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Role of Khardal (*Brassica Nigra*) in Non-Communicable Diseases: An Overview

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Abstract:
Medicinal plants have an enormous contribution in the primary healthcare systems of local communities, particularly in developing countries like India. The World Health Organisation (WHO) estimates that up to 80% of the world's population in developing countries depends on locally available plant resources. The conventional pharmaceuticals are often expensive or inaccessible, and toxic too. Among the diversity of medicinal plants, Khardal (*Brassica nigra*) is one of the medicinal plants used extensively in various non-communicable/ chronic and degenerative diseases. It is an annual weedy plant which has immense edible as well as medicinal value. The use of Khardal has been in practice right from pre-historic period in the form of mustard plaster which was first described by Dioscorides (Circa 1st CE). Khardal also finds its mention in the holy Quran. The Unani physicians recommend Khardal in a number of ailments. In the light of current scientific literature, the pharmacological actions of Khardal in various non-communicable diseases (NCDs) such as diabetes, cardiovascular diseases, neurological disorders, respiratory diseases, joint diseases, cancer, vitiligo and alopecia have been revalidated. A review on Khardal has been undertaken, especially in order to establish its role in NCDs.

Keywords: Khardal, *Brassica nigra*, Non-communicable diseases, Unani medicine.

1. Introduction

Plant based drugs have a long history in both traditional and modern societies. A number of modern drugs shave been isolated or derived from natural sources based on their use in traditional medicine as crude drugs or as purified compound formulations approved by various regulatory agencies (Butler, 2004; Jones et al, 2006). The use of plants in the indigenous cultures of various countries forms an important socio-economic base of the country (Abdel-Wahab, 2009). Medicinal plants therefore have a significant contribution in the primary healthcare systems of local communities, particularly in developing countries like India (Amri et al, 2012; Muthu et al, 2006). The World Health Organisation (WHO) estimates that up to 80% of the world's population in developing countries depends on locally available plant resources (Anonymous, 2002). Population rise, insufficient supply of drugs, unaffordable cost of treatments, side effects of several conventional/ synthetic drugs and development of resistance to currently used drugs for diseases have led to increased emphasis on the use of plant materials as a source of medicines for a wide variety of human ailments particularly in non-communicable diseases (NCDs).

By definition, NCDs also known as chronic diseases or lifestyle diseases, are not passed from person to person. They are of long duration and generally slow progression. NCDs kill more than 36 million people each year and nearly 80% of NCD deaths - 29 million - occur in low and middle-income countries. The four main types of NCDs are cardiovascular diseases, cancers, chronic respiratory diseases and diabetes. Cardiovascular diseases account for most NCD deaths, or 17.3 million people annually, followed by cancers (7.6 million), respiratory diseases (4.2 million), and diabetes (1.3 million). These four groups of

diseases account for around 80% of all NCD deaths. NCDs are projected to exceed the combined deaths of communicable and nutritional diseases and maternal and perinatal deaths as the most common causes of death by 2030 (Lim et al, 2012).

Several herbs consist of powerful natural ingredients, helpful in curing various NCDs. For instance, Khardal (*Brassica nigra*) is one of the important medicinal plants used extensively for the treatment of NCDs/ chronic and other degenerative disorders (Velisek et al, 1995). The use of Khardal has been in practice right from pre-historic period in the form of mustard plaster which was first described by Dioscorides (Ewing, 1999). Khardal also finds its mention in the holy Quran (Azarpour et al, 2014). Its use in a number of disorders/ diseases has been mentioned in the Unani classical literature (Baitar, ynm). Khardal belongs to family Brassicaceae. It is an annual weedy plant which has immense edible as well as medicinal value. It grows upto 0.6 – 1.2 m height. It is in flower from Jun to August, and the seeds ripen from July to September. The flowers are hermaphrodite and are pollinated by Bees, flies. The plant is self-fertile. It prefers light (sandy), medium (loamy) and heavy (clay) soils and requires well-drained soil. The plant prefers acidic, neutral and alkaline soils but can grow in very acid soils too. It can grow in semi-shade (light woodland) or no shade. The plant can tolerate maritime exposure (Kumar et al, 2013). Current advancements in the drug discovery technology and search for novel chemical diversity have intensified the efforts for exploring and revalidating the role of Unani drugs in various ailments.

2. Phytochemical Screening of Khardal

Khardal seeds contain about 4% of isothiocynate glycoside called sinigrin (potassium myronate) and myrosin, which yield after maceration with water 0.7-1.3% of volatile liquid, known as the essence of mustard or volatile oil of mustard. This oil contains over 90% of allyl isothiocyanate. The seeds also contain about 27% of fixed oil, 30% of proteins, lecithin, inosite, albumins, gums, mucilage and colouring matters. An alkaloid, sinapine hydrogen sulphate is also present in trace amount in seeds. Fixed oil obtained by expression contains glycerides of oleic, stearic and erucic or brassic acids. It is yellowish-green, non-drying, slightly odorous and of bland mild taste. It solidifies on cooling (Evans, 2007; Kirtikar & Basu, 2005; Kokate et al, 2007; Nadkarni, 1994).

The leaf is reported to contain 31 calories, 89.5 g H_2O, 3.0 g protein, 0.5 g fat, 5.6 g total carbohydrate, 1.1 g fiber, 1.4 g ash, 183 mg Ca, 50 mg P, 3.0 mg Fe, 32 mg Na, 377 mg K, 4200 □g □-carotene equivalent, 0.11 mg thiamine, 0.22 mg riboflavin, 0.8 mg niacin, and 97 mg ascorbic acid; and the mature seed is reported to contain 7.6 g H_2O, 29.1 g protein, 28.2 g fat, 30.2 g total carbohydrate, 11.0 g fiber, and 0.5 g ash, in 100 gm respectively (Matai et al, 1973).

In a recent study, seven flavanoids were separated from *Brassica nigra*, and these isolated compounds were identified as: kaempferol- 3,7-di-O-β-D-glucopyranoside, 7-O-β-Dglucopyranosyl kaempferol 3-O-a-L-rhamnopyranosyl-β-D-glucopyranoside, kaempferol 3-O-β-Dglucopyranoside, kaempferol 3-O-β-Dgalactopyranoside, kaempferol 3-O-a-Lrhamnopyranosyl-β-D-glucopyranoside, Kaempferol and kaempferol 7-methyl ether. All of

these compounds were isolated for the first time from this species (Kamel & Ahmed, 2013).

3. Physico-chemical standards of Khardal

Seeds:

Ash value	4.2 – 5.7%
Acid insoluble ash	Approx. 1.5%
Moisture content	Not more than 5%
Fixed oil	Not less than 25%
Volatile oil	Not less than 0.6%

Fixed Oil:

Specific gravity	0.914 – 0.923
Saponification value	173 – 184˚C
Unsaponifiable matter	0.9 – 1%
Refractive index	1.472 – 1.473
Solidifying point	-11 – 17˚C
Iodine value	96 – 194

Volatile oil:

Specific gravity	1.014 – 1.030
Refractive index	1.527 – 1.529
Optical rotation	Inactive

(Kokate et al, 2007; Kulkarni et al, 1997)

4. Indications of Khardal in various NCDs

NCDs described in Unani	Conventional equivalents	Reference
Amraz-e-sina	Respiratory diseases	Sina, 2007; Khan, 1892; Kirtikar & Basu, 2005; Nadkarni, 1994; Ghani, ynm; Baitar, ynm
Asabi dard	Neuralgia	Kirtikar & Basu, 2005; Ghani, ynm; Rothe, 2012
Bars	Leukoderma/ Vitiligo	Ghani, ynm; Baitar, ynm
Da us salab	Alopecia	Khan, 1892; Ghani, ynm; Baitar, ynm; Rothe, 2012
Falij	Paralysis	Khan, 1892; Ghani, ynm
Irq-un-nisa	Sciatica	Sina, 2007; Nadkarni, 1994; Baitar, ynm; Anonymous, 2000
Ishal-e-muzmin	Chronic Diarrhoea	Khan, 1892; Ghani, ynm
Juzam	Leprosy	Khan, 1892
Khanazir	Parotitis	Sina, 2007; Khan, 1892; Nadkarni, 1994; Ghani, ynm
Muharrik-e-qalb	Cardiac stimulant	Baitar, ynm; Anonymous, 2000
Niqras	Gout	Nadkarni, 1982; Nadkarni, 1994; Ghani, ynm; Baitar, ynm
Nisyan	Dementia	Ghani, ynm
Quba	Dermatophysis/ Eczema	Khan, 1892
Qulanj	Colitis	Ghani, ynm
Rasha	Chorea	Ghani, ynm
Sara	Epilepsy	Khan, 1892; Ghani, ynm; Baitar, ynm; Rothe, 2012
Shaqeeqa	Migraine	Ghani, ynm
Waja-ul-mafasil	Arthritis	Sina, 2007; Khan, 1892; Nadkarni, 1982; Kirtikar & Basu, 2005; Nadkarni, 1994; Baitar, ynm; Ghani et al, 2012; Anonymous, 2000; Rothe, 2012; Punjaji, 2012
Warm wa izm e tihal	Splenitis and Splenomegaly	Sina, 2007; Khan, 1892; Kirtikar & Basu, 2005; Ghani, ynm; Baitar, ynm
Zat ul janb	Pleurisy	Anonymous, 1992; Anonymous, 2000
Zat ur riya	Pneumonia	Anonymous, 1992; Vanila et al, 2008; Anonymous, 2000

5. Scientific studies of Khardal in most common NCDs in world

5.1 Cardiovascular diseases

The potential of Khardal as a natural source of the antioxidant alpha-tocopherol has already been established (Yusuf et al, 2007). In a study, the aqueous extracts of Khardal inhibited lipid peroxidation induced by ferrous sulphate ascorbate on human erythrocyte membranes (Sujatha et al, 1995). In another study, no differences were found in serum cholesterol or triglyceride levels in rats fed with mucilaginous fraction of Khardal (Eskin et al, 2007).

In a 12-month randomized-placebo-controlled trial, the effects of fish oil versus Khardal oil was examined in 360 patients with suspected acute myocardial infarction (MI). The treatment was administered to all patients approximately 18 hours after symptoms of an acute MI. Patients in

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group A (n=122) received fish oil 1.08g/day orally, group B (n=120) received Khardal oil 2.9 g/day orally, and 118 patients received placebo. Results indicated a reduction in total cardiac events in patients treated with fish oil or Khardal oil compared with placebo. Also in comparison with the placebo group, patients treated with fish oil or Khardal oil showed a reduction in total angina pectoris, cardiac arrhythmias and left ventricular enlargement (Singh et al, 1997).

In another randomized-single-blind clinical trial enrolling 1000 patients with angina pectoris, MI or surrogate risk factors for coronary heart disease, similar results were documented in patients with increased intake of whole grains and Khardal oil (Singh et al, 2002).

5.2 Cancer

Numerous mechanisms of action have been proposed regarding the potential of Khardal and its derivatives, particularly organic isothiocyanates, for cancer chemoprotective activity. The cytotoxicity of Khardal derivatives on neuroblastoma cells has been investigated (Coggiola et al, 2005).

In a study, cytotoxic activity of the ethanolic, ethyl acetate and hexane extracts of Khardal was evaluated against five cancer cell lines, and it was found to exhibit significant growth inhibitory activities, in a dose dependent manner against HepG2 (Human cell line of a well differentiated hepatocellular carcinoma isolated from a liver), HeLa (Cervical carcinoma cells), HCT (Colon carcinoma cells), MCF-7 (Breast carcinoma cells) and Hep2 (Human epidermoid larynx carcinoma cells) tumour cells, using 3-[4,5-dimethylthiazol-2-yl]-2,5-diphenyl tetrazolium bromide (MTT) dye assay (Kamel & Ahmed, 2013).

Khardal juice was found to be protective against benzo[a]pyrene induced DNA damage in human derived cells in a dose dependent manner. The chemoprotective activities may be associated with induction of detoxifying enzymes (Uhl et al, 2003).

In another study, the effects of organic isothiocyanates on P-glycoprotein and multidrug, resistance-associated, protein (MRP1)- mediated transport in multidrug resistant (MDR) human cancer cell lines, were examined. Both P-glycoprotein and MRP1 were involved in the bioavailability, distribution and elimination of many drugs. Dietary organic isothiocyanates inhibited the P-glycoprotein and MRP1-mediated efflux of daunomycin and vinblastine in MDR human cancer cells, enhancing the efficacy of cancer chemotherapy. The study also found evidence of organic isothiocyanates inhibiting tumour formation in breast, colon, lung and skin tissue in animal models (Tseng et al, 2002).

Essential oil of Khardal reduced tumour cell proliferation through apoptotic and antiangiogenesis mechanisms in mice, while the mucilage fraction inhibited colonic preneoplastic changes in rats (Kumar et al, 2009; Eskin et al, 2007).

5.3 Diabetes

Different studies in rats exhibited a hypoglycemic effect in normal animals as well as decreased serum glucose and increased insulin responses on post-prandial glucose in diabetic induced animals, using both the whole plant and mucilaginous extracts of Khardal. The proposed mechanisms included modulation of gluconeogenic and glucolytic enzymes (Srinivasan, 2005; Grover et al, 2002; Grover et al, 2003; Yadav et al, 2004).

In an experimental study, streptozotocin induced diabetic rats were treated separately with aqueous, ethanol, acetone and chloroform

extracts of the seeds of Khardal. The increase in serum glucose value between 0 and 1 hour of glucose tolerance test (GTT) was the least (29 mg/dl) in aqueous extract treated animals. In further studies carried out with aqueous extract, the effective dose was found to be 200 mg/kg body weight in GTT. Administration of 200 mg/kg body weight of aqueous extract to diabetic animals daily once for one month brought down fasting serum glucose (FSG) levels. Also, the increase in glycosylated heamoglobin (HbA1c) and serum lipids was much less as compared to the untreated group (Anand et al, 2007).

In another study, aqueous extract of Khardal has been shown to have good antidiabetic effect along with significant decrease of abnormal serum lipid levels. To understand the mechanism of action, effect of oral administration of extract for two months on glycolytic and gluconeogenic enzymes was studied in liver and kidney tissues of rats with streptozotocin (STZ) induced diabetes mellitus. The activities of gluconeogenic enzymes were higher and of glycolytic enzymes were decreased in both the liver and kidney tissues during diabetes (Anand et al, 2009).

5.4 Neurological disorders

The study experimentally investigated the anticonvulsant effect of Khardal by using kindling method. Sixty male mice were randomly selected and divided into six experimental groups (n = 10) including: 1-control, 2-pentylentetrazole (PTZ)-kindled mice, 3-positive control group received valproate (100 mg/Kg) as anti-convulsant drug, 4-5 and 6 received Khardal seed extract in three doses (75, 150 and 300 mg/Kg; IP). All groups except for the control ones were kindled by 11 period injections of PTZ (35 mg/Kg; IP). In the 12th injection, all groups except for the control group were tested for PTZ challenge dose (75 mg/Kg). However, the exhibited phases of seizure (0-6) were observed and noted till 30 minutes after the PTZ injection. At last, the brains of all the mice were removed and then malondialdehyde (MDA), superoxide dismutase (SOD) and nitric oxide (NO) levels of the brain tissues were determined. Statistical analysis of the data shows that the seed extract could reduce the intensity, improvement and duration of seizure. In addition, the Khardal extract increased the SOD and NO levels and decreased the MDA level in the brain tissues. Attained results show that the extract of Khardal seed can be used in grand mal seizure treatment. Moreover, the antiepileptic effect of this extract is probably caused by its antioxidant properties which acts via enzyme activity mechanism (Kiasalari et al, 2012).

In another investigation, Acetylcholinesterase inhibitory (AChEI) activity of aquous and total extracts of Khardal was assessed by using Ellman method with acetylthiocholine iodide as substrate and dithiodinitrobenzoic acid as reagent in 96-well plates at 405nm. AChEIs are the usual drugs for Alzheimer's. The results demonstrated that only total extract of Khardal showed 13.4% inhibition at concentration of 300µg/ml (Hajimehdipoor et al, 2013).

5.5 Joint diseases/ disorders

A study was done to assess the anti-arthritic activity of Khardal. Arthritis was induced in albino rats by inducing the freunds complete adjuvant. The seeds of freunds adjuvant were coarsely powdered and extracted with ethanol (95%) and water using soxhlet. The effect of this plant extracts on arthritic rats were assessed by the various blood parameters and also taking the changes in paw volume. The Khardal suppressed the arthritic changes induced in rats and results were statistically significant (Vinyas et al, 2012).

6. Discussion and conclusion

The inaccessibility and insufficient response of conventional drugs in the management of NCDs is a big challenge. Use of plants and plant products in the form of crude drugs as well as in various compound formulations for combating NCDs has been a major strength of Unani drugs. Khardal is one such herbal drug which is highly effective in a wide variety of NCDs. Due to its potent antioxidant property, it inhibits and prevents the oxidative stress and protects from many diseases, such as cardiovascular diseases, diabetes, tumors, joint diseases, epilepsy, carcinogenesis, Alzheimer's disease, respiratory diseases, skin diseases, etc. According to the Unani classical literature as well as current scientific studies, Khardal has proved to be a significant Unani drug, particularly in case of NCDs. Although, the clinical trials of Khardal are limited and are lacking in various aspects, and they must be carried out in order to revalidate other entities as well.

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8. Conflict of Interest

None declared.

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