

# **Effects of Caffeine and Coffee on Cardiovascular Diseases Including High Blood Pressure, Arrhythmias & High Cholesterol**

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Heart disease is currently the number one cause of death for both men and women in the United States and in many other Western countries. Studies show that nine factors contribute to a significant percentage of heart attacks: smoking, abnormal lipoprotein ratios, high blood pressure, diabetes, abdominal obesity, low daily fruit and vegetable consumption, exercise and stress.<sup>1</sup> Caffeine and coffee consumption adversely affects a number of these factors which include cholesterol and other lipid levels, homocysteine, blood pressure, arrhythmias and stress levels, increasing the risk of heart disease.

## **Cholesterol:**

Cholesterol is an essential fat present in the diet and produced by the body. It is an important component and precursor to steroid hormones, including cortisol, epinephrine, estrogen, progesterone and testosterone. It is also useful in the synthesis of Vitamin D. Cholesterol is a sticky substance that can collect on the insides of arteries when in excess. Over time, this buildup can contribute to the hardening and narrowing of the arteries, reducing the flow of blood to the vital organs, brain and the heart itself. If the heart's blood supply is cut off, the result is a heart attack, or myocardial infarction. For this reason, high serum cholesterol is a primary factor contributing to the increased risk of heart attacks.<sup>2</sup> Both diet and genetics are important factors affecting cholesterol levels. Other lifestyle factors such as exercise, smoking, weight management and coffee drinking all influence cholesterol levels. Experimentally, coffee consumption significantly contributes to variation in levels of total cholesterol.<sup>3</sup>

## **Homocysteine:**

Cholesterol is not the only contributor to increased risk of heart attacks. High levels of homocysteine, an amino acid naturally present in the bloodstream, are associated with greater susceptibility of developing cardiovascular disease. Folic acid, vitamin B6 and B12 help break down excess homocysteine, but coffee has been implicated as a factor that raises plasma levels of this amino acid.<sup>4</sup>

## **Arrhythmias:**

Arrhythmias are changes from the normal pattern of electrical impulses in the heart, leading to abnormal rhythms. They can be so brief as to be barely noticeable, or their length can be significant. Arrhythmias disrupt the normal efficiency and effectiveness of the heartbeat. Heart rate rapidity, or tachycardia, is one of these disruptions; heart rate increases have been noted after coffee consumption.<sup>5</sup> In people who are susceptible to arrhythmias, the safety of coffee consumption is questionable.<sup>6</sup>

## **High Blood Pressure:**

Nearly one in three Americans have blood pressure that is higher than normal. Like cholesterol, high blood pressure is a silent disease which can create devastating complications, including hardening of the

arteries, kidney and heart problems, eye difficulties, aneurysms, heart attacks and strokes. High blood pressure is widely acknowledged to be one of the most significant risk factors for other cardiovascular diseases.<sup>7,8</sup> Lifestyle modifications, including modifications in diet and exercise, can make significant changes in blood pressure.<sup>9</sup> An important lifestyle adjustment involves coffee: studies show that when male regular coffee drinkers ceased drinking coffee, they experienced significant reductions in measured blood pressure.<sup>10</sup>

Of all the dietary habits that people find difficult to change, coffee drinking is one of the most challenging because it is so entrenched in cultural habits and caffeine addiction.<sup>11</sup> Withdrawal symptoms can involve painful headaches, nausea, vomiting, and loose stools, as well as depression, fatigue and anxiety.<sup>12,13</sup> People whose health problems would be ameliorated if they gave up coffee can improve their chance for successfully quitting coffee if they have both a satisfying alternative and a method to slowly decrease their caffeine intake to reduce withdrawal symptoms.

**The following characteristics of coffee have an adverse effect on the cardiovascular system:**

- **Coffee Raises Blood Pressure**
  - Acute caffeine intake has been shown to significantly increase central blood pressure as well as systolic and diastolic blood pressure while people are drinking coffee at work.<sup>14,15</sup> Drinking coffee, within three hours, causes a measurable rise in both systolic and diastolic blood pressure, and that effect can persist even into the following day.<sup>16, 17</sup> In people prone to hypertension, drinking coffee may be harmful.<sup>18</sup>
- **Coffee Drinking Is Associated with the Presence of Heart Rhythm Irregularities**
  - Coffee drinking is shown to be a predictor for the incidence of heart palpitations.<sup>19,20</sup> Due to its effects on raising cortisol, it increases heart rate. It is also implicated in the potential to produce cardiac arrhythmias.<sup>21</sup>
- **Coffee Increases Serum Cholesterol Levels**
  - Coffee drinking is linked to higher levels of serum cholesterol, with particularly high levels noted in people who drink boiled coffee or coffee processed at high temperatures (which includes espresso and espresso drinks).<sup>22, 23</sup> Other forms of coffee have also been shown to increase serum cholesterol levels including decaffeinated coffee, and studies show that replacement of regular coffee with decaffeinated coffee does not affect lipid levels.<sup>24,25,26</sup> Coffee drinking also demonstrably raised blood levels of low density lipoproteins in one lipid research study<sup>27</sup>, although results in other studies are inconclusive.
- **Coffee Drinking Raises Homocysteine Levels**
  - Increased plasma homocysteine increases a person's risk of suffering from a heart attack. Coffee drinking significantly increases homocysteine in the bloodstream, even more so than caffeine alone. The negative effect of coffee occurs with both caffeinated and decaffeinated coffee, and is noted within hours of coffee consumption.<sup>28</sup> Filtering the coffee did not affect homocysteine; unfiltered coffee as well as filtered coffee increased homocysteine levels, and did not change plasma concentrations of the B vitamins 6, 12 and folate.<sup>29, 30</sup>

- **Coffee Drinking Aggravates the Body’s Inflammation Processes**
  - Coffee drinkers exhibit increased presence of inflammatory markers, including significantly higher interleukin 6, C-reactive protein, serum amyloid-A, higher tumor necrosis factor alpha and higher white blood cell counts. This effect is observed at levels of 200 ml or 6 oz of coffee per day. It is suggested that this inflammatory response contributes to the negative effects of coffee on the cardiovascular system.<sup>31</sup>
  
- **Coffee Drinking is Associated with Increased Heart Attack Risk**
  - Independent of any other risk factors for heart disease, heavy coffee consumption has been shown to increase the short-term risk of heart attack, coronary death, or acute myocardial infarction.<sup>32</sup> A J-shaped association is suggested for the link between coffee drinking and risk of developing acute coronary disease: the more coffee consumed, the greater the risk.<sup>33</sup> A large scale epidemiological study looking at heart attacks and risk factors showed that coffee drinking increases the risk of succumbing to an acute myocardial infarction in people with diabetes.<sup>34</sup>
  
- **Caffeine Increases Blood Vessel Stiffness**
  - Caffeine has been demonstrated to negatively affect stiffness in the aorta as well as aortic pressure, in healthy adults as well as in adults with hypertension. Increased arterial stiffness is a contributing factor in coronary artery disease and is involved in the process of arteriosclerosis or hardening of the arteries.<sup>35,36,37</sup>
  
- **Caffeine Causes Mineral Excretion**
  - Coffee drinking is associated with decreased absorption of magnesium resulting in lower blood levels of magnesium.<sup>38</sup> Caffeine reduces the reabsorption of calcium and magnesium in the kidney, causing minerals to be excreted in the urine.<sup>39,40</sup> Magnesium is an essential mineral utilized in more than 300 enzymatic reactions and physiological processes including energy metabolism, effective utilization of glucose, hormonal balance and proper heart function.<sup>41</sup>
  - Epidemiological studies demonstrate that magnesium has a beneficial effect on blood pressure.<sup>42</sup> Deficiency of magnesium is associated with risk factors and complications of heart failure and adequate magnesium has a protective effect on the development of arrhythmias and cardiac abnormalities.<sup>43</sup>
  - Adequate levels of calcium and potassium are essential to cardiovascular health.<sup>44</sup> Low levels of potassium, in particular, have been linked to increased incidence of high blood pressure, and potassium supplementation is recommended as an intervention to help reduce high blood pressure.<sup>45</sup> Potassium intake has also been linked to incidence of strokes; specifically, low dietary potassium intake is associated with increased risk of developing a stroke.<sup>46</sup> Although caffeine and coffee intake does not directly influence potassium absorption, caffeine has a diuretic effect, and diuretics increases excess excretion of potassium as well as magnesium from the kidneys.<sup>47</sup>
  
- **Coffee Elevates Stress Hormones**
  - Caffeine in coffee elevates the stress hormones cortisol, epinephrine (also known as adrenaline) and norepinephrine.<sup>48</sup> This elevation is present even hours after consumption.<sup>49</sup> These hormones are responsible for increased heart rate and blood pressure, and a sense of “emergency alert”. Circulation of oxygen to the brain and extremities is decreased and the immune system is suppressed.

- The purpose of this “fight or flight” response is to provide the body with a temporary energy boost for intense physical activity. With today’s sedentary lifestyle, the continual state of increased stress resulting from caffeine consumption can chronically increase blood pressure and affect normal heart rate and rhythm.
- **Caffeine Interferes with GABA Metabolism**
  - GABA (Gamma-aminobutyric acid) is a neurotransmitter naturally produced in the brain and nervous system as well as the heart. It plays an important role in mood and stress management and influences heart rate and function.
  - Caffeine has been found to interfere with binding of GABA to GABA receptors, preventing it from performing its calming function.<sup>50</sup> GABA’s role in stress management is compromised in the presence of caffeine. Presence of psychological and social stress is associated with increased risk of suffering a heart attack.<sup>51</sup>

### **Recommendation:**

Individuals who suffer from or are susceptible to disorders of the cardiovascular system would do well to avoid coffee. Dietary changes that include weaning off of coffee and all other sources of caffeine can help relieve symptoms of these disorders as caffeine both increases the reactivity of the body to the stress of everyday life as well as increases blood pressure and heart rate.<sup>52</sup> Nutrition professionals can support cardiovascular patients by guiding them through the process of substituting a non-caffeinated, alkaline herbal coffee that brews and tastes just like coffee.

### **Kicking the Caffeine Habit:**

The social prevalence of coffee drinking and the addictive side effects of caffeine can cause problems with patient compliance. Caffeine-free herbal coffee marketed under the brand name of Teeccino<sup>®</sup> helps coffee drinkers replace their regular or decaf coffee with a satisfying alternative. Coffee drinkers need a dark, full-bodied, robust brew to help satisfy their coffee craving. Teeccino satisfies the 4 needs coffee drinkers require in a coffee alternative:

- 1) Teeccino brews just like coffee, allowing coffee drinkers to keep their same brewing ritual.
- 2) It has a delicious, deep roasted flavor that is very coffee-like.
- 3) It wafts an enticing aroma.
- 4) People experience a natural energy boost from nutritious Teeccino.

**Teecino offers the following health benefits to people suffering from heart conditions:**

<u><b>Beneficial Features of Teecino</b></u>	<u><b>Teecino Ingredients:</b></u> <small>54,55,56,57,58,59,60,61,62,63</small>
<ul style="list-style-type: none"> <li>▪ Inulin fiber from chicory                             <ul style="list-style-type: none"> <li>• Unlike coffee, Teecino has nutritional value, including soluble inulin fiber, a pre-biotic that helps support a healthy population of beneficial microflora.</li> <li>• Inulin improves mineral absorption</li> </ul> </li> <li>▪ 65 mg of Potassium                             <ul style="list-style-type: none"> <li>• Teecino is a source of potassium. In liquid form, potassium is easily absorbed to help relieve muscle fatigue, maintain normal heart rhythm and blood pressure, and help prevent strokes.</li> </ul> </li> <li>▪ Alkaline – helps reduce acidity                             <ul style="list-style-type: none"> <li>• As opposed to acidic coffee, Teecino is alkaline, which reduces stomach acidity.</li> </ul> </li> <li>▪ Gluten Free                             <ul style="list-style-type: none"> <li>• Gluten does not extract into boiling water. Tests show Teecino is gluten free although it contains barley.</li> </ul> </li> <li>▪ Naturally Caffeine-free                             <ul style="list-style-type: none"> <li>• No chemical processing like decaffeinated coffee.</li> </ul> </li> </ul>	<ul style="list-style-type: none"> <li>▪ Carob                             <ul style="list-style-type: none"> <li>• Consumption of water-soluble fiber from carob lowers elevated blood cholesterol in healthy people.</li> </ul> </li> <li>▪ Barley                             <ul style="list-style-type: none"> <li>• Contains niacin, a B vitamin important for healthy heart function.</li> <li>• Shown to have a beneficial effect on lipid metabolism.</li> </ul> </li> <li>▪ Almond                             <ul style="list-style-type: none"> <li>• Has a beneficial effect on serum lipid levels.</li> </ul> </li> <li>▪ Figs                             <ul style="list-style-type: none"> <li>• Contain polyphenols, plant compounds that act as antioxidants.</li> <li>• A good source of potassium.</li> </ul> </li> <li>▪ Dates                             <ul style="list-style-type: none"> <li>• Contains potassium and magnesium, important for maintaining heart rhythm.</li> </ul> </li> <li>▪ Chicory root                             <ul style="list-style-type: none"> <li>• Has been shown to improve mineral absorption, including magnesium.</li> </ul> </li> </ul>

**The Pain-free Way to Wean off of Coffee**

Start by mixing normal coffee 3/4 to 1/4 Teecino Herbal Coffee. Gradually reduce the percentage of coffee over a two to three week period until only 100% Teecino Herbal Coffee is brewed. Gradual reduction of caffeine is recommended.<sup>53</sup> Side effects such as headaches, fatigue, and brain foginess can be avoided as the body gradually adjusts to less reliance on stimulants.

**Example:** Use the following proportions if you make a 10-cup pot of coffee daily:

<b>DAY</b>	<b>Regular Coffee</b>	<b>Teecino</b>
<b>Day 1-3:</b>	4 tablespoons	1 tablespoon
<b>Day 4-6:</b>	3 tablespoons	2 tablespoons
<b>Day 7-9:</b>	2 tablespoons	3 tablespoons
<b>Day 10:</b>	1 1/2 tablespoons	3 1/2 tablespoons
<b>Day 11:</b>	1 tablespoon	4 tablespoons
<b>Day 12-13:</b>	1/2 tablespoon	4 1/2 tablespoons
<b>Day 14:</b>	0	5 tablespoons

## References

- <sup>1</sup> Yusuf, S., Hawken, S., Ounpuu, S., Dans, T., Avezum, A., Lanas, F., McQueen, M., Budaj, A., Pais, P., Varigos, J., Lisheng, L. and the INTERHEART Study Investigators. 2004. Effect of potentially modifiable risk factors associated with myocardial infarction in 52 countries (the INTERHEART study): case-control study. *Lancet*. 364(9438):937-52.
- <sup>2</sup> US Department of Health and Human Services, Public Health Service, National Institutes of Health, NIH Publication Number 01-3290. Copyright 2001.
- <sup>3</sup> Thelle, D.S., Arnesen, E. and Forde, O.H. 1983. The TromsÅ, heart study. Does coffee raise serum cholesterol? *New England Journal of Medicine*. 308(24):1454-7.
- <sup>4</sup> Olthof, M.R., Hollman, P.C., Zock, P.L. and Katan, M.B. 2001. Consumption of high doses of chlorogenic acid, present in coffee, or of black tea increases plasma total homocysteine concentrations in humans. *American Journal of Clinical Nutrition*. 73(3):532-8.
- <sup>5</sup> Green, P.J. and Suls, J. 1996. The effects of caffeine on ambulatory blood pressure, heart rate, and mood in coffee drinkers. *Journal of Behavioral Medicine*. 19(2):111-28.
- <sup>6</sup> Frishman, W.H., Del Vecchio, A., Sanal, S. and Ismail, A. 2003. Cardiovascular manifestations of substance abuse: part 2: alcohol, amphetamines, heroin, cannabis, and caffeine. *Heart Disease*. 5(4):253-71.
- <sup>7</sup> National Heart, Lung and Blood Institute, High Blood Pressure. Copyright 2004.
- <sup>8</sup> Miura, K. 2004. Strategies for prevention and management of hypertension throughout life. *Journal of Epidemiology*. 14(4):112-7.
- <sup>9</sup> Miller, E.R. 3rd, Erlinger, T.P., Young, D.R., Jehn, M., Charlestonm J., Rhodes, D., Wasan, S.K. and Appel, L.J. 2002. Results of the Diet, Exercise, and Weight Loss Intervention Trial (DEW-IT). *Hypertension*. 2002;40:612.
- <sup>10</sup> Superko, H.R., Myll, J., DiRicco, C., Williams, P.T., Bortz, W.M. and Wood, P.D. 1994. Effects of cessation of caffeinated-coffee consumption on ambulatory and resting blood pressure in men. *American Journal of Cardiology*. 73(11):780-4.
- <sup>11</sup> Braun, S. Buzz: The Science and Lore of Alcohol and Caffeine. Copyright 1996.
- <sup>12</sup> Strain, E.C., G.K. Mumford, K. Silverman, and R.R. Griffiths. 1994. Caffeine dependence syndrome. *Journal of the American Medical Association*, 272:1043-1048.
- <sup>13</sup> Silverman, K., Evans, S.M., Strain, E.C. and Griffiths, R.R. 1992 Withdrawal Syndrome after the Double-Blind Cessation of Caffeine Consumption. *The New England Journal of Medicine*. 16(327): 1109-14.
- <sup>14</sup> Waring, W.S., Goudsmit, J., Marwick, J., Webb, D.J. and Maxwell, S.R.J. 2003. Acute caffeine intake influences central more than peripheral blood pressure in young adults. *American Journal of Hypertension*. 16(11): 919-24.
- <sup>15</sup> Jeong, D.U. and Dimsdale, J.E. 1990. The effects of caffeine on blood pressure in the work environment. *American Journal of Hypertension*. 3(10): 749-53.
- <sup>16</sup> Shirlow, M.J., Berry, G. and Stokes, G. 1988. Caffeine consumption and blood pressure: an epidemiological study. *International Journal of Epidemiology*. 17(1):90-7.
- <sup>17</sup> James, J.E. 1994. Chronic effects of habitual caffeine consumption on laboratory and ambulatory blood pressure levels. *Journal of Cardiovascular Risk*. 1(2): 159-64.
- <sup>18</sup> Nurminen, M.L., Niittynen, L., Korpela, R. and Vapaatalo, H. 1999. Coffee, caffeine and blood pressure: a critical review. *European Journal of Clinical Nutrition*. 53(11):831-9.

- 
- <sup>19</sup> Lochen ML, Rasmussen K. 1996. Palpitations and lifestyle: impact of depression and self-rated health. The Nordland Health Study. Scandinavian journal of social medicine. 24(2):140-4.
- <sup>20</sup> Shirlow, M.J. and Mathers, C.D. 1985. A study of caffeine consumption and symptoms: indigestion, palpitations, tremor, headache and insomnia. International Journal of Epidemiology. 14(2):239-48.
- <sup>21</sup> Rosmarin PC. 1989. Coffee and coronary heart disease: a review. Progress in Cardiovascular Diseases. 32(3):239-45.
- <sup>22</sup> Lindahl, B., Johansson, I., Huhtasaari, F., Hallmans, G. and Asplund, K. 1991. Coffee drinking and blood cholesterol--effects of brewing method, food intake and life style. Journal of Internal Medicine. 230(4):299-305.
- <sup>23</sup> Salvaggio, A., Periti, M., Miano, L., Quaglia, G. and Marzorati, D. 1991. Coffee and cholesterol, an Italian study. American Journal of Epidemiology. 134(2):149-56.
- <sup>24</sup> Aro A, Pietinen P, Uusitalo U, Tuomilehto J. 1989. Coffee and tea consumption, dietary fat intake and serum cholesterol concentration of Finnish men and women. Journal of Internal Medicine. 226(6):127-32.
- <sup>25</sup> Green MS, Harari G. 1992. Association of serum lipoproteins and health-related habits with coffee and tea consumption in free-living subjects examined in the Israeli CORDIS Study. Preventive medicine. 21(4):532-45.
- <sup>26</sup> van Dusseldorp, M., Katan, M.B. and Demacker, P.N. 1990. Effect of decaffeinated versus regular coffee on serum lipoproteins. A 12-week double-blind trial. American Journal of Epidemiology. 132(1):33-40.
- <sup>27</sup> Kark JD, Friedlander Y, Kaufmann NA, Stein Y. 1985. Coffee, tea, and plasma cholesterol: the Jerusalem Lipid Research Clinic prevalence study. British Medical Journal (Clinical Research Edition). 291(6497):699-704.
- <sup>28</sup> Verhoef, P., Pasman, W.J., Van Vliet, T., Urgert, R. and Katan, M.B. 2002. Contribution of caffeine to the homocysteine-raising effect of coffee: a randomized controlled trial in humans. American Journal of Clinical Nutrition. 76(6):1244-8.
- <sup>29</sup> Urgert, R., van Vliet, T., Zock, P.L. and Katan, M.B. 2000. Heavy coffee consumption and plasma homocysteine: a randomized controlled trial in healthy volunteers. American Journal of Clinical Nutrition. 72(5):1107-10.
- <sup>30</sup> Grubben, M.J., Boers, G.H., Blom, H.J., Broekhuizen, R., de Jong, R., van Rijt, L., de Ruijter, E., Swinkels, D.W., Nagengast, F.M. and Katan, M.B. 2000. Unfiltered coffee increases plasma homocysteine concentrations in healthy volunteers: a randomized trial. American Journal of Clinical Nutrition. 71(2):480-4.
- <sup>31</sup> Zampelas, A., Panagiotakos, D.B., Pitsavos, C., Chrysohoou, C. and Stefanadis, C. 2004. Associations between coffee consumption and inflammatory markers in healthy persons: the ATTICA study. American Journal of Clinical Nutrition. 80(4):862-7.
- <sup>32</sup> Happonen P, Voutilainen S, Salonen JT. 2004. Coffee drinking is dose-dependently related to the risk of acute coronary events in middle-aged men. Journal of Nutrition. 134(9):2381-6.
- <sup>33</sup> Panagiotakos, D.B., Pitsavos, C., Chrysohoou, C., Kokkinos, P., Toutouzas, P. and Stefanadis, C. 2003. The J-shaped effect of coffee consumption on the risk of developing acute coronary syndromes: the CARDIO2000 case-control study. Journal of Nutrition. 133(10):3228-32.
- <sup>34</sup> Tavani, A., Bertuzzi, M. Gallus, S., Negri, E. and La Vecchia, C. 2002. Diabetes mellitus as a contributor the risk of acute myocardial infarction. Journal of Clinical Epidemiology. 55(11):1082-7.
- <sup>35</sup> Vlachopoulos C, Hirata K, Stefanadis C, Toutouzas P, O'Rourke MF. 2003. Caffeine increases aortic stiffness in hypertensive patients. American Journal of Hypertension. 16(1):63-6.

- 
- <sup>36</sup> Vlachopoulos C, Hirata K, O'Rourke MF. 2003. Effect of caffeine on aortic elastic properties and wave reflection. Journal of Hypertension. 21(3):563-70.
- <sup>37</sup> Mahmud A, Feely J. 2001. Acute effect of caffeine on arterial stiffness and aortic pressure waveform. Hypertension. 38(2):227-31.
- <sup>38</sup> Johnson, S. 2001. The multifaceted and widespread pathology of magnesium deficiency. Medical Hypothesis. 56(2):163-70.
- <sup>39</sup> Bergman, E.A., Massey, L.K., Wise, K.J. and Sherrard, D.J. 1990. Effects of dietary caffeine on renal handling of minerals in adult women. Life Sciences. 47(6):557-64.
- <sup>40</sup> Kynast-Gales, S.A. and Massey, L.K. 1994. Effect of caffeine on circadian excretion of urinary calcium and magnesium. Journal of the American College of Nutrition. 13(5):467-72.
- <sup>41</sup> Gums, J. 2004. Magnesium in cardiovascular and other disorders. American Journal of Health System Pharmacy. 61(15):1569-76.
- <sup>42</sup> Yamori, Y., Nara, Y., Mizushima, S., Sawamura, M. and Horie, R. 1994. Nutritional factors for stroke and major cardiovascular diseases: international epidemiological comparison of dietary prevention. Health Report. 6(1):22-7.
- <sup>43</sup> Douban, S., Brodsky, M.A., Whang, D.D. and Whang, R. 1996. Significance of magnesium in congestive heart failure. The American Heart Journal, 132(3):664-71.
- <sup>44</sup> McCarron, D.A. and Reusser ME. 2001. Are low intakes of calcium and potassium important causes of cardiovascular disease? American Journal of Hypertension. 14(6 Pt 2): 206S-212S.
- <sup>45</sup> Whelton, P.K., He, J., Cutler, J.A., Brancati, F.L., Appel, L.J., Follmann, D. and Klag, M.J. 1997. Effects of oral potassium on blood pressure. Meta-analysis of randomized controlled clinical trials. JAMA. 277(20):1624-32.
- <sup>46</sup> Bazzano, L.A., He, J., Ogden, L.G., Loria, C., Vupputuri, S., Myers, L. and Whelton, P.K. 2001. Dietary potassium intake and risk of stroke in US men and women: National Health and Nutrition Examination Survey I epidemiologic follow-up study. Stroke, 32(7):1473-80.
- <sup>47</sup> Dyckner, T. and Wester, P.O. 1987. Potassium/magnesium depletion in patients with cardiovascular disease. The American Journal of Medicine. 82(3A):11-7.
- <sup>48</sup> al'Absi, M., Lovallo, W.R., McKey, B., Sung, B.H., Whitsett, T.L. and Wilson, M.F. 1998. Hypothalamic-pituitary-adrenocortical responses to psychological stress and caffeine in men at high and low risk for hypertension. Psychosomatic Medicine, 60(4):521-7.
- <sup>49</sup> Lovallo, W.R., Al'Absi, M., Blick, K., Whitsett, T.L. and Wilson, M.F. 1996. Stress-like adrenocorticotropin responses to caffeine in young healthy men. Pharmacology, Biochemistry and Behavior. 55(3):365-9.
- <sup>50</sup> Roca, D.J., G.D. Schiller, and D.H. Farb. 1988. Chronic Caffeine or Theophylline Exposure Reduces Gamma-aminobutyric Acid/Benzodiazepine Receptor Site Interactions. Molecular Pharmacology, May;33(5):481-85.
- <sup>51</sup> Rosengren A, Hawken S, Ounpuu S, Sliwa K, Zubaid M, Almahmeed WA, Blackett KN, Sitthi-amorn C, Sato H, Yusuf S; INTERHEART investigators. 2004. Association of psychosocial risk factors with risk of acute myocardial infarction in 11119 cases and 13648 controls from 52 countries (the INTERHEART study): case-control study. Lancet. 364(9438):953-62.
- <sup>52</sup> Lane, J.D., Pieper, C.F., Phillips-Bute, B.G., Bryant, J.E. and Kuhn, C.M. 2002. Caffeine affects cardiovascular and neuroendocrine activation at work and home. Psychosomatic Medicine. 64(4):595-603.
- <sup>53</sup> Silverman, K., Evans, S.M., Strain, E.C. and Griffiths, R.R. 1992 Withdrawal Syndrome after the Double-Blind Cessation of Caffeine Consumption. The New England Journal of Medicine. 16(327): 1109-14.

- 
- <sup>54</sup> Physicians Desk Reference for Herbal Medicines. Second Edition. Copyright 2000.
- <sup>55</sup> Roehl, E. Whole Foods Facts: The Complete Reference Guide. Copyright 1996.
- <sup>56</sup> Roberfroid MB. 1997. Health benefits of non-digestible oligosaccharides. Advances in experimental medicine and biology. 427: 211-9.
- <sup>57</sup> Biddle, W. 2003. Gastroesophageal reflux disease: current treatment approaches. Gastroenterology nursing : the official journal of the Society of Gastroenterology Nurses and Associates. 26(6):228-36.
- <sup>58</sup> Kim M, Shin HK. 1996. The water-soluble extract of chicory reduces glucose uptake from the perfused jejunum in rats. Journal of Nutrition. 126(9):2236-42.
- <sup>59</sup> Al-Shahib W, Marshall RJ. (2003) The fruit of the date palm: its possible use as the best food for the future? International Journal of Food Sciences and Nutrition. 54(4):247-59.
- <sup>60</sup> Gums JG. 2004. Magnesium in cardiovascular and other disorders. American journal of health-system pharmacy : AJHP : official journal of the American Society of Health-System Pharmacists. 61(15):1569-76.
- <sup>61</sup> Li, J., Kaneko, T., Qin, L.Q., Wang, J. and Wang, Y. 2003. Effects of barley intake on glucose tolerance, lipid metabolism, and bowel function in women. Nutrition. 19(11-12). 926-9.
- <sup>62</sup> Lovejoy, J.C., Most, M.M., Lefevre, M., Greenway, F.L. and Rood, J.C. 2002. Effect of diets enriched in almonds on insulin action and serum lipids in adults with normal glucose tolerance or type 2 diabetes. 76(5):1000-6.
- <sup>63</sup> Haskell, W.L., Spiller, G.A., Jensen, C.D., Ellis, B.K. and Gates, J.E. 1992. Role of water-soluble dietary fiber in the management of elevated plasma cholesterol in healthy subjects. American Journal of Cardiology. 69(5):433-9.