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Special Article

Anticoagulant activity of select dietary supplements

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This review considers the potential of certain dietary supplements, including garlic, Ginkgo biloba*, ginger, ginseng, fish oil, and vitamin E, to interfere with hemostasis. Dietary supplements are common components of the diet in the United States, with about half the US adult population taking some type of dietary supplement regularly. It has been suggested that some supplements could adversely affect coagulation when taken alone or in combination with antiplatelet medications. Supplements could alter hemostasis by a variety of mechanisms, such as reducing platelet aggregation or inhibiting arachidonic acid, a cellular signaling messenger and inflammatory intermediate. To conduct this review, multiple databases were searched using a variety of search terms to ensure relevant papers were located. Moderate to severe adverse events, such as spinal epidural hematoma, spontaneous intracerebral hemorrhage, retrobulbar hemorrhage, subarachnoid hemorrhage, spontaneous hyphema, and postoperative bleeding, have occasionally been anecdotally associated with consumption of dietary supplements. However, the number of controlled studies in the literature is too limited to demonstrate consistent anticoagulant effects of dietary supplements alone or in combination with drug therapy.*

INTRODUCTION

More than half of the adult population in the United States regularly takes dietary supplements.[1] Consequently, a concern is whether dietary supplements affect hemostasis, and if so, to what degree. Hemostasis is the process by which blood flow is halted by a complex chain of events, one of which is the coagulation cascade (Figure 1).[2] Some dietary supplements currently available in the United States alter hemostasis in vitro, but whether such effects are present in vivo is less certain.

Dietary supplements could alter coagulation at various points in the cascade, particularly via platelet aggregation (Table 1). Treatment with supplements with antiplatelet/anticoagulant activity could be beneficial for some individuals with cardiovascular illnesses or for preventing such diseases, hence their potential popularity. The effects of some dietary supplements on the coagulation cascade may be due to their putative ability to lower arachidonic acid levels (Figure 2), providing an anti-inflammatory effect of potential benefit to individuals suffering from arthritis, similar to the effects of aspirin and other non-steroidal anti-inflammatory drugs (NSAIDs). However, if these products have anticoagulant activity, they may increase bleeding, especially if used in combination with other anticoagulants, for example, coumadin, NSAIDs, or aspirin.

This review is focused on popular dietary supplements such as garlic, ginkgo biloba, ginger, ginseng, fish oil, and vitamin E, as well as other supplements that have been reported to alter hemostasis in humans. When appropriate, animal studies reporting relevant findings are discussed. The various points in the coagulation cascade at which dietary supplements may modify hemostasis and the potential consequences of such effects are discussed. Descriptions of the databases that were searched to prepare this review can be found in Table 2.

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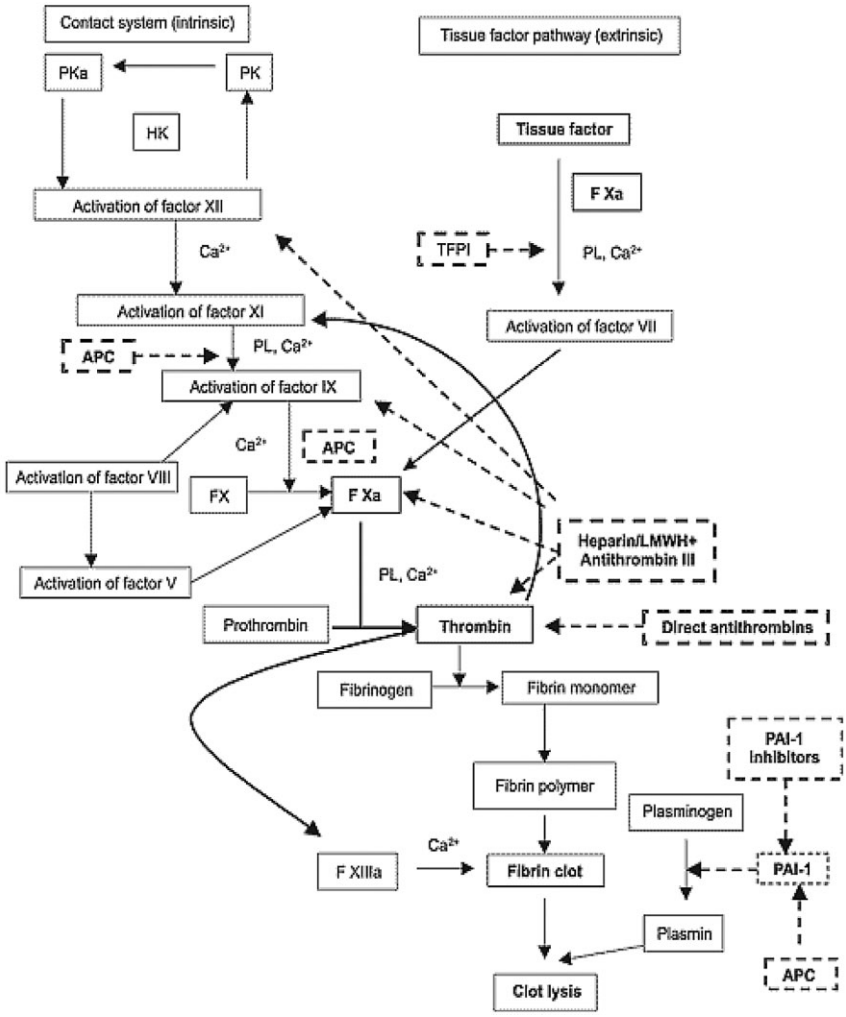

Figure 1 **Coagulation cascade.** Reproduced from Raghavan and Dikshit[2] with permission. Copyright © Prous Science, S.A.U. or its licensors. All rights reserved.

It should be noted that intravenous administration of a supplement can have a greater effect on coagulation at smaller doses than oral supplementation due to the greater bioavailability of the supplement. Therefore, data from such studies should be interpreted with caution.

Garlic

Garlic (*Allium sativum*) is reported to be the third most popular herbal supplement in the United States, with sales exceeding 19 million US dollars per year.[3] It is used raw as a seasoning or condiment, and as an extract in dietary supplements. Fresh garlic and garlic in dietary supplement form may have different physiological effects and properties, with both forms purported to have antibacterial and cholesterol-lowering properties. Dosages generally recommended in the literature for adults are 4 g (one to two cloves) of raw garlic per day, one 300 mg dried garlic powder tablet (standardized to 1.3% allicin or 0.6% allicin yield) two to three times per day, or 7.2 g of aged garlic extract per day.[4]

Two types of compounds in garlic may be bioactive. S-allylcysteine is a water-soluble compound found in garlic that is excreted in the urine in the form of the metabolite N-acetyl-S-allycysteine. Oil-soluble compounds also present in garlic, mainly allicin, sulfides, ajoenes, and vinyldithins, are quickly metabolized by the body after consumption and are not found in the urine and blood.[5]

Three compounds of garlic, allicin, adenosine, and paraffinic sulfide, are hypothesized to have antiplatelet properties.[6] Adenosine and allicin both inhibit platelet aggregation without affecting cyclooxygenase and lipoxygenase metabolism of arachidonic acid.[7] In vivo human studies have documented garlic's effect on hemostatic parameters such as adenosine diphosphate (ADP)-

Table 1 **Mechanism(s) of anticoagulant activity of select dietary supplements.**

Supplement	Action	Reference
Garlic	Reduces ADP-induced platelet aggregation; thromboxane reduction; reduces clotting time	Makheja and Bailey (1990)[6]; Rahman and Billingham (2000)[8]; Steiner and Li (2001)[9]; Gadkari et al. (1991)[10]; Srivastava (1986)[12]
Gingko biloba	Inhibits binding of platelet activation factor to receptors	Koch (2006)[35]
Ginseng	Inhibits thromboxane function	Teng et al. (1989)[44]
Ginger	Alters thromboxane synthesis; inhibits arachidonic acid-induced platelet activation	Verma et al. (1993)[46]; Srivastava et al. (1984)[47]; Koo et al. (2001)[48]
Fish oil	Increases bleeding time; reduction in platelet aggregation	Agren et al. (1997)[54]; Cobiac et al. (1991)[55]
Vitamin E	Reduces platelet adhesion to endothelial cells; increases bleeding time; prevents platelet aggregation	Steiner et al. (1995)[74]; Szuwart et al. (2000)[75]; Freedman et al. (1996)[77]
Policosanol	Inhibits arachidonic acid production; reduces collagen- and ADP-induced platelet activation	Valdes et al. (1996)[83]; Carbajal et al. (1998)[84]; Castano et al. (1999)[85]; Arruzazabala et al. (2002)[86]
Magnesium	Reduces platelet aggregation; increases bleeding time	Gawaz et al. (1994)[89]; Ravn et al. (1996)[91]
Feverfew	Inhibits cyclo-oxygenase production and arachidonic acid; reduces serotonin release by collagen- and ADP- induced platelet aggregating agents	Makheja and Bailey (1982)[95]; Heptinstall et al. (1985, 1987)[96,97]
Dong quai	Inhibits thromboxane and prostacyclin synthetase	Norred and Brinker (2001)[100]
Coenzyme Q_{10}	Reduction in platelet receptors and size	Serebruany et al. (1997)[103]
Glucosamine	Inhibition of ADP-induced platelet aggregation	Hua et al. (2004)[105]
Lycopene	Inhibits platelet aggregation	Hsiao et al. (2005)[108]
L-arginine	Inhibits platelet response	Anfossi et al. (1999)[109]
Taurine	Reduces platelet aggregation	Hayes et al. (1989)[110]; Miglis et al. (2002)[111]
Selenium	Inhibits thromboxane synthesis	Perona et al. (1990)[112]
Passion flower	Contains coumarin, an anticoagulant	Aoyagi et al. (1974)[114]
Chamomile	Contains coumarin, an anticoagulant	Segal and Pilote (2006)[115]

induced platelet aggregation[8–10] (5 mL extract/day), thromboxane reduction[11] (5.46 g/day), and clotting time (10 g/day).[12] In vitro studies have shown a reduction in ADP-induced platelet aggregation,[8] thromboxane reduction,[13] Ca+ mobilization (doses not provided),[14] and inhibition of the synthesis of thromboxane B2.[7]

Ingestion of garlic at amounts much greater than the recommended dose is anecdotally linked in case reports to spinal epidural hematoma[15,16] as well as spontaneous bilateral and postoperative bleeding.[17] Furthermore, the results of two studies indicate that garlic increases the anticoagulant properties of NSAIDs or blood-thinning medications.[18,19] Other studies have not shown any statistically significant effect of garlic on ADP- or collagen-induced aggregation ex vivo[20] and in vivo[21,22] when given in a 305 mg/L garlic-oil extract.

Overall, it appears that garlic supplements when taken at recommended doses by individuals who are not taking anticoagulant medication do not have anticoagulant properties. However, consuming higher than recommended doses or using garlic in combination with anticoagulants cannot be ruled out as a risk factor for increased bleeding.

Ginkgo biloba

Ginkgo *(Ginkgo biloba)* is among the top ten best-selling herbs in the United States, with sales exceeding $17 million per year.[3] Several manufacturers have added ginkgo to their multivitamin and other multi-component products in amounts that vary from 40 mg to 240 mg a day.[23] Gingko can also be found in energy drinks in varying amounts. For example, Original Rockstar™ energy drink contains 150 mg of gingko, which exceeds the doses present in many of the studies discussed below which found excessive bleeding to be associated with gingko consumption.

Of the 33 known flavone glycosides in ginkgo, the main bioavailable components are the terpenoides, i.e., gingkolides A, B, C and bilobalide.[24] Purported benefits of taking ginkgo include prevention of the onset of Alzheimer's disease and dementia, increased mental

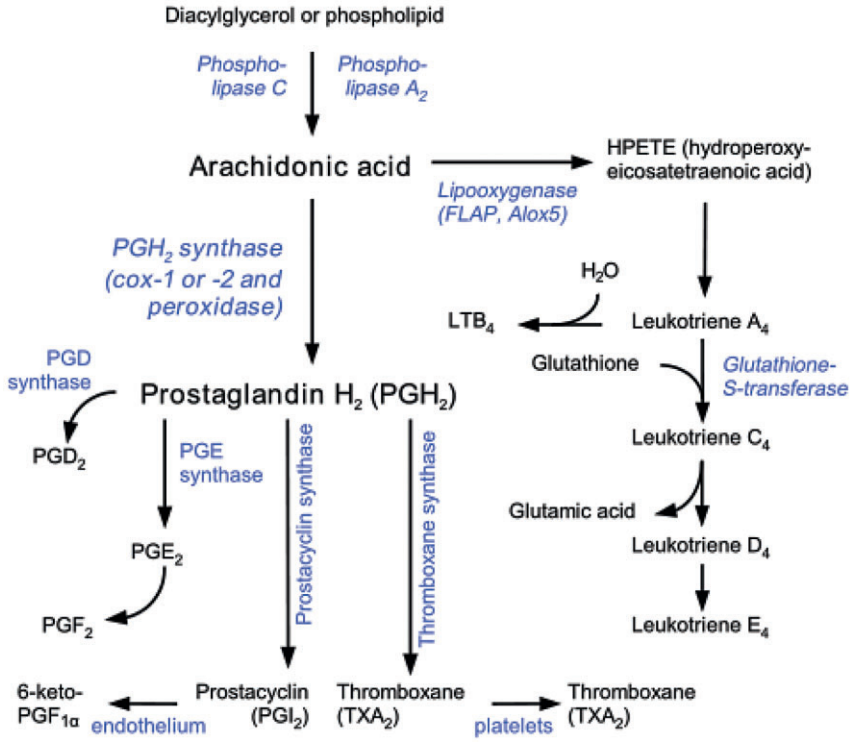

Figure 2 **The influence of arachidonic acid on platelet function.** Reproduced with permission under the terms of the GNU Free Documentation License, Version 1.2 or any later version published by the Free Software Foundation.

concentration, prevention of vertigo, and improved blood flow through platelet inhibition. Terpene ginkgolide B is believed to be the active component in ginkgo responsible for its purported platelet-inhibiting qualities.[25]

There are several case reports of potential associations between ginkgo use and hemorrhage, including spontaneous intracerebral hemorrhage,[26] retrobulbar hemorrhage,[27] subarachnoid hemorrhage,[28] subdural

Table 2 **Description of the databases searched for the present literature review.**

Database	Description
PubMed/NCBI	PubMed comprises more than 20 million citations for biomedical literature from MEDLINE, life science journals, and online books. Citations may include links to full-text content from PubMed Central and publisher websites
International Bibliographic Information on Dietary Supplements	IBIDS provides access to bibliographic citations and abstracts from published, international, and scientific literature on dietary supplements. IBIDS is a collaboration between two US government agencies: the Office of Dietary Supplements of the National Institutes of Health, and the Food and Nutrition Information Center of the United States Department of Agriculture's National Agricultural Library
Cat.inist	This database of The Institute for Scientific and Technical Information of the French Center for Scientific Research contains 15 million bibliographic references in science, technology, medicine, humanities, and social sciences
The Cochrane Library	The Cochrane Library contains high-quality, independent evidence to inform healthcare decision-making. It includes reliable evidence from Cochrane and other systematic reviews, clinical trials, and more. Cochrane reviews bring you the combined results of the world's best medical research studies, and are recognized as the gold standard in evidence-based health care
Google Scholar	Provides a search of scholarly literature across many disciplines and sources, including theses, books, abstracts, and articles
Defense Technical Information Center	Serves the Department of Defense community as the largest central resource for Department of Defense and government-funded scientific, technical, engineering, and business related information available
Defence Research Reports	A database of scientific and technical research produced by and for Defence Research & Development Canada (DRDC) over the past 60 years

hematoma,[29] and spontaneous hyphema.[30] In these case reports, ginkgo was used in combination with warfarin or with NSAIDs such as aspirin, so the independent and/or interactive effects of these latter drugs cannot be isolated from the effects attributable solely to ginkgo.

A few case reports document bleeding with *Ginkgo biloba* supplementation, at 120 mg, 80 mg, and 75 mg, respectively.[31–33] A study of 12 healthy males showed no excessive bleeding when 125 mg extract of ginkgo was taken in combination with warfarin for 7 consecutive days.[34] Other studies with healthy male volunteers also did not show any significant effect of ginkgo on platelet activating factor (at 1,200–2,400 mg/day)[35] or platelet function in vivo (at 120 mg/day).[22]

A study to determine the effects of taking ginkgo in combination with cilostazol (a drug used to alleviate symptoms of claudication in peripheral vascular disease) reported lower sheer-induced platelet aggregation, but no effects on bleeding time.[36] A 52-week study conducted to determine the efficacy of ginkgo for dementia found no adverse events in the ginkgo-treated subjects who received 120 mg/day, but one hemorrhage in the placebo group.[37]

In conclusion, controlled studies have shown that short-term, low doses of ginkgo below 120 mg/day appear to alter platelet aggregation, especially when taken with certain medications such as cilostazol, but they may or may not increase bleeding time. Nevertheless, due to the large number of case reports describing bleeding with ginko supplementation, caution is warranted.

Ginseng

Ginseng (*Panax ginseng*) is a perennial herb found in Korea and China. It has been used in eastern Asian herbal remedies for thousands of years as a stimulant and aphrodisiac and is presently marketed in the United States and many other countries to increase alertness and energy.[38] Globally, sales of ginseng exceeded 1.5 billion US dollars in 2008.[2] Various beverages contain ginseng, including energy drinks. For example, Original Rockstar™ contains 25 mg of ginseng and SoBe® Green Tea contains 50 mg of ginseng.

Ginsenosides are reportedly the bioactive components in ginseng.[39] Saponin complexes within the ginsenosides are metabolized in various parts of the body, mainly the hypothalamus-pituitary-adrenal axis and immune system, and are responsible for ginseng's purported benefits.[40] Saponin may act on the immune system by inhibiting platelet-activating factor, thereby potentially reducing platelet volume.

There are a few case reports in the literature stating that ginseng consumption, in doses ranging from 120 to 200 mg daily, is associated with vaginal bleeding[41] and increased blood-clotting time.[42] One article reported that ginseng alters the efficacy of anticoagulant therapy.[43] Ginseng at a concentration of 0.1 mg/mL has been reported to inhibit in vitro thromboxane formation.[44] In another study, no effect on platelet function in vivo was found (dose not provided).[45]

Ginseng appears to be safe when taken alone. Its interaction with NSAIDs does not appear to have been examined; therefore, caution should be exercised when taking ginseng with these drugs.

Ginger

Ginger is the rhizome of the plant *Zingeber officinale*. Medicinally, it has been used to alleviate nausea. The recommended daily dose of ginger is 1 g daily. Amounts exceeding 4 g may cause stomach discomfort and nausea.

Recently, ginger has been reported to lower cholesterol levels and to have blood-thinning properties.[46] One of its active components, gingerol, is reported to inhibit platelet aggregation in vitro by acting on prostaglandin and thromboxane synthesis[47] and inhibiting arachidonic acid-induced platelet aggregation.[48] Ginger's effect on in vitro platelet aggregation has led to research on its potential adverse effects if used with blood thinners such as NSAIDs and warfarin. One study showed a single dose of 2 g of ginger had no significant effect on platelet aggregation[49] within a 24-h period and another showed that a single dose of 25 mg of ginger did not affect clotting status in individuals taking warfarin.[50] No case reports of ginger interacting with warfarin or NSAIDs were located. Therefore, ginger supplements do not have confirmed anticoagulant properties.

Fish oil

In 1970, Danish researchers discovered that the Inuit in Greenland had a low incidence of heart disease despite their high-fat diets.[51] They also found that the Inuit bruised easily, had long bleeding times, and low levels of triglyceride, lipoprotein, and total cholesterol compared to individuals consuming standard Western diets. Furthermore, when platelets from Inuits were compared to those of Caucasians, they appeared to be less adhesive and did not clump together as easily.[52] In 1985, it was suggested that consumption of fish oil lowered levels of certain plasma lipids, lipoproteins, and apoproteins.[53] Later, researchers found that docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA), the bioactive ingredients in fish oil, were responsible for its purported antiplatelet properties through absorption by platelets and leukocytes.[54] Most commercially available fish oil supplements contain, on average, 1,000 mg of fish oil.

Numerous studies have investigated the effects of fish oil on hemostasis. Results of several studies provide

evidence of fish oil's reported antiplatelet effect. The hemostatic properties observed have varied, with some studies reporting a hypocoagulant effect,[55] reduction in in vitro platelet aggregation,[56] and moderate effects on extending bleeding time in humans.[57] However, nine studies of fish oil found no significant effects on hemostatic parameters such as bleeding time,[58,59] abnormal bleeding during surgery,[60,61] platelet aggregation,[62] prothrombin formation,[63] or platelet activating factor.[64] The dosages employed in these studies ranged from 1 to 5 g per day.

Given fish oil's popularity, concern has arisen regarding its effects on hemostasis when it is taken daily in combination with NSAIDs or warfarin. A few studies have shown that fish oil supplementation in combination with aspirin at doses of 10 g of fish oil and 325 mg of aspirin,[65] 5 g of fish oil and 325 mg of aspirin,[66] and 4.5 g of fish oil and 480 mg of aspirin[67] increases bleeding time. In addition, a study with non-human primates reported that fish oil supplementation increased bleeding time and interrupted vascular thrombus formation.[68]

Thus, fish oil taken alone appears to have a marginal effect on coagulation; however, when taken with NSAIDs or other anticoagulants, such as warfarin, bleeding time may increase; therefore, caution is warranted.

Vitamin E

Vitamin E is a generic name used for a group of fat-soluble vitamins with certain antioxidant properties. It occurs naturally in eight chemical forms: alpha-, beta-, gamma-, and delta-tocopherol and alpha-, beta-, gamma-, and delta-tocotrienol. Of the eight, alpha-tocopherol has the highest bioavailability in humans.[69] For US adults, the recommended dietary allowance of vitamin E is 22.4 IU (15 mg) per day, and the tolerable upper intake level is 1500 IU (1000 mg) per day.[68,70] Through a search of common commercially available dietary supplements, the range of vitamin E supplementation doses was found to be 200 IU (134 mg) to 1,000 IU (670 mg), with 400 IU (268 mg) being the most common. Although one study found that a dose of only 50 mg/day of vitamin E resulted in an increase in subarachnoid hemorrhage,[71] most other studies did not observe such an association, even at higher doses.

For example, two studies, one with 20 healthy adults receiving vitamin E supplementation at doses of 530 mg/day for 5 consecutive weeks[72] and another with 42 healthy adults receiving 530 mg/day for 2 consecutive weeks,[73] failed to show any reduction in in vivo platelet aggregation. Another study found no significant effect of 45 mg/day of vitamin E on platelet aggregation when it was taken for 8 consecutive weeks.[74]

Other human studies do suggest that vitamin E possesses platelet antiaggregation properties. For example, two studies reported a reduction in in vitro platelet adhesion to endothelial cells.[75,76] Furthermore, a randomized, double-blind study of 100 volunteers found a significant decrease in platelet adhesion in volunteers that took 265 mg/day of vitamin E with 325 mg aspirin for 2 years compared with 48 volunteers that took 325 mg of aspirin alone for the same length of time.[77] Another study with 15 volunteers measured the ability of vitamin E at various doses (400, 800, and 1,200 IU/day) to inhibit platelet aggregation. All three dose levels inhibited platelet aggregation, and the 1,200 IU/day dosage was found to inhibit platelet aggregation by altering arachidonic acid production.[78] Another study reported that alpha-tocopherol inhibited platelet aggregation in vitro in a dose dependent manner.[79] Furthermore, gamma-tocopherol was reported to ameliorate effects of exercise-induced platelet aggregation, while alpha-tocopherol did not.[80]

Therefore, overall, it appears vitamin E may have dose-dependent anticoagulant properties. Doses lower than 400 IU/day have inconsistent antiplatelet activity. However, doses closer to the tolerable upper intake level may inhibit platelet aggregation when taken in the form of either alpha- or gamma-tocopherol.

Policosanol

Although policosanol is not a popular dietary supplement according to published surveys,[81,82] it has been investigated for beneficial effects on cardiovascular health, such as reducing low-density lipoprotein (LDL) levels and increasing high-density lipoprotein (HDL).[83] Policosanol is a natural extract of waxes derived from plants like sugar cane and yams and from beeswax. It is composed of several fatty alcohols, including octocosanol and tricontanol.

Policosanol at a dose of 10 mg/day is reported to reduce arachidonic acid production and collagen- and ADP-induced platelet aggregation.[84–86] When policosanol is taken in conjunction with aspirin, it has been reported to decrease ADP-induced platelet aggregation by 10% and collagen-induced platelet aggregation by 35% compared to aspirin alone.[87] No studies have demonstrated that policosanol causes excessive bleeding. Moreover, no case reports of bleeding due to policosanol supplementation were located. Policosanol may cause bleeding when taken with aspirin or other NSAIDs, but this has not been established definitely,

Magnesium

Magnesium is the fourth most abundant mineral in the human body[88] and is essential for adenosine triphosphate (ATP) metabolism. In commercially available oral supplements, magnesium is found in doses ranging from 250 to 500 mg.

One study of magnesium supplementation found that an intravenous infusion of 192 mg/dL at a dose of 3 mL/h for 24 hours (for a total dose of 138 mg) increased bleeding time by roughly 40% in vivo and ex vivo in eight healthy volunteers.[89] Another study administered the same concentration of magnesium for the same duration intravenously to 14 volunteers and reported that it increased bleeding time by 48% and decreased platelet aggregation in vitro.[90] A third study administered the same concentration and duration of intravenous magnesium with 100 mg of aspirin in 12 volunteers and found the combination inhibited platelet adhesion ex vivo.[91] Daily doses of magnesium (800–1,200 mg tablets) in combination with a daily dose of 81 mg aspirin in 42 volunteers for 3 months decreased platelet-dependent thrombosis 35% more than aspirin alone (there was no magnesium-only supplement group in this study).[92] Intravenous infusion of magnesium in combination with aspirin does appear to alter hemostasis; however, the oral dietary supplement formulation and dosage of magnesium has not been extensively studied.

Feverfew

Feverfew (*Tanacetum parthenium*) has been used as an herbal remedy for migraine headaches since medieval times.[93] Sesquiterpene lactones in feverfew are reported to be responsible for its purported effects on platelets.[94] Feverfew reduces in vitro serotonin release by ADP- and collagen-induced platelet aggregating agents.[95] It also prevents thromboxane synthesis in vitro by inhibiting cyclo-oxygenase production[96] and arachidonic acid production.[97] No clinical evidence that feverfew is an anticoagulant was located and feverfew does not appear to interact with NSAIDs. However, due to its possible antiplatelet properties, caution should be exercised when taking feverfew with NSAIDs.

Dong quai

Dong quai (*Radix Angelicae sinensis*) is a fragrant perennial herb that grows at high altitudes in China, Korea, and Japan. It has been used in Eastern medicine to treat migraine headache, irregular menstruation, and menstrual pain.[98]

Six biochemical constituents related to the anticoagulant coumarin have been identified in dong quai. These are osthole, ferulic acid, bergapten, imperatorin, oxypeucedonin, and psoralin.[99] There is no predominant component, and the concentration of each component in dong quai varies considerably in different lots. Osthole and ferulic acid are the primary components that appear to affect platelet aggregation through inhibition of in vitro thromboxane A_2 and prostacyclin synthetase.[100]

There are anecdotal accounts implicating dong quai in hemorrhage and suggesting it interacts with warfarin,[101] but no studies were found that examined the effects of dong quai on coagulation. Because dong quai contains coumarin derivatives, it should be used with caution, especially by patients being treated with warfarin or NSAIDs.

Coenzyme Q_{10}

Coenzyme Q_{10} is increasing in popularity as a dietary supplement. It is found in mitochondria and is involved in aerobic cellular respiration. Coenzyme Q_{10} is necessary for cell function.[102] When administered as a dietary supplement in doses of 400 mg/day, it appears to affect platelet size, but it does not alter platelet aggregation in vitro.[103] Coenzyme Q_{10} does not appear to interact with warfarin[104] or have any harmful effects on coagulation. Insufficient evidence currently exists in the literature to recommend against coenzyme Q_{10} supplementation for individuals receiving coumadin-containing drugs.

Glucosamine

Glucosamine is naturally present in shellfish shells, animal bone, and bone marrow. It is also present in some fungi, such as *Aspergillus niger*. It is used to treat arthritis, typically in doses of 1,500 mg/day. It suppresses ADP-mediated platelet activation in humans[105] and appears to reduce platelet aggregation in guinea pigs.[106] A recent review noted 21 case reports describing a glucosamine and warfarin interaction resulting in an increased international normalized ratio.[107] No studies were found that showed an interaction between glucosamine and NSAIDs. Glucosamine appears to exhibit antiplatelet properties and may interact with NSAIDs. Although glucosamine appears to interact with warfarin, it does not appear to cause excessive bleeding itself.

Other supplements

Several dietary supplements have occasionally been reported to possess anti-platelet/anti-coagulation properties.

Lycopene. Lycopene is a bioactive ingredient in tomatoes reported to inhibit platelet aggregation.[108]

L-arginine. The amino acid L-arginine may also inhibit platelet response.[109]

Taurine. Taurine is an amino acid added to energy drinks and two studies indicate it may reduce platelet aggregation.[110,111]

Selenium. The essential mineral selenium appears to inhibit thromboxane synthesis in vitro[112] and has been shown to interact with warfarin.[113]

Passion flower. Passion flower (*Passiflora incarnata*) contains small amounts of coumarin[114] and, theoretically, may increase bleeding; however, no documented cases of excessive bleeding have been reported with its use.

Chamomile. Chamomile (*Matricaria recutita*) also contains small amounts of coumarin.[115] Theoretically, it may potentiate the effect of warfarin and NSAIDs, but no reports have documented this.

CONCLUSION

Although there has been considerable research examining potential adverse or beneficial effects of various dietary supplements on hemostasis, there is no definitive clinical data demonstrating that any unadulterated dietary supplement adversely affects hemostasis when taken alone or in combination with blood-thinning medications in the doses typically provided by reliable manufacturers. However, there are numerous reports in the literature suggesting several supplements may affect coagulation; therefore, future research is necessary.

Acknowledgment

The views, opinions and/or findings in this report are those of the authors, and should not be construed as an official Department of the Army position, policy, or decision, unless so designated by other official documentation. Citation of commercial organization and trade names in this report do not constitute an official Department of the Army endorsement or approval of the products or services of these organizations.

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