Evidence-Based Strategy for Cancer Prevention: Advocating for the Adoption of Black Cumin (*Nigella sativa*) Herbal Gardens in Zimbabwe

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**ABSTRACT**

**Introduction:** Cancer has become the world’s biggest killer. The developing world has not been spared of the effects, a clear sign of migration in diets and social activities and possible the effects of industrialization on clean environments for example, China. Zimbabwe and Sub-Saharan Africa have not been spared, it is reported that but 70% of cancer-related deaths are taking pace in low-to-medium-income countries (LMICs). In Zimbabwe alone, recent data points out that there was a 7% increase in the number of reported new cases (to 7018) with prostate and cervical cancer being the most frequently occurring cancers.

**Objective:** We sought out to review the present cancer situation in Zimbabwe and in line with the national cancer strategy, advocate for low cost, evidence-based and effective ways of dealing with cancer.

**Methods:** We reviewed Data from the WHO fact sheets and Zimbabwe Cancer Registry on the current situation and trends on cancer.

**Results:** Zimbabwe, like any other LMIC country is faced with a growing cancer burden. The major limitations in cancer, diagnosis, therapy and care is mainly due to poor detection limitations (65%) and technically related (equipment, patient awareness and personnel (35%). Prostate cancer (9%) has recently overtaken Kaposi sarcoma (7%) as the most frequently occurring cancer in Zimbabwe among men. Among females cervical cancer remains the frequently occurring cancer (19%). In 2014, cancer emerged as the biggest cause of mortality in Zimbabwe ahead of HIV/AIDS and TB. Black Cumin (*Nigella sativa*) is a traditional herb that can cure a number of cancers. The active compound of *Nigella sativa*, Thymoquinone (TQ) was found to be active against the following listed cancer types: Blood Cancer, Breast Cancer, Pancreatic Cancer, Renal Cancer, Skin cancer, Lung Cancer, Hepatic Cancer, Colon Cancer, Fibrosarcoma and Prostate Cancer.

**Discussion and conclusion:** The mechanism of action of Thymoquinone against cancers has been reviewed and TQ has been identified with modulation of p53 pathway, upregulating apoptosis genes p21 and Brca. We are also calling for a shift in cancer alertness in the primary healthcare systems, and the advocacy of traditional medicine, such as the black seed which has been proved to be efficacious against major cancers. We hypothesise that black seed will also be able to fight against the undocumented cancers prevalent in the poor African populations.

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INTRODUCTION

Cancer has been for a long time, associated with the developed world as the biggest killer. Of late, the third world has not been spared of the effects [1], a clear sign of migration in diets and social activities and possible the effects of industrialization on clean environments for example, China [2]. Up to one third of cancers are preventable, and this can be done through behavioural change [3] (accounting for 30% of global cancers) in terms of tobacco—which caused about 22% cancer deaths in 2004, dietary adjustments, alcohol abuse, and physical activity initiation [4]. Tobacco alone causes other multiple cancers. Other infections may also result in cancers. Occupational hazards such as dust and radiation can also be causes of various cancers [4]. Cancer-related deaths are expected to remain on the increase with 13.1 million deaths projection by 2030 [4].

In Africa, due to poverty and culture, diets have been mainly vegetable-based and a starch-main source of carbohydrates. Recent developments have seen urbanization and adoption of western cultures among the African population, which is the main reason for dietary migration. The abandonment of traditional diets by Africa, for the fast foods diet, could be among other causes, the cause of the surge in cancers. Plants are invaluable sources of new drugs and have been a major source of therapeutic agents since ancient times to cure human disease.

Zimbabwe and Sub-Saharan Africa have not been spared, it is reported that but 70% of cancer-related deaths are taking pace in low-to-medium-income countries (LMICs) [4]. In Zimbabwe alone, recent data points out that there was a 7% increase in the number of reported new cases (to 7018) with prostate and cervical cancer being the most frequently occurring cancers [5]. Zimbabwe, like other health systems in the LMIC countries has a big setback in the fight against cancer due to poor cancer diagnosis, prevention, treatment and care. Over 50% of their health budgets are foreign aid grants and they have been focusing mainly on communicable diseases like Malaria, TB and HIV. This is inadequate resource allocation towards cancer diagnosis, prevention, treatment and care. The WHO has come up with a strategy for prevention, which is to avoid and reduce the risk factors, vaccinate, control of occupational hazards and reduced exposure to UV. Other key preventive measures include early detection, early diagnosis, screening, treatment (of early cancers and preventable cancers) and palliative care. The WHO states that, cancer is a preventable disease to a larger extent, meaning we can reduce its impact on human lives.

Prostate cancer (9%) has recently overtaken Kaposi sarcoma (7%) as the most frequently occurring cancer in Zimbabwe among men. Among females cervical cancer remains the frequently occurring cancer (19%). In 2014, cancer emerged as the biggest cause of mortality in Zimbabwe ahead of HIV/AIDS and TB. In Zimbabwe, there are two major government run cancer referral centers for chemotherapy, radiotherapy and surgery that is, Harare Hospital, Mopelo teaching Hospital and Parirenyatwa hospital. Other private hospitals are also involved, for example, 3 private hospitals are involved in cancer diagnosis and treatment, but these are expensive. In terms of chemotherapy, patients buy the drug on prescription and bring back to the doctor for administration. Health workers in this area are overwhelmed because of the number of cases vis a vis the resources available, and in many instances the radiotherapy equipment at the referral centers usually breakdown for longer periods.

Despite having active cancer registries, diagnosis remains poor. Detection of cancers is slowed down mainly due to poverty. Many patients are dying because they do not receive necessary cancer treatment due to misdiagnosis/late diagnosis and lack of treatment. Most patients present at a late stage, making care and treatment vary expensive (NCSD 2013). Patients spend a lot of time at home trying traditional medicine because they cannot afford a doctor, and if they can afford they may not afford the prescribed medicine, hence there is a lot of traditional herbs being used to relieve pain. When diagnosis is done the cancer would have progressed to higher stages, making it difficult and expensive to cure. More so, the lack of sufficient knowledge on the need for early screening for example in the case of cervical cancer and pap smears is also a cause of the huge cancer burden (Figure 1).

- Lack of access to early detection (screening and diagnosis) facilities
- Advanced stage presentation of patients with cancers, increasing the cost of management and leading to avoidable premature deaths
- Inadequate resources (human, equipment and technology) negatively impact on cancer early diagnosis
- Lack of information on need for regular cancer screening and where services are available reduced utilization of those services that are available both in the public and private sector
- Prohibitive costs of screening services
- An effective national mechanism, such as a national cancer screening committee, is needed to motivate for, organize and co-ordinate cancer screening activities
- Provision of cancer early detection services (early diagnosis and screening) is necessary at all levels, accompanied by a sound referral system (referral centers with capacity to take up the referral case)
- There is need to conduct a formal assessment of the reasons for delays in early detection of cancers, focusing on who is affected and why
Programs to encourage earlier presentation of disease need to be developed, including training of primary care workers on cancer prevention, early diagnosis, and early recognition of symptoms and signs of cancer (early warnings) and taking appropriate action – referral to next level for further management.

- Lack of current cancer treatment guidelines and resulting lack of standardization of cancer management across institutions.
- Increasing incidence of common cancers and anticipated further rise in incidence with the introduction of effective surveillance, early detection and screening measures.
- Few centralized functional diagnostic and treatment facilities.
- Most health workers have no basic training in cancer management and care.
- Funding for cancer related activities is given a low priority.
- Shortage of and need for rehabilitation of essential diagnostic and treatment equipment and consumables.
- There are limited human resources and lack of retention incentives of skilled staff in cancer diagnosis and treatment.
- There is poor availability of cancer medicines, notably chemotherapy and opioid analgesics.
- Clinical research is very limited, hence the limited availability of a local evidence base.
- There are limitations in paediatric cancer diagnosis and treatment.

These issues are not new to Africa, hence there is need to adopt evidence based approaches, for example from the scientific arena [6].

**Making Use of Scientific Data and Traditional Knowledge**

**Black Seed**

Black seed or Black Cumin is a small elegant annual herb distributed and cultivated all over India. The plant is a small prostrate annual herb about 45 cm high 2-3 slender leaves pinnatisect, 2-4 cm long cut into linear segment, segments oblong. Flowers pale, blue on solitary long peduncles, seeds trigonous and black in colour. It belongs to the kingdom **Plantae**, division **Magnoliophyta**, order **Ranunculales**, family **Ranunculaceae**, genus **Nigella** and species **sativa**.

**Compositions of Nigella sativa**

Black Seed contains the phytochemicals Thymoquinone (TQ) and crystalline nigellone as well as anti-oxidants, amino acids, proteins, carbohydrates, Essential fatty acids (3, 6 and 9) volatile oils, alkaloids, saponin and fiber, as well as minerals such as calcium, iron, sodium and potassium [7]. Still many components in Black Seed are to be thoroughly investigated for their composition and functions. The seed contain numerous esters of structurally unusual unsaturated fatty acids with terpene alcohols (7%); traces of alkaloids are found which belong to two different types: isochinoline alkaloids are represented by nigellimin...
Thymoquinone (TQ) has been found to modulate the physiological and biochemical processes involved in reactive oxygen species (ROS) generation both in normal and tumor cells where it acts as antioxidant and pro-oxidant, respectively. Many of these activities have been attributed to the quinone-constituents of the seed \[^{[14-24]}\]. Salomi et al. \[^{[25]}\] showed that a crude methanol extract of black seed exhibited a strong cytotoxic action on Erlich ascites carcinoma, Dalton’s ascites lymphoma and sarcoma 180 cells with minimal cytotoxicity to normal lymphocytes. These investigations have also described cytotoxic property of extracts in vivo as shown by inhibition of the growth of Erlich ascites carcinoma in mice receiving 2 mg of the extract per mouse per day for 10 days \[^{[20]}\].

In in vitro cell studies, \textit{N. sativa} has been found to have anticancer properties inhibiting the growth of colon cancer cells specifically. In animal studies the seed was able to fight colon cancer in rats successfully with no observable side effects \[^{[11]}\].

Statistics show that the success rates of people using chemotherapy over a five year period is only 2.1% USA and 2.3% Australia \[^{[15]}\]. \textit{N. sativa} on the other hand was proven to annihilate pancreatic tumor cells. Chemotherapy has many side effects and one of the side effects is the possibility of secondary cancers. Secondary cancers are very aggressive and may occur from tumor reseeding \[^{[7]}\]. \textit{N. sativa} not only rebuilds the immune system and destroys cancer cells; it reinforces the good cells to fight the cancer.

Studies have reported use in traditional cancer therapy and antitumor activity of some crude and purified components of \textit{Nigella sativa} including action on colorectal cancer \[^{[19]}\].

Other investigators have recently reported that TQ triggers apoptotic cell death in human colorectal cancer cells which were correlated with G1 phase arrest of the cell cycle. Table \textbf{1} summarizes findings on cancers which black cumin had been reported to have action on.

\textbf{SUMMARY OF CANCER TYPES ON WHICH BLACKSEED HAS AN EFFECT}

<table>
<thead>
<tr>
<th>Cancer type</th>
<th>Active ingredient</th>
<th>Mechanism and action/Side effects</th>
<th>Author, Year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Leukemia</td>
<td>Thymoquinone (TQ)</td>
<td>TQ exhibits anti-proliferative effect of human myeloblastic leukemia HL-60 cells. Derivatives induce apoptosis and a decrease in mitochondrial membrane. α-hederin induce death of murine leukemia.</td>
<td>Effenberger et al. [^{[21]}]</td>
</tr>
<tr>
<td>Pancreatic Cancer</td>
<td>TQ</td>
<td>Induced apoptosis and inhibited proliferation in PDA cells</td>
<td>El Aziz et al. (2005)</td>
</tr>
<tr>
<td>Cervical cancer</td>
<td>TQ</td>
<td>Terpene-terminated 6 alkyl residues induced cell death by apoptosis.</td>
<td>Effenberger et al. (2010) [^{[21]}]</td>
</tr>
</tbody>
</table>
Methanol, n-hexane and chloroform extracts effectively killed the HeLa cells by inducing apoptosis.

<table>
<thead>
<tr>
<th>Cancer Type</th>
<th>Treatment</th>
<th>Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Renal cancer</td>
<td>Crude oil</td>
<td>Oral treatment resulted in significant decrease in $H_2O_2$, DNA synthesis and incidence of tumors. Chemo-preventive effects against FeNTA induced report oxidative stress, hyperproliferative report and renal carcinogenesis.</td>
</tr>
<tr>
<td>Skin</td>
<td>Topical application</td>
<td>Inhibited two stage initiation dimethlbenz[a]anthracene skin carcinogenesis. Intraperitoneal administration restricted soft tissue sarcomas.</td>
</tr>
<tr>
<td>Lung</td>
<td>$\alpha$-hederin from N. sativa</td>
<td>Antitumor activity against LL/2 in BDF1 mice. Supplementation of diet with honey and N. sativa protects against MNRI.</td>
</tr>
<tr>
<td>Hepatic</td>
<td>Extract had 88% inhibitory effect on Hep G2 cell line.</td>
<td>Oral administration effective in increasing the activities of quinone reductase and glutathione transferase promising prophylactic agent against chemical carcinogenesis and toxicity.</td>
</tr>
<tr>
<td>Colon</td>
<td>TQ</td>
<td>Antineoplastic and pro-apoptotic against colon cancer cell line HCT 116. Act as chemo-preventive agent on SW 626 cancer cells.</td>
</tr>
<tr>
<td>Fibrosarcoma</td>
<td>TQ</td>
<td>Inhibited the survival of fibrosarcoma cells with IC$_{50}$ of 15 mM. 0.01% TQ one week before and after MCA treatment inhibited tumor incidence by 43% and 34%, respectively. Oil decreased fibrinolytic potential of human fibrosarcoma cell line HT1080.</td>
</tr>
<tr>
<td>Prostate</td>
<td>TQ</td>
<td>Inhibited DNA synthesis, proliferation and viability of cancerous prostate epithelial cells(LN CaO, C4-B, DU145 and PC-3) Effective in treating hormone sensitive as well as hormone refractory prostate cancer. TQ inhibited vascular endothelial growth factor</td>
</tr>
</tbody>
</table>

**DISCUSSION**

Cancer has risen to be a non-communicable disease of high importance throughout the world, and particularly in the third-world countries. In 2014, cancer was the biggest killer in Zimbabwe and extrapolating that result to the third and developing world, we see that we are faced with a huge task. The rate of growth in the burden of cancer alone is such a scare that improved cancer treatment and care alone will not be sufficient to curtail the raging veld fire [17]. In the third world, the fight has been largely on infectious diseases than the non-communicable diseases, and the shift from the infectious front to the non-communicable front cannot come that easily. Low to medium income countries (LMICs) governments are hugely dependent on donor aid to keep their health departments going. The small national budgets are not even enough to supplement.

The scare that cancer poses calls for an early awakening and concerted efforts now. Africa needs to invest in cancer clinics, diagnostic and care centres. Most of the African based cancers are undocumented and in many cases, people perish due to misdiagnosis. The diagnosis of cancer will happen later in a patients’ life and the cancer will be terminal at that point. We are also calling for a shift in cancer alertness in the primary healthcare systems and the advocacy of traditional medicine, such as the black seed which has been proved to be efficacious against major cancers. We suggest opening of dialogue to facilitate partnerships, for example, the AMPATH-Oncology, a North American-Europe-Kenyan partnership that was forged to develop a comprehensive cancer care model encompassing diagnosis, treatment and care [18]. More would be achieved by prevention, whereby we arrest the emergency of new cases while we handle current cases, thus we hypothesise that black seed will also be able to fight against the undocumented cancers prevalent in the poor African populations. Therefore, planting and maintaining an herbal garden and using the herb for its bioactive components in a daily diet for health improvement can slow down emergence and progression of cancers [19,20,31,32].

The mechanism of action of Thymoquinone the active ingredient of Black Cumin, against cancers has been reviewed elsewhere [20], briefly TQ has been identified with modulation of p53 pathway, upregulating apoptosis genes p21 and Brca. Challenges associated with cancer will remain and are expected to escalate (about 85% increase in cancer burden by 2030). Therefore, all efforts and avenues are needed in the fight against cancer.
CONCLUSION

The anti-cancer properties of *Nigella sativa* were discovered a long time ago but scientific research for this traditional herb is very recent. Research has shown that it is very safe and has a few or no side effects thus it is a promising anticancer agent. Extensive research with *N. sativa* may contribute to the discovery of new anticancer strategies.

REFERENCES


