

A review of biologically active oxime ethers

Tomasz Kosmalski ^{1*}, Daria Kupczyk ², Szymon Baumgart ¹, Renata Paprocka ¹ and Renata Studzińska ^{1*}

¹ Nicolaus Copernicus University in Toruń, Collegium Medicum in Bydgoszcz, Faculty of Pharmacy, Department of Organic Chemistry, 2 Jurasza Str., 85–089 Bydgoszcz, Poland; tkosm@cm.umk.pl, rstud@cm.umk.pl, sz.baumgart@cm.umk.pl, renata.bursa@cm.umk.pl

² Nicolaus Copernicus University in Toruń, Collegium Medicum in Bydgoszcz, Faculty of Medicine, Department of Medical Biology and Biochemistry, 24 Karłowicza Str., 85–092 Bydgoszcz, Poland; dariak@cm.umk.pl

* Correspondence: tkosm@cm.umk.pl, rstud@cm.umk.pl

Table S1. Minimal inhibitory concentrations (µg/mL) of the selected antifungal oxime ethers inhibiting growth of 80% and 90% of fungal strains (MIC₈₀ and MIC₉₀, respectively).

	MIC ₈₀			MIC ₉₀	
	11a	11b	11c	12a	12b
<i>C. albicans</i>	0.004	0.016	0.016	2	16
<i>C. parapsilosis</i>	0.004	0.0625	0.0625	>128	>128
<i>T. rubrum</i>	0.0625	0.016	0.0625	-	-
<i>A. niger</i>	-	-	-	2	2
<i>A. fumigatus</i>	1	1	1	-	-
<i>C. tropicalis</i>	0.001	0.0625	-	-	-
<i>C. krusei</i>	0.0625	0.25	0.25	-	-
<i>C. neoformans</i>	0.016	0.001	0.004	32	16

Table S2. Minimal inhibitory concentrations ($\mu\text{g/mL}$) of the selected oxime ethers with antifungal activity.

MIC	5a	5b	5c	6	7a	7b	7c	8a	8b	9	10a	10b	13a	13b	14	38
<i>C. albicans</i>	4	2	1	2	4	16	16	0.25	0.5	>64	1	1	6.25	64	1	31.25
<i>C. glabrata</i>	0.5	1	0.06	4	-	-	-	-	-	-	-	-	-	-	-	-
<i>C. parapsilosis</i>	1	0.25	0.004	8	-	-	-	-	-	-	-	-	-	-	2	-
<i>A. fumigatus</i>	8	2	32	>128	-	-	-	-	-	-	-	-	-	-	-	-
<i>A. flavus</i>	32	8	32	>128	-	-	-	-	-	-	-	-	25	32	-	-
<i>T. mentagrophytes</i>	8	4	4	64	-	-	-	-	-	-	-	-	-	-	-	-
<i>T. rubrum</i>	8	2	2	64	-	-	-	-	-	-	-	-	-	-	-	-
<i>S. cerevisiae</i>	-	-	-	-	8	>64	32	0.5	2	-	-	-	-	-	-	-
<i>A. niger</i>	-	-	-	-	64	1	64	8	4	-	-	-	50	>128	-	-
<i>M. gypseum</i>	-	-	-	-	8	1	16	1	8	-	-	-	-	-	-	-
<i>C. gatti</i>	-	-	-	-	-	-	-	-	-	0.5	-	-	-	-	-	-
<i>A. fumigatus</i>	-	-	-	-	-	-	-	-	-	32	-	-	-	-	-	-
<i>E. dermatitidis</i>	-	-	-	-	-	-	-	-	-	64	-	-	-	-	-	-
<i>C. krusei</i>	-	-	-	-	-	-	-	-	-	-	-	-	-	-	1	-
<i>Candida-51</i>	-	-	-	-	-	-	-	-	-	-	-	-	6.25	32	-	-
<i>Rhizopus</i>	-	-	-	-	-	-	-	-	-	-	-	-	25	-	-	-

Table S3. Minimal inhibitory concentrations (µg/mL) of the selected oxime ethers with antibacterial activity.

	30	31	32a	32b	36a	36b	37	38	40	41a	41b	42a	42b	42c	43
<i>S. aureus</i>	0.19	0.78 1	32	32	62.5	62.5	1	7.81	6.25	3.125	12.5	0.5	0.5	0.5	-
MRSA	>100	-	-	-	-	-	-	-	-	-	-	-	-	-	-
<i>S. epidermidis</i>	0.19	-	-	-	-	-	-	-	-	-	-	-	-	-	-
<i>B. subtilis</i>	0.39	-	-	-	-	-	-	-	-	-	-	-	-	-	-
<i>E. coli</i>	0.39	0.39 1	32	32	125	125	-	125	12.5	50	25	>64	>64	>64	-
<i>K. pneumoniae</i>	0.19	1.56 3	-	-	-	-	>64	62.5	-	-	-	-	-	-	-
<i>P. aeruginosa</i>	25	>50	-	-	-	-	>64	-	6.25	>100	50	>64	>64	>64	-
<i>S. pyogenes</i>	-	-	32	32	-	-	-	-	-	-	-	-	-	-	-
<i>S. typhimurium</i>	-	-	32	64	-	-	-	-	-	-	-	-	-	-	-
<i>A. baumannii</i>	-	-	-	-	-	-	>64	-	-	-	-	-	-	-	-
<i>M. tuberculosis</i>	-	-	-	-	-	-	32	-	-	-	-	-	-	-	0.04
<i>S. typhi</i>	-	-	-	-	-	-	-	-	25	-	-	-	-	-	-
<i>B. cereus</i>	-	-	-	-	-	-	-	-	-	3.125	6.25	-	-	-	-
<i>B. subtilis</i>	-	-	-	-	-	-	-	15.62	-	-	-	-	-	-	-

MRSA: methicillin-resistant *Staphylococcus aureus*

Table S4. Cytotoxicity (IC₅₀, μ M) of the selected oxime ethers against selected human cancer cell lines

Line	80a	80b	83	87	88	89a	89b	91a	91b	92a	92b	93
K562	0.37	0.11	-	-	-	-	-	-	-	-	-	-
A549	-	-	-	2.0	-	40.2	47.4	-	-	-	-	-
HT-29	-	-	-	3.3	-	-	-	-	-	-	-	-
HeLa	-	-	8.43	22.6	5.63	-	-	6.6	7.5	-	-	-
MCF-7	-	-	11.06	>100	>30	-	-	6.6	7.5	-	-	0.075
MDA-MB-231	-	-	12.63	4.7	-	28.7	40.4	5.1	7.2	-	-	-
G-361	-	-	-	8.9	-	-	-	-	-	-	-	-
A431	-	-	-	-	13.25	-	-	-	-	-	-	-
A2780	-	-	-	-	25.05	-	-	-	-	-	-	-
PC-3	-	-	-	-	-	47.8	43.6	-	-	-	-	-
DU145	-	-	-	-	-	-	-	9.5	9.0	-	-	-
Ishikawa	-	-	-	-	-	-	-	6	12	-	-	-
SMMC-7721	-	-	-	-	-	-	-	-	-	0.64	0.63	-

Table S5. Selected mechanisms of action of the oxime ethers with the anticancer activity.

	Mechanism of action
80a, 80b	inhibition of tubulin polymerization
87	apoptosis
88	decrease in the G1 phase
92a, 92b	inhibition of migration and DNA replication, inducing irreversible apoptosis by regulating the expression level of apoptose-related proteins
91b	apoptosis, inhibition of migration and invasion, inhibition of cancer stem cell population, abrogation of EGF-induced proliferation, migration, and tyrosine kinase (TK) signaling in breast cancer cells
93	estrogen receptor agonist, antiproliferative activities via ER-independent mechanism