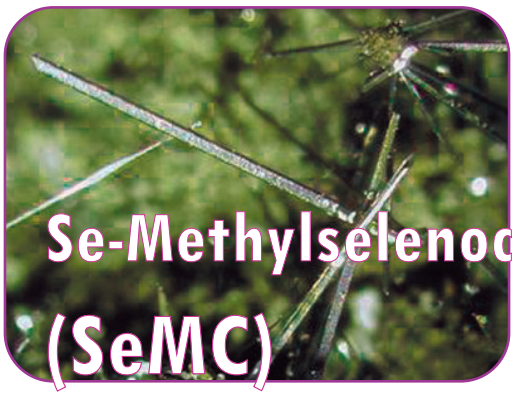
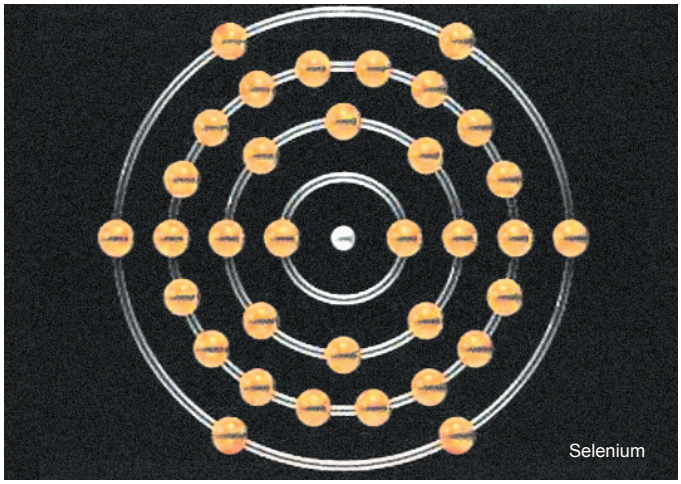


Se-Methylselenocysteine (SeMC)

Beyond selenate ... beyond selenomethionine ... beyond whole selenized yeast ...

Heart disease remains the number one cause of death in the developed world ... yet dying of **cancer** continues to evoke the greater fear. Indeed, many people who wouldn't otherwise become health-conscious will suddenly change their lifestyles when this killer breaks into their lives.

We know a lot about the lifestyle choices that can protect a person against cancer: a diet rich in fruits and vegetables, regular exercise, and avoiding carcinogenic compounds from cigarette smoke to fungal toxins are proven ways to reduce your risk. But today's science lets us be a lot more specific than these broad guidelines. Beyond making shifts in consumption of *whole food groups*, there's quite a bit of evidence that getting more of certain *specific* vitamins, minerals, and phytonutrients reduces your risk of cancer. And at the top of the list is **selenium**.


Selenium

Starting in the 1960s[1] and continuing through to today,[2] a mountain of evidence – from animal and test-tube studies, to research comparing the risk of cancer among and within populations with different dietary selenium intakes or soil, water, or crop selenium levels – has accumulated to back up selenium's cancer-fighting reputation.[3] The most powerful evidence to date has come in the form of the "gold standard" of scientific proof: a large-scale, randomized, double-blind, placebo-controlled trial.[4]

This study – in which over 1300 patients with existing skin cancer participated – found that, while it had no effect against skin cancer, **a 200 microgram selenium supplement cut the incidence of *new* cancers by 37%, slashed cancer *deaths* by 50%, and reduced death *from all causes* by a remarkable 17%** as compared to a placebo.[4] The trial was able to document *specific* reductions in **lung and colon cancers**,[4] and an especially remarkable effect against **prostate cancer**: later analysis revealed that men taking the selenium supplement were only *37%* as likely to suffer this fate as were men who had received the dummy pill.[5]

That's the good news. Now get ready for *even better* news. As scientists have learned how selenium is metabolized in the body, they've also come to a new understanding of the biochemical processes that underlie selenium's anti-cancer effects. And with these insights, researchers have been able to do what they've never been able to do before: to identify *specific forms* of selenium whose biochemical characteristics make them most readily used by the body to create potent cancer-fighting metabolites. The bottom line: over the course of the last decade, **science has discovered a naturally-occurring form of selenium which is simultaneously *more potent* in its cancer-battling prowess, *and less toxic per unit of cancer-fighting punch*, than any other selenium supplement available.**

Selenium which is simultaneously *more potent* in its cancer-battling prowess, *and less toxic* than any other selenium supplement available.

This breakthrough selenium compound is **Se-methylselenocysteine** – often referred to by its initials as **SeMC**. And with the coming of the twenty-first century, its time has come.

It's *Not* the Antioxidant Effect!

The first thing to get your head around is the fact that **selenium's most important anti-cancer effects – and the unique combination of cancer-fighting prowess and low toxicity seen in SeMC – have *nothing to do* with the mineral's antioxidant activity**. Popular books and magazines are still trotting out the notion that selenium fights cancer because it's an antioxidant, used as part of the antioxidant enzymes **glutathione peroxidase (GSH-Px)** and **thioredoxin reductase (TrxR)**. By fighting off free

radicals, it's said, these selenium-containing enzymes could prevent the damage to DNA that can ultimately turn a healthy cell into a consuming enemy within. But while selenium is certainly important as an antioxidant, the idea that antioxidant activity explains selenium's *anti-cancer* effects has been abandoned by researchers, because it just can't be squared with the latest science on how selenium is handled in the body.

Totally Untested

In this article, we'll be focusing on the different cancer-fighting potency and toxicities of several different forms of selenium. Two forms which we will not be discussing are undefined "selenium proteinates" and "selenium amino acid chelates." This is because there is *absolutely no scientific data available* on the toxicity of these forms of selenium, or on their effect on cancer;[15] indeed, they don't even represent a clearly-defined form of selenium to begin with. In the complete absence of reliable information on these forms of selenium, we strongly recommend avoiding supplements which contain these uncharacterized selenium compounds.

Selenium's most important anti-cancer effects have *nothing to do* with the mineral's antioxidant activity.

Careful studies in the role of selenium in protecting animals from experimental cancer clearly show that **the strongest anti-cancer effect is achieved at intakes far greater than the dosages at which antioxidant enzymes max out.** That is, your body doesn't just keep pumping out more and more selenium-dependent proteins as you take in more and more selenium: at surprisingly low levels, the production of these enzymes reaches a plateau. In humans, levels of key selenium-based enzymes reach a plateau level when your whole-blood or plasma selenium concentrations reach about 90 to 100 nanograms per milliliter[6-9] – levels achievable after[8] consuming just 40 micrograms of supplemental selenium a day.[8,9] As intake of selenium increases beyond this basic nutritional level, there is a *temporary* jump in TrxR's levels and/or activity, but the increase fades away with time.[10-12] Yet the amount of selenium which maximizes the *anti-cancer* effect is much greater than this – and also greater than the amount needed for detoxification of some cancer-causing chemicals, or for the enhancement of the immune system, which were also once put forward as possible explanations for selenium's cancer-quashing effect (see **Figure 1**).

In fact, there is even more direct proof that boosting antioxidant and detoxification enzymes are not the basis for selenium's anticarcinogenic prowess. When you feed laboratory animals the same amount of selenium in either an organic form (**selenomethionine**, the form used in most supplements and the main form of selenium in selenium-yeast supplements) or the two common inorganic forms (**selen*ite* and selen*ate***), selenomethionine gives the animals the greatest boost in antioxidant glutathione peroxidase activity … yet the two inorganic forms are the more effective cancer-fighters.[13,14] Likewise, inorganic selenium's greater cancer-battling properties can't be explained by its effects on detoxification enzymes like **glutathione transferases**, because these forms of selenium are equal to selenomethionine in their ability to elevate this enzyme.[13]

Furthermore, there is a disconnect between the *tissue levels* of selenium that you get after consuming a given amount of a particular form of the mineral, and the strength of the anti-cancer effect of that form of selenium. Again using the more common forms of the supplement, scientists have shown that, over a wide range of doses, taking a given amount of selenium in the form of selenomethionine causes more selenium to accumulate in your tissues than taking the same amount of selenium as selenite or selenate– yet, once again, selenite and selenate consistently outperform selenomethionine when tested as cancer shields.[13,14] In one study, in fact, either selenite or selenate provided a measure of protection against the earliest stages in cancer development at dosages where selenomethionine was *totally without effect*.[16]

An even stronger rebuttal of the idea that simple *levels* of selenium were decisive in the mineral's anti-cancer effect came from feeding animals a constant level of selenomethionine, but in combination with either a standard diet, or a diet designed to inhibit the body's accumulation of selenium from this form of the mineral. The result: the diet that *reduced* the body's retention of selenomethionine actually *enhanced* its anti-cancer effect![17] Yet when animals were fed selenite (whose tissue accumulation is not affected by the same dietary manipulation), the mineral's

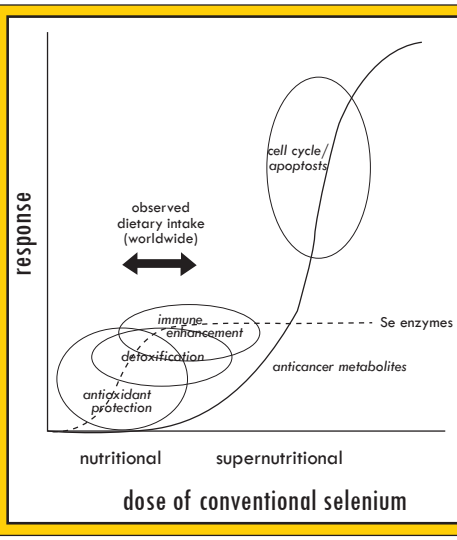


Figure 1. Intake of selenium, antioxidant enzymes, and anti-cancer effect. Redrawn from (3).

cancer-shielding capacity was unaffected by the same changes in the diet.[17]

SeMC, the selenium supplement that maximizes the body's production of a key anti-cancer metabolite.

These studies parallel findings in studies of the relationship between selenium status and vulnerability to cancer in large human populations. In these studies, when selenium status is measured using higher intake of the mineral in the diet, a protective relationship is almost always reported.[2,3,18] Yet when the amount of selenium that has been accumulated by the body is measured, there is no consistent association.[2,3,18] In one especially revealing study,[18] women with the highest *dietary* intake of selenium were nearly 38% less likely to suffer breast cancer than were women whose intake was lowest … yet there was *no connection* between breast cancer risk and plasma, red blood cell, or toenail selenium levels *in the same women!*

But if immune enhancement, carcinogen detoxification, antioxidant action, and even tissue concentrations don't explain selenium's vigilance on the "enemy within," what does? To answer this question, scientists asked the next question. *What happens metabolically to all of that "other" selenium* – the selenium that is *not* being accumulated in the tissues, and which is *not* incorporated into proteins or into enzymes with antioxidant or detoxifying properties?

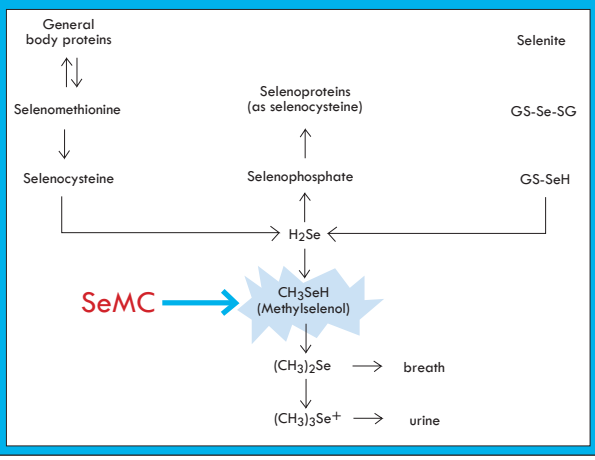
As it turned out, the painstaking work of uncovering the answer to this question was not just an excuse for researchers to ask the government for more grant money. Understanding the way that selenium is processed by the body has led to a revolution in our understanding of how selenium fights cancer. And with this knowledge in hand, scientists have identified **SeMC**, the selenium supplement that maximizes the body's production of a key anti-cancer metabolite, yet which minimizes the toxicity associated with some other forms of the mineral.

While many scientists contributed to the ultimate revelation, the breakthrough insights and key experiments have come out of the labs of Dr. Clement Ip of the Roswell Park Cancer Institute and Dr. Howard Ganther of the University of Wisconsin's Department of Nutritional Sciences.[14,17,19-29] Other key research (spearheaded by Dr. John W. Finley of the USDA's Grand Forks Human Nutrition Research Center,[30-33] Dr. Henry Thompson of the AMC Cancer Research Center,[25,34-39] Dr. Ranabir Sinha of the Baylor College of Medicine,[40-43] and Dr. Julian Spallholz of the Texas Tech University Health Sciences Center,[44-46]) has helped make the full importance of these findings clear, integrating them into unexpected corners of cancer-nutrition research and revealing the mechanisms that underlie **SeMC**'s superiority.

The Fork in the Road

The metabolic pathways of different forms of selenium are pictured in **Figure 2**. As you can see, both selenomethionine and sodium selenite *can* be converted into **hydrogen selenide (H_2Se)**. However, much of the selenium in selenomethionine gets tied up into general body proteins, while this doesn't happen with inorganic selenium salts (such as selenate or selenite). As a result, more hydrogen selenide is formed when you take selenate

Figure 2: The Selenium Metabolic Pathway. Redrawn from (24).



or selenite than when you take the same amount of selenium as selenomethionine. Since their research had shown that inorganic forms of selenium is the stronger cancer-fighter of the two,[13,14,17] and that inhibiting selenomethionine's incorporation into general bodily proteins (which frees up more selenium to be metaboblized into hydrogen selenide) makes it more effective in protecting against cancer,[17] it seemed clear that the anti-cancer effect of these two forms of selenium was somehow dependent on their being converted into hydrogen selenide.

If the formation of hydrogen selenide is a critical step in the ability of inorganic forms of selenium and selenomethionine to fight cancer, then the next logical question is whether this fact is due to the hydrogen selenide *itself*, or is instead related to something that the body forms *out of* it. To answer this question, Ganther and Ip looked at its two major metabolic fates (see **Figure 2**). Much of the hydrogen selenide in the body is used to make the selenium-dependent antioxidant and detoxification enzymes. But once these enzymes are fully topped up, the body protects itself from the inherent toxicity of hydrogen selenide by using a biochemical reaction known as **methylation** to form the dramatically less-toxic **methylselenol (CH_3SeH)** metabolite. And methylselenol, in turn, is metabolized into further, even *more* methylated

derivatives (see **Figure 2**).

Don't Try This at Home, Kids!

More evidence for methylselenol's place as the critical selenium metabolite came from experiments combining different forms of selenium with the toxic metal **arsenic**. Arsenic alters selenium compounds by removing methyl groups, so giving animals various selenium compounds combined with arsenic allowed scientists to further demonstrate the importance of methylselenol, versus metabolites which are more or less methylated, in preventing cancer. Thus, combining arsenic with selenite results in less methylselenol being formed – and it blocks selenite's anti-cancer effect.[47,48] At the other end of the selenium metabolic pathway (see **Figure 2**), the heavily-methylated trimethylselenonium form of selenium is so hard to break down into methylselenol that it offers no protection against cancer; but when you combine it with arsenic, the methyl groups are stripped off and some methylselenol is formed. The dumbfounding result: the **trimethylselenonium-plus-arsenic cocktail *protects experimental animals against cancer*,**[48] even though by themselves trimethylselenonium is useless – and arsenic is a known carcinogen, which *causes* cancer of the bladder, lungs, skin, kidney, liver, and prostate!

Of the three possible anticancer selenium compounds – hydrogen selenide itself, selenium-containing antioxidant and detoxification enzymes, or methylated selenium metabolites – Ganther and Ip were able to rule out the enzymes, as we've already discussed.[13,14] So now there were two possibilities: hydrogen selenide, or one of the methylated selenium compounds. Ip and Ganther resolved the question simply and elegantly. They identified a series of forms of selenium which the body *directly converts* into the methylated forms of selenium, *without* passing through the hydrogen selenide step. If hydrogen selenide itself was the essential selenium metabolite, then these forms of selenium would be ineffective in fighting cancer. But if one of the methylated selenium compounds were the true secret of selenium's dynamic protective activity, then the compound that most readily formed this metabolite would be pointing at the center of the labyrinth.

The SeMC Solution

The results of this research can be seen in **Table 1**. The bottom line: compounds which are most directly converted into methylselenol, such as methylseleninic acid, selenobetaine, and **Se-Methylselenocysteine (SeMC), proved to be the most potent, and among the least toxic, forms of selenium.** Using **SeMC** and other immediate precursors of methylselenol, less selenium is needed to get the same anti-cancer effect … and yet these forms of selenium are safe at doses where inorganic selenium is toxic. In fact, **SeMC** has a lack of toxicity similar to that of selenomethionine, which is *much* less effective at fighting cancer. And unlike selenomethionine, **SeMC** doesn't build up in your tissues – a fact which resolves the curious finding that you can predict a person's cancer risk from the amount of selenium in his or her diet or in the local soil and water, but *not* from the amount of the mineral in his or her tissues.

In terms of *sheer potency,* **SeMC** is clearly the best selenium source to use. But when you consider the potential toxicity of selenium, and the evidence from animal studies that the amount of selenium that's most effective in fighting cancer is much higher than the doses usually used in supplements (see **Figure 1**),[3] **SeMC** looks even better. If we think in terms of a "therapeutic window" between the toxic and the effective dose, there is nearly no room to maneuver when using inorganic selenium or selenomethionine, while a wide gap separates the therapeutic dose of **SeMC** and the dose at which toxicity emerges (**Table 1**). To put it another way: if we think **in terms of a potency-to-toxicity ratio, SeMC undeniably comes out on top,** its ratio being about *twice* as good as either selenite or selenomethionine.

Table 1. SeMC: The Superior Selenium Against Experimental Breast Cancer.
Adapted from (23,26).

Form Of Selenium	Metabolite	Dose (ppm) Needed To Cut Tumors by 50%	Toxic Dose (ppm)
SeMC	Methylselenol	2	5
Selenobetaine	Methylselenol	2	5
Selenobetaine methyl ester	Dimethylselenide	2–3	?
Selenite	H2Se	3	4
Selenomethionine	H2Se + Enzymes	4–5	5-6
Selenocystine	H2Se + Enzymes	4–5	?
Dimethylselenoxide	Dimethylselenide*	>10	?
Trimethylselenonium	(Itself)	>80†	Nontoxic

* A biochemically inefficient conversion. †No effect at this dose

Forms of selenium (such as selenite, selenate, and selenomethionine), which must jump through the hoops of first forming hydrogen selenide and being methylated before they can form methylselenol are less effective than those forms (such as **SeMC**) whose path to methylselenol has no obstacles. Likewise, selenium compounds (such as selenobetaine methyl ester, dimethylselenoxide, and trimethylselenonium) which can only be "retroconverted" into methylselenol by stripping them of their "extra" methyl groups (see the sidebar, **Don't Try This at Home, Kids!**) are poor cancer-fighters.[23,26] There's only one conclusion that you can draw from all of

this: methylselenol is the critical metabolite for cancer prevention. Since methylselenol *itself* can't be used as an anti-cancer supplement (because this critical metabolite is too chemically unstable to be used in this way), a direct methylselenol precursor such as **SeMC constitutes the most potent form of selenium for cancer prevention.**[25]

The Secret of Cancer-Fighting Foods

It's long been known that people who live in areas with higher concentrations of selenium in their soil and crops are much less likely to die of cancer.[1,3] And it's well-established that a diet rich in fruits and vegetables is one of your best defenses against this killer – and especially certain *specific* fruits and veggies.[49] The plant foods that have most consistently been found to lower your risk of cancer are cruciferous vegetables (such as broccoli and cabbage) and *Allium* vegetables (like onions and garlic), along with tomatoes.[49] The usual explanation for these foods' unique cancer-fighting properties is that aside from their vitamin content, these vegetables are vibrant sources of cancer-fighting phytonutrients.[49] Thus, broccoli is a rich source of **D-glucarate**[50] and **sulforaphane**[51] (which support the detoxification of many cancer-causing compounds) as well as **indole-3-carbinol**[52] (**I3C**, which supports the safer metabolism of potentially cancer-promoting estrogens), while garlic and onions are packed with **diallyl disulfide**, which favorably modulates your body's handling of carcinogens.[53]

Once the remarkable cancer-fighting effects of **SeMC** came to light, however, scientists began to wonder if there might be a connection between the cancer-fighting powers of these vegetables and selenium – not just the *amount* of the mineral, but the *kind*. If the *amount* of selenium in a food was a reliable estimate of its anticancer effect, then wheat, barley, and corn would be more strongly associated with cancer protection than Brussels sprouts or chives, because these grains actually accumulate *more* selenium than cruciferous or *Allium* vegetables when grown in high-selenium soil.[54] Yet the reverse is true. Likewise, if simple selenium *concentration* were the critical factor, then people who eat a lot of beef might be expected to be immune from the disease, since beef is the single largest source of selenium in the North American diet![55,56] So since Ganther and Ip had shown that different forms of selenium have widely varying cancer-fighting potencies, might the explanation for the cancer protection provided by these vegetables relate to the *kind* of selenium that they contain?

It would make sense. Even before Ip and Ganther had zeroed in on **SeMC** as the superior selenium supplement, it was known that different plants stored the selenium they drew in from the Earth in different biochemical forms.[54] When soil selenium is low, most of the selenium in a plant appears as selenate; but as concentrations increase, plants protect themselves against the possible toxicity of inorganic forms of the mineral by storing it in relatively nontoxic forms, such as selenomethionine and **SeMC**. So if, in high-selenium areas, one plant stored selenium in a form which had a greater cancer-fighting potential, that plant would be more protective than another plant which contained more *total* selenium in a less effective form.

The hypothesis proved correct. Once again, **SeMC** provided the key to unlock the mystery – by proving once again its superior anticancer shield.

It turns out that when soil selenium levels are high enough, **SeMC is the selenium that dominates in cancer-fighting foods like broccoli, onions, and garlic,** while cereal grains and other foods which are not especially linked to reduced cancer risk store most of their "excess" selenium as selenomethionine.[57] And in a series of experiments, researchers have shown conclusively that **the SEMC in these foods lies behind much of the unique defense against cancer which they provide.**

SeMC is the selenium that dominates in cancer-fighting foods like broccoli, onions, and garlic.

Scientists at the Grand Forks Human Nutrition Research Center designed an ingenious study[33] to determine how much of the anti-cancer effects of high-selenium broccoli and broccoli sprouts is attributable to the *phytonutrients* in these plants, and how much is the result of the *kind* of selenium which they contain. The researchers exposed six groups of laboratory animals to **dimethylhydrazine (DMH)**, a deadly colon-cancer carcinogen. One group was given a basic, nutritionally-adequate diet. A second group was given the same diet along with a "megadose" selenium supplement in the form of sodium selenite. A third group was given the basic diet along with low-selenium broccoli sprouts. A fourth group ate a diet with the same "megadose" of selenite given to the second group, *combined with* the low-selenium broccoli sprouts. And the fifth and sixth groups received enough broccoli and broccoli sprouts (respectively) grown in high-selenium conditions to provide the same high dose of selenium as the animals in the "megadose" selenium groups. But while the other animals received their selenium supplement as inorganic selenium, most of the selenium in the diets of animals consuming high-selenium broccoli was **SeMC**.

You can see the results of this experiment in **Figure 3.** The colons of animals whose diets were unsupplemented quickly became riddled with precancerous lesions. The phytonutrients in low-selenium broccoli sprouts provided some protection against the formation of these lesions, reducing their numbers by about a quarter. Compared to

this, "megadose" inorganic selenium *seemed* to provide less protection, reducing the burden of abnormal growths by only 16%, but in fact the difference between the two could not be distinguished when analyzed with statistical methods. And indeed, *adding* the low-selenium sprouts to the "megadose" selenite didn't actually provide more protection against precancerous lesions than the selenite alone.

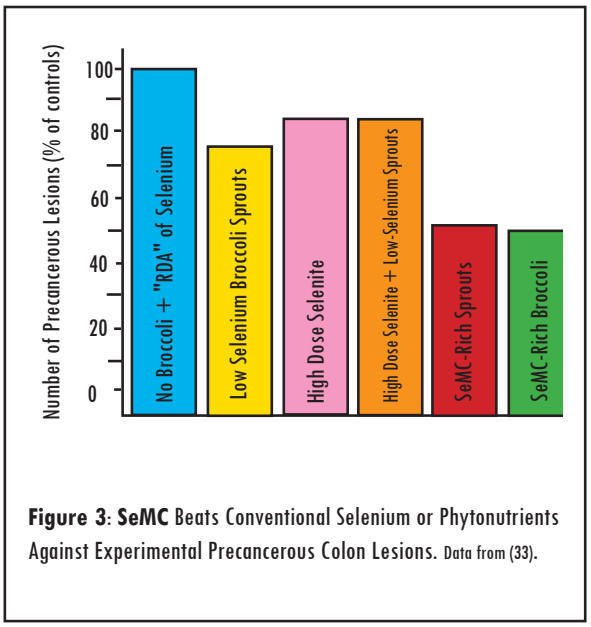


Figure 3: **SeMC** Beats Conventional Selenium or Phytonutrients Against Experimental Precancerous Colon Lesions. Data from (33).

Yet high-selenium broccoli or broccoli sprouts, containing the *same* amount of selenium but mostly in the form of **SeMC**, ***slashed* the incidence of cancer-forming cells**, cutting the burden of precancerous growths roughly in *half*.[33] And this difference was deemed significantly different from *all* of the other diets – including those with the added low-selenium broccoli foods. Bottom line: **the SeMC in high-selenium broccoli and broccoli sprouts plays a greater a role in their anti-cancer effect than their phytonutrients** or the absolute amount of selenium![33]

Dr. Finley's group has shown the same effect in breast cancer: the high-selenium broccoli, rich in **SeMC, potently lowers the rate of developing early breast cancer lesions – much more effectively than the same dose of selenium as selenate, or of selenite-supplemented broccoli.**[32,33] Likewise, in an animal model of **familial adenomatous polyposis** (FAP – an inherited vulnerability to colon cancer), high-**SeMC** broccoli was dramatically more active in protecting against tumors of the intestines and colon than conventional broccoli, cutting the rate of intestinal tumors by 39%, and massively lowering the risk of tumors in the colon (a *79%* reduction!).[30]

SeMC, lies behind the protective effects of eating foods from high-selenium soil; the fact that foods like garlic and broccoli produce SeMC is responsible for much of their well-earned anticancer reputation.

And similar experiments have demonstrated that the same is true of other **SeMC**-rich vegetables, such as high-selenium garlic,[36,58-61] ramps (wild leeks),[62] and (to a very limited extent) onions (which don't accumulate as much **SeMC** as these other vegetables).[60] Whether you compare the selenium in **SeMC**-rich vegetables to the same amount of selenium from other selenium-enriched foods which do *not* contain **SeMC** (such as yeast,[58] wheat,[31] and even Brazil nuts,[60] which are widely famed as a food source for selenium (see **Table 2**)), or to lower-selenium versions of the same plant, or even to a low-selenium crop *plus* added selenium from the usual supplemental sources, a high-**SeMC** diet consistently mounts a better defense against cancer. The inescapable conclusion seems to be that, on the one hand, **SeMC, and not simple selenium content, lies behind the protective effects of eating foods from high-selenium soil; and that, on the other hand, the fact that foods like garlic and broccoli produce SeMC (and not other forms, like selenomethionine) is responsible for much of their well-earned anticancer reputation.**

Table 3. Effects of Different Selenium Sources on Chemically-Induced Breast Cancer. Adapted from (60).

Selenium Group	% With Tumors	Total Tumor Count
"RDA" of Selenium	83.3	81
"Megadose" Selenium From:		
Selenomethionine	60.0	54
Inorganic Selenium	50.0	42
Brazil Nuts*	46.7	38
Onion (Low SeMC)	46.7	44
Garlic (High SeMC)	33.3	26

**Contains Mostly Selenomethionine and other Selenoaminoacids and Selenopeptides; no SeMC*[63]

So what is it about **SeMC** – acting through methylselenol – that makes it at once less toxic *and* more potent as a cancer-fighting selenium supplement?

The Demolitionist and the Arsonist

To answer this question, teams of scientists centered at the AMC Cancer Research Center,[25,34-39] the Baylor College of Medicine,[40-43] and elsewhere have gone down to the cellular level, exploring the difference between the effects of **SeMC** on cultured cancer cells and the effects of the forms of selenium found in common selenium supplements. To explain what they've discovered, imagine that a cancer cell is an abandoned old tenement tower, rotting from within and in danger of collapsing into neighboring, well-maintained, functional apartments (healthy cells). To

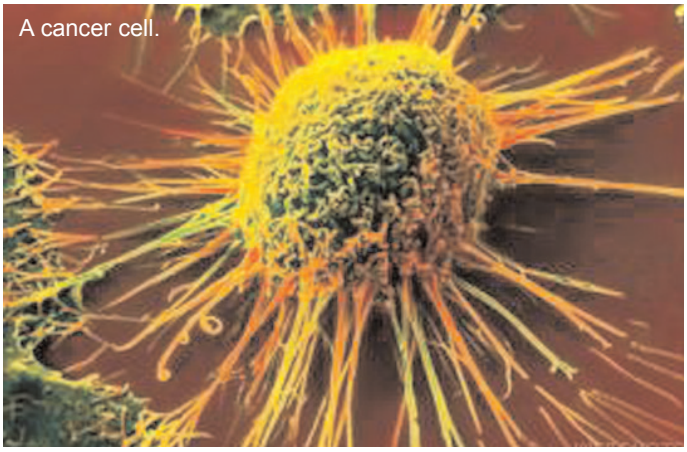
protect the people living in the well-maintained apartments, the city administration plans to remove the dilapidated wreck using a clean pulldown process in which the building is collapsed *from within,* ensuring that its collapse will not damage the surrounding homes.

SeMC takes out cancer cells with the precision professionalism of a "demolitions expert."

Now imagine that there is a *double* threat. The building has been abandoned as hazardous because of its weakened state of repair. But this has made it attractive to a bored gang of youth, who have been on a terror campaign of torching old wrecks for kicks. Of course, indiscriminately setting condemned structures alight may get rid of derelict buildings – but it can also maim or kill innocent people living in the neighborhood if the fire spreads or as the building collapses as its supports burn.

To get to the point of this morality tale: scientists have found that **SeMC takes out cancer cells with the precision professionalism of a "demolitions expert,"** targeting cancer cells for destruction without harming healthy surrounding tissue. By contrast, **regular selenium supplements act, at the cellular level, like an arson gang,** killing cancer cells in an inefficient and indiscriminate fashion that inevitably harms healthy cells, too.

Every cell in your body has a "self-destruct button," like the ones in James Bond's Aston Martins: a carefully-regulated process known as **apoptosis** (or "programmed cell death"). The apoptotic "death program" is built into your cells for a variety of reasons: for one thing, it helps the body to get rid of cells which are only needed for brief periods during our development, like the webbing between an embryo's fingers. But **apoptosis is also a critical defense against cancer,** allowing the body to automatically shut down cells on the verge of malignant transformation because of DNA damage or the activation of "cancer genes."


A cancer cell.

Apoptosis takes malignant cells step by step through a series of well-laid-out stages which end in its removal – *without* inflicting damage on surrounding, healthy tissue. The cell's dysfunctional DNA is fragmented; its mitochondria are shut down; the cell crumples inward and is cleanly consumed by immune cells that home in on the imploding cell.

By studying cancer cells in culture, scientists have demonstrated that **SeMC destroys cancer cells through activating the "programmed cell death" of apoptosis:**[19,35,36,38,40-42,64] it's the expert demolitionist in the analogy we used above, removing the dangers of a cell that poses a carcinogenic threat to the body with surgical precision, leaving healthy surrounding tissue unscarred (see **Table 3**).

Table 3. In vitro Effects of SeMC vs. Conventional Selenium Sources. Adapted from (26).

Parameter	Effect of Conventional Selenium Sources (eg Selenite)	Effect of SeMC-Type Forms
Cell structure	Cytoplasmic vacuolization, cell detachment	Normal
Membrane damage?	Yes	No
Inhibition of cell growth	Extreme	Moderate
Inhibition of DNA synthesis	Extreme	Moderate
Intervention in cell cycle	Late-stage	Early-stage
Genotoxicity	Extreme	None
Cause of cell death	Necrosis	Apoptosis

But apoptosis is not the only way that cells can be destroyed. Cells can also be laid waste by the ravaging chaos of **necrosis.** While apoptosis is a carefully-orchestrated process, built into the essence of every cell in your body as a protective self-destruct mechanism, necrosis is the simple vandalizing of the cell by toxins and free radicals.

Necrosis usually begins when a harmful compound agent ruptures cellular membranes, unleashing enzymes present in the cell's **lysosomes** (the cellular "garbage incinerators") from their carefully-sequestered compartments. These enzymes chew up the cell from within. The cell's DNA is mutated and otherwise damaged, *without* being protectively deactivated. The "I-beams" that support the structure of the cell (**cytoskeleton**) are severed. Mitochondria swell as they become dysfunctional, like nuclear plants entering meltdown.

In short, when a cell falls prey to necrosis, all hell breaks loose – and it spreads. As the cell bursts, its churning contents trigger an inflammatory overreaction which spreads the havoc of necrosis to surrounding, healthy cells.

It's an ugly, indiscriminate assault, with plenty of innocent bystanders getting caught in the crossfire.

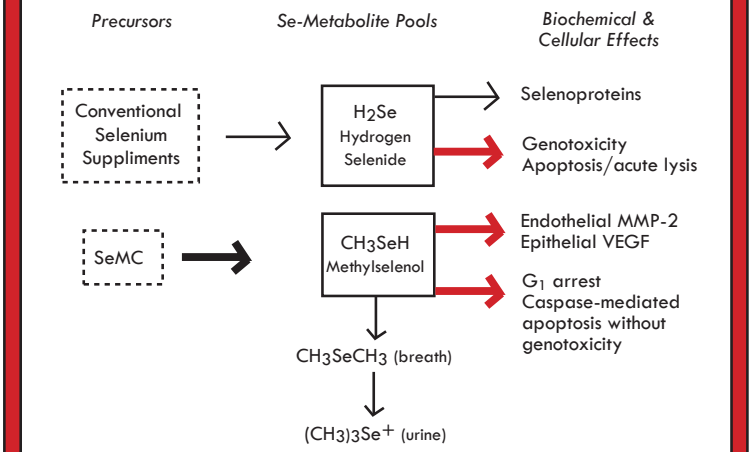
Believe it or not, **necrosis is the *direct* effect of inorganic selenium supplements on healthy and cancerous cells *alike*** (see **Table 3**). Selenium's toxicity was recognized long before its nutritional essentiality was, and the ability of these forms of selenium to kill cancer cells is fundamentally related to their greater toxicity. Compared to healthy cells, cancerous cells are more susceptible to necrotic attack from these more venomous forms of the mineral: in our analogy, they're like decaying buildings made more vulnerable to fire – tinderboxes filled with fire hazards, just waiting for a spark to set them ablaze. But healthy cells are damaged by inorganic selenium too, either directly (by being poisoned themselves) or indirectly (through the collateral damage inflicted by necrosis and the resulting inflammatory inferno). In the metaphor we used above, **conventional selenium supplements are reckless kids playing "pyro" games,** engaging in wholesale arson which harms normal cells even as it kills some cancerous ones.

Fortunately, as we've seen, the body normally detoxifies some of the selenite or selenate in your diet and

Regular selenium supplements act, at the cellular level, like an arson gang.

supplements by converting it first to hydrogen selenide and then to methylselenol – the same cancer-fighting metabolite formed more directly by **SeMC.** But the *immediate* effects of inorganic forms of selenium, and their inefficient conversion into the less-toxic methylselenol metabolite, go a long way toward explaining both their higher toxicity and their lower anti-cancer activity.

Figure 3: Mechanisms which may Underlie SeMC's Superior Benefits. Redrawn from (27).



From Benchtop to Bottle

As research into the critical role of key selenium metabolites continues, researchers are learning even more about the protective powers of **SeMC.** They've shown how this form of the mineral steps in to shut down the growth of cancer cells early on in their reproductive cycle while conventional forms only become active in the later stages, once the process is already underway.[19,34,41,43] And they've seen evidence to suggest that, in addition to its *direct* effects on the tumor, **SeMC may also fight cancer by inhibiting angiogenesis,**[20,27-29] cutting off the growing tumor's blood supply more effectively than the common selenium supplements, *without* interfering with the growth of blood vessels in normal, healthy tissue.

For years, we've heard the good news about selenium repeated over and over again – until it seems like an old story. But the **SeMC** is news that most people haven't heard, and *this* selenium story is even more exciting than the early reports. Compared to conventional selenium sources, **SeMC** is more effective. It's safer. And it doesn't build up in your tissues.

By any measure, **SeMC** has proved itself to be the *best* selenium you can take. The National Cancer Institute apparently agrees: it is in the process of filing "Investigational New Drug" documents to use **SeMC** instead of other selenium supplements in future human trials.[65] But while the restricted use of **SeMC** in research laboratories across the United States has brought us some very good news on the selenium front, and can be expected to bring us even more good news in the near future, the fact that **you now have the power to choose SeMC as *your* selenium supplement** is, in the end, the best news of all.

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