Chapter 10

References

10 References

1. Sarker, S.D. and Nahar, L., *An Introduction to Natural Products Isolation,* in *Natural Products Isolation,* S.D. Sarker and L. Nahar, Editors. 2012, Humana Press. p. 1-25.

2. Koehn, F.E. and Carter, G.T., *The evolving role of natural products in drug discovery.* Nature Reviews Drug Discovery, 2005. **4**(3): p. 206-220.

3. Zhang, M.M., Qiao, Y., Ang, E.L., and Zhao, H., *Using natural products for drug discovery: the impact of the genomics era.* Expert Opinion on Drug Discovery, 2017. **12**(5): p. 475-487.

4. Newman, D.J. and Cragg, G.M., *Natural Products as Sources of New Drugs from 1981 to 2014.* Journal of Natural Products, 2016. **79**(3): p. 629-661.

5. Entzeroth, M., Flotow, H., and Condron, P., *Overview of High-Throughput Screening.* Current Protocols in Pharmacology, 2009. **44**(1): p. 9.4.1-9.4.27.

6. Kingston, D.G.I., *Modern Natural Products Drug Discovery and Its Relevance to Biodiversity Conservation.* Journal of Natural Products, 2011. **74**(3): p. 496-511.

7. Li, J.W.H. and Vederas, J.C., *Drug Discovery and Natural Products: End of an Era or an Endless Frontier?* Science, 2009. **325**(5937): p. 161-165.

8. Ganesan, A., *The impact of natural products upon modern drug discovery.* Current Opinion in Chemical Biology, 2008. **12**(3): p. 306-317.

9. Ortholand, J.-Y. and Ganesan, A., *Natural products and combinatorial chemistry: back to the future.* Current Opinion in Chemical Biology, 2004. **8**(3): p. 271-280.

10. Chen, M.S. and White, M.C., *A Predictably Selective Aliphatic C–H Oxidation Reaction for Complex Molecule Synthesis.* Science, 2007. **318**(5851): p. 783-787.

11. Harvey, A.L., *Natural products in drug discovery.* Drug Discovery Today, 2008. **13**(19): p. 894-901.

12. Newman, D.J., Cragg, G.M., and Snader, K.M., *Natural Products as Sources of New Drugs over the Period 1981−2002.* Journal of Natural Products, 2003. **66**(7): p. 1022-1037.

13. Newman, D.J. and Cragg, G.M., *Natural Products as Sources of New Drugs over the Nearly Four Decades from 01/1981 to 09/2019.* Journal of Natural Products, 2020. **83**(3): p. 770-803.

14. Chen, Y. and Kirchmair, J., *Cheminformatics in Natural Product-based Drug Discovery.* Molecular Informatics, 2020. **39**(12): p. 2000171.

15. Mullard, A., *2023 FDA approvals.* Nat Rev Drug Discov, 2024. **23**(2): p. 88-95.

16. Miethke, M., Pieroni, M., Weber, T., Brönstrup, M., Hammann, P., Halby, L., Arimondo, P.B., et al., *Towards the sustainable discovery and development of new antibiotics.* Nature Reviews Chemistry, 2021. **5**(10): p. 726-749.

17. Ling, L.L., Schneider, T., Peoples, A.J., Spoering, A.L., Engels, I., Conlon, B.P., Mueller, A., et al., *A new antibiotic kills pathogens without detectable resistance.* Nature, 2015. **517**(7535): p. 455-459.

18. Imai, Y., Meyer, K.J., Iinishi, A., Favre-Godal, Q., Green, R., Manuse, S., Caboni, M., et al., *A new antibiotic selectively kills Gram-negative pathogens.* Nature, 2019. **576**(7787): p. 459-464.

19. Kozioł, A., Mroczko, L., Niewiadomska, M., and Lochyński, S., *γ-lactones with potential biological activity.* Polish Journal of Natural Sciences, 2017. **32**(3): p. 495-511.

20. Mathema, V.B., Koh, Y.-S., Thakuri, B.C., and Sillanpää, M., *Parthenolide, a Sesquiterpene Lactone, Expresses Multiple Anti-cancer and Anti-inflammatory Activities.* Inflammation, 2012. **35**(2): p. 560-565.

21. Feltenstein, M.W., Schühly, W., Warnick, J.E., Fischer, N.H., and Sufka, K.J., *Anti-inflammatory and anti-hyperalgesic effects of sesquiterpene lactones from Magnolia and Bear's foot.* Pharmacology Biochemistry and Behavior, 2004. **79**(2): p. 299-302.

22. Pae, H.O., Jeong, G.S., Kim, H.S., Woo, W.H., Rhew, H.Y., Kim, H.S., Sohn, D.H., et al., *Costunolide inhibits production of tumor necrosis factor-α and interleukin-6 by inducing heme oxygenase-1 in RAW264.7 macrophages.* Inflammation Research, 2007. **56**(12): p. 520-526.

23. Lee, J., Tae, N., Lee, J.J., Kim, T., and Lee, J.-H., *Eupatolide inhibits lipopolysaccharide-induced COX-2 and iNOS expression in RAW264.7 cells by inducing proteasomal degradation of TRAF6.* European Journal of Pharmacology, 2010. **636**(1): p. 173-180.

24. Formisano, C., Sanna, C., Ballero, M., Chianese, G., Sirignano, C., Rigano, D., Millán, E., et al., *Anti-inflammatory sesquiterpene lactones from Onopordum illyricum L. (Asteraceae), an Italian medicinal plant.* Fitoterapia, 2017. **116**: p. 61-65.

25. Pan, L., Hu, L., Zhang, L., Xu, H., Chen, Y., Bian, Q., Zhu, A., et al., *Deoxyelephantopin decreases the release of inflammatory cytokines in*

macrophage associated with attenuation of aerobic glycolysis via modulation of PKM2. International Immunopharmacology, 2020. **79**: p. 106048.

26. Scarponi, C., Butturini, E., Sestito, R., Madonna, S., Cavani, A., Mariotto, S., and Albanesi, C., *Inhibition of Inflammatory and Proliferative Responses of Human Keratinocytes Exposed to the Sesquiterpene Lactones Dehydrocostuslactone and Costunolide.* PLOS ONE, 2014. **9**(9): p. e107904.

27. Paço, A., Brás, T., Santos, J.O., Sampaio, P., Gomes, A.C., and Duarte, M.F. *Anti-Inflammatory and Immunoregulatory Action of Sesquiterpene Lactones*. Molecules, 2022. **27**, 1142.

28. Matos, M.S., Anastácio, J.D., and Nunes dos Santos, C. *Sesquiterpene Lactones: Promising Natural Compounds to Fight Inflammation*. Pharmaceutics, 2021. **13**, 991.

29. Viennois, E., Xiao, B., Ayyadurai, S., Wang, L., Wang, P.G., Zhang, Q., Chen, Y., et al., *Micheliolide, a new sesquiterpene lactone that inhibits intestinal inflammation and colitis-associated cancer.* Laboratory Investigation, 2014. **94**(9): p. 950-965.

30. Ninomiya-Tsuji, J., Kajino, T., Ono, K., Ohtomo, T., Matsumoto, M., Shiina, M., Mihara, M., et al., *A Resorcylic Acid Lactone, 5Z-7-Oxozeaenol, Prevents Inflammation by Inhibiting the Catalytic Activity of TAK1 MAPK Kinase Kinase.* Journal of Biological Chemistry, 2003. **278**(20): p. 18485-18490.

31. Kuttikrishnan, S., Prabhu, K.S., Al Sharie, A.H., Al Zu'bi, Y.O., Alali, F.Q., Oberlies, N.H., Ahmad, A., et al., *Natural resorcylic acid lactones: A chemical biology approach for anticancer activity.* Drug Discovery Today, 2022. **27**(2): p. 547-557.

32. Buskuhl, H., de Oliveira, F.L., Blind, L.Z., de Freitas, R.A., Barison, A., Campos, F.R., Corilo, Y.E., et al., *Sesquiterpene lactones from Vernonia scorpioides and their in vitro cytotoxicity.* Phytochemistry, 2010. **71**(13): p. 1539-1544.

33. Ashour, M.L., El-Readi, M.Z., Tahrani, A., Eid, S.Y., and Wink, M., *A novel cytotoxic aryltetraline lactone from Bupleurum marginatum (Apiaceae).* Phytochemistry Letters, 2012. **5**(2): p. 387-392.

34. Toyang, N.J., Wabo, H.K., Ateh, E.N., Davis, H., Tane, P., Sondengam, L.B., Bryant, J., et al., *Cytotoxic sesquiterpene lactones from the leaves of Vernonia guineensis Benth. (Asteraceae).* Journal of Ethnopharmacology, 2013. **146**(2): p. 552-556.

35. Xiao, W., Li, X., Li, N., Bolati, M., Wang, X., Jia, X., and Zhao, Y., *Sesquiterpene lactones from Saussurea involucrata.* Fitoterapia, 2011. **82**(7): p. 983-987.

36. Taylor, P.G., Dupuy Loo, O.A., Bonilla, J.A., and Murillo, R., *Anticancer activities of two sesquiterpene lactones, millerenolide and thieleanin isolated from Viguiera sylvatica and Decachaeta thieleana.* Fitoterapia, 2008. **79**(6): p. 428-432.

37. Cao, S., Hou, Y., Brodie, P., Miller, J.S., Randrianaivo, R., Rakotobe, E., Rasamison, V.E., et al., *Antiproliferative Compounds of Cyphostemma greveana from a Madagascar Dry Forest.* Chemistry & Biodiversity, 2011. **8**(4): p. 643-650.

38. Sassa, T., Nukina, M., and Ikeda, M., *Electrophilic Reactivities and Biological Activities of trans- and cis-Resorcylides.* NIPPON KAGAKU KAISHI, 1981. **1981**(5): p. 883-885.

39. Kumar, C.G., Mongolla, P., Sujitha, P., Joseph, J., Babu, K.S., Suresh, G., Ramakrishna, K.V.S., et al., *Metabolite profiling and biological activities of bioactive compounds produced by Chrysosporium lobatum strain BK-3 isolated from Kaziranga National Park, Assam, India.* SpringerPlus, 2013. **2**(1): p. 122.

40. He, J., Wijeratne, E.M.K., Bashyal, B.P., Zhan, J., Seliga, C.J., Liu, M.X., Pierson, E.E., et al., *Cytotoxic and Other Metabolites of Aspergillus Inhabiting the Rhizosphere of Sonoran Desert Plants.* Journal of Natural Products, 2004. **67**(12): p. 1985-1991.

41. Meng, L.-H., Li, X.-M., Lv, C.-T., Li, C.-S., Xu, G.-M., Huang, C.-G., and Wang, B.-G., *Sulfur-Containing Cytotoxic Curvularin Macrolides from Penicillium sumatrense MA-92, a Fungus Obtained from the Rhizosphere of the Mangrove Lumnitzera racemosa.* Journal of Natural Products, 2013. **76**(11): p. 2145-2149.

42. Prieto-Martínez, F.D., Norinder, U., and Medina-Franco, J.L., *Cheminformatics Explorations of Natural Products*, in *Progress in the Chemistry of Organic Natural Products 110: Cheminformatics in Natural Product Research*, A.D. Kinghorn, et al., Editors. 2019, Springer International Publishing. p. 1-35.

43. Banerjee, P., Erehman, J., Gohlke, B.-O., Wilhelm, T., Preissner, R., and Dunkel, M., *Super Natural II—a database of natural products.* Nucleic Acids Research, 2015. **43**(D1): p. D935-D939.

44. Chen, C.Y.C., *TCM Database@Taiwan: The World's Largest Traditional Chinese Medicine Database for Drug Screening In Silico.* PLOS ONE, 2011. **6**(1): p. e15939.

45. van Santen, J.A., Jacob, G., Singh, A.L., Aniebok, V., Balunas, M.J., Bunsko, D., Neto, F.C., et al., *The Natural Products Atlas: An Open Access Knowledge Base for Microbial Natural Products Discovery.* ACS Central Science, 2019. **5**(11): p. 1824-1833.

46. Zeng, X., Zhang, P., Wang, Y., Qin, C., Chen, S., He, W., Tao, L., et al., *CMAUP: a database of collective molecular activities of useful plants.* Nucleic Acids Research, 2019. **47**(D1): p. D1118-D1127.

47. Mohamed, A., Nguyen, C.H., and Mamitsuka, H., *Current status and prospects of computational resources for natural product dereplication: a review.* Briefings in Bioinformatics, 2016. **17**(2): p. 309-321.

48. Chanana, S., Thomas, C.S., Braun, D.R., Hou, Y., Wyche, T.P., and Bugni, T.S. *Natural Product Discovery Using Planes of Principal Component Analysis in R (PoPCAR).* Metabolites, 2017. **7**, 34.

49. Harn, Y.-C., Su, B.-H., Ku, Y.-L., Lin, O.A., Chou, C.-F., and Tseng, Y.J., *NP-StructurePredictor: Prediction of Unknown Natural Products in Plant Mixtures.* Journal of Chemical Information and Modeling, 2017. **57**(12): p. 3138-3148.

50. Rodrigues, T., *Harnessing the potential of natural products in drug discovery from a cheminformatics vantage point.* Organic & Biomolecular Chemistry, 2017. **15**(44): p. 9275-9282.

51. Chen, Y., Garcia de Lomana, M., Friedrich, N.-O., and Kirchmair, J., *Characterization of the Chemical Space of Known and Readily Obtainable Natural Products.* Journal of Chemical Information and Modeling, 2018. **58**(8): p. 1518-1532.

52. Chen, H., Engkvist, O., Blomberg, N., and Li, J., *A comparative analysis of the molecular topologies for drugs, clinical candidates, natural products, human metabolites and general bioactive compounds.* MedChemComm, 2012. **3**(3): p. 312-321.

53. Chávez-Hernández, A.L., Sánchez-Cruz, N., and Medina-Franco, J.L., *A Fragment Library of Natural Products and its Comparative Chemoinformatic Characterization.* Molecular Informatics, 2020. **39**(11): p. 2000050.

54. Schäfer, T., Kriege, N., Humbeck, L., Klein, K., Koch, O., and Mutzel, P., *Scaffold Hunter: a comprehensive visual analytics framework for drug discovery.* Journal of Cheminformatics, 2017. **9**(1): p. 28.

55. Wetzel, S., Schuffenhauer, A., Roggo, S., Ertl, P., and Waldmann, H., *Cheminformatic Analysis of Natural Products and their Chemical Space.* CHIMIA, 2007. **61**(6): p. 355.

56. Rosén, J., Lövgren, A., Kogej, T., Muresan, S., Gottfries, J., and Backlund, A., *ChemGPS-NPWeb: chemical space navigation online.* Journal of Computer-Aided Molecular Design, 2009. **23**(4): p. 253-259.

57. Pascolutti, M., Campitelli, M., Nguyen, B., Pham, N., Gorse, A.-D., and Quinn, R.J., *Capturing Nature's Diversity.* PLOS ONE, 2015. **10**(4): p. e0120942.

58. Van der Maaten, L. and Hinton, G., *Visualizing data using t-SNE.* Journal of Machine Learning Research, 2008. **9**(11): p. 2579-2605.

59. McInnes, L., Healy, J., and Melville, J., *UMAP: Uniform Manifold Approximation and Projection for Dimension Reduction.* arXiv:1802.03426, 2018. **10**: p. 1802.

60. González-Medina, M., Prieto-Martínez, F.D., Owen, J.R., and Medina-Franco, J.L., *Consensus Diversity Plots: a global diversity analysis of chemical libraries.* Journal of Cheminformatics, 2016. **8**(1): p. 63.

61. Sánchez-Cruz, N. and Medina-Franco, J.L., *Statistical-based database fingerprint: chemical space dependent representation of compound databases.* Journal of Cheminformatics, 2018. **10**(1): p. 55.

62. Yu, M.J., *Druggable chemical space and enumerative combinatorics.* Journal of Cheminformatics, 2013. **5**(1): p. 19.

63. Ertl, P., Roggo, S., and Schuffenhauer, A., *Natural Product-likeness Score and Its Application for Prioritization of Compound Libraries.* Journal of Chemical Information and Modeling, 2008. **48**(1): p. 68-74.

64. Chen, Y., Stork, C., Hirte, S., and Kirchmair, J. *NP-Scout: Machine Learning Approach for the Quantification and Visualization of the Natural Product-Likeness of Small Molecules*. Biomolecules, 2019. **9**, 43.

65. Seo, M., Shin, H.K., Myung, Y., Hwang, S., and No, K.T., *Development of Natural Compound Molecular Fingerprint (NC-MFP) with the Dictionary of Natural Products (DNP) for natural product-based drug development.* Journal of Cheminformatics, 2020. **12**(1): p. 6.

66. Kirchweger, B. and Rollinger, J.M., *Virtual Screening for the Discovery of Active Principles from Natural Products*, in *Natural Products as Source of Molecules with Therapeutic Potential: Research & Development, Challenges and Perspectives*, V. Cechinel Filho, Editor. 2018, Springer International Publishing. p. 333-364.

67. Warren, G.L., Andrews, C.W., Capelli, A.-M., Clarke, B., LaLonde, J., Lambert, M.H., Lindvall, M., et al., *A Critical Assessment of Docking Programs and Scoring Functions.* Journal of Medicinal Chemistry, 2006. **49**(20): p. 5912-5931.

68. Grisoni, F., Merk, D., Friedrich, L., and Schneider, G., *Design of Natural-Product-Inspired Multitarget Ligands by Machine Learning.* ChemMedChem, 2019. **14**(12): p. 1129-1134.

69. Chaudhari, R., Tan, Z., Huang, B., and Zhang, S., *Computational polypharmacology: a new paradigm for drug discovery.* Expert Opinion on Drug Discovery, 2017. **12**(3): p. 279-291.

70. Reker, D., Rodrigues, T., Schneider, P., and Schneider, G., *Identifying the macromolecular targets of de novo-designed chemical entities through self-organizing map consensus.* Proceedings of the National Academy of Sciences, 2014. **111**(11): p. 4067-4072.

71. Moumbock, A.F.A., Li, J., Mishra, P., Gao, M., and Günther, S., *Current computational methods for predicting protein interactions of natural products.* Computational and Structural Biotechnology Journal, 2019. **17**: p. 1367-1376.

72. Cockroft, N.T., Cheng, X., and Fuchs, J.R., *STarFish: A Stacked Ensemble Target Fishing Approach and its Application to Natural Products.* Journal of Chemical Information and Modeling, 2019. **59**(11): p. 4906-4920.

73. Karageorgis, G., Foley, D.J., Laraia, L., Brakmann, S., and Waldmann, H., *Pseudo Natural Products—Chemical Evolution of Natural Product Structure.* Angewandte Chemie International Edition, 2021. **60**(29): p. 15705-15723.

74. Hartenfeller, M., Zettl, H., Walter, M., Rupp, M., Reisen, F., Proschak, E., Weggen, S., et al., *DOGS: Reaction-Driven de novo Design of Bioactive Compounds.* PLOS Computational Biology, 2012. **8**(2): p. e1002380.

75. Kratz, J.M., Grienke, U., Scheel, O., Mann, S.A., and Rollinger, J.M., *Natural products modulating the hERG channel: heartaches and hope.* Natural Product Reports, 2017. **34**(8): p. 957-980.

76. Wang, Y., Xing, J., Xu, Y., Zhou, N., Peng, J., Xiong, Z., Liu, X., et al., *In silico ADME/T modelling for rational drug design.* Quarterly Reviews of Biophysics, 2015. **48**(4): p. 488-515.

77. Kirchmair, J., Göller, A.H., Lang, D., Kunze, J., Testa, B., Wilson, I.D., Glen, R.C., et al., *Predicting drug metabolism: experiment and/or computation?* Nature Reviews Drug Discovery, 2015. **14**(6): p. 387-404.

78. Šícho, M., Stork, C., Mazzolari, A., de Bruyn Kops, C., Pedretti, A., Testa, B., Vistoli, G., et al., *FAME 3: Predicting the Sites of Metabolism in Synthetic Compounds and Natural Products for Phase 1 and Phase 2 Metabolic Enzymes.* Journal of Chemical Information and Modeling, 2019. **59**(8): p. 3400-3412.

79. Annunziata, F., Pinna, C., Dallavalle, S., Tamborini, L., and Pinto, A., *An Overview of Coumarin as a Versatile and Readily Accessible Scaffold with Broad-Ranging Biological Activities*. International Journal of Molecular Sciences, 2020. **21**, 4618.

80. Maria João, M., Lourdes, S., Eugenio, U., Orlando, A.A., Enrique, M., and Estela Guardado, Y., *Coumarins — An Important Class of Phytochemicals*, in *Phytochemicals*. 2015, IntechOpen. p. 533-538.

81. Sharifi-Rad, J., Cruz-Martins, N., López-Jornet, P., Lopez, E.P.-F., Harun, N., Yeskaliyeva, B., Beyatli, A., et al., *Natural Coumarins: Exploring the Pharmacological Complexity and Underlying Molecular Mechanisms.* Oxidative Medicine and Cellular Longevity, 2021. **2021**: p. 6492346.

82. Önder, A., *Chapter 3 - Anticancer activity of natural coumarins for biological targets*, in *Studies in Natural Products Chemistry*, R. Atta Ur, Editor. 2020, Elsevier. p. 85-109.

83. Abolibda, T.Z., Fathalla, M., Farag, B., Zaki, M.E.A., and Gomha, S.M., *Synthesis and Molecular Docking of Some Novel 3-Thiazolyl-Coumarins as Inhibitors of VEGFR-2 Kinase*. Molecules, 2023. **28**, 689.

84. Alshabanah, L.A., Al-Mutabagani, L.A., Gomha, S.M., and Ahmed, H.A., *Three-Component Synthesis of Some New Coumarin Derivatives as Anticancer Agents.* Frontiers in Chemistry, 2022. **9**: p. 762248.

85. Gomha, S.M., Abdel-aziz, H.M., and El-Reedy, A.A.M., *Facile Synthesis of Pyrazolo[3,4-c]pyrazoles Bearing Coumarine Ring as Anticancer Agents.* Journal of Heterocyclic Chemistry, 2018. **55**(8): p. 1960-1965.

86. Küpeli Akkol, E., Genç, Y., Karpuz, B., Sobarzo-Sánchez, E., and Capasso, R., *Coumarins and Coumarin-Related Compounds in Pharmacotherapy of Cancer*. Cancers, 2020. **12**, 1959.

87. Naderi Alizadeh, M., Rashidi, M., Muhammadnejad, A., Moeini Zanjani, T., and Ziai, S.A., *Antitumor Effects of Umbelliprenin in a Mouse Model of Colorectal Cancer.* Iranian Journal of Pharmaceutical Research, 2018. **17**(3): p. 976-985.

88. Al-Warhi, T., Sabt, A., Elkaeed, E.B., and Eldehna, W.M., *Recent advancements of coumarin-based anticancer agents: An up-to-date review.* Bioorganic Chemistry, 2020. **103**: p. 104163.

89. Lugano, R., Ramachandran, M., and Dimberg, A., *Tumor angiogenesis: causes, consequences, challenges and opportunities.* Cellular and Molecular Life Sciences, 2020. **77**(9): p. 1745-1770.

90. Pinedo, H.M. and Slamon, D.J., *INTRODUCTION: Translational Research: The Role of VEGF in Tumor Angiogenesis.* The Oncologist, 2000. **5**(S1): p. 1-2.

91. Hicklin, D.J. and Ellis, L.M., *Role of the Vascular Endothelial Growth Factor Pathway in Tumor Growth and Angiogenesis.* Journal of Clinical Oncology, 2005. **23**(5): p. 1011-1027.

92. Wang, X., Bove, A.M., Simone, G., and Ma, B., *Molecular Bases of VEGFR-2-Mediated Physiological Function and Pathological Role.* Frontiers in Cell and Developmental Biology, 2020. **8**: p. 599281.

93. Nilsson, M. and Heymach, J.V., *Vascular Endothelial Growth Factor (VEGF) Pathway.* Journal of Thoracic Oncology, 2006. **1**(8): p. 768-770.

94. Peng, F.-W., Liu, D.-K., Zhang, Q.-W., Xu, Y.-G., and Shi, L., *VEGFR-2 inhibitors and the therapeutic applications thereof: a patent review (2012-2016).* Expert Opinion on Therapeutic Patents, 2017. **27**(9): p. 987-1004.

95. S, V., Kajal, K., Mondal, S., Wahan, S.K., Das Kurmi, B., Das Gupta, G., and Patel, P., *Novel VEGFR-2 Kinase Inhibitors as Anticancer Agents: A Review Focusing on SAR and Molecular Docking Studies (2016–2021).* Chemistry & Biodiversity, 2023. **20**(2): p. e202200847.

96. Aziz, M.A., Serya, R.A.T., Lasheen, D.S., Abdel-Aziz, A.K., Esmat, A., Mansour, A.M., Singab, A.N.B., et al., *Discovery of Potent VEGFR-2 Inhibitors based on Furopyrimidine and Thienopyrimidne Scaffolds as Cancer Targeting Agents.* Scientific Reports, 2016. **6**(1): p. 24460.

97. Sorokina, M., Merseburger, P., Rajan, K., Yirik, M.A., and Steinbeck, C., *COCONUT online: Collection of Open Natural Products database.* Journal of Cheminformatics, 2021. **13**(1): p. 1-13.

98. Berthold, M.R., Cebron, N., Dill, F., Gabriel, T.R., Kötter, T., Meinl, T., Ohl, P., et al. *KNIME: The Konstanz Information Miner*. in *Data Analysis, Machine Learning and Applications*. 2008. Springer.

99. Berman, H.M., Westbrook, J., Feng, Z., Gilliland, G., Bhat, T.N., Weissig, H., Shindyalov, I.N., et al., *The Protein Data Bank.* Nucleic Acids Research, 2000. **28**(1): p. 235-242.

100. Tukiran, T., Mahmudah, F., Hidayati, N., and Shimizu, K., *Gallic acid: A phenolic acid and its antioxidant activity from stem bark of chloroform extracts of syzygium litorale (blume) amshoff (myrtaceae).* Molekul, 2016. **11**(2): p. 180-189.

101. Sunseri, J. and Koes, D.R., *Pharmit: interactive exploration of chemical space.* Nucleic Acids Research, 2016. **44**(W1): p. W442-W448.

102. Skariyachan, S. and Garka, S., *Chapter 1 - Exploring the binding potential of carbon nanotubes and fullerene towards major drug targets of multidrug resistant bacterial pathogens and their utility as novel therapeutic agents*, in *Fullerens, Graphenes and Nanotubes*, A.M. Grumezescu, Editor. 2018, William Andrew Publishing. p. 1-29.

103. Kumar, R. and Sharma, A., *Chapter 15 - Computational strategies and tools for protein tertiary structure prediction*, in *Basic Biotechniques for Bioprocess and Bioentrepreneurship*. 2023, Academic Press. p. 225-242.

104. Pettersen, E.F., Goddard, T.D., Huang, C.C., Couch, G.S., Greenblatt, D.M., Meng, E.C., and Ferrin, T.E., *UCSF Chimera—A visualization system for exploratory research and analysis.* Journal of Computational Chemistry, 2004. **25**(13): p. 1605-1612.

105. Waterhouse, A., Bertoni, M., Bienert, S., Studer, G., Tauriello, G., Gumienny, R., Heer, F.T., et al., *SWISS-MODEL: homology modelling of protein structures and complexes.* Nucleic Acids Research, 2018. **46**(W1): p. W296-W303.

106. Dolinsky, T.J., Nielsen, J.E., McCammon, J.A., and Baker, N.A., *PDB2PQR: an automated pipeline for the setup of Poisson–Boltzmann electrostatics calculations.* Nucleic Acids Research, 2004. **32**(2): p. W665-W667.

107. Tripathi, N., Goel, B., Bhardwaj, N., Sahu, B., Kumar, H., and Jain, S.K., *Virtual screening and molecular simulation study of natural products database for lead identification of novel coronavirus main protease inhibitors.* Journal of Biomolecular Structure and Dynamics, 2022. **40**(8): p. 3655-3667.

108. O'Boyle, N.M., Banck, M., James, C.A., Morley, C., Vandermeersch, T., and Hutchison, G.R., *Open Babel: An open chemical toolbox.* Journal of Cheminformatics, 2011. **3**(1): p. 33.

109. Morris, G.M., Huey, R., Lindstrom, W., Sanner, M.F., Belew, R.K., Goodsell, D.S., and Olson, A.J., *AutoDock4 and AutoDockTools4: Automated docking with selective receptor flexibility.* Journal of Computational Chemistry, 2009. **30**(16): p. 2785-2791.

110. Singh, R., Pokle, A.V., Ghosh, P., Ganeshpurkar, A., Swetha, R., Singh, S.K., and Kumar, A., *Pharmacophore-based virtual screening, molecular docking and molecular dynamics simulations study for the identification of LIM kinase-1 inhibitors.* Journal of Biomolecular Structure and Dynamics, 2022. **41**(13): p. 1-15.

111. Subramaniam, S., Mehrotra, M., and Gupta, D., *Virtual high throughput screening (vHTS)--a perspective.* Bioinformation, 2008. **3**(1): p. 14-17.

112. Daina, A., Michielin, O., and Zoete, V., *SwissADME: a free web tool to evaluate pharmacokinetics, drug-likeness and medicinal chemistry friendliness of small molecules.* Scientific Reports, 2017. **7**(1): p. 42717.

113. Lee, S., Lee, I.H., Kim, H.J., Chang, G.S., Chung, J.E., and No, K.T., *The PreADME Approach: Web-based program for rapid prediction of physico-*

chemical, drug absorption and drug-like properties. euro QSAR 2002 - Designing Drugs and Crop Protectants: Processes Problems and Solutions, 2002: p. 418-420.

114. Durrant, J.D. and McCammon, J.A., *Molecular dynamics simulations and drug discovery.* BMC Biology, 2011. **9**(1): p. 71.

115. Tripathi, N., Bhardwaj, N., Singh, B., and Jain, S.K., *In-silico identification of Coumarin-based natural compounds as potential VEGFR-2 inhibitors.* Chemical Papers, 2024: p. 1-14.

116. Sobolev, O.V., Afonine, P.V., Moriarty, N.W., Hekkelman, M.L., Joosten, R.P., Perrakis, A., and Adams, P.D., *A Global Ramachandran Score Identifies Protein Structures with Unlikely Stereochemistry.* Structure, 2020. **28**(11): p. 1249-1258.e2.

117. Davis, I.W., Leaver-Fay, A., Chen, V.B., Block, J.N., Kapral, G.J., Wang, X., Murray, L.W., et al., *MolProbity: all-atom contacts and structure validation for proteins and nucleic acids.* Nucleic Acids Research, 2007. **35**(2): p. W375-W383.

118. Williams, C.J., Headd, J.J., Moriarty, N.W., Prisant, M.G., Videau, L.L., Deis, L.N., Verma, V., et al., *MolProbity: More and better reference data for improved all-atom structure validation.* Protein Science, 2018. **27**(1): p. 293-315.

119. Colovos, C. and Yeates, T.O., *Verification of protein structures: Patterns of nonbonded atomic interactions.* Protein Science, 1993. **2**(9): p. 1511-1519.

120. Jitendra, S. and Vinay, R., *Structure based drug designing of a novel antiflaviviral inhibitor for nonstructural 3 protein.* Bioinformation, 2011. **6**(2): p. 57-60.

121. Ma, X.-l., Chen, C., and Yang, J., *Predictive model of blood-brain barrier penetration of organic compounds.* Acta Pharmacologica Sinica, 2005. **26**(4): p. 500-512.

122. Ganeshpurkar, A., Singh, R., Gore, P.G., Kumar, D., Gutti, G., Kumar, A., and Singh, S.K., *Structure-based screening and molecular dynamics simulation studies for the identification of potential acetylcholinesterase inhibitors.* Molecular Simulation, 2020. **46**(3): p. 169-185.

123. Tu, Y., Yang, Y., Li, Y., and He, C., *Naturally occurring coumestans from plants, their biological activities and therapeutic effects on human diseases.* Pharmacological Research, 2021. **169**: p. 105615.

124. Dutta, S., Mahalanobish, S., and Sil, P.C., *Chapter 8 - Phytoestrogens as Novel Therapeutic Molecules Against Breast Cancer*, in *Discovery and Development of Anti-Breast Cancer Agents from Natural Products*, G. Brahmachari, Editor. 2021, Elsevier. p. 197-229.

125. Chopra, B., Dhingra, A.K., and Dhar, K.L., *Psoralea corylifolia L. (Buguchi) — Folklore to modern evidence: Review.* Fitoterapia, 2013. **90**: p. 44-56.

126. Liu, X., Nam, J.-W., Song, Y.S., Viswanath, A.N.I., Pae, A.N., Kil, Y.-S., Kim, H.-D., et al., *Psoralidin, a coumestan analogue, as a novel potent estrogen receptor signaling molecule isolated from Psoralea corylifolia.* Bioorganic & Medicinal Chemistry Letters, 2014. **24**(5): p. 1403-1406.

127. Qi, S.-Z., Li, B.-B., Liu, M.-S., Zhang, Z., Miao, S., and Gong, K.-K., *Chemical constituents from the seeds of Cullen corylifolium and their inhibitory activity on diacylglycerol acyltransferase.* Natural Product Research, 2023. **37**(10): p. 1601-1607.

128. Zhang, X., Zhao, W., Wang, Y., Lu, J., and Chen, X., *The Chemical Constituents and Bioactivities of Psoralea corylifolia Linn.: A Review.* The American Journal of Chinese Medicine, 2016. **44**(01): p. 35-60.

129. Sigismund, S., Avanzato, D., and Lanzetti, L., *Emerging functions of the EGFR in cancer.* Molecular Oncology, 2018. **12**(1): p. 3-20.

130. Uribe, M.L., Marrocco, I., and Yarden, Y., *EGFR in Cancer: Signaling Mechanisms, Drugs, and Acquired Resistance*. Cancers, 2021. **13**, 2748.

131. Masuda, H., Zhang, D., Bartholomeusz, C., Doihara, H., Hortobagyi, G.N., and Ueno, N.T., *Role of epidermal growth factor receptor in breast cancer.* Breast Cancer Research and Treatment, 2012. **136**(2): p. 331-345.

132. Liu, T.C., Jin, X., Wang, Y., and Wang, K., *Role of epidermal growth factor receptor in lung cancer and targeted therapies.* Am J Cancer Res, 2017. **7**(2): p. 187-202.

133. Bhuyan, M.S.I. and Gao, X., *A protein-dependent side-chain rotamer library.* BMC Bioinformatics, 2011. **12**(14): p. S10.

134. Chaudhary, N. and Aparoy, P., *Application of per-residue energy decomposition to identify the set of amino acids critical for in silico prediction of COX-2 inhibitory activity.* Heliyon, 2020. **6**(10): p. e04944.

135. Tripathi, N., Shah, H., Bhardwaj, N., Sarkar, R., and Jain, S.K., *In silico analysis, isolation, and cytotoxicity evaluation of the coumestans from Cullen corylifolium (L.) Medik.* Natural Product Research, 2023: p. 1-8.

136. Pahari, P. and Rohr, J., *Total Synthesis of Psoralidin, an Anticancer Natural Product.* The Journal of Organic Chemistry, 2009. **74**(7): p. 2750-2754.

137. Sarkar, R., Mukherjee, S., Biswas, J., and Roy, M., *Phenethyl isothiocyanate, by virtue of its antioxidant activity, inhibits invasiveness and metastatic potential of*

breast cancer cells: HIF-1α as a putative target. Free Radical Research, 2016. **50**(1): p. 84-100.

138. Sarkars, R., Mukherjee, S., and Roy, M., *Targeting Heat Shock Proteins by Phenethyl Isothiocyanate Results in Cell-Cycle Arrest and Apoptosis of Human Breast Cancer Cells.* Nutrition and Cancer, 2013. **65**(3): p. 480-493.

139. Meng, X.-Y., Zhang, H.-X., Mezei, M., and Cui, M., *Molecular Docking: A Powerful Approach for Structure-Based Drug Discovery.* Current Computer-Aided Drug Design, 2011. **7**(2): p. 146-157.

140. Danker, T. and Möller, C., *Early identification of hERG liability in drug discovery programs by automated patch clamp.* Frontiers in Pharmacology, 2014. **5**: p. 87849.

141. Hospital, A., Goñi, J.R., Orozco, M., and Gelpí, J.L., *Molecular dynamics simulations: advances and applications.* Advances and Applications in Bioinformatics and Chemistry, 2015. **8**: p. 37-47.

142. Case, D., Ben-Shalom, I., Brozell, S., Cerutti, D., Cheatham III, T., Cruzeiro, V., Darden, T., et al., *AMBER 2020.* University of California, San Francisco, 2020.

143. Gómez-Outes, A., Suárez-Gea, M.L., Calvo-Rojas, G., Lecumberri, R., Rocha, E., Pozo-Hernández, C., Terleira-Fernández, A.I., et al., *Discovery of anticoagulant drugs: a historical perspective.* Current Drug Discovery Technologies, 2012. **9**(2): p. 83-104.

144. Stefanachi, A., Leonetti, F., Pisani, L., Catto, M., and Carotti, A., *Coumarin: A Natural, Privileged and Versatile Scaffold for Bioactive Compounds.* Molecules, 2018. **23**(2).

145. Alam, F., Khan, G.N., and Asad, M.H.H.B., *Psoralea corylifolia L: Ethnobotanical, biological, and chemical aspects: A review.* Phytotherapy Research, 2018. **32**(4): p. 597-615.

146. Uikey, S.K., Yadav, A.S., Sharma, A.K., Rai, A.K., Raghuwanshi, D.K., and Badkhane, Y., *The Botany, Chemistry, Pharmacological and Therapeutic Application of Psoralea corylifolia L.–A Review.* International Journal of Phytomedicine, 2010. **2**: p. 100-107.

147. Khushboo, P.S., Jadhav, V.M., Kadam, V.J., and Sathe, N.S., *Psoralea corylifolia Linn.-"Kushtanashini".* Pharmacognosy Reviews, 2010. **4**(7): p. 69-76.

148. Tripathi, N., Parmar, A., Pandey, N., Bhardwaj, N., Chakrabarty, S., Sarkar, R., Kumar, H., et al., *Isolation, Cytotoxicity, and In-silico Screening of Coumarins from Psoralea corylifolia Linn.* Chemistry & Biodiversity, 2024. **21**(2): p. e202301841.

149. Oueslati, M.H., Guetat, A., Bouajila, J., Alzahrani, A.K., and Basha, J., *Deverra tortuosa (Desf.) DC from Saudi Arabia as a new source of marmin and furanocoumarins derivatives with α-glucosidase, antibacterial and cytotoxic activities.* Heliyon, 2021. **7**(4): p. e06656.

150. Mukandiwa, L., Ahmed, A., Eloff, J.N., and Naidoo, V., *Isolation of seselin from Clausena anisata (Rutaceae) leaves and its effects on the feeding and development of Lucilia cuprina larvae may explain its use in ethnoveterinary medicine.* Journal of Ethnopharmacology, 2013. **150**(3): p. 886-891.

151. Marumoto, S. and Miyazawa, M., *Biotransformation of Bergapten and Xanthotoxin by Glomerella cingulata.* Journal of Agricultural and Food Chemistry, 2010. **58**(13): p. 7777-7781.

152. Chang, H., Okada, Y., Okuyama, T., and Tu, P., *1H and 13C NMR assignments for two new angular furanocoumarin glycosides from Peucedanum praeruptorum.* Magnetic Resonance in Chemistry, 2007. **45**(7): p. 611-614.

153. Bergendorff, O., Dekermendjian, K., Nielsen, M., Shan, R., Witt, R., Ai, J., and Sterner, O., *Furanocoumarins with affinity to brain benzodiazepine receptors in vitro.* Phytochemistry, 1997. **44**(6): p. 1121-1124.

154. Steck, W. and Bailey, B.K., *Characterization of plant coumarins by combined gas chromatography, ultraviolet absorption spectroscopy, and nuclear magnetic resonance analysis.* Canadian Journal of Chemistry, 1969. **47**(19): p. 3577-3583.

155. Shawl, A.S., Raina, V.K., Kumar, T., Srivastava, S.K., Tripathi, S., and Kumar, S., *Furanocoumarins from Platytaenia lasiocarpa.* Journal of Medicinal and Aromatic Plant Sciences.

156. Joo, S.-H., Lee, S.-C., and Kim, S.-K., *UV absorbent, marmesin, from the bark of Thanakha,Hesperethusa crenulata L.* Journal of Plant Biology, 2004. **47**(2): p. 163-165.

157. Liu, R., Li, A., Sun, A., and Kong, L., *Preparative isolation and purification of psoralen and isopsoralen from Psoralea corylifolia by high-speed counter-current chromatography.* Journal of Chromatography A, 2004. **1057**(1): p. 225-228.

158. Hashmi, A.A., Naz, S., Hashmi, S.K., Irfan, M., Hussain, Z.F., Khan, E.Y., Asif, H., et al., *Epidermal growth factor receptor (EGFR) overexpression in triple-negative breast cancer: association with clinicopathologic features and prognostic parameters.* Surgical and Experimental Pathology, 2019. **2**(1): p. 6.

159. Ali, R. and Wendt, M.K., *The paradoxical functions of EGFR during breast cancer progression.* Signal Transduction and Targeted Therapy, 2017. **2**(1): p. 16042.

160. Yang, C.-H., Chou, H.-C., Fu, Y.-N., Yeh, C.-L., Cheng, H.-W., Chang, I.-C., Liu, K.-J., et al., *EGFR over-expression in non-small cell lung cancers harboring EGFR mutations is associated with marked down-regulation of CD82.* Biochimica et Biophysica Acta (BBA) - Molecular Basis of Disease, 2015. **1852**(7): p. 1540-1549.

161. Bethune, G., Bethune, D., Ridgway, N., and Xu, Z., *Epidermal growth factor receptor (EGFR) in lung cancer: an overview and update.* Journal of Thoracic Disease, 2010. **2**(1): p. 48-51.

162. Paço, A., Brás, T., Santos, J.O., Sampaio, P., Gomes, A.C., and Duarte, M.F., *Anti-Inflammatory and Immunoregulatory Action of Sesquiterpene Lactones*. Molecules, 2022. **27**(3): p. 1142.

163. Chaturvedi, D., *Chapter 6 - Recent developments in the anti-inflammatory potential of sesquiterpene lactones and their semisynthetic analogs*, in *Discovery and Development of Anti-Inflammatory Agents from Natural Products*, G. Brahmachari, Editor. 2019, Elsevier. p. 185-205.

164. Shi, C., Li, H., Yang, Y., and Hou, L., *Anti-Inflammatory and Immunoregulatory Functions of Artemisinin and Its Derivatives.* Mediators of Inflammation, 2015. **2015**: p. 435713.

165. Li, X., Yuan, W., Wu, J., Zhen, J., Sun, Q., and Yu, M., *Andrographolide, a natural anti-inflammatory agent: An Update.* Frontiers in Pharmacology, 2022. **13**: p. 920435.

166. Zhang, L., Fang, X., Sun, J., Su, E., Cao, F., and Zhao, L., *Study on Synergistic Anti-Inflammatory Effect of Typical Functional Components of Extracts of Ginkgo Biloba Leaves*. Molecules, 2023. **28**, 1377.

167. Niu, T.T., Yuan, B.Y., and Liu, G.Z., *Ginkgolides and bilobalide for treatment of Alzheimer's disease and COVID-19: potential mechanisms of action.* European Review for Medical and Pharmacological Sciences, 2022. **26**(24): p. 9502-9510.

168. Goldie, M. and Dolan, S., *Bilobalide, a unique constituent of Ginkgo biloba, inhibits inflammatory pain in rats.* Behavioural Pharmacology, 2013. **24**(4): p. 298-306.

169. Cho, J.Y., Baik, K.U., Jung, J.H., and Park, M.H., *In vitro anti-inflammatory effects of cynaropicrin, a sesquiterpene lactone, from Saussurea lappa.* European Journal of Pharmacology, 2000. **398**(3): p. 399-407.

170. Furman, D., Campisi, J., Verdin, E., Carrera-Bastos, P., Targ, S., Franceschi, C., Ferrucci, L., et al., *Chronic inflammation in the etiology of disease across the life span.* Nature Medicine, 2019. **25**(12): p. 1822-1832.

171. Ahmed, A.U., *An overview of inflammation: mechanism and consequences.* Frontiers in Biology, 2011. **6**(4): p. 274-281.

172. Medzhitov, R., *Origin and physiological roles of inflammation.* Nature, 2008. **454**(7203): p. 428-435.

173. Feghali, C.A. and Wright, T.M., *Cytokines in acute and chronic inflammation.* Frontiers in Bioscience, 1997. **2**(4): p. 12-26.

174. Williams, C.S., Mann, M., and DuBois, R.N., *The role of cyclooxygenases in inflammation, cancer, and development.* Oncogene, 1999. **18**(55): p. 7908-7916.

175. Noor, F., Tahir ul Qamar, M., Ashfaq, U.A., Albutti, A., Alwashmi, A.S.S., and Aljasir, M.A. *Network Pharmacology Approach for Medicinal Plants: Review and Assessment*. Pharmaceuticals, 2022. **15**, 572.

176. Sakle, N.S., More, S.A., and Mokale, S.N., *A network pharmacology-based approach to explore potential targets of Caesalpinia pulcherima: an updated prototype in drug discovery.* Scientific Reports, 2020. **10**(1): p. 17217.

177. Chandran, U., Mehendale, N., Patil, S., Chaguturu, R., and Patwardhan, B., *Chapter 5 - Network Pharmacology*, in *Innovative Approaches in Drug Discovery*, B. Patwardhan and R. Chaguturu, Editors. 2017, Academic Press: Boston. p. 127-164.

178. Ibrahim, R.S. and El-Banna, A.A., *Network pharmacology-based analysis for unraveling potential cancer-related molecular targets of Egyptian propolis phytoconstituents accompanied with molecular docking and in vitro studies.* RSC Advances, 2021. **11**(19): p. 11610-11626.

179. Peng, X., Wang, J., Peng, W., Wu, F.-X., and Pan, Y., *Protein–protein interactions: detection, reliability assessment and applications.* Briefings in Bioinformatics, 2017. **18**(5): p. 798-819.

180. Sengupta, D. and Kundu, S., *Role of long- and short-range hydrophobic, hydrophilic and charged residues contact network in protein's structural organization.* BMC Bioinformatics, 2012. **13**(1): p. 142.

181. Daina, A., Michielin, O., and Zoete, V., *SwissTargetPrediction: updated data and new features for efficient prediction of protein targets of small molecules.* Nucleic Acids Research, 2019. **47**(W1): p. W357-W364.

182. Shannon, P., Markiel, A., Ozier, O., Baliga, N.S., Wang, J.T., Ramage, D., Amin, N., et al., *Cytoscape: a software environment for integrated models of biomolecular interaction networks.* Genome Research, 2003. **13**(11): p. 2498-504.

183. Tuller, T., Atar, S., Ruppin, E., Gurevich, M., and Achiron, A., *Common and specific signatures of gene expression and protein–protein interactions in autoimmune diseases.* Genes & Immunity, 2013. **14**(2): p. 67-82.

184. Asthagiri, D., Neal, B.L., and Lenhoff, A.M., *Calculation of short-range interactions between proteins.* Biophysical Chemistry, 1999. **78**(3): p. 219-231.

185. Gromiha, M.M. and Selvaraj, S., *Importance of long-range interactions in protein folding.* Biophysical Chemistry, 1999. **77**(1): p. 49-68.

186. Szklarczyk, D., Gable, A.L., Nastou, K.C., Lyon, D., Kirsch, R., Pyysalo, S., Doncheva, N.T., et al., *The STRING database in 2021: customizable protein–protein networks, and functional characterization of user-uploaded gene/measurement sets.* Nucleic Acids Research, 2021. **49**(D1): p. D605-D612.

187. Bindea, G., Mlecnik, B., Hackl, H., Charoentong, P., Tosolini, M., Kirilovsky, A., Fridman, W.H., et al., *ClueGO: a Cytoscape plug-in to decipher functionally grouped gene ontology and pathway annotation networks.* Bioinformatics, 2009. **25**(8): p. 1091-3.

188. Ahmad, A., Abuzinadah, M.F., Alkreathy, H.M., Banaganapalli, B., and Mujeeb, M., *Ursolic acid rich Ocimum sanctum L leaf extract loaded nanostructured lipid carriers ameliorate adjuvant induced arthritis in rats by inhibition of COX-1, COX-2, TNF-α and IL-1: Pharmacological and docking studies.* PLOS ONE, 2018. **13**(3): p. e0193451.

189. Tripathi, N., Saraf, P., Bhardwaj, N., Shrivastava, S.K., and Jain, S.K., *Identifying inflammation-related targets of natural lactones using network pharmacology, molecular modeling and in vitro approaches.* Journal of Biomolecular Structure and Dynamics, 2024: p. 1-16.

190. Martín-Vázquez, E., Cobo-Vuilleumier, N., López-Noriega, L., Lorenzo, P.I., and Gauthier, B.R., *The PTGS2/COX2-PGE2 signaling cascade in inflammation: Pro or anti? A case study with type 1 diabetes mellitus.* International Journal of Biological Sciences, 2023. **19**(13): p. 4157-4165.

191. Thorn, C.F., Grosser, T., Klein, T.E., and Altman, R.B., *PharmGKB summary: very important pharmacogene information for PTGS2.* Pharmacogenetics and Genomics, 2011. **21**(9): p. 607-613.

192. Andersen, V., Holst, R., Kopp, T.I., Tjønneland, A., and Vogel, U., *Interactions between Diet, Lifestyle and IL10, IL1B, and PTGS2/COX-2 Gene Polymorphisms in Relation to Risk of Colorectal Cancer in a Prospective Danish Case-Cohort Study.* PLOS ONE, 2013. **8**(10): p. e78366.

193. Alexanian, A. and Sorokin, A., *Cyclooxygenase 2: protein-protein interactions and posttranslational modifications.* Physiological Genomics, 2017. **49**(11): p. 667-681.

194. Boraschi, D., Italiani, P., Weil, S., and Martin, M.U., *The family of the interleukin-1 receptors.* Immunological Reviews, 2018. **281**(1): p. 197-232.

195. Panga, V. and Raghunathan, S., *A cytokine protein-protein interaction network for identifying key molecules in rheumatoid arthritis.* PLOS ONE, 2018. **13**(6): p. e0199530.

196. Pula, G., Crosby, D., Baker, J., and Poole, A.W., *Functional Interaction of Protein Kinase Cα with the Tyrosine Kinases Syk and Src in Human Platelets*.* Journal of Biological Chemistry, 2005. **280**(8): p. 7194-7205.

197. Wee, P. and Wang, Z. *Epidermal Growth Factor Receptor Cell Proliferation Signaling Pathways*. Cancers, 2017. **9**, 52.

198. Blaukat, A., *Src Kinase*, in *xPharm: The Comprehensive Pharmacology Reference*, S.J. Enna and D.B. Bylund, Editors. 2007, Elsevier. p. 1-14.

199. Irwin, M.E., Bohin, N., and Boerner, J.L., *Src family kinases mediate epidermal growth factor receptor signaling from lipid rafts in breast cancer cells.* Cancer Biology & Therapy, 2011. **12**(8): p. 718-726.

200. Molla, M.D., Akalu, Y., Geto, Z., Dagnew, B., Ayelign, B., and Shibabaw, T., *Role of Caspase-1 in the Pathogenesis of Inflammatory-Associated Chronic Noncommunicable Diseases.* Journal of Inflammation Research, 2020. **13**: p. 749-764.

201. Chen, M., Wang, L., Li, M., Budai, M.M., and Wang, J., *Mitochondrion-Mediated Cell Death through Erk1-Alox5 Independent of Caspase-9 Signaling*. Cells, 2022. **11**, 3053.

202. Ghanbarian, A.T. and Hurst, L.D., *Neighboring Genes Show Correlated Evolution in Gene Expression.* Molecular Biology and Evolution, 2015. **32**(7): p. 1748-1766.

203. Yang, W., Ng, P., Zhao, M., Wong, T.K.F., Yiu, S.-M., and Lau, Y.L., *Promoter-sharing by different genes in human genome – CPNE1 and RBM12 gene pair as an example.* BMC Genomics, 2008. **9**(1): p. 456.

204. Kyrchanova, O. and Georgiev, P., *Mechanisms of Enhancer-Promoter Interactions in Higher Eukaryotes*. International Journal of Molecular Sciences, 2021. **22**, 671.

205. Li, S., Peng, Y., and Panchenko, A.R., *DNA methylation: Precise modulation of chromatin structure and dynamics.* Current Opinion in Structural Biology, 2022. **75**: p. 102430.

206. Moosavi, S., Rahgozar, M., and Rahimi, A., *Protein function prediction using neighbor relativity in protein–protein interaction network.* Computational Biology and Chemistry, 2013. **43**: p. 11-16.

207. McAdam, B.F., Mardini, I.A., Habib, A., Burke, A., Lawson, J.A., Kapoor, S., and FitzGerald, G.A., *Effect of regulated expression of human cyclooxygenase isoforms on eicosanoid and isoeicosanoid production in inflammation.* The Journal of Clinical Investigation, 2000. **105**(10): p. 1473-82.

208. Ricciotti, E. and FitzGerald, G.A., *Prostaglandins and Inflammation.* Arteriosclerosis, Thrombosis, and Vascular Biology, 2011. **31**(5): p. 986-1000.

209. Kimura, R., Nishioka, T., Soemantri, A., and Ishida, T., *Cis-acting effect of the IL1B C−31T polymorphism on IL-1β mRNA expression.* Genes & Immunity, 2004. **5**(7): p. 572-575.

210. Adamik, J., Wang, K.Z.Q., Unlu, S., Su, A.-J.A., Tannahill, G.M., Galson, D.L., O'Neill, L.A., et al., *Distinct Mechanisms for Induction and Tolerance Regulate the Immediate Early Genes Encoding Interleukin 1β and Tumor Necrosis Factor α.* PLOS ONE, 2013. **8**(8): p. e70622.

211. Paraboschi, E.M., Cardamone, G., Rimoldi, V., Gemmati, D., Spreafico, M., Duga, S., Soldà, G., et al., *Meta-Analysis of Multiple Sclerosis Microarray Data Reveals Dysregulation in RNA Splicing Regulatory Genes*. International Journal of Molecular Sciences, 2015. **16**, 23463-23481.

212. A.G. Agundez, J., L. Gonzalez-Alvarez, D., A. Vega-Rodriguez, M., Botello, E., and Garcia-Martin, E., *Gene Variants and Haplotypes Modifying Transcription Factor Binding Sites in the Human Cyclooxygenase 1 and 2 (PTGS1 and PTGS2) Genes.* Current Drug Metabolism, 2014. **15**(2): p. 182-195.

213. Ingley, E., *Src family kinases: Regulation of their activities, levels and identification of new pathways.* Biochimica et Biophysica Acta (BBA) - Proteins and Proteomics, 2008. **1784**(1): p. 56-65.

214. Qiao, Y., Wang, P., Qi, J., Zhang, L., and Gao, C., *TLR-induced NF-κB activation regulates NLRP3 expression in murine macrophages.* FEBS Letters, 2012. **586**(7): p. 1022-1026.

215. Habermann, N., Ulrich, C.M., Lundgreen, A., Makar, K.W., Poole, E.M., Caan, B., Kulmacz, R., et al., *PTGS1, PTGS2, ALOX5, ALOX12, ALOX15, and FLAP SNPs: interaction with fatty acids in colon cancer and rectal cancer.* Genes & Nutrition, 2013. **8**(1): p. 115-126.

216. Gebhardt, F., BÜrger, H., and Brandt, B., *Modulation of EGFR Gene Transcription by a Polymorphic Repetitive Sequence – a Link between Genetics and Epigenetics.* The International Journal of Biological Markers, 2000. **15**(1): p. 105-110.

217. Ghoula, M., Janel, N., Camproux, A.-C., and Moroy, G. *Exploring the Structural Rearrangements of the Human Insulin-Degrading Enzyme through Molecular Dynamics Simulations*. International Journal of Molecular Sciences, 2022. **23**, 1746.

218. Martin, J. and Frezza, E., *A dynamical view of protein-protein complexes: Studies by molecular dynamics simulations.* Frontiers in Molecular Biosciences, 2022. **9**: p. 970109.

219. Vakser, Ilya A., *Protein-Protein Docking: From Interaction to Interactome.* Biophysical Journal, 2014. **107**(8): p. 1785-1793.

220. Macalino, S.J.Y., Basith, S., Clavio, N.A.B., Chang, H., Kang, S., and Choi, S. *Evolution of In Silico Strategies for Protein-Protein Interaction Drug Discovery*. Molecules, 2018. **23**, 1963.

221. Singh, R., Mandrah, K., Asati, A., Patel, D.K., Goel, B., Vishwakarma, R.A., Roy, S.K., et al., *Transformation of Santonin to a Naproxen Analogue with Anti-Inflammatory Activity.* Journal of Natural Products, 2019. **82**(6): p. 1710-1713.

222. Chaplan, S.R., Bach, F.W., Pogrel, J.W., Chung, J.M., and Yaksh, T.L., *Quantitative assessment of tactile allodynia in the rat paw*. Journal of Neuroscience Methods, 1994. **53**(1): p. 55-63.

223. Tiwari, V., Anderson, M., Yang, F., Tiwari, V., Zheng, Q., He, S.-Q., Zhang, T., et al., *Peripherally Acting μ-Opioid Receptor Agonists Attenuate Ongoing Pain-associated Behavior and Spontaneous Neuronal Activity after Nerve Injury in Rats.* Anesthesiology, 2018. **128**(6): p. 1220-1236.

224. Uniyal, A., Akhilesh, Singh Rathore, A., Kumari Keshri, P., Pratap Singh, S., Singh, S., and Tiwari, V., *Inhibition of pan-Aurora kinase attenuates evoked and ongoing pain in nerve injured rats via regulating KIF17-NR2B mediated signaling.* International Immunopharmacology, 2022. **106**: p. 108622.

225. Gadepalli, A., Ummadisetty, O., Akhilesh, Chouhan, D., Yadav, K.E., and Tiwari, V., *Peripheral mu-opioid receptor activation by dermorphin [D-Arg2, Lys4] (1–4) amide alleviates behavioral and neurobiological aberrations in rat model of chemotherapy-induced neuropathic pain.* Neurotherapeutics, 2024. **21**(1): p. e00302.

226. Ummadisetty, O., Akhilesh, Gadepalli, A., Chouhan, D., Patil, U., Singh, S.P., Singh, S., et al., *Dermorphin [D-Arg2, Lys4] (1-4) Amide Alleviates Frostbite-*

Induced Pain by Regulating TRP Channel-Mediated Microglial Activation and Neuroinflammation. Molecular Neurobiology, 2024: p. 1-12.

227. Hargreaves, K., Dubner, R., Brown, F., Flores, C., and Joris, J., *A new and sensitive method for measuring thermal nociception in cutaneous hyperalgesia.* PAIN, 1988. **32**(1): p. 77-88.

228. Uniyal, A., Gadepalli, A., Modi, A., and Tiwari, V., *Modulation of KIF17/NR2B crosstalk by tozasertib attenuates inflammatory pain in rats.* Inflammopharmacology, 2022. **30**(2): p. 549-563.

229. Zhou, H.-H., Zhang, L., Zhang, H.-X., Xu, B.-R., Zhang, J.-P., Zhou, Y.-J., Qian, X.-P., et al., *Tat-HA-NR2B9c attenuate oxaliplatin-induced neuropathic pain.* Experimental Neurology, 2019. **311**: p. 80-87.

230. Yoon, C., Wook, Y.Y., Sik, N.H., Ho, K.S., and Mo, C.J., *Behavioral signs of ongoing pain and cold allodynia in a rat model of neuropathic pain.* PAIN, 1994. **59**(3): p. 369-376.

231. Tiwari, V., He, S.-Q., Huang, Q., Liang, L., Yang, F., Chen, Z., Tiwari, V., et al., *Activation of μ-δ opioid receptor heteromers inhibits neuropathic pain behavior in rodents.* PAIN, 2020. **161**(4): p. 842-855.

232. Uniyal, A., Akhilesh, Tiwari, V., Gadepalli, A., Ummadisetty, O., and Tiwari, V., *Epigallocatechin-3-gallate improves chronic alcohol-induced cognitive dysfunction in rats by interfering with neuro-inflammatory, cell death and oxido-nitrosative cascade.* Metabolic Brain Disease, 2021. **36**(7): p. 2141-2153.

233. Zheng, C.-J., Lan, X.-P., Cheng, R.-B., Huang, B.-K., Han, T., Zhang, Q.-Y., Zhang, H., et al., *Furanofuran lignans from Vitex negundo seeds.* Phytochemistry Letters, 2011. **4**(3): p. 298-300.

234. Zheng, C.-J., Li, H.-Q., Ren, S.-C., Xu, C.-L., Rahman, K., Qin, L.-P., and Sun, Y.-H., *Phytochemical and Pharmacological Profile of Vitex negundo.* Phytotherapy Research, 2015. **29**(5): p. 633-647.

235. Ahuja, S., Ahuja, S., and Ahuja, U., *Nirgundi (Vitex negundo)–nature's gift to mankind.* J Asian Agri-History, 2015. **19**(1): p. 5-32.

236. Bello, M.O., Zaki, A.A., Aloko, S., Fasinu, P.S., Bello, E.O., Ajao, U.L., and Oguntoye, O.S., *The genus Vitex: An overview of iridoids as chemotaxonomic marker.* Beni-Suef University Journal of Basic and Applied Sciences, 2018. **7**(4): p. 414-419.

237. Dutta, P.K., Chowdhury, U.S., Chakravarty, A.K., Achari, B., and Pakrashi, S.C., *Nishindaside, a novel iridoid glycoside from Vitex negundo.* Tetrahedron, 1983. **39**(19): p. 3067-3072.

238. Roy, S.K., Bairwa, K., Grover, J., Srivastava, A., and Jachak, S.M., *Determination of negundoside and agnuside in Vitex negundo by qNMR and method validation.* Journal of Analytical Chemistry, 2015. **70**(5): p. 639-646.

239. Biedermann, D., Buchta, M., Holečková, V., Sedlák, D., Valentová, K., Cvačka, J., Bednárová, L., et al., *Silychristin: Skeletal Alterations and Biological Activities.* Journal of Natural Products, 2016. **79**(12): p. 3086-3092.

240. Shaker, E., Mahmoud, H., and Mnaa, S., *Silymarin, the antioxidant component and Silybum marianum extracts prevent liver damage.* Food and Chemical Toxicology, 2010. **48**(3): p. 803-806.

241. AbouZid, S. and Ahmed, O.M., *Chapter 14 - Silymarin Flavonolignans: Structure–Activity Relationship and Biosynthesis*, in *Studies in Natural Products Chemistry*. 2013, Elsevier. p. 469-484.

242. Abenavoli, L., Izzo, A.A., Milić, N., Cicala, C., Santini, A., and Capasso, R., *Milk thistle (Silybum marianum): A concise overview on its chemistry, pharmacological, and nutraceutical uses in liver diseases.* Phytotherapy Research, 2018. **32**(11): p. 2202-2213.

243. Valentová, K., Biedermann, D., and Křen, V., *2,3-Dehydroderivatives of Silymarin Flavonolignans: Prospective Natural Compounds for the Prevention of Chronic Diseases.* Proceedings, 2019. **11**(1): p. 21.

244. Abbasi, B.H., Khan, M.A., Mahmood, T., Ahmad, M., Chaudhary, M.F., and Khan, M.A., *Shoot regeneration and free-radical scavenging activity in Silybum marianum L.* Plant Cell, Tissue and Organ Culture (PCTOC), 2010. **101**(3): p. 371-376.

245. Tripathi, N., Naik, A., Kumar, D.N., Bhardwaj, N., Goel, B., Kumar, S., Chakrabarty, S., et al., *Unveiling the healing properties of 2,3-dehydrosilychristin: a potential silymarin-derived flavonolignan from Vitex negundo.* Natural Product Research, 2024: p. 1-9.

246. Parmar, V.S., Bisht, K.S., Sharma, S.K., Jain, R., Taneja, P., Singh, S., Simonsen, O., et al., *Highly oxygenated bioactive flavones from Tamarix.* Phytochemistry, 1994. **36**(2): p. 507-511.

247. Garcia, M.G., Gomes, R.F., Nascimento, C.C., Oliveira, L.M., Thomasi, S.S., Ferreira, A.G., and Lima, M.P., *Isolation of New Compounds from Andira parviflora and Inga alba Wood Residues Using LC-DAD-SPE/NMR.* Chemistry of Natural Compounds, 2021. **57**(2): p. 300-305.

248. Lin, L.-C., Pai, Y.-F., and Tsai, T.-H., *Isolation of Luteolin and Luteolin-7-O-glucoside from Dendranthema morifolium Ramat Tzvel and Their*

Pharmacokinetics in Rats. Journal of Agricultural and Food Chemistry, 2015. **63**(35): p. 7700-7706.

249. Tavakoli, S., Khalighi-Sigaroodi, F., Khosravi Dehaghi, N., Yaghoobi, M., Hajiaghaee, R., Gholami, A., and Ghafarzadegan, R., *Isolation and purification of apigenin, quercetin and apigenin 7-O-glycoside from Apium graveolens L., Petroselinum crispum (Mill.) Fuss, Allium cepa L., respectively.* Journal of Medicinal Plants, 2022. **21**(83): p. 72-86.

250. Sajjadi, S.E., Shokoohinia, Y., and Moayedi, N.S., *Isolation and Identification of Ferulic Acid From Aerial Parts of Kelussia odoratissima Mozaff.* Jundishapur Journal of Natural Pharmaceutical Products, 2012. **7**(4): p. 159-62.

251. Shoeb, M., Jaspars, M., MacManus, S.M., Celik, S., Nahar, L., Kong-Thoo-Lin, P., and Sarker, S.D., *Anti-colon cancer potential of phenolic compounds from the aerial parts of Centaurea gigantea (Asteraceae).* Journal of Natural Medicines, 2007. **61**(2): p. 164-169.

252. Kırmızıbekmez, H. and Demir, D., *Iridoid Glycosides and Phenolic Compounds from the Flowers of Vitex agnus-castus.* Helvetica Chimica Acta, 2016. **99**(7): p. 518-522.

253. Sharma, R.L., Prabhakar, A., Dhar, K.L., and Sachar, A., *A new iridoid glycoside from Vitex negundo Linn (Verbenacea).* Natural Product Research, 2009. **23**(13): p. 1201-1209.

254. Jassbi, A.R., Singh, P., Krishna, V., Gupta, P.K., and Tahara, S., *Antioxidant Study and Assignments of NMR Spectral Data for 3',4',7-Trihydroxyflavanone 3',7-Di-O-β-D-glucopyranoside (Butrin) and Its Hydrolyzed Product.* Chemistry of Natural Compounds, 2004. **40**(3): p. 250-253.

255. Wu, T.-H., Yen, F.-L., Lin, L.-T., Tsai, T.-R., Lin, C.-C., and Cham, T.-M., *Preparation, physicochemical characterization, and antioxidant effects of quercetin nanoparticles.* International Journal of Pharmaceutics, 2008. **346**(1): p. 160-168.

256. Seebacher, W., Simic, N., Weis, R., Saf, R., and Kunert, O., *Complete assignments of 1H and 13C NMR resonances of oleanolic acid, 18α-oleanolic acid, ursolic acid and their 11-oxo derivatives.* Magnetic Resonance in Chemistry, 2003. **41**(8): p. 636-638.

257. Rodrigues, F., Lima, J., Oliveira, M., Vasconcelos, J., Santiago, G., Mafezoli, J., Braz-Filho, R., et al., *Diterpene and other constituents from Stemodia maritima (Scrophulariaceae).* Journal of the Brazilian Chemical Society, 2010. **21**(8): p. 1581-1586.

258. Sholichin, M., Yamasaki, K., Kasai, R., and Tanaka, O., *13C Nuclear magnetic resonance of lupane-type triterpenes, lupeol, betulin and betulinic acid.* Chemical Pharmaceutical Bulletin, 1980. **28**(3): p. 1006-1008.

259. Chen, H., Wang, C., Ye, J., Zhou, H., and Tao, R., *Isolation of Sulfuretin and Butin from Rhus verniciflua Stokes Using Medium-pressure Liquid Chromatography and their Tyrosinase Inhibitory Effects.* BioResources, 2016. **11**(1): p. 759-771.

260. Lee, S.W., Kim, J.H., Song, H., Seok, J.K., Hong, S.S., and Boo, Y.C., *Luteolin 7-Sulfate Attenuates Melanin Synthesis through Inhibition of CREB- and MITF-Mediated Tyrosinase Expression*. Antioxidants, 2019. **8**, 87.

261. Fajriah, S., Megawati, M., and Darmawan, A., *Apigenin, an anticancer isolated from Macaranga gigantifolia leaves.* Journal of Tropical Life Science, 2016. **6**(1): p. 7-9.

262. López-Martínez, L.M., Santacruz-Ortega, H., Navarro, R.E., Sotelo-Mundo, R.R., and González-Aguilar, G.A., *A ¹H NMR Investigation of the Interaction between Phenolic Acids Found in Mango (Manguifera indica cv Ataulfo) and Papaya (Carica papaya cv Maradol) and 1,1-diphenyl-2-picrylhydrazyl (DPPH) Free Radicals.* PLOS ONE, 2015. **10**(11): p. e0140242.

263. Petrásková, L., Kristýna, K., David, B., Vladimír, K., and Kateřina, V., *Simple and Rapid HPLC Separation and Quantification of Flavonoid, Flavonolignans, and 2,3-Dehydroflavonolignans in Silymarin*. Foods, 2020. **9**, 116.

264. Dharmasiri, M.G., Jayakody, J.R.A.C., Galhena, G., Liyanage, S.S.P., and Ratnasooriya, W.D., *Anti-inflammatory and analgesic activities of mature fresh leaves of Vitex negundo.* Journal of Ethnopharmacology, 2003. **87**(2): p. 199-206.

265. Tiwari, O.P. and Tripathi, Y.B., *Antioxidant properties of different fractions of Vitex negundo Linn.* Food Chemistry, 2007. **100**(3): p. 1170-1176.

266. Jain, S.K., Singh, S., Khajuria, A., Guru, S.K., Joshi, P., Meena, S., Nadkarni, J.R., et al., *Pyrano-isochromanones as IL-6 Inhibitors: Synthesis, in Vitro and in Vivo Antiarthritic Activity.* Journal of Medicinal Chemistry, 2014. **57**(16): p. 7085-7097.

267. Shaik-Dasthagirisaheb, Y.B., Varvara, G., Murmura, G., Saggini, A., Potalivo, G., Caraffa, A., Antinolfi, P., et al., *Vascular Endothelial Growth Factor (VEGF), Mast Cells and Inflammation.* International Journal of Immunopathology and Pharmacology, 2013. **26**(2): p. 327-335.

268. Boloor, V.A., Hosadurga, R., Rao, A., Jenifer, H., and Pratap, S., *Unconventional Dentistry in India – An Insight into the Traditional Methods.* Journal of Traditional and Complementary Medicine, 2014. **4**(3): p. 153-158.