Caroline Wood

Could purple tomatoes help us be healthier?

Key words
genetic engineering
cancer
superfoods

One of the greatest global health challenges we face is the obesity epidemic. In 2014, the World Health Organisation (WHO) estimated that worldwide 39% of adults over 18 years were overweight (with a BMI of 25+) and 13% were obese (with a BMI of 30+). This has led to a dramatic surge in the levels of non-communicable diseases such as type II diabetes, cardiovascular heart disease (CVD) and certain cancers. We've all heard that certain 'superfoods' contain compounds that can help combat these diseases, but these are often expensive and not accessible to everyone. If only everyday foods could be engineered to have these enhanced health effects... but thanks to genetic engineering, scientists have started to do just that, giving us purple tomatoes!

Our changing diet

When humans lived as hunter-gatherers, we would have consumed a much wider range of fruit and vegetables, whereas today our diets are heavily based on cereal crops (***Figure 1***). In fact, despite there being thousands of species of edible plants, just three crops – rice, wheat and maize – provide an estimated 60% of the world's energy intake. Yet as our dietary repertoire has shrunk, levels of obesity and its associated diseases have rapidly climbed. In fact, a lack of fruit and vegetables is ranked as the second highest risk factor for cancer in men, and the fifth highest in women in the UK (***Figure 2***). This is thought to be because plants produce many products as part of their natural metabolism that are beneficial for our health.

BMI (body mass index) is mass (in kg) / height (in m) squared

Andrew Davis, John Innes Centre

Figure 1 *A comparison between what our hunter-gatherer ancestors may have eaten (left) and our modern diets today (right), which are heavily based on cereals and animal products.*

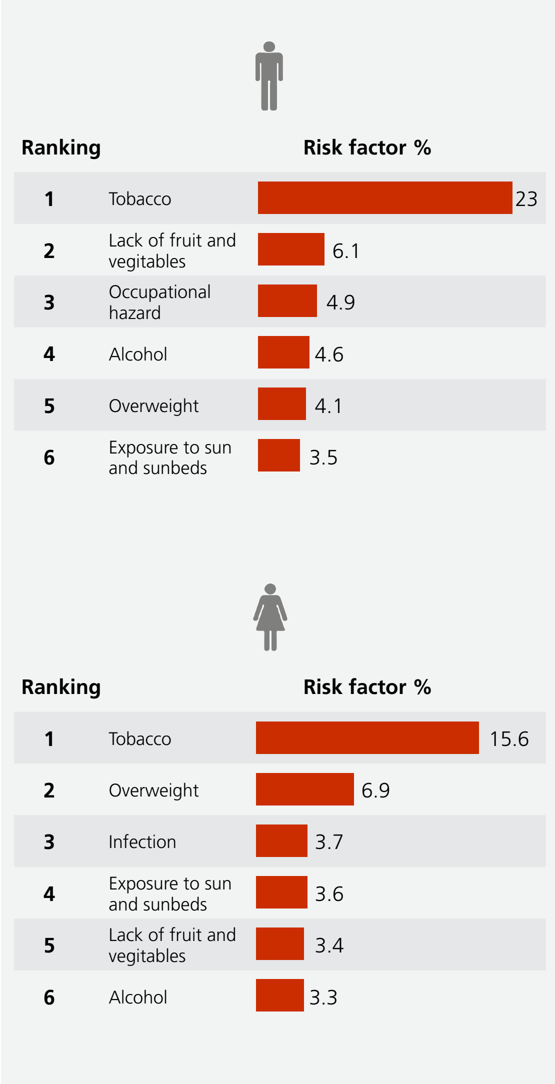

Figure 2 *The top six causes of all cancers in men and women in the UK. Source: Cancer Research UK*

Of particular interest are anthocyanins, a group of compounds found in red-orange and blue-violet fruits and vegetables. Epidemiological studies (studies of the distribution of diseases across different populations) have indicated that higher anthocyanin consumption is associated with decreased risk of cardiovascular disease, obesity and certain cancers. However, the foods containing high levels of anthocyanins – e.g. cherries, blackcurrants, blueberries and cranberries – tend to be expensive, and you would need to eat a lot of them every day to get a significant benefit. So, a group of researchers at the John Innes Centre in Norwich decided to use genetic engineering technology to see if anthocyanin levels could be increased in a more common crop that is easier to grow.

"We decided to use tomatoes because they are a very versatile food, can be grown in many places and are relatively easy to transform using GM techniques," says Professor Cathie Martin, a plant biotechnologist who led the study at the John Innes Centre for plant science in Norwich. A gene from snapdragon was introduced into the tomato plants that caused them to accumulate anthocyanins in the fruits, making them turn purple (*see Box above*).

How do you make a purple tomato?

Genes are typically divided up into different elements – the coding region, and a promoter which controls how they are turned off/on. The genes the scientists introduced into the purple tomato contained the coding sequences of regulatory proteins from *Antirrhinum majus* (garden snapdragon) that control anthocyanin biosynthesis, which gives the flowers their purple colour. These genes were driven by a fruit-specific promoter from tomato, so that they would be activated only in the tomato fruits and not in the whole plant, to make sure there were no side effects on the development of the tomato plants. The genes were introduced into the tomato plants using *Agrobacterium tumefaciens*, a species of bacteria that infects plants by inserting a segment of its DNA into the plant cell which becomes incorporated into the plant's genome. Researchers can use *Agrobacterium* to introduce desired genes into plants by cloning the gene into the segment of DNA which the bacteria transfer to the plant.

Will it work?

To test the health benefits of the tomatoes, the researchers used a genetically modified strain of mice that is prone to developing cancers. This is because they lack both copies of the *p53* gene which helps to control cell division. "Normally these mice only live for an average of 142 days," says Cathie. "But when we supplemented their diet with 10% purple tomatoes, their average lifespan increased to 182 days." Crucially, the mice didn't live significantly longer if they were fed a diet supplemented with 10% normal red tomatoes, showing that the benefit came from the anthocyanins in the genetically modified fruits (***Figure 3***).

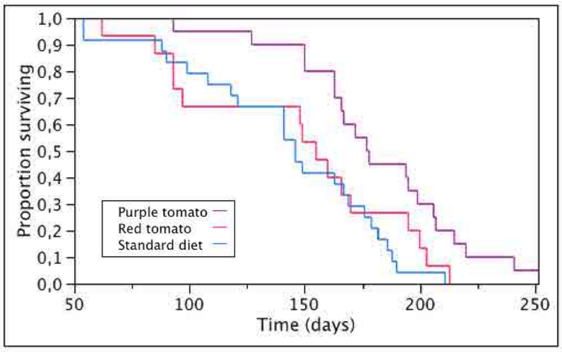

Figure 3 *Graph to show how the lifespan of tumour-prone p53-/p53- mice if affected when they are fed diets supplemented with either normal red tomatoes or high-anthocyanin purple tomatoes. Published in Butelli et al Nature Biotechnology 2008 doi:10.1038/nbt.1506*

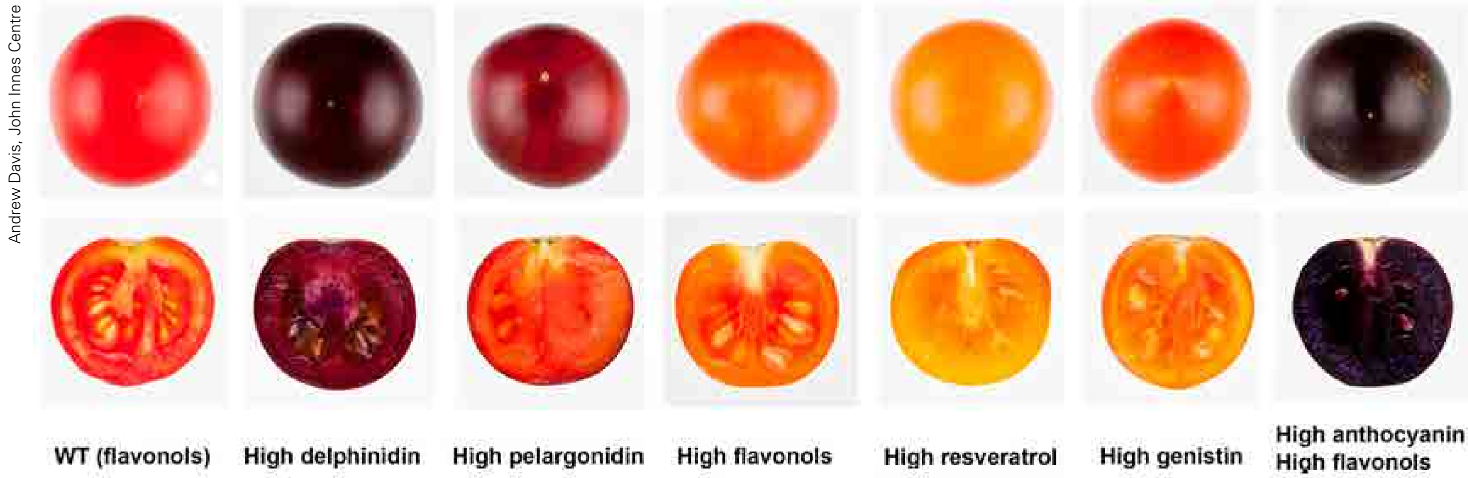

Figure 4 *A range of super-fortified tomatoes produced using GM technology. WT = 'Wild type' (normal)*

Since then, the researchers have used the same technology to make tomatoes that accumulate high levels of a whole range of beneficial compounds. These include flavonols: antioxidants that are thought to protect against cancer, cardiovascular disease and other age-related illnesses. In this case, the high concentration of flavonols makes the tomatoes turn orange (***Figure 4***). Another type of tomato has high levels of resveratrol – the 'miracle compound' that is supposedly the cause of the anti-ageing effects associated with moderate red wine consumption. In fact, just one GM tomato contains as much resveratrol as 50 bottles of red wine!

Given the strict regulations on GM foods in Europe, it could be a while before we see fortified tomatoes, or indeed other engineered crops, on our supermarket shelves. At the moment, purple tomato juice is being presented to the Food and Drink Association (FDA) of the United States to establish that it is safe to consume and can be marketed in the USA. Cathie believes that we shouldn't just rely on one or two "super foods" but instead make changes to our diets as a whole. "I personally don't see the future as being "eat all the junk food you like and take a pill or a special tomato at the end" she says. "Improving our whole diets is better for long term health." When plants have so much natural goodness in them, increasing our fruit and vegetable intake is surely one of the easiest ways to start to improve our health.

A fishy story

GM crops are also being explored for their potential to make fortified animal feeds. Omega-3 polyunsaturated fatty acids – particularly eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) - are widely known to have a crucial role in protecting against heart disease and also for developing a healthy brain and nervous system. One of the best sources of these is oily fish such as salmon, mackerel and trout. But these fish do not produce omega-3 fatty acids themselves; instead they accumulate up the food chain from marine phytoplankton that do make them – in other words, fish oils are not made by fish, but algae. Consequently, when oily fish are farmed, they are typically fed on fishmeal and fish oil made from smaller ocean fish, to ensure that the final product contains all the essential fatty acids and proteins. This puts pressure on wild stocks of fish.

Figure 5 *False flax (Camelina sativa) has been genetically modified so that it produces omega-3 fatty acids. The unmodified plant is already grown as a source of biofuel.*

But scientists at Rothamsted Research have used genetic engineering to alter the metabolism of false flax (*Camelina sativa* – ***Figure 5***) to make EPA and DHA. This plant naturally makes some shorter-chain omega-3 fatty acids: the researchers introduced a set of seven synthetic genes based on those present in marine phytoplankton to convert these into EPA and DHA. It is hoped that these plants could become a sustainable, land-based source of fish meal in the future.

Caroline Wood is a postgraduate research student in the Department of Animal and Plant Sciences, University of Sheffield.