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A COMPUTATIONAL SCREENING OF QUINAZOLINONE DERIVATIVES AS POTENTIAL ANTIFUNGAL AGENTS

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INTRODUCTION

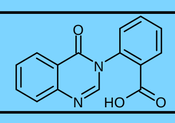
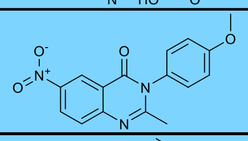
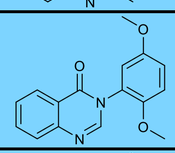
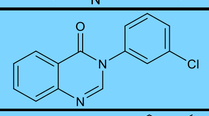
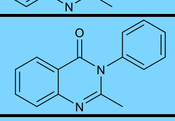
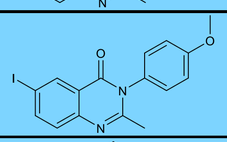
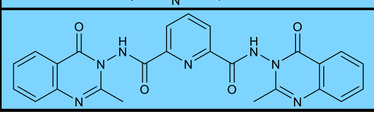
Phytopathogenic fungi are causing many plant diseases that reduce crop quality and lead to huge yield losses. The excessive use of available fungicides over a long period of time has increased the fungal resistance and become a major ecological issue, giving the incentive to find new antifungal agents. Possible targets for these agents are enzymes involved in fungal cell growth. Chitinases (EC 3.2.1.14) cleave the *β*-(1,4) glycosidic bond in chitin, a major component in all fungal cell walls. Thus, fungal chitinases are important for cell wall degradation and remodeling [1].
Quinazolinone is a common heterocyclic nitrogen scaffold whose derivatives exert antifungal, antiviral, and antibacterial activity. The aim of this study was to evaluate the feasibility of several structurally different quinazolinone derivatives [2] to form the complex with catalytic domain of fungal chitinases by performing a molecular docking analysis.

EXPERIMENTAL

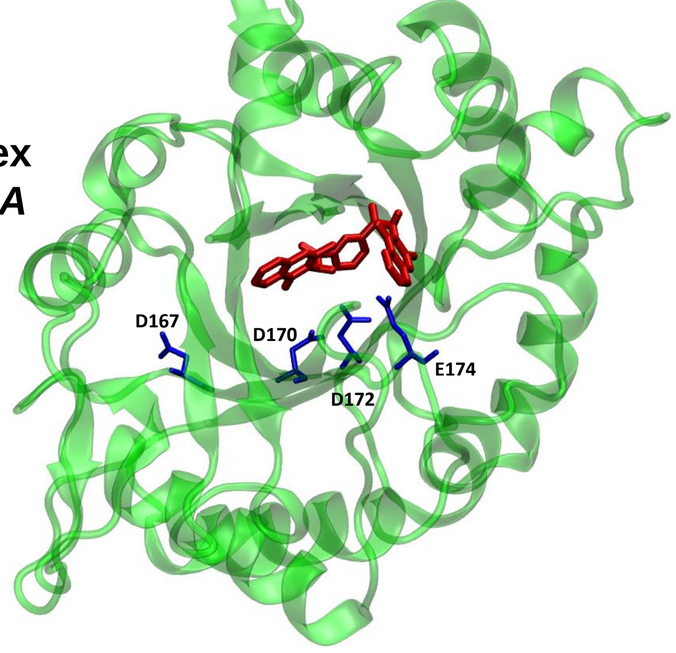
Eight quinazolinone derivatives (Q1-Q8) and two fungal chitinases from glycosidase family 18: type A (*ChA*, PDB ID: 2XUC) and type B (*ChB*, PDB ID: 2IUZ), were chosen for the study. Prior to analysis, structures of tested derivatives were optimised using Avogadro 1.2.0. Afterwards, docking was performed using AutoDock Vina 1.1.2 and the best-scoring ligand pose for each enzyme was chosen and visualised with VMD 1.9.3 software.

RESULTS

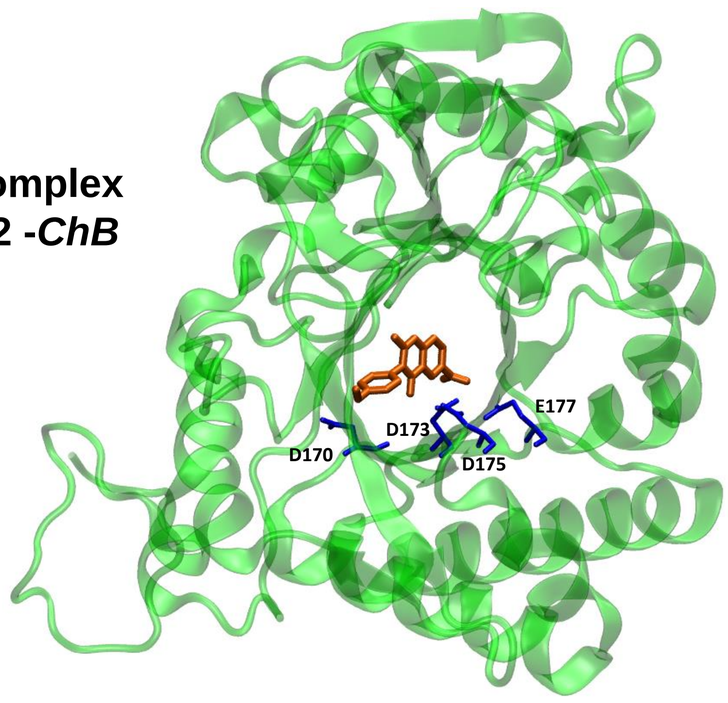
Docking revealed that all selected quinazolinone derivatives form complexes with docking scores between -8.8, and -5.8 kcal mol^{-1}.The best affinity scores were obtained for compounds Q8 and Q2 with *ChA* and *ChB*, respectively. Both compounds bind near the substrate-binding cleft and conserved catalitic DxxDxDxE motif.

Compound	Structure	Binding affinity kcal mol^{-1}	
		ChA	*ChB*
Q1		-6.2	-8.4
Q2		-7.0	**-8.8**
Q3		-5.8	-8.0
Q4		-6.6	-6.8
Q5		-6.6	-7.5
Q6		-6.3	-8.6
Q7		-6.3	-7.5
Q8		**-8.7**	-8.7

Complex Q8 -*ChA*



Complex Q2 -*ChB*



REFERENCES

[1] J.-W. Peng et al, *J. Agric. Food Chem*. 69 (2021) 16, 4604–4614.
[2] M. Komar et al, *Croat. Chem. Acta* 92 (2019) 4, 511–517.

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CONCLUSIONS

Given that the results of this computational study showed the feasibility of the quinazolinone derivatives to form a complex with the catalytic domain of chitinases, it can be assumed that this type of compounds could serve as potential antifungal agents. This should be confirmed by further *in vitro* experiments.