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REVIEW ARTICLE ON PROSTATE CANCER

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Abstract

Background: Homeopathy and other complementary and alternative therapies are frequently used to improve cancer patients' quality of life and lessen the side effects of standard medical care. Homeopathy is an integrative part of medical system which uses Ultra high diluted preparations for various kind of treatments. Various preclinical laboratory studies are conducted to explain the mechanism of action of ultra-high diluted homeopathic medicine against prostate cancer cell lines. There aren't many research on the use of homeopathic remedies to treat the illness itself, in contrast. However, over the past 20 years, studies have been published that suggest homeopathic high dilutions may be useful against cancer in experimental models.

Prostate cancer is the most frequently diagnosed cancer worldwide and the sixth largest cause of cancer-related death among males. Prostate tissue biopsies, MRI scans, and prostate-specific antigen (PSA) testing are the mainstays of diagnosis; however, the value of PSA testing for screening is still debatable. There are now new diagnostic tools accessible, such as different types of PET scans, risk stratification bioassay tests, and germline testing. When a cancer just affects the prostate, it is said to be localised and perhaps treatable. Bisphosphonates, rank ligand inhibitors, hormone therapy, chemotherapy, radiopharmaceuticals, immunotherapy, concentrated radiation, and other targeted therapies may be employed if the disease has spread outside the prostate

Objective: The objective of the study was to conduct a comprehensive review of basic science studies on homeopathic high dilutions in cancer.

Method: Following the Preferred Reporting Items for Review, we conducted a literature search in the database for original publications, from 2011 to 2022 and in English Kinds of literature were searched in web databases Pubmed, Research gate, Google scholar, and Scopus from year 2011 to 2022.

Result: The main focus of the research was on apoptotic processes' role in cytotoxic effects. To highlight the distinctiveness of such effects, experimental designs should take into account characteristics of homeopathy that are inherent. From various literatures it shows that ultra-high diluted homeopathic medicines are prepared according to homeopathic principles. Homeopathic medicine stops the cell proliferation and improves the quality of life of patient from prostate cancer.

Conclusion: These homeopathic medicines are effective against prostate cancer. These medicines are supposed to be anti-cancerous as they cause malignant cell death or size deduction by inhibition of proliferative cells, apoptotic signally, enhancing mitochondrial membrane permeability and lowering cancer marker enzymes. This studies provides scientific evidence of the ability of homeopathic dilutions to induce apoptosis in the breast cancer cell line which encourages a possible use as supportive medicines in cancer therapy.

Keywords: Homeopathy, Prostate cancer, invitro, cell line studies, ultra high dilutions.

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INTRODUCTION

Prostate cancer is the second most frequent cancer in males worldwide and a very common disease that only affects men. Thus, it has become crucial for medicine to explore new therapeutic options for prostate cancer. The inherent androgenic, glucocorticoid, and oestrogenic-like properties of medicinal plants or herbs have the potential to be used in the treatment of prostate cancer because this disease is so highly susceptible to androgens. Apoptosis signalling intermediates seem to be the target of numerous anticancer drugs in recent years^[1]. Worldwide, prostate cancer is the most commonly diagnosed malignancy and the sixth leading cause of cancer death in men. Diagnosis is primarily based on prostate-specific antigen (PSA) testing, MRI scans, and prostate tissue biopsies, although PSA testing for screening remains controversial. New diagnostic technologies including risk stratification bioassay tests, germline testing, and various PET scans are now available^[2].

The second most frequent reason for cancer-related death is prostate cancer. The American Cancer Society predicts that in 2004, this cancer will be diagnosed in about 221,000 Americans. Prostatectomy, radiation therapy, and hormone therapy are examples of traditional treatments for prostate cancer^[3]. However, because to the heterogeneous population of hormone-sensitive and hormone-insensitive cells that make up prostate carcinomas, which dictate how well a patient responds to androgen restriction, issues can occur in individuals receiving hormonal therapy. Patients with prostate cancer are increasingly turning to alternative medical remedies, with herbal medicines being the most popular, especially those with metastatic disease^[4].

Prostate cancer, the fifth leading cause of death worldwide, is the second most common cancer diagnosis for men, according to data analysis. There will be 1.4 million entirely new cases of prostate

cancer in 2020^[5]. Prostate cancer in its early stages rarely causes symptoms and advances slowly, calling for careful observation. 12,76,106 new cases of prostate cancer were reported globally in 2019, according to GLOBOCAN 2018 estimates, with industrialised countries having a higher prevalence^[5]. Different ways to diagnostic testing are the cause of variations in incidence rates across the globe. The highest incidence and fatality rates are found in men over 65, and both are strongly associated with age. African American men experience the highest incidence rates and the most severe conditions compared to white men^[6].

Samuel Hahnemann created the homeopathic medical system in the late 18th century. It is founded on the idea that "like cures like" and frequently employs extremely high dilutions of remedies. Critical studies of the clinical literature in homeopathy generally, but not always, show significant benefits that go beyond placebo, but there is not enough data in any one condition to show specific efficacy or to comprehend causes. There aren't many high-quality studies on homeopathy and cancer in the literature^[7].

The application of homeopathy in the treatment of cancer depends on the type of cancer, its stage, and the patient's overall health. Here are some elements of homeopathic cancer treatment^[8]

1. The excruciating pain experienced by some cancer types is among the most upsetting symptoms. Conventional medications can reduce pain, but only to a limited degree, and they also have adverse effects. Additionally, there is always a cap on the maximum dosage that can be given to a patient without risk.
2. The advantage of administering Homeopathic medicines in such cases is that there can be effective pain control without inducing any side effects.

3. Homeopathy can help in improving the general wellbeing and vitality of the patient.
4. Conventional treatment options for cancer (surgery, chemotherapy, radiotherapy, etc) are associated with distressing side effects and homeopathy can play a definite role to counter these side effects.
5. The diagnosis of cancer often leaves the patient with a sense of depression, anxiety, and fear. The treatment may induce additional irritability, impatience and mood fluctuations. Homeopathy can influence the psyche of the patient and help him/her to deal with these emotions in a better way (8-14) Prostate cancer is the most frequently diagnosed male cancer and the sixth most prevalent cause of cancer mortality in males worldwide. In 2020, there were 1,414,249 newly discovered cases and 375,000 annual fatalities from this illness worldwide. Prostate cancer is the most prevalent malignancy detected globally in more than 50% of countries.

Age, ethnicity, obesity, and family history are the most well-known significant risk factors. [15]. Fortunately, cancer aggressiveness declines with age while the total incidence rises as people age. [14]. Male gender, advanced age, a favourable family history, increased height, obesity, hypertension, lack of exercise, consistently high testosterone levels, exposure to Agent Orange, and ethnicity are all risk factors for prostate cancer. [17]

The second most typical cancer diagnosis for males is prostate cancer, which is also the fifth highest cause of death globally. Early-stage prostate cancer frequently has no symptoms and progresses slowly, necessitating only vigilant surveillance. Early-stage prostate cancer frequently has no symptoms and progresses slowly, necessitating only vigilant surveillance. According to GLOBOCAN statistics for 2018, there were 1,276,106 new cases of

prostate cancer. reported globally in 2018, with wealthier nations having a higher prevalence. Worldwide variations in incidence rates are a result of diverse approaches to diagnostic testing. Men over the age of 65 are most likely to get prostate cancer, and fatality rates are also significantly correlated with age. In comparison to White men, African-American men have the highest incidence rates and the most severe form of prostate cancer. Although there is currently no known way to prevent prostate cancer, the risk can be decreased by consuming less high-fat foods, more fruits and vegetables, and engaging in more physical activity. For men with a family history and men of colour, screening should start at age 45. For the primary prevention of this illness, up-to-date data on prostate cancer incidence and mortality as well as a deeper comprehension of the aetiology and causative risk factors are crucial.

CELL LINE STUDIES WITH ULTRA HIGH DILUTED MEDICINE:

Various studies focusing on the genes that homoeopathic medicines target and studies investigating the cellular mechanisms of homoeopathic medicines for establishing precise, suitable medicine selection. Evidence from such experimental and clinical trials strongly points to homoeopathic medicine's efficacy in the treatment of cancer. Studies on this cell line are a useful pre-clinical tool for making a preliminary assessment of the efficacy of homoeopathic medications in the treatment of cancer. Homoeopathic medications have been shown to have cytotoxic and apoptosis-inducing characteristics in investigations on cell lines.

NEED FOR THE STUDY:

The greatest evidence-based care must be given to patients with cancer in the earliest stages of the disease because the incidence of the disease is always rising. Although homoeopathy has a wide range of prescribed medications, investigations demonstrating the precise mechanism of

action of these medications are sadly lacking. In order to identify the best, indicated, scientifically based action potential of homoeopathic medications in various prostate cancers, which enables us to provide the best recommended care, there is an expanding necessity to get focused on such studies. To examine the therapeutic effects of homoeopathic medications, cell line studies will be the best alternative

RISK FACTORS – (18)Prostate Cancer Risk Factors

CAUSES:

Genetics is undoubtedly a factor in prostate cancer, despite the fact that the exact causation is unknown. Prostate cancer risk is known to vary depending on race, genetic background, and family history. [24] In general, people with genetic or hereditary prostate cancer have malignancies that manifest earlier in life, progress more rapidly, are more likely to be locally advanced, and have a higher chance of recurrence following surgery. [25] The highest heritability of any serious malignancy in men is inherited prostate cancer. [26] There may be a genetic link between prostate cancer and a family history of Lynch syndrome, hereditary breast or ovarian cancer, or both. [27] [28]

DIET-The normal Western diet has a general link to prostate cancer. Little to no evidence exists to support a link between trans fat, saturated fat, or carbohydrate consumption and prostate cancer. However, it has been demonstrated in a mouse model that a lard diet (rich in unsaturated fats) greatly accelerates the progression of prostate cancer. Supplemental vitamin intake doesn't reduce risk; in fact, some vitamins may make it higher. An advanced prostate cancer risk factor is high calcium intake. Milk products and diets high in saturated fat appear to increase the risk of

cancer. Prostate cancer risk may be increased by low vitamin D blood levels. Patients with prostate cancer who are vitamin D deficient die more frequently overall and from the disease alone.

Chemical Exposure and Medications-Some prescription drugs, surgical procedures, and medical conditions are associated with prostate cancer.

Sexual Activity-Prostate cancer risk is increased by having multiple sexual partners over one's lifetime or beginning sexual activity at a young age. Regular ejaculation may lower the overall risk of prostate cancer, but less frequent ejaculation is not linked to an increase in the prevalence of advanced illness. [11] [12]

INFECTION-The occurrence and progression of prostate cancer may be influenced by infections. [13] Prostate cancer risk appears to be increased by chlamydia, gonorrhoea, or syphilis infections. [14] Although it has been suggested that the Human Papilloma Virus (HPV) contributes to the occurrence of prostate cancer, the evidence is conflicting. [15]

Epidemiology-The second-leading cause of cancer-related deaths in males in the United States, prostate cancer is the most frequently diagnosed organ cancer in men. [77] The first is lung cancer. [78] [79] Although there will still be 268,490 new cases of prostate cancer detected and a projected 34,500 fatalities in the United States in 2022, the American Cancer Society reports that comparatively few men with prostate cancer pass away from the condition. In the developed world, prostate cancer is more prevalent. [80] In the US, the overall 5-year survival rate is 99%. [81] Since 1992, when PSA testing became widely accessible, the incidence has generally grown but the fatality rate has gradually declined.

MORE LIKELY	AGE	Chance of having prostate cancer rises rapidly after age 50 Prostate cancer is rare in men younger than 40.
	RACE	more often in African American men and in Caribbean men occurs less often in Asian American and Hispanic/Latino men
	GEOGRAPHY	Prostate cancer is most common in North America, northwestern Europe, Australia, and on Caribbean islands. It is less common in Asia, Africa, Central America, and South America.
	FAMILY HISTORY	INHERITED GENETIC FACTOR
	GENE CHANGES	<i>BRCA1</i> or <i>BRCA2</i> genes Lynch syndrome

LESS LIKELY	DIET
	OBESITY
	SMOKING
	CHEMICAL EXPOSURE
	PROSTATE INFLAMMATION
	SEXUALLY TRANSMITTED DISEASE
	VASECTOMY

INVITRO HOMOEOPATHUC EXPERIMENTS:

SR.NO	AUTHOR	YEAR	CELL LINE	MEDICINE	FINIDNG
1.	Rajesh L. Thangapazham, MS, Jaya P. Gaddipati, PhD, N. V. Rajeshkumar, PhD, Anuj Sharma, MS, Anoop K. Singh	2015	(DU-145, LNCaP, MAT-LyLu	s Conium maculatum, Sabal serrulata, Thuja occidentalis, Asterias, Phytolacca, and	: The results demonstrate that the highly diluted homeopathic remedies used by homeopathic practitioners for cancer show no measurable effects on cell growth or gene expression in vitro using currently available methodologies

				Carcin osin	
2.	Rajesh L. Thangapazham, MS, N. V. Rajeshkumar, PhD, Anuj Sharma, MS, Jim Warren, MS, Anoop K. Singh, PhD, John A. Ives	2015	MAT-LyLu	Conium maculatum, Sabal serrulata, Thuja occidentalis, and a MAT-LyLu Carcin osin nosode	: There were no significant changes in mRNA levels of the apoptotic genes bax, bcl-2, bcl-x, caspase-1, caspase2, caspase-3, Fas, FasL, or the cytokines interleukin (IL)-1 α , IL-1 β , tumor necrosis factor (TNF)- β , IL-3, IL-4, IL-5, IL-6, IL-10, TNF- α , IL-2, and interferon- γ in prostate tumor and lung metastasis after treatment with homeopathic medicines.
3.	Çisil ÇAMLI PULAT 1,	2021	Prostate cancer	Tarantula cubensis	These results indicated that T. cubensis alcoholic extract might be utilized as an anticancer biotherapeutic and should be further examined for its potential
4.	RANKO MIOCINOVIC1 ' 2 , N. PATRICK MCC ABE12 , RICK W. KECK1,2 , JERZY JANKUN1 ' 2 ' 4 , JAMES A. HAMPTON3	2004	lines DU-145 and PC-3	Baical ein	, induced a dose-dependent growth inhibition of prostate cancer cell lines DU-145 and PC-3, as well as HUVECs.
5.	Hui-Hsuan Lin a,b , Kuei-Chuan Chan c,d , Jenn-Yuan Sheu e , Shu-Wen Hsuan f ,	2011		Hibiscus sabdariffa	
6.	Brian W. MacLaughlin, BS, Babet Gutsmuths, PharmD, PhD, Ewald Pretner, MD	2015	n PC-3 and DU-145	Sabal serrulata, Thuja occidentalis, and Conium	Treatment with Sabal serrulata in vitro resulted in a 33% decrease of PC-3 cell proliferation at 72 hours and a 23% reduction of DU-145 cell proliferation at 24 hours (P < .01). Thuja occidentalis and Conium maculatum did not have any effect on human prostate

				m macula tum	cancer cell proliferation. . In vivo, prostate tumor xenograft size was significantly reduced in Sabal serrulata-treated mice compared to untreated controls (
7.	Lucero Delgado Pastelín, Cynthia Ordaz Pichardo, Gustavo Aguilar Velázquez	2015	PC-3 (Prostate cancer)	Echina cea angusti folia	This study provides scientific evidence of the ability of E. angustifolia homeopathic dilutions to induce apoptosis
8.	Botkina, Olga ; Plotnikov, Evgenii	2022	prostate cancer PC-3,	Hydras tis, Coniu m and Carcin osinu m	The results obtained in vitro indicated the absence of a direct cytotoxic effect in the studied homeopathic preparations
9.	Marina Julia ^[17]	2012	PC3 Cells	Sabal Serrula ta	Popular phytotherapeutic Sabal Serrulata is used to treat urological conditions like prostate cancer. Various research supporting and refuting Sabal Serrulata's efficacy are described in the literature. MTT assay used to assess cytotoxicity. o Trypan blue exclusion assay used to measure the anti-proliferative activity. o Cells can be double- stained with ethidium bromide (EB) and acridine orange (AO) dyes to detect apoptosis, or FACS can be used. o Ribonuclease protection assay and multiprobe sets for mRNA expression detection o Protein expression was discovered using a Western blot. According to this research, there is not enough scientific data to support Sabal serrulata as the best treatment option for prostate cancer due to the lack of agreement
10.	MacLaughlin et al	2015	prostate cancer cell	Sabal Serrula ta	This study demonstrated that the size of the prostate tumour xenograft was dramatically decreased in mice treated with Sabal serrulata as compared to

					untreated controls. <i>S. serrulata</i> alone caused the response in the human prostate cancer; other homoeopathic treatments were ineffective. The study's findings support future investigation into <i>S. serrulata</i> as a specialised homoeopathic treatment for prostate cancer.
11.	MacLaughlin et al	2006	PC-3 and DU-145 human prostate cancer cell lines prostate cancer LNCaP cells, as well as MDA-MB-231 human breast cancer cell	Sabal serrulata, Thuja occidentalis, and Conium maculatum,	The authors' research examined the antiproliferative properties of homoeopathic preparations of Sabal serrulata, Thuja occidentalis, and Conium maculatum in vitro on PC-3 and DU-145 human prostate cancer cell lines prostate cancer LNCaP cells, as well as MDA-MB-231 human breast cancer cell lines and in vivo on naked mouse xenografts. Sabal serrulata treatment inhibited PC-3 cell proliferation by 33% after 72 hours and DU-145 cell growth by 23% after 24 hours (P .01). The distinct doubling time of each cell line is probably to blame for the variation in decrease. On human breast cancer cells MDA-MB-231, no impact was seen.
12.	Tilbe ÖZAR et al	2020	PC-3 human prostate cancer cell line		The anticancer effect of whitebeam (<i>Sorbus aria</i>) extract was demonstrated on PC-3 human prostate cancer cells in vitro in this in vitro investigation. The MTT cell proliferation assay was used to assess the anticancer efficacy of the ethanol extract produced from whitebeam fruits. Additionally, the total phenol content and antioxidant capacity of whitebeam fruits were determined using the Folin-Ciocalteu assay and the CUPRAC method, respectively. Prostate cancer in vitro was significantly inhibited by whitebeam fruit extract. In vitro

					research reveals the obtained ethanol extract to be a promising natural anticancer drug. Whitebeam is a highly effective anticancer agent on PC-3 cancer cells in vitro, according to results
13.	Çisil Çamli Pulat	2021	Lung cancer cell line H69AR, prostate cancer cell line PC-3 and breast cancer cell line MCF-7	Tarantula cubensis alcoholic extract Theranekron®	Due to their high peptide composition, spider venoms are well known to have significant promise for their antibacterial, antifungal, and anticancer properties. In this study, four different human cancer cell lines and one non-cancerous human cell line were used to assess the cytotoxic effect of Theranekron®. By conducting an invitro test for Theranekroncytotoxic ®'s effect, it was hoped to lay the groundwork for future research. Theranekron® exhibits a high level of cytotoxicity on human breast cancer cell lines, according to the results. As opposed to breast cancer cells, it was discovered that human small cell lung cancer, glioblastoma, and prostate cancer cell lines had a considerably lower rate of cytotoxicity. These findings suggested a potential use for T. cubensis alcoholic extract.
14.	Amarnath K, et al	2013	prostate cancer cell line (PC3)	Ethanol extract of Acalypha indica	This research will determine how homoeopathic medicine affects cell viability. MTT and LDH assays were run after treating PC3 cells with either free ETAI or ETAI loaded CS-CT microparticles. After 24 hours of incubation, there was a negligible difference between the values of untreated PC3 cells and those treated with CS/CT/ETAI microparticles. This suggests that both free ETAI and CS/CT/ETAI microparticles are equipotent during the first time course of incubation. However, it was discovered that CS/CT/ETAI

					<p>microparticles were more efficient than free ETAI after 72 hours of incubation. By doing so, it is possible to improve its overall effects on cell cytotoxicity and increase bioavailability. The effects of exposure to a homoeopathic substance of plant origin recognised to have anticancer potentials</p>
15.	Jonas et al[2006	Prostate cancer cell lines. MAT-LyLu, LNCaP and DU 145 cells.	Thuja occidentalis, Conium maculatum, and Sabal serrulata and Carcinogen	<p>Homeopathic remedies for T. occidentalis, C. maculatum, and S. serrulata and 1000 c for MAT-LyLu Carcinogen were applied to various sets of plates in concentrations of 100 L, 30 c, 200 c, and 1000 c.</p> <p>Control cells came from wells that weren't treated. The growth of the cells was allowed for 24, 48, 72, and 96 hours. Then, using the MTT assay and a rAPO-1 multiprobe, we assessed the viability of the cells and the expression of the apoptotic genes. On any cell line, with any medication, no appreciable variations in cell survival or gene expression were observed. Therefore, these medications do not directly cause cytotoxicity or apoptosis in prostate cancer cell lines</p>

CONCLUSION

This review provides evidences on the cytotoxic and anti-proliferative activity of potentised Homoeopathic medicines in cell lines. These significant results necessitate further in vitro and in vivo studies to evaluate the applicability of Homoeopathic medicines in the treatment of Breast cancer.

CONFLICT OF INTERESTS

The author have not declared any conflict of interests.

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