

# Dietary Habits: Role in the Development and Treatment of Cervical Cancer

Apurva<sup>1</sup>, Pracheta Janmeda<sup>2</sup>, Srishti Gangwar<sup>1</sup>, Yuvraj Singh Yadav<sup>1</sup>, Aryan Singh<sup>1</sup>, Priya<sup>1</sup>,  
and Priya Chaudhary<sup>1\*</sup>

<sup>1</sup>Department of Biotechnology, School of Applied and Life Sciences, Uttarakhand University,  
Dehradun-248007, Uttarakhand, India

<sup>2</sup>Department of Bioscience and Biotechnology, Banasthali Vidyapith, Banasthali-304022,  
Rajasthan, India

\*Corresponding Author Email: [priyachaudhary@uumail.in](mailto:priyachaudhary@uumail.in)

## Abstract

Cervical cancer is one of the major cancers in females. As a worldwide concern, determining crucial factors of cervical cancer is beneficial for the prevention strategies. Due to the function of nutrition factors or diet for cancer, the aim was to describe the effect of vitamin, non-nutritional, and nutritional factors in cervical cancer phases. It is observed that micronutrients, trace elements, and Mediterranean diet have a crucial effect in minimizing the chances of cervical cancer, as well as, westernized diet, milk, snacks, and salt were determined as high-risk food factors. Thus, a diet enrich in nutrition can prove to be helpful for the cure of cervical cancer and may decrease the chances of getting this disease. However, additional investigation is also required for different countries.

**Keywords:** Cervical cancer, Diet, Nutrition, Prevention, Vitamins

## Introduction

One of the major types of cancer that affects the cervical cells, the lower portion of uterus that joins the vagina is referred as cervical cancer. Various investigations have pointed out the function of human papillomavirus (HPV) as a major cause of cervical cancer. Economic status, education level, multiparity, family history, smoking, age of first pregnancy, marital status, and marriage age are also mentioned as the risk factors in various other investigations (Okunade, 2020). Nutritional and dietary factors have been determined to contribute 20-60% of cancer across the globe. Among which, the involvement of diet to the risk of cancer in developed nations has been determined to be greater, whereas that in developing nations has been estimated to be 20% (Madan et al., 2023). Thus, cancer is referred as a disorder of developed nations.

Cervical cancer may not cause any symptoms in initial stages but as it progressed, it may result in symptoms like pain while sexual activity, pelvic discomfort, and irregular vaginal bleeding

(Hull et al., 2020). In latest research, dietary antioxidants such as vitamins E, D, A, and nutrition holds a greater share while contributing in the prevention of cervical cancer. There are number of proofs associated with the impact of nutrients on the prevention of cancer. Encouraging access and knowledge of these preventive measures is important to preserve the women health across the worldwide (Nazari et al., 2023). On the other side as there are geographical differences in the incidence, mortality and risk factors of cervical cancer, investigations in various countries are essential. Thus, the aim of this review is to briefly describe the role of different diets, dietary components in the cause and treatment of cervical cancer along with some dietary recommendations.

### **Risk Factors and Predisposing Conditions of Cervical Cancer**

Various predisposing conditions and risk factors affect the initiation of cervical cancer (Figure 1) which is discussed as follows:

#### **HPV Infection**

Persistent type of infection involving high-risk strains of HPV such as type 18, and 16, is the major risk factor of cervical cancer. After causing infection to the cervical cells, the virus start causing genetic alterations that initiates the mechanism of carcinogenesis (Della Fera et al., 2021). The immune system is capable in eradicating the HPV infection but high-risk strains that acquired persistently increases the chances of getting cancer. Above 200 associated viruses make up the HPV group, most of them are transferred via a sexual contact. Most of the HPV strains causes skin wart but some might results in genital warts or even cancer (Oyouni, 2023).

#### **Western Diet**

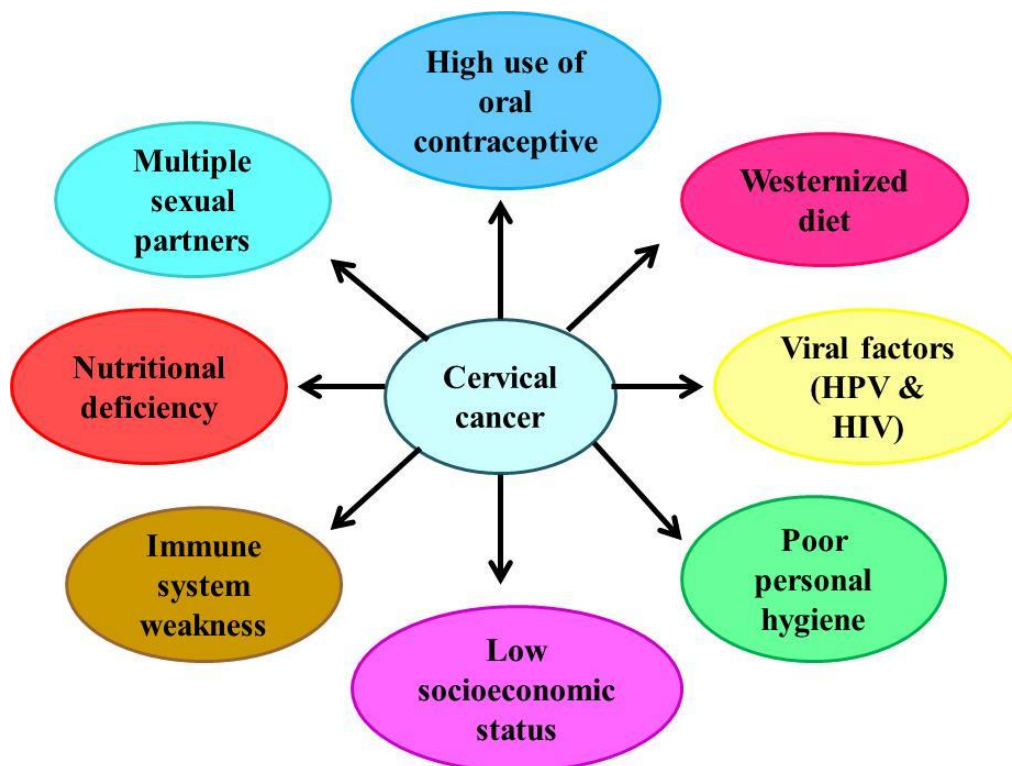
Higher intake of high-fructose goods, high-fat dairy items, animal products, fried meals, sweets, candies, high-sugar beverages, processed meat, red meat, refined cereals, and pre-packaged foods are the features of Westernized diet. According to estimation, one-third of cancer mortality is due to the obesity and poor dietary habits (Drake et al., 2018). These observations are consistent with the findings of evolutionary theory which state that the human body is evolved to some dietary habits and the latest diet, which is far differ from the ancestral one may lead to chronic illness. There are number of investigations that report the harmful consequences of Western diet on non-communicable disorders such as cancer (Clemente-Suárez et al., 2023).

However, the Westernized diet is still consider as a diet option that put health status at risk by causing inflammation, increases the chances of disorders, and raising their mortality, and morbidity (Ruiz-Núñez et al., 2013). Various studies have reported that inflammation, and oxidative stress is two biological factors that influence the cervical cancer. Similarly, due to

the higher oxidative stress that a cell experience, various researchers associated the raised generation of reactive species to a various types of cancer (Dash et al., 2024). For instance, cervical cancer can also rise as the outcome of endogenously created reactive species via the activation of signalling mechanism such as MAPK, and PI3K/AKT. This finding can be determined by the reactive species capacity to both decrease the function of tumor suppressor proteins, and direct the mechanism of oncogenes (Khan et al., 2021).

### Other Related Factors

Remarkable risks factors also comprise of weaken immune system due to smoking, and HIV/AIDS which worsen the effects of HPV. A history of early sexual activity as well as multiple sexual partners also raises the chances of getting cervical cancer. Females who have a family history of cancer or a history of precancerous lesions are more vulnerable. This cancer is also raised by socioeconomic variables like restricted access to routine analysis and preventive treatments (Schabath et al., 2013).



**Figure 1:** Risk factors and predisposing conditions of cervical cancer

### Effect of Micronutrients on Cervical Cancer

Dietary antioxidants and nutrition involves vitamins E, D, C, and A which have a remarkable role in the prevention of cervical cancer. Essential vitamins, trace elements or micronutrients have a potential to promote health and cure or avert illness (Fagbohun et al., 2023). The antioxidant activity of most of the micronutrients neutralizes the free radicals and provides

protection against the DNA damages. Furthermore, it also stabilizes the p53 protein, lowers the immunosuppression, regulates the methylation process, and controls the genomic regulators. It also has the capability to influence the carcinogenic mechanism in different animal models (Sablina et al., 2005). Manganese (Mn), selenium (Se), iron (Fe), zinc (Zn), and copper (Cu) are the trace elements that plays an important role in the elimination of cancer. These factors provide support to the antioxidant enzymes by behaving as co-factors. The crucial trace elements have anti-cancer properties and they show their therapeutic impact by helping in the formation of antioxidant enzymes and elimination of reactive species (Hosseinimehr et al., 2015).

### **Impact of Mediterranean Diet on Cervical Cancer**

In the case of HPV infection and cervical cancer, Mediterranean diet (MD) plays a crucial role in causing or in directing protective effect. In real, MD affects the infection and if it gets minimized and does not rise the chances of cervical cancer. Thus, it slows down the infection and advancement of HPV. Diets depends majorly on plants have gathered focus lately due to their therapeutic effect and recommended health benefits (Nautiyal et al., 2023). Diet depends on plants referred as vegan diets; vegetarian diet involving dairy products and egg referred as lacto-ovo vegetarian diets; and diet which are totally plant-based with or without egg and dairy items except intake of shellfish, and fish are called as pescovegetarian diets. Meat (like birds, chicken, deer, lamb, hog, and cattle) and meat related products are not involved in vegetarian diets (Mariotti and Gardner, 2019). The preliminary dietary supply of bioactive agents or fiber is plant associated food which involves vegetable oil, legumes, seeds and nuts, cereals, vegetables, and fruits. In general, phytochemicals with anti-cancer properties include polyphenols, carotenoids, sulphur compounds, and fiber; these foods comprises of whole grain cereals, green tea, tomatoes, allium, and cruciferous vegetables (Vignesh et al., 2024). As a result, plant-associated diet may have anti-oxidant and anti-inflammatory activities that avoid the initiation of cancer. According to latest report, consuming plant-based food to secure healthful diet has been linked with a decreased cancer risk, despite of the fact that an unhealthy diet is a major risk factor for most of the cancer types (Molina-Montes et al., 2020).

### **Role of Diet in HPV Persistence and Clearance**

It is well understood that oxidative damage or antioxidant deficiency is associated with the cervical cancer. This circumstance produces reactive species which results in the damage of DNA of normal healthy cells. In this condition, cervical cells become more sensitive to the infection of HPV and the ultimate rise in the occurrence of cervical cancer. Antioxidants

present in diet such as vitamins have gathered a lot of focus in current years for their ability to cure cancer (Preci et al., 2021) as shown in Figure 2 and briefed as follows:

### **Vitamin A**

Retinyl esters, retinyl, and retinol are the major fat-soluble retinoids in combination determined as vitamin A. The organ liver has the ability to convert beta-carotene into vitamin A on the basis of body's requirement. Oxidative stress created by the deficiency of vitamin A prevents repair of cells and causes damage to cells. The initial stages of cervical carcinoma, for instance HPV infection and the development of CIN 1, may be restricted by vitamin A (Carazo et al., 2021).

### **Vitamin D**

For the proper mineralization of bone, vitamin D regulates sufficient amount of phosphate and calcium in the blood and also directs the absorption of calcium in the small intestine. In addition, osteoclasts and osteoblasts also require vitamin D for the remodelling and development of bone (Voulgaridou et al., 2023). Thus, vitamin D reported to have anti-inflammatory properties that increases the expression of genes which encodes for insulin receptors or proteins included in the signalling pathway of insulin. Vitamin D also helps persons with HPV infection with their metabolic and clinical symptoms due to its anti-inflammatory activities and also has a great impact on improving insulin resistance. Higher consumption of vitamin D can also suppress the persistent infection of HPV and prevent the occurrence of CIN 1 (Fenercioglu, 2024).

### **Carotenoids**

Carotenoids are the colourful pigments in photosynthetic bacteria, algae, and plants that are responsible for the orange, red, and yellow color found in fruits, vegetables, and plants. On consumption, these are converted into vitamin A. Among various carotenoids, the most prevalent one are lycopene, zeaxanthin, and lutein. Carotenoids majorly restrict the infection of HPV and lycopene may restrict the occurrence of CIN 3 (Ono et al., 2020).

### **Folate**

Cell proliferation, DNA methylation, DNA repair, DNA synthesis and red blood cells are all majorly affected by folate. It is hypothesized that, in individuals having higher level of folate, the infection of HPV is lowered and the elimination of HPV is enhanced as folate limits the integration mechanism of HPV (Piyathilake et al., 2014).

### **Greens**

Greens such as cauliflower, cabbage, and broccoli are some of the examples of cruciferous greens. These greens comprise of sulforaphane, and indole-3-carbinol that aids in the

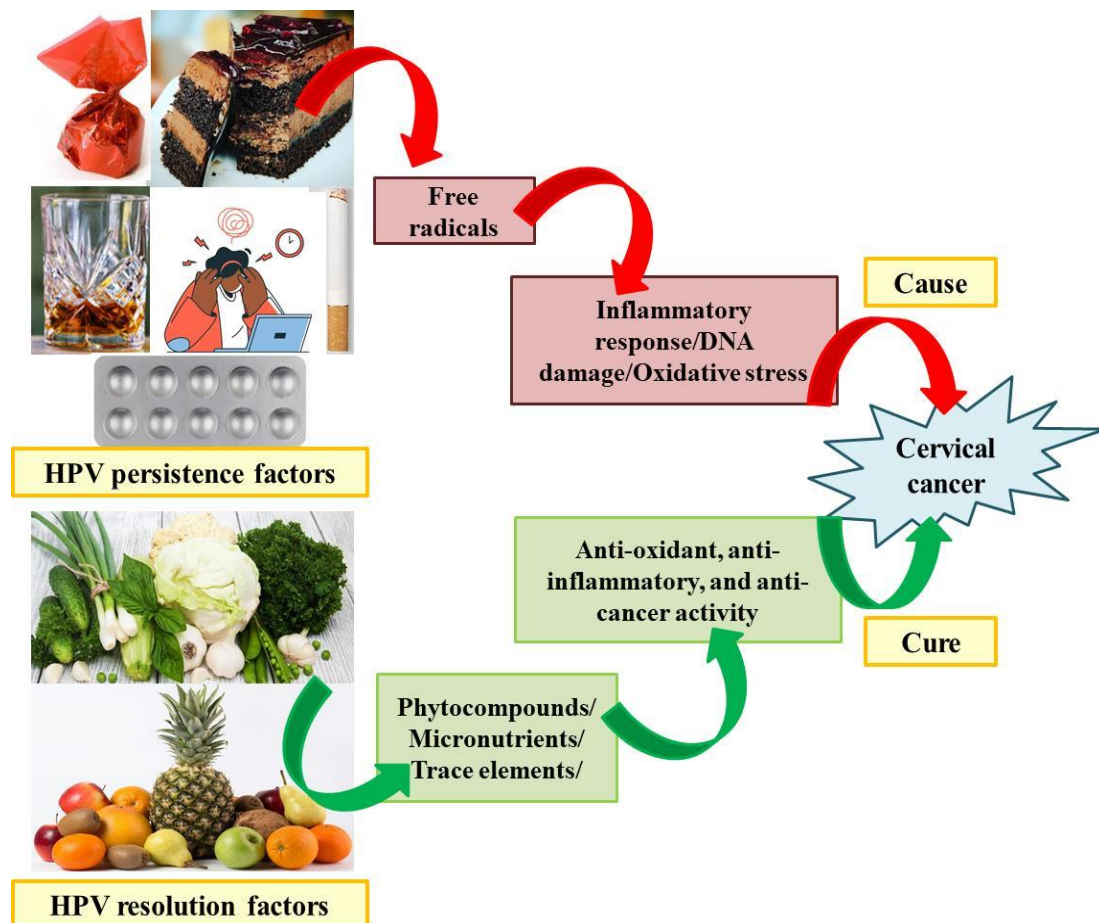
mechanism of detoxification of harmful substances and also avoid the generation of cancer cells. According to some investigations, the consumption of these veggies may also help in decreasing the progression of cervical dysplasia (Higdon et al., 2007).

### Fatty Acids Omega-3

Fatty fish, walnuts, and flaxseeds are the major sources of omega-3 fatty acids that comprises of anti-inflammatory properties which further regulates the immune system and reduces the inflammation. They can also help in delaying the cell alterations associated to cervical dysplasia (Zivkovic et al., 2011).

### Zinc and Selenium

For the health of the immune system and cells, selenium and zinc both are the essential elements. Food items having higher content of zinc involve shellfish, nuts, and seeds whereas food higher in selenium involves Brazil nuts (Zavros et al., 2023).



**Figure 2:** Persistence and resolution factors of cervical cancer

### Potential Mechanism

Cervical cancer progresses and develops in larger part due to the free radicals directed oxidative stress. It usually occurs when the ability of body to scavenge reactive species is disrupted.

Oxidative stress has been associated with signalling pathway activation, mutations, and DNA damage that support metastasis, survival, and growth of cancer. Reactive species also comprises of a capability that mutates the DNA and provide harm to nearby cellular constituents (Preci et al., 2021). This damage initiates the mechanism of converting normal cervical cells into cancerous one if the healing ability of the body is disrupted. Tumor growth and cell proliferation pathways involved in cellular survival and inflammation, for instance mitogen-activated protein kinase (MAPKs) and nuclear factor-kappa B (NF-kB) can be activated by oxidative damage. Cancer cell now proliferates uncontrollably by avoiding apoptosis by the help of various routes. Latent HPV infection is a major factor in the cervical cancer, mainly when it comes to highly-risk strains like HPV-18 and 16. Proteins generated by HPV obstructed the tumor suppressor proteins that worsen the damages induced by oxidative stress (Zhao et al., 2021).

By scavenging reactive species, antioxidants lessen or limit the oxidative stress directed damages. Antioxidants provide shields to healthy cells so that they get protected from oxidative stress, which decreases the after effects of the therapy. Furthermore, there is a concern about the consumption of too many antioxidant supplement may conflict with the treatment of cancer, which usually based on directing oxidative stress in order to eliminate cancer cells (Chaudhary et al., 2023a). Antioxidant timing and dose are therefore important in these types of treatments. Cervical cancer majorly progresses due to the oxidative stress, although antioxidant molecule may lower the load and improves the results of therapy. To fully grasp the major applications of these antioxidants in the therapy of cancer, additional investigation is required (Chaudhary et al., 2023b).

### **Dietary Recommendations**

The risk of cervical cancer can be lowered down by following a healthy diet, mainly one that comprises of food items rich in some nutrient factors that enhance the immunity, decreases the inflammation, and fight against the free radicals directed oxidative damage (Koshiyama, 2019). The below mentioned (Table 1) is a brief discussion of the major nutrients, and food habits that may lower down the chances of cervical cancer.

**Table 1:** Dietary recommendations to lower down the risk of cervical cancer

<b>Dietary recommendations</b>	<b>Associated benefits</b>	<b>References</b>
Citrus fruits, leafy greens, berries, sweet potatoes, and carrots	Antioxidant molecules such as vitamin E, C, and A can provide protection to cells	Koshiyama, 2019

	against free radicals and decreases the spread of HPV infection, that is one of the significant factor responsible for cervical cancer	
Lettuce, kale, spinach, fortified grains, and legumes	Considered to be the better source of folate and can remarkably lower down the risk of HPV infection and development of cervical cancer	Hajiesmaeil et al., 2022
Cabbage, cauliflower, and broccoli	Reported to have anti-cancer activity due to the presence of indole-3-carbinol and sulforaphane compounds in these veggies	Katz et al., 2018
Pumpkins, sweet potatoes, and carrots	Considered to be the good source of beta-carotene that reported to enhance the immune system and ultimately provide protection against oxidative stress directed damages	Grune et al., 2010
Walnuts, Omega-3 flaxseeds, and fatty acids	These substances reported to have anti-inflammatory property that decreases the chances of cervical cancer by lowering the inflammatory response	Koshiyama, 2019
Green tea	Polyphenols specifically found only in green tea reported to have anti-cancer activity	Cao et al., 2016



Yogurt, and probiotic fermented foods	Reported to have the ability that strengthen the immune system and restore the healthy environment of gut flora, both of these are capable in providing protection against HPV infection	Mazziotta et al., 2023
Whole grains, vegetables, fruits, and fiber	Favours normal digestion that lowers the inflammatory response in the organism body	He et al., 2022

### Conclusion

With the development of stringent strategies, cervical cancer can be effectually regulated. Different risk factors causing cervical cancer make possible treatment, diagnosis, and prevention. In the current review, all factors responsible for the cause of cervical cancer were determined in order to develop a suitable preventive method. In investigations during recent time period, antioxidants have gained much focus in the cervical cancer prevention. As they provide protection to the cell against oxidative stress directed DNA alterations and improves the immune system mechanism. On the basis of the present review, healthcare officials should educate communities, families, and female to include vitamins and important nutrition in their diet plan to avoid the development of cervical cancer.

### References

1. Cao J., Han J., Xiao H., Qiao J., Han M. (2016). Effect of Tea Polyphenol Compounds on Anticancer Drugs in Terms of Anti-Tumor Activity, Toxicology, and Pharmacokinetics. *Nutr.*, 8(12):762. doi: 10.3390/nu8120762.
2. Carazo A., Macáková K., Matoušová K., Krčmová L.K., Protti M., Mladěnka P. (2021). Vitamin A Update: Forms, Sources, Kinetics, Detection, Function, Deficiency, Therapeutic Use and Toxicity. *Nutr.*, 13(5):1703. doi: 10.3390/nu13051703.
3. Chaudhary P., Janmeda P., Docea A.O., Yeskaliyeva B., Razis A.F.A., Modu B., Calina D., Sharifi-Rad J. (2023a). Oxidative stress, free radicals and antioxidants: potential crosstalk in the pathophysiology of human diseases. *Front. Chem.*, 11:1158198. <http://dx.doi.org/10.3389/fchem.2023.1158198>.

4. Chaudhary P., Janmeda P., Setzer W.N., Aldahish A., Sharifi-Rad J., Calina D. (2023b). Breaking free from free radicals: harnessing the power of natural antioxidants for health and disease prevention. *Chem. Pap.*, 78(7):2061-2077. <http://dx.doi.org/10.1007/s11696-023-03197-1>.
5. Clemente-Suárez V.J., Beltrán-Velasco A.I., Redondo-Flórez L., Martín-Rodríguez A., Tornero-Aguilera J.F. (2023). Global Impacts of Western Diet and Its Effects on Metabolism and Health: A Narrative Review. *Nutr.*, 15(12):2749. doi: 10.3390/nu15122749.
6. Dash U.C., Bhol N.K., Swain S.K., Samal R.R., Nayak P.K., Raina V., Panda S.K., Kerry R.G., Duttaroy A.K., Jena A.B. (2024). Oxidative stress and inflammation in the pathogenesis of neurological disorders: Mechanisms and implications. *Acta Pharm. Sin. B*. <https://doi.org/10.1016/j.apsb.2024.10.004>.
7. Della Fera A.N., Warburton A., Coursey T.L., Khurana S., McBride A.A. (2021). Persistent Human Papillomavirus Infection. *Viruses.*, 13(2):321. doi: 10.3390/v13020321.
8. Drake I., Sonestedt E., Ericson U., Wallström P., Orho-Melander M. (2018). A Western dietary pattern is prospectively associated with cardio-metabolic traits and incidence of the metabolic syndrome. *Br J Nutr.*, 119(10):1168-1176. <http://dx.doi.org/10.1017/S000711451800079X>.
9. Fagbohun O.F., Gillies C.R., Murphy K.P.J., Rupasinghe H.P.V. (2023). Role of Antioxidant Vitamins and Other Micronutrients on Regulations of Specific Genes and Signaling Pathways in the Prevention and Treatment of Cancer. *Int J Mol Sci.*, 4(7):6092. doi: 10.3390/ijms24076092.
10. Fenercioglu A.K. (2024). The Anti-Inflammatory Roles of Vitamin D for Improving Human Health. *Curr. Issues Mol. Biol.*, 46(12):13514-13525. <https://doi.org/10.3390/cimb46120807>.
11. Grune T., Lietz G., Palou A., Ross A.C., Stahl W., Tang G., Thurnham D., Yin S.A., Biesalski H.K. (2010). Beta-carotene is an important vitamin A source for humans. *J Nutr.*, 140(12):2268S-2285S. doi: 10.3945/jn.109.119024.
12. Hajjesmaeil M., Mirzaei Dahka S., Khorrani R., Rastgoo S., Bourbour F., Davoodi S.H., Shafiee F., Gholamalizadeh M., Toriki S.A., Akbari M.E., Doaei S. (2022). Intake of food groups and cervical cancer in women at risk for cervical cancer: A nested case-control study. *Caspian J Intern Med.*, 13(3):599-606. doi: 10.22088/cjim.13.3.599.

13. He Y., Wang B., Wen L., Wang F., Yu H., Chen D., Su X., Zhang C. (2022). Effects of dietary fiber on human health. *Food Sci. Hum. Wellness.*, 11(1):1-10. <https://doi.org/10.1016/j.fshw.2021.07.001>.
14. Higdon J.V., Delage B., Williams D.E., Dashwood R.H. (2007). Cruciferous vegetables and human cancer risk: epidemiologic evidence and mechanistic basis. *Pharmacol Res.*, 55(3):224-36. doi: 10.1016/j.phrs.2007.01.009.
15. Hosseinimehr S.J. (2015). The protective effects of trace elements against side effects induced by ionizing radiation. *Radiat Oncol J.*, 33(2):66-74. doi: 10.3857/roj.2015.33.2.66.
16. Hull R., Mbele M., Makhafola T., Hicks C., Wang S.M., Reis R.M., Mehrotra R., Mkhize-Kwitshana Z., Kibiki G., Bates D.O., Dlamini Z. (2020). Cervical cancer in low and middle-income countries. *Oncol Lett.*, 20(3):2058-2074. doi: 10.3892/ol.2020.11754.
17. Katz E., Nisani S., Chamovitz D.A. (2018). Indole-3-carbinol: a plant hormone combatting cancer. *F1000Res.*, 7:F1000 Faculty Rev-689. doi: 10.12688/f1000research.14127.1.
18. Khan A.Q., Rashid K., AlAmodi A.A., Agha M.V., Akhtar S., Hakeem I., Raza S.S., Uddin S. (2021). Reactive oxygen species (ROS) in cancer pathogenesis and therapy: An update on the role of ROS in anticancer action of benzophenanthridine alkaloids. *Biomed Pharmacother.*, 143:112142. <https://doi.org/10.1016/j.biopha.2021.112142>.
19. Koshiyama M. (2019). The Effects of the Dietary and Nutrient Intake on Gynecologic Cancers. *Healthcare.*, 7(3):88. doi: 10.3390/healthcare7030088.
20. Madan A., Pathak K., Naaz A., Pokhriyal R., Paheriya Y., Badoni H. (2023). Medicinal properties of Himalayan Marsh Orchid: *Dactylorhiza hatagirea* (D.Don) Soó (Garud Panja). *U. J. App. Life. Sci.*, 4(1):108-114
21. Mariotti F., Gardner C.D. (2019). Dietary Protein and Amino Acids in Vegetarian Diets-A Review. *Nutr.*, 11(11):2661. doi: 10.3390/nu11112661.
22. Mazziotta C., Tognon M., Martini F., Torreggiani E., Rotondo J.C. (2023). Probiotics Mechanism of Action on Immune Cells and Beneficial Effects on Human Health. *Cells.*, 12(1):184. doi: 10.3390/cells12010184.
23. Molina-Montes E., Salamanca-Fernández E., Garcia-Villanova B., Sánchez M.J. (2020). The Impact of Plant-Based Dietary Patterns on Cancer-Related Outcomes: A Rapid Review and Meta-Analysis. *Nutr.*, 12(7):2010. doi: 10.3390/nu12072010.

24. Mwaka A.D., Orach C.G., Were E.M., Lyratzopoulos G., Wabinga H., Roland M. (2016). Awareness of cervical cancer risk factors and symptoms: cross-sectional community survey in post-conflict northern Uganda. *Health Expect.*, 19(4):854-67. doi: 10.1111/hex.12382.
25. Nautiyal S., Kalia M., Rautela I., Moity R.K., Singh T., Kalia S. (2023). Evaluation of food products with integrated *Solanum nigrum*: A review. *U. J. App. Life. Sci.*, 4(1):115-125.
26. Okunade K.S. (2020). Human papillomavirus and cervical cancer. *J Obstet Gynaecol.*, 40(5):602-608. doi: 10.1080/01443615.2019.1634030.
27. Ono A., Koshiyama M., Nakagawa M., Watanabe Y., Ikuta E., Seki K., Oowaki M. (2020). The Preventive Effect of Dietary Antioxidants on Cervical Cancer Development. *Medicina.*, 56(11):604. doi: 10.3390/medicina56110604.
28. Oyouni, A.A.A. (2023). Human papillomavirus in cancer: Infection, disease transmission, and progress in vaccines. *J. Infect. Public Health.*, 16(4):626-631. <https://doi.org/10.1016/j.jiph.2023.02.014>.
29. Piyathilake C.J., Macaluso M., Chambers M.M., Badiga S., Siddiqui N.R., Bell W.C., Edberg J.C., Partridge E.E., Alvarez R.D., Johanning G.L. (2014). Folate and vitamin B12 may play a critical role in lowering the HPV 16 methylation-associated risk of developing higher grades of CIN. *Cancer Prev Res (Phila.)*, 7(11):1128-37. doi: 10.1158/1940-6207.CAPR-14-0143.
30. Preci D.P., Almeida A., Weiler A.L., Mukai Franciosi M.L., Cardoso A.M. (2021). Oxidative damage and antioxidants in cervical cancer. *Int J Gynecol Cancer.*, 31(2):265-271. doi: 10.1136/ijgc-2020-001587.
31. Preci D.P., Almeida A., Weiler A.L., Mukai Franciosi M.L., Cardoso A.M. (2021). Oxidative damage and antioxidants in cervical cancer. *Int J Gynecol Cancer.*, 31(2):265-271. doi: 10.1136/ijgc-2020-001587.
32. Ruiz-Núñez B., Pruijboom L., Dijck-Brouwer D.A.J., Muskiet F.A.J. (2013). Lifestyle and nutritional imbalances associated with Western diseases: causes and consequences of chronic systemic low-grade inflammation in an evolutionary context. *J Nutr Bioschem.*, 24(7):1183-1201. <https://doi.org/10.1016/j.jnutbio.2013.02.009>.
33. Sablina A.A., Budanov A.V., Ilyinskaya G.V., Agapova L.S., Kravchenko J.E., Chumakov P.M. (2005). The antioxidant function of the p53 tumor suppressor. *Nat Med.*, 11(12):1306-13. doi: 10.1038/nm1320.

34. Schabath M.B., Villa L.L., Lazcano-Ponce E., Salmerón J., Quiterio M., Giuliano A.R. (2012). HIM Study. Smoking and human papillomavirus (HPV) infection in the HPV in Men (HIM) study. *Cancer Epidemiol Biomarkers Prev.*, 21(1):102-10. doi: 10.1158/1055-9965.EPI-11-0591.
35. Vignesh A., Amal T.C., Sarvalingam A., Vasanth K. (2024). A review on the influence of nutraceuticals and functional foods on health. *Food Chem. Adv.*, 5:100749. <https://doi.org/10.1016/j.focha.2024.100749>.
36. Voulgaridou G., Papadopoulou S.K., Detopoulou P., Tsoumana D., Giaginis C., Kondyli F.S., Lymperaki E., Pritsa A. (2023). Vitamin D and Calcium in Osteoporosis, and the Role of Bone Turnover Markers: A Narrative Review of Recent Data from RCTs. *Diseases.*, 11(1):29. doi: 10.3390/diseases11010029.
37. Zavros A., Andreou E., Aphas G., Bogdanis G.C., Sakkas G.K., Roupa Z., Giannaki C.D. (2023). The Effects of Zinc and Selenium Co-Supplementation on Resting Metabolic Rate, Thyroid Function, Physical Fitness, and Functional Capacity in Overweight and Obese People under a Hypocaloric Diet: A Randomized, Double-Blind, and Placebo-Controlled Trial. *Nutr.*, 15(14):3133. doi: 10.3390/nu15143133.
38. Zhao H., Wu L., Yan G., Chen Y., Zhou M., Wu Y., Li Y. (2021). Inflammation and tumor progression: signaling pathways and targeted intervention. *Signal Transduct Target Ther.*, 6(1):263. doi: 10.1038/s41392-021-00658-5.
39. Zivkovic A.M., Telis N., German J.B., Hammock B.D. (2011). Dietary omega-3 fatty acids aid in the modulation of inflammation and metabolic health. *Calif Agric (Berkeley).*, 65(3):106-111. doi: 10.3733/ca.v065n03p106.