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ACST ARCHIVES OF CANCER SCIENCE AND THERAPY
ISSN 2766-273X

Short Communication

Anticancer Activity of Genistin: A Short Review

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Abstract

Genistein is an isoflavone glycoside that provides a variety of health advantages. The possibility of cancer chemopreventive drugs derived from natural sources, such as polyphenols, may constitute a novel, cost-effective strategy to reduce the rising burden of cancer throughout the world. A soy-rich diet was linked to cancer prevention in several epidemiological studies, which was explained by the presence of the phenolic component genistein in soy-based foods. Inhibiting metastasis and changing apoptosis, the cell cycle, and angiogenesis are the key ways that genistin fights various cancers. It acts as a chemotherapeutic agent against different types of cancer, mainly by altering apoptosis, the cell cycle, and angiogenesis and inhibiting metastasis. This study critically evaluates the literature that is currently available on the therapeutic benefits of genistin for various cancers.

More Information

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Submitted: May 16, 2023
Approved: June 15, 2023
Published: June 16, 2023

How to cite this article: Rahaman MM, Sikder MI, Khan MA, Islam MT. Anticancer Activity of Genistin: A Short Review. Arch Cancer Sci Ther. 2023; 7: 010-013.

DOI: 10.29328/journal.acst.1001035

Keywords: Genistin; Cancer; Isoflavone protective effect

Introduction

The term "cancer" refers to a class of illnesses indicated by uncontrolled cell proliferation and the capacity to invade or spread to different body parts (WHO) [1]. More than a hundred different diseases are compiled due to cancer. The most typical cancer signs and symptoms include a lump, irregular bleeding, chronic cough, unusual weight loss, and changes in bowel habits (WHO) [1]. The growth of cancer cells is different from normal cell growth.

High intakes of animal fat and alcohol increase the risk of developing cancer, whereas foods of plant origin protect against the disease due to the presence of phytochemicals through a variety of mechanisms of action (such as antioxidant capacity, hormonal activity, enzyme stimulation, and interference with DNA replication) [2,3]. In addition to vitamins and minerals, plant foods also contain secondary plant metabolites like polyphenols [4,5]. The most investigated substances over the past 20 years were polyphenols, which have been looked into for their potential to protect human health. Flavonoids and nonflavonoids are the two main subgroups of polyphenols. Genistin is one of the most significant isofavones [6,7]. Genistin (4′, 5, 7-Trihydroxyisofavone 7-glucoside) is a crucial isoflavone that is frequently present in agriculturally significant legume plants which are indigenous to various Pacific islands, East Asia, and Southeast Asia [8,9]. Numerous diseases, including cancers, are improved by genistin's biological component [10]. Genistein is a phytoestrogen that shares structural similarities with both organic and synthetic estrogens since it contains 17-μs-estradiol [11]. The prevention of cancer is significantly aided by phytoestrogens Mishra, et al. 2003. The literature states that genistin is biologically active and is also a well-described isoflavone, and the most recent research backs up its beneficial effects. Numerous in vitro and in vivo studies have also provided evidence that genistein holds promise as a chemopreventive agent for the treatment of various cancers. We discuss the anticancer effects of genistin compounds in this review.

Methodology

A search was conducted in well-established scientific databases including PubMed, Science Direct, MedLine, and Google Scholar using the keywords Genistin, anticancer, and activity/effect. There were no linguistic limitations.

Inclusion criteria

The following criteria for inclusion were used:

1. Studies with anticancer effects from various sources
2. Studies carried out *in vivo*, *in vitro*, or *ex vivo* with or without experimental animals

3. Studies that include or exclude the mechanism of activity

Exclusion criteria

The following criteria for exclusion were used:

1. Titles and/or abstracts that do not match the inclusion requirements, data duplication

2. Anticancer activity, with other research obscuring the current topic of study

Anticancer effects of genistin (Table 1).

Discussion

A range of medications have been used to treat cancer, including chemotherapy, hormone therapy, radiation, surgery, immunotherapy, and targeted therapy [12]. Choosing the most effective therapy is important despite the fact that there are numerous therapeutic modalities available. It has been predicted that isofavones lower the risk of breast cancer and colon cancer brought on by hormone-mediated processes. The anticancer properties of genistin have been consistently shown by a number of studies. Given that soy isofavones and endogenous estrogens share a similar structural makeup, it has been suggested that using them may help prevent cancers that are hormone-dependent. Genistin is a substance found in soybeans [13]. Genistin inhibited matrix metalloproteinase-3 (MMP-3) concentration-dependent activity and cell invasion, according to an in vitro study using the human invasive breast carcinoma MDA-MB-231 cells [14]. Combination therapies using genistein and genistin, genistein and beta-sitosterol, and beta-sitosterol and genistin inhibit the invasion and migration of breast cancer cells and have demonstrated anti-cancer activity through the regulation of the phosphatidylinositol 3-kinase/mammalian target of rapamycin (PI3K/Akt/mTOR) pathways [15]. Another in vivo investigation utilizing rats revealed that 12-dimethylbenz (a) anthracene

Table 1: Effects of Genistin on cancer cell lines.

Cell line	Dose/Conc.	Activity (Mechanism of action)	References
MCF-7 and MDA-MB- 231	0-150 μM	Suppressed cell proliferation (suppress ERα signaling)	Hwang, et al. 2020 [26]
MDA-MB-231 and MCF-7	0-200 μM; EC_{50} = 72.82 ± 2.66 μM	Inactivation of PI3K/Akt/mTOR pathway	Zhu, et al. 2018 [27]
MDA-MB- 231	31.5-500 μg/ml; IC_{50}= 219 μg/mL	Blocks or inhibits cells when they pass through the G1 to S transition, which reduces the rate of cell division.	Funing, et al. 2021 [28]
SCC-9	0.1-200 μM; MEC= 100 μM	Inhibit cell proliferation	Browning, et al. 2005 [29]
	1200 mg/kg diet for 3 months	-	Hamdy et al. 2011 [30]
MCF-7	20 mg/kg	Suppressing methyl nitrosourea-induced mammary carcinogenesis as well as the lipid environment within the tumor cells, which affects the growth of tumors or proliferation.	Hooshmand, et al. 2008 [31]
SCC-9	1-100 μmolL–1 MEC = 100 μM.	Prevention of cell proliferation	Browning, et al. 2005 [32]
253J B-V		Suppression of tumor angiogenesis and activation of tumor apoptosis in cells	Singh, et al. 2006 [33]
MCF-7 and MDA-MB-231	50 or 100 mg/kg/day for 5 weeks (weekend off) orally phytoestrogens-containing soy extract	Suppressed cell proliferation	Gallo, et al. 2006 [34]
	0.1% genistin for 40 weeks	Androgen-independent PLS10 rat prostate cancer growth is dose-dependently inhibited.	Kato, et al. 2000 [35]
MDA-MB-231	0-100 μM	High-invasive breast cancer cell's ability to migrate was dose-dependently suppressed.	Valachovicova, et al. 2004 [36]
LNCaP	AIN-76 with genistin at 0.14% of the diet	Increased tumor cell apoptosis and decreased tumor angiogenesis	Zhou, et al. 2002 [37]
BCap-37	3×10^5 mol/L	Antiproliferative	Zhenzhou, et al. 2000 [38]
LNCaP and C4-2B	10 mM (genistin); 100 μg/ml, 200 μg/ml, 500 μg/ml, 1000 μg/ml of soy extracts	Induction of prostate cancer cell apoptosis	Dong, et al. 2012 [39]
MCF-7	0.028% and 0.14% GSI (genistin-rich soy isofavones),	Prevention of cancer cell growth	Zhou, et al. 2004 [40]
	20 mg/kg body weight/day	Displayed the highest prevalence of palpable tumors.	Amin, et al. 2006 [41]
MCF-7	fed 1200 ppm for 11 weeks	The size of tumors has grown as a result of an increasing percentage of cell proliferation.	Allred, et al. 2001 [42]
SK-OV-3	1 to 100 μM	Disrupt the cell cycle to prevent cell division, causing cell cycle arrest not only during the G2/M phase but also at the G1 phase.	Choi, et al. 2007 [43]
Human melanoma cell line (M14)	100, 200, and 400 μM	Able to lower the viability of M14 cells, protecting against DNA (pBR322) damage and having a superoxide dismutase-like effect.	Russo, et al. 2006 [44]
LNCaP	AIN-93M with the addition of genistin at 0.14%	Reduced tumor angiogenesis and increased tumor cell death were linked to genistin tumor inhibition, although tumor metastasis was not significantly inhibited.	Zhou, et al. 2002 [45]
253J B-V	AIN-93M with the addition of genistin at 0.14%	Decreased tumor angiogenesis and induced tumor cell death to prevent the orthotopic development of bladder tumors.	Singh, et. al 2006 [46]
MCF-7	750.3 ppm diet	Increase pS2 mRNA expression and encourage cell division in MCF-7 tumors transplanted into athymic mice.	Allred, et al 2004 [47]
HT-29	200 and 300 μg/mL	Enhanced DNA damage and suppress the growth of cancer cells.	Plewa, et al. 2001 [48]
RGC-5	5-50 μM	Not only mitigated cell death but also prevented the activation of mitochondria-associated apoptosis and reduced ROS generation.	Ondricek, et al. 2012 [49]

(DMBA) increased tumorigenicity, endocrine dysregulation, and oxidative stress indicators and caused breast cancer. However, genistin (1200 mg/kg diet) treatment for 3 months increased antioxidant defense levels with highly prospective chemopreventive efficacy [16]. A combination of genistin and iprifavone is effective in reducing mammary cancer brought on by methyl nitrosourea [17]. Additionally, genistin prevented the growth of human ovarian cancer SK-OV-3 cells by disrupting the cell cycle in either the Gap 1 (G1) or G2/M phase and inducing death [18]. Genistin has demonstrated protective effects against Ultraviolet (UV)-induced pBR322 DNA damage and significantly reduced the viability of M14 cells [19]. Additionally, it decreased the growth of SCC-9 human oral squamous cell carcinoma [20]. Through the stimulation of tumor cell death and the inhibition of angiogenesis in 253J B-V tumors in an orthotopic tumor model in mice, genistin therapy decreased the fnal weights of bladder tumors by 56% [21]. In an *in vitro* experiment, it also reduced the growth of myosarcoma, liver, and colon cancer cells [22]. In mice with the LNCaP human prostate tumor, dietary supplements of genistin with soy phytochemical concentrate (SPC) containing food significantly slowed tumor development by 57%, along with decreased tumor angiogenesis and increased tumor cell death [23]. Genistin, which was isolated from a PCC70 soybean fraction, inhibited the proliferation of HT-29 human colon cancer cells in a number of different ways [24]. The estrogen-stimulated gene's expression was dramatically decreased in the mouse uteri by the soybean isofavone genistin, which may halt estrogen-related endometrial carcinogenesis [25].

Conclusion

There are many health benefits associated with genistin. Genistin significantly reduces the risk of developing cancer, according to a number of experimental studies. To further substantiate the claims of activity against cancer, more standardization and documentation of genistin clinical trial data are required.

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