

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

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## Research Article

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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 place 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.

## 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 <sup>[1]</sup>, a clear sign of migration in diets and social activities and possible the effects of industrialization on clean environments for example, China <sup>[2]</sup>. Up to one third of cancers are preventable, and this can be done through behavioural change <sup>[3]</sup> (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 <sup>[4]</sup>. 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 <sup>[4]</sup>. Cancer-related deaths are expected to remain on the increase with 13.1 million deaths projection by 2030 <sup>[4]</sup>.

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) <sup>[4]</sup>. 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 <sup>[5]</sup>. 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.

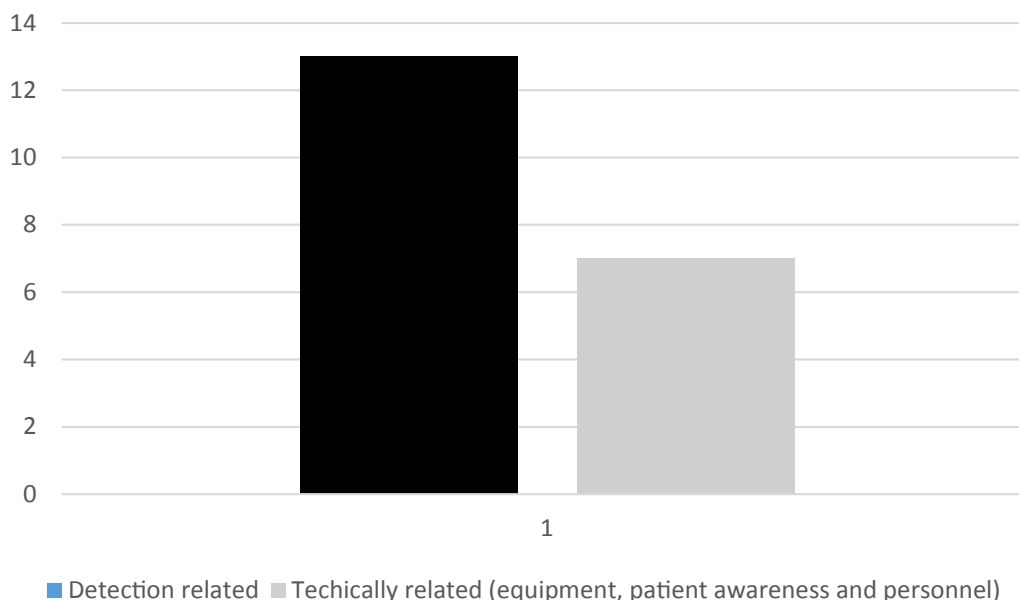
Prostate cancer (9%) has recently overtaken Kaposi sarcoma (7%) as the most frequently occurring cancer in Zimbabwe among men. Among females cervical cancer remains the frequently occurring cancer (19%). In 2014, cancer emerged as the biggest cause of mortality in Zimbabwe ahead of HIV/AIDS and TB. In 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

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- 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.



**Figure 1.** Identified limitations to effective cancer care in Zimbabwe.

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

### 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 <sup>[7]</sup>. 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

and nigellimin-N-oxide. Thymoquinone was identified as the main component (up to 50%) besides p-cymene (40%), pinene (up to 15%), dithymoquinone (DTQ) and thymohydroquinone. Other terpene derivatives were found only in trace amounts [8]. The essential oil contains significant (10%) amounts of fatty acid ethyl esters. On storage, thymoquinone yields dithymoquinone and higher oligocondensation products. The seeds also contain a fatty oil rich in unsaturated fatty acids, mainly linoleic acid (50-60%), oleic acid (20%), eicodadienoic acid (3%) and dihomolinoleic acid (10%). Saturated fatty acids (palmitic, stearic acid) amount to about 30% or less. Also contain parts of the essential oil, mostly thymoquinone, by which it acquires an aromatic flavour. The seeds give on steam-distillation a yellowish brown volatile oil with an unpleasant odour. The oil contains carvone, D-limonene and a carbonyl compound, nigellone [9].

## USES OF BLACK SEED

Among other traditional uses such as spicing, food preservation and curative remedy for numerous disorders thus it helps to restore the natural balance of the body's vital organs and strengthen its natural defences [10]. Black Seed also exhibits properties such as antioxidant, antibacterial, anti-fungal, anticancer [11]. Traditionally, it has been used to bolster vitality, aid digestion, respiratory, kidney, liver, inflammatory, analgesic, anti-diabetic and circulatory support [12]. The herb has also been employed for skin diseases such as, jaundice, fever, paralysis, diarrhoea and cough Worthen. Its oil has been used to treat skin conditions such as eczema and boils and is used topically to treat cold symptoms. The extracts have also been used to relieve respiratory diseases such as bronchial asthma and bronchitis, rheumatism and related inflammatory diseases. The bioactive constituent of *N. sativa* oil extract is Thymoquinone (TQ) and it has been found to have many health benefits [13].

## THYMOQUINONE EXTRACTS IN CANCER TREATMENT

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 [10].

In *in vitro* cell studies, *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]. *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]. *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 *Nigella sativa* including action on colorectal cancer [16].

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 1** summarizes findings on cancers which black cummin had been reported to have action on.

## SUMMARY OF CANCER TYPES ON WHICH BLACKSEED HAS AN EFFECT

**Table 1.** Findings on cancers which black cummin had been reported to have action.

Cancer type	Active ingredient	Mechanism and action/Side effects	Author, Year
Leukemia	Thymoquinone (TQ)	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.	Effenberger et al. [21]
Breast	TQ	Terpene-terminated 6-alkyl residues induce cell death by apoptosis in MCF-7/Topo breast carcinoma.	Effenberger et al. (2010) [21] Farah and Begum (2003) [22]
Pancreatic Cancer	TQ	Induced apoptosis and inhibited proliferation in PDA cells	El Aziz et al. (2005)
Cervical cancer	TQ	Terpene-terminated 6 alkyl residues induced cell death by apoptosis.	Effenberger et al. (2010) [21]

		Methanol, n-hexane and chloroform extracts effectively killed the HeLa cells by inducing apoptosis.	Shafi et al. (2009) [23]
Renal cancer	Crude oil	Oral treatment resulted in significant decrease in H <sub>2</sub> O <sub>2</sub> , DNA synthesis and incidence of tumors. Chemo-preventive effects against FeNTA induced report oxidative stress, hyperproliferative report and renal carcinogenesis.	Khan and Sultana (2005) [24]
Skin		Topical application inhibited two stage initiation dimethylbenz[a]anthracene skin carcinogenesis. Intraperitoneal administration restricted soft tissue sarcomas.	Salomi et al. (1991) [25]  Swamy and Haut (2003) [26]
Lung		α-hederin from <i>N. sativa</i> has antitumor activity against LL/2 in BDF1 mice. Supplementation of diet with honey and <i>N. sativa</i> protects against MNRI.	Mabrouk et al. (2002) [27] Swamy and Haut (2003) [26]
Hepatic		Extract had 88% inhibitory effect on Hep G2 cell line. Oral administration effective in increasing the activities of quinone reductase and glutathione transferase promising prophylactic agent against chemical carcinogenesis and toxicity.	Thabrew et al. (2005) [28] Nagi and Imaki (2009)
Colon	TQ	Antineoplastic and pro-apoptotic against colon cancer cell line HCT 116. Act as chemo-preventive agent on SW 626 cancer cells.	Gali-Muhtasib et al. (2004) [11]
Fibrosarcoma		TQ inhibited the survival of fibrosarcoma cells with IC <sub>50</sub> 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.	Badary and Gamal (2011) [29]
Prostate	TQ	TQ 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	Kaseb et al. [30]

## 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

1. Kingham TP, et al. Treatment of cancer in sub-Saharan Africa. *Lancet Oncol.* 2013;14:58-167.
2. Jia H, et al. Peering into China's thick haze of air pollution. Scientists are teasing out which emissions contribute most and the chemical reactions that create smog filled with particulates. *ACS Cent Sci.* 2017;95:19-22.
3. Baum A, et al. Successful behavioral interventions to prevent cancer: The example of skin cancer. *Annu Rev Public Health.* 1998;1:319-333.
4. [http://www.afro.who.int/sites/default/files/2017-06/who-fctc-10-year\\_report\\_web.pdf](http://www.afro.who.int/sites/default/files/2017-06/who-fctc-10-year_report_web.pdf)
5. Chokunonga E, et al. Pattern of cancer in Zimbabwe. *Zimbabwe National Cancer Registry.* 2012;1:1-41.
6. Anorlu RI. Cervical cancer: The sub-Saharan African perspective. *Reprod Health Matters.* 2008;16:41-49.
7. Ali B and Blunden. Pharmacological and toxicological properties of *N. sativa*. *Phytother Res.* 2003;17:299-305.
8. Entok E, et al. Anti-inflammatory and anti-oxidative effects of *Nigella sativa* L: 18FDG-PET imaging of inflammation. *Mol Biol Rep.* 2014;41:2827-2834.
9. El-Mahdy MA, et al. Thymoquinone induces apoptosis through activation of caspase-8 and mitochondrial events in p53-null myeloblastic leukemia HL-60 cells. *Int J Cancer.* 2005;117:409-417.
10. Chopra R, et al. Supplement to glossary of Indian medicinal plants. 3rd Edition. New Delhi, Council of Industrial and Scientific Research, India. 1992;3:333.
11. Gali-Muhtasib H, et al. Thymoquinone extracted from black seed triggers apoptotic cell death in human colorectal cancer cells via a p53-dependent mechanism. *Int J Oncol.* 2004;25:857-866.
12. Atal C and Kapur. Cultivation on utilization of medicinal plants. *Royal Botanical Garden.* 1982;22:877.
13. El-Aziz MAA, et al. The biochemical and morphological alterations following administration of melatonin, retinoic acid and *Nigella sativa* in mammary carcinoma: An animal model. *Int J Exp Pathol.* 2005;86:383-396.
14. Mahfouz M and Dakhakhny. The isolation of crystalline active principle from *Nigella sativa* seed. *Pharm Sci United Arab Rep.* 1960;1:14-17.
15. Morgan G, et al. The contribution of cytotoxic chemotherapy to 5-year survival in adult malignancies. *Clin Oncol (R Coll Radiol).* 2004;16:549-560.
16. Khalife R, et al. Thymoquinone from *Nigella sativa* seeds promotes the antitumor activity of non-cytotoxic doses of topotecan in human colorectal cancer cells *in vitro*. *Planta Medica.* 2016;82:312-321.
17. Sylla BS and Wild. A million Africans dying a year from cancer by 2030: What can cancer research and control offer to the continent? *Int J Cancer.* 2012;2:245-250.
18. Strother RM, et al. AMPATH-oncology: A model for comprehensive cancer care in sub-Saharan Africa. *J Cancer Policy.* 2013;1:42-48.
19. Butt M and Sultan. *Nigella sativa*: Reduces the risk of various maladies. *Crit Rev Food Sci Nutr.* 2010;7:654-665.
20. H El-Far A. Thymoquinone anticancer discovery: Possible mechanisms. *Curr Drug Discov Technol.* 2015;12:80-89.
21. Effenberger K, et al. Erpene conjugates of the *Nigella sativa* seed-oil constituent thymoquinone with enhanced efficacy in cancer cells. *Chem Biodivers.* 2010;7:129-139.
22. Farah I, et al. Effect of *Nigella sativa* (*N. sativa* L.) and oxidative stress on the survival pattern of MCF-7 breast cancer cells. *Biomed Sci Instrum.* 2003;39:359-364.
23. Shafi G, et al. Induction of apoptosis in HeLa cells by chloroform fraction of seed extracts of *Nigella sativa*. *Cancer Cell Int.* 2009;9:29.
24. Khan N and Sultana. Inhibition of two stage renal carcinogenesis, oxidative damage and hyperproliferative response by *Nigella sativa*. *Eur J Cancer Prev.* 2005;14:159-168.

## Research and Reviews Journal of Medical and Clinical Oncology

25. Salomi M, et al. Inhibitory effects of *Nigella sativa* and saffron (*Crocus sativus*) on chemical carcinogenesis in mice. *Nutr Cancer*. 1991;16:67-72.
26. Swamy S, et al. Intracellular glutathione depletion and reactive oxygen species generation are important in alpha-hederin induced apoptosis of P388 cells. *Mol Cell Biochem*. 2003;24:127-139.
27. Mabrouk GM, et al. Inhibition of methylnitrosourea (MNU) induced oxidative stress and carcinogenesis by orally administered bee honey and *Nigella* grains in Sprague Dawely rats. *J Exp Clin Cancer Res*. 2002;21:341-346.
28. Thabrew M, et al. Cytotoxic effects of a decoction of *Nigella sativa*, *Hemidesmus indicus* and *Smilax glabra* on human hepatoma HepG2 cells. *Life Sci*. 2005;77:1319-1330.
29. Badary O, et al. Inhibitory effects of thymoquinone against 20-methylcholanthrene-induced fibrosarcoma tumorigenesis. *Cancer Detect Prev*. 2001;25:362-368.
30. Kaseb AO, et al. Androgen receptor and E2F-1-targeted thymoquinone therapy for hormone-refractory prostate cancer. *Cancer Res*. 2007;67:7782-7788
31. <http://www.iccpportal.org/sites/default/files/plans/cancer%20strategy%20final%202013%202017.pdf>
32. Morhason-Bello IO, et al. Challenges and opportunities in cancer control in Africa: A perspective from the African Organisation for Research and Training in Cancer. *Lancet Oncol*. 2013;14:42-151.