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Review article

Antitumor Effects of Flaxseed in Iranian Traditional Medicine and Contemporary Medicine; a Brief Review

N. Masoudi[1], M. Tabarrai[2], Z. Niktabe[2], S. Dehghan[1], M. Khodadoost[1*]

[1]Department of Traditional Medicine, School of Traditional Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran.
[2]Department of Traditional Medicine, School of Traditional Medicine, Tehran University of Medical Sciences, Tehran, Iran.

Abstract

Cancers are the result of uncontrollable multiplication of abnormal cells. In order to control progression of cancers, various therapeutic regiments are used that have side effects and are costly. Iranian traditional medicine (ITM) contains comprehensive subjects regarding cancerous tumors. In the present study, the nature and development of cancer from ITM point of view and the effect of flax as an easily accessible medicinal herb which has been mentioned in several ancient prescriptions and has been used in the management of dropsies and tumors has been discussed. In a library search through the valid ITM references and Avicenna and other scholars texts, explanations of ITM regarding cancer has been investigated and flax and its therapeutic effects in the cancer management has been described. A number of medical databases were searched for contemporary medicine articles; finally, the findings in these two systems of medicine were compared. Flax possesses a cleansing effect in the whole body according to ITM and can be used for management of dropsies inside the body especially hard tumors and cancers. The present work has shown its uses in cancers of breast, prostate, ovary, small intestine and colon as well as its analgesic effects. New studies have approved the anti-cancerous effects of flaxseed that have been reported by ITM scholars. Since they believed that flax was beneficial for tumors of all organs, investigations of its effects against cancerous tumors of other organs is recommended.

Keywords: flaxseed; Iranian traditional medicine; tumour

Introduction

Cancer is a prolonged disease with the uninhibited growth and extent of abnormal cells producing masses of tissues which are called tumors. The special possessions of environmental agents on a certain genetic context lead to development of cancer [1]. The American Cancer Society and the International Union against Cancer have reported nearly 27 million diagnoses and 17 million deaths by 2030 worldwide [2]. In 2015, 1658370 new cases of cancer have been identified in USA. As estimated by the Agency for Healthcare Research and Quality (AHRQ), the total cost of cancer management in United States has been about 88.7

*Corresponding author: khodadost.m@gmail.com

billion dollars in 2011 [3].
Cancer can spread like a silent pandemic disease [4]. While most cancers do not have a definite cure, there are approaches like surgery, chemotherapy, radiotherapy, hormonal therapy and bone marrow transplantation which can control the progression of the disease [5]. Interventions have their own limitations like resistance to therapy and side effects along with being a financial burden for the patient [6]. Recently, there has been an interest in research activities towards traditional and complementary medicine due to lower costs and fewer side effects. Ancient systems of medicine such as Unani, Egyptian, Indian, Chinese and Iranian traditional medicine (ITM) can be useful sources of knowledge for further understanding of cancer [7]. In ITM manuscripts the word cancer (in reference to crab) has been used since 500 BC at the time of Hippocrates to describe incurable solid swellings. Celsus (25 BC – 50 AD) in the first century AD used the word tumor instead of solid swelling [5]. Cancer has been described by Avicenna (ITM clinician, 5th century AH) as a growing and disturbing tumor which could infiltrate in various organs [8]. There are several ITM books discussing the diagnosis and treatment of cancerous tumors and according to the particular condition a range of therapeutic methods and herbal remedies such as violet, garlic, fenugreek and asafetida have been used in the management of cancerous tumors [8,9].
Flax is a medicinal plant which has been mentioned in various ITM texts as having wide range of use for management of cancerous tumors. Recent studies have also approved the use of flax regarding cancer. In the present article the nature and pathophysiology of cancer has been discussed according to ITM and the role of flax in the management of cancerous tumors has been explained; finally, the findings have been compared with the results of contemporary medical researches.

Methods

The data were collected in a library search using the keywords tumor, "Varam" (swelling), "Sarataan" (cancer), "Khelt" (humor), "Soda" (black bile), "Merreh Soda" (burned black bile), and "Kataan" (flaxseed)" from the major ITM references such as Canoon of medicine (5th century AH), "Al-shamel fi-alsanaat-altebyah" (7th century AH), "Mojarabaate-ielate-jaghtaee" (10th century AH), "Makhzan-aladveeh" (12th century AH), "Kholasat-alhekmat*"* (12th century AH) along with published articles about ITM since 2000 found in PubMed, Web of science, Google scholar and Scopus databases using keywords tumor, swelling, cancer, humor, soda, black bile, and flaxseed. In this investigation, the process of production of normal and abnormal humors, the nature and types of tumor and the mechanisms involving its development along with the relation to the modern concept of cancer was evaluated. Thereafter, flax and its therapeutic effects regarding cancer were presented. Contemporary medicine articles were searched using keywords "cancer" with any of these words; definition, prevalence, etiology, treatment, cost, cancer and flax and cancer of liver, prostate, breast, spleen, skin, bladder, intestine, colon, lung, ovary. Articles with subjects of cancer's pathophysiology and its prevalence and complications and also nutritional and therapeutic uses of flax were selected. Among the 56 articles, 23 which were more relevant were reviewed**.** Later on, the findings in the two systems of medicine were compared.

Results and Discussion

Risk factors for cancer in ITM and contemporary medicine

Although a lot of factors have been mentioned in the development of cancer smoking, unhealthy diet and lack of physical activity seem to be the major risk factors for the disease [3]. One third of deaths due to cancer in developed countries are connected to obesity, lack of exercise and poor diet [3]. The negative effects of these factors have been clearly mentioned in ITM. In Iranian traditional medicine, the risk of cancer has been related to factors such as sleep pattern, physical

activity, digestive function and stress from social or personal conditions and previous infection or inflammation [7]. Contemporary medical findings also point to the role of inflammation at the start point of the cancer [10]. Proposing a relation between cancer and inflammation is not new. In 1863, Virchow presented his theory that the origin of cancer lied in the location of chronic inflammation. According to a part of his theory, tissue damage and inflammation could lead to cell proliferation. This proliferation alone cannot induce cancer but in an environment of inflammatory cells, growth factors, activated stroma and DNA-damage promoting agents the risk of cancer can increase. In case of tissue damage with ulcer, cell proliferation will increase at the time of healing. This proliferation and inflammation will decrease by the time of complete healing. Those proliferated cells that have experienced DNA damage or have experienced mutagenesis will continue to proliferate in microenvironments of inflammatory cells and growth factors. In other words, tumors are like ulcers that have not undergone healing [10]. Since flaxseed oil inhibits the production of inflammatory agents including prostaglandin E2, leukotriene B4, histamine, bradykinin and arachidonic acid, [11] its role in control of the inflammatory process leading to cancer is plausible.

Terminologies in ITM

Most literatures of ITM books described unnatural humor and burned black bile as etiologies of cancer [2]. For better understanding of ITM view about cancer, a number of terminologies need to be explained.

Humoral theory: according to ITM, body is composed of four humors that are made out of the ingested food by different proportions in the liver. They include "Dam" (blood), "Balgham" (phlegm), "Safra" (yellow bile) and "Soda" (black bile) and they should have a balance in the body. Any disturbance in the balance and quality can lead to diseases in our body [8,12].

Production of abnormal humors in the body: there are circumstances under which abnormal humors can be produced in the forms of mixtures of abnormal material with a normal humor or as a result of exposure of humor to sever coldness or hotness [8].

Swelling and its types: swellings are the result of distemperament. In swellings there is a transformation in the shape and pattern of tissues, cells and organs. Then dislocation of organs and tissues can happen as well as entrance of waste materials to the swollen region leading to separation of some parts of the tissue. When pathological changes in metabolism of humors happened, swellings can develop. While according the affected humor they can present with different types and shapes [8].

Cancer according to Avicenna

Avicenna believed that accumulation of abnormal "Soda*"* such as burned black bile, could produce swellings some of which were known as cancer. In Avicenna's view cancer was a growing and disturbing type of swelling that infiltrated the organs. If this swelling became chronic the sense of the organ would be lost and the organ would be finally destroyed. The reason behind accumulation of harmful "Soda" and development of cancer was the abnormal changes in the metabolism of humors [8]. Humors other than "Soda" could also become accumulated and result in swellings which would transform into harmful "Soda" under abnormal conditions and increase the risk of cancer [8,13]. In Canon of medicine Avicenna mentioned examples of transformation of swellings into cancer. About solid swellings of uterus he has explained that if these swellings would not dissolve quickly, they could become cancerous [8]. According to this view, a number of other swellings described in the Canon of medicine and other ITM texts could be included in cancerous or pre-cancerous conditions in modern medicine. Accordingly, remedies which were used for treatment of swellings in ITM might be helpful in the management of some cancers. One of the important medicinal herbs used for this purpose was flax therefore, its functions, properties and medicinal uses in the management of swellings

has been discussed and compared with modern findings.

Flax and its antitumor effects in ITM and contemporary medicine

According to ITM herbal texts, flax length is about one meter with narrow stems and leaves. Its flowers are cobalt-blue color. The seeds are small, soft and broad. Flaxseed can be yellow or red, sometimes black or even white. Their oil could be prepared in various oral and topical forms [9]. Flaxseed has the ability to mature the waste and harmful carcinogen substances in the body and prepare them for expulsion [8,14]. Furthermore, it can dissolve these substances along with swellings of liver and other organs without leaving a trace [9]. It seems that these properties along with other ones that will be discussed are comparable to anti-cancerous and immune boosting effects indicated by contemporary research [15].

Flaxseed has been used in meals of many people around the world. It has four main useful constituents: alpha linoleic acid (omega 3 fatty acid) in high amounts, fiber and water soluble and insoluble vitamins and finally very high amount of lignan. The content of lignan in flaxseed is 75-800 times more compared to other oily seeds, cereals, beans, fruits and vegetables. Lignan metabolites function like anti-oxidants and free radical scavengers and therefore decrease the risk of carcinogenesis and protect the cells from DNA damage by free radicals [16].

The ITM scholars believe that flax causes easy defecation and cleans the organs and tissues from waste [9]. It not only prepares and matures the accumulated carcinogens but also expels them through its laxative action along with cleaning the surface of organs and tissues [13]. This means that flax has the potential to control metastasis of cancer tumors [17. Recent studies have shown the presence of high fiber in flaxseed which can justify its laxative action [16]. Flax has a role in the management of solid tumors [8,9,14] and can also soften the consistency of the swellings [8,14]. In fact in ITM loosening the consistency of a tumor is considered a part of the treatment [8]. By increasing the softness in the involved tissue, flax would facilitates the expulsion of waste and poisonous and pre-cancerous materials from the swellings [9,14].

Decoction of flax in a sitz bath or as vaginal douche has been suggested to be beneficial for cleaning the uterus and vagina as well as inflammation of intestines and swellings and inflammation of uterus [8,9,14].

Our investigation in modern databases regarding the effect of flax in cancer of uterus showed no results; however, there were several articles about the effect of flax in ovarian cancer. Dietary intervention with flaxseed which is a good source of omega3 fatty acid and its phytoestrogen lignans have shown the potential of these seeds in prevention and management of ovarian cancer through inflammatory prostaglandin pathways targeting. Omega3 fatty acid itself has been reported to be effective in prevention of several types of cancers [18].

Flax has been also used for ulcers of kidneys and bladder by ITM physicians [8,9,14]; however, we did not find any recent article supporting this subject.

Among the flax's reports of anticancer property we came across a cancer of prostate research [18]. Phytolignans present in flaxseed supplements had controlled the growth of malignant cells and decreased the tumor angiogenesis in patients suffering from prostatic cancer [19]. Physiological concentration of enterolignans has been strongly related to Ki-67 marker which is very sensitive to cellular proliferation in cancer of prostate. The results showed that enterolignans present in flax possessed anti-proliferative properties [20].

Another use of flax mentioned in Canon of medicine was resolving the coagulated milk developed in the ducts of mammary glands as well as some types of swelling of the breast [8,9].

A study on postmenopausal breast cancer patients who were candidates for surgery showed that consuming 25 g flaxseed each day 32 days prior to the surgery led to reduction of cell proliferation in the breast tumor. Flax has been

also mentioned in ITM texts as a pain reliever [8, 9, 14]. In animal models too, local application of flaxseed oil has produced analgesic property in joint pain [21]. New studies have indicated that alpha linoleic acid (ALA) present in flaxseed oil has analgesic and anti-inflammatory properties [22]. The anti-inflammatory [23, 24], antioxidant [25,26] and analgesic [11] effects of flaxseed oil has been also discussed in the recent studies.

Inflammatory colic (called *"Ghoolanj-e-varami"* in ITM) was a painful condition due the presence of a swelling in the intestine. Flax has been one of the suggested remedies for this condition [8,9] and was also used for the ulcers of intestines especially in the form of enema [8,9]. Recent researches have shown the inhibitory effect of flaxseed in the tumors of small as well as large intestine [18].

Flax is a rich source of a lignan known as secoisolariciresinol diglycoside (SDG). The action of bacteria present in the intestinal lumen of human and other animals can change SDG to a mammal lignan. This action will lead to production of lignan metabolites Enterolactone and Enterodiol. These metabolites have antioxidant and free radical scavenging activities therefore they can reduce the risk of carcinogenesis and DNA damage [16].

There are a number of medicinal uses for flax mentioned in ITM which have not been investigated in contemporary medicine yet. These include management of head ulcer (flax in the form of poultice) [9], testicular swelling and stiffness "Salabat" of the spleen (again in the form of poultice) [27] and swelling of the spleen [9].

Conclusion

Many different risk factors of cancer such as lack of physical activity, smoking and unhealthy regimen have been reported in contemporary medicine. On the other hand ITM mentions the impact of these factors clearly, too. Also ITM expresses that swelling, inflammation and chronic irritation can develop cancers. The impact of swelling in the onset of cancer has been studies in contemporary medicine. On the basis of ITM, any humor accumulation can cause swelling, also abnormal "Soda" increases the risk of developing cancer. It seems that different types of dropsies that have been investigated in ITM can be in the list of cancer or pre-cancerous tumors; thereupon, the drugs in ITM that were effective in the treatment of dropsies (like flax) could be helpful in the treatment of cancer.

In ITM point of view, flax has a cleansing effect in the whole body and can be used in the management of swellings of liver and other internal organs as well as solid tumors located in any part of the body. In the present article the analgesic effect as well as therapeutic effect of flax in management of cancers of breast, prostate, ovary, small intestine and large intestine has been mentioned.

Contemporary medical research approves the anti-cancerous effect of flax mentioned by ITM. There are other medicinal uses of flax according to ITM which have not been investigated yet. These can be interesting subjects for future evaluations. Since Avicenna recommended flax for tumors of all organs, evaluation of the effect of flax in tumors of other organs is suggested as well.

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Declaration of interest

The authors declare that there is no conflict of interest. The authors alone are responsible for the content of the paper.

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