

[Home](#)[Journals](#)[Books](#)[Conferences](#)[News](#)[About Us](#)[Jobs](#)[Home](#) > [Journal](#) > [Chemistry & Materials Science](#) | [Medicine & Healthcare](#) > [PP](#)[Indexing](#) [View Papers](#) [Aims & Scope](#) [Editorial Board](#) [Guideline](#) [Article Processing Charges](#)[PP](#) > [Vol.4 No.1, January 2013](#)

OPEN ACCESS

Hepatoprotective Effect of Vitamin C (Ascorbic Acid)

PDF (Size: 182KB) PP. 84-92 DOI : 10.4236/pp.2013.41012

Author(s)

Elias Adikwu, Oputiri Deo

ABSTRACT

Human and animal studies have shown that some drugs and chemical agents have potential hepatotoxic effects. The hepatotoxic effect of drugs and some chemical agents is reported to be associated with the generation of reactive oxygen species (ROS). These ROS are reported to be associated with lipid peroxidation in the liver. This mechanism has led to continuous evaluation of the hepatoprotective effect of antioxidants in humans and animals. Among the antioxidants been evaluated is vitamin C which is a water soluble antioxidant. Reports have linked vitamin C with hepatoprotective property in animals and humans. It synergistic hepatoprotective effect with other antioxidants was also reported. Due to these reports a comprehensive literature review on the hepatoprotective property of vitamin C in humans and animals was performed. It was observed that vitamin C exhibited a reputable hepatoprotective effect in humans and animals. Research showed that vitamin C inhibited hepatotoxicity induced by drugs, heavy metals, organophosphate insecticides and some chemical agents. Vitamin C was reported to normalized levels of serum alanine aminotransferase, aspartate aminotransferase, gamma glutamine, alkaline phosphatase, lactate dehydrogenase and malondialdehyde and serum bilirubin in intoxicated animals. It potentiates the activities of free radical scavengers, superoxide dimutase, and catalase glutathione peroxidase thereby preventing microsomal lipid peroxidation, liver fibrosis, liver necrosis and hepatic inflammation. In humans vitamin C was reported to be beneficial in non alcoholic steatohepatitis and in patients with fatty liver disease. Hepatoprotective property of vitamin C is attributed to it antioxidant property. Vitamin C (ascorbic acid) which is a major water-soluble antioxidant is believed to decrease lipid peroxidation either directly or indirectly by regenerating vitamin E. Vitamin C is an important free radical scavenger in extracellular fluids, trapping radicals and protecting biomembranes from peroxide damage. Vitamin C effectively scavenges singlet oxygen, superoxide, hydroxyl, water soluble peroxy radical and hypochlorous acid. It is also reported to be an excellent source of electrons and therefore can donate electrons to free radicals such as hydroxyl and super oxide radicals and quench their activity. Vitamin C is an essential co-factor involved in many biochemical functions and acts as an electron donor or reducing agent. In this review it is observe that vitamin C has hepatoprotective effect which increases when co administered with other agents precisely antioxidants.

KEYWORDS

Vitamin C; Hepatoprotection; Antioxidant

Cite this paper

E. Adikwu and O. Deo, "Hepatoprotective Effect of Vitamin C (Ascorbic Acid)," *Pharmacology & Pharmacy*, Vol. 4 No. 1, 2013, pp. 84-92. doi: 10.4236/pp.2013.41012.

References

- [1] I. B. Chatterjee, " The History of Vitamin C Research in India," *Journal of Biosciences*, Vol. 34. No. 2, 2009, pp. 185-194. doi:10.1007/s12038-009-0021-7
- [2] T. Stangeland, S. F. Remberg and K. A. Lye, " Total Antioxidant Activity in 35 Ugandan Fruits and Vegetables," *Elsevier*, Vol. 113, No. 1, 2008, pp. 85-91.
- [3] S. J. Padayatty, H. Sun, Y. Wang and H. D. Riordan, " Vitamin C Pharmacokinetics: Implication for Oral and Intravenous Use," *Annals of Internal Medicine*, Vol. 140, No. 7, 2004, pp. 533-537.
- [4] Expert groups on vitamins and mineral, 2003.

[• Open Special Issues](#)[• Published Special Issues](#)[• Special Issues Guideline](#)[PP Subscription](#)[Most popular papers in PP](#)[About PP News](#)[Frequently Asked Questions](#)[Recommend to Peers](#)[Recommend to Library](#)[Contact Us](#)

Downloads: 83,617

Visits: 195,359

[Sponsors >>](#)

- [5] T. R. Wandzilak S. D. D' Andre, P. A. Davis and H. E. Williams, " Effect of High Dose Vitamin C on Urinary Oxalate Levels," *Journal of Urology*, Vol. 151, 1994, pp. 834-837.
- [6] M. Levine, C. Conry-Cantilena, Y. Wang, R. W. Welch and P. W. Washko, " Vitamin C Pharmacokinetics in Healthy Volunteers," *Proceedings of the National Academy of Sciences*, Vol. 93, No. 8, 1996, pp. 3704-3709. doi:10.1073/pnas.93.8.3704
- [7] M. Levine, S. C. Rumsey, R. Daruwala, J. B. Park and Y. Wang, " Criteria and Recommendations for Vitamin C Intake," *Journal of the American Medical Association*, Vol. 281, No. 15, 1999, pp. 1415-1423. doi:10.1001/jama.281.15.1415
- [8] E. Cameron and A. Campbell, " The Ortho-Molecular Treatment of Cancer, II, Clinical Trial of High Dose Ascorbic Acid Supplements in Advanced Human Cancer," *Chemical and Biological Interactions*, Vol. 9, 1974, pp. 285-315. doi:10.1016/0009-2797(74)90019-2
- [9] M. Urivetsky, D. Kessarar and A. D. Smith, " Ascorbic Acid Overdosing: A Risk for Calcium Oxalate Nephrolithiasis," *Journal of Urology*, Vol. 147, 1992, pp. 1215-1218.
- [10] N. Sminoroff and G. L. Wheeler, " Ascorbic Acid in Plants Biosynthesis and Function," *Critical Reviews in Biochemistry and Molecular Biology*, Vol. 19, 2000, pp. 267-290.
- [11] A. Bendich, " Antioxidant Micronutrients and Immune Responses," In: Bendich and R. K. Chandra, Eds., *Micronutrients and Immune Functions*, Academy Sciences, New York, 1990, p. 175.
- [12] L. R. McDowell, " Vitamins in Animal Nutrition Comparative Aspects to Human Nutrition Vitamin C," Academic. Press, London, 1989, pp. 93-131.
- [13] H. Sies, W. Stahl and A. R. Sundquist, " Antioxidant Functions of Vitamins Vitamin E and C, Carotene and Other Carotenoids," *Annals of New York Academy of Sciences*, Vol. 669, 1992, pp. 7-20. doi:10.1111/j.1749-6632.1992.tb17085.x
- [14] C. A. Burtis and E. R. Ashwood, " Tietz Textbook of Clinical Chemistry," 2nd Edition, WB Saunders Co., Philadelphia, 1994, pp. 1275-1512.
- [15] S. P. Netke., M. V. Roomi, C. Tsao and A. Niedzwiecki, " Ascorbic Acid Protects Guinea Pigs from Acute Aflatoxin Toxicity," *Toxicology and Applied Pharmacology*, Vol. 143, No. 2, 1997, pp. 429-435. doi:10.1006/taap.1996.8091
- [16] S. A. Bashandy and S. H. Alwasel, " Carbon Tetrachloride-Induced Hepatotoxicity and Nephrotoxicity in Rats: Protective Role of Vitamin C," *Journal of Pharmacology and Toxicology*, Vol. 6, No. 3, 2011, pp. 283-292. doi:10.3923/jpt.2011.283.292
- [17] O. Ademuyiwa, O. Ade-sanya and O. R. Ajuwon, " Vitamin C in CC14 Hepatotoxicity-A Preliminary Report," *Human Experimental Toxicology*, Vol. 13, No. 2, 1994, pp. 107-109. doi:10.1177/096032719401300208
- [18] T. Kataoka, Y. Ni-shiyama, K. Yamato, J. Teraoka, Y. Morii, A. Sakoda, Y. Ishimori, T. Taguchi and K. Yamaoka, " Comparative Study on the Inhibitory Effects of Antioxidant Vitamins and Radon on Carbon Tetrachloride-Induced Hepatopathy," *Journal of Radiation Research*, 2012, pp. 1-10.
- [19] P. Grajeda-Cota, M. V. Ramirez-Mares and E. González de Mejía, " Vitamin C Protects against in Vitro Cytotoxicity of Cypermethrin in Rat Hepato-cytes," *Toxicology in vitro*, Vol. 18, No. 1, 2004, pp. 13-19. doi:10.1016/S0887-2333(03)00077-8
- [20] S. Mongi, S. Mah-foud, M. Amel, B. Kamel and J. Abdelfattahel, " Protective Effects of Vitamin C against Haematological and Biochemical Toxicity Induced by Deltamethrin in Male Wistar Rats," *Ecotoxicology and Environmental Safety*, Vol. 74, No. 6, 2011, pp. 1765-1769. doi:10.1016/j.ecoenv.2011.04.003
- [21] A. H. Mossa, A. A. Refaie and A. Ramadan, " Effect of Exposure to Mixture of Four Organophosphate Insecticides at No Observed Adverse Effect Level Dose on Rat Liver: The Protective Role of Vitamin C," *Research Journal of Environmental Toxicology*, Vol. 5, No. 6, 2011, pp. 323-335. doi:10.3923/rjet.2011.323.335
- [22] S. F. Ambali, C. Onukak, S. B. Idris, L. S. Yaqub, M. Shittu, H. Aliyu and M. U. Kawu, " Vitamin C Attenuates Short-Term Hematological and Biochemical Alterations Induced by Acute Chlorpyrifos Exposure in Wistar Rats," *Journal of Medicine and Medical Sciences*, Vol. 1, No. 10, 2010, pp. 465-477.

- [23] I. C. Ozturk, F. Ozturk and M. Gul, " Protective Effects of Ascorbic Acid on Hepatotoxicity and Oxidative Stress Caused by Carbon Tetrachloride in the Liver of Wistar Rats," *Cell Bio-chemistry and Function*, Vol. 27, No. 5, 2009, pp. 309-315. doi: 10.1002/cbf.1575
- [24] H. H. Kamel, H. Azza, A. Walaa, M. S. Ahmed and A. H. Mohamed, " Protective Effect of Some Antioxidants against Ccl4-Induced Toxicity in Liver Cells from BRL3A Cell Line," *Journal of American Science*, Vol. 6, No. 10, 2010, pp. 992-1003.
- [25] A. M. Attar, " hepatoprotective Influence of Vitamin c on Thioacetamide Induce Liver Cirrhosis in Wistar Male Rats," *Journal of Pharmacology and Toxicology*, Vol. 6, No. 3, 2011, pp. 218-233. doi: 10.3923/jpt.2011.218.233
- [26] H. K. Hussein, M. H. El-naggar and J. M. Al-Dailamy, " Protective Role of Vitamin C against Hepatorenal Toxicity of Fenvalerate in Male Rats," *Global Advanced Research Journal of Environmental Science and Toxicology*, Vol. 1, No. 4, 2012, pp. 60-65.
- [27] K. S. El-Gendy, N. M. Aly, F. H. mohammed, A. Kenawy and A. H. Sebae, " The Role of Vitamin c as Antioxidant in Protection of Oxidative Stress Induced by Imidacloprid," *Food and Chemical Toxicology*, Vol. 48, No. 1, 2010, pp. 215-221. doi: 10.1016/j.fct.2009.10.003
- [28] O. S. Eissa, " Protective Effect of Vitamin C and Glutathione against the Histopatho-logical Changes Induced by Imidacloprid in the Liver and Testis of Japanese Quail," *The Egyptian Journal of Hospital Medicine*, Vol. 16, 2004, pp. 39-54.
- [29] P. A. Abhilash, R. Hari-krishnan and M. Indira, " Ascorbic Acid Supplementation Causes Faster Restoration of Reduced Glutathione Content in the Regression of Alcohol-Induced Hepatotoxicity in Male Guinea Pigs," *Redox Report*, Vol. 17, No. 2, 2012, pp. 72-79. doi: 10.1179/1351000212Y.0000000010
- [30] V. Rajamanickam and N. Muthuswamy, " Effect of Heavy Metals Induced Toxicity on Metabolic Biomarkers in Common Carp (*Cyprinus carpio* L.)," *Maejo International Journal of Science and Technology*, Vol. 2. No. 1, 2008, pp. 192-200.
- [31] M. M. El-Tohamy and W. S. El-Nattat, " Effect of Antioxidant on Lead-Induced Oxidative Damage and Reproductive Dysfunction in Male Rabbits," *Journal of American Science*, Vol. 6, No. 1, 2010, pp. 613-622.
- [32] P. Banerjee, S. S. Bhattacharyya and N. Bhattacharjee, " Ascorbic Acid Combats Arsenic-Induced Oxidative Stress in Mice Liver," *Ecotoxicology and Environmental Safety*, Vol. 72, No. 2, 2009, pp. 639-649. doi: 10.1016/j.ecoenv.2008.07.005
- [33] F. M. El-Demerdash, M. I Yousef and M. A. Zoheir, " Stannous Chloride Induces Alterations in Enzyme Activities, Lipid Peroxidation and Histopathology in Male Rabbit: Antioxidant Role of Vitamin C," *Food and Chemical Toxicology*, Vol. 43, No. 12, 2005, pp. 1743-1752. doi: 10.1016/j.fct.2005.05.017
- [34] M. I. Yousef, T. I. Awad, F. A. Elhag and F. A. Khaled, " Study of the Protective Effect of Ascorbic Acid against the Toxicity of Stannous Chloride on Oxidative Damage, Antioxidant Enzymes and Biochemical Parameters in Rabbits," *Toxicology*, Vol. 25, No. 3, 2007, pp. 194-202. doi: 10.1016/j.tox.2007.03.017
- [35] S. Gajawat, G. Sancheti and P. K. Goyal, " Vitamin C against Concomitant Exposure to Heavy Metal and Radiation: A Study on Variations in Hepatic Cellular Counts," *Asian Journal of Experimental Sciences*, Vol. 19, No. 2, 2005, pp. 53-58.
- [36] N. J. Chinoy, A. K. Sharma, T. N. Patel, R. Memon and D. D. Jhala Ahmedabad, " Recovery from Fluoride and Aluminium Induced Free Radical Liver Toxicity in Mice," *Fluoride*, Vol. 37, No. 4, 2004, pp. 257-263.
- [37] N. J. Chinoy, " Studies on Fluoride, Aluminium and Arsenic Toxicity in Mammals and Amelioration by Some Antidotes," In: G. Tripathi, Ed., *Modern Trends in Experimental Biology*, CBS Publisher, New Delhi, 2002, pp. 164-193.
- [38] A. Sharma and N. J. Chinoy, " Fluoride Induced Ultrastructural and Histopathological Changes in Liver of Mice and Its Reversal by Antidotes [Abstract]," *Proceedings of International Conference on Probing in Biological Systems*, Mumbai, 7-11 February 2000, p. 113.
- [39] P. Krishnamoorthy and M. Sangeetha, " Hepatoprotective Effect of Vitamin C on Sodium Nitrite-Induce Lipid Peroxidation in Albino Rats," *Indian Journal of Biochemistry and Biophysics*, Vol. 45, No. 3, 2008, pp. 206-208.

- [40] M. R. Al-shathly, M. I. Mujallid, E. A. Al-Sharif and M. M. Alqurashi, " The Preventive Effect of Vi-tamin C upon Added Methyl Tertiary Butyl Ether (MTBE) in Drinking Water on the Liver of Albino Mice," *International Journal of Research in Chemistry and Environment*, Vol. 2, No. 2, 2012, pp. 214-228.
- [41] K. M. Gaafa, M. M. Badawy and A. A. Hamza, " The Protective Effects of Ascorbic Acid, Cimetidine, and Nifedipine on Diethyldithiocarbamate-Induced Hepatic Toxicity in Albino Rats," *Drug and Chemical Toxicology*, Vol. 34, No. 4, 2011, pp. 405-419. doi:10.3109/01480545.2011.586035
- [42] O. Awodele, A. Akintowa, O. V. Osunkalu and H. A. Coker, " Modulatory Ac-tivity of Antioxidant against the Toxicity of Rifampicin in Vivo," *Instituto de Mediana Tropica de Sao Paulo*, Vol. 52, No. 1, 2010, pp. 43-46. doi:10.1590/S0036-46652010000100007
- [43] A. Mitra, V. C. Ravikumar, W. M. Bourn and D. R. Bourcier, " Influence of Ascorbic Acid Esters on Acetaminophen-Induced Hepatotoxicity in Mice," *Toxicological Letter*, Vol. 44, No. 1-2, 1988, pp. 39-46. doi:10.1016/0378-4274(88)90127-0
- [44] F. G. Peterson and R. G. Knodell, " Ascorbic Acid Protects against Acetaminophen- and Cocaine-Induced Hepatic Damage in Mice," *Drug-Nutrient Interactions*, Vol. 3, No. 1, 1984, pp. 33-41.
- [45] C. M. Remi?o, F. Milhazes, N. Borges, F. Fernandes, E. Carvalho and F. Bastos, " The Toxicity of N-Methyl-Alpha-Methyldopamine to Freshly Isolated Rat Hepatocytes Is Prevented by Ascorbic Acid and N-Acetylcysteine," *Toxicology*, Vol. 5, No. 2-3, 2004, pp. 193-203.
- [46] Y. Ergul, T. Erkan and H. Uzun, " Effect of Vi-tamin C on Oxidative Liver Injury Due to Isoniazid in Rats," *Pediatrics International*, Vol. 52, No. 1, 2010, pp. 69-74. doi:10.1111/j.1442-200X.2009.02891.x
- [47] A. Z. Karakilcik, A. Hayat, N. Aydilek, M. Zerir and M. Cay, " Effects of Vitamin C on Liver Enzymes and Biochemical Parameters in Rats Anesthetized with Halothane," *General Physiology and Bio-physics*, Vol. 24, No. 1, 2005, pp. 47-55.
- [48] S. Thakur and E. Maheswari, " Carbamazepine Provoked Hepatotoxicity: Attenu-ation by Vitamin C," *2nd International Conference on Medical, Biological and Pharmaceutical Sciences*, Singapore City, 28-29 April 2012.
- [49] M. H. Omar, E. A. Ahmed, S. Abdel-Ghafar, S. Mohammed and A. Y. Nasser, " Hepatoprotective Effects of Vitamin C, DPPD, and L-Cysteine against Cisplatin-Induced Oxidative Stress in Male Rats," *Journal of Biology and Earth Sciences*, Vol. 2, No. 1, 2012, pp. 28-36.
- [50] M. Mohsenikia, B. Hajipour, M. H. Somi, A. Khodadadi and M. Noori " Proph-ylactic Effect of Vitamin C on Cyclosporine A-induced Liver Toxicity," *Thrita Student Journal of Medical Science*, Vol. 1, No. 1, 2012, pp. 24-26.
- [51] S. W. Park and S. M. Lee, " An-tioxidant and Prooxidant Properties of Ascorbic Acid on Hepatic Dysfunction Induced by Cold Ischemia/Reperfusion," *European Journal of Pharmacology*, Vol. 580, No. 3, 2008, pp. 401-406. doi:10.1016/j.ejphar.2007.11.023
- [52] M. Y. Seo and S. M. Lee, " Protective Effect of Low Dose of Ascorbic Acid on He-patobiliary Function in Hepatic Ischemia/Reperfusion in Rats," *Journal of Hepatology*, Vol. 36, No. 1, 2002, pp. 72-77. doi:10.1016/S0168-8278(01)00236-7
- [53] H. Matsukawa, T. Yagi, H. Matsuda, H. Kawahara, I. Yamamoto, J. Matsuoka and N. Tanaka, " Ascorbic Acid 2-Glucoside Prevents Sinusoidal Endothelial Cell Apoptosis in Supercooled Preserved Grafts in Rat Liver Transplantation," *Transplantation Proceedings*, Vol. 32, No. 2, 2000, pp. 313-317. doi:10.1016/S0041-1345(99)00967-7
- [54] M. O. Taha, H. S. Souza, C. A. Carvalho, D. J. Faqundes, M. J. Simoes, N. J. Novo and A. Caricati-Neto, " Cytoprotective Effects of Ascorbic Acid on the Ischemia-Reperfusion Injury of Rat Liver," *Transplantation Proceedings*, Vol. 36, No. 2, 2004, pp. 296-300.
- [55] V. De Tata, S. Brizzi, M. Saviozzi, A. Lazzarotti, V. Fierabracci, G. Malvaldi and A. Casini, " Protective Role of Dehydroascorbate in Rat Liver Ischemia-Reperfusion Injury," *Journal of Surgical Research*, Vol. 123, No. 2, 2005, pp. 215-221. doi:10.1016/j.jss.2004.08.008
- [56] C. Rojas, S. Ca-denas, R. Pérez-Campo, M. López-Torres and G. Barja, " Effect of Vitamin C on Antioxidants, Lipid Peroxidation, and GSH System in the Normal Guinea Pig Heart," *Journal of Nutritional Science Vitaminology Tokyo*, Vol. 40, No. 5, 1994, pp. 411-420.
- [57] S. Cedenas C. Rojas and G. Barja, " Endotoxin Increases Oxidative Injury to Proteins in Guinea Pig

[58] G. Barja, M. López-Torres, R. Pérez-Campo, C. Rojas, S. Cadenas, J. Prat and R. Pamplona, "Dietary Vitamin C Decreases Endogenous Protein Oxidative Damage, Malondialdehyde, and Lipid Peroxidation and Maintains Fatty Acid Unsaturation in the Guinea Pig Liver," *Free Radical Biology and Medicine*, Vol. 17, No. 2, 1994, pp. 105-115. doi:10.1016/0891-5849(94)90108-2

[59] M. A. Ibrahim, G. O. Buhari and A. B. Aliyu, "Amelioration of Monosodium Glutamate-Induced Hepatotoxicity by Vitamin C," *European Journal of Scientific Research*, Vol. 60, No. 1, 2011, pp. 159-165.

[60] H. B. Calleja and R. H. Brooks, "Acute Hepatitis Treated with High Doses of Vitamin C Report of a Case," *Ohio State Medical Journal*, Vol. 56, 1960, pp. 821-823.

[61] G. G. Willis, "The Influences of Ascorbic Acid upon the Liver," *Canadian Medical Association Journal*, Vol. 76, 1957, p. 1044.

[62] C. A. Oyinbo, W. N. Dare, G. R. A. Okogun, L. C. Anyanwu, N. M. Ibeabuchi, C. C. Noronha and O. A. Okanlawon, "The Hepatoprotective Effect of Vitamin C and E on Hepatotoxicity Induced by Ethanol in Sprague Dawley Rats," *Pakistan Journal of Nutrition*, Vol. 5, No. 6, 2006, pp. 507-511. doi:10.3923/pjn.2006.507.511

[63] S. Ozdil, S. Bolkent, R. Yanardag and P. Arda-Pirincci, "Protective Effects of Ascorbic Acid, DL-Alpha-Tocopherol Acetate, and Sodium Selenate on Ethanol-Induced Liver Damage of Rats," *Biological Trace Element Research*, Vol. 97, No. 2, 2011, pp. 149-162. doi:10.1385/BTER:97:2:149

[64] Y. Yanadarg, O. OzsoySacan, S. Ozdil and S. Bolkent, "Combined Effects of Vitamin C, Vitamin E, and Sodium Selenate Supplementation on Absolute Ethanol-Induced Injury in Various Organs of Rats," *International Journal of Toxicology*, Vol. 26, No. 6, 2007, pp. 513-523. doi:10.1080/10915810701707296

[65] M. G. Shalan, D. H. Abdaliw and A. G. Shalan, "The Protective Efficacy of Vitamins (c and e), Selenium and Silymarin Supplements against Alcohol Toxicity," *World Rabbit Science*, Vol. 15, No. 2, 2007, pp. 103-110

[66] F. A. Morsy, A. Gamal el Din, N. M. Shaffie and M. A. Badawi, "Histopathologic Study of the Antiestrogenic Nolvadex Induced Liver Damage in Rats and Vitamins Ameliorative Effect," *Nature and Science*, Vol. 8, No. 5, 2010, pp. 1-15.

[67] A. R. Soylu, N. Aydogdu, U. N. Basaran, S. Altaner, O. Tarcin, N. Gedik, H. Umit, A. Tezel, G. Dokmeci, H. Baloglu, M. Ture, K. Kutlu and K. Kaymak, "Antioxidants Vitamin E and C Attenuate Hepatic Fibrosis in Biliary-Obstructed Rats," *World Journal of Gastroenterology*, Vol. 14, No. 12, 2006, pp. 6835-6841.

[68] C. Oliveira, L. C. Gayotto, C. Tatai, B. I. Della Nina, E. S. Lima, D. Abdalla and F. P. Lopasso, "Vitamin C and Vitamin E in Prevention of Nonalcoholic Fatty Liver Disease (NAFLD) in Choline Deficient Diet Fed Rats," *Nutrition Journal*, Vol. 2, No. 9, 2003, pp. 1-5.

[69] G. O. Gullek, S. O. Guek and E. Altuntas, "The Effects of Methydatheon on Liver: Role of Vitamin E and C," *Toxicology and Industrial Health*, Vol. 19, No. 2-6, 2003, pp. 63-67.

[70] M. Tawfik and N. Al-Badr, "Adverse Effects of Monosodium Glutamate on Liver and Kidney Functions in Adult Rats and Potential Protective Effect of Vitamins C and E," *Food and Nutrition Sciences*, Vol. 3, No. 5, 2012, pp. 651-659. doi:10.4236/fns.2012.35089

[71] M. Jurima-Rome, F. S. Abbott, W. Tang, H. S. Huang and L. W. Whitehouse, "Cytotoxicity of Unsaturated Metabolites of Valproic Acid and Protection by Vitamins C and E in Glutathione-Depleted Rat Hepatocytes," *Toxicology*, Vol. 112, No. 1, 1996, pp. 69-85. doi:10.1016/0300-483X(96)03352-5

[72] R. Sutcu, I. Altuntas, B. Yildirim, N. Karahan, H. Demirin and N. Delibas, "The Effects of Subchronic Methidathion Toxicity on Rat Liver: Role of Antioxidant Vitamins C and E," *Cell Biology and Toxicology*, Vol. 22, No. 3, 2006, pp. 221-227. doi:10.1007/s10565-006-0039-7

[73] D. Califima, "Histologic Examination of the Protective Effect of Vitamin E and C in Cisplatin-Induced Hepatotoxicity," *Trakya Universitesi Tip Fakultesi Dergisi*, Vol. 22, No. 3, 2005, pp. 124-131.

[74] F. E. Uboh, P. E. Ebong, H. D. Akpan and I. F. Usuh, "Hepatoprotective Effect of Vitamin C and E against Gasoline Vapour Induced Liver Injury in Male Rats," *Turkish Journal of Biology*, Vol. 36, 2012, pp. 217-223.

- [75] S. Y. A1-Awthan, A. M. A1-Douis, G. H. El-Sokkary and A. E. Aglan, " Dimethoate Induced Oxidative Stress and Morphological Changes in the Liver of Guinea Pig and the Protective Effect of Vitamin C and E," *Asian Journal of Biological sciences*, Vol. 5, No. 1, 2012, pp. 9-19.
- [76] A. J. Velaganni and C. Balasundaram, " Effect of Antioxidant A, Cand E and Their Analogues on Azo Dye Binding Proteins in Liver of Rats Treated with P-Dimethyla-minoazobenzene," *Indian Journal of Experimental Biology*, Vol. 48, 2010, pp. 373-377.
- [77] E. D. Eze, F. A. Dawud, A. A. Zainab, A. Jimoh, I. S. Malgwi and A. S. Isa, " Preliminary Studies of Effects of Vitamin C and Zinc on Some Liver En-zymes in Alloxan-Induced Diabetic Wistar Rats," *Asian Journal of Medical Sciences*, Vol. 4, No. 1, 2012, pp. 17-22.
- [78] K. Hamden, M. A. Boujbiha, H. Masmoudi, F. M. Ayadi, K. Ja-moussi and A. Elfeki, " Combined Vitamins (C and E) and In-sulin Improve Oxidative Stress and Pancreatic and Hepatic Injury in Alloxan Diabetic Rats," *Biomedicine and Pharma-cotherapy*, Vol. 63, No. 2, 2009, pp. 95-99. doi:10.1016/j.biopha.2008.02.001
- [79] D. Samir, Z. Kechrid and M. R. Djabar, " Combined Protective Effect of Zinc and Vitamin C on Nickel-Induced Oxidative Liver Injury in Rats," *Annals of Biological Research*, Vol. 3, No. 7, 2010, pp. 3278-3286.
- [80] R. Patra, D. Swarup and S. Dwivedi, " Anti-oxidant Effects of Tocopherol, Ascorbic Acid and L-Methionine on Lead Induced Oxidative Stress to the Liver, Kidney and Brain in Rats," *Toxicology*, Vol. 162, No. 2, 2001, pp. 81-88. doi:10.1016/S0300-483X(01)00345-6
- [81] K. Ramanathan, B. Balakumar and C. Panneerselvam, " Effects of Ascorbic Acid and Alpha Tocopherol on Arsenic Induced Oxidative Stress," *Human Experimental Toxicology*, Vol. 21, No. 12, 2002, pp. 675-680. doi:10.1191/0960327102ht307oa
- [82] M. G. Shalana, M. S. Mostafa and M. M. Hassouna, " Amelioration of Lead Toxicity on Rat Liver with Vitamin C and Silymarin Supplements," *Toxicology*, Vol. 206, 2005, pp. 1-15. doi:10.1016/j.tox.2004.07.006
- [83] K. K. Das, S. N. Das and S. Das Gupta, " The Influence of Ascorbic Acid on Nickel Induced Hepatic Lipid Peroxidation on Rats," *Journal of Basic and Clinical Physiology and Pharmacology*, Vol. 12, No. 3, 2001, pp. 187-195. doi:10.1515/JBCPP.2001.12.3.187
- [84] K. Chen, J. Suh and A. C. Carr, " Vitamin C Suppresses Oxidative Lipid Damage in Vivo, Even in the Presence of iron Overload," *American Journal of Physiology, Endocrinology and Metabolism*, Vol. 279, No. 6, 2000, pp. 1406-1412.
- [85] M. Sabzevarizadeh and H. Najafzadeh, " Comparison Effect of Silymarin and Vitamin C on Liver Function in Myoglobinuric Status in Rats," *World Applied Sciences Journal*, Vol. 17, No. 2, 2012, pp. 228-232.
- [86] S. J. Flora, M. Pande and A. Mehta, " Beneficial Effect of Combined Administration of Some Naturally Occurring Antioxidants (Vitamins) and Thiol Chelators in the Treatment of Chronic Lead Intoxication," *Chemico-Biological Interactions*, Vol. 145, No. 3, 2003, pp. 267-280.
- [87] S. A. Harrison, S. Torgerson, P. Hayashi, J. Ward and S. Schenker, " Vitamin E and Vitamin C Treatment Improves Fibrosis in Patients with Nonalcoholic Steatohepatitis," *American Journal of Gastroenterology*, Vol. 98, No. 11, 2003, pp. 2485-2490. doi:10.1111/j.1572-0241.2003.08699.x
- [88] G. Ersoz, F. Gun-sar, Z. Karasu and S. Akay, " Management of Fatty Liver Disease with Vitamin E and C Compared to Ursodeoxycholic Acid Treatment," *Turkish Journal of Gastroenterology*, Vol. 16, No. 3, 2005, pp. 124-128.
- [89] M. Babich, " Efficacy of Vitamin E and Vitamin C in the Treatment of Nonalcoholic Steatohepatitis," *Practical Gastroenterology*, 2010, pp. 20-27.
- [90] M. M. Attia, A. M. Sayed, F. A. Ibrahim, A. S. Mohammed and M. S. El-Alfy, " Effects of Antioxidant Vitaminson the Oxi-dant/Antioxidant Status and Liver Function in Homozygous Beta-Thalassemia," *Romanian Journal of Biophysics*, Vol. 21, No. 2, 2011, pp. 93-106.
- [91] T. Foster, M. J. Budoff, S. Saab, N. Ahmadi, C. Gordon and A. D. Guerci, " Atorvastatin and Antioxidants for the Treatment of Nonalcoholic Fatty Liver Disease: The St. Francis Heart Study Randomized Clinical Trial," *American Journal of Gastroenterology*, Vol. 106, 2011, pp. 71-77. doi:10.1038/ajg.2010.299

[92] S. J. Padayatty and A. Katz Y. Wang, P. Eck, O. Kwon, P. Eck, O. Kwon, J. H. Lee, S. Chen, C. Corpe, A. Dutta, S. K. Dutta and M. Levine, " Vitamin C as an Antioxidant: Evaluation of Its Role in Disease Prevention," Journal of the American College of Nutrition, Vol. 22, No. 1, 2003, pp. 18-35.

[93] B. Frei, L. England and B. N. Ames, " Ascorbate Is an Outstanding Antioxidant in Human Blood Plasma," Proceedings of the Natural Academy of Sciences, Vol. 86, No. 16, 1989, pp. 6377-6381.