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The Role of Galactose-induced Oxidative Stress on Cellular Aging: A Literature Review

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Abstract: Aging is a complex process impacted by both internal and external causes. Nutrition is a crucial extrinsic factor in the development of aging and degenerative disorders. D-galactose is involved in many aging mechanisms in the brain, heart, liver, kidney, and skin. Galactose-induced cellular aging is primarily caused by oxidative stress. Production of ROS can damage proteins, lipids, and DNA. The recommended daily dietary limit for D-galactose is 50 grams for healthy people who can completely remove it within 8 hours. An in vivo study revealed that consuming 150 mg/kg/day of galactose led to metabolic issues, heightened blood pressure, and disrupted cardiac sympathovagal balance. These outcomes resulted from compromised cardiac mitochondrial activity, elevated oxidative stress, inflammation, and mitochondrial dysfunction, which caused cell death and eventually cardiac failure. A diet high in carbohydrates, particularly those derived from dairy products and their derivatives, can lead to the accumulation of galactose and its metabolites within cells. This buildup subsequently increases reactive oxygen species and reduces antioxidant capacity, resulting in mitochondrial dysfunction and heightened oxidative and osmotic stress. The culmination of these processes is a decline in cellular function, senescence, and accelerated organ aging.

Keywords: Cellular aging, Galactose, Molecular, Nutrition, Oxidative stress

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Introduction

The global population is increasingly aging biologically, leading to a rise in degenerative diseases. Aging, defined as a gradual decline in the body's physiological functions, is a major risk factor for the progression of degenerative conditions, including cardiovascular diseases, neurodegenerative disorders, and the decline of organ function (Bo-Htay et al., 2018; Niccoli & Partridge, 2012). Aging is a complex process influenced by various intrinsic and extrinsic factors (Farage et al., 2008). Nutrition plays a critical extrinsic factor in the onset of aging and degenerative diseases. An unbalanced and high in carbohydrates diet has been associated with the development of obesity and related metabolic

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syndromes (Umbayev et al., 2020).

Galactose is a monosaccharide sharing the same chemical formula as glucose, $C_6H_{12}O_6$. However, it differs from glucose in the position of the hydroxyl group on the fourth carbon atom (Williams, 2003). In nature, it exists as two optical isomers: L-galactose and D-galactose, but humans can only digest the D-form due to enzyme specificity (Umbayev et al., 2020). Galactose plays vital roles in various physiological processes, including the galactosylation of ceramides involved in myelin sheath formation in Schwann cells, the synthesis of heparin and heparin sulfate, lactose production during breastfeeding, and serving as a substitute for glycolipids (cerebrosides), proteoglycans, and glycoproteins (Chichlowski et al., 2011; Mills et al., 2011; Prado & Dewey, 2014). Notably, galactosylceramide is the predominant glycosphingolipid in the brain and nervous tissue, although it is present in smaller amounts in other tissues (Bender & Mayes, 2018).

Oxidative stress occurs when the balance between oxidation and antioxidant defenses is disrupted, leading to increased production of reactive oxygen species (ROS). This imbalance damages cellular components, including DNA, proteins, and lipids (Jiang et al., 2016). Usually, ROS levels are kept in check by antioxidant systems, including non-enzymatic factors and enzymes like glutathione peroxidase (GSH-Px), catalase (CAT), and superoxide dismutase (SOD) (Yahata & Hamaoka, 2017).

Numerous studies have established the link between types of sugar and the acceleration of cellular aging (Noordam et al., 2013). Galactose (especially D-galactose) is a more potent glycation agent than glucose, thus having a higher capability of inducing oxidative stress (Budni et al., 2016; Delwing-de Lima et al., 2017). This review discusses how galactose induces oxidative stress, ultimately contributing to cellular aging and organ dysfunction.

Galactose

Structure

Monosaccharides (glucose, galactose, fructose) are important dietary components mainly serving as energy sources. Enzymes converted more complex saccharides into monosaccharides for energy and other vital functions. Louis Pasteur first identified galactose in milk in 1856, naming it "lactose"—later known as "galactose"—from the Greek "galakt," meaning "milk". Galactose is a natural aldohexose prevalent in nature as D-Galactose and, together with glucose, forms the disaccharide lactose (Coelho et al., 2015). As an aldohexose, galactose contains an aldehyde group on carbon 1, with the other end attached to a hydroxyl group. Notably, galactose is an epimer of glucose at carbon 4 (Qi & Tester, 2019).

Dietary Sources of Galactose

The primary source of galactose is disaccharide lactose. Type of sugar exclusively present in milk, including breast milk. Consequently, after weaning, dietary lactose comes from dairy products. Certain dairy products contain lower levels of lactose than whole milk because lactose is enzymatically broken down by microbes used during production (Williams, 2003). Additionally, sources of free galactose beyond milk include fruits and vegetables such as tomatoes, Brussels sprouts, bananas, and apples (Acosta & Gross, 1995). Lactose can also be enzymatically hydrolyzed to produce lactose hydrolysate syrup, which comprises lactose, glucose, and galactose. This syrup is utilized as a sweetening agent in the manufacture of biscuits, confectionery, and milk-based snacks, thereby indicating that galactose is present in foods beyond those derived solely from milk (Qi & Tester, 2019).

The galactose content in milk varies significantly among mammalian species, reflecting adaptations to their environments and the nutritional needs of their infants (Chichlowski et al., 2011; Georgi et al., 2013). Human milk is distinct in its sugar composition, containing 55-70 g/L of lactose and 5-8 g/L of complex oligosaccharides (Coelho et al., 2015). Over 100 different oligosaccharide structures are present in breast milk, with galactose being the predominant component (Mills et al., 2011). This sugar level is maintained due to its critical role in infant development, including postnatal processes such as myelin sheath formation on nerve cells, providing a prebiotic defense mechanism, and serving as a vital energy source (Chichlowski et al., 2011; Mills et al., 2011; Prado & Dewey, 2014). Lactose supplies about 40% of an infant's energy and makes up 90% of their total daily sugar intake (Coelho et al., 2015).

Galactose can also be produced naturally within human cells (Umbayev et al., 2020). A 70 kg adult male can synthesize approximately 2 grams of galactose daily (Berry et al., 1995). This endogenous production occurs via the hydrolysis of glycoproteins, glycolipids, and proteoglycans that contain galactose groups in lysosomes (Coelho et al., 2015).

The FDA recommends a daily intake limit of 50 grams of added sugar (including galactose) for healthy adults (Bo-Htay et al., 2018). When galactose metabolism enzymes function correctly, the body can efficiently process galactose within 8 hours after

consumption. Elevated galactose levels may result from two main mechanisms: (a) higher consumption of foods containing galactose, and (b) genetic mutations causing metabolic disorders in enzymes of the Leloir pathway (Lai et al., 2009). Research has shown that D-galactose also influences the aging process in living organisms. Numerous studies indicate that D-galactose plays a significant role in aging mechanisms across brain, heart, liver, kidney, and skin cells (Umbayev et al., 2020).

Absorption and Metabolism

Galactose is attached to complex molecules and must be broken down before absorption. This process is facilitated by *lactase*, a *disaccharidase* primarily located in the brush border of the small intestine's mucosal epithelial cells. Human lactase functions optimally at a pH of 5.5-6, which corresponds to the pH of the jejunum. Although minor absorption of monosaccharides can also happen in the duodenum and ileum, this is less common (Williams, 2003).

Apical cells (brush border) and basolateral membranes of enterocytes in the small intestine lumen, particularly within the jejunum, contain specific transporter proteins that facilitate the absorption of monosaccharides (Wright et al., 2012). Glucose and galactose share the same carrier; therefore, disruption of this carrier impairs the absorption of both compounds (Qi & Tester, 2019). The rate of monosaccharide absorption in the intestinal lumen varies; several studies indicate that galactose and glucose are absorbed significantly faster than other monosaccharides. Furthermore, galactose is absorbed slightly more rapidly than glucose (Bender, 2003). It is noteworthy that galactose absorption is an active process requiring ATP and can be inhibited by metabolic inhibitors (Williams, 2003).

Specific transporters responsible for monosaccharide absorption in the small intestine include isoforms of sodium-driven sugar co-transporters (SGLTs) and concentration gradient-dependent glucose transporters (GLUTs) (Qi & Tester, 2019). Galactose is absorbed through co-transport with sodium ions via SGLT1 and enters the circulation by diffusion through GLUT1 (Bender & Mayes, 2018).

Galactose metabolism occurs primarily via the Leloir pathway, converting galactose into glucose-1-phosphate, which then enters glycolysis. The intermediates from this process are utilized in glycogen formation, mucopolysaccharide production, and glycoprotein synthesis. This pathway primarily takes place in the cytoplasm, especially in the hepatocite (Holden et al., 2003). An alternative route, known as the Isselbacher pathway, metabolizes galactose-1-phosphate, a toxic byproduct, by reducing it to galactitol and converting it to galacturonic acid via dehydrogenation (Coelho et al., 2015). A deficiency in this pathway, called galactosemia, results in the buildup of galactose-1-phosphate in tissues, leading to liver problems, cataracts, intellectual disability, and growth failure (Bender & Mayes, 2018).

Before entering the Leloir pathway, β-galactose is converted into α-galactose by the enzyme galactose mutarotase (GALM; enzyme 1). Afterward, once in the path, α-galactose is phosphorylated to galactose-1-phosphate (Gal-1-P) by galactokinase (GALK; enzyme 2). The enzyme galactose-1-phosphate uridylyltransferase (GALT; enzyme 3) then transfers the uridine monophosphate (UMP) group from UDP-Glucose (UDP-glc) to Gal-1-P, producing glucose-1-phosphate (Glc-1-P) and UDP-galactose (UDP-gal). In the third step of the Leloir pathway, UDP-galactose 4'-epimerase (GALE; enzyme 4) catalyzes the reversible conversion between UDP-galactose and UDP-glucose. Both nucleotides act as donors in glycosylation reactions, which play a significant biological role in glycoconjugate production. The formation of Glc-1-P is crucial in the production of Glc-6-P and glucose (Umbayev et al., 2020). Alternative to the Leloir pathway, aldose reductase (enzyme 5) converts galactose to galactitol, galactose dehydrogenase (enzyme 6) converts galactose to galactose, and UDP-glucose pyrophosphorylase (UGP; enzyme 7) converts Gal-1-P to UDP-gal (Bender & Mayes, 2018).

Biological Functions

Galactose is involved in the galactosylation of ceramides during the formation of myelin sheaths in Schwann cells, as well as in the synthesis of heparin and heparin sulfate. It also contributes to lactose production during breastfeeding and can serve as a substitute for glycolipids (such as cerebrosides), proteoglycans, and glycoproteins. The main glycosphingolipid in the brain and nervous tissues is galactosylceramide, although it appears in smaller amounts in other tissues (Bender & Mayes, 2018).

The glycaemic index is a system for classifying carbohydrate-rich foods based on their effect on blood sugar levels. Foods that digest more slowly lead to smaller blood sugar spikes, resulting in a lower overall glycaemic index. An index of 70 or higher is considered high, 56-69 is medium, and 55 or below is low. Glucose has a glycaemic index of 100. Lactose's glycaemic index is significantly lower

than sucrose's, which reflects the glycaemic index of galactose (Qi & Tester, 2019).

Overconsumption of plant-derived sugars or those produced by the hydrolysis of polysaccharides is considered to have adverse health effects. During commercial extraction, hydrolysis, or purification of starch, other dietary components such as fiber, minerals, vitamins, proteins, antioxidants, and others are typically omitted. Consequently, the energy source becomes more concentrated and is absorbed more readily by the intestines. This perspective, however, does not extend to sugars naturally present in fruits and vegetables (Qi & Tester, 2019). Health issues related to sugar typically include dental problems, obesity, diabetes, and deficiencies in nutrients that are not commonly found in carbohydrate-rich foods (Goldenberg & Punthakee, 2013).

Galactose and Oxidative Stress

Galactose-induced cellular aging mainly results from oxidative stress and a weakened antioxidant system (Bo-Htay et al., 2018). This heightened oxidative stress leads to increased production of lipid peroxides. The damage caused by galactose buildup involves hydrogen peroxide and superoxide anions, produced by excessive galactose metabolism, which accelerate aging (Aydin et al., 2012; Yanar et al., 2011). An excess of ROS can damage proteins, lipids, and DNA through peroxidation. Redox homeostasis disruption due to increased ROS formation is a main feature of the aging process (Li et al., 2016; Liang et al., 2017).

D-Galactose is a reducing sugar that, when accumulated, reacts with proteins and amino acids to create unstable Schiff bases (Wu et al., 2017). If this state persists for several months, the Schiff bases can solidify and converted into Advanced Glycation End-products (AGEs) (Hegab et al., 2012). When AGEs attach to their receptors (RAGEs) in numerous organs, they activate the nuclear factor kappa-B (NF-κB) pathway, causing inflammation and the formation of reactive oxygen species (Frimat et al., 2017).

A rat study revealed that consuming 150 mg/kg/day of galactose led to metabolic issues, heightened blood pressure, and disrupted cardiac sympathovagal balance. These outcomes resulted from compromised cardiac mitochondrial activity, elevated oxidative stress, inflammation, and mitochondrial dysfunction, which caused cell death and eventually cardiac failure (Bo-Htay et al., 2018).

The accumulation of galactose also reduces the myocardial antioxidant capacity, particularly affecting thiol groups, including non-protein thiol groups (Cebe et al., 2014; Chang et al., 2017). Concurrently, there is an elevation in protein oxidation products, including protein carbonyl groups, dityrosine-bound proteins, and kynurenine (Umbayev et al., 2020)

Persistent oxidative stress induced by D-galactose also diminishes the antioxidant capacity of ferric ions and decreases the activity of Cu-Zn superoxide dismutase (SOD) (Chang et al., 2017; Wu et al., 2017). An elevation in lipid peroxide markers, including lipid hydroperoxides, conjugated dienes, and malondialdehyde, is observed with six weeks of D-galactose administration in rats (Baraibar et al., 2012; Bo-Htay et al., 2018; Eaton et al., 2001).

Mitochondria serve as the primary targets and producers of reactive oxygen species (ROS). Damage inflicted by ROS results in mitochondrial dysfunction, which, in turn, leads to increased ROS production. The activation of nicotinamide adenine dinucleotide phosphate (NADPH) oxidase (Nox) promotes excessive generation of ROS (Chang et al., 2017). Additionally, galactose diminishes oxidative phosphorylation efficiency by reducing the transmembrane potential, decreasing ATP synthesis, and altering respiratory function. Prolonged exposure to galactose results in a reduction in mitochondrial quantity and a decline in mitochondrial DNA copies, indicating mitochondrial DNA damage (Aydin et al., 2011).

Another mechanism involves the build-up of galactose, leading to osmotic shock in cells. This occurs because galactitol accumulates, which should typically be metabolized into Gal-1-P. The excess galactitol activates aldose reductase, depletes the NADPH system, and reduces glutathione reductase activity. Such a build-up can also alter the cellular oxidative balance (Kubo et al., 1999).

D-galactose within the cell is enzymatically converted by galactose reductase into galactitol, which may induce osmotic stress. Elevated D-galactose levels can be oxidized by galactose oxidase to hydrogen peroxide, and increased hydrogen peroxide concentrations can reduce antioxidant enzyme activity. Furthermore, d-galactose can initiate non-enzymatic glycation, leading to the formation of advanced glycation end products (AGEs) over weeks or months. Accumulated AGEs interact with their receptor (RAGE), and the activation of NADPH can generate reactive oxygen species (ROS) (Askarova et al., 2013; Wautier et al., 2001).

In galactose metabolism disorders, Gal-1-P accumulates in various tissues, leading to increased nitric oxide and iNOS levels. Additionally, increased Gal-1-P impairs the conversion of inositol

phosphate to inositol, which is involved in antioxidant activity (Umbayev et al., 2020).

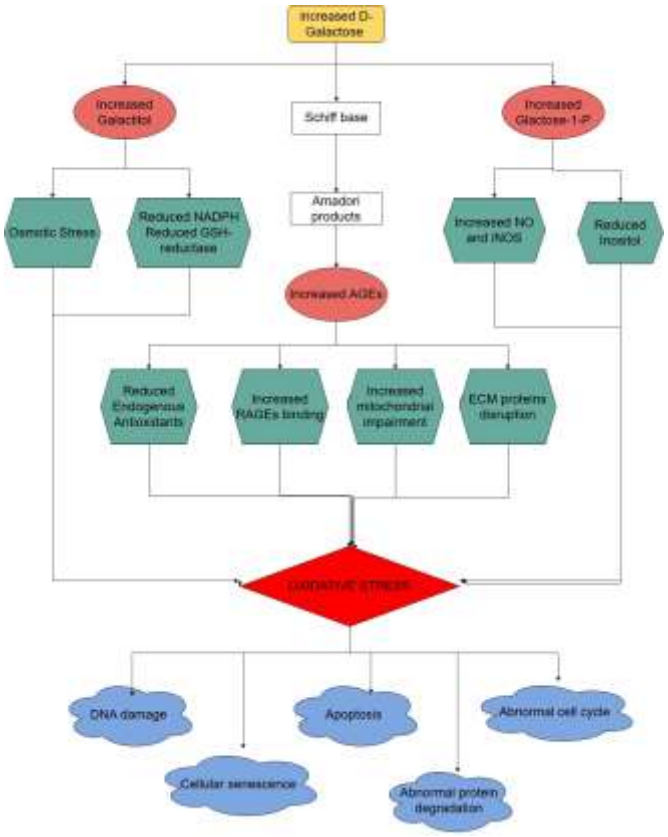

Figure 1. Summary of the Mechanism of Cellular Aging by D-Galactose (modified from (Bo-Htay et al., 2018; Umbayev et al., 2020)

Conclusion

A diet high in carbohydrates, particularly those derived from dairy products, may lead to the accumulation of galactose and its metabolites within cells. This accumulation increases reactive oxygen species and reduces antioxidant capacity, resulting in mitochondrial dysfunction and elevated oxidative stress. Consequently, these effects contribute to a decline in cellular function, increased senescence, and accelerated organ aging. Further research is essential to assess the risks and benefits of milk and dairy products for patients with chronic conditions.

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Conflict of Interest

The authors declare that they have no conflict of interest.

References

Acosta, P. B., & Gross, K. C. (1995). Hidden sources of galactose in the environment. *European Journal of Pediatrics*, *154*(7 Suppl 2). https://doi.org/10.1007/BF02143811

Askarova, S., Tsoy, A., & Lee, J. C.-M. (2013). RAGE targeted strategies for Alzheimer's amyloid β peptide induced blood-brain barrier dysfunctions. *Molecular Neurodegeneration*, *8*(Suppl 1), P5. https://doi.org/10.1186/1750-1326-8-S1-P5

Aydin, S., Yanar, K., Atukeren, P., Dalo, E., Sitar, M. E., Uslu, E., Caf, N., & Çkatay, U. (2011). Comparison of oxidative stress biomarkers in renal tissues of d-galactose-induced, naturally aged, and young rats. *Biogerontology 2011 13:3*, *13*(3), 251–260. https://doi.org/10.1007/S10522-011-9370-3

Baraibar, M. A., Liu, L., Ahmed, E. K., & Friguet, B. (2012). Protein oxidative damage at the crossroads of cellular senescence, aging, and age-related diseases. *Oxidative Medicine and Cellular Longevity*, *2012*. https://doi.org/10.1155/2012/919832

Bender, D. A. (2003). GLUCOSE | Function and Metabolism. *Encyclopedia of Food Sciences and Nutrition*, 2904–2911. https://doi.org/10.1016/B0-12-227055-X/00558-7

Bender, D. A., & Mayes, P. A. (2018). Carbohydrates of Physiological Significance. In V. W. Rodwell, D. A. Bender, K. M. Botham, P. J. Kennelly, & P. A. Weil (Eds.), *Harper's Illustrated Biochemistry* (31st ed., pp. 141–149). McGraw-Hill Education.

Berry, G. T., Nissim, I., Lin, Z., Mazur, A. T., Gibson, J. B., & Segal, S. (1995). Endogenous synthesis of galactose in normal men and patients with hereditary galactosaemia. *The Lancet*, *346*(8982), 1073–1074. https://doi.org/10.1016/S0140-6736(95)91745-4

Bo-Htay, C., Palee, S., Apaijai, N., Chattipakorn, S. C., & Chattipakorn, N. (2018). Effects of <scp>d</scp> -galactose-induced ageing on the heart and its potential interventions. *Journal of Cellular and Molecular Medicine*, *22*(3), 1392–1410. https://doi.org/10.1111/jcmm.13472

Budni, J., Pacheco, R., da Silva, S., Garcez, M. L., Mina, F., Bellettini-Santos, T., de Medeiros, J., Voss, B. C., Steckert, A. V., Valvassori, S. da S., & Quevedo, J. (2016). Oral administration of D-galactose induces cognitive impairments and oxidative damage in rats. *Behavioural Brain Research*, *302*, 35–43. https://doi.org/10.1016/j.bbr.2015.12.041

Cebe, T., Yanar, K., Atukeren, P., Ozan, T., Kuruç, A. I., Kunbaz, A., Sitar, M. E., Mengi, M., Aydın, M. Ş., Eşrefoğlu, M., Aydın, S., & Çakatay, U. (2014). A

comprehensive study of myocardial redox homeostasis in naturally and mimetically aged rats. *AGE 2014 36:6*, *36*(6), 9728-. https://doi.org/10.1007/S11357-014-9728-Y

Chang, Y. M., Chang, H. H., Lin, H. J., Tsai, C. C., Tsai, C. Te, Chang, H. N., Lin, S. L., Padmaviswanadha, V., Chen, R. J., & Huang, C. Y. (2017). Inhibition of Cardiac Hypertrophy Effects in D-Galactose-Induced Senescent Hearts by Alpinate Oxyphyllae Fructus Treatment. *Evidence-Based Complementary and Alternative Medicine : ECAM*, *2017*. https://doi.org/10.1155/2017/2624384

Chichlowski, M., German, J. B., Lebrilla, C. B., & Mills, D. A. (2011). The influence of milk oligosaccharides on microbiota of infants: opportunities for formulas. *Annual Review of Food Science and Technology*, *2*, 331–351. https://doi.org/10.1146/ANNUREV-FOOD-022510-133743

Coelho, A. I., Berry, G. T., & Rubio-Gozalbo, M. E. (2015). Galactose metabolism and health. *Current Opinion in Clinical Nutrition and Metabolic Care*, *18*(4), 422–427. https://doi.org/10.1097/MCO.0000000000000189

Delwing-de Lima, D., Hennrich, S. B., Delwing-Dal Magro, D., Aurélio, J. G. M., Serpa, A. P., Augusto, T. W., & Pereira, N. R. (2017). The effect of d-galactose induced oxidative stress on in vitro redox homeostasis in rat plasma and erythrocytes. *Biomedicine & Pharmacotherapy = Biomedecine & Pharmacotherapie*, *86*, 686–693. https://doi.org/10.1016/J.BIOPHA.2016.12.011

Eaton, P., Hearse, D. J., & Shattock, M. J. (2001). Lipid hydroperoxide modification of proteins during myocardial ischaemia. *Cardiovascular Research*, *51*(2), 294–303. https://doi.org/10.1016/S0008-6363(01)00303-0

Farage, M. A., Miller, K. W., Elsner, P., & Maibach, H. I. (2008). Intrinsic and extrinsic factors in skin ageing: a review. *International Journal of Cosmetic Science*, *30*(2), 87–95. https://doi.org/10.1111/J.1468-2494.2007.00415.X

Frimat, M., Daroux, M., Litke, R., Nevière, R., Tessier, F. J., & Boulanger, E. (2017). Kidney, heart and brain: three organs targeted by ageing and glycation. *Clinical Science (London, England : 1979)*, *131*(11), 1069–1092. https://doi.org/10.1042/CS20160823

Georgi, G., Bartke, N., Wiens, F., & Stahl, B. (2013). Functional glycans and glycoconjugates in human milk. *American Journal of Clinical Nutrition*, *98*(2). https://doi.org/10.3945/ajcn.112.039065

Goldenberg, R., & Punthakee, Z. (2013). Definition, Classification and Diagnosis of Diabetes, Prediabetes and Metabolic Syndrome. *Canadian Journal of Diabetes*, *37*(SUPPL.1). https://doi.org/10.1016/j.jcjd.2013.01.011

Hegab, Z., Gibbons, S., Neyses, L., & Mamas, M. A. (2012). Role of advanced glycation end products in cardiovascular disease. *World Journal of Cardiology*, *4*(4), 90. https://doi.org/10.4330/WJC.V4.I4.90

Holden, H. M., Rayment, I., & Thoden, J. B. (2003). Structure and Function of Enzymes of the Leloir Pathway for Galactose Metabolism. *Journal of Biological Chemistry*, *278*(45), 43885–43888. https://doi.org/10.1074/jbc.R300025200

Jiang, T., Sun, Q., & Chen, S. (2016). Oxidative stress: A major pathogenesis and potential therapeutic target of antioxidative agents in Parkinson's disease and Alzheimer's disease. *Progress in Neurobiology*, *147*, 1–19. https://doi.org/10.1016/j.pneurobio.2016.07.005

Kubo, E., Miyoshi, N., Fukuda, M., & Akagi, Y. (1999). Cataract Formation through the Polyol Pathway is associated with Free Radical Production. *Experimental Eye Research*, *68*(4), 457–464. https://doi.org/10.1006/EXER.1998.0624

Lai, K., Elsas, L. J., & Wierenga, K. J. (2009). Galactose toxicity in animals. *IUBMB Life*, *61*(11), 1063–1074. https://doi.org/10.1002/IUB.262

Li, X., Zhang, Y., Yuan, Y., Sun, Y., Qin, Y., Deng, Z., & Li, H. (2016). Protective Effects of Selenium, Vitamin E, and Purple Carrot Anthocyanins on D-Galactose-Induced Oxidative Damage in Blood, Liver, Heart and Kidney Rats. *Biological Trace Element Research*, *173*(2), 433–442. https://doi.org/10.1007/S12011-016-0681-8

Liang, C. yan, Liang, Y. min, Liu, H. zhen, Zhu, D. mei, Hou, S. zhen, Wu, Y. yun, Huang, S., & Lai, X. ping. (2017). Effect of Dendrobium officinale on D-galactose-induced aging mice. *Chinese Journal of Integrative Medicine 2017*, 1–9. https://doi.org/10.1007/S11655-016-2631-X

Mills, S., Ross, R. P., Hill, C., Fitzgerald, G. F., & Stanton, C. (2011). Milk intelligence: Mining milk for bioactive substances associated with human health. *International Dairy Journal*, *21*(6), 377–401. https://doi.org/10.1016/J.IDAIRYJ.2010.12.011

Niccoli, T., & Partridge, L. (2012). Ageing as a Risk Factor for Disease. *Current Biology*, *22*(17), R741–R752. https://doi.org/10.1016/J.CUB.2012.07.024

Noordam, R., Gunn, D. A., Tomlin, C. C., Maier, A. B., Mooijaart, S. P., Slagboom, P. E., Westendorp, R. G. J., De Craen, A. J. M., & Van Heemst, D. (2013). High serum glucose levels are associated with a higher perceived age. *Age (Dordrecht, Netherlands)*, *35*(1), 189–195. https://doi.org/10.1007/S11357-011-9339-9

Prado, E. L., & Dewey, K. G. (2014). Nutrition and brain development in early life. *Nutrition Reviews*, *72*(4), 267–284. https://doi.org/10.1111/NURE.12102

Qi, X., & Tester, R. F. (2019). Fructose, galactose and glucose – In health and disease. *Clinical Nutrition ESPEN*, *33*, 18–28. https://doi.org/10.1016/j.clnesp.2019.07.004

Umbayev, B., Askarova, S., Almabayeva, A., Saliev, T., Masoud, A. R., & Bulanin, D. (2020). Galactose-Induced Skin Aging: The Role of Oxidative Stress. *Oxidative Medicine and Cellular Longevity*, *2020*(1), 7145656. https://doi.org/10.1155/2020/7145656

Wautier, M. P., Chappey, O., Corda, S., Stern, D. M., Schmidt, A. M., & Wautier, J. L. (2001). Activation of NADPH oxidase by AGE links oxidant stress to altered gene expression via RAGE. *American Journal of Physiology. Endocrinology and Metabolism*, *280*(5). https://doi.org/10.1152/AJPENDO.2001.280.5.E685

Williams, C. A. (2003). GALACTOSE. *Encyclopedia of Food Sciences and Nutrition*, 2843–2846. https://doi.org/10.1016/B0-12-227055-X/00544-7

Wright, E. M., Sala-Rabanal, M., Loo, D. D. F., & Hirayama, B. A. (2012). Sugar Absorption. *Physiology of the Gastrointestinal Tract, Two Volume Set*, 1583–1593. https://doi.org/10.1016/B978-0-12-382026-6.00058-0

Wu, W., Hou, C. L., Mu, X. P., Sun, C., Zhu, Y. C., Wang, M. J., & Lv, Q. Z. (2017). H2S Donor NaHS Changes the Production of Endogenous H2S and NO in D-Galactose-Induced Accelerated Ageing. *Oxidative Medicine and Cellular Longevity*, *2017*. https://doi.org/10.1155/2017/5707830

Yahata, T., & Hamaoka, K. (2017). Oxidative stress and Kawasaki disease: how is oxidative stress involved from the acute stage to the chronic stage? *Rheumatology (Oxford, England)*, *56*(1), 6–13. https://doi.org/10.1093/RHEUMATOLOGY/KEW044

Yanar, K., Aydin, S., Çakatay, U., Mengi, M., Buyukpinarbaşili, N., Atukeren, P., Sitar, M. E., Sönmez, A., & Uslu, E. (2011). Protein and DNA oxidation in different anatomic regions of rat brain in a mimetic ageing model. *Basic & Clinical Pharmacology & Toxicology*, *109*(6), 423–433. https://doi.org/10.1111/J.1742-7843.2011.00756.X