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dark horse

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There are many proteins crouching in the recesses of databanks whose role *in vivo* eludes researchers. Despite similarities of all kinds they may share with other proteins, they seem to have been designed for another purpose. A few of them may even have an unexpected function in an organism that does not synthesize them at all – much in the way a pair of scissors can be used to hammer a nail into the wall. This is precisely the case of a protein known as gamma-conglutin, found in the seeds of lupins. Unlike the majority of proteins in lupin seeds, gamma-conglutin does not seem to be used as a source of nourishment for seedlings. However, it does have an effect on sugar levels in our blood! Lupin seeds have been part of our diet in various parts of the world for centuries and their beneficial effects on our health long acknowledged. Today, thanks to technological advances, scientists are able to discern what is going on at the molecular level.



Lupin Hills, by Erin Hanson

Courtesy of the artist

Lupins are tall-stemmed plants with flowers of many colours that grow on almost any soil but – in the wild – mainly around the Mediterranean, in the Northern regions of Africa and across the American continent. They have been used as animal fodder, soil fertilizers and food in the Mediterranean and the Andes for thousands of years, and their medicinal and cosmetic use dates back to Hippocrates (400-356 BC) when they were mixed with honey, vinegar, goat galls or lemon juice to treat indigestion, appetite loss and sciatica, or to deal with pimples, scabs and scars left by small pox. The seeds of white lupins, *Lupinus albus*, were also of social value in Rome and used as counters or counterfeit money in games, and distributed to crowds on special occasions – the way we throw rice over the newly-wed in some parts of the world today. The catch phrase "Lupins for the people!" stems from these times, and is no doubt the source of one of Monte Python's Flying Circus sketches in which Dennis Moore (played by John Cleese) stops a coach and asks its occupants to hand over the lupins.

There are at least two hundred different species of lupins, though only a few are actually cultivated for animal fodder or soil fertilizers, and more recently for human consumption and the health industry. Besides lauding lupin seeds for their potential health benefits, scientists are beginning to consider lupin seeds of greater nutritional value than soybeans and, currently, 85% of the world's lupin crops intended for human consumption are grown in Australia. The protein content of a lupin seed ranges from 33 to 44% of its dry weight - which is similar to that of soybeans. However, there is less fat in lupin seeds than in soybeans, which makes them a good candidate for people suffering from cardiovascular disease for example. Furthermore, there seems to be a direct link between lupin seeds and glycaemia, which could help in the battle against diabetes.

Lupin seeds are packed with storage proteins, i.e. proteins that are degraded for seedling growth. There are two types of storage protein: albumins and globulins. Globulins outnumber albumins and constitute the bulk of seed storage proteins *senso* *stricto*. Based on their physicochemical properties, globulins are now classified into four different categories – the alpha-, beta-, delta- and gamma-conglutins – all of which have their structural and post-translational subtleties. Gamma-conglutins seem to dance to their own tune. Unlike their alpha-, beta- and delta-counterparts, they are very compact and apparently not hydrolysed for early seedling growth. In fact, their role in lupin seeds is not known.

On the molecular front, gamma-conglutins are made of two subunits - one large, one small - that arise from the same protein sequence. The two subunits bind to one another in one of two ways: one compact, the other less compact. These monomers of two subunits - then unite to form dimers, tetramers or hexamers, all of which are reversible depending on the surrounding pH. Why different gamma-conglutin oligomers exist, why they are reversible, why they do not share the same fate as the other storage proteins remains a mystery. Based on sequence comparisons, they show signs of having derived from hydrolase inhibitors or proteases that could have been involved in the plant's defence mechanisms or protein turnover, but they no longer present either of these activities.

What we do know, however, is that gammaconglutins are so tough they resist digestion in our gastro-intestinal tract and can cross into the bloodstream, where they are able to influence the level of glucose. How? Endomembrane vesicles could transfer them from the intestinal tract into the bloodstream. Once there, gamma-conglutins may monitor glucose level not by affecting insulin secretion itself but by binding to the hormone or to its receptor. What is more, as gamma-conglutins are low in fat, they do not add to body weight. Consequently, not only do gamma-conglutins help to regulate sugar levels in the blood but also fat – a godsend for those prone to diabetes and cardiovascular disease. The role of gammaconglutin in glycaemia begs the question: are there insulin-like hormones in plants that regulate sugar (sucrose) levels in sap? It is an intriguing notion but one that has met with much controversy, and the current answer is a big: no.

No one knows what gamma-conglutins do in lupin seeds, but they could become a source of functional food in that they have component parts that are beneficial to human health. This should not be cast aside light-heartedly in societies where diabetes and cardiovascular disease affect hundreds of millions of people worldwide, and treatment is costly. Leguminous plants such as lupins could help to keep these rates down, and perhaps even prevent the development of either disease in the first place. Some forms of diabetes and cardiovascular disease are genetic, but the great majority are due to years of sugar or cholesterol intake that is not healthy for the patient, and has been ignored or left undetected. Besides these afflictions, lupin seeds could become an alternative source of nourishment for humans whose population is growing exponentially while the globe's resources are evolving in the opposite direction.

Cross-references to UniProt

Gamma conglutin 1, Lupinus albus (White lupine) : Q9FSH9

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