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Review Article

Prophetic medicine as potential functional food elements in the intervention of cancer: A review



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ABSTRACT

Amounting scientific evidences have revealed the antitumor, antimetastatic, antiangiogenic, anti-proliferative, chemopreventive and neo-adjuvant efficacy of Prophetic Medicine in various *in vitro*, *in vivo* and clinical cancer models. Prophetic Medicine includes plants, dietary materials or spices that were used as remedy recipes and nutrition by the great Prophet Mohammed (peace be upon him) to treat various ailments. Prophetic medicine is the total authentic Hadith narrated by the Prophet (PBUH) in relation to medicine, whether Qur'anic verses or honourable Prophetic Hadith. The ability of functional foods from Prophetic Medicine to modulate various signalling pathways and multidrug resistance conferring proteins with low side-effects exemplify their great potential as neo-adjuvants and/or chemotherapeutics. The present review aims to provide the collective *in vitro*, *in vivo*, clinical and epidemiology information of Prophetic Medicines, and their bioactive constituents and molecular mechanisms as potential functional foods for the management of cancer.

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1. Introduction

The global prevalence of cancer and the mortality rate remains high despite numerous extensive advancements and progress in the last decade [1,2]. Factors such as bad dietary habits, smoking status, alcohol consumption, genetic predisposition, diabetes and sedentary lifestyle significantly increase the risk of developing cancer. The rate of cancer mortality was reported to drop by 23% since 1991, nonetheless the mortality incidences are increasing for liver, pancreas, uterine cancer. The cancer statistics by American Cancer Society reported that prostate cancer (43%), colorectal cancer (9%), and melanoma (8%) as the most prevalent types of cancer in males whereas breast (41%), uterine corpus (8%), and colon and rectum (8%) in females [3]. The most recent cancer statistics in 2016 predicted a total of 1,685,210 new cancer cases and 595,690 cancer deaths in the United States. The report estimated that prostate (21%), lung (14%) and colon (8%) to be the three most common new cancer cases in men whereas breast (29%), lung (13%) and colon (7%) as new commonly diagnosed in women. The overall cancer incidence trends are found to stable in females whereas a declined trend in males (3.1% per year from 2009 to 2012) was recorded due to the reduced diagnosis of prostate cancer. Nevertheless, prostate cancer is estimated to contribute up to 8% of death cases in males while breast and genital (ovary and uterine) are projected to contribute up to 14% and 9% of mortality cases in females. Furthermore, respiratory (lung, 26–27%) and digestive system (colon and pancreas, 15%) are projected to be cause the highest mortality cases among other cancers [4].

The development of new anticancer drugs that possess potent cytotoxic property towards the cancer cells still denote as the main mode of chemotherapy [5]. Nevertheless, the therapeutic efficacy of chemotherapeutic drugs faces insurmountable challenges due to the notable toxicities, high acquired resistance and poor therapeutic index [3,6]. Furthermore, processes such as decrease in drug uptake, increase in drug efflux, activation of DNA repair mechanisms and evasion of drug-induced apoptosis contribute to the increasing resistance against chemotherapeutics drugs among patients with a variety of blood cancers and solid tumors. For instance, in Glioblastoma multiforme, the glioma cells developed resistant towards temozolomide through their ability to repair the DNA damage by expressing proteins such as O6-alkylguanine DNA alkyltransferase (AGT) that demethylates temozolomide-methylated guanosine encoded in humans by the O-6-methylguanine-DNA methyltransferase (MGMT) gene [7]. This ultimately lead to the growth of tumor again with potent resistant and ultimately, multidrug resistance and failure in chemotherapy [8–10]. Moreover, newer anticancer agents and regimes are expected to target cancerous cells exclusively since current chemotherapeutic drugs are unable to discriminate healthy cells and cause adverse side-effects such as bleeding, diarrhea, hair loss and immunosuppression [10,11]. Over the last century, natural products served as the main source of pharmaceutical industry that drives the ground-breaking drug discovery. In the last decade, functional foods have attracted great attention among the researchers and physicians for the prevention and management of chronic diseases such as cancer, and diabetes owing to their nutritional benefits beyond basic nutrition and ability to specifically target malfunctioned genes and modulate various signalling pathways [12–14].

A food is considered to be 'functional' if it or any of its elements (added, removed or modified/technologically developed

ingredients) provides specific health benefits such as preventive, protective and/or curative functions against one or more diseases [15]. Furthermore, the use of dietary materials and natural products as part of functional foods offer great advantages in the discovery of novel approaches for safer and effective treatment of cancer and immunity with marginal side-effects and toxicity [13,14,16]. Among these uprising functional food elements are the Prophetic medicines which includes the intake of dietary materials or plants or herbals such as *Nigella sativa*, *Cymbogon citratus*, ginger, honey and truffles that were used as remedy recipes and consumed as food element by the Prophet Mohammed (PBUH) [17]. In addition, Prophetic medicine have been largely documented to possess wide-ranging pharmacological activities, particularly, antitumor [18,19], antiangiogenic [20,21], antiproliferative [22,23] and antimetastatic [24,25] effects that serve them as potential anticancer agents. Various reports have demonstrated ethnopharmacological information, discovery of novel phytochemicals, pharmacological activities and potential molecular mechanisms of these Prophetic medicine elements from foods, spices and plants [22,26–28]. More importantly, the affordability, reduced side-effects and easy availability of these Prophetic Medicines further accentuate their popular selection in combating various chronic diseases [17,29,30].

Despite the various *in vitro*, *in vivo*, clinical reports and specific reviews on the functional food potentiality of Prophetic medicines, there is no review that discusses their preventive and curative potential collectively in the management of cancer. Furthermore, several of these Prophetic medicines such as dates, gingers, lemongrass, bitter melon, black cumin and olives and their bioactive constituents have been used and/or are currently developed as in the preparation and as component of functional foods ingredients such as cereals, yogurts, juices, herbal and concoctions [31–34]. Thus, the present review aims to provide the collective information of various and common Prophetic medicinal foods, drinks, spices and fruits as anticancer, antiangiogenic, neo-adjuvant and chemotherapeutic agents from various *in vitro* and *in vivo* cancer models reports. The present review provided the epidemiology reports and the synergistic studies of between these Prophetic medicines. Moreover, this review provides the latest scientific information and/or primary anticancer review on some of the PMAC foods, spices, drinks, and frits and further underlines the roles, mechanistic studies and their uses as functional foods. The elements of Prophetic medicines (from functional foods & drinks) included in this review were provided by the MABL Chair for Scientific Miracles of Prophetic Medicines, Faculty of Medicine, Taibah University, KSA and as described by Sheikh BY [17] (Table 1). From this list, the Prophetic medicinal elements only which have been reported to have anticancer activities were included in this review. Above all, the information from this review would guide the scientific community and industry to further investigate (mainly, *in vivo* and clinical studies) and potentially develop Prophetic medicines as anticancer functional foods.

2.1. Black cumin

Nigella sativa or commonly known as Habbatul Sawdaa (in Arabic) or black cumin (Fig. 1A) is one of the Prophetic medicinal plant and has been used traditionally for various ailments [17,35]. Listed in the family of Ranunculaceae, *N. sativa* is ethnomedicinally used in the Northern Africa, India and Middle East regions to cure

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