What You Should Know About Taking Herbs with

PrTaro-Warfarin

(Warfarin sodium tablets, USP)

Patient Education Booklet

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Introduction

The use of natural health products including herbs has dramatically increased in Canada over the past several years. According to recent surveys, up to 50% of Canadians use natural health products every year.

Although people take herbal products to prevent or treat various diseases, there is often little high quality scientific evidence that they are effective. Since January 2004, herbals and other natural supplements have been regulated as natural health products under new regulations developed by the Natural Health Products Directorate (Health Canada). The new regulations require that each product be reviewed by Health Canada and given a license (noted on the label as a NPN or Natural Product Number). Manufacturers of natural health products must also be licensed and follow specific "Good Manufacturing Practice" standards as explained in the new regulations. Finally, the new regulations outline what information must be provided to consumers on the labels of all natural health products. For more information about the new regulations visit the Natural Health Product Directorate website at:
http://www.hc-sc.gc.ca/dhp-mps/prodnatur/index_e.html

Many natural health products, including herbs, are advertised as being safe because they are "natural." Being "natural" does not mean that side effects will not occur or that herbal products will not interact with medications you may be taking.

How Herbs Can Interact With Warfarin

Herbs contain hundreds of ingredients, which can cause unwanted side effects and interact with prescription medications. Although some research has been done on how herbs interact with prescription medications, not enough is known. That is why you should be cautious about taking herbs with warfarin sodium tablets[3].

Some herbs can interact with warfarin, causing it to increase its effectiveness, which may cause bleeding problems. Other herbs may cause warfarin to be less effective, which may lead to blood clotting problems. Still other herbs prevent platelets from forming a clot after an injury, similar to the way aspirin does. When these products are taken with warfarin there is a greater chance of excess bleeding.

The purpose of this booklet is to identify some common herbs and other natural health products, and describe what is currently known about how they interact with warfarin. It also briefly describes some of the common uses, and possible side effects of these herbs and natural health products. The information presented is based on a review of the scientific literature available at the time this booklet was prepared.

The authors of this booklet do not claim to have reviewed all the literature and believe there is additional literature that has not come to our attention. Further, the authors make no judgments as to the truthfulness of the literature or the accuracy of any claims. The "Purpose/Use" for each herbal product is based on unsubstantiated claims in literature as well as historical claims, the truthfulness of which has not been subjected to rigorous review by the Natural Health Products Directorate (Health Canada). Such claims are included in this booklet only as a background to their possible interaction with warfarin.

[3] You should always talk to your doctor, pharmacist, and other healthcare providers before you take any prescription medication, over-the-counter product, or herbal product with warfarin.

Black Cohosh (Cimicifugaracemosa)

Purpose/Use: Black cohosh is claimed to relieve hot flashes, mood disturbances and other symptoms associated with menopause. The few clinical trials completed to date suggest that any positive effects are likely to be small. Side effects of black cohosh are generally mild, but few studies have investigated its use for longer than 6 months.

Interactions with warfarin: Raw black cohosh plants have been reported to contain salicylic acid in small amounts and thus theoretically may increase the effects of drugs like warfarin. We are not aware of any clinically relevant reports of interactions between black cohosh and warfarin. However, you should always talk to your doctor, pharmacist or other healthcare providers before taking black cohosh with warfarin.

Boldo and Fenugreek (Peumus boldo and Trigonelle foenum-graecum)

Purpose/Use: Boldo is reportedly used to treat gallstones, to stimulate digestion, and as an anti-parasitic agent. Boldo is considered safe when ingested in the amounts normally found in foods. When used in higher medicinal doses, diarrhea has been reported and more recently a case of possible liver problems was published.

Fenugreek is reportedly used to stimulate the appetite, lower blood sugar in patients with diabetes, for gastrointestinal conditions, atherosclerosis, and high blood cholesterol. Side effects of fenugreek include developing body odor that resembles maple syrup, diarrhea or gas, low blood sugar (when taken at high doses) and allergic skin reactions.

Interactions with warfarin: We are aware of a case report of a patient with a history of hypertension who was taking boldo and fenugreek (two different products) with warfarin therapy and experienced an increase in INR[4]. During warfarin therapy, an increase in INR means that boldo and fenugreek combined may potentiate the effects of warfarin and bleeding problems could occur. Therefore, be cautious about taking boldo and fenugreek while you are taking warfarin. Talk to your doctor, pharmacist or other healthcare providers before taking these products together with warfarin.

Chamomile (Matricariarecutita)

Purpose/Use: Chamomile has a long tradition of medicinal use for a wide range of conditions including sleep disorders, anxiety, infections or inflammation of the skin, colic in infants, stomach ailments and teething pain. However there are very few clinical trials assessing the scientific efficacy of chamomile for these conditions. It appears relatively safe; however, there are reported cases of allergic reactions from people who used chamomile medicinally (or came into physical contact with the plant) including some that were life-threatening.

Interactions with warfarin: Chamomile is known to contain a compound (called coumarin) which may increase the risk of bleeding. That means that ingesting chamomile together with warfarin may increase your INR and thus your risk of experiencing side effects such as bleeding problems. There are several cases of this happening to patients. Therefore, talk to your doctor, pharmacist or other healthcare providers before taking chamomile together with warfarin.

Chitosan

Purpose/Use: Chitosan comes from chitin which forms the exoskeleton of crustaceans such as crabs, lobsters and crayfish, as well as many insects and spiders. It is used in the management of high cholesterol and as a dietary fiber. Since it is often made from shellfish, patients with shellfish allergies may also be allergic to chitosan products.

Interactions with warfarin: There is one case report (supported by some laboratory studies) of a patient taking warfarin whose INR significantly increased after self-medication with 1200mg twice per day of chitosan. Higher INR levels suggest that the patient is at risk for bleeding. Therefore, talk to your doctor, pharmacist or other healthcare providers before taking chitosan together with warfarin.

Coenzyme Q10 (Ubiquinone)

Purpose/Use: Coenzyme Q10 is involved in many different chemical reactions in the body. It has a chemical structure similar to vitamin K that is known to counteract the effects of anticoagulants like warfarin. It is considered to be a powerful antioxidant. There is some evidence that it may be beneficial for those diagnosed with cardiovascular diseases (i.e., congestive heart failure). Side effects are rare and mainly confined to stomach upset, nausea and rash.

Interactions with warfarin: In our review of the literature, we have discovered conflicting findings on the effect of coenzyme Q10 on blood clotting response. There have been a number of case reports of possible interactions between warfarin and coenzyme Q10. In several cases, ingestion of coenzyme Q10 has been associated with decreased INR values. A drop in INR value means that coenzyme Q10 decreases the effect of warfarin and could lead to blood-clotting problems. Two animal studies report that coenzyme Q10 increases the metabolism of warfarin in the body, supporting the findings described in the human cases. Other cases reported an increase in INR (and thus an increase in the risk of side effects such as bleeding) when patients took warfarin and coenzyme Q10 together. However, a recent double-blind crossover study in middle-aged patients taking long-term warfarin treatment reported that those patients taking coenzyme Q10 experienced no decrease in INR values compared with those taking an inactive treatment (placebo). Given these conflicting findings, it is recommended that you be cautious taking coenzyme Q10 and warfarin at the same time. You should always talk to your doctor, pharmacist or other healthcare providers before taking coenzyme Q10.

Cranberry

Purpose/Use: Drinking cranberry juice appears to help prevent urinary tract infections. Cranberry tablets/capsule may also have this effect. Cranberry products are not generally associated with any side effects, but some types of cranberry juice do contain a lot of sugar and drinking too much juice can lead to diarrhea.

Interactions with warfarin: There are multiple case reports of possible interactions between cranberry juice and warfarin. Overall, cranberry juice appears to increase INRs, but one case report found a decrease in INR. This is supported by a non-blinded randomized trial reporting that cranberry alters the way warfarin is used by the body and has the potential to increase its effects. However, a randomized, double-blind study could not find any change in INR in patients stabilized on warfarin who drank 250 mL of cranberry juice daily for 7 days. Nor did a laboratory study looking at how cranberry might impact the way warfarin is broken down in the body. In warfarin treatment, an increase in INR means that cranberry juice could potentiate the effects of warfarin and bleeding problems could occur. Given the conflicting evidence, it is best to be cautious about taking cranberry products while you are taking warfarin. Talk to your doctor, pharmacist or other healthcare providers before taking cranberry products with warfarin.

Curbicin

Purpose/Use: Curbicin is a traditional herbal formula from Sweden reportedly used for urination difficulties and benign prostatic hypertrophy. The active ingredients of curbicin are extracts from saw palmetto (Serenoa repens), pumpkin seeds (Curcubita pepo) and dwarf palm plants (Sabal serrulata). Curbicin also contains vitamin E. We are not aware of any reported side effects.

Interactions with warfarin: We are aware of at least two published cases of patients developing an increase in INR while taking curbicin and warfarin. In warfarin treatment, an increase in INR means that curbicin could potentiate the effects of warfarin and bleeding problems could occur. Therefore, be cautious about taking curbicin while you are taking warfarin. Talk to your doctor, pharmacist or other healthcare providers before taking curbicin with warfarin.

Danshen (Salvia miltiorrhiza)

Purpose/Use: Danshen is a Chinese herbal product reportedly used for a range of medical complaints, especially heart problems, such as angina and heart attacks. Side effects of danshen can include nausea, stomach pain, and diarrhea.

Interactions with warfarin: Danshen has been reported to increase the effectiveness of warfarin on blood clotting. There have been at least two reports of patients on warfarin that developed a significantly increased INR (>8 in one case) when they started taking danshen. In warfarin treatment, an increase in INR means that danshen could potentiate the effects of warfarin and bleeding problems could occur. Several laboratory studies also showed that this herbal product raises the level of warfarin in the body, or has effects that could increase the impact of warfarin, leading to bleeding. Do not take danshen while you are taking warfarin.

Dong Quai (Angelica sinensis)

Purpose/Use: Dong quai is a Chinese herbal supplement reportedly used for menstrual cramps, irregular menstrual periods, and menopausal symptoms. It contains a natural type of coumarin that may work like warfarin to prevent blood clots. Side effects of dong quai may include nausea, constipation and diarrhea.

Interactions with warfarin: There have been at least two reports of patients whose INR/PT increased while taking dong quai and warfarin. In one case, a patient stabilized on warfarin experienced a doubled INR after taking dong quai for four weeks. In another case, a patient previously stable on warfarin experienced widespread bruising and her INR increased to 10 after taking dong quai for a month. Given these findings, do not take dong quai while taking warfarin.

Echinacea (Echinacea angustifolia, Echinacea pallida, Echinacea purpurea, Purple coneflower)

Purpose/Use: This herb has been used extensively in Native North American healing traditions and in other countries to help heal wounds, fight infection, boost the immune system, and treat the common cold. Several studies claim that echinacea may shorten the duration of cold, but we are not aware of good evidence that it can prevent a cold. Side effects of echinacea are rare but include allergic reactions.

Interactions with warfarin:
In our literature search, we did not find any published case reports describing echinacea-warfarin interactions or any theoretical explanation of how these two products might interact. However, you should always talk to your doctor, pharmacist or other healthcare providers before taking any herbal product, including Echinacea, with warfarin.

Ephedra/Ma Huang (Ephedra sinica)

Purpose/Use:
Ephedrine is the active agent of ephedra also known by its Chinese name -ma huang. Although it has been included in weight loss products, Health Canada has issued a warning against this use. Other reported uses include relieving asthma and as a decongestant. Reported side effects include insomnia, nervousness, tremors, seizures, headaches, high blood pressure, irregular heartbeat, heart attacks, stroke, and death. Side effects appear to occur more often if it is taken together with caffeine.

Interactions with warfarin: While we are not aware of any reported interactions between ephedra and warfarin, since ephedra can cause high blood pressure, a patient taking ephedra and warfarin could be at risk for bleeding in the brain as well as the side effects listed above. For this reason, you should be cautious about taking ephedra and warfarin. Talk to your doctor, pharmacist or other healthcare providers before you take ephedra.

Evening Primrose Oil (Oenothera biennis)

Purpose/Use: The main active ingredient in evening primrose oil is an omega-6 fatty acid called gamma-linolenic acid (GLA). It has been used to treat atopic dermatitis and for a number of medical conditions including rheumatoid arthritis, premenstrual syndrome and diabetes. It appears generally safe at recommended doses, but patients diagnosed with seizure disorders or taking a class of drugs called neuroleptics (e.g., chorpormazine, thioridazine) should use this product with caution.

Interactions with warfarin: Laboratory studies have reported that the GLA in evening primrose oil may increase bleeding times in animals which means it may increase the effects of drugs like warfarin. It is not clear if there will be a clinically significant interaction. Until more research is available, you should be cautious about taking evening primrose oil and warfarin. Talk to your doctor, pharmacist or other healthcare providers before you take evening primrose oil.

Feverfew
(Tanacetum parthenium)

Purpose/Use: The leaf of feverfew is reportedly used for fever and arthritis. It is also used for the prevention of migraine headaches. Side effects of feverfew can include nervousness, tension, nausea, tiredness, and joint pains.

Interactions with warfarin: We are not aware of any reports of interactions between feverfew and warfarin. However, studies have shown that feverfew can cause bleeding similar to the way aspirin does. For this reason, you should be cautious about taking feverfew and warfarin. Talk to your doctor, pharmacist or other healthcare providers before you take feverfew.

Flaxseed
(Linum usitatissimum)

Purpose/Use: Flaxseed and flaxseed oil (also known as linseed oil) are rich sources of the essential fatty acid alpha-linolenic acid, which the body uses to make omega-3 fatty acids such as eicosapentaenoic acid. Omega-3 fatty acids in general are thought to be good for patients with cardiovascular disease, but evidence from human trials of flaxseed and flaxseed oil products are mixed regarding its efficacy. Flaxseed (but not flaxseed oil) has also been used as a laxative. Flaxseed products are generally well tolerated, but ingestion of raw flaxseeds should be avoided. Also, flaxseed products can cause bowel obstructions if not taken with sufficient water.

Interactions with warfarin: We are not aware of any reports of interactions between flaxseed products and warfarin. However, studies have shown that flaxseed decreases the blood's ability to clot and thus may increase the effects of warfarin. For this reason, you should be cautious about taking flaxseed and warfarin. Talk to your doctor, pharmacist or other healthcare providers before you take flaxseed.

Garlic
(Allium sativum)

Purpose/Use: Garlic has been used for centuries as a folklore medicine. Recently it has become popular for its alleged ability to lower cholesterol levels. Other claimed effects include a mild lowering of blood pressure and antiviral effects. Side effects of garlic are normally mild but can include nausea, stomach pain, diarrhea, headache, and odour.

Interactions with warfarin: We are aware of a report of two patients previously stabilized on warfarin who developed an increase in their INRs when they started taking garlic. However, two clinical trials (one a randomized double-blind study) could not find any impact on warfarin metabolism in patients taking garlic. An increased INR means that the garlic may be enhancing the effects of warfarin and there is a risk of bleeding. Given the conflicting evidence, you should be cautious about taking garlic while you are taking warfarin. Talk to your doctor, pharmacist or other healthcare providers before you start taking garlic products.

Ginger
(Zingiber officinale)

Purpose/Use: Ginger has been claimed to reduce nausea, prevent spasms in the gastrointestinal tract, and decrease the symptoms associated with inflammatory musculoskeletal conditions such as arthritis. No significant side effects have been reported other than mild headaches and digestive upset.

Interactions with warfarin:
Laboratory studies have reported that ginger may decrease the blood's ability to clot. One non-blinded, observational study of patients taking ginger and warfarin together reported that ginger was associated with an increased risk of bleeding. Another non-blinded study in healthy adults did not find any significant effect on the metabolism of warfarin when it was taken together with ginger. Given the conflicting information, it is best to be cautious about taking ginger with warfarin. Talk to your doctor, pharmacist or other healthcare providers before you take ginger.

Ginkgo
(Ginkgo biloba)

Purpose/Use: Ginkgo is claimed to improve blood flow to the brain and blood vessels in the legs, improve thinking, and the memory. It is reported to be relatively safe when not mixed with medications. The most common unwanted side effects are mild stomach upset, diarrhea, restlessness and headache.

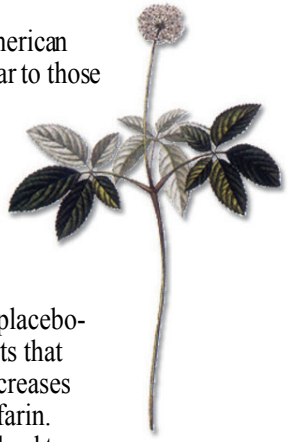
Interactions with warfarin: There has been at least one report of a patient having increased bleeding while taking a ginkgo product with warfarin. In addition, there have been at least four reported cases of bleeding problems in patients who were taking ginkgo alone. However, a recent double-blind crossover study in middle aged patients on stable long-term warfarin treatment reported that those patients taking ginkgo experienced no increase in INR values or major bleeding compared with those taking an inactive treatment (placebo). This lack of significant interaction is supported by three other studies in healthy adults. Animal and laboratory studies have also reported conflicting findings. Overall, it seems unlikely that there will be a clinically significant interaction between warfarin and ginkgo at regular doses; however, given the conflicting evidence, it is best to be cautious about taking ginkgo if you are taking warfarin. Talk to your doctor, pharmacist or other healthcare providers before taking ginkgo.

Ginseng, Asian
(Panax ginseng)

Purpose/Use: Asian ginseng is claimed to increase resistance to infection and stress, improve sexual function, and delay the aging process. Asian ginseng's side effects have been reported to include, high blood pressure, trouble sleeping, headache, nausea, nervousness, heart palpitations, and rashes.

Interactions with warfarin: We are aware of at least two reports of patients whose INR/PT decreased when they took Asian ginseng and warfarin. A randomized, double-blind clinical trial reported similar findings. A decrease in the INR/PT may lead to blood-clotting problems. However, an animal study and a study in healthy humans showed that ginseng had no significant impact on the metabolism of warfarin raising doubts about how ginseng and warfarin might interact. Until more information is available, you should be cautious about using Asian ginseng if you are taking warfarin. Talk to your doctor, pharmacist or other healthcare providers before you start taking Asian ginseng.

Ginseng, Canadian/American (Panax quinquefolius)



Purpose/Use: Canadian or American ginseng has reported uses similar to those for Asian ginseng. There is some evidence that it has fewer adverse effects, but that it might lower blood glucose levels.

Interactions with warfarin:
One randomized, double-blind, placebo-control in healthy patients reports that Canadian/American ginseng decreases the anticoagulant effects of warfarin. A decrease in the INR/PT may lead to blood-clotting problems. You should be cautious about using Canadian/American ginseng if you are taking warfarin. Talk to your doctor, pharmacist or other healthcare providers before you start taking Canadian/American ginseng.

Ginseng, Siberian (Eleutherococcus senticosus)

Purpose/Use: Siberian ginseng is reportedly used to increase the body's resistance to stress, strengthen the body's immune response, and increase vitality. Reported side effects of Siberian ginseng are rare but include increased blood pressure, increase in heart rate, insomnia, irritability, and allergic reactions.

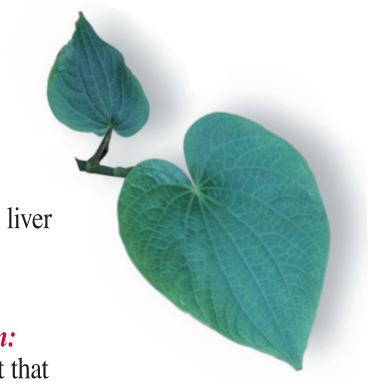
Interactions with warfarin: In our literature search, we did not find any published case reports describing an interaction between Siberian ginseng and warfarin. However, it is claimed (based on laboratory studies) that it can lead to bleeding problems, similar to the way aspirin does. For this reason you should be cautious about taking Siberian ginseng with warfarin. Talk to your doctor, pharmacist or other healthcare providers before you take siberian ginseng with warfarin.

Glucosamine/Chondroitin

Purpose/Use: Glucosamine and chondroitin are used for treating the symptoms of osteoarthritis. Glucosamine is found in human tissue, including the cartilage in the joints. Studies have reported that glucosamine and chondroitin may improve the structure of the cartilage and may have an anti-inflammatory effect. The side effects of glucosamine and chondroitin are rare and include nausea, diarrhea and stomach pain.

Interactions with warfarin: Health Canada has issued a report that describes patients that experienced an increase in INR when taking glucosamine with warfarin. In addition there are several case reports that suggest taking glucosamine/chondroitin combination products can increase a patient's INR. An increased INR means that glucosamine and chondroitin may be enhancing the effects of warfarin and there is a risk of bleeding. Be cautious while taking glucosamine or chondroitin with warfarin. Talk to your doctor, pharmacist or other healthcare providers before you start taking glucosamine or chondroitin.

Kava
(Piper methysticum)



Purpose/Use: Kava is used for relief of anxiety and as a sedative. Kava is not currently available for sale in Canada due to concerns that it may cause liver toxicity. Health Canada is currently investigating.

Interactions with warfarin:
Laboratory studies suggest that compounds found in kava prevent blood clots from forming or growing larger. In our review of the literature, we have not found reports of interactions between warfarin and kava. You should be cautious about taking kava with warfarin. Talk to your doctor, pharmacist or other healthcare providers before you start taking kava.

Mango
(Mangifera indica)

Purpose/Use: Mango fruit is native to southern Asia and is commonly consumed for its sweet flavour, fiber, and high vitamin A and C content. Historical and anecdotal reports suggest that mango fruit may help fight viral and parasitic infections, coughs, and act as a laxative. Side effects of mango include allergic contact dermatitis similar to poison ivy and very rarely anaphylactic allergic reactions.

Interactions with warfarin: We are aware of a report of thirteen male patients stabilized on anticoagulant therapy who experienced increased INR values after ingesting mango fruit and warfarin together (1-6 mangos daily, for 2 days to 1 month before the anticoagulation clinic appointment). An increase in INR after mango intake suggests you could have bleeding problems if you take mango and warfarin together. Therefore, be cautious about taking mango while you are taking warfarin. Talk to your doctor, pharmacist or other healthcare providers before eating/ingesting mango with warfarin.

Methyl Salicylate
(Oil of wintergreen)

Purpose/Use: Methyl salicylate is a volatile oil found in a variety of plants that reportedly attracts pollinating bees and protects the plants from pests. Oil of wintergreen contains 98% methyl salicylate and is a common source of this volatile oil. It is the active ingredient in many over-the-counter analgesic topical preparations used for musculoskeletal pains and aches. Side effects include allergic contact dermatitis and rarely anaphylactic reactions.

Interactions with warfarin: We are aware of multiple case reports of interactions between methyl salicylate and warfarin. Four of these reported that the patients developed an elevated INR while using topical methyl salicylate and warfarin. One resulted in a life-threatening bleed. An increase in INR means that methyl salicylate may potentiate the effect of warfarin, and cause bleeding problems. Do not use methyl salicylate while you are taking warfarin.

Milk Thistle (Silybum marianum)

Purpose/Use: Milk thistle has a long history of traditional uses for many different types of liver disorders. Although, more research is needed to ascertain whether it is useful clinically, the available studies suggest that it is generally safe. It is possible to be allergic to milk thistle (as with any other plant).

Interactions with warfarin:
One laboratory study suggests that compounds found in milk thistle have the potential to affect the metabolism of warfarin if the two products are taken together. It is not clear if this is a clinically-significant interaction. Until more information is available, it is probably best to use caution and talk to your doctor, pharmacist or other healthcare providers before taking milk thistle with warfarin.

Nettle (Urtica dioica)

Purpose/Use: Nettle has been used medicinally to help manage benign prostatic hyperplasia, urinary tract disorders and arthritis among other things. It is likely safe when used in normally recommended medicinal doses, but should not be used by women who are pregnant, as it has been reported to cause contractions of the uterus in animals.

Interactions with warfarin: Nettle root contains a compound (coumarin) that is known to increase the effects of anticoagulants such as warfarin. Nettle leaves also contain a compound (vitamin K) that can in high doses impact the activity of warfarin. A laboratory study reported that nettle has the potential to interact with a number of medications including drugs like warfarin.
It is not clear if this is a clinically-significant interaction. Until more information is available, it is probably best to use caution and talk to your doctor, pharmacist or other healthcare providers before taking nettle with warfarin.

Omega 3 Fatty Acids (Fish oils)

Purpose/Use: Omega 3 fatty acids, most commonly found in fish oil, include alpha-linolenic acid, docosahexaenoic acid, and eicosapentaenoic acid. There is growing literature suggesting that they may be beneficial for a wide range of cardiovascular conditions and arthritis. Allergic reactions are possible to supplements containing omega 3 fatty acids, and mild, transient gastrointestinal upset are the most commonly reported adverse effects.

Interactions with warfarin: There are a number of case reports in which patients taking warfarin and omega 3 fatty acids together have experienced increased INRs or bleeding. Diets high in fatty fish content have also been reported to be associated with prolonged bleeding times. The research is conflicting with some studies reporting the potential for an interaction with drugs like warfarin and others concluding such an interaction is unlikely. Until more information is available, it is probably best to use caution and talk to your doctor, pharmacist or other healthcare providers before taking omega 3 fatty acids with warfarin.

Quercitin

Purpose/Use: Quercitin is a flavonol found in many different kinds of plants. It has been used as a medicinal product in the management of many conditions including those of cardiovascular origin. However, there are not a lot of good studies about its effectiveness. It is generally considered safe at doses consistent with normal dietary intake. Higher doses have been associated with a range of side effects including nausea, vomiting, and headaches.

Interactions with warfarin: A laboratory study suggests that quercitin may decrease the blood's ability to clot and thus possibly increase the effects of warfarin. It is not clear if this is a clinically significant interaction. Until more information is available, it is probably best to use caution and talk to your doctor, pharmacist or other healthcare providers before taking quercitin with warfarin.

Quilinggao

Purpose/Use: Quilinggao is a Chinese herbal product from the "essence of a tortoise shell" reportedly used for enhancing skin complexion, reducing "internal heat", and improving general health. The combination of herbs in quilinggao varies between different brands but often includes the following herbs which may have anti-platelet activity: Chuanbeimu (Fritillaria cirrhosa), Beimu (Fritillaria spp.), Chishao (Paeoniae rubra, Chinese peony), Jinyinhua (Lonicera japonica), and Jishi (Poncirus trifoliata). We are not aware of any published reports on the side effects of quilinggao.

Interactions with warfarin: We are aware of at least one case report of a patient on stable warfarin therapy who consumed quilinggao and developed an increase in INR and experienced bleeding from the gums and nose as well as skin bruising. An increase in INR while taking warfarin means that quilinggao may potentiate the effect of warfarin and bleeding problems could occur. Do not use quilinggao with warfarin.

Red Clover (Trifolium pratense)

Purpose/Use: Red clover contains phytoestrogens and is commonly used in an attempt to treat symptoms associated with menopause like hot flashes. It is also sometimes used for high cholesterol and osteoporosis. It is likely safe in the usual recommended medicinal doses, but should be used with caution by children and anyone not able to take estrogen products.

Interactions with warfarin:
Red clover contains multiple compounds that have been reported in laboratory studies to decrease platelet aggregation and thus theoretically may increase the effects of drugs like warfarin which do the same thing. There is one case report of a woman taking a combination herbal product that contained red clover, dong quai and siberian ginseng who experienced bleeding in her brain. It is not clear if the herbal product was the cause of the bleeding. However, until more information is available, it is best to use caution and talk to your doctor, pharmacist or other healthcare providers before taking red clover with warfarin.

Royal Jelly

Purpose/Use: Royal jelly is the nutrient-rich substance that worker honey bees produce to feed to their queen bee. It has been purported to be useful to enhance energy, stamina and longevity; however, scientific evidence to support these claims are lacking. It should be avoided by anyone allergic to bees or bee products.

Interactions with warfarin: There is one case report of a gentleman previously stabilized on warfarin whose INR increased significantly when he began taking royal jelly for 1 week. Until further research is available, it is best to use caution and talk to your doctor, pharmacist or other healthcare providers before taking royal jelly with warfarin.

Saw Palmetto (Serenoa repens)

Purpose/Use: Saw palmetto is taken to help men with symptoms of prostate enlargement. Side effects of saw palmetto are generally rare and mild, but include nausea or upset stomach, headache, and diarrhea.

Interactions with warfarin: We are not aware of any reports of interactions between saw palmetto and warfarin. However, there is one report of a patient who experienced prolonged bleeding during surgery while taking saw palmetto. Although the PT and PTT values during and after surgery in this patient were normal, the increased bleeding time is a cause for concern. Animal studies have shown that saw palmetto can cause bleeding by a mechanism similar to aspirin. Be cautious about taking saw palmetto with warfarin. Talk to your doctor, pharmacist or other healthcare providers before taking saw palmetto and warfarin together.

Soy (Glycine soja, Glycine max)

Purpose/Use: Soy products are claimed to promote cardiovascular health, treat menopausal symptoms, and prevent breast cancer. Side effects of soy are rare but include constipation, bloating, nausea, and allergic skin rash. It has been reported to trigger asthma and hypothyroidism in susceptible individuals.

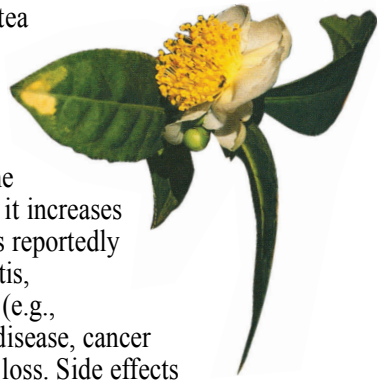
Interactions with warfarin: We are aware of at least one recent case report of a patient taking 240 ml soymilk daily for four weeks while on warfarin therapy whose INR decreased. In patients taking warfarin, a decrease in INR means that warfarin is not working as effectively and that blood clots could develop. Therefore, be cautious about consuming soy while you are taking warfarin. Talk to your doctor, pharmacist or other healthcare providers before taking soy and warfarin together.

St. John's Wort (Hypericum perforatum)

Purpose/Use: St. John's Wort is used for the management of mild to moderate depression. Side effects of St. John's Wort occur in 1-3% of people and can include dry mouth, dizziness, confusion, fatigue, and skin rash, especially with sun exposure.

Interactions with warfarin: We are aware of a report of nine patients who developed a decrease in their INR when they started taking St. John's Wort. Although none of the patients developed clotting problems, the decline in INR was thought to be significant. The finding that St. John's Wort increases the metabolism of warfarin is supported by an un-blinded clinical trial in healthy patients. However, there are two additional case reports that found that taking St John's Wort and warfarin together led to an increased INR. It is important to note that the St. John's Wort products taken by these patients were not tested for purity and thus may have contained contaminants responsible for this unusual reaction. In patients taking warfarin, a decrease in INR means warfarin is not working effectively and that blood clots could develop. Recently, the United Kingdom's Committee on Safety on Medicine warned that St. John's Wort should not be used with warfarin. Talk to your doctor, pharmacist or other healthcare providersb efore taking these products together. You may need to have your INR/PT blood test performed more frequently, or you may be counseled not to take them together.

Tea - Black or Green (Camellia sinensis)



Purpose/Use: Black tea is a common source of caffeine and thus can have stimulant effects as well as have medicinal effects on the heart and kidney (e.g., it increases urination). Green tea is reportedly used for chronic gastritis, cardiovascular disease (e.g., atherosclerosis), liver disease, cancer prevention and weight loss. Side effects of both appear to be rare and include allergy and gastrointestinal upset.

Interactions with warfarin: We are aware of one case report each of patients who may have experienced interactions between black or green tea and warfarin. One patient experienced an increase in her INR when she stopped drinking black tea, meaning that she was at risk for side effects from the warfarin. Another patient developed decreased INR values after taking warfarin together with one and a half gallons of green tea each day for one week prior to his INR test. While taking warfarin, a decrease in INR means that warfarin may not be working properly and you may experience blood-clotting problems. Therefore, be cautious while taking green tea with warfarin. Talk to your doctor, pharmacist or other healthcare providers before taking black or green tea with warfarin.

Vitamin K

Purpose/Use: Vitamin K is an essential co-factor for several compounds that are part of the coagulation process in the human body. It is found in many dietary sources such as green leafy vegetables and fruits.

Interactions with warfarin: Increased intake of vitamin K has been shown to decrease the effect of warfarin in patients. Therefore, be cautious with your vitamin K intake from dietary and other sources while you are taking warfarin. Talk to your doctor, pharmacist or other healthcare providers if you have any questions.

Wolf Berry or Goji Berry
(Lycium barbarum)

Purpose/Use: Wolf berry is a Chinese herbal supplement reportedly used for the treatment of back and leg aches, impotence, visual problems, and vertigo. We are not aware of any reported side effects for this herb.

Interactions with warfarin: We are aware of a case report of a patient previously stabilized on warfarin taking wolf berry tea who developed an elevated INR. In patients taking warfarin, an increase in INR means that its anticoagulant effect is potentiated and bleeding problems could occur. Therefore, be cautious about taking wolf berry and warfarin together. Talk to your doctor, pharmacist or other healthcare providers before taking wolf berry or goji berry together with warfarin.

Summary

It is clear that more research studies need to be conducted to learn if herbal products are effective and if they are safe to take with warfarin and other medications. **Tell your doctor and other healthcare providers the names and amounts of any herbal products you are taking. You should always talk to your doctor, pharmacist or other healthcare providers before you start taking any herbal products - especially if you are taking warfarin.**

If you take herbal products with warfarin you may need to have your INR/PT checked more frequently to be sure your warfarin is working well. You may also need to have your dose of warfarin increased or decreased.

If you notice any of the following problems, call your doctor:

- nose bleeds
- bleeding gums
- easy bruising
- bleeding that does not stop after a cut
- heavy or prolonged menstrual period
- red or dark brown urine
- coughing up blood
- chest pain
- headache, dizziness and/or weakness
- swelling in arms or legs

The authors of this booklet do not claim to have reviewed all the literature and believe there is additional literature that may not have come to our attention. Further, the authors make no judgments as to the truthfulness of the literature or the accuracy of any claims. The Purpose/Use for each herbal product is based on unsubstantiated claims in literature as well as historical claims, the truthfulness of which has not been subject to rigorous review by the Natural Health Products Directorate (Health Canada). Such claims are included in this booklet only as a background to their possible interaction with warfarin.

Notes:

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