

Clinical Studies – Safety of Germanium-132

[Home](#) » [Research](#) » Clinical Studies – Safety of Germanium-132

A great deal of controversy has unnecessarily lingered for decades regarding the alleged lack of safety regarding Germanium-132 and its inclusion in dietary supplements. Much of this misinformation can be attributed to mistakes made years ago concerning the accidental or careless classification of organic germanium-132 (bis beta-carboxyethyl germanium sesquioxide) as being analogous or the same thing as elemental Germanium—a toxic metalloid utilized in a variety of industrial applications.

This false conclusion stems primarily from several unfortunate incidents occurring several decades ago. Basically, a handful disreputable manufacturers imported impure quantities of Germanium-132, that had been tainted with the elemental form perhaps to save money or increase their “product” volume, from Asian sources and a few subsequent deaths occurred.

The complete truth is—the *organic* form of Germanium-132 (in untainted, pure samples) has never caused any negative health reactions, illness, or death.

In clinical research, organic Germanium-132 has demonstrated efficacy for:

- Lowering or stabilizing blood pressure and serum cholesterol (LDL)
- Stimulating Interferon production (to block HIV virus replication)
- Encouraging suppressor T-Cell and NK-Lymphocyte production
- Activating dormant Macrophages to kill cytotoxins
- Promoting attraction and efficient absorption of oxygen by various bodily organs
- Protecting against radiation damage and free radicals
- Inhibiting the growth of harmful flora and invading organisms
- Rejuvenating development of blood vessels for improved vision
- Helping the body retain bone density while reducing sensitivity
- Diminishing parathyroid secretions leading to decreased bone strength
- Acting as a potent pain relieving agent

Essentially, organic Germanium-132 boosts the immune system by activating dormant

macrophages to phagocytize (digest) cellular debris and viruses and also motivate other immune cells into action. This organic mineral may also provide some benefit as well for improved neural response and resistance to germs. Many alternative health practitioners and experienced researchers assert all disease results directly from the under-oxygenation of cellular tissue; and Germanium-132 greatly enhances both the presence and absorption of oxygen in the body's various organs.

Although you may not be used to reading empirical data-oriented research, the clinical studies below provide verifiable information regarding both the safety and efficacy of Germanium-132 for supporting the immune system and natural body processes against a variety of negative health conditions. Criteria for these type of studies include the application of unbiased observation methods without adherence to preconceptions, strict protocols of the scientific method for experimental design, and most importantly, results that can be reproduced (and thus measured) over and over again.

In other words, these data cannot be refuted easily, not without presenting conflicting findings for peer review along with detailed explanations of why the earlier experiment failed in some respect. At the very least, the articles below provide a starting point for further study and consideration of this effective and *safe* health-promoting mineral.

Immunological control of methicillin-resistant *Staphylococcus aureus* (MRSA) infection in an immunodeficient murine model of thermal injuries.

Summary: GE-132 Can Protect Against MRSA Infections.

“*Staphylococcus aureus*, especially methicillin-resistant *S. aureus* (MRSA), is a major cause of sepsis in patients who are immunosuppressed by their burns. In this study, an immunological regulation of MRSA infection was attempted in a mouse model of thermal injury. SCIDbg mice were resistant to MRSA infection, while SCIDbgMN mice (SCIDbg mice depleted of neutrophils and macrophages (Mphi)) were susceptible to the same infection. Also, thermally injured SCIDbg mice were shown to be susceptible to MRSA infection. On the other hand, the resistance of SCIDbgMN mice to the infection was completely recovered after an inoculation with Mphi from normal mice.

However, anti-MRSA resistance was not shown in SCIDbgMN mice inoculated with

Mphi from thermally injured mice. Mphi from MRSA-infected thermally injured mice were identified as alternatively activated Mphi, and Mphi from MRSA-infected unburned mice were characterized as classically activated Mphi.

Mphi from thermally injured SCIDbg mice previously treated with 2-carboxyethylgermanium sesquioxide (Ge-132) protected SCIDbgMN mice against MRSA infection. Ge-132 has been described as an inhibitor of alternatively activated Mphi generation. These results suggest that MRSA infection in thermally injured patients is controlled immunologically through the induction of anti-MRSA effector cells and elimination of burn-associated alternatively activated Mphi, which are cells that inhibit the generation of classically activated Mphi.”^[1]

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^[1]Katakura, T., Yoshida, T., Kobayashi, M., Herndon, D. N. and F. Suzuki. “Immunological control of methicillin-resistant *Staphylococcus aureus* (MRSA) infection in an immunodeficient murine model of thermal injuries.”

Clinical and experimental immunology. Vol. 142, Issue 3. (419-25). Dec 2005. Online. Accessed: 9 May 2007. (Highlighted text by *The Editors*).

Available: <http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?CMD=search&DB=pubmed> PMID: 16297152 [PubMed - indexed for MEDLINE]

DNA binding specificity and cytotoxicity of novel antitumor agent Ge132 derivatives.

Summary: GE-132 Shows Enhanced Anti-Tumor Activity.

“A series of Ge132 derivatives have shown enhanced anti-tumor activity. Previous studies suggest that DNA can be their primary target. Here we show direct evidence that two newly synthesized Ge132 derivatives can intercalate into DNA. Unexpected methyl substitution effect of the novel derivatives on DNA sequence selectivity and cytotoxicity was observed.”^[1]

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[1]Shangguan, G., Xing, F., Qu, X., Mao, J., Zhao, D., Zhao, X. and J. Ren. "DNA binding specificity and cytotoxicity of novel anti-tumor agent Ge132 derivatives."

Bioorganic & medicinal chemistry letters. Vol. 15, Issue 12. (2962-5). 2005 Jun 15. Online. Accessed: 9 May 2007. (Highlighted text by *The Editors*).

Available: <http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?CMD=search&DB=pubmed> PMID: 15914003 [PubMed - indexed for MEDLINE]

Prevention of trabecular bone loss in the mandible of ovariectomized rats.

Summary: GE-132 Shows Increased Bone Mineral Density and Bone Mineral Content.

"The effect of therapeutic agents on trabecular bone loss in the mandible was investigated in ovariectomized rats. Eighty-seven Wistar SPF female rats were ovariectomized (OVX) or given a sham operation (Sham), and maintained on a diet containing 0.1% calcium. Four weeks later, groups of OVX rats were treated with estriol (E3), calcitonin (CT), etidronate, or 2-carboxyethylgermanium sesquioxide (Ge-132).

The Basal group was maintained on a diet containing 1.0% calcium, and the OVX and sham groups on a diet containing 0.1% calcium. The trabecular bone mineral density (BMD) and trabecular bone mineral content (BMC) in 11 mandibular slices from 0.5 mm at the mesial margin of the first molar to 0.5 mm at the distal margin of the third molar, were measured using peripheral Quantitative Computed Tomography (pQCT).

The BMD in the OVX group was lower than that in the Sham group, and decreased BMC was observed only in the molar region. BMD and BMC were increased in the etidronate-treated group, but only BMC was increased in the CT group. E3 treatment increased BMD and BMC; significant increases were also observed beneath the molar. Ge-132 treatment increased both BMD and BMC, especially the latter."^[1]

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Chiba, Japan.**

[1]Jiang, G., Matsumoto, H., Yamane, J., Kuboyama, N., Akimoto, Y. and A. Fujii. "Prevention of trabecular bone loss in the mandible of ovariectomized rats." *Journal of oral science*. Vol. 46, Issue 2. Jun 2004. (75-85). Online. Accessed: 9 May 2007. (Highlighted text by *The Editors*). Available: <http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?CMD=search&DB=pubmed> PMID: 15287540 [PubMed - indexed for MEDLINE]

Germane facts about germanium sesquioxide:

I. Chemistry and anticancer properties.

Summary: GE-132 – Anti-Cancer Properties and why more Studies have not been Performed!

“This paper reviews the history, chemistry, safety, toxicity, and anticancer effects of the organogermanium compound bis (2-carboxyethylgermanium) sesquioxide (CEGS). A companion review follows, discussing the inaccuracies in the scientific record that have prematurely terminated research on clinical uses of CEGS. CEGS is a unique organogermanium compound first made by Mironov and coworkers in Russia and, shortly thereafter, popularized by Asai and his colleagues in Japan.

Low concentrations of germanium occur in nearly all soils, plants and animal life; natural occurrence of the CEGS form is postulated but not yet demonstrated. The literature demonstrating its anticancer effect is particularly strong: CEGS induces interferon-gamma (IFN-gamma), enhances natural killer cell activity, and inhibits tumor and metastatic growth—effects often detectable after a single oral dose.

In addition, oral consumption of CEGS is readily assimilated and rapidly cleared from the body without evidence of toxicity. Given these findings, the absence of human clinical trials of CEGS is unexpected. Possible explanations of why the convincing findings from animal research have not been used to support clinical trials are discussed. Clinical trials on CEGS are recommended.”^[1]

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Calgary, Alberta, Canada**

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[1]Kaplan, B. J., Parish, W. W., Andrus, G. M., Simpson, J. S. and C. J. Field. "Germane facts about germanium sesquioxide: I. Chemistry and anticancer properties."

Journal of alternative and complementary medicine. Vol. 10, Issue 2. Apr 2004. (337-44). Online. Accessed: 9 May 2007. (Highlighted text by *The Editors*).

Available: <http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?CMD=search&DB=pubmed> PMID: 15165414 [PubMed - indexed for MEDLINE]

Germane facts about germanium sesquioxide:

II. Scientific error and misrepresentation.

"The preceding paper reviewed the anticancer properties and safety of bis (2-carboxyethylgermanium) sesquioxide (CEGS). An examination of those data leads one to question why this information has not stimulated clinical trials in patients with cancer. The answer is discussed in this paper, which traces the history to an error published in the scientific literature in 1987.

The reliance by subsequent authors on secondary sources, citing only the error and not the correction published in 1988, constitutes part of the explanation of why CEGS has been neglected. A second factor is also considered: careless reporting about any germanium-based compound as if the many thousands of germanium compounds were all the same. This combination of a publication error, careless writing, and the reliance on secondary sources appears to be responsible for the neglect of the potential clinical use of this unique germanium compound."^[1]

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[1]Kaplan, B. J., Andrus, G. M. and W. W. Parish. "Germane facts about germanium sesquioxide: II. Scientific error and misrepresentation."

Journal of alternative and complementary medicine. Vol. 10, Issue 2. Apr 2004 (345-8). Online. Accessed: 9 May 2007. (Highlighted text by *The Editors*).

Available: <http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?CMD=search&DB=pubmed> PMID: 15165415 [PubMed - indexed for

MEDLINE]

[Studies on the hydroxyl free radical-scavenging effect of combined selenium and germanium.]

[Article in Chinese]

Summary: GE-132 – Free Radical Scavenging Ability with Selenium!

“The effect of selenium, carboxyethyl-germanium sesquioxide (Ge-132) and the combination of selenium and Ge-132 on the production of hydroxyl free radical in liver microsomes of rats treated with Fe₂SO₄-NADPH system was studied with electron spin resonance technique (ESR). The results showed that the production of hydroxyl free radical was decreased significantly by adding selenium, Ge-132 and combined selenium and Ge-132, indicating a direct scavenging effect on hydroxyl free radical. It was also observed a enhanced scavenging effect at the low concentration of combined selenium and Ge-132.”^[1]

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Wuhan 430030, China.

^[1]Wu, Z., Chen, X., Yang, K. and T. Xia. “[Studies on the hydroxyl free radical-scavenging effect of combined selenium and germanium].” (Article in Chinese).

Wei sheng yan jiu. (Journal of hygiene research.) Vol. 30, Issue 4. Jul 2001 (208-10). Online. Accessed: 9 May 2007. (Highlighted text by *The Editors*).

Available: <http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?CMD=search&DB=pubmedPMID:12561515> [PubMed - in process]

2-Carboxyethylgermanium sesquioxide, a synthetic organogermanium compound, as an inducer of contrasuppressor T cells.

Summary: GE-132 Induces Contrasuppressor T-Cell Activity!

“2-Carboxyethylgermanium sesquioxide (Ge-132), a synthesized organogermanium compound with immunomodulating activities, was shown to be an inducer of anti-suppressor T cells in normal mice. The suppressor cell activity of T6S cells, a clone of burn-

induced CD8+ IL-4-producing suppressor T cells, was clearly inhibited when a mixed lymphocyte-tumor cell reaction of the clone was conducted with splenic mononuclear cells from mice treated orally with a 100 mg/kg dose of Ge-132. The activity of anti-suppressor cells was demonstrated in spleens of mice 2 days after treatment with Ge-132 and reached its peak on day 3.

The anti-suppressor cells induced by the compound were of a contrasuppressor T cell-lineage, because they were characterized as CD4+ CD28+ TCRalpha/beta+ Vicia villosa lectin-adherent T cells. These cells produced IFN-gamma but did not produce IL-2, IL-4, IL-6 or IL-10 in their culture fluids. CD4+ anti-suppressor T cells induced by Ge-132 may be different from other subsets of CD4+ T cells because Th1 and Th2 cells generated in our laboratory did not adhere to Vicia villosa lectin-coated petri dishes, and each produced specific cytokines.

Th1 cells produced IFN-gamma and IL-2 while Th2 cells produce IL-4 and IL-10 in vitro. These results suggest that Ge-132 may be useful as an inducer of contrasuppressor T cells in immunocompromised individuals bearing suppressor T cells. To eliminate suppressor T cells from immunocompromised hosts may result in improved resistance from various opportunistic infections.“^[1]

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Yamaguchi University of Medical School
Japan.**

^[1]Ikemoto, K., Kobayashi, M., Fukumoto, T., Morimatsu, M., Pollard R. B. and F. Suzuki. “2-Carboxyethylgermanium sesquioxide, a synthetic organogermanium compound, as an inducer of contrasuppressor T cells.” *Experientia*. Vol. 52, Issue 2. Feb 1996 (159-66). Online. Accessed: 9 May 2007. (Highlighted text by *The Editors*). Available: <http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?CMD=search&DB=pubmedPMID: 8608818> [PubMed - indexed for MEDLINE]

Effect of organic germanium compound (Ge-132) on experimental osteoporosis in rats.

Summary: GE-132 – May be Beneficial for Osteoporosis!

“The therapeutic effect of organic germanium compound, 2-carboxyethylgermanium-

sesquioxide (Ge-132), for experimental osteoporosis was studied using ovariectomized rats maintained on a low calcium containing diet. 2. Serum calcitonin (sCT) level was decreased and serum parathyroid hormone (sPTH) level was increased by ovariectomy and the decrement and increment rates, respectively, were reduced by administration of Ge-132.

Thus, the sCT/sPTH ratio was greater in the groups given Ge-132, indicating that the resorption [sic] was somehow inhibited by Ge-132. 3. The transverse strength of femur bone was significantly enhanced by Ge-132. 4. A trend was found in the group given Ge-132 for a larger femur cortical bone index. 5. The relative femur bone wet weight was greater in the group given Ge-132. 6. These results indicate that Ge-132 prevents decreased bone strength, and affects the femur cortical bone index, and bone mineral mass caused by osteoporosis.“^[1]

**Department of Pharmacology
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Chiba, Japan.**

^[1]Fujii, A., Kuboyama, N., Yamane, J., Najao, S. and Y. Furukawa. "Effect of organic germanium compound (Ge-132) on experimental osteoporosis in rats."

General pharmacology. Vol. 24, Issue 6. Nov 1993 (1527-32). Online. Accessed: 9 May 2007. (Highlighted text by *The Editors*). Available: <http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?CMD=search&DB=pubmed> PMID: 8112531 [PubMed - indexed for MEDLINE]

Antiviral activity of carboxyethylgermanium sesquioxide (Ge-132) in mice infected with influenza virus.

Summary: GE-132 – Immunomodulating activities. May have Anti-Viral Properties.

“The protective effect of carboxyethylgermanium sesquioxide (Ge-132) in mice infected with a mouse-adapted strain of influenza virus (H2N2) was investigated. When mice were exposed to a 10 LD50 dose of influenza virus via aerosol and were treated orally with 20 or 100 mg/kg of Ge-132 daily for 6 consecutive days, a significant protective effect was demonstrated.

The antiviral effect of Ge-132 was indicated by an increase of survivors, a prolongation of mean survival days, an inhibition of the development of lung consolidation, and a decrease of virus titer in lung tissues, as compared to infected control mice treated with phosphate-buffered saline.

Natural killer (NK) cell activity in the spleens and lungs of the infected mice was also significantly augmented after the oral administration of Ge-132. In addition, NK cells stimulated with Ge-132 in vivo showed killing activity against NK-insensitive Meth-A cells infected with influenza virus.

Because no virucidal or virustatic activities of Ge-132 on the virus were found in vitro, this protective effect in mice against influenza virus infection may be displayed through immunomodulating activities of this compound such as the augmentation of NK cell activity.”^[1]

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Sendai, Japan.**

^[1]Aso, H., Suzuki, F., Ebina, T. and N. Ishida. “Antiviral activity of carboxyethylgermanium sesquioxide (Ge-132) in mice infected with influenza virus.”

Journal of biological response modifiers. Vol. 8, Issue 2. Apr 1989 (180-9). Online. Accessed: 11 May 2007. (Highlighted text by *The Editors*).

Available: <http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?CMD=search&DB=pubmed> PMID: 2471817 [PubMed - indexed for MEDLINE]

Induction of interferon production by natural killer cells by organogermanium compound, Ge132.

Summary: GE-132 – Study shows increased Interferon production by Natural Killer Cells.

“Interferon (IFN)-inducing activity of the organogermanium compound Ge132 in human peripheral mononuclear cells was investigated. By using Percoll discontinuous density gradient centrifugation, peripheral blood nonphagocytic and nonadherent mononuclear cells were divided into the low-and high-density fractions. Natural killer

(NK)-enriched low-density fractions, but not the T-cell-enriched high-density fractions, showed IFN production by the stimulation of Ge132.

The maximal titer of IFN by NK-enriched fractions (F1 + F2) was observed after a 74-h cultivation in the presence of 200 micrograms/ml Ge132. IFN production by the NK-enriched fractions was abrogated by treatment of the cells with monoclonal antibody against human NK cells in the presence of complement. The treatment with antiserum-neutralizing human IFN-gamma resulted in a marked reduction, indicating that a major part of IFN was IFN-gamma. These results suggested that Ge132 might possess affinity to NK cells, inducing IFN production by NK cells.“^[1]

^[1]Munakata, T., Arai, S., Kuwano, K., Furukawa, M. and Y. Tomita. “Induction of interferon production by natural killer cells by organogermanium compound, Ge132.”
Journal of interferon research. Vol. 7, Issue 1. Feb 1987 (69-76). Online. Accessed: 11 May 2007. (Highlighted text by *The Editors*). Available: <http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?CMD=search&DB=pubmed> PMID: 3108417 [PubMed - indexed for MEDLINE]

[Inhibitive effects of spirulina on aberrant crypts in colon induced by dimethylhydrazine]

[Article in Chinese]

Summary: GE-132 – Study shows protective ability on Colon Aberrant Cysts.

“Precancerous pathological changes of colon was induced by single injection in a short-term and multiple injection in a long-term intraperitoneally with 1,2-dimethylhydrazine (DMH) in NIH mice and Sprague-Dawley rats. And, protective effects of spirulina, germanium-132 and vitamin E on colon aberrant crypts induced by DMH were observed.

Results showed either single injection or multiple injection with DMH could induce aberrant crypts in colon. The number of aberrant crypts scattered by short-term single injection was less than that by multiple one, and less of the aberrant crypts foci were formed by short-term single injection.

Spirulina powder, germanium-132 and vitamin E all could inhibit the function of aber-

rant crypts of colon. In the ninth week during multiple injection with DMH, a lot of aberrant crypts of colon had been induced, and a certain amount of aberrant crypts foci had been generated. The number of aberrant crypts and aberrant crypts foci in the animals with tumor increased with the length of DMH injection. In the ninth-, 13th- and 16th-week, respectively, the number of aberrant crypts and aberrant crypts foci was significantly less in animals protected by spirulina than in positive controls ($P < 0.01$), but there was no significant difference between them during 21st- and 24th-week of injections.”^[1]

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Hengyang Hunan.**

^[1]Chen, F. and Q. Zhang. “[Inhibitive effects of spirulina on aberrant crypts in colon induced by dimethylhydrazine].” (Article in Chinese).

Zhonghua yu fang yi xue za zhi. (Chinese journal of preventive medicine). Vol. 29, Issue 1. Jan 1995 (13-7). Online. Accessed: 11 May 2007. (Highlighted text by *The Editors*).

Available: <http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?CMD=search&DB=pubmed> PMID: 7600882 [PubMed - indexed for MEDLINE]

[An observation of antiproliferative effect of germanium-132 on cultured pterygium fibroblasts]

[Article in Chinese]

Summary: GE-132 – Study shows effect on Pterygium Fibroblasts.

“OBJECTIVE: To detect the antiproliferation of carboxyethyl germanium sesquioxide (Ge-132) on fibroblasts of pterygium in vitro and try to find a potentially effective agent for treatment of primary pterygium and prevention of its postoperative recurrence.

METHODS: Primary culture and subculture of pterygium fibroblasts were established in vitro. Different concentrations of Ge-132 (39 – 5,000 mg/L) or mitomycin-C (3.13 – 4.00 mg/L, the control) were added to the fibroblast culture of the third or fourth passage respectively. The inhibitory effect was determined by MTT (tetrazolium bromide) method. The influence of addition of Ge-132 on the growth curve of fibroblasts was observed, and the changing expression of proliferating cell nuclear antigen (PCNA) in

fibroblasts was studied by immunohistochemical method

RESULTS: The addition of Ge-132 in the culture caused significant inhibition of the fibroblast proliferation in dose dependent manner (625 – 50,000 mg/L) without cytotoxicity (IC(50) = 3,000 mg/L), the marked descent of growth curve and suppression of the expression of PCNA in cultured cells (P < 0.01). **CONCLUSION:** Ge-132 can inhibit the proliferation of pterygium fibroblast in vitro significantly.“^[1]

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^[1]Liu, Y., Sun, X., Li, B. and J. Wang. “[An observation of antiproliferative effect of germanium-132 on cultured pterygium fibroblasts]” (Article in Chinese).

[Zhonghua yan ke za zhi]. (Chinese journal of ophthalmology). Vol. 36, Issue 4. Jul 2000 (263-6), 16. Online. Accessed: 11 May 2007. (Highlighted text by *The Editors*).

Available: <http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?CMD=search&DB=pubmed> PMID: 11853609 [PubMed - indexed for MEDLINE]

Effect of germanium-132 on low-density lipoprotein oxidation and atherosclerosis in Kurosawa and Kusanagi hypercholesterolemic rabbits.

Summary: GE-132 – Study shows Antioxidant Ability of Germanium-132.

“Germanium-132 (Ge-132) was given at 200 mg/kg of body weight to 8-week-old Kurosawa and Kusanagi hypercholesterolemic (KHC) rabbits. Thirty-six weeks later, the susceptibility of plasma low-density lipoprotein to oxidation and the morphology of atherosclerosis in the aorta and coronary artery were investigated. Treatment with Ge-132 resulted in decreases in the oxidation rate and in the formation rate of thiobarbituric acid-reactive substances following copper-induced oxidation of LDL. Ge-132 is suggested to possess antioxidative properties, but this did not lead to any attenuation of atherosclerotic progression in the KHC rabbits.“^[1]

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[1]Wakabayashi Y. "Effect of germanium-132 on low-density lipoprotein oxidation and atherosclerosis in Kurosawa and Kusana-gi hypercholesterolemic rabbits."
Bioscience, biotechnology, and biochemistry. Vol. 65, Issue 8. Aug 2001 (1893-6). Online. Accessed: 11 May 2007. (Highlighted text by *The Editors*).
Available: <http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?CMD=search&DB=pubmed> PMID: 11577738 [PubMed - indexed for MEDLINE]