

## **Rationale for a Novel Nutraceutical Complex: Potassium Taurine Bicarbonate**

Mark F. McCarty, Natural Alternatives International,  
1185 Linda Vista Dr., San Marcos, CA 92078

### **Abstract**

Potassium taurine bicarbonate (PTB), an equimolar blend of potassium bicarbonate and taurine, provides a convenient and feasible means of delivering physiologically significant doses of potassium, taurine, and organic base when dissolved in water (“K-water”). This brief essay reviews the versatile and complementary health benefits that likely would accrue in individuals making regular use of K-water; in particular, an adequate intake of PTB could be expected to aid blood pressure control, lessen risk for atherosclerosis and its thromboembolic complications (particularly stroke), promote maintenance of bone density, help to prevent calcium renal stones, and possibly reduce risk for weight gain and diabetes.

### **Potassium Taurine Bicarbonate**

Potassium taurine bicarbonate (PTB) is a mineral complex that provides three dietary compounds that are suboptimally supplied by most modern diets: potassium, taurine, and base (as bicarbonate ion). It consists of an equimolar blend of potassium bicarbonate and taurine. When added to water, these compounds form a soluble ionic complex which has a slightly lower pH than that of potassium bicarbonate alone, and that is less prone than potassium bicarbonate to evolve carbon dioxide when small amounts of acid are added to the solution. (J. Zielinski, personal communication). Most likely, this reflects formation of an ionic complex in which potassium is attracted to the negatively charged sulfonic acid group of the taurine zwitterion, the bicarbonate ion is attracted to the positively charged amine group of taurine, and potassium and bicarbonate are attracted to each other. When incorporated in this complex, bicarbonate is less prone to extract protons from solution, thus explaining the pH characteristics of this complex.

When added to a liter of water, 60 mmol of PTB (13.5 g) provides 2.35 g potassium and 7.5 g taurine. The first sip of the resulting solution can have a mildly acrid flavor, but this flavor rapidly down-regulates such that there is very little detectable flavor in subsequent sips: in other words, it tastes like ordinary water. Thus, an aqueous solution of PTB – designated “K-water” – represents a convenient, feasible means of administering PTB. K-water can be blended with neutral or mildly alkaline ingredients to produce soft drinks, teas, and modified juices. Acidic additives generate free potassium ion, ruining the flavor; thus, K-water cannot be used to make coffee.

Potassium, taurine, and organic base are each distinguished by the fact that daily multi-gram doses are required to provide optimal physiological benefit. Furthermore, consumption of potassium in a concentrated form – as in tablets or capsules – risks injury

to the gastrointestinal mucosa. For these reasons, K-water represents a practical, convenient means of achieving physiologically significant intakes of each of the constituents of PTB.

Although clinical research with PTB remains to be accomplished, the health benefits conferred by this complex can likely be inferred from the known properties of its individual constituents:

### **Potassium**

Owing to the promiscuous use of refined grains, sugars, oils, and fatty animal products in modern diets, as well as the relative paucity of fruits and vegetables in many of these diets, potassium intakes today are far lower than they were in Paleolithic hunter-gatherers who consumed no refined foods but had exceptionally high intakes of fruits and vegetables.<sup>1</sup> There is considerable evidence that increased intakes of potassium can lower elevated blood pressure to a worthwhile extent, especially in the context of high salt diets.<sup>2</sup> This effect has been demonstrated in numerous controlled studies, and validated in meta-analyses;<sup>3;4</sup> most of these studies assessed supplemental potassium intakes of 60 mmol daily or higher. Furthermore, epidemiology suggests that, independent of any impact on blood pressure, higher potassium intakes decrease risk for myocardial infarction and, more substantially, stroke.<sup>5-11</sup> A portion of this protection reflects the fact that potassium has a natriuretic effect, thus offsetting some of the adverse health effects of salty diets.<sup>12-15</sup> In addition, the modest increase in serum potassium associated with potassium-rich diets acts to increase the membrane potential of vascular endothelium – thereby boosting activity of nitric oxide synthase while inhibiting that of the superoxide-generating NADPH oxidase.<sup>16-18</sup>

Salt promotes loss of bone mineral by inducing renal calcium loss (calciuria); the natriuretic effect of potassium tends to counteract this effect, thus helping to preserve bone density.<sup>19-24</sup> Hence, improved potassium nutrition can be expected to benefit the healthful structure and function of the vascular system as well as of bone. And it is not unlikely that potassium, owing to its natriuretic activity, has a favorable impact on other pathologies linked to high-salt diets, such as cardiac hypertrophy and asthma.<sup>25</sup>

### **Bicarbonate**

Owing to a high intake of proteins rich in sulfhydryl amino acids – which generate sulfuric acid when catabolized in vivo – modern diets tend to generate metabolic acidosis, which is compensated in part by dissolution of bone mineral; bone phosphate acts as a buffer.<sup>1;26-28</sup> This problem is exacerbated by the fact that many diets are relatively low in organic anions – associated primarily with potassium, calcium, and magnesium in natural foods, especially fruits and vegetables – that are can be metabolized in vivo to yield bicarbonate ion, an effective buffer for metabolic acidosis that spares bone mineral.<sup>1</sup> In cross-sectional studies, high consumption of fruits and vegetables – rich in organic potassium salts – has been linked to increased bone density in men and women.<sup>29-31</sup> Researchers have repeatedly demonstrated that ample supplemental intakes (usually 60 mmol daily or more) of potassium bicarbonate or potassium citrate can substantially slow

bone turnover and renal calcium loss in postmenopausal women, in all likelihood postponing the onset of osteoporosis and fracture.<sup>32-36</sup> The bicarbonate component of PTB is intended to provide this important benefit. The ability of potassium bicarbonate to decrease calciuria – which in part reflects the natriuretic action of the potassium – should have the added benefit of decreasing risk for calcium-based renal stones.<sup>34;37</sup>

A further potential drawback of the mild metabolic acidosis associated with protein-rich modern diets is that it promotes increased cortisol production – a “side effect” of an up-regulation of adrenocortical activity that functions to boost the efficiency of renal acid secretion by stimulating renal production of ammonia.<sup>38-41</sup> Increased cortisol production would be expected to increase risk for visceral obesity and insulin resistance syndrome. Perhaps this explains why increased dietary potassium – typically associated with organic anions in foods – has been linked to decreased risk for diabetes in prospective epidemiology.<sup>42;43</sup> Furthermore, the modest improvement in nitrogen balance observed during supplementation with potassium bicarbonate<sup>44</sup> possibly reflects decreased cortisol production, as well as a decrease in renal ammonia production. The alkalinizing impact of PTB can be expected to have a down-regulatory impact on cortisol secretion in those eating acid-forming diets.<sup>45</sup>

## **Taurine**

This neglected nutrient appears to have extraordinarily versatile potential for promoting vascular health when administered in multi-gram daily doses. Clinical studies have evaluated taurine supplementation in doses up to 6 g daily, and no hint of adverse effects has emerged in these studies, presumably because excess taurine is rapidly cleared by the kidneys. Moreover, the body pool of taurine is very high, inasmuch as muscle, the heart, neurons, phagocytes and various other tissues contain taurine in millimolar concentrations. Although taurine contains a sulfonic acid group, it is not metabolized to yield sulfonic acid, and thus does not promote calciuria.<sup>46</sup> The potential vascular benefits of high-dose taurine include: a platelet-stabilizing effect that is complementary to that of aspirin;<sup>47-49</sup> an anti-hypertensive effect that, at least in part, appears to reflect a moderate down-regulation of elevated sympathetic activity;<sup>50-57</sup> an anti-inflammatory anti-atherosclerotic effect (independent of modulation of serum lipids) demonstrated in rodent models of atherogenesis;<sup>58-60</sup> a positive inotropic effect in patients with congestive heart failure that does not appear to entail the increased risk for arrhythmia associated with digitalis therapy;<sup>61-63</sup> and a possible beneficial impact on the symptoms of cardiac angina and intermittent claudication, as suggested by Italian clinical reports published in the 1960s.<sup>64</sup>

The anti-atherogenic impact of taurine in rodents possibly reflects taurine’s ability to detoxify hypochlorous acid,<sup>65</sup> a potent oxidant that is the chief product of myeloperoxidase, an enzyme active in intimal macrophages. A high-expression polymorphism of myeloperoxidase has been linked to increased risk for coronary atherosclerosis in recent epidemiology,<sup>66</sup> and hypochlorite-modified proteins are prominent in human atheromatous lesions.<sup>67;68</sup> Hypochlorous acid is capable of oxidizing LDL particles to high-uptake forms;<sup>69-71</sup> the fact that taurine is protective in certain

rodent models of atherogenesis that fail to respond to vitamin E,<sup>72-74</sup> suggests that hypochlorous acid may play a more important role than hydroxyl radical in promoting pathogenic modifications of LDL *in vivo*. (This in turn might explain why supplemental vitamin E has failed to confer cardiovascular protection in prospective supplementation trials).<sup>75;76</sup> It has also been suggested that taurine's ability to quench hypochlorous acid might promote plaque stabilization, since hypochlorous acid functions to activate metalloproteases.<sup>77;78</sup> Furthermore, the product of taurine's interaction with hypochlorous acid, taurochloramine, can suppress activation of NF-kappaB<sup>79;80</sup> - an anti-inflammatory effect which would antagonize atherogenesis. The possible utility of taurine in other inflammatory disorders merits further investigation.

In diabetic rodents, taurine-enriched diets have been shown to ameliorate neuropathy and nephropathy.<sup>81-83</sup> There is a small amount of suggestive evidence that taurine may have a favorable impact on bone health; it impedes the multiplication of osteoclasts *in vitro*, and, when administered orally to hamsters, is reported to slow loss of periodontal bone in a model of periodontal bone loss.<sup>84</sup> Taurine may also have neuroprotective potential, helping neurons to survive the excitotoxicity that accompanies ischemia and plays a pathogenic role in many neurodegenerative disorders. Under conditions that give rise to excitotoxicity, taurine is released from neurons into the extracellular space, where it can act as an agonist for GABA(A) receptors that promote neuron hyperpolarization by boosting chloride conductance; this in turn tends to protect neurons by moderating the excessive calcium influx that characterizes excitotoxicity.<sup>85-90</sup> Since supplemental taurine can increase brain taurine levels,<sup>91</sup> it can be expected to potentiate this protective feedback mechanism. Supplemental taurine has in fact shown brain-protective activity in some<sup>92;93</sup> but not all<sup>94</sup> rodent models of excitotoxicity.

In light of the fact that high intakes of taurine may be required to optimize its health benefits, a solution of PTB represents a very practical means of achieving this high intake. Supplemental taurine may be of particular value to vegetarians, whose diets are virtually devoid of this nutrient; suboptimal taurine status may account for the platelet hyperaggregability that has been observed in vegetarians.<sup>95</sup>

### **Clinical Prospects**

Drinking up to a liter of K-water daily, providing 60 mmol of PTB, can thus be expected to help preserve vascular health by a range of complementary mechanisms, help maintain bone density, prevent renal stones, and possibly reduce risk for weight gain and insulin resistance. Its practicality is enhanced by the fact that both potassium bicarbonate and taurine are quite inexpensive. It is contraindicated in patients experiencing renal failure, taking potassium sparing diuretics, or with other medical conditions in which increased potassium intakes would be considered inappropriate. Clinical studies examining the impact of K-water consumption in various clinical conditions – most notably essential hypertension – appear to be warranted.

## Disclosure

The author owns stock in the company – Nutrition Company of America - to which the patent rights have been assigned.

## References

1. Frassetto L, Morris RCJ, Sellmeyer DE, Todd K, Sebastian A. Diet, evolution and aging--the pathophysiologic effects of the post-agricultural inversion of the potassium-to-sodium and base-to-chloride ratios in the human diet. *Eur J Nutr JID* - 100888704 2001;40:200-13.
2. Smith SJ, Markandu ND, Sagnella GA, MacGregor GA. Moderate potassium chloride supplementation in essential hypertension: is it additive to moderate sodium restriction? *Br Med J (Clin Res Ed)* 1985;290:110-13.
3. Cappuccio FP, MacGregor GA. Does potassium supplementation lower blood pressure? A meta-analysis of published trials. *J Hypertens JID* - 8306882 1991;9:465-73.
4. Whelton PK, He J, Cutler JA, Brancati FL, Appel LJ, Follmann D *et al.* Effects of oral potassium on blood pressure. Meta-analysis of randomized controlled clinical trials. *JAMA JID* - 7501160 1997;277:1624-32.
5. Khaw KT, Barrett-Connor E. Dietary potassium and stroke-associated mortality. A 12-year prospective population study. *N Engl J Med JID* - 0255562 1987;316:235-40.
6. Suter PM. The effects of potassium, magnesium, calcium, and fiber on risk of stroke. *Nutr Rev JID* - 0376405 1999;57:84-88.
7. Iso H, Stampfer MJ, Manson JE, Rexrode K, Hennekens CH, Colditz GA *et al.* Prospective study of calcium, potassium, and magnesium intake and risk of stroke in women. *Stroke JID* - 0235266 1999;30:1772-79.
8. Fang J, Madhavan S, Alderman MH. Dietary potassium intake and stroke mortality. *Stroke JID* - 0235266 2000;31:1532-37.
9. Bazzano LA, He J, Ogden LG, Loria C, Vupputuri S, Myers L *et al.* Dietary potassium intake and risk of stroke in US men and women: National Health and Nutrition Examination Survey I epidemiologic follow-up study. *Stroke JID* - 0235266 2001;32:1473-80.

10. Law MR, Morris JK. By how much does fruit and vegetable consumption reduce the risk of ischaemic heart disease? *Eur J Clin Nutr JID* - 8804070 1998;52:549-56.
11. Joshipura KJ, Hu FB, Manson JE, Stampfer MJ, Rimm EB, Speizer FE *et al.* The effect of fruit and vegetable intake on risk for coronary heart disease. *Ann Intern Med JID* - 0372351 2001;134:1106-14.
12. Dietz R. The role of potassium in hypertension. Discovery of potassium as a natriuretic and antihypertensive agent. *Am J Nephrol JID* - 8109361 1983;3:100-08.
13. Smith SR, Klotman PE, Svetkey LP. Potassium chloride lowers blood pressure and causes natriuresis in older patients with hypertension. *J Am Soc Nephrol JID* - 9013836 1992;2:1302-09.
14. Krishna GG, Kapoor SC. Potassium supplementation ameliorates mineralocorticoid-induced sodium retention. *Kidney Int JID* - 0323470 1993;43:1097-103.
15. Zhou MS, Nishida Y, Yoneyama H, Chen QH, Kosaka H. Potassium supplementation increases sodium excretion and nitric oxide production in hypertensive Dahl rats. *Clin Exp Hypertens JID* - 9305929 1999;21:1397-411.
16. McCabe RD, Bakarich MA, Srivastava K, Young DB. Potassium inhibits free radical formation. *Hypertension* 1994;24:77-82.
17. Young DB, Lin H, McCabe RD. Potassium's cardiovascular protective mechanisms. *Am J Physiol JID* - 0370511 1995;268:R825-R837.
18. McCarty MF. Endothelial membrane potential regulates production of both nitric oxide and superoxide--a fundamental determinant of vascular health. *Med Hypotheses* 1999;53:277-89.
19. Cappuccio FP, Kalaitzidis R, Duneclift S, Eastwood JB. Unravelling the links between calcium excretion, salt intake, hypertension, kidney stones and bone metabolism. *J Nephrol JID* - 9012268 2000;13:169-77.
20. Lemann JJ, Pleuss JA, Gray RW, Hoffmann RG. Potassium administration reduces and potassium deprivation increases urinary calcium excretion in healthy adults [corrected]. *Kidney Int JID* - 0323470 1991;39:973-83.
21. Lemann JJ, Pleuss JA, Gray RW. Potassium causes calcium retention in healthy adults. *J Nutr JID* - 0404243 1993;123:1623-26.
22. Lemann JJ, Pleuss JA, Hornick L, Hoffman RG. Dietary NaCl-restriction prevents the calciuria of KCl-deprivation and blunts the calciuria of KHCO<sub>3</sub>-deprivation in healthy adults. *Kidney Int JID* - 0323470 1995;47:899-906.

23. Wasserstein AG, Stolley PD, Soper KA, Goldfarb S, Maislin G, Agus Z. Case-control study of risk factors for idiopathic calcium nephrolithiasis. *Miner Electrolyte Metab JID* - 7802196 1987;13:85-95.
24. Hall WD, Pettinger M, Oberman A, Watts NB, Johnson KC, Paskett ED *et al.* Risk factors for kidney stones in older women in the southern United States. *Am J Med Sci JID* - 0370506 2001;322:12-18.
25. Antonios TF, MacGregor GA. Deleterious effects of salt intake other than effects on blood pressure. *Clin Exp Pharmacol Physiol* 1995;22:180-84.
26. Wachman A, Bernstein DS. Diet and osteoporosis. *Lancet* 1968;1:958-59.
27. Frassetto LA, Todd KM, Morris RCJ, Sebastian A. Worldwide incidence of hip fracture in elderly women: relation to consumption of animal and vegetable foods. *J Gerontol A Biol Sci Med Sci JID* - 9502837 2000;55:M585-M592.
28. Sellmeyer DE, Stone KL, Sebastian A, Cummings SR. A high ratio of dietary animal to vegetable protein increases the rate of bone loss and the risk of fracture in postmenopausal women. Study of Osteoporotic Fractures Research Group. *Am J Clin Nutr JID* - 0376027 2001;73:118-22.
29. New SA, Bolton-Smith C, Grubb DA, Reid DM. Nutritional influences on bone mineral density: a cross-sectional study in premenopausal women. *Am J Clin Nutr JID* - 0376027 1997;65:1831-39.
30. Tucker KL, Hannan MT, Chen H, Cupples LA, Wilson PW, Kiel DP. Potassium, magnesium, and fruit and vegetable intakes are associated with greater bone mineral density in elderly men and women. *Am J Clin Nutr JID* - 0376027 1999;69:727-36.
31. New SA, Robins SP, Campbell MK, Martin JC, Garton MJ, Bolton-Smith C *et al.* Dietary influences on bone mass and bone metabolism: further evidence of a positive link between fruit and vegetable consumption and bone health? *Am J Clin Nutr JID* - 0376027 2000;71:142-51.
32. Lemann JJ, Pleuss JA, Gray RW. Potassium causes calcium retention in healthy adults. *J Nutr JID* - 0404243 1993;123:1623-26.
33. Sebastian A, Morris RCJ. Improved mineral balance and skeletal metabolism in postmenopausal women treated with potassium bicarbonate. *N Engl J Med JID* - 0255562 1994;331:279-Sebastian, A.
34. Morris RCJ, Schmidlin O, Tanaka M, Forman A, Frassetto L, Sebastian A. Differing effects of supplemental KCl and KHCO<sub>3</sub>: pathophysiological and clinical implications. *Semin Nephrol JID* - 8110298 1999;19:487-93.

35. Sellmeyer DE, Schloetter M, Sebastian A. Potassium citrate prevents increased urine calcium excretion and bone resorption induced by a high sodium chloride diet. *J Clin Endocrinol Metab* JID - 0375362 2002;87:2008-12.
36. Pak CY, Peterson RD, Poindexter J. Prevention of spinal bone loss by potassium citrate in cases of calcium urolithiasis. *J Urol* JID - 0376374 2002;168:31-34.
37. Rodman JS. Prophylaxis of uric acid stones with alternate day doses of alkaline potassium salts. *J Urol* JID - 0376374 1991;145:97-99.
38. Welbourne TC. Acidosis activation of the pituitary-adrenal-renal glutaminase I axis. *Endocrinology* 1976;99:1071-79.
39. Welbourne TC, Francoeur D. Influence of aldosterone on renal ammonia production. *Am.J.Physiol* 1977;233:E56-E60.
40. Perez GO, Oster JR, Katz FH, Vaamonde CA. The effect of acute metabolic acidosis on plasma cortisol, renin activity and aldosterone. *Horm.Res.* 1979;11:12-21.
41. Henger A, Tutt P, Riesen WF, Hulter HN, Krapf R. Acid-base and endocrine effects of aldosterone and angiotensin II inhibition in metabolic acidosis in human patients. *J.Lab Clin.Med.* 2000;136:379-89.
42. Colditz GA, Manson JE, Stampfer MJ, Rosner B, Willett WC, Speizer FE. Diet and risk of clinical diabetes in women. *Am J Clin Nutr* 1992;55:1018-23.
43. McCarty MF. Acid-base balance may influence risk for insulin resistance syndrome by modulating cortisol output. *Med Hypotheses* 2005;64:380-84.
44. Frassetto L, Morris RC, Jr., Sebastian A. Potassium bicarbonate reduces urinary nitrogen excretion in postmenopausal women. *J Clin Endocrinol.Metab* 1997;82:254-59.
45. Maurer M, Riesen W, Muser J, Hulter HN, Krapf R. Neutralization of Western diet inhibits bone resorption independently of K intake and reduces cortisol secretion in humans. *Am.J.Physiol Renal Physiol* 2003;284:F32-F40.
46. Wang XB, Zhao XH. The effect of dietary sulfur-containing amino acids on calcium excretion. *Adv Exp Med Biol* JID - 0121103 1998;442:495-99.
47. Hayes KC, Pronczuk A, Addesa AE, Stephan ZF. Taurine modulates platelet aggregation in cats and humans. *Am J Clin Nutr* JID - 0376027 1989;49:1211-16.
48. Franconi F, Bennardini F, Mattana A, Miceli M, Ciuti M, Mian M *et al.* Plasma and platelet taurine are reduced in subjects with insulin-dependent diabetes mellitus: effects of taurine supplementation. *Am J Clin Nutr* JID - 0376027 1995;61:1115-19.



49. Franconi F, Miceli M, Bennardini F, Mattana A, Covarrubias J, Seghieri G. Taurine potentiates the antiaggregatory action of aspirin and indomethacin. *Adv Exp Med Biol JID* - 0121103 1992;315:181-86.
50. Kohashi N, Okabayashi T, Hama J, Katori R. Decreased urinary taurine in essential hypertension. *Prog Clin Biol Res* 1983;125:73-87.
51. Fujita T, Ando K, Noda H, Ito Y, Sato Y. Effects of increased adrenomedullary activity and taurine in young patients with borderline hypertension. *Circulation* 1987;75:525-32.
52. Yamori Y, Nara Y, Ikeda K, Mizushima S. Is taurine a preventive nutritional factor of cardiovascular diseases or just a biological marker of nutrition? *Adv Exp Med Biol* 1996;403:623-29.
53. Nara Y, Yamori Y, Lovenberg W. Effect of dietary taurine on blood pressure in spontaneously hypertensive rats. *Biochem Pharmacol JID* - 0101032 1978;27:2689-92.
54. Sato Y, Ogata E, Fujita T. Hypotensive action of taurine in DOCA-salt rats-- involvement of sympathoadrenal inhibition and endogenous opiate. *Jpn Circ J JID* - 7806868 1991;55:500-08.
55. Ideishi M, Miura S, Sakai T, Sasaguri M, Misumi Y, Arakawa K. Taurine amplifies renal kallikrein and prevents salt-induced hypertension in Dahl rats. *J Hypertens JID* - 8306882 1994;12:653-61.
56. Anuradha CV, Balakrishnan SD. Taurine attenuates hypertension and improves insulin sensitivity in the fructose-fed rat, an animal model of insulin resistance. *Can J Physiol Pharmacol JID* - 0372712 1999;77:749-54.
57. Harada H, Kitazaki K, Tsujino T, Watari Y, Iwata S, Nonaka H *et al.* Oral taurine supplementation prevents the development of ethanol-induced hypertension in rats. *Hypertens Res JID* - 9307690 2000;23:277-84.
58. Petty MA, Kintz J, DiFrancesco GF. The effects of taurine on atherosclerosis development in cholesterol-fed rabbits. *Eur J Pharmacol* 1990;180:119-27.
59. Kondo Y, Murakami S, Oda H, Nagate T. Taurine reduces atherosclerotic lesion development in apolipoprotein E-deficient mice. *Adv Exp Med Biol JID* - 0121103 2000;483:193-202.
60. Murakami S, Kondo Y, Sakurai T, Kitajima H, Nagate T. Taurine suppresses development of atherosclerosis in Watanabe heritable hyperlipidemic (WHHL) rabbits. *Atherosclerosis JID* - 0242543 2002;163:79-87.

61. Azuma J, Sawamura A, Awata N, Ohta H, Hamaguchi T, Harada H *et al.* Therapeutic effect of taurine in congestive heart failure: a double-blind crossover trial. *Clin Cardiol* 1985;8:276-82.
62. Azuma J, Sawamura A, Awata N. Usefulness of taurine in chronic congestive heart failure and its prospective application. *Jpn Circ J* 1992;56:95-99.
63. Azuma J, Takihara K, Awata N, Ohta H, Sawamura A, Harada H *et al.* Beneficial effect of taurine on congestive heart failure induced by chronic aortic regurgitation in rabbits. *Res Commun Chem Pathol Pharmacol* 1984;45:261-70.
64. McCarty MF. The reported clinical utility of taurine in ischemic disorders may reflect a down-regulation of neutrophil activation and adhesion. *Med Hypotheses JID - 7505668* 1999;53:290-99.
65. Wright CE, Lin TT, Lin YY, Sturman JA, Gaull GE. Taurine scavenges oxidized chlorine in biological systems. *Prog Clin Biol Res JID - 7605701* 1985;179:137-47.
66. Nikpoor B, Turecki G, Fournier C, Theroux P, Rouleau GA. A functional myeloperoxidase polymorphic variant is associated with coronary artery disease in French-Canadians. *Am Heart J JID - 0370465* 2001;142:336-39.
67. Hazell LJ, Arnold L, Flowers D, Waeg G, Malle E, Stocker R. Presence of hypochlorite-modified proteins in human atherosclerotic lesions. *J Clin Invest* 1996;97:1535-44.
68. Hazell LJ, Baerenthaler G, Stocker R. Correlation between intima-to-media ratio, apolipoprotein B-100, myeloperoxidase, and hypochlorite-oxidized proteins in human atherosclerosis. *Free Radic.Biol.Med* 2001;31:1254-62.
69. Hazell LJ, Stocker R. Oxidation of low-density lipoprotein with hypochlorite causes transformation of the lipoprotein into a high-uptake form for macrophages. *Biochem J* 1993;290 ( Pt 1):165-72.
70. Hazell LJ, Davies MJ, Stocker R. Secondary radicals derived from chloramines of apolipoprotein B-100 contribute to HOCl-induced lipid peroxidation of low-density lipoproteins. *Biochem J* 1999;339 ( Pt 3):489-95.
71. Jerlich A, Fritz G, Kharrazi H, Hammel M, Tschabuschnig S, Glatter O *et al.* Comparison of HOCl traps with myeloperoxidase inhibitors in prevention of low density lipoprotein oxidation. *Biochim Biophys Acta* 2000;1481:109-18.
72. Morel DW, Llera-Moya M, Friday KE. Treatment of cholesterol-fed rabbits with dietary vitamins E and C inhibits lipoprotein oxidation but not development of atherosclerosis. *J Nutr* 1994;124:2123-30.

73. Fruebis J, Carew TE, Palinski W. Effect of vitamin E on atherogenesis in LDL receptor-deficient rabbits. *Atherosclerosis* 1995;117:217-24.
74. Jacobsson LS, Yuan XM, Zieden B, Olsson AG. Effects of alpha-tocopherol and astaxanthin on LDL oxidation and atherosclerosis in WHHL rabbits. *Atherosclerosis* 2004;173:231-37.
75. Pruthi S, Allison TG, Hensrud DD. Vitamin E supplementation in the prevention of coronary heart disease. *Mayo Clin Proc JID* - 0405543 2001;76:1131-36.
76. Marchioli R, Schweiger C, Levantesi G, Tavazzi L, Valagussa F. Antioxidant vitamins and prevention of cardiovascular disease: epidemiological and clinical trial data. *Lipids JID* - 0060450 1902;36 Suppl:S53-S63.
77. Fu X, Kassim SY, Parks WC, Heinecke JW. Hypochlorous acid oxygenates the cysteine switch domain of pro-matrix metalloproteinase (MMP-7). A mechanism for matrix metalloproteinase activation and atherosclerotic plaque rupture by myeloperoxidase. *J Biol Chem JID* - 2985121R 2001;276:41279-87.
78. McCarty MF. Supplementary taurine may stabilize atheromatous plaque by antagonizing the activation of metalloproteinases by hypochlorous acid. *Med Hypotheses* 2004;63:414-18.
79. Barua M, Liu Y, Quinn MR. Taurine chloramine inhibits inducible nitric oxide synthase and TNF-alpha gene expression in activated alveolar macrophages: decreased NF-kappaB activation and IkappaB kinase activity. *J Immunol JID* - 2985117R 2001;167:2275-81.
80. Kanayama A, Inoue J, Sugita-Konishi Y, Shimizu M, Miyamoto Y. Oxidation of Ikappa Balpha at methionine 45 is one cause of taurine chloramine-induced inhibition of NF-kappa B activation. *J Biol Chem JID* - 2985121R 2002;277:24049-56.
81. Hansen SH. The role of taurine in diabetes and the development of diabetic complications. *Diabetes Metab Res Rev JID* - 100883450 2001;17:330-46.
82. Pop-Busui R, Sullivan KA, Van Huysen C, Bayer L, Cao X, Towns R *et al*. Depletion of taurine in experimental diabetic neuropathy: implications for nerve metabolic, vascular, and functional deficits. *Exp Neurol JID* - 0370712 2001;168:259-72.
83. Trachtman H, Futterweit S, Maesaka J, Ma C, Valderrama E, Fuchs A *et al*. Taurine ameliorates chronic streptozocin-induced diabetic nephropathy in rats. *Am J Physiol JID* - 0370511 1995;269:F429-F438.
84. Koide M, Okahashi N, Tanaka R, Kazuno K, Shibasaki K, Yamazaki Y *et al*. Inhibition of experimental bone resorption and osteoclast formation and survival by 2-aminoethanesulphonic acid. *Arch Oral Biol JID* - 0116711 1999;44:711-19.

85. Saransaari P, Oja SS. Mechanisms of ischemia-induced taurine release in mouse hippocampal slices. *Brain Res.* 1998;807:118-24.
86. Saransaari P, Oja SS. Taurine and neural cell damage. *Amino.Acids* 2000;19:509-26.
87. Bureau MH, Olsen RW. Taurine acts on a subclass of GABAA receptors in mammalian brain in vitro. *Eur.J.Pharmacol.* 1991;207:9-16.
88. Zhao P, Huang YL, Cheng JS. Taurine antagonizes calcium overload induced by glutamate or chemical hypoxia in cultured rat hippocampal neurons. *Neurosci.Lett.* 1999;268:25-28.
89. O'Byrne MB, Tipton KF. Taurine-induced attenuation of MPP+ neurotoxicity in vitro: a possible role for the GABA(A) subclass of GABA receptors. *J.Neurochem.* 2000;74:2087-93.
90. Louzada PR, Lima AC, Mendonca-Silva DL, Noel F, De Mello FG, Ferreira ST. Taurine prevents the neurotoxicity of beta-amyloid and glutamate receptor agonists: activation of GABA receptors and possible implications for Alzheimer's disease and other neurological disorders. *FASEB J.* 2004;18:511-18.
91. Dawson R, Jr., Liu S, Eppler B, Patterson T. Effects of dietary taurine supplementation or deprivation in aged male Fischer 344 rats. *Mech.Ageing Dev.* 1999;107:73-91.
92. Rivas-Arancibia S, Rodriguez AI, Zigova T, Willing AE, Brown WD, Cahill DW *et al.* Taurine increases rat survival and reduces striatal damage caused by 3-nitropropionic acid. *Int.J.Neurosci.* 2001;108:55-67.
93. Guo J, Li R, Zhao P, Cheng J. Effect of taurine in combination with electroacupuncture on neuronal damage following transient focal cerebral ischemia in rats. *Acupunct.Electrother.Res.* 2002;27:129-36.
94. Shuaib A. The role of taurine in cerebral ischemia: studies in transient forebrain ischemia and embolic focal ischemia in rodents. *Adv.Exp.Med.Biol.* 2003;526:421-31.
95. McCarty MF. Sub-optimal taurine status may promote platelet hyperaggregability in vegetarians. *Med Hypotheses* 2004;63:426-33.