

Potential Roles and Mechanisms of Avena Sativa in Cancer Prevention

Mohammad Kordkatouli¹, Seyed Abolghassem Mohammadi Bondarkhilli^{1*}, Aryan Sateei¹, Audrius Dulskas²

¹ Department of Biology, Gorgan Branch, Islamic Azad University, Gorgan, Iran

² Department of Abdominal and General Surgery and Oncology, National Cancer Institute, Vilnius, Lithuania

***Corresponding Author:** Abolghassam Mohammadi Bondarkhilli, Department of Biology, Gorgan Branch, Islamic Azad University, Gorgan, Iran. E-mail: sambondar2@gmail.com

Submitted: 26 July 2024

Revised: 18 August 2024

Accepted: 29 August 2024

In Press

Keywords:

Antioxidants

Avena Sativa

Cancer

COX-2

miRNA

The protective effects of dietary fiber are attributed to several mechanisms: it regulates bowel movements by increasing stool bulk and speeding up gastrointestinal transit, which minimizes the contact time between carcinogens and the intestinal lining, thus reducing cancer risk; it dilutes fecal carcinogens due to increased stool volume, lessening their interaction with the colonic epithelium; the fermentation of fiber by gut microbiota produces short-chain fatty acids (SCFAs) like butyrate, which protect against cancer by serving as an energy source for colonocytes, maintaining mucosal integrity, and exhibiting anti-inflammatory properties; dietary fiber also modulates gut microbiota, encouraging the growth of beneficial bacteria that can outcompete harmful, carcinogen-producing bacteria; it enhances immune function by influencing gut immune cells, aiding in the removal of cancer cells and preventing inflammation, a known cancer risk factor; fiber binds to bile acids, leading to their excretion and preventing the formation of more carcinogenic secondary bile acids implicated in colorectal cancer development; and SCFAs, particularly butyrate, affect cell proliferation and differentiation, inducing apoptosis in cancer cells and inhibiting the growth of neoplastic cells. Flavonoids, polyphenolic compounds in Avena Sativa, display antioxidant, anti-inflammatory, and antiproliferative activities, modulating enzyme function, inhibiting cell growth, and inducing apoptosis in cancer cells. Avenanthramides and other anti-inflammatory compounds in Avena Sativa modulate multiple inflammatory pathways, including inhibiting the activity of enzymes like COX-2 and reducing the production of pro-inflammatory cytokines, potentially lowering the risk of chronic inflammation-related cancers.

Copyright © 2024 Pirkani et al. Published by Breast Cancer Research Center, ACECR. This work is licensed under a Creative Commons Attribution - NonCommercial 4.0 International License (<https://creativecommons.org/licenses/by-nc/4.0/>) non-commercial uses of the work are permitted, provided the original work is properly cited.

INTRODUCTION

Avena Sativa is recognized as a whole grain and is rich in proteins, lipids, carbohydrates, vitamins, minerals, and various phytochemicals, including

polyphenols, flavonoids, and saponins. Recent research has increasingly focused on the health benefits of oat consumption, particularly its role in reducing the risk of numerous diseases [1, 2]. Studies

have shown that a diet rich in Avena Sativa can provide several biological benefits, such as preventing cardiovascular diseases, lowering blood glucose levels, and promoting intestinal health [2, 3]. Additionally, Avena Sativa has been found to have anti-allergic, antioxidant, and cancer-preventive properties. Cancer remains the second leading cause of death globally the natural compounds found in Avena Sativa represent a significant breakthrough in developing new cancer prevention strategies. These compounds can interact with multiple cellular targets, addressing the complex nature of cancer pathogenesis. Consequently, the study of the cancer-preventive activities and potential mechanisms of oat nutrients and phytochemicals has become a prominent area of research [2, 4-6].

Avena Sativa harbors a spectrum of antioxidants, chiefly avenanthramides, and beta-glucans, bolster their potential to thwart cancer [1]. Avenanthramides, phenolic alkaloids exclusive to Avena Sativa, comprise anthranilic acid amides fused with hydroxycinnamic acids and are synthesized in response to stress, boasting anti-inflammatory, antioxidant, and anti-itching properties. They combat oxidative stress and potential DNA damage by scavenging free radicals and impeding pro-inflammatory pathways like NF- κ B, linked to cancer progression. Furthermore, avenanthramides prompt apoptosis in cancer cells and stymie angiogenesis, forming new blood vessels that nourish tumors. Beta-

glucans, polysaccharides in oat cell walls, consist of glucose molecules connected by β -1,3 and β -1,4 glycosidic bonds and are lauded for their immunomodulatory effects. They activate macrophages and other immune cells, fortifying the body's defenses against cancerous cells, and aid in maintaining gut health [1, 2, 5]. They are pivotal for colorectal cancer prevention by binding carcinogens and facilitating their excretion. Avena Sativa also contains phenolic acids like ferulic, caffeic, and sinapic acids, alongside phytochemicals such as sterols and saponins, which collectively scavenge free radicals, chelate metal ions, and modulate immune function—integral to cancer prevention. Avenanthramides specifically block reactive species, trigger apoptosis and senescence, halt cell proliferation by diminishing cyclins, and inhibit epithelial-mesenchymal transition (EMT) and metastasis. Beta-glucans mobilize cancer-fighting molecules, particularly natural killer (NK) cells, during cancer's promotional stage and counteract angiogenesis. These multifaceted mechanisms underscore the antioxidants in Avena Sativa as a promising avenue in cancer prevention, necessitating continued research to leverage their capabilities within a comprehensive cancer prevention framework fully [5, 6] [Figure1].

Peptides found in Avena Sativa can inhibit proteolytic enzymes and regulate cellular signaling pathways, thereby inhibiting the growth of cancer cells. These

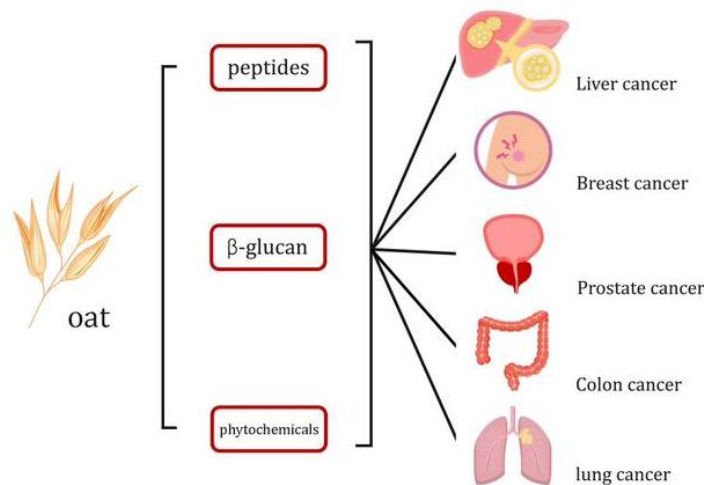


Figure 1. The effect of Avena Sativa on cancers and its type of mechanism.

peptides can help reduce tumor growth by inhibiting specific enzymes, such as metalloproteinases, which play a role in cancer cell invasion and metastasis [6–8]. Dietary fibers in *Avena Sativa* can reduce the risk of colorectal cancer by increasing stool bulk and decreasing transit time through the gut. Additionally, fibers can ferment in the colon to produce short-chain fatty acids like butyrate, which have anticancer properties. Polyphenols and flavonoids in *Avena Sativa* can help prevent cancer by scavenging free radicals and reducing oxidative stress. These compounds can inhibit the growth and proliferation of cancer cells by regulating cellular signaling pathways such as MAPK and PI3K/Akt cellular signaling pathways such as MAPK, PI3K/Akt, NF- κ B, Wnt/ β -catenin, and AMPK play crucial roles in the mechanisms of cancer prevention by oat compounds. These pathways regulate the growth, proliferation, apoptosis, and survival of cancer cells, and their inhibition or regulation can help reduce cancer cell growth and proliferation and increase apoptosis. Further research in this area could lead to developing new and more effective cancer prevention and treatment strategies [7, 8].

1. Antioxidant Activity

Avena sativa is rich in antioxidant compounds, particularly avenanthramides, which are unique to *Avena sativa* and have been studied for their health benefits, including anti-inflammatory and antiproliferative properties. Hydroxyl radicals can cause oxidative DNA damage and potentially initiate cancer. In addition, *Avena Sativa* boosts the body's antioxidant enzymes, such as superoxide dismutase (SOD) and catalase, which are important for detoxifying reactive oxygen species (ROS) and protecting cells from oxidative stress [9]. They also modulate cell signaling pathways, including downregulating the NF- κ B pathway, which is often overactive in cancer cells and contributes to inflammation and cell survival. *Avena Sativa*'s direct effects on cancer cells include inducing cell cycle arrest, particularly in the G2/M phase, preventing cancer cell proliferation. Stimulating apoptosis through activating pathways such as the caspase cascade helps eliminate potential cancer cells.

Inhibition of angiogenesis by reducing pro-angiogenic factors such as vascular endothelial growth factor (VEGF) is necessary for tumor growth and spread [10, 11]. The clinical relevance of these findings suggests that *Avena Sativa* can be part of a cancer-prevention diet and, when combined with other healthy lifestyle choices, can help reduce the risk of certain types of cancer [12]. These mechanisms are the specific antioxidant activities of *Avena sativa*, especially those attributed to avenanthramides, by neutralizing free radicals, enhancing antioxidant defenses, modulating cell signals, inducing cell cycle arrest, stimulating apoptosis, and inhibiting angiogenesis. They play a role in preventing cancer [13].

Avena Sativa harbors a spectrum of antioxidants, chiefly avenanthramides, and beta-glucans, bolsters their potential to thwart cancer [9]. Avenanthramides, phenolic alkaloids exclusive to *Avena Sativa*, comprise anthranilic acid amides fused with hydroxycinnamic acids and are synthesized in response to stress, boasting anti-inflammatory, antioxidant, and anti-itching properties [14]. They combat oxidative stress and potential DNA damage by scavenging free radicals and impeding pro-inflammatory pathways like NF- κ B, linked to cancer progression [15]. Furthermore, avenanthramides prompt apoptosis in cancer cells and stymie angiogenesis—forming new blood vessels that nourish tumors. Beta-glucans, polysaccharides in oat cell walls, consist of glucose molecules connected by β -1,3 and β -1,4 glycosidic bonds and are lauded for their immunomodulatory effects [16]. They activate macrophages and other immune cells, fortifying the body's defenses against cancerous cells, and aid in maintaining gut health, pivotal for colorectal cancer prevention, by binding carcinogens and facilitating their excretion [17]. *Avena Sativa* also contains phenolic acids like ferulic, caffeic, and sinapic acids, alongside phytochemicals such as sterols and saponins, which collectively scavenge free radicals, chelate metal ions, and modulate immune function—integral to cancer prevention [18]. Avenanthramides specifically block reactive species, trigger apoptosis and senescence, halt cell proliferation by diminishing cyclins, and inhibit epithelial-mesenchymal transition

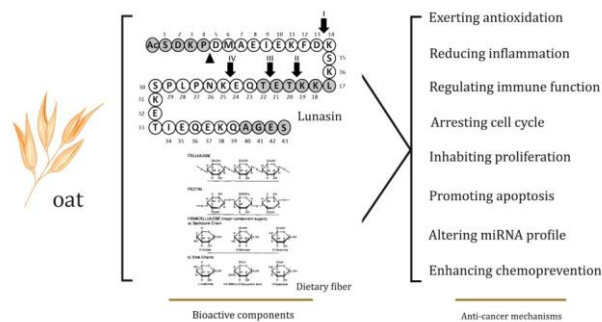


Figure 2. Antioxidant activity in cancer treatment.

(EMT) and metastasis [19]. Beta-glucans fight cancer-fighting molecules, especially natural killer (NK) cells, in the stage of cancer cell metastasis through angiogenesis [20]. These mechanisms mentioned by other researchers to the antioxidants present in *Avena Sativa* have been carried out by researchers in this regard for their use as a cancer preventive agent [21] [Figure 2].

2. Dietary Fiber Content

Dietary fiber in *Avena Sativa* plays a crucial role in cancer prevention, especially concerning colorectal cancer [22]. The protective effects of dietary fiber are attributed to several mechanisms: it regulates bowel movements by increasing stool bulk and speeding up gastrointestinal transit, which minimizes the contact time between carcinogens and the intestinal lining, thus reducing cancer risk; it dilutes fecal carcinogens due to increased stool volume, lessening their interaction with the colonic epithelium; the fermentation of fiber by gut microbiota produces short-chain fatty acids (SCFAs) like butyrate, which protect against cancer by serving as an energy source for colonocytes, maintaining mucosal integrity, and exhibiting anti-inflammatory properties; dietary fiber also modulates gut microbiota, encouraging the growth of beneficial bacteria that can outcompete

harmful, carcinogen-producing bacteria; it enhances immune function by influencing gut immune cells, aiding in the removal of cancer cells and preventing inflammation, a known cancer risk factor; fiber binds to bile acids, leading to their excretion and preventing the formation of more carcinogenic secondary bile acids implicated in colorectal cancer development; and SCFAs, particularly butyrate, affect cell proliferation and differentiation, inducing apoptosis in cancer cells and inhibiting the growth of neoplastic cells [22-24]. These mechanisms underscore the complex interplay between dietary fiber, gut microbiota, and the immune system, contributing to the potential cancer-preventive effects of *Avena Sativa*, with the most pronounced benefits observed when the fiber is part of an overall healthy diet and lifestyle [25].

3. Compounds found in Avena Sativa

The *Avena Sativa* provides a comprehensive overview of various flavonoids and their anticancer properties. Myricetin, Apigenin, Kaempferol, Rutin, Quercetin, general flavonoids, and Catechin are highlighted for their roles in inhibiting cancer cell growth, inducing apoptosis (programmed cell death), and reducing inflammation these compounds are effective against multiple cancer types, including

breast, colon, prostate, lung, liver, ovarian, pancreatic, and stomach cancers. Each flavonoid operates through different mechanisms, such as inhibiting signaling pathways, reducing oxidative stress, and preventing metastasis and angiogenesis (formation of new blood vessels). This detailed understanding underscores the potential of these natural compounds in cancer prevention and treatment [15, 18-20, 23, 26, 27].

Myricetin is known for its ability to inhibit cancer cell growth, reduce inflammation, induce apoptosis, and prevent metastasis. It has shown efficacy against breast, colon, prostate, and lung cancers [1-3, 7, 25, 27].

Apigenin is particularly effective in inducing apoptosis and autophagy, causing cell cycle arrest, and inhibiting the migration and invasion of cancer cells. It also stimulates the immune response, making it a potent compound against breast, prostate, lung, colon, liver, ovarian, and pancreatic cancers [2, 23-26].

Kaempferol works by inhibiting various signaling pathways, reducing inflammation, inducing apoptosis, and preventing metastasis and angiogenesis. It is effective against breast, colon, prostate, lung, and ovarian cancers [2, 15, 18].

Rutin induces apoptosis, inhibits cancer cell growth, reduces oxidative stress, and prevents angiogenesis and inflammation. It has potential against breast, colon, prostate, and lung cancers [1, 2, 25, 26].

Quercetin increases apoptosis and autophagy, inhibits the PI3K/Akt/mTOR and MAPK/ERK pathways, and reduces metastasis and angiogenesis. It is effective against breast, colon, prostate, and lung cancers [15, 25-27].

General flavonoids inhibit cell proliferation, induce apoptosis, prevent metastasis and angiogenesis, and reduce inflammation. They are effective against stomach, breast, prostate, and colon cancers [21, 22, 25].

Catechin inhibits cell proliferation, induces apoptosis, prevents metastasis and angiogenesis, and reduces inflammation. It has shown efficacy against breast, colon, prostate, and lung cancers.

These flavonoids operate through multiple

mechanisms, making them promising candidates for cancer prevention and treatment. Their ability to target various pathways and processes in cancer progression highlights their potential as natural therapeutic agents [Table 1] [23-25].

4. Bioactive Compounds

Avena Sativa harbors a variety of bioactive compounds that contribute to their anticancer potential. Avenanthramides, unique phenolic compounds in *Avena Sativa*, consist of hydroxycinnamic acid linked to anthranilic acid and are known for their antioxidant and anti-inflammatory effects [9,10,26]. They scavenge harmful free radicals and inhibit inflammatory cytokines like TNF- α , influencing cell signaling pathways that govern cancer cell proliferation and apoptosis [27]. Beta-glucans, soluble fibers found in *Avena Sativa*, bolster the immune response against cancer by activating macrophages and natural killer cells and are also beneficial for gut health, which is inversely related to colorectal cancer risk [28]. Saponins, characterized by their foaming properties, can induce apoptosis in cancer cells, lower cholesterol, and enhance immune function, along with their anti-inflammatory properties that contribute to cancer prevention [29]. Phenolic acids, such as ferulic, caffeic, and sinapic acids, act as antioxidants that may protect cells from DNA damage leading to cancer, have anti-inflammatory effects, and can modulate the gut microbiota [30]. Flavonoids, polyphenolic compounds in *Avena Sativa*, display antioxidant, anti-inflammatory, and antiproliferative activities, modulating enzyme function, inhibiting cell growth, and inducing apoptosis in cancer cells [31]. Lignans, phytoestrogens similar to estrogen, are converted by intestinal bacteria into enterolignans, which are associated with a reduced risk of hormone-related cancers and possess antioxidant properties [32]. These compounds interact to reduce the risk of cancer by protecting against oxidative stress, strengthening the immune response, modulating the level of hormones, maintaining intestinal health, and emphasizing the importance of a proper diet and the consumption of this type of oat bran and its bioactive components. They emphasize food to prevent cancer [33].

5. Anti-inflammatory Properties

and natural killer cells, which are crucial in the body's

Table 1. Substances extracted from arena sativa in its effect on cancer.

compound	Cancer Types			Properties and Effects
Myricetin	Breast, Lung	Colorectal,	Prostate,	Inhibits cancer cell growth, reduces inflammation induces apoptosis, inhibits metastasis
Apigenin	Breast, Colorectal, Pancreatic	Prostate, Liver,	Lung, Ovarian,	Induces apoptosis and autophagy, cell cycle arrest, inhibits migration and invasion, stimulates immune response
Keampferol	Breast, Lung, Ovarian	Colorectal,	Prostate,	Inhibits signaling pathways, reduces inflammation, induces apoptosis, inhibits metastasis and angiogenesis
Rutin	Breast, Lung	Colorectal,	Prostate,	Induces apoptosis, inhibits cancer cell growth, reduces oxidative stress, inhibits angiogenesis and inflammation
Quercetin	Breast, Lung	Colorectal,	Prostate,	Increases apoptosis and autophagy, inhibits PI3KL/Akt/mTOR and MAPK/ERK pathways, reduces metastasis and angiogenesis
Flavonoids	Stomach, Colorectal	Breast,	Prostate,	Inhibits cell proliferation, induces apoptosis, inhibits metastasis and angiogenesis, reduces inflammation
Catechin	Breast, Lung	Colorectal,	Prostate,	Inhibits cell proliferation, induces apoptosis, inhibits metastasis and angiogenesis, reduces inflammation

The anti-inflammatory properties of Avena sativa play a crucial role in its potential for cancer prevention, as chronic inflammation is a well-established risk factor for various malignancies. Avena sativa contains bioactive compounds that mitigate this risk by inhibiting the production of pro-inflammatory cytokines such as tumor necrosis factor-alpha (TNF-α) and interleukin-6 (IL-6), which are pivotal in the inflammatory process and are linked to cancer progression. Additionally, these compounds modulate the NF-κB signaling pathway, which is significant in inflammation and oncogenesis [34, 35]. Antioxidants in Avena sativa, including avenanthramides, combat oxidative stress by neutralizing free radicals, thereby reducing the risk of chronic inflammation and DNA damage associated with carcinogenesis. Beta-glucans in Avena sativa enhance immune function by activating macrophages

defense against tumors and mitigating inflammation; the dietary fiber in Avena sativa also positively impacts the gut microbiota, promoting the growth of the normal flora and probiotics that produce anti-inflammatory compounds, which is associated with a reduced risk of colorectal cancer [35, 36]. Furthermore, Avena sativa may contain compounds that inhibit enzymes such as cyclooxygenase-2 (COX-2), which are involved in the inflammatory process and implicated in cancer. These anti-inflammatory properties contribute significantly to Avena Sativa's role as a functional food in cancer prevention, suggesting that reducing inflammation may help lower the risk of cancer initiation and progression. By incorporating Avena sativa into the diet, individuals may benefit from its multifaceted role in modulating inflammation, supporting immune function, and fostering a healthy gut microbiota through the action

of probiotics, thereby potentially reducing the overall risk of cancer development [37, 38].

6. Synergistic Effects

The bioactive compounds in *Avena Sativa*, such as avenanthramides, phenolic acids, flavonoids, beta-glucans, and phytoestrogens, work in synergy to enhance their potential anticancer effects [39,41]. These compounds do not act in isolation; instead, they interact to form a more potent defense against oxidative stress, effectively neutralizing free radicals and protecting cells from oxidative damage, a key factor in cancer development [42]. The dietary fiber in *Avena Sativa*, especially beta-glucans, works alongside phytochemicals to promote gut health and immune function. Beta-glucans encourage the growth of beneficial gut bacteria that can metabolize phytochemicals into compounds with anticancer properties, fostering a healthy gut microbiome essential for cancer prevention [43]. Avenanthramides and other anti-inflammatory compounds in *Avena Sativa* modulate multiple inflammatory pathways, including inhibiting the activity of enzymes like COX-2 and reducing the production of pro-inflammatory cytokines, potentially lowering the risk of chronic inflammation-related cancers [44]. Beta-glucans and other immunomodulatory compounds activate various immune cells, such as macrophages and natural killer cells, essential for identifying and destroying cancer cells, resulting in a more robust immune response against potential tumors [45]. The bioactive compounds in *Avena Sativa* also inhibit the proliferation of cancer cells and prevent their spread; for instance, avenanthramides can induce apoptosis in cancer cells, while saponins can inhibit the metastatic process [46]. Lignans and other phytoestrogens in *Avena Sativa* influence hormone levels in the body, binding to estrogen receptors and modulating the effects of estrogen, which is associated with the risk of hormone-related cancers [47]. The presence of these compounds in *Avena Sativa* adds another layer to the cereal's cancer-preventive properties; these synergistic effects illustrate how the combination of different bioactive compounds in *Avena Sativa* can lead to a more comprehensive anticancer effect, enhancing their individual effects and contributing to the potential of *Avena Sativa* as a functional food in

cancer prevention [48].

7. Clinical Evidence

Clinical evidence on the potential roles and mechanisms of *Avena Sativa* in cancer prevention comes from epidemiological studies, clinical trials, and experimental research [49]. Epidemiological studies have explored the relationship between oat consumption and cancer risk, suggesting a slight protective effect with relative risks around 0.9. However, these studies grapple with challenges like dietary exposure misclassification, limited statistical power, and potential residual confounding. Clinical trials have highlighted the preventive effect of resistant starch found in *Avena Sativa*, showing significant benefits in individuals with a high hereditary risk of cancer [50]. Consistent research indicates that whole grain intake, including *Avena Sativa*, is associated with reduced cancer odds, attributed to whole grains' vitamins, minerals, phytochemicals, and fiber that lower the risk of colorectal cancer and other chronic diseases. Specific studies on oatmeal point to its role in combating colon cancer, with its soluble fiber, especially beta-glucan, being beneficial for lowering blood cholesterol and potentially reducing colorectal cancer risk [51]. Systematic reviews and meta-analyses examining the link between ultra-processed food consumption and cancer risk suggest a significant association between ultra-processed foods and the development of cancers, such as breast, pancreatic, and colorectal cancers, while underscoring the protective effects of whole grains like *Avena Sativa* [52]. This clinical evidence supports the beneficial effects of *Avena Sativa* in cancer prevention. However, it's crucial to recognize that *Avena Sativa* should complement a balanced diet, regular exercise, and healthy lifestyle choices for effective cancer risk reduction, with ongoing research essential to full understanding these protective effects [53].

8. Molecular Pathways

To provide a comprehensive academic perspective on the potential functions and mechanisms of *Avena Sativa* in cancer prevention, we delve into the molecular pathways affected by their bioactive compounds [54]. Avenanthramides, unique antioxidants in *Avena Sativa*, prevent cancer by

blocking reactive species, reducing oxidative stress, and potential DNA damage [55]. They modulate cell signaling pathways, including apoptosis and senescence, block cell proliferation, and inhibit epithelial-mesenchymal transition (EMT) and metastasis. The combined action of various antioxidants in Avena Sativa provides a stronger defense against oxidative stress, enhancing the overall anticancer effect [56]. Avena Sativa also modulates inflammation through compounds that suppress the activation of the NF- κ B pathway, a key regulator of inflammation and cell survival in cancer, and inhibit the production of pro-inflammatory cytokines like TNF- α and IL-6 [57]. Beta-glucans in Avena Sativa activate immune cells such as macrophages and natural killer (NK) cells, enhancing the body's defense against tumors and reducing inflammation. The fiber in Avena Sativa influences the composition of the gut microbiota, promoting the growth of beneficial bacteria that produce anti-inflammatory compounds crucial for cancer prevention [58].

Additionally, Avena Sativa may contain compounds that inhibit enzymes like cyclooxygenase-2 (COX-2), which are involved in the inflammatory process and are implicated in cancer [59]. These anti-inflammatory properties contribute to Avena Sativa's role as a functional food in cancer prevention, suggesting that reducing inflammation may help lower the risk of cancer initiation and progression [60]. However, these effects should be part of a comprehensive approach to cancer prevention that includes a balanced diet and healthy lifestyle choices [61]. The synergistic effects of the bioactive compounds in Avena Sativa lead to a more comprehensive anticancer effect, enhancing their individual effects and contributing to the potential of Avena Sativa as a functional food in cancer prevention; while these synergistic effects are promising, they should be part of a comprehensive approach to cancer prevention that includes a balanced diet and healthy lifestyle choices [62].

The anticancer potential of Avena sativa is further enhanced by its impact on transcription regulation, microRNAs (miRNAs), and cell signaling pathways. Avena sativa contains bioactive compounds that modulate gene expression by influencing transcription factors and signaling pathways in cancer progression. These compounds can inhibit the nuclear

factor kappa-light-chain-enhancer of activated B cells (NF- κ B) pathway, which plays a crucial role in inflammation and cancer. Additionally, Avena sativa affects the expression of miRNAs, small non-coding RNAs that regulate gene expression post-transcriptionally [57, 58]. By modulating miRNAs, Avena sativa can suppress oncogenes and enhance tumor suppressor genes, inhibiting cancer cell proliferation and inducing apoptosis (programmed cell death). Research studies have shown that Avena sativa can influence several key cell signaling pathways in cancer. For example, it can modulate the phosphatidylinositol 3-kinase (PI3K)/Akt pathway, which is crucial for cell survival and growth, and the mitogen-activated protein kinase (MAPK) pathway, which is involved in cell proliferation and differentiation. These pathways are often dysregulated in cancers such as breast, colon, and prostate cancer [57, 59-62].

In a study conducted by other researchers in England, the effect of Avena sativa on miRNA expression in colorectal cancer was investigated. Their findings showed that Avena sativa can modulate the expression of specific miRNAs and lead to the suppression of oncogenes and the increase of tumor suppressor genes. Similarly, another study conducted by researchers in Denmark investigated the effects of Avena sativa on breast cancer and showed its ability to affect the NF- κ B pathway and reduce inflammation. Furthermore, the fiber in Avena sativa promotes healthy gut microbiota, fostering the growth of the normal flora and probiotics that produce anti-inflammatory compounds associated with a reduced risk of colorectal cancer. Avena sativa may also contain compounds that inhibit enzymes such as cyclooxygenase-2 (COX-2), which are involved in the inflammatory process and implicated in cancer [57-63].

These anti-inflammatory properties contribute significantly to Avena Sativa's role as a functional food in cancer prevention, suggesting that reducing inflammation may help lower the risk of cancer initiation and progression. By incorporating Avena sativa into the diet, individuals may benefit from its multifaceted role in modulating inflammation, supporting immune function, and fostering a healthy gut microbiota through the action of probiotics, thereby potentially reducing the overall risk of cancer

development. This detailed understanding underscores the potential of *Avena sativa* as a dietary component in cancer prevention strategies, highlighting its multifaceted role in modulating inflammation, supporting immune function, regulating transcription and miRNA activity, and influencing key cell signaling pathways to combat cancer effectively [60, 62-63].

Furthermore, when researchers are conducting their research, in conclusion, cellular senescence is a possible therapeutic tool in the fight against cancer [63, 64]. One barley component, avenanthramide C (AVN C), exhibits anti-tumor, anti-inflammatory, anti-atherosclerotic, and antioxidant properties. Further research is necessary since the connection between AVN C and cellular senescence in malignancies is not entirely understood [63]. The senescence phenotype, characterized by flattened and expanded form, increased activity of senescence-associated β -galactosidase (SA- β -Gal), and G1 phase arrest, is substantiated by the same researchers' suggestion that AVN C therapy predisposes cancer cells, specifically colorectal cancer. The researchers also mentioned the potential benefits of using miRNAs as gene regulators [64]. Additionally, it has been demonstrated in earlier research that AVN C induced cellular senescence by suppressing the miR-

183/96/182 cluster transcriptionally, which in turn reduced maturity. Through the mechanism of attenuating β -catenin-mediated transactivation of the miR-183/96/182 cluster to release its common target FOXO1 and two others, AVN C causes its senescence. It also activated two more targets, SMAD4 and FOXO3, which upregulates the expression of p21 and p16. Furthermore, via suppressing β -catenin, AVN C has also been observed to aid p53-mediated p21 activation. Our findings together reveal a unique β -catenin/miR-183/96/182/FOXO1-mediated CRC cell senescence method, suggesting AVN C functions as a CRC therapeutic adjuvant [62] (Figure 3)

CONCLUSION

Furthermore, when researchers conduct their research, cellular senescence is a possible therapeutic tool in the fight against cancer. One barley component, avenanthramide C (AVN C), exhibits anti-tumor, anti-inflammatory, anti-atherosclerotic, and antioxidant properties. Further research is necessary since the connection between AVN C and cellular senescence in malignancies is not entirely understood. The senescence phenotype, characterized by flattened and expanded form, increased activity of senescence-associated β -galactosidase (SA- β -Gal),

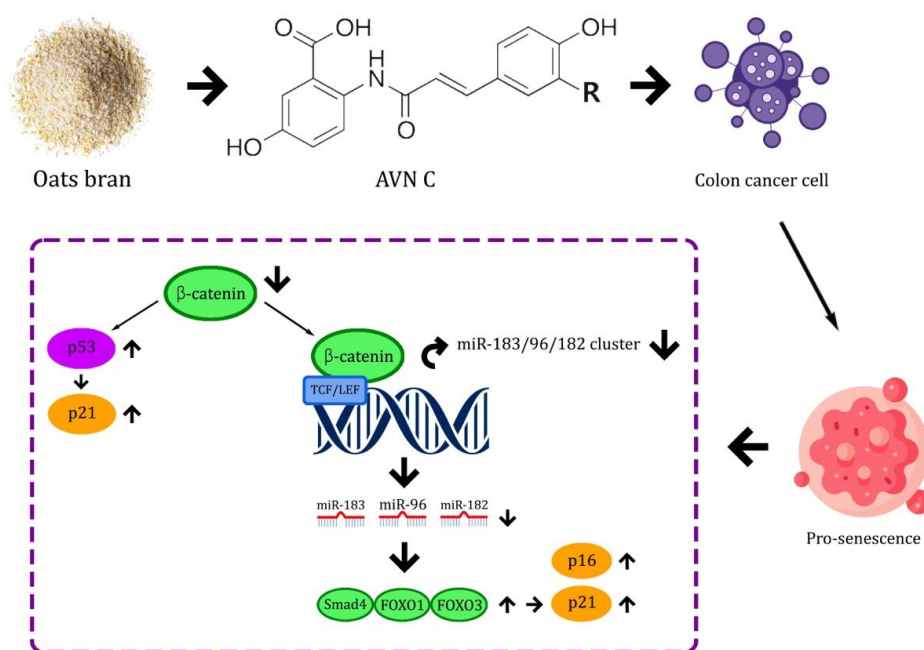


Figure 3. Effect of *Avena Sativa* on gene regulation in colon cancer.

and G1 phase arrest, is substantiated by the same researchers' suggestion that AVN C therapy predisposes cancer cells, specifically colorectal cancer. The researchers also mentioned the potential benefits of using miRNAs as gene regulators. Additionally, it has been demonstrated in earlier research that AVN C induced cellular senescence by suppressing the miR-183/96/182 cluster transcriptionally, which in turn reduced maturity. Through the mechanism of attenuating β -catenin-mediated transactivation of the miR-183/96/182 cluster to release its common target FOXO1 and two others, AVN C causes its senescence. It also activated two more targets, SMAD4 and FOXO3, which upregulates the expression of p21 and p16. Furthermore, via suppressing β -catenin, AVN C has also been observed to aid p53-mediated p21 activation. Our findings together reveal a unique B-catenin/miR-183/96/182/FOXO1-mediated CRC cell senescence method, suggesting AVN C functions as a CRC therapeutic adjuvant.

ACKNOWLEDGMENTS

None declared.

CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

ETHICS APPROVAL

This study does not need an ethical approval number.

REFERENCES

- Meydani M. Potential health benefits of avenanthramides of Avena Sativa. *Nutrition reviews*. 2009;67(12):731-5. DOI: [10.1111/j.1753-4887.2009.00256.x](https://doi.org/10.1111/j.1753-4887.2009.00256.x).
- George S, Abrahamse H. Redox Potential of Antioxidants in Cancer Progression and Prevention. *Antioxidants*. 2020;9. DOI: [10.3390/antiox9111156](https://doi.org/10.3390/antiox9111156).
- Aldubayan M, Elgharabawy R, Ahmed A, Tousson E. Antineoplastic Activity and Curative Role of Avenanthramides against the Growth of Ehrlich Solid Tumors in Mice. *Oxidative Medicine and Cellular Longevity*. 2019. DOI: [10.1155/2019/5162687](https://doi.org/10.1155/2019/5162687).
- Wang P, Chen H, Zhu Y, McBride J, Fu J, Sang S. Oat avenanthramide-C (2c) is biotransformed by mice and the human microbiota into bioactive metabolites. *The Journal of nutrition*. 2015;145(2):239-45. DOI: [10.3945/jn.114.206508](https://doi.org/10.3945/jn.114.206508).
- Damazo-Lima M, Rosas-Pérez G, Reynoso-Camacho R, Pérez-Ramírez I, Rocha-Guzmán N, Ríos E, et al. Chemopreventive Effect of the Germinated Oat and Its Phenolic-AVA Extract in Azoxymethane/Dextran Sulfate Sodium (AOM/DSS) Model of Colon Carcinogenesis in Mice. *Foods*. 2020;9. DOI: [10.3390/foods9020169](https://doi.org/10.3390/foods9020169).
- Turrini E, Maffei F, Milelli A, Calcabrini C, Fimognari, C. Overview of the Anticancer Profile of Avenanthramides from Oat. *International Journal of Molecular Sciences*. 2019;20. DOI: [10.3390/ijms20184536](https://doi.org/10.3390/ijms20184536).
- Borek C. Dietary Antioxidants and Human Cancer. *Integrative Cancer Therapies*. 2004;3:333-41. DOI: [10.1177/1534735404270578](https://doi.org/10.1177/1534735404270578).
- Chen C, Milbury P, Collins F, Blumberg J. Avenanthramides are bioavailable and have antioxidant activity in humans after acute consumption of an enriched mixture from Avena Sativa. *The Journal of nutrition*. 2007;137(6):1375-82. DOI: [10.1093/JN/137.6.1375](https://doi.org/10.1093/JN/137.6.1375).
- Wang H, Hung C, Hsu J, Yang M, Wang S, Wang C. Inhibitory effect of whole oat on aberrant crypt foci formation and colon tumor growth in ICR and BALB/c mice. *Journal of Cereal Science*. 2011;53:73-7. DOI: [10.1016/J.JCS.2010.09.009](https://doi.org/10.1016/J.JCS.2010.09.009).
- Stāka A, Bodnieks E, Puķīti, A. Impact of Oat-Based Products on Human Gastrointestinal Tract. *Proceedings of the Latvian Academy of Sciences. Section B. Natural, Exact, and Applied Sciences*. 2015;69:145-51. DOI: [10.1515/prolas-2015-0021](https://doi.org/10.1515/prolas-2015-0021).
- Boffetta P, Thies F, Kris-Etherton P. Epidemiological studies of Avena Sativa consumption and risk of cancer and overall mortality. *British Journal of Nutrition*. 2014;112:S14-S18. DOI: [10.1017/S0007114514002268](https://doi.org/10.1017/S0007114514002268).
- Dioum E, Schneider K, Vigerust D, Cox B, Chu Y, Zachwieja J, et al. Avena Sativa Lower Age-Related Systemic Chronic Inflammation (iAge) in Adults at Risk for Cardiovascular Disease. *Nutrients*. 2022;14. DOI: [10.3390/nu14214471](https://doi.org/10.3390/nu14214471).
- Martínez-Villaluenga C, Peñas E. Health benefits of oat: current evidence and molecular mechanisms. *Current opinion in food science*. 2017;14:26-31. DOI: [10.1016/J.COFS.2017.01.004](https://doi.org/10.1016/J.COFS.2017.01.004).
- Kim I, Hwang C, Yang W, Kim C. Multiple Antioxidative and Bioactive Molecules of Avena Sativa (Avena sativa L.) in Human Health. *Antioxidants*. 2021;10. DOI: [10.3390/antiox10091454](https://doi.org/10.3390/antiox10091454).
- Wu W, Tang Y, Yang J, Idehen E, Sang S. Avenanthramide Aglycones and Glucosides in Oat Bran: Chemical Profile, Levels in Commercial Oat Products, and Cytotoxicity to Human Colon Cancer Cells. *Journal of agricultural and food chemistry*. 2018;66(30):8005-14. DOI: [10.1021/acs.jafc.8b02767](https://doi.org/10.1021/acs.jafc.8b02767).
- Li X, Zhou L, Yu Y, Zhang J, Wang J, Sun B. The Potential Functions and Mechanisms of Oat on Cancer Prevention: A Review. *Journal of agricultural and food chemistry*. 2022. DOI: [10.1021/acs.jafc.2c06518](https://doi.org/10.1021/acs.jafc.2c06518).
- Meydani M. Potential health benefits of avenanthramides of Avena Sativa. *Nutrition reviews*. 2009;67(12):731-5. DOI: [10.1111/j.1753-4887.2009.00256.x](https://doi.org/10.1111/j.1753-4887.2009.00256.x).

- [10.1111/j.1753-4887.2009.00256.x](https://doi.org/10.1111/j.1753-4887.2009.00256.x).
18. Alfieri M, Redaelli R. Oat phenolic content and total antioxidant capacity during grain development. *Journal of Cereal Science*. 2015;65:39-42. DOI: [10.1016/J.JCS.2015.05.013](https://doi.org/10.1016/J.JCS.2015.05.013).
 19. Daniels D, Martin H. Isolation of a New Antioxidant from *Avena Sativa*. *Nature*. 1961;191:1302-2. DOI: [10.1038/1911302A0](https://doi.org/10.1038/1911302A0).
 20. Mohammadi Bondarkhilli SA, Kordkatouli M, Maroufi M. Oncogenic and anticancer roles of miRNAs in colorectal cancer: A review. *Micro Nano Bio Aspects*. 2024;3:14-22. doi: 10.22034/mnba.2024.429195.1053.
 21. Li Y, Chen X, Kwan T, Loh Y, Singer J, Liu Y, et al. Dietary Fiber Protects against Diabetic Nephropathy through Short-Chain Fatty Acid-Mediated Activation of G Protein-Coupled Receptors GPR43 and GPR109A. *Journal of the American Society of Nephrology: JASN*. 2020. DOI: [10.1681/ASN.2019101029](https://doi.org/10.1681/ASN.2019101029).
 22. Zou J, Chassaing B, Singh V, Pellizzon M, Ricci M, Fythe M, et al. Fiber-Mediated Nourishment of Gut Microbiota Protects against Diet-Induced Obesity by Restoring IL-22-Mediated Colonic Health. *Cell host & microbe*. 2018;23(1):41-53. DOI: [10.1016/j.chom.2017.11.003](https://doi.org/10.1016/j.chom.2017.11.003).
 23. Donohoe D, Holley D, Collins L, Montgomery S, Whitmore A, Hillhouse A, et al. A gnotobiotic mouse model demonstrates that dietary fiber protects against colorectal tumorigenesis in a microbiota- and butyrate-dependent manner. *Cancer discovery*. 2014;4(12):1387-97. DOI: [10.1158/2159-8290.CD-14-0501](https://doi.org/10.1158/2159-8290.CD-14-0501).
 24. Paudel D, Dhungana B, Caffé M, Krishnan P. A Review of Health-Beneficial Properties of *Avena Sativa*. *Foods*. 2021;10. DOI: [10.3390/foods10112591](https://doi.org/10.3390/foods10112591).
 25. Turrini E, Maffei F, Milelli A, Calcabrini C, Fimognari C. Overview of the Anticancer Profile of Avenanthramides from Oat. *International Journal of Molecular Sciences*. 2019;20. DOI: [10.3390/ijms20184536](https://doi.org/10.3390/ijms20184536).
 26. Gangopadhyay N, Hossain M, Rai D, Brunton N. A Review of Extraction and Analysis of Bioactives in Oat and Barley and Scope for Use of Novel Food Processing Technologies. *Molecules*. 2015;20:10884-909. DOI: [10.3390/molecules200610884](https://doi.org/10.3390/molecules200610884).
 27. Khan I, Huang G, Li X, Liao W, Leong W, Xia W, et al. Mushroom polysaccharides and jiaogulan saponins exert cancer preventive effects by shaping the gut microbiota and microenvironment in *ApcMin/+* mice. *Pharmacological research*. 2019;104448. DOI: [10.1016/j.phrs.2019.104448](https://doi.org/10.1016/j.phrs.2019.104448).
 28. Espley R, Butts C, Laing W, Martell S, Smith H, McGhie T, et al. Dietary flavonoids from modified apple reduce inflammation markers and modulate gut microbiota in mice. *The Journal of nutrition*. 2014;144(2):146-54. DOI: [10.3945/jn.113.182659](https://doi.org/10.3945/jn.113.182659).
 29. Chan K, Ismail M, Esa N, Alitheen N, Imam M, Ooi D, et al. Defatted Kenaf (*Hibiscus cannabinus* L.) Seed Meal and Its Phenolic-Saponin-Rich Extract Protect Hypercholesterolemic Rats against Oxidative Stress and Systemic Inflammation via Transcriptional Modulation of Hepatic Antioxidant Genes. *Oxidative Medicine and Cellular Longevity*. 2018. DOI: [10.1155/2018/6742571](https://doi.org/10.1155/2018/6742571).
 30. Huang G, Wang Z, Wu G, Zhang R, Dong L, Huang F, et al. Lychee (*Litchi chinensis* Sonn.) Pulp Phenolics Activate the Short-Chain Fatty Acid-Free Fatty Acid Receptor Anti-inflammatory Pathway by Regulating Microbiota and Mitigate Intestinal Barrier Damage in Dextran Sulfate Sodium-Induced Colitis in Mice. *Journal of agricultural and food chemistry*. 2021. DOI: [10.1021/acs.jafc.0c07407](https://doi.org/10.1021/acs.jafc.0c07407).
 31. Khan M, Karima G, Khan M, Shin J, Kim J. Therapeutic Effects of Saponins for the Prevention and Treatment of Cancer by Ameliorating Inflammation and Angiogenesis and Inducing Antioxidant and Apoptotic Effects in Human Cells. *International Journal of Molecular Sciences*. 2022;23. DOI: [10.3390/ijms231810665](https://doi.org/10.3390/ijms231810665).
 32. Li X, Zhou L, Yu Y, Zhang J, Wang J, Sun B. The Potential Functions and Mechanisms of Oat on Cancer Prevention: A Review. *Journal of agricultural and food chemistry*. 2022. DOI: [10.1021/acs.jafc.2c06518](https://doi.org/10.1021/acs.jafc.2c06518).
 33. Sur R, Nigam A, Grote D, Liebel F, Southall M. Avenanthramides, polyphenols from *Avena Sativa*, exhibit anti-inflammatory and anti-itch activity. *Archives of Dermatological Research*. 2008;300:569-74. DOI: [10.1007/s00403-008-0858-x](https://doi.org/10.1007/s00403-008-0858-x).
 34. Kim S, Jung C, Anh N, Kim S, Park S, Kwon S, et al. Effects of *Avena Sativa* (*Avena sativa* L.) on Inflammation: A Systematic Review and Meta-Analysis of Randomized Controlled Trials. *Frontiers in Nutrition*. 2021;8. DOI: [10.3389/fnut.2021.722866](https://doi.org/10.3389/fnut.2021.722866).
 35. Daou C, Zhang H. Oat Beta-Glucan: Its Role in Health Promotion and Prevention of Diseases. *Comprehensive Reviews in Food Science and Food Safety*. 2012;11:355-65. DOI: [10.1111/J.1541-4337.2012.00189.X](https://doi.org/10.1111/J.1541-4337.2012.00189.X).
 36. Bai J, Ren Y, Li Y, Fan M, Qian H, Wang L, et al. Physiological functionalities and mechanisms of β -glucans. *Trends in Food Science & Technology*. 2019. DOI: [10.1016/J.TIFS.2019.03.023](https://doi.org/10.1016/J.TIFS.2019.03.023).
 37. Jayachandran M, Chen J, Chung S, Xu B. A critical review on the impacts of β -glucans on gut microbiota and human health. *The Journal of nutritional biochemistry*. 2018;61:101-10. DOI: [10.1016/j.jnutbio.2018.06.010](https://doi.org/10.1016/j.jnutbio.2018.06.010).
 38. Volman J, Ramakers J, Plat J. Dietary modulation of immune function by β -glucans. *Physiology & Behavior*. 2008;94:276-84. DOI: [10.1016/j.physbeh.2007.11.045](https://doi.org/10.1016/j.physbeh.2007.11.045).
 39. Sang S, Landberg R, Chu Y. Whole grain *Avena Sativa*, more than just a fiber: Role of unique phytochemicals. *Molecular Nutrition & Food Research*. 2017;61. DOI: [10.1002/mnfr.201600715](https://doi.org/10.1002/mnfr.201600715).
 40. Gangopadhyay N, Hossain M, Rai D, Brunton N. A Review of Extraction and Analysis of Bioactives in Oat and Barley and Scope for Use of Novel Food Processing Technologies. *Molecules*. 2011;20:10884-909. DOI: [10.3390/molecules200610884](https://doi.org/10.3390/molecules200610884).
 41. Trabalzini L, Ercoli J, Trezza A, Schiavo I, Macri G, Moglia

- A, et al. Pharmacological and In Silico Analysis of Oat Avenanthramides as EGFR Inhibitors: Effects on EGF-Induced Lung Cancer Cell Growth and Migration. *International Journal of Molecular Sciences*. 2022;23. DOI: [10.3390/ijms23158534](https://doi.org/10.3390/ijms23158534).
42. Paudel D, Dhungana B, Caffé M, Krishnan P. A Review of Health-Beneficial Properties of Avena Sativa . *Foods*. 2021;10. DOI: [10.3390/foods10112591](https://doi.org/10.3390/foods10112591).
43. Jayachandran M, Chen J, Chung S, Xu B. A critical review on the impacts of β -glucans on gut microbiota and human health. *The Journal of nutritional biochemistry*. 2018;61:101-10 . DOI: [10.1016/j.jnutbio.2018.06.010](https://doi.org/10.1016/j.jnutbio.2018.06.010).
44. Daou C, Zhang H. Oat Beta-Glucan: Its Role in Health Promotion and Prevention of Diseases. *Comprehensive Reviews in Food Science and Food Safety*. 2012;11:355-65. DOI: [10.1111/J.1541-4337.2012.00189.X](https://doi.org/10.1111/J.1541-4337.2012.00189.X).
45. Basu P, Maier C. Phytoestrogens and breast cancer: In vitro anticancer activities of isoflavones, lignans, coumestans, stilbenes and their analogs and derivatives.. *Biomedicine & pharmacotherapy = Biomedecine & pharmacotherapie*. 2018;107:1648-66. DOI: [10.1016/j.biopha.2018.08.100](https://doi.org/10.1016/j.biopha.2018.08.100).
46. Hedelin M, Löf M, Andersson T, Adlercreutz H, Weiderpass E. Dietary Phytoestrogens and the Risk of Ovarian Cancer in the Women's Lifestyle and Health Cohort Study. *Cancer Epidemiology, Biomarkers & Prevention*. 2011;20:308-17. DOI: [10.1158/1055-9965.EPI-10-0752](https://doi.org/10.1158/1055-9965.EPI-10-0752).
47. Paudel D, Dhungana B, Caffé M, Krishnan P. A Review of Health-Beneficial Properties of Avena Sativa. *Foods*. 2021;10. DOI: [10.3390/foods10112591](https://doi.org/10.3390/foods10112591).
48. Martínez-Villaluenga C, Peñas E. Health benefits of oat: current evidence and molecular mechanisms. *Current opinion in food science*. 2017;14:26-31. DOI: [10.1016/J.COFS.2017.01.004](https://doi.org/10.1016/J.COFS.2017.01.004).
49. Mätkki Y, Virtanen E. Gastrointestinal Effects of Oat Bran and Oat Gum: A Review. *Lwt - Food Science and Technology*. 2001;34:337-47. DOI: [10.1006/FSTL.2001.0795](https://doi.org/10.1006/FSTL.2001.0795).
50. Xu D, Feng M, Chu Y, Wang S, Shete V, Tuohy K, et al. The Prebiotic Effects of Avena Sativa on Blood Lipids, Gut Microbiota, and Short-Chain Fatty Acids in Mildly Hypercholesterolemic Subjects Compared With Rice: A Randomized, Controlled Trial. *Frontiers in Immunology*. 2021;12. DOI: [10.3389/fimmu.2021.787797](https://doi.org/10.3389/fimmu.2021.787797).
51. Li X, Zhou L, Yu Y, Zhang J, Wang J, Sun B. The Potential Functions and Mechanisms of Oat on Cancer Prevention: A Review. *Journal of agricultural and food chemistry*. 2022. DOI: [10.1021/acs.jafc.2c06518](https://doi.org/10.1021/acs.jafc.2c06518).
52. Paudel D, Dhungana B, Caffé M, Krishnan P. A Review of Health-Beneficial Properties of Avena Sativa . *Foods*. 2021;10. DOI: [10.3390/foods10112591](https://doi.org/10.3390/foods10112591).
53. Paudel D, Dhungana B, Caffé M, Krishnan P. A Review of Health-Beneficial Properties of Avena Sativa. *Foods*. 2021;10. DOI: [10.3390/foods10112591](https://doi.org/10.3390/foods10112591).
54. Thies F, Masson L, Boffetta P, Kris-Etherton P. Avena Sativa and bowel disease: a systematic literature review. *British Journal of Nutrition*. 2014;112:S31-S43. DOI: [10.1017/S0007114514002293](https://doi.org/10.1017/S0007114514002293).
55. Chu Y, Wise M, Gulvady A, Chang T, Kendra D, Klinken B, et al. In vitro antioxidant capacity and anti-inflammatory activity of seven common Avena Sativa. *Food chemistry*. 2013;139(1-4):426-31. DOI: [10.1016/j.foodchem.2013.01.104](https://doi.org/10.1016/j.foodchem.2013.01.104).
56. Guo W, Kong E, Meydani M. Dietary Polyphenols, Inflammation, and Cancer. *Nutrition and Cancer*. 2009;61:807-10. DOI: [10.1080/01635580903285098](https://doi.org/10.1080/01635580903285098).
57. Thies F, Masson L, Boffetta P, Kris-Etherton P. Avena Sativa and bowel disease: a systematic literature review. *British Journal of Nutrition*. 2014;112:S31-S43. DOI: [10.1017/S0007114514002293](https://doi.org/10.1017/S0007114514002293).
58. Li X, Zhou L, Yu Y, Zhang J, Wang J, Sun B. The Potential Functions and Mechanisms of Oat on Cancer Prevention: A Review. *Journal of agricultural and food chemistry*. 2022. DOI: [10.1021/acs.jafc.2c06518](https://doi.org/10.1021/acs.jafc.2c06518).
59. Yu Y, Zhou L, Li X, Liu J, Li H, Gong L. The Progress of Nomenclature, Structure, Metabolism, and Bioactivities of Oat Novel Phytochemical: Avenanthramides. *Journal of agricultural and food chemistry*. 2022. DOI: [10.1021/acs.jafc.1c05704](https://doi.org/10.1021/acs.jafc.1c05704).
60. Fu Rong D, Li Z, Zhang Jinqi Li N. Avenanthramide C induces cellular senescence in colorectal cancer cells via suppressing β -catenin-mediated the transcription of miR-183/96/182 cluster. *Biochemical Pharmacology* 2022;199:115021.
61. Kordkatouli M, CHO WC, Bondarkhilli SAM, Dulskas A, Qureshi SAM. Oct-4 and Its Role in the Oncogenesis of Colorectal Cancer. *Middle East Journal of Cancer*. 2024;15: -. https://mejcs.sums.ac.ir/article_49918_25eefc8c3eb0cd9d543213163f2a0624.pdf
62. Kordkatouli M, Mohammadi Bondarkhilli SA, Sateei A, Mahmood Janlou MA. Roles of miR-21 in the Onset and Advancement of Colorectal Cancer (CRC). *Multidisciplinary Cancer Investigation*. 2024;8 0-0. doi: 10.61186/mci.8.1.3. <http://mcijournal.com/article-1-394-en.html>
63. Sadeghi Z, Maleki P, Mohammadi Bondarkhilli SA, Mohammadi M, Raheb J. Dataset on cytotoxicity effect of polyethylenimine-functionalized graphene oxide nanoparticles on the human embryonic carcinoma stem cell, NTERA2 cell line. *Data in brief*. 2019;26:104487. DOI: [10.1016/j.dib.2019.104487](https://doi.org/10.1016/j.dib.2019.104487)