ReadiSorb Liposomal Glutathione Research Studies

1. Atherosclerosis. 2007 Dec;195(2):e61-8. Epub 2007 Jun 22.

Anti-oxidant and anti-atherogenic properties of liposomal glutathione: studies in vitro, and in the atherosclerotic apolipoprotein E-deficient mice.

Rosenblat M[1], Volkova N, Coleman R, Aviram M.

Abstract

Liposomal glutathione, but not the control liposomes (with no glutathione), dose-dependently inhibited copper ion-induced low density lipoprotein (LDL) and HDL oxidation. As peroxidase activity was found to be present in both LDL and HDL, it has contributed to the anti-oxidative effects of liposomal glutathione. In-vitro, no significant effect of liposomal glutathione on J774 A.1 macrophage cell-line oxidative stress and on cellular cholesterol metabolism was observed. In contrast, in the atherosclerotic apolipoprotein E-deficient (E(0)) mice, consumption of liposomal glutathione (12.5 or 50mg/kg/day, for 2 months), but not control liposomes, resulted in a significant reduction in the serum susceptibility to AAPH-induced oxidation by 33%. Liposomal glutathione (50mg/kg/day) consumption also resulted in an increment (by 12%) in the mice peritoneal macrophages (MPM) glutathione content, paralleled by a significant reduction in total cellular lipid peroxides content (by 40%), compared to placebo-treated mice MPM. MPM paraoxonase 2 activity was significantly increased by 27% and by 121%, after liposomal glutathione consumption (12.5 or 50mg/kg/day, respectively). Analyses of cellular cholesterol fluxes revealed that, liposomal glutathione (12.5mg/kg/day) consumption, decreased the extent of oxidized-LDL (Ox-LDL) uptake by 17% and the cellular cholesterol biosynthesis rate, by 34%, and stimulated HDL-induced macrophage cholesterol efflux, by 19%. Most important, a significant reduction in macrophage cholesterol mass (by 24%), and in the atherosclerotic lesion area (by 30%) was noted. We thus conclude that liposomal glutathione possesses anti-oxidative and anti-atherogenic properties towards lipoproteins and macrophages, leading to attenuation of atherosclerosis development.

PMID:
17588583
[PubMed - indexed for MEDLINE]

2. Health Phys. 2010 Jan;98(1):53-60. doi: 10.1097/HP.0b013e3181b9dbbc.

Aminothiol receptors for decorporation of intravenously administered (60)Co in the rat.

Levitskaia TG[1], Morris JE, Creim JA, Woodstock AD, Luders T, Curry TL, Thrall KD.

Abstract

This report provides a comparison of the oral decorporation efficacy of L-glutathione (GSH), L-cysteine (Cys), and a liposomal GSH formulation (ReadiSorb) toward systemic (60)Co to that observed following intravenous administration of GSH and Cys in F344 rats. Aminoacid L-histidine (His) containing no thiol functionality was tested intravenously to compare in vivo efficacy of the aminothiol (GSH, Cys) chelators with that of the aminoimidazole (His) chelator. In these studies, (60)Co was administered to animals by intravenous injection, followed by intravenous or oral gavage doses of a chelator repeated at 24-h intervals for a total of 5 doses. The results suggest that GSH and Cys are potent decorporation agents for (60)Co in the rat model, although the efficacy of treatment depends largely on the systemic availability of the chelator. The intravenous route of administration of GSH or Cys was most effective in reducing tissue (60)Co levels and in increasing excretion of radioactivity compared to control animals. Liposomal encapsulation was found to markedly enhance the oral bioavailability of GSH compared to non-formulated GSH. The oral administration of liposomal GSH reduced (60)Co levels in nearly all tissues by 12-43% compared to that observed for non-formulated GSH. Efficacy of oral Cys was only slightly reduced in comparison with intravenous Cys. Further studies to optimize the dosing regimen in order to maximize decorporation efficiency are warranted.

PMID:
19959951
[PubMed - indexed for MEDLINE]
PMCID:
PMC2818207

3. Neurochem Res. 2010 Oct;35(10):1575-87. doi: 10.1007/s11064-010-0217-0. Epub 2010 Jun 10.

Liposomal-glutathione provides maintenance of intracellular glutathione and neuroprotection in mesencephalic neuronal cells.

Zeevalk GD[1], Bernard LP, Guilford FT.

Abstract

A liposomal preparation of glutathione (GSH) was investigated for its ability to replenish intracellular GSH and provide neuroprotection in an in vitro model of Parkinson's disease using paraquat plus maneb (PQMB) in rat mesencephalic cultures. In mixed neuronal/glial cultures depleted of intracellular GSH, repletion to control levels occurred over 4 h with liposomal-GSH or non-liposomal-GSH however, liposomal-GSH was 100-fold more potent; EC(50s) 4.75 μM and 533 μM for liposomal and non-liposomal-GSH, respectively. Liposomal-GSH utilization was also observed in neuronal cultures, but with a higher EC(50) (76.5 μM), suggesting that glia facilitate utilization. Blocking γ-glutamylcysteine synthetase with buthionine sulfoxamine prevented replenishment with liposomal-GSH demonstrating the requirement for catabolism and resynthesis. Repletion was significantly attenuated with endosomal inhibition implicating the endosomal system in utilization. Liposomal-GSH provided dose-dependent protection against PQMB with an EC(50) similar to that found for repletion. PQMB depleted intracellular GSH by 50%. Liposomal-GSH spared endogenous GSH during PQMB exposure, but did not require

GSH biosynthesis for protection. No toxicity was observed with the liposomal preparation at 200-fold the EC(50) for repletion. These findings indicate that glutathione supplied in a liposomal formulation holds promise as a potential therapeutic for neuronal maintenance.

PMID:
20535554
[PubMed - indexed for MEDLINE]

4. Med Sci Monit. 2011 Dec;17(12):CR677-82.

A clinical trial of glutathione supplementation in autism spectrum disorders.

Kern JK[1], Geier DA, Adams JB, Garver CR, Audhya T, Geier MR.

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Abstract

BACKGROUND:

Recent evidence shows that subjects diagnosed with an autism spectrum disorder (ASD) have significantly lower levels of glutathione than typically developing children. The purpose of this study was to examine the use of two commonly used glutathione supplements in subjects diagnosed with an ASD to determine their efficacy in increasing blood glutathione levels in subjects diagnosed with an ASD.

MATERIAL/METHODS:

The study was an eight-week, open-label trial using oral lipoceutical glutathione (n=13) or transdermal glutathione (n=13) in children, 3-13 years of age, with a diagnosis of an ASD. Subjects underwent pre- and post-treatment lab testing to evaluate plasma reduced glutathione, oxidized glutathione, cysteine, taurine, free and total sulfate, and whole-blood glutathione levels.

RESULTS:

The oral treatment group showed significant increases in plasma reduced glutathione, but not whole-blood glutathione levels following supplementation. Both the oral and transdermal treatment groups showed significant increases in plasma sulfate, cysteine, and taurine following supplementation.

CONCLUSIONS:

The results suggest that oral and transdermal glutathione supplementation may have some benefit in improving some of the transsulfuration metabolites. Future studies among subjects diagnosed with an

ASD should further explore the pharmacokinetics of glutathione supplementation and evaluate the potential effects of glutathione supplementation upon clinical symptoms.

PMID: 22129897

[PubMed - indexed for MEDLINE]

PMCID: PMC3628138

5. J Cardiovasc Pharmacol. 2013 Mar;61(3):233-9. doi: 10.1097/FJC.0b013e31827c0f02.

Oral pretreatment with liposomal glutathione attenuates reperfusion injury in rabbit isolated hearts.

Lauver DA[1], Kaissarian NM, Lucchesi BR.

Abstract

Reactive oxygen species are a key mediator of myocardial reperfusion injury. Endogenous cellular defenses against reactive oxygen species often become overwhelmed after ischemia and reperfusion. Therefore, exogenous supplementation of various antioxidant compounds has been hypothesized to protect against reperfusion. Reduced glutathione (GSH) is an important endogenous antioxidant that affords protection against oxidative damage. Oral administration of GSH is limited due to poor gastrointestinal absorption. A liposomal preparation of glutathione (lipGSH) capable of oral administration was investigated for its ability to attenuate tissue injury and increase myocardial glutathione levels in an isolated heart model of reperfusion injury. Male, New Zealand white rabbits were assigned randomly among 4 groups as follows: control and daily oral administration of lipGSH for 3, 7, or 14 days. At completion of the dosing regimen, hearts were harvested and perfused in a retrograde manner with the use of a Langendorff apparatus. The hearts were subjected to 30 minutes of global ischemia followed by 60 minutes of reperfusion. Hearts from lipGSH-treated rabbits exhibited better recovery of left ventricular contractile function during reperfusion and had attenuated oxidative damage. Furthermore, hearts from lipGSH-treated animals had increased myocardial tissue levels of GSH demonstrating effective absorption of lipGSH.

PMID:

23188132

[PubMed - indexed for MEDLINE]

6. J Interferon Cytokine Res. 2013 May;33(5):270-9. doi: 10.1089/jir.2012.0103. Epub 2013 Feb 14.

Glutathione supplementation improves macrophage functions in HIV.

Morris D[1], Guerra C, Khurasany M, Guilford F, Saviola B, Huang Y, Venketaraman V.

Abstract

In this study, we determined the effects of glutathione (GSH)-enhancing agents in restoring the levels of GSH in isolated macrophages from individuals with HIV infection thereby resulting in improved control of Mycobacterium tuberculosis. Our results indicate that treatment with N-acetyl cysteine or a liposomal formulation of glutathione (lGSH) resulted in replenishment of reduced also known as free GSH (rGSH), and correlated with a decrease in the intracellular growth of M. tuberculosis. Finally, we observed differences in the amount of the catalytic subunit of glutamine-cysteine ligase (GCLC), glutathione synthase, and glutathione reductase present in macrophages derived from healthy and HIV-infected individuals. These changes correlated with changes in free radicals as well as rGSH levels. Our results indicate that HIV infection leads to increased production of free radicals and decreased production of GCLC resulting in depletion of rGSH and this may lead, in part, to the loss of innate immune function observed in HIV patients. These findings represent a novel mechanism for control of M. tuberculosis infection, and a possible supplement to current HIV treatments.

PMID:

23409922

[PubMed - indexed for MEDLINE]

7. Biomed Res Int. 2013;2013:402827. doi: 10.1155/2013/402827. Epub 2013 May 23.

Characterization of dendritic cell and regulatory T cell functions against Mycobacterium tuberculosis infection.

Morris D[1], Gonzalez B, Khurasany M, Kassissa C, Luong J, Kasko S, Pandya S, Chu M, Chi PT, Bui S, Guerra C, Chan J, Venketaraman V.

Abstract

Glutathione (GSH) is a tripeptide that regulates intracellular redox and other vital aspects of cellular functions. GSH plays a major role in enhancing the immune system. Dendritic cells (DCs) are potent antigen presenting cells that participate in both innate and acquired immune responses against microbial infections. Regulatory T cells (Tregs) play a significant role in immune homeostasis. In this study, we investigated the effects of GSH in enhancing the innate and adaptive immune functions of DCs against Mycobacterium tuberculosis (M. tb) infection. We also characterized the functions of the sub-populations of CD4+T cells such as Tregs and non-Tregs in modulating the ability of monocytes to control the

intracellular M. tb infection. Our results indicate that GSH by its direct antimycobacterial activity inhibits the growth of intracellular M. tb inside DCs. GSH also increases the expressions of costimulatory molecules such as HLA-DR, CD80 and CD86 on the cell surface of DCs. Furthermore, GSH-enhanced DCs induced a higher level of T-cell proliferation. We also observed that enhancing the levels of GSH in Tregs resulted in downregulation in the levels of IL-10 and TGF- β and reduction in the fold growth of M. tb inside monocytes. Our studies demonstrate novel regulatory mechanisms that favor both innate and adaptive control of M. tb infection.

PMID:

23762843

[PubMed - indexed for MEDLINE]

PMCID:

PMC3676983

8. Clin Dev Immunol. 2013;2013:959650. doi: 10.1155/2013/959650. Epub 2013 Nov 7.

An elucidation of neutrophil functions against Mycobacterium tuberculosis infection.

Morris D[1], Nguyen T, Kim J, Kassissa C, Khurasany M, Luong J, Kasko S, Pandya S, Chu M, Chi PT, Ly J, Lagman M, Venketaraman V.

Abstract

We characterized the functions of neutrophils in response to Mycobacterium tuberculosis (M. tb) infection, with particular reference to glutathione (GSH). We examined the effects of GSH in improving the ability of neutrophils to control intracellular M. tb infection. Our findings indicate that increasing the intracellular levels of GSH with a liposomal formulation of GSH (L-GSH) resulted in reduction in the levels of free radicals and increased acidification of M. tb containing phagosomes leading to the inhibition in the growth of M. tb. This inhibitory mechanism is dependent on the presence of TNF-α and IL-6. Our studies demonstrate a novel regulatory mechanism adapted by the neutrophils to control M. tb infection.

PMID:

24312131

[PubMed - in process]

PMCID: PMC3838815

9. J Environ Public Health. 2012;2012:835059. doi: 10.1155/2012/835059. Epub 2011 Dec 29.

A review of the diagnosis and treatment of Ochratoxin A inhalational exposure associated with human illness and kidney disease including focal segmental glomerulosclerosis.

Hope JH[1], Hope BE.

Abstract

Ochratoxin A (OTA) exposure via ingestion and inhalation has been described in the literature to cause kidney disease in both animals and humans. This paper reviews Ochratoxin A and its relationship to human health and kidney disease with a focus on a possible association with focal segmental glomerulosclerosis (FSGS) in humans. Prevention and treatment strategies for OTA-induced illness are also discussed, including cholestyramine, a bile-acid-binding resin used as a sequestrant to reduce the enterohepatic recirculation of OTA.

PMID:

22253638

[PubMed - indexed for MEDLINE]

PMCID:

PMC3255309

10. The Scientific World Journal

Volume 2013 (2013), Article ID 767482, 20 pages

http://dx.doi.org/10.1155/2013/767482

Review Article

A Review of the Mechanism of Injury and Treatment Approaches for Illness Resulting from Exposure to Water-Damaged Buildings, Mold, and Mycotoxins

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Received 15 January 2013; Accepted 10 February 2013

Academic Editors: O. Aruoma, P. Maček, and J. B.T. Rocha

Abstract

Physicians are increasingly being asked to diagnose and treat people made ill by exposure to water-damaged environments, mold, and mycotoxins. In addition to avoidance of further exposure to these environments and to items contaminated by these environments, a number of approaches have been used to help persons affected by exposure to restore their health. Illness results from a combination of factors present in water-damaged indoor environments including, mold spores and hyphal fragments, mycotoxins, bacteria, bacterial endotoxins, and cell wall components as well as other factors. Mechanisms of illness include inflammation, oxidative stress, toxicity, infection, allergy, and irritant effects of exposure. This paper reviews the scientific literature as it relates to commonly used treatments such as glutathione, antioxidants, antifungals, and sequestering agents such as Cholestyramine, charcoal, clay and chlorella, antioxidants, probiotics, and induced sweating.