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THE SCIENCE BEHIND ISAGENIX



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A WORD FROM THE CHIEF

Have you ever stopped to think about how many chemicals and toxins you are exposed to every day? Not just pollution outdoors, but in every space you enter—your house, a restaurant, the beauty salon, or the grocery store. While most of these toxins may be “harmless” in the short-term, chronic exposure and accumulation in our fat cells, as evidenced by large studies such as the National Human Adipose Tissue Survey, may lead to significant health complications.

Isagenix has been at the forefront of the research behind Cleanse Days for restoring, nourishing, and detoxifying the body since 2002. Now, new research findings discussed in this publication show that performing Cleanse Days may offer countless health benefits to the body. Not only do Cleanse Days help with detoxification, studies show they also support improved body composition, fat loss, brain health, and insulin sensitivity. No matter what your health goals are, Cleanse Days as part of an Isagenix system can help you succeed.

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Isagenix Chief Science Officer



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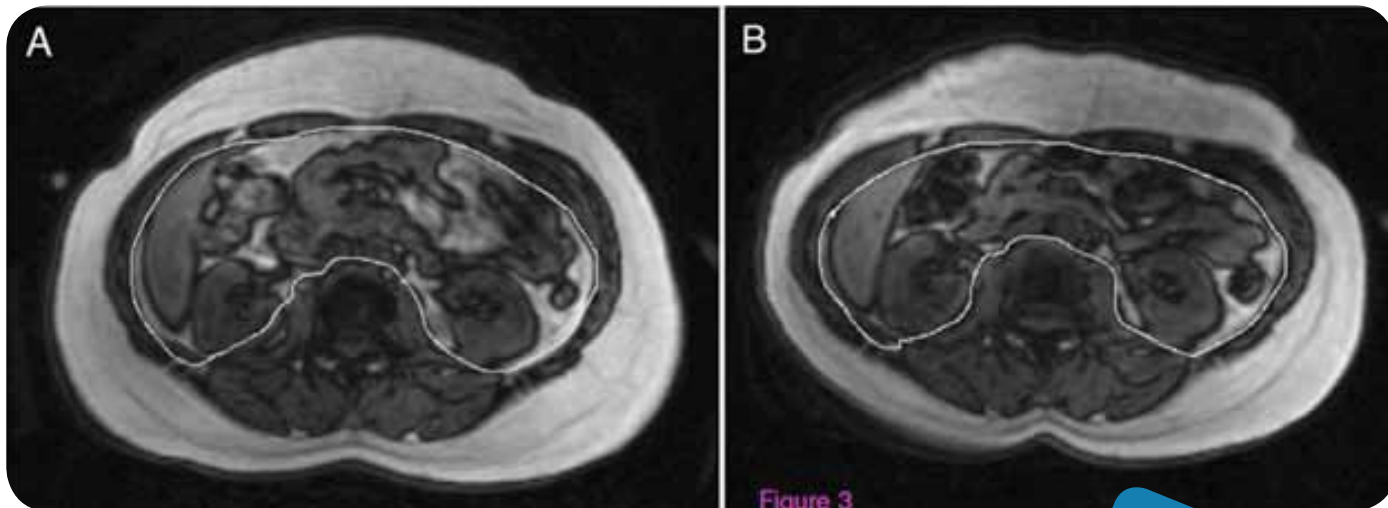
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UIC Study Earns Top Recognition at Scientific Conference

Isagenix is pleased to announce that the University of Illinois at Chicago (UIC) study that involved our Isagenix system is receiving excellent recognition within the field of nutritional science.

The UIC study's abstract won the American Society for Nutrition (ASN) Obesity Research Interest Section abstract competition. In addition, the study was selected for an oral presentation in April at ASN's annual meeting at the Experimental Biology conference in Boston.

Experimental Biology is one of the largest annual scientific conferences to take place in the world. The event brings together scientists and researchers from fields of anatomy, physiology, biochemistry, pathology, nutrition, and pharmacology to discuss strides and contributions in the field of science.

"It's very impressive that we won, considering the competition," said Krista Varady, Ph.D., assistant professor at the UIC College of Applied Health Sciences and the study's principal investigator. She explains that the abstract was chosen along with four others as winners among hundreds of abstracts submitted within the research interest section.

According to Isagenix Chief Science Officer Suk Cho, Ph.D., "It's exciting and an honor for these researchers to receive this type of recognition. The study with Dr. Varady is novel with quality outcomes that make winning this obesity research interest competition well-deserved."

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The 10-week study demonstrated clear, clinical validation for the use of an Isagenix system using Cleanse Days and Shake Days. The study showed superior results when compared with a “heart-healthy” dietary plan based on nationally recognized guidelines.

The Isagenix system led to a 56 percent greater reduction in average weight loss, 47 percent greater reduction in average body fat loss, twice as much visceral fat loss, and 35 percent greater reduction of oxidative stress. The study subjects also reported greater adherence on the Isagenix plan and that they considered it convenient and easy to follow.

The study’s results were published in two peer-reviewed journals, *Nutrition and Metabolism* and *Nutrition Journal* (1, 2).

Notably, the results published in *Nutrition Journal* include before (figure A) and after (figure B) cross-sectional abdominal scans (shown at the top of Page 3) of a subject who was in the Isagenix group in the study. When viewed side by side, there is a noticeable decrease in visceral fat—the fat that surrounds the internal organs—in figure B compared to figure A (the white area within the outlined section). On average, the MRI scans showed that the group taking Isagenix products lost twice the amount of

visceral fat when compared to those who followed a “heart-healthy” diet. The group also had reductions in subcutaneous fat—the thick white outer layer outside of the outlined section.

Nicholas Messina, M.D., former medical director and principal investigator of numerous clinical trials, recently praised the study for its randomized, double-arm design, as well as its appropriate inclusion and exclusion criteria and clear objectives.

“The bottom line is that this is a well-designed, scientifically sound protocol that was carried out at a major university research center by a skilled, published researcher. This was not the common observational study that is often seen when evaluating nutritional products,” Dr. Messina said.



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Science Behind Cleansing

Cleansing is one of the many reasons that Isagenix systems are different from other “diets”. In fact, diet is really the wrong word to use to describe Isagenix. We offer a collection of systems that can be customized to your own health goals and adopted as a lifestyle, meaning these are habits and tools you’ll have for the long haul. Cleansing is one of those habits within an Isagenix lifestyle.

Isagenix has been leading the way to health by advocating the practice of cleansing for more than a decade. Now, recent scientific findings are leading nutritional researchers to believe that this practice of “cleansing”—a combination of intermittent fasting with herbs and vitamins that support detoxification—provides surprising health benefits.

A body of evidence in both animals and humans has been steadily building to support cleansing in combination with herbal supplementation and calorie restriction as a foundation for weight control, appetite regulation, improved insulin sensitivity, brain health, cell and tissue maintenance, and detoxification.

WEIGHT CONTROL

One of the first things that people notice when they embark on Cleanse Days is the weight loss. Studies on intermittent fasting have shown that it is just as an effective approach for weight loss as compared to cutting calories (1). In one study, overweight women who fasted intermittently for six months lost more weight than women who restricted their calories each day (2).

RESET FOOD CRAVINGS

It would seem that after a day of not eating, one would be more likely to gorge on food when it was re-introduced. Not so. Evidence suggests that when intermittent fasting becomes a habit, less food

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is commonly eaten during normal calorie days (3). Some theories imply that this could be due to shrinking of the stomach on fast days so that you are less likely to overindulge at meal time. Along the same concept, Isagenix Cleaners proclaim that Cleanse Days practically erase any previous food cravings they used to have.

RESET INSULIN SENSITIVITY

Insulin sensitivity—how well insulin does its job of ushering glucose in the blood (after eating food) into the appropriate body tissues where it is used for energy—also looks to be “reset” by fasting. One study showed that healthy men who fasted for 20 hours every other day for 15 days had increased rates of glucose uptake, signifying improved insulin sensitivity and better blood sugar control (4).

BRAIN PROTECTION

Research on fasting’s effect on brain and mood has so far been done on animals, but the results are still promising. It appears that fasting stimulates the production of brain-derived neurotrophic factor (BDNF), which increases the resistance of

brain neurons to degeneration and preserves learning and memory (5). Fasting has also shown to be beneficial in the brain for stimulating growth of new brain neurons, called neurogenesis (6). When levels of BDNF increase, so do levels of serotonin, otherwise known as the “feel good” neurotransmitter (7). This could help explain why one study among aging men found that after two-day fasts, their moods and perceptions of quality of life were improved (8).

TIME FOR THE BODY TO GO TO WORK—ON ITSELF

One of the most important defense mechanisms the body has to guard itself against aging is a process called autophagy (8). Autophagy can be thought of as the body doing its own internal “housekeeping” so that all organ systems and processes continue to run smoothly. Old, damaged cell components are repaired or discarded so that cells can continue to function optimally. Autophagy in the body decreases as we age, so the body’s ability to self-help itself is reduced as well. Calorie restriction, including fasting, has been found to promote autophagy to repair the body’s cells

(9). It’s as if the consumption of fewer calories allows the body to rest and to go into repair mode. This has been proposed to be the reason why calorie restriction and fasting have an “anti-aging” effect.

DETOXIFICATION

Lastly, there is the detoxification that can take place on Cleanse Days. Often misunderstood, improved detoxification (or the increased efficiency of phase 1, 2, and 3 enzyme systems) while on Cleanse Days may be one of the most fascinating parts of the scientific story behind Cleanse Days—worth an entire article in itself. (Read more on Page 9.)

Isagenix Cleanse Days do more than just help you lose weight. As science has shown, cleansing benefits aspects of the entire body, helping it to repair, reset, and restore. By including Isagenix Cleanse Days in your lifestyle, you are committing to living healthier and for longer.

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UK's “Fast Diet”? Not So Fast



There's something oddly familiar about the premise of Britain's latest diet craze that is now reaching U.S. shores, wouldn't you think?

The Fast Diet, a UK best-selling book that has just been published in the U.S., promises that you can eat whatever you want, but still lose weight, and even live longer as long as you employ “intermittent fasting”. Ah, now you see the connection—Isagenix has been extolling the virtues of intermittent fasting as “Cleanse Days” for more than a decade.

The book outlines a 5:2 approach—unrestricted eating for five days of the week and two non-consecutive days spent fasting, which counts as 500 calories a day for women and 600 calories a day for men. That's somewhat similar to the Isagenix plan, which encourages adoption of Shake Days for five to six days and one or two Cleanse Days per week.

In their book, Dr. Michael Mosley and Mimi Spencer do a fine job building a case for intermittent fasting as a method for better weight-control, improved health, and even longer life. For example, they review the research produced by nutritionist Krista Varady, Ph.D., of University of Illinois at Chicago, who was the principal investigator for UIC's study evaluating Isagenix products. They also discuss the findings of Valter Longo, Ph.D., and Mark Mattson, Ph.D., that show calorie restriction and intermittent fasting in rodents can potentially protect the brain and increase lifespan.

HOWEVER, THE WEIGHT-LOSS PLAN HAS HAD CRITICS PUTTING UP THEIR WARNING SIGNALS AND FOR GOOD REASON:

Eating whatever you want (and as much as you want) has its consequences. One of the biggest negatives is the endorsement to eat without restraint for five days of the week. The book does propose some healthy eating guidelines, but with the main attraction being “Eat anything you want!”, there's likelihood that many people will live by those words. That kind of promotion is bound to be harmful as people are given license to grossly overeat and to eat the wrong types of foods as often as possible—think greasy hamburgers, French fries, and sugary sodas. Even two days of intermittent fasting can't undo a lifetime of making unhealthy choices like these.

Another problem is potential muscle loss. When the body is taking in fewer calories, it goes into what's called a catabolic state (meaning “breakdown”; the opposite is anabolic, which means “build-up”). Catabolism is fine for the breakdown of fat, but if calorie-deficient bouts are not followed up with the right type of muscle-building protein in the right amount, the result can be breakdown of muscle. Studies have found that during weight loss, a diet higher in quality protein preserves muscle mass more than a diet higher in carbohydrate (2). Research has also found that protein from dairy, such as whey, may be the superior protein for increased fat loss and muscle retention during weight loss (3).

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Then, there's the issue of complete nutrition. As we've mentioned many times in previous articles, most Americans already eat too much, yet do not receive adequate amounts of micronutrients (vitamins and minerals) from their foods for optimal health. Mainly, this is because too many people don't eat enough fruits and vegetables or may not know how to properly choose foods for adequate amounts of micronutrients. Even those who think they know what foods to eat in combination for better health haven't fared well in achieving weight loss and improved health. One study compared weight loss groups consuming either fresh, healthy foods for the majority of their diet or nutrient-rich meal replacement shakes and found that meal replacement shakes resulted in more weight loss, better improvement to health biomarkers, and better adherence based on the convenience of the shakes (4).

How can you take advantage of the benefits of intermittent fasting without the drawbacks of the 5:2 diet approach that include eating too

much, losing muscle, and not getting enough vitamins and minerals? Look to Isagenix for the perfect program that takes the guesswork out of intermittent fasting and how to do it right.

What you get with Isagenix is intermittent fasting combined with additional nutritional, antioxidant, and detoxification support in Cleanse Days, which are part of a fully guided system that won't leave you eating everything in sight one day followed by wanting to eat your arm off the next. An Isagenix system means moderate calorie control on Shake Days and appropriate fasting with nutritional support on Cleanse Days.

The Isagenix system, unlike the Fast Diet, is also backed by clinical data showing that it leads to healthy weight loss, fat loss (without the muscle loss, especially if exercise is

included), and better cardiovascular health. The end result is curbed food cravings, successful weight loss and maintenance, preservation of muscle mass, and finally, a long-term lifestyle that will keep you healthier than ever before.



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THE BASICS OF DETOXIFICATION

Whether out for a run, grilling your favorite meats on a hot summer day, or spring cleaning the house, our bodies are exposed to millions of chemicals considered “toxins”. These toxins in our environment (exotoxins) and that our bodies produce (endotoxins) have the ability to disrupt the essential biological structures needed for the body to function such as DNA, cellular membranes, and protein. Repeated exposure to various toxins can contribute to adverse health effects in the short-term such as headaches, nausea, and fatigue; and in the long-term can contribute to weight gain and chronic health outcomes.

Detoxification is essential for ridding the body of toxins and preventing their “health robbing” effects. Although all cells have the ability to detoxify toxins, the most important organ for detoxification is the liver—known as the body’s filter and purification system.

Fat Cells House Toxins

Toxins enter the liver as either water- or fat-soluble molecules. Water-soluble toxins are rather easily metabolized and excreted into the urine. In contrast, fat-soluble toxins can be stored in fat cells where they are protected from the body’s detoxification systems.

Excess fat stores, especially organ-bathing visceral fat, are linked to several diseases such as diabetes, cardiovascular disease, and metabolic dysfunction. The addition of toxin exposure to an overweight or obese individual may only serve to increase these risks (1).

Three Phases of Detoxification

There are three phases of detoxification (2). In the first step, the toxin is metabolized by phase I detoxifying enzymes resulting in an intermediary metabolite. Although there are several phase I enzymes, the most abundant and important are the cytochrome P-450s (P-450s).

During detoxification P-450s perform two functions: 1) they make toxins more water-soluble, and 2) they convert the toxin into a molecule usually less toxic and, therefore, less reactive towards our DNA, proteins, etc. (Interestingly,

sometimes this reaction converts a less toxic molecule into a more toxic molecule, which is where phase II detoxification steps in.) The result is a more water-soluble, less toxic molecule easily transported into the blood, through our kidneys, and out into the urine for elimination.

After undergoing phase I detoxification many toxins are then subject to phase II detoxification. At its most basic level, phase II enzymes place a water-soluble small molecule onto the toxin.

One of the most important phase II detoxifying enzymes is known as glutathione (GSH) transferase. As the name implies, the GSH transferases transfer a GSH molecule onto the toxin. Like phase I detoxification, this step also serves to make the toxin water-soluble and less toxic to the body.

Besides GSH, the body uses several other molecules to bind to the toxin and increase its solubility including sulfates, amino acids, and glucuronic acid. The use of these water-soluble small molecules makes sense considering that our cells have a surplus of these molecules inside or outside the cell. However, if we’re exposed to excessive amounts of toxins they could rapidly deplete our GSH levels resulting in too little GSH to do what it does best, which is to protect against free radicals and detoxify toxins.

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Finally, phase III of detoxification involves the elimination of toxins from cells. In this step, the products of phase I and II reactions are transported out of cells and into the bloodstream for elimination.

Proper Nutrition Essential for Detoxification

To ensure optimal functioning of our detoxification systems it is essential to have an adequate dietary intake of vitamins (B vitamins, vitamins C, and E), minerals (selenium, zinc, copper), and other bioactive nutrients such as coenzyme Q10 and polyphenols. These nutrients bolster our detoxification defenses either through their roles in phases I, II or III of detoxification or by providing antioxidant support (3). Nutritional support is essential in the detoxification process because some toxins are produced as the result of free radicals. Additionally, nutritional support is needed to counteract the oxidative damage caused by toxins.

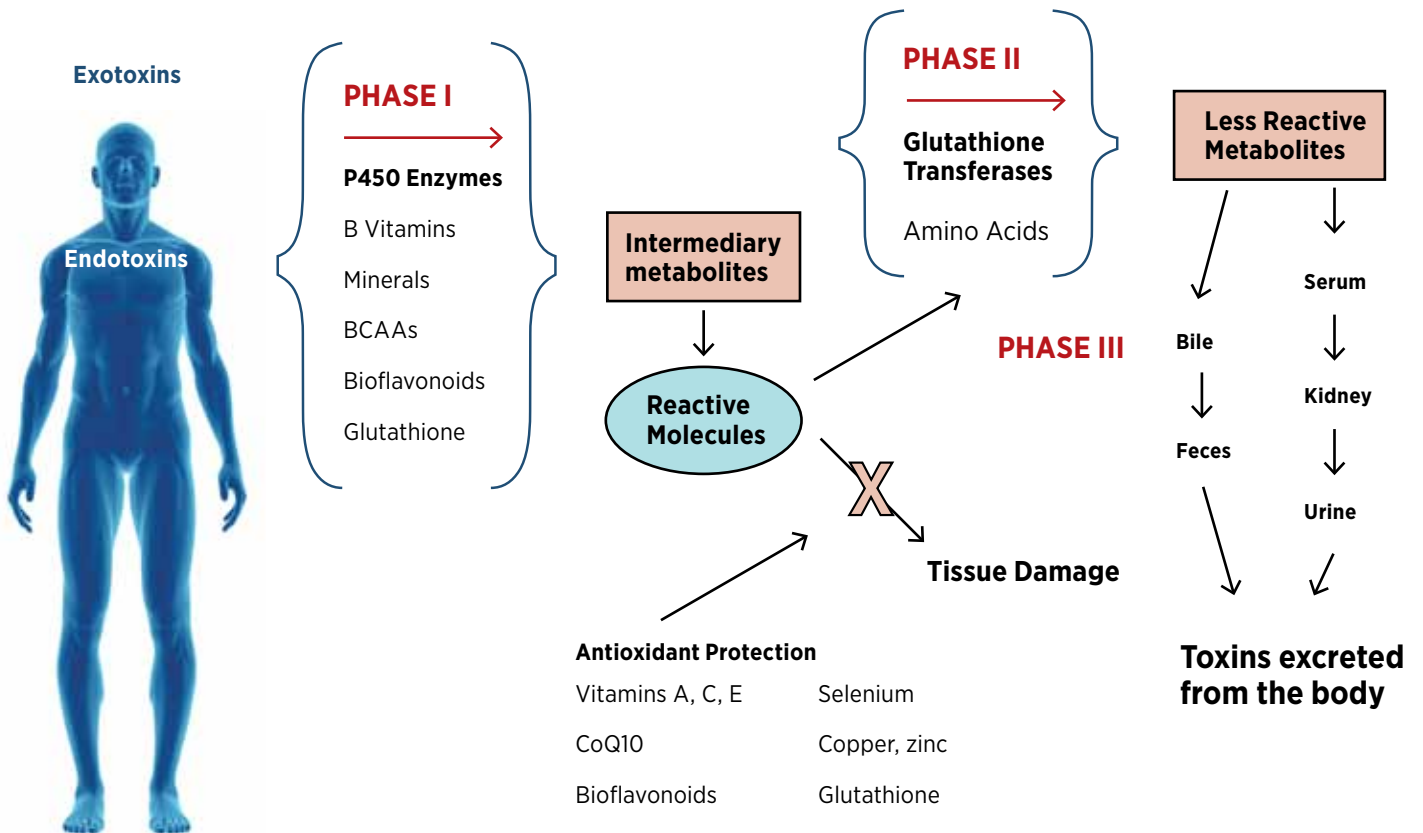
Plant botanicals including ashwagandha, aloe vera, and turmeric (Cleanse for Life), milk thistle (Product B), resveratrol, and other antioxidant vitamins and botanicals (Ageless Essential Daily Pak) have all been shown to improve detoxification. Beyond these micronutrients, the detoxification system also needs an adequate source of the amino acid cysteine, the sulfur-containing amino acid essential for GSH production. Luckily, cysteine is abundant in whey protein found in IsaLean Shakes, Bars, and Soups.

Calorie Restriction and Intermittent Fasting Stimulate Detoxification

Although not yet extensively examined in humans, subjecting animals to calorie restriction (CR) or intermittent fasting (IF) has also been shown to increase efficiency of detoxification pathways. The precise mechanisms responsible for the benefits of CR or IF on detoxification are unclear, but it's

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THREE PHASES OF DETOXIFICATION



Adapted from: Liska, DJ. The detoxification enzyme systems. Altern Med Rev. 1998;3(3):189.

thought that these two cleansing protocols “turn on” genes that increase synthesis of our detoxification enzymes within the phase I, II or III pathways.

Additionally, the reduction of fat mass—the primary target for toxin storage—stimulates the release of toxins into the circulation. Once in the bloodstream toxins are more easily metabolized and excreted from the body. When the body has the additional nutritional support of amino acids, vitamins, polyphenols, and other bioactive ingredients, the detoxification enzymes can perform at peak function.

The Isagenix system ingeniously incorporates both intermittent fasting on Cleanse Days and calorie restriction on Shake Days to help you burn fat and stimulate the release of fat-stored toxins. The polyphenol-rich nutrients and plant extracts found in Cleanse For Life provide plant-based antioxidant support (4-7) that supports the detoxification enzymes responsible for toxin elimination. Also, the whey protein in IsaLean Shake supplies essential amino acids such as cysteine that can boost GSH production (8;9) and facilitate toxin removal.



Collectively, the Isagenix system provides the perfect combination of nutritional support for optimizing your detoxification system.

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How Do Isagenix Cleanse Days Work?

Cleanse Days on the Isagenix system are periods of reduced calorie intake in combination with the nutritional support from **Cleanse for Life**. Evidence from the scientific literature shows Cleanse Days can help you reach your weight loss goals and provide many additional health benefits.



IMPROVE INSULIN SENSITIVITY: Improve regulation of blood sugar levels²

LOSE FAT: Melt away fat, especially deadly visceral fat that bathes internal organs³



ACTIVATE LONGEVITY GENES: Activate the expression of detoxification and longevity genes that play a role in healthy aging^{4,5}



RESET CALORIE INTAKE: Less food is commonly consumed after Cleanse Days suggesting a “reset” to the food intake center in the brain¹

BOOST MOOD AND PROTECT YOUR BRAIN:

Increase levels of brain-derived neurotrophic factor (BDNF) to protect and stimulate growth of brain cells, which is correlated with elevated mood^{6,7}



RECYCLE: Stimulate autophagy, the recycling of old and tired cells⁸



LOWER OXIDATIVE STRESS:

Shrinking fat cells leads to release of fewer inflammatory cytokines⁹

FAST FACT: Most fad diets such as water or juice fasting can put your body in a catabolic state that breaks down both fat and muscle.

By following Cleanse Days with the high-quality protein provided by Shake Days, you can burn fat and maintain muscle.

WHAT MAKES ISAGENIX CLEANSE FOR LIFE UNIQUE?

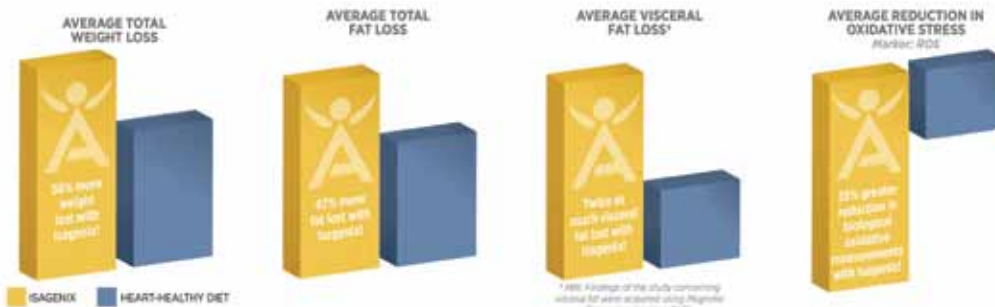
The polyphenol-rich nutrients and plant extracts increase efficiency of the enzymes responsible for toxin metabolism and elimination, especially when used in combination with intermittent fasting.

Unlike other “cleanses,” such as laxatives or diuretics that can deplete your body of nutrients, Cleanse for Life nourishes your body with vitamins, minerals, and botanicals.



THE EVIDENCE:

A recently published clinical trial has shown that Isagenix Cleanse Days (intermittent fasting with Cleanse for Life) along with Shake Days (calorie restriction with IsaLean Shake) are a winning combination for visceral fat loss.



For more information, visit IsagenixHealth.net

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