Executive summary of the report of major research project of University Grants Commission (UGC) entitled '*Rational Therapy With Glutamine Analogs As Possible Anticancer Agents*' [Ref. No. **41-747/2012 (SR)**] of Prof. Tarun Jha

Derivatives and analogs of glutamine may act as anticancer agents by inhibiting phosphate dependent kidney type glutaminase (KGA), matrix metalloproteinase-2 (MMP-2) and histone deacetylase-8 (HDAC-8) enzymes. One of these glutamines inhibited phosphate dependent kidney type glutaminase (KGA) and two of them showed anticancer activity about 90%. Moreover, quantitative structure-activity relationship (QSAR) study directed some leads may be obtained. Some of these glutamines were found to inhibit MMP-2 enzyme selectively (activity in lower nanomolar concentration) whereas some of the isoglutamines (derivatives of glutamines) may act as dual MMP-2/HDAC-8 inhibitors (activity in lower micromolar concentration). Multi chemometric modeling techniques were tried to design and develop such glutamines and isoglutamines. These designed compounds were synthesized and subsequently screened for biological evaluation. Apart from exerting potent enzyme inhibition (KGA, MMP-2 and HDAC-8), these compounds showed anti-migratory and anti-invasive properties. These compounds may be used as adjuvant therapeutic agents in cancer after detailed study.

List of Publications

Number of Books/Book Chapters published:

1. T. Jha, N. Adhikari, A. K. Halder, A. Saha (2015) Ligand- and Structure- Based Drug Design of Non- Steroidal Aromatase Inhibitors (NSAIs) in Breast Cancer *In* Quantitative Structure -Activity Relationships in Drug Design, Predictive Toxicology, and Risk Assessment. Edited by: K. Roy, IGI Global, USA, In press.
2. T. Jha, A.K. Halder, N. Adhikari (2014) Epstein–Barr Virus and Treatment of Its Infection *In* Cancer Causing Viruses and Their Inhibitors. Edited by: S. P. Gupta CRC Press, Taylor and Francis Group, New York, pp.157-205.

Journal Publications:

National:

1. C. Mondal, N. Adhikari, A. K. Halder, T. Jha (2014) Structural exploration of 2, 6, 9-trisubstituted purine derivatives as potent CDK2 inhibitors in cancer through validated molecular modeling studies. *Journal of Engineering, Science and Management Education*, 7, 228-238.

International:

1. A. K. Halder, A. Mukherjee, N. Adhikari, A. Saha, T. Jha (2015) Nitric oxide synthetase (NOS) inhibitors in cancer angiogenesis, *Current Enzyme Inhibition*, In Press.
2. T. Jha, S. Samanta, A. K. Halder, N. Adhikari, A. Sanyal, T. Mukherjee (2015) Synthesis, biological evaluation, enzyme assay and molecular modeling studies on some 5-N-substituted- 2-N-(substituted benzenesulphonyl)-L(+)glutamines as possible anticancer agents. Communicated.
3. T. Jha, S. Basu, A. K. Halder, N. Adhikari, S. Samanta (2015) Possible Anticancer Agents: Synthesis, Pharmacological Activity and Molecular Modeling Studies on some 5-N-Substituted-2-N-(Substituted Benzenesulphonyl)- L(+)Glutamines. Communicated.
4. A. K. Halder, S. Mallick, D. Shikha, A. Saha, K. D. Saha, T. Jha (2015) Design of dual MMP-2/HDAC-8 inhibitors by pharmacophore mapping, molecular docking, synthesis and biological activity. *RSC Advances*, 5: 72373-72386.
5. N. Adhikari, A. K. Halder, S. Mallick, A. Saha, K. D. Saha, T. Jha (2015) Structure activity relationship study on some selective matrix metalloproteinase-2 inhibitors designed through in silico /fragment-based lead identification, de novo lead modification, syntheses and biological assays. Communicated.
6. N. Adhikari, A. K. Halder, A. Saha, K. Das Saha, T. Jha (2015) Structural findings of phenylindoles as cytotoxic antimitotic agents in human breast cancer cell lines through multiple validated QSAR studies. *Toxicology in vitro,* 29: 1392-1404.

7. A. K. Halder, A. Saha, K. Das Saha, T. Jha, (2015) Stepwise development of structure–activity relationship of diverse PARP-1 inhibitors through comparative and validated in silico modeling techniques and molecular dynamics simulation. *Journal of Biomolecular Structure and Dynamics*, 33: 1756-1779. Impact Fcator: 2.983
8. C. Mondal, A. K. Halder, N. Adhikari, A. Saha, K. Das Saha, S. Gayen, T. Jha (2015) Comparative validated molecular modeling of p53-HDM2 inhibitors as antiproliferative agents. *European Journal of medicinal Chemistry*, 90: 860-875. Impact Factor: 3.432
9. C. Mondal, A. K. Halder, N. Adhikari, T. Jha, (2014) Structural findings of cinnolines as anti-schizophrenic PDE10A inhibitors through comparative chemometric modeling. *Molecular Diversity*, 18: 655-671. Impact Factor: 2.544
10. N. Adhikari, A.K. Halder, C. Mondal, T. Jha (2014) Structural findings of quinolone carboxylic acids in cytotoxic, antiviral, and anti-HIV-1 integrase activity through validated comparative molecular modeling studies. *Medicinal Chemistry Research*, 23: 3096-3127. Impact Factor: 1.612
11. N. Adhikari, A.K. Halder, C. Mondal, T. Jha (2013) Exploring structural requirements of aurone derivatives as antimalarials by validated DFT based QSAR, HQSAR and COMFA-COMSIA approach. *Medicinal Chemistry Research*, 22: 6029-6045. Impact Factor: 1.612
12. A.K. Halder, A. Saha, T. Jha (2013) Exploring QSAR and pharmacophore mapping of structurally diverse selective matrix-metalloproteinase inhibitors. *Journal of Pharmacy and Pharmacology*, 65: 1541-1554. Impact Factor: 2.003
13. N. Adhikari, A.K. Halder, C. Mondal, T. Jha (2013) Ligand based validated comparative chemometric modeling and pharmacophore mapping of aurone derivatives as antimalarial agents. *Current Computer-Aided Drug Design*, 9: 417-432. Impact Factor: 1.942
14. C. Mondal, A.K. Halder, N. Adhikari, T. Jha (2013) Cholesteryl ester transfer protein inhibitors in coronary heart disease: Validated comparative QSAR modeling of N, N-disubstituted trifluoro-3-amino-2-propanols. *Computers in Biology and Medicine*, 43: 1545-1555. Impact Factor: 1.269

15. A.K. Halder, A. Saha, T. Jha (2013) The Role of 3D Pharmacophore Mapping Based Virtual Screening for Identification of Novel Anticancer Agents: An Overview. *Current Topics in Medicinal Chemistry*, 13: 1098-1126. Impact Factor: 4.269
16. A.K. Halder, A. Saha, T. Jha (2013) Exploration of Structural and Phisocochemical Requirements and Search for Virtual Hits for Aminopeptidase N inhibitors. Mol. Divers., 17: 123-137. Impact Factor: 2.544