

DAFTAR PUSTAKA

- Ahmed, W.S. *et al.* 2021. Phosphodiesterase 5 (PDE5): Structure-function regulation and therapeutic applications of inhibitors. *Biomedicine & Pharmacotherapy* 1;134:111128.
- Akhvlediani, N. D. *et al.* 2018. Current role of sildenafil sitrat in the management of erectile dysfunction. *Urologia*. 2018 May;(2):142-146. Russian. PMID: 29901310.
- Almannie, R. *et al.* 2023. Recreational use of oral erectile dysfunction medications among male physicians-A cross-sectional study. *Urology Annals*, 15(2), pp.148-157.
- Amaral, S. *et al.* 2008. Diabetes and the impairment of reproductive function: possible role of mitochondria and reactive oxygen species. *Current Diabetes Reviews*, 4(1), 46-54.
- Ameli, M. *et al.* 2018. Protective effect of tadalafil and verapamil on testicular function and oxidative stress after torsion/detorsion in adult male rat. *Andrologia*, 50(8), p.e13068.
- Andersson, K.E. 2018. PDE5 inhibitors–pharmacology and clinical applications 20 years after sildenafil sitrat discovery. *British journal of pharmacology*, 175(13), pp.2554-2565.
- Atsbeha B.W., Kebede B.T., Birhanu B.S., Yimenu D.K., Belay W.S., Demeke C.A. The weekend drug; recreational use of sildenafil citrate and concomitant factors: a cross-sectional study. *Front. Med.* 2021;8 doi: 10.3389/fmed.2021.665247. <https://www.frontiersin.org/articles/10.3389/fmed.2021.665247> 08, 25, 2022. [Online].
- Barnett, C.F. *et al.* 2006. Sildenafil sitrat in the treatment of pulmonary hypertension. *Vasc Health Risk Manag.* 2006;2(4):411-22. doi: 10.2147/vhrm.2006.2.4.411. PMID: 17323595; PMCID: PMC1994020.
- Berman-Rosenzweig, E. *et al.* 2014. Effects of dose and age on adverse events associated with tadalafil in the treatment of pulmonary arterial hypertension. *Pulmonary Circulation*, 4(1), pp.45-52.
- Blount, M.A. *et al.* 2004. Binding of tritiated sildenafil sitrat, tadalafil, or vardenafil to the phosphodiesterase-5 catalytic site displays potency, specificity, heterogeneity, and cGMP stimulation. *Molecular Pharmacology*, 66(1), pp.144-152.
- Bruunsgaard, H. *et al.* 2000. Ageing, tumour necrosis factor-alfa (TNF- α) and atherosclerosis. *Clinical & Experimental Immunology*, 121(2), pp.255-260.

- Bui, T.M. *et al.* 2020. ICAM-1: A master regulator of cellular responses in inflammation, injury resolution, and tumorigenesis. *Journal of Leucocyte Biology*, 108(3), pp.787-799.
- Cai, Y. *et al.* 2016. Involvement of ICAM- 1 in impaired spermatogenesis after busulfan treatment in mice. *Andrologia*, 48(1), pp.37-44..
- Campolo, F. *et al.* 2023. Once upon a Testis: The Tale of Cyclic Nucleotide Phosphodiesterase in Testicular Cancers. *International Journal of Molecular Sciences*, 24(8), p.7617.
- Celino, F.T. *et al.* 2011. Tolerance of spermatogonia to oxidative stress is due to high levels of Zn and Cu/Zn superoxide dismutase. *PLoS One*;6(2):e16938. doi: 10.1371/journal.pone.0016938. PMID: 21364994; PMCID: PMC3041797.
- Cornejo-Guerra C. *et al.* 2024. Consequences of Exposure to Hypobaric Hypoxia Associated with High Altitude on Spermatogenesis and Seminal Parameters: A Literature Review. *Cells*;13(7):592. doi: 10.3390/cells13070592. PMID: 38607031; PMCID: PMC11011536.
- D Ramirez, A. *et al.* 2014. Regulation of dopamine signaling in the striatum by phosphodiesterase inhibitors: novel therapeutics to treat neurological and psychiatric disorders. *Central Nervous System Agents in Medicinal Chemistry (Formerly Current Medicinal Chemistry-Central Nervous System Agents)*, 14(2), pp.72-82.
- Dhaliwal A. *et al.* 2023 PDE5 Inhibitors. [Updated 2023 Apr 10]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 Jan-. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK549843/>
- Domiaty, S. *et al.* 2022. Molecular Mechanics Simulations and Experimental Investigation of the Effect of Tadalafil on Various Inflammatory Pain Mediators. *ACS omega*, 7(48), pp.43747-43758.
- Duranti, G. *et al.* 2017. Influence of the PDE5 inhibitor tadalafil on redox status and antioxidant defense system in C2C12 skeletal muscle cells. *Cell stress and chaperones*, 22(3), pp.389-396.
- Eaton, C.B. *et al.* 2007. A retrospective study of the relationship between biomarkers of atherosclerosis and erectile dysfunction in 988 men. *International journal of impotence research*, 19(2), pp.218-225.
- Elkerdasy, H.I. *et al.* 2019. The toxic effect of sildenafil sitrat citrate on adult albino rat testis and the possible protective role of royal jelly (histological and immunohistochemical study). *Egyptian Journal of Histology*, 42(2), pp.381-392.
- Elterman, D.S. *et al.* 2021. The quality of life and economic burden of erectile dysfunction. *Research and Reports in Urology*, pp.79-86.
- Frajese, G.V. *et al.* 2006. Tadalafil in the treatment of erectile dysfunction; an overview of the clinical evidence. *Clinical interventions in aging*, 1(4), pp.439-449.

- Gong, B. *et al.* 2017. Direct comparison of tadalafil with sildenafil sitrat for the treatment of erectile dysfunction: a systematic review and meta-analysis. *International urology and nephrology*, 49(10), pp.1731-1740.
- Griswold, M.D. 2016. Spermatogenesis: the commitment to meiosis. *Physiological reviews*, 96(1), pp.1-17.
- Hasan, H. *et al.* 2022. Mechanism of inflammatory associated impairment of sperm function, spermatogenesis and steroidogenesis. *Frontiers in endocrinology*, 13, p.897029.
- Jahin, E.S.E.S. *et al.* 2022. Effects of sildenafil sitrat on the testes of the nondiabetic and diabetic adult albino rats (Light and Electron Microscopic Study). *Al-Azhar International Medical Journal*, 3(12), pp.37-42.
- Janjic, M.M. *et al.* 2012. Transient rise of serum testosterone level after single sildenafil sitrat treatment of adult male rats. *The Journal of Sexual Medicine*, 9(10), pp.2534-2543.
- Kaleta, B. *et al.* 2019. Sildenafil sitrat upregulates tumor necrosis factor α production in peripheral blood mononuclear cells of healthy men-preliminary report. *Acta Poloniae Pharmaceutica-Drug Research*, 76(1), pp.123-128.
- Kent, T. and Griswold, M.D. 2014. Checking the pulse of vitamin A metabolism and signaling during mammalian spermatogenesis. *Journal of developmental biology*, 2(1), pp.34-49.
- Kim, B. *et al.* 2020. The long-term protective effect of tadalafil on spermatogenesis following testicular ischemia-reperfusion injury in a rat model.
- Koshi D(Ed.). 2017. The male external genital organs. *Cunningham's Manual of Practical Anatomy, Volume 2: Thorax and Abdomen*, 16th Edition. Oxford University Press. <https://accessmedicine.mhmedical.com/content.aspx?bookid=3475§ionid=286445970>
- Kozłowska, A. *et al.* 2020. The role of oxidative stress in the pathogenesis of erectile dysfunction in patients with type 2 diabetes. *International Journal of Impotence Research*, 32(2), 171-178
- Kumar, V., Abbas, A.K. and Aster, J.C., 2017. *Robbins & Cotran Pathologic Basis of Disease-General Pathology, Vol 1: First Bangladesh Edition-E-Book*. Elsevier Health Sciences.
- Li, M. W. *et al.* 2006. Cytokines and their role in spermatogenesis. *Frontiers in Bioscience*, 11, 1227-1246.
- Limoncella, S. *et al.* 2022. Phosphodiesterase (PDE) 5 inhibitors sildenafil sitrat, tadalafil and vardenafil impact cAMP-specific PDE8 isoforms-linked second messengers and steroid production in a mouse Leydig tumor cell line. *Molecular and cellular endocrinology*, 542, p.111527.

- Liu, W. *et al.* 2024. Microenvironment of spermatogonial stem cells: a key factor in the regulation of spermatogenesis. *Stem Cell Research & Therapy*, 15(1), p.294.
- Lysiak, J.J. 2004. The role of tumor necrosis factor-alfa and interleukin-1 in the mammalian testis and their involvement in testicular torsion and autoimmune orchitis. *Reproductive Biology and Endocrinology*, 2, pp.1-10.
- María, E. F. *et al.* 2019. The inflammatory mediators TNF- α and nitric oxide arrest spermatogonia GC-1 cell cycle, *Reproductive Biology*, Volume 19, Issue 4, 2019, Pages 329-339, ISSN 1642-431X, <https://doi.org/10.1016/j.repbio.2019.11.001>.
(<https://www.sciencedirect.com/science/article/pii/S1642431X18304157>)
- Matzkin, M.E. *et al.* 2021. Hallmarks of testicular aging: the challenge of anti-inflammatory and antioxidant therapies using natural and/or pharmacological compounds to improve the physiopathological status of the aged male gonad. *Cells*, 10(11), p.3114.
- Mayur S. J. *et al.* 2023. Phosphodiesterase-5 (PDE5) Inhibitors in the Treatment of Erectile Dysfunction: A Review. *Asian Journal of Pharmaceutical Research*; 13(1):63-7. doi: 10.52711/2231-5691.2023.00012 Available on: <https://asianjpr.com/AbstractView.aspx?PID=2023-13-1-12>
- McCabe, M.P. *et al.* 2016. Definitions of sexual dysfunctions in women and men: a consensus statement from the Fourth International Consultation on Sexual Medicine 2015. *The journal of sexual medicine*, 13(2), pp.135-143.
- Mescher, A.L. 2018. Junqueira's basic histology: text and atlas. New York: McGraw Hill.
- Middendorff, R. *et al.* 2000. Multiple roles of the messenger molecule cGMP in testicular function. *Andrologia*, 32(1), pp.55-59.
- Middendorff, R., Davidoff, M.S., Behrends, S., Mewe, M., Miethens, A. and Müller, D., 2000. Multiple roles of the messenger molecule cGMP in testicular function. *Andrologia*, 32(1), pp.55-59.
- Monalisa F. A. *et al.* 2014 Clinical and Molecular Genetics of the Phosphodiesterases (PDEs), *Endocrine Reviews*, Volume 35, Issue 2, 1 April 2014, Pages 195–233, <https://doi.org/10.1210/er.2013-1053>
- Mostafa, T. *et al.* 2022. Recreational Use of Oral PDE5 Inhibitors: The Other Side of Midnight. *Sex Med Rev.* 2022 Jul;10(3):392-402. doi: 10.1016/j.sxmr.2021.10.004. Epub 2021 Dec 10. PMID: 34903486.
- Oh, S. S. & Narver, H. L. 2024. Mouse and rat anesthesia and analgesia. *Current Protocols*, 4, e995. doi: 10.1002/cpz1.995
- Osterloh, I.H., 2004. The discovery and development of Viagra®(sildenafil citrate). In *Sildenafil* (pp. 1-13). Basel: Birkhäuser Basel.

- Pohl, E. *et al.* 2021. Healthy ageing and spermatogenesis. *Reproduction*, 161(4), pp.R89-R101.
- Puşçaşu, C. *et al.* 2023. Exploring the Multifaceted Potential of Sildenafil sitrat in Medicine. *Medicina*, 59(12), p.2190.
- Raj, C.J. *et al.* 2022. Deciphering the nexus between oxidative stress and spermatogenesis: A compendious overview. *Oxidative Stress and Toxicity in Reproductive Biology and Medicine: A Comprehensive Update on Male Infertility Volume II*, pp.1-16.
- Saraiva, K.L. *et al.* 2009. Chronic treatment with sildenafil sitrat stimulates Leydig cell and testosterone secretion. *Int J Exp Pathol*;90(4):454-62. doi: 10.1111/j.1365-2613.2009.00660.x. PMID: 19659904; PMCID: PMC2741156.
- Shah, W. *et al.* 2021. The molecular mechanism of sex hormones on Sertoli cell development and proliferation. *Frontiers in endocrinology*, 12, p.648141.
- Shamloul, R. *et al.* 2013. Erectile dysfunction. *The Lancet*, 381(9861), pp.153-165.
- Sharlip, I.D. *et al.* 2008. Tadalafil is efficacious and well tolerated in the treatment of erectile dysfunction (ED) in men over 65 years of age: Results from Multiple Observations in Men with ED in National Tadalafil Study in the United States. *The Journal of Sexual Medicine*, 5(3), pp.716-725.
- Sharma, P. *et al.* 2019. Epigenetics and oxidative stress: A twin- edged sword in spermatogenesis. *Andrologia*, 51(11), p.e13432.
- Shindel A.W., & Lue T.F. (2021). Evaluation and management of erectile dysfunction. Bhasin S, & O’Leary M.P., & Basaria S.S.(Eds.), *Essentials of Men’s Health*. McGraw Hill.
<https://accessmedicine.mhmedical.com/content.aspx?bookid=2950§ionid=248296753>
- Simsek, A. *et al.* 2014. Effects of the recreational use of PDE5 inhibitors on the corpus cavernosum of young, healthy rats. *International urology and nephrology*, 46, pp.1889-1893.
- Sokanovic, S.J. *et al.* 2014. Age related changes of cAMP and MAPK signaling in Leydig cells of Wistar rats. *Experimental gerontology*, 58, pp.19-29.
- Suede, S. H. *et al.* 2023 Histology, Spermatogenesis. In: *StatPearls [Internet]*. Treasure Island (FL): StatPearls Publishing; 2025 Jan–. PMID: 31985935.
- Sweetman, S.C. ed., 2009. *The complete drug reference (Vol. 1)*. London: Pharmaceutical Press.
- Tomita, N. *et al.* 2020. The phosphodiesterase 5 inhibitor tadalafil has renoprotective effects in a rat model of chronic kidney disease. *Physiological reports*, 8(17), p.e14556.

- Toor, J.S. and Sikka, S.C. 2017. Developmental and reproductive disorders—role of endocrine disruptors in testicular toxicity. In Reproductive and developmental toxicology (pp. 1111-1121). Academic Press.
- Ückert, S. *et al.* 2006. Update on phosphodiesterase (PDE) isoenzymes as pharmacologic targets in urology: present and future. *European urology*, 50(6), pp.1194-1207.
- Ueda, P. *et al.* 2020. Trends in frequency of sexual activity and number of sexual partners among adults aged 18 to 44 years in the US, 2000-2018. *JAMA network open*, 3(6), pp.e203833-e203833.
- Valatsou, A. *et al.* 2017. Beneficial effects of sildenafil sitrat on tissue perfusion and inflammation in a murine model of limb ischemia and atherosclerosis. *Current Vascular Pharmacology*, 15(3), pp.282-287.
- Vlachopoulos, C. *et al.* 2015. Acute effect of sildenafil sitrat on inflammatory markers/mediators in patients with vasculogenic erectile dysfunction. *International Journal of Cardiology*, 182, pp.98-101.
- Wang, Y. *et al.* 2018. Tadalafil 5 mg once daily improves lower urinary tract symptoms and erectile dysfunction: a systematic review and meta- analysis. *LUTS: Lower Urinary Tract Symptoms*, 10(1), pp.84-92.
- Wang, Y.Y. *et al.* 2021. Protein kinases regulate hyperactivated motility of human sperm. *Chinese Medical Journal*, 134(20), pp.2412-2414.
- Weinbauer, G.F. *et al.* 2010. Physiology of testicular function. *Andrology: Male reproductive health and dysfunction*, pp.11-59.
- Xiao, X. *et al.* 2012. Intercellular adhesion molecule-1 is a regulator of blood–testis barrier function. *Journal of cell science*, 125(23), pp.5677-5689.
- Yildiz, H. *et al.* 2011 Effects of sildenafil sitrat citrate on torsion/detorsion-induced changes in red blood cell and plasma lipid peroxidation, antioxidants, and blood hematology of male rats. *Eur J Obstet Gynecol Reprod Biol.* 159(2):359-63. doi: 10.1016/j.ejogrb.2011.07.023. Epub 2011 Aug 9. PMID: 21831505.
- Zhao, S.G. *et al.* 2015. Association between sildenafil sitrat and inflammation markers/mediators. *International Journal of Cardiology*, 198, pp.178-179.