

REVIEW ARTICLE

Diet based on oil of seeds of *Brassica napus*. Implications for the prevention and treatment of prostate diseases

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## Summary

In last centuries, human diet has been modified due to changes in the technological, economic, and cultural mode of the social life. The rapid development of the technology and advances in food production and processing of plants resulted in changes in the structure of consumption. The consequence is an growing interest among researchers, but also among consumers in searching for new alternatives to classical pharmacology, preventive solutions, and therapeutic strategies of age related, chronic diseases and cancer. In this paper, the authors have attempted to assess the benefits of usage in diet cold-pressed oils extracted from the seeds of *Brassica napus* (oilseed rape) with particular emphasis on the evidence of possible use of *B. napus* oil, and other bio-active substances contained therein, in the prevention and symptomatic treatment of prostate diseases, including benign prostatic hyperplasia (BPH). The authors postulate that the information presented in this paper may be important and helpful in the development of new, effective and safe forms of prevention and treatment of progressive age-related disorders (phytotherapeutics) and nutritional strategies (dietary supplements) based on seeds oil of *Brassicaceae* family representatives, especially *Brassica napus* (pollen).

**Keywords:** diet, cold+pressed oil, chemoprevention, *Brassicaceae*, *Brassica napus*

## INTRODUCTION

Nutrition in human history passed a dramatic change of abandoning the natural foods at the expense of processed foods due to changes in technological, economic, and cultural mode of the social life [1]. Nowadays, it is well known that nutrition has important long-term consequences for health. Moreover, more and more epidemiological data indicate that the mismatch between our physiology, type of diet and lifestyle is a major cause of many chronic diseases, including coronary heart disease, hypertension, type 2 diabetes, autoimmune disease and cancers [2, 3]. In the aging populations of developed countries, an increased frequency of so-called lifestyle diseases is observed. Thus, the need of the development of novel forms of prevention strategies through education of healthy lifestyles and the introduction of healthy dietary practices are emphasized. The growing consumer awareness makes them start to pay more attention to those aspects of life that help improve its quality. As a consequence, in recent years there has been an increase of interest of a nutrition with pro-healthy properties and of adequate nutrition.

In this paper the authors have made a thorough review of the scientific literature concerning use of *Brassica* sp., especially *B. napus* seeds oil, in context of prevention of prostate disease and have made a complex analysis of pharmacological properties of this plant.

## FATTY ACIDS IN OILS WITH HEALT-PROMOTING PROPERTIES

Vegetable and plant oils are a key component of diet in all continents. In past decades, the growing popularity of pro-healthy activity promoted with effective advertising, considerably increased their consumption. A well-balanced diet, including slimming diet, provides the optimal quantity of fats, enabling the course of many cellular processes [4].

Recently, cold-pressed oils are of special interests among many consumers as well as many researchers [5]. Such oils, characterized by a relatively high fat content – over 15% – are obtained from beans, seeds, fruit or vegetable sprouts. Moreover, these oils possess many more nutritive properties than refined ones. Hence, many of these ingredients are present in products intended directly for human consumption, other components can be partially or completely lost during the refining process (purification) of oil [6]. Taking into account the chemical composition of plant oils, in general, they are abundant in free fatty acids, phenolic compounds, tocopherols, sterols, stanols, phospholipids and other components [7]. Moreover, in cold-pressed oils additional bio-active compounds were identified, such as: triacylglycerols (approx. 95%), a small amount of diacylglycerols, monoacylglycerols, and free fatty acids. Other compounds are phospholipids, tocopherols and tocotrienols, free and esterified sterols, hydrocarbons (squalene), triterpene alcohols, carotenoids and chlorophylls [6].

Improper food model based on high consumption of highly processed food and low consumption of fruit and vegetables increases the risk of the development of many disorders, for example cardiovascular diseases, hypertension or hyperlipidemia. Regular consumption of small amounts of fish oils as well as flaxseed oil rich in polyunsaturated fatty acids may decrease the risk of these kind of diseases. Fatty acids (especially omega-3 and omega-6) are subject of intensive scientific studies that every year show a new positive effects on human organism. It has been already proved that their regular consumption is involved with blood circulation improvement, reduction of cholesterol, lowering of blood pressure [9], and may have a neuroprotective effects [10]. Recent studies, especially on animal models as well as some clinical trials also indicate that consumption of an adequate amounts of omega-fatty acids may help fight cancers, including colon, rectum, pancreas, breast and prostate cancer [11, 12].

## SELECTED ISSUES ON PHARMACOTHERAPY AND PHYTOTHERAPY OF PROSTATE DISEASES. PHYTOCHEMICAL PROFILE AND CHEMOPROTECTIVE PROPERTIES OF *BRASSICACEAE* SP. REPRESENTATIVES

### Aging, prostate diseases, pharmacology of benign prostatic hyperplasia

Several studies have shown that andropause is involved in prostate gland hypertrophy of benign or neoplastic origin. Despite the progress of knowledge in this field, the ethiology of lower urinary tracts syndroms (LUTS), associated with benign prostatic hyperplasia (BPH) and prostate cancer (PC) remains not fully understood. Currently, for the first-line pharmacologic treatment of BPH and moderate to severe LUTS as well as for adjuvant therapy of prostate cancer, two classes of drugs are used: (1) selective  $\alpha_1$ -adrenergic receptor blockers ( $\alpha$ -blockers) and (2)  $5\alpha$ -reductase inhibitors (5-ARI; azasteroids, e.g. finasteride and dutasteride) [13-15]. Indeed, over past two decades, numerous randomized, placebo-controlled clinical trials confirmed the effectiveness of those 5-ARIs and  $\alpha_1$ -blockers (terazosin, doxazosin, tamsulosin, alfuzosin, and silodosin) [16]. However, despite many scientific papers supporting the efficacy of synthetic drugs used in monotherapy of prostate diseases or, in particular, in combination [14, 16], there is lack of complex data explaining the molecular mechanisms of potential interactions between these synthetic drugs and herbal drugs and also dietary components. Researchers interested in or involved in the studies of the efficacy of BPH/LUTS treatment emphasize that the management of all those sexual dysfunctions in men treated for prostate diseases should involve assessment of co-morbidities and concomitant medications, and consideration of lifestyle interventions, including healthy diet, to decrease risk factors [17].

### Significance of chemoprevention and the rational phytotherapy of prostate diseases

Early detection of prostate disease progress, especially during andropause, as well as searching for new alternative forms of prevention and therapy are important issues for health care institutions [18]. Hence, a considerable interest in the modification of diet with use of herbs has arisen [19].

According to physicians dealing with the issue of rational, safe and effective prophylaxis and therapy of prostate disorders, the principle components used in the chemoprevention strategy are often closely connected to the natural history of prostate diseases and include i.e. agents and their molecular targets; strategic intermediate endpoint biomarkers (IEBs) and their critical pathways.

Analysis of scientific literature shows that more and more intensive studies are undertaken to search for new plant materials with properties that can be used in prophylaxis and chemoprevention of prostate disorders, as well as attempting to clarify the molecular basis, efficacy and safety of the phytotherapy of such diseases [20-27]. As examples of plants with examined potential phytotherapeutic activities are *Pygeum africanum*, *Zea mays*, *Cucurbita pepo* [28], *Angelica koreana* [29], *Torilis japonica* [30], *Epilobium* sp. [21,24,27], and especially *Serenoa repens* can be given [31]. The mechanism of action of herbal extracts of above mentioned plants is not fully understood, but the knowledge about them increases every year. In general, they have been described to inhibit androgen regulating enzymes (i.e. 5 $\alpha$ -reductase, aromatase), possessing anti-inflammatory, anti-oxidant properties and inhibiting cell proliferation [21, 22]. It was also proven that these properties are attributed mainly to phytosterols, fatty acids [22, 27, 32, 33], as well as tannins [22, 27, 34], flavonoids [3, 20, 22, 27] and glucosinolates [35]. For example, it was experimentally *in vitro* proven that free fatty acids (approx. 80%: mainly oleic, lauric, linoleic and myristic acids) may inhibit both types of 5 $\alpha$ -steroid reductase activities [36].

## Health-promoting properties of representatives of Brassicaceae family

*Brassicaceae* is the major group of plants belonging to Angiosperms (flowering plants) containing over 300 (349) plant genera, and about 3700 species. It owes its name to the genus *Brassica* [37].

Numerous epidemiological studies and experiments in animals have shown that high intake of cruciferous vegetables such as broccoli, Brussels sprouts, cauliflower, and cabbage, can protect the human body against the development of cancer [38, 39]. Therefore, these vegetables attracted the interests of researchers as a potential source of potential chemopreventive agents in age related diseases and tumorigenesis [39, 40]. Chemopreventive properties of several representatives from *Brassicaceae* family, including protective activities in prostate cancer have been investigated for a long time [35, 41, 42].

One of main and best known chemopreventive constituents of *Brassicaceae* plants are isothiocyanates – generated by hydrolysis of their precursors, glucosinolates, for example sulforaphane [1-isothiocyanato-4-(methyl-sulfinyl)butane; SFN] present in broccoli and broccoli sprouts [43, 44]. Recent studies demonstrated that SFN blocked cancer development at postinitiation phases, inhibiting proliferation and inducing cancer cells apoptosis [43, 44]. What is especially important and already highlighted, there are no published data so far explaining at molecular level, the possibility of occurrence of interactions between extracts obtained from plant materials mentioned above and synthetic drugs belonging to the 5 $\alpha$ -steroid reductase inhibitors (i.e. finasteride and dutasteride) which belong to the androgen regulating enzymes.

## ***Brassica* sp. with emphasis on *Brassica napus* – herbal material and nutritional properties, phytochemistry**

Many phytochemicals present in plant-derived preparations and plant foods are poorly absorbed in humans. After absorption these compounds usually are being metabolised and rapidly excreted. Despite of this, some of them still exert many beneficial effects, including anti-aging, free-radical scavenging, anti-inflammatory, and anti-proliferative effects. These include compounds found in cruciferous vegetables and especially berries of *Brassica* sp. Currently, the profile of different *Brassica* species is quite well established [35, 41, 42]. The functional and nutritional values of different vegetable oils from seeds and leaves depend on the nature of different fatty acids incorporated into the oil (triacylglycerols and smaller amounts of mono- and di-glycerols), free fatty acids, phytosterols such as brassicasterol (belonging to the brassinosteroids or brassicasteroids, BRs), campesterol, stigmasterol,  $\beta$ -sitosterol and avenasterol [52, 53] and sphingolipids, e.g. ceramides, cerebrosides [54]. Apart from these beneficial substances, other bioactive compounds such as: terpenoids, flavones, long chain hydrocarbons have been reported from the EtOAc-soluble fraction [55], as well as polysaccharides, for example LBPP, were extracted and isolated from the oil from seeds and pollen of *B. napus* [56].

The oil content of the seed varies from 30 to 45%, depending on the species, the variety and climatic conditions under which the plant is grown. The *B. napus* has been known as a rich source of oil with a low content of saturated fatty acids (5–7%) and a high content of polyunsaturated fatty acids (PUFA, with about 7–10%  $\alpha$ -linolenic and 17–21% linoleic acids), with a good balance between the omega-6 and omega-3 fatty acids. That is why it is considered as healthy, edible oil: the ratio of linoleic to linolenic acid amounts 2 and is higher balanced than in soybean oil [49-51]. This 7% of saturated fatty acids from canola oil is about half the level present in corn oil, olive oil or cottonseed oil. The most important in nature is the monounsaturated fatty acid (MUFA), an oleic acid. It is present in many plant oils; in some of them, such as olive and canola oil, it is the major fatty acid. The most important canola oil components are also vitamins E and K, stigmasterol, campesterol and  $\beta$ -sitosterol. Tocopherols, present in canola oil, are natural antioxidants present in different amounts in many vegetable oils. Tocopherols content in canola oil ranges from 0.5 to 0.9% [57]. Canola oil contains mostly  $\alpha$ - and  $\gamma$ -tocopherol. Different tocopherols have different antioxidant activity *in vitro* and *in vivo*. The lowest content of tocopherols was found in cold pressed canola oil.

Additionally, brassinosteroids (BRs), belonging to the steroid plant hormones present in *Brassica* family plants play important regulatory roles in various physiological processes, including growth and differentiation [58, 59]. They have been detected and isolated from seeds, fruits, leaves, galls and pollen [60]. In recent years, there is a growing interest in them due to gradually discovered pro-health, beneficial properties [59].

## Biological, chemoprotective and antitumor properties of *Brassica napus* preparations and fractions

In recent years, it has been postulated that *Brassica napus* (pollen) may possess chemoprotective and tumor suppressive properties [56,61] which stimulate massive research in biochemical, nutritional and medical sciences. Some researchers suggest that potential antitumor effects could be attributed to efficient reactive oxygen species scavenging by *Brassica* extracts [62]. A cytotoxic activity of two sphingolipids: cerebroside (1-O-( $\beta$ -D-glucopyranosyl)-(2S,3S,4R,8E)-2-[(2'R)-2'-hydroxytetracosenoilamino]-8-octadecene-1,3,4-triol) and ceramide ((2S,3S,4R,8E)-2-[(2'R)-2'-hydroxytetracosenoilamino]-8-octadecene-1,3,4-triol), isolated from ethyl acetate extract of pollen, was detected in human lung tumor Tca8113 cell line [54]. Studies from Heggen et al. proved that sterols from tall and rapeseed oils similarly reduce atherogenic lipids and lipoproteins [63]. A few studies concerning potential chemoprotective and anticancer properties were conducted on brassinosteroids (BRs). Furthermore, experimental work carried out by Wu et al. has shown that steroid fraction of a chloroform extract from *Brassica campestris* L. (CPBC) could display a differing extent of cytotoxic activity on several human cancer cell lines (PC-3, LNCaP, MCF-7, Hela, BEL-7402, BCG-823, KB, A549 and HO8910). The mechanism of cell death appeared to be apoptosis via caspase activity induction and the inhibition of Bcl-2 protein, especially in prostate cancer cells (PC-3) [64,65]. Further analysis revealed that a sterol - brassinolide could be responsible for these effects, which in turn could provide a potential use for the treatment of prostate diseases, including cancer [65]. In other prostate cancer cells, LNCaP, ethyl acetate extract from pollen decreased the secretion of prostate specific antigen (PSA) [65]. What is more important, canola oil composition is of particular importance in the treatment of cancer because this oil has been positively associated with prevention and treatment of such disorders including cancer [66]. Some results suggest that diet rich in omega-3 fatty acid (also from canola oil) slows down prostate tumorigenesis by lowering estradiol, testosterone and AR levels, promoting apoptosis and suppressing cell proliferation in C3(1)Tag mice [67]. *Brassica napus* L. roots have been investigated for antioxidant and anticancer effect on human tumor cells (Hep G2). Extract of the plant inhibited the tumor cell line Hep G2 proliferation. Potentially, plant material from *Brassica napus* can be used as a nutritional supplement in cancer prevention [68]. Different data indicate that intake of  $\gamma$ -tocopherol may reduce prostate cancer risk, and several *in vitro* studies have demonstrated that  $\gamma$ -tocopherol can inhibit prostate cancer cell growth. It is known that  $\gamma$ -tocopherol suppresses prostate tumor progression in an *in vivo* TRAP model, and could be a chemopreventive agent for human prostate cancer [69]. Other examinations have shown that gamma tocopherol upregulates the expression of 15-S-HETE and induces growth arrest through a PPAR  $\gamma$ -dependent mechanism in PC-3 human prostate cancer cells [70]. Moreover, the potential role of  $\gamma$ -tocotrienol (GT3) in reducing prostate cancer proliferation were examined in prostate cancer cells. Authors were found that the  $\gamma$



and  $\delta$  isoforms of tocotrienol from different plants were more effective at inhibiting the growth of prostate cancer cell lines (PC-3 and LNCaP) compared with the  $\gamma$  and  $\delta$  forms of tocopherol [71].

## CONCLUSIONS

Despite the increasing knowledge of the biological and pharmacological properties of components from seeds oil of *Brassica napus*, their molecular mechanisms of action in prostate gland are still not fully understood, especially in model organisms and in humans. Also the mechanism of potential interactions within the prostate gland resulting from cross-reaction between synthetic drugs used in pharmacotherapy of prostate diseases and diet rich in fatty acids, sphingolipids and/or phytosterols from the oil of pollen is unknown. Thus, further studies on the molecular mechanism of the potential anticancer and chemopreventive activities of oil from *Brassicaceae* sp. representatives in prostate cancer should be taken into the consideration.

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## DIETA NA BAZIE OLEJU Z NASION *BRASSICA NAPUS*. IMPLIKACJE W PREWENCJI I TERAPII SCHORZENÍ PROSTATY

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## Streszczenie

W ostatnich stuleciach ludzka dieta została istotnie zmodyfikowana w wyniku zmian trybu technologicznych, ekonomicznych i kulturalnych. Szybki rozwój technologii i postęp w produkcji i przetwórstwie żywności z roślin spowodował zmiany w strukturze konsumpcji. Konsekwencją tych zdarzeń jest wzrost zainteresowania naukowców oraz konsumentów poszukiwaniem nowych, alternatywnych strategii żywieniowych, a także profilaktyką schorzeń towarzyszących okresowi starzenia się, jak również chorób przewlekłych i nowotworowych. W niniejszej pracy autorzy podjęli próbę przybliżenia korzyści wynikających ze stosowania diety zawierającej tłoczony na zimno olej uzyskiwany z nasion *Brassica napus* (rzepak), ze szczególnym uwzględnieniem dowodów świadczących o możliwości wykorzystania oleju z *B. napus*, substancji bioaktywnych w nim zawartych w prewencji i leczeniu objawowym schorzeń prostaty, w tym BPH. Autorzy sugerują, że informacje zawarte w niniejszej pracy mogą być istotne i pomocne w opracowaniu nowych, skutecznych i bezpiecznych form prewencji i leczenia objawowego schorzeń postępujących wraz z wiekiem (fitoterapeutyki) oraz strategii żywieniowych (suplementy diety) opartych na bazie oleju z nasion wybranych przedstawicieli rodziny *Brassicaceae*, w tym *Brassica napus*.

**słowa kluczowe:** dieta, olej tłoczony na zimno, chemoprewencja, *Brassicaceae*, *Brassica napus*