

## REPORT

### Critical Need For a Multi-Modal Approach to Combat Obesity

By Julius Goepf, MD

If we travel back to the early 1980s, a diagnosis of **AIDS** resulted in near-certain death within a year or two. The development of single-agent antiviral drugs provided HIV-infected individuals with only a brief reprieve. It was not until the implementation of **multi-modal** drug “cocktails” that HIV became a manageable disease.

The successful use of “multi-modal” therapy is by no means limited to HIV treatment. Cardiologists often prescribe **multiple** drugs (including prescription fish oil and niacin) that function via a wide range of **mechanisms** to restore the health of those stricken with severe heart disease.



Likewise, progressive oncologists long ago realized that successful cancer treatment mandated the implementation of **multi-modal** approaches to control malignant cell proliferation.

The scientific community now recognizes the role that **obesity** plays in the induction of age-related diseases and early death.<sup>1</sup> The lethal consequences of even a few extra pounds have led to public outcries that Americans have to shed excess fat.



In this article, we introduce a novel **multi-modal** nutritional strategy to remove **excess body fat** stores, especially in the **abdominal** region. Peer-reviewed scientific studies substantiate impressive results using the individual components of this program. This **multi-modal** approach is an important first step that overweight and obese individuals should initiate to achieve **maximal weight loss**.

A question middle-age people ask is why they amass so much body fat while eating *less* than when they were younger and thinner. Scientists have identified a number of biological factors to explain age-related weight gain, yet effective programs to restore youthful body contours remain elusive.

A major impediment to circumventing the *causes* of weight gain is the simple fact that there are so many causes. The encouraging news is that there are more scientifically documented weight-loss compounds to neutralize these *obesity factors* than ever before.

When used in controlled clinical studies, these compounds have demonstrated modest to impressive fat-loss effects. These same benefits are not always duplicated in real world settings. What has yet to be done, up until now, is combine scientifically validated compounds into a **multi-modal** program that circumvents *every* known factor involved in excess *age-related* fat storage.

#### THE AGE-RELATED DECREASE IN CELLULAR ENERGY EXPENDITURE

We know that one factor involved in age-related weight gain is a decrease in *resting energy expenditure* at the cellular level. What this means in simple terms is that we are not burning fat as energy and instead are storing it in our adipocytes (fat cells). Our bloated outer appearance reflects this *relentless* engorgement of surplus fat into our adipocytes.

Scientists have found that the **decrease** in energy expenditure with aging may cause **120-190 excess calories** to be stored in the body every day.<sup>2</sup> This translates to an **extra 13-20 pounds** of stored body fat each year.

Based on these data, the restoration of a more **youthful metabolic rate** is one critical factor in inducing weight loss in aging people. Fortunately, a patented **green tea delivery system** has been documented to **significantly enhance weight loss** and **reduce abdominal waist circumference** in humans.

As you will read, however, this remarkable new **green tea phytosome** delivery system is only one part of a **multi-modal** solution to do away with surplus **body fat**.



## THE MAKING OF A SUPERIOR GREEN TEA COMPOUND

A number of published studies demonstrate weight-loss effects in response to ingesting green tea or specific tea extracts. A problem identified early on is getting *enough* of green tea's active constituents absorbed into the bloodstream and delivered to cells throughout the body.

The key components responsible for green tea's weight-loss benefits are the *polyphenol* compounds that increase *metabolic energy expenditure* and hence calorie consumption.<sup>3-7</sup> Scientists realized that these *polyphenols* would be more effective if their absorption from the intestinal tract could be *increased* and thus deliver more of the metabolically active agent to the tissues.<sup>8-11</sup>



A group of Italian researchers created biological *complexes* of purified *green tea polyphenols* combined with *phospholipids*. This unique **green tea phytosome** was shown to increase the polyphenols' ability to be absorbed after oral ingestion and increase peak plasma levels of the critical green tea polyphenol *epigallocatechin gallate* (EGCG). After oral ingestion of an equal dose of EGCG complexed with phospho-lipids, the peak plasma level was **138% greater** than for EGCG alone! Furthermore, the total amount of EGCG measured over time was about **three times greater** for the phospholipid complex than for the free form alone!<sup>8</sup>

## DRAMATIC WEIGHT LOSS!

When this purified **green tea phytosome** was tested on human subjects, the weight-loss effects were rapid and substantial. This in-depth multicenter clinical trial involved 100 significantly overweight participants.<sup>8</sup> Half the group received the **green tea phytosome** (two **150 mg** tablets daily). Both groups were placed on reduced calorie diets (approximately 1,850 calories/day for men and 1,350 calories/day for women).

After **45** days, the control group lost an average of around **four** pounds. The group receiving the **green tea phytosome** supplement dropped an average of 13 pounds—more than **triple** the amount of the control group.

After **90** days, the results were virtually unprecedented! The control group that followed the restricted calorie diet alone lost **9.9** pounds. The **green tea phytosome**-supplemented group shed a total of **30.1 pounds**—again more than triple the amount of weight loss compared with the control group!<sup>8</sup>

## IMPRESSIVE REDUCTION IN ABDOMINAL CIRCUMFERENCE

Study subjects in the group receiving the **green tea phytosome** had a **12% decrease** in their *body mass index* (BMI) compared with only **5% decrease** in the diet-alone group.<sup>8</sup>

In the all-important measurement of waist circumference (abdominal girth), there was a **10% reduction** in the **green tea phytosome** group compared with a **5% reduction** in the diet-alone group. Male participants did even better in this category, showing a **14% reduction** in waist circumference compared with a **7%** reduction in the control group.<sup>8</sup>

## GREEN TEA DOES MORE THAN BOOST METABOLIC RATE

If increasing *resting metabolic rates* is all it took to remove excess body fat stores, today's obesity epidemic would largely disappear. We now know that this is only one part of a **multi-modal** solution.

Aging diminishes the ability of our cells to utilize even the *reduced* amounts of fats and sugars we ingest. This phenomenon is clearly demonstrated by the age-induced increase of glucose, triglycerides, cholesterol, and dangerous fat remnants in our blood. Simply stated, as we age, we have a reduced **metabolic capacity** to make use of the fats and sugars we eat throughout the day. The result is that our bloodstreams become chronically *bloated* with artery-clogging and obesity-inducing dietary byproducts.



A proven way to *reverse* the chronic **fat-sugar overload** in our blood is to impede its *absorption* from the digestive tract. While there are drugs that effectively do this, *green tea extracts* have demonstrated promise as inhibitors of fat absorption.<sup>12,13</sup> The ability of green tea to inhibit *absorption* of ingested fat calories may explain some of the observed vascular risk reduction that had been previously ascribed purely to its antioxidant effects.<sup>14</sup>

## HOW GREEN TEA INHIBITS FAT ABSORPTION AND FAT ACCUMULATION IN CELLS

French researchers released a landmark paper demonstrating that a **green tea extract** inhibited the breakdown of fat molecules in the digestive tract that enable these fats to be absorbed from the intestine.<sup>12</sup>

They found that green tea extract could inhibit fat-digesting enzymes in the stomach and small intestine in animal studies, concluding that **“green tea extract exhibiting marked inhibition of digestive lipases is likely to reduce fat digestion in humans.”**<sup>12</sup>

Researchers at *Rutgers University* demonstrated much more recently that these fat-absorption-reducing effects of green tea extracts could inhibit the development of obesity, the metabolic syndrome, and fatty liver disease in mice.<sup>15</sup> Korean researchers last year showed that *green tea extracts* could reduce weight gain in mice by impeding dietary fat absorption and by modulating activity of the gene target PPAR-*gamma*.<sup>16</sup> In another **2008** report, the same team demonstrated that certain *green tea extracts* prevent fat from accumulating inside fat cells.<sup>17</sup>

## REDUCTION OF OBESITY FACTOR BLOOD MARKERS

The new **green tea phytosome** demonstrated still other benefits that help to explain how it induced so much **fat loss** in the human study (**described on the previous page**).

In the diet-alone control group, total **cholesterol** dropped **10%** and **triglycerides** by **20%**. These reductions are expected in response to a reduction in calorie intake.<sup>8</sup> In the **green tea phytosome**-supplemented group, however, total cholesterol dropped **25%** and **triglycerides** by **33%**.<sup>8</sup>

As will be discussed in this issue of **Life Extension®**, an important element involved in successful *weight loss* is to purge excess fat (triglycerides) from the bloodstream. Study subjects taking this **green tea phytosome** significantly reduced their **blood levels of triglycerides** (and cholesterol). This may help explain the remarkable reduction of **30.1 pounds** of body weight experienced by those receiving this novel polyphenol compound most aptly named **TeaSlender™ Green Tea Phytosome**.

There has been a veritable explosion of research into how green tea extracts affect every aspect of obesity, from inhibition of fat breakdown and absorption in the digestive tract, to reduction in fat storage within cells, to enhancement of metabolic rate with concomitant increased energy consumption.<sup>3,16-18</sup> All of these benefits indicate an important role for green tea in helping to prevent the deadly *metabolic syndrome*, a constellation of disease risk factors that are often initiated by obesity.<sup>19,20</sup>

## HOW CARBOHYDRATES INDUCE WEIGHT GAIN

The weight-loss effects of blocking dietary fat absorption are not as profound as one might expect. One reason is that in the aging body, **carbohydrates** absorbed into the bloodstream are readily transformed into *triglycerides*, which is the primary form that fat is stored in the adipocytes.

The aging body develops a resistance to the ability of insulin to transport glucose into the body's energy-producing cells. This excess glucose promotes chronic secretion of **insulin** into the bloodstream (*hyper-insulinemia*), and chronically elevated insulin levels are associated with excess fat storage and degenerative diseases. As excess glucose accumulates in the blood, it is converted by an enzyme (*glycerol-3-phosphate dehydrogenase*) into triglycerides for storage in the adipocytes (fat cells).

Scientists refer to the chronic bloodstream-overload of sugars and fats as *postprandial disorders*. The term *postprandial* is defined as “after meal.” For significant and sustained fat loss to occur, one should reduce postprandial blood levels of both sugar (glucose) and fat (triglycerides).



# REPORT

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By Julius Goepp, MD

### IMPEDING CARBOHYDRATE ABSORPTION

Blocking the breakdown and absorption of carbohydrates are important points of intervention for losing weight. The objective is to target specific *enzymes* in the intestine, *before* calorie-rich carbohydrates enter the circulation.

Researchers at the innovative Integrative Medicine Program at the *UCLA School of Medicine* have been actively exploring this area, using extracts from the common white kidney bean (*Phaseolus vulgaris*).<sup>21</sup> The bean extract attains its effect by blocking the alpha-amylase starch-digesting enzymes in the intestine.<sup>22</sup> In order to validate this theory, a study was done where 27 obese adults took either a placebo or the *Phaseolus vulgaris* extract known to “neutralize” the amylase enzyme.<sup>21</sup> After eight weeks, those taking the white bean extract lost **3.8 pounds** in weight, and **1.5 inches** of abdominal fat. Other important benefits were observed in those taking the *Phaseolus vulgaris* such as a **three-fold reduction** in *triglyceride* levels compared with the placebo recipients. Suppressing blood *triglyceride* levels is often an important component of a long-term weight-loss program.



In another human study of *Phaseolus vulgaris*,<sup>23</sup> researchers discovered that those who consumed the most carbohydrates lost the most weight. Those study subjects consuming the highest levels of dietary starch and supplemented with *Phaseolus vulgaris* lost **8.7 pounds** compared with only **1.7 pounds** in the control group. Even more impressive was the **3.3 inches** of belly fat lost in the *Phaseolus vulgaris* group versus only **1.3 inches** in the controls. The conclusions showed that weight loss is attainable with diet modification, exercise, and behavioral interventions and it can be enhanced in people with high starch intakes through the addition of *Phaseolus vulgaris* to impede absorption of carbohydrate calories.

In a remarkable double-blind study on 60 overweight volunteers, half the study participants received **445 mg** a day of *Phaseolus vulgaris* while the other half were given a placebo.<sup>24</sup> Both groups were placed on a 2,000-2,200/day-calorie, carbohydrate-rich diet. After only **30 days**, those taking *Phaseolus vulgaris* lost **6.5 pounds** of weight and **1.2 inches** in waist size compared with **0.8 pounds** and **0.2 inches** in the placebo group.

These kinds of studies show the futility of trying to lose weight by restricting caloric intake alone, yet demonstrate remarkable effects when just one natural weight loss compound is combined with reductions in food intake.

### IMPEDING THE ALPHA-GLUCOSIDASE ENZYME

While inhibiting intestinal *amylase* enzyme activity has demonstrated some fat-loss results, it may be equally important to impede another enzyme needed for carbohydrate absorption called *alpha-glucosidase*.

European researchers working with extracts of several seaweed species found that extracts of the *Fucus vesiculosus* (bladder wrack) caused significant *reductions* in blood glucose eight hours after being given to rabbits.<sup>25</sup> Subsequent research has uncovered a host of health benefits from seaweed extracts, including powerful antioxidant, anti-tumor, and vascular health-promoting effects.<sup>26-29</sup>

Intrigued by these findings, researchers began exploring the antidiabetic properties of various seaweeds, including *bladder wrack* and *Ascophyllum nodosum*, also known as *brown algae*. What they discovered was that these seaweeds were capable of strongly inhibiting the carbohydrate-digesting *alpha-glucosidase* enzyme in rat intestines.<sup>28</sup> Given to diabetic rats in the laboratory, the extracts reduced fasting glucose levels significantly at 14 days and blunted the sharp rise in blood glucose (postprandial effect) following an oral glucose tolerance test. Interestingly, the animals also experienced decreases in total cholesterol and sugar-damaged (glycated) protein levels.

A proprietary combination of extracts from *bladder wrack* and *brown seaweed* known as **InSea2™** has been shown to help modulate dangerous *postprandial* sugar swings that lead to increased protein (glycation) damage, abdominal obesity, and food cravings that often come after a meal rich in carbohydrates.<sup>30-32</sup> While these results have not yet been published, they reveal important aspects of how these extracts may work to improve metabolic health, a critical component of achieving normal weight.



The formulator of **InSea2™** first conducted a series of studies to demonstrate the effect of the extracts on inhibiting the digestive enzymes, *amylase* and *glucosidase*. Both enzymes were powerfully inhibited within a few minutes of being exposed to the seaweed extracts. Additionally, they found that when **InSea2™** was fed to laboratory animals, glucose levels were reduced by up to **90%** following a meal compared with non-supplemented animals. Insulin levels (a measure of insulin sensitivity) were as much as **40%** lower in the **InSea2™** supplemented rats.<sup>33</sup> Clearly, this supplement may provide important benefits in reducing metabolic parameters that impact both systemic health issues as well as weight gain.

Upon further review of the study data, scientists found another interesting effect in the group supplemented with **InSea2™**. The normal response to an after-meal spike in blood glucose is a *surge* in **insulin** secretion. This insulin surge often causes blood glucose to be driven down too low. This can then create artificial hunger for more calories to elevate the depressed glucose blood levels. In lab animals taking **InSea2™**, the dramatic post-meal drop in glucose levels did not occur, and their glucose levels returned to baseline levels in a more gradual and natural fashion.

The after-meal drop in blood sugar produces a feeling of fatigue and can foster a sense of increased hunger leading to additional caloric intake. By “smoothing out” the postprandial sugar drop, **InSea2™** exerts both biochemical and behavioral benefits on overall calorie intake. In the researchers’ words, **“InSea2™ was able to change the absorption profile of a highglycemic index (GI) food towards that of a low-GI food.”**<sup>33</sup>

## THE MULTIPLE BIOLOGICAL EFFECTS OF *IRVINGIA GABONENSIS*

*Irvingia gabonensis* has been used in food preparation for millennia in Africa, where it is prized for its nutritional potential.<sup>34,35</sup> Based on its known therapeutic properties, scientists began to examine *Irvingia* extracts for their ability to achieve glucose control.<sup>36</sup> The researchers found that *Irvingia* supplements produced a reduction in plasma lipid levels, especially the dangerous very low-density lipoprotein (VLDL), LDL, and triglycerides.<sup>37</sup> The team went on to study *Irvingia*’s effect in rats, seeking to understand the molecular reasons for these impressive results.<sup>38</sup> What they found was that *Irvingia* produced a marked reduction in levels of a host of *amylase* enzymes, culminating in reduced absorption of glucose and concomitantly lower levels in blood and urine.

While *Irvingia* research continued to focus on its antioxidant and antimicrobial effects,<sup>39-42</sup> scientists began exploring its potential for combating obesity. The results of these investigations on weight loss and lipid control were eventually published.<sup>43</sup> In the first study, 28 people received the *Irvingia* supplement and 12 were given a placebo. All subjects stayed with their regular diets. After the month-long study period, the *Irvingia* group had lost **5.26%** of their body weight, whereas placebo recipients shed only **1.32%**. As in the older studies, supplemented patients, but not placebo patients, experienced decreases in total cholesterol, LDL, and triglycerides and an increase in HDL.

Stimulated by these findings of *Irvingia* in human trials, researchers set out to discover exactly how these effects were being obtained. They did this armed with new knowledge about the complex interactions of fat tissue in the metabolic processes, including its influence by, and on, various biochemicals involved in inflammation.<sup>44</sup> The researchers focused on three key elements: 1) a substance called *PPAR gamma*, produced by a gene known to contribute to human obesity; 2) the hormone *leptin* (which suppresses appetite and increases triglyceride breakdown in adipocytes); and 3) *adiponectin* (which reduces fat deposition).

Using fat cells from mice, the researchers examined the effects of *Irvingia* extract on these three important players in the obesity-generating process. After just eight days of treatment, the cells were found to have significantly reduced their production of fat stores. This result occurred in response to the inhibition of an enzyme (*glycerol-3-phosphate dehydrogenase*) responsible for converting glucose to stored triglyceride in adipocytes. This was accompanied by a decrease in expression of *PPAR gamma*, with a corresponding increase in the production of the insulin-sensitizing compound *adiponectin*. These were compelling results—as the researchers concluded that, **“[Irvingia] may play an important multifaceted role in the control of adipogenesis [fat production] and have further implications in in-vivo anti-obesity effects.”**<sup>44</sup>

Encouraged by these findings, the researchers progressed to larger human studies. In a recently published study in the journal *Lipids in Health and Disease*,<sup>45</sup> human subjects who supplemented with *Irvingia* enjoyed significant improvements in body weight, body fat, and waist circumference, while their plasma lipid, adiponectin, and leptin levels were all improved. Interestingly, supplemented subjects also experienced decreases in levels of the inflammatory marker **C-reactive protein**, which is a known cardiovascular risk factor.<sup>46</sup> Reduction of inflammation is now gaining the attention of scientists around the world as another

important component for controlling weight and metabolic disorders. The authors' conclusion is "***Irvingia gabonensis extract may prove to be a useful tool in dealing with the emerging global epidemics of obesity, hyperlipidemia, insulin resistance, and their co-morbid conditions.***"<sup>45</sup>

Perhaps one of the most consistent benefits of *Irvingia* supplementation was a *reduction* in **appetite** among study subjects. Avoiding over-consumption of calories remains a critical aspect of a science-based weight-loss program.

## SUMMARY

Scientists now recognize many biochemical pathways and control mechanisms that help regulate how we absorb, distribute, and expend ingested food throughout the body. With each new discovery we identify additional points for intervention that can tip the scales in favor of successful reductions in body fat.

Natural supplements whose mechanisms of action are clearly understood are available to help in controlling body weight. Used responsibly and in combination, these nutrients may complement one another and have the potential to yield maximum control over abdominal fat, obesity, and cardiovascular health.

Advances in our understanding of the causes of obesity are paying off on multiple fronts. While the nutrients described in this article provide many components of a **multi-modal** weight-loss program, we encourage members to carefully review all the articles in this month's issue to fully take advantage of today's wealth of knowledge about shedding excess fat pounds.

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