Development of Noscapine Derivatives for Evaluation of Anticancer Efficacy

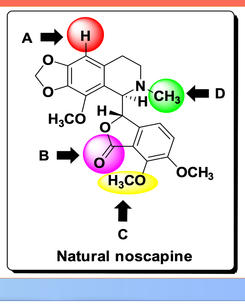
Prajna P. Mohanta[1], Pratyush Pragyandipta[1], Amiya K. Patel[1], Pradeep K. Naik[1]

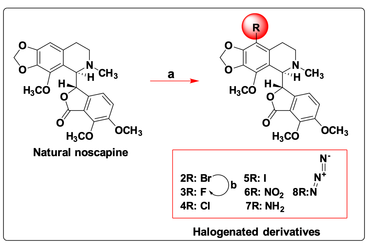
[1]Centre of Excellence in Natural Products and Therapeutics, Department of Biotechnology and Bioinformatics,
Sambalpur University, Jyoti Vihar,
Burla, Sambalpur-768 019, Odisha, India

Rationale & Objective

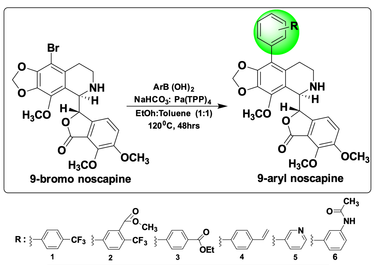
DEVELOPMENT OF NOVEL DERIVATIVES OF NOSCAPINE

In Quest of making novel derivatives of noscapine, nine new classes of noscapinoids were developed by coupling active pharmacophore such as (a) First generation of noscapine derivatives (b) biaryl derivatives of noscapine (c) α-noscapine derivatives of noscapine (d) arylimino groups (Schiff bases) (e) N-aryl methyl, (f) 1,3-diynl, (g) Imidazo [1,2- α] pyridine and (h) Urea group (i) amido-thiadizole at the various diversity at the various diversity points of noscapine scaffold (Figure 1) based on *in silico* combinatorial approach, followed by chemical synthesis and exhaustive experimental as potent anticancer agents.

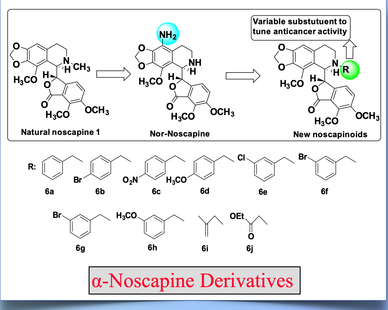




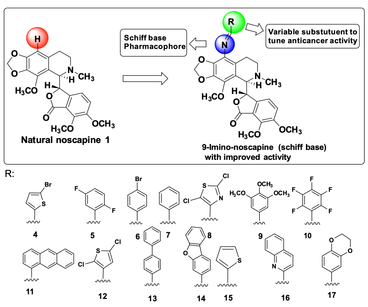
First Generation Noscapine Derivatives



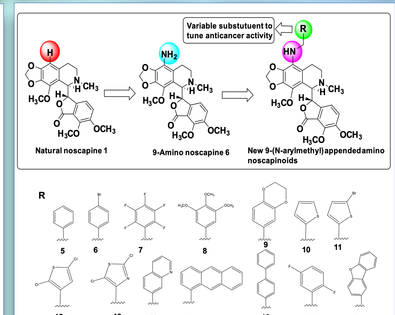
Biaryl Derivatives of Noscapine



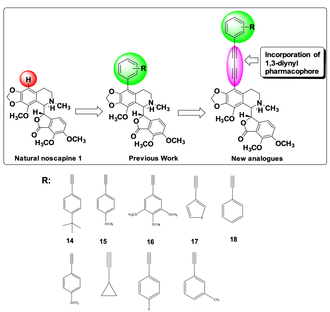
α-Noscapine Derivatives



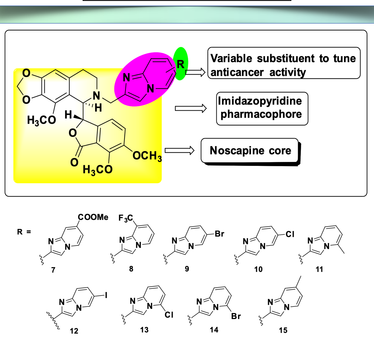
9-arylimino Derivatives



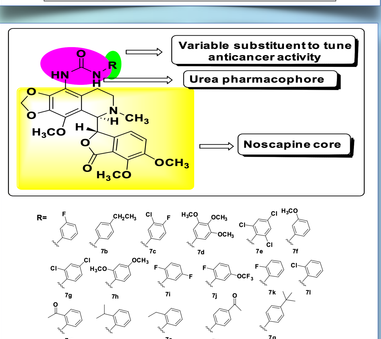
9-N-arylmethylamino Derivatives



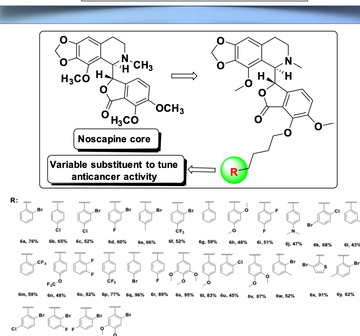
9-(1,3-diynyl) Derivatives



Imidazo[1,2-a]pyridine Derivatives



Urea Derivatives



Amido-thiadiazole Derivatives

List of Publications

i. Pragyandipta, P., Pedapati, R. K., Reddy, P. K., Nayek, A., Meher, R. K., Guru, S. K., ... & Naik, P. K. (2023). Rational design of novel microtubule targeting anticancer drugs N-imidazopyridine noscapinoids: Chemical synthesis and experimental evaluation based on in vitro using breast cancer cells and in vivo using xenograft mice model. Chemico-Biological Interactions, 110606. https://doi.org/10.1016/j.cbi.2023.110606

ii. *Pragyandipta, P., Naik, M. R., Bastia, B., & Naik, P. K. (2023). Development of 9-(N-arylmethylamino) congeners of noscapine: the microtubule targeting drugs for the management of breast cancer. 3 Biotech, 13(2), 38. https://doi.org/10.1007/s13205-022-03445-3*

iii. *Cheruvanachari, P., Pattnaik, S., Mishra, M., Pragyandipta, P., & Naik, P. K. (2022). Terpinen-4-ol, An Active Constituent of Kewda Essential Oil, Mitigates Biofilm Forming Ability of Multidrug Resistant Staphylococcus aureus and Klebsiella pneumoniae. Journal of Biologically Active Products from Nature, 12(5), 406-420. https://doi.org/10.1080/22311866.2022.2154264*

iv. *Meher, R. K., Pragyandipta, P., Pedapati, R. K., Nagireddy, P. K. R., Kantevari, S., Nayek, A. K., & Naik, P. K. (2021). Rational design of novel N-alkyl amine analogues of noscapine, their chemical synthesis and cellular activity as potent anticancer agents. Chemical biology & drug design, 98(3), 445–465. https://doi.org/10.1111/cbdd.13901*

v. *Meher RK, Pragyandipta P, Reddy NPK, Bastia B, Kantevari S, Naik PK. Development of 1,3-diynyl derivatives of noscapine as potent tubulin binding anticancer agents for the management of breast cancer. Journal of Biomolecular Structure and Dynamics (2021), DOI: https://doi.org/10.1080/07391102.2021.1982008*

vi. *Pragyandipta, P., Meher, R. K., Naik, M. R., Nagireddy, P. K., Pedapati, R. K., Kantevari, S., & Naik, P. K. (2021). In-Silico-Inspired Design of 1, 3-Diynyl Congeners of Noscapine as Promising Tubulin-Binding Anticancer Agent: Chemical Synthesis and Cellular Activity with Breast Cancer Cell Lines. ChemistrySelect, 6(14), 3500-3511. https://doi.org/10.1002/slct.202004723*

vii. *Patel, A. K., Meher, R. K., Reddy, P. K., Pedapati, R. K., Pragyandipta, P., Kantevari, S., Naik, M. R., & Naik, P. K. (2021). Rational design, chemical synthesis and cellular evaluation of novel 1,3-diynyl derivatives of noscapine as potent tubulin binding anticancer agents. Journal of molecular graphics & modelling, 106, 107933. https://doi.org/10.1016/j.jmgm.2021.107933*

viii. *Patel, A. K., Meher, R. K., Nagireddy, P. K., Pragyandipta, P., Pedapati, R. K., Kantevari, S., & Naik, P. K. (2021). 9-Arylimino noscapinoids as potent tubulin binding anticancer agent: chemical synthesis and cellular evaluation against breast tumour cells. SAR and QSAR in environmental research, 32(4), 269–291. https://doi.org/10.1080/1062936X.2021.1891567*

ix. *Pragyandipta, P., Meher, R. K., Reddy, P. K., Pedaparti, R., Kantevari, S., & Naik, P. K. (2022). Structure Based Design of Tubulin Binding 9-Arylimino Noscapinoids: Chemical Synthesis and Experimental Validation Against Breast Cancer Cell Lines. Analytical Chemistry Letters, 12(1), 29-43.*

x. *Meher, R. K., Nagireddy, P. K. R., Pragyandipta, P., Kantevari, S., Singh, S. K., Kumar, V., & Naik, P. K. (2022). Insilico design of novel tubulin binding 9-arylimino derivatives of noscapine, their chemical synthesis and cellular activity as potent anticancer agents against breast cancer. Journal of biomolecular structure & dynamics, 40(15), 6725–6736. https://doi.org/10.1080/07391102.2021.1889668*

xi. *Pragyandipta, P., Pedapati, R., Reddy, P. K., Kantevari, S and Naik, P.K (2022) Urea noscapine congeners as anticancer agent: chemical synthesis and experimental evaluation based on in vitro using breast cancer cells and in vivo using xenograft mice model. Submitted to Life Sciences.*

xii. *Santoshi, S., & Naik, P. K. (2014). Molecular insight of isotypes specific β-tubulin interaction of tubulin heterodimer with noscapinoids. Journal of computer-aided molecular design, 28, 751–763.*

xiii. *Santoshi, S., Manchukonda, N. K., Suri, C., Sharma, M., Sridhar, B., Joseph, S., Lopus, M., Kantevari, S., Baitharu, I., & Naik, P. K. (2015). Rational design of biaryl pharmacophore inserted noscapine derivatives as potent tubulin binding anticancer agents. Journal of computer-aided molecular design, 29, 249–270.*

xiv. *Santoshi, S., Naik, P. K., & Joshi, H. C. (2011). Rational design of novel anti-microtubule agent (9-azido-noscapine) from quantitative structure activity relationship (QSAR) evaluation of noscapinoids. Journal of biomolecular screening, 16, 1047–1058*

xv. *Lopus, M., & Naik, P. K. (2015). Taking aim at a dynamic target: Noscapinoids as microtubule-targeted cancer therapeutics. Pharmacological reports: PR, 67, 56–62.*

xvi. *Naik, P. K., Chatterji, B. P., Vangapandu, S. N., Aneja, R., Chandra, R., Kanteveri, S., & Joshi, H. C. (2011a). Rational design, synthesis and biological evaluations of amino-noscapine: a high affinity tubulin-binding noscapinoid. Journal of computer-aided molecular design, 25, 443–454.*

xvii. *Naik, P. K., Santoshi, S., Rai, A., & Joshi, H. C. (2011b). Molecular modelling and competition binding study of Br-noscapine and colchicine provide insight into noscapinoid-tubulin binding site. Journal of molecular graphics & modelling, 29, 947–955.*

List of Collaborators

Dr. Pradeep Kumar Naik,
Professor & Head
Dept. of Biotechnology & Bioinformatics,
Sambalpur University

Dr. Srinivas Kantevari,
Principal Scientist
Indian Institute of Chemical Technology, Hyderabad

Dr. Manu Lopus,
Reader 'F'
School of Biological Sciences,
UM-DAE, CEBS