Feverfew and Cancer

Many readers know the feverfew plant (*Tanacetum parthenium*), a member of the Chrysanthemum family, sometimes called bachelor's buttons. This is a cheerful-looking perennial, with a profusion of white pompon-like blooms – like a shower of tiny daisies. Feverfew is often included in mixed bouquets and, to me, is the essence of summer.

Others know this plant as a source of herbal relief. One traditional usage, as a febrifuge (or fever-reducer) is apparent from its name. It is also a well-known folk remedy for migraine. I keep a feverfew product in my medicine chest, in anticipation of the summertime visits of a friend who is prone to these massive headaches (Pfaffenrath 2002; Murphy 1988).

Now scientists at the University of Rochester Medical Center have found that an extract of feverfew is effective against a type of human leukemia. Monica L. Guzman, PhD, and Craig T. Jordan, PhD, report that feverfew extracts kill malignant stem cells like no other single therapy they have tested. The active ingredient is derived from parthenolide, one of a class of sesquiterpene lactones found in the plant. The US National Cancer Institute is sufficiently excited by this work to have accepted it into the rapid access program, which aims to move experimental drugs from the laboratory to human clinical trials as quickly as possible.

“Research is a very important step in setting the stage for future development of a new therapy for leukemia,” said Dr. Jordan. “We have proof that we can kill leukemia stem cells with this type of agent, and that is good news.”

A Focus on Stem Cells

What is particularly exciting is that this feverfew extract is the first agent known to destroy myeloid leukemia at the level of the stem cells. Increasingly, cancer research is homing in on these primordial cells as the source of cancer. This is the level at which malignancy is born, and unless it is attacked at this level it can rarely be controlled, much less cured.

In the 19th century there were many intimations that primitive cells, called “embryonal rests,” were fundamentally connected with the development of cancer. A high point came over a century ago, when University of Edinburgh, Scotland, embryologist John Beard, DSc (1858-1924) put forward the theory that cancer was in fact caused by the malignant transformation of what he called pluripotent germ cells. It now seems almost certain that Beard was giving an early description of stem cells and their propensity to undergo malignant change. Beard’s idea was initially greeted with interest, but was later marginalized, and finally all but forgotten. However, his philosophy was kept alive through the work of a few maverick biologists, such as Ernst T. Krebs, Sr. and Jr., H.H. Beard, William D. Kelley, DDS, and others. Click or go to the following for information on Prof. John Beard: http://www.cancerdecisions.com/062602.html

In recent years, academic scientists have identified cancer stems cells in blood cancers as well as in brain and breast tumors. The work of Michael Clarke, MD, and his post-doctoral student, Mohammed Al-Hajj, PhD, at the University of Michigan, has been particularly influential. Clarke and Al-Hajj have shown that, contrary to what is generally assumed, not all tumor cells are equally capable of causing metastatic cancer. In fact, they found that in experimental breast tumors only a tiny fraction — less than one percent — of tumor cells are actually capable of causing metastasis. These highly malignant cells are identifiable as stem cells.

Research in 2005 by JeanMarie Houghton, MD, PhD, of the University of Massachusetts, Worcester, showed that in certain stomach cancers the cells that initiate the malignancy originate not in the tissues of the stomach itself, but are actually stem cells that have migrated there from the bone marrow. The initiating event in this sequence is a low-grade infection in the stomach, typically caused by *Helicobacter pylori*. Bone marrow derived cells (BMDCs) are sent to the stomach in response to this infection, as part of the body’s attempt to heal itself. Once in the stomach, BMDCs assume the characteristics of the surrounding tissues, but under the influence of hormonal signals emitted by the inflamed tissue, they undergo malignant change.

The latest University of Rochester findings on feverfew, while interesting from the point of view of pharmacology, are even more important in terms of basic science. They have deepened the scientific understanding of how stem cells are involved in the origin and progression of cancer.

Currently, other treatments for acute myelogenous leukemia (AML), including the recently approved drug Gleevec, are only moderately effective. That may be because they do not affect the malignant stem cells, so “you’re pulling the weed without getting to the root,” as Dr. Craig T. Jordan of the University of Rochester said. In laboratory experiments, the Rochester scientists have now shown that parthenolide is in fact more selective at stopping cancer through apoptosis (programmed cell death) than was the standard drug cytarabine (Ara-C).

There have been some prior experiments showing that feverfew compounds halt the growth of cancer cells. A phase I trial found that it was also relatively non-toxic, laying the groundwork for future studies of its effectiveness (Curry 2004).

Feverfew Available

According to a University of Rochester press release, a person with leukemia would not be able to take enough of the over-the-counter herbal remedy to halt the disease. It is not
clear how this information has been established in the absence of clinical trials. In fact, patients with leukemia might want to discuss this information with their hematologist-oncologist.

Standardized feverfew products are widely available for the treatment of migraine and other conditions. Many brands describe their products as "high parthenolide." One needs to read the labels carefully, however. I have found various products claiming to have 2, 5 or even 7% parthenolide by weight. Some of these come from obscure companies. One should definitely look for a product marketed by a reputable company which would have something substantial to lose by deceiving the public about the strength and purity of its product. One such company is Nature's Way. This company markets three separate feverfew products: feverfew leaves, feverfew extract and an even more concentrated product called MygraFew. This claims to have a standardized content of 2% parthenolide. Thus, a 30 milligram tablet contains 600 micrograms of parthenolide.

Cautions

The label cautions that feverfew is not recommended for use by pregnant or lactating women, or children under two years of age. Certain individuals may also experience oral discomfort or irritation when using the product. If irritation does occur, the manufacturer advises discontinuing the use of the product immediately. According to the website www.intelhealth.com:

"Feverfew has been well tolerated in studies. The most common side effects are mouth inflammation or ulcers, including swelling of the lips, bleeding of the gums, and loss of taste. When stopped suddenly after being used for long periods of time, feverfew may cause rebound headaches, anxiety, sleep disturbances, muscle stiffness or pain. Some people may experience more rapid or pounding heart rates. Skin irritation or eczema may occur in those with feverfew allergies. Photosensitivity (sensitivity to sunlight or sunlamps) has been reported with other herbs in the Compositae plant family and may be possible with feverfew as well. Less common side effects may include stomach upset, such as indigestion, nausea, gas, constipation, diarrhea, bloating or heartburn."

It is not at all clear how often these adverse events occur. The website further cautions that feverfew may combine adversely with certain drugs: "In theory, feverfew may increase the risk of bleeding when used with anticoagulants (blood thinners) or anti-platelet drugs. Examples include warfarin (Coumadin), heparin and clopidogrel (Plavix). Feverfew may also increase the risk of bleeding when used with anti-inflammatory pain relievers, such as aspirin, ibuprofen (Motrin, Advil) and naproxen (Naprosyn, Aleve, Anaprox). However, it is possible that feverfew may increase the effectiveness of these pain relievers."

"Based on the results from some animal studies, it has been suggested that feverfew could worsen symptoms of depression or reduce the effectiveness of antidepressants such as fluoxetine (Prozac). Feverfew should be used with caution in individuals with a history of depression or other psychiatric illnesses."

The current research work on the use of feverfew in the treatment of AML is extremely good news. Apart from anything else, it strengthens the argument that what is at the root of cancer is not a transformed body (somatic) cell, but a special type of stem cell. This concept has the potential to revolutionize the understanding of cancer, and its treatment. However, even with the help of NCI, it may be years before this flower derivative makes it to the market. One thing is certain. At around 20c per tablet, the cost is reasonable, and compares favorably with patented Gleevec, which, although better researched, costs around $100 per day.

National Debate

There is a major national debate in the US over stem cell research. The use of stem cells has been restricted by government decree. The National Institutes of Health (NIH) in principle is in favor of stem cell research. An NIH news release states:

"Research involving human pluripotent stem cells...promises new treatments and possible cures for many debilitating diseases and injuries. The NIH believes the potential medical benefits of human pluripotent stem cell technology are compelling and worthy of pursuit in accordance with appropriate ethical standards."

Yet there is a curious lack of support for stem cell research, at least at NCI. For instance, when I searched the NCI's financial year 2006 budget proposal I could find only one glancing reference to stem cells in that entire document.

I could also find no references whatsoever to stem cells in Andrew C. von Eschenbach's "A vision for the National Cancer Program in the United States." This is the statement in which the NCI director put forward his views on how to eliminate the death and suffering due to cancer by the year 2015. "A new era is now within our grasp," he stated, "a time when no one suffers or dies as a result of cancer." It is hard to imagine how the NCI intends to accomplish this without a serious involvement in the most important and exciting research initiative of our time.

Moss Reports

My approach is not to prejudge or to disparage unfairly, but simply to determine whether or not there is a solid scientific basis for the claims made on behalf of these various treatments for cancer — CAM as well as orthodox. I take the same strictly objective, evidence-based approach in the nearly 200 Moss Reports, each one of which is an in-depth study of the available conventional and alternative treatments for a particular type of cancer. My goal in writing these reports is to present an impartial and clear-eyed analysis of the most promising treatment options. People dealing with cancer need a reliable source of up-to-date information, a source they can count on to be honest and even-handed in assessing the many conflicting claims that assail them. The Moss Reports are designed to do just that. If you would like to order a Moss Report for yourself or a patient, you can do so from our website, www.cancerdecisions.com, or by calling Diane at 1-800-980-1234 (814-238-3367 from outside the US). We look forward to helping you.

Bibliography


