

Why so Many Cancer Drugs Are Made From Periwinkle

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STORY AT-A-GLANCE

- > Compounds found in rosy periwinkle (Catharanthus roseus), a perennial plant native to Madagascar, form the basis for a number of commonly used cancer drugs that have been in use since the 1960s
- > Of the 70 different alkaloids found in periwinkle, the two primary compounds used in anticancer drugs are the powerful vinca alkaloids vinblastine and vincristine
- > Vincristine and vinblastine are both included in the World Health Organization's list of essential medicines
- Other medicinal applications include the treatment of diabetes and hypertension. Their cytotoxic effects have gained the greatest attention, however
- > Vinblastine is an integral part of anticancer regimens against testicular cancer, Hodgkin and Non-Hodgkin lymphomas, breast cancer and germ cell tumors. Vincristine is approved for the treatment of acute leukemia, rhabdomyosarcoma, neuroblastoma, Wilm's tumor, Hodgkin's disease and other lymphomas, as well as several nonmalignant blood disorders

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Many modern drugs are derived from purified and concentrated plant compounds (although compared to 20 years ago, few drug companies expend time and money looking at medicinal plant chemistry these days). Rosy periwinkle (Catharanthus

roseus), for example, a perennial plant native to Madagascar, is the basis for a number of commonly used cancer drugs that have been in use since the 1960s.¹

Of the 70 different alkaloids found in periwinkle, the two primary compounds used in anticancer drugs are the powerful vinca alkaloids² vinblastine and vincristine.³ Alkaloids are nitrogen-containing compounds shown to be very important for human health. Within the family of alkaloids, there are those with antiparasitic, antidiabetic, anticancer, antihypertensive and/or antiasthma properties, just to name a few. Others benefit your mood.

Even the humble daffodil contains a valuable alkaloid with anticancer properties called haemanthamine. This alkaloid inhibits the protein production cancer cells depend on to grow and flourish. Berberine is yet another powerful alkaloid found in plants such as goldenseal, goldthread, Oregon grape root and barberry. These plants have traditionally been used in the treatment of Type 2 diabetes, gastrointestinal infections, liver problems and a number of other health conditions.

Berberine is particularly beneficial for mitochondrial function and is a powerful activator of AMPK, a metabolic master switch. Interestingly, glyphosate — the most widely used herbicide in the world — robs the plant of the ability to make these important medicinal compounds.

Vinca Alkaloids Are Powerful Cancer Fighters

Aside from vinblastine and vincristine, two others known for their cancer-fighting powers are vinorelbine and vindesine.⁴ All but vindesine have been approved for use in the U.S., and vincristine and vinblastine are included in the World Health Organization's list of essential medicines.⁵

A synthetic vinca alkaloid called vinflunine, developed in 2008, has since been approved in Europe for the treatment of certain types of bladder cancer. It's also being investigated for the use against other malignancies. Other medicinal applications include the treatment of diabetes and hypertension (high blood pressure). Their

cytotoxic effects have gained the greatest attention, however. As explained in a 2013 paper in the International Journal of Preventive Medicine:

"The main mechanisms of vinca alkaloid cytotoxicity is due to their interactions with tubulin and disruption of microtubule function ... directly causing metaphase arrest ... [T]he vinca alkaloids and other antimicrotubule agents also have an effect on both nonmalignant and malignant cells in the non-mitotic cell cycle, because microtubules are involved in many non-mitotic functions ...

The vinca alkaloids and other microtubule disrupting agents have power to inhibit malignant angiogenesis in vitro. For example, [vinblastine] with concentrations range from 0.1 to 1.0 pmol/L blocked endothelial proliferation, chemotaxis and spreading on fibronectin, all essential steps in angiogenesis, but other normal fibroblasts and lymphoid tumors were unaffected at these minute concentrations.

In combination with antibodies against vascular endothelial growth factor, low doses of [vinblastine] increased antitumor response considerably, even in tumors resistant to direct cytotoxic effects of the drug. Vinca alkaloids inhibit cell proliferation by binding to microtubules, which can cause a mitotic block and apoptosis ...

Side effects of [vinblastine] consist of toxicity to white blood cells, nausea, vomiting, constipation, dyspnea, chest or tumor pain, wheezing and fever. It is also rarely associated with antidiuretic hormone secretion."

Historical Overview

Vinca alkaloids are the second most-used class of cancer drugs today. They've also been used the longest. Vinca alkaloids were originally discovered by two Canadian scientists, Robert Noble and Charles Beer, in the 1950s.⁷

During that time, Gordon Svoboda, a medical researcher at Eli Lilly, also added periwinkle to his list of research subjects, having heard reports of its use for diabetes

during World War II. In 1958, Gordon discovered extract from the plant also performed remarkably well in anticancer tests.

That same year, Noble and Beer presented their own anticancer findings at a research symposium at the New York Academy of Sciences. Notably, the two teams (Eli Lilly and Noble/Beer) concluded that since periwinkle extract lowered white blood cell counts, it might be useful against leukemia — a disease characterized by white blood cell proliferation.

Beer was responsible for isolating vinblastine, which he named. Eventually, Eli Lilly and Noble/Beer established a joint research collaboration, which led to the development of two chemotherapy drugs. Vincristine gained approval as a chemotherapeutic agent by the U.S. Food and Drug Administration (FDA) in 1961. Vinblastine gained FDA approval in 1963. Many other countries around the world approved the two drugs shortly thereafter.

Vinca Alkaloids in Conventional Cancer Treatment

Vinblastine is an integral part of anticancer regimens against testicular cancer, Hodgkin and Non-Hodgkin lymphomas, breast cancer and germ cell tumors. Vinorelbine has been shown to have "significant antitumor activity" in those with breast cancer, and is also used in bone cancer treatments, and is approved for the initial treatment of advanced lung cancer in the U.S.

Vincristine, meanwhile, is approved for the treatment of acute leukemia, rhabdomyosarcoma, neuroblastoma, Wilm's tumor, Hodgkin's disease and other lymphomas, as well as several nonmalignant blood disorders, including refractory autoimmune thrombocytopenia, hemolytic uremic syndrome and thrombotic thrombocytopenia purpura.

Common side effects for vincristine include peripheral neuropathy, suppressed activity of bone marrow, constipation, nervous system toxicity, nausea and vomiting.

As you can see, toxicity is an issue. While the toxicological profile of each alkaloid is different, all vinca alkaloids have peripheral neurotoxicity — vincristine being the most potent. As noted in the featured paper on vinca alkaloids, this neurotoxicity is "related to axonal degeneration and decreasing of axonal transport, most likely caused by a druginduced perturbation of microtubule function."

The only ways to counteract these toxic effects are to either lower the dose, decrease the frequency of drug administration, or to discontinue use altogether. "Although a number of antidotes, including thiamine, vitamin B12, folinic acid, pyridoxine and neuroactive agents, have been applied, these treatments have not been obviously shown to be effective," the authors note.

All vinca alkaloids, but vincristine⁸ and vinblastine in particular, also have notable toxicity on the gastrointestinal tract, as noted in a recent study.⁹ All of them can also cause severe tissue damage, and are associated with acute heart problems, as well as lung and blood toxicity. The featured paper also specifies that vaccinations should not be administered while on a vinca alkaloid drug, as they weaken your immune system.

Your Lifestyle Choices Can Offer Potent Cancer Prevention

While anticancer drugs have their place, it's important to remember that the lifestyle choices you make on a daily basis will influence your overall cancer risk in the first place. The good news is there's a lot you can do to lower your risk. In fact, I believe you can virtually eliminate your risk of cancer and chronic disease, and radically improve your chances of recovering from cancer if you currently have it, by addressing foundational lifestyle factors.

The following — starting with diet-related pointers, followed by other lifestyle recommendations — is by no means an exhaustive list.

There are many other strategies that can be useful as well, and several really great books have been written just on the topic of natural cancer prevention, including "Waking the Warrior Goddess: Dr. Christine Horner's Program to Protect Against and

Fight Breast Cancer" by Dr. Christine Horner, "The Cancer Revolution: A Groundbreaking Program to Reverse and Prevent Cancer" by Dr. Leigh Erin Connealy and "The Healing Platform: Build Your Own Cure!" by Annie Brandt.

Another excellent book for those who want to understand more about the role of diet and the metabolic underpinnings of cancer is "Tripping Over the Truth: The Return of the Metabolic Theory of Cancer Illuminates a New and Hopeful Path to a Cure" by Travis Christofferson.

Eat real food, ideally organic or biodynamic; avoid processed foods and sugars, especially processed fructose — All forms of sugar are detrimental to health in general and promote cancer. Processed fructose, however, is one of the most harmful and should be avoided as much as possible.

Reduce nonfiber carbs but have large volumes of fresh organic veggies along with high amounts of healthy fats from avocados, raw butter, seeds, nuts and raw cacao nibs. Consider adding cancer-fighting whole foods such as broccoli and **fermented foods**, and drinking a pint to a quart of organic green vegetable juice daily.

Eating certified organic or biodynamic foods will help you avoid genetically engineered foods and ingredients, which are typically loaded with glyphosate, a suspected carcinogen that also has antibiotic activity and has been shown to harm health in a number of different ways.

Implement a cyclical ketogenic diet — In my book, "Fat for Fuel," I describe a metabolic mitochondrial therapy program that I believe is a core foundation for a healthy life. Most people simply eat far too many processed foods, net carbs and too few healthy fats, and too many unhealthy fats, which results in gaining and retaining extra body fat and becoming increasingly insulin resistant.

Most also eat too much protein for optimal health and, while exercise cannot compensate for the damage done by a high-carb, low-fat diet, most do not get enough physical movement either. These factors set in motion metabolic and biological

cascades that deteriorate your health and "predispose" you to cancer and other chronic diseases.

Oncologists in Turkey are also using a stacked ketogenic treatment protocol that has been proven effective even in many stage 4 cancer patients.

By using metabolic support strategies such as ketogenic diet and fasting, a minimal dose of chemotherapy can be used, thereby eliminating many side effects and risks of treatment, while actually improving outcomes.

Limit protein — Newer research has emphasized the importance of the mTOR pathway. When activated, cancer growth is accelerated. To quiet this pathway, I believe it may be wise to limit your protein to 1 gram of protein per kilogram of lean body mass, or roughly one-half gram of protein per pound of lean body weight. Replace excess protein with high quality fats such as eggs from organic free-range hens, high quality meats, avocados and coconut oil.

Avoid unfermented soy products — Unfermented soy is high in plant estrogens, or phytoestrogens, also known as isoflavones. In some studies, soy appears to work in concert with human estrogen to increase breast cell proliferation, which increases the chances for mutations and cancerous cells.

Optimize your omega-3 level — Omega-3 deficiency is a common underlying factor for cancer,¹⁰ so make sure you get plenty of high quality animal-based omega-3 fats. I recommend getting an omega-3 index test done annually. For optimal health and disease prevention, your index should be above 8%.

Use curcumin — This is the active ingredient in turmeric and in high concentrations can be very useful adjunct in the treatment of cancer. For example, it has demonstrated major therapeutic potential in preventing breast cancer metastasis.¹¹

Avoid drinking alcohol — At minimum, limit your alcoholic drinks to one per day.

Avoid charring your meats and steer clear of all processed meats — Charcoal or flame broiled meat is linked with increased breast cancer risk. Acrylamide — a carcinogen created when starchy foods are baked, roasted or fried — has been found to increase cancer risk as well. I recommend eating at least one-third of your food raw. Avoid frying or charbroiling; boil, poach or steam your foods instead.

Processed meats of all kinds also contain acrylamide, along with nitrites that may form harmful N-nitroso compounds in your body. The evidence against processed meat is so strong, it was, as a group, classified as a Group 1 carcinogen by the International Agency for Research on Cancer in 2015.

Stop eating at least three hours before bedtime — Compelling evidence suggests that fueling the mitochondria in your cells at a time when they don't need it leads to the production of reactive oxygen species (free radicals) that damage mitochondrial and eventually nuclear DNA. There is also evidence to indicate that cancer cells uniformly have damaged mitochondria, so the last thing you want to do is eat before you go to bed.

Water fasting — Multiday water fasting, even when you do not have a weight or insulin problem, provides powerful metabolic benefits that help lower your disease risk. Importantly, fasting radically improves your body's ability to digest damaged cells (autophagy) and increases stem cells.

Optimize your gut microbiome — Optimizing your gut flora will reduce inflammation and strengthen your immune response, both of which are important for cancer prevention. Researchers have found a microbe-dependent mechanism through which some cancers mount an inflammatory response that fuels their development and growth.

So, inhibiting inflammatory cytokines may also slow cancer progression and improve the response to chemotherapy. Adding naturally fermented food to your daily diet is an easy way to prevent cancer or speed recovery. You can always add a high quality probiotic supplement as well, but naturally fermented foods are best. Make sure you're not iodine deficient — There's compelling evidence linking iodine deficiency with certain forms of cancer. Dr. David Brownstein,¹² author of "Iodine: Why You Need it, Why You Can't Live Without it," is a proponent of iodine for breast cancer. It actually has potent anticancer properties and has been shown to cause cell death in breast and thyroid cancer cells.

For more information, I recommend reading his book. One caveat: While I believe the bulk of what he states is spot on, I'm not convinced his dosage recommendations are ideal. I believe they may in fact be five or six times higher than optimal. So, do your homework before starting iodine loading.

Improve your insulin and leptin receptor sensitivity — The best way to do this is by avoiding sugar and grains and restricting carbs primarily to fiber-rich vegetables. Exercise will also help normalize your insulin and leptin sensitivity.

Maintain a healthy body weight — This will come naturally when you begin eating right for your nutritional type and exercising. It's important to lose excess body fat because fat produces estrogen.

Optimize your vitamin D level — Vitamin D influences virtually every cell in your body and is one of nature's most potent cancer fighters. Vitamin D is actually able to enter cancer cells and trigger apoptosis (cell death). For general health and disease prevention, you should ideally maintain a vitamin D level of 60 to 80 ng/ml year-round. Vitamin D also works synergistically with every cancer treatment I'm aware of, with no adverse effects.

Get plenty of restorative sleep — Make sure you are getting enough restorative sleep. Poor sleep can interfere with your melatonin production, which is associated with an increased risk of insulin resistance and weight gain, both of which contribute to cancer's virility.

The link between lack of sleep and cancer is so strong that the World Health Organization, since 2007, has tagged shift work as a "probable human carcinogen"

because it causes circadian disruption.¹³ As a general rule, adults need between seven and nine hours of sleep each night.

Exercise regularly — Researchers and cancer organizations increasingly recommend making regular exercise a priority in order to reduce your risk of cancer, and help improve cancer outcomes. One of the primary reasons exercise works to lower your cancer risk is because it drives your insulin levels down, and controlling your insulin levels is one of the most powerful ways to reduce your cancer risks.

Research has also found evidence suggesting exercise can help trigger apoptosis (programmed cell death) in cancer cells. Studies have also found that the number of tumors decrease along with body fat, which may be an additional factor.

This is because exercise helps lower your estrogen levels, which explains why exercise appears to be particularly potent against breast cancer.

Finally, exercise increases mitochondrial biogenesis, which is essential to fight cancer. Ideally, your exercise program should include balance, strength, flexibility, high intensity interval training (HIIT).

Limit electromagnetic field (EMF) exposure — In 2011, the International Agency for Research on Cancer classified cellphones as a Group 2B "possible carcinogen," and the evidence supporting the theory that EMF radiation from wireless technologies can trigger abnormal cell growth and cancer is just keeps growing and getting stronger.

Among the latest evidence are two government-funded animal studies¹⁶ that linked cellphone radiation to brain and heart tumors, as well as DNA and cellular damage. These findings are further supported by a lifetime exposure study¹⁷ by the highly respected Ramazzini Institute in Italy, which also found a clear link between cellphone radiation and these types of tumors.^{18,19,20}

A core problem is the fact that EMF triggers potent oxidant stress, which is at the heart of not only cancer but most chronic diseases. To learn more, including how to lower your EMF exposure, not only from cellphones and wireless technologies but

also from standard household wiring, see "Cellphones Strongly Linked to Cancer — New Study Reproduces Government Findings."

Avoid BPA, phthalates and other xenoestrogens — These are estrogen-like compounds that have been linked to increased breast cancer risk.

Avoid synthetic hormone replacement therapy, especially if you have risk factors for breast cancer — Breast cancer is an estrogen-related cancer, and according to a study²¹ published in the Journal of the National Cancer Institute, breast cancer rates for women dropped in tandem with decreased use of hormone replacement therapy.

Similar risks also exist for younger women who use oral contraceptives. Birth control pills, which also comprise synthetic hormones, have been linked to cervical and breast cancers.

If you are experiencing excessive menopausal symptoms, consider bioidentical hormone replacement therapy instead, which uses hormones that are molecularly identical to the ones your body produces and do not wreak havoc on your system. This is a much safer alternative.

Implement stress-reduction strategies — Stress from all causes is a major contributor to disease. Even the CDC states that 85% of disease is driven by emotional factors. It is likely that stress and unresolved emotional issues may be more important than the physical ones, so make sure this is addressed.

My favorite tool for resolving emotional challenges is **Emotional Freedom Techniques** (**EFT**). Other helpful strategies include meditation, mindfulness practice, prayer and yoga, just to name a few.

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