The science behind slimming drugs

**Slimming drugs may seem like a straightforward solution to weight loss, but how do they work? And are they safe? Jennifer Trent Staves finds out**

Our mass is increasing. In 2013, 26 per cent of men and 23.8 per cent of women were classified as obese in England. Twenty years earlier, obesity affected only 13.2 per cent of men and 16.4 per cent of women.

With busy lives, losing weight can be difficult – and the combination of exercise and a healthy diet can take longer than some would like.

Some people look for slimming pills to give them a quick fix to the problem. The pills work in many different ways and on different parts of the body.

They can also have dangerous – sometimes lethal – side-effects, so it's important that they are taken only with advice from a medical professional.

**Reducing fat absorption**

When you eat, your pancreas produces lipase enzymes that break down the fat in your food so that the duodenum can absorb it.

One type of slimming drug essentially blocks your body from breaking down and absorbing these nutrients. The most popular drug of this type is called orlistat, a competitive inhibitor of lipases. Orlistat, which is available in prescription and non-prescription forms, prevents the enzymes produced by your pancreas from doing their job. Small amounts of fat can still be absorbed by your body – but the rest of it passes through your body.

You don’t have to cut down the amount of food you eat while you’re taking orlistat, but the less fat you eat, the fewer side-effects you’re likely to encounter. One of the most commonly reported side-effects is oily poo, which is essentially all of the fat your body didn’t absorb. Your body will also have trouble absorbing other nutrients, such as vitamin A, vitamin D, vitamin E, and vitamin K.

Orlistat can be used over a long period of time, in combination with diet and exercise. Weight loss with orlistat has been found to be 50 per cent higher than weight loss while taking a placebo.

**ABOUT THIS RESOURCE**

This resource first appeared in ‘Fat’ in December 2015. Published by the Wellcome Trust, a charity registered in England and Wales, no. 210183. bigpictureeducation.com
Other drugs try to do a similar thing. For example, laxatives try to loosen up the poo in your system and increase the number of times you need to go to the toilet. The idea here is that your body has less time to absorb the food you’ve eaten. But they do not specifically target the fat in your food, so much of the weight you will lose is water – and the side-effects can be very painful. Laxative abuse, where laxatives are used frequently in an attempt to lose weight, can lead to permanent damage to the colon and severe dehydration, which can be fatal.

**Telling you to stop eating**

When you’re full, your gut sends messages to your brain so you know to stop eating.

This state of feeling full – known as satiety – is complex, involving hormones and other factors. For example, when you’ve eaten enough, your intestines release a hormone called leptin, which signals to your brain that you can stop eating for now. But these hormones can be muted by other physiological, psychological and environmental factors.

Some researchers are looking at pills that can mimic the effects of bariatric restriction, a surgery that reduces the size of the stomach, so that you feel fuller sooner. One company has created a so-called ‘smart gel’ that fills your stomach.

Another pill that can be bought over the counter (without a prescription) is called Appesat. It’s made from a seaweed extract. The substances in this pill expand when they reach your stomach.

These may help you to feel full, but if you struggle with stopping eating when you are full or get many cravings between meals they won’t help you lose weight.

**Telling you that you’re not hungry**

Other slimming pills work directly on the brain, rather than in the gut.

Sibutramine is a drug that was originally developed as an antidepressant. It increases the concentration of serotonin and noradrenaline in the brain by not allowing them to be reabsorbed by the neurons that released them. A side-effect of this is suppressed appetite. This drug was withdrawn in 2010 because of a high incidence of heart attack and stroke.

Fen-phen was another drug – also pulled from the shelves – that works in this way. It is a combination of phentermine, which blocks the reabsorption of dopamine, and fenfluramine, which increases serotonin.
Both of these drugs work like amphetamines (‘speed’), which also increase the concentration of dopamine in the brain. Appetite suppression (and the resulting weight loss) is a side-effect, but so are seizures, stomach pain and, in some cases, death.

Respiring fat at a higher rate

The rate at which you respire fat is down to a number of different factors, one of which is your metabolic rate.

Some drugs work by increasing your metabolic rate, so that you respire fat more quickly. While this might sound enticing to a bodybuilder or someone wanting to lose weight, it can have devastating effects. For example, in 2015, a 21-year-old student bought diet pills over the internet. The pills contained dinitrophenol, or DNP.

This chemical has long been known for its weight-loss effects, but it was pulled from the shelves more than 80 years ago because it was “not fit for human consumption”. The problem is that when your rate of metabolism increases, your body temperature rises. That may boost the respiration of fat, but it will also cause fever and dehydration. The young woman who took DNP ultimately died because her body became too hot and could not be cooled down. DNP has been linked to at least five deaths in the UK since 2007.

The future

So far, orlistat appears to be the safest slimming pill on the market, and other drugs similar to it are in development.

Is it possible to develop a slimming pill that doesn’t cause damage to the rest of the body? With obesity on the rise, researchers are certainly trying.

In 2015, a group of researchers at the Salk Institute said they have created a ‘fat-burning’ pill that doesn’t have to be dissolved into the blood like other appetite suppressants.

It works on the FXR protein, which our body turns on when we eat, causing the body to respire fat. These researchers have looked at how their pill, called fexaramine, can switch on FXR, but only in the intestines, and not in the liver, kidneys and adrenal glands. So far, fexaramine has prevented weight gain in a mouse model. Human clinical trials are next.

Another interesting idea is in RNA interference, where RNA inhibits the expression of a particular gene. Some studies have shown that knocking out a specific gene in mice keeps them from accumulating fat, even on a high-fat diet.
REFERENCES

- Health and Social Care Information Centre: Statistics on obesity, physical activity and diet
- Mode of action of orlistat (1997)
- MedExpress: How does orlistat work?
- Guardian: Woman dies after taking ‘diet pills’
- Cambridge Polymer Group: Smart-gel for non-surgical bariatric treatment
- The Brain from Top to Bottom: How amphetamines affect neurotransmitters
- NHS Choices: Warnings issued over deadly DNP ‘diet drug’
- Salk Institute: ‘Imaginary meal’ tricks the body into losing weight
- Nuclear receptor corepressor RIP140 regulates fat accumulation (2004)

FURTHER READING

- Guardian: DNP – the return of a deadly weight-loss drug

ABOUT THIS RESOURCE

This resource first appeared in ‘Fat’ in December 2015. Published by the Wellcome Trust, a charity registered in England and Wales, no. 210183.
bigpictureeducation.com