

Tguxgtcvtqn Uwuegrvkdknkv { qh *Streptococcus pneumoniae* cpf *Neisseria meningitidis* Uvtckpu Iuqncvgf kp vjg Uvcvg qh Mkpcu Ggtcku, Btc |kn, htq o 4227 vq 4235

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3

patients with meningitis, which have been identified using standard methods and maintained in the certified strains collection of Ezequiel Dias Foundation. In addition, one reference strain of *S. pneumoniae* (ATCC 49619) was also included in this study. The susceptibility to Resveratrol (Sigma-Aldrich, St Louis, MO), expressed as the minimum inhibitory concentration (MIC), was determined on blood agar containing this drug at eight concentrations ranging from 25 to 200 mg/L diluted in 0.5% ethanol, and control plates with blood agar with 0.5% ethanol [4]. All strains were tested in duplicates and incubated at 37°C, for 24 h, under ambient air or atmosphere with 5% CO₂. MIC₁₀₀ was defined as the lowest concentration of Resveratrol that completely inhibited any visible growth.

Pneumococci were also tested for susceptibility to ceftriaxone and penicillin using E-test method, and to chloramphenicol, clindamycin, erythromycin, ofloxacin, oxacylin, rifampicin, tetracycline, trimethoprim-sulfamethoxazole, and vancomycin using the disc diffusion method (Probac, São Paulo, Brazil). Experimental procedures and interpretation of results were performed according to clinical and laboratory standards institute (CLSI) clinical breakpoints [9]. In order

to shed light on the mode of action of Resveratrol, we tested the association between the susceptibility to this drug and to the antibiotics mentioned above. Briefly, *pneumococci* were divided into two groups according to their MIC₁₀₀ to Resveratrol: a) 200 mg/L; b)

175 mg/L. Then, a confusion matrix was built for each antibiotic tested distributing the strains into the groups "a" and "b" above according to their susceptibility or resistance to the respective antibiotic (Table 1 exemplifies a confusion matrix). Associations were assessed with chi-square test using GraphPad 5.0 (GraphPad Software, San Diego, CA).

Aiming to determine the toxic doses of Resveratrol upon L929

Strain ID	Year of isolation	Age (years)	Gender	Serotype	CEF	CLI	CO	ERI	OF	OXA	PE N	RIF	ST	TT	VAN	MIC100 RSV (mg/L)-ambient air	MIC100 (mg/L) atmosphere with 5% CO	RSV -
883/07	2007	41	F	11A	S	S	S	S	S	S	S	S	R	S	S	200	200	
1070/07	2007	57	M	11F	S	S	S	S	S	S	S	S	R	S	S	200	200	
1180/07	2007	29	M	6A/C	S	S	S	S	S	S	S	S						

chloramphenicol; ERI: erythromycin; OF: ofloxacin; OXA: oxacillin; PEN: penicillin; RIF: rifampicin; TT: tetracycline; ST: trimethoprim-sulfamethoxazole; VAN: vancomycin; RSV: Resveratrol

The lack of association between pneumococcal susceptibility to Resveratrol and the antibiotics tested herein suggests that the former does not share the same mode of action with the currently available antimicrobials used to treat meningitis. Our results, despite the low

selectivity indices observed, may warrant further studies to assess the potential of Resveratrol derivatives as antimicrobial alternatives to treat meningococcal and pneumococcal infections.

Strain ID	Year of isolation	Age (years)	Gender	Sero group	MIC100 RSV (mg/L) - ambient air	MIC100 RSV (mg/L) - atmosphere with 5% CO
78/08	2008	7	F	Y	50	50
92/08	2008	73	M	W135	75	75
264/08	2008	14	F	B	75	75
563/08	2008	58	F	W135	75	75
100/09	2009	NA	NA	W135	75	75
119/09	2009	NA	NA	W135	75	50
281/09	2009	15	M	Y	75	75
24/10	2010	12	F	C	50	75
35/10	2010	50	M	C	50	75
57/10	2010	57	F	C	50	50
56/10	2010	11	M	C	50	50
108/10	2010	44	F	C	75	75
131/10	2010	5	F	B	75	75
132/10	2010	1	F	Y	50	50
138/10	2010	64	M	C	50	50
177/10	2010	5	F	C	75	75
201/10	2010	6	F	B	50	75
215/10	2010	10	M	C	50	50
42167	2012	21	F	C	50	75
42320	2012	6	F	C	75	75
15/12	2012	4	M	B	75	75
78/12	2012	30	M	C	50	75
86/12	2012	15	F	C	75	75
96/12	2012	22	M	C	50	75
101/12	2012	40	M	C	50	75
170/12	2012	NA	NA	NA	50	50
175/12	2012	<1	M	B	50	50
326/12	2012	73	F	W135	75	75
345/12	2012	18	M	B	75	75
616/12	2012	<1	F	B	50	75

843/12	2012	18	F	B	75	75
17/13	2013	39	M	C	75	75

Table 3 Epidemiological data and Resveratrol susceptibility of *Neisseria meningitidis* strains. Epidemiological data and results of susceptibility test to Resveratrol of *meningococci* strains causing meningitis in Minas Gerais, Brazil