Pea, *Pisum sativum*, and Its Anticancer Activity

Runchana Rungruangmaitree, Wannee Jiraungkoorskul

Mahidol University International College, Mahidol University, Salaya Campus, Nakhon Pathom, 1Department of Pathobiology, Faculty of Science, Mahidol University, Bangkok, Thailand

ABSTRACT

*Pisum sativum* (Family: Fabaceae), as known as green pea or garden pea, has long been important in diet due to its content of fiber, protein, starch, trace elements, and many phytochemical substances. It has been shown to possess antibacterial, antidiabetic, antifungal, anti-inflammatory, antihypercholesterolemia, and antioxidant activities and also shown anticancer property. Its nonnutritive biologically active components include alkoalides, flavonoids, glycosides, isoflavones, phenols, phytosterols, phytic acid, protease inhibitors, saponins, and tannins. This plant is rich in apigenin, hydroxybenzoic, hydroxycinnamic, luteolin, and quercetin, all of which have been reported to contribute to its remedial properties including anticarcinogenesis property. Based on established literature on the anticancer property of *P. sativum* and possible mode of action, this review article has focused to demonstrate that *P. sativum* could be further explored for the development of anticancer treatment.

Key words: Anticancer, pea, *Pisum sativum*, plant, traditional medicine

LEGUME

Legume or pulse is one of the traditional medicines used globally because it has the amount of nutritional substances and has the efficiency of therapeutic treatments. Legumes include beans, grains, and peas as well as alfalfa, carob, clover, copaifera, fenugreek, indigo, lentil, licorice, lupin, mesquite, natto, soybean, peanut, rosewood, and tamarind are the member of the Fabaceae family. The nutritional values of legume are low fat, high protein, dietary fiber, and various of micronutrients and phytochemical substances which exhibit the medicinal properties, especially anticancer property. Pea is one of the major food legumes that can grow in different regions, and it ranks the fourth in world food legume productions next to soybean, peanut, and dry bean. Seed and sprout of pea have become increasingly consumed because people concern about their health problem by changing dietary habits. The present review explores scientific evidences to provide updated information about the properties of green pea or garden pea (*Pisum sativum*), one of the anticancer plants that is being investigated for its mechanism.

TAXONOMICAL CLASSIFICATION

The taxonomy of *P. sativum* is in the Kingdom (*Plantae*); Subkingdom (*Viridiplantae*); Infrakingdom (*Embryophyta*); Division (*Tracheophyta*); Superdivision (*Embryophyta*); Division (*Tracheophyta*); Subdivision (*Spermatophyta*); Class (*Magnoliopsida*); Superorder (*Rosanae*); Order (*Fabales*); Family (*Fabaceae*); Genus (*Pisum*); and Species (*P. sativum*)

NOMENCLATURE

The origin of *Pisum* spp. is in Southwestern Asia including Afghanistan, India, Pakistan, and then spreads to subtropic and tropic regions.

The vernacular names of *P. sativum* include Chinese pea, edible pod pea, field pea, garden pea, green pea, honey pea, sugar pea, and sweet pea (English); ertjic (Afrikaans); katar (Bengali); ervilha (Brazil); jia wan dou (Chinese); doperwten (Dutch); petit pois (French); erbsen (German); kacang ertis (Indonesian); endo (Japanese); sancak (Khem); kacang manis (Malaysia); ervilha (Portuguese); gorach (Russian); aroja (Spanish); spritart (Swiss); thua lan tao (Thai); bezelye (Turkish); ropox (Ukrainian); and dau hoa lan (Vietnamese).

PLANT DESCRIPTION OF *PISUM SATIVUM*

*P. sativum* is an herbaceous annual, with a climbing hollow stem growing up to 2–3 m long. Leaves are alternate, pinnately compound, and consist of 2–3 pairs of 1.5–8 cm long large leaf-like stipules. Flowers have five green fused sepals and five white to reddish-purple petals of different sizes. Fruit grows into a pod, 2.5–10 cm long that often has a rough inner membrane. The pod is a seed container which composed by two sealed valves and split along the seam which connects the two valves. Seeds are round, smooth, and green color [Figure 1].

PHYTOCHEMICAL SUBSTANCES

The active phytochemical substances of *P. sativum* are as follows: Asparaginase,[9] flavonoids including apigenin, daidzein, genistein, and kaempferol[10] lectin,[11-13] phenolic compounds including caffeic, catechin, coumaric acids, genticis acids, ferulic, protocatechuic, and vanillic acids[14,15] pisatin and an allelopathic active substances[16,17] proanthocyanidin,[18] saponins,[19,20] and steroid phytohormone including brassinosteroid[21,22] and tannins[23]

This is an open access article distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 3.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as the author is credited and the new creations are licensed under the identical terms.

For reprints contact: reprints@medknow.com
TRADITIONAL USES

P. sativum can be consumed in raw form as well as cooked or frozen form. The various bioactive compounds’ current uses or phytochemical properties of P. sativum from several literature reviews are antibacterial,[24,25] anti-Helicobacter pylori,[26,27] anticancer,[28] antidiabetic,[29,30] antifungal,[31] anti-inflammatory,[32,33] antilipidemic,[34,35] and antioxidant[36,37] activities. Moreover, it can act as insecticidal activity.[38-40]

ANTICANCER ACTIVITY

The extracts of P. sativum have been investigated and found to be pharmacologically active inducing anticancer activity. Clemente et al.[41,42] compared the effect of Bowman-Birk trypsin-chymotrypsin inhibitor, a potential cancer chemopreventive agent, with the protease inhibitors, rTl1B and rTl2B, from P. sativum seed from the United Kingdom. They studied the inhibitory activities on the growth of human colorectal adenocarcinoma HT-29. The rTl1B showed the effective 46 μM of IC50. El-Aassar et al.[43] studied the P. sativum extracted lectins from Egypt exhibited the antiproliferative property to liver cancer cell line. Patel[44] extracted lectin from leaves and buds of P. sativum from Saudi Arabia and studied cytotoxicity to many cancer cell lines such as MCF-7 (breast), HepG-2 (liver), HEP-2 (larynx), and HCT-116 (colon). In recently, Stanisavljevic et al.[45] identified the amount of phenolic compounds from pea seeds in different colors from Croatia. They reported the darker seed color, the higher total phenolic content in the form of gallic acid, epigallocatechin, naringenin, and apigenin. The seed extracts also showed the cytotoxic effect on malignant cell lines, for example, LS174 (colon), MDA-MB-453 (breast), A594 (lung), and K562 (blood). In several review articles have mentioned the health benefits of P. sativum due to its concentration and properties of starch, protein, fiber, vitamins, minerals, and phytochemicals.[46-48] In addition, the plants in the same Fabaceae family also show the anticancer activities such as alfalfa, Medicago sativa;[49] carob, Ceratonia siliqua;[50] lentil, Lens culinaris;[51] and soybean, Glycine max.[52]

PHYTOCHEMICAL SUBSTANCES ACT AS ANTICANCER ACTIVITY

Several studies found that a diet high in whole grains including legumes may reduce the risk of cancer such as breast cancer,[53] colorectal cancer,[54,55] and endometrial cancer.[56,57] Various phytoconstituents in legumes have been reported their anticancer activities.

Isoflavones

The most abundant isoflavones in the legume sprouts were found as genistein followed by daidzein. Sukanya and Gayathri[58] studied the growth inhibitory properties of isoflavones extract of legume sprout from India on breast cancer MCF-7. Moreover, Pudenz et al.[59] reported that isoflavones worked as phytoestrogens and could inhibit tumorigenesis both in vitro and in vivo studies. Their mechanisms were DNA repair, induction of apoptosis, cell proliferation, migration, and invasion.

Lectins

There are the most abundant lectin proteins in several legume tree barks, and they have great potential as antitumor and anticancer properties.[60] Other legume lectins also have antiproliferative and anticancer properties such as concanavalin A, a lectin from Jack bean seed.[61] Several studies have suggested the cytotoxicity or tumor inhibition mechanisms of lectins to various tumor cell lines such as skin,[62,63] liver, bile duct, and bone cell lines.[64]

Saponins

A number of legumes contain saponins such as soybean, chickpea, peanut, and lentil, which have reported to exhibit anticancer activities. Several studies suggest that legume saponins may possess anticancer activities in melanoma cell,[65] colon cancer,[66,67] and cervical cancer.[68] The mechanism of suppressing the metastatic of cancer was mentioned by Chang et al.[69] using sialyltransferase inhibition activity of saponin on the cell surface. The other mechanism was saponin regulation of the apoptosis pathway enzymes, leading to programmed cell death of cancer cells.[70,71]

Phenolic compounds

It has been recognized that phenolic compounds act as antioxidants and were found high amount in peas.[72] The association of antioxidant properties of plant phenolic compounds and their effects in the prevention of various oxidative stress diseases, for example, cancer or cardiovascular diseases were explained by Dai and Mumper.[73]

CONCLUSION

Legume is considered as a good and nonexpensive of plant foods. It plays important roles in human nutrition and also in prevention in many diseases, especially cancer. Several researchers reported that P. sativum is rich in many nutritional and nonnutritional components which can prove to be prevention and inhibition cancer. This review article has attempted to compile the new medicinal plant P. sativum, to be one of the choices of anticancer plants.

Acknowledgement

A special thanks to the members of the Fish Research Unit, Department of Pathobiology, Faculty of Science, Mahidol University, for their support. The author would like to thank anonymous reviewers and editors of this review article for their perceptive comments and positive criticism in this review article.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.
REFERENCES

1. Schneider AV. Overview of the market and consumption of pulses in Europe. Br J Nutr 2002;88 Suppl 3:5243-50.

2. Vohra K, Dureja H, Garg V. An insight of pulses: From food to cancer treatment. J Pharmacogn Nat Prod 2015;1:108.

3. Vidal-Valverde C, Frias J, Hernandez A, Martin-Alvarez P, Sierra I, Rodriguez C, et al. Assessment of nutritional compounds and anti-nutritional factors in pea (Pisum sativum) seeds. J Sci Food Agric 2003;83:298-306.

4. Chon SU. Total polyphenols and bioactivity of seeds and sprouts in several legumes.Curr Pharm Des 2013;19:6112-24.

5. Integrated Taxonomic Information System (ITIS). *Pisum sativum* L. Taxonomic Serial No. 24.

6. Majed H, Safdar W, Ali B, Mohanna A, Ahmad I, Mumtaz A. Genetic assessment of the genus *Pisum* L. based on sequence specific amplification polymorphism data. J Med Plants Res 2012;6:956-67.

7. Lim T. Edible Medicinal and Non-Medicinal Plants. Vol. 2. Fruits. Netherlands: Springer; 2012.

8. Pavel PN. Plant fact sheet for pea (*Pisum sativum* L.). USDA-Natural Resources Conservation Service, Pullman, Washington; 2012.

9. Chagas E, Sodex L. Purification and properties of asparaginase from the testa of immature seeds of pea (*Pisum sativum* L.). Braz Arch Biol Technol 2001;44:239-45.

10. Timoarcă M, Voilmannova A. Determination of flavonoid content in coloured peas (*Pisum sativum* L.), in relation to cultivars dependence and storage duration under natural conditions. Povarăvaristva 2010;4:58-62.

11. Bala M, Nag T, Mathur K, Kumar S, Vyas M, Saini A, Tomar B. In vitro callus induction for determination of lectin activity in pea (*Pisum sativum* L.) variety (AP-1). Rom Biotechnol Lett 2010;15:5781-7.

12. Patel A. Isolation, characterization and production of a new recombinant lectin protein from leguminous plants. Biochem Comp 2014;2:1-9.

13. Ng TB, Chan YS, Ng CC, Wong JH. Purification and characterization of a lectin from green leguminous plants. Biochem Comp 2014;2:1‑9.

14. Chong SU. Total polyphenols and bioactivity of seeds and sprouts in several legumes. J Sci Food Agric 2003;83:298‑306.

15. Saha H, Prakash A, Venkat Kumar S, Manimgalar S, Devi Rajeswari V. Evaluation of antioxidant activity of *Pisum sativum* (pod and grain) and detection of its bioactive compounds by GCMS analysis. Pharm. Lib 2014;6:369-65.

16. Taylor VG, Fields PG, Sutherland DH. Insecticidal components from field pea extracts: Soyasaponins and lycostilcins. J Agric Food Chem 2004;52:7484-90.

17. Sahito H, Amin M, Mal B, Channa M, Dhillo K. Efficacy of different insecticides against thrips on peas, *Pisum sativum* (L.) in vivo condition. J Agric Sustain 2013;3:56-77.

18. Preethep Kumar P, Balasubramanian A, Mohan S. Efficacy of extracts of pea (*Pisum sativum* L.) in the management of saw-toothed beetle, *Oryzaephilus surinamensis* (L.) infesting stored neem (*Azadirachta indica*) Jussi seeds. Sky J Agric Res 2015;4:67-71.

19. Clemente A, Gee JM, Johnson IT, Mackenzie DA, Domoney C. Pea (*Pisum sativum* L.) protease inhibitors from the Bowman-Birk class influence the growth of human colorectal adenocarcinoma HT29 cells in vitro. J Agric Food Chem 2005;53:8979-86.

20. Clemente A, Carmen Marin-Manzano M, Jiménez E, Carmen Arques M, Domoney C. The anti-proliferative effect of T11B, a major Bowman-Birk isooinhibitor from pea (*Pisum sativum* L.), on HT29 colon cancer cells is mediated through protease inhibition. Br J Nutr 2012;108 Suppl 1:135-44.

21. El-Aassar MR, Hafez EE, El-Deeb NM, Fouda MM. Microencapsulation of lectin anti-cancer agent and controlled release by alginate beads, biosafety approach. Int J Macromol 2005;36:94-98.

22. Dahl WJ, Foster LM, Tyler RT. Review of the health benefits of peas (*Pisum sativum* L.). Br J Nutr 2012;108 Suppl 1:53-10.

23. Rosenthal GA, Nikorno P. The natural abundance of Lecanasavin, an active anti-cancer agent, in alfalfa, Medicago sativa (L.). Pharm Biol 2000;38:1-6.

24. Custódio L, Escapa A, Patarra J, Aligue R, Albericio F, Neng N, et al. Sapwood of carob tree (*Carobia xilosa* L.) as a potential source of bioactive compounds. Proc Nat Acad Sci 2013;7:225-9.

25. Chan YS, Yu H, Lai N, Ng TB. Lectin from green speckled lentil seeds (*Lens culinaris*) triggered apoptosis in nasopharyngeal carcinoma cell lines. Chin Med 2016;10:25.

26. Suthar AC, Banavalikar MV, Bhoyni MK. Pharmacological activities of Genistin, an isoflavone from soy (*Glycine max*): Part I – Anti-cancer activity. Indian J Exp Biol 2001;39:511-9.

27. Thompson MD, Thompson HJ, Brick MA, McGinley JN, Jiang W, Zhu Z, et al. Mechanisms associated with dose-dependent inhibition of rat mammary carcinogenesis by dry bean (*Phaseolus vulgaris*, L.). J Nutr 2008;138:2091-7.

28. Wang Y, Wang Z, Fu L, Chen Y, Fang J. Legume consumption and colorectal adenoma risk: A meta-analysis of observational studies. PLoS One 2013;8:e73355.

29. Zhu B, Sun Y, Qi L, Zhong R, Miao X. Dietary legume consumption reduces risk of colorectal cancer: Evidence from a meta-analysis of cohort studies. Sci Rep 2015;5:8797.
52. Terry P, Vanio H, Welk A, Weiderpass E. Dietary factors in relation to endometrial cancer: A nationwide case-control study in Sweden. Nutr Cancer 2002;42:25-32.

53. Ollberding NJ, Lim U, Wilkens LR, Setiawan WV, Shvetsov YB, Henderson BE, et al. Legume, soy, tofu, and isoflavone intake and endometrial cancer risk in postmenopausal women in the multiethnic cohort study. J Natl Cancer Inst 2012;104:67-76.

54. Sukanya S, Gayathri G. Variability in the distribution of daidzein and genistein in legume sprouts and their anticancer activity with mcf-7 breast cancer cells. Acad J Cancer Res 2014;7:173-8.

55. Pudenz M, Roth K, Gerhauser C. Impact of soy isoflavones on the epigenome in cancer prevention. Nutrients 2014;6:4218-72.

56. Liu B, Bian HJ, Bao JK. Plant lectins: Potential antineoplastic drugs from bench to clinic. Cancer Lett 2010;287:1-12.

57. Lei HY, Chang CP. Lectin of concanavalin A as an anti-hepatoma therapeutic agent. J Biomed Sci 2009;16:10.

58. Sames K, Schumacher U, Halla Z, Van Damme EJ, Peumans WJ, Asmus B, et al. Lectin and proteoglycan histochemistry of Merkel cell carcinomas. Exp Dermatol 2001;10:100-9.

59. Wang H, Ng TB, Ooi VE, Liu WK. Effects of lectins with different carbohydrate-binding specificities on hepatoma, choriocarcinoma, melanoma and osteosarcoma cell lines. Int J Biochem Cell Biol 2000;32:385-72.

60. Chang WW, Yu CY, Lin TW, Wang PH, Tsai YC. Soyasaponin I decreases the expression of alpha2,3-linked sialic acid on the cell surface and suppresses the metastatic potential of B16F10 melanoma cells. Biochem Biophys Res Commun 2006;341:614-9.

61. Gurkinkel DM, Rao AV. Soyasaponins: The relationship between chemical structure and colon anticarcinogenic activity. Nutr Cancer 2003;47:24-33.

62. Ellington AA, Berhow MA, Singletary KW. Inhibition of Akt signaling and enhanced ERK1/2 activity are involved in induction of macroautophagy by triterpenoid B-group soyasaponins in colon cancer cells. Carcinogenesis 2006;27:298-306.

63. Xiao JK, Huang GQ, Zhu CP, Ren DD, Zhang SH. Morphological study on apoptosis Hela cells induced by soyasaponins. Toxicol In Vitro 2007;21:820-6.

64. Zhu J, Xiong L, Yu B, Wu J. Apoptosis induced by a new member of saponin family is mediated through caspase-8-dependent cleavage of Bcl-2. Mol Pharmacol 2005;68:1831-8.

65. Khang D, Dung T, Elzaawely A, Xuan T. Phenolic profiles and antioxidant activity of germinated legumes. Foods 2016;5:27.

66. Dai J, Mumper RJ. Plant phenolics: Extraction, analysis and their antioxidant and anticancer properties. Molecules 2010;15:7313-52.