



## Muscadine Research

This paper is a brief description of the research on Muscadine fruit seeds and skin extracts on various cancers and other studies. The studies have been conducted mostly in-vitro. Some have been conducted in-vivo on animals. They have been conducted by major universities and the United States government. These are mostly abstracts of the original research which can be found on Pubmed.gov.

Muscadine seeds contain 40 times the Resveratrol of normal grape seeds and have 4 times the anti-oxidation effects of grapes. But not all Muscadines are the same. The effectiveness of the Muscadine fruit depends on whether it was grown organically and the composition of the soil in which it is grown. Muscadines are a fruit that looks like a grape, but Muscadines have two extra chromosomes that grapes do not have.

**Nature's Pearl** double tests every new batch of fruit to be certain it contains the highest levels of nutraceuticals. Samples are even sent to Brunswick labs for independent third party verification!

The Nature's Pearl manufacturing process has been certified by the Food and Drug Administration. However it is not intended to diagnose, treat, cure, or prevent any disease. It is not a drug. It is an all-natural, vegetarian, organic, whole food supplement.

Page two is a brief description of the results of research on colon cancer from University of Florida.

Page three is a brief description of the results of research on E. Coli from Mississippi State University.

Page four is a brief description of the results of research on diabetes from Clemson University.

Page five is a brief description of the Anti-Cancer possibilities from Colorado State University.

Page six is a brief description of the results on Alzheimer's from Mount Sinai School of Medicine.

Page seven Anti-inflammatory effects of Muscadines from the Journal of Ag. and Food Chemistry.

Page eight effects on Leukemia from the University of Kentucky.

Page nine Muscadines can inhibit growth of prostate cancer in the laboratory.

Page eleven American Association for Cancer Research Muscadine effect on seven different cancers.

Page twelve is the Brunswick laboratory ORAC value comparison chart.

Page thirteen effects on neck squamous cell carcinoma cells from the University of Colorado.

Page fifteen is the Resveratrol level of grapes vs. Muscadines from Mississippi State University.

Page sixteen marketing Business Associates Introductory letter.



## Muscadine Research

### Induction of Cell Death in Caco-2 Human Colon Carcinoma Cells by Ellagic Acid Rich Fractions from Muscadine Grapes (*Vitis rotundifolia*)

Susanne U. Mertens-Talcott,<sup>†</sup> Joon-Hee Lee,<sup>‡</sup> Susan S. Percival,<sup>‡</sup> and Stephen T. Talcott<sup>\*‡</sup>

Department of Pharmaceutics, University of Florida, P. O. Box 110494, Gainesville, Florida 32610-0494, and Department of Food Science and Human Nutrition, Institute of Food and Agricultural Sciences, University of Florida, P. O. Box 110370, Gainesville, Florida 32611-0370

*J. Agric. Food Chem.*, 2006, 54 (15), pp 5336–5343

DOI: 10.1021/jf060563f

Publication Date (Web): June 23, 2006

Copyright © 2006 American Chemical Society

### Abstract

Possible anticancer mechanisms exerted by polyphenolic compounds contained in fruits and vegetables include antioxidant activity, the inhibition of proliferation, and the induction of apoptosis in cancer cells. This study examined the effects of four isolated polyphenolic extracts from red muscadine grapes (*Vitis rotundifolia*) on vital cell parameters and the induction of apoptosis in Caco-2 colon carcinoma cells. The magnitude of effects in cell culture was then correlated to polyphenolic composition and antioxidant capacity. Whereas anticancer effects of individual polyphenolic compounds have been demonstrated multiple times, information relating to anticancer effects of polyphenolic extracts is not available in abundance. All four extracts induced apoptosis, decreased cell number, and caused alterations in cell cycle kinetics in a concentration-dependent manner. The efficacy of the polyphenolics on vital cell parameters correlated well to the presence of ellagic acid glycosides and flavonoids and also to the antioxidant capacity. **This study demonstrated the anticancer properties of ellagic acid rich extracts from red muscadine juice.**

Keywords: Polyphenols; anticancer; red wine; apoptosis



## Muscadine Research

J Appl Microbiol. 2009 Aug;107(2):533-9. Epub 2009 Mar 19.

### **Antibacterial activity of fresh and processed red muscadine juice and the role of their polar compounds on Escherichia coli O157:H7.**

Kim TJ, Silva JL, Jung YS.

#### **Source**

Department of Food Science, Nutrition and Health Promotion, Mississippi State University, Mississippi 39762, USA. tkim@foodscience.msstate.edu

#### **Abstract**

##### **AIMS:**

The objectives of this research were to show the anti-*Escherichia coli* O157:H7 effect of fresh (FRMJ) and processed red muscadine (*Vitis rotundifolia*) juice (PRMJ) and to discern the active compounds responsible for anti-*E. coli* O157:H7.

##### **METHODS AND RESULTS:**

Polar and phenolic compounds of FRMJ and PRMJ were analysed by high-performance liquid chromatography. Antibacterial activity of FRMJ, PRMJ, their polar and polyphenol fractions, individual synthetic acids and their mixture with or without sugars were investigated on *E. coli* O157:H7. FRMJ and PRMJ inactivated ( $P < \text{or} = 0.05$ ) 5-log cocktail cells of *E. coli* O157:H7 within 4 h at 37 degrees C. Polar fractions that contained malic, tartaric and tannic acids showed strong antimicrobial activity ( $P < \text{or} = 0.05$ ) against *E. coli* O157:H7. Tannic acid among the synthetic acids showed the highest antimicrobial activity against *E. coli* O157:H7.

##### **CONCLUSIONS:**

FRMJ, PRMJ and their polar compounds showed strong anti-*E. coli* O157:H7 activity.

##### **SIGNIFICANCE AND IMPACT OF THE STUDY:**

Earlier findings have failed to show any anti-*E. coli* O157:H7 effect of grape juice without adding preservatives. Our findings show that red muscadine juice has natural antibacterial substances and suggest that these can be used as active antimicrobial ingredients against *E. coli* O157:H7 in nonalcoholic beverages.



## Muscadine Research

J Agric Food Chem. 2011 Sep 14;59(17):9506-11. Epub 2011 Aug 9.

### **Inhibitory effects of muscadine anthocyanins on $\alpha$ -glucosidase and pancreatic lipase activities.**

You Q, Chen F, Wang X, Luo PG, Jiang Y.

#### **Source**

Department of Food, Nutrition and Packaging Sciences, Clemson University, Clemson, South Carolina 29634, United States.

#### **Abstract**

Inhibitory effects of the Noble muscadine grape extracts and the representative phytochemicals for anthocyanins (i.e., cyanidin and cyanidin-3,5-diglucoside) on two enzymes, that is,  $\alpha$ -glucosidase and pancreatic lipase, were investigated regarding their antidiabetic activities. The study demonstrated that the anthocyanin extracts and the selected chemicals obeyed the competitive mode against the enzymes. The methanolic extracts of whole fruit and skin of the muscadine showed inhibitory activities against the  $\alpha$ -glucosidase with their IC(50) values at 1.50 and 2.73 mg/mL, and those against the lipase at 16.90 and 11.15 mg/mL, respectively, which indicated that **the muscadine extracts possessed strong antidiabetic activities.** Particularly, the ethyl acetate (EtoAc) extract and the butanol (BuOH) extract exhibited much higher inhibitory activities against both enzymes than the CHCl<sub>3</sub> and water extracts, while the majority of anthocyanins existed in the BuOH fractions. Moreover, cyanidin exhibited a much stronger antidiabetic activity than cyanidin-3,5-diglucoside, suggesting that anthocyanins may have higher inhibitory activities after being digested. Further chromatographic analysis by high-performance liquid chromatography-mass spectrometry identified five individual anthocyanins, including cyanidin, delphinidin, petunidin, peonidin, and malvidin glycosides.



## Muscadine Research

J Nutr. 2009 Sep;139(9):1806S-12S. Epub 2009 Jul 29.

### **Anticancer and cancer chemopreventive potential of grape seed extract and other grape-based products.**

Kaur M, Agarwal C, Agarwal R.

#### **Source**

Department of Pharmaceutical Sciences, School of Pharmacy, University of Colorado, Denver, CO 80045, USA.

#### **Abstract**

With emerging trends in the incidence of cancer of various organ sites, additional approaches are needed to control human malignancies. Intervention or prevention of cancer by dietary constituents, a strategy defined as chemoprevention, holds great promise in our conquest to control cancer, because it can be implemented on a broader population base with less economic burden. 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**

[ added by MBA ... Remember that Muscadines contain 4 times the resveratrol of regular grapes. So, an equal amount of Muscadine based consumption would provide more of the above compounds.]



## Muscadine Research

J Alzheimers Dis. 2009;16(1):59-72.

### **Heterogeneity in red wine polyphenolic contents differentially influences Alzheimer's disease-type neuropathology and cognitive deterioration.**

Ho L, Chen LH, Wang J, Zhao W, Talcott ST, Ono K, Teplow D, Humala N, Cheng A, Percival SS, Ferruzzi M, Janle E, Dickstein DL, Pasinetti GM.

#### **Source**

Department of Psychiatry, Mount Sinai School of Medicine, NY, USA. Lap.Ho@mssm.edu

#### **Abstract**

We recently found that moderate consumption of two unrelated red wines generate from different grape species, a Cabernet Sauvignon and a muscadine wine that are characterized by distinct component composition of polyphenolic compounds, significantly attenuated the development of Alzheimer's disease (AD)-type brain pathology and memory deterioration in a transgenic AD mouse model. Interestingly, our evidence suggests that the two red wines attenuated AD phenotypes through independent mechanisms. In particular, we previously found that treatment with Cabernet Sauvignon reduced the generation of AD-type amyloid-beta (Abeta) peptides. In contrast, evidence from our present study suggests that **muscadine treatment attenuates Abeta neuropathology and Abeta-related cognitive deterioration in Tg2576 mice** by interfering with the oligomerization of Abeta molecules to soluble high-molecular-weight Abeta oligomer species that are responsible for initiating a cascade of cellular events resulting in cognitive decline. Collectively, our observations suggest that distinct polyphenolic compounds from red wines may be bioavailable at the organism level and beneficially modulate AD phenotypes through multiple Abeta-related mechanisms. Results from these studies suggest the possibility of developing a "combination" of dietary polyphenolic compounds for AD prevention and/or therapy by modulating multiple Abeta-related mechanisms.



## Muscadine Research

### Anti-inflammatory Properties of the Muscadine Grape (*Vitis rotundifolia*)

The muscadine grape possesses one of the highest antioxidant levels among fruits; yet, the effect of this fruit on mammalian metabolic systems has not received significant attention. To examine the anti inflammatory properties of the muscadine, grape skins were dried, pulverized, and extracted (10% w/v) with 50% ethanol. The extract was then tested in two different assays: the release of superoxide in phorbol myristate acetate-activated neutrophils and the release of cytokines [tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ), interleukin-1 $\beta$  (IL- $\beta$ ), and interleukin-6 (IL-6)] by lipopolysaccharide-activated peripheral blood mononuclear cells. The release of superoxide and cytokines was inhibited by increasing concentrations of the extract. A 1:100 dilution of the extract inhibited superoxide release by approximately 60% while the release of TNF- $\alpha$  and IL-1 $\beta$  was reduced at a dilution of 1:200 by approximately 15 and 90%, respectively (all  $P < 0.05$ ). The inhibition pattern on the release of IL-6 was similar to that seen with TNF- $\alpha$ . In a related in vivo study, rats were fed a diet containing 5% (wt/wt) dried muscadine grape skins for 14 days and then were injected with carrageenan in the foot pad. After 3 h, paw edema was measured and the rats on the grape skin diet had approximately 50% less paw edema than controls ( $P < 0.05$ ). These results demonstrate that the muscadine grape skin powder possesses significant in vitro and in vivo anti inflammatory properties.

Journal of Agricultural and Food Chemistry  
<http://pubs.acs.org/doi/pdf/10.1021/jf058015%2B>

Keywords: Muscadine grape (*Vitis rotundifolia*); superoxide; anti inflammatory; interleukin-1 $\beta$ ; interleukin-6; TNF- $\alpha$ ; edema



## Muscadine Research

### University of Kentucky research on Leukemia

An extract from grape seeds forces laboratory leukemia cells to commit cell suicide, according to researchers from the University of Kentucky. They found that within 24 hours, 76 percent of leukemia cells had died after being exposed to the extract.

The investigators, who report their findings in the January 1, 2009, issue of *Clinical Cancer Research*, a journal of the American Association for Cancer Research, also teased apart the cell signaling pathway associated with use of grape seed extract that led to cell death, or apoptosis. They found that the extract activates JNK, a protein that regulates the apoptotic pathway.

While grape seed extract has shown activity in a number of laboratory cancer cell lines, including skin, breast, colon, lung, stomach and prostate cancers, no one had tested the extract in hematological cancers nor had the precise mechanism for activity been revealed.

"These results could have implications for the incorporation of agents such as grape seed extract into prevention or treatment of hematological malignancies and possibly other cancers," said the study's lead author, Xianglin Shi, Ph.D., professor in the Graduate Center for Toxicology at the University of Kentucky.

"What everyone seeks is an agent that has an effect on cancer cells but leaves normal cells alone, and this shows that grape seed extract fits into this category," he said. Shi adds, however, that the research is not far enough along to suggest that people should eat grapes, grape seeds, or grape skin in excess to stave off cancer. "This is very promising research, but it is too early to say this is chemo-protective."

Hematological cancers – leukemia, lymphoma and myeloma – accounted for an estimated 118,310 new cancer cases and almost 54,000 deaths in 2006, ranking these cancers as the fourth leading cause of cancer incidence and death in the U.S. Given that epidemiological evidence shows that eating vegetables and fruits helps prevent cancer development, Shi and his colleagues have been studying chemicals known as proanthocyanidins in fruits that contribute to this effect. Shi has found that apple peel extract contains these flavonoids, which have antioxidant activity, and which cause apoptosis in several cancer cell lines but not in normal cells. **Based on those studies, and findings from other researchers that grape seed extract reduces breast tumors in rats and skin tumors in mice, they looked at the effect of the compound in leukemia cells.**

Using a commercially available grape seed extract, Shi exposed leukemia cells to the extract in different doses and found the marked effect in causing apoptosis in these cells at one of the higher doses. They also discovered that the extract does not affect normal cells, although they don't know why.

The researchers then used pharmacologic and genetic approaches to determine how the extract induced apoptosis. They found that the extract strongly activated the JNK pathway, which then led to up-regulation of Cip/p21, which controls the cell cycle.

They checked this finding by using an agent that inhibited JNK, and found that the extract was ineffective. Using a genetic approach – silencing the JNK gene – also disarmed grape seed extract's lethal attack in leukemia cells. "This is a natural compound that appears to have relatively important properties," Shi said.

American Association for Cancer Research (2008, December 31).

Grape-seed Extract Kills Laboratory Leukemia Cells, Proving Value Of





## Muscadine Research

### Unique Grape Skin Extract Inhibits Prostate Cancer Cell Growth in the Laboratory

Laboratory experiments show that an extract of the skin of muscadine grapes can inhibit growth of prostate cancer cells in the laboratory. Investigators from the **National Cancer Institute (NCI)**, part of the National Institutes of Health, and their research partners also show that muscadine grape skin extract (MSKE) does not contain significant amounts of resveratrol, another grape skin component that has been widely studied and shown to be of potential benefit in preventing prostate cancer growth. The results appear in the September 1, 2007, issue of *Cancer Research*.

Using a series of human prostate cancer cells, representing different stages of prostate cancer progression, the researchers showed that MSKE significantly inhibits the growth of cancerous, but not normal, prostate cells, primarily by inducing a process called apoptosis, or programmed cell death. Programmed cell death is one of the mechanisms the body uses to rid itself of cells with unrepaired genetic damage before those cells can duplicate themselves. In contrast, resveratrol seems to act by blocking the cell cycle, a sequence of steps that a cell passes through when it grows and divides into two identical cells. Both mechanisms are used by the body to prevent the development of cancer.

According to Jeffrey E. Green, M.D., chief of the Transgenic Oncogenesis and Genomics Section in NCI's Center for Cancer Research (CCR), "These results show that MSKE may have potent antitumor activities in the lab that differ from the effects of resveratrol. Further studies of MSKE will be necessary to determine if this extract has potential as a chemopreventive or therapeutic agent."

The fact that all of the cells studied, which cover the different stages of prostate cancer tumor progression, responded to MSKE suggests that the active compounds in this extract potentially may inhibit tumor development at very early stages.

The muscadine grape (*Vitis rotundifolia*) is distinct from the more common red grapes used to produce red wines, a major source of resveratrol. The chemical constituents of muscadine grapes differ from most other grape varieties, as they are richer in chemicals called anthocyanins. Anthocyanins, which produce the red and purple colors of the grapes, have strong antioxidant activity and have shown several antitumor effects, including inhibition of DNA synthesis in breast cancer cells, of blood vessel growth in some tumors, and of enzymes involved in tumor spread. Muscadine grapes can be found growing wild from Delaware to the Gulf of Mexico and westward from Missouri to Texas.



## Muscadine Research

**(Continued)**

### **Unique Grape Skin Extract Inhibits Prostate Cancer Cell Growth in the Laboratory**

While previous studies suggested that anthocyanins might suppress the cancer process, no rigorous study of the mechanisms underlying these effects has yet been done. Resveratrol, by contrast, has been widely examined. Although earlier studies showed that it can induce programmed cell death in prostate cancer cells, resveratrol did not significantly induce cell death in the prostate cell model system used for this muscadine study. The results of this study suggest that resveratrol may activate different antitumor mechanisms than MSKE.

Even though MSKE had significant inhibitory effects on the prostate cancer cells studied, it did not alter the growth rate of the normal human prostate cells in the lab, which served as controls. Ongoing studies of MSKE in animals will help to determine the underlying mechanisms of MSKE's inhibitory effects in prostate cancer cells. The researchers hope that the lab effects of MSKE will be reproducible in testing on cancerous and normal prostate cells in animals. Should MSKE move on to trials in humans, Green says that since "muscadine grape products, including grape juice and grape wine, have been used in human studies without reported side effects, they may be relatively safe for use in clinical trials."

###

Inhibition of prostate cancer growth by muscadine grape skin extract and resveratrol through distinct mechanisms. Hudson TS, Hartle DK, Hursting SD, Nunez NP, Wang TTY, Young, HA, Arany P, and Green JE. *Cancer Res.* 2007; 67(17).

For more information about cancer, please visit the NCI Web site at [www.cancer.gov](http://www.cancer.gov), or call NCI's Cancer Information Service at 1-800-4 CANCER (1-800-422-6237).

For more information on Dr. Green's research at NCI, please go to <http://ccr.cancer.gov/staff/staff.asp?profileid=5721>.



## Muscadine Research

### Inhibition of cancer cell growth by muscadine grape seed and grape skin extracts

Presented at the annual convention of the American Association for Cancer Research

E. Ann Tallant, Charisse H. Holmes, Patricia E. Gallagher.  
Wake Forest University School of Medicine, Winston-Salem, NC

The muscadine grape (*Vitis rotundifolia*) is native to the Southeastern United States and muscadine grape seed products are marketed as dietary supplements, based upon their antioxidant properties. Extracts from muscadine grapes contain a number of antioxidants, including resveratrol and ellagic acid; however, the natural antioxidants found in grape seed extracts are predominantly procyanidins, while the grape skin extracts contain more anthocyanins. We investigated the effect of muscadine grape seed extracts (MSE) and muscadine grape skin extracts (MSKE) on the growth of human lung, colon, prostate, skin, brain and breast cancers as well as human leukemias.

Cells were incubated with increasing concentrations (from 0.5 to 50 µg/mL) of aqueous extracts of either MSE or MSKE and the total number of cells was quantified after 7 days. Both the MSE and MSKE inhibited the growth of A549 and SK-LU-1 human lung adenocarcinoma cancer cells (81.8% inhibition at the highest concentration) and HT29 and HCT116 human colon cancer cells (80.5% inhibition at the highest dose).

Similarly, extracts from both muscadine grape seeds and skins inhibited the growth of LNCaP and PC3 human prostate cancer cells. The growth of U87 and U373 human glioblastoma cells and RPMI 7951 and SKMEL28 human skin cancer cells was dose-dependently reduced by treatment with the MSE or MSKE. Human leukemia cells were also incubated with increasing concentrations of the extracts; the growth of THP-1 human acute monocytic leukemia cells, HL-60 human acute promyelocytic cells, and K562 human chronic myelogenous leukemia cells was reduced by both muscadine grape extracts (average of 74.2% inhibition at the highest dose).

Both the MSE and MSKE inhibited the growth of estrogen receptor-dependent ZR-75-1, HER2 over-expressing SKBR3, and triple negative MDA-MB-231 human breast cancer cells. The inhibition of growth by either extract was highest in the triple negative breast cancer cells (92.6% inhibition at the highest concentration). The reduction in human breast cancer cell growth was accompanied by a significant decrease in the phosphorylation and activation of the mitogen-activated protein kinases ERK1 and ERK2; MAP kinase activities were reduced 91% by MSE and 80% by MSKE in ZR-75-1 estrogen receptor-dependent breast cancer cells and 73% by MSE and 66% by MSKE in MDA-MB-231 triple negative breast cancer cells.

There were no significant differences between the effects of the grape seed extract compared to the grape skin extract with any of the cell lines. These results demonstrate that extracts from muscadine grape seeds and muscadine grape skins inhibit the growth of human lung, colon, prostate, breast, skin, brain and leukemia cells *in vitro*, suggesting that further studies are warranted to investigate their potential use in the prevention or treatment of cancer.

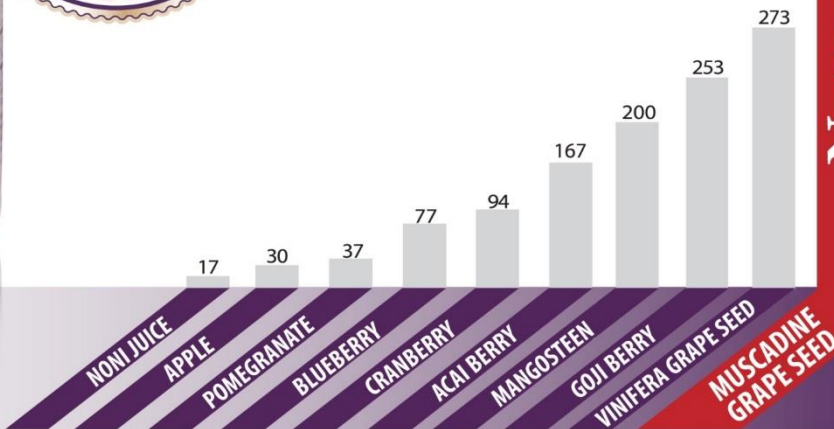


## Muscadine Research

# ANTIOXIDANT RATINGS

ORAC Scale – Oxygen Radical Absorbing Capacity

895\*



To compare the antioxidant values of various foods and nutrients, scientists developed a unit of measure called ORAC (Oxygen Radical Absorbing Capacity). The higher the ORAC rating of a substance, the more free radicals it can neutralize. Beware as you compare ORAC values. Always check to see that you are comparing gram to gram as shown here.  
\* Brunswick Laboratories 2006. ORAC ratings may vary slightly from batch to batch. All ORAC ratings are measured by Brunswick Laboratories, and expressed as micromole TE per 1 gram.



## Muscadine Research

### Grape Seed Extract Causes Irreparable DNA Damage to Cancer Cells

From: Oxford Journals >> Life Sciences & Medicine >> Carcinogenesis

Generation of reactive oxygen species by grape seed extract causes irreparable DNA damage leading to G2/M arrest and apoptosis selectively in head and neck squamous cell carcinoma cells

Study Abstract:

Head and neck squamous cell carcinoma (HNSCC) accounts for 6% of all malignancies in United States, and unfortunately, the recurrence of secondary primary tumors and resistance against conventional treatments decrease the overall 5-year survival rate in HNSCC patients. Thus, additional approaches are needed to control HNSCC. Here, for the first time, employing human HNSCC Detroit 562 and FaDu cells as well as normal human epidermal keratinocytes (NHEK), **we investigate grape seed extract (GSE) efficacy and associated-mechanism in both cell culture and nude mice xenografts. GSE selectively inhibited the growth, and caused cell cycle arrest and apoptotic death** in both Detroit 562 and FaDu cells by activating DNA damage check-point cascade including ATM/ATR-Chk1/2-Cdc25C as well as caspases 8, 9 and 3. Consistent with these results, GSE treatment resulted in a strong DNA damage, and a decrease in the levels of DNA repair molecules Brca1 and Rad51 and DNA repair foci. GSE-caused accumulation of intra-cellular reactive oxygen species (ROS) was identified as a major mechanism of its effect for growth inhibition, DNA damage and apoptosis, which was remarkably reversed by antioxidant N-acetylcysteine. GSE feeding to nude mice decreased Detroit 562 and FaDu xenograft tumor growth by 67% and 65% ( $p < 0.001$ ), respectively. In IHC analysis, xenografts from GSE-fed groups showed decreased proliferation but increased DNA damage and apoptosis.

Together, these findings show that GSE targets both DNA damage and repair, and provide mechanistic insights for its efficacy selectively against HNSCC both in cell culture and mouse xenograft; supporting its translational potential against HNSCC.

From press release:

Nearly 12,000 people will die of head and neck cancer in the United States this year and worldwide cases will exceed half a million. A study published this week in the journal Carcinogenesis shows that in both cell lines and mouse models, grape seed extract (GSE) kills head and neck squamous cell carcinoma cells, while leaving healthy cells unharmed.

“It’s a rather dramatic effect,” says Rajesh Agarwal, PhD, investigator at the University of Colorado Cancer Center and professor at the Skaggs School of Pharmaceutical Sciences. It depends in large part, says Agarwal, on a healthy cell’s ability to wait out damage. “Cancer cells are fast-growing cells,” Agarwal says. “Not only that, but they are necessarily fast growing. When conditions exist in which they can’t grow, they die.”



## Muscadine Research

Grape seed extract creates these conditions that are unfavorable to growth. Specifically, the paper shows that grape seed extract both damages cancer cells' DNA (via increased reactive oxygen species) and stops the pathways that allow repair (as seen by decreased levels of the DNA repair molecules Brca1 and Rad51 and DNA repair foci). "Yet we saw absolutely no toxicity to the mice, themselves," Agarwal says.

Again, the grape seed extract killed the cancer cells but not the healthy cells. "I think the whole point is that cancer cells have a lot of defective pathways and they are very vulnerable if you target those pathways. The same is not true of healthy cells," Agarwal says.

The Agarwal Lab hopes to move in the direction of clinical trials of grape seed extract, potentially as an addition to second-line therapies that target head and neck squamous cell carcinoma that has failed a first treatment.

### Study Information:

S. Shrotriya, G. Deep, M. Gu, M. Kaur, A. K. Jain, S. Inturi, R. Agarwal, C. Agarwal. Generation of reactive oxygen species by grape seed extract causes irreparable DNA damage leading to G2/M arrest and apoptosis selectively in head and neck squamous cell carcinoma cells Carcinogenesis 2012 January - University of Colorado Cancer Center and professor at the Skaggs School of Pharmaceutical Sciences.



## Muscadine Research

### *Resveratrol Concentrations*

#### **Grape Seed Varieties**

#### **Levels**

Pinot Seed (red)	1.10 µg/g
Chardonnay Seed (white)	1.10 µg/g
Gamay Seed (red)	1.00 µg/g
Muscadine Seed (white)	43.65 µg/g
Muscadine Seed (red)	44.57 µg/g

\* Mississippi State University,  
Dr. Betty Ector.

## **Muscadines**

***Over 40 X the Resveratrol concentration of wine grape seeds!***



## Muscadine Research

MBA is dedicated to helping people develop a personal business enterprise. The American Dream does not come from working for someone else. We'll help you start your own business.

### **Why did we start Marketing Business Associates?**

Too many people are sick and broke and dying. We humans need to reduce stress and cortisol levels in the blood. We need to increase our immune system functions so the body can heal itself. We need to eat right and exercise. We believe we can help with some of those tasks.

### **Who are we looking for?**

You want to make more money (who doesn't) and help other people. Are you worth more than you get paid? Are you better than your boss thinks you are? You may be young - just getting started, or you may be retired or a decade from retirement - without enough in the bank to live as comfortably as you would like. Are you a self-starter? Are you ambitious? Are you driven? Do you have a small amount of time so we can help you build a successful residual income? Then we are looking for you! We want to help you increase or even double your income. You can live almost anywhere in the world and we can help you start a business for a lot less than you think. Contact us, we will be glad to discuss it with you.

Forbes magazine indicated that "direct marketing" was the best kept secret in the business world. Direct sales (of which network marketing is a part) has experienced 91-percent growth in the last 10 years with annual sales in excess of \$30 billion in the United States, and \$100 billion worldwide. Financial experts say it's a "recession proof" industry. Billionaire Warren Buffet, after purchasing a network marketing company, called it the best investment he'd ever made. Tom Peters, author of *In Search of Excellence*, calls it the first truly revolutionary shift in marketing in the last 50 years.

All of the reasearch in this pamphlet can be found on the net at the National Intstitute of Health - Pubmed.gov





## Muscadine Research

Many people over 50 are looking at retirement and wondering how they are going to make it on Social Security because they have no saving to speak of. A residual income business is less than \$500 to start and can provide the income boost you need with very little effort. Both Forbes and NPR recommend a residual income business for the boomers looking at or already in retirement. Residual income is money you continue to accumulate after you perform the work.

Nature's Pearl has FDA certification and is made from Muscadine seeds.

Nature's Pearl has over 30 million dollars in research backing up its product

Some research shows that Muscadine extract kills skin cancer in the laboratory.

The product is an all-natural, vegetarian, whole food supplement.

It is grown, stored and bottled in North Carolina (a real American product)!

It is sold person to person all over the United States and Canada.

It is loaded with antioxidants, anti-inflammatory and anticancer nutrients.

Research on Nature's Pearl supplements shows very positive results.

If you are interested in more information about the product,  
or want to start a business in Nature's Pearl,  
call or email me and I will be happy to discuss it with you.

The Nature's Pearl manufacturing process has been certified by the Food and Drug Administration. However it is not intended to diagnose, treat, cure, or prevent any disease. It is not a drug. It is an all-natural, vegetarian, organic, whole food supplement.

Rodger Rossman

Managing Partner

Marketing Business Associates

Nature's Pearl is "Made by Nature, Proven by Science"

Youngevity Independent Distributor #101683075

Phone: 252-340-5714

[rodgerrossman@gmail.com](mailto:rodgerrossman@gmail.com)