ASIAN JOURNAL OF PHARMACEUTICAL AND CLINICAL RESEARCH

INNOVARE ACADEMIC SCIENCES
Knowledge to Innovation

Vol 16, Issue 7, 2023

Online - 2455-3891
Print - 0974-2441

Review Article

RAPHANUS SATIVUS - A REVIEW OF ITS TRADITIONAL USES, PHYTOCHEMISTRY, AND PHARMACOLOGY

SAHA S[1], PAUL S[1], AFROZ A[1], DEY A[1], CHATTERJEE A[2], KHANRA R[1]*

[1]Department of Pharmaceutical Technology, JIS University, Kolkata, West Bengal, India. [2]Department of Pharmaceutical Technology, Bengal School of Technology, Hooghly, West Bengal, India. Email: Mail-ritukhanra@yahoo.co.in

Received: 01 February 2023, Revised and Accepted: 24 March 2023

ABSTRACT

Raphanus sativus (R. sativus) is a widely used vegetable belonging to the family *Brassicaceae*, generally grown as annual or biennial plants, with a taproot which is much enlarged when it is cultivated. In Yemenite folk medicines, *R. sativus* juice is used in eliminating kidney stones. Few people, specifically in the Middle East, prefer to drink its juice in pursuit of certain health benefits. In Unani, Greeko-Arab, and Indian folk medicine, It is used as a home remedy for the treatment of many diseases such as jaundice, gallstone, liver diseases, rectal disorder, indigestion, and other gastric pains. This article has reviewed the information available on *R. sativus* ethnopharmacology, geographical distribution, chemical composition, and pharmacological uses. The information on botanical description, distribution, traditional uses, chemical composition, bioactive components, and therapeutic investigations was gathered from a comprehensive literature search of electronic databases such as Science Direct, PubMed, Web of Science, Wiley, ACS, Springer, Google Scholar, and SCOPUS until 2020 for publications. An elaborative study has been done on botanical characterization, traditional uses, chemical composition, and various pharmacological or therapeutic uses. Mainly this plant is fully loaded with polyphenolic compounds which exert a promising antioxidant property. This plant possesses various therapeutic benefits such as anti-inflammatory, anti-microbial, anti-tumorogenesis, anti-cancer, anti-diabetic, and anti-nephrotoxicity activity. The comprehensive literature analysis shows that a wide range of populations has utilized various parts of *R. sativus* around the globe. The above information shows that the plant holds a variety of hidden and unknown potentials which can be studied extensively for its phytoconstituents and therapeutic outcomes. However, while searching through the literature available, it was observed that there is a lack of information on its phytochemical profiling and its corresponding pharmacological benefits. It is believed that this review will help lay the groundwork for encouraging pharmacological and pharmaceutical studies.

Keywords: *Raphanus sativus*, Ethnopharmacological, Radish.

 DOI: http://dx.doi.org/10.22159/ajpcr.2023v16i7.47468. Journal homepage: https://innovareacademics.in/journals/index.php/ajpcr

INTRODUCTION

Plants have been used in therapy since the ancient ages, and they can be the solution to various diseases and among them *Raphanus sativus*. It is one of the most important vegetables which has enormous activities. *R. sativus* belong from the *Brassicaceae* family which is generally grown as annual or biennial plants, with a taproot which is much enlarged when it is cultivated [1]. *R. sativus* sprouts contain polar and non-polar compounds that could possibly possess antimicrobial activity [2]. Crude juice of the *R. sativus* inhibited the growth of *Escherichia coli, Pseudomonas pyocyaneus, Salmonella typhi,* and *Bacillus subtilis in vitro* [3]. It has been also found that *R. sativus* helps to fight cancer as it contain sulforaphane having quinone reductase activity which inhibits the groth of colon cancer cells [4]. Saponin-also found in cruciferous plants-was reported to cause some necrotic cell death [5]. *R. sativus* has also significant antioxidant activity and anthocyanin named cyanidin glycosides has an o-dihydroxy structure, and cyanidin glycosides have a high antioxidant capacity [6]. Research shows that *R. sativus* has a big impact on the kidney and ethanolic and water extract of *R. sativus* have a nephroprotective effect against rifampicin [7]. *R. sativus* crude extract when tested on the blood pressure and heart rate of normotensive rats under anesthesia, exhibited a dose-dependent inhibition, which is in line with its traditional use in hypertension [8]. The extract caused a dose-dependent (0.13 mg/kg) fall in the blood pressure and heart rate of rats that was mediated through an atropine-sensitive pathway [9].

TAXONOMICAL CHARACTERISTICS [10]

- Kingdom-Plantae-plantes, Planta, Vegetal, plants
- Subkingdom-Viridiplantae-Green plants
- Infrakingdom- Streptophyta-land plants
- Super division-Embryophyta
- Division -Tracheophyta-vascular plants, tracheophytes
- Subdivision-Spermatophytina-spermatophytes, seed plants, phanérogames
- Class-Magnoliopsida
- Superorder-Rosanae
- Order-Brassicales
- Family-*Brassicaceae*
- Genus-Raphanus L.-*R. sativus*
- Species-*Raphanus sativus L*

BOTANICAL CHARACTERIZATION

R. sativus is having few specific morphological characteristics which may help in identifying the plant/fruit. *R. sativus* (Radish) belongs to the family *Brassicaceae*. Radish plants grow annually or biannually, specifically in the season of winter. It is generally grown from March to August in the hills and is available all over the world. The external features of radish plants include variation in leaves type, leaves arrangement, flower petal color, flower symmetry, and fruit type. It is observed that the flowers of the *R. sativus* used to be symmetrical in nature. The color of the *R. sativus* flower petals are pink, white, and light red. There are two types of leaves. One is called a compound leaf (made up of two or more discrete leaflets) and another is called a simple leaf (lobed or un-lobed but not separated into leaflets). The leaf arrangement used to be an alternative arrangement that is there is one leaf per node along the stem. The edge of the leaf blade has lobes and a teeth kind of structure. The fruit of *R. sativus* used to be dry with the range of the weight 10–250 mm but does not split into pieces when ripe. The farmers usually cultivate the radish in the season of winter as it needs a clear sunlight and low temperature for better growth [11].

TRADITIONAL USES ACCORDING TO LOCALITY BASIS OR COUNTRY BASIS

R. sativus has multi-purpose uses in terms of food or medicinal properties. As for being a edible plant *R. sativus* leaf and fruit are generally cooked or sometimes eaten raw. It is having astringent and diuretic properties that's why used traditionally to increase bile flow. *R. sativus* juice is an old home remedy for cough, rheumatic arthritis, and gallbladder stones [12]. Usually, people eat raw radishes mainly in salad, while it is also seen in many European dishes. Few people, specifically in the Middle East, prefer to drink its juice in pursuit of certain health benefits. In Unani, Greeko-Arab, and Indian folk medicine, *R. sativus* is used as a home remedy for the treatment of many diseases such as jaundice, gallstone, liver diseases, rectal disorder, indigestion, and other gastric pains. The leaves which generally have been discarded are containing 10 times more vitamin C than roots thus containing more anti-oxidant properties. In Yemenite folk medicines, *R. sativus* juice is used in eliminating kidney stones [13].

The leaves, and roots can be used in asthma, chest tightness, and even in the infection by intestinal parasites. The root is antiscorbutic, antispasmodic, astringent, cholagogue and digestive. The plant contains raphanin, which is antibacterial and antifungal in nature, thus inhibiting the growth of *Staphylococcus aureus, E. coli, streptococci,* and *Pneumococci*. The plant also shows anti-tumor activity.

Eating *R. sativus* also enhances your body's natural adiponectin (a protein hormone) production. Higher levels of this hormone can help to protect against insulin resistance. *R. sativus* is rich in antioxidants and minerals such as calcium and potassium. Together, these nutrients help to lower high blood pressure and reduce your risk for heart disease. *R. sativus* is also a great source of natural nitrates that improve blood flow.

R. sativus contains an ample amount of glucosinolates-sulfur compounds which show a protective effect toward the cells from genetic mutations that cause cancer and also prevent the growth of tumor cells [13,14].

PHYTOCHEMISTRY [15]

R. sativus is containing a lot of phytoconstituents that show a wide range of biological activities. Various parts of it consisting various phytochemicals. The predominant phytoconstituents are shown in Fig. 1.

PHARMACOLOGICAL ACTIVITIES OF *R. SATIVUS* PLANT

Anti-oxidant activity

R. sativus plant is potential as antibacterial, antiinflammation, and also as antioxidant because of its saponin, flavonoid, polyphenol, glycoside, essential oil, vitamin A, and vitamin C content [11]. The presence of antioxidants is needed to prevent the oxidation process and maintain the quality of food products from rancidity, discoloration, and other physical spoilage [12]. *R. sativus* extract had 10.5% (w/v) glucosinolate glucoraphasatin activity and 154.5% anti-radical power by the presence of 0.098 flavonoid and 24.32 µg/mL phenolic compound [13]. Previous reports confirmed that antioxidants and tyrosinase from foods were one of the main causes of most vegetables and fruits quality and can promote health as well as prevent diseases [14]. The antioxidant activity and tyrosinase inhibition of many vegetables and fruits has been widely studied. This study indicated that the antioxidant and antityrosinase capacity of these vegetables in Thailand, including white *R. sativus,* garlic and ginger due to the presence of radical scavenging, phenolic flavonoids and antityrosinase compounds [15]. Antioxidant activity is generally based on the number and location of hydroxyl groups present as well as the presence of a 2–3 double bond and 4-oxofunction [16]. Flavonoids inhibit enzymes such as prostaglandin synthase, lipoxygenase, and cycloxygenase, closely related to tumorigenesis, and may induce detoxifying enzymes such as glutathione S-transferase [17]. Anthocyanin is named cyanidin glycosides having o-dihydroxy structure, cyanidin glycosides have a high antioxidant capacity [18].

Anti-inflammatory Activity

R. sativus crude extract when tested on the blood pressure and heart rate of normotensive rats under anesthesia, exhibited a dose-dependent inhibition, which is in line with its traditional use in hypertension [19]. The hypotensive effect of the plant extract was briefly similar to that of acetylcholine or carbachol [20]. Acetylcholine is known to cause a fall in blood pressure by activation of the muscarinic receptors located on the endothelium of blood vessels [21]. The plant extract tested positive for the presence of different classes of compounds such as saponins, flavonoids, tannins, phenols, and alkaloids [6]. Some of these classes of compounds, such as saponins were responsible for cholinergic receptor-mediated cardiovascular inhibitory activities [22]. The extract caused a dose-dependent (0.13 mg/kg) fall in the Blood Pressure and Heart Rate of rats that was mediated through an atropine-sensitive pathway [20]. The study showed that the cardiovascular inhibitory effects of the plant are mediated through the activation of muscarinic receptors, thus possibly justifying its use in Hypertension [23]. Hypertension in SHRs was suppressed after 4 weeks of feeding with R. sativus leaf powder. We also confirmed the inhibitory activity of *R. sativus* leaf powder for ACE measured in a previous study [24]. Ethanolic extracts of *R. sativus* leaves is identified with Sinapic acid which is considered as the main ingredient for anti-inflammatory effects. The addition of active fraction markedly inhibited LPS-stimulated production of inflammatory mediators by suppressing p38 Mitogen-activated protein kinase and nuclear factor-κB activation [25].

Anti-microbial activity

Plants have been used in therapy since ancient ages, and they can be the solution to all previously mentioned problems using the different anticancer and antimicrobial products found naturally in plants. Many plants are known to exhibit antioxidant activity, and consuming them reduces the risk of free radicals. Furthermore, plants that possess anticancer activity can be a safer replacement for chemotherapy with fewer side effects [9]. *R. sativus* sprouts contain polar and non-polar compounds that could possibly possess antimicrobial and anticancer activity [26]. Crude juice of the *R. sativus* inhibited the growth of *E. coli, P. pyocyaneus, S. typhi*, and *B. subtilis in vitro*. This common plant may be an important source of antimicrobial substances [27]. The cysteine-rich peptides (Rs-AFP1 and Rs-AFP2) isolated from *R. sativus* showed substantial antifungal activity against several fungal species with minimal inhibitory concentration of 30–60 µg/mL. Both Rs-AFPs are among the most potent antifungal proteins characterized. Moreover, their antibiotic activity shows a high degree of specificity to filamentous fungi [28]. The active region of the antifungal protein appears to involve ß-strands 2 and 3 in combination with the loop connecting those strands [2]. Two purified antifungal proteins RAP-1 and RAP-2 isolated from Korean *R. sativus* seeds (*R. sativus*) exhibited growth-inhibitory activities against *Candida albicans* and *Saccharomyces cerevisiae* [3]. The protein AFP1 isolated from the *R. sativus* showed antifungal activity against *Fusarium culmorum* [29]. The *R. sativus* released biocidal compounds, mainly isothiocyanates, produced during the enzymic degradation of glucosinolates present in the plant cell. The highest fungicidal activity depended on the concentration of isothiocyanates [30]. A neutral fraction of kaiware *R. sativus* extract aqueous in vitro showed proliferation inhibition of mouse embryo fribroblast 3T3 cells and papovavirus SV40 transformed 3T3 cells with IC50 of 17.4 and 8.7 µg/mL [31]. Diaminotoluene (2,4-D) showed highest cytotoxic activity against HeLa cells, 4,4´-methylenedianiline (4,4-D) intermediate, and 1,6-hexanediamine (1,6-D) lowest cytotoxicity. However,the phytotoxicity decreased in the order of 4,4-D >2,4-D>1,6-D [32]. Acetosyringone is an important monocyclic phenolic signal inducer molecule produced by the plant in response to wounding, which influences the transformation rate of infected plants through the activation of virulence genes [33]. Plant bioactive compounds such as polyphenols and flavonoids are associated with various biological properties including antioxidant activity. These antioxidants act as a redox potential, reducing agents, hydrogen donors, unpaired electrons, singlet oxygen quenchers, or chelate metal cations [34]. The molecular structure and the position of hydroxyl group

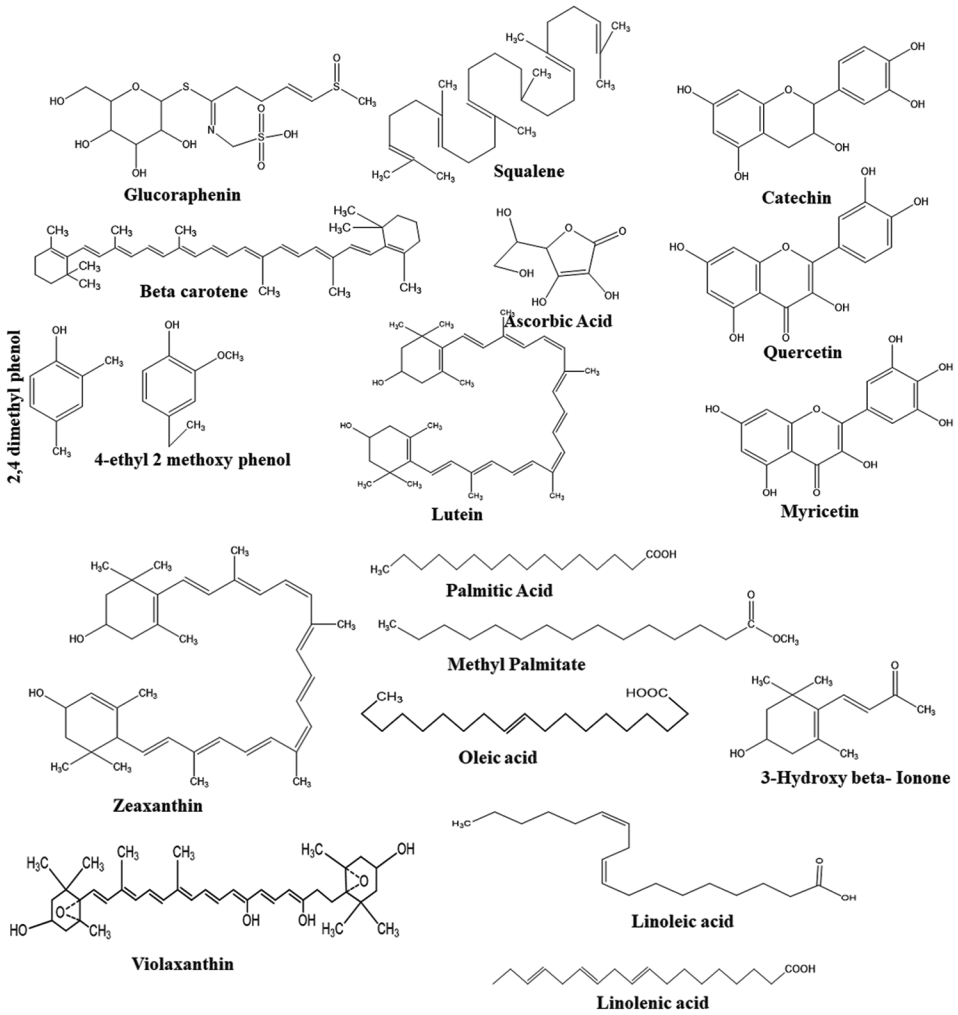

Fig. 1: Structure of various phyto-constituents existing in the *Raphanus sativus* L

Table 1: Effects of *Raphanus sativus L* extract on various cancer cell line

S. No.	Cell line	Pharmacological effect	References
1.	MDA-MB-231 human breast cancer cells	Reduces expression of ERB2 and ERB3 expression in breast cancer cell line. Over expression of these 2 genes have been identified in most of the breast cancer	[64,65]
2.	MDA-MB-231	This breast cancer cell line shows reduction in cell viability on treatment with *R. sativus* leaf and root as well which proves its anti-proliferative activity. *R. sativus* leaf shows IC50 value 453.2±1.9 mcg/mL and *R. sativus* root shows IC_{50} value 470±2.6 lg/mL, where the standard Doxorubicin shows 1.1±0.04	[66,67]
3.	A549 (Epithelial carcinoma cell line)	This adenocarcinomic human alveolar basal epithelial cell line shows reduction in cell viability on treatment with *R. sativus* leaf and root as well which proves its anti-proliferative activity. *R. sativus* leaf shows IC50 value 217±2.1 mcg/ml and *R. sativus* root shows IC50 value 250.6±3.1 lg/mL, where the standard Doxorubicin shows 1±0.02	[68]
4.	HepG2 (Hepatic Cancer Cell line)	This hepatocellular carcinoma cell line shows reduction in cell viability on treatment with *R. sativus* leaf and root as well which proves its anti-proliferative activity.	[68]
5.	MCF-7 (Cell line named after Michigan Cancer Foundation)	MCF-7 is a human breast cancer cell line which can be inhibited by the treatment of *R. sativus* root and leaves, proving its anti-carcinogenic activity.	[68]
6.	NIH-3T3 (Fibroblast Cell line)	*R. sativus* leaf extract has shown inhibitory effect at 703.6 µg/mL on NIH -3T3 which is a I fibroblast cell line	[69]
7.	DL	DL cell line is a cell line for lymphoma, on which *R. sativus* leaf has shown very good anti-proliferative effect in the concentration of 423.3 µg/mL	[69]

R. sativus: Raphanus sativus

in flavonoids determine their antioxidant potential [35]. The phenolic and flavonoid compounds have been reported act as an antimicrobial activity particularly against gram-negative bacteria [36]. The hairy root extract possessing antimicrobial activity against gram-positive Plant Cell, Tissue and Organ Culture and gram-negative bacteria have been reported in several studies [37]. Plant extracts possessing a significant

amount of poly Phenolic compounds often inhibits cell adherence [38]. Among flavonoids, quercetin has the most potent antibiofilm property as it has the ability to inhibit DNA-gyrase, bacterial energy metabolism, and cell membrane function [39].

Anti-diabetic activity

Diabetes mellitus is an alarming disease which is caused by loss of glucose homeostasis resulting in high blood glucose level [40]. It is a metabolic disorder & one of the main causes of death every year [41]. The hypoglycemic effect of red *R. sativus* roots may be due to its content of flavonoids and anthocyanins [42]. The consumption of flavonoids or flavonoid-rich foods may reduce the risk of diabetes [43]. Dried red *R. sativus* roots at a concentration 7.5% was identified as the most effective in lowering urine glucose level [44]. *R. sativus* increases the lipid metabolism and lowers the lipid plasma by increasing the activity of lipoprotein lipase [45]. *R. sativus* significantly reduced the starch-induced-postprandial glycemic load, suggesting that it has a potent antidiabetic activity [46]. Pelargonidin which is an anthocyanin has been found to be effective to reduce blood sugar level [47]. By various mechanism *R. sativus* root extracts have shown the effect in reducing the blood sugar like regulation of hormones related to glucose metabolism, preventing oxidative stress, balancing out sugar uptake and absorption. *R. sativus* root extract has been shown to increase the level of adiponectin which is involved in the regulation of glucose and fat metabolism. Adiponectin found to increase insulin sensitivity, enhancing the bodyweight reduction, increasing fatty acid oxidation, and increasing gluconeogenesis [48].

Anti-nephrotoxicity activity

Dimethoate-intoxicated rats showed a constellation of disorders in renal function witnessed by increased urea, creatinine, and uric acid levels [49]. *R. sativus* and leek juices have a high potent protective effect against oxidative stress [50]. *R. sativus* extract and zearalenone succeeded in restoring the antioxidant enzyme activities since it caused a significant increase in GSH and SOD activity in the liver and kidney which may be due to the higher content of isothiocyanate, kaempferol glycosides, and L-tryptophan compounds in R. sativus extract and their ability to scavenge free radicals [51]. *R. sativus* methanolic extract reversed the decreased levels of reduced GSH and SOD which may be due to the presence of polyphenolic compounds [52]. *R. sativus* and leek juices to dimethoate intoxicated mice restored these altered biochemical parameter levels to within normal limits and improved kidney dysfunction [52]. *R. sativus* exhibits nephroprotection against nephrotoxicity induced by gentamicin. They concluded that this may be due to its potent antioxidant effect [53]. Rifampicin causes acute renal failure and other renal or nephrotoxicity problems [54]. Ethnomedicinal plants reduce nephrotoxicity may be due to their antioxidant properties due to flavonoids, alkaloids, saponins, and tannins present in these plants [55]. Flavonoids like quercetin, is nephroprotective and have been depicted as inhibiting drug-induced nephrotoxicity in experimental animals [56]. Leaves of *R. sativus* contain quercetin which protects the cell lining and hence with the treatments of water extract and ethanolic extract maintained the normal morphology of the kidney [57]. Diuretics are drugs that increase the formation of urine. They act either by increasing the glomerular filtration rate and thus increasing the production of urine. *R. sativus* has excellent diuretic properties [58]. Ethanolic and water extract of *R. sativus* have a nephroprotective effect against rifampicin [59].

Anti-cancer activity

Cancer is one of the main causes of death and almost one-third of cancers are related to dietary factors [7]. Young *R. sativus* which is a cruciferous vegetable, is rich in vitamin A,vitamin C, and essential minerals which can prevent blood acidification [60]. It contains sulforaphane having quinone reductase activity which inhibits the growth of colon cancer cells [7]. The chemotherapeutic drug like mitomycin C, was used as the positive control for comparing the sensitivity of the cancer cell line to the clinical and conventional anticancer drug as well as with the extract. Mitomycin C possessed a cytotoxicity against the HCT116 cells. The presence of sulforaphane and sulforaphane has already been reported for cruciferous plants [61]. Sulforaphane and Sulforaphane demonstrated a stronger cytotoxicity on PC3 prostate cancer cell line and HCT116 (Table 1), colon cancer cell line than the chemotherapeutic drug (IC50 = 6.67±0.07 and 10.67±2.27 lg/mL, respectively). The Thai rat-tailed *R. sativus* extract possessed a low IC_{50}-indicating its cytotoxicity and suggesting a strong anticancer activity. Saponin-also found in cruciferous plants-was reported to cause some necrotic cell death [62]. Isothiocyanates are reported to inhibit carcinogenesis by various mechanisms [16]. Sulforaphane increases many phase II metabolic enzymes responsible for the reduction of oxidative stress molecules including carcinogens [63]. Sulforaphane reportedly enhances cytokine-TRAIL-mediated apoptosis through down-regulation of ERK and Akt in lung adenocarcinomas [5]. *R. sativus* leaves have been used to see anti-cancer effects using various cell lines.

CONCLUSION

It becomes very much easy to justify the multi-disciplinary property of *R. sativus* from the above-mentioned detailed discussion. *R. sativus* is such a easily available vegetable for almost all seasons which has got some phytochemical properties in each of the part of it like fruit and leaf which makes it more potent to work against various lifestyle disorders and also opens a wide path for the intense research on various life-threatening diseases to the world of science.

AUTHOR'S CONTRIBUTION

Sakshar Saha, Subham Paul, SK Aman Afroz, Ahana Dey, Atanu Chatterjee, and Ritu Khanra. All gave the same effort to complete the manuscript.

CONFLICT OF INTEREST

The researchers claim no conflict of interests.

AUTHOR'S FUNDING

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

REFERENCES

1. Hanlon PR, Barnes DM. Phytochemical composition and biological activity of 8 varieties of radish (*Raphanus sativus* L.) sprouts and mature taproots. J Food Sci 2011;76:C185-92. doi: 10.1111/j.1750-3841.2010.01972.x, PMID 21535648
2. Tang D, Dong Y, Ren H, Li L, He C. A review of phytochemistry, metabolite changes, and medicinal uses of the common food mung bean and its sprouts (*Vigna radiata*). Chem Cent J 2014;8:4. doi: 10.1186/1752-153X-8-4, PMID 24438453
3. Abdou IA, Abou-Zeid AA, El-Sherbeeny MR, Abou-El-Gheat ZH. Antimicrobial activities of *Allium sativum*, *Allium cepa*, *Raphanus sativus*, *Capsicum frutescens*, *Eruca sativa*, *Allium kurrat* on bacteria. Qual Plant Mater Veg 1972;22:29-35. doi: 10.1007/BF01099735
4. Lim S, Ahn JC, Lee EJ, Kim J. Antiproliferation effect of sulforaphene isolated from radish (*Raphanus sativus* L.) seeds on A549 cells. Appl Biol Chem 2020;63:1-8.
5. Thakur M, Melzig MF, Fuchs H, Weng A. Chemistry and pharmacology of saponins: Special focus on cytotoxic properties. Bot Targets Ther 2011;1:19-29.
6. Rice-Evans CA, Miller NJ, Bolwell PG, Bramley PM, Pridham JB. The relative antioxidant activities of plant-derived polyphenolic flavonoids. Free Radic Res 1995;22:375-83. doi: 10.3109/10715769509145649, PMID 7633567
7. Khalid R, Anwar MI, Ambreen A. Nephroprotective effects of *Raphanus sativus* (Radish) in rifampicin induced nephrotoxicity in adult albino rabbits. J Toxicol Pharm Sci 2018;2:7-12.
8. Kirtikar KR, Basu BD. Indian Medicinal Plants. Vol. 1993. Allahabad: Lalit Mohan Publication; 1935. p. 1347-8.
9. Ghayur MN, Gilani AH. Radish seed extract mediates its cardiovascular inhibitory effects via muscarinic receptor activation. Fundam Clin Pharmacol 2006;20:57-63. doi: 10.1111/j.1472-8206.2005.00382.x, PMID 16448395

10. Integrated Taxonomic Information System - Report. Available from: https://www.itis.gov/servlet/SingleRpt/SingleRpt?search_topic=TSN&search_value=23290#null [Last accessed on 2022 May 09].
11. *Raphanus sativus* (Cultivated *R. sativus*): Go Botany. Native Plant Trust; n.d. Available from: https://gobotany.nativeplanttrust.org/species/raphanus/sativus [Last accessed on 2022 May 09].
12. *Raphanus sativus*; n.d. Useful Tropical Plants. Available from: https://tropical.theferns.info/viewtropical.php?id=Raphanus+sativus [Last accessed on 2022 May 09].
13. Banihani SA. Radish (*Raphanus sativus*) and diabetes. Nutrients 2017;9:1014. doi: 10.3390/nu9091014, PMID 28906451
14. Information about Nutrients and Herbs - Uses, Benefits. Planet Ayurveda; 2019. Available from: https://www.planetayurveda.com/R. sativus [Last accessed on 2022 May 09].
15. Gamba M, Asllanaj E, Raguindin PF, Glisic M, Franco OH, Minder B, *et al*. Nutritional and phytochemicaln characterization of radish (*Raphanus sativus*): A systematic review. Trends Food Sci Technol 2021;113:205-18. doi: 10.1016/j.tifs.2021.04.045
16. Barillari J, Iori R, Papi A, Orlandi M, Bartolini G, Gabbanini S, *et al*. Kaiware Daikon (*Raphanus sativus* L.) extract: A naturally multipotent chemopreventive agent. J Agric Food Chem 2008;56:7823-30. doi: 10.1021/jf8011213, PMID 18665601
17. Charoensiri R, Kongkachuichai R, Suknicom S, Sungpuag P. Beta-carotene, lycopene, and alpha-tocopherol contents of selected Thai fruits. Food Chem 2009;113:202-7. doi: 10.1016/j.foodchem.2008.07.074
18. Yin MC, Cheng WS. Antioxidant activity of several Allium members. J Agric Food Chem 1998;46:4097-101. doi: 10.1021/jf980344x
19. Bozin B, Mimica-Dukic N, Samojlik I, Goran A, Igic R. Phenolics as antioxidants in garlic (*Allium sativum* L., *Alliaceae*). Food Chem 2008;111:925-9. doi: 10.1016/j.foodchem.2008.04.071
20. Vargas R, Perez RM, Perez S, Zavala MA, Perez C. Antiurolithiatic activity of *Raphanus sativus* aqueous extract on rats. J Ethnopharmacol 1999;68:335-8. doi: 10.1016/s0378-8741(99)00105-1, PMID 10624898
21. Lee Y, Howard LR, Villalón B. Flavonoids and antioxidant activity of fresh pepper (*Capsicum annuum*) cultivars. J Food Sci 1995;60:473-6. doi: 10.1111/j.1365-2621.1995.tb09806.x
22. Singh D, Chaudhuri PK. Structural characteristics, bioavailability and cardioprotective potential of saponins. Integr Med Res 2018;7:33-43. doi: 10.1016/j.imr.2018.01.003, PMID 29629289
23. Furchgott RF, Zawadzki JV. The obligatory role of endothelial cells in the relaxation of arterial smooth muscle by acetylcholine. Nature 1980;288:373-6. doi: 10.1038/288373a0, PMID 6253831
24. Gilani AH, Aftab K, Saeed SA, Ahmad VU, Noorwala M, Mohammad FV. Pharmacological characterization of symphytoxide-A, a saponin from *Symphytum officinale*. Fitoterapia (Milano) 1994;65:333-9.
25. Gilani AH, Ghayur MN, Houghton PJ, Jabeen Q, Kazim SF, Jumani MI, *et al*. Studies on the hypotensive, cardio-suppressant, vasodilator and antiplatelet activities of betel nut crude extract and its constituents. Int J Pharmacol 2005;2:33-41. doi: 10.3923/ijp.2006.33.41
26. Kim BR, Park JH, Kim SH, Cho KJ, Chang MJ. Antihypertensive properties of dried radish leaves powder in spontaneously hypertensive rats. Korean J Nutr 2010;43:561-9. doi: 10.4163/kjn.2010.43.6.561
27. Kook SH, Choi KC, Lee YH, Cho HK, Lee JC. *Raphanus sativus* L. seeds prevent LPS-stimulated inflammatory response through negative regulation of the p38 MAPK-NF-κB pathway. Int Immunopharmacol 2014;23:726-34. doi: 10.1016/j.intimp.2014.11.001, PMID 25467201
28. Khamees AH. Phytochemical and pharmacological analysis for seeds of two varieties of Iraqi *Raphanus sativus*. Int J Pharm Sci Rev Res 2017;43:237-42.
29. Terras FR, Schoofs HM, De Bolle MF, Van Leuven F, Rees SB, Vanderleyden J, *et al*. Analysis of two novel classes of plant antifungal proteins from radish (*Raphanus sativus* L.) seeds. J Biol Chem 1992;267:15301-9. doi: 10.1016/S0021-9258(19)49534-3, PMID 1639777
30. De Samblanx GW, del Carmen AF, Sijtsma L, Plasman HH, Schaaper WM, Posthuma GA, *et al*. Antifungal activity of synthetic 15-mer peptides based on the Rs-AFP2 (*Raphanus sativus* antifungal protein 2) sequence. Pept Res 1996;9:262-8. PMID 9048418
31. Park JH, Shin KK, Hwang CW. New antimicrobial activity from Korean radish seeds (*Raphanus sativus* L.). J Microbiol Biotechnol 2001;11:337-41.
32. Hans MR, Cornelis PW, Martinus SW, Lolke S, Broekaert WF, Bronwen RS, *et al*. Antifungal Protein Fragment-Derived Peptides and their Agricultural, Therapeutic, or Preservative Uses. Vil. 21. UK: PCT Appl Wo; 1997. p. 97.
33. Smolinska U, Horbowicz M. Fungicidal activity of volatiles from selected cruciferous plants against resting propagules of soil-borne fungal pathogens. J Phytopathol 1999;147:119-24. doi: 10.1111/j.1439-0434.1999.tb03817.x
34. Akihiro M, Koji K, Hiroyoshi O, Kazuaki K, Yoshiko A. Antitumor substances from vegetables, their manufacture, and pharmaceutical compositions. Jpn Kokai Tokkyo Koho 1993;49:99.
35. Kim MN, Jang JC, Lee IM, Lee HS, Yoon JS. Toxicity and biodegradation of diamines. J Environ Sci Health B 2002;37:53-64. doi: 10.1081/PFC-120002897, PMID 11990359
36. Gelvin SB. *Agrobacterium* and plant genes involved in T-DNA transfer and integration. Annu Rev Plant Physiol Plant Mol Biol 2000;51:223-56. doi: 10.1146/annurev.arplant.51.1.223, PMID 15012192
37. Rice-Evans CA, Miller NJ, Paganga G. Structure-antioxidant activity relationships of flavonoids and phenolic acids. Free Radic Biol Med 1996;20:933-56. doi: 10.1016/0891-5849(95)02227-9, PMID 8743980
38. Kumar S, Pandey AK. Chemistry and biological activities of flavonoids: An overview. ScientificWorldJournal 2013;2013:162750. doi: 10.1155/2013/162750, PMID 24470791
39. Caillet S, Côté J, Sylvain JF, Lacroix M. Antimicrobial effects of fractions from cranberry products on the growth of seven pathogenic bacteria. Food Control 2012;23:419-28. doi: 10.1016/j.foodcont.2011.08.010
40. Yoon JY, Chung IM, Thiruvengadam M. Evaluation of phenolic compounds, antioxidant and antimicrobial activities from transgenic hairy-root cultures of gherkin (*Cucumis anguria* L.). S Afr J Bot 2015;100:80-6. doi: 10.1016/j.sajb.2015.05.008
41. Papuc C, Goran GV, Predescu CN, Nicorescu V, Stefan G. Plant polyphenols as antioxidant and antibacterial agents for shelf-life extension of meat and meat products: Classification, structures, sources, and action mechanisms. Compr Rev Food Sci Food Saf 2017;16:1243-68. doi: 10.1111/1541-4337.12298, PMID 33371586
42. Ouyang J, Sun F, Feng W, Sun Y, Qiu X, Xiong L, *et al*. Quercetin is an effective inhibitor of quorum sensing, biofilm formation and virulence factors in *Pseudomonas aeruginosa*. J Appl Microbiol 2016;120:966-74. doi: 10.1111/jam.13073, PMID 26808465
43. Scheen AJ. Drug treatment of non-insulin-dependent diabetes mellitus in the 1990s. Achievements and future developments. Drugs 1997;54:355-68. doi: 10.2165/00003495-199754030-00001, PMID 9279500
44. Gispen WH, Biessels GJ. Cognition and synaptic plasticity in diabetes mellitus. Trends Neurosci 2000;23:542-9. doi: 10.1016/s0166-2236(00)01656-8, PMID 11074263
45. Vinayagam R, Xu B. Antidiabetic properties of dietary flavonoids: A cellular mechanism review. Nutr Metab (Lond) 2015;12:60. doi: 10.1186/s12986-015-0057-7, PMID 26705405
46. Bahadoran Z, Mirmiran P, Azizi F. Dietary polyphenols as potential nutraceuticals in management of diabetes: A review. J Diabetes Metab Disord 2013;12:43.
47. Shin T, Ahn M, Kim GO, Park SU. Biological activity of various radish species. Orient Pharm Exp Med 2015;15:105-11. doi: 10.1007/s13596-015-0183-9
48. Yoshida M, Kimura H, Kyuki K, Ito M. Effect of combined Vitamin E and insulin administration on renal damage in diabetic rats fed a high cholesterol diet. Biol Pharm Bull 2005;28:2080-6. doi: 10.1248/bpb.28.2080, PMID 16272693
49. Tiwari AK. Revisiting "Vegetables" to combat modern epidemic of imbalanced glucose homeostasis. Pharmacogn Mag 2014;10:S207-13. doi: 10.4103/0973-1296.133211, PMID 24991093
50. Valenti L, Riso P, Mazzocchi A, Porrini M, Fargion S, Agostoni C. Dietary anthocyanins as nutritional therapy for nonalcoholic fatty liver disease. Oxid Med Cell Longev 2013;2013:145421. doi: 10.1155/2013/145421, PMID 24282628
51. Manivannan A, Kim JH, Kim DS, Lee ES, Lee HE. Deciphering the nutraceutical potential of *Raphanus sativus*--a comprehensive overview. Nutrients 2019;11:402. doi: 10.3390/nu11020402, PMID 30769862
52. Moram GS, Kholief TE, Ahmed AT. Antioxidant effect of radish (*Raphanus sativus* L.) and leek (*Allium porrum* L.) juices against hepatotoxicity and nephrotoxicity induced by dimethoate in male albino mice. World J Pharm Res 2015;4:215-46.
53. Salah-Abbès JB, Abbès S, Ouanes Z, Houas Z, Abdel-Wahhab MA, Bacha H, *et al*. Tunisian radish extract (*Raphanus sativus*) enhances the antioxidant status and protects against oxidative stress induced by zearalenone in BALB/c mice. J Appl Toxicol 2008;28:6-14. doi: 10.1002/jat.1240, PMID 17385802
54. Van Assendelft AH. Rifampicin and nephrotoxicity. Arch Intern Med 1988;148:1228b. doi: 10.1001/archinte.148.5.1228b, PMID 3365091
55. Abed SA, El-Shazely MO, Ahmed KA, Abdelmawla EM, Ibrahim AK. Pathological, immunohistochemical and biochemical studies on the therapeutic effect of *Raphanus sativus* Oil on streptozotocin induced

diabetic rats, Egyptain. J Comp Pathol Clin Pathol 2015;28:1-17.
56. Chen YQ, Chen HY, Tang QQ, Li YF, Liu XS, Lu FH, *et al*. Protective effect of quercetin on kidney diseases: From chemistry to herbal medicines. Front Pharmacol 2022;13:968226. doi: 10.3389/fphar.2022.968226, PMID 36120321
57. Muthukumar T, Jayakumar M, Fernando EM, Muthusethupathi MA. Acute renal failure due to rifampicin: A study of 25 patients. Am J Kidney Dis 2002;40:690-6. doi: 10.1053/ajkd.2002.35675, PMID 12324902
58. Borrelli F, Izzo AA. The plant kingdom as a source of anti-ulcer remedies. Phytother Res 2000;14:581-91. doi: 10.1002/1099-1573(200012)14:8<581:aid-ptr776>3.0.co;2-s, PMID 11113992
59. Devi PS, Shyamala DC. Protective effect of quercetin in cisplatin-induced cell injury in the rat kidney. Indian J Pharmacol 1999;31:422-6.
60. Kumar BS, Swamy BV, Archana S, Anitha M. A review on natural diuretics. Res J Pharm Biol Chem Sci 2010;1:615-34.
61. Keck AS, Finley JW. Cruciferous vegetables: Cancer protective mechanisms of glucosinolate hydrolysis products and selenium. Integr Cancer Ther 2004;3:5-12. doi: 10.1177/1534735403261831, PMID 15035868
62. Pocasap P, Weerapreeyakul N, Barusrux S. Cancer preventive effect of Thai rat-tailed radish (*Raphanus sativus* L. var. caudatus Alef). J Funct Foods 2013;5:1372-81. doi: 10.1016/j.jff.2013.05.005
63. Clarke JD, Dashwood RH, Ho E. Multi-targeted prevention of cancer by sulforaphane. Cancer Lett 2008;269:291-304. doi: 10.1016/j.canlet.2008.04.018, PMID 18504070
64. Gross-Steinmeyer K, Stapleton PL, Tracy JH, Bammler TK, Lehman T, Strom SC, *et al*. Influence of Matrigel-overlay on constitutive and inducible expression of nine genes encoding drug-metabolizing enzymes in primary human hepatocytes. Xenobiotica 2005;35:419-38. doi: 10.1080/00498250500137427, PMID 16012075
65. Zhang Y, Munday RE, Jobson HE, Munday CM, Lister C, Wilson P, *et al*. Induction of GST and NQO1 in cultured bladder cells and in the urinary bladders of rats by an extract of broccoli (*Brassica oleracea* italica) sprouts. J Agric Food Chem 2006;54:9370-6. doi: 10.1021/jf062109h, PMID 17147420
66. Jin CY, Moon DO, Lee JD, Heo MS, Choi YH, Lee CM, *et al*. Sulforaphane sensitizes tumor necrosis factor-related apoptosis-inducing ligand-mediated apoptosis through down regulation of ERK and Akt in lung adenocarcinoma A549 cells. Carcinogenesis 2007;28:1058-66. doi: 10.1093/carcin/bgl251, PMID 17183064
67. Kim WK, Kim JH, Jeong DH, Chun YH, Kim SH, Cho KJ, *et al*. Radish (*Raphanus sativus* L. leaf) ethanol extract inhibits protein and mRNA expression of ErbB2 and ErbB3 in MDA-MB-231 human breast cancer cells. Nutr Res Pract 2011;5:288-93. doi: 10.4162/nrp.2011.5.4.288, PMID 21994522
68. Noman OM, Nasr FA, Alqahtani AS, Al-Zharani M, Cordero MA, Alotaibi AA, *et al*. Comparative study of antioxidant and anticancer activities and HPTLC quantification of rutin in white radish (*Raphanus sativus* L.) leaves and root extracts grown in Saudi Arabia. Open Chem 2021;19:408-16. doi: 10.1515/chem-2021-0042
69. Jamuna KS, Suma MS, Ramesh CK, Mahmood R, Nanjundaswamy L. Studies on *in vitro* antiproliferative activities in Cruciferae vegetables. J Appl Hortic 2017;19:230-4. doi: 10.37855/jah.2017.v19i03.39