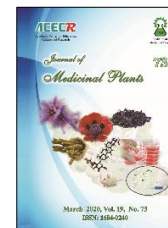




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Review Article

Review of skin cancers terminology, etiology and treatment from ancient persian medicine view point

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ABSTRACT

Background: Skin cancers are the most prevalent type among the white with an increasing trend of incidence around the world and Iran. Scientific developments in diagnosing these cancers and using screening methods and utilizing treatment methods have contributed to the relative control of the cancer. Hence, it is necessary to consider other suggested approaches of complementary and traditional medicine to prevent and treat these cancers. **Objective:** The purpose of this review is to investigate the alternative remedies from the Persian Medicine; as a pioneer medical approach with an old history. **Methods:** In this review study, the medical textbooks of the golden era of Persian Medicine (9th to 19th centuries AD), i.e., the times of Razes and Avicenna, were explored and interesting opinions on skin malignancies were found. In addition, the phrase “skin cancers” was searched in databases like PubMed, Science Direct, Scopus, and Google Scholar. The gleaned data were analyzed and compared. **Results:** The ancient Persian scholars knew the cancers and were forerunners in the description, classified, etiology and treatment of skin cancers. This study explored interesting opinions like nutrition and black bile clearance on skin malignancies treatment, also found no contradictory views between the Persian and modern medicine on the topic of skin cancers. **Conclusion:** Paying attention to the neglected areas can makes useful theories and hypotheses fore achievement to new more effective and safe remedies.

1. Introduction

Skin malignancies are the most common cancers among the white race. These cancers

have an increasing incidence around the world and account for many disabilities and morbidities [1]. Many attempts have been made to achieve

Abbreviations: PM, Persian Medicine

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effective screening and therapeutic methods for these diseases [2].

However, the applications of these methods have been restrained due to numerous complications, prolonged treatment responses, and heavy costs [3-5]. The therapeutic deficiencies, and inability in controlling the skin cancers along with untoward side effects of anti-cancer procedures, the alternative and complementary adjunct care has been highly considered round the world [6]. The public celebration of traditional and complementary medicine has progressively increased round the world over the past decade. According to WHO, about 70-80 percent of people in the developing countries use traditional and complementary medicine [7].

This branch of medicine uses a collection of information including knowledge, science, skills, and practices that originate from theories, beliefs, and local experiences of various cultures aimed at, justifiably or unjustifiably, maintaining health and also diagnosing and treating physical and mental disorders [8, 9].

The Persian medicine (PM) is one of the richest traditional medicines of the world considered as our invaluable research literature and reservoir [10]. This branch of medicine not only corresponds to the WHO definition of traditional medicine, but also possesses unique characteristics such as an ancient history and content of ethical issues that discriminate it from other types of medicine.

Some historical evidence indicates that medicine was first transmitted from Persia to Greece [11]. It was recorded and classified by Hippocrates during 355-460 BC. It was transferred again to Persia by Alexander's invasion in 330 BC [12]. Greece experienced a medical stagnancy era after Galen, a pupil of Hippocrates (129-199 AD) and a number of

monotheist physicians who were followers of Galen school resorted to Jundishapour University of Persia (242 AD). These physicians translated parts of their scientific reservoir into Persian [13]. During the collapse of the Roman Empire, when the Christian West was going through its dark period of science and civilization during the Middle Ages (395 AD), Jundishapour University was at the zenith of its scientific growth and a place for scientific controversial debates by the Persian, Arab, Indian, and Greek scholars from all over the world. In 636 AD, PM was transferred to Moslem Arabs after their invasion of Jundishapour. The movement of translation of medicine into Arabic began by the establishment of Baghdad Hospital by Abbasids (762 AD) [14-16].

After Islam, the Persian Moslem physicians and scientists like Razes (the 9th and 10th centuries AD), Avicenna (the 10th and 11th centuries AD), and Jorjani complemented the PM via innovative interpretations, inventions, and discoveries [12]. The PM was subsequently transferred to Europe after the onset of the crusade wars and translated into Latin [15]. After the emergence of Renaissance, the well-known outstanding texts of PM such as Razes, Al-Hawi and Avicenna's Canon were taught in more than 900 years in European universities [17].

Humans have been known with cancer since the early historical eras and the papyruses discovered in ancient Egypt have accounts of cancer and methods for its surgery [18]. Scientific developments in diagnosing cancer and using screening methods and utilizing treatment methods such as operation, chemotherapy, radiotherapy, etc have contributed to the relative control of the cancer and longer life of the patients [19]. However, in terms of control and treatment, this disease is among the unknown [20].

Ancient medicine like Greek, Egyptian, Indian, Chinese and Persian is precious sources of research. Paying attention to thousands-year-old approaches, especially PM scholars experiences and treatment suggestions of the past in describing cancer, its etiology, signs and treatment methods, and, most important of all, recommendations to keep health for preventing this disease might be quite valuable [21].

Hence, future research can focus on the multi-thousand-year approaches of PM scholars and scientists toward description of various kinds of cancer such as skin malignancies, their etiology, symptoms, and therapeutic methods, especially health maintenance recommendations for preventing affliction with these conditions as a dynamic context.

2. Methods

In this review study, the keywords “malignant and malignancy” and all their Persian and Arabic equivalents were explored in chapters on dermal disorders in valid texts of PM (from 9th to 19th centuries AD) such as Al-Hawi (9th and 10th centuries), Canon of Medicine (11th century), Zakhireye Kharzam Shahi (12th century), Sharholasbab -va- Alalamat, Teb -e- Akbari (12th and 13th centuries) and Exir-e-Azam (19th century).

In addition, the phrase “skin cancers” was searched in databases including PubMed, Science Direct, Scopus, and Google Scholar.

Studies that included the evidences of mentioned information were selected for review. The gleaned data were analyzed and compared.

3. Results

3.1. Definition and terminology of various skin malignancies

Cancer is derived from the Latin word “Crab”, meaning adherence to each other like crabs in each part of the body that attack [21]. Ancient scientists referred to cancer as solid dark lesions visible and tangible on the surface of the skin with or without invading the surrounding tissues provided that they are chronic and do not respond to conventional treatment [22]. These lesions may be painful or painless [23]. Although the word “cancer” is mentioned as a subcategory of skin disorders, this term does not entail all malignancies of skin; rather, there are other terms that refer to skin malignancies [24]. Generally, dermal and physical problems of the appearance fall into two categories in PM texts: “Owraam” and skin diseases. Various types of injuries are discussed in a separate chapter called “Ghorouh” since they may penetrate the deeper tissues like muscles [22]. A subset of each chapter refers to various types of skin malignancies (Diagram 1). PM scholars accurately describe these malignancies and based on their definition they can be linked to some of skin cancers in modern medicine (Table 1).

3.2. Etiology of skin malignancies

On the basis of PM, the human body consists of four humors called cardinal humors. These include yellow bile, blood, phlegm, and black bile. Humans need a correct proportion of these substances to remain healthy. Whenever the balance of quality and quantity between the four humors is impaired, the person gets sick. Cancer is also considered as the result of imbalance in the quality and consistency of these humors induced by these changes in human body [28].

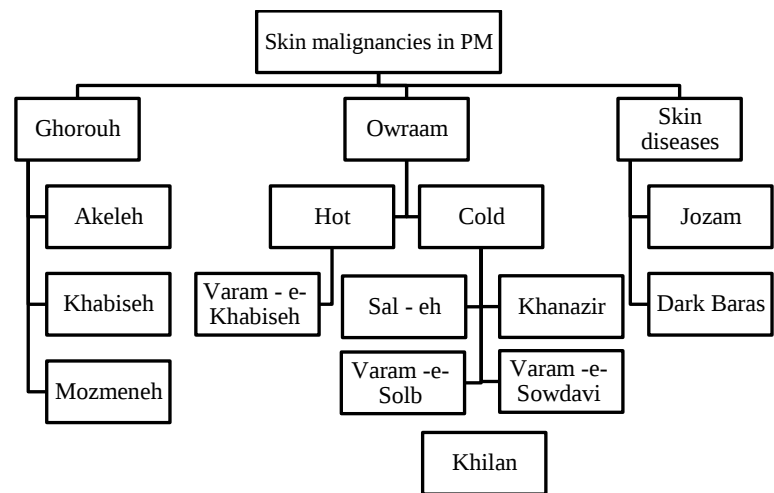


Fig. 1. Classification of skin malignancies from the viewpoint of PM

Table 1. Definition and terminology of skin malignancies from the viewpoint of PM and relation Skin cancers

PM Terms in Arabic	PM Terms in English	Relation Skin cancers	Terms Definitions
Sal-eh	Like solid tumor	Cystic BCC	It is of the dermal phlegm swelling type mostly created in older ages. The sclerotic type resembles sclerosis and if left untreated may get malignant. Deficient surgery may lead to recurrence and poor prognosis [25].
Varam-e-khabiseh	Horrid tumor	BCC SCC	This great swelling results from thick blood or plethora and is not easily eliminated till it blocks all the lumen of veins and arteries and the organ gets rotten and necrotic. It is called malignant or evil due to the thickness and magnitude of the substances [26].
Varam-e-solb	Solid tumor	BCC	This is a solid sclerotic swelling that is created by a combination of phlegm and black bile and includes the benign and malignant types. The malignant type is characterized by lack of painfulness. The Greek term for it is Soqirus. Sometimes, it metastasizes to other organs, a condition called Qunus. Its color is lighter than melancholic swelling due to its combination with phlegm and has often a lead-like appearance [22].
Varam-e-sowdavi	Black bile solid tumor	Pigmented BCC SCC Melanoma	This is a mass in any body organ, whether overt or covert, superficial or deep, that originates from abnormal black bile resulting from the oxidation of the humors and is characterized by a stiff hard mass, dark color, deep penetration, and difficult healing [27].

Table 1. Definition and terminology of skin malignancies from the viewpoint of PM and relation Skin cancers
(Continued)

PM Terms in Arabic	PM Terms in English	Relation Skin cancers	Terms Definitions
Khanazir	Pig scrofula	Metastatic Lymphoma	This is a kind of cold swelling created from thick phlegm or black bile substances due to transformed quality. It mostly involves the loose flabby parts of the body like the cervical and axillary regions. It attaches to the adjacent organs and increases in number like warts. Hence, it is called Khanazir (plural of Khenzir) meaning pigs because pigs are multi-offspring at each breed [22].
Khilan	Atypical Nevi	Melanoma	These are transformed nevi with malignancy susceptibility. Avicenna believes that some nevi may sometimes undergo changes and turn to black bile sclerotic swelling [27].
Jozam	Like Leprosy	Untreated BCC	This a kind of skin disease that is untreated and chronic. Finally lead to tissue damage and amputation [25].
Dark Baras	Black Vitelligo	Melanoma Superficial SCC	This is a kind of Baras (Vitelligo) with dark color that originated from black bile and resistant to treatment [22].
Ghorouh-e-akeleh	Cankers	Types of SCC	Sometimes, the cancers invade the surrounding tissues and produce malformed ulcers with reddish or greenish edges that are resistant to treatment [24].
Ghorouh-e-khabiseh	Horrid ulcer	Types of SCC	These are a kind of malignant ulcers created by the presence of abnormal humors and transmitted to skin. They are mostly untreatable and culminate in death [24].
Ghorouh-e-mozmeneh	Chronic ulcer	Types of SCC	These infectious chronic ulcers cannot be treated promptly and may get malignant [24].

Among the four humors, abnormal black bile has a greater share in producing cancer than other humors. This type of black bile is produced by chemical changes in other humors. This type of reaction is called “Ehteraq” means oxidation in traditional medicine [29].

Skin malignancies cover a wide range of high-risk, fatal, and refractory disorders in traditional medicine that either originate from the skin or are transferred to skin from other organs. If an increased amount of abnormal black bile is produced in the body for any reason, if the resulting metabolites are not eliminated via natural routes and thus reach the skin, or if the skin is not able to eliminate them completely, various types of malignancies will be induced [30].

Consequently, the causes of dermal malignancies from the perspective of PM fall into two categories: external and internal causes.

One of the most important internal causes of black bile is nutrition. The excessive consumption of black bile-inducing materials may render the individual susceptible to malignancy. For example, egg plants, lentils, mushroom, stale/spoiled foods, fried foods and processed meat are among the black bile-producing food items.

Other factors contributing to oxidation of humors and production of abnormal black bile are long-term exposure to dry hot climates, mental stress, difficult conditions of industrialized civil life, and prolonged insomnia [25]. Moreover, incomplete elimination of abnormal black bile, deposition of redundant metabolites, and migration of these substances to the skin render the individual susceptible to malignancy. In this regard, liver dysfunction and

inability of the spleen in eliminating black bile are the most important factors [31].

The external factors include prolonged exposure to sunlight, chronic skin disorders, past history of injury, damage, and pain in different parts of the body and chronic ulcers [4]. Avicenna, in his Canon, refers to ulceration, transformation and atypical form of naevi as etiologic causes of affliction with skin cancer [27].

3.3. Treatment of Skin Malignancies

Avicenna believes that destroying skin cancers is a stubborn task. The principles of treatment and recurrent inhibition according to PM, are Reducing carcinogenic factors by modifying lifestyle especially corrected nutrition and depletion of carcinogenic substance by clearance of black bile, modifies liver and spleen function, and empowerment of the organ.

The therapeutic goals are prevention of increased swelling, prevention of increased inflammation and ulcer, inhibition of invasive behavior of tumor and curative treatment of them [27]. In order to achieve these therapeutic goals, they simultaneously used topical and systemic drugs.

Topical drugs included "Rade" (Drugs that prevent the absorption of abnormal materials to the site of tumor and reduce swelling) and "Mohallel" (Drugs that dissolve the mass and destroy it). One of the most used topical drugs by the PM scholars in "Rade" group is "*Solanum nigrum*". Persian physicians, avoided topical "Mohallel" with high lytic activity and usually used mild or moderate lytic activity topical medications like "*Iris germanica*". They believed that high lytic drugs could damage healthy skin tissue in addition to destroying and dissolve cancerous lesion [25].

Oral drugs are most effective in controlling and treating cancer through clearing the body

from abnormal black bile. Clearance via exsanguinations like phlebotomy (Fasd) and blood-letting (Wet cupping) not recommended while they cannot correct the condition by themselves since the disturbance resides more in the quality of substances than in their quantity in this disorder. Furthermore, clearing the body from black bile must be done rapidly in treating cancer [23].

Some ancient scientists believed that surgery and manipulation of the tumor or its site may enhance the infiltration of the cancer and its metastasis to other tissues. Nevertheless, surgery is suggested in cases of minor tumors that can be surgically removed completely while maintaining the healthy edges of the tumor provided that no cancer cells remain in the body [25, 32].

4. Discussion

According to WHO, cancer is the most life-threatening health challenge and one of the leading causes of mortality and disability round the globe. It has an increasing course in developing countries [33]. The annual rate of incidence of cancer in Iran is more than 90,000 cases [34]. Skin cancers are the most prevalent type among the white with an increasing trend of incidence around the world [35]. Studies conducted in Iran indicate the high rate of incidence of skin cancer in the Iranian community so that it ranks second in frequency among cancers in 2007 [36].

Unfortunately, the current treatment modalities impose high costs and are associated with many complications [3]. Hence, it is necessary to consider other suggested approaches of traditional medicine to prevent and treat cancers. The PM as a pioneer medical approach with an old history, may pave the alternative way.

The Edwin Smith and Ebers Papyrus are two of the oldest medical documents describing the treatment of cancer patients. After Hippocrates, over the next centuries, medical science did not develop because of religious concerns about autopsy and surgical procedures. The 17th century is a period in which there were new information about how to treat such oral cancer [37]. While, Persian scientists knew the types of cancers from the 9th century. Describe them and used of topical and systemic remedies in addition surgical procedures for several types of cancers [25, 27].

In this study, the medical textbooks of the golden era of PM (9th to 19th centuries AD), i.e., the times of Razes and Avicenna, were explored and interesting opinions on skin malignancies were found. These can complement the findings of modern medicine.

In modern medicine, the skin cancers are divided into two main categories on the basis of their origin: melanocytic (malignant melanoma) and non-melanocytic (basal cell carcinoma and squamous cell carcinoma). Each of these categories is divided into some subcategories on the basis of the involved site, morphology, histopathology and clinical signs and symptoms [38].

The Persian physicians knew the cancers and were forerunners in the description of these disorders.

For the first time in history, Avicenna introduced transformed ulcerous nevi as a kind of skin malignancy [39]. Today, the atypical nevi are considered as a factor contributing to melanoma [40].

The ancient Persian scholars classified the dermal malignancies more on the basis of etiology and morphologic features of the mass while the modern medicine classifies them on the basis of cellular origin.

In term of PM, Sal-eh, Varam-e-khabiseh, Varam-e-solb, Varam-e-sowdavi, Khanazir and Khilan in subcategory of "Owraam". Ghorouh-e-akele, Ghorouh-e-khabiseh, Ghorouh-e-mozmeneh in subcategory of Ghorouh and Jozam and Baras subtype of skin diseases have relative correspondent to new definition of skin cancers [Fig. 1].

Although an exact correspondence between these cancers is not feasible due to differences in disease classification, the old and new definitions are consistent and various common skin malignancies fall under the subcategory of old skin malignancies (Table 1).

Hence, are not significantly contradictory between ancient Persian medicine concept and new definition of skin cancers.

From the perspective of PM scholars, affliction with skin cancer or susceptibility for its incidence depends on several parameters among which are disturbed life style such as nutrition, living in dry and hot climate, prolonged exposure to sunlight, healthful sleep, body clearance, and noting the black bile excretory paths such as digestive function and constipation. The predisposing factors to skin cancer incidence are mental and spiritual stress due to personal and social conditions of humans along with organ susceptibility like infectious ulcers, chronic scars, and numerous nevi. The effect of many of these factors on affliction with skin cancer is approved and known by modern medicine [41-44].

The PM highlights the early diagnosis of cancer and believes that cancer is curable if it is treated early so that the more its treatment is delayed, the more stabilized it becomes in the body [23, 25, 27]. Today, scientists offer various screening modalities to help diagnose skin cancer early, especially melanoma that is the most malignant type [45].

Briefly, the PM recommends the following treatments:

1. Prevention of growth and infiltration of the tumor using topical, local, and systemic drugs.
2. Surgical removal of the cancerous mass.
3. Diminishing the general susceptibility of the body for recurrent affliction with cancer and preventing its recurrence.

The modern methods like radiotherapy, chemotherapy, gene therapy, and immunotherapy along with surgical interventions, may control the recurrence of the primary tumor for some time, they do not guarantee the patient's life quality or elimination of the susceptibility to cancer affliction due to untoward complications. Nonetheless, combination of modern and traditional medicine both controls and clears the carcinogenic factors and balances humors to reduce the chance of recurrence with increased life quality and expectancy [30].

5. Conclusion

The PM with its multi-thousand-year history has been pioneer in describing and treating many

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maladies such as cancers. This study also found no contradictory views between the old and modern scholars on the topic of skin cancers. Therefore, paying due attention to the neglected areas like nutrition and black bile clearance is very important. Some useful theories and hypotheses may be formulated by integrating and adjusting the theories, experiences, and attitudes of Persian scholars of traditional medicine and the laboratory, therapeutic, and clinical findings of modern medicine.

Author contributions

All authors participated in designing the overall approach to gleand data and analysis and in writing the article.

Conflict of interest

The authors have no conflict of interest to disclose.

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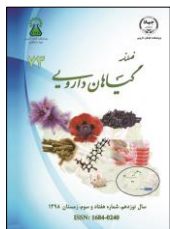
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مقاله مروری

مروری بر واژه‌شناسی، سبب‌شناسی و درمان بدخیمی‌های پوستی از دیدگاه طب کهن ایران

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چکیده

اطلاعات مقاله

گل‌واژگان:

طب کهن ایرانی

سودا

بدخیمی پوست

مقدمه: بدخیمی‌های پوست، از شایع‌ترین سرطان‌ها در میان سفید پوستان هستند که بروز فزاینده‌ای در جهان و ایران دارند. دستاوردهای علمی در تشخیص، غربالگری و روش‌های درمانی در کنترل این سرطان‌ها موفقیت نسبی داشته است. از اینرو لازم است، رویکردهای پیشنهادی سایر طب‌های مکمل و سنتی مورد توجه قرار گیرد. **هدف:** هدف از این مقاله مروری بررسی درمان‌های جایگزین و مکمل از دیدگاه طب ایرانی به عنوان طب پیشگام با سابقه تاریخی طولانی است. **روش بررسی:** در این مطالعه مروری، منابع پزشکی دوره طلایی طب ایرانی (قرن نهم تا نوزدهم میلادی)، یعنی زمان رازی و ابن‌سینا مورد بررسی قرار گرفت و نظرات آنها در مورد بدخیمی‌های پوستی استخراج شد. علاوه بر این، عبارت "سرطان پوست" در پایگاه داده‌ها مانند PubMed، Science Direct، Scopus و Google Scholar جستجو شد. داده‌های جمع‌آوری شده مورد تجزیه و تحلیل و مقایسه قرار گرفت. **نتایج:** دانشمندان پارسی باستان انواع سرطان‌ها را می‌شناختند و در توصیف، طبقه‌بندی، سبب‌شناسی و درمان سرطان‌های پوست پیشگام بودند. در این مطالعه ایده‌های جالبی در مدیریت سرطان‌ها یافت شد. همچنین هیچ دیدگاهی متناقض بین طب ایرانی و مدرن در مورد سرطان‌های پوست وجود نداشت. **نتیجه‌گیری:** توجه به سایر مواردی که امروزه مورد غفلت واقع شده است، مثل تغذیه و پاکسازی از خلط سودا، می‌تواند با ارائه تئوری‌ها و فرضیه‌های جدید در دستیابی به درمان‌های مؤثرتر و ایمن‌تر راهگشا باشد.

مخفف‌ها: PM، طب ایرانی

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