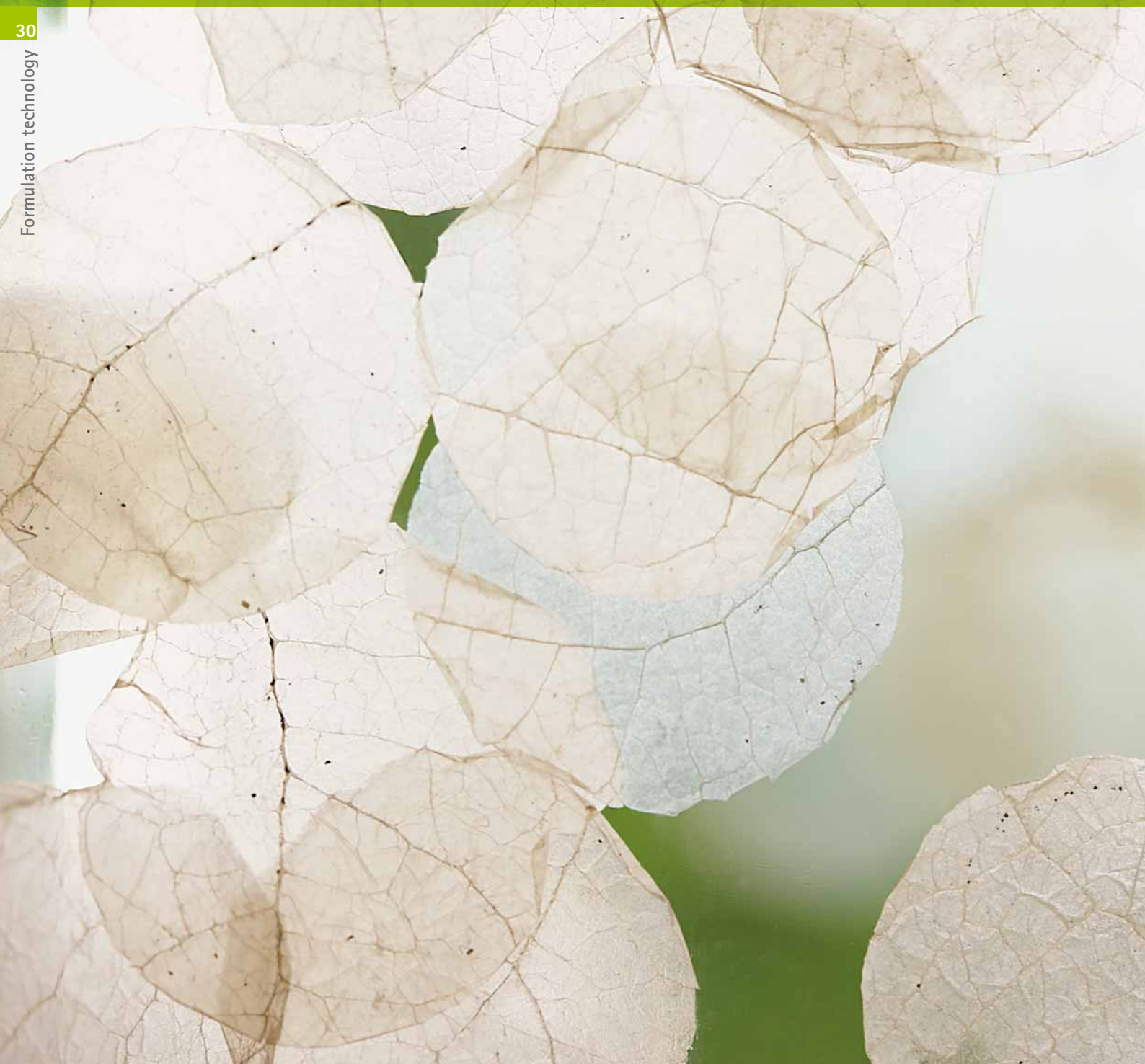
Optimum formulations for pesticidal active substances

Selectively **through any barrier**

Hairy leaf surfaces, sticky stalks or a humid climate: if a pesticide is to be effective it needs to be optimally adapted to its purpose and suited to the growing conditions and the crop concerned. With a cleverly devised mixture of substances, formulation technicians at Bayer CropScience help active substances reach their targets more effectively and thus safeguard crop yields all over the world – even under extreme conditions.



Their mission: to spread out and infiltrate foreign worlds and then eliminate the enemy. No, they aren't a squad of starship troopers, they are crop protection agents and the action is on a much smaller scale. The objective is to distribute a host of active ingredients as evenly as possibly over the leaves in a giant cereal field to control harmful fungi, weeds or insects. Like futuristic humans traveling through space in a fleet of space ships searching for new worlds, tiny molecules enclosed in droplets drift through the air. Yet many of their potential landing strips, the leaves for example, are covered in water-repellent wax crystals, causing most liquids to simply bounce off them. To ensure that the substance can land safely, scientists add other substances which cushion the impact or reduce the surface tension. These ensure that the spray mist droplets adhere firmly to the leaves and also wet large areas so that the active substance can penetrate quickly. Sometimes the substances follow a well-honed strategy, attaching themselves to the leaf and gradually seeping into the plant in the right dosage over a period of many days. However, it is no space travel authority that is planning the pesticides' journey, but about 150 Bayer CropScience employees in Monheim and Frankfurt am Main. They are formulation technicians: experts who manage time and time again to deliver increasingly complex fungicides, insecticides or herbicides safely to their target – their site of action.

These formulators working unobtrusively in the background are using their ingenuity to play a central role in the second green revolution. The ever-shrinking area of agricultural land available for a constantly increasing world population makes it necessary to find new ways of safeguarding or even increasing crop yields. Bayer's scientists not only keep product prices down but also help the environment; thanks to their individual solutions, the potential burden on soil and plants is kept to a minimum, and their work makes the use of many new substances possible. "New pesticides usually contain highly effective molecules with more and more complex structures and their synthesis is very elaborate, making them extremely expensive," says Dr. Rolf Pontzen, a laboratory manager in Bayer CropScience's Formulation Technology department. "Our task is not made any easier by the fact that we have to try simultaneously to protect as many plants as possible with as little active substance as possible." Theoretically, five to ten grams of substance are sufficient to coat all the leaves in a one-hectare field – equivalent to the size of a football pitch – with the finest imaginable film. Indeed, modern products are now so efficient that a film like this really could work. "Our work has made it possible for Bayer to now get amazingly close to this objective," says Professor Peter Baur, Group Leader for Bioavailability Optimization at Bayer CropScience. With his team, he has already developed agents of which ten to 20 grams of active substance, mixed into granules or liquid, are sufficient, after dilution with water, for a hectare of agricultural land.

Traveling with the sap through all parts of the plant

When chemists have discovered a new ingredient or a new substance has been acquired, Pontzen, Baur and their colleagues step into the picture. "Without the right formulation, even the best active substance is useless," says Dr. Hilmar Wolf, Head of the Fungicide Formulations group. He is proud that Bayer CropScience has one of the leading formulation departments in the world. "New pests or harmful fungi which have become insensitive to conventional products and increased demands for optimum protection of crops even under extreme conditions make it necessary to constantly develop new pesticides. Formulation is one of the crucial components of this." The herbicide Laudis®, for example, only works because the formulation technicians found two additives which help the active substance to penetrate the leaf quickly and effectively so that it can ultimately be distributed throughout the plant in the sap flow, thereby preventing further weed growth over a prolonged period.

Another example is the insecticide Movento®: Bayer CropScience scientists concealed an additive in plant oil and added it to the preparation in an especially finely tuned dose. As a result, the active substance is delivered gently but continuously via the sap to its target – the places where aphids or white flies suck.

Effective penetration of the membrane: the wafer-thin surface layer of leaves called the cuticle (large photo) prevents active ingredients from gaining access into the plant. Dr. Rolf Pontzen (left) and Dr. Hilmar Wolf search for additives that make it easier to penetrate this green barrier.

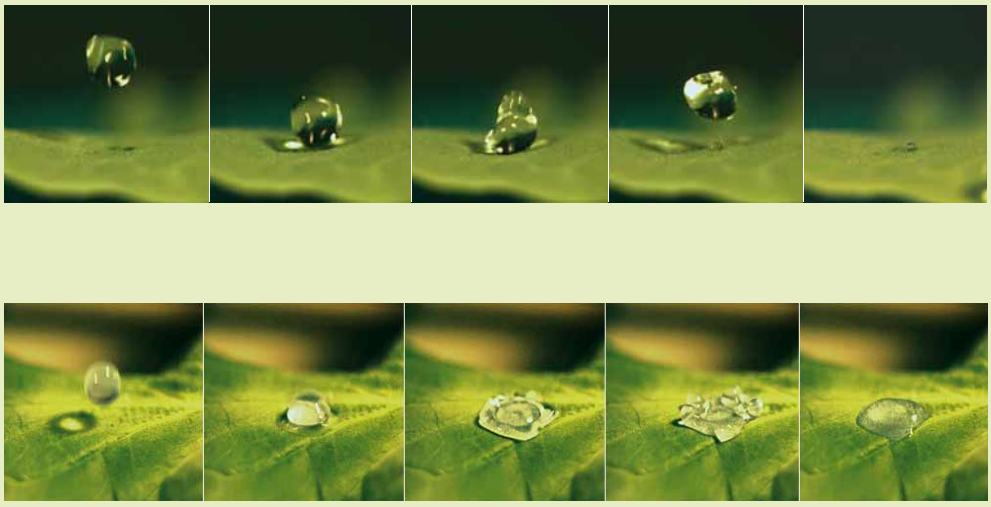
A good formulation consists of numerous substances contained in the pesticide in addition to the active substance itself. Dispersants, for example, ensure that the farmer has to do very little stirring when diluting the product, while emulsifiers ensure even distribution of the product in water. Other substances make the mixture last longer, or prevent it from becoming lumpy and so blocking the nozzles. In addition, there are adjuvants which help the active substance on its journey to its target. These affect droplet size and deformability or make it easier for the pesticide to coat a leaf. "The climate in which the products are used also affects their success, as do the types of fertilizer and other additives which farmers add to the spray mixture," explains Baur. "We also have to consider whether the product is applied from the air or on the ground."

Finding the most effective mixture of thousands of substances

Thus it can happen that the same active substance can be produced in completely different formulations for different applications or areas of use: droplets adhere easily to hairy tomato leaves or even smooth apple leaves, but if there are a large number of small wax crystals on the leaf, as in the case of barley, for example, all the water simply drips off. "Our fungicide Folicur is available for water-repellent cereals in a mixture with a special additive which reduces surface tension and at the same time promotes uptake through the leaves. For more sensitive fruit plants, on the other hand, we offer a variant which ensures delayed uptake of the active substance through the leaves," says Wolf.

In order to ensure that they always find the optimum cocktail, the scientists have collected an inexhaustible supply of adjuvants. "Our main tool is the many substances which we have got to know and value over the past decades," says Baur. Most of all, it requires a lot of patience and even more experience to select the right mixture from the thousands of potential substances. With meticulous attention to detail, the experts test new adjuvants over and over again in different concentrations and changing combinations. The Bayer formulators use two unique methods to accelerate this phase. Firstly they look at the treated leaves through a scanning electron microscope. "This allows us to watch what the preparations in the spray coating are actually doing on the leaf," says Pontzen.

The second process optimized by Bayer is used to evaluate the penetration of the substance through the repellent layer of the plant called the cuticle. Pontzen clamps the wafer-thin cuticle – less than one tenth the thickness of a hair – in a metal cylinder about the size of a thumb. He then adds some test liquid and measures at regular intervals how much active substance comes through the cuticle. Thanks to this standard procedure, technicians can compare potential products and quickly optimize them. Sometimes they are able to help penetration of the active substance with the use of special additives which soften the cuticle and sometimes they prevent penetration by ensuring that the active substance forms insoluble crystals. Both of these can be crucial: if a substance is intended to attack germinating fungal spores or mites by direct contact, it has to work on the leaf surface. If, however, it is intended to control insects



Slow-motion drops: crop protection agents are generally distributed on fields as aqueous solutions. When the tiny droplets land on the water-repelling surface of rapeseed leaves, they simply bounce off (top sequence of images) and do not reach their intended target, the site of action in the plant. To ensure that the agent remains on the plant, Bayer scientists mix it with special substances that cushion the fall or reduce the surface tension. This ensures that the spray mist droplets remain firmly attached to the leaves (bottom sequence of images) and generally also coat them to a large extent so that the active ingredient can quickly penetrate the plant. It then travels to all parts of the plant via the sap. The more effectively this is done, the less crop protection agent the farmer has to spray on his fields.

which suck on the plants – aphids for example – it has to penetrate the plant and be distributed through the plant as well as possible via the sap.

At the end of the optimization process, there is always the practical test. "Extensive biological screening in the greenhouse, in which the specific effect is tested, is followed by numerous field trials to find the best formulation. Especially important here are trials under extreme conditions, as it is then in particular that optimized formulations display an improved biological effect," explains Wolf. An effect which gives hope for the future: in view of the world-wide shortage of agricultural land and the constantly increasing population, it is becoming more and more important to provide optimum crop protection even under extreme conditions. Thus today's formulation technicians are already working on tomorrow's problems – a genuine advantage over rocket scientists, who cannot practice the colonization of distant worlds in advance.

http://hcs.osu.edu/hcs300/
This link contains general information about plant biology.

Checking success: biology lab assistant Sascha Teitscheid (left) and laboratory technician Nicole Enders check a vine scheduled to undergo spraying with a crop protection agent in the laboratory.

Wafer-thin protection

Some crop protection agents need a special formulation to be able to penetrate the leaf. This is because the outer layer of cells – the epidermis – is covered by a wafer-thin, water-repellent membrane called the cuticle. The cuticle is generally only about a micrometer thick and its task is to protect the plant against water loss through evaporation via the leaves. This makes the cuticle an extremely difficult barrier for crop protection agents to penetrate. Scientists at Bayer CropScience use special formulations to help active ingredients quickly and effectively penetrate the leaf, or ingeniously encapsulate the active ingredients so that they remain on the cuticle for longer and can be released over an extended period of time. This scanning electron microscope image (small photo, 900-fold enlargement) shows a layer of spray on a cotton leaf with the typical rippled cuticle.