A Novel Combination of Plant Extracts with Promising Anti-Prostate Cancer Activity

by J.L. Hall, PhD, N. Springer, MSc, and D.L. Bemis, PhD

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Introduction
Prostate cancer is the most common cancer in men. The causes of this disease are not well understood, but prostate cancer is clearly associated with age, making it seem like an almost inevitable affliction for older men. The diagnosis of prostate cancer is based on analysis of a tissue biopsy – microscopic examination of a tiny sample of prostate tissue. A positive biopsy means that cancer cells are present and the conventional treatments include hormonal therapy, radiation therapy, and surgery with the actual regimen keyned to the stage of cancer detected in the prostate and whether there is evidence that it has spread.

The majority of biopsies are negative. The good news for these men – that they don’t have cancer – is tempered by the fact that they remain at high risk for developing prostate cancer, especially those with a family history of the disease. Moreover, they must cope with the symptoms that indicated prostate problems in the first place, including elevated PSA (Prostate Specific Antigen, a marker for prostate cancer) and BPH (Benign Prostatic Hyperplasia or swollen prostate, often associated with urinary and sexual problems).

There is no widely accepted conventional treatment for the prevention of prostate cancer in high-risk men or for the alleviation of the symptoms associated with enlarged prostate. The significant side effects frequently associated with hormones and surgery has generated considerable interest in the potential of alternative treatments including herbal remedies and nutritional supplements for alleviating symptoms and promoting prostate health. One of the challenges for anyone surveying the growing list of vitamins, herbs, and minerals claimed to keep the prostate healthy is to sort out whether the various promises are evidence-based. In other words: is there any science that supports the use of the product, what is the quality of the research, and what do the data tell us? This report summarizes the development of a novel combination of herbal supplements with anti-prostate cancer activity and describes the scientific methods behind the product.

The Scientific Procedures for Testing and Validating Potential Remedies
While the ultimate goal of identifying and researching natural compounds is to justify their use for promoting or restoring the health of human beings, there are a series of laboratory experiments that are essential before any of these compounds can be evaluated for clinical use. These experiments, broadly referred to as pre-clinical, have evolved into a relatively standardized progression starting with in vitro or test tube procedures, followed by cell-based assays, and culminating with in vivo or animal-based studies, and finally, when justified, clinical trials in human populations. This series of experiments is focused both on assuring that the compound may be safely tolerated by humans as well as on providing a scientific rationale for its application, hopefully to include some understanding of how the compound exerts its effect.

For natural compounds proposed for use in humans, the priority is to determine whether they exhibit toxicity and if so, to what extent. Considerable information can be gained from toxicity studies in which various cells maintained in tissue culture are exposed to a range of concentrations of the compound. The lower the concentration at which cells are killed, the higher the toxicity and the less likely the compound is to be tolerated by animals. Compounds with limited toxicity may be further tested in a vast array of in vitro studies. These might include assays for their effect on cell proliferation (important for cancer), for examining whether their effect is tissue specific (important if the goal is to target a specific cancer), and for localizing their site of action in the cell and for determining their biochemical impact (important if there is an indication of a specific anti-cancer activity). Many of these biochemical experiments, including enzyme assays, can be performed in cell-free systems that take place in a miniature test tube containing test compounds and their molecular targets.

What emerges from these in vitro studies is a series of observations constituting a profile of the compound’s toxicity, physiological effect, and mechanism of action. This profile will dictate whether further tests and animal studies are worthwhile. The decision to pursue animal studies is critical because these studies serve as a ‘proof of principle’ enabling examination of a compound’s effect in an organism, often a mammal, whose biology closely resembles that of a human being. These tests can reveal both the true potential of a compound’s
benefits as well as unanticipated side effects that are only evoked in a complex organism. The options for the design of animal studies are too numerous and diverse to summarize here so a single relevant example of an animal model system that has proven useful for cancer research will be reviewed.

Geneticists have developed strains of mice that have proven to be valuable in vivo models for studying the biological response to treatments for human cancers. Some of these specialized mice lack a thymus and hence cannot mount an immune response. When human cancer cells are transplanted into these mice, a process called a graft, the cells will grow into a tumor without interference from the host. Since the first successful transplantation of human tumors into athymic mice, many different human tumor cell lines (e.g., mammary, lung, genitourinary, gastro-intestinal, head and neck, glioblastoma, bone, and malignant melanomas) have been transplanted and successfully grown in these animals. The mice are then treated with compounds to assess their affect on the transplanted tumor cells. Positive results in these experiments, meaning that the compound reduces or abolishes the tumor with little or no harm to the mice, provides an extremely powerful argument for testing the compounds in human clinical trials.

The experimental procedures briefly summarized above represent the pathway for establishing a scientific basis for the safety and activity of any extract or supplement intended for improving human health. Products that have been subjected to these procedures stand apart from those that have not been rigorously tested. It is precisely this scientific lineage that was followed for the development of the novel combination of plant extracts described below.

Beljanski's Experiments with Pao Pereira and Rauwolfia Vomitoria; Anti-Cancer Activity

Both Pao Pereira, a tree that grows in the Amazon rain forest and Rauwolfia Vomitoria, a plant that grows in Africa, have a history of use as herbal remedies for a variety of ailments. The fact that extracts from these plants contain compounds with anti-cancer activity was first demonstrated by the French biochemist, Mirko Beljanski, working at the Pasteur Institute.

Beljanski developed a cell-free in vitro assay called the Oncotest which he used to test compounds for their propensity to act as carcinogens. This test, at once simple and powerful, was based on his observation that the DNA isolated from cancer cells is different from the DNA from healthy cells in two respects: cancer cell DNA absorbs more UV light and is more active as a template for in vitro DNA synthesis. These observations are consistent with the cancer DNA double helix being relatively more open or relaxed in structure resulting in more frequent loops of single stranded DNA. Beljanski saw this destabilization of the DNA duplex as an inherent property of cancer DNA and reasoned that it accounts for the characteristic enhancement of UV absorption and template activity. When Beljanski added known carcinogens to the cancer DNA he found that both the hyperchromicity (elevated UV absorption) and the rate of DNA synthesis were further increased whereas the results with normal DNA were almost unchanged. Compounds without cancer causing effects were neutral in the Oncotest, having no significant effect on chromicity or template activity of either cancer or healthy DNA.

Having established the validity of the Oncotest to identify carcinogens, Beljanski went on to use the test to try and identify compounds that inhibit or reduce the UV absorption and template activity of cancer DNAs while at the same time have no effect on normal DNAs. In a sense, this innovation amounts to using the Oncotest in reverse and enables screening for compounds that counteract the effects of carcinogens. Any compounds found in these screens could be considered potential anti-cancer agents. In the course of these experiments, Beljanski found that extracts from Pao Pereira and Rauwolfia Vomitoria reduced UV absorption and template activity of cancer DNA in the Oncotest. The potential of these compounds was first observed in these in vitro experiments.

Beljanski proceeded to test the Pao and Rauwolfia extracts in a fairly extensive series of cell-based assays. The extracts showed several consistent and noteworthy properties. First, at optimal concentrations, they stopped the proliferation of cancer cell lines maintained in the laboratory, while sparing healthy cells. This selectivity was maintained across a broad spectrum of cell types including brain, colon, liver, kidney, and skin. In the course of these experiments Beljanski showed that the extracts were active against the prostate cancer cell line, PC3.

Finally, Beljanski performed in vivo tests to explore the effects of the active compound in the Rauwolfia extract on cancer cells transplanted into mice. In these experiments mouse cancer cell lines from a lymphoma were transplanted into mice of the same strain in which the cancer originated. This ensured that the mice did not develop an immune response to the transplanted cells, thus enabling the effects of the Rauwolfia compound to be clearly discerned. At the highest doses, up to 80% of the mice treated with the Rauwolfia compound survived for ninety days whereas all of the untreated mice were dead by day
Plant Extracts with Anti-Prostate Cancer Activity

As noted in the report of this study: “All mice that did not survive developing tumors (average weight 8.6 +/-2.1 grams). Cured mice survived in excellent condition.” These data clearly demonstrated the anti-cancer activity of the Rauwolfia compound in an animal model system. Perhaps, most striking was the absence of deleterious side effects.

Based on their track record in these and other experiments, the Pao and Rauwolfia extracts were successfully used in numerous human case studies and ultimately developed as dietary supplements by Natural Source International, Ltd. These products, called Pao V® and Rovol V®, respectively, have been sold in Europe for many years and have recently been introduced in the United States. As described below, the anti-cancer activity of both these extracts remains the subject of ongoing research and development.

New Research with Pao Pereira and Rauwolfia Vomitoria: Anti-Prostate Cancer Activity

As part of an effort to develop natural products targeted toward prostate health, Natural Source established a collaboration with Drs. Katz and Bemis in the Department of Urology at Columbia University. The goal of these studies was to examine the potential activity of the Pao and Rauwolfia extracts specifically with regard to prostate cancer. The preliminary results of these experiments were presented at the First International Conference of the Society of Integrative Oncology. The preliminary results of these experiments were presented at the First International Conference of the Society of Integrative Oncology.

The experiments, carried out by Dr. Bemis, encompass in vitro cell-based assays that confirm the anticancer activity of the extracts in the human prostate cancer cell line LNCaP. These results justified an animal study involving transplantation of LNCaP cells into athymic mice and subsequent administration of the Pao extract to the mice. The results of these experiments were positive. Dr. Bemis also performed a series of cell free in vitro assays that shed new light on the mechanism of action of the Pao and Rauwolfia extracts. These experiments, the details of which can be found in the abstract, suggest that while the mechanisms of the antiprostate cancer action of the two extracts overlap, they are nevertheless distinct. This observation supported the concept of combining the two extracts together in the form of a new product. This product, called Prostabel®, is designed to take advantage of the activity of both Pao and Rauwolfia as well as any synergistic effect afforded by their different mechanisms of action. A clinical trial to examine the effects of Prostabel® in men with elevated PSA is expected to begin next year.

Conclusion

The demonstration of the antiprostate cancer activity of the Pao Pereira and Rauwolfia Vomitoria extracts and the development of a combination of the two extracts in the form of Prostabel® represents a formidable example of the application of scientific methods to the analysis and validation of natural products for promoting health.

For Further Information on Natural Source Products and Dr. Beljanski’s scientific research please visit the following websites:

www.natural-source.com
www.beljanski.com
www.mbschachter.com
http://www.findarticles.com/cf_dls/m0ISW/244/111271889/p1/article.jhtml

References

1. See the following websites:
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