

Research Article

A Meta analysis of different herbs (leaves, roots, stems) used in treatment of cancer cells

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The initial step in the progression of cancer is the deformation of normal cells, which is caused by mutations in the DNA of the cell. This abnormal cell, during the process of its asexual reproduction, acquires invasion characteristics and causes alterations in the tissues that are around it, while at the same time ignoring signals linked to the regulation of cell growth that are present in its immediate environment. It would appear that a significant number of the chemical compounds that are created by plants do not play any direct role in the growth of plants. These kinds of molecules are referred to by the phrase "secondary metabolite," which is short for "secondary metabolites." Essential components include alkaloids, terpenoids, flavonoids, pigments, and tannins. Secondary metabolites are responsible for a wide variety of biological effects, including those on hematopoietic cells, lipids, and the cardiovascular system. Other biological effects can also be linked to secondary metabolites.

Keywords: Cancer, Herbal treatment, Chemical Constituents, Alkaloids compounds.

1. Introduction

Cancer is one of the leading causes of death around the world, coming in at a close second to cardiovascular diseases. The initial step in the progression of cancer is the distortion of a normal cell, which is caused by mutations in the DNA of the cell [1]. During its process of asexual reproduction, this aberrant cell takes on the characteristics of an invading cell and causes alterations in the tissues that are nearby, while at the same time it is oblivious to signals in its immediate environment that are related to the regulation of cell growth.

Because of how common cancer is all throughout the world, it has become a significant problem for public health [2]. Every year, an estimated 182 out of every 100,000 people are diagnosed with cancer, and of those, an average of 102 people pass away as a direct result of the disease. According to the World Health Organization (WHO), each year there are 14 million new cases of cancer identified worldwide, and the disease is responsible for the deaths of 8 million people. At some time in their life, seven out of every one hundred thirty-four persons in Iran will be given a cancer diagnosis [3]. These statistics show that each year in Iran there are 85,000 newly diagnosed instances of cancer, which ultimately results in 55,000 deaths. Cancer is one of the top causes of mortality, and it is anticipated that the disease would claim the

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lives of about 13.1 million additional people by the year 2030.

Chemotherapy is just one of the many current methods that may be used to treat cancer; however, due to the fact that the chemicals that are used are not selective, along with the cancerous cells, a significant number of healthy cells will also be destroyed. The fundamental obstacle that must be overcome in the treatment of cancer is destroying cancer cells in the presence of normal cells without causing damage to the normal cells. In order to generate anticancer drugs from natural resources like plants, testing cytotoxic compounds and screening raw extracts of plants is required [4,5].

As a result of this, it would be beneficial if there were natural therapies that were both more effective and had fewer adverse effects. Medicinal plants are a great source of potential new drugs that can combat cancer because of the many chemical compounds that they contain.

It would appear that a significant number of the chemical compounds produced by plants do not have a direct role in the development of plants. These kinds of molecules are referred to by the phrase "secondary metabolite," which is short for "secondary metabolites." Essential components include alkaloids, terpenoids, flavonoids, pigments, and tannins [6]. Secondary metabolites are responsible for a wide variety of biological effects, including those on hematopoietic cells, lipids, and the circulatory system, amongst other things.

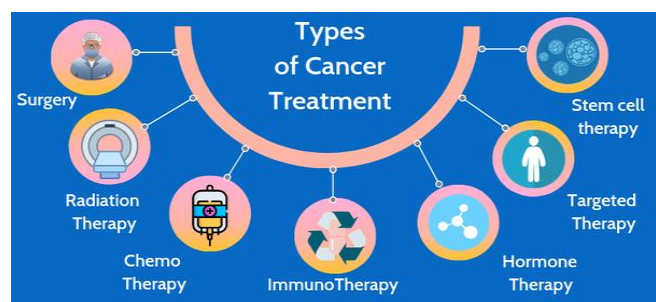


Fig. 1. Types of Cancer Treatment

The discovery of secondary compounds in naturally occurring goods and plants used for therapeutic purposes has been connected to a number of reported advances in conventional cancer treatments. It is believed that plants can inhibit enzymes that drive

cancer, repair DNA, increase manufacture of cellular antitumor enzymes, raise immunity, and provide antioxidant effects. These are the main ways in which plants are thought to have anticancer advantages [7].

Cancer is a debilitating disease, and effective measures to combat cancer are essential to improving the overall health of the society. Herbal medicines are becoming increasingly popular as potential cancer treatments as more information is uncovered about the phytochemicals contained in various herbs. The initial cancerous tumours will either undergo chemical supplement therapy or surgical removal in order to undergo treatment. On the other hand, metastatic cancers are extraordinarily challenging to cure [8]. However, because to the nonselective nature of the chemicals that are used in chemotherapy, a significant proportion of healthy cells will be eliminated along with cancer cells during the treatment process. Fig;1 & 2. The anticancer chemicals that are employed in cancer treatment today originate from plants, the sea, and microorganisms at a rate that is greater than sixty percent.

The use of plants as a treatment for cancer has been the subject of a significant amount of research, which has produced some encouraging findings. Plants have been shown to be useful in treating a variety of health conditions, including diabetes, infertility, thyroid disorders, anaemia, and mental health concerns, according to a large number of research and investigations [9]. It is of the utmost importance to locate plants with cytotoxic effects that have the potential to serve as substitutes for chemotherapy and other time-consuming and uncomfortable cancer therapies [10].

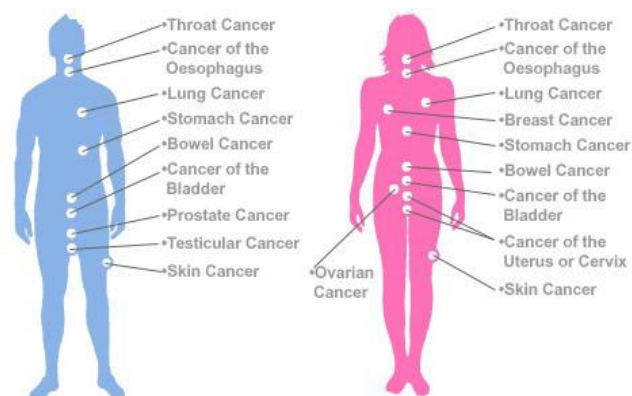


Fig. 2. Different types of Cancer

2. Materials and Methods

We found the information that we used in our inquiry in a variety of places, including PubMed, ScienceDirect, and Google Scholar, to name just a few of those places. We searched for information about cancer using the terms "plant," "herb," and "herbal medicine" in the database that we accessed.



Fig. 3. Achillea wilhelmsii

Achillea wilhelmsii:

There is some evidence to support the hypothesis that prostate cancer (PCa) has an elevated level of human telomerase reverse transcriptase (hTERT) (PCa). Since ancient times, the *Achillea wilhelmsii* (AW) herb has been highly regarded for the curative effects it possesses [11]. Learn how the AW extract influenced a PCa cell line and write out your findings. The MTT assay was used to investigate whether or not a hydroalcoholic extract of AW possessed cytotoxic properties against the PCa PC3 cell line. Fig; 3 Flow cytometry was utilised in order to evaluate the effect that the extract had on apoptosis [12]. The expression of hTERT mRNA was analysed through the technique of reverse transcription-quantitative polymerase chain reaction. The ELISA test was utilised in order to determine the telomerase enzyme concentrations. Following treatment for 48 hours with hydroalcoholic AW extract, the proliferation of PC3 cell lines was reduced at an IC₅₀ level of 150 g/ml. In a dose-dependent manner, treatment of the PC3 cells with AW led to an increase in the proportion of early and late apoptotic cells as well as a reduction in the number of viable cells ($P < 0.001$) in both of these time frames. A startling gap could also be seen between the numbers of early and late apoptotic cells in the sample. The expression of hTERT mRNA was not affected by treatment with AW extract for 2, 4, 8, or 12 hours; however, treatment with AW extract for 24, 48, or 72

hours resulted in a reduction in hTERT mRNA expression [13]. In addition, the concentration of hTERT was significantly reduced after being treated with AW extract for a period of 24 hours, despite the fact that the P-value was relatively low. There was no noticeable difference in hTERT concentration between treatments lasting 2, 4, 8, and 12 hours, as well as 24, 48, and 72 hours. It is possible that the great effectiveness of the hydroalcoholic extract of AW in inhibiting expression of the critical oncogene hTERT in PCa is responsible for the powerful antiproliferative and apoptotic effects that it elicited in the PC3 cell line [14]. Therefore, it is encouraging to use telomerase inhibition as a therapeutic method for treating PCa, and AW may have a lot of potential as a novel natural anticancer medication.



Fig. 4. Allium sativum

Allium sativum:

Garlic, scientifically known as *Allium sativum*, has been used as a dietary supplement and traditional medicine for many years, and its popularity among cancer patients and survivors continues to grow. In vitro studies showed that the development of human breast cancer cell lines MCF-7 and MDA-MB-231 was suppressed by the *allium sativum* L. (ASB) compound. Both the trypan blue assay and the LDH assay were utilised to conduct the quantitative analysis of the cytotoxic effects that ASB extract had on BCa cell lines [15]. After cytotoxicity experiments, assays measuring the activities of caspase-3 and -9 were carried out in order to acquire mechanistic insight into the underlying molecular pathways. After incubation with the ASB extract, the antiproliferative activity was demonstrated using the MTT assay, and the migratory capacity of the BCa cells was evaluated using the lateral motility assay [16]. The bioactive compounds in

the ASB extract were analysed with GC-MS in order to identify them. The cytotoxic effects of ASB extract were felt most acutely by the MCF-7 and MDA-MB-231 cell lines [17]. Both of the cell lines that were tested revealed considerable activation of caspase-9, which lends credence to the theory that the cytotoxic activity is brought about via apoptosis. According to the results of the MTT test, both cell lines exhibited a strong antiproliferative effect at each of the time points tested [18]. The ability of the ASB extract to inhibit motility was demonstrated by the significant slowing down of BCa cell movement that was seen in assays measuring lateral motility. Researchers were able to detect a large number of bioactive compounds in ASB with the help of GC-MS. A good number of these chemicals had previously been associated with cancer-fighting qualities [19]. In general, the bioactive compounds found in *Allium sativum* exhibit significant anticancer and antimotility effects on human breast cancer cell lines MDA-MB-231 and MCF-7.



Fig. 5. Ginger

Ginger:

NFB expression was drastically reduced in the choline-deficient diet supplemented with ginger group, going from 88.3 ± 1.83 percent of samples in the choline-deficient diet group showing positive staining to 32.35 ± 1.34 percent of samples in the choline-deficient diet group showing positive staining ($p < 0.05$). Positive staining for tumour necrosis factor alpha (TNF- α) was seen in 83.3 percent 4.52 percent of samples in the group that consumed a diet low in choline [20-23]. However, this figure reduced substantially to 7.94 percent 1.32 percent after the ginger was applied to the samples ($p < 0.05$). It was revealed that there was a strong link between NF-B

and TNF- in the group that consumed less choline in their diet, but this was not the case in the group that consumed less choline and was treated with ginger extract. As can be seen in Figure 5, the treatment with ginger extract resulted in a significant reduction in the amount of NF κ B and TNF- α expression in the rats with liver cancer [24]. Ginger has the potential to fight cancer and reduce inflammation thanks to its ability to inhibit the production of the cytokine TNF- α , which is associated with inflammation.



Fig. 6. Trigonella foenum graecum

Trigonella foenum graecum:

Every treatment for cancer comes with some sort of undesirable side effects or consequences. Possible toxicities include behavioural dysfunction, cachexia, malaise, anorexia, and weariness (among many others), as well as tissue-specific toxicities such as kidney and lung fibrosis, hepatic cytolysis, mucositis, azoospermia, and myelosuppression [25]. Other possible toxicities include behavioural dysfunction, anorexia, and fatigue. Additional resources are available One such example is the powerful chemotherapy medication cisplatin, which is utilised in the treatment of cancer (see Figure 6). Over the course of the last decade, a significant amount of data has become accessible regarding the efficacy of fenugreek in animal models and in vitro settings for the prevention and treatment of cancer [26]. The anticancer properties of fenugreek have been the subject of much investigation, and a large number of studies have demonstrated that fenugreek extracts and their individual components are both useful in preventing and treating cancer. Fenugreek has a number of anticancer compounds, the most effective of which have been identified to date as being trigonelline, diosgenin, protodioscin, and dioscin.

However, they can be targeted by chemicals that transmit signals [27].



Fig. 7. *Taxus baccata*

Taxus baccata:

One of these plants, the *Taxus baccata*, has been the subject of research for a considerable amount of time. There are alkaloid structures present in certain components of the plant. Despite their structural similarity to those of other plants, their alkaloids have a unique taxane ring that distinguishes them from those of other plants [28]. These alkaloids accelerate and stabilise the production of microtubules, which results in a disruption of the mitosis process. Fig ;7 The microtubules that are the product of dimeric proteins are the target of the drug taxol [29]. Tubulins polymerize into microtubules when joined with microtubule associated protein (MAP) and GTP. Microtubules are necessary for the division of cells and are required for this process. There is a possibility that taxol will stabilise microtubules [30]. The result of this is that the microtubules lose their usual activity, which in turn disturbs the cell cycle and stops the cell from dividing [31]. As a consequence of the creation of aberrant clusters, microtubules that are not working as they should are disseminated throughout the cell.



Fig. 8. *Rosa damascena* Mill

Rosa damascena Mill:

(Damask rose) is a member of the Rosaceae family and has been utilised for the treatment of a variety of conditions in the practise of traditional medicine. However, there hasn't been a lot of research done on whether or not it has any potential anti-cancer capabilities [32]. This research was conducted with the intention of determining whether or not the hexane (RA-HE) and methanolic (RA-ME) extracts of *R. damascena* were cytotoxic to human breast (MCF-7) and lung epithelial (A-549) as well as cervical (HeLa) cancer cells. Fig;8 Both RA-HE and RA-ME had cytotoxic effects on HeLa cells; however, the IC₅₀ values for RA-HE was 819.6 µg/ml while the IC₅₀ value for RA-ME was 198.4 µg/ml [33]. In addition, the cytotoxic mechanism in HeLa cells was investigated by applying cytotoxic doses of the most efficient extract (RA-ME). HeLa cells that were treated with RA-ME at concentrations ranging from 250 to 1000 g/ml showed a concentration-dependent increase in lipid peroxidation (LPO) as well as a reduction in glutathione (GSH), supporting the relationship between oxidative stress and lipid peroxidation. In RA-ME-exposed HeLa cells, we also saw a decrease in mitochondrial membrane potential (MMP) and an increase in the formation of reactive oxygen species (ROS) [34]. Using flow cytometry, an investigation into the subG1 phase of the cell cycle in HeLa cells indicated a significant dose-response link between RA-ME treatment and the induction of cell death. In addition, the Annexin V assay demonstrated a concentration-dependent rise in the number of late-stage apoptotic HeLa cells [35]. Our findings indicate that oxidative stress is the underlying mechanism behind RA-ability ME's to kill HeLa cells and cause cytotoxicity.

Olive tree:

Olive leaf extract, also known as *Olea europaea* L., has a long history of usage in the treatment of a wide variety of medical ailments in traditional medicine. Additionally, the benefits of *Olea europaea* have been linked to longer life expectancy. You have been asked to offer a summary of the current research on the therapeutic potential of *Olea europaea* products in the treatment of cancer [37-39].



Fig. 9. Olive tree

This summary should include a discussion of the hypothesised compounds responsible for the plant's chemotherapeutic activities.

Myrtus communis L:

Researchers in Yemen evaluated the anticancer effects of MC extracts prepared with methanol and hot water on two different cancer cell lines (5637 and MCF-7) [40].



Fig. 10. Myrtus communis L

The authors also investigated the antibacterial and antioxidant properties of plant extracts. Although considerable antioxidant activity and antibacterial activity with MIC values ≤ 125 $\mu\text{g/mL}$ against Gram-positive bacteria were determined for MC, IC₅₀ values for anticancer activity test were computed as >50 $\mu\text{g/mL}$ (see fig. 10) [41-44]. Myrtucommulone is one of the most intriguing chemicals in MC since it is a nonprenylated acylphloroglucinol. In addition to its other features, it was recently demonstrated that myrtucommulone-A triggered apoptosis in cancer cell lines via the mitochondrial cytochrome c/Apaf-1/caspase-9 pathway [45]. The authors of the cited study demonstrated that apoptosis was the underlying mechanism of cell death and observed that myrtucommulone was significantly less cytotoxic for

non-transformed human peripheral blood mononuclear cells (PBMC) or foreskin fibroblasts (EC₅₀ cell death = 20-50 μM). They found that myrtucommulone produced loss of the mitochondrial membrane potential in MM6 cells and provoked release of cytochrome c from mitochondria, suggesting that myrtucommulone induced apoptosis was mediated by the intrinsic rather than the extrinsic death pathway [46]. Myrtucommulone was discovered to promote cell death, but Jurkat cells lacking caspase-9 were resistant to this and neither PARP nor caspase-8 were processed [47]. Myrtucommulone was found to strongly trigger cell death and PARP cleavage even in cell lines lacking CD95 (Fas, APO-1) signalling, FADD, or caspase-8. Aromatic phloroglucinol core was found to be crucial for cytotoxic activity when testing myrtucommulones against various cancer cell lines, as myrtucommulones lacking this core were found to be ineffective against certain cancer cell lines, while myrtucommulones containing this core were found to be effective against these same lines [48]. All of these discoveries seem like the first steps of the pioneer of an ideal and selective anti-cancer therapy, which is why they are so significant and promising. However, additional research is required to bolster and enhance the findings for creating a much-anticipated cancer therapy.

3. Natural Active compound present in herbs

Cancer is a collective term used to refer to a group of diseases that are characterised by the unregulated growth and spread of malignant tumours (through the blood and lymph systems). The disease has a cataclysmic impact on those who are afflicted with it and is one of the leading causes of death across the world [49]. There are more than a hundred distinct types of cancer, and most of the time, these cancers get their names from the organ or cell type in which they are discovered for the first time. Having a population that is getting older correlates to a rise in the incidence of chronic diseases, which creates a significant burden on the public health system [50]. It is believed that more than thirty percent of the population has cancer, and that cancer is responsible for more than twenty percent of all deaths. Mutations in the DNA of the cells that are impacted by cancer often lead to the development of tumours, which are the clinical manifestation of the disease. The primary categories of

tumours are categorised as either benign or malignant [51]. It's possible that chronic inflammation raises the risk of cancer in multiple tissues (e.g., all gastrointestinal). Cells that overexpress antiapoptotic proteins have an increased risk of developing cancer because these cells have a higher chance of being selected for resistance to inflammatory substances [52]. Aside from surgical procedures, the majority of modern cancer treatments depend on cytotoxic regimens. These treatments involve the use of chemicals and radiation in an effort to primarily target quickly dividing cells by interfering with the process that controls cellular reproduction [53]. Because these treatments lack selectivity, they are associated with unfavorable side effects and, more importantly, they

are becoming less effective as resistance to them develops up. The development of new medications with the potential to block the resistance mechanism of cancer is an innovative and intriguing approach to the treatment of the disease [54]. Herbal drugs (such as polyphenols, brassinosteroids, and taxol) are in high demand for the treatment of cancer since they are both all-natural and simple to acquire. A limited number of medicines derived from plants are now being utilised in the treatment of cancer [55]. In order to establish the molecular mechanism that is responsible for the anticancer action of some of these plant components and to deconstruct novel molecules that are derived from these plants, additional research is required.

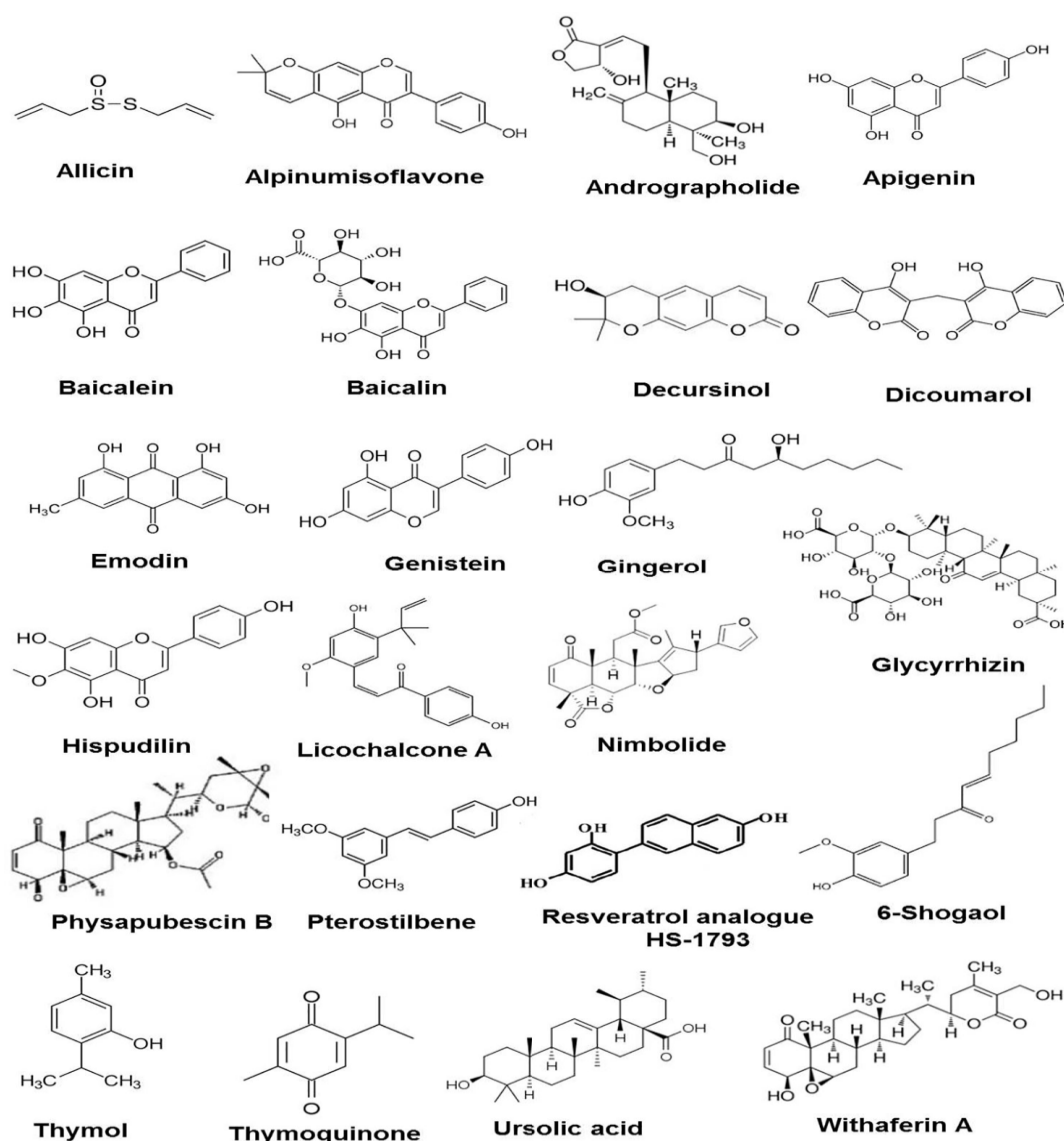


Figure 11. Natural Active compound present in herb for treatment of cancer

4. Conclusion

The disease has devastating effects on those who contract it and is one of the leading causes of death across the world. There are more than a hundred distinct types of cancer, and most of the time, these cancers get their names from the organ or cell type in which they are discovered for the first time. Having a population that is getting older correlates to a rise in the incidence of chronic diseases, which creates a significant burden on the public health system. Because medicinal herbs often have a large number of chemical components, these plants are important resources for the development of novel molecules that are active in the fight against cancer. There are many chemical substances that are created by plants, but it would appear that they do not directly contribute to the growth of the plant. These chemical molecules are called secondary metabolites, and that is the name that is used to describe them. These chemicals are made up of a variety of essential components, including as alkaloids, terpenoids, flavonoids, pigments, and tannins, amongst others. Secondary metabolites are known to have a wide variety of biological effects, including those that are anti-inflammatory, anti-cancer, contraceptive, and varied influences on hematopoietic cells, lipids, and the cardiovascular system. Standard cancer treatments have made significant strides forward as a direct result of the identification of secondary compounds present in naturally occurring products and medicinal plants. It is hypothesised that the anticancer effects of plants stem from their inherent capabilities to repair damaged DNA, inhibit enzymes that promote the growth of cancer, raise the cellular manufacturing of antitumor enzymes, stimulate the immune system, and generate antioxidant effects.

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