

## Documents

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**Unveiling the impact of *Chlorella vulgaris* supplementation on liver metabolisms of aged rats – A preclinical study** (2024) *Journal of Functional Foods*, 121, art. no. 106383, .

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**Abstract**

*Chlorella vulgaris* is renowned for its rich nutritional composition and has been associated with various health benefits. This study aimed to look into the effect of CV on liver metabolomes and metabolic pathways in aged Sprague Dawley (SD) rats. Three and 21-month-old male SD rats were divided into control and treated groups. Results showed that carbohydrates such as maltose/lactose and mannose/fructose were downregulated in old rats. These metabolites were downregulated in young rats supplemented with CV. Interestingly, taurine was upregulated in old rats, while the trend was reversed in old rats supplemented with CV at 300 mg/kg/d. The differentially expressed metabolites in different age groups and CV supplementation were mapped to starch and sucrose metabolism, galactose metabolism, and taurine and hypotaurine metabolism. Further research is needed to understand the long-term effects of CV supplementation on ageing and determine optimal dosage levels, especially regarding its potential to mitigate age-related diseases. © 2024 The Author(s)

**Author Keywords**

Ageing; *Chlorella vulgaris*; Liquid Chromatography-Mass Spectrometry; Liver; Metabolomics

**References**

- (2020), World Health Organisation Decade of healthy ageing: The global strategy and action plan on ageing and health 2016–2020: Towards a world in which everyone can live a long and healthy life: Report by the director-general. Geneva: World Health Organization.,;
- Chao, C.-C., Shen, P.-W., Tzeng, T.-Y., Kung, H.-J., Tsai, T.-F., Wong, Y.-H. **Human iPSC-derived neurons as a platform for deciphering the mechanisms behind brain aging** (2021) *Biomedicines*, 9.
- Kim, H., Kisseleva, T., Brenner, D.A. **Aging and liver disease** (2015) *Current Opinion in Gastroenterology*, 31, p. 184.
- Schmucker, D.L. **Age-related changes in liver structure and function: Implications for disease?** (2005) *Experimental Gerontology*, 40, pp. 650-659.
- Tanaka, T., Biancotto, A., Moaddel, R., Moore, A.Z., Gonzalez-Freire, M., Aon, M.A., Candia, J., Fantoni, G. **Plasma proteomic signature of age in healthy humans** (2018) *Aging Cell*, 17, p. e12799.
- Rutledge, J., Oh, H., Wyss-Coray, T. **Measuring biological age using omics data** (2022) *Nature Reviews Genetics*, 23, pp. 715-727.

- Horvath, S., Raj, K.  
**DNA methylation-based biomarkers and the epigenetic clock theory of ageing**  
(2018) *Nature Reviews Genetics*, 19, pp. 371-384.
- Fleischer, J.G., Schulte, R., Tsai, H.H., Tyagi, S., Ibarra, A., Shokhirev, M.N., Huang, L., Navlakha, S.  
**Predicting age from the transcriptome of human dermal fibroblasts**  
(2018) *Genome Biology*, 19, p. 221.
- Fang, W., Chen, S., Jin, X., Liu, S., Cao, X., Liu, B.  
**Metabolomics in aging research: Aging markers from organs**  
(2023) *Frontiers in Cell and Developmental Biology*, 11.
- Liu, Y., Weng, W., Gao, R., Liu, Y.  
**New insights for cellular and molecular mechanisms of aging and aging-related diseases: Herbal medicine as potential therapeutic approach**  
(2019) *Oxidative Medicine and Cellular Longevity*, 2019.
- Kitada, K., Machmudah, S., Sasaki, M., Goto, M., Nakashima, Y., Kumamoto, S., Hasegawa, T.  
**Supercritical CO<sub>2</sub> extraction of pigment components with pharmaceutical importance from *Chlorella vulgaris***  
(2009) *Journal of Chemical Technology and Biotechnology*, 84, pp. 657-661.
- Panahi, Y., Pishgoo, B., Jalalian, H.R., Mohammadi, E., Taghipour, H.R., Sahebkar, A., Abolhasani, E.  
**Investigation of the effects of *Chlorella vulgaris* as an adjunctive therapy for dyslipidemia: Results of a randomised open-label clinical trial**  
(2012) *Nutrition and Dietetics*, 69, pp. 13-19.
- Makpol, S., Yeoh, T.W., Ruslam, F.A.C., Arifin, K.T., Yusof, Y.A.M.  
**Comparative effect of Piper betle, *Chlorella vulgaris* and tocotrienol-rich fraction on antioxidant enzymes activity in cellular ageing of human diploid fibroblasts**  
(2013) *BMC Complementary and Alternative Medicine*, 13, pp. 1-10.
- Sulaiman, S.; N.A.S.; W.Z.W.N.; Y.A.M.Y. Chemopreventive Effect of *Chlorella vulgaris* in Choline Deficient Diet and Ethionine Induced Liver Carcinogenesis in Rats. *International Journal of Cancer Research*. 2006, 2, 234–241, doi:10.3923/ijcr.2006.234.241.
- Saberbaghi, T., Abbasian, F., Mohd Yusof, Y.A., Makpol, S.  
**Modulation of cell cycle profile by *Chlorella vulgaris* prevents replicative senescence of human diploid fibroblasts**  
(2013) *Evidence-Based Complementary and Alternative Medicine*, 2013.
- Zainul Azlan, N., Mohd Yusof, Y.A., Alias, E., Makpol, S.  
***Chlorella vulgaris* improves the regenerative capacity of young and senescent myoblasts and promotes muscle regeneration**  
(2019) *Oxidative Medicine and Cellular Longevity*, 2019.
- Zainul Azlan, N., Mohd Yusof, Y.A., Makpol, S.  
***Chlorella vulgaris* ameliorates oxidative stress and improves the muscle regenerative capacity of young and old sprague-dawley rats**  
(2020) *Nutrients*, 12.
- Zhao, Y., Yang, Y., Li, Q., Li, J.  
**Understanding the unique microenvironment in the aging liver**  
(2022) *Frontiers in Medicine*, 9.
- Ibrahim, M.A., Eraqi, M.M., Alfaiz, F.A.  
**Therapeutic role of taurine as antioxidant in reducing hypertension risks in rats**  
(2020) *Heliyon*, 6.

- Singh, P.; Gollapalli, K.; Mangiola, S.; Schraner, D.; Yusuf, M.A.; Chamoli, M.; Shi, S.L.; Lopes Bastos, B.; Nair, T.; Riermier, A.; Taurine deficiency as a driver of aging. *Science* 2023, 380, eabn9257, doi:10.1126/science. abn9257.
- Wen, C., Li, F., Zhang, L., Duan, Y., Guo, Q., Wang, W., He, S., Yin, Y.  
**Taurine is involved in energy metabolism in muscles, adipose tissue, and the liver**  
(2019) *Molecular Nutrition and Food Research*, 63.
- Maughan, R.  
**Carbohydrate metabolism**  
(2009) *Surgery (Oxford)*, 27, pp. 6-10.
- Chandel, N.S. Carbohydrate Metabolism. *Cold Spring Harbor Perspectives in Biology*. 2021, 13, doi:10.1101/cshperspect. a040568.
- Lee, H., Kim, M.  
**Effect of Chlorella vulgaris on glucose metabolism in Wistar rats fed high fat diet**  
(2009) *Journal of Medicinal Food*, 12, pp. 1029-1037.
- Huang, Y., Lu, J., Zhao, Q., Chen, J., Dong, W., Lin, M., Zheng, H.  
**Potential therapeutic mechanism of traditional Chinese medicine on diabetes in rodents: A review from an NMR-based metabolomics perspective**  
(2022) *Molecules*, 27, p. 5109.
- Shi, Y., Zhong, L., Zhong, H., Zhang, J., Liu, X., Peng, M., Fu, G., Hu, Y.  
**Taurine supplements in high-carbohydrate diets increase growth performance of Monopterus albus by improving carbohydrate and lipid metabolism, reducing liver damage, and regulating intestinal microbiota**  
(2022) *Aquaculture*, 554.
- Goon, D.E.; Ab-Rahim, S.; Mohd Sakri, A.H.; Mazlan, M.; Tan, J.K.; Abdul Aziz, M.; Mohd Noor, N.; Ibrahim, E.; Sheikh Abdul Kadir, S.H. Untargeted serum metabolites profiling in high-fat diet mice supplemented with enhanced palm tocotrienol-rich fraction using UHPLC-MS. *Scientific Reports*. 2021, 11, 21001, doi:10.1038/s41598-021-00454-9.
- van den Berg, R.A., Hoefsloot, H.C.J., Westerhuis, J.A., Smilde, A.K., van der Werf, M.J.  
**Centering, scaling, and transformations: Improving the biological information content of metabolomics data**  
(2006) *BMC Genomics*, 7, p. 142.
- Xia, J., Wishart, D.S.  
**Using MetaboAnalyst 3.0 for comprehensive metabolomics data analysis**  
(2016) *Current Protocols in Bioinformatics*, 55, pp. 10-14.

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