CHAPTER 8:

BIBLIOGRAPHY

8. Bibliography:

1. Jihyun J. The Role of Nephrons in Renal Physiology. Journal of Molecular Histology & Medical Physiology. 2024 Nov 28;9(6):1–2. doi:10.37421/2684-494X.2024.9.263
2. Theodorou C, Leatherby R, Dhanda R. Function of the nephron and the formation of urine. Anaesthesia & Intensive Care Medicine. 2021 Jul 1;22(7):434–8. doi:10.1016/J.MPAIC.2021.05.004
3. Ogobuiro I, Tuma F. Physiology, Renal. StatPearls. 2023 Jul 24. PubMed PMID: 30855923.
4. Willig SP. Kidney anatomy and physiology. Biomedical instrumentation & technology / Association for the Advancement of Medical Instrumentation. 1993 Jul;27(4):342–4. doi:10.1007/978-3-319-23458-8_1 PubMed PMID: 8369870.
5. Fortnum D. Introduction to Kidney Functions and Pathophysiology. 2024;1–11. doi:10.1007/978-3-031-30320-3_1
6. Brunton LL, Chabner BA, Knollmann BC. Goodman & Gillman's The Pharmacological Basic Of Therapeutics. In: Goodman and Gilman's The Pharmacological Basis of Therapeutics. 13th ed. McGraw-Hill Education; 2018.
7. Ferri C, Del Pinto R. Diuretics. In: Encyclopedia of Endocrine Diseases. 2018. doi:10.1016/B978-0-12-801238-3.66129-9
8. Gilbert SJ. Sodium and Water Disorders. Advances in Kidney Disease and Health. 2025 Jan 1;32(1):41–9. doi:10.1053/j.akdh.2024.09.002
9. Martin K, Tan SJ, Toussaint ND. Total Body Sodium Balance in Chronic Kidney Disease. Int J Nephrol. 2021 Jan 1;2021(1):7562357. doi:10.1155/2021/7562357
10. Borrelli S, Provenzano M, Gagliardi I, Ashour M, Liberti ME, De Nicola L, et al. Sodium Intake and Chronic Kidney Disease. International Journal of Molecular Sciences 2020, Vol 21, Page 4744. 2020 Jul 3;21(13):4744. doi:10.3390/IJMS21134744 PubMed PMID: 32635265.
11. Borrelli S, Provenzano M, Gagliardi I, Ashour M, Liberti ME, De Nicola L, et al. Sodium Intake and Chronic Kidney Disease. Int J Mol Sci. 2020 Jul 1;21(13):4744. doi:10.3390/IJMS21134744 PubMed PMID: 32635265.
12. Kotchen TA, Cowley AW, Frohlich ED. Salt in Health and Disease — A Delicate Balance. New England Journal of Medicine. 2013 Mar 28;368(13):1229–37. doi:10.1056/NEJMRA1212606 PubMed PMID: 23802533.

13. de Bhailis ÁM, Kalra PA. Hypertension and the kidneys. Br J Hosp Med (Lond). 2022 May 2;83(5). doi:10.12968/HMED.2021.0440 PubMed PMID: 35653320.
14. Townsend RR. Pathophysiology of Hypertension in Chronic Kidney Disease. Chronic Renal Disease. 2020 Jan 1;313–22. doi:10.1016/B978-0-12-815876-0.00021-8
15. Lala A, Levin A, Khunti K. The interplay between heart failure and chronic kidney disease. Diabetes Obes Metab. 2025 Jul 1;27(7):3568. doi:10.1111/DOM.16371 PubMed PMID: 40259497.
16. Ter Maaten JM, Bansal N. Kidneys Under Pressure: The Consequence of Heart Failure and Elevated Filling Pressures. American Journal of Kidney Diseases. 2025 Sep 1;86(3):298–300. doi:10.1053/j.ajkd.2025.06.005
17. Shiba N, Shimokawa H. Chronic kidney disease and heart failure—Bidirectional close link and common therapeutic goal. J Cardiol. 2011 Jan 1;57(1):8–17. doi:10.1016/J.JJCC.2010.09.004 PubMed PMID: 21030212.
18. Ahmed K, Dubey MK, Kajal, Dubey S, Pandey DK. Chronic kidney disease: causes, treatment, management, and future scope. Computational Intelligence for Genomics Data. 2025 Jan 1;99–111. doi:10.1016/B978-0-443-30080-6.00010-9
19. Ammar A, Edwin SB, Whitney R, Lipari M, Giuliano C. Updates in chronic kidney disease management: A systematic review. Pharmacotherapy: The Journal of Human Pharmacology and Drug Therapy. 2025 May 1;45(5):291–306. doi:10.1002/PHAR.70014 PubMed PMID: 40152479.
20. Supramanian K, Sekar M, Afendi NSHN, Supramanian K, Sekar M, Afendi NSHN. Chronic Kidney Disease: Etiology, Pathophysiology, and Management Strategies to Increase Quality of Life. Chronic Kidney Disease - Novel Insights into Pathophysiology and Treatment. 2024 May 9. doi:10.5772/INTECHOPEN.1005083
21. Higueras L. Understanding Kidney Failure: Causes, Symptoms, and Treatment Options. J Clin Exp Nephrol. 2023;8(4):207. doi:10.36648/2472-5056.8.4.207
22. Blebea NM, Pușcașu C, Ștefănescu E, Stăniguț AM. Diuretic Therapy: Mechanisms, Clinical Applications, and Management. Journal of Mind and Medical Sciences 2025, Vol 12, Page 26. 2025 May 2;12(1):26. doi:10.3390/JMMS12010026
23. Chakraverty R, Samanta K, Mandal P, Karmakar S. Mechanism of action of diuretic and anti-diuretic drugs. How Synthetic Drugs Work: Insights into Molecular Pharmacology of Classic and New Pharmaceuticals. 2023 Jan 1;369–90. doi:10.1016/B978-0-323-99855-0.00016-6

24. Konstam MA. The Journey Toward Advances in Diuretics Management: Quite Far and Not Far Enough. J Card Fail. 2020 Sep 1;26(9):802–5. doi:10.1016/j.cardfail.2020.07.021 PubMed PMID: 32829018.
25. Felker GM, Ellison DH, Mullens W, Cox ZL, Testani JM. Diuretic Therapy for Patients With Heart Failure: JACC State-of-the-Art Review. J Am Coll Cardiol. 2020 Mar 17;75(10):1178–95. doi:10.1016/J.JACC.2019.12.059 PubMed PMID: 32164892.
26. Roush GC, Kaur R, Ernst ME. Diuretics. J Cardiovasc Pharmacol Ther. 2014 Jan;19(1):5–13. doi:10.1177/1074248413497257 PubMed PMID: 24243991.
27. Arumugham VB, Shahin MH. Therapeutic Uses of Diuretic Agents. StatPearls. 2023 May 29. PubMed PMID: 32491770.
28. Puthenpura MM, Wilcox J, Keane R, Demirjian S, Auron M, Williams JB, et al. Diuretic management protocol to improve quality and safety in managing acute heart failure in an integrated health system: An implementation science approach. Int J Cardiol. 2025 Feb 15;421:132920. doi:10.1016/j.ijcard.2024.132920 PubMed PMID: 39708902.
29. Coppola S, Chiumello D, Adnan A, Pozzi T, Forni LG, Gattinoni L. Diuretics in critically ill patients: a narrative review of their mechanisms and applications. Br J Anaesth. 2025 Jun 1;134(6):1638–47. doi:10.1016/J.BJA.2025.02.032 PubMed PMID: 40221314.
30. Fră;ţilă; GV, Obrişcă B, Ismail G. A practical approach to sequential nephron blockade in acute decompensated heart failure. Romanian Journal of Cardiology / Revista Romana de Cardiologie. 2023 Sep 1;33(3):83–92. doi:10.2478/RJC-2023-0021
31. Van Poelgeest E, Prokopidis K, Erdogan T, Kwak MJ, Piotrowicz K, Paoletti L, et al. Effectiveness and safety of chronic diuretic use in older adults: an umbrella review of recently published systematic reviews and meta-analyses of randomized-controlled trials. Eur Geriatr Med. 2025 Aug 1;16(4):1353. doi:10.1007/S41999-025-01229-5 PubMed PMID: 40413712.
32. Kosicka Klinika Hipertensjologii T, Chorób Wewnętrznych im Karola Marcinkowskiego Poznaniu AU, Głuszek J, Kosicka T. Difficulties in treatment with thiazide diuretics in the elderly. Arterial Hypertension. 2023;27(2):63–72. doi:10.5603/AH.A2023.0006
33. Li G, Hu R. Concerns about Diuretics as the First-line Treatment of Hypertension in the Elderly. Aging Dis. 2021 Oct 1;12(7):1541. doi:10.14336/AD.2021.0224 PubMed PMID: 34631204.

34. Van Poelgeest EP, Handoko ML, Muller M, van der Velde N. Diuretics, SGLT2 inhibitors and falls in older heart failure patients: to prescribe or to deprescribe? A clinical review. Eur Geriatr Med. 2023 Aug 1;14(4):659. doi:10.1007/S41999-023-00752-7 PubMed PMID: 36732414.
35. Hoenders R, Ghelman R, Portella C, Simmons S, Locke A, Cramer H, et al. A review of the WHO strategy on traditional, complementary, and integrative medicine from the perspective of academic consortia for integrative medicine and health. Front Med (Lausanne). 2024;11:1395698. doi:10.3389/FMED.2024.1395698 PubMed PMID: 38933107.
36. World Health Organization. WHO establishes the Global Centre for Traditional Medicine in India [Internet]. 2022. Available from: https://www.who.int/news/item/25-03-2022-who-establishes-the-global-centre-for-traditional-medicine-in-india
37. Dutta K, Chetia P, Lahkar S, Das S. Herbal plants used as diuretics: A comprehensive review. J Pharm Chem Biol Sci. 2014 Jan 1;2:27–32.
38. Snigdha M, Satish Kumar S, Sharmistha M, Lalit S, Tanuja S. An overview on herbal medicines as diuretics with scientific evidence. saspublishers.com. 2013;1(3).
39. Wright CI, Van-Buren L, Kroner CI, Koning MMG. Herbal medicines as diuretics: A review of the scientific evidence. J Ethnopharmacol. 2007 Oct 8;114(1):1–31. doi:10.1016/J.JEP.2007.07.023 PubMed PMID: 17804183.
40. Rajanivetha R. Plants with Diuretic effect. Research Journal of Pharmacy and Technology. 2013.
41. Akram M, Asif M, Naveed A, Shah P, Uzair M, Shaheen D, et al. *Tribulus terrestris* Linn.: A review article. Journal of Medicinal Plants Research. 2011 Feb;5:3601–5.
42. Meena P, Anand A. A comprehensive overview of Gokshura (*Tribulus terrestris* Linn.). Journal of Ayurveda and Integrated Medical Sciences. 2019;4(06).
43. Ministry for Health and Family Welfare, Ministry for Health and Family Welfare, Ministry for Health and Family Welfare. The Ayurvedic Pharmacopoeia of India, Part-I, Volume-I. The Ayurvedic Pharmacopoeia of India. 2010;2:171.
44. Pillai CK. Siddha Materia Medica - Vegetable Kingdom (Tamil). Chennai: Raththina Nayakkar & Sons, Chennai, India (P) Ltd.; 2006.
45. Vijai N, Singh L, Kumar L. Lithotriptic and anti-lithogenic effect of Tila-Dhatri Kshara along with Gokshura Kashaya in ethylene glycol-induced nephrolithiasis in adult male Charles Foster rats. Volume 17, Issue 1, Pages 85 - 91. 2024 Jan 7;85–91. doi:10.22159/ajpcr.2024.v17i1.48641

46. Kaushik J, Tandon S, Bhardwaj R, Kaur T, Singla SK, Kumar J, et al. Delving into the Antiurolithiatic Potential of *Tribulus terrestris* Extract Through –In Vivo Efficacy and Preclinical Safety Investigations in Wistar Rats. Sci Rep. 2019;9(1). doi:10.1038/s41598-019-52398-w
47. Kaliaperumal K, Bhat BA, Subramanian K, Ramakrishnan T, Chakravarthy E, Al-Keridis LA, et al. In-vivo anti-hyperglycemic effect of herbal extracts *Tribulus terrestris* (L) and Curcuma amada (R) on streptozotocin-induced diabetic rats and its associated histopathological studies. Heliyon. 2024;10(1). doi:10.1016/j.heliyon.2024.e24009
48. Misiakiewicz-Has K, Maciejewska-Markiewicz D, Rzeszotek S, Pilutin A, Kolasa A, Szumilas P, et al. The obscure effect of *Tribulus terrestris* saponins plus inulin on liver morphology, liver fatty acids, plasma glucose, and lipid profile in SD rats with and without induced type 2 diabetes mellitus. Int J Mol Sci. 2021;22(16). doi:10.3390/ijms22168680
49. Samani NB, Jokar A, Soveid M, Heydari M, Mosavat SH. Efficacy of *Tribulus terrestris* Extract on the Serum Glucose and Lipids of Women with Diabetes Mellitus. Iran J Med Sci. 2016;41(3 Suppl).
50. Chhatre S, Nesari T, Somani G, Kanchan D, Sathaye S. Phytopharmacological overview of *Tribulus terrestris*. Pharmacognosy Reviews. 2014. doi:10.4103/0973-7847.125530
51. Neumann J, Líbalová K, Konvalina P, Smetana P, Vráblík P, Šoch M. *Tribulus terrestris* L.-a review. Journal of Central European Agriculture. 2024. doi:10.5513/JCEA01/25.1.4119
52. Wu TS, Shi LS, Kuo SC. Alkaloids and other constituents from *Tribulus terrestris*. Phytochemistry. 1999;50(8). doi:10.1016/S0031-9422(97)01086-8
53. Abbas MW, Hussain M, Akhtar S, Ismail T, Qamar M, Shafiq Z, et al. Bioactive Compounds, Antioxidant, Anti-Inflammatory, Anti-Cancer, and Toxicity Assessment of *Tribulus terrestris*—In Vitro and In Vivo Studies. Antioxidants. 2022;11(6). doi:10.3390/antiox11061160
54. Hammoda HM, Ghazy NM, Harraz FM, Radwan MM, ElSohly MA, Abdallah II. Chemical constituents from *Tribulus terrestris* and screening of their antioxidant activity. Phytochemistry. 2013;92:153–9. doi:https://doi.org/10.1016/j.phytochem.2013.04.005
55. Waseem M, Rauf A, Rehman S. A scientific review on phyto-pharmacological properties of *Tribulus terrestris* Linn. Indian Drugs. 2018. doi:10.53879/id.55.10.11439

56. Wile D. Diuretics: A review. Annals of Clinical Biochemistry. 2012. p. 419–31. doi:10.1258/acb.2011.011281 PubMed PMID: 22783025.
57. Aswini E, Vivek D, Swathilakshmi S. Role of phytochemicals in diuresis management. World Journal of Pharmaceutical Research www.wjpr.net │. 2020;9.
58. Katzung Bertram G., Trevor Anthony J. Bertram G. Katzung: Basic and Clinical Pharmacology. McGraw-Hill Education - Europe. 14th ed. McGraw-Hill Education; 2018.
59. Tripathi K. Essentials of Medical Pharmacology. Essentials of Medical Pharmacology. 8th ed. New Delhi: Jaypee Brothers Medical Publishers (P) Ltd; 2019.
60. Kehrenberg MCA, Bachmann HS. Diuretics: a contemporary pharmacological classification? Naunyn Schmiedebergs Arch Pharmacol. 2022 Jun 1;395(6):619–27. doi:10.1007/S00210-022-02228-0/FIGURES/2 PubMed PMID: 35294605.
61. Patel P, Preuss CV. StatPearls Publishing [Internet]. StatPearls Publishing; 2025. Thiazide Diuretics. Available from: https://www.ncbi.nlm.nih.gov/books/NBK532918/
62. Crane P, Wiegand TJ. Thiazide Diuretics. Encyclopedia of Toxicology, Fourth Edition: Volume 1-9. 2025 Apr 26;9:V9-43-V9-51. doi:10.1016/B978-0-12-824315-2.00732-6 PubMed PMID: 30422513.
63. Anisman SD, Erickson SB, Fodor KM. Thiazide diuretics. BMJ. 2024 Feb 5;384:e075174. doi:10.1136/BMJ-2023-075174 PubMed PMID: 38316445.
64. Ernst ME, Fravel MA. Thiazide and the Thiazide-Like Diuretics: Review of Hydrochlorothiazide, Chlorthalidone, and Indapamide. Am J Hypertens. 2022 Jul 1;35(7):573–86. doi:10.1093/AJH/HPAC048 PubMed PMID: 35404993.
65. Sakalauskiene G, Civinskiene G, Antuševas A, Civinskas P. Pharmacological properties of loop diuretics and their clinical effects. Kardiologiya. 2018;58(1):72–83. doi:10.18087/CARDIO.2018.1.10084 PubMed PMID: 29466174.
66. Oh SW, Han SY. Loop Diuretics in Clinical Practice. Electrolytes & Blood Pressure. 2015 Jun 1;13(1):17–21. doi:10.5049/EBP.2015.13.1.17
67. Sica DA, Carter B, Cushman W, Hamm L. Thiazide and loop diuretics. J Clin Hypertens. 2011 Sep;13(9):639–43. doi:10.1111/J.1751-7176.2011.00512.X PubMed PMID: 21896142.
68. Patibandla S, Heaton J, Kyaw H. Spironolactone. StatPearls. 2023 Jul 4. PubMed PMID: 32119308.

69. Pitt B, Pfeffer MA, Assmann SF, Boineau R, Anand IS, Claggett B, et al. Spironolactone for Heart Failure with Preserved Ejection Fraction. New England Journal of Medicine. 2014 Apr 9;370(15):1383–92. doi:10.1056/NEJMoa1313731
70. Farzam K, Abdullah M. Acetazolamide. xPharm: The Comprehensive Pharmacology Reference. 2023 Jul 2;1–5. doi:10.1016/B978-008055232-3.61158-4 PubMed PMID: 30335315.
71. Patel P, Patel R, Thorell W. Mannitol. StatPearls Publishing LLC. 2024 Jun 8. PubMed PMID: 29262205.
72. Yi K, Chen TC. Medical treatment: Osmotic agents. Pearls of Glaucoma Management: Second Edition. 2016 Jan 1;253–8. doi:10.1007/978-3-662-49042-6_27/FIGURES/4
73. Ray SD, Mirza M, Ramlakhan K, Elayan I, D'Souza MS. Clinical studies on the adverse effects of diuretics. Side Effects of Drugs Annual. 2024 Jan 1;46:249–57. doi:10.1016/BS.SEDA.2024.07.014
74. Sica DA. Diuretic-Related Side Effects: Development and Treatment. The Journal of Clinical Hypertension. 2007;6(9):532. doi:10.1111/J.1524-6175.2004.03789.X PubMed PMID: 15365284.
75. Greenberg A. Diuretic Complications. Am J Med Sci. 2000 Jan 1;319(1):10–24. doi:10.1016/S0002-9629(15)40676-7 PubMed PMID: 10653441.
76. D Craig Brater, David H. Ellison. UpToDate [Internet]. 2025. Loop diuretics: Dosing and major side effects - UpToDate. Available from: https://www.uptodate.com/contents/loop-diuretics-dosing-and-major-side-effects?search=loop%20diuretics&source=search_result#H1
77. Waller DG, Sampson AP. Diuretics. Medical Pharmacology and Therapeutics. 2018 Jan 1;219–29. doi:10.1016/B978-0-7020-7167-6.00014-2
78. Sica DA. Diuretic-Related Side Effects: Development and Treatment. The Journal of Clinical Hypertension. 2007;6(9):532. doi:10.1111/J.1524-6175.2004.03789.X PubMed PMID: 15365284.
79. Roush GC, Kaur R, Ernst ME. Diuretics: A review and update. Journal of Cardiovascular Pharmacology and Therapeutics. 2014. doi:10.1177/1074248413497257
80. Palmer BF. Metabolic complications associated with use of diuretics. Semin Nephrol. 2011 Nov;31(6):542–52. doi:10.1016/j.semnephrol.2011.09.009 PubMed PMID: 22099511.
81. Khan TM, Patel R, Siddiqui AH. Furosemide. StatPearls. 2023 May 8. PubMed PMID: 29763096.

82. Huang X, Dorhout Mees E, Vos P, Hamza S, Braam B. Everything we always wanted to know about furosemide but were afraid to ask. Am J Physiol Renal Physiol. 2016 May 15;310(10):F958–71. doi:10.1152/AJPRENAL.00476.2015/ASSET/IMAGES/LARGE/ZH20091678730004.JPEG PubMed PMID: 26911852.
83. Group TAO and C for the ACR. Major Outcomes in High-Risk Hypertensive Patients Randomized to Angiotensin-Converting Enzyme Inhibitor or Calcium Channel Blocker vs DiureticThe Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT). JAMA. 2002 Dec 18;288(23):2981–97. doi:10.1001/jama.288.23.2981
84. Adomako EA, Sambandam KK. Challenges in diuretic therapy: A case-based discussion. American Journal of the Medical Sciences. 2022 Oct 1;364(4):386–93. doi:10.1016/J.AMJMS.2022.04.021/ASSET/5858435E-4A61-45BE-A0BD-A3C8D95C1201/MAIN.ASSETS/GR4.JPG PubMed PMID: 35472337.
85. Garg N, Abdel-Aziz SM, Aeron A. Health Benefits and Possible Risk of Herbal Medicine. In: Microbes in Food and Health. 2016.
86. Martín-Herrera D, Abdala S, Benjumea D, Gutiérrez-Luis J. Diuretic activity of some Withania aristata Ait. fractions. J Ethnopharmacol. 2008;117(3). doi:10.1016/j.jep.2008.03.004
87. Ntchapda F, Bonabe C, Kemeta Azambou DR, Talla E, Dimo T. Diuretic and antioxidant activities of the aqueous extract of leaves of Vepris heterophylla (Engl.) R. Let (Rutaceae) in rats. BMC Complementary and Alternative Medicine. 2016. doi:10.1186/s12906-016-1439-8
88. Wright CI, Van-Buren L, Kroner CI, Koning MMG. Herbal medicines as diuretics: A review of the scientific evidence. Journal of Ethnopharmacology. 2007. p. 1–31. doi:10.1016/j.jep.2007.07.023 PubMed PMID: 17804183.
89. Phillips OA, Mathew KT, Oriowo MA. Antihypertensive and vasodilator effects of methanolic and aqueous extracts of *Tribulus terrestris* in rats. J Ethnopharmacol. 2006 Apr 6;104(3):351–5. doi:10.1016/J.JEP.2005.09.027 PubMed PMID: 16289603.
90. Saeed M, Munawar M, Bi JB, Ahmed S, Ahmad MZ, Kamboh AA, et al. Promising phytopharmacology, nutritional potential, health benefits, and traditional usage of *Tribulus terrestris* L. herb. Heliyon [Internet]. 2024. Available from: https://www.sciencedirect.com/science/article/pii/S2405844024015809?via%3Dihub doi:10.1016/j.heliyon.2024.e25549

91. Kasote DM, Jagtap SD, Thapa D, Khyade MS, Russell WR. Herbal remedies for urinary stones used in India and China: A review. J Ethnopharmacol. 2017 May 5;203:55–68. doi:10.1016/J.JEP.2017.03.038 PubMed PMID: 28344029.
92. Ștefănescu R, Tero-Vescan A, Negroiu A, Aurică E, Vari CE. A comprehensive review of the phytochemical, pharmacological, and toxicological properties of *Tribulus terrestris* l. Biomolecules. 2020. doi:10.3390/biom10050752
93. Zhu W, Du Y, Meng H, Dong Y, Li L. A review of traditional pharmacological uses, phytochemistry, and pharmacological activities of *Tribulus terrestris*. Chemistry Central Journal. 2017. doi:10.1186/s13065-017-0289-x
94. Al-Ali M, Wahbi S, Twaij H, Al-Badr A. *Tribulus terrestris*: Preliminary study of its diuretic and contractile effects and comparison with Zea mays. J Ethnopharmacol. 2003;85(2–3):257–60. doi:10.1016/S0378-8741(03)00014-X PubMed PMID: 12639749.
95. Xu YJ, Xu TH, Zhou HO, Li B, Xie SX, Si YS, et al. Two new furostanol saponins from *Tribulus terrestris*. J Asian Nat Prod Res. 2010;12(5). doi:10.1080/10286021003747458
96. Tyagi P, Ranjan R. Comparative study of the pharmacological, phytochemical and biotechnological aspects of *Tribulus terrestris* Linn. and Pedalium murex Linn: An overview. Acta Ecologica Sinica. 2023 Apr 1;43(2):223–33. doi:10.1016/J.CHNAES.2021.07.008
97. Singh RC, Sisodia CS. Effect of *Tribulus terrestris* fruit extracts on chloride and creatinine renal clearances in dogs. Indian J Physiol Pharmacol. 1971;15(3).
98. Al-Ali M, Wahbi S, Twaij H, Al-Badr A. *Tribulus terrestris*: preliminary study of its diuretic and contractile effects and comparison with Zea mays. J Ethnopharmacol. 2003 Apr 1;85(2–3):257–60. doi:10.1016/S0378-8741(03)00014-X PubMed PMID: 12639749.
99. Hannah Rachel Vasanthi A, Muthulakshmi V, Gayathri V, Manikandan R, Ananthi S, Kuruvilla S. Antiurolithiatic effect of Sirupeelai Samoola Kudineer: A polyherbal siddha decoction on ethylene glycol-induced renal calculus in experimental rats. Pharmacogn Mag. 2017 Apr 1;13(50s):S273–9. doi:10.4103/pm.pm_454_16
100. Povydysh MN, Titova M V., Ivanov IM, Klushin AG, Kochkin D V., Galishev BA, et al. Effect of phytopreparations based on bioreactor-grown cell biomass of *Dioscorea deltoidea, Tribulus terrestris* and *Panax japonicus* on carbohydrate and lipid metabolism in type 2 diabetes mellitus. Nutrients. 2021 Nov 1;13(11):3811. doi:10.3390/NU13113811/S1 PubMed PMID: 34836067.

101. Chhatre S, Nesari T, Somani G, Kanchan D, Sathaye S. Comparative evaluation of diuretic activity of different extracts of *Tribulus terrestris* fruits in experimental animals. J Res Phytochem Pharmacol. 2012;2(3).
102. Sharma I, Khan W, Ahmad S. In vitro and ex vivo approach for anti-urolithiatic potential of bioactive fractions of gokhru with simultaneous HPLC analysis of six major metabolites and their exploration in rat plasma. Pharm Biol. 2017;55(1). doi:10.1080/13880209.2016.1266671
103. Khan S, Kabir H, Jalees F, Asif M, Naquvi K. Antihyperlipidemic potential of fruits of *Tribulus terrestris* linn. Int J Biomed Res. 2011 Oct 11;2. doi:10.7439/ijbr.v2i1.79
104. Tilwari A, Shukla NP, Uma Devi P. Effect of five medicinal plants used in Indian system of medicines on immune function in Wistar rats. Afr J Biotechnol. 2011;10(73). doi:10.5897/AJB10.2168
105. Ercan P, El SN. Inhibitory effects of chickpea and *Tribulus terrestris* on lipase, α-amylase and α-glucosidase. Food Chem. 2016;205. doi:10.1016/j.foodchem.2016.03.012
106. Zhang S, Li H, Yang S jie. Tribulosin protects rat hearts from ischemia/reperfusion injury. Acta Pharmacol Sin. 2010;31(6):671–8. doi:10.1038/aps.2010.45
107. Sivapalan SR. Biological and pharmacological studies of *Tribulus terrestris* Linn-A review. International Journal of Multidisciplinary Research. 2016;3(1).
108. Do J, Choi S, Choi J, Hyun JS. Effects and mechanism of action of a *Tribulus terrestris* extract on penile erection. Korean J Urol. 2013;54(3). doi:10.4111/kju.2013.54.3.183
109. Heidari MR, Mehrabani M, Pardakhty A, Khazaeli P, Zahedi MJ, Yakhchali M, et al. The analgesic effect of *Tribulus terrestris* extract and comparison of gastric ulcerogenicity of the extract with indomethacine in animal experiments. In: Annals of the New York Academy of Sciences. 2007. doi:10.1196/annals.1397.045
110. Baburao B, Rajyalakshmi G, Allenki V, Gangarapu K, Anchuri shyam sunder, Rao B, et al. Anti-inflammatory and antimicrobial activities of methanolic extract of *Tribulus terrestris* Linn plant. International journal of chemical science. 2009 Jan 1;7:1867–72.
111. Oh HK, Park SJ, Moon HD, Jun SH, Choi NY, You YO. *Tribulus terrestris* inhibits caries-inducing properties of *Streptococcus mutans*. J Med Plant Res. 2011;5(25). doi:10.5897/JMPR11.1008
112. Goranova T, Bozhanov S, Lozanov V, Mitev V, Kaneva R, Georgieva E. Changes in gene expression of CXCR4, CCR7 and BCL2 after treatment of breast cancer cells with

saponin extract from *Tribulus terrestris*. Neoplasma. 2015;62(1). doi:10.4149/neo_2015_004

113. Al-Bayati FA, Al-Mola HF. Antibacterial and antifungal activities of different parts of *Tribulus terrestris* L. growing in Iraq. J Zhejiang Univ Sci B. 2008;9(2). doi:10.1631/jzus.B0720251
114. Osman W, Shantier S, Mohamed M. Evaluation of Anti-inflammatory Activity and Identification of a Monoterpenoidhydroxylactone (-)-loliolide from *Tribulus terrestris* L.: In vivo and In silico Approaches. Volume 44, Issue 2, Pages 131 - 142. 2024 Jun 1;44(2):131–42. doi:10.52794/hujpharm.1179460
115. Abbas MW, Hussain M, Akhtar S, Ismail T, Qamar M, Shafiq Z, et al. Bioactive Compounds, Antioxidant, Anti-Inflammatory, Anti-Cancer, and Toxicity Assessment of *Tribulus terrestris*—In Vitro and In Vivo Studies. Antioxidants. 2022;11(6). doi:10.3390/antiox11061160
116. Singh N, Kumhar IP, Salim M. Phytochemical analysis of *Tribulus terrestris*. Journal of Medicinal Plants Studies. 2022;10(2):188–90. Available from: www.plantsjournal.com
117. Patel A, Bhatt M, Soni A, Sharma P. Identification of steroidal saponins from *Tribulus terrestris* and their in silico docking studies. J Cell Biochem. 2021;122(11). doi:10.1002/jcb.30113
118. Muniasamy R, Venkataraman R. Pharmacognostical studies on *Tribulus terrestris* and *Tribulus alatus*. Der Pharmacia Sinica. 2011 Jan 1;2:136–9.
119. Urkude AS, Acharya R, Pawar SD, Patel BR, Alam Q. In Silico Evaluation of Bioactive Compounds from Gokshura (*Tribulus terrestris* L.) and Punarnava *(Boerhavia diffusa* L.) for their Nephroprotective Activity in Chronic Kidney Disease and Related Complications. Toxicol Int. 2024 Apr 8;31(2):227–37. doi:10.18311/TI/2024/V31I2/35525
120. Guo W, Wang Y, Fan M, Xie S, Zhao H, Wang J, et al. Integrating metabolomics and network pharmacology to explore the protective effect of gross saponins of *Tribulus terrestris* L. fruit against ischemic stroke in rat. J Ethnopharmacol. 2020 Dec 5;263:113202. doi:10.1016/j.jep.2020.113202 PubMed PMID: 32768639.
121. Tian C, Chang Y, Liu X, Zhang Z, Guo Y, Lan Z, et al. Anti-inflammatory activity in vitro, extractive process and HPLC-MS characterization of total saponins extract from *Tribulus terrestris* L. fruits. Ind Crops Prod. 2020 Aug 1;150:112343. doi:10.1016/J.INDCROP.2020.112343

122. Evstatieva L, Tchorbanov B. Complex investigations of *Tribulus terrestris* L. for sustainable use by pharmaceutical industry. Biotechnology and Biotechnological Equipment. 2011;25(2). doi:10.5504/bbeq.2011.0035
123. Vinay CM, Mehta CH, Bhat C, Kamath A, B Joshi M, Paul B, et al. Integrated LC-MS/MS and network pharmacology approach for predicting active ingredients and pharmacological mechanisms of *Tribulus terrestris* L. against cardiac diseases. J Biomol Struct Dyn. 2023 Jan 1;41(21):11930–45. doi:10.1080/07391102.2023.2199076 PubMed PMID: 37042962.
124. Sudheendran A, Shajahan MA, Premlal S. A comparative diuretic evaluation of fruit and root of Gokshura (*Tribulus terrestris* Linn.) in albino rats. Ayu. 2021 Jan 1;42(1):52–6. doi:10.4103/AYU.AYU_154_17 PubMed PMID: 36743273.
125. Nalwaya N, Jarald EE, Asghar S, Ahmad S. Diuretic activity of a herbal product UNEX. International Journal of Green Pharmacy (IJGP). 2009;3(3). doi:10.22377/IJGP.V3I3.88
126. Arasaratnam V, Balakumar S, Senthuran A, Rajendraprasad R. A study of *Tribulus terrestris* extract on risk factors for urinary stone in normal subjects and urolithic patients. J Natl Sci Found. 2010;38(3). doi:10.4038/jnsfsr.v38i3.2308
127. Nair AB, Jacob S. A simple practice guide for dose conversion between animals and human. J Basic Clin Pharm. 2016 Mar;7(2):27–31. doi:10.4103/0976-0105.177703
128. Abubakar AR, Haque M. Preparation of medicinal plants: Basic extraction and fractionation procedures for experimental purposes. Journal of Pharmacy and Bioallied Sciences. 2020. doi:10.4103/jpbs.JPBS_175_19
129. Huie CW. A review of modern sample-preparation techniques for the extraction and analysis of medicinal plants. Analytical and Bioanalytical Chemistry. 2002. doi:10.1007/s00216-002-1265-3
130. Vogel HG. Drug Discovery and Evaluation: Pharmacological Assays. 3rd ed. Vogel HG, editor. Vol. 1. New York: Springer-Verlag Berlin Heidelberg; 2008. 458–461 p. Available from: https://link.springer.com/referencework/10.1007/978-3-540-70995-4
131. Lakshmanan M, Shewade DG, Raj GM. Introduction to Basics of Pharmacology and Toxicology: Volume 3: Experimental Pharmacology: Research Methodology and Biostatistics. Introduction to Basics of Pharmacology and Toxicology: Volume 3: Experimental Pharmacology: Research Methodology and Biostatistics. 2022. doi:10.1007/978-981-19-5343-9
132. Druzhilovskiy DS, Rudik A V., Filimonov DA, Lagunin AA, Gloriozova TA, Poroikov V V. Online resources for the prediction of biological activity of organic compounds.

Russian Chemical Bulletin. 2016 Feb 1;65(2):384–93. doi:10.1007/S11172-016-1310-6/METRICS

133. Vithalkar MP, Sandra KS, Bharath HB, Krishnaprasad B, Fayaz SM, Sathyanarayana B, et al. Network Pharmacology-driven therapeutic interventions for Interstitial Lung Diseases using Traditional medicines: A Narrative Review. Int Immunopharmacol. 2025 Feb 6;147:113979. doi:10.1016/J.INTIMP.2024.113979
134. Byregowda BH, Baby K, Maity S, Nayak UY, S G, Fayaz SM, et al. Network pharmacology and in silico approaches to uncover multitargeted mechanism of action of *Zingiber zerumbet* rhizomes for the treatment of idiopathic pulmonary fibrosis. F1000Res. 2024 Mar 22;13:216. doi:10.12688/F1000RESEARCH.142513.1 PubMed PMID: 39931327.
135. Bateman A, Martin MJ, Orchard S, Magrane M, Adesina A, Ahmad S, et al. UniProt: the Universal Protein Knowledgebase in 2025. Nucleic Acids Res. 2025 Jan 6;53(D1):D609–17. doi:10.1093/NAR/GKAE1010 PubMed PMID: 39552041.
136. Stelzer G, Rosen N, Plaschkes I, Zimmerman S, Twik M, Fishilevich S, et al. The GeneCards suite: From gene data mining to disease genome sequence analyses. Curr Protoc Bioinformatics. 2016;2016. doi:10.1002/cpbi.5
137. Oliveros JC. Venny 2.1. BioinfoGP, CNB-CSIC. 2021.
138. Shannon P, Markiel A, Ozier O, Baliga NS, Wang JT, Ramage D, et al. Cytoscape: A software Environment for integrated models of biomolecular interaction networks. Genome Res. 2003 Nov;13(11):2498–504. doi:10.1101/GR.1239303, PubMed PMID: 14597658.
139. Dennis G, Sherman BT, Hosack DA, Yang J, Gao W, Lane HC, et al. DAVID: Database for Annotation, Visualization, and Integrated Discovery. Genome Biol. 2003;4(5). doi:10.1186/gb-2003-4-5-p3
140. Cao EH, Zhao YX. human sodium chloride cotransporter NCC S344E in the phosphorylation state and in complex with hydrochlorothiazide. Worldwide Protein Data Bank. 2024 Sep 4. doi:10.2210/PDB9BWT/PDB
141. Human NKCC1 state Fu-II [Internet]. 2022 Sep 28. doi:10.2210/PDB7SFL/PDB
142. Goodsell DS, Sanner MF, Olson AJ, Forli S. The AutoDock suite at 30. Protein Science. 2021;30(1). doi:10.1002/pro.3934
143. Cosconati S, Forli S, Perryman AL, Harris R, Goodsell DS, Olson AJ. Virtual screening with AutoDock: Theory and practice. Expert Opinion on Drug Discovery. 2010. doi:10.1517/17460441.2010.484460

144. Morris G.M., Dallakyan S. AutoDock — AutoDock. 02-27. 2013;1(1).
145. Rose PW, Prlić A, Bi C, Bluhm WF, Christie CH, Dutta S, et al. The RCSB Protein Data Bank: Views of structural biology for basic and applied research and education. Nucleic Acids Res. 2015;43(D1). doi:10.1093/nar/gku1214
146. Rose PW, Beran B, Bi C, Bluhm WF, Dimitropoulos D, Goodsell DS, et al. The RCSB Protein Data Bank: Redesigned web site and web services. Nucleic Acids Res. 2011;39(SUPPL. 1). doi:10.1093/nar/gkq1021
147. Goodsell DS, Zardecki C, Di Costanzo L, Duarte JM, Hudson BP, Persikova I, et al. RCSB Protein Data Bank: Enabling biomedical research and drug discovery. Protein Science. 2020. doi:10.1002/pro.3730
148. Berman HM, Battistuz T, Bhat TN, Bluhm WF, Bourne PE, Burkhardt K, et al. The protein data bank. Acta Crystallogr D Biol Crystallogr. 2002;58(6 I). doi:10.1107/S0907444902003451
149. Berman HM, Westbrook J, Feng Z, Gilliland G, Bhat TN, Weissig H, et al. The Protein Data Bank. Nucleic Acids Research. 2000. doi:10.1093/nar/28.1.235
150. Baroroh, S.Si., M.Biotek. U, Muscifa ZS, Destiarani W, Rohmatullah FG, Yusuf M. Molecular interaction analysis and visualization of protein-ligand docking using Biovia Discovery Studio Visualizer. Indonesian Journal of Computational Biology (IJCB). 2023;2(1). doi:10.24198/ijcb.v2i1.46322
151. Biovia. Biovia Discovery Studio® 2020: Comprehensive Modeling and Simulations for Life Sciences Datasheet. Dassault Systemes: The 3D Experience Company. 2020.
152. Dassault Systemes. Dassault Systemes. 2023. Biovia Discovery Studio Comprehensive Modeling and Simulations for Life Sciences.
153. BIOVIA. Dassault Systèmes BIOVIA, Discovery Studio Modeling Environment, Release 2017. Dassault Systèmes. 2017;San Diego(Calif).
154. Kim S, Chen J, Cheng T, Gindulyte A, He J, He S, et al. PubChem 2023 update. Nucleic Acids Res. 2023;51(D1). doi:10.1093/nar/gkac956
155. Kim S, Thiessen PA, Bolton EE, Chen J, Fu G, Gindulyte A, et al. PubChem substance and compound databases. Nucleic Acids Res. 2016;44(D1). doi:10.1093/nar/gkv951
156. Kim S, Chen J, Cheng T, Gindulyte A, He J, He S, et al. PubChem in 2021: New data content and improved web interfaces. Nucleic Acids Res. 2021;49(D1). doi:10.1093/nar/gkaa971
157. Kim S. Exploring Chemical Information in PubChem. Curr Protoc. 2021;1(8). doi:10.1002/cpz1.217

158. Spessard GO. ACD Labs/LogP dB 3.5 and ChemSketch 3.5. J Chem Inf Comput Sci. 1998;38(6). doi:10.1021/ci980264t
159. Listyarini RV. Implementation of Molecular Visualization Program for Chemistry Learning. Prisma Sains : Jurnal Pengkajian Ilmu dan Pembelajaran Matematika dan IPA IKIP Mataram. 2021;9(1). doi:10.33394/j-ps.v9i1.3941
160. O'Boyle NM, Banck M, James CA, Morley C, Vandermeersch T, Hutchison GR. Open Babel: An Open chemical toolbox. J Cheminform. 2011;3(10). doi:10.1186/1758-2946-3-33
161. Abreu PA, Carvalho K de L, Rabelo VWH, Castro HC. Computational strategy for visualizing structures and teaching biochemistry. Biochemistry and Molecular Biology Education. 2019;47(1). doi:10.1002/bmb.21199
162. Johansson MU, Zoete V, Michielin O, Guex N. Defining and searching for structural motifs using DeepView/Swiss-PdbViewer. BMC Bioinformatics. 2012;13(1). doi:10.1186/1471-2105-13-173
163. OECD. Guideline for Testing of Chemicals. 2022. Test Guideline 425: Acute Oral Toxicity - Up-and-Down Procedure. Available from: https://www.oecd.org/en/publications/2022/06/test-no-425-acute-oral-toxicity-up-and-down-procedure_g1gh2953.html
164. S Kim Suvarna, Layton C, Bancroft JD. Bancroft's Theory and Practice of Histological Techniques. 8th ed. Suvarna SK, Layton C, Bancroft JD, editors. Elsevier Limited; 2019. 557 p.
165. Kiran A, Kumar P, Mandal T, Ganesh Shenoy K, Pai VR, Sharma S, et al. Acute Toxicity Study of the Crude Aqueous Extract of *Tribulus terrestris* Dried Fruit with Potential Diuretic Effect. Original Article Pharmacogn J. 2025;17(5):566–76. doi:10.5530/pj.2025.17.70
166. Earnest Oghenesuvwe E, Daniel Lotanna A. Guidelines on dosage calculation and stock solution preparation in experimental animals' studies. Journal of Natural Sciences; 2014. Available from: https://www.google.com.ng/search?q=Silymarin+tablet,+photos&tbm.
167. Saxena S, Chakraborty D. Antimicrobial Activity and GC-MS Analysis of Bioactive Compounds of *Tribulus terrestris* L. Asian Journal of Research in Botany. 2023 Dec 22;6(2):352–61. Available from: https://journalajrib.com/index.php/AJRIB/article/view/202

168. Zhang H, Kuang Y, Shahrajabian MH, Wang N, Sun W. Study of puncture vine (*Tribulus terrestris* L.), and the important roles of its chemical ingredients. Not Sci Biol. 2025 Feb 27;17(1):12194–12194. doi:10.55779/NSB17112194
169. Mishra P, Mandlik D, Arulmozhi S, Mahadik K. Nephroprotective role of diosgenin in gentamicin-induced renal toxicity: biochemical, antioxidant, immunological and histopathological approach. Futur J Pharm Sci. 2021;7(1). doi:10.1186/s43094-021-00318-z
170. Farsalinos K. Electronic cigarettes as a harm reduction concept for public health. Toxicological Risk Assessment and Multi-System Health Impacts from Exposure. 2021 Jan 1;617–43. doi:10.1016/B978-0-323-85215-9.00036-2
171. Bashir A, Sizar O. Laxatives. Therapeutic Management of Incontinence and Pelvic Pain: Pelvic Organ Disorders. 2024 Jan 30;227–30. doi:10.1007/978-1-84628-756-5_35 PubMed PMID: 30725931.
172. Nau R. Osmotherapy for elevated intracranial pressure: A critical reappraisal. Clin Pharmacokinet. 2000 Sep 13;38(1):23–40. doi:10.2165/00003088-200038010-00002/FIGURES/TAB4 PubMed PMID: 10668857.
173. Human Metabolome Database: Showing metabocard for Sorbitol (HMDB0000247). Available from: https://hmdb.ca/metabolites/HMDB0000247#biological_properties
174. Borges-Grisi MH de S, Brito ACM, Bezerra IM, Martorano-Fernandes L, Cavalcanti YW, Almeida L de FD de. Antimicrobial Effect of Cinnamaldehyde and α-Terpineol on Endodontic Biofilms of Candida albicans and Enterococcus faecalis. Int J Microbiol. 2025;2025(1). doi:10.1155/IJM/4769807,
175. Aborah M, Scarano F, Neto C. Gas Chromatography/Mass Spectrometry Chemical Profiling of Volatile Compounds from Cranberry Plant Byproducts as Potential Antibacterials, Antifungals, and Antioxidants. Molecules. 2025 May 1;30(9). doi:10.3390/MOLECULES30092047,
176. Chinnappan D, Krishnan M, Kuppamuthu A, Elangovan N. Developmental and Neuroprotective Effects of α-Terpineol in MPTP-Induced Parkinsonism in Zebrafish Larvae. Neurochem Res. 2025 Jun 1;50(3). doi:10.1007/S11064-025-04407-W,
177. Bakrim S, Benkhaira N, Bourais I, Benali T, Lee LH, El Omari N, et al. Health Benefits and Pharmacological Properties of Stigmasterol. Antioxidants 2022, Vol 11, Page 1912. 2022 Sep 27;11(10):1912. doi:10.3390/ANTIOX11101912
178. Goswami M, Priya, Jaswal S, Gupta G Das, Verma SK. A comprehensive update on phytochemistry, analytical aspects, medicinal attributes, specifications and stability of

stigmasterol. Steroids. 2023 Aug 1;196:109244. doi:10.1016/J.STEROIDS.2023.109244 PubMed PMID: 37137454.

179. Food Standards Australia New Zealand. Systematic review of the evidence for relationships between saturated, cis monounsaturated, cis polyunsaturated fatty acids and selected individual fatty acids, and blood cholesterol concentration. 2016 Jul. Available from: https://www.foodstandards.gov.au/sites/default/files/consumer/labelling/nutrition/Documents/Systematic%20review%20fatty%20acids%20cholesterol.pdf
180. Marangoni F, Agostoni C, Borghi C, Catapano AL, Cena H, Ghiselli A, et al. Dietary linoleic acid and human health: Focus on cardiovascular and cardiometabolic effects. Atherosclerosis. 2020 Jan 1;292:90–8. doi:10.1016/J.ATHEROSCLEROSIS.2019.11.018 PubMed PMID: 31785494.
181. Li J, Guasch-Ferré M, Li Y, Hu FB. Dietary intake and biomarkers of linoleic acid and mortality: systematic review and meta-analysis of prospective cohort studies. Am J Clin Nutr. 2020 Jul 1;112(1):150. doi:10.1093/AJCN/NQZ349 PubMed PMID: 32020162.
182. Mousavi SM, Jalilpiran Y, Karimi E, Aune D, Larijani B, Mozaffarian D, et al. Dietary Intake of Linoleic Acid, Its Concentrations, and the Risk of Type 2 Diabetes: A Systematic Review and Dose-Response Meta-analysis of Prospective Cohort Studies. Diabetes Care. 2021 Sep 1;44(9):2173–81. doi:10.2337/DC21-0438 PubMed PMID: 34417277.
183. Ryu CM, Faragt MA, Hu CH, Reddy MS, Wei HX, Paré PW, et al. Bacterial volatiles promote growth in Arabidopsis. Proc Natl Acad Sci U S A. 2003 Apr 15;100(8):4927–32. doi:10.1073/PNAS.0730845100/ASSET/AF411A34-41A2-45BB-B0A3-F5EF9FB8E781/ASSETS/GRAPHIC/PQ0730845004.JPEG PubMed PMID: 12684534.
184. Cortes-Barco AM, Hsiang T, Goodwin PH. Induced systemic resistance against three foliar diseases of Agrostis stolonifera by (2R,3R)-butanediol or an isoparaffin mixture. Annals of Applied Biology. 2010 Sep 1;157(2):179–89. doi:10.1111/J.1744-7348.2010.00417.X;JOURNAL:JOURNAL:17447348;PAGE:STRING:ARTICLE/CHAPTER
185. Kong HG, Shin TS, Kim TH, Ryu CM. Stereoisomers of the bacterial volatile compound 2,3-butanediol differently elicit systemic defense responses of pepper against multiple viruses in the field. Front Plant Sci. 2018 Feb 22;9:333556. doi:10.3389/FPLS.2018.00090/BIBTEX

186. Semwal P, Painuli S, Abu-Izneid T, Rauf A, Sharma A, Daştan SD, et al. Diosgenin: An Updated Pharmacological Review and Therapeutic Perspectives. Oxid Med Cell Longev. 2022;2022:1035441. doi:10.1155/2022/1035441 PubMed PMID: 35677108.
187. Singh Chaudhary P, Shukla KS, Akhtar J, Ahmad M, Irfan Khan M. Diosgenin: Ethnopharmacology, Mechanism of Actions, and Formulations. Journal of Chemical Health Risks. 2024 May 3;14(3):2669–92. doi:10.52783/JCHR.V14.I3.5025
188. Traber MG, Atkinson J. Vitamin E, antioxidant and nothing more. Free Radic Biol Med. 2007 Jul 1;43(1):4–15. doi:10.1016/j.freeradbiomed.2007.03.024 PubMed PMID: 17561088.
189. Forouzanfar F, Pourbagher-Shahri AM, Ghazavi H. Evaluation of Antiarthritic and Antinociceptive Effects of Cedrol in a Rat Model of Arthritis. Oxid Med Cell Longev. 2022;2022:4943965. doi:10.1155/2022/4943965 PubMed PMID: 35509836.
190. Kagawa D, Jokura H, Ochia R, Tokimitsu I, Tsubone H. The sedative effects and mechanism of action of cedrol inhalation with behavioral pharmacological evaluation. Planta Med. 2003 Jul 1;69(7):637–41. doi:10.1055/S-2003-41114, PubMed PMID: 12898420.
191. Shoskes JJ, Wilson MK, Spinner ML. Pharmacology of testosterone replacement therapy preparations. Transl Androl Urol. 2016;5(6):834. doi:10.21037/TAU.2016.07.10 PubMed PMID: 28078214.
192. Bansal M, Ramakrishnan C, Ramachandran GN. Stabilization of the collagen structure by hydroxyproline residues. Proceedings of the Indian Academy of Sciences - Section A. 1975 Oct;82(4):152–64. doi:10.1007/BF03046724/METRICS
193. Xu S, Gu M, Wu K, Li G. Unraveling the Role of Hydroxyproline in Maintaining the Thermal Stability of the Collagen Triple Helix Structure Using Simulation. Journal of Physical Chemistry B. 2019 Sep 12;123(36):7754–63. doi:10.1021/ACS.JPCB.9B05006/ASSET/IMAGES/LARGE/JP9B05006_0008.JPEG PubMed PMID: 31418574.
194. Crawford F, Hollis S. Topical treatments for fungal infections of the skin and nails of the foot. Cochrane Database Syst Rev. 2007;2007(3):CD001434. doi:10.1002/14651858.CD001434.PUB2 PubMed PMID: 17636672.
195. Groza N V., Yarkova TA, Gessler NN, Rozumiy A V. Synthesis of Benzoic Acid Esters and Their Antimicrobial Activity. Pharm Chem J. 2024 Jul 1;58(4):625–30. doi:10.1007/S11094-024-03186-Y/FIGURES/1

196. Ciesielski V, Legrand P, Blat S, Rioux V. New insights on pentadecanoic acid with special focus on its controversial essentiality: A mini-review. Biochimie. 2024 Dec 1;227:123–9. doi:10.1016/J.BIOCHI.2024.10.008 PubMed PMID: 39395658.
197. Rosenfeld RM, Schwartz SR, Cannon CR, Roland PS, Simon GR, Kumar KA, et al. Clinical Practice Guideline: Acute Otitis Externa. Otolaryngology-Head and Neck Surgery. 2014;150:S1–24. doi:10.1177/0194599813517083 PubMed PMID: 24491310.
198. Barkovskaya A, Buffone A, Žídek M, Weaver VM. Proteoglycans as Mediators of Cancer Tissue Mechanics. Front Cell Dev Biol. 2020 Nov 30;8:569377. doi:10.3389/FCELL.2020.569377/FULL
199. Iozzo R V., Sanderson RD. Proteoglycans in cancer biology, tumour microenvironment and angiogenesis. J Cell Mol Med. 2011 May;15(5):1013. doi:10.1111/J.1582-4934.2010.01236.X PubMed PMID: 21155971.
200. KEGG PATHWAY: Proteoglycans in cancer - Homo sapiens (human). Available from: https://www.kegg.jp/pathway/hsa05205
201. KEGG PATHWAY: AGE-RAGE signaling pathway in diabetic complications - Homo sapiens (human). Available from: https://www.kegg.jp/pathway/hsa04933
202. Zhou M, Zhang Y, Shi L, Li L, Zhang D, Gong Z, et al. Activation and modulation of the AGEs-RAGE axis: Implications for inflammatory pathologies and therapeutic interventions – A review. Pharmacol Res. 2024 Aug 1;206. doi:10.1016/j.phrs.2024.107282 PubMed PMID: 38914383.
203. Ministry of AYUSH. Ministry of AYUSH, Government of India, New Delhi, 2019. Siddha System of Medicine: The Science of Holistic Health. Available from: www.ayush.gov.in
204. Monica G. Siddha Medicine: The Ancient Science of Healing in Southern India. 2024. doi:10.4172/2573-4555.1000441
205. Semerdjieva IB, Zheljazkov VD. Chemical Constituents, Biological Properties, and Uses of *Tribulus terrestris*: A Review. Nat Prod Commun. 2019;14(8). doi:10.1177/1934578X19868394
206. Rehman MHU, Saleem U, Ahmad B, Rashid M. Phytochemical and toxicological evaluation of *Zephyranthes citrina*. Front Pharmacol. 2022;13. doi:10.3389/fphar.2022.1007310
207. Sharma S, Varsha KK, Kumari S, Gopalakrishnan V, Jose AE, Choudhary B, et al. Acute toxicity analysis of Disarib, an inhibitor of BCL2. Sci Rep. 2020;10(1). doi:10.1038/s41598-020-72058-8

208. Bondarchuk YA, Alekseeva O V., Shakhmatov II, Krinitsina IN. Response of the Hemostatic System to Acute Vital Stress in Rats. Bull Exp Biol Med. 2020 Apr 1;168(6):724–6. doi:10.1007/S10517-020-04788-8/METRICS PubMed PMID: 32328939.

209. Gavage Techniques in Small Animals, Animals in Science. Available from: https://www.queensu.ca/animals-in-science/policies-procedures/sop/rats/10-8

210. University of California SF. Oral Gavage In Mice and Rats IACUC Standard Procedure. 2023. Available from: https://iacuc.ucsf.edu/sites/g/files/tkssra751/f/wysiwyg/STD%20PROCEDURE%20-%20Misc%20Rodent%20Procedures%20-%20Oral%20Gavage%20In%20Mice%20and%20Rats.pdf

211. Mantel-Teeuwisse AK, Kloosterman JME, Maitland-van der Zee AH, Klungel OH, Porsius AJ, De Boer A. Drug-induced lipid changes: A review of the unintended effects of some commonly used drugs on serum lipid levels. Drug Safety. 2001. doi:10.2165/00002018-200124060-00003

212. Abbas MW, Hussain M, Akhtar S, Ismail T, Qamar M, Shafiq Z, et al. Bioactive Compounds, Antioxidant, Anti-Inflammatory, Anti-Cancer, and Toxicity Assessment of *Tribulus terrestris*—In Vitro and In Vivo Studies. Antioxidants 2022, Vol 11, Page 1160. 2022 Jun 13;11(6):1160. doi:10.3390/ANTIOX11061160

213. Yasmeen S, Yasmeen S, Qamar F, Khattak SUR, Naveed S, Mughal M, et al. Acute and Sub-Acute Toxicity of Spray-Dried Extract of *Tribulus terrestris*. Journal of Hunan University Natural Sciences. 2022 Sep 30;49(9):58–66. doi:10.55463/ISSN.1674-2974.49.9.8

214. Kanakia S, Toussaint JD, Mullick Chowdhury S, Tembulkar T, Lee S, Jiang YP, et al. Dose ranging, expanded acute toxicity and safety pharmacology studies for intravenously administered functionalized graphene nanoparticle formulations. Biomaterials. 2014;35(25):7022–31. doi:10.1016/j.biomaterials.2014.04.066 PubMed PMID: 24854092.

215. Zarei MH, Lorigooini Z, Khoei HA, Bijad E. Acute oral toxicity assessment of galbanic acid in albino rat according to OECD 425 TG. Toxicol Rep. 2023;11:111–5. doi:10.1016/j.toxrep.2023.07.001

216. Rispin A, Farrar D, Margosches E, Gupta K, Stitzel K, Carr G, et al. Alternative Methods for the Median Lethal Dose (LD50) Test: The Up-and-Down Procedure for Acute Oral Toxicity. ILAR J. 2002;43(4):233–43.

217. Suvarna R, Suryakanth VB, Bakthavatchalam P, Kalthur G, Nayak M D, Prabhu MM, et al. Acute and sub-chronic toxicity of *Liberin*, an anti-diabetic polyherbal formulation in rats. J Ayurveda Integr Med. 2023;14(6):100804. doi:10.1016/j.jaim.2023.100804
218. Turner P V., Wheler CL, Beaufrère H, Fabian N, Harkness JE. Harkness and Wagner's: Biology and Medicine of Rabbits and Rodents, Sixth Edition. Harkness and Wagner's: Biology and Medicine of Rabbits and Rodents, Sixth Edition. 2025. doi:10.1002/9781119290506
219. Vigneshwar R, Arivuchelvan A, Mekala P, Imayarasi K. Sex-specific reference intervals for Wistar albino rats: hematology and clinical biochemistry. Vol. 60. 2021;60(1):58–65. doi:10.36062/ijah.60.1.2021.58-65
220. Di Fulvio M, Rathod YD, Khader S. Diuretics: a review of the pharmacology and effects on glucose homeostasis. Front Pharmacol. 2025;16:1513125. doi:10.3389/FPHAR.2025.1513125 PubMed PMID: 40223924.
221. Rehman A, Setter SM, Vue MH. Drug-Induced Glucose Alterations Part 2: Drug-Induced Hyperglycemia. Diabetes Spectrum. 2011 Nov 1;24(4):234–8. doi:10.2337/DIASPECT.24.4.234
222. Buscemi S, Nicolucci A, Lucisano G, Galvano F, Grosso G, Massenti FM, et al. Impact of chronic diuretic treatment on glucose homeostasis. Diabetol Metab Syndr. 2013 Dec 13;5(1):80. doi:10.1186/1758-5996-5-80 PubMed PMID: 24330854.
223. Ames RP. A comparison of blood lipid and blood pressure responses during the treatment of systemic hypertension with indapamide and with thiazides. Am J Cardiol. 1996 Feb 22;77(6):B12–6. doi:10.1016/S0002-9149(97)89233-8 PubMed PMID: 8848987.
224. Weidmann P, De M, Ferrari P. Effect of diuretics on the plasma lipid profile. Eur Heart J. 1992;13:61–7.
225. Akhtar F, Khalid F, Wang H, Zhang D, Gong X. The Effect of Thiazide Diuretics on Blood Lipid Profile in Hypertensive Adults: A Meta-analysis of Randomized Controlled Trials. Cureus. 2018 May 18;10(5):e2651. doi:10.7759/CUREUS.2651 PubMed PMID: 30034973.
226. Pollock JS, Ryan MJ, Samson WK, Brooks DP. Water and electrolyte homeostasis brings balance to physiology. https://doi.org/101152/ajpregu002462014. 2014 Sep 1;307(5). doi:10.1152/AJPREGU.00246.2014 PubMed PMID: 25031231.
227. Poursharif S, Hamza S, Braam B. Changes in Proximal Tubular Reabsorption Modulate Microvascular Regulation via the TGF System. Int J Mol Sci. 2022 Oct 1;23(19):11203. doi:10.3390/IJMS231911203 PubMed PMID: 36232506.

228. Fogo AB, Harris RC. Crosstalk between glomeruli and tubules. Nature Reviews Nephrology. 2025;21:189–99. doi:10.1038/s41581-024-00907-0
229. Layton AT, Layton HE. A computational model of epithelial solute and water transport along a human nephron. PLoS Comput Biol. 2019 Feb 1;15(2):e1006108. doi:10.1371/JOURNAL.PCBI.1006108 PubMed PMID: 30802242.
230. Van Bruggen JT, Chalmers B, Muller M. Effects of solvent and solute drag on transmembrane diffusion. J Gen Physiol. 1982 Mar 1;79(3):507. doi:10.1085/JGP.79.3.507 PubMed PMID: 6804595.
231. Günzel D. Is there a molecular basis for solvent drag in the renal proximal tubule? Pflügers Archiv - European Journal of Physiology 2022 475:2. 2022 Nov 23;475(2):277–81. doi:10.1007/S00424-022-02773-W PubMed PMID: 36418493.
232. Hahn RG. Effects of diet, habitual water intake and increased hydration on body fluid volumes and urinary analysis of renal fluid retention in healthy volunteers. Eur J Nutr. 2020 Mar 1;60(2):691. doi:10.1007/S00394-020-02275-4 PubMed PMID: 32430554.
233. Salis A, Monduzzi M. Not only pH. Specific buffer effects in biological systems. Curr Opin Colloid Interface Sci. 2016 Jun 1;23:1–9. doi:10.1016/J.COCIS.2016.04.004
234. Ralston SH. Bone structure and metabolism. Medicine. 2021 Sep 1;49(9):567–71. doi:10.1016/J.MPMED.2021.06.009
235. Murshed M. Mechanism of Bone Mineralization. Cold Spring Harb Perspect Med. 2018 Dec 1;8(12):a031229. doi:10.1101/CSHPERSPECT.A031229 PubMed PMID: 29610149.
236. Pham TD, Verlander JW, Wang Y, Romero CA, Yue Q, Chen C, et al. Aldosterone regulates pendrin and epithelial sodium channel activity through intercalated cell mineralocorticoid receptor–dependent and –independent mechanisms over a wide range in serum potassium. Journal of the American Society of Nephrology. 2020;31(3):483–99. doi:10.1681/ASN.2019050551/-/DCSUPPLEMENTAL PubMed PMID: 32054691.
237. Natarajan A, Jose PA. Renal Modulation: The Renin-Angiotensin-Aldosterone System (RAAS). Nephrology and Fluid/Electrolyte Physiology: Neonatology Questions and Controversies. 2013;107. doi:10.1016/B978-1-4160-3163-5.50013-0
238. Kanugula AK, Kaur J, Batra J, Ankireddypalli AR, Velagapudi R. Renin-Angiotensin System: Updated Understanding and Role in Physiological and Pathophysiological States. Cureus. 2023 Jun 21;15(6):e40725. doi:10.7759/CUREUS.40725 PubMed PMID: 37350982.

239. Leung EKY. Parathyroid hormone. Adv Clin Chem. 2021 Jan 1;101:41–93. doi:10.1016/BS.ACC.2020.06.005 PubMed PMID: 33706890.
240. Alexander RT, Lee JJ, Plain A, Beggs MR, Dimke H. Effects of phospho- and calciotropic hormones on electrolyte transport in the proximal tubule. F1000Res. 2017;6:1797. doi:10.12688/F1000RESEARCH.12097.1 PubMed PMID: 29043081.
241. Oh MS. External Balance of Electrolytes and Acids and Alkali. Seldin and Giebisch's The Kidney: Physiology and Pathophysiology. 2013 Jan 1;291–317. doi:10.1016/B978-0-12-381462-3.00010-0
242. Pollock JS, Ryan MJ, Samson WK, Brooks DP. Water and electrolyte homeostasis brings balance to physiology. Am J Physiol Regul Integr Comp Physiol. 2014 Sep 1;307(5):R481. doi:10.1152/AJPREGU.00246.2014 PubMed PMID: 25031231.
243. Neligan PJ. Fluid and electrolyte balance. Anaesthesia & Intensive Care Medicine. 2024 Feb 1;25(2):107–11. doi:10.1016/J.MPAIC.2023.10.011
244. Wilcox CS, Testani JM, Pitt B. The Pathophysiology of Diuretic Resistance And Its Implications For The Management of Chronic Heart Failure. Hypertension. 2020 Oct 1;76(4):1045. doi:10.1161/HYPERTENSIONAHA.120.15205 PubMed PMID: 32829662.

LIST OF PUBLICATIONS FROM THESIS

9. List of publications from thesis:

- Kiran A, Kumar PSE, Mandal T, Shenoy KG, Pai VR, Sharma S, Amuthan A. Acute Toxicity Study of the Crude Aqueous Extract of *Tribulus terrestris* Dried Fruit with Potential Diuretic Effect. Pharmacogn J. 2025;17(5): 566-576.

Pharmacogn J. 2025; 17(5): 566-576
A Multifaceted Journal in the field of Natural Products and Pharmacognosy
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Original Article

Acute Toxicity Study of the Crude Aqueous Extract of Tribulus terrestris Dried Fruit with Potential Diuretic Effect

Amruth Kiran[1], Praveen Kumar S E[2], Tatiyana Mandal[1], K Ganesh Shenoy[1], Vasudev R Pai[3], Swati Sharma[4], Arul Amuthan[1,5,*]

ABSTRACT

Introduction: *Tribulus terrestris* is an important medicinal plant used in Indian traditional medicine, the crude aqueous extract of the plant is primarily used to induce diuresis for treating cardiovascular diseases and managing renal stones, etc... The safe dose and adverse effect profile of the extract was not explored adequately in preclinical studies. Hence, the present study was undertaken. **Methods:** The acute toxicity was assessed based on the OECD guideline number 425: Acute Oral Toxicity – Up-and-Down-Procedure. A total of 11 animals were used in the study. Initially, one animal was administered with a dosage of 2000 mg/kg; and as the animal survived, four more animals were dosed and were observed for survival and other possible adverse drug reactions. The animals' body weight was measured before experimenting and at the end of the study. Biochemical and haematological examinations were done on normal control and test groups. Animals from the test group were sacrificed, and histopathological examinations of the vital organs were carried out. **Results:** No signs of toxicity or changes in the behaviour were observed in the treatment group. As all the animals survived, it was decided that the LD_{50} was greater than 2000 mg/kg. However, the changes observed with platelets, total cholesterol and LDL were within the normal limits. Histological examination of the vital organs did not reveal any changes in the architecture of the organs. **Conclusion:** Our study demonstrated that the crude aqueous extract of Tribulus terrestris dried fruit does not cause toxicity under the 2000 mg/kg dose limit.

KEYWORDS: *Tribulus terrestris,* crude aqueous extract, acute toxicity study, Wistar rats, Indian traditional medicine, Siddha system of medicine

Amruth Kiran[1], Praveen Kumar S E[2], Tatiyana Mandal[1], K Ganesh Shenoy[1], Vasudev R Pai[3], Swati Sharma[4], Arul Amuthan[1,5,*]

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History

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INTRODUCTION

In traditional and folklore medicine, various medicinal plants have been used for centuries, which are known to have diuretic property. Mono and poly-herbal drugs are used extensively in traditional Indian medicines such as Ayurveda, Siddha, and Unani for diuretic purpose. There are several mono and poly-herbal medicines in the form of pills, tinctures, decoctions, and capsules that are currently in therapeutic use[1].

Diuretic substances that increase water excretion may be helpful in a variety of illnesses, including oedema, cardiovascular diseases, nephritis, toxaemia during pregnancy, premenstrual tension and pulmonary congestion. Plants with medicinal properties have been used in traditional medicine for centuries to cure numerous diseases and disorders. The multiple therapeutic actions and uses of these medicinal plants are described in classical literature on Indigenous medicines and Pharmacopoeias[1].

Herbal medications are widely used in certain regions due to their local availability, affordability, and the common perception that they are safer than Western medicine. Medicinal plants association with other plants in their habitat can affect their therapeutic benefits. Researchers and healthcare practitioners are increasingly focused on this field as they acknowledge the genuine health advantages of these therapies. Several studies have reported plants having strong diuretic efficacy and their uses in various cardiovascular diseases, especially hypertension[2].

The crude aqueous extract (CAE) of *Tribulus terrestris* (*TT*) is a renowned Siddha and Ayurvedic herbal medicine widely used in the Indian subcontinent of Asia. In Siddha, it is popularly known as Nerunjil; in Ayurveda, it is popular by Gokshura. Its therapeutic potentials are well described in Brahatrayi and Ayurvedic Nighantus. *TT* has been reported to possess antimicrobial, antihypertensive, diuretic, anti-lithotrophic[3,4], and antidiabetic[5-7] properties. It is also known to stimulate spermatogenesis[8], treat erectile dysfunction[1] and show antitumour activity[8]. The diuretic efficacy of *TT* is well documented in the literature. However, there is a lack of conclusive reports regarding its adverse effects, as represented in Table 1.

METHODS

Aim: The study aimed to assess the acute toxicity of CAE of TT dried fruit in Wistar rats as per Organisation for Economic Co-operation and Development (OECD) guideline number 425[14].

Test drug extract preparation: TT dried fruits were procured from a local medicinal plant shop. With deionised water, the fruits were washed thoroughly and dried in a hot air oven at 40°C for five days. The dried sample was partially crushed and soaked in distilled water overnight with a solid-to-solvent ratio of 1 100. The sample was heated for six hours at 40°C with constant stirring (500 rpm). The resultant extract was centrifuged at 2000 g for 5 mins, and the supernatant was concentrated through vacuum evaporation to obtain the final extract of 9.2% concentrated extract.

Cite this article: Kiran A, Kumar PSE, Mandal T, Shenoy KG, Pai VR, Sharma S, Amuthan A. Acute Toxicity Study of the Crude Aqueous Extract of Tribulus terrestris Dried Fruit with Potential Diuretic Effect. Pharmacogn J. 2025;17(5): 566-576.

- Arul A, Amruth K, Praveen K S E, Devasrita D, Govindasamy S, Vasudev R P, Shenoy KG. *Tribulus terrestris*: A Revisit to a Promising Herbal Diuretic. Pharmacogn J. 2025;17(5): 653-661.

Pharmacogn J. 2025; 17(5): 653-661
A Multifaceted Journal in the field of Natural Products and Pharmacognosy
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Review Article

Tribulus terrestris: A Revisit to a Promising Herbal Diuretic

Amruth Kiran[1], Praveen Kumar S E[2], Devasrita Dash[1], Govindasamy Suresh[1], Vasudev R Pai[3], Arul Amuthan[1,4]*, K Ganesh Shenoy[1]

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History
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Article Available online
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ABSTRACT

Background: Standard diuretics are essential for managing fluid as well as electrolyte overload and hypertension but are frequently associated with adverse effects such as electrolyte imbalances, renal dysfunction, and metabolic disturbances. This has prompted increased interest in safer, plant-based alternatives. *Tribulus terrestris*, a medicinal herb used as a diuretic agent in traditional systems, has shown promising diuretic activity in recent experimental studies. **Objective:** To provide an outline and assess the reported diuretic effects of *Tribulus terrestris*, including its phytochemical profile, mechanisms of action, and findings from in vivo, in vitro, and in silico studies. **Methods:** An extensive literature survey was performed on the PubMed, Scopus, ScienceDirect, and Google Scholar databases for studies published between 2000 and 2025. The inclusion criterion was original articles evaluating the diuretic activity of *Tribulus terrestris*. Articles without diuretic activity were excluded. Data extraction included the plant part used, extract type, dosage, model used and observed effects. **Results:** This review highlights the diuretic properties and phytoconstituents of *Tribulus terrestris*. Most studies have used aqueous or ethanolic extracts of fruits or whole plants and reported significant increases in urine output and urinary sodium excretion, which are often comparable to those of standard diuretics such as furosemide. **Conclusion:** This review highlights the preclinical diuretic activity of *Tribulus terrestris*. It has shown effective and well-tolerated diuretic potential in preclinical and human subjects. It is a promising, likely herbal-based diuretic, natural alternative or complement, adjunct to conventional diuretics, which warrants further investigation through clinical studies.

Keywords: diuresis, diuretic agent, herbal medicine, Indian traditional medicine, Siddha system of medicine, *Tribulus terrestris*

INTRODUCTION

Diuretics are pharmacologically active substances that promote the excretion of water and electrolytes, primarily sodium and chloride, through the kidneys, increasing urine output[1]. They play pivotal roles in modern clinical medicine, serving as first-line therapies for managing various cardiovascular, renal, and hepatic conditions, such as hypertension, congestive heart failure, nephrotic syndrome, chronic kidney disease, and liver cirrhosis, where fluid overload and blood pressure regulation are of paramount importance. Conventional diuretics such as thiazides, loop diuretics, potassium-sparing agents, osmotic diuretics, and carbonic anhydrase inhibitors have proven highly effective in managing such clinical conditions. However, despite their efficacy, these agents are not without limitations, and they exhibit a wide array of adverse effects, including electrolyte imbalances (e.g., hypokalemia, hyponatremia), dehydration, hypotension, metabolic disturbances (e.g., hyperuricemia, hyperglycemia), renal dysfunction, and ototoxicity, which significantly hamper long-term compliance and quality of life in vulnerable (especially elderly) populations[2-4].

The adverse drug reaction profile of conventional diuretics has prompted a need for safer, equally effective, and more holistic alternatives. The World Health Organization (WHO) has emphasized the integration of traditional medicine into national health systems, recognizing the potential of herbal drugs in preventive and therapeutic healthcare[5]. Numerous medicinal plants have been studied in this context for their diuretic potential[6-8]. One plant that has drawn considerable attention is *Tribulus terrestris* (*TT*), an herbaceous plant widely distributed in tropical and subtropical regions across Asia, Africa, Europe, and Australia[9]. It has long held a revered place in various traditional medicine systems, including Ayurveda, Traditional Chinese Medicine (TCM), Siddha and Unani, and its use has been indicated in the treatment of urinary tract infections, edema, sexual dysfunction, kidney stones, and inflammation[10,11].

TT contains a rich repertoire of phytochemicals, including saponins, flavonoids, alkaloids, tannins, and glycosides, many of which are biologically active and are associated with diuretic properties. In particular, its fruit and root extracts have demonstrated notable renal and cardiovascular effects in preclinical studies. The therapeutic potential of plants as natural diuretic lies in its efficacy, favorable safety profile, and additional antioxidant, anti-inflammatory, and adaptogenic activities. These multifaceted actions may contribute synergistically to its diuretic potential, making it a strong candidate for integration into evidence-based herbal therapeutics[12-18].

This review aims to systematically explore and synthesize existing scientific literature on the diuretic properties of *TT*, focusing on its phytochemical composition, mechanisms of action, experimental outcomes, and potential clinical relevance. We hope to contribute to the growing discourse on plant-

Cite this article: Arul A, Amruth K, Praveen K S E, Devasrita D, Govindasamy S, Vasudev R P,. *Tribulus terrestris*: A Revisit to a Promising Herbal Diuretic. Pharmacogn J. 2025;17(5): 653-661.

CONFERENCE PRESENTATIONS FROM THESIS

10.Conference presentations:

- Attended the MPSCON2024 International conference jointly organised by the Medical Pharmacologists Society and Department of Pharmacology, Saveetha Medical College and Hospital, Chennai, Tamil Nadu, India, on August 29 and 30, 2024.

Title of oral presentation: Dose-dependent diuretic action of the crude aqueous extract of *Tribulus terrestris* fruit

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INSTITUTE OF MEDICAL AND TECHNICAL SCIENCES
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MPSCON2024

INTERNATIONAL CONFERENCE OF THE MEDICAL PHARMACOLOGISTS SOCIETY (MPS)

In Association with

Department of Pharmacology, Saveetha Medical College and Hospital, Chennai, India

Certificate of Participation

This certificate is proudly presented to

AMRUTH KIRAN

For his/her participation as **ORAL PAPER PRESENTER** in the MPSCON2024-International Conference of the Medical Pharmacologists Society at Saveetha Medical College and Hospital (SMCH), Chennai, India on August 29 th-30th 2024

He/ She presented the topic: ***Dose-dependent diuretic action of the crude aqueous extract of Tribulus terrestris fruit***

Dr. J. Kumutha
Dean, SMCH, SIMATS

Dr. J Thirunavukkarasu
Organizing Chairman, Professor & Head
Dept of Pharmacology, SMCH

Dr. Syed Shehnaz Ilyas
Organizing Secretary, Professor,
Dept of Pharmacology, SMCH

Dr. Shiva Murthy N
Joint Organising Secretary, Founder President, MPS
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MPSCON2024

INTERNATIONAL CONFERENCE OF THE MEDICAL PHARMACOLOGISTS SOCIETY (MPS)

In Association with

Department of Pharmacology, Saveetha Medical College and Hospital, Chennai, India

Certificate of Participation

This certificate is proudly presented to

Amruth Kiran

For his/her securing ~~FIRST~~/SECOND PRIZE in an ORAL/ ~~POSTER~~ ~~PAPER~~ PRESENTATION under UG/PG/FACULTY category in the MPSCON 2024 - International Conference of the Medical Pharmacologists Society at Saveetha Medical College and Hospital (SMCH), Chennai, India on August 29th-30th 2024

He/ She presented the topic: Dose dependent diuretic action of the crude aqueous extract of Tribulus terristris fruit

Dr. J. Kumutha
Dean, SMCH, SIMATS

Dr. J Thirunavukkarasu
Organizing Chairman, Professor & Head
Dept of Pharmacology, SMCH

Dr. Syed Shehnaz Ilyas
Organizing Secretary, Professor,
Dept of Pharmacology, SMCH

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Joint Organising Secretary, Founder President, MPS
Professor of Pharmacology, CDSIMER.

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- Attended IPC-IPSCON 2024 National conference jointly organised by the International Pharmacology Conference, Indian Pharmacology Society, and Department of Pharmacology, AIIMS, New Delhi, India, from 28th to 30th November 2024

Title of the poster presentation: Molecular Docking Studies of Phytoconstituents from *Tribulus terrestris* Against Human NKCC1 state Fu-II (7SFL)

विज्ञान एवं प्रौद्योगिकी विभाग
DEPARTMENT OF SCIENCE & TECHNOLOGY

IUPHAR INTERNATIONAL UNION OF BASIC AND CLINICAL PHARMACOLOGY

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Human Resource Development Group
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Council of Scientific & Industrial Research

IPC-IPSCON 2024

International Pharmacology Conference (IPC)
&
54th Annual Conference of Indian Pharmacological Society 2024
28th - 30th November 2024
Organized By: Department of Pharmacology, AIIMS, NEW DELHI

TODAY'S RESEARCH – TOMORROW'S MEDICINE

Certificate of Participation

Ref no. 3901/DMC/CME/16C/2/2024/327356
DMC has AWARDED 14.2 Credit Hours

This is to certify that

Dr./Mr./Ms **AMRUTH KIRAN**

participated as Invited Speaker/ Chairperson/ Judge/ Resource Person/ Panelist/ Delegate in IPC-IPSCON-2024, Organized by the Department of Pharmacology, All India Institute of Medical Sciences, New Delhi.

Dr. Shiv Prakash	Dr. D. S. Arya	Dr. Harlokesh Narayan Yadav	Dr. B. Kalakumar
President - IPS	Organizing Chairman	Organizing Secretary	General Secretary - IPS

विज्ञान एवं प्रौद्योगिकी विभाग
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&
54th Annual Conference of Indian Pharmacological Society 2024
28th - 30th November 2024
Organized By: Department of Pharmacology, AIIMS, NEW DELHI

TODAY'S RESEARCH – TOMORROW'S MEDICINE

Certificate of Participation

This is to certify that

Dr./Mr./Ms Amruth Kiran

participated in the Oral/ Poster Presentation/Quiz competition in the IPC-IPSCON-2024, Organized by the Department of Pharmacology, All India Institute of Medical Sciences, New Delhi.

Dr. Shiv Prakash	Dr. D. S. Arya	Dr. Harlokesh Narayan Yadav	Dr. B. Kalakumar
President - IPS	Organizing Chairman	Organizing Secretary	General Secretary - IPS

ANNEXURES

11. Annexures:

KASTURBA MEDICAL COLLEGE
MANIPAL
(A constituent unit of MAHE, Manipal)

IAEC Registration NO. 94/PO/RReBi/S/99/CPCSEA.

25.08.2023

Certificate

This is to certify that the project proposal no. IAEC/KMC/69/2023 titled **"Evaluation of Diuretic Activity of *Tribulus terrestris* fruit in Wistar Rats - A Bioactivity Guided Approach"** submitted by Mr. Amruth Kiran, Research Associate, Division of Pharmacology, Department of Basic Medical Sciences, MAHE, Manipal, has been approved/recommended by the IAEC of Kasturba Medical College, Manipal, MAHE in its meeting dated 25th August, 2023 and has sanctioned 200-250g, 8 weeks old, **female** wistar rats, 20nos under this proposal for a duration of next 12 months.

Authorized by	Name	Signature	Date
Chairman:	Dr. Vandana K.E		04/09/2023
Member Secretary:	Dr. Amrita Parida		4.09.2023
Main Nominee of CPCSEA:	Dr. Jayaprakash Shetty K.		8.9.23

KASTURBA MEDICAL COLLEGE * MAHE, MANIPAL * IAEC

1 of 2

Kasturba Medical College, Madhav Nagar, Manipal 576104, Karnataka, India
dir. 91 820 2922325, 2922367, 2571201 *fax.* 91 820 2571927 *email.* office.kmc@manipal.edu www.manipal.edu

KASTURBA MEDICAL COLLEGE
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IAEC Registration NO. 94/PO/RReBi/S/99/CPCSEA.

17.05.2024

Certificate

This is to certify that the project proposal no. IAEC/KMC/69/2023 titled "**Evaluation of Diuretic Activity of *Tribulus terrestris* fruit in Wistar Rats. A Bioactivity Guided Approach**" submitted by Mr. Amruth Kiran, Research Associate, Division of Pharmacology, Department of Basic Medical Sciences, MAHE, Manipal, has been approved/recommended by the IAEC of Kasturba Medical College, Manipal, MAHE in its meeting dated 17th May, 2024.

Based on the pilot study results from the previously approved 20 rats, IAEC has approved 150g, male Wistar rats, 100nos, under this proposal for a duration of the next 12 months.

Authorized by	Name	Signature	Date
Chairman:	Dr. Vandana K.E		31/5/24.
Member Secretary:	Dr. Amrita Parida		31/5/24
Main Nominee of CPCSEA:	Dr. Jayaprakash Shetty K.		4/6/24

KASTURBA MEDICAL COLLEGE * IAEC * MAHE, MANIPAL

Kasturba Medical College, Madhav Nagar, Manipal 576104, Karnataka, India
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MANIPAL
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MAHE/CDS/PHD/2023

Date: 30-09-2023

Mr. Amruth Kiran
Research Associate and PhD Candidate
DBMS, MAHE-Manipal

Through:
The Head, DBMS, MAHE, Manipal

HEAD
Department of Basic Medical Sciences
MAHE, Manipal - 576 104

Dear Mr. Amruth,

Sub: Transfer of PhD Candidate admitted at KMC, MAHE, Manipal to DBMS, MAHE, Manipal
Ref: Request dated 18-08-2023; sub: request to change the PhD topic

With regard to the above subject, please note the following changes:

Name of Candidate	Mr. Amruth Kiran
New Registration Number	**196600001**
New Institution	DBMS, MAHE, Manipal
Category	Part time
Date of Registration	24-12-2019
Name of the New Guide	Dr. Arul L Amuthan, Assistant Professor, Division of Pharmacology, DBMS, MAHE, Manipal
Name of the New Co-Guide	Dr. Vasudev R Pai, Assistant Professor – Senior Scale, Department of Pharmacology, MCOPS, MAHE, Manipal
Old Registration Number	190100019
Old Institution	KMC, MAHE, Manipal

- The Doctoral Advisory Committee to be re-constituted and the same to be communicated to the undersigned.
- PhD protocol to be submitted to CDS for university presentation and approval.
- Rest of the terms and conditions mentioned in the registration letter dated 04-01-2020 remains the same.

Regards

Dr. Vasudha Devi
Deputy Director – Centre for Doctoral Studies

Copy to:
- The Registrar, MAHE, Manipal
- The Registrar – Evaluation, MAHE, Manipal
- The Dean, KMC, MAHE, Manipal
- Dr. Arul L Amuthan, Assistant Professor, Division of Pharmacology, DBMS, MAHE, Manipal
- Dr. Vasudev R Pai, Assistant Professor – Senior Scale, Department of Pharmacology, MCOPS, MAHE, Manipal
- PhD Coordinator, KMC, MAHE, Manipal
- PhD Coordinator, DBMS, MAHE, Manipal

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MAHE/CDS/PHD/2023

Date: December 04, 2023

Mr. Amruth Kiran
PhD Scholar
Division of Pharmacology
Department of Basic Medical Sciences (DBMS)
MAHE, Manipal

Research Associate
Division of Pharmacology
Department of Basic Medical Sciences (DBMS)
MAHE, Manipal

Dear Mr. Amruth,

Sub: PhD protocol approval
Refs:

1. Registration letter dated 04-January-2020
2. Transfer letter dated 16-November-2022
3. Transfer letter dated 30-September-2023

With regard to the above subject, MAHE has approved the new PhD protocol as detailed below.

Name of Candidate	Mr. Amruth Kiran
Admission/Registration Number	196600001
Date of Joining/Registration	24th December 2019
Name of the Guide	Dr. Arul Amuthan L, Assistant Professor, Division of Pharmacology, Department of Basic Medical sciences, MAHE, Manipal
Name of the Co-Guide	Dr. Vasudev R Pai, Assistant Professor-Senior Scale, Department of Pharmacognosy, Manipal College of Pharmaceutical Sciences, MAHE, Manipal
New PhD Topic	Evaluation of Diuretic Activity of Tribulus terrestris fruit in Wistar Rats – A Bioactivity Guided Approach
Date of PhD Protocol Approval	27th October 2023

The guidelines regarding DAC reports and other details are as follows:

- You are required to present your half yearly DAC report at the institution in person and DAC meeting minutes and progress report to be submitted to the undersigned as per timeline.
- The maximum duration of PhD program is 7 years from the date of Registration. The Admission stands cancelled after the completion of maximum duration. Fee is applicable for the extended period.

Failing to fulfil any of the above conditions your registration stands cancelled.

With regards,

Dr. Vasudha Devi
Deputy Director, Centre for Doctoral Studies

Copy to:

- Registrar, MAHE, Manipal
- Registrar-Evaluation, MAHE, Manipal
- The Dean, DBMS, MAHE, Manipal
- Dr. Arul Amuthan L, Assistant Professor, Division of Pharmacology, Department of Basic Medical sciences, MAHE, Manipal
- Dr. Vasudev R Pai, Assistant Professor-Senior Scale, Department of Pharmacognosy, Manipal College of Pharmaceutical Sciences, MAHE, Manipal
- Dr. Indira Adiga K, Professor and PhD Coordinator, Department of Biochemistry, Department of Basic Medical Sciences, MAHE, Manipal
- Dr. Chandrika Nayak, Professor and PhD Coordinator, Department of Biochemistry, Department of Basic Medical Sciences, MAHE, Manipal
- Sr. Manager, Student Finance, MAHE, Manipal

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21/08/25 LD

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Annexure 46; Version2; 11 Sept 2023

Centre for Doctoral Studies, MAHE, Manipal

Request for Modification of PhD Thesis Title

(Please type, handwritten applications will not be considered)

Date: 20/08/2025

Name of the PhD scholar	Amruth Kiran	
Registration Number	196600001	
Date of Admission	24/12/2019	**Date of protocol approval:** 27/10/2023
Category (Please tick relevant)	TMA Pai Scholar/ Self Sponsored/ Project Fellow/National Scholar/**Part Time (MAHE employees)**/ Part Time (working professionals)/Research Centre scholar (Full time)/ Research Centre scholar (Part time)/Integrated MD-MS PhD/ Any other (Specify).....	
Mode (Please tick relevant)	**Part Time**/ Full Time	
Name of the Institution/ Research Centre	Department of Basic Medical Sciences (DBMS), MAHE, Manipal	
Number of DAC presentations completed till date	08	
Original approved title	Evaluation of Diuretic Activity of Tribulus terrestris fruit in Wistar Rats – A Bioactivity Guided Approach	
New Title	Experimental and Computational Elucidation of the diuretic action of *Tribulus terrestris*: An integrated in vivo and in silico approach	
To what extent the objectives and methodology that were approved by university have been revised to accommodate the new title (denote in %)		5%
Objectives as per original protocol	I. To evaluate and compare the diuretic action of various extracts, fractions and subfractions of *Tribulus terrestris* fruit in rats. II. To evaluate the phytochemistry of highly active diuretic extract / fraction / subfraction of *Tribulus terrestris* dried fruit via GC-MS method. III. To evaluate the long-term effect of highly active diuretic extract / fraction / subfraction of *Tribulus terrestris* fruit extract. IV. iv. To evaluate the combined effect of highly active extract / fraction / subfraction of *Tribulus terrestris* fruit with standard diuretic drugs.	
Revised objectives as per new title (if any)	I. To evaluate and compare the diuretic action of the crude aqueous extract of *Tribulus terrestris* dried fruit in rats **(modified)** II. To predict the possible phytochemical targets and pathways for the diuretic action of the phytoconstituents of the crude aqueous extract of *Tribulus terrestris* dried fruit using network pharmacology **(new objective was added)**	

Signature of the PhD scholar with date: Amruth Kiran 20/Aug/2025

Signature of the Guide with date: 20/8/2025

Signature of the HOI with date:

HEAD
Department of Basic Medical Sciences
MAHE, Manipal - 576 104

Process flow: PhD scholar → submission of request → CDS → Registrar Evaluation, HOI, PhD coordinator, Guide, PhD scholar

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Annexure 46; Version2; 11 Sept 2023

Note: -

- DAC recommendation is mandatory.
- Title can be revised only once during the entire course duration.
- If there is a major change in the title, objectives and methodology, the revised protocol is to be presented to the DAC for approval. Following this, DAC approval to be submitted to Institution for Institutional Protocol Approval Committee (IPAC) presentation and approval. IPAC meeting minutes to be submitted to CDS for the final confirmation of revised title/protocol.

CDS Office Use: -

Verification status: Verified **Date:** 22/08/2025

Remarks:

Approved ☑ **/ Not Approved** ☐

for Dr.

Deputy Director
Centre for Doctoral Studies
Dr. SHOBHA D'ARA

Deputy Director
Centre for Doctoral Studies
MAHE, Manipal - 576104

To:
To:

PhD scholar

CC:

e-7/7/21

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(Deemed to be University under Section 3 of the UGC Act, 1956)

Ph. D. Course Work Grade Sheet

Name of the Candidate	**Amruth Kiran**
Registration Number	**191300008**
Date of Registration	**24 December 2019**
Title of Thesis	**Establishing the cardioprotective activity of rapamycin in angiotensin–II induced maladaptive changes in myocardium and an exploration into its time course of effects in mice**
Name of the Supervisor	**Dr. Vasudha Devi**
Name of Co-Supervisor (if any)	**Dr. Dhandapani Kuppuswamy and Dr. Abhinav Kanwal**

Sl. No.	Title of Course Work	Credits	Grade Obtained
1.	Systematic review and meta-analysis	4	A
2.	A Primer to Medical Genetics	2	A
3.	Biostatistics, Epidemiology and Research methodology	6	D

Grade Values

Grade	A+	A	B	C	D	E	F
Grade Value	10	9	8	7	6	5	0

DEAN
Melaka Manipal Medical College
(Manipal Campus)
Manipal - 576104

Head of the Institution
(Name, Signature with Seal)

Guide
(Name, Signature)
DR. VASUDHA DEVI

Deputy Director - Centre for Doctoral Studies

Deputy Director
Centre for Doctoral Studies
MAHE, Manipal - 576104