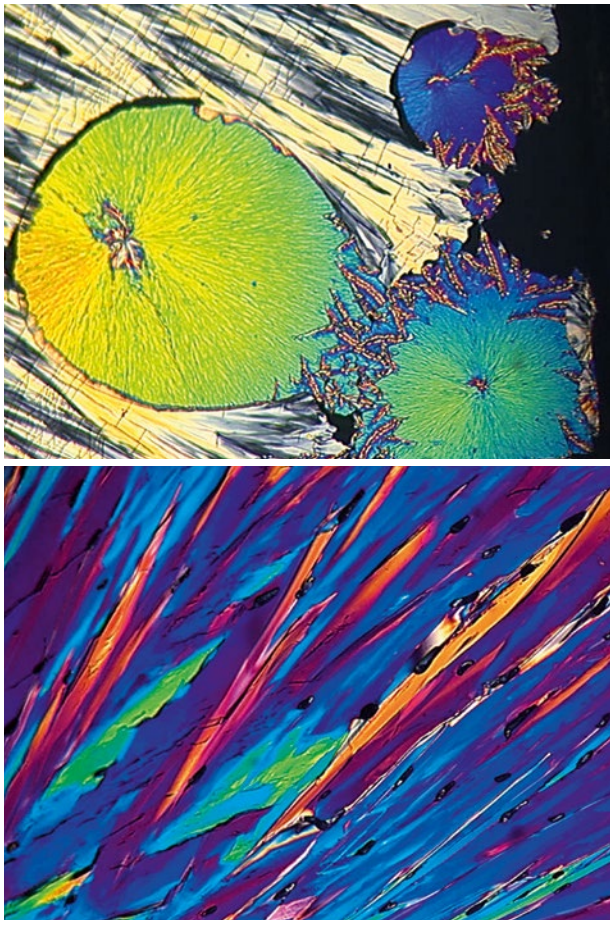
Crystalline form influences the quality and efficacy

Together with her team, Olenik therefore takes a very close look at the candidate molecules identified in research: she examines the physical and chemical properties of each substance and tests the different salts to determine which display, say, the best solubility. Then she analyzes the crystals, for example under the microscope. In a process known as polymorphism screening, Olenik tries to identify and characterize all crystalline forms of candidate active substances. "With the help of thermomicroscopy, we observe how our substances melt on exposure to polarized light to form new and different crystals. We can actually see how the bonds change and the molecules re-organize to form new lattice structures," Olenik explains. "Because the light is refracted to different degrees by the areas of a crystal, we often obtain very colorful images – mosaic-like surfaces, thin needles, or feathery structures in all sorts of colors."

Selectively changing active ingredient properties

Polymorphism screening plays a critical role in process engineering, chemical development and production. "It can be problematic if a compound in a formulation changes its crystal structure," the Bayer expert explains. Researchers attempt to prevent such occurrences by using a thermodynamically stable crystalline form that no longer will convert into a different crystal.

In some cases, it is also necessary to specifically alter other properties of an active substance, such as its solubility. Active substance molecules can only detach from their solid structure and reach the target location if they are in the right form.



Colorful patterns under the microscope: the crystalline structure of a crop protection agent changes as it warms up and cools down, altering the light refraction and therefore its color.

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