White Paper

SoZo®

A Platform of Antioxidant Science
White Paper #1

SoZo Global, Inc.

Empowering People Worldwide Through Superior Wellness Products

Research has shown antioxidants from fruits and vegetables exert beneficial effects that can help fight oxidation and its damaging downstream effects.

SoZo® Background

Free Radicals, Oxidation and Bio-rusting

To date, a large body of scientific research suggests that oxidation plays a central role in the initiation and progression of many chronic diseases.[1] Fruits and vegetables are a rich source of antioxidants that have been shown to counteract the effects of oxidation in the body. A correlation has been found between fruit and vegetable consumption and a decreased risk for heart disease, stroke, cancer, gastrointestinal issues, and eye disease.[2] Research has shown antioxidants from fruits and vegetables exert beneficial effects that can help fight oxidation and its damaging downstream effects.

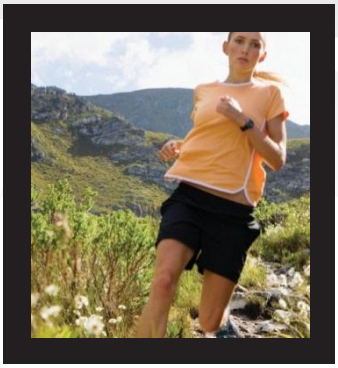
Oxidation plays a major role in the destruction and alteration of cells and cellular components if not kept under control.[3] Oxidation is caused by free radicals that are created endogenously by the body during various bodily functions or are ingested exogenously when consumed as part of the diet. Inefficiencies in dealing with oxidative stress caused by excesses of free radicals of various types can disrupt healthy cellular tissue and organ function.

Oxidation in biological systems (in the body) can most simply be described as a form of "bio-rusting", a chemical process that is similar to the chemical oxidation that occurs when metal rusts or when a match "burns". Free-radicals, highly charged molecules that circulate through the body, cause bio-rusting of a number of macromolecules important for the proper functioning of cells, tissues and organs. Free radicals are highly reactive chemical entities (molecules, ions) containing one or more unpaired electrons. Once formed, these highly reactive radicals can start a reaction chain that produces many more radicals. The process is known as a "radical cascade". In biological systems, oxygen free radicals, particularly superoxide radical-anions and hydroxyl radicals, are the most common and dangerous.

These molecules can do many types of damage to human cells and to human cell systems. Bio-rusted molecules create conditions that can lead to loss of cellular integrity, functionality and, ultimately, viability. Excesses of free radicals can even affect the proper function of DNA, RNA and their important associated proteins. Chronic and excessive oxidation, if allowed to continue unchecked, can initiate pro-inflammatory pathways that ultimately lead to degenerative diseases.

What are Endogenous Sources of Free Radicals?

Endogenous (internally generated) free radicals are produced within the cell and can be released into surrounding areas. The primary source of endogenous free radicals is the cellular energy-yielding "burning process" of various nutrients with oxygen. Endogenous free radicals are produced when: a.) cells metabolize oxygen in the mitochondria and free radicals are spun out as by-products; b.) cells are invaded by foreign (often toxic) compounds; c.) the immune system mobilizes to kill or deactivate foreign proteins, viruses, bacteria or parasites.



Plant-based phenolic compounds from fruits and vegetables are the best sources of exogenous antioxidants.

What are Exogenous Sources of Free Radicals?

Exogenous (externally ingested) free radicals are introduced to the body: a.) in cooked food (especially animal products and refined goods). Oxidized and hydrogenated oils can significantly contribute to free radical buildup; b.) in certain food additives (preservatives, colorings, etc.); c.) due to nutritional deficiencies; d.) by consumption of alcohol or by smoking (including passive inhalation of smoke); e.) from environmental pollution (from air, water, household chemicals, asbestos, pesticide residues and other man-made pollutants including plastics and other synthetics; f.) by exposure to excessive heat or cold; g.) by invasion of pathogenic bacteria and parasites; h.) due to chemotherapy, prescription drugs and over- the-counter remedies; i.) by exposure to various types of radiation; and j.) depression and other emotional stress.

Clearly, our bodies are under a constant assault by many oxidative agents. Generally speaking, most young and healthy bodies do a relatively good job of minimizing the effects of this onslaught of oxidation. As we age, however, our bodies often become less and less able to fight the build-up of oxidation and conditions of bio-rust begin to accumulate. Consequently, additional support may be required from a healthier diet and supplementation.

That's where antioxidants become important.

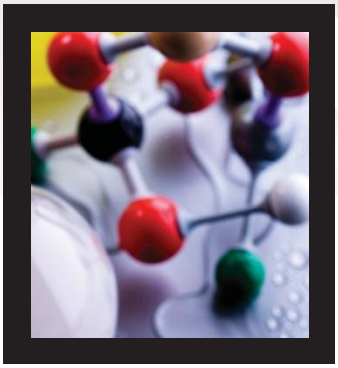
Antioxidants

Antioxidants are compounds that can reduce or even eliminate bio-rusting. Plants and animals maintain complex systems of multiple types of antioxidants, such as glutathione, vitamin C and vitamin E as well as enzymes such as catalase, superoxide dismutase and various peroxidases as part of their "natural" defense systems to combat oxidative damage. Antioxidants are believed to produce beneficial effects in the body by eliminating the causes of oxidative stress.

Antioxidants have been shown to fight oxidation through 3 main mechanisms: a.) by trapping free radicals; b.) by donating electrons and thereby neutralizing free radicals; and c.) by repairing damaged molecules. Detoxification of free radicals is another way the body protects itself against oxidative stress.

Plant-based phenolic compounds from fruits and vegetables are the best sources of exogenous (ingested from outside of the body) antioxidants. The high concentrations of antioxidants in these plant foods are believed to be one of the main reasons that diets rich in fruits and vegetables have been shown to lower the risk for development of numerous age-related conditions and diseases.

During their life cycle, plants generate an abundance of antioxidants in order to protect against the damaging rays of the sun and highly oxidative cellular processes such as photosynthesis. Understandably, plant antioxidants often accumulate in the brightly-colored skin of fruits and vegetables in order to protect the seeds of the plant.



Polyphenols are some of the most exciting substances in food nutrition research. This family of food components does not include vitamins or minerals, yet they have been reported to exert strong benefits for human health.

Our Consumption of Food-Based Antioxidants is Insufficient

Every major health organization recommends increasing fruit and vegetable intake to decrease the risk for most of the major diseases. It has been estimated that fewer than 25% of Americans get the recommended amounts of fruits and vegetables.[4] To make matters worse, many of the vegetables and fruits consumed today have been exposed to heat, light and air during processing and storage. All three of these elements can decrease the amount or effectiveness of various antioxidants found in these foods. Many antioxidants can also be removed during the processing of fruits and vegetables. Along with the many known beneficial compounds that are removed during food processing, many unknown compounds, whose beneficial properties have yet to be discovered, may also be destroyed or removed.

Nutritionists and other scientists believe that plant nutrients can exert a "synergistic" effect when all of the antioxidant components of food are allowed to remain together in the natural, original matrix of the fruit or vegetable rather than overly extracting and concentrating any specific compound. This synergistic effect may be increased by blending certain whole fruit and vegetable materials.

Some nutritionists would say that it may be short-sighted to believe that isolated nutrients could cover all the antioxidant needs of our bodies. Many isolated or synthetic nutrients have shown initial promise in the lab, but have often failed to show consistent or measurable benefits in subsequent human studies.

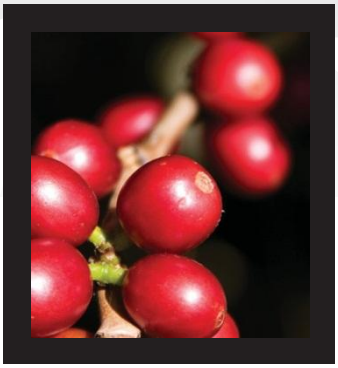
We Are Still Learning New Things about the Health Properties of Food

Science has yet to fully understand the entire story of how the food we eat affects our health. Over 100 years ago, we began to discover that food had many beneficial components. Around this time we discovered the macronutrients: carbohydrates, protein and fat. Later, we discovered essential minerals, vitamins, trace minerals, and recently, phytochemicals such as polyphenols. It is likely that numerous components of food have yet to be discovered. To ensure that all of these important known and unknown food nutrients are left intact, it is best to preserve as many components of food during processing as possible.

One of the biggest classes of phytochemicals, polyphenols, are some of the most exciting substances in food nutrition research. This family of food components does not include vitamins or minerals, yet they have been reported to exert strong benefits for human health. There are thousands of polyphenols found in nature, each exhibiting different properties.[5] Notable sources of polyphenols include berries, grapes/wine, olive oil, chocolate/cocoa, coffee, walnuts, peanuts, pomegranates and other fruits and vegetables.

The effects of polyphenols on health and disease are well documented. The evidence now suggests that polyphenols play a preventative role in major disease states such as cancer, cardiovascular disease and osteoporosis.[6] The research also shows that polyphenols may also play a role in preventing diabetes and neurodegenerative diseases.[7]

Specialized processing is needed to preserve these beneficial phytochemicals. Freeze-drying is one the best ways to concentrate and preserve the beneficial compounds in food.



Concentrated freeze-dried, "whole food" preparations have been created to help supplement diets that may lack adequate consumption of antioxidants from fruit and vegetable sources. These preparations are created using advanced processing designed to preserve the nutrients originally found in the fruits and vegetables.

SoZo®

SoZo is a polyphenol-rich nutritional supplement beverage that has been scientifically designed to incorporate a full spectrum of the most antioxidant-laden fruit and vegetable whole food powders and extracts available in the world today. SoZo is a hand-picked combination of well-studied freeze dried whole foods, fruit and vegetable concentrates, and effective, patented ingredients.

The following polyphenols and phenolic acids are present in SoZo:

Ellagic acid	Shown to be effective at preventing DNA oxidation[8]
Antocyanins	Shown to offer neuroprotective benefits and anti-inflammatory benefits[9]
Chlorogenic Acids	Shown to inhibit oxidation of LDL[10] (oxLDL is the most harmful form)
Proanthocyanins	Shown to have beneficial anticancer and cardioprotective properties[11]

SoZo contains the following whole food concentrates and patented ingredients:

Coffeeberry® whole coffee fruit extract – CoffeeBerry® whole coffee fruit is the king of the "superfruits". CoffeeBerry® represents the most exciting new development in coffee technology since freeze dried coffee crystals. This exciting patented and trademarked technology produces a one-of-a-kind coffee fruit extract that, in acute discovery clinical trials, has been shown to increase Peroxinase 1, (PON-1), a beneficial human blood enzyme that published research has associated with management of oxidative stress, oxidized LDL, longevity and severity of coronary artery disease. Whole coffee fruit is known to contain high levels of various isomers of chlorogenic acid, ferulic acid and trigoneline.

FruiteX-B® calcium fructoborate – Patented FruiteX-B is an exact mimetic of a naturally-occurring plant mineral complex commonly found in certain fruits, vegetables, nuts and legumes. The calcium fructoborate molecule contains the micronutrient boron. A body of science, including much research generated by scientists at the USDA has suggested that boron, in the form of boro-carbohydrates, is essential for proper functioning of many bodily systems, especially for the maintenance of healthy bones and joints. Due to the generally inadequate intake of fruits and vegetables in the Western diet, many individuals may be not be consuming adequate levels of these boro-carbohydrates or "borates". Emerging research suggests that FruiteX-B may support healthier levels of calcium and vitamin D.

VitaVeggie® high ORAC vegetable blend – A nature's basket of broccoli, broccoli sprouts, tomato, carrot, spinach, kale, brussel sprouts and onion extract; VitaVeggie all-vegetable

SoZo is a polyphenol-rich nutritional supplement beverage that has been scientifically designed to incorporate a full spectrum of the most antioxidant-laden fruit and vegetable whole food powders and extracts available in the world today.

One 3oz dose of SoZo delivers 360mg of polyphenols and 250mg of phenolic acids (chlorogenic acid derivatives)

antioxidant blend provides quality, high-ORAC antioxidants from vegetable concentrates plus a liberal helping of fully-intact whole vegetable phytochemicals from concentrated freeze-dried vegetable powders. A single gram of VitaVeggie provides 5000 ORAC units. VitaVeggie brings much more to the table than high ORAC values—it has also been standardized for specific glucosinolate and sulphoraphane levels producing a well-rounded robust blend that sets the industry standard. VitaVeggie has been shown to increase quinone reductase in liver cells. This enzyme is part of the phase II detoxification system of the liver that helps to rid the body of harmful substances that increase oxidative stress.

VitaGranate® pomegranate concentrate – VitaGranate is standardized to a very high content of antioxidants, particularly tannins and flavonoids. Research indicates that pomegranate may offer powerful support for improved coronary and cardiovascular health. The pomegranate has been reported to influence healthy inflammatory status, anti-oxidative conditions, and microbial status. Pomegranates have also been reported to reduce LDL oxidation and inhibit angiotensin coverting enzyme (ACE).

VitaBerry® Plus® high antioxidant fruit blend – A potent combination of wild North American blueberries, bilberries, grapes, grapeseeds, tart cherries, raspberry seeds, strawberries, cranberries, resveratrol and quercitin, VitaBerry provides a blend of high antioxidant berries chosen for their antioxidant content and potency that supplies a combination of the most powerful fruit antioxidant phytochemicals in order to deliver a diverse array of physiological benefits.

VitaGrape® high ORAC extract - Grapes are one of the few natural sources of resveratrol, a compound reported to be implicated in healthier aging.

The 2010 SoZo® Study

SoZo has gone through rigorous *in vitro* and *in clinico* testing to explore its beneficial properties for human nutrition.

SoZo Polyphenol Analysis

As part of the scientific development of SoZo, a complete chemistry analysis was conducted to determine the phenolic composition. One 3-oz dose of SoZo delivers 360mg of polyphenols and 250mg of phenolic acids (chlorogenic acid derivatives).

SoZo Free Radical Absorbance Capacity

SoZo also underwent free radical absorbance capacity testing. These tests were performed to find out the antioxidant capacity of SoZo. The most widely used form of antioxidant testing is the Oxygen Radical Absorption Capacity (ORAC) testing. This test has been used as a standard for understanding the antioxidant value of foods for over a decade. To gain a fuller picture of the antioxidant capabilities of SoZo, more comprehensive antioxidant testing was carried out.

The body undergoes oxidative stress from multiple free radicals on a daily basis. The most common free radicals and oxidants are superoxide, peroxynitrite, singlet oxygen and the

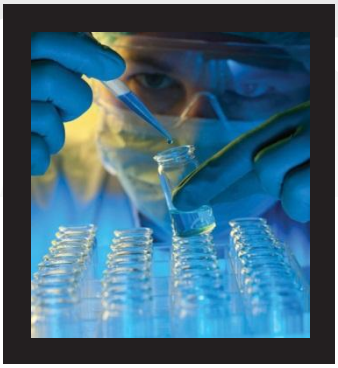
hydroxyl radical. Therefore studying SoZo's effects on multiple free radicals and oxidants will give a much fuller understanding of its antioxidant capabilities. SoZo was tested for Hydroxyl Radical Absorbance Capacity, Peroxynitrite Radical Absorbance Capacity (NORAC) assay, Superoxide Radical Absorbance Capacity (SORAC) assay, and Singlet Oxygen Absorbance Capacity (SOAC) assay, as illustrated in the chart below:

Free Radical/ Oxidant	Association with human health	Antioxidant Assay	Sozo Results
Hydrophilic oxygen radicals	Oxidative stress, inflammation, and aging	ORAC	10,292 µmole TE/Serving size
Hydroxyl radical	DNA damage and cancer	HORAC	31,032 µmole TE/Serving size
Peroxynitrite	Neuro degenerative diseases	NORAC	643 µmole TE/Serving size
Superoxide radical	Mitochondrial disease	SORAC	11,430 µmole TE/Serving size
Singlet oxygen	Diseases of the eye	SOAC	7,457 µmole TE/Serving size
		Total Antioxidant Capacity	**60,854 µmole TE/Serving size**

In vitro testing is beneficial for obtaining some initial understanding of how a compound may affect certain free radicals. *In vitro* tests, however, are conducted in test tubes outside of the body and often provide a limited scope of physiological relevance. Therefore, in order to obtain a fuller understanding of how (and if) a substance actually works in the body, it is necessary to conduct *in clinico* testing. Consequently, this study was set up as an acute, discovery study in order to find out for the first time what SoZo can do in the human body as measured by blood levels and activities of selected biomarkers and bio-targets.

SoZo Placebo-Controlled Double-Blind Study

Consequently, a placebo-controlled study was conducted to explore SoZo's effects on various oxidative blood biomarkers in humans. 20 men and women were randomly selected to partake in this double-blind study. All participants arrived fasted and were evenly assigned to be in either the study (SoZo) group or the control (placebo) group. The study group received 3 oz of SoZo, and the control group received 3 oz of a placebo beverage (pear juice). The participants' blood was drawn before administration of the beverages in order to establish a baseline value for each of the blood markers being studied. Blood was subsequently drawn every hour for 4 hours. The blood was then analyzed for blood levels and/or activities of various biomarkers and bio-targets: Hydroxyl Radical Antioxidant Capacity (HORAC), 8-iso-Prostaglandin F2α (isoprostanes), advanced oxidation protein products



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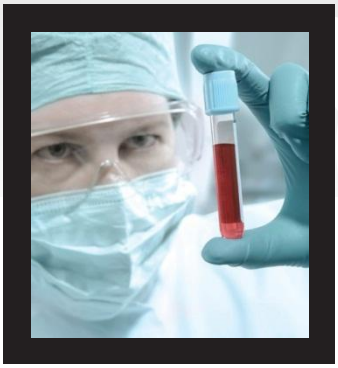


SoZo significantly acutely raised the hydroxyl radical absorbance capacity and this effect was sustained throughout the 4 hours of treatment.

(AOPP), nitric oxide (NO) and C-Reactive Proteins (CRP). These bio-target blood entities were of particular interest due to their known effects on oxidation, inflammation and cardiovascular disease as well as bio-markers since they are associated (if changed) with onset of specific chronic conditions such as cardiovascular disease and inflammation.

Testing these bio-markers and bio-targets in a clinical setting gave us insight into the physiological potency and efficacy of SoZo. This type of testing directly addresses any potency and efficacy of tested material in human participants.

Bio-marker: Hydroxyl Radical Absorbance Capacity

One of the most exciting conclusions in this *in clinico* study was the verification of the previously-observed *in vitro* effects of SoZo on the Hydroxyl R adical Absorbance Capacity. The hydroxyl radical has been shown to play a role in muscle function, fatigue and inflammation.[12, 13, 14, 15] It has also been shown to be a mediator in DNA damage.[16] The earlier *in vitro* test of SoZo on the Hydroxyl Radical Absorbance Capacity yielded significant results. This raised curiosity to understand whether SoZo would exhibit similar effects in the body.

In this human study, SoZo significantly acutely raised the Hydroxyl Radical Absorbance Capacity, and this effect was sustained throughout the 4 hours of treatment.

Bio-marker: 8-iso-Prostaglandin F2α

8-iso-Prostaglandin F2α (8-IP F2 α), one of the most studied isoprostanes, is created from the peroxidation of arachidonic acid. A study sponsored by the National Institute of Health showed isoprostanes to be the best bio-marker for oxidative stress in animals.[17] Isoprostanes have been shown to be the best indicator of oxidative stress in animals and also in humans.[1819]

Animal research has shown older animals can have amounts of isoprostanes that are 30 times higher than younger animals.[20] Isoprostanes have shown a correlation with inflammation.[21] They were also found to be a beneficial predictor of cardiac events outcomes in patients with acute coronary syndrome.[22] Higher levels of isoprostanes have also been found to be increased in a number of risk factors for atherosclerosis such as cigarette smoking, high cholesterol, diabetes, and obesity.[23] In addition, there is evidence to believe isoprostanes may be an independent predictor for risk of atherosclerosis.[24]

In this study, SoZo acutely decreased the level of 8-IP F2 α found in the blood and continued to maintain a reduction throughout the 4 hours of the study. The placebo actually increased 8-IP F2 α throughout the duration of the test. The results from this study warrant further investigation into SoZo's long-term effects on cardiovascular disease and other chronic diseases associated with oxidation.

Bio-marker: Advanced Oxidation Protein Products

Advanced Oxidation Protein Products (AOPP) are pro-inflammatory mediators that have been shown to impair HDL metabolism.[25] AOPP combines with albumin to create complexes that have been shown to contribute to foam cell formation in the walls of the arteries. SoZo significantly reduced AOPP levels at the 1 hour interval and maintained the reduction

throughout the study. The placebo did not reduce the levels of AOPP in the blood, and in fact increased these levels.

Bio-marker: Nitric Oxide

Nitric oxide works in the body as a vasodilator, increasing blood flow and lowering blood pressure. Those with atherosclerosis, diabetes and hypertension have been shown to have impaired nitric oxide pathways.[26] SoZo showed a sustained increase in NO over the 4 hour period from baseline as opposed to the placebo.

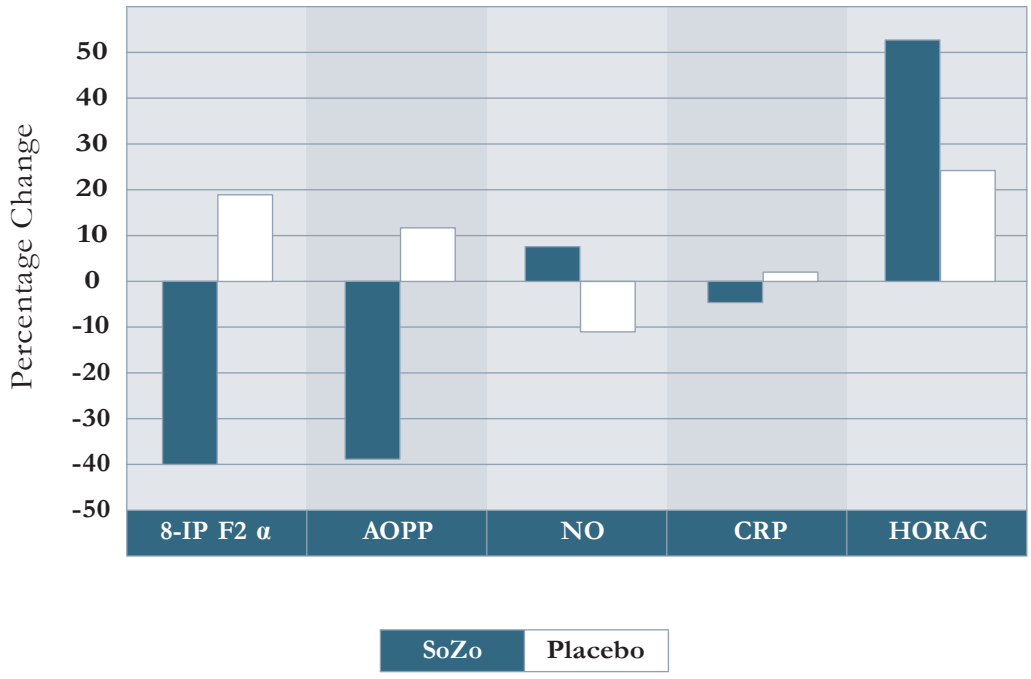
SoZo showed a sustained increase in NO levels over the 4 hour period from baseline. The placebo showed a reduction in NO under these experimental conditions.

Bio-marker: C - reactive protein

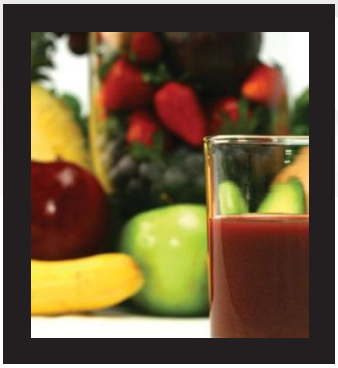
C - reactive protein (CRP) is a well-established biomarker for inflammation in the body. In 2 large studies CRP was shown to be a strong predictor for heart disease.[27]

SoZo showed a small reduction in CRP whereas the placebo slightly increased CRP. While this response is admittedly slight, it suggests a trend towards a beneficial effect. It is possible that prolonged and repeated dosages with SoZo could more greatly affect this marker. Additional studies will help confirm this.

SoZo Study Results Summary



SoZo acutely decreased the level of 8-IP F2 **α** found in the blood and continued to maintain a reduction throughout the 4 hours of the study.



The present study showed that SoZo not only exhibits powerful in vitro antioxidant activity, but also physiologically relevant in clinico effects.

Discussion

Oxidation is found at the core of many chronic diseases such as atherosclerosis, cancer, Alzheimer's and other chronic degenerative disease.[28] It is also believed to be an important contributing factor to the aging process.[29] While there is much we have yet to discover about the causative nature of oxidation in disease, mounting evidence warrants increased attention into fighting the effects of oxidation in the body.

Antioxidants are known to play a major role in counteracting the effects of oxidative stress in the body. Fruits and vegetables are nutrient dense sources of antioxidants. Their antioxidant content is believed to be one of the main reasons why those that consume the highest amounts of fruits and vegetables have lower risk for most of the major chronic diseases.

Polyphenols are the most abundant antioxidants found in fruits and vegetables. Though they are ubiquitous in fruits and many vegetables, polyphenols can be destroyed or removed during food processing.[30] The effect of food processing on polyphenols is compounded by the lack of fruit and vegetable consumption. The US government and major health organizations have worked hard over the past few decades to promote the consumption of fruits and vegetables with very little effect.

Whole food fruits and vegetables in their concentrated and least-processed forms are a possible way to deliver the benefits of polyphenols in a physiologically significant dose. Polyphenol antioxidant research presents some of the newest and most exciting research in the fight against oxidative stress. *In vitro* research shows polyphenols to be some of the most potent antioxidant agents in the diet. The present study showed that SoZo not only exhibits powerful in *vitro* antioxidant activity, but also physiologically relevant *in clinico* effects.

Although the effects of the ingredients of SoZo are well documented and understood, this study was performed in order to confirm the synergistic effects of this scientifically- designed blend. Instead of merely estimating the polyphenol content of SoZo solely from previous testing of its components, a full comprehensive analysis was done to find the actual concentration of the phenolics available in this beverage. *In vitro* testing was also undertaken to find out the antioxidant capacity of SoZo using the most widely accepted form of testing, ORAC. In order to better understand the possible effects on superoxide, peroxynitrite, singlet oxygen and the hydroxyl radical, SoZo underwent HORAC, NORAC, SORAC and SOAC testing.

In summary, SoZo was shown to have significant and sustained effects on 8-IP F2 α and Hydroxyl Radical Absorbance Capacity. SoZo was also shown to have positive effects on AOPP, NO, and CRP. All bio-makers were affected at the first hour interval, which means SoZo was fast-acting and likely had a primary and direct effect on the studied bio-markers. These bio-markers are directly associated with inflammation in the body as well as cardiovascular and other chronic diseases. This study did not show SoZo to have any adverse effects.

Generally, it is clear that SoZo elicited a positive response in its first discovery clinical study. This study warrants further investigation into SoZo's long term effects on the oxidative status of humans and into SoZo's obvious potential for exerting a positive impact upon the health status of its users.

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For more information about SoZo, contact: