EXPLORING THE ANTIFUNGAL EFFECT OF QUINAZOLINONE-Cu(II) COMPLEXES AGAINST YEAST INFECTIONS

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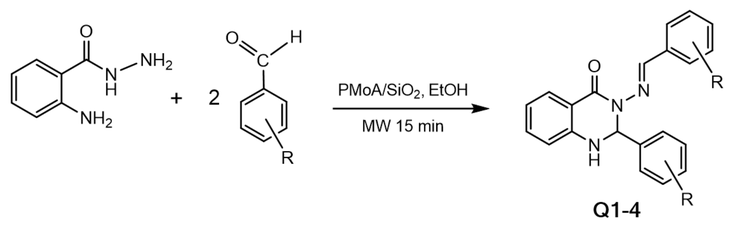
Yeasts are an important group of single-celled microorganisms employed in the traditional fermentation, biotechnology and life science. However, some yeasts act as pathogens in humans, causing serious infections and even death. Other yeasts can cause spoilage of food and significant economic losses. Various preservatives are utilized to suppress yeast growth, and several antifungal medications are used to treat infections. But increasing resistance of yeasts to commonly used organic compounds pose a challenge in search for new drugs and preservatives [1-2]. Quinazolinones and their transition-metal complexes are a subject of considerable interest due to their wide range of biological activities and therapeutic effects [3-4]. Taking into consideration their application in pharmaceutical and food industry, a series of quinazolinone Schiff base ligands, and corresponding Cu(II) complexes were screened as potentially useful antifungal agents.

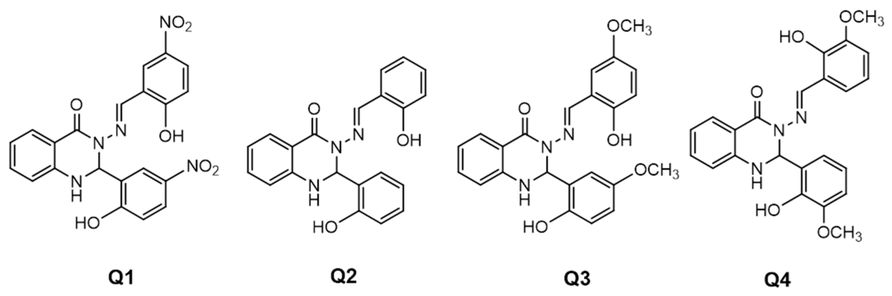
Methods

- Quinazolinone Schiff bases were prepared by MW-assisted PMoA/SiO_2 catalysed condensation of 2-amino-benzhydrazide and the corresponding aldehydes [5].
- Cu(II) complexes were prepared by the reaction of copper chloride with equimolar amount of corresponding quinazolinone Schiff base ligand.
- Antifungal activity was evaluated against a panel of 15 pathogenic yeast species. The sensitivity of the yeast culture was determined by measuring the diameter (mm) of a clear zone around the individual ligands and Cu(II) complexes.

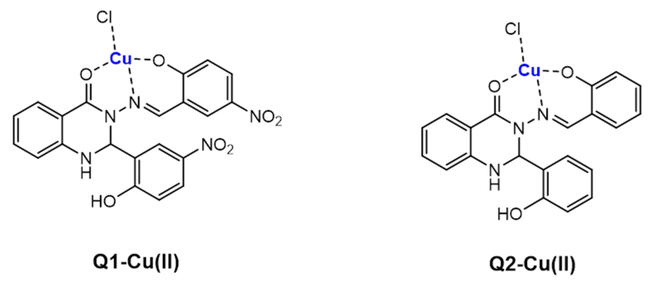


Q1-4

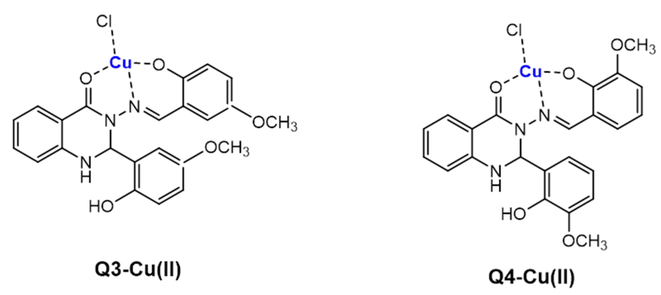
Studied compounds: 2,3-disubstituted-quinazolinone Schiff bases **Q1**, **Q2**, **Q3**, **Q4** and Copper(II) complexes **Q1-Cu**, **Q2-Cu**, **Q3-Cu**, **Q4-Cu**.



Q1 Q2 Q3 Q4



Q1-Cu(II) Q2-Cu(II)



Q3-Cu(II) Q4-Cu(II)

References

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Results and Discussion

- Pathogenic yeast strains of human origin and 10 yeast cultures that commonly cause spoilage of fruits and vegetables were screened for sensitivity to quinazolinone ligands and Cu(II) complexes.
- All copper complexes **Q1-Cu**, **Q2-Cu**, **Q3-Cu** and **Q4-Cu** showed significant antifungal activity against different pathogenic yeast species (**Table 1, Figure 1**)
- The largest spectrum of inhibition activities was found with **Q4-Cu**. It inhibited 80 % of the yeast cultures tested.

Table1. Inhibitory activities of ligands Q1 -Q4 and copper complexes Q1-Cu, Q2-Cu,Q3-Cu and Q4-Cu against pathogenic yeasts species expressed as inhibition coefficients (IC).

Yeast Species	CCY No.	Origin	Q1	Q1-Cu	Q2	Q2-Cu	Q3	Q3-Cu	Q4	Q4-Cu
Candida albicans	29-3163	Hemoculture	0	0	0	0	0	0	0	1.33
Candida glabrata	26-20-24	Cervix	0	0	0	0	0	0	0	1.33
Candida parapsilosis	29-20-31	Tonsiles	0	0	0	0	0	0	0	0
Candida tropicalis	29-7-68	Tongue	0	0	0	1.00	0	0	0	1.33
Debaryomyces hansenii	41-10-4	Mayonnaise	1.86	0	1.70	0	1.7	1.50	1.70	1.17
Hanseniaspora uvarum	25-6-32	Plum tree fruit	1.33	0	0	1.70	0	1.70	0	1.67
Pichia kudriavzevii	29-9-25	Fodder yeast contaminant	1.00	1.70	0	1.65	0	2.70	0	2.04
Pichia kudriavzevii	29-9-40	Tonsiles	0	0	0	1.70	0	0	0	1.70
Pichia membranifaciens	39-1-30	Pear tree fruit	0	0	0	3.50	0	4.25	0	1.10
Rhodotorula mucilaginosa	20-1-38	Apricot tree soil adjacent	1.33	0	0	0	0	0	0	2.00
Schizosaccharo-myces pombe	44-1-3	unknown	2.60	1.70	0	0	0	0	0	0
Torulaspora delbrueckii	41-24-1	Grape juice	1.33	0	0	1.70	0	1.17	0	1.50
Yarrowia lipolytica	29-26-5	Olives	0	1.33	0	0	0	0	0	0
Zygosaccharo-myces bailii	35-6-9	Wine contaminant	0	1.67	0	1.33	0	3.00	0	2.50
Zygosaccharo-myces rouxii	35-5-2	Grape must contaminant	0	1.67	0	2.00	0	1.50	0	1.33

Notes: Inhibition coefficient (IC) of compound against yeast culture was calculated as a ratio of a clear zone around the tested compound to a diameter of the quinazolinone compound colony [6]. IC values higher than 2 indicated strong inhibition activity.

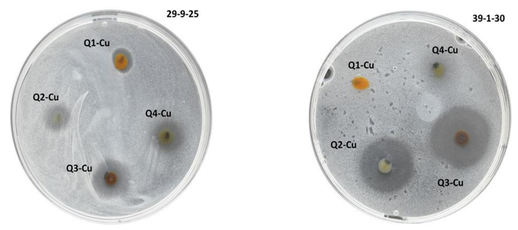

Fig.1. Inhibition activity of complexes Q1-Cu – Q4-Cu (concentration 20 mM) against yeast species *Pichia kudriavzevii* (29-9-25) and *Pichia membranifaciens* (39-1-30).

Conclusions

- **Efficient approach to quinazolinone Schiff bases - high yields, reusable catalyst, mild reaction conditions**
- **Cu(II) omplexes inhibited the growth of pathogenic yeast species in various extent**
- **Ligand Q1 and all Cu(II) complexes are strong inhibitors of selected spoilage yeast found in the food industry Q4-Cu was the most active compound against *Candida* and other yeast infections**
- **Cu(II) complexes derived from quinazolinone ligands are promising candidates for development of new antifungal agents**

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