

## MOLECULES TARGETING CANCER STEM CELLS

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The aim of the present project was to synthesize novel derivatives of diphylline glycoside of Cleistanthin A (SBGB-0001-000) and to screen them for anticancer activity (by MTT, Soft Agar Assay) and anticancer stem cell activity (by tumorsphere assay) on breast cancer cell lines. In all 70 novel derivatives of SBGB-0001-000 were synthesized and screened for anticancer and anticancer stem cell activity. Out of 70, two derivatives namely, SBGB-0001-014 and SBGB-0001-023 exhibited better anticancer and anticancer stem cell activity compared to standard chemotherapeutic drug Cisplatin. Since, cancer stem cells (CSCs) are subpopulation of cells within the cancer tissues with drug resistance and metastatic properties, these two candidates were further tested for its anticancer stem cell activity on drug (Paclitaxel) resistant population on highly metastatic breast cancer cell line MDAMB231 (with high number of CSCs) compared to standard chemotherapeutic drug Cisplatin and a target drug therapy sunitinib. Our sphere assay results indicate that the candidate molecules have better anticancer stem cell potential, inhibiting spheres at 25 nM compared to Cisplatin and sunitinib. In (figure 1), briefly describes that, our in-vitro data supports the anticancer stem cell effect of two novel candidates on breast cancer cell lines. Further, these candidates do not exhibit any toxic effect on normal cells (peripheral blood lymphocytes) compared to Cisplatin. The molecules show good hepatocyte stability and have been taken further for the preclinical studies like PK-PD, MTD and Xenograft studies.

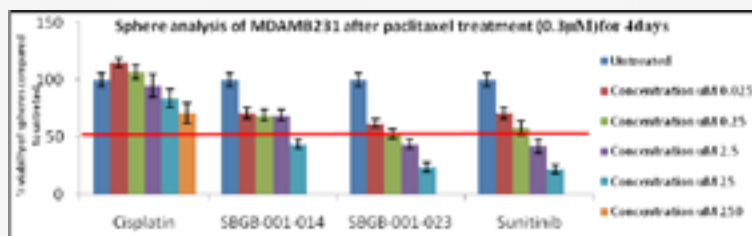


Figure 1: Indicates that the candidate molecules SBGB-0001-014 and SBGB-0001-023 are effective on paclitaxel treated MDAMB231 cells compared to Cisplatin at 25 nM (0.025 µM).

## BIOGRAPHY

Maithili A Athavale has completed her PhD from National Institute for Research in Reproductive Health, Mumbai University, India. She has handled various Projects in Research and Development of various Pharma companies. She has publications in national and international journals. Currently, she is working as Senior Manager R&D of Biotech Division, of Godavari Biorefineries Ltd. Her lab is into in-vitro screening of many novel synthetic molecules for anticancer and anticancer stem cell activity on breast, prostate and oral cancer cell lines. The lab has screened and found eight novel molecules having potent anticancer and anticancer stem cell activity. Two of the lead molecules have entered preclinical studies.

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