Antiadhesion Herbs

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Abstract

Herbal medicines that block bacteria or cancer cells from adhering to their target cells offer a novel therapeutic approach. These medicines can potentially help prevent and treat a range of infections or cancers. *Vaccinium macrocarpon* (cranberry) is the best-studied of these medicines. It has been shown to be useful both in prevention and treatment of urinary-tract infection in some patients. There is growing interest in using cranberry or its close relatives—*V. angustifolium* or *V. corymbosum* (blueberry); *V. myrtillus* (bilberry); and *V. ovalifolium, V. ovatum,* or *V. parvifolium* (huckleberry)—to block *Helicobacter pylori* and *Streptococcus* spp. adhesion. *Camellia sinensis* (tea) also has promise as an antiadhesion agent, particularly against *Streptococcus mutans*. Other herbs with antiadhesion effects in vitro or in animal studies include *Panax ginseng* (Asian ginseng), *Artemisia capillaris* (yin-chen wormwood), *Humulus lupulus* (hops), propolis, *Asarum sieboldii* (xi xin), *Asarum canadense* (wild ginger), *Asarum europaeum* (European wild ginger), *Cladosiphon okmuranus* (mozuku), *Fucus vesiculosus* (bladderwrack), and *Fucus evanescens*.

Introduction

Some herbal medicines block adhesion of pathogenic microbes to epithelial cells. This mechanism of action demonstrates the diversity of antimicrobial activity in medicinal herbs and provides a therapeutic approach not available in antibiotic drugs. The continued failure of most of conventional medicine to appreciate the value of antiadhesive botanicals, even if they are not as potent or immediate in their actions as drugs, does a disservice to patients. Some studies have shown that common antibiotics such as trimethoprim-sulfamethoxazole do not inhibit bacterial adhesion directly and actually seem to increase levels of more virulent uropathogens after cessation of treatment.[1]

There is some evidence that the antiadhesive properties of botanicals also affect movements of cancer cells and may provide protection against local invasion and metastasis.

Vaccinium spp. and Urinary-Tract Infection

Vaccinium macrocarpon (cranberry) fruit is one of the best-studied and most well-known antiadhesion herbs. This Ericaceae family herb contains proanthocyanidins that have been shown to block the adhesion of *Escherichia coli* to human urothelium in vitro and in clinical trials.[2] This same effect has been demonstrated by other members of the same genus, notably blueberry (*V. angustifolium* and *V. corymbosum*).[3–5] *V. myrtillus* and (bilberry), and various huckleberries (*V. ovalifolium, V. ovatum* and *V. parvifolium*) contain similar constituents and are presumed to have antiadhesive activity. Table 1 presents clinical trials that have provided some degree of quantification of how effectively cranberry reduces *E. coli* adhesion.

Cranberry clearly does not deliver the same immediate results as antibiotics in most patients with uncomplicated UTIs. As a monotherapy, cranberry juice or various encapsulated products have not been rigorously proven effective for treating UTIs.[6] This is not surprising as cranberries do not have potent, direct toxicity to bacterial cells and antiadhesive effects are less likely to be helpful in an already-established infection.

Trials on prevention of UTI, however, at least in women with recurrent UTIs, show that cranberry products (juice and various powdered extracts) can, over 12 months' time, effectively reduce the incidence of UTI.[7,8] These products achieve this effect with minimal toxicity, though long-term studies have fairly high levels of dropouts, mainly because patients stop taking cranberry juice as a result of time and taste issues.

Vaccinium corymbosum (blueberry).

Vaccinum macrocarpum (cranberry).

Cranberry has also been assessed for cost effectiveness. In a 12-month trial, 150 sexually active women were randomly assigned to drink cranberry juice and take placebo tablets, take cranberry tablets and drink placebo cranberry-flavored juice, or drink placebo cranberry-flavored juice and take placebo tablets.[9] Juice doses were 250 mL, three times per day; tablets containing a dried extract of juice (30:1) were taken twice per day.

Table 1. A Sample of Studies Quantifying *Escherichia coli* Antiadhesive Effects of Cranberry

Trial (type)	Daily dose	Results
Sobota[a] 1984 (open, n = 22)	15 oz juice	15 of 22 subjects had significantly decreased adhesion 1–3 hours after drinking juice.
Valentova, et al.[b] 2007 (controlled, n = 65)	400 or 1200 mg dried juice	1200 mg only reduced adhesion significantly compared with placebo.
Greenberg, et al.[c] 2005 (controlled, n = 5)	42.5 g dried fruit	3 of 5 subjects had reduced adhesion after cranberries, none after raisins or at baseline.
Di Martino, et al.[d] 2006 (randomized double-blind, n = 20)	8.5 or 25 oz cranberry juice	8.5 oz of cranberry juice reduced adhesion 45% and 25 oz 62% compared with placebo drink.

Latin binomial for cranberry is *Vaccinium macrocarpon.*
[a]Ref. 2; [b]Valentova K, Stejskal D, Bednar P, et al. Biosafety, antioxidant status, and metabolites in urine after consumption of dried cranberry juice in healthy women: A pilot double-blind placebo-controlled trial. J Agric Food Chem 2007;55:3217–3224; [c]Greenberg JA, Newmann SJ, Howell AB. Consumption of sweetened dried cranberries versus unsweetened raisins for inhibition of uropathogenic *Escherichia coli* adhesion in human urine: A pilot study. J Altern Complement Med 2005;11:875–878; [d]Di Martino P, Agniel R, David K, et al. Reduction of *Escherichia coli* adherence to uroepithelial bladder cells after consumption of cranberry juice: A double-blind randomized placebo-controlled cross-over trial. World J Urol 2006;24:21–27.

Participants taking either form of cranberry had significantly fewer UTIs compared with the placebo group. Because of reduced antibiotic use and less time off work, the cranberry-treated groups spent less money on treatment than the placebo group. Tablets proved to be twice as cost effective as juice in this trial. Though these results need to be independently replicated, they provide strong evidence that ongoing use of cranberry products can provide a significant benefit in women with recurrent UTIs.[9]

Vaccinium spp. and *Helicobacter pylori*

Adhesion of *Helicobacter pylori* to stomach epithelium and possibly mucus is important to this bacterium's ability to stay in the body and create disease.[10] In vitro, cranberry extract has been shown to reduce *H. pylori* adhesion to human gastric mucus.[11] Cranberry extracts also blocked adhesion directly to gastric epithelium in vitro.[12] Cranberry extracts showed additive inhibitory effects on *H. pylori* in vitro when combined with *Origanum vulgare* (oregano) extracts.[13] The mechanisms of action shown in this study included inhibition of urease and disruption of energy production by blocking proline dehydrogenase.

In a double-blind, randomized clinical trial, 225 adults in Linqu County, China, took either 250 mL of cranberry juice twice daily or an artificially cranberry-flavored juice.[14] This area of China has one of the highest stomach cancer rates in the world. Only 189 subjects completed the trial with full compliance. All participants had positive 13C-urea breath tests documenting *H. pylori* infection at the outset of the trial. By the end of the 90-day trial, significantly more subjects who drank real cranberry juice had negative breath tests compared with the placebo group (14.4% versus 5.4% were negative in each group, respectively).

While clearly much less effective than antibiotics, the lack of side-effects and ability to incorporate the treatment regularly suggest cranberry could, if the results of this trial are durable,[14]

Organisms Against Which Cranberry Has Shown Antiadhesive Activity

Escherichia coli

Helicobacter pylori

Influenza

Proteus mirabilus

Pseudomonas aeruginosa

Streptococcus mutans

Sources: Ref. 11; Schmidt DR, Sobota AE. An examination of the anti-adherence activity of cranberry juice on urin ary and non-urinary bacterial isolates. Microbios 1988;55:173–181; Weiss EI, Houri-Haddad Y, Greenbaum E, Hochman N, et al. Cranberry juice constituents affect influenza virus adhesion and infectivity. Antiviral Res 2005;66:9–12.

Vaccinum spp. (huckleberry).

represent a potentially huge reduction in gastric cancer rates in an endemic area. It is not known if these results would apply to western populations, particularly because the Chinese villagers in this study had no prior exposure to antibiotics, not to mention the enormous dietary and cultural differences between China and the West.

In a double-blind clinical trial in Israel, 177 adults with breath test–confirmed *H. pylori* infection drank 250 mL twice daily of either cranberry juice or a cranberry-flavored placebo drink (during drug treatment and for 2 weeks after).[15] All subjects took a combination of clarithromycin, amoxicillin, and omeprazole for 7 days. An additional unblinded control group of 712 adults took the drugs without placebo or cranberry. Overall, cranberry was no more effective than placebo or no additional treatment in eradicating *H. pylori* as assessed by breath testing. However, when looking at just women in the trial, cranberry was associated with a nonsignificant, 8% higher rate of eradication compared with placebo, and a significant 15% higher rate of eradication compared with the antibiotic-only group. Women did have higher levels of *H. pylori* growth than men in this trial. More work is needed, and higher doses probably need to be used, but this trial provides evidence that women undergoing *H. pylori* eradication treatment may benefit from adding cranberry to their regimens.

Vaccinium spp. and Oral Flora

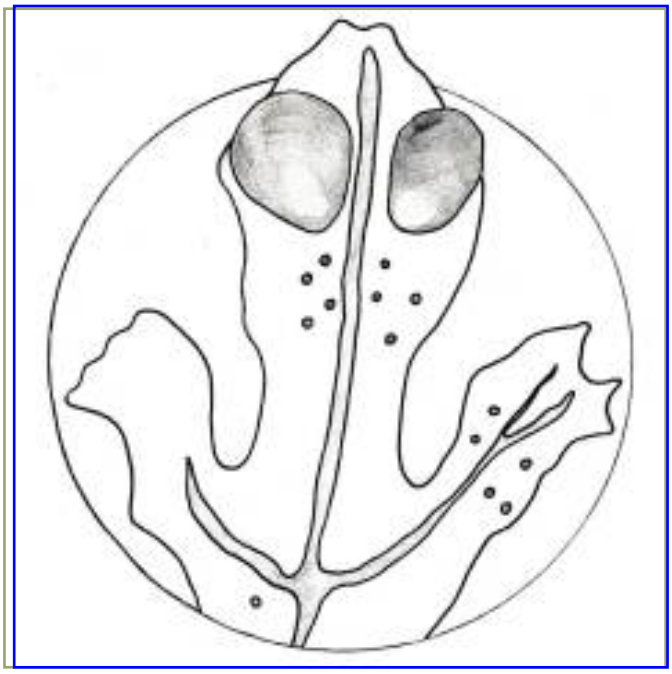
Various extracts and constituents from cranberry have been studied for their effect on oral microbes that can play a role in gingivitis, cavity formation, periodontal disease, and other problems. Flavonoids and proanthocyanidins from fresh cranberry fruit were found to moderately block glycosyltransferases and acid production by *Streptococcus mutans*.[16] Glycosyltransferases are critical enzymes for this microbe to form compounds that let it adhere to tooth surfaces. A combination of quercetin-3-arabinofuranoside, myricetin, and procyanidin A2 extracted from cranberry was more effective than any one component in isolation.

A similar study found the same constituents active also at inhibiting biofilm development by *S. mutans* in vitro.[17] Crude cranberry juice has also been shown to block glycosyltransferases, inhibit binding to teeth, and reduce acidogenicity of *S. mutans*.[18] High molecular weight compounds in cranberry reduce the hydrophobicity of streptococci, which has been shown to be directly related to inhibiting biofilm formation.[19] Cranberry does not kill *S. mutans* directly.[20]

Another question is whether cranberry can break up a biofilm. In vitro, high molecular weight materials from cranberry, presumed to be high in proanthocyanidins, have been shown to promote *Streptococcus sobrinus* actually breaking out of biofilms ("desorption").[21] This same extract has previously been shown to help prevent biofilm formation in the first place.[22]

Only 1 human trial was located on the effect of cranberry on oral health. A mouthwash with high molecular weight cranberry compounds added was compared with placebo mouthwash in 59 healthy volunteers for 6 weeks.[23] The count of *S. mutans* was significantly lower in the cranberry group compared with placebo, while no differences in plaque or gingival indices were noted. This provides preliminary evidence for the value of cranberry in helping with various dental diseases.

Highly sweetened cranberry juices should be avoided, as sugar is simply not healthy. (However, most studies on cranberry for UTIs have been done using a sweetened cranberry drink.) Some patients tolerate unsweetened juice, but most will not. Rather than using synthetic sweeteners with unknown long-term consequences and scant evidence of reduced weight gain,[24,25] we suggest that patients either try mixing blueberry and cranberry juice in equal parts or diluting cranberry juice with water and the lowest amount of grape juice possible. For patients who cannot or will not tolerate juice or find it too expensive, encapsulated products should be used (combinations of juice and capsules are of course possible). We generally recommend 2–4 oz of juice twice per day for prevention, increasing the dose to 4 times per day or more for acute problems. For capsules, 1000 mg twice per day for prevention and 2000 mg four or more times per day for acute problems are recommended.



Fucus vesiculosus (bladderwrack). Drawing© Kathy Abascal, B.S., J.D., R.H. (AHG).

Camellia sinensis

Camellia sinensis (tea) is a subshrub native to China, now widespread there and in India, Sri Lanka, Indonesia, and many other parts of the world. The popularity of its leaves (in various forms) as a beverage globally is rivaled only by water, coffee, and soft drinks. Of these, only green tea and water offer major health benefits with minimal risks at reasonable doses.[26] This is not to say that black tea is not bioactive, but that it has more potential for increasing the risk of gastrointestinal (GI) cancers with long-term regular use. Among the most overlooked of green tea's effects are its antiadhesive properties.

An acidic polysaccharide from green tea inhibited *H. pylori* adhesion to gastric cells at very low concentrations (0.01 mg/mL).[27] The polysaccharide was also highly active in this study against adhesion of *Staphylococcus aureus* and *Propionibacterium acnes*, but did not interfere with adhesion of normal gut microbes. Ethanol (50% or 95%) extracts of black tea were very effective, even at 0.5% dilution, at inhibiting *S. mutans* adhesion in vitro.[28] The tea extracts clearly inhibited glycosyltransferases of this microbe as well.

Epigallocatechin gallate and other polyphenols from green tea potently blocked in vitro adhesion of *Porphyromonas gingivalis*, which plays a role in dental disease.[29] Oolong tea, which contains partially fermented tea leaves, has been shown to reduce caries formation in rats infected with *S. mutans*.[30]

Antiadhesive effects of *C. sinensis* may extend beyond their utility against microbes. Theaflavins, polyphenolic compounds related to flavonoids, from black tea have shown the interesting ability in vitro to block adhesion of monocytes to vascular endothelium.[31] Blocking this oxidized low density lipoprotein–stimulated process could be key to preventing formation or worsening of arteriosclerotic lesions. A green-tea extract has been shown to induce annexin-I expression in lung-cancer cells in vitro.[32] This compound is believed to play a role in normal cell–cell adhesion, and to help prevent cancer cells from spreading locally and/or distantly. Further study is clearly warranted in these areas.

Human research on tea as a preventive against dental caries is fairly extensive. A review of several clinical trials involving several thousand subjects found that various forms of tea did have a preventive effect against caries.[33] Typically 3–5 g of green, Oolong, or black tea leaf or powder, are mixed with 1 cup of water and 3–5 cups are drunk per day. For oral disease prevention or treatment, the tea should be swished around in the mouth before being swallowed for optimal efficacy.

Miscellaneous Antiadhesive Herbs

Panax ginseng (Asian ginseng) root carbohydrates have shown some ability to interfere with *H. pylori* binding to human cells based on a qualitative in vitro assay.[34] A quantitative assay as well as scanning electron microscopy has confirmed that concentrations as low as 0.2 mg/mL of Asian ginseng carbohydrates can significantly reduce *H. pylori* adhesion.[35] The immune- and inflammation-modulating actions of Asian ginseng may also have some relevance in mitigating the effects of *H. pylori* infection.[36,37] Human trials should be undertaken.

Artemisia capillaris (yin-chen wormwood, capillary mugwort), a bitter herb used primarily in traditional Asian medicine, contains polysaccharides that block *H. pylori* adhesion to erythrocytes; this has been noted in a quantitative in vitro assay.[38] Yin-chen wormwood polysaccharides were approximately one third as potent as Asian ginseng polysaccharides at blocking *H. pylori* adhesion in vitro.[35] Yin-chen wormwood, like its European cousin *Artemisia absinthium* (wormwood), contains terpenoids that are also antimicrobial with some potential to attack *H. pylori* directly.[39] This herb's bitter qualities improve digestive function, which creates a less-hospitable environment for this microbe.[40,41]

Humulus lupulus (hops) bracts yield polyphenolic compounds, which were shown to be significantly more potent than green or Oolong tea leaves at blocking adhesion of *S. mutans* and *S. sorbinus* in vitro.[42] Other compounds in hops have been shown to be directly antimicrobial against *S. mutans*.[43]

An extract of these compounds at a 0.1% concentration was formulated into a mouthwash and tested in 29 healthy male volunteers.[44] After total plaque removal, they refrained from any oral hygiene for 3 days except using the hops mouthwash or a placebo. New plaque formation was significantly lower in the hops group compared with the placebo group at the end of this period.

Propolis, which is a bee-harvested mixture of plant and tree resins, is a well-known and often-used herbal antimicrobial. It is simultaneously quite active at inhibiting adhesion of a wide

range of microbes, including *Candida albicans*, streptococci, staphylococci, and enterococci, in vitro, and at killing these organisms outright.[45]

Asarum sieboldii (xi xin) root finds use in traditional Asian medicine for respiratory-tract infections. Ethanolic and aqueous extracts of this medicinal plant have been shown to inhibit glycosyltransferases, acid production, growth, and adhesion of *S. mutans* in vitro.[46] There are similar species of this genus native to the United States (*Asarum canadense*) and Europe (*A. europaeum*), generally known as wild ginger because of their spicy taste (though they have no relationship to *Zingiber officinale* or true ginger otherwise). These herbs should be used with caution as they contain the carcinogenic and nephrotoxic compound aristolochic acid.

Numerous medicinal algae have also shown potential as antiadhesive agents. Fucosylated Lewis b antigen is a receptor to which *H. pylori* strains can bind.[47] Numerous algae contain fucoidans, glycosaminoglycans that may interfere with *H. pylori* adhesion, including *Cladosiphon okmuranus* (mozuku) and *Fucus vesiculosus* (bladderwrack). In vitro, fucoidans from these algae blocked *H. pylori* adhesion to human gastric cells.[48] Presumably the fucoidans are acting as "false receptors," looking like what *H. pylori* wants to bind to but not actually being attached to anything, so the microbe just drifts away down the GI tract. Though unproven in human trials, fucoidans from *Cladosiphon* and *Fucus* have been shown to protect Mongolian gerbils from infection and those that were infected from developing gastritis.[49]

Fucoidan from *Fucus evanescens*, native to the Okhotsk sea, has been shown to moderately inhibit metastasis of lung cancer cells in mice.[50] Though fucoidan had some direct antineoplastic activity, it also had antiadhesive activity. This was true of fucoidans from a range of algae in a separate study that looked at breast-cancer adhesion.[51]

Conclusion

Antiadhesive herbal medicines represent an intriguing and unique approach to helping patients with a range of infections and cancers. Because these agents do not necessarily kill the microbes or cancer cells directly, the agents may be less likely to promote evolution of resistance. They may also represent a significantly useful synergistic addition to treatment with direct antimicrobial and antineoplastic agents, because they act through such distinctive mechanisms. Much research remains to be done, but some antiadhesive herbs (cranberry and tea) are already in widespread use, have been validated clinically to varying degrees, and can realistically be prescribed now for clinical benefit with minimal risk. ■

References

1. Reid G, Bruce AW, Beheshti M. Effect of antibiotic treatment on receptivity of uroepithelial cells to uropathogens. Can J Microbiol 1988;34:327–331.

2. Sobota AE. Inhibition of bacterial adherence by cranberry juice: Potential use for the treatment of urinary tract infections. J Urol 1984;131:1013–1016.

3. Howell AB, Vorsa N, Marderosian AD, Foo LY. Inhibition of the adherence of P-fimbriated *Escherichia coli* to uroepithelial-cell surfaces by proanthocyanidin extracts from cranberries. N Engl J Med 1998;339:1085–1086.

4. Ofek I, Goldhar J, Sharon N. Anti–*Escherichia coli* adhesin activity of cranberry and blueberry juices. In: Kahane I, Ofek I, eds. Toward Anti Adhesion Therapy for Microbial Diseases. New York: Plenum Press, 1996:179–183.

5. Schmidt BM, Howell AB, McEniry B, et al. Effective separation of potent antiproliferation and antiadhesion components from wild blueberry (*Vaccinium angustifolium* Ait.) fruits. J Agric Food Chem 2004;52:6433–6442.

6. Jepson RG, Mihaljevic L, Craig J. Cranberries for treating urinary tract infections. Cochrane Database Syst Rev 2000;2:CD001322.

7. Jepson RG, Craig JC. A systematic review of the evidence for cranberries and blueberries in UTI prevention. Mol Nutr Food Res 2007;51:738–745.

8. Jepson R, Craig J. Cranberries for preventing urinary tract infections. Cochrane Database Syst Rev 2008;1:CD001321.

9. Stothers L. A randomized trial to evaluate effectiveness and cost effectiveness of naturopathic cranberry products as prophylaxis against urinary tract infection in women. Can J Urol 2002;9:1558–1562.

10. Tzouvelekis LS, Mentis AF, Makris M, et al. In vitro binding of *Helicobacter pylori* to human gastric mucin. Infect Immun 1991;59:4252–4254.

11. Burger O, Ofek I, Tabak M, et al. A high molecular mass constituent of cranberry juice inhibits *Helicobacter pylori* adhesion to human gastric mucus. FEMS Immunol Med Microbiol 2000;29:295–301.

12. Shmuely H, Burger O, Neeman I, et al. Susceptibility of *Helicobacter pylori* isolates to the antiadhesion activity of a high–molecular-weight constituent of cranberry. Diagn Microbiol Infect Dis 2004;50:231–235.

13. Lin YT, Kwon YI, Labbe RG, Shetty K. Inhibition of *Helicobacter pylori* and associated urease by oregano and cranberry phytochemical synergies. Appl Environ Microbiol 2005;71:8558–8564.

14. Zhang L, Ma J, Pan K, et al. Efficacy of cranberry juice on *Helicobacter pylori* infection: A double-blind, randomized placebo-controlled trial. Helicobacter 2005;10:139–145.

15. Shmuely H, Yahav J, Samra Z, et al. Effect of cranberry juice on eradication of *Helicobacter pylori* in patients treated with antibiotics and a proton pump inhibitor. Mol Nutr Food Res 2007;51:746–751.

16. Gregoire S, Singh AP, Vorsa N, Koo H. Influence of cranberry phenolics on glucan synthesis by glucosyltransferases and *Streptococcus mutans* acidogenicity. J Appl Microbiol 2007;103:1960–1968.

17. Duarte S, Gregoire S, Singh AP, et al. Inhibitory effects of cranberry polyphenols on formation and acidogenicity of *Streptococcus mutans* biofilms. FEMS Microbiol Lett 2006;257:50–56.

18. Koo H, Nino de Guzman P, et al. Influence of cranberry juice on glucan-mediated processes involved in *Streptococcus mutans* biofilm development. Caries Res 2006;40:20-27.

19. Yamanaka A, Kimizuka R, Kato T, Okuda K. Inhibitory effects of cranberry juice on attachment of oral streptococci and biofilm formation. Oral Microbiol Immunol 2004;19:150–154.

20. Leitão DP, Polizello AC, Ito IY, Spadaro AC. Antibacterial screening of anthocyanic and proanthocyanic fractions from cranberry juice. J Med Food 2005;8:36–40.

21. Steinberg D, Feldman M, Ofek I, Weiss EI. Cranberry high molecular weight constituents promote *Streptococcus sobrinus* desorption from artificial biofilm. Int J Antimicrob Agents 2005;25:247–251.

22. Steinberg D, Feldman M, Ofek I, Weiss EI. Effect of a high–molecular-weight component of cranberry on constituents of dental biofilm. J Antimicrob Chemother 2004;54:86–89.

23. Weiss EI, Kozlovsky A, Steinberg D, et al. A high molecular mass cranberry constituent reduces mutans streptococci level in saliva and inhibits in vitro adhesion to hydroxyapatite. FEMS Microbiol Lett 2004;232:89–92.

24. Soffritti M, Belpoggi F, Degli Esposti D, et al. First experimental demonstration of the multipotential carcinogenic effects of aspartame administered in the feed to Sprague-Dawley rats. Environ Health Perspect 2006;114:379–385.

25. Vermunt SH, Pasman WJ, Schaafsma G, Kardinaal AF. Effects of sugar intake on body weight: A review. Obes Rev 2003;4:91–99.

26. Gardner EJ, Ruxton CH, Leeds AR. Black tea—helpful or harmful? A review of the evidence. Eur J Clin Nutr 2007;61:3–18.

27. Lee JH, Shim JS, Lee JS, et al. Inhibition of pathogenic bacterial adhesion by acidic polysaccharide from green tea (*Camellia sinensis*). J Agric Food Chem 2006;54:8717–8723.

28. Limsong J, Benjavongkulchai E, Kuvatanasuchati J. Inhibitory effect of some herbal extracts on adherence of *Streptococcus mutans*. J Ethnopharmacol 2004;92(2–3):281–289.

29. Sakanaka S, Aizawa M, Kim M, Yamamoto T. Inhibitory effects of green tea polyphenols on growth and cellular adherence of an oral bacterium, *Porphyromonas gingivalis*. Biosci Biotechnol Biochem 1996;60:745–749.

30. Ooshima T, Minami T, Aono W, et al. Oolong tea polyphenols inhibit experimental dental caries in SPF rats infected with mutans streptococci. Caries Res 1993;27:124–129.

31. Lü H, Hua P, Yu J, et al. Study on the effect of theaflavins on the adhesion between monocyte and endothelial cells [in Chinese]. Zhong Yao Cai 2005;28:304–306.

32. Lu QY, Jin YS, Zhang ZF, et al. Green tea induces annexin-I expression in human lung adenocarcinoma A549 cells: Involvement of annexin-I in actin remodeling. Lab Invest 2007;87:456–465.

33. Hamilton-Miller JM. Anti-cariogenic properties of tea (*Camellia sinensis*). J Med Microbiol 2001;50:299–302.

34. Belogortseva NI, Yoon JY, Kim KH. Inhibition of *Helicobacter pylori* hemagglutination by polysaccharide fractions from roots of *Panax ginseng*. Planta Med 2000;66:217–220.

35. Lee JH, Park EK, Uhm CS, et al. Inhibition of *Helicobacter pylori* adhesion to human gastric adenocarcinoma epithelial cells by acidic polysaccharides from *Artemisia capillaris* and *P anax ginseng*. Planta Med 2004; 70:615–619.

36. Park S, Yeo M, Jin JH, et al. Inhibitory activities and attenuated expressions of 5-LOX with red ginseng in *Helicobacter pylori*–infected gastric epithelial cells. Dig Dis Sci 2007;52:973–982.

37. Park S, Yeo M, Jin JH, et al. Rescue of *Helicobacter pylori*–induced cytotoxicity by red ginseng. Dig Dis Sci 2005;50:1218–1227.

38. Woo JS, Ha BH, Kim TG, et al. Inhibition of *Helicobacter pylori* adhesion by acidic polysaccharide fractions from *Artemisia capillaris*. J Microbiol Biotechnol 2003;13:853–858.

39. Cha JD, Jeong MR, Jeong SI, et al. Chemical composition and antimicrobial activity of the essential oils of *Artemisia scoparia* and *A. capillaris*. Planta Med 2005;71:186–190.

40. Okuno I, Uchida K, Kadowaki M, Akahori A. Choleretic effect of *Artemisia capillaris* extract in rats. Jpn J Pharmacol 1981;31:835–838.

41. Zhang LH, Wang JZ, Zhou XB, Wu BJ. A comparative study on cholagogic effect of *Artemisia* [in Chinese]. Chung Kuo Chung Yao Tsa Chih 1993;18:560–561,575.

42. Tagashira M, Uchiyama K, Yoshimura T, et al. Inhibition by hop bract polyphenols of cellular adherence and water-insoluble glucan synthesis of mutans streptococci. Biosci Biotechnol Biochem 1997;61:332–335.

43. Gerhäuser C. Broad spectrum anti-infective potential of xanthohumol from hop (*Humulus lupulus* L.) in comparison with activities of other hop constituents and xanthohumol metabolites. Mol Nutr Food Res 2005;49:827–831.

44. Shinada K, Tagashira M, Watanabe H, et al. Hop bract polyphenols reduced three-day dental plaque regrowth. J Dent Res 2007;86:848–851.

45. Koo H, Gomes BP, Rosalen PL, et al. In vitro antimicrobial activity of propolis and *Arnica montana* against oral pathogens. Arch Oral Biol 2000;45: 141–148.

46. Yu HH, Seo SJ, Hur JM, et al. *Asarum sieboldii* extracts attenuate growth, acid production, adhesion, and water-insoluble glucan synthesis of *Streptococcus mutans*. J Med Food 2006;9:505–509.

47. Boren T, Falk P, Roth KA, et al. Attachment of *Helicobacter pylori* to human gastric epithelium mediated by blood group antigens. Science 1993;262:1892–1895.

48. Shibata H, KimuraTakagi I, Nagaoka M, et al. Inhibitory effect of *Cladosiphon fucoidan* on the adhesion of *Helicobacter pylori* to human gastric cells. J Nutr Sci Vitaminol (Tokyo) 1999;45:325–336.

49. Shibata H, Iimuro M, Uchiya N, et al. Preventive effects of *Cladosiphon fucoidan* against *Helicobacter pylori* infection in Mongolian gerbils. Helicobacter 2003;8:59–65.

50. Alekseyenko TV, Zhanayeva SY, Venediktova AA, et al. Antitumor and antimetastatic activity of fucoidan, a sulfated polysaccharide isolated from the Okhotsk Sea *Fucus evanescens* brown alga. Bull Exp Biol Med 2007;143:730–732.

51. Cumashi A, Ushakova NA, Preobrazhenskaya ME, et al. A comparative study of the anti-inflammatory, anticoagulant, antiangiogenic, and antiadhesive activities of nine different fucoidans from brown seaweeds. Glycobiology 2007;17:541–552.

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