# CERTIFICATE

I certify that the thesis entitled **"Exploring the Anti-Cancer Potential of *Rhododendron arboreum* Sm. in Gastric Cancer using *In vitro* and *In vivo* Models"** submitted for the award of **Doctor of Philosophy (Ph.D)** by **Yangchen Dolma Kom** is the record of research work carried out by her during the period from **January 2020** to **April 2025** under my guidance and supervision and that this work has not formed the basis for the award of any Degree, Diploma, Associateship, Fellowship or other Titles in this Institute or any other University or Institution of Higher Learning.

A. Vijayabal 7/4/25

**Signature of the HoD**

07/04/2025

**Signature of the Supervisor**

**with Designation**

Dr.R.KARTHIYAYINI
Assistant Professor
Department of Botany
Avinashilingam Institute for Home Science
and Higher Education for Women
Coimbatore - 641 043

7/4/2025

**Signature of the Dean of Respective School**

# DECLARATION

I declare that the thesis entitled **"Exploring the Anti-Cancer Potential of *Rhododendron arboreum* Sm. in Gastric Cancer using *In vitro* and *In vivo* Models"** submitted by me for the award of Doctor of Philosophy (Ph.D) is the record of work carried out by me during the period from 2020 to 2025 under the guidance of **Dr. R. Karthiyayini, Assistant Professor (SS), Department of Botany, Avinashilingam Institute of Home Science and Higher Education For Women, Coimbatore** and has not formed the basis for the award of any Degree, Diploma, Associateship, Fellowship, Titles in this Institute or any other University or other similar Institution of Higher Learning.

**Signature of the Research Scholar**

04/04/2025

**Signature of the Supervisor**

# ACKNOWLEDGEMENT

*First and foremost, I owe my profound gratitude to* ***God Almighty,*** *the author of knowledge and wisdom, for showering countless blessings throughout my research work to complete the thesis successfully.*

*I take this opportunity to sincerely thank* ***Padma Bhusan Dr. T. S. Avinashilingam Ayya Avargal,*** *Founder and First Chancellor of Avinashilingam Institute for Home Science and Higher Education for Women, Coimbatore and* ***Padma Shri Dr. Rajammal P. Devadas Amma Avargal*** *for giving me this opportunity to gain knowledge in this institution.*

*I express my sincere thanks to our Chancellor,* ***Dr. T. S. K. Meenakshi Sundaram,*** *Former and Revered Chancellors,* ***Dr. S. P. Thyagarajan*** *and late* ***Dr. P. R Krishna Kumar,*** *Avinashilingam Institute for Home Science and Higher Education for Women, Coimbatore, for all their good wishes and permission to carry out my work in this eminent institution.*

*I express my reverential thanks to* ***Dr. V. Bharathi Harishankar****, Vice Chancellor, and Former Vice Chancellor,* ***Dr. Premavathy Vijayan,*** *Avinashilingam Institute for Home Science and Higher Education for Women, Coimbatore, for permitting me to utilize the infrastructure of the University and rendering benevolent support during the tenure of my study.*

*I acknowledge* ***Dr. H. Indu (i/c),*** *Registrar, and* ***Dr. S. Kowsalya,*** *Former Registrar, Avinashilingam Institute for Home Science and Higher Education for Women, Coimbatore, for extending all the possible help towards the completion of this study.*

*My heartfelt thanks to the Controller of Examinations,* ***Dr. K. Sampath Rani,*** *Professor, and former Controller of Examinations* ***Dr. K. Manimozhi****, Professor, Avinashilingam Institute for Home Science and Higher Education for Women, Coimbatore, for her valuable suggestions and the help given for the successful completion of the study.*

*I am thankful to **Dr. P. Lalitha**, Professor, Director of Research and Development Cell, and my special thanks to **Dr. G.P. Jeyanthi,** Professor, Former Director R&D, Avinashilingam Institute for Home Science and Higher Education for Women, Coimbatore, for all the prudent suggestions and for the immense help rendered.*

*I am indebted to **Dr. Anitha Subash,** Professor, and Dean, School of Biosciences, and **Dr. A. Vijayalakshmi,** Dean Academics, Professor and Head, Department of Botany, Avinashilingam Institute for Home Science and Higher Education for Women, Coimbatore, for their constant encouragement, timely help and tremendous support rendered in carrying out the research work.*

*I extend my profound and earnest gratitude to my Supervisor, **Dr. R. Karthiyayini,** Assistant Professor (SS), Department of Botany, for her meticulous guidance and effective management in the execution of each part of my research. Her unwavering support, insightful feedback, and dedication to pushing the boundaries of knowledge have not only enriched my research but have also inspired me to strive for excellence in everything I do. Her encouragement, moral support and constant rational counseling during every step of the research work and working under her mentorship have been a privilege and a transformative experience that I will always cherish.*

*I am thankful to **Dr. Parimelazhagan Thangaraj,** Professor and Head, Department of Botany, Bharathiar University, the Subject Expert for my Doctoral Committee, for his constructive criticisms and valuable suggestions given for the study.*

*My profound thanks to all the **Staff members** of the Department of Botany, Avinashilingam Institute for Home Science and Higher Education for Women, Coimbatore, who have created a congenial atmosphere to work in throughout my thesis.*

*I am grateful to thank **Dr. Jubie Selvaraj** Associate Professor, Department of Pharmaceutical Chemistry & **Dr. Raman Rajeshkumar** Assistant Professor, Department of Pharmaceutical Biotechnology. JSS College of Pharmacy Ooty. **Dr. G. Ariharasivakumar** Professor, Department of Pharmacology. KMCH College of Pharmacy Coimbatore, for all the possible help rendered and valuable*

*01747) for funding my Ph.D. research work.*

*My sincere and special thanks to my fellow Researchers* ***Surya S, Vasandhlakshmi R*** *and* ***Indumathi B*** *for their encouragement and timely support.*

*On a personal note, I thank my beloved Father, Mother, Sister and Brother and my dear friends for their unshakeable support, prayers, care, motivation, sacrifice, trust, cooperation and untiring patience. They were the strong pillars who supported me to complete this work with determination.*

*I also acknowledge the contributions of all other unseen hands during the study for the help rendered in the successful completion of the study.*

***Yangchen Dolma Kom***

## LIST OF TABLES

## LIST OF FIGURES

## ABBREVIATIONS

| S.No. | Abbreviations | Full Form |
|---|---|---|
| 1. | **1B3D** | Crystal Structure of the Human Matrix Metalloproteinase-9 |
| 2. | **1ERR** | Crystal Structure of the Human Estrogen Receptor Alpha (Erα) Ligand-Binding Domain Complexed with an Agonist |
| 3. | **$^{1}$H NMR** | Proton Nuclear Magnetic Resonance |
| 4. | **6GQ0** | Crystal Structure of the Human Insulin-Like Growth Factor 1 Receptor (IGF-1R) Kinase Domain in Complex with an Inhibitor |
| 5. | **6S9B** | Crystal Structure of Human Glycogen Synthase Kinase-3 Beta (GSK-3β) in Complex with an Inhibitor |
| 6. | **Å** | Ångström |
| 7. | **ABTS** | 2,2'-azino-bis-3-ethyl benzthiazoline-6-sulphonic Acid |
| 8. | **ACP** | Acid Phosphatase |
| 9. | **ADME** | Absorption, Distribution, Metabolism and Excretion |
| 10. | **AE/g** | Atropine Equivalents Per Gram |
| 11. | **AGS** | Human Gastric Adenocarcinoma Cells |
| 12. | **ALA** | Alanine |
| 13. | **$AlCl_3$** | Aluminium Chloride |
| 14. | **$AlCl_3.6H_2O$** | Aluminum Chloride Hexahydrate |
| 15. | **ALP** | Alkaline Phosphatase |
| 16. | **amu** | Atomic Mass Units |
| 17. | **ASN** | Asparagine |
| 18. | **ASP** | Aspartic Acid |
| 19. | **BBB** | Blood Brain Barrier |
| 20. | **BCG** | Bromocresol Green Solution |
| 21. | **BMRB** | Biological Magnetic Resonance Data Bank |
| 22. | **BSI** | Botanical Survey of India |
| 23. | **BW** | Body Weight |

| | | |
|---|---|---|
| 24. | **C-H** | Carbon Hydrogen Bond |
| 25. | **C=O** | Carbonyl Group |
| 26. | **C≡N** | Carbon-Nitrogen Triple Bond |
| 27. | **CAFs** | Cancer-Associated Fibroblasts |
| 28. | **CAT** | Catalase |
| 29. | **$CD_3OD$** | Deuterated Methanol |
| 30. | **$CH_3OH$** | Methanol |
| 31. | **ChEMBL** | Chemical European Molecular Biology Laboratory |
| 32. | **$Cm^{-1}$** | Reciprocal Centimeters (wavenumber) |
| 33. | **Conc** | Concentration |
| 34. | **ctDNA** | Circulation Tumor DNA |
| 35. | **$Cu^{++}$** | Copper II Ion |
| 36. | **CYP19A1** | Cytochrome P450 Family 19 Subfamily A Member 1 |
| 37. | **$D.H_2O$** | Distilled Water |
| 38. | **$D_2O$** | Deuterium Oxide |
| 39. | **DAVID** | Database for Annotation, Visualization and Integrated Discovery |
| 40. | **dL** | Deciliter |
| 41. | **DMEM** | Dulbecco's Modified Eagle Medium |
| 42. | **DMSO** | Dimethyl Sulfoxide |
| 43. | **DNPH** | 2,4-Dinitrophenylhydrazine |
| 44. | **DPPH** | 2,2-Diphenyl-1-picrylhydrazyl |
| 45. | **DTNB** | (5,5'-Dithiobis(2-nitrobenzoic acid)) |
| 46. | **ECM** | Extracellular Matrix |
| 47. | **EDTA** | Ethylenediaminetetraacetic Acid |
| 48. | **EGFR** | Epidermal Growth Factor Receptor |
| 49. | **ELISA** | Enzyme-linked Immunosorbent Assay |
| 50. | **ESR1** | Estrogen Receptor 1 |
| 51. | **ESR2** | Estrogen Receptor 2 |
| 52. | **FACS** | Fluorescence-Activated Cell Sorter |
| 53. | **FBS** | Fetal Bovine Serum |
| 54. | **FDR** | False Discovery Rate |
| 55. | **$Fe^{3+}$** | Ferric Ion |

| | | |
|---|---|---|
| 56. | **$FeCl_3$** | Ferric Chloride |
| 57. | **$FeSO_4$** | Ferrous Sulfate |
| 58. | **FITC** | Fluorescein Isothiocyanate |
| 59. | **FRAP** | Ferric Reducing Antioxidant Power Assay |
| 60. | **FT-IR** | Fourier Transform Infrared Spectroscopy |
| 61. | **GAE** | Gallic Acid Equivalents |
| 62. | **GB/SA** | Generalized-Born and Solvent Accessible Surface Area |
| 63. | **GC** | Gastric Cancer |
| 64. | **GC-MS** | Gas Chromatography-Mass Spectrometry |
| 65. | **GC/TQ** | Gas Chromatography/ Triple Quadrupole |
| 66. | **GLU** | Glutamic Acid |
| 67. | **GO** | Gene Ontology |
| 68. | **GPx** | Glutathione Peroxidase |
| 69. | **GSH** | Reduced Glutathione |
| 70. | **GSK3B** | Glycogen Synthase Kinase 3 Beta |
| 71. | **GSSG** | Glutathione Disulphide |
| 72. | **H&E** | Haematoxylin & Eosin |
| 73. | **$H_2O$** | Water |
| 74. | **$H_2O_2$** | Hydrogen Peroxide |
| 75. | **$H_2SO_4$** | Sulfuric Acid |
| 76. | **Hb** | Haemoglobin |
| 77. | **HCl** | Hydrochloric Acid |
| 78. | **HDL** | High Density Lipoprotein |
| 79. | **HER2** | Human Epidermal Growth Factor Receptor 2 |
| 80. | **HIS** | Histidine |
| 81. | **HMGCR** | 3-Hydroxy-3-Methylglutaryl-CoA Reductase |
| 82. | **Hz** | Hertz |
| 83. | **IAEC** | Institutional Animal Ethics Committee |
| 84. | **$IC_{50}$** | Half-maximal Inhibitory Concentration |
| 85. | **IGF1R** | Insulin-like Growth Factor 1 Receptor |
| 86. | **intraHB** | Intramolecular Hydrogen Bonds |
| 87. | **$K_2Cr_2O_7$** | Potassium Dichromate |

| | | |
|---|---|---|
| 88. | **KBr** | Potassium Bromide |
| 89. | **KDR** | Kinase Insert Domain Receptor |
| 90. | **KEGG** | Kyoto Encyclopaedia of Genes and Genomes |
| 91. | **KOH** | Potassium Hydroxide |
| 92. | **LB** | Lower Band |
| 93. | **LDL** | Low Density Lipoprotein |
| 94. | **LEU** | Leucine |
| 95. | **LPO** | Lipid Peroxidation Assay |
| 96. | **m/z** | Mass-to-Charge Ratio |
| 97. | **MAPK** | Mitogen-Activated Protein Kinase |
| 98. | **MDA** | Malondialdehyde |
| 99. | **MDS** | Molecular Dynamic Simulation |
| 100. | **MET** | Mesenchymal-Epithelial Transition Factor |
| 101. | **MHz** | Megahertz |
| 102. | **mM** | Millimolar |
| 103. | **$mm^3$** | Cubic Milli Meter |
| 104. | **MMP9** | Matrix Metalloproteinase 9 |
| 105. | **MolSA** | Molecular Surface Area |
| 106. | **MPO** | Myeloperoxidase |
| 107. | **MTT** | 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide |
| 108. | **$NaCO_2$** | Sodium Carbonate |
| 109. | **NADPH** | Nicotinamide Adenine Dinucleotide Phosphate |
| 110. | **$NaNO_2$** | Sodium Nitrite |
| 111. | **NaOH** | Sodium Hydroxide |
| 112. | **NCCS** | National Centre for Cell Sciences |
| 113. | **NIST** | National Institute of Standards and Technology |
| 114. | **nm** | Nanometre |
| 115. | **NMA** | N-methyl -Amino Acid |
| 116. | **NMR** | Nuclear Magnetic Resonance |
| 117. | **NPT** | Isothermal-Isobaric Ensemble |
| 118. | **NRotB** | Number of Rotatable Bonds |
| 119. | **ns** | Nanoseconds |

| | | |
|---|---|---|
| 120. | **O-H** | Hydroxyl Group |
| 121. | **$O^{\bullet}_2$** | Superoxide Radical |
| 122. | **$O_2^-$** | Superoxide Anion |
| 123. | **$OH^{\bullet}$** | Hydroxyl Radical |
| 124. | **OPLS-3** | Optimized Potentials for Liquid Simulations 3 |
| 125. | **PBS** | Phosphate Buffer Solution |
| 126. | **PDB** | Protein Data Bank |
| 127. | **PI** | Propidium Iodine |
| 128. | **PI3K/AKT** | Phosphoinositide 3-Kinase (PI3K) / Protein Kinase B (AKT) |
| 129. | **PPI** | Protein-Protein Interaction |
| 130. | **ppm** | Part Per Million |
| 131. | **PubChem** | Public Database of Chemical Molecules and their Biological Activities |
| 132. | **PUFAs** | Polyunsaturated Fatty Acids |
| 133. | **$R^{\bullet}$** | Superoxide Dismutase Activity |
| 134. | **RBCs** | Red Blood Cells |
| 135. | **RCSB** | Research Collaboratory for Structural Bioinformatics |
| 136. | **RE/g** | Rutin Equivalents Per Gram |
| 137. | **RFA** | *Rhododendron* Flower Acetone |
| 138. | **RFD** | *Rhododendron* Flower DMSO |
| 139. | **RFE** | *Rhododendron* Flower Ethanol |
| 140. | **RFM** | *Rhododendron* Flower Methanol |
| 141. | **rGyr** | Radius of Gyration |
| 142. | **RLA** | *Rhododendron* Leaf Acetone |
| 143. | **RLD** | *Rhododendron* Leaf DMSO |
| 144. | **RLE** | *Rhododendron* Leaf Ethanol |
| 145. | **RLM** | *Rhododendron* Leaf Methanol |
| 146. | **RMSD** | Root Mean Square Deviation |
| 147. | **RMSF** | Root Mean Square Fluctuations |
| 148. | **ROS** | Reactive Oxygen Species |
| 149. | **rpm** | Revolutions Per Minute |
| 150. | **SAR** | Structure-Activity Relationship |

| | | |
|---|---|---|
| 151. | **SASA** | Solvent Accessible Surface Area |
| 152. | **SER** | Serine |
| 153. | **SGOT** | Serum Glutamic Oxaloacetic Transaminase |
| 154. | **SGPT** | Serum Glutamic Pyruvic Transaminase |
| 155. | **SOD** | Superoxide Dismutase |
| 156. | **STRING** | Search Tool for the Retrieval of Interacting Genes/Proteins |
| 157. | **T1/T2** | Relaxation Parameters |
| 158. | **TAC** | Total Alkaloid Content |
| 159. | **TAE/g** | Tannic Acid Equivalents Per Gram |
| 160. | **TBA** | Thiobarbituric Acid |
| 161. | **TBARS** | Thiobarbituric Acid Reactive Substances |
| 162. | **TCA** | Trichloroacetic Acid |
| 163. | **TFC** | Total Flavonoid Content |
| 164. | **TIP4P** | Transferable Intermolecular Potential with 4 Points |
| 165. | **TPC** | Total Phenolic Content |
| 166. | **TPSA** | Topological Polar Surface Area |
| 167. | **TPTZ** | 2,4,6-tris(2-pyridyl)-s-triazine |
| 168. | **TSP** | 3-(trimethylsilyl)-1-propanesulfonic Acid |
| 169. | **TWBC** | Total White Blood Cells |
| 170. | **U/mg** | Units Per Milligram |
| 171. | **UV** | Ultraviolet |
| 172. | **v/v** | Volume/Volume |
| 173. | **VEGF** | Vascular Endothelial Growth Factor |
| 174. | **VLDL** | Very Low Density Lipoprotein |
| 175. | **WBCs** | White Blood Cells |
| 176. | **δ** | Chemical Shift |
| 177. | **µL** | Microliter |
| 178. | **µm** | Micrometre |