

Producing biomolecules from plants: Artbiochem, Archena (Murcia), Spain

Vegetabology

Artbiochem is neither a new biochemical discipline nor a new artistic trend. It is the name of a Spanish biotech company dedicated to the production of enzymes and other biomolecules from artichoke.

In the south-eastern corner of Spain, on the shores of the Mediterranean, is the region of Murcia. For many visitors this region is synonymous with beaches, sun and holidays; and much of the regional economy is indeed based on tourism. But there is more to Murcia than buckets and spades. Over a thousand years ago, the Arabs found inland Murcia's real treasure, the fertile valley of the Segura river. For the Moors, an appropriate combination of sun, water and fertile land was the source of wealth and happiness. So they settled in Murcia, drained off the swamps and created a network of channels and dams

to bring water to every corner of the valley. The agrarian culture they inaugurated has, since then, marked the way of life and the character of the people of this region. In fact, Murcia is still one of Spain's main agricultural producers, and the fruits of its orchards are commonly found in markets all over Europe.

Tradition meets biotechnology

Artbiochem is a Murcian company in which this old agrarian tradition meets the modern techniques of biotechnology. Their goal is the purification and commercialisation of enzymes and other biomolecules

derived from plants, especially those cultivated in the area. Of these plants, they have focused their attention on the globe artichoke (*Cynara cardunculus*). According to Francisco Palazón, quality assurance manager of the company, the artichoke is a plant with potential, "beside its culinary and health promoting properties, artichoke contains a surprisingly high number of enzymes and molecules of potential interest. They are rich in diverse phenolic compounds, ranging from benzoic and cinnamic derivatives, to flavonoids and tannins. Among them, for example, the luteolin and the sylimarin. Many of these phe-



Francisco Palazón, of the Murcian biotech company Artbiochem, looking out for quality.

nols show antioxidant activity and could result a good source of dietary antioxidants or be used to preserve and stabilize the freshness, nutritive value, flavour and colour of foods. Artichoke is also a good source of inulin, a dietary fiber with prebiotic properties, and interesting enzymes like cynarases (endopeptidases with milk-clotting properties), polyphenol oxidases and peroxidases, with diverse industrial applications. Among all these artichoke molecules, by now Artbiochem produces inulin and peroxidases and keeps running research programs on some others”.

The A-(rtichoke) Team

Artbiochem is a very young company, founded in 2002. It was born as a spin-off (in fact the first spin-off) of the University of Murcia. Previous research carried out by the University showed that artichoke inulin (*Phytochem.* 66: 1476) and peroxidases (*J. Inorg. Biochem.* 94: 243) had unique properties and were abundant in the artichoke waste produced by the vegetable conserve industry. These findings prompted the company’s creation. A small group of experts in biochemistry, nutrition and enzymology began to develop the required industrial processes. They optimised purification methods and escalated them to industrial levels, then they acquired appropriate equipment and moved into new facilities, that were built for the company. Important economic support came from institutional funds, such as those of the Institute of Promotion and the Directorate General of Science and Technology of the Region of Murcia. Artbiochem’s web page claims that, “our aim is to repay these institutions their confidence in us in the form of clean biotechnology”.

The globe artichoke is a thistle native to the Mediterranean, where it has been cultivated and consumed from ancient times. The edible portion of the plant consists mainly of the involucre bracts and fleshy heart of the immature large floral head, the capitulum. Cooked in various different ways, artichokes are ingredients in many traditional Mediterranean dishes. Most of

the artichoke produced in Murcia is locally processed by the canning industry. The artichoke hearts are selected, boiled and bottled ready to eat. The raw material that feeds Artbiochem projects are the byproducts of this industry, consisting mainly of

From the beginning, Artbiochem has benefitted from the NEOTEC programme, organised by the Centre for the Development of Industrial Technology, CDTI (a Spanish public organisation under the Ministry of Science and Innova-



Photo: Artbiochem

Artbiochem’s business premises in Archena’s *Polígono Industrial ‘la Capellanía’* (roughly translated as *The Chaplaincy Business Park*).

bracts and stems. And there is quite a lot. Spain is, after Italy, Europe’s main producer of artichokes and Murcia churns out 45% of Spanish production. This means that the Murcian canning industry processes about 80,000 tons of artichoke a year.

80,000 tons of artichoke a year

“Well,” says Palazón, “it is like the dream of any biochemist made true: an abundant and cheap raw material which is not expected to become the limiting factor during the extraction and purification processes”.

Palazón adds: “However the yield of these processes is usually very low and they require huge amounts of plant leftovers. Recent innovations in our company make us able to process almost all the artichoke residue generated in our region”.

NEOTEC supports new technology-based Spanish companies with funding and counsel.

Squeezing the vegetable

Artbiochem’s facilities are located in Archena, a village at the heart (no pun intended) of the area that produces artichokes (see photo above). They consist of a 5,000 m² three-floor building, housing labs and administrative offices, and a 1,000 m² processing plant. The latter is like a supersized biochemistry lab with huge extraction tanks, centrifuges, chromatographers, freeze dryers and everything required for the large scale purification of plant products.

“Artbiochem is, in addition, quite a clean industry” says Palazón. “We reuse and revalue an industrial by-product. Our

extraction and purification processes are environmentally friendly. The solid residues we produce are recovered and reused as food for animals. The liquid residues are pre-depurated and analyzed before their final release”.

The Spanish company is relatively slimline. Artbiochem's staff consists of only 15 people; four technicians at the processing plant, three administrative assistants in the offices and four PhDs in the labs. The latter control the running processes and look for new products and production improvements. There are, in addition, four executives. Francisco Palazón is one of them.

Multi-purpose plant

Artichoke peroxidase is the company's first product. In nature, peroxidases are a crucial part in increasing a plant's defences against pathogens. These enzymes form a large family that catalyze the oxidation of a wide range of organic and inorganic substrates. This catalytic capacity has various industrial applications. In clinical biochemistry, for example, peroxidases are used in immunoassays (like ELISA) to detect viruses and other pathogens, or in coupled enzymatic assays to detect and quantify metabolites such as glucose and cholesterol in biological fluids.



Extraction of enzymes from artichokes at Artbiochem in Archena (Murcia), Spain.

Peroxidases have also been used in the elaboration of biotechnological and industrial products ranging from phenolic resins, adhesives, antioxidants, and antistatic and electromagnetic radiation protective materials to food colourings and biological detergents.

The most widely used peroxidase is obtained from horseradish. However, peroxidases with different properties are required



A field of peroxidase and inulin (otherwise known as artichoke).

in different processes. “The peroxidase isolated from artichoke by Artbiochem,” says Palazón, “is a highly glycosylated isoenzyme offering certain advantages in industrial applications where peroxidase is immobilized in bioreactors. It has an optimum activity at 60-70°C and high thermal stability, making it ideal for industrial processes at elevated temperatures. Its optimum pH is in the range of 4-6 with appreciable activity remaining at pH 8-9”.

Bioethanol venture gets started

In addition to peroxidase, Artbiochem's other major product is artichoke inulin. They call it (what a surprise!) “Artinulin”. Inulin is a storage polysaccharide present in significant quantities in certain commonly eaten fruit and vegetables, the artichoke among them. It has numerous applications. As a food ingredient, it acts as a dietary fibre with probiotic effects, since it reaches the lower intestinal tract undigested, where it promotes the growth of the gut's bacterial flora. This makes it suitable for diabetics. Inulin has also been shown to increase the bioavailability of calcium. The resistance of inulin to hydrolysis (both in the gut and bloodstream) make it a promising candidate material for the encapsulation of medicines to be delivered into the body and then undergo a process of controlled release.

“Artinulin,” says Palazón, “has a higher mean degree of polymerization than most of the other commercially available inulins. This makes it very suitable for the food industry. Artinulin may replace fats and carbohydrates from certain foods, not compromising its taste and texture and enhancing some of its nutritional properties”.

Service as an additional foothold

“By now,” says Palazón, “our main objective is to get our products into the international markets. This is also our main problem. It is very hard to compete with big companies and products that have dominated the market for many years”.

In fact research, and not production, is the main current activity at Artbiochem. The search for new applications, new products, new markets and new clients. As an additional foothold, the Spanish offer research and development as a service for companies and organizations that need to purify a protein or enzyme but lack in-house skills or equipment. Meanwhile, Artbiochem is also participating in a national project on bioethanol production.

“Biotechnological enterprises like this used to require huge investments and years of hard work with no income,” says Palazón. Fortunately, the company can count on the tenacity and enthusiasm of its founders and employees. “That keeps our project alive”.

RAFAEL FLORÉS