

Nutritionals Nutraceuticals Functional Foods Dietary Supplements

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Nutraceuticals and metabolic syndrome

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Nutraceuticals is an area of pharmacology regarding food components or active ingredients that may be used as therapeutic agents. This includes a large number of compounds, such as an active ingredient, food supplements, and functional foods, as well as preparations based on medicinal herbs. Most compounds are vegetable originated, but there are also substances with animal origin (e.g., fish oil). Recent studies have shown promising results for these drugs in various pathological complications such as diabetes, atherosclerosis, cardiovascular diseases, cancer, and neurological disorders. These conditions involve many changes, including alterations redox state, and most of nutraceuticals have antioxidant activity with ability to counteract this situation. Hence, nutraceuticals are considered as sources of health promotion, and they, nowadays, have received a considerable interest.

Since nutraceuticals are generally considered like 'foods', their use does not strictly follow the same rules of classical drugs and have no patent protection. The process of market release for a drug is a very lengthy, starting from 'in vitro' demonstration of possible effects, followed by evaluation in animal models and then

in humans analyzing effectiveness and tolerability of therapies. Following approval and market availability, there is strict monitoring of side effects.

In contrast, nutraceuticals are used in therapy without relevant evidence. They might be involved in a wide variety of biological processes, but the mechanistic actions are not always fully clear and sometimes they are not, or not particularly robust, for the theoretical basis of their effectiveness.

Extensive research within the past two decades has revealed that obesity is a proinflammatory disease. Several spices have been shown to exhibit activity against obesity through antioxidant and anti-inflammatory mechanisms. Among them, curcumin has been investigated most extensively as a treatment for obesity and obesity-related metabolic diseases.

The tasks of essential nutrient selenium in the living organism are still not fully understood. The most important task is its important role in the functioning of glutathione peroxidase (GPx). GPx is an enzyme which is indispensable in the breakdown of various radicals and other metabolites (intermediate products of metabo-

lism). These are produced physiologically in the metabolism and occur particularly in physiological states. Without the enzyme GPx these waste products of metabolism would gradually destroy the cells in the body.

Carbohydrates will be in the news for their health effects for the indefinite future. While dietary fibre remains a mainstay nutrient, high fibre foods have not exactly been flying off the shelf. Carbohydrates are valuable part of our diet. They cannot be excluded without considerable amount of effort and health consequences. New research is showing that carbohydrates have a major role in both sugar and fat metabolism. Carbohydrate metabolism is far more complicated than the release of glucose as energy.

Research with one particular type of dietary fibre — unmodified resistant starch — is proving the importance of large intestinal fermentation to metabolism via insulin sensitivity than





anyone had previously theorised.

More often discussions regarding metabolic effects of carbohydrates are broken down into two chapters: digestibility and release of blood sugar in the small intestine and dietary fibre within the large intestine. It is as if there is a wall of separation between blood sugar and small intestinal effects and the large intestinal effects. We typically think of sugar consumption when we consider blood sugar management. For instance, if we eat less sugar, we will have better blood sugar levels, right?

However, eating fewer glycemic carbohydrates will cause less sugar to be circulating in the blood from that particular meal. There is evidence that consistently eating low glycemic food helps maintain healthy blood sugar levels over the course of one's lifetime. As we already know, food formulators have replaced high glycemic carbohydrates with lower glycemic alternatives for quite some time: alternative sweeteners and sugar alcohols have replaced sugar, while protein and fibres have replaced flour. However, lowering the glycemic response of one meal will not change the metabolism or the way the body manages blood glucose over the short run. The primary benefits are applicable to that one meal.

Over the past decade, there has been a growing awareness that bacteria and other organisms that live in our gut — called microbiome — are important. In addition to diet and exercise, certain gut bacteria are correlat-

ed with, and potentially contribute to, numerous health conditions. What we eat significantly changes the composition of the microbiome, as bacteria consume almost everything that ends up in the large intestine.

Thousands of researchers around the world are trying to unravel relationships not only between microbiome and health conditions — particularly in areas of obesity, inflammation and diabetes — but also between dietary components and microbiome. But since there are different bacteria species and other organisms that live in our gut, and our dietary consumption varies around the world, this is no easy task.

Research has shown that eating unmodified resistant starch changes the composition of the microbiome within the large intestine and actually improves how the entire body metabolises glucose and manages blood sugar. It consistently increases *Ruminococcus bromii*, among other types of bacteria. It also results in shifts in the profile of short chain fatty acids produced by the bacteria. These massive shifts in bacteria and fatty acid levels change the expression of hundreds of genes within the intestinal tract: some genes are turned on while others are turned off.

It is not clear which biomarker or combination of biomarkers is responsible for changes in the gene expression, as there is a lot happening in the intestinal soup. It is not like there is one pathway to target — there are literally thousands of pathways being impacted with changes in the intestinal food.

There are a variety of nutraceuticals with a potential lipid-lowering effect and therefore useful in the cardiovascular prevention. Nevertheless, in relation to scarcity of experimental studies, these molecules do not always have solid scientific evidence with

regard to both mechanisms of action and clinical efficacy. Data produced by small studies were often disavowed by larger and controlled studies or meta-analytic data. Some nutraceuticals are also able to enhance the action of the classic drugs, due to different mechanisms of action.

Finally, except for the red yeast rice, there are no clinical trials which may document the relationship between any of these treatments and the reduction of clinical events, and this represents a great limit in their reasoned prescription.

Different nutraceuticals may have different mechanisms of action. Based on different mechanisms of action, some nutraceuticals are then able to enhance the action of statins. Nutraceuticals are often used without relevant evidence: mechanisms of action are not clearly confirmed; most of clinical data is derived from small, uncontrolled studies, and finally, except for fermented red rice, there are no clinical trials which may document the relationship between these interventions and reduction of clinical events.

Therefore, among all nutraceuticals, it is necessary to extrapolate those having a really documentable efficacy. However, these kind of treatments are usually well-tolerated by patients. Overall, subjects with a middle or low cardiovascular risk are the best indication of nutraceuticals, but they may also be useful for patients experiencing side effects during classical therapies.

Finally, in consideration of the additive effect of some nutraceuticals, a combination therapy with classical drugs may improve the achievement of clinical targets. Thus, nutraceuticals may be a helpful alternative in hypolipidemic treatment and, if properly used, might represent a valid strategy of cardiovascular prevention. **INS**