Bioflavonoids are a group of plant pigments that are responsible for the colors of many flowers and fruits. Citrus bioflavonoids are those bioflavonoids, or flavonoids, found in citrus fruits such as lemon, orange, tangerine, grapefruit, etc. These substances possess antioxidant activities, which help fight poor health and aging.

Citrus bioflavonoids have been investigated for their biological activity, with both anti-inflammatory and anti-carcinogenic effects being reported. Flavonoids are a subset of a larger group of beneficial plant substances known as polyphenols.

The common citrus bioflavonoids include:
Apigenin, Hesperidin, Hesperitin, Naringenin, Naringin, Narirutin, Nobiletin, Quercetin, Rutin, Tangeretin, Tangeritin

Heart and blood vessel health

Citrus bioflavonoids are polyphenolic compounds with powerful biological properties. This review aims to summarize recent advances towards understanding the ability of citrus flavonoids to regulate lipid metabolism and other metabolic parameters relevant to the metabolic syndrome, type 2 diabetes and cardiovascular disease. Recent studies suggest an important role of citrus flavonoids in the treatment of dyslipidemia, insulin resistance, hepatic steatosis, obesity and atherosclerosis. The favorable outcomes are achieved through multiple mechanisms. Human studies focused on dose, bioavailability, efficacy and safety are required to propel the use of these promising therapeutic agents into the clinical arena.

Skin health

Ultraviolet radiation absorbed by the epidermis is the major cause of various cutaneous disorders, including photoaging and skin cancers. Although topical sunscreens may offer proper skin protection, dietary plant compounds may significantly contribute to lifelong protection of skin health, especially when unconsciously sun UV exposed. A combination of rosemary and citrus bioflavonoids extracts was used to inhibit UV harmful effects on human HaCaT keratinocytes and in human volunteers after oral intake. Survival of HaCaT cells after UVB radiation was higher in treatments using the combination of extracts than in those performed with individual extracts, indicating potential synergic effects. The combination of extracts also decreased UVB-induced intracellular radical oxygen species (ROS) and prevented DNA damage in HaCaT cells by comet assay and decreased chromosomal aberrations in X-irradiated human lymphocytes. The oral daily consumption of 250 mg of the combination by human volunteers revealed a significant minimal erythema dose (MED) increase after eight weeks. Stronger protection was achieved after 12 weeks. The combination of citrus flavonoids and rosemary polyphenols and diterpenes may be considered as an ingredient for oral photoprotection.

More at: [www.raysahelian.com/citrusbioflavonoids.html](http://www.raysahelian.com/citrusbioflavonoids.html)
ABSTRACT

To document that grape seed extract taken orally will decrease plasma estrogen levels (estrone (E1), estradiol (E2), and E1-conjugates) and increase precursor androgen levels (testosterone and androstenedione) in healthy postmenopausal women. [Time Frame: 12 weeks]

Brief Summary:
The role of estrogens in the pathogenesis of breast cancer has been well documented. This has led to the development of "Anti-Estrogens" (selective estrogens receptor modulators and Aromatase Inhibitors), used for treatment and prevention of breast cancer. These agents, however, have significant side effects, which are not acceptable to many healthy high-risk women. There is preliminary evidence that grape seed extract acts as "natural" aromatase inhibitor (1). This study has the potential to quantify the effectiveness of a natural substance that mimics the action of pharmaceutical aromatase inhibitors.

Detailed Description:
Early detection of breast cancer with screening mammography and the use of more effective medical therapies have led to a decrease in breast cancer mortality. However, breast cancer is still the second leading cause of cancer death in women (2). Therefore, the future lies in not only early detection but prevention of breast cancer. Currently available chemopreventive agents are associated with potentially serious side effects and can be quite costly, especially when taken for extended periods of time. Therefore, they are usually targeted only to women at high risk of disease. Identification of an inexpensive, efficacious preventive therapy with few or no side effects would represent a major advance in reducing the morbidity and mortality due to breast cancer. One exciting possibility is grape seed extract. Grapes and grape seeds contain procyanidins, a highly active subclass of flavonoids with actions similar to pharmaceutical aromatase inhibitors (AIs). These procyanidin dimers have been found to suppress estrogen biosynthesis both in vitro and in animal models (1). Based upon this knowledge we proposed this dose finding pilot study.

More at:
www.clinicaltrials.gov/ct2/show/record/NCT00566553
Reduce Fat Absorption with Grape Seed Extract

BONNIE SINGLETON, LIVESTRONG.COM | OCTOBER 2017

Modern research is finding that grapes and grape seed extracts contain potent antioxidant and anti-inflammatory properties that may improve overall health and also prove to be an effective tool in fighting obesity and assisting in weight loss.

Identification:
Red and purple grapes contain powerful antioxidants known as anthocyanins. The University of Maryland Health Center states that the seeds from red and purple grapes contain high levels of vitamin E, flavonoids, linoleic acid and the powerful antioxidant compounds known as oligomeric proanthocyanidin complexes, or OPC's.

Significance:
According to an article authored by K.M. Flegal, et al., published in the “Journal of the American Medical Association” in January 2010, the rate of obesity is 32.2 percent among adult men and 35.5 percent among adult women in the U.S., with the authors noting that obesity raises your risk factor for developing cardiovascular disease, diabetes and cancer. A joint 2009 study by the Centers for Disease Control and Prevention and RTI International found that the direct and indirect cost of obesity may reach as high as $147 billion annually.

Significance:
Researchers at Maastricht University in the Netherlands, in a study published in 2004 in “European Journal of Clinical Nutrition,” discovered that grape seed extract reduced the calorie intake of healthy people by 4 percent over a 24-hour period, which led the scientists to conclude that grape seed extract may reduce energy intake in overweight subjects and play a significant role in body-weight management.

A study in Spain by Gemma Montaguta, et al., published in June 2010 in the “Journal of Nutritional Biochemistry” found that grape seed extract improved insulin resistance by making insulin receptors switch back on again and restore more youthful function, a finding that could be helpful in treating weight gain in people with diabetes and pre-diabetes.

Diego A. Moreno, Ph.D., led research published in 2003 in “Nutrition” that showed bioactive phytochemicals in grape seed extract inhibited the fat-metabolizing enzymes pancreatic lipase and lipoprotein lipase, suggesting the grape seed extract may be useful as a treatment to limit dietary fat absorption and the accumulation of fat in adipose tissue.

Considerations:
Grape seed extract is available in drug stores, grocery stores and health food stores in capsule, tablet and liquid form. The University of Maryland Health Center recommends looking for products that state they are standardized to 40 to 80 percent proanthocyanidins, or an OPC content of not less than 95 percent.

More at:
www.livestrong.com/article/300567-grape-seed-extract-and-weight-loss/
Anticancer and Cancer Chemopreventive Potential of Grape Seed Extract and Other Grape-Based Products

MANJINDER KAUR, CHAPLA AGARWAL, RAJESH AGARWAL | SEPTEMBER 2009

ABSTRACT

With cancer on the rise, additional steps are needed to control human malignancies. Chemoprevention, a strategy of cancer prevention by dietary means, is showing great promise in this area as it can be implemented to a broader population with less of an economic burden.

Introduction:
Consistent with this, several epidemiological studies have shown that populations that consume diets rich in fruits and vegetables have an overall lower cancer incidence. Based on these encouraging observations, research efforts from across the globe have focused on identifying, characterizing, and providing scientific basis to the efficacy of various phytonutrients in an effort to develop effective strategy to control various human malignancies. Cancer induction, growth, and progression are multi-step events and numerous studies have demonstrated that various dietary agents interfere with these stages of cancer, thus blocking malignancy. Fruits and vegetables represent untapped reservoir of various nutritive and nonnutritive phytochemicals with potential cancer chemopreventive activity. Grapes and grape-based products are one such class of dietary products that have shown cancer chemopreventive potential and are also known to improve overall human health. This review focuses on recent advancements in cancer chemopreventive and anticancer efficacy of grape seed extract and other grape-based products. Overall, completed studies from various scientific groups conclude that both grapes and grape-based products are excellent sources of various anticancer agents and their regular consumption should thus be beneficial to the general population.

GSE and Cancer:
Cancer is a disease in which the cell presents itself with unrestricted proliferative potential. As reviewed by Hanahan and Weinberg (20), the transition of normal cell toward cancerous phenotype is due to the occurrence of 6 basic defects in normal cell physiology, which culminate in giving an added growth advantage to the transformed cell (20). Because these defects are mostly due to aberrant signaling cascades involving numerous molecular players, targeting them by chemopreventive agents could be a rationalized approach in cancer control; indeed, GSE targets these signaling cascades for its anticancer and/or chemopreventive efficacy.

Other Parts of the Grape:
Although the above-cited literature strongly suggests that grape seeds are a potential source of anticancer and cancer chemopreventive phytochemicals, the other parts of the grape such as the skin, the whole grape by itself, grape-derived raisins, and phytochemicals present within the grapes have also demonstrated potential anticancer efficacy in various preclinical and clinical studies.

More at:
www.ncbi.nlm.nih.gov/pmc/articles/PMC2728696/
Grape seed extract is considered to be one of the most effective natural skin care ingredients available. A natural byproduct of the equally popular wine industry, it provides a wide range of benefits to all skin types helping with reducing oxidization and increasing the suppleness of skin.

Grape seed extract has been carefully studied by biochemists and physicians to confirm these properties, and in fact, the more it is researched the more benefits are discovered! Grape seed extract is now accepted as a compound which protects, heals and beautifies skin.

Grape seed contains flavonoids believed to act as the pigment in plants, and it’s suggested that the purpose of flavonoids in grapes are to protect the plant and its seeds from the damaging effects of ultraviolet radiation and oxidation. When applied to your skin the properties of the grape seed still provide strong antioxidant benefits, binding with free radicals and protecting your skin from premature aging and damage caused within the cells.

Found inside Grape seed (and used in many beauty products) is also the chemical Resveratrol, which when massaged into the skin helps to protect and repair. Grape seed extract also acts as a mild alpha-hydroxy acid (AHA), which works in a variety of ways to nourish and strengthen the skin; helping to remove dead skin cells, improving the condition of the skin (particularly the collagen and elastin structures) and helping to keep the skin firm and youthful in appearance. AHA also improves the moisture barrier of skin cells, which allows them to accept and retain necessary moisture so that they remain healthy.

So if you’re looking for a naturally sourced ingredient in your skincare which offers protection from environmental damage and premature ageing, grape seed is it.
Resveratrol is a potent member of the class of natural, plant-derived chemicals known as polyphenols. These help explain in part why a diet high in fruit and vegetables confers health benefits and are associated with reduced risk of common complex conditions such as cardiovascular disease, cancer, diabetes, and Alzheimer’s disease.

We present the latest molecular findings that account for the beneficial actions of resveratrol. The intracellular pathways activated are crucial for anti-oxidant defence, regulation of the cell cycle, mitochondrial energy production, vascular tone, oncogene suppression, and many other phenomena which if unchecked lead to morbidity and mortality from onset and progression of these various diseases. While a healthy diet and lifestyle is strongly recommended in prevention of such conditions, the future bodes well for the use of resveratrol and analogues of higher potency than the natural form for treatment of diseases that afflict humans, particularly as they age.

Resveratrol (trans-3,5,4’-trihydroxystilbene or 5-[(E)-2-(4-hydroxyphenyl)-ethenyl]benzene-1,3-diol; C14H12O3), is a polyphenolic flavonoid found in the seeds and skins of grapes, red wine, mulberries, peanuts, and rhubarb. Polyphenols exert a diversity of health benefits by activating intracellular pathways, many of which are the same as those activated by calorie restriction, an intervention long known to enhance health and prolong lifespan (Wood et al 2004). An early target of resveratrol is the sirtuin class of nicotinamide adenine dinucleotide (NAD)-dependent deacetylases. Seven sirtuins have been identified in mammals, of which SIRT-1 is believed to mediate the beneficial effects on health and longevity of both calorie restriction and resveratrol (Guarente and Picard 2005).

A number of intracellular pathways are activated by SIRT-1. The extent to which the sirtuin-activating actions of resveratrol are direct or indirect is still not resolved completely (Denu 2005). The pathways regulated by sirtuins include gluconeogenesis and glycolysis in the liver, fat metabolism, and cell survival. Depending on cell type and circumstances, sirtuins activate or suppress members of the forkhead box O (FOXO) group of transcription factors. FOXOs then activate or suppress specific genes, leading to a decrease in apoptosis, an increase in antioxidant activities, DNA protection, anti-inflammatory effects, and modulation of various other mechanisms so as to promote the health of the cell, and thus the organism (reviewed by Morris 2005, 2008). It may be that sirtuins benefit survival by ramping up stress resistance pathways in cells in times of adversity (Guarente and Picard 2005). Several recent reports presented evidence that SIRT-1 interacts directly and deacetylates the metabolic regulator and transcriptional coactivator, peroxisome proliferator-activated receptor-γ co-activator 1α (PGC-1α). By doing so it improves mitochondrial function, induces genes for mitochondrial and fatty acid oxidation and increases mitochondrial membrane potential (Lagouge et al 2006; Gerhart-Hines et al 2007; Anderson et al 2008).

More at: www.ncbi.nlm.nih.gov/pmc/articles/PMC2546476/