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Supplementary Information

2D Chemometric Studies of a Series of Azole Derivatives Active against Fluconazole-Resistant *Cryptococcus gattii*

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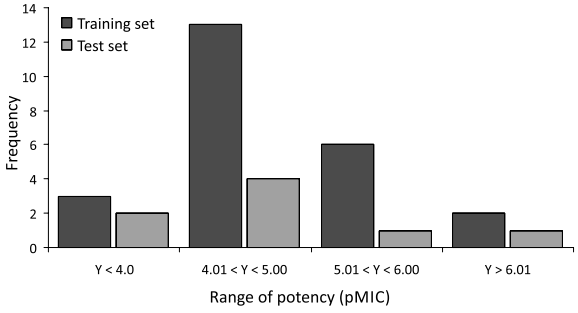

Figure S1. Frequency histogram of compounds of the training and test sets in relation to range of potency (pMIC).

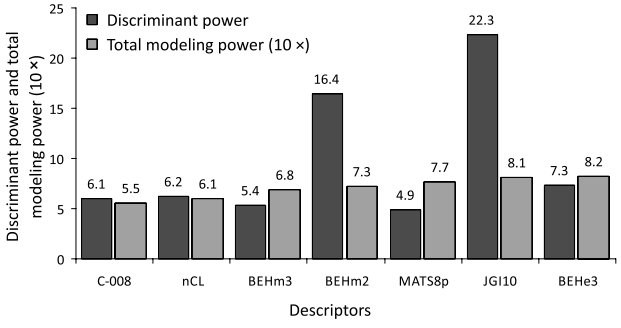

Figure S2. Coefficients of discriminant power (black bar) and total modeling power (10 ×) (gray bar) to the descriptors present in the final SIMCA model.

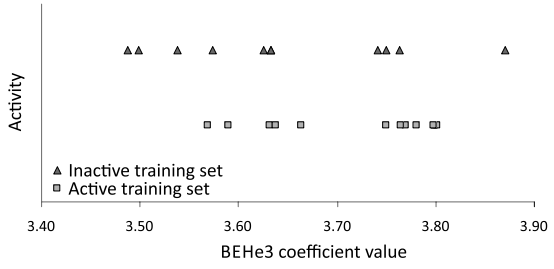

Figure S3. Profile of activity coefficients *vs.* BEHe3 for compounds of the training and test sets.

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Table S1. Chemical structure of the azole derivatives used in chemometric studies

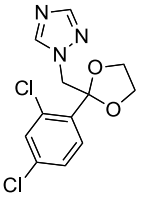
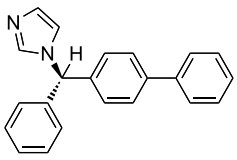
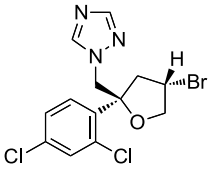
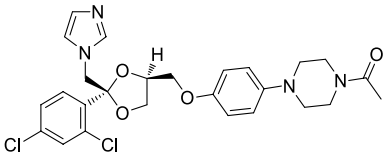
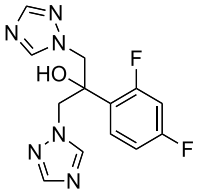
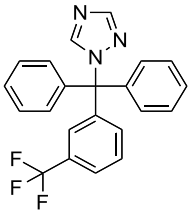
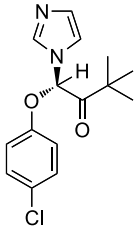
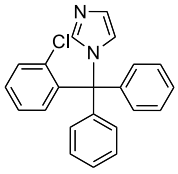
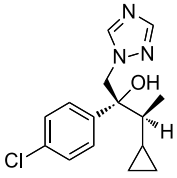
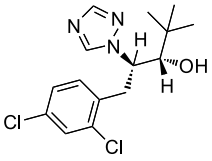
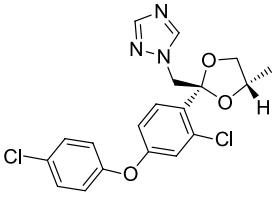
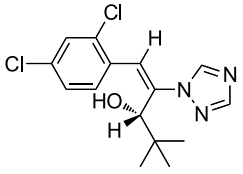
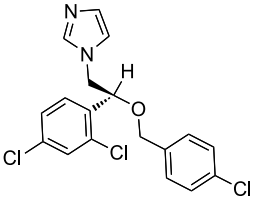
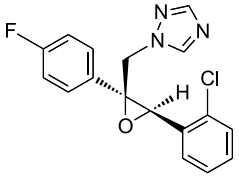
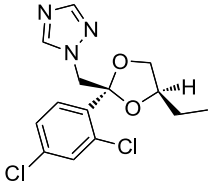
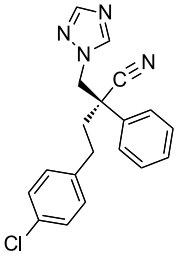
Name	Structure	Name	Structure
Azaconazole		Bifonazole	
Bromuconazole		Ketoconazole	
Climbazole		Clotrimazole	
Ciproconazole		Diclobutrazole	
Difenoconazole		Diniconazole	
Econazole		Epoxiconazole	
Etaconazole		Fenbuconazol	
Fluconazole		Fluotrimazol	

Table S1. continuation

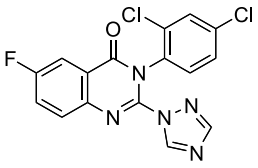
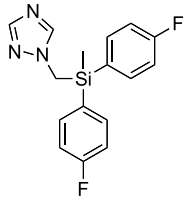
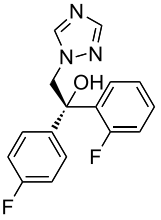
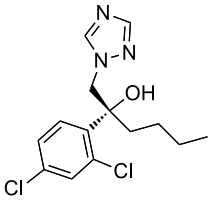
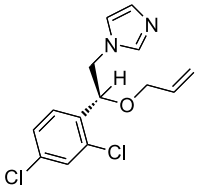
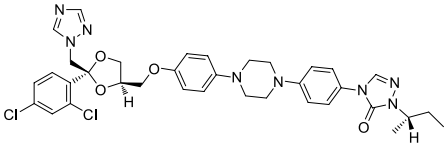
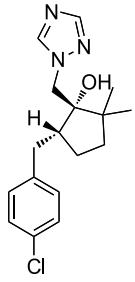
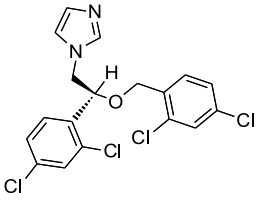
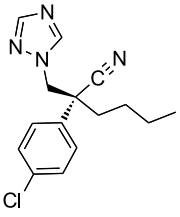
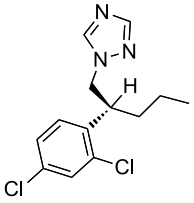
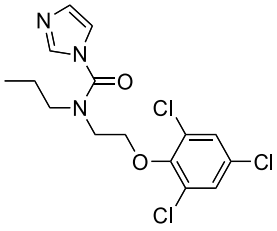
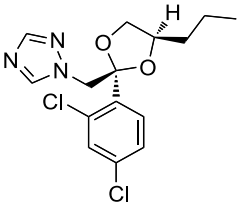
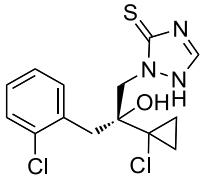
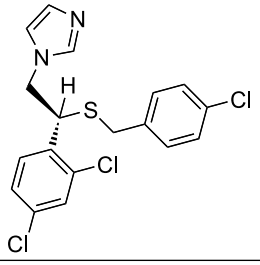
Name	Structure	Name	Structure
Fluquinconazole		Flusilazol	
Flutriafol		Hexaconazol	
Imazalil		Itraconazole	
Metconazole		Miconazole	
Myclobutanil		Penconazole	
Prochloraz		Propiconazole	
Prothioconazole		Sulconazole	

Table S1. continuation

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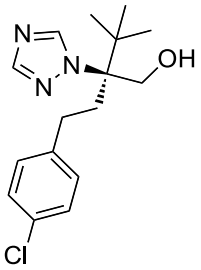
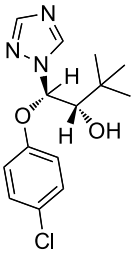
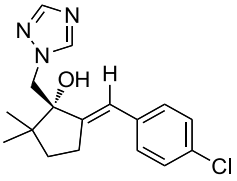
Tebuconazole		Triadimenol	
Triticonazole			

Table S2. All the descriptors pre-selected by RLM model using MOBYDIGS 1.0. The descriptors highlighted in gray were used in final 2D QSAR model

Descriptor	Meaning
Me	mean atomic Sanderson electronegativity (scaled on Carbon atom)
Ms	mean electrotopological state
nDB	number of double bonds
J	Balaban distance connectivity index
MAXDN	maximal electrotopological negative variation
PW3	path/walk 3 - Randic shape index
T(F..F)	sum of topological distances between F..F
X2v	valence connectivity index chi-2
X5v	valence connectivity index chi-5
X2Av	average valence connectivity index chi-2
IC3	information content index (neighborhood symmetry of 3-order)
SIC2	structural information content (neighborhood symmetry of 2-order)
ATS5e	Broto-Moreau autocorrelation of a topological structure - lag 5 / weighted by Sanderson electronegativities
ATS6p	Broto-Moreau autocorrelation of a topological structure - lag 6 / weighted by atomic polarizabilities
MATS7m	Moran autocorrelation - lag 7 / weighted by atomic masses
MATS8m	Moran autocorrelation - lag 8 / weighted by atomic masses
MATS2e	Moran autocorrelation - lag 2 / weighted by atomic Sanderson electronegativities
GATS1m	Geary autocorrelation - lag 1 / weighted by atomic masses
GATS8m	Geary autocorrelation - lag 8 / weighted by atomic masses
GATS1e	Geary autocorrelation - lag 1 / weighted by atomic Sanderson electronegativities
GATS5e	Geary autocorrelation - lag 5 / weighted by atomic Sanderson electronegativities
GATS4p	Geary autocorrelation - lag 4 / weighted by atomic polarizabilities
GATS6p	Geary autocorrelation - lag 6 / weighted by atomic polarizabilities
GATS3v	Geary autocorrelation - lag 6 / weighted by
ESpm03u	spectral moment 03 from edge adj. Matrix
BELe8	lowest eigenvalue n. 8 of burden matrix / weighted by atomic sanderson electronegativities

Table S2. continuation

Descriptor	Meaning
GGI1	topological charge index of order 1
SEigZ	eigenvalue sum from Z weighted distance matrix (Barysz matrix)
nArX	number of halogen linked to aromatic ring
C-003	atom-centred fragments - CHR3[a]
C-040	atom-centred fragments - R-C(=X) –X / R-C#X / X=C=X[b,c]
H-052	atom-centred fragments - H attached to C^0(sp3) with 1X attached to next C[d]
N-072	atom-centred fragments - RCO–N< / >N–X=X
nCONN	number of urea (–thio) derivatives
nN=C–N<	number of number of amidine derivatives
nCXr	number of halogens on ring C(sp3)

[a]R stands for any group linked through carbon; [b]X stands for any electronegative atom (O, N, S, P, Se, halogens); [c]# stands for triple bond; [d]the superscript number represents the formal oxidation number of the atoms (example, C0).