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Research article

# Ginseng consumption and risk of cancer: A meta-analysis

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ABSTRACT

*Background:* The findings of currently available studies are not consistent with regard to the association between the risk of cancer and ginseng consumption. Therefore, we aimed to evaluate this association by conducting a meta-analysis of different studies.
*Methods:* To systematically evaluate the effect of ginseng consumption on cancer incidence, six databases were searched, including PubMed, Ovid Technologies, Embase, The Cochrane Library, China National Knowledge Infrastructure, and Chinese VIP Information, from 1990 to 2014. Statistical analyses based on the protocol employed for a systematic review were conducted to calculate the summary relative risks (RRs) and 95% confidence intervals (CIs).
*Results:* We identified nine studies, including five cohort studies, three case-control studies, and one randomized controlled trial, evaluating the association between ginseng consumption and cancer risk; these studies involved 7,436 cases and 334,544 participants. The data from the meta-analysis indicated a significant 16% lower risk of developing cancer in patients who consumed ginseng (RR = 0.84, 95% CI = 0.76–0.92), with evidence of heterogeneity ($p = 0.0007$, $I^2 = 70\%$). Stratified analyses suggested that the significant heterogeneity may result from the incidence data for gastric cancer that were included in this study. Publication bias also showed the same result as the stratified analyses. In addition, subgroup analyses for four specific types of cancer (colorectal cancer, lung cancer, gastric cancer, and liver cancer) were also performed. The summary RRs for ginseng intake versus no ginseng consumption were 0.77 for lung cancer, 0.83 for gastric cancer, 0.81 for liver cancer, and 0.77 for colorectal cancer.
*Conclusion:* The findings of this meta-analysis indicated that ginseng consumption is associated with a significantly decreased risk of cancer and that the effect is not organ specific.


## 1. Introduction

Cancer imposes a global threat to public health. According to the Global Cancer Statistics estimates, there were about 14.1 million new cancer cases and 8.2 million cancer deaths in 2012 [1]. Importantly, these numbers have rapidly increased with increased population growth and environmental pollution. Malignancy results from complex interactions among multiple genes, the intracellular environment, and neighboring tissues [2]. The basic theory of tumorigenesis suggests that the process starts with a normal cell that is transformed through the activation of proto-oncogenes and the suppression of tumor suppressor genes. After the transformation, the cell does not behave like a normal cell, but instead begins to exhibit the properties of a cancer cell. These transformed cells acquire the capability to proliferate uncontrollably through self-sufficiency in growth signals and are insensitive to antigrowth signals. In addition, they are able to evade apoptosis, eventually resulting in tumor growth. As the tumor continues to develop, its growth is aided by the development of new blood vessels that provide it with nutrients, thereby allowing it to sustain itself and

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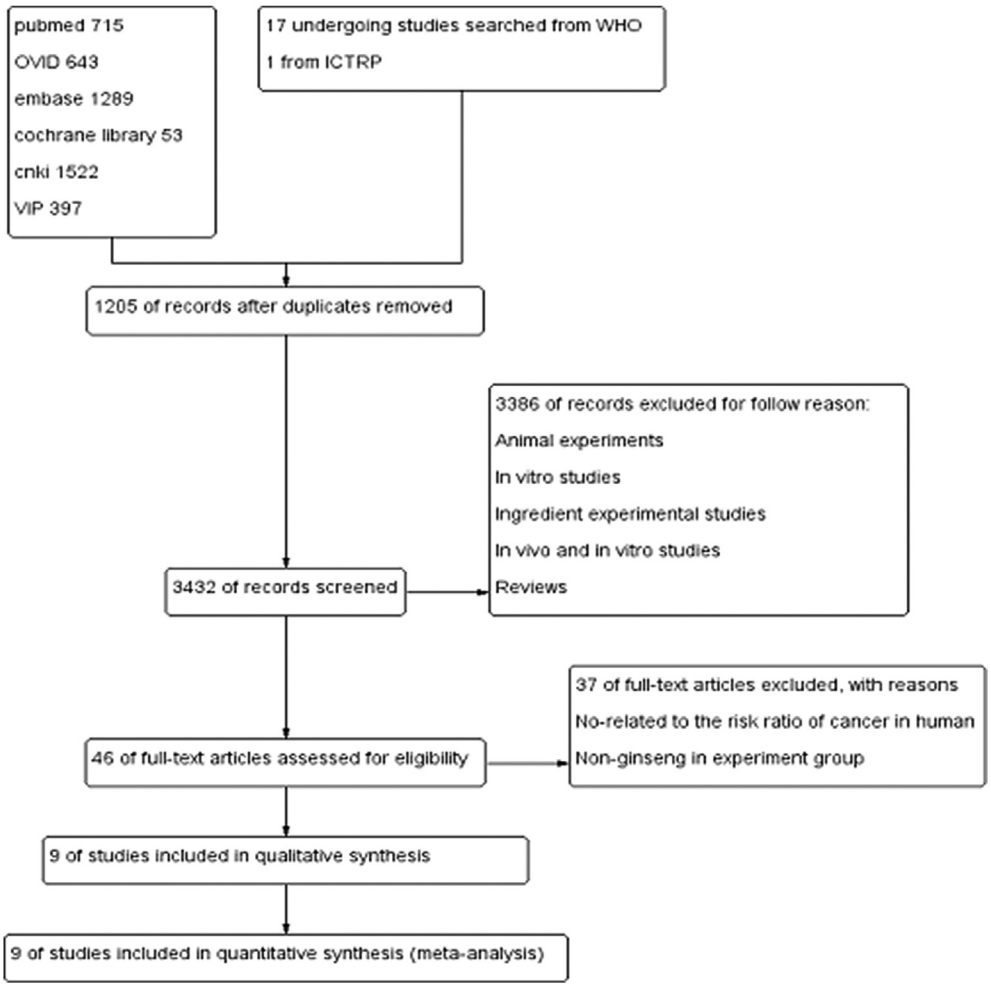


**Fig. 1.** Flowchart of study selection. ICTRP, International Clinical Trials Registry Platform; WHO, World Health Organization.

even invade other tissues, resulting in metastasis that is ultimately lethal [2–5].

Chemoprevention is defined as the use of natural, synthetic, or biological agents to prevent, suppress, and reverse the carcinogenic progression. It is ideally effective in prevention of the disease and should be nontoxic. Chemoprevention is characterized by the disruption of, or at least the delay of, multiple pathways and processes in the three stages of carcinogenesis, namely, initiation, promotion, and progression [6,7]. Chemicals or biomolecules that inhibit the initiation stage are necessary for the preservation of DNA [8,9]. In contrast to compounds that preserve DNA, compounds that affect the later stages of carcinogenesis (promotion and progression) are known for their ability to decrease the proliferative capacity of initiated cells. They interfere with cancer cell proliferation by downregulating the expression of the molecules involved in signal-transduction pathways, such as nuclear factor kappa-light-chain enhancer of activated B cells (NF-kB), mammalian target of rapamycin, and signal transducer and activator of transcription 3, and by inhibiting cytochrome $P_{450}$ enzymes that modulate signal transduction to hormone-responsive elements [10]. In addition, suppressing agents are likely to reduce or delay the ability of cancer cells to acquire metastatic properties by promoting pathways leading to apoptosis [11] and inhibiting pathways leading to angiogenesis, epithelial mesenchymal transition, invasion, and dissemination [12].

Traditional herbal medicine used for thousands of years is advantageous in maintaining a balanced health status and help prevent further diseases in a safe and effective manner. Ginseng (*Panax ginseng* Meyer) is widely used and has been included in pharmacopoeias in China, Japan, Germany, France, Austria, and the United Kingdom. It is widely available as an over-the-counter drug and also commonly used as an adjuvant to increase human immunity [13,14]. Furthermore, the protective effect of ginseng in cancer chemoprevention has been shown by extensive laboratory and preclinical studies [15]. Ginseng is chemoprophylactic and often acts on its cellular and molecular targets through various signaling pathways, thereby inhibiting the tumor by regulation of the cell cycle, induction of apoptosis, and inhibition of angiogenesis and invasion [16,17]. The anticancer effects of ginseng involve modulation of diverse signaling pathways, including regulation of cell proliferation mediators (cyclin-dependent kinases and cyclins), growth factors (c-myc, epidermal growth factor receptor, and vascular endothelial growth factor), tumor suppressors (p53 and p21), oncogenes (*MDM2*), cell death mediators [B-cell lymphoma 2 (Bcl-2), B-cell lymphoma-extra large (Bcl-xL), X-linked inhibitor of apoptosis protein (XIAP), caspases, and death receptors], inflammatory response molecules (NF-κB and cyclooxygenase-2), and protein kinases (c-Jun N-terminal protein kinase, Akt, and adenosine monophosphate-activated protein kinase) [18]. During the past decade, although a series of epidemiologic studies had