

The Homeopathic Effects of *Sabal Serrulata* against Prostate Cancer: an *in vitro* approach

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Introduction

The concept

Homeopathy is a medical system considered as a part of the Complementary and Alternative Medicine. **Samuel Hahnemann** is its founder and he formulated the basic principles in the early 19th century.

Homeopathy is based on two central principles:

- **Principle of similarity.** It states that a substance able to cause a symptom in healthy subjects can also be used to cure that symptom.
- **Principle of infinitesimals.** It states that a therapeutic substance becomes more potent as it is diluted and vigorously shaken (*succussion*).

The homeopathic preparations are done by a process known as **potentization** which involves repeated dilutions with *succussion* at each step (see Figure 1).

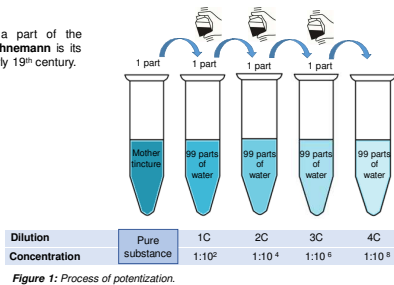
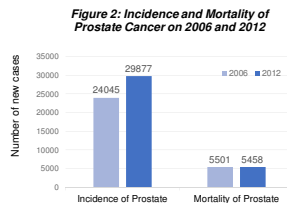


Table 1: Nomenclature of the most used homeopathic remedies. Potencies are abbreviated with a letter. The number preceding the letter indicates the number of times the substance has been diluted.

Name and potency	Dilution	Example	Meaning	Concentration
Mother tincture (MT)			Pure substance	-
Decimal X or D	1:10	30X	30 consecutive dilutions of 1:10	1:10 ³⁰
Centesimal C or CH	1:100	30C	30 consecutive dilutions of 1:100	1:10 ⁶⁰
Fifty millesimal (LM)	1:50000	30LM	30 consecutive dilutions of 1:50000	1:9.3·10 ¹⁴⁰

Homeopathy in cancer

Prostate cancer is the second most frequent cancer affecting men (15% of male cancer cases). In Figure 2 there is shown the number of new cases of prostate cancer on 2006 and 2012.



Among prostate cancer patients, approaching cancer with homeopathy is becoming increasingly popular

Placebo effect

In any pharmacologic treatment, the therapeutic effects have two aspects: **specific effects** (dosage, duration, interactions, etc.) and **nonspecific effects** (expectations and beliefs, non-pharmacologic characteristics, placebo effect etc.)

Some evidences suggest that the **placebo effect** is a genuine **psychobiological event** conditioned by the overall therapeutic context (see Figure 3).

In homeopathy, the process of choosing the right medicine for a patient needs not only a skilled homeopath but also an **open-minded patient** willing to present his or her physical and mental symptoms with a lot of details. Due to this, it has been hypothesized that:

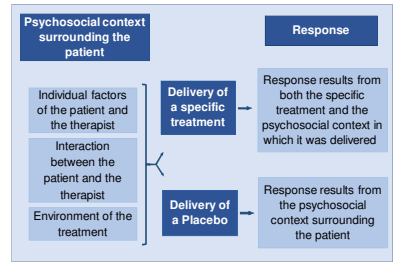


Figure 3: Contribution of the psychosocial context.

The placebo phenomenon can have a possible influence on effectiveness rates of homeopathy

How to choose the proper treatment?

- **Materia medica (MM):** Homeopathic Remedy Reference Guide that lists all homeopathic remedies with their associated symptomatology.
- **Repertory:** Index of diseases with its associate symptomatology. Per each symptom there is a remedy that according to MM fits the most.

Depending on the patient's symptomatology the therapist has a list of remedies. Among them he/she has to choose the most suitable/s for the patient.

This review will focus on the study of *Sabal Serrulata*. The choice of this remedy was made following two criteria:

- It is one of the most prescribed remedies for prostate cancer by the pioneers of homeopathy.
- According to the repertory Synthesis the most suitable remedies for prostate cancer are: *Conium Maculatum* (CON), *Sabal Serrulata* (SABAL) and *Thuja Occidentalis* (THUJ), (see Figure 4)

This review will focus on the study of *Sabal Serrulata* which has effects against prostate pain, emission of prostatic secretions and swelling, induration and inflammation

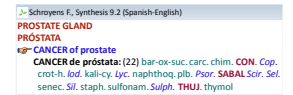


Figure 4: Search result from "Synthesis" Repertory

Objective

Present an overview about current studies that test the effects of *Sabal Serrulata* on cells and animal models.

1. Analyse the *in vitro* studies published in scientific sources that evaluate the effectiveness of *Sabal serrulata*.
2. The administration of the drug to cells will **fully minimise the possible placebo effect** observed in patients. Therefore, the specific therapeutic effects of the drugs will be demonstrated.
3. *In vivo* studies with animal models will complement *in vitro* studies.

Methods

All studies are published in peer-reviewed journals with **impact factor**. The **selection criteria** required for this review are:

- **Cytotoxicity** measured using MTT assay.
- **Anti-proliferative activity** measured by trypan blue exclusion assay
- **Apoptosis** determined by dual staining the cells with ethidium bromide (EB) and acridine orange (AO) dyes or FACS
- **Detection of mRNA expression** by ribonuclease protection assay and multiprobe sets
- **Expression of proteins** detected by Western blot

Results

Sabal Serrulata is a popular phytotherapeutic agent for the treatment of urologic problems like prostate cancer. The literature describes various studies in favour and against *Sabal Serrulata*'s efficiency (see Figure 5).

In Table 2 are shown the main results obtained and their possible underlying mechanisms (see Table 2).

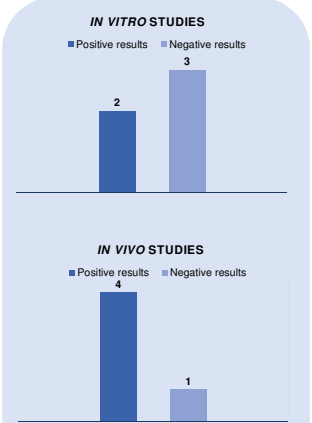


Figure 5: Number of reviewed studies showing positive and negative results about *Sabal Serrulata* efficiency (in vitro and in vivo)

Title	Dilution	Cell lines/strain	Main results	P value
Effects of Homeopathic Preparations on Human Prostate Cancer Growth in Cellular and Animal Models	MT 12CH 30CH 100CH 200CH 300CK 1000CK	PC-3 DU-145 Male nude BALB/c nu+ mice	Reduction of cell proliferation (%) PC-3: 33% at 72h; DU-145: 23% at 24h	<0.01; <0.01
			Tumour incidence (%) Control: 100%; MT: 94.5%; 200C: 75%	-
Effect of Homeopathic Treatment on Gene Expression in Copenhagen Rat Tumor Tissues	200C	MAT-LyLu Copenhagen rats	mRNA expression of apoptotic genes: No significant results	>0.05
			Expression of cytokines: No significant results	>0.05
Can Homeopathic Treatment Slow Prostate Cancer Growth?	200C	DU 145 LNCaP MAT-LyLu Copenhagen rats	Reduction of tumour incidence: 23%	-
			Reduction of tumour volume: 45%	-
Saw Palmetto induces growth arrest and apoptosis of androgen-dependent prostate cancer LNCaP cells via inactivation of STAT 3 and androgen receptor signaling	0.5-1 µl/ml	LNCaP	Reduction of tumour weight: 33%	-
			Cell viability: No significant results	>0.05
Homeopathic Medicines Do Not Alter Growth and Gene Expression in Prostate and Breast Cancer Cells In Vitro	30C 200C 1000C	MAT-LyLu MDA-MB-231	Apoptotic genes expression: No significant results	>0.05
			Reduction of tumour incidence: 23%	<0.0001
Saw Palmetto induces growth arrest and apoptosis of androgen-dependent prostate cancer LNCaP cells via inactivation of STAT 3 and androgen receptor signaling	0.5-1 µl/ml	LNCaP	Reduction of tumour weight: 13%	<0.05
			Increase of apoptotic cell death: 19%	<0.05
Homeopathic Medicines Do Not Alter Growth and Gene Expression in Prostate and Breast Cancer Cells In Vitro	30C 200C 1000C	MAT-LyLu MDA-MB-231	Inhibition of cells growth: ED ₅₀ =2µl/ml	-
			Apoptotic effect 0.5µl/ml: 8.7±2.0%(24h); 9.9±1.6%(48h) 1µl/ml: 14.3±2.2%(24h); 35.1±4.4%(48h)	P<0.005
Homeopathic Medicines Do Not Alter Growth and Gene Expression in Prostate and Breast Cancer Cells In Vitro	30C 200C 1000C	MAT-LyLu MDA-MB-231	Increase of expression: p21 and p53	-
			Down-regulation of IL-6-induced level of pSTAT 3: 60%	P<0.005
Homeopathic Medicines Do Not Alter Growth and Gene Expression in Prostate and Breast Cancer Cells In Vitro	30C 200C 1000C	MAT-LyLu MDA-MB-231	Inhibition of xenografts growth and weight	p<0.05; p=0.02
			Cell growth and viability: No significant results	>0.05
Homeopathic Medicines Do Not Alter Growth and Gene Expression in Prostate and Breast Cancer Cells In Vitro	30C 200C 1000C	MAT-LyLu MDA-MB-231	mRNA expression of apoptotic genes: No significant results	>0.05
			mRNA expression of apoptotic genes: No significant results	>0.05

Table 2: Main results. Studies in favour and against *Sabal Serrulata*'s efficiency and its possible underlying mechanisms

Permixon



Permixon® is a liposterolic extract of *Sabal Serrulata* used to treat some of lower urinary tract symptoms associated with BPH.

Permixon® has an antiproliferative effect against prostate cancer cell lines. Some suggested mechanisms of action are:

- Inhibition of both type 1 and type 2 isoenzymes of 5 alpha-reductase
- Interference with binding of dihydrotestosterone to cytosolic androgen receptors
- Intrinsic pathway of apoptosis
- Activation of the mitochondrial permeability transition pore
- Down-regulation of inflammatory-related genes and of the activation of NF-κB pathway
- Changes in cell membrane organisation

A lot of *in vitro* studies prove many effects of *Sabal Serrulata* against different prostatic cancer cell lines.

Conclusions

- Homeopathy one of the most controversial subjects in CAM: the mode of action of the homeopathic potentization is still unknown, the assumptions upon which homeopathy is based are not supported from the modern scientific principles and the placebo effect has a possible influence on effectiveness rates of homeopathy.
- There is a very limited number of reports in the scientific literature. None of the studies are conducted by a blind researcher
- Given the lack of mechanism to explain most of the effects of *Sabal Serrulata*, any interpretation of these data should be done cautiously.
- Permixon® could be an interesting tool for new applications such as prostate cancer.
- The administration of *Conium maculatum* and *Thuja Occidentalis* along with *Sabal Serrulata* could show more positive effects on cancer.

This review suggests that due to the lack of consensus, there are insufficient scientific evidences to ensure that *Sabal serrulata* is the right remedy of choice for prostate cancer