

Disease type/risk	First Author	Study Title Complete Citation	Date	Abstract	Human	Human cell	Animal	Animal cell
	Chatterjee, A.	Chatterjee, A.; Yasmin, T.; Bagchi, D.; Stohs, S. J., Inhibition of Helicobacter pylori in vitro by various berry extracts, with enhanced susceptibility to clarithromycin. <i>Mol Cell Biochem</i> 2004 , 265, (1-2), 19-26.		The objective of this study was to evaluate the effects of various berry extracts, with and without clarithromycin on Helicobacter pylori. Resistance to clarithromycin by H. pylori has been reported, leading to interest in alternatives/adjuncts to therapy with clarithromycin. H. pylori American type culture collection (ATCC) strain 49503 was grown, cell suspensions were made in PBS and diluted 10-fold. One hundred microl of the suspension was then incubated for 18 h with extracts of raspberry , strawberry, cranberry, elderberry, blueberry, bilberry, and OptiBerry, a blend of the six berries, at 0.25-1% concentrations. Serially diluted cell suspensions were exposed for 1 h to clarithromycin at 15 microg/ml. Ten microl of bacterial samples from the 10(-7) dilution tube were plated and incubated for 18 h and the number of colonies were counted. Growth of H. pylori was confirmed by the CLO test. All berry extracts significantly (p < 0.05) inhibited H. pylori, compared with controls , and also increased susceptibility of H. pylori to clarithromycin, with OptiBerry demonstrating maximal effects.				
	Chung, J. G.	Chung, J. G., Inhibitory actions of ellagic acid on growth and arylamine N-acetyltransferase activity in strains of Helicobacter pylori from peptic ulcer patients. <i>Microbios</i> 1998 , 93, (375), 115-127.		Arylamine N-acetyltransferase (NAT) activity in Helicobacter pylori was inhibited by ellagic acid, a possible chemopreventive drug. The NAT activity was determined using an acetyl CoA recycling assay and high pressure liquid chromatography. Inhibition of growth studies using H. pylori demonstrated that ellagic acid elicited a dose-dependent bactericidal effect in H. pylori cultures, i.e. the greater the concentration of ellagic acid, the greater the inhibition of growth of H. pylori. The IC50 value was 1 mM for inhibition of growth of H. pylori. Cytosols or suspensions of H. pylori with and without selected concentrations of ellagic acid co-treatment showed different percentages of 2-aminofluorene and p-aminobenzoic acid acetylation. The data indicated that there was decreased NAT activity associated with increased ellagic acid in H. pylori cytosols and intact cells. For the cytosol and intact bacteria examinations, the apparent values of K-m and V-max decreased after co-treatment with 1 mM ellagic acid. This report is the first demonstration of ellagic acid inhibition of arylamine NAT activity and ellagic acid inhibition of growth in the bacterium H. pylori.				

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	Funatogawa, K.	Funatogawa, K.; Hayashi, S.; Shimomura, H.; Yoshida, T.; Hatano, T.; Ito, H.; Hirai, Y., Antibacterial activity of hydrolyzable tannins derived from medicinal plants against <i>Helicobacter pylori</i> . <i>Microbiology and Immunology</i> 2004 , 48, (4), 251-261.		<p><i>Helicobacter pylori</i> is a major etiological agent in gastroduodenal disorders. In this study, we isolated 36 polyphenols and 4 terpenoids from medicinal plants, and investigated their antibacterial activity against <i>H. pylori</i> in vitro. All hydrolyzable tannins tested demonstrated promising antibacterial activity against H. pylori. Monomeric hydrolyzable tannins revealed especially strong activity. Other compounds demonstrated minimal antibacterial activity with a few exceptions. A monomeric hydrolyzable tannin, Tellimagrandin I demonstrated time- and dose-dependent bactericidal activity against <i>H. pylori</i> in vitro. On the other hand, hydrolyzable tannins did not affect the viability of MKN-28 cells derived from human gastric epithelium. Hydrolyzable tannins, therefore, have potential as new and safe therapeutic regimens against <i>H. pylori</i> infection. Furthermore, we investigated effects of hydrolyzable tannins on lipid bilayer membranes. All the hydrolyzable tannins tested demonstrated dose-dependent membrane-damaging activity. However, it remains to be elucidated whether their membrane-damaging activity directly contributes to their antibacterial action.</p>				
	Gotteland, M.	Gotteland, M.; Brunser, O.; Cruchet, S., Systematic review: are probiotics useful in controlling gastric colonization by <i>Helicobacter pylori</i> ? <i>Alimentary</i> <i>Pharmacology & Therapeutics</i> 2006 , 23, (8), 1077-1086.		<p><i>Helicobacter pylori</i> is a highly prevalent pathogen considered as an aetiological factor for gastroduodenal ulcers, and a risk factor for gastric adenocarcinoma and lymphoma in humans. Most subjects colonized by this micro-organism are asymptomatic and remain untreated. In symptomatic patients, the antibiotic treatment has a high cost and is not 100% effective because of resistance to antibiotics and to moderate patient compliance. This review discusses the role of probiotics as alternative solutions to assist in the control of <i>H. pylori</i> colonization in at-risk populations. The evidence that some strains of <i>Lactobacillus</i> and <i>Bifidobacterium</i> are able to inhibit <i>H. pylori</i> growth through the release of bacteriocins or organic acids, and may also decrease its adhesion to epithelial cells, is reviewed. In addition, probiotics have a possible role in the stabilization of the gastric barrier function and the decrease of mucosal inflammation. Other aspects that are considered are the contribution of probiotics to the healing of the gastric mucosa linked to their antioxidant and anti-inflammatory properties. Clinical trials in colonized adults and children are reviewed, and suggest that probiotics do not eradicate <i>H. pylori</i> but maintain lower levels of this pathogen in the stomach; in combination with antibiotics, probiotics may increase eradication rate and/or decrease adverse effects. Papers suggesting similar effects on H. pylori by foodstuffs such as berry juice and some milk proteins are quoted. Regular intake of these and other dietary products might constitute a low-cost, large-scale alternative solution applicable for populations at-risk for <i>H. pylori</i> colonization.</p>				

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	Kamiji, M. M.	Kamiji, M. M.; de Oliveira, R. B., Non-antibiotic therapies for Helicobacter pylori infection. <i>European Journal of Gastroenterology & Hepatology</i> 2005 , 17, (9), 973-981.		Despite years of experience with Helicobacter pylori treatment the ideal regimen for treating the infection has not been found. The most effective eradication treatment is the combination of a proton pump inhibitor with antibiotics, but 10-20% of the patients fail to obtain eradication of the infection. Antibiotic resistance is a major factor affecting the outcome of treatment. Non-antibiotic therapies, including phytomedicines, probiotics, and antioxidants, have been increasingly investigated as potential alternatives for the treatment of H. pylori. In this article, we review the non-antibiotic therapies for H. pylori infection.				
	Lin, Y. T.	Lin, Y. T.; Kwon, Y. I.; Labbe, R. G.; Shetty, K., Inhibition of Helicobacter pylori and associated urease by oregano and cranberry phytochemical synergies. <i>Applied and Environmental Microbiology</i> 2005 , 71, (12), 8558-8564.		Ulcer-associated dyspepsia is caused by infection with Helicobacter pylori. H. pylori is linked to a majority of peptic ulcers. Antibiotic treatment does not always inhibit or kill H. pylori with potential for antibiotic resistance. The objective of this study was to determine the potential for using phenolic phytochemical extracts to inhibit H. pylori in a laboratory medium. Our approach involved the development of a specific phenolic profile with optimization of different ratios of extract mixtures from oregano and cranberry. Subsequently, antimicrobial activity and antimicrobial-linked urease inhibition ability were evaluated. The results indicated that the antimicrobial activity was greater in extract mixtures than in individual extracts of each species. The results also indicate that the synergistic contribution of oregano and cranberry phenolics may be more important for inhibition than any species-specific phenolic concentration. Further, based on plate assay, the likely mode of action may be through urease inhibition and disruption of energy production by inhibition of proline dehydrogenase at the plasma membrane.				

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	Lin, Y. T.	Lin, Y. T.; Vatter, D.; Labbe, R. G.; Shetty, K., Enhancement of antioxidant activity and inhibition of Helicobacter pylori by phenolic phytochemical-enriched alcoholic beverages. <i>Process Biochemistry</i> 2005 , 40, (6), 2059-2065.		Ulcer-associated dyspepsia;is caused by,an infection of Helicobacter pylori. H. pylori is a food-related pathogen that infects the stomach and weakens the stomach lining and is linked to a, majority of peptic ulcers. Antibiotic treatment does not always inhibit or kill H. pylori as it has side effects with potential for antibiotic resistance. Previous research has indicated that phytochemical-enriched wines have therapeutic benefits. The objective of this study was to determine the potential of phenolic phytochemical-enriched wine and vodka to inhibit H. pylori in laboratory medium. This offers,a novel approach to couple antioxidant-enriched benefits of alcoholic beverages with synergistic antimicrobial effectiveness and can be considered as,'generally regarded as safe' (GRAS). This approach involved the development of phenolic phytochemical-enriched alcoholic beverages through release from dry botanicals enclosed in tea bags. Phenolic phytochemical-enriched alcoholic beverages were then assayed for total phenolics, antioxidant activity, and phenolic profile by HPLC. Various phenolic-enriched concentrations were then used for antioxidant assay and corresponding antimicrobial activity against H. pylori. Results indicate that total phenolics increased from 86 mu g/ml in control to an average of 186 mu g/ml in phenolic-enriched white wine. Corresponding antioxidant activity increased from 38% 1, 1 -Diphenyl-2-picrylhydrazyl (DPPH) free radical inhibition in control to an average of 83% in phenolic-enriched white wines. Total phenolics increased from 5.7 mu g/ml in control to an average of 289 mu g/ml in phenolic-enriched vodka. The antioxidant activity increased from 2% DPPH inhibition in control to 69% inhibition in phenolic-enriched vodka. Phenolic-enriched wine enhanced the inhibitory activity against H. pylori but there was no concentration-dependent correlation. Raspberry, cinnamon and peppermint-enriched wines had the highest antimicrobial activity. In the case of phytochemicals-enriched vodka, raspberry was most inhibitory. Results indicate that the synergistic contribution of phenolics and antioxidant activity may be more important for inhibition than any specific phenolic concentration. This research has implications for diet- based management of H. pylori.				
	Mahady, G. B.	Mahady, G. B.; Pendland, S. L.; Stoia, A.; Hamill, F. A.; Fabricant, D.; Dietz, B. M.; Chadwick, L. R., In vitro susceptibility of Helicobacter pylori to botanical extracts used traditionally for the treatment of gastrointestinal disorders. <i>Phytotherapy Research</i> 2005 , 19, (11), 988-991.		The gram-negative bacterium Helicobacter pylori (HP), identified in 1982, is now recognized as the primary etiological factor associated with the development of gastritis and peptic ulcer disease. In addition, HP infections are also associated with chronic gastritis, gastric carcinoma and primary gastric B-cell lymphoma. For centuries, herbals have been used in traditional medicine to treat a wide range of ailments, including gastrointestinal (GI) disorders such as dyspepsia, gastritis and peptic ulcer disease (PUD). However, the mechanism of action by which these botanicals exert their therapeutic effects has not been completely elucidated. As part of an ongoing screening program, the study assessed the in vitro susceptibility of 15 HP strains to botanical extracts, which have a history of traditional use in the treatment of GI disorders. Methanol extracts of Myristica fragrans (seed) had a MIC of 12.5 mu g/mL; Zingiber officinale (ginger rhizome/root) and Rosmarinus officinalis (rosemary leaf) had an MIC of 25 mu g/mL. Methanol extracts of botanicals with a MIC of 50 mu g/mL included Achillea millefolium, Foeniculum vulgare (seed), Passiflora incarnata (herb), Origanum majorana (herb) and a (1:1) combination of Curcuma longa (root) and ginger rhizome. Botanical extracts with a MIC of 100 mu g/mL included Carum carvi (seed), Elettaria cardamoinum (seed), Gentiana lutea (roots), Juniper communis (berry), Lavandula angustifolia (flowers), Melissa officinalis (leaves), Mentha piperita (leaves) and Pimpinella anisum (seed). Methanol extracts of Matricaria recutita (flowers) and Ginkgo biloba (leaves) had a MIC > 100 mu g/mL.				

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	Nohynek, L. J.	<p>Nohynek, L. J.; Alakomi, H. L.; Kahkonen, M. P.; Heinonen, M.; Helander, I. M.; Oksman-Caldentey, K. M.; Puupponen-Pimia, R. H.,</p> <p>Berry phenolics: antimicrobial properties and mechanisms of action against severe human pathogens.</p> <p><i>Nutr Cancer</i> 2006, 54, (1), 18-32.</p>	2006	<p>Antimicrobial activity and mechanisms of phenolic extracts of 12 Nordic berries were studied against selected human pathogenic microbes. The most sensitive bacteria on berry phenolics were <i>Helicobacter pylori</i> and <i>Bacillus cereus</i>. <i>Campylobacter jejuni</i> and <i>Candida albicans</i> were inhibited only with phenolic extracts of cloudberry, raspberry, and strawberry, which all were rich in ellagitannins. Cloudberry extract gave strong microbicidal effects on the basis of plate count with all studied strains. However, fluorescence staining of liquid cultures of virulent <i>Salmonella</i> showed viable cells not detectable by plate count adhering to cloudberry extract, whereas <i>Staphylococcus aureus</i> cells adhered to berry extracts were dead on the basis of their fluorescence and plate count. Phenolic extracts of cloudberry and raspberry disintegrated the outer membrane of examined <i>Salmonella</i> strains as indicated by 1-N-phenyl-naphthylamine (NPN) uptake increase and analysis of liberation of [¹⁴C]galactose- lipopolysaccharide. Gallic acid effectively permeabilized the tested <i>Salmonella</i> strains, and significant increase in the NPN uptake was recorded. The stability of berry phenolics and their antimicrobial activity in berries stored frozen for a year were examined using <i>Escherichia coli</i> and nonvirulent <i>Salmonella enterica</i> sv. Typhimurium. The amount of phenolic compounds decreased in all berries, but their antimicrobial activity was not influenced accordingly. Cloudberry, in particular, showed constantly strong antimicrobial activity during the storage.</p>				
	Puupponen-Pimia, R.	<p>Puupponen-Pimia, R.; Nohynek, L.; Alakomi, H. L.; Oksman-Caldentey, K. M.,</p> <p>Bioactive berry compounds-novel tools against human pathogens.</p> <p><i>Appl Microbiol Biotechnol</i> 2005, 67, (1), 8-18.</p>	2005	<p>Berry fruits are rich sources of bioactive compounds, such as phenolics and organic acids, which have antimicrobial activities against human pathogens. Among different berries and berry phenolics, cranberry, cloudberry, raspberry, strawberry and bilberry especially possess clear antimicrobial effects against, e.g. <i>Salmonella</i> and <i>Staphylococcus</i>. Complex phenolic polymers, like ellagitannins, are strong antibacterial agents present in cloudberry and raspberry. Several mechanisms of action in the growth inhibition of bacteria are involved, such as destabilisation of cytoplasmic membrane, permeabilisation of plasma membrane, inhibition of extracellular microbial enzymes, direct actions on microbial metabolism and deprivation of the substrates required for microbial growth. Antimicrobial activity of berries may also be related to antiadherence of bacteria to epithelial cells, which is a prerequisite for colonisation and infection of many pathogens. Antimicrobial berry compounds may have important applications in the future as natural antimicrobial agents for food industry as well as for medicine. Some of the novel approaches are discussed.</p>				

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	Puupponen-Pimia, R.	<p>Puupponen-Pimia, R.; Nohynek, L.; Alakomi, H. L.; Oksman-Caldentey, K. M.,</p> <p>The action of berry phenolics against human intestinal pathogens.</p> <p><i>Biofactors</i> 2005, 23, (4), 243-51.</p>	2005	<p>Phenolic compounds present in berries selectively inhibit the growth of human gastrointestinal pathogens. Especially cranberry, cloudberry, raspberry, strawberry and bilberry possess clear antimicrobial effects against e.g. salmonella and staphylococcus. Complex phenolic polymers, such as ellagitannins, are strong antibacterial agents present in cloudberry, raspberry and strawberry. Berry phenolics seem to affect the growth of different bacterial species with different mechanisms. Adherence of bacteria to epithelial surfaces is a prerequisite for colonization and infection of many pathogens. Antimicrobial activity of berries may also be related to anti-adherence activity of the berries. Utilization of enzymes in berry processing increases the amount of phenolics and antimicrobial activity of the berry products. Antimicrobial berry compounds are likely to have many important applications in the future as natural antimicrobial agents for food industry as well as for medicine.</p>				
	Puupponen-Pimia, R.	<p>Puupponen-Pimia, R.; Nohynek, L.; Hartmann-Schmidlin, S.; Kahkonen, M.; Heinonen, M.; Maatta-Riihinen, K.; Oksman-Caldentey, K. M.,</p> <p>Berry phenolics selectively inhibit the growth of intestinal pathogens.</p> <p><i>J Appl Microbiol</i> 2005, 98, (4), 991-1000.</p>	2005	<p>AIMS: To investigate the effects of berries and berry phenolics on pathogenic intestinal bacteria and to identify single phenolic compounds being responsible for antimicrobial activity. METHODS AND RESULTS: Antimicrobial activity of eight Nordic berries and their phenolic extracts and purified phenolic fractions were measured against eight selected human pathogens. Pathogenic bacterial strains, both Gram-positive and Gram-negative, were selectively inhibited by bioactive berry compounds. Cloudberry and raspberry were the best inhibitors, and Staphylococcus and Salmonella the most sensitive bacteria. Phenolic compounds, especially ellagitannins, were strong inhibitory compounds against Staphylococcus bacteria. Salmonella bacteria were only partly inhibited by the berry phenolics, and most of the inhibition seemed to originate from other compounds, such as organic acids. Listeria strains were not affected by berry compounds, with the exception of cranberry. Phenolic compounds affect the bacteria in different mechanisms. CONCLUSIONS: Berries and their phenolics selectively inhibit the growth of human pathogenic bacteria. SIGNIFICANCE AND IMPACT OF THE STUDY: Antimicrobial properties of berries could be utilized in functional foods. Furthermore these compounds would be of high interest for further evaluation of their properties as natural antimicrobial agents for food and pharmaceutical industry.</p>				

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	Puupponen-Pimia, R.	<p>Puupponen-Pimia, R.; Nohynek, L.; Meier, C.; Kahkonen, M.; Heinonen, M.; Hopia, A.; Oksman-Caldentey, K. M.,</p> <p>Antimicrobial properties of phenolic compounds from berries.</p> <p><i>J Appl Microbiol</i> 2001, 90, (4), 494-507.</p>	2001	<p>AIMS: To investigate the antimicrobial properties of phenolic compounds present in Finnish berries against probiotic bacteria and other intestinal bacteria, including pathogenic species. METHODS AND RESULTS: Antimicrobial activity of pure phenolic compounds representing flavonoids and phenolic acids, and eight extracts from common Finnish berries, was measured against selected Gram-positive and Gram-negative bacterial species, including probiotic bacteria and the intestinal pathogen Salmonella. Antimicrobial activity was screened by an agar diffusion method and bacterial growth was measured in liquid culture as a more accurate assay. Myricetin inhibited the growth of all lactic acid bacteria derived from the human gastrointestinal tract flora but it did not affect the Salmonella strain. In general, berry extracts inhibited the growth of Gram-negative but not Gram-positive bacteria. These variations may reflect differences in cell surface structures between Gram-negative and Gram-positive bacteria. Cloudberry, raspberry and strawberry extracts were strong inhibitors of Salmonella. Sea buckthorn berry and blackcurrant showed the least activity against Gram-negative bacteria. CONCLUSION: Different bacterial species exhibit different sensitivities towards phenolics. SIGNIFICANCE AND IMPACT OF THE STUDY: These properties can be utilized in functional food development and in food preservative purposes.</p>				
	Puupponen-Pimia, R.	<p>Puupponen-Pimia, R.; Aura, A. M.; Oksman-Caldentey, K. M.; Myllarinen, P.; Saarela, M.; Mattila-Sandholm, T.; Poutanen, K.,</p> <p>Development of functional ingredients for gut health.</p> <p><i>Trends in Food Science & Technology</i> 2002, 13, (1), 3-11.</p>	2002	<p>Microbial reactions in the gut have an essential role not only in gut health, but in general human health. The gut is the site of active fermentation of non-digestible diet components, as well as bioconversions and absorption of plant-derived compounds, such as phenolics. When developing nutritionally designed foods that promote health through gut microbial reactions, three different types of food ingredients can be used: living micro-organisms (probiotics), non-digestible carbohydrates (dietary fiber and prebiotics) and bioactive plant secondary metabolites (e.g. phenolics).</p>				

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	Rauha, J. P.	<p>Rauha, J. P.; Remes, S.; Heinonen, M.; Hopia, A.; Kahkonen, M.; Kujala, T.; Pihlaja, K.; Vuorela, H.; Vuorela, P.,</p> <p>Antimicrobial effects of Finnish plant extracts containing flavonoids and other phenolic compounds.</p> <p><i>Int J Food Microbiol</i> 2000, 56, (1), 3-12.</p>	2000	<p>Plant phenolics, especially dietary flavonoids, are currently of growing interest owing to their supposed functional properties in promoting human health. Antimicrobial screening of 13 phenolic substances and 29 extracts prepared from Finnish plant materials against selected microbes was conducted in this study. The tests were carried out using diffusion methods with four to nine microbial species (<i>Aspergillus niger</i>, <i>Bacillus subtilis</i>, <i>Candida albicans</i>, <i>Escherichia coli</i>, <i>Micrococcus luteus</i>, <i>Pseudomonas aeruginosa</i>, <i>Saccharomyces cerevisiae</i>, <i>Staphylococcus aureus</i> and <i>Staphylococcus epidermidis</i>). Flavone, quercetin and naringenin were effective in inhibiting the growth of the organisms. The most active plant extracts were purple loosestrife (<i>Lythrum salicaria</i> L.) against <i>Candida albicans</i>, meadowsweet (<i>Filipendula ulmaria</i> (L.) Maxim.), willow herb (<i>Epilobium angustifolium</i> L.), cloudberry (<i>Rubus chamaemorus</i> L.) and raspberry (<i>Rubus idaeus</i> L.) against bacteria, and white birch (<i>Betula pubescens</i> Ehrh.), pine (<i>Pinus sylvestris</i> L.) and potato (<i>Solanum tuberosum</i> L.) against gram-positive <i>Staphylococcus aureus</i>.</p>				
	Ruggiero, P.	<p>Ruggiero, P.; Tombola, F.; Rossi, G.; Pancotto, L.; Lauretti, L.; Del Giudice, G.; Zoratti, M.,</p> <p>Polyphenols reduce gastritis induced by <i>Helicobacter pylori</i> infection or VacA toxin administration in mice.</p> <p><i>Antimicrobial Agents and Chemotherapy</i> 2006, 50, (7), 2550-2552.</p>	2006	<p><i>Helicobacter pylori</i> colonizes the human gastric mucosa, causing inflammation that leads to atrophic gastritis, and it can cause peptic ulcer and gastric cancer. We show that polyphenol administration to mice experimentally infected by <i>H. pylori</i> or treated with VacA toxin can limit gastric epithelium damage, an effect that may be linked to VacA inhibition.</p>				

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	Ryan, T.	<p>Ryan, T.; Wilkinson, J. M.; Cavanagh, H. M.,</p> <p>Antibacterial activity of raspberry cordial in vitro.</p> <p><i>Res Vet Sci</i> 2001, 71, (3), 155-9.</p>	2001	<p>Raspberry juice cordial has a long anecdotal use in Australia for the prophylaxis and treatment of gastroenteritis in livestock, cage birds and humans. The antimicrobial properties of raspberry juice cordial, raspberry juice, raspberry leaf extract and a commercial brand of raspberry leaf tea were investigated against five human pathogenic bacteria and two fungi. Raspberry cordial and juice were found to significantly reduce the growth of several species of bacteria, including Salmonella, Shigella and E. coli, but demonstrated no antifungal activity. No antimicrobial activity was detected in the leaf extract or tea.</p>				
	Tombola, F.	<p>Tombola, F.; Campello, S.; De Luca, L.; Ruggiero, P.; Del Giudice, G.; Papini, E.; Zoratti, M.,</p> <p>Plant polyphenols inhibit VacA, a toxin secreted by the gastric pathogen <i>Helicobacter pylori</i>.</p> <p><i>Febs Letters</i> 2003, 543, (1-3), 184-189.</p>	2003	<p>VacA is a major virulence factor of the widespread stomach-dwelling bacterium <i>Helicobacter pylori</i>. It causes cell vacuolation and tissue damage by forming anion-selective, urea-permeable channels in plasma and endosomal membranes. We report that several flavone derivatives and other polyphenols present in vegetables and plants inhibit ion and urea conduction and cell vacuolation by VacA. Red wine and green tea, which contain many of the compounds in question, also potently inhibit the toxin. These observations suggest that polyphenols or poly-phenol derivatives may be useful in the prevention or cure of H. pylori-associated gastric diseases.</p>				

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	Tsou, M. F.	<p>Tsou, M. F.; Hung, C. F.; Lu, H. F.; Wu, L. T.; Chang, S. H.; Chang, H. L.; Chen, G. W.; Chung, J. G.,</p> <p>Effects of caffeic acid, chlorogenic acid and ferulic acid on growth and arylamine N-acetyltransferase activity in <i>Shigella sonnei</i> (group D).</p> <p><i>Microbios</i> 2000, 101, (398), 37-46.</p>	2000	<p>Arylamine N-acetyltransferase (NAT) activities with a-aminofluorene (2-AF) as substrates were determined in <i>Shigella sonnei</i> (group D) collected from patients with diarrhoeal disease. The NAT activity was determined using an acetyl CoA recycling assay and high pressure liquid chromatography. Inhibition of growth studies from <i>S. sonnei</i> (group D) demonstrated that caffeic acid (CA), chlorogenic acid (CGA) and ferulic acid (FA) elicited a dose-dependent bactericidal effect in <i>S. sonnei</i> (group D) cultures, i.e. the greater the concentration of CA, CGA and FA, the greater the inhibition of growth of <i>S. sonnei</i>(group D). Cytosols or suspensions of <i>S. sonnei</i>(group D) with and without selected concentrations of CA, CGA and FA co-treatment showed different percentages of 2-AF acetylation. The data indicated that there was reduced NAT activity associated with increased CA, CGA and FA in <i>Shigella dysenteriae</i> (group D) cytosols and intact cells. For the cytosol and intact bacteria examinations, the apparent values of K-m and V-max decreased after being co-treated with 400 mu M CA, CGA and FA. This report is the first demonstration of plant phenolic inhibition (CA, CGA and FA) of arylamine NAT activity and growth in the bacterium <i>S. sonnei</i> (group D).</p>	X			
	Vuorela, S.	<p>Vuorela, S.; Kreander, K.; Karonen, M.; Nieminen, R.; Hamalainen, M.; Galkin, A.; Laitinen, L.; Salminen, J. P.; Moilanen, E.; Pihlaja, K.; Vuorela, H.; Vuorela, P.; Heinonen, M.,</p> <p>Preclinical evaluation of rapeseed, raspberry, and pine bark phenolics for health related effects.</p> <p><i>J Agric Food Chem</i> 2005, 53, (15), 5922-31.</p>	2005	<p>Rapeseed, raspberry, and pine bark are promising bioactive sources of plant phenolics selected from among ca. 100 previously screened plant materials for in vitro preclinical evaluation of health related effects. Phenolic extracts and isolated fractions of the selected materials were investigated for antioxidant, antimicrobial, antiinflammatory, and antimutagenic properties as well as for cell permeability. It was shown that rapeseed and pine bark phenolics and raspberry anthocyanins were good or excellent antioxidants toward oxidation of phosphatidylcholine membrane (liposomes), rapeseed oil (crude) phenolics were effective radical scavengers (DPPH test), and both raspberry and pine bark phenolics inhibited LDL oxidation. Rapeseed oil phenolics, principally vinylsyringol, raspberry anthocyanins, and pinoresinol and matairesinol, the principal components of pine bark phenolic isolate, were effective against formation of the proinflammatory mediator, prostaglandin E(2). Raspberry ellagitannins inhibited the growth of <i>Proteus mirabilis</i> and <i>Klebsiella oxytoca</i>. Pine bark and rapeseed had minor effects on the permeability of model drugs in Caco-2 experiments. None of the tested extracts were mutagenic nor toxic to Caco-2 cells or macrophages. Thus, phenolic isolates from rapeseed, raspberry, and pine bark and are safe and bioactive for possible food applications including functional foods intended for health benefit.</p>	X			

Disease type/risk	First Author	Study Title Complete Citation	Date	Abstract				
	Yanagawa, Y.	<p>Yanagawa, Y.; Yamamoto, Y.; Hara, Y.; Shimamura, T.,</p> <p>A combination effect of epigallocatechin gallate, a major compound of green tea catechins, with antibiotics on Helicobacter pylori growth in vitro.</p> <p><i>Current Microbiology</i> 2003, 47, (3), 244-249.</p>	2003	<p>Since green tea catechins are known to have antimicrobial activity against a variety of microorganisms, their possible effects on Helicobacter pylori in combination with antibiotics were examined. Fifty-six clinical isolates of H. pylori, including 19 isolates highly resistant to metronidazole (MTZ) and/or clarithromycin (CLR), were used to determine in vitro sensitivity to tea catechins. The MIC₉₀ of both epigallocatechin gallate (EGCg) and epicatechin gallate (ECg) was 100 µg/ml. However, other tea catechins tested did not show any anti-H. pylori activity. Highly antibiotic-resistant clinical isolates showed a similar sensitivity to both EGCg and ECg. The kinetic study of antibacterial activity in liquid cultures revealed a relatively slow but strong activity on the growth of H. pylori. In combination with sub-MIC of amoxicillin (AMX), the antibacterial activity of AMX was significantly enhanced by the presence of EGCg. To estimate the general combination effect between EGCg and other antibiotics, such as MTZ and CLR, on the antibacterial activity against clinical isolates, the fraction inhibitory concentration (FIC) was determined by checkerboard study. The FIC indexes showed additive effects between EGCg and antibiotics tested. These results indicate that EGCg may be a valuable therapeutic agent against H. pylori infection.</p>				
	Yoda, Y.	<p>Yoda, Y.; Hu, Z. Q.; Zhao, W. H.; Shimamura, T.,</p> <p>Different susceptibilities of Staphylococcus and Gram-negative rods to epigallocatechin gallate.</p> <p><i>J Infect Chemother</i> 2004, 10, (1), 55-8.</p>	2004	<p>We examined the antibacterial effects of epigallocatechin gallate (EGCg, the main constituent of tea catechins) against various strains of Staphylococcus and Gram-negative rods. Compared to the minimum inhibitory concentrations (MICs) of EGCg against S. aureus, S. epidermidis, S. hominis, and S. haemolyticus (50-100 µg/ml), higher MICs (>or=800 µg/ml) were observed against Gram-negative rods, including Escherichia coli, Klebsiella pneumoniae, Salmonella typhi, Proteus mirabilis, Pseudomonas aeruginosa, and Serratia marcescens. And difference was observed between the binding abilities of EGCg with viable S. aureus and with E. coli. The bactericidal activity of EGCg for S. aureus was blocked dose-dependently by purified peptidoglycan but not by lipopolysaccharide or dextran. It was also found that peptone and protein, but not amino acids, in the culture medium greatly affected the antibacterial activity of EGCg. These results indicate that the structure of the bacterial cell wall and the different affinities of EGCg with the various cell wall components are responsible for the different susceptibilities of Staphylococcus and Gram-negative rods to EGCg.</p>				

Disease type/risk	First Author	Study Title Complete Citation	Date	Abstract	Human	Human cell	Animal	Animal cell
	Cavanagh, H. M.	Cavanagh, H. M.; Hipwell, M.; Wilkinson, J. M., Antibacterial activity of berry fruits used for culinary purposes. J Med Food 2003, 6, (1), 57-61.	2003	Increasing interest in the health benefits of various culinary berries has led to investigation of their antibacterial activity. Commercial raspberry, blackcurrant, cranberry, and blackberry cordials (100% fruit) as well as fresh berries were assessed for their ability to inhibit the growth of various bacteria and the yeast Candida albicans . Three of the six raspberry cordials and the blackcurrant cordial inhibited all 12 bacteria and C. albicans at dilutions of 1:5. Bacteria showed varying susceptibilities to the remaining cordials. All cordials inhibited the growth of Mycobacterium phlei. Of the fresh berries, mulberries and boysenberries did not inhibit any bacteria, and the remaining berries inhibited the growth of varying numbers of bacteria. There was no correlation between gram-positive or gram-negative bacterial status and susceptibility to the berries. It is suggested that the antibacterial activity of these berries may be of benefit as a means of water purification for suspect water supplies or to enhance shelf life when incorporated into food products .				