NUTRACEUTICAL PLATFORMS

Obesity: A New Role for Anti-Inflammatory Nutraceuticals

Immune and metabolic pathways have been shown to affect cell function in obese states. Anti-inflammatory therapies may be useful in inhibiting the engagement of these pathways.

by Coriander Stone

Classic inflammation is a well known occurrence in response to injury, infection or trauma, but what are the exact physiological processes that occur and is classic inflammation the same as the inflammation that occurs in obesity? As obesity is rapidly becoming recognized as an inflammatory disease, it may be interesting to look at how anti-inflammatory nutraceuticals could positively impact on this state.

Classic inflammation involves redness, swelling, pain and heat due to a rapid immune response targeted at the injury site. It serves to protect the area against further injury or attack the infection and usually, when the infection or injury have improved, the inflammation subsides and disappears; it is a rapid, acute response.

Metaflammation

In obesity, the inflammatory pathway is dysregulated and inflammation is of a different nature to classical. Obese inflammation has been termed "metaflammation," for the following reasons. The inflammatory trigger is metabolic and thought to be caused by an excess of nutrients – as weight loss reverses the inflammation. As fat cells start to grow with excess nutrient intake, they begin to behave abnormally and metabolic cells (adipose tissue) secrete cytokines called "adipokines," which mediate inflammation. These signals from metabolic cells damage metabolic homeostasis, leading to a dysfunctional response.

The major difference here is that this is a low grade, chronic inflammation that only resolves with weight loss. Increased levels of classic inflammatory cytokines such as TNF-α and IL-6 have been found in both obese mouse and human models – IL-6 is involved in whole body energy homeostasis as well as inflammation and appetite. In addition to this, not only is adipose tissue involved, but the pancreas, brain, liver and muscles have all been found to experience inflammation where metaflammation occurs.

The adipokines secreted also inhibit insulin signaling, which is why obesity is so intricately associated with type-2 diabetes. Nutrient excess stimulates multiple signaling pathways in metabolic cells to activate an inflammatory response, which in turn leads to insulin resistance and disrupts nutrient and energy metabolism. Metaflammation seems to respond particularly to nutrients from high fat and high carbohydrate sources. This is illustrated in figure 1. It is this metaflammation that causes obesity-related pathologies such as cardiovascular disease, cancer and other inflammatory diseases, and it is for this reason that tackling inflammation may be key to maintaining health.

Immune Response

When the immune response is triggered by adipose tissue over time, not only does it result in metaflammation, but the white blood cells and cytokines involved in the inflammation dysregulate the metabolic pathways. This results in incorrect signaling between hormones and an inability to accept satiety signals. So not only do obese people need more calories to maintain their basal metabolic rate, but the interference in hormonal signaling (namely leptin and insulin resistance) also feeds the obesity cycle. While many of the mechanisms are not yet understood, it is clear that it is an impossible vicious cycle, which needs several factors to help break it.

While it is unlikely that merely addressing inflammation would

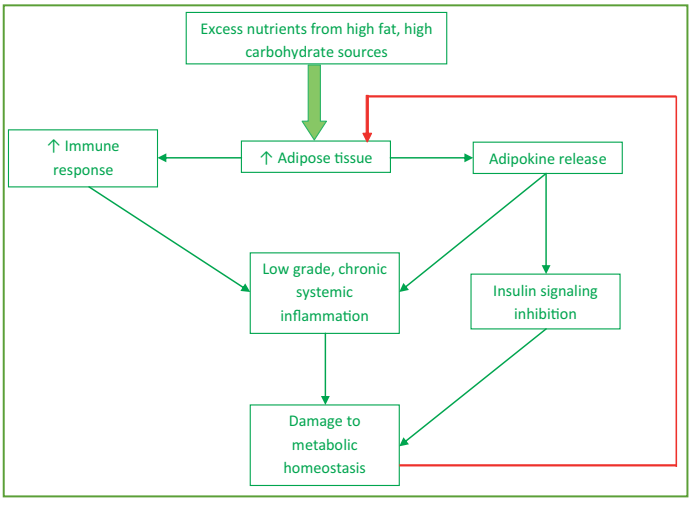

Figure 1: Metaflammation seems to respond particularly to nutrients from high fat and high carbohydrate sources.

› *The active component of the well-known Asian spice turmeric, has been shown time and again to be a potent anti-inflammatory.*

be enough to combat obesity, it is certainly an interesting and worthwhile approach. It is almost certainly effective alongside other weight loss strategies, in order to maintain a healthy weight and, above all, avoid the obesity-related pathologies which pose such a danger to health.

Combating Inflammation

While it is clear that there are several mechanisms in place contributing to metaflammation in obesity, there is another hypothesis. Nutrients of all kinds are naturally inflammatory, as they are considered foreign bodies. Therefore, whenever we eat food of any kind, there is some degree of inflammation. In lean people, this inflammation is usually resolved when the nutrients are metabolized, but in obese people this is not the case, as there are more nutrients being consumed, more frequently. It is just a hypothesis, but it is interesting that the first step in combating inflammation and reducing weight needs to be calorie restriction of some sort.

However, reducing inflammation alongside calorie restriction might be a worthwhile approach and has already had some interest in research. Reducing TNF-α has been shown to be useful in increasing insulin resistance and inhibiting IL-1 has also been effective in the same way. From a purely nutrient standpoint, the best way to reduce inflammation is to balance meals properly, reducing or eliminating sugars and animal proteins, increasing plant foods and natural antioxidants.

There are also a number of nutraceuticals which have been proven to be anti-inflammatories, some of which are discussed below. These may also be worth considering as part of the approach in combating obesity and its' related pathologies.

Omega 3 Fatty Acids: Omega 3 fats have long been shown to possess potent anti-inflammatory properties and have been widely studied in this respect. Mouse and human studies have shown a decrease in inflammatory cytokines and an increase in insulin sensitivity with omega 3 supplementation. They have also been shown to decrease the risk of cardiovascular disease and reduce triglycerides in type-2 diabetes.

Omega 3 supplementation seems to have the most effect in trials where inflammation is already present, whereas individuals with healthy biomarkers saw little difference. But this is also to be expected, as inflammatory markers cannot be reduced where there is no inflammation. In individuals with inflammatory conditions and those at risk of heart disease, levels of TNF-α, IL-6 and other pro-inflammatory cytokines were reduced. Since these are some of the most important and abundant adipokines, omega 3 may well be a very interesting therapy alongside calorie restriction in weight loss.

Curcumin: The active component of the well-known Asian spice turmeric, has been shown time and again to be a potent anti-inflammatory. Not only that, curcumin is also an antioxidant – necessary in all inflammatory disorders to "mop up" detrimental by-products, or waste, produced during the inflammatory process. Curcumin has also been shown to reduce the immune response in adipose tissue, making it a potentially important therapeutic intervention in the battle against obesity and its' related pathologies. Curcumin is readily available, not only as a spice for cooking but also as a standardized 95% pure curcuminoid preparation for therapeutic use and has not been shown to have

Table 1: Clinical Trials on Selected Anti-Inflammatory Nutraceuticals

Nutraceutical	Trial Design	Result
Omega 3	Single-blind, randomized placebo controlled trial with people over 60 years with heart failure were given 2g of omega 3 per day for 3 months.	Pro-inflammatory cytokines IL-6 and TNF-α were reduced and risk of future complications deemed to be significantly reduced.
	Randomized, double-blinded placebo controlled trial in diabetics were given 0.85g EPA and 3.4g DHA daily for 8 weeks.	Levels of triglycerides significantly reduced over 8 weeks although no change in inflammatory status. NOTE, 8 weeks would not be considered clinically sufficient time for these changes to occur.
Curcumin	Wild type and obese mice were fed either 3% by weight 95% standardized curcumin extract or normal chow for 8 weeks.	Curcumin significantly reduced glycemic status, insulin sensitivity, inflammatory markers and body weight.
Palmitoleic Acid	39 overweight and obese men and women were divided into insulin resistant and sensitive groups and were measured for palmitoleic acid levels.	There was no significant difference in plasma palmitoleate levels between the 2 groups.
	100 subjects at increased risk of T2 diabetes had plasma palmitoleate levels measured and insulin sensitivity was determined using oral glucose tolerance testing.	Circulating palmitoleate was associated with increased insulin sensitivity, suggesting its' positive role in insulin management.
Resveratrol	High fat diet fed mice were separated into 2 groups, with one supplemented with 0.4% resveratrol.	Resveratrol supplemented nice showed lower body weight and inflammatory cytokines.

› Natural Fertility & Conception Toolkit for Couples

Israeli company Fruitful Way Ltd. has pioneered a new, natural fertility and conception toolkit for couples who are trying to get pregnant. It includes a unique, science-backed dietary supplement, scientifically mated with a sophisticated fertility app. Of nearly 50 million couples struggling to conceive worldwide, almost half of them are trying to conceive their first child. A woman's fertility rate drops from 86% at ages 20-24 to 52% at 35-38. By age 45 (a time when more and more women are trying to conceive) fertility rates plummet to about 5%.

"Multiple risk factors impact fertility," notes Dr. Sharon Shmueli, Fruitful Family Practitioner. "These include: age, diet, stress, overweight, excessive alcohol, smoking and a stressful 21st century lifestyle. "Our fertility toolkit can help couples get pregnant naturally and safely," she says.

For couples living a busy, around-the-clock lifestyle, using the scientifically designed Fruitful supplements in conjunction with the Fruitful iPhone app can increase the chances for conceiving during the first 12 months of trying. "The Fruitful app uses proprietary technology, push messages and data sharing as well as daily reminders and assisting in define your fertility window," explains Dr. Shmueli. "It evaluates your status and helps you take control of the most important task of your life: getting pregnant."

The Fruitful fertility supplements help optimize and prepare the mother's body to conceive, and prepare the father's to make it happen. Each tailored supplement contains effective levels of scientifically backed healthy ingredients to optimize the process of getting pregnant and support safe conception and pregnancy.▼

any toxic side-effects. However, it should be considered that curcumin is generally poorly absorbed and that it is worth considering one either mixed with piperine – the major component of black pepper, or the extract known as BCM-95, which has been shown to more readily absorbed. Curcumin has been shown to significantly reduce both blood glucose levels and body weight after just 2 weeks treatment and may be a very interesting intervention in obesity.

Palmitoleic Acid: Also known as palmitoleate or omega 7, this fatty acid is a lipid-controlling hormone (lipokine) with insulin-sensitising properties and has also been shown to reduce the detrimental effects of inflammation, as well as regulate the metabolism of inflammation in obesity. It occurs naturally in animal, marine and vegetable oils, with some of the richest sources being macadamia nuts and sea buckthorn oil. Contrary to popular belief, nuts may actually help with weight loss rather than contribute to gain. It has already been used as an added ingredient to ready meals in the US military, with the prospect of increasing energy levels and reducing the risk of heart disease.

However, not all trials have shown positive correlation with insulin response in humans, so more study in this interesting area is required. It could well be an interesting intervention alongside other therapeutic techniques, as table 1 shows.

Resveratrol: Resveratrol is a natural polyphenolic compound found in fruit, nuts and particularly in the skin of red grapes. It is a potent antioxidant and anti-inflammatory, but its effects on white adipose tissue inflammation has not been widely investigated. However, initial studies show lower body weight gain, glucose, cholesterol and triglyceride levels in resveratrol fed mice, as well as significantly inhibiting pro-inflammatory cytokines, including IL-6 and TNF-α, suggesting its' potential benefits in inflammatory obesity.▼