Drugs against cancer from whey and bacterial plastic

Plastic from bacteria

In 1926 French microbiologist Maurice Lemoigne observed that some bacteria are able to form granules inside their cells when environment becomes unfavorable. Such a "behavior" can be compared to bears gathering fat for preparation to hibernate during the winter time. Curious about his discovery, Lamoigne dag further and isolated the material that was enclosed in the granules He characterized it in terms of its chemical structure and found out that the material was built in the form of a long chain of identical repeating units – monomers – with its structure reassembling synthetic polymers. Lemoigne called this material polyhydroxybutyrate (PHB). Over the following decades, scientists have been answering questions on how, when and why bacteria accumulate this biopolymer and also learned how to produce it on an industrial scale. In the meantime, researchers discovered other similar polyesters with a range of various monomers – they have named these compounds polyhydroxyalkanoates (PHA).

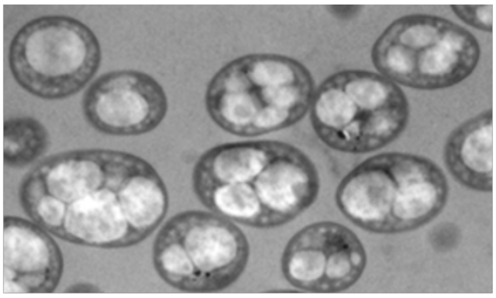

Figure 1 Dark grey bacteria with white granules containing PHA (source Biocatalysis Group, UCD)

PHAs found their uses in many industrial applications due to the magnitude of properties they have to offer and relatively easy production. For example, hard PHB is used to produce bottles, pens or credit cards. Other PHAs are very elastic or, in some cases, their consistency and stickiness even resembles this of the honey. These polymers have another undisputable advantage compared to conventional plastics – they are biodegradable! This means that a bottle made of PHB or a piece of paper fixed together with a PHA-based glue can be thrown into a compost hip and will disappear within 3 months.

The scientific world found interest in PHA to such an extent that these days it is not only polymers that are being studied, but also their constituents – fatty acids that possess an additional alcohol group in their structure. As mentioned before, up to this day around 130 different PHA building blocks have been discovered. These acids have been tested for their activity as surface active molecules (i.e. substances enhancing solubility of fats in water), medicines that kill unwanted microbes, or as in my previous lab in Ireland – anticancer agents. In Dublin we have discovered that attaching a PHA monomer to a peptide (a small protein) enhances its activity in killing cancerous cells..

Fight with cancer

Cancer affects more and more people and also becomes one of the most common cause of death globally. Having this in mind, scientists from all around the world constantly put their efforts in discovering new anticancer drugs. One of the many examples of these drugs are esters of fatty acids and sugars. Currently they are made mainly using chemical synthesis but these processes do not guarantee pure medicine. In our project we will use biological catalysts in order to produce the said esters.

Bio-catalysts – in our case enzymes – have already started displacing the traditional chemical counterparts in industrial production. Green catalysts offer environmentally friendly synthesis and production of only one ultra-pure product. Our research idea is to employ enzymes from the family of lipases, which in living organisms, including human beings, digest fats into fatty acids and glycerin, or, in other words, perform reaction of fats hydrolysis. For many years lipases have been used to produce biofuels. They are added to washing powders to aid in the removal of greasy stains. In certain conditions, these enzymes can perform a reverse reaction to hydrolysis – they are able to stick together a molecule of an organic acid to another, containing alcohol group (for example glycerin, ethanol or a sugar), thus creating a new ester bond.

From whey to anticancer drugs

In Poland we have a large and well-functioning dairy industry, which unfortunately generates huge amounts of liquid wastes – whey. Its surplus, which is still rich in lactose, is in most of the cases underutilized and is used as a feedstock for cattle. Thinking about these locally generated waste streams, and having in mind sustainable development of our country, we have chosen lactose to make sugar esters using lipases. We will test a range of enzymes originating from a variety of organisms thanks to which we will get several differently build esters made from lactose and monomers coming from bioplastics.

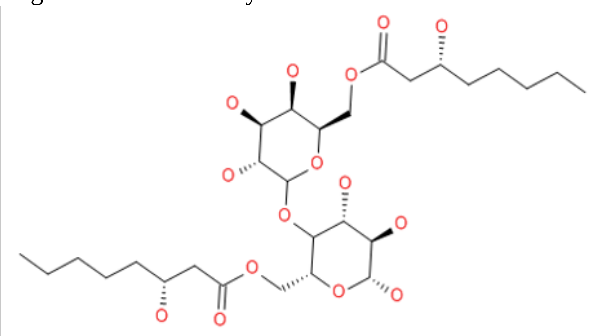

Figure 2 A molecule of a new drug – the middle part is built of lactose and the said chains come from PHA monomers

One may ask – why would we look into making such exotic molecules built from whey lactose and polyhydroxyalkanoates monomers? It is common knowledge that cancerous cells munch on sugars more greedily than normal cells do and our new compounds are built from a sugar. In addition, scientists have shown that, once taken up by a cell, sugar esters completely mess up their energy production system. On top of that, the Irish research has shown that an addition of a PHA monomer to an anticancer drug largely improves the latter's therapeutic effect. These facts provide quite an optimistic premise that we are on a right track to create not only a new drug to fight cancer, but also to equip the scientific society with methods for novel esters preparation and their characterization.