

SCIENTIFIC REFERENCES BEHIND SUPPLAMINE®

January 23, 2007

3DG is the Result of Protein Glycation

Dyer, D. G., J. A. Blackledge, et al. (1991). "Formation of pentosidine during nonenzymatic browning of proteins by glucose. Identification of glucose and other carbohydrates as possible precursors of pentosidine in vivo." J Biol Chem 266(18): 11654-60.

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Brownlee, M. (1994). "Lilly Lecture 1993. Glycation and diabetic complications." Diabetes 43(6): 836-41.

Kikuchi, S., K. Shinpo, et al. (1999). "Neurotoxicity of methylglyoxal and 3-deoxyglucosone on cultured cortical neurons: synergism between glycation and oxidative stress, possibly involved in neurodegenerative diseases." J Neurosci Res 57(2): 280-9.

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3DG Causes AGEs in Skin

Baynes, J. W., S. R. Thorpe, et al. (1984). "Nonenzymatic glycosylation of lysine residues in albumin." Methods Enzymol 106: 88-98.

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Monnier, V. M., O. Bautista, et al. (1999). "Skin collagen glycation, glycooxidation, and crosslinking are lower in subjects with long-term intensive versus

conventional therapy of type 1 diabetes: relevance of glycated collagen products versus HbA1c as markers of diabetic complications. DCCT Skin Collagen Ancillary Study Group. Diabetes Control and Complications Trial." Diabetes 48(4): 870-80.

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Monnier, V. M. and D. R. Sell (2006). "Prevention and repair of protein damage by the Maillard reaction in vivo." Rejuvenation Res 9(2): 264-73.

3DG Crosslinks Proteins Including Collagen

Niwa, T., N. Takeda, et al. (1993). "Presence of 3-deoxyglucosone, a potent protein crosslinking intermediate of Maillard reaction, in diabetic serum." Biochem Biophys Res Commun 196(2): 837-43.

Prabhakaram, M. and B. J. Ortwerth (1994). "Determination of glycation crosslinking by the sugar-dependent incorporation of [¹⁴C]lysine into protein." Anal Biochem 216(2): 305-12.

Niwa, T., T. Katsuzaki, et al. (1996). "Modification of beta 2m with advanced glycation end products as observed in dialysis-related amyloidosis by 3-DG accumulating in uremic serum." Kidney Int 49(3): 861-7.

Niwa, T., T. Katsuzaki, et al. (1997). "Amyloid beta 2-microglobulin is modified with imidazolone, a novel advanced glycation end product, in dialysis-related amyloidosis." Kidney Int 51(1): 187-94.

Thornalley, P. J. (2002). "Glycation in diabetic neuropathy: characteristics, consequences, causes, and therapeutic options." Int Rev Neurobiol 50: 37-57.

Su, Schwartz, Tobia, and Kappler 2002, Dynamis Therapeutics - in house studies.

3DG Reduces Collagen Type I Production

Su, Schwartz, Tobia, and Kappler 2004, Dynamis Therapeutics - in house studies. Done in tissue culture with fibroblasts.

Artlett C. 2004, Thomas Jefferson University - unpublished studies. Done in tissue culture with fibroblasts.

3DG Causes an Inflammatory Response

Bierhaus, A., M. A. Hofmann, et al. (1998). "AGEs and their interaction with AGE-receptors in vascular disease and diabetes mellitus. I. The AGE concept." Cardiovasc Res 37(3): 586-600.

Hofmann, M. A., S. Drury, et al. (1999). "RAGE mediates a novel proinflammatory axis: a central cell surface receptor for S100/calgranulin polypeptides." Cell 97(7): 889-901.

Thornalley, P. J. (2002). "Glycation in diabetic neuropathy: characteristics, consequences, causes, and therapeutic options." Int Rev Neurobiol 50: 37-57.

Welten, A. G., C. G. Schalkwijk, et al. (2003). "Single exposure of mesothelial cells to glucose degradation products (GDPs) yields early advanced glycation end-products (AGEs) and a proinflammatory response." Perit Dial Int 23(3): 213-21.

Yan, S. F., R. Ramasamy, et al. (2003). "Glycation, inflammation, and RAGE: a scaffold for the macrovascular complications of diabetes and beyond." Circ Res 93(12): 1159-69.

Artlett C. 2006, Thomas Jefferson University - unpublished studies

3DG Causes Reactive Oxygen Species and Free Radical Production and Impairs the Body's ability to Remove ROS

Takahashi, M., J. Fujii, et al. (1995). "Elevation of aldose reductase gene expression in rat primary hepatoma and hepatoma cell lines: implication in detoxification of cytotoxic aldehydes." Int J Cancer 62(6): 749-54.

Araki, A. (1997). "[Oxidative stress and diabetes mellitus: a possible role of alpha- dicarbonyl compounds in free radical formation]." Nippon Ronen Igakkai Zasshi 34(9): 716-20.

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Eriksson, U. J., P. Wentzel, et al. (1998). "Teratogenicity of 3-deoxyglucosone and diabetic embryopathy." Diabetes 47(12): 1960-6.

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Hofmann, M. A., S. Drury, et al. (1999). "RAGE mediates a novel proinflammatory axis: a central cell surface receptor for S100/calgranulin polypeptides." Cell 97(7): 889-901.

Shinpo, K., S. Kikuchi, et al. (2000). "Selective vulnerability of spinal motor neurons to reactive dicarbonyl compounds, intermediate products of glycation, in vitro: implication of inefficient glutathione system in spinal motor neurons." Brain Res 861(1): 151-9.

Niwa, T. and S. Tsukushi (2001). "3-deoxyglucosone and AGEs in uremic complications: inactivation of glutathione peroxidase by 3-deoxyglucosone." Kidney Int Suppl 78: S37-41.

Shimoi, K., A. Okitsu, et al. (2001). "Oxidative DNA damage induced by high glucose and its suppression in human umbilical vein endothelial cells." Mutat Res 480-481: 371-8.

Thornalley, P. J. (2002). "Glycation in diabetic neuropathy: characteristics, consequences, causes, and therapeutic options." Int Rev Neurobiol 50: 37-57.

Inactivating 3DG Prevents Collagen Crosslinking

Su, Schwartz, Tobia, and Kappler 2002, Dynamis Therapeutics - in house studies. Done in vitro using arginine to stop 3DG from crosslinking collagen.

Reducing 3DG Protects Diabetic Skin from Loss of Elasticity

Su, Schwartz, Tobia, and Kappler 2002, Dynamis Therapeutics - in house studies. Inhibiting F3K with DYN 12 and therefore reducing 3DG levels in diabetic rats prevented the loss of skin elasticity seen in non-treated diabetic rats.

Inhibition of F3K Increases Collagen Production

Su, Schwartz, Tobia, and Kappler 2004, Dynamis Therapeutics - in house studies. Done in tissue culture with fibroblasts using DYN 12.

Meglumine Reduces AGE Products in Skin

Schwartz, Menter, Tobia, Marcy, and Kappler – Morehouse College of Medicine, Dynamis Therapeutics, Inc – in house studies. Rats placed on 50 mM meglumine in their drinking water for over 1 year developed 60% fewer AGE products than untreated rats.

Meglumine Prevents Proinflammatory Response

Artlett C. 2006, Thomas Jefferson University - unpublished studies.