REVIEW ARTICLE

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A review of the most important herbal drugs effective in chest pain due to cardiac disease

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ABSTRACT

Cardiovascular diseases is currently one of the most important health issues. Chest pain is one of the most common disorders due to cardiovascular diseases that can be a warning sign for myocardial infarction. Chest pain can be due to heart and otherwise diseases. Bioactive compounds or medicinal herbs are a rich source of antioxidant compounds, biologically active ingredients, phenols, and other substances that inhibit oxidative stress and reduce free radicals through certain mechanisms, and therefore prevent cardiovascular diseases and reduce chest pains. Medicinal plants play the role of the traditional medicine in the treatment and prevention of cardiovascular diseases and other disorders affecting myocardial and vascular tissues. Based on the results obtained from the review of numerous articles indexed in the databases *ISI*, *Scopus*, *PubMed*, *Google Scholar*, etc, a number of plants have been reported to be used for the treatment and prevention of cardiovascular diseases and chest pain due to cardiac disease, including *Curcuma longa*, *Sophora flavescens*, *Calendula officinalis*, *Carthamus tinctorius*, *Tripterygium wilfordi*, *Salvia miltiorrhiza*, *Ampelopsis grossedentata*, *Pseudotsuga menziesii*, *Vitis vinifera*, *Styphnolobium japonicum*, *Allium sativum*. Pharmacological studies have also investigated the therapeutic effects of medicinal herbs, and also their clinical effects and the use of their active ingredients in the production of useful natural drugs. The results of phytochemical investigations on these plants have shown that the most important compounds of the plants include flavonoids,phenolics, Alkaloids, flavonoids and phenolics, saponin and other bioactive compounds can be anti-chest pain hrugs. Due to main active ingredients and flavonoids of these plants, they can be used to produce natural drugs that reduce cardiovascular diseases and thus chest pain due to cardiac diseases, and therefore relieve the suffering of patients. The purpose of this study was to identify and report medicinal plants with potential for anti-chest pain.

Key words: Chest pain; Cardiovascular disease; Medicinal herbs; Phytotherapy

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INTRODUCTION

Chest pain is due to various causes including heart pain, stomach pain, stomach acid back, trauma, and other factors that cause pain and suffering to the patient. Because chest pain usually increases in people in the community and can be a concern for the individual and the family. Waking up at night with chest pain often leads to a heart attack. A heart attack is one of the deadliest diseases, one of the symptoms of which is chest pain. However, an attack is not always felt with chest pain and this can be misleading.

CHEST PAIN

Chest is an important part of our body, in which the

heart, lungs and blood vessels are maintained and supported. The energizing movement of the human life is directed from this part to the whole body. The chest is located between the ribs and there are various problems that can occur for this part of the body (1, 2). There are usually a few signs and symptoms that are warning signs for chest diseases, most notably of which is chest pain (3, 4). The cause of chest pain can be cardiac, digestive, lung and chest wall diseases, anxiety and fear. The treatment is selected based on the cause of pain (5-10). Chest pain is a discomfort or pain affecting the neck to the upper abdomen (the last rib of the chest). Chest pain, depending on its origin, can be a serious warning or safe. Chest pain can be due to various causes divided into six main categories (11-18):

1. **Cardiac causes**: Cardiovascular diseases are one of the most important causes of chest pain, including pericarditis, mitral valve prolapse, valvular cardiac disease, and syndrome X.
2. **Chest wall diseases:** Chest wall diseases are due to severe trauma to the area, muscle spasm, and neck arthrosis that are also causes of pain in the area. This type of chest pain is less dangerous than other pains due to cardiac disease.
3. **Gastrointestinal symptoms**, gastric reflux, bile duct diseases, , inflammation of the pancreas and esophagus, and increased sensitivity to pain can also be the causes of chest pain.
4. **Pulmonary causes**: Pulmonary infections, pneumonia, increased blood pressure in the pulmonary arteries, pulmonary abscess, pulmonary embolism, and asthma are the causes of the chest pain due to pulmonary diseases.
5. **Mental and psychological causes**: Anxiety and panic attack or fear-induced shock may also cause chest pain. Some of the symptoms associated with them may include dizziness and imbalance, dyspnea, heart palpitations and trembling, etc.
6. **Non cardiac chest pain** (**NCCP**) is a pain due to a variety of causes other than cardiac factors. People who are affected by this kind of pain often have signs of pressure and pain in the areas of the lower back, neck, arms and jaw (19-21).

CARDIAC PAIN

Chest pain due to a cardiac origin is referred to as angina. This pain usually occurs when adequate blood and oxygen do not reach the heart. A heart attack is one of the most common types of cardiac pains. A heart attack occurs when fatty deposits or blood clots block the blood flow to the heart and do not allow enough food and oxygen to reach the myocardium. This attack is usually accompanied by a fullness sensation, pain, pressure, and sometimes a burning sensation in the chest. The pain due to heart attack usually takes a few minutes. This pain may spread to other parts of the body. A squeezing sensation is usually experienced in the waist, neck, chin, shoulder, and arms, especially the left arm in heart attack (22-25). Apart from heart attack, there are other cardiac causes that can lead to chest pain including the inflammation of the pericardium that surrounds the heart. The disease, referred to as pericarditis, is usually due to a viral infection. In this case, chest pain is very severe and usually affects a certain point, and is accompanied by symptoms such as fever and fatigue .Coronary artery spasm, vascular diseases, especially aortic disease, etc., are among other cardiac causes of chest pain (24-31).

HERBAL TREATMENTS FOR CHEST PAIN DUE TO CARDIAC DISEASES

Historical background

In ancient Iran, herbs used to treat heart disease, pain and suffering from it. Diet and consumption of medicinal herbs play an important role in reducing chest pain due to cardiac and non-cardiac diseases, including digestive disorders, anxiety and depression (32-34).

Lavender oil can help lower blood pressure and heart rate. It has a relaxing effect on the mind. Massaging is a method for calming and healing the mind (35-37).

Garlic: Research has shown that garlic plays an important role in treating cardiac diseases and reducing vascular deposition. The use of garlic is very useful to relieve chest pain in hypertensive patients and the people whose chest pain is due to a heart attack and the following recovery period (38-40). Chest pain treatment with turmeric:

Turmeric causes relief of chest pain due to its anti-inflammatory properties. Turmeric consumption for the long term will prevent cardiac disease. In addition, spices reduce high cholesterol levels (41-44).

Pomegranate juice: Pomegranate juice is useful for cardiac disease patients and the patients with chest pain and angina, and is a good cardiotonic agent (45, 46).

Parsley: The leaf and fruit of parsley have similar properties to the coumarin drug. Coumarin is present in parsley fruit and acts as an anticoagulant and therefore does not allow the cellular elements in the blood to stiffen. The brewed leaf and fruit of parsley is useful for cardiac disease patients with atherosclerosis (47-49).Chest pain treatment with

ginger: **Ginger** is very beneficial due to its anti-inflammatory properties. In addition, based on research findings, ginger relieves gastrointestinal diseases and prevents vomiting (50-52). In general, treatments for chest pain depend on the cause of the pain. Drug therapy, non-invasive procedure, or a combination of the above-mentioned can be considered a therapeutic approach for patients with more severe and dangerous chest pain, but herbal therapy and the use of medicinal herbs and natural antioxidants to reduce the complications of the chest pain due to cardiac diseases can be a less dangerous and effective solution for the treatment and reduction of chronic and severe chest pain and cardiovascular diseases (32-52).

The present review article is to introduce medicinal herbs effective on cardiovascular diseases and the mechanism of therapeutic actions of the most important medicinal herbs occurring across the world for the chest pain due to cardiovascular disease, and to report medicinal herbs used to treat common cardiovascular diseases in the world.

METHODOLOGY

The information in this review article was obtained using the search terms chest anatomy, chronic chest pain, cardiovascular disease, chest pain due to cardiac disease, effective medicinal herbs on chest pain, effective medicinal herbs on cardiovascular diseases, medicinal herbs and Atherosclerosis, effect of herbal therapy on chest pain due to cardiac disease, effect of extracts and essential oils of medicinal herbs on myocardial tissue in mouse and human, abd effect of herbal extracts on chest pain due to non-cardiac diseases in humans to retrieve indexed articles in the databases such as Iran Medex, Irandoc, ISI, PubMed, Scopus, Web of Science, Scientific Information Database, Magiran, and Google Scholar.

In this study, a total of 100 articles were reviewed. After the preliminary review, 25 articles were found

Table 1: Action mechanisms of effective medicinal herbs on cardiovascular diseases

Scientific Name	Family Name	Common Name	Action Mechanisms of Effective Medicinal Herbs on Cardiovascular Diseases	Reference
Curcuma longa	Zingiberaceae	Turmeric	Anti-inflammatory, anti-oxidizing, anti-cancer, anti-thrombotic, and cardiovascular protective agents. Turmeric with NF-kB inhibition prevents heart embolism and also prevents hyperthyroidism by inhibiting p300. It has antioxidant properties And by controlling eNOS and iNOS, the mucosal stability of the heart's myocardium prevents the effects of diabetes on the heart, and also prevents Adriamycin from inducing cardiomyopathy, and turmeric also inhibits sarcalplasmic Ca2 + -ATPase and corrects calcium defects. Turmeric also acts by induction of HO-1 (oxygenase-1), which is an antiproliferative agent, and also decreases serum cholesterol and inhibits NF-kB as an anti-aterogenic agent, and prevents heart attacks and chest pain from heart attacks he does.	53
Panax	Araliaceae	Ginseng	The effective ingredient of this plant is Ginsenosides, which is a saponin and used to treat heart disease. It has vasorelaxant properties, antioxidants, anti-inflammatory, anti-diabetes, cytoprotective, proangiogenic. This plant activates protein kinase A and stabilizes hypoxia-inducible factor-1. It also activates the signaling pathway of PI3K/Akt. It also prevents cardiac fibrosis by controlling the NFkB pathway and decreases the chest wall chest pain From cardiac fibrosis.	54
Coptis	Ranuncul-aceae	Goldthread	The original compound of this plant is Berberine, an alkaloid that has been used to treat heart disease from the past. It has Positive inotropic properties; vasodilator; cardiac cytoprotective; is antiapoptotic and causes blockage of potassium channels, also activates AMP-activated protein kinase, also activates the PI3K/Akt pathway.	54
Sophora flavescens	Fabaceae	Shrubby sophora	This plant contains active matrine alkaloids and oxymatrine, which is considered as the active ingredient of this plant. The plant has a strong protective effect on the heart, and it increases the hERG by conduction of the potassium (hERG-mediated K + conducance) and also increases its expression. The compounds in this plant reduce enzyme conversion and transforming growth factor-β and collagen. It also inhibits mitogen activation of protein kinase. This plant can positively regulate the expression of β3-adrenoreceptors, endothelial nitric oxide and anti-apoptotic proteins, and prevent heart disorders and complications such as chest pain.	54
Calendula officinalis	Asteraceae	Marigold	A dose of 50mM of this plant extract is used to treat ischemia and has a cardiac effect by stimulating left ventricular pressure and aortic flow, as well as reducing the size of myocardial infarction and cardiomyocytes apoptosis. The protection of the heart appears to be achieved by changing the death signal from an ischemic reperfusion to a survival signal by modulating the antioxidant and anti-inflammatory pathways shown by activating Akt (Protein kinase B) and B-cell lymphoma 2 and decreasing TNFα.	55

Carthamus tinctorius	Asteraceae	Safflower	It probably inhibits the dose of this extract (2.5 and 0.625 g/kg of cardiac arrhythmias and increased cardiac palpitations, decreases the concentration of IL-6 and TNF-α in the serum, and suppresses excess expression of the Bax protein and It also decreases BCl-2 expression and greatly reduces the Bax/Bcl-2 ratio.	55
Tripterygium wilfordi	Celastraceae	Thunder god vine	Triptolide is the active ingredient of this plant that suppresses the immune system and anti-inflammatory drugs. The extract dose of this plant is 20 μg/kg/d and 100 μg/kg/d, probably myocardial fibrosis, reduces hypertrophy and reduces cardiac dysfunction Which reduces the production of pro-vibrotic factors of TNF-α and IL-1β. A dose of 20 ng/ ml (20 ng/ml) of inflammation of H9c2 heart cells in high glucose exposure by reducing the activation of NF-κB The mechanism by which the plant protects the body against a heart attack is probably through the inhibition of NF-κB / IL-1β and NF-κB/ TNF-α cascades.	56
Astragalus	Fabaceae	Milkvetch	APSA is a part of the plant that is active in this plant. APS improves cardiac function and myocardial collagen by inhibiting chymase-Ang II system Ang II-activated ERK1/2. Also, APS can improve glucose metabolism disorders in diabetic hamster by increasing the expression of the GLUT-4 gene and controlling the level of Peroxisome proliferator-activated receptor alpha. Pre-treatment with 0.8 mg/ml polysaccharide (APS) can inhibit high-glucose apoptosis in H9c2 cells by reducing the expression of the Caspases and releasing cytochrome C from mitochondria to the cytoplasm by modulating the ratio of BCL-2 to BCL2 Associated X in the mitochondria.	56
Salvia miltiorrhiza	Lamiaceae	Chinese sage	Intraperitoneal injection of salvia miltiorrhiza at a dose of 100 mg/kg/d for 4 weeks improved the cardiac performance of diabetic rats and compared with low-level thrombospondin-1 (TSP-1) and Transforming growth factor beta 1 cardiomyopathy. Protects the heart tissue. Cryptotanshinone is a major active ingredient isolated from this plant. Oral doses of 10 mg/ kg/d for 28 days reduce heartbeat in diabetic rats with streptozotocin by inhibiting the STAT3 pathway and expressing MMP-9.	56
Ampelopsis grossedentata	Vitaceae	Moyeam	Myricitrin is a flavone isolated from the root of Ampelopsis grossedentata. Pre-treatment with this flavone dose of 25 μg /ml for 12 hours significantly reduced AGE-induced inflammatory cytokines and cell apoptosis by activating nrf2 and inhibiting NF-κB. Oral administration of 300 mg/kg/d for 8 weeks reduced cardiomyocytes apoptosis and inflammation of the diabetic mouse heart by regulating the route Protein kinase B and ERK-mediated nuclear transcription factor-erythroid 2-related factor 2.	56
Pseudotsuga menziesii	Pinaceae	Douglas fir	Taxifolin flavonoids found in Pseudotsuga taxifolia At concentrations of 40 μg/ml and 20 can reduce the apoptosis of H9c2 cells with high blood sugar by inhibiting Reactive oxygen species production. Taxifolin reduces structure and function disorders by blocking the oxidative activity of Nicotinamide adenine dinucleotide phosphate.	56
Vitis vinifera	Vitaceae	Grape vine	Resveratrol (3, 5, 4'-trihydroxylstilbene) is a combination of natural polyphenols in grapes that prevents myocardial infarction apoptosis in a newborn's high blood sugar by inhibiting NADPH-induced ROS production and reducing activity levels An antioxidant enzyme in the heart that is probably done by the 5' AMP-activated protein kinase signaling pathway.	56
Passiflora	Passifloraceae	Passion flowers	Chrysin is a natural flavonoid present in this plant and a PPAR-γ agonist Isoproterenol-induced cardiac damage in diabetic rats reduces oxidative stress by activating PPAR-γ and inhibiting AGE-RAGE-mediating inflammation and signaling pathways.	56
Styphnolobium japonicum	Fabaceae	Japanese pagoda tree	Troxerutin is a bioflavonoid that protects against diseases and cardiac disorders, which effect through the suppression of NF-κB and JNK in diabetic rats.	56
Citrus	Rutaceae	Citrus	Nobiletin Flavonoids found in Citrus Skin is a treatment with this combination 50mg/kg/d in. 11 weeks) reduces diabetic heart damage through oxidative stress suppression, JNK pathways, p38 MAPK, and NF-κB.	56
Grapefruit	Rutaceae	Grapefruit	Naringin (4, 5, 7-trihydroxyflavonone-7-rhamnoglycoside) is the most flavonoid glycoside present in grapefruit, causing its bitter taste. This combination with 80 μM dose of cardiopulmonary bypass grafts contributes to high glucose damage by ROS and inhibition of waterfalls. MAPK protects.	56
Allium sativum	Amaryllidaceae	Garlic	The Allian substance present in this plant, as an inhibitor of plaque atherosclerosis and vasodilator enhancer. NO is produced by nitric oxide synthase (NOS) from L-arginine. NO stimulates Guanillac cyclase to modify GTP (Guanosine Triphosphate) to c-GMP to activate protein kinase G, which reactivates Ca + 2 and activates potassium channel, which is activated by calcium. Reducing the concentration of myosin light chain kinase (MLCK), Ca + 2 can not be phosphorylated for longer myosin, thus the bridge cycle is stopped and the smooth muscle of the blood vessels is relaxed so that vasodilation occurs.	57

Table 2: Effective material of the herbal plant

Scientific Name	Effective material	Ref.
Curcuma longa	Diarylheptanoids, curcumin, demethoxycurcumin, bisdemethoxycurcumin, germacrone, atlantone, zingiberene	53
Panax	Ginsenosides, saponin, polyacetylenic alcohols	54
Coptis	Berberin, Alkaloids, isoquinoline alkaloids berberine, palmatine, and coptisine	54
Sophora flavescens	Alkaloids, Matrine, oxymatrine, kurarinol, kushenol I/N and kurarinone.	54
Calendula officinalis	flavonol glycosides, triterpene oligoglycosides, oleanane-type triterpene glycosides, saponins, sesquiterpene glucoside.	55
Carthamus tinctorius	linoleic acid, adiponectin, flavonoids and phenolics.	55
Tripterygium wilfordi	Triptolide, Celastrol, pentacyclic triterpenoid, diterpene	56
Astragalus	lavonoids, saponins, polysaccharides	56
Salvia miltiorrhiza	salvianolic acid, dihydrotanshinone, tanshinone I, tanshinone IIA	56
mpelopsis grossedentata	Myricitrin, flavonoids, dihydromyricetin, epigallocatechin-3-gallate	56
Pseudotsuga menziesii	Taxifolin, daglesioside II [kaempferol 3-O-[2", 5"-O-(4"'-hydroxy)-beta-truxinoyl]-alpha-L-arabinofuranoside] (2), daglesioside III [kaempferol 3-O-[2", 5"-di-O-(E)-p-coumaroyl]-alpha-L-arabinofuranoside] (3), and daglesioside IV [kaempferol 3-O-[3", 6"-di-O-(E)-cinnamoyl]-beta-D-glucopyranoside] (4). In addition, the known flavonoids (E)-tiliroside, (E)-ditiliroside, astragalin (kaempferol 3-O-beta-D-glucopyranoside), isorhamnetin, kaempferol, and quercetin	56
Vitis vinifera	Resveratrol (3, 5, 4′-trihydroxylstilbene), Anthocyanins, hydroxycinnamic acids proanthocyanidins, Stilbenoids	56
Passiflora	Chrysin, formic, butyric, linoleic, linolenic, malic, myristic, oleic, palmitic acids, phenolic, amino acid α-alanine. Esters, ethyl butyrate, ethyl caproate, n-hexyl butyrate and n-hexyl caproate	56
Styphnolobium japonicum	Troxerutin, rutin, quercetin., flavonoid glycosides sophoricoside, genistin, rutin, flavonoid aglycones genistein, kaempferol, sophorabioside, sophoricoside, genistein-7-diglucoside, genistein-7-diglucorhamnoside, glycosides kaempferol-3-sophoroside, kaempferol-3-rhamnodiglucoside., cytisine, N-methylcytisine, sophocarpine, matrine, stizolamine	56
Citrus	Nobiletin, flavonoids, limonoids	56
Grapefruit	Naringin (4, 5, 7-trihydroxyflavonone-7-rhamnoglucoside)	56
Allium sativum	Alliin, ajoene, polysulfides, vinyldithiins, S-allylcysteine, saponins, flavonoids	57

to address the subject of our study and were selected for analysis.

RESULTS

medicinal herbs that were addressed in this article are effective in some way on the treatment and prevention of cardiovascular diseases (atherosclerosis, heart attacks, etc.) and chest pain due to cardiac and non-cardiac diseases (Table 1). Based on the results of this review, a number of plants have been reported to prevent cardiovascular diseases (atherosclerosis, heart attack, etc.) and chest pain due to cardiac and non-cardiac disease, Including, Curcuma longa, Panax, Coptis, Sophora flavescens, Calendula officinalis, Carthamus tinctorius, Tripterygium wilfordi, Astragalus, Salvia miltiorrhiza, Ampelopsis grossedentata, Pseudotsuga menziesii, Vitis vinifera, Passiflora, Styphnolobium japonicum, Citrus, grapefruit and Allium sativum.

Additional information on medicinal and therapeutic plants is given in Table 1. The results from phytochemical investigations of plants have shown that the most important compounds of the plants include total flavonoids and phenolics, steroids, Alkaloids, linoleic acid, adiponectin, flavonoids and phenolics., Myricitrin, Nobiletin, flavonoids, limonoids, Naringin(4, 5, 7 trihydroxyflavonone-7-rhamnoglucoside), Alliin, Alkaloids, isoquinoline alkaloids berberine, palmatine, and coptisine, gallic acid, rutin and saponin, ect. The most important active ingredients and important flavonoids in these plants are shown in Table 2.

DISCUSSION

Today, phytotherapy, referred to as the use of plant-based products and herbal extracts, is widespread around the world, even in industrialized countries that are the pioneers of technology and science in the use of synthetic herbal drugs. Medicinal herbs have important antioxidant and anticancer properties due to their strong phenolic compounds and flavonoids, and these plants reduce oxidative markers, such as ROS and NOS, that damage free radicals that are the cause of certain diseases such as liver injury, gum tissue damage, atherosclerosis, cardiovascular disease, and chest pain (58-72).Today, cardiovascular diseases are one of the most important health issues. Bioactive compounds or medicinal herbs, which are a rich source of antioxidant substances, reduce free radicals and control oxidative stress. As the phytochemical investigations of medicinal herbs effective to reduce cardiovascular disorders have shown, these plants have numerous flavonoids and antioxidants that, through certain mechanisms and by means of antioxidant substances, inhibit oxidative stress and prevent dyslipidemia and cardiac diseases (64-78). Antioxidant properties of medicinal herbs are due to the presence of many active ingredients, including flavonoids, phytosterols, vitamins, quercetin, terpenoids, carotenoids, curcumin, lignin and saponin, etc. However, the phenolic compounds and polyphenols contribute most significantly to this action; therefore, there is a significant relationship between the polyphenolic compounds in the extract and its antioxidant activity (53-57). Besides, medicinal herbs Curcuma longa, Sophora flavescens, Calendula officinalis, Carthamus tinctorius, Tripterygium wilfordi, Salvia miltiorrhiza, Ampelopsis grossedentata, Pseudotsuga menziesii, Vitis vinifera, Styphnolobium japonicum and Allium sativum. have strong antioxidant activity and produce protective effects against cardiovascular diseases by inhibiting hyperglycemia and oxidative stress. These plants produce protective effects against cardiovascular damage and chest pain due to cardiac diseases induced by free radicals, as well as against damaging agents to cardiovascular tissues by inhibiting apoptosis signaling and triggering apoptosis pathways in cardiovascular system cells, and therefore reduce chest pain and improve cardiac function.

The results from phytochemical investigations of the medicinal herbs have indicated that their antioxidant and functional properties may be due to active ingredients and flavonoids, such as, total flavonoids, phenolics, steroids, alkaloids, linoleic acid, adiponectin, phenolics, myricitrin, nobiletin, limonoids, naringin (4,5,7-trihydroxyflavonone-7-rhamnoglucoside), Alliin, alkaloids, isoquinoline alkaloids berberine, palmatine, and coptisine, gallic acid, rutin and saponin, etc. which produce potent antioxidant effects and reduce chest pain due to cardiac diseases (53-57). Since illnesses associated with neurological and psychiatric illness cause suffering to the patient, the use of medicinal herbs that can reduce these diseases and pain is a good therapeutic approach and medicinal herbs are used not only in the treatment of diseases, but also in the prevention and control of diseases and as cosmetics (79-91). Therefore, the available observations are important for the treatment of cardiovascular diseases and the reduction of chronic chest pain, as well as for future studies on traditional medicine for the development of herbal drugs.

Declaration of conflicting interests

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Authors' contributions

All authors searched, studies, reviewed and contributed to the design of the research. All authors reviewed, commented and approved the final draft.

Ethical Approval

In preparation of this review article we tried to consider all ethical issues.

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