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Novel Chalcone Derivatives as Potent Lyn Tyrosine Kinase Inhibitors: A Promising In Silico Approach for Targeted Therapy in Triple-Negative Breast Cancer

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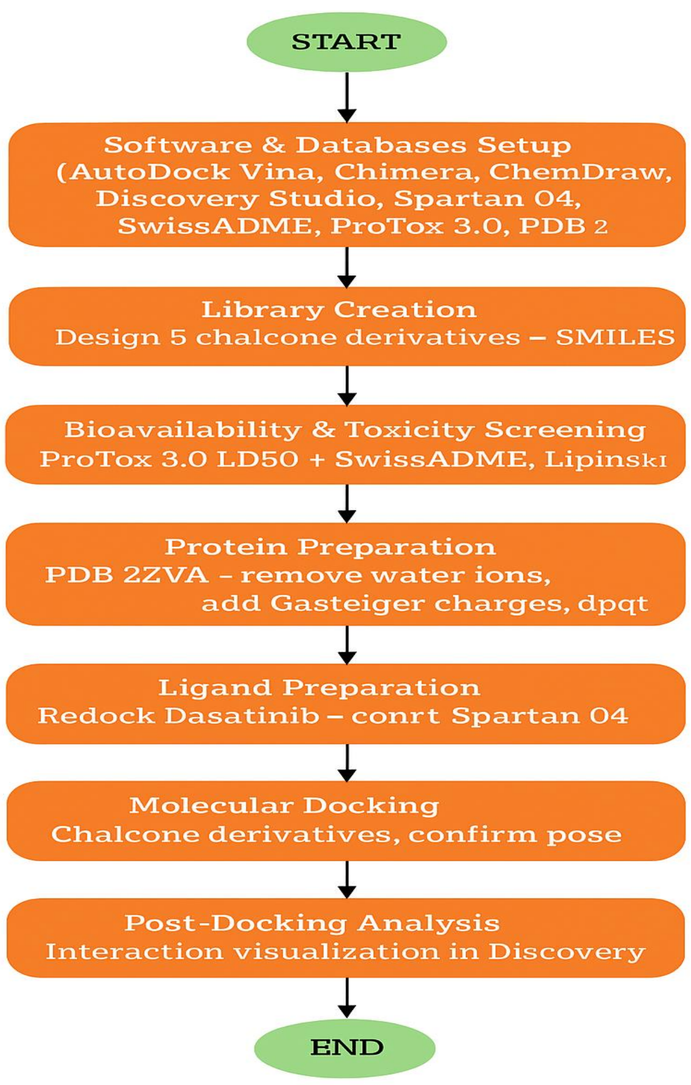
INTRODUCTION & AIM

- **TNBC Background & Lyn Kinase Role: Breast cancer remains the most common cancer in women, with TNBC making up ~15% of cases. TNBC is highly aggressive, and Lyn tyrosine kinase particularly its splice isoform ratio has been linked to invasion, metastasis, and poor survival outcomes.**

- **Chalcones as Potential Therapy: Chalcones, natural plant-derived compounds with anticancer activity, have shown cytotoxicity against TNBC cell lines. This study explores novel chalcone derivatives as potential Lyn kinase inhibitors using in silico methods, aiming to identify new therapeutic candidates for TNBC.**

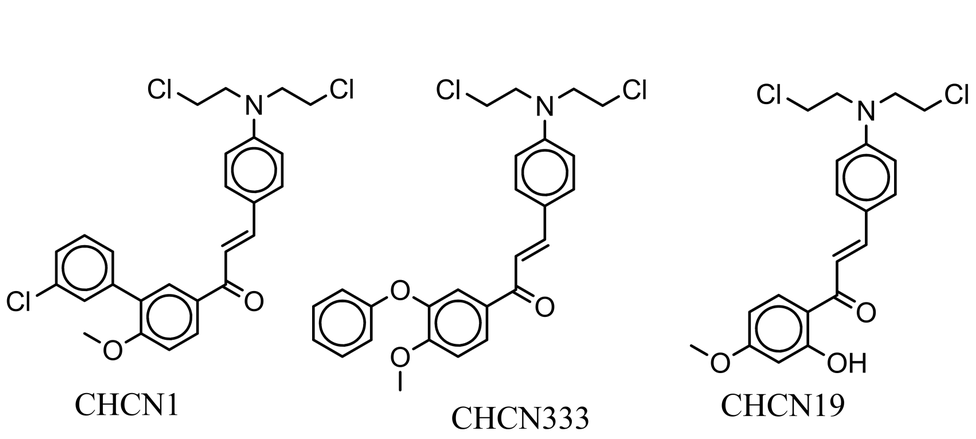
Aim: To identify hits from novel designed chalcone derivatives targeting lyn tyrosine kinase receptor in the management of Triple Negative Breast Cancer

METHOD



RESULTS & DISCUSSION

Table 1. 2D structure of selected novel chalcone deriatives



RESULTS & DISCUSSION

Table 2. Oral bioavailability of novel chalcone derivatives based on lipinski's rule of five and toxicity studies (LD_{50})

Parameter	CHCN1	CHCN19	CHCN48	CHCN333	CHCN94
Molecular Weight (g/mol)	488.83	394.29	391.89	470.39	407.89
H-bond Acceptors	2	3	2	3	3
H-bond Donors	0	1	0	0	1
LogP (MLOGP)	5.28	3.22	4.21	4.50	3.61
Lipinski's Violation	1	0	0	0	0
Oral Acute Toxicity Class	V	V	IV	IV	IV

(a) Molecular weight in g/mol, (b) (20) (Mwt ≤ 500, MLogP ≤ 5, HbAS 10, and HbD ≤ 5
Class IV= LD50 ≤ 2000 mg/kg; Class V= LD50 ≤ 5000 mg/kg.

Table 3. Binding energies of co-crystalysed ligand (Lig 0) & novel chalcone derivatives against lyn tyrosin kinase receptor (CHCN1 - CHCN 94)

Compound name	Dock scores (kcal/mol)
Lig 0	-9.8
CHCN1	-8.6
CHCN19	-7.1
CHCN48	-8.3
CHCN333	-8.1
CHCN94	-8.0

PDB ID: 2ZVA; lyn tyrosin kinase enzyme ; Co-crystallysed ligand: Dasatinib

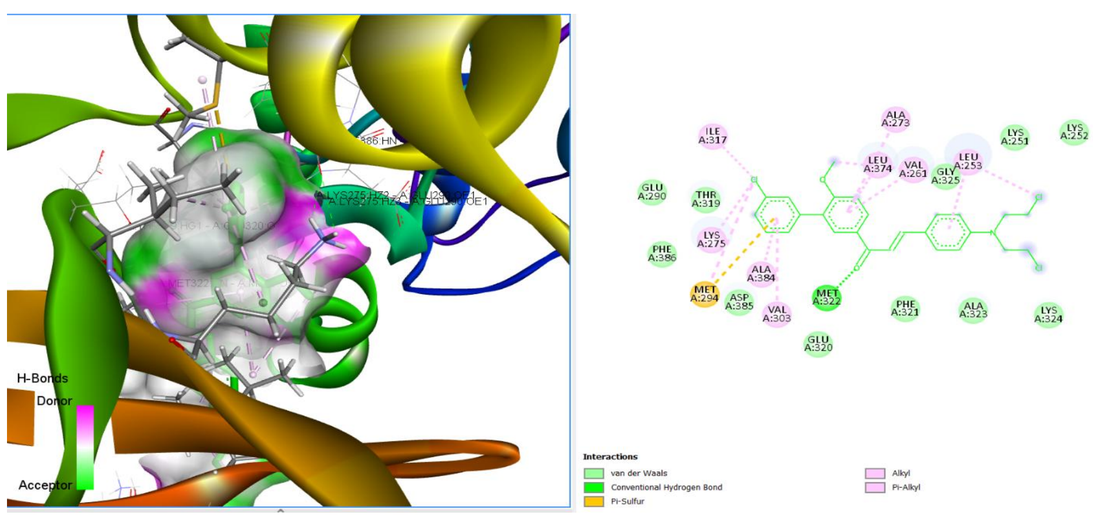


Figure 1. Three-dimensional molecular pose (left) and 2D (right) interactions of CHCN1 on binding cavity of Lyn tyrosine kinase enzyme

CONCLUSION

- **The chalcone derivatives showed favorable ADME profiles (MW 391.89–488.83 g/mol, TPSA 29.54–49.77 Å², bioavailability score 0.55) with low predicted toxicity (LD50 ≤ 2000–5000 mg/kg). Docking scores ranged from –7.1 to –8.6 kcal/mol, with CHCN1 being the most promising candidate. Key interactions were observed with Lys275, Glu290, Asp385, and Phe386, underscoring its potential as Lyn kinase inhibitor.**

FUTURE WORK / REFERENCES

- **Further analysis to elucidate the anti cancer activities of lyn tyrosine kinase enzyme of CHCN1 with dock score comparable to co-crystalised ligand dasatinib in TNB cancer.**

Reference

- **[1] Arnold M, Morgan E, Rumgay H, Mafra A, Singh D, Laversanne M, et al. Current and future burden of breast cancer: Global statistics for 2020 and 2040. The Breast 2022;66:15–23. https://doi.org/10.1016/j.breast.2022.08.010.**
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- **[3] Waks AG, Winer EP. Breast Cancer Treatment. JAMA 2019;321:288. https://doi.org/10.1001/jama.2018.19323.**