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Mini Review

Promising Results: Efficacy of Two Plant Extracts for Benign Prostatic Hyperplasia (BPH)

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Abstract

The prostate gland is a major source of serious health problems for men. It is susceptible to the most common chronic inflammatory condition, benign prostatic hyperplasia (BPH), and prostate cancer is the most common malignancy. Age is a key risk factor for both BPH and prostate cancer, but diet, physical activity, and exposure to toxins also contribute to risk. BPH is specifically associated with hormonal changes that occur as men age. Family history is a predictor of prostate cancer.

Chronic inflammation is itself a risk factor for cancer and there is evidence that BPH is a forerunner of prostate cancer. At the molecular level, alterations in DNA structure characteristic of all cancers, are detected in the DNA from BPH tissues independently of the more extensive damage seen in the DNA from prostate tumors [1]. At the level of therapy, two plant extracts (*Pao pereira* and *Rauwolfia vomitoria*) that react with this damaged DNA and induce apoptosis in cancer cells have demonstrated effectiveness against prostate cancer and advanced prostate cancer [2-5]. Recent research from Dr. Jun Yan's laboratory at Nanjing University, sponsored by the Beljanski Foundation, shows that both extracts are also remarkably effective for BPH in an animal model: the androgen imbalance seen in older men is corrected, the prostate is reduced to normal size and the inflammatory condition is directly suppressed [6-9]. The effects of the extracts demonstrate that BPH is reversible.

Keywords: *Benign Prostatic Hyperplasia (BPH); Prostate Gland; Prostate Cancer; Pao pereira; Rauwolfia vomitoria*

Pao pereira and *Rauwolfia vomitoria* plant extracts resolve BPH by reducing 5α-reductase and androgen receptor

Levels of the male hormone testosterone normally decrease as men age, leading to a compensatory increase in the activity of the enzyme 5α-reductase. This enzyme converts testosterone to its more aggressive form, dihydrotestosterone. When dihydrotestosterone binds to the androgen receptor, overgrowth of prostate cells is triggered, the gland increases in size and the well-known urinary symptoms occur. Interfering with the conversion of testosterone to dihydrotestosterone by inhibiting 5α-reductase is the focus of therapies for BPH and several drugs accomplish this, albeit with a variety of negative side effects. Surprising results from recent studies indicate that both the *Pao pereira* and *Rauwolfia vomitoria* extracts are effective for BPH, while showing no evidence of negative side effects.

The extracts reduce BPH prostate weight and size as seen in figure 1. The statistically significant reduction in the levels of 5α-reductase and androgen receptor is shown in figure 2. The extracts restore normal prostate size by suppressing the levels of both 5α-reductase and androgen receptor thereby removing the trigger for BPH. The well-known marker for prostate inflammation/cancer, PSA (prostate specific antigen), is also reduced. The data show that the plant extracts exert the same effects as finasteride and are just as effective, but

unlike this commonly prescribed drug they do not appear to cause side effects. For example, finasteride significantly diminishes sperm counts whereas the plant extracts do not.

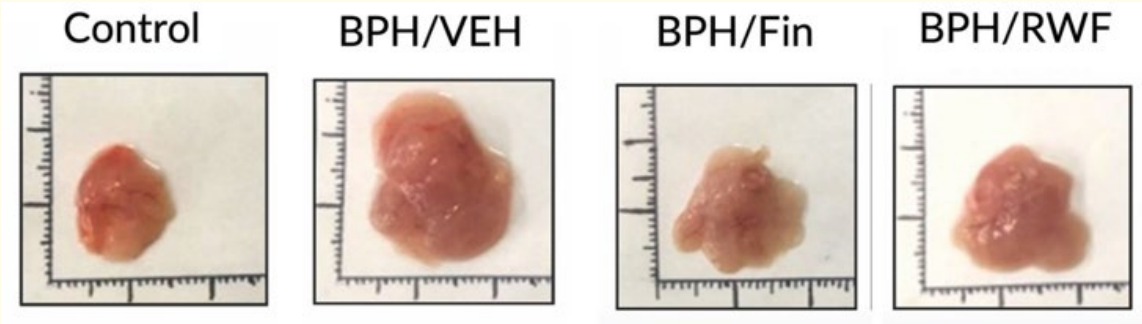

Figure 1: *Rauwolfia vomitoria extract reduces weight of BPH prostates to normal range in BPH animal model. Control (no BPH, no treatment), BPH/Veh is BPH with saline, BPH/FN is BPH with finasteride treatment, and BPH/Pao is BPH with Rauwolfia (RWF) extract treatment. The figure shows representative photographs of the dissected prostate glands from the four groups. Statistical analysis shows that the weights of BPH/FN and BPH/RWF prostates are not significantly different from the control [8].*

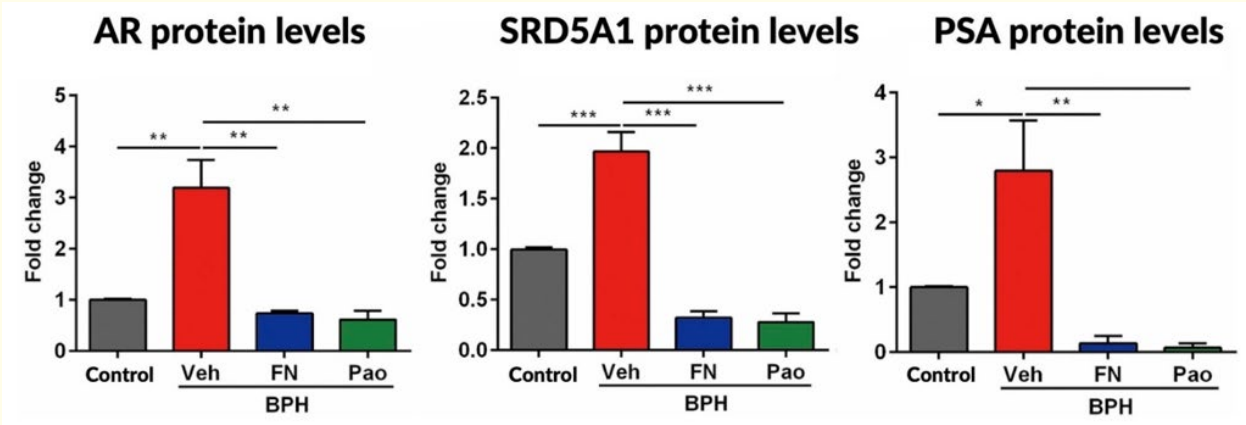

Figure 2: *Pao pereira extract reduces protein expression of androgen receptor (AR), 5α -reductase (SRDA1), and prostate specific antigen (PSA) in BPH animal model. The control is no BPH, no treatment; Veh is BPH with saline treatment; FN is BPH with finasteride treatment; and Pao is BPH with Pao pereira treatment. The y axis indicates the extent of protein increases for the vehicle treated group and the extent of protein reduction by FN and Pao relative to the control [6].*

Pao pereira and *Rauwolfia vomitoria* suppress BPH by inhibiting inflammation-associated NFκB signaling

Additional studies with the *Pao* and *Rauwolfia* extracts revealed a direct impact on a major control point of inflammation, the NFκB pathway. The NFκB complex controls expression of numerous genes that promote inflammation, and activation of this complex is correlated with BPH progression. Inhibition of NFκB provides a mechanism to attenuate inflammation of the prostate and this is exactly what the *Pao pereira* and *Rauwolfia vomitoria* extracts do. For example, two pro-inflammatory chemokines (CXCL5 and CXCL12) that are

induced by NFκB in BPH are down regulated by the *Pao pereira* extract. These cytokines are also activated in prostate cancer, revealing just how interlinked prostate inflammation and prostate cancer really are. One study points out that the inflammatory mediator, CXCL5, "may play multiple roles in the etiology of both benign and malignant proliferative diseases in the prostate" [10]. The fact that the *Pao* and *Rauwolfia* extracts can subdue these chemokines in BPH by suppressing NFκB suggests a role in preventing the transition from BPH to prostate cancer.

Rauwolfia vomitoria triggers autophagic apoptosis in BPH

Cells can recycle their proteins and organelles in a process called autophagy-literally 'self-digestion". This process promotes survival of cells that contain misfolded proteins or damaged structures-as the recovered components can be reused to make correct proteins and healthy structures. When a cell is in chronic inflammation like BPH, persistent autophagy leads to apoptosis or cell death, a way to rid the body of the defective cell. Induction of autophagic apoptosis is a pathway to resolve the serious inflammation of BPH by removing the affected cells from the prostate.

How does *Rauwolfia* extract induce autophagic apoptosis?

The *Rauwolfia* extract triggers a process called ER stress by changing gene expression in the 'unfolded protein response' (UPR) pathway. UPR normally controls correct folding of cellular proteins for maintenance of homeostasis. In BPH cells, continued stimulation of the UPR pathway by the extract, causes persistent ER stress, which leads to autophagy, apoptosis and cell death (See diagram in Figure 3). Autophagy in BPH cells induced by the *Rauwolfia* extract does not foster repair and survival of the cells (the cytoprotective effect of autophagy), rather it terminates the inflamed cells (the cytotoxic effect of autophagy).

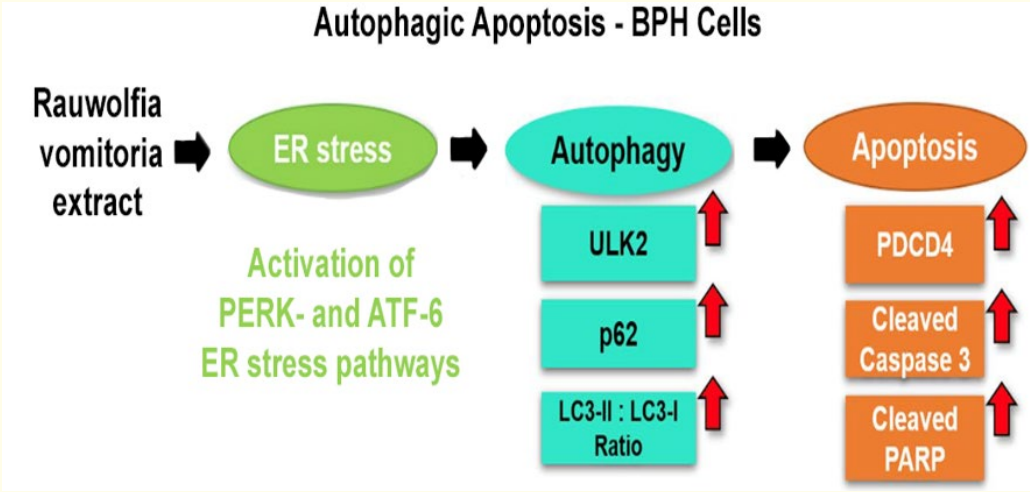

Figure 3: *Rauwolfia vomitoria extract induces apoptosis in stromal and epithelial BPH cells via endoplasmic reticulum (ER) stress. ER stress is activated by PERK- and ATF-6 pathways followed by downstream: 1) autophagy (increase in ULK2 and p62 gene expression and LC3-II:LC3-I ratio); and 2) apoptosis (increase in PDCD4 protein and cleavage of Caspase 3 and PARP) [9].*

Conclusion

The broad-spectrum anticancer activity of the *Pao pereira* and *Rauwolfia vomitoria* extracts was originally discovered by Dr. Mirko Beljanski, a scientist who was committed to developing effective nontoxic natural plant extracts for cancer [11]. The new research summarized here demonstrates that the extracts also have profound anti-inflammatory effects not just on the NFκB pathway and but also on androgen balance and autophagy.

Further Reading

Further information and links can be found on the Beljanski Foundation website: www.beljanski.org.

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