

Potential antibiotic and anti-infective effects of rhodomirtone from *Rhodomyrtus tomentosa* (Aiton) Hassk. on *Streptococcus pyogenes* as revealed by proteomics

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Rhodomirtone (Fig. 1) from *Rhodomyrtus tomentosa* (Aiton) Hassk. (Fig. 2) has a strong antibacterial activity against the bacterial pathogen *Streptococcus pyogenes*. Our previous studies indicated that the bactericidal activity of rhodomirtone might involve intracellular targets. In the present studies we followed a proteomics approach to investigate the mode of action of rhodomirtone on *S. pyogenes*. For this purpose, *S. pyogenes* was cultivated in the presence of 0.39 µg/ml rhodomirtone, which corresponds to 50% of the minimal inhibitory concentration. The results show that the amounts of various enzymes associated with important metabolic pathways were strongly affected, which is consistent with the growth-inhibiting effect of rhodomirtone. Additionally, cells of *S. pyogenes* grown in the presence of rhodomirtone produced reduced amounts of known virulence factors, such as the glyceraldehyde-3-phosphate dehydrogenase, the CAMP factor, and the streptococcal pyrogenic exotoxin C.

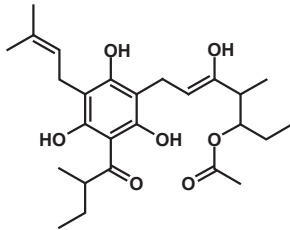
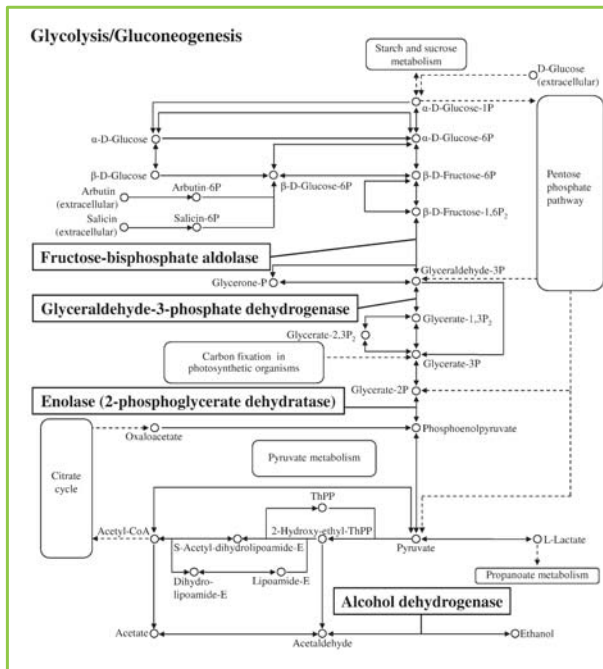


Fig. 1: Rhodomirtone



Fig. 2: *Rhodomyrtus tomentosa*

Mode of action



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Results

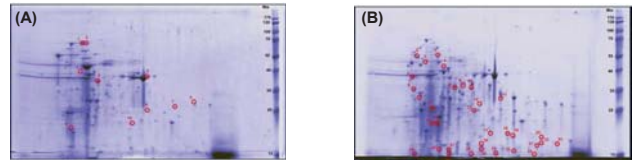


Fig 2. Two-dimensional gel electrophoresis profiles of cellular proteins of *S. pyogenes* grown in the absence (A) and presence (B) of rhodomirtone (50% MIC). Spots selected for MALDI-TOF MS analyses are numbered.

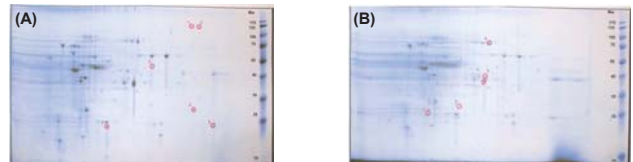


Fig 2. Two-dimensional gel electrophoresis profiles of culture supernatant proteins of *S. pyogenes* grown in the absence (A) or presence (B) of rhodomirtone (50% MIC). Spots selected for MALDI-TOF MS analyses are numbered.

Spot No.	Protein name	Mascot score	Organism
Untreated cells			
4	Alcohol dehydrogenase	89 (78)*	<i>S. pyogenes</i> M6
5	Glyceraldehyde-3-phosphate dehydrogenase (GAPDH) (Plaminogen-binding protein)	71 (67)	<i>S. pyogenes</i> M3
6	Hypothetical protein Spy0770 (salt-stress induce protein)	18 (67)	<i>S. pyogenes</i>
7	Streptokinase (fragment)	30 (67)	<i>S. pyogenes</i>
8	Transposase	41 (67)	<i>S. pyogenes</i> M3
9	Organic phosphate binding CYTH family protein	58 (67)	<i>S. pyogenes</i> M3
10	AE006516 NID	56 (78)	<i>S. pyogenes</i> M1
	AE014074 NID	56 (78)	<i>S. pyogenes</i>
Treated cells			
1	Xaa-His dipeptidase	78 (78)	<i>S. pyogenes</i> M28
2	Chaperone protein dnaK (Heat shock protein 70) (Heat shock 70 kDa protein) (HSP70)	76 (78)	<i>S. pyogenes</i> M1
4	60 kDa chaperonin (protein Cpn60) (groEL protein)	85 (67)	<i>S. pyogenes</i> M3
5	Heat shock protein (Fragment)	77 (67)	<i>S. pyogenes</i>
7	Glyceraldehyde-3-phosphate dehydrogenase	64 (67)	<i>S. pyogenes</i> M3
8	AE006516 NID	56 (67)	<i>S. pyogenes</i> M1
10	Ornithine carbamoyltransferase	75 (67)	<i>S. pyogenes</i> M28
11	Putative O-acetylserine lyase	171 (67)	<i>S. pyogenes</i> M18
12	Glyceraldehyde-3-phosphate dehydrogenase	73 (78)	<i>S. pyogenes</i> M3
	Enolase (2-phosphoglycerate dehydratase) (2-phospho-D-glycerate)	73 (67)	<i>S. pyogenes</i>
13	Peptide deformylase	106 (67)	<i>S. pyogenes</i> M3
14	Xaa-His dipeptidase	54 (67)	<i>S. pyogenes</i> M1
16	Fructose-bisphosphate aldolase	78 (67)	<i>S. pyogenes</i>
20	AE006516 NID	59 (67)	<i>S. pyogenes</i> M1
21	Glyceraldehyde-3-phosphate dehydrogenase	64 (67)	<i>S. pyogenes</i> M3
26	Triosephosphate isomerase (TIM) (Triose-phosphate isomerase)	45 (67)	<i>S. pyogenes</i> M1
Untreated supernatant			
1	Phage protein	17 (67)	<i>S. pyogenes</i> M3
	NrdI protein	17 (67)	<i>S. pyogenes</i> M3
	Hypothetical protein nrdI	17 (67)	<i>S. pyogenes</i> M28
4	CAMP factor	89 (78)	<i>S. pyogenes</i> M3
6	Streptococcal pyrogenic exotoxin C	114 (78)	<i>S. pyogenes</i>
	Exotoxin C precursor	107 (78)	<i>S. pyogenes</i>
	Exotoxin type C	106 (78)	<i>S. pyogenes</i> M28
	Enterotoxin	106 (78)	<i>S. pyogenes</i> M3
Treated supernatant			
1	SpeC protein (Fragment)	100 (78)	<i>S. pyogenes</i>
2	Cysteine synthase	68 (67)	<i>S. pyogenes</i> M3
	Putative O-acetylserine lyase	146 (78)	<i>S. pyogenes</i> M18
5	Glyceraldehyde-3-phosphate dehydrogenase	57 (78)	<i>S. pyogenes</i> M3

*Significant matching score (P>0.05)

Fig 3. Identified proteins of *S. pyogenes* that were present in distinct amounts when cells were grown in the absence or presence of rhodomirtone at 50% MIC. Proteins with the highest Mascot protein scores are listed.