In-silico identification of potential antagonists for human Casein kinase II sub-unit alpha'(CK2α2)

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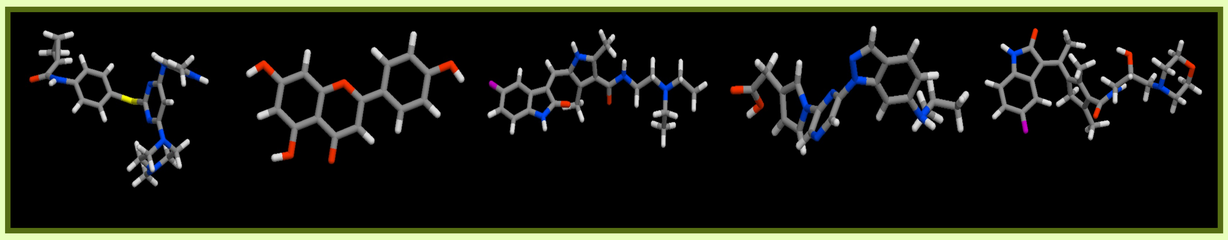
KEY POINTS

> Human CK2α2 is an enzyme that belongs to the Serine/threonine protein kinase family which is involved in signal transduction.

> Over expression of human CK2α2 leads to kidney cancer.

>Apigenin, VX680, Sunitinib, CCK and SUI4813 were the existing inhibitors of human CK2α2 showing side effects.



VX680 Apigenin Sunitinib CCK SUI481

Five existing inhibitors of human CK2α2

MATERIALS AND METHODS

Retrieval of co–crystal structure of human CK2α2

PDB PROTEIN DATA BANK

Prediction of ligand binding site

CASTp

Structural analogue search through Virtual screening

Ligand.Info

Harvard ChemBank, E-MSD ChemPDB, KEGG Ligand, Anti-HIV NCI, Druglikeness NCI, Unannotated NCI, Akos GmbH, Asinex Ltd.

Docking analysis through Schrodinger software

Maestro

Docking complex

RESULTS

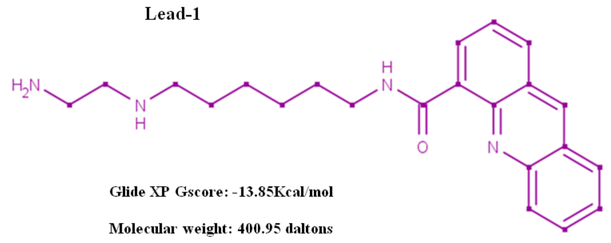
Lig Prep (1942) → Post Lig Prep (2636) → Qik Prop (2474)

GLIDE HTVS (281) → SP Docking (52) → XP Docking (39)

CONCLUSION:

Human CK2α2-lead 1 docking complex was well correlated with native co-crystal structure and the residues Ile 117, Asn 119 are participated in forming H-bond network. Hence, lead 1 with good docking score and binding affinity to human CK2α2 was proposed as novel antagonist against cancer.

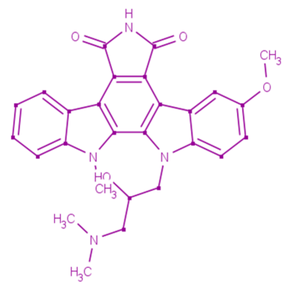
Lead-1



Glide XP Gscore: -13.85Kcal/mol

Molecular weight: 400.95 daltons

Lead-3

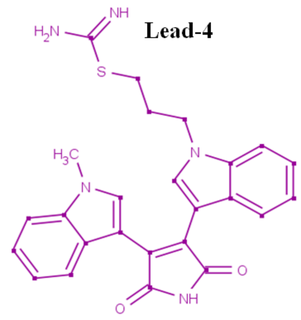


Glide XP Gscore: -12.94Kcal/mol

Molecular weight: 470.53 daltons

Proposed leads

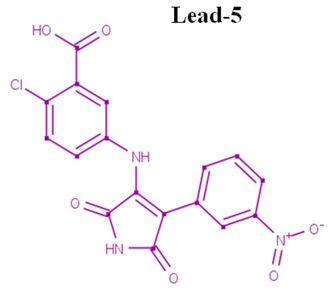
Lead-4



Glide XP Gscore: -12.70Kcal/mol

Molecular weight: 457.56 daltons

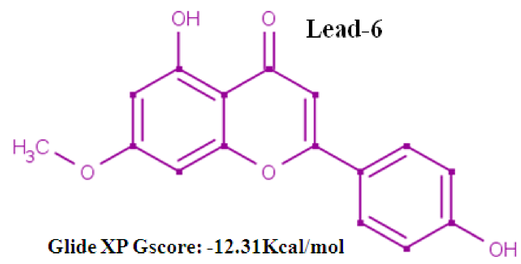
Lead-5



Glide XP Gscore: -12.63Kcal/mol

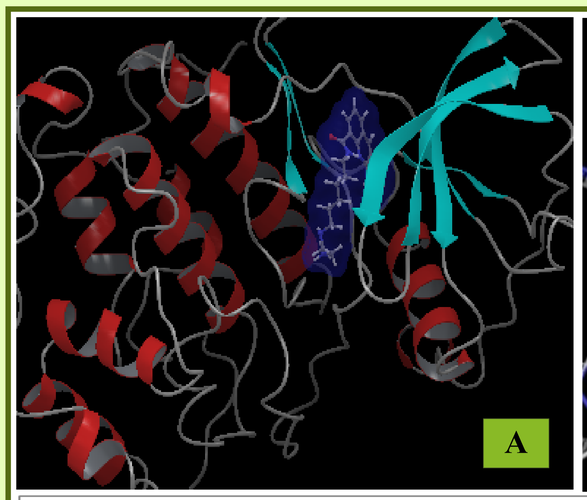
Molecular weight: 387.74 daltons

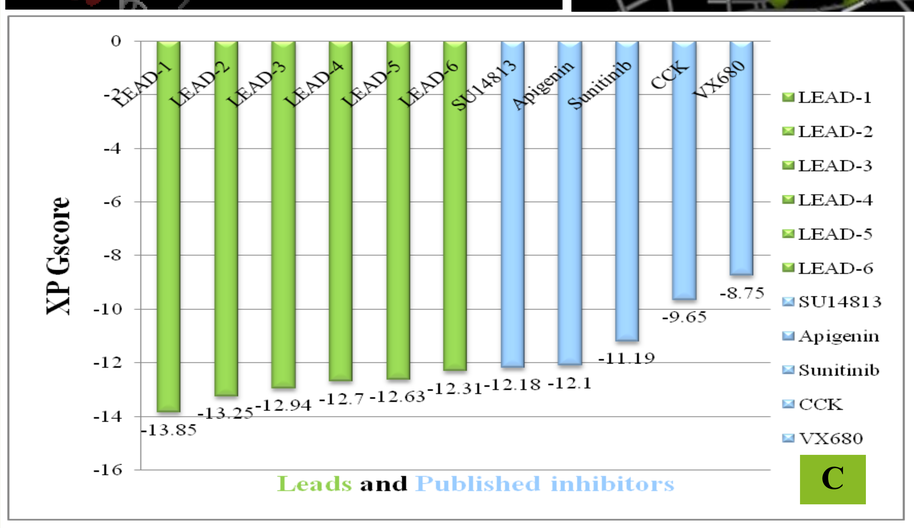
Lead-6



Glide XP Gscore: -12.31Kcal/mol

Molecular weight: 284.27





Active site residues

Arg 44, Leu 46, Val 54, Val 67, Lys 69, Ile 96, Phe114, Tyr 116, Ile 117, Asn 119 , His 161, Met 164, Ile 175 and Asp 176

A) Docking complex of human CK2α2 with lead 1.

B) H-bond network in the docking complex

C) Comparison of lead docking scores with published inhibitors

ACKNOWLEDGMENTS:

My deep sense of gratitude to honorable Dr.A.Umamaheswari, Associate professor & Coordinator of BIF, Dept of Bioinformatics, SVIMS, Tirupati for her guidance and DBT, ministry of science and technology, Govt. of India for providing traineeship.