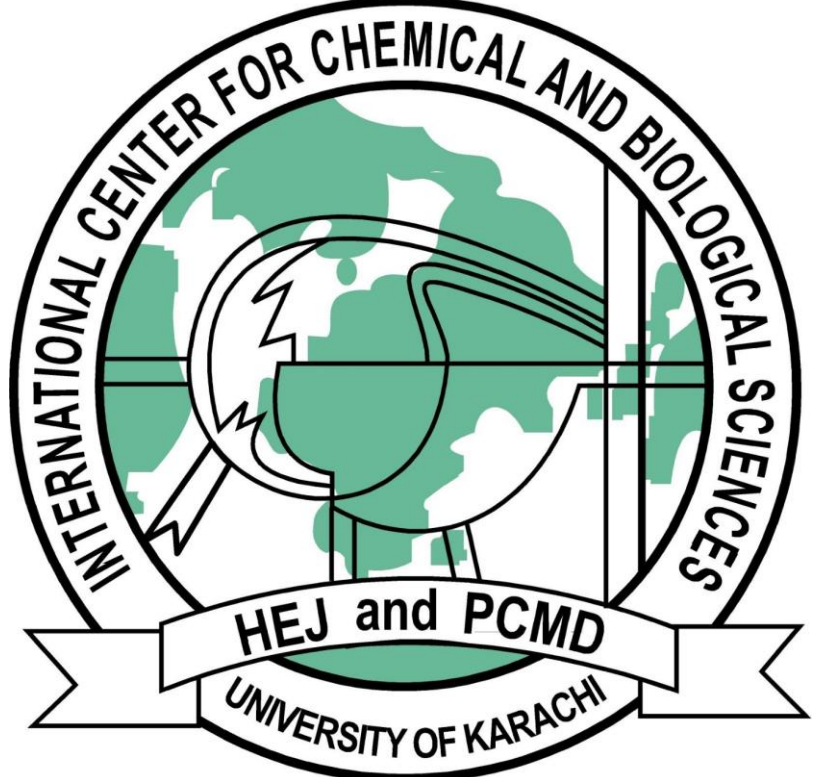




# Furan-Conjugated Peptidomimetic as Potentially Selective Inhibitor of HeLa Cancer Cell Lines

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## CERVICAL CANCER

Cervical cancer, which is a cancer of cervix, has higher mortality rate. It is third most prevalent form of cancer among women in Pakistan.

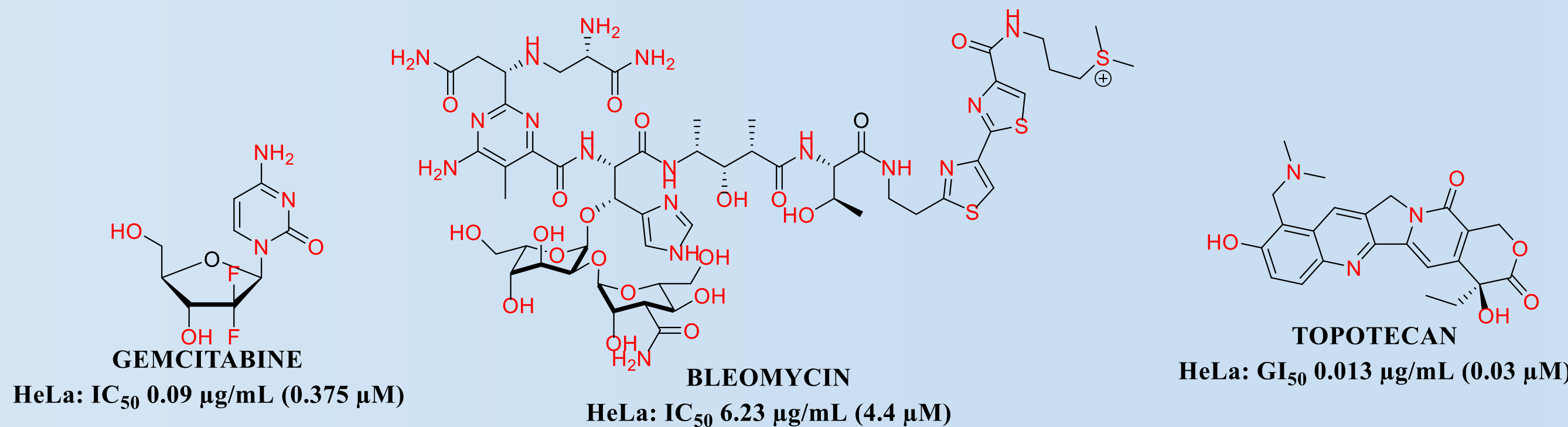
Treatments available for cervical cancer include surgery, chemotherapy, radiotherapy and vaccination.

Chemotherapy, used to treat cancer are all associated with severe side effects and lacks cancer cells targeting specificity.

## STRUCTURES OF SOME APPROVED MEDICINES

The drugs contain heterocyclic moieties and one of them is glycopeptide.

They are cytotoxic, expensive and synthetically complexed.

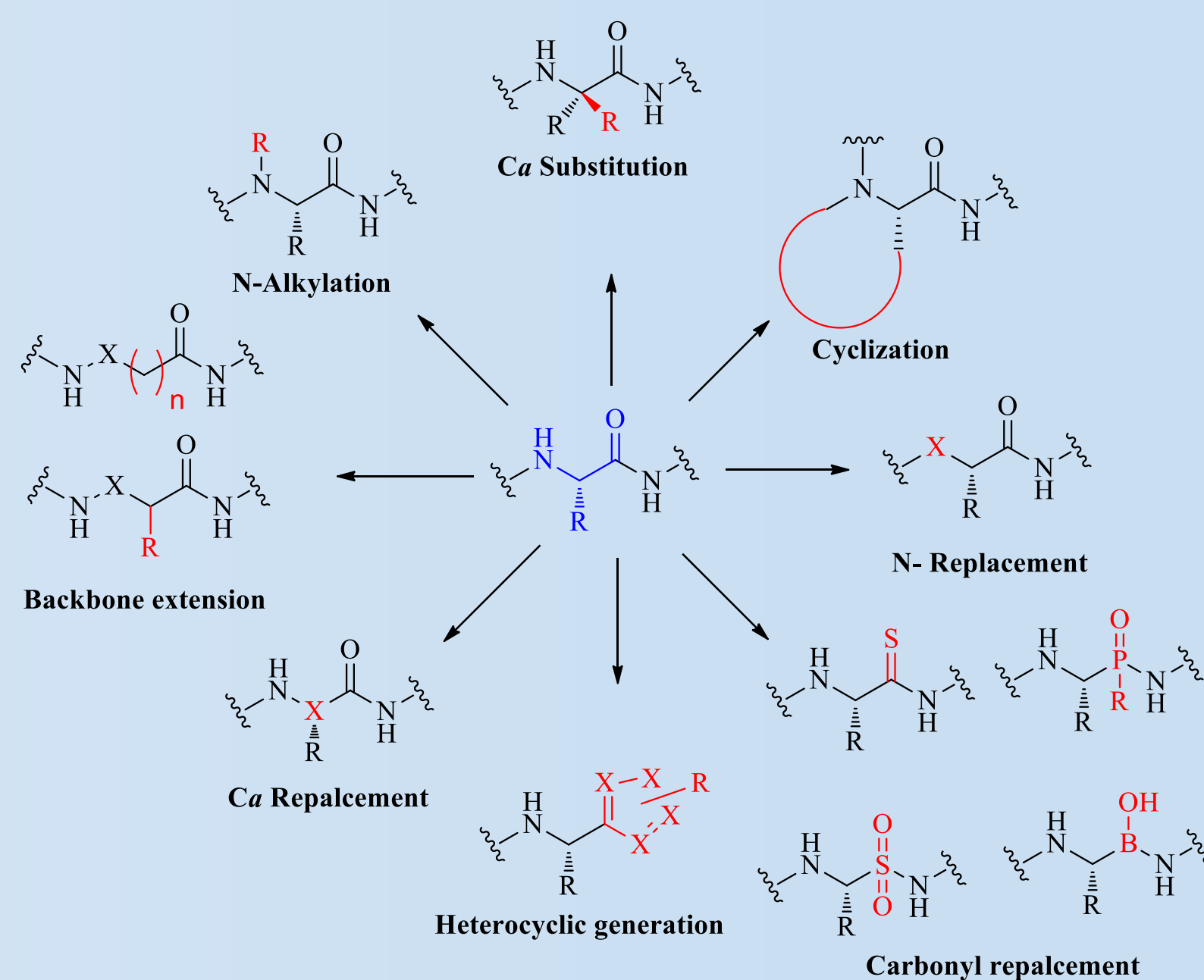


All these drugs are cytotoxic on normal cells and associated with multiple harmful side effects.

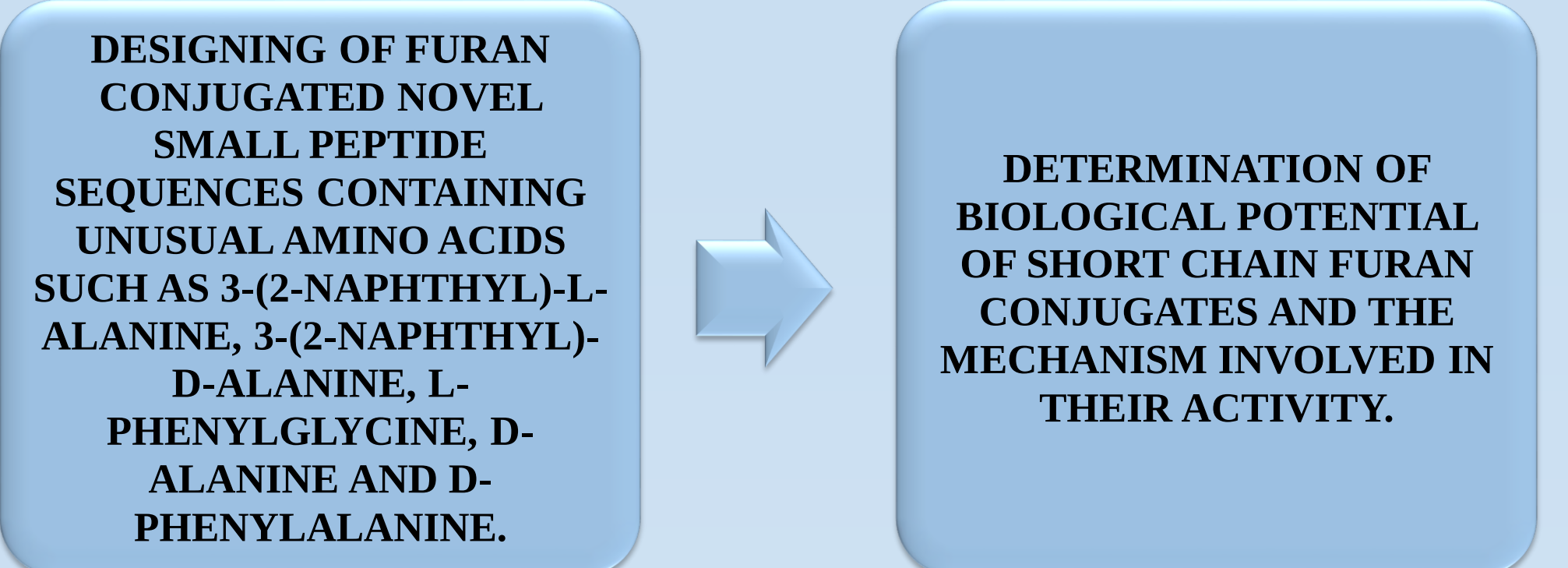
## PEPTIDES THERAPEUTICS AND PEPTIDOMIMETICS

Peptides are an important class of therapeutically important compounds having great advantage as a drug candidate due to its greater selectivity, lower toxicity, high potency and safe mode of action. They are now used as a direct therapeutic agent, in targeted drug delivery and as a diagnostic tool in cancer biology. Peptides containing D-amino acid residues / unusual building blocks or conjugated with heterocyclic moieties of entirely different characteristics are considered better drug candidates with improved therapeutic potential and bio-stability.

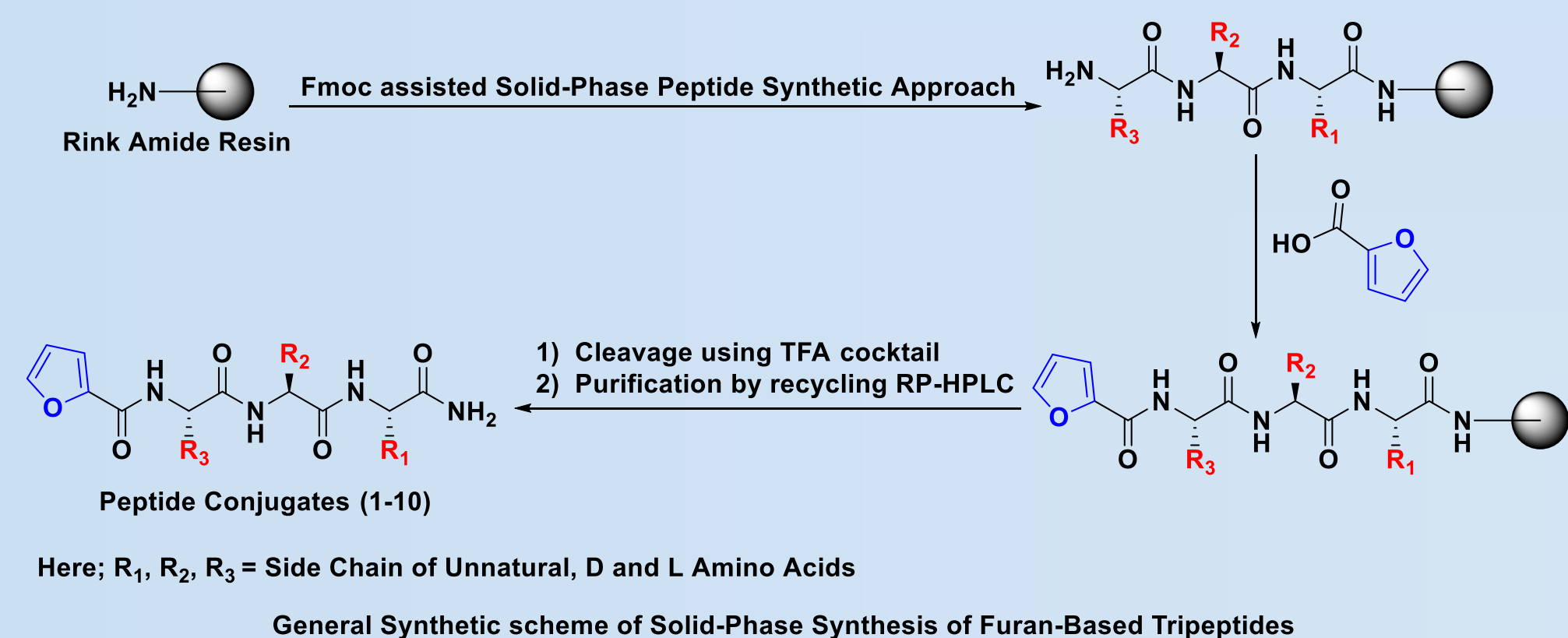
## METHODS OF DEVELOPING NEW PEPTIDOMIMETICS



## CURRENT STUDY



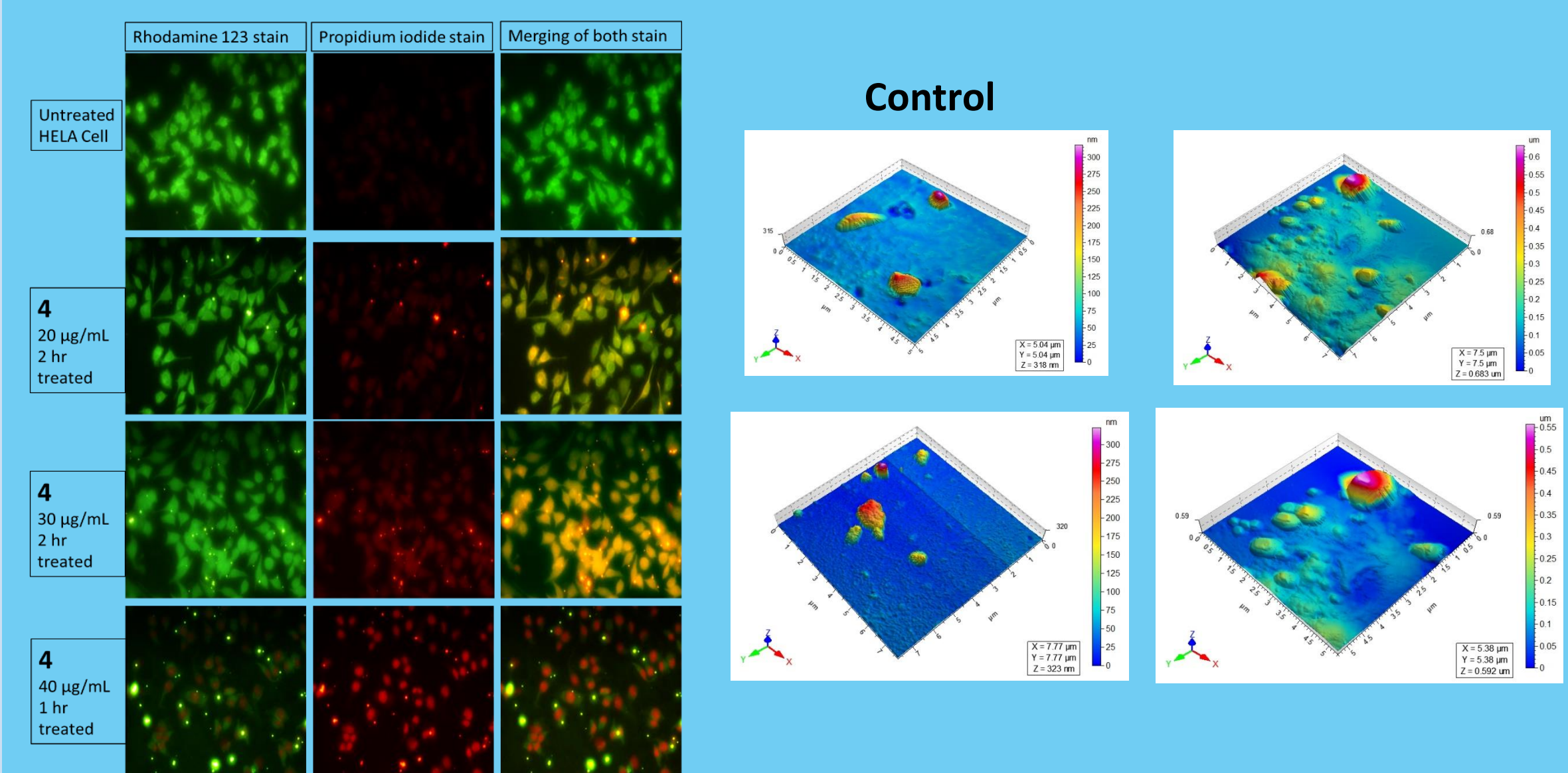
## METHODOLOGY



## RESULTS AND DISCUSSION

### In-vitro Screening on Other Cell Lines

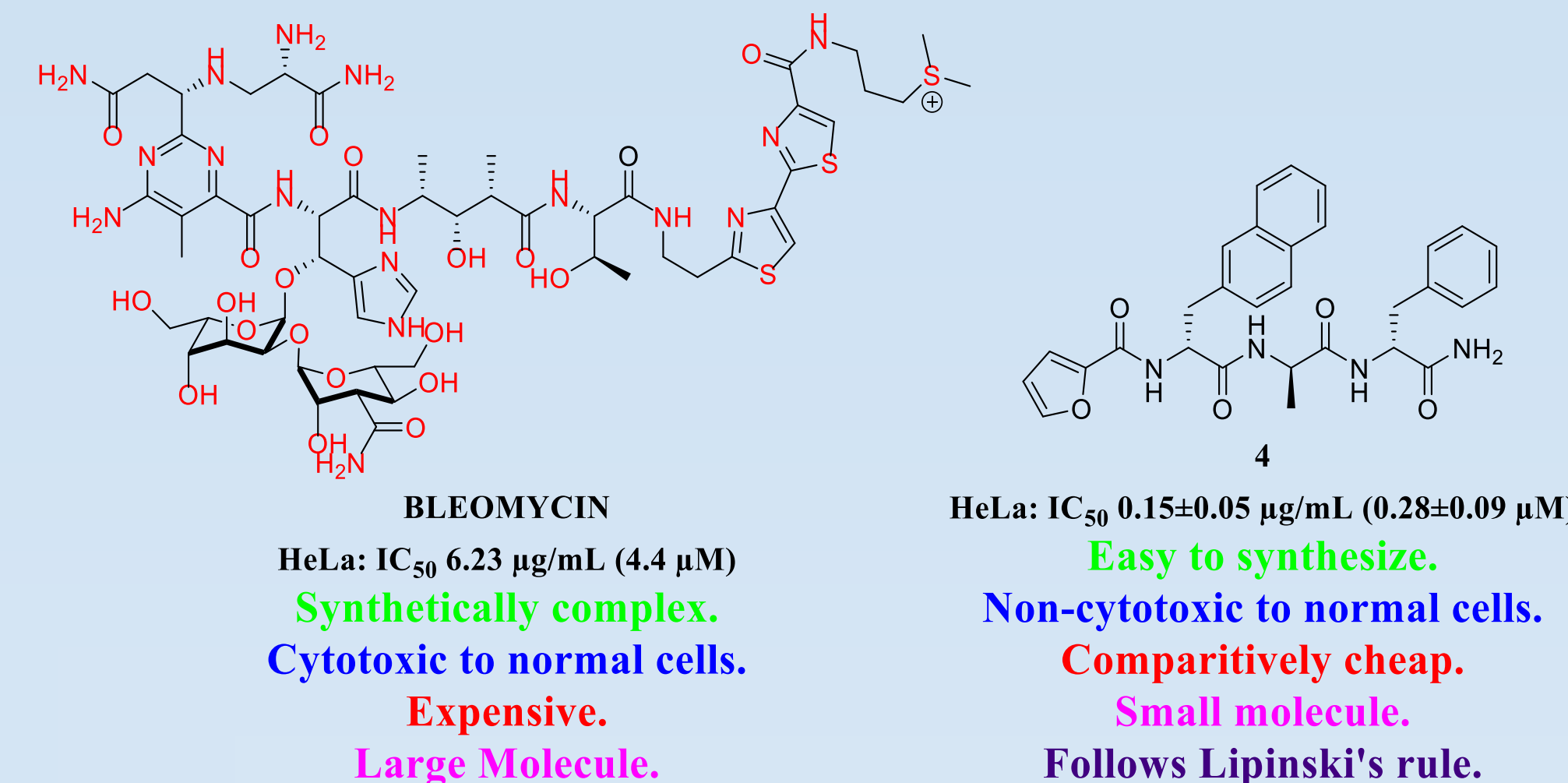
| Peptide 4   | Anti-Proliferative Effect of Peptide-4 IC <sub>50</sub> µg/mL |            |             |              |             |         |
|-------------|---------------------------------------------------------------|------------|-------------|--------------|-------------|---------|
|             | HeLa                                                          | HUVEC      | IMR-90      | MCF-7        | MDA-MB-231  | NIH 3T3 |
| Peptide 4   | 0.15±0.05                                                     | >100       | >100        | >100         | >100        | >100    |
| Doxorubicin | 3.09±0.16                                                     | 0.02±0.005 | 0.06 ± 0.01 | 0.01 ± 0.005 | 0.21 ± 0.03 | <1      |



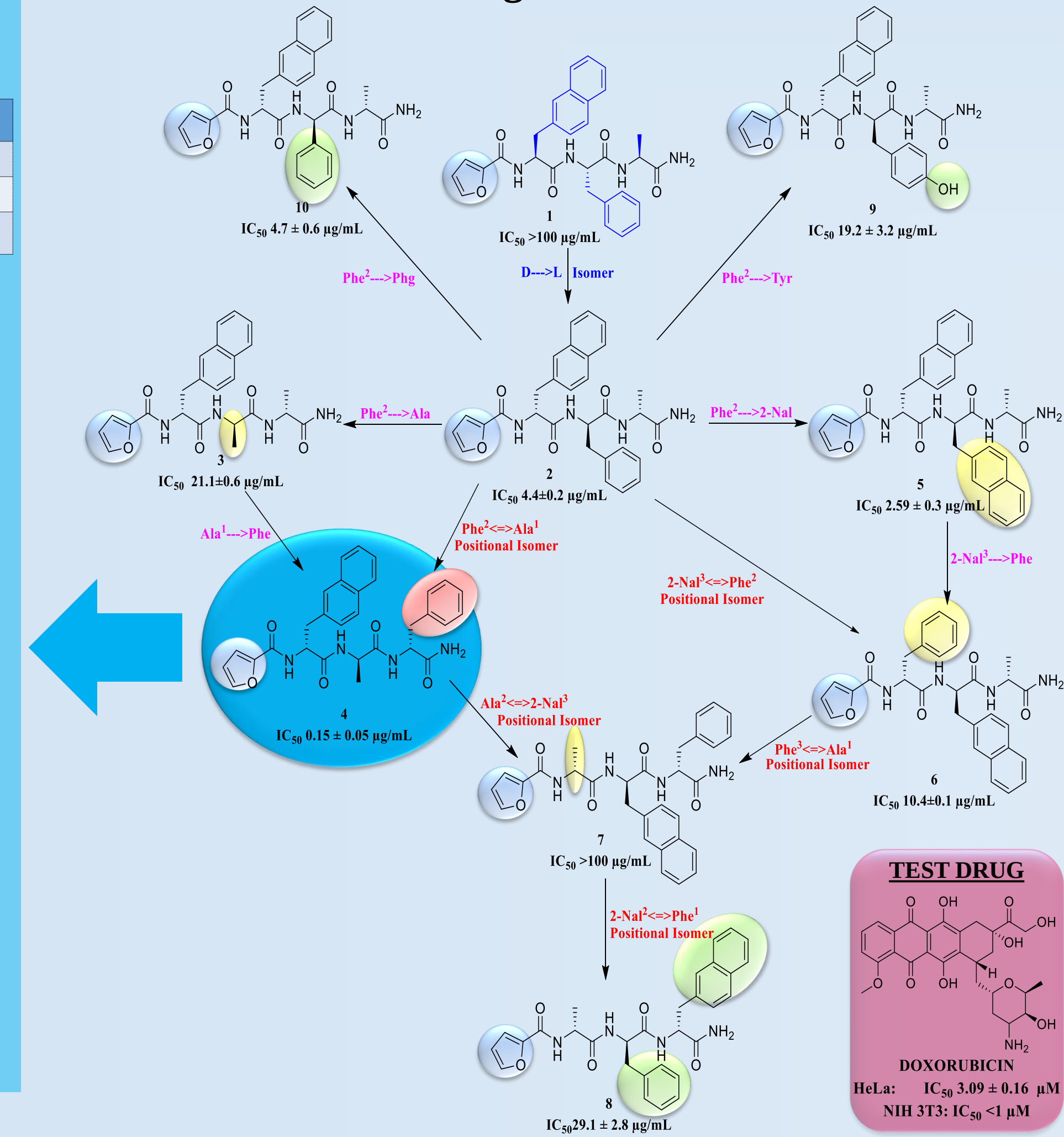
- ❖ AFM at 20 µg/mL showed Membranolytic Effect.
- ❖ PI Staining confirmed Membranolytic Effect.

## SIGNIFICANCE OF STUDY

- ❖ Easy, short and efficient synthesis of library of novel short chain peptide sequences conjugated with furan nucleus in high yield.
- ❖ Potent inhibitor of HeLa cancer cell lines based on novel peptide conjugates were discovered.
- ❖ The synthesized library of novel short chain peptide conjugates were found to be non-cytotoxic on normal 3T3 cell lines.
- ❖ All novel short chain peptide conjugates follow Lipinski's rule of five. Hence, can act as novel drug candidates.



### In-vitro Screening on HeLa Cancer Cell Line



## CONCLUSION

- ❖ Peptide library (furan conjugated peptides 1-10) was synthesized using Fmoc-assisted solid-phase peptide methodology.
- ❖ Structure-activity relationship among various peptide conjugates was developed.
- ❖ Furan conjugated peptide (4) was identified as selective anticancer agent against HeLa cancer cell lines. AFM and staining with rhodamine 123 and propidium iodide of peptide conjugate 4 showed membranolytic effect of this peptide conjugate.



## ACKNOWLEDGEMENT

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