

A computational-based Polyphenol therapy for Non-Small Cell Lung Cancer:  
Naringin co-amorphous systems for solubility and bioavailability enhancement.

*Dani Lakshman Yarlagadda <sup>a</sup>, Subham Das <sup>b</sup>, Vullendula Sai Krishna Anand <sup>a</sup>, Suman Manandhar <sup>c</sup>, Swapnil J Dengale <sup>d</sup>, K Sreedhara Ranganath Pai <sup>c</sup>, Krishnamurthy Bhat <sup>a\*</sup>*

- a. Department of Pharmaceutical Quality Assurance, Manipal College of Pharmaceutical Sciences, Manipal Academy of Higher Education (MAHE), Manipal, Karnataka – 576104, India.
- b. Department of Pharmaceutical Chemistry, Manipal College of Pharmaceutical Sciences, Manipal Academy of Higher Education (MAHE), Manipal, Karnataka – 576104, India.
- c. Department of Pharmacology, Manipal College of Pharmaceutical Sciences, Manipal Academy of Higher Education (MAHE), Manipal 576104, India.
- d. Department of Pharmaceutical Analysis, National Institute of Pharmaceutical Education and Research (NIPER), Guwahati, Changsari 781101, India



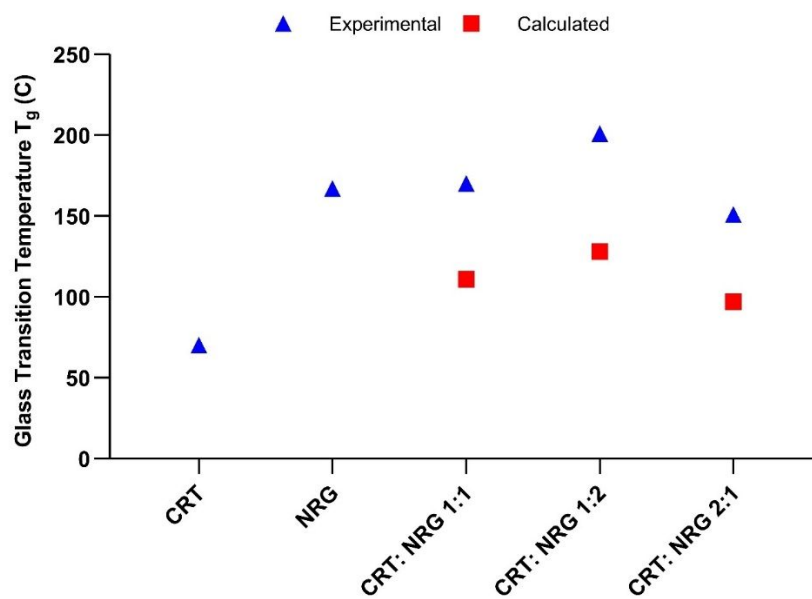


Figure S3. Experimental and Theoretical glass transition temperature (T<sub>g</sub>) of Ceritinib (CRT), Naringin (NRG), and co-amorphous systems using Gordon Taylor equation.

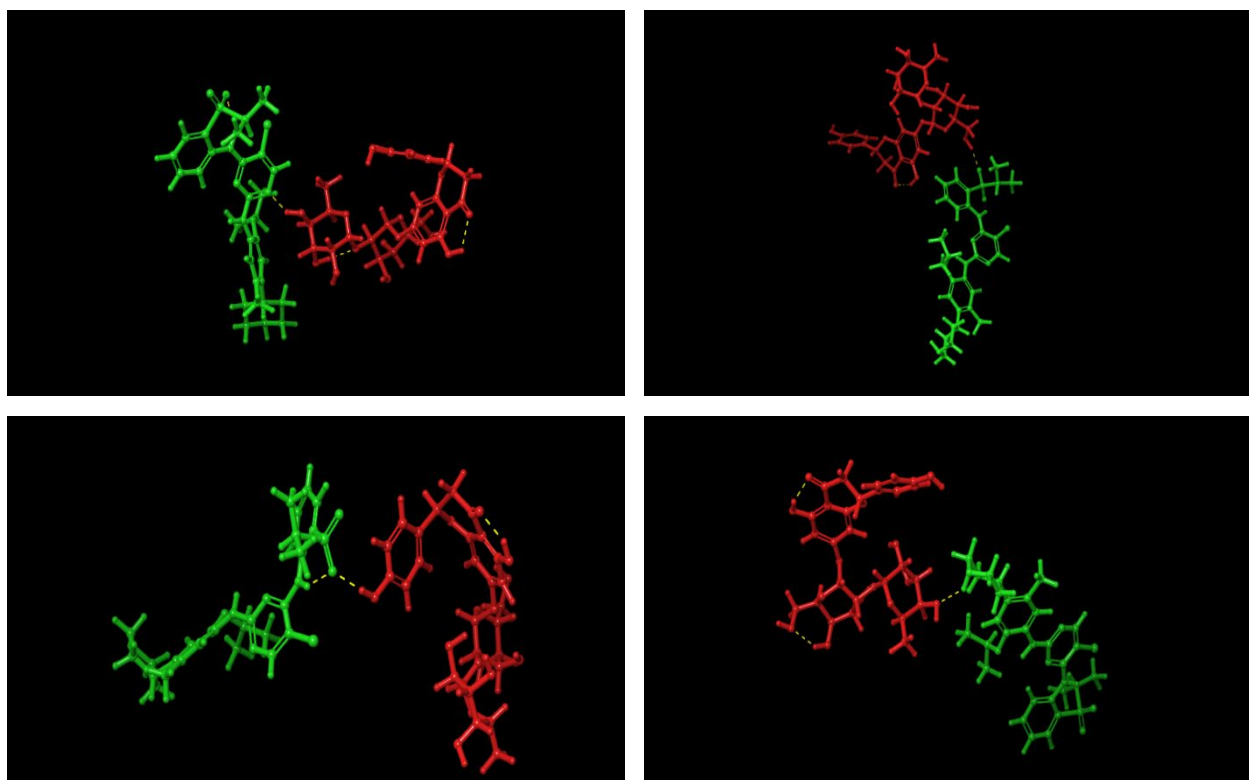
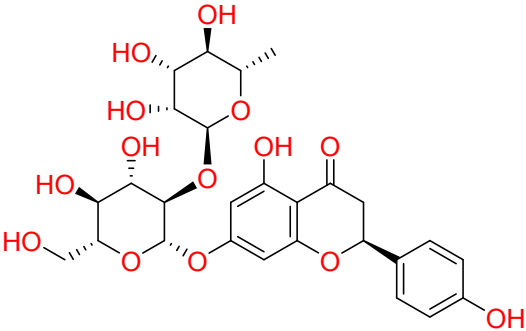
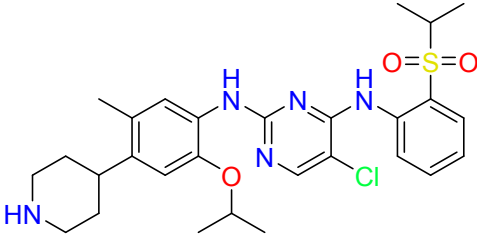
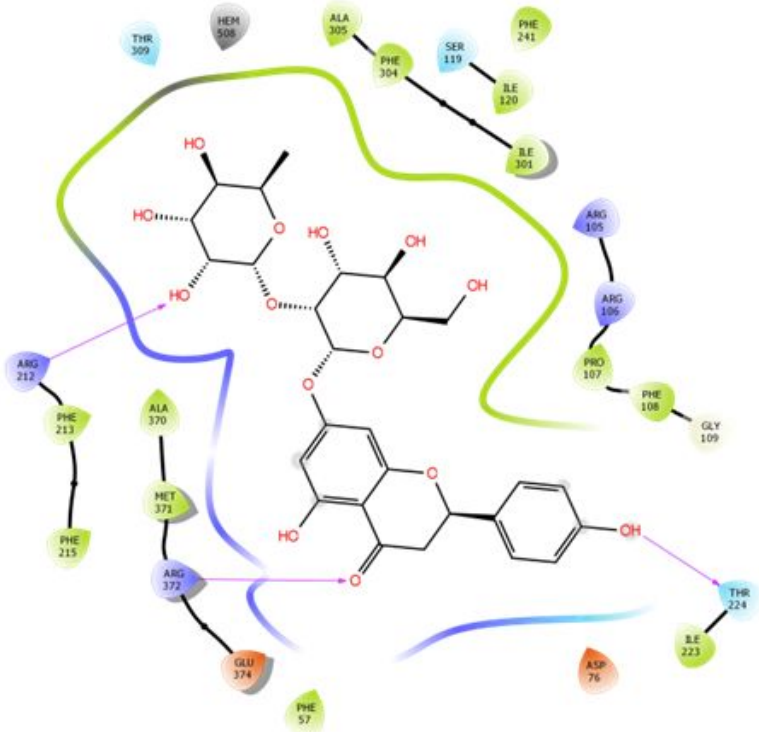


Figure S4. pi-pi interactions between CRT-RTH systems from MD simulation. (Red-CRT, Green- RTH, Blue- pi-pi interactions, Yellow- Hydrogen bonds)

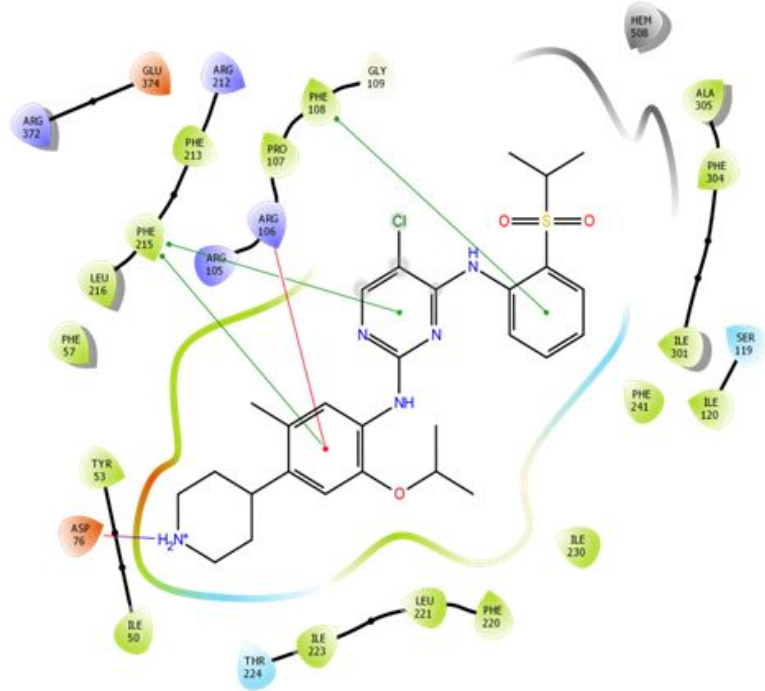
**Table S1.** NRG and CRT, along with their chemical structure and docking score.

Compound name	Chemical structure	Docking score (Kcal/mol)
Naringin		-10.970
Ceritinib		-9.035

**Table S2.** 2D interaction diagram alongwith binding interaction of NRG and CRT at the binding site of the CYP3A4 protein

Compound name	Chemical structure	Binding interactions
Naringin		ARG212, THR224, ARG372 (H-bond interaction)

Ceritinib



ASP76 (salt  
bridge),  
ARG106  
(pi-cation),  
PHE108,  
PHE215  
(pi-pi  
stacking)