Fitness from Within:  
Nature-Identical Hydroxytyrosol

Fresh fish, lots of fruits and vegetables, a serving of walnuts every day and, most importantly, olive oil. People who regularly put these foods on their menu are following what is known as the Mediterranean diet – and making very healthy eating choices. What makes this a healthy diet is that these foods contain plant secondary metabolites, a category of substances that includes hydroxytyrosol. This antioxidant is much sought after as an active agent, and WACKER can now produce a nature-identical version of it via a new, patented synthesis route. The process improves purity with no unwanted byproducts, while keeping the content of the active agent at a defined level – opening up entirely new possibilities for manufacturers of nutritional supplements and cosmetics.

Healthy and fit with the Mediterranean diet

Thinly sliced carrots combined with layers of bell peppers and tomatoes, seasoned with olive oil and grated Parmesan – while certainly delicious, a colorful vegetable carpaccio like this also serves up a course of important vitamins, minerals and fiber. That eating an abundance of fruits and vegetables keeps mind and body in good shape is fairly well known, as is the promise of longevity that the Mediterranean diet offers. A large number of studies have put Southern European eating habits under the microscope and investigated physical health within these populations. What they have concluded is that the Mediterranean diet has a positive effect on our bodies – an effect due to the com-
Plant secondary metabolites ward off disease

Hydroxytyrosol is a powerful antioxidant...

...but is expensive in its natural form and difficult to produce

The solution: chemical synthesis

pounds these foods contain. Nutrition experts have been paying particularly close attention to the plant secondary metabolites in bell peppers, olives and the like, owing to the health benefits of these chemicals. Examples of what these “natural wonders” are supposed to do include protecting against cardiovascular diseases, diabetes and Alzheimer’s, strengthening immune system response, and inhibiting inflammatory processes.

Plant secondary metabolites – polyphenols, to be precise – include hydroxytyrosol, a compound that is among the most powerful antioxidants, protecting human cells from harmful oxygen radicals. Olives and olive leaves are the most common naturally occurring source of this substance. “There are already a few suppliers out there who obtain this active agent via extraction,” explains Dr. Sebastian Schuck, senior manager for business development at WACKER BIOSOLUTIONS, “and they sell it to manufacturers of nutritional supplements and cosmetics who use it in their product formulations.” Their olive extract, however, is a blend of a wide range of polyphenols rather than pure hydroxytyrosol. Olive harvests are also subject to seasonal fluctuations, which affects more than just the composition of the product ingredients – it also has an impact on the price of these valuable extracts.

Nevertheless, demand for this health superstar is on the rise, which gave WACKER experts an idea: “We follow trends on the nutritional-supplement market very closely, of course. That’s what got us to thinking about developing a synthesis route for making hydroxytyrosol – a method that could supply the market
An efficient process...

...independent of harvests and weather...

...yielding high purity and quality

with this coveted active in large enough amounts and at high levels of purity," Schuck recalls. No sooner said than done. Within just a year and a half, WACKER researchers had managed to prepare a nature-identical hydroxytyrosol – a feat that included selecting the most suitable synthesis route, scaling up the process and ultimately submitting a successful patent application.

That these chemists were able to develop a route in such a short period of time was primarily due to the enormous treasure trove of experience that has been gained over a great many decades in the laboratories at the main plant in Burghausen. And thanks to the new multistage synthesis method, the company now has a cost-effective process for manufacturing a highly pure form of the active. Because a great deal of expertise has gone into the process, Schuck can only reveal so much: “There are a lot of ways of synthesizing a natural substance – but, as far as we’re concerned, our researchers found the best, most efficient method currently available,” says the WACKER expert. Another advantage is that the route is based on commercially available raw materials and practical process conditions, ensuring that the compound can be produced on a large scale.

“Plus, we don’t end up with a mixture of natural substances any more – now we can directly produce metric tons of the molecule we want, without having to rely on harvests. Our hydroxytyrosol meets a precise set of specifications, and the quality is consistent and exceptionally high,” Schuck is pleased to report. And that opens up the possibility of other applications: the active is highly concentrated, making it suitable, for instance, as a nutritional supplement in more compact forms, such as tablets and cap-
The global market for nutritional supplements is growing. In addition, WACKER also hopes that nature-identical hydroxytyrosol – marketed under the name HTEssence® – will be more widely accepted among food manufacturers. “Cost pressures are especially high in that industry – and HTEssence® means we can offer these manufacturers a cost-effective, high-quality alternative,” Schuck points out. The food industry is the most important market for WACKER BIOSOLUTIONS, constituting 61 percent of the division’s sales. Experts estimate global sales of food supplements to be around 96 billion US dollar, a figure that rises to 112 billion US dollar when functional foods are taken into account. It is a promising market – and it is precisely the market that WACKER’s new, nature-identical hydroxytyrosol is intended to serve and, in so doing, expand the company’s functional ingredients business.

Hydroxytyrosol protects cells from free radicals...

Its unusually powerful antioxidant properties are what make hydroxytyrosol such an interesting plant secondary metabolite for use in foods and cosmetics. The compound is exceptionally good at capturing free radicals, which can damage our cells. At 45,000 micromol Trolox equivalents\(^1\) per gram, the oxygen radical absorbance capacity of hydroxytyrosol is nearly ten times that of green tea and over twice as high as that of coenzyme Q10. As Schuck notes, “That means that hydroxytyrosol protects human cells and blood lipids from oxidative stress – a key factor influencing the development of cardiovascular diseases.”

Also attributed to this active substance is the ability to strengthen...
immune system response, lower blood pressure, inhibit inflammatory processes, and exert a positive effect on the bones and joints – interesting properties that could be put to use in nutritional supplements or applications in sports nutrition, such as power bars or functional beverages.

The cosmetics industry, however, discovered hydroxytyrosol some time ago as a useful additive in products such as anti-aging formulations. “Hydroxytyrosol affects melanin production in human cells, suppressing dark pigmentation and making the skin lighter and more uniform. Antioxidants are also used for protecting the skin, where they counteract the aging process,” Schuck explains.

Light skin is particularly desirable for many people in Asia, which is why so many products there advertise a lightening effect. Pharmacies already carry a number of creams and lotions utilizing the active substance in olives in order to lighten the skin. Industry experts expect the market for these skin-lightening products to grow to some 20 billion US dollar by 2018. “Our HTEssence® is the perfect product for this market, since it doesn’t contain any undesirable byproducts or impurities at all,” Schuck observes. The substance will be sold as an odorless, water-soluble powder, although it will also be available in liquid form.

WACKER anticipates approval for HTEssence® by the end of the year. The company has already sent out samples of the product to a few customers for research and development purposes – and initial feedback on nature-identical hydroxytyrosol has put
Schuck and his team in a very good mood.

**Background Information on Hydroxytyrosol:**
A compound found in olives and olive leaves, hydroxytyrosol is a plant secondary metabolite – a phenol to be precise. Phenols and polyphenols are aromatic compounds present as bioactive substances in plants, where they produce color or flavor, or act as an antioxidant. Their considerable antioxidant power makes them interesting for the food and cosmetics industries: as free-radical scavengers, antioxidants prevent oxidative stress, which is associated with a number of diseases and signs of aging.

Antioxidants are present in many plants, but not all of these exhibit the same levels of activity – this is why hydroxytyrosol is considered so important: Olive oil polyphenols, which include hydroxytyrosol, are said to contribute to the protection of blood lipids from oxidative stress – a factor often linked to human aging and many diseases, including cancers or cardiovascular diseases.
A WACKER employee is filling pure, nature-identical hydroxytyrosol dissolved in water in a spray dryer. Thanks to the controlled production process, HTEssence® is free of allergens and pesticides and does not contain any unwanted byproducts or contaminants (photo: Wacker Chemie AG).

Spray-dried nature-identical hydroxytyrosol: The odorless, water-soluble powder HTEssence® is available in great purity and with a defined amount of active ingredient (photo: Wacker Chemie AG).
Ideal for cosmetic products: Hydroxytyrosol is able to influence the melanin pigments in human cells, so that the skin becomes lighter and dark patches disappear. As a free radical scavenger it can further prevent wrinkle formation and skin aging (photo: Wacker Chemie AG).

Note:
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The company in brief:
WACKER is a globally-active chemical company with some 16,000 employees and annual sales of around €4.48 billion (2013).
WACKER has a global network of 25 production sites, 21 technical competence centers and 52 sales offices.

WACKER SILICONES
Silicone fluids, emulsions, rubber and resins; silanes; pyrogenic silicas; thermoplastic silicone elastomers

WACKER POLYMERS
Polyvinyl acetates and vinyl acetate copolymers in the form of dispersible polymer powders, dispersions, solid resins and solutions used as binders for construction chemicals, paints and coatings, adhesives, plasters, textiles and nonwovens, as well as for polymeric materials based on renewable resources

WACKER BIOSOLUTIONS
Biotech products such as cyclodextrins, cysteine and biologics, as well as fine chemicals and PVAc solid resins

WACKER POLYSILICON
Polysilicon for the semiconductor and photovoltaic industries

Siltronic
Hyperpure silicon wafers and monocrystals for semiconductor components