The ‘Unimportant’ Molecule Curing Cancer

Do-It-Yourself Tips for Boosting Your Levels – Without Big Pharma’s Help

by Jonathan V. Wright, MD

Editor’s Note: This article first appeared in Dr. Jonathan V. Wright’s Nutrition & Healing newsletter, February 2008.

In February 2007, you may have read about Panzem, one of “Big Pharma’s” aggressive moves into bioidentical hormones. But for decades before the pharmaceutical industry changed its name and spent hundreds of millions of dollars trying for FDA “approval,” Panzem was actually known by its real name, 2-methoxyestradiol.

For much of that time, no one really knew the function of 2-methoxyestradiol; and since there are such tiny quantities of it in our bodies, it was dismissed (as scientists so often do when they don’t yet know what one of Nature’s “minor” molecules is for) as “unimportant.”

But now the gold rush of research is on for 2-methoxyestradiol, because it appears that it may be able to actually cure – or at least significantly slow – many types of cancer, including some of the most commonly feared forms, such as prostate, breast, and ovarian.

An ‘Inactive’ Hormone Shows Its True Cancer-Fighting Potential

As usual with patent medicine research, the emphasis (and the rush) is on the “gold” that can be produced by selling an “approved” form of this entirely natural molecule (at an unnaturally high price), rather than learning how to work with Nature as closely as possible, which would offer the most benefit at the least possible cost to patients everywhere. But that’s just one of many “fatal flaws” of the current “health care” system here in these United States. And even though that’s unlikely to change anytime soon, we still may be able to salvage something from this situation.

Before turning the spotlight on 2-methoxyestradiol itself, it’s always important to have a little bit of general background on how these things work in the body. Estrogens and androgens are steroid hormones (Nature’s own original steroids, not the “extraterrestrial-molecule,” pumped-up-to-be-patentable, pseudo-steroids currently scandalizing professional athletics). These natural steroids are produced by the ovaries or testes, adrenal cortices, and other body tissues of both men and women.

But, as you may have read in the December 2007 issue of Nutrition & Healing, too much estrogen, especially too much of the “wrong kind” of estrogen, increases the risk of new cancers and promotes the development of any tumors that are already present. This occurs primarily when two of the “major” forms of estrogen, estradiol and estrone, follow a pathway that metabolizes them into estrogen compounds that promote tumor formation. Other pathways produce estrogen metabolites that protect against tumors.

As it turns out, 2-methoxyestradiol isn’t inactive, as the “experts” once assumed. In fact, it’s one of the most potent anticarcinogenic estrogen metabolites. This metabolite is formed from the hydroxylation of 17ß-estradiol followed by O-methylation in the liver. (I know that’s highly technical, but remember the word methylation for later.)

Some recent studies have shown that 2-methoxyestradiol inhibits the growth of prostate cancer cells by inducing apoptosis (cell “suicide”) and preventing tumor growth in rapidly growing cells. It showed similar benefits for both breast and prostate cancer when it was used in combination with other chemotherapeutic therapies. And, speaking of its role among chemotherapy drugs, not only does 2-methoxyestradiol have potent effects against pancreatic and gastric cancers that have become resistant to other chemotherapeutic drugs, but it also reduced the amount...
of other chemotherapeutic drugs needed in cases of ovarian cancer by enhancing their antitumor effects.\(^7,8\)

Researchers have seen similar results using 2-methoxyestradiol in many other kinds of cancer, including osteosarcoma, leukemia, and chondrosarcoma, a type of cancer affecting the cartilage.\(^9-12\)

In addition to promoting apoptosis in cancer cells and working with chemotherapy drugs to boost their effects with lower doses (which, hopefully, will help minimize the harsh effects of these drugs), 2-methoxyestradiol also works against cancers by inhibiting angiogenesis, the formation of new blood vessels, which is how many cancers nourish themselves.\(^13,14\) To top off this roster of benefits, 2-methoxyestradiol has also shown the ability to inhibit the spread of cancer through metastasis.

All of these various approaches to fighting cancer (and likely some that haven’t even been discovered yet) make 2-methoxyestradiol an extremely promising tool for treating the disease at many different stages.\(^15,16\)

**Giving Nature the Cancer-Curing Credit It’s Due**

The study results I listed above are really just the tip of the proverbial iceberg when it comes to the clinical trials being done on 2-methoxyestradiol. As a matter of fact, just as I was sitting down to write this article, yet another “2-methoxyestradiol might cure cancer” study was released – and made quite a splash in the media (probably because it was done at one of the most mainstream of mainstream institutions, the Mayo Clinic). The press report started:

> A new study of an estrogen-derived drug shows promise as a treatment for breast cancer and breast cancer metastases to bone. A drug that has shown promise in treating sarcoma, lung and brain cancers, demonstrates that the drug may also be effective in treating breast cancer, in particular the spread of breast cancer.\(^17\)

I’m sure you’ve noticed the typical patent medicine company language “spin” right away. 2-methoxyestradiol is a natural estrogen, not a “drug,” but the word *drug* is used three times in the first two sentences. And the spin didn’t stop there.

[Mayo Clinic researchers] studied the effect of 2-methoxyestradiol on the bone. ... In breast cancer, the cancer commonly lodges in the bone, destroying it in a debilitating painful process called osteolysis. Osteolysis can lead to bone fractures and causes patients to feel tired, or even to lose consciousness.

According to one of the researchers, 2-methoxyestradiol is potentially very important in the treatment of breast cancer metastatic to bone because it has few of the unpleasant side effects of most chemotherapy drugs and targets both bone resorption and the cancerous tumor cells. According to another researcher, “We were expecting the ‘drug’ [quotation marks added] to have an effect, but we were not expecting to have as big of an effect as it did.”

I suppose getting the mainstream to credit Nature instead of “drugs” is too much to hope for. But at least they haven’t tried twisting all-natural 2-methoxyestradiol into a patentable, space-alien version – yet.

And these researchers did make one other bit of progress: They appear to be among the first to notice that swallowing steroids is not Nature’s preferred route of administration. Of course, that should have been obvious from the start to any MD, PhD, or intelligent student of the human body. But, obvious or not, nearly all other researchers have had their volunteers swallow 2-methoxyestradiol, which may be one of the reasons such enormous doses have been required in the research to-date. According to the news report on the Mayo Clinic study:

> Take the guess-work out of balancing hormones!

Meridian Valley Lab offers a cutting-edge **Comprehensive 24 hour Urinary Hormone Panel.**

This test is invaluable for the treatment of the following conditions:

- Menopause
- Andropause
- Adrenal Fatigue
- Infertility
- Breast Cancer Prevention
- Hypothyroidism
- Growth Hormone Deficiency
- Polycystic Ovarian Syndrome
- And many more......

We offer free peer-to-peer physician consultations for physicians practicing in the field of Bioidentical hormone replacement therapy.

**Call to order your tests today!**

425.271.8689

Visit our website for more details

www.meridianvalleylab.com
Clinical trials of 2ME2 for breast cancer patients are in progress. These trials are based on an oral version of 2ME2 to treat primary tumors, but this method has limitations as the oral version of 2ME2 is poorly suited to getting into the blood system and reaching tumors. Researchers resolved this problem by delivering 2ME2 by injection and found it was much more effective.

To put it simply, the Mayo Clinic study found that 2-methoxyestradiol can:
- effectively target breast cancer cells
- prevent the spread of breast cancer cells to bone
- protect bone from osteolysis, which is a type of bone metastasis in which the bone is eaten away by cancer cells
- be much more effective in smaller quantities when not swallowed, but (in this case) injected.\textsuperscript{18}

Safety in Numbers – and Larger-than-Normal Doses

The Mayo Clinic study may be the most recent – and accurately conducted – research on 2-methoxyestradiol so far, but there are lots of other studies on this estrogen metabolite as well that show just as much promise, even with some wrinkles in the methodology.

In a phase I clinical trial of 2-methoxyestradiol in 15 women with metastatic breast cancer, 10 patients stabilized in their disease progression, and two reported reductions in bone pain and the use of painkillers. And there were no adverse effects from daily oral doses of 200, 400, 600, or 800 milligrams, although at 1,000 mg per day, all 15 patients in the study reported hot flashes.\textsuperscript{19}

Another phase I study of 2-methoxyestradiol examined its effects when combined with the cancer drug docetaxel in 15 patients with metastatic breast cancer. This time, no adverse effects were observed when oral 2-methoxyestradiol was administered in concentrations between 200 and 1,000 mg per day for 28 days following 4 to 6 weeks of docetaxel therapy.\textsuperscript{20}

The next clinical trial on 2-methoxyestradiol’s résumé involved 11 men and 9 women who were given oral doses of the metabolite to find the maximum-tolerated dose and determine any level of toxicity. To be enrolled in the study, patients had to have malignant, metastatic, inoperable solid tumors and to have exhausted standard treatment options. Prostate and ovarian cancers were the most commonly represented tumors in the study group. Patients were initially given a specific oral dose of 2-methoxyestradiol over the course of 28 days. When a treatment cycle was completed without adverse effects or progression of disease, doses were escalated to the next highest dose. Results of the study determined that 2-methoxyestradiol was well tolerated orally at dose levels ranging from 400 mg to 3,000 mg, though side effects, such as hot flashes and thrombosis, did occur in some participants.\textsuperscript{21}

As the previous study indicated, 2-methoxyestradiol may be as beneficial for men as it is for women. In one randomized, placebo-controlled study specifically on PSA (prostate specific antigen) levels and prostate cancer, 33 patients were given either 400 or 1,200 milligrams per day of oral 2-methoxyestradiol over the course of 16 weeks. PSA numbers either stabilized or declined by as much as 40 percent in many of the patients receiving the 1,200-milligram dose. Several patients did develop abnormalities in liver function that resolved when 2-methoxyestradiol was discontinued, but other than those few instances, the 2-methoxyestradiol was well tolerated in the study participants.\textsuperscript{22}

Once again, no matter how the media – or the patent medicine industry – tries to spin it, 2-methoxyestradiol is a naturally occurring estrogen metabolite, not a “drug.” And this natural substance has enormous potential as an anticancer agent for a wide
The ‘Unimportant’ Molecule

variety of cancers, particularly when it's administered properly (into the bloodstream first, before the liver gets a chance to change it and destroy it, which is actually the liver's job with steroid hormones.) But even the studies that used the wrong method of administration demonstrated that 2-methoxyestradiol has few adverse effects and little toxicity.

The Good News and Bad News about this Revolutionary Cancer Therapy

The good news we can take away from the 2-methoxyestradiol research to date is that a much safer and effective form of cancer treatment is coming. Now for the bad news: Given the “approval” process, it's still years away. And, unfortunately, like all other newly introduced “approved drugs,” it will be enormously expensive (although more likely to be covered by insurance than non-approved natural treatments).

But by now you might be wondering why you need to wait around for approval at all. Since 2-methoxyestradiol is a naturally occurring estrogen, doctors, especially ones skilled and knowledgeable in the safe and effective use of bioidentical hormones, should be able to order it through their compounding pharmacies and prescribe it for you just like the other estrogens used in an overall bioidentical hormone replacement therapy (BHRT) program.

Not to mention the fact that even though they've been proven safe, it's also very likely that you wouldn't need doses as large as the ones used in the research studies: There's every reason to believe that much lower doses of 2-methoxyestradiol will be just as effective if they're used as part of an overall, natural anticancer approach, in combination with excellent diet, detoxification, immune support and stimulation, and many other safe and natural anticancer compounds. So why not just talk to your doctor about adding this safe and all-natural hormone to your current BHRT regimen now?

Well, unfortunately, it's not that easy—and, believe me, I've tried. One compounding pharmacist told me that chemical supply sources advertising 2-methoxyestradiol for sale on line refused to sell to compounding pharmacies, giving various excuses. Another compounding pharmacist actually was able to purchase a very small amount, which arrived in a package emblazoned with a skull and crossbones, accompanied by a “safety sheet” that cautioned about potentially toxic effects of 2-methoxyestradiol! Either these sources don't have a clue what they're selling, or the fix is in (but most likely it's a mixture of both).

Since 2-methoxyestradiol is in fact a relatively harmless natural metabolite with great potential for good, I'm hoping it becomes available through the same sources as other bioidentical hormones at a reasonable price sometime in the near future. Otherwise, it'll be the same ol' story: if you develop cancer, don’t call your doctor; call your travel agent!

In the meantime, though, there are some things you can do to increase your body's own 2-methoxyestradiol levels.

Stockpiling Your Own Internal Reserves

2-methoxyestradiol is one of the metabolites monitored in the 24-hour urine evaluation we wrote about in the December 2007 issue of Nutrition & Healing. Even though it's present in very tiny quantities, don't be fooled by the research studies using huge doses by unnatural means (oral administration). As I mentioned above, even tiny quantities can be pivotal as “signaling molecules" when they occur naturally in your body.

For example, one research study found that an exceptionally tiny quantity — 1 micromole — has "anti-proliferative, antiangiogenic, and apoptotic effects" on uterine fibroid cells. Although there’s no concrete proof, it's very likely that one function of the very tiny quantities of 2-methoxyestradiol in our bodies is to prevent both benign hormone-related tumors such as fibroids as well as hormone-related cancers before they get started.

So how can you increase your own level of 2-methoxyestradiol? Remember the term methylation from the beginning of this article? It's the process that produces 2-methoxyestradiol from other forms of estrogen. Methylation relies on certain enzymes and molecules called methyl donors to function properly. Making sure you're supplying your body with enough of these methyl donor molecules is key to raising your 2-methoxyestradiol levels.

The list of foods that contain the necessary methyl donor molecules will probably look familiar: green leafy vegetables, legumes, citrus, berries, and nuts. Although in this particular case, it's very important that the foods have been processed as little as possible before you eat them — and that includes heating and freezing. Keeping these foods as fresh and "raw" as possible helps preserve the methyl donor molecules they contain.

There are also a few supplements that supply methyl groups, including particularly S-adenosylmethionine (SAMe), followed by methylsulfonylmethane (MSM), betaine (including the betaine from betaine hydrochloride), 5-methyltetrahyrofolate (a "new-in-the-stores" and more natural form of folic acid), and methylcobalamin (a form of vitamin B12).

If your 24-hour urine test reveals that your levels of 2-methoxyestradiol are low, increase your consumption of the foods listed above, and check with a physician skilled and knowledgeable in bioidentical hormone replacement therapy about which and how much of these supplements to take.
The ‘Unimportant’ Molecule

And on a nonsupplemental note: stress, especially prolonged stress, reduces methylation of estrogens, since the required “methyl groups” get used by the body to make adrenaline instead. Meditation, biofeedback, and other stress and “adrenaline reducing” techniques can make more methyl groups available to make 2-methoxyestradiol, and reduce your risk of cancer at the same time.

Thanks to Lauren Rüssel, ND, for her organization and summary of the data collected for this article.

Notes


22. Jonathan V. Wright, MD, has degrees from both Harvard University (cum laude) and the University of Michigan. More than any other doctor, he practically invented the modern science of applied nutritional biochemistry, and he has advanced nutritional medicine for nearly three decades. Dr. Wright is credited with introducing the nutritional remedy for benign prostate disease (BPH), the first successful treatment to reverse macular degeneration, the safe medical use of DHEA therapy, natural hormone replacement therapy for women, and many other revolutionary natural cures.

To learn more about Dr. Wright's seven-volume Library of Nutritional Cures and his newsletter Nutrition & Healing and/or to subscribe to the newsletter, please visit www.wrightnewsletter.com, or call 888-213-0685 (ask for code WNAHWEB).