Update on the Activity of a Topical Triple Antibiotic Ointment Against Cutaneous Pathogens

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ABSTRACT

Background: Triple antibiotic ointment (TAO) containing neomycin, polymyxin B and bacitracin has been widely utilized over-the-counter (OTC) for decades (USA) to prevent superficial wound or burn infections. In Australia (AUS), TAO is restricted to prescription use. This study determined: cross-resistance patterns of neomycin compared to other aminoglycosides; the level and trend of resistance to TAO and individual components (USA) especially versus mupirocin-resistant strains; and established the baseline of TAO activity level against AUS pathogens.
Methods: 200 strains (≥ 50% gentamicin-resistant) from the USA were used for the cross-resistance study including *S. aureus* (SA; 110), coagulase-negative staphylococci (CoNS; 50), *P. aeruginosa* (PSA; 10), *E. coli* (EC; 20) and other Enterobacteriaceae (EBS; 10) tested against TAO, bacitracin, polymyxin B, neomycin, amikacin, gentamicin, streptomycin, tobramycin and mupirocin. 50 gentamicin-resistant isolates from each year (1997 - 2002) were used to determine the activity of TAO over time. Baseline resistance rates of TAO among 300 AUS isolates (AGARS Program, 2002 - 2003) were studied. This study used reference broth microdilution methods.
Results: At a 1:100 dilution of the ointment concentration, TAO inhibited all CoNS, PSA and EBS and resistance to TAO among SA was 13.5% for the cross-resistance study. Polymyxin B inhibited all Gram-negative species. Patterns of susceptibility did not significantly vary from 1997 to 2002. AUS pathogens showed that TAO activity was 94% (MRSA), 98% (EBS) and 100% against MSSA, CoNS and PSA. These rates were equal to that observed in the USA. Mupirocin-resistant SA (5%) and CoNS (47%) were all TAO-susceptible. All Gram-negative species were also mupirocin-resistant, but inhibited by neomycin or polymyxin B.
Conclusions: Aminoglycoside-resistance patterns differ significantly and none of them could predict neomycin-resistance. TAO-resistance was rare in the USA after extensive OTC use and was not adversely influenced by decades of parenteral aminoglycoside use. AUS surveillance showed high levels of TAO susceptibility in sampled isolates as a baseline for possible OTC availability. TAO maintains a significantly superior spectrum compared to mupirocin and was usable against mupirocin-resistant strains.

INTRODUCTION

The use of the "Triple Antibiotic Ointment (TAO)" containing neomycin, polymyxin B and bacitracin was initially described in the mid-1950's although each component had been available in various geographic locations since 1943 - 1949. The product has been marketed by various pharmaceutical companies and currently the branded name Neosporin is promoted by Pfizer Consumer Healthcare. TAO is promoted as a topical "first-aid" agent to minimize/prevent infections in superficial wounds or burns (21CFR Part 333). By combining antimicrobial agents with narrower spectrums targeting either Gram-positive or -negative pathogens, a wide-spectrum of preventative activity has been achieved that includes: staphylococci, pyogenic streptococci, Enterobacteriaceae (*E. coli*, *Klebsiella* spp., etc.), *Pseudomonas aeruginosa* and several other organisms of environmental origin commonly observed as co-pathogens or opportunists of cutaneous wounds.

The advantage of these compounds, applied as non-prescription topicals, has been the lack of wide spread use by the parenteral route. Therefore, TAO use in the over-the-counter (OTC) environment presents minimal resistance-based compromise to the subsequent therapy of any prominently used antimicrobial or class. In fact, the National Committee for Clinical Laboratory Standards (NCCLS; currently the CLSI) withdrew all in vitro testing criteria from their disk diffusion and MIC dilution standards in the early 1980's as these drugs were no longer used for systemic infections or routinely tested in medical centers in the USA. This fact presents problems of monitoring the continued potency of these agents in the USA since limited data exists from direct testing of any TAO component.

Breakpoints utilized for susceptibility to TAO components were not rigorously validated (NCCLS) in the years prior to 1980 and were selected for the prediction of success versus systemic infections, not for topical formulations with very high concentrations (3.5 mg neomycin base; 5,000 IU polymyxin B; 400 U bacitracin/gm). The historical breakpoints for neomycin have varied from ≤ 3 µg/ml (*S. aureus*) to ≤ 10 µg/ml (all pathogens); for polymyxin B have been ≤ 2 µg/ml without an intermediate susceptibility definition; and for bacitracin have also been placed at ≤ 2 µg/ml. Debate continues about appropriate breakpoints for susceptibility to topical agents, but a safe or conservative definition of the TAO concentration should be used, but only for comparing topical products. An example of a topical product with a widely published breakpoint would be mupirocin (susceptible at ≤ 8 µg/ml and high-level resistance at > 256 µg/ml). Many experts believe that only the high-level resistance may have clinical significance, and this breakpoint corresponds to an approximately 1:100 dilution of the marketed product (2.0%). These facts will be taken into consideration in this report.

The purpose of this multi-phased study was to:

1. Determine the contemporary cross resistance or co-resistance patterns of neomycin compared to routinely tested aminoglycosides when testing USA cutaneous pathogens;
2. Determine the level and trends of resistance to TAO and its three components using USA isolates selected to enhance detection of resistance to the neomycin component; and
3. Establish the baseline level of TAO activity against contemporary clinical isolates from medical centers in Australia, a country not using OTC TAO.

These results would indicate the long-term resistance effects (if any) of TAO-OTC use in the USA and establish the baseline level of susceptibility in Australia to TAO. The use of such in vitro surveillance results and continued monitoring should provide a mechanism to detect significant trends toward resistances as TAO or other topical antimicrobials move toward OTC use (Australia) and be continued in the USA.

MATERIALS AND METHODS

Study sites: JMI Laboratories, North Liberty, Iowa, USA (Phase I and Phase II) and Women's and Children's Hospital, Adelaide, Australia (Phase III).

Susceptibility methods: NCCLS M7-A6 [2003] reference broth microdilution method and interpretations by NCCLS M100-S14 [2004], were available.

Quality control (QC) using NCCLS [2003 and 2004] recommended QC strains including: *S. aureus* ATCC 29213, *E. faecalis* ATCC 29212, *E. coli* ATCC 25922, and *P. aeruginosa* ATCC 27853. All QC results were within published/established ranges for the tested agents. The commercial producer of the frozen, reference panels (TREK Diagnostics, Cleveland, Ohio, USA) also obtained acceptable QC results prior to distribution to Iowa and Australia.

Organism collection:

Phase I - for the determination of aminoglycoside cross-resistance patterns, the following strains were selected (200 targeted strains): *S. aureus*, oxacillin-susceptible and -resistant (110; 70 gentamicin-susceptible); CoNS, oxacillin-susceptible and -resistant (50; 25 gentamicin-susceptible); *P. aeruginosa* (10; seven gentamicin-susceptible); *E. coli* (20; 10 gentamicin-susceptible); and Other Enterobacteriaceae (10; three gentamicin-susceptible). A total of 115 of these strains (57.5%) were susceptible to gentamicin.

Phase II - for the determination of antimicrobial activity of TAO versus pathogens by year taken from isolates in 1997 through 2002, emphasizing aminoglycoside resistance and then adjusting to the true resistance rates for TAO and components by comparing to the observed gentamicin rates within each species in surveillance trials. Fifty samples per year (300 total strains).

Phase III - for the determination of neomycin, polymyxin B, bacitracin and TAO rates of resistance in year 2002 - 2003 "community-acquired" isolates from Australia (AGARS Program).

Results from these phases should be compared to the pathogen and antimicrobial resistance summaries from the following programs: AGARS (Australia); SENTRY Antimicrobial Surveillance Program, worldwide including USA and Australia; and selected other literature references.

Table 1. Summary of Phase I results for nine agents or combinations tested against a selected group of strains including those with elevated gentamicin resistance.

Organism (no. tested)	Antimicrobial agent	MIC (µg/ml or Iu/ml) 50%	MIC (µg/ml or Iu/ml) 90%	% by category[a] Susceptible	% by category[a] Resistant
S. aureus (110)	Neomycin	0.6	78	63.6	30.9
	Bacitracin	25	100	0.9	-[b]
	Polymyxin B	78	157	-	-
	TAO[c]	-	-	-	30.0(13.6)[d]
	Amikacin	4	16	96.4	0.0
	Gentamicin	≤0.5	64	63.6	36.4
	Streptomycin	4	8	98.2	0.9
	Tobramycin	16	256	45.5	51.8
	Mupirocin	≤0.5	≤0.5	95.5	2.7
CoNS (51)[d]	Neomycin	0.06	9.8	90.2	5.9
	Bacitracin	25	50	0.0	-
	Polymyxin B	20	78	-	-
	TAO[c]	-	-	-	5.9(0.0)[c]
	Amikacin	≤1	4	100.0	0.0
	Gentamicin	8	32	49.0	33.3
	Streptomycin	2	4	98.0	2.0
	Tobramycin	8	128	47.1	39.2
	Mupirocin	≤0.5	>1024	52.9	25.5
P. aeruginosa (10)	Neomycin	4.9	20	70.0	10.0
	Bacitracin	>200	>200	0.0	-
	Polymyxin B	1.2	1.2	100.0	0.0
	TAO[c]	-	-	-	0.0(0.0)[c]
	Amikacin	2	4	100.0	0.0
	Gentamicin	2	64	70.0	30.0
	Streptomycin	32	128	20.0	40.0
	Tobramycin	≤0.5	32	70.0	30.0
	Mupirocin	>1024	>1024	-	-
E. coli (20)	Neomycin	1.2	78	85.0	15.0
	Bacitracin	>200	>200	0.0	-
	Polymyxin B	0.6	0.6	100.0	0.0
	TAO[c]	-	-	-	0.0(0.0)[c]
	Amikacin	≤1	4	100.0	0.0
	Gentamicin	1	64	50.0	45.0
	Streptomycin	32	512	45.0	45.0
	Tobramycin	1	32	65.0	20.0
	Mupirocin	128	512	-	-
Other enteric bacilli (10)	Neomycin	0.6	2.4	100.0	0.0
	Bacitracin	>200	>200	0.0	-
	Polymyxin B	0.3	0.6	100.0	0.0
	TAO[c]	-	-	-	0.0(0.0)[c]
	Amikacin	≤1	16	90.0	10.0
	Gentamicin	8	128	30.0	30.0
	Streptomycin	32	128	40.0	40.0
	Tobramycin	8	32	40.0	50.0
	Mupirocin	256	1024	-	-

a. Susceptibility as defined by the NCCLS or cited criteria.
b. - = no interpretive criteria.
c. TAO = triple antibiotic ointment and the calculated resistance rate for the most active component based on parenteral therapy breakpoints. Percentage in parenthesis is the proportion of strains resistant to a 1:100 dilution of TAO.
d. CoNS = coagulase-negative staphylococci.

Table 2. Summary of Phase II results for 10 agents or combinations tested against a selected group of strains with elevated gentamicin MICs (≥ 8 µg/ml).

Organism (no. tested)	Antimicrobial agent	MIC (µg/ml or Iu/ml) 50%	MIC (µg/ml or Iu/ml) 90%	% by category[a] Susceptible	% by category[a] Resistant
S. aureus (159)	Neomycin	20	78	34.6	47.8
	Polymyxin B	157	157	-[b]	-
	Bacitracin	50	400	0.0	-
	TAO	39	78	28.9	64.8(27.0)[c]
	Mupirocin	≤0.5	1024	82.4	11.3
	Oxacillin	>2	>2	23.9	76.1
CoNS (65)	Neomycin	2.4	20	89.2	6.2
	Polymyxin B	39	78	-	-
	Bacitracin	50	100	0.0	-
	TAO	2.4	20	89.2	4.6(3.1)[c]
	Mupirocin	≤0.5	>1024	61.5	18.5
	Oxacillin	>2	>2	23.1	76.9
Enteric bacilli (68)	Neomycin	2.4	78	70.6	25.0
	Polymyxin B	≤1.2	20	88.2	11.8
	Bacitracin	>400	>400	0.0	-
	TAO	≤1.2	≤1.2	97.1	2.9(2.9)[c]
	Mupirocin	256	1024	-	-

a. Susceptibility as defined by the NCCLS or cited criteria.
b. - = no criteria have been published.
c. TAO tested as the topical formulation using the neomycin component as the MIC. Percentage susceptible or resistant was based on the coverage of the most active component. The percentage in parenthesis is for the proposed topical breakpoint of resistance at > 39 µg/ml (1:100 dilution).

RESULTS

- Against the *S. aureus* strains (Table 1), the aminoglycoside resistance rates varied widely from 51.8% (tobramycin) to nil (amikacin). At a breakpoint of ≤ 10 (9.8) or ≤ 16 (20) µg/ml, neomycin inhibited 63.6 to 69.1% of isolates with 30.9% of strains with MIC values of ≥ 39 µg/ml. Judgments of potency and spectrum of TAO were made by using the lowest resistance rate for the most active component (neomycin) i.e. 30.9% resistance. As noted earlier, if one uses a 1:100 dilution of the ointment concentration to indicate susceptibility, the resistance rate was only 13.5% for this collection enriched (four-fold greater, see Phase II) with gentamicin-resistant strains.
- *P. aeruginosa* (30.0% resistance to gentamicin) isolates showed no resistance to TAO, to the polymyxin B component of TAO, or to amikacin (Table 1).
- *E. coli* and other Enterobacteriaceae strains (30 isolates; Table 1) were very susceptible to neomycin and/or polymyxin B. No resistant isolates were identified to TAO (most active component), although 10 to 50% of the strains were resistant to aminoglycosides (per protocol) depending on the organism group. Overall, no single surrogate aminoglycoside was identified for testing neomycin. On an average, using Phase I results for gentamicin:
  - 6.1% of gentamicin-susceptible strains were neomycin-resistant.
  - 86.0% of gentamicin-resistant strains were neomycin-susceptible.
- Table 2 lists all strains (USA) tested across the six year interval by reference MIC methods (Phase II). Only 11.8% of enteric bacilli strains were resistant to the TAO most active component (polymyxin B), but only a single strain of *P. mirabilis* in 1998 and *S. marcescens* in 2000 were resistant to both neomycin and polymyxin B. The overall susceptibility rate for the TAO was 97.1% using a published breakpoint for components or the proposed 1:100 dilution of the formulation (Table 2).
- In Table 3, the TAO activity versus the staphylococci shows excellent coverage of CoNS (resistance rates of 3.1 [TAO] to 6.2% [neomycin only]). In contrast, mupirocin high-level resistance was 18.5%; 11.3% for *S. aureus*. The collection of *S. aureus* was highly resistant overall with 76.1% MRSA isolates. TAO achieved 96 - 100% inhibition of these multi-resistant *S. aureus* strains. The TAO coverage/activity was greater than any single TAO component at this level indicating an enhanced (synergy) interaction between the three agents.
- Table 4 shows the rates of gentamicin resistance for the SENTRY Antimicrobial Surveillance Program isolates of *S. aureus*, CoNS, *E. coli* and *P. aeruginosa* for 1997 through 2003 (USA). A clear trend was observed that lower resistance rates for gentamicin have been detected in recent years for *S. aureus* (11.1 to 4.4%), CoNS (32.8 to 18.7%) and *P. aeruginosa* (11.8 to 7.1%).
- Using all data presented, one can calculate the probability of encountering a TAO- or neomycin-resistant isolate from among the most at-risk grouping of bacteria, gentamicin-resistant isolates of staphylococci or Gram-negative bacilli. Example calculations follow:
  - For *S. aureus* in 2002, 6.4% gentamicin resistance (Table 4) with a neomycin resistance rate among them of 47.8% (3.1% resistance adjusted) and a TAO-resistant rate of 27.0% (1.7% resistance). A second calculation could combine Phase I and II results for a neomycin resistance rate (0.14 x 6.4%) of only 0.9%. Both methods of calculations show a very low rate of TAO-resistant strains, far less than the rates of documented mupirocin resistance.
  - For the Enterobacteriaceae in 2002, the gentamicin resistance rate increased using *E. coli* as a marker species (Table 4). This increase of 2.9 to 4.2% (2002) combined with the 11.8% resistance rate to polymyxin B results in a TAO component resistance rate of 0.5%, but a TAO combination resistance rate of only (2.9 x 0.042) 0.1%. This very low rate was achieved via the low endemic aminoglycoside resistance among contemporary enteric bacilli and the enhanced interactions of the neomycin and polymyxin components of TAO.

Table 3. MIC result distribution by year (1997-2002) for topical antimicrobial agents against 159 isolates of *S. aureus* non-susceptible to gentamicin.

Year (no. isolates)	Antimicrobial agent	Cumulative % inhibited at MIC (µg/ml or Iunits/ml) of:[a] ≤4.9	6.25	9.8	12.5	20	25	39	50	78	100	157	313	≥400
1997 (32)	Neomycin	41	-	47	-	56	-	81	-	91	-	94	94	-
	Polymyxin B	0	-	0	-	0	-	0	-	53	-	97	100	-
	Bacitracin	-	0	-	3	-	19	-	88	-	94	-	-	100
	TAO[c]	38	-	38	-	41	-	78	-	97	-	100	100	-
1998 (26)	Neomycin	31	-	39	-	58	-	81	-	96	-	96	96	-
	Polymyxin B	0	-	4	-	4	-	8	-	50	-	100	100	-
	Bacitracin	-	4	-	12	-	31	-	92	-	100	-	-	100
	TAO	31	-	31	-	42	-	81	-	100	-	100	100	-
1999 (28)	Neomycin	14	-	18	-	46	-	75	-	96	-	96	100	-
	Polymyxin B	0	-	0	-	4	-	4	-	43	-	93	100	-
	Bacitracin	-	4	-	7	-	11	-	86	-	86	-	-	100
	TAO	11	-	11	-	21	-	64	-	96	-	100	100	-
2000 (25)	Neomycin	20	-	32	-	52	-	84	-	96	-	96	100	-
	Polymyxin B	0	-	0	-	0	-	0	-	68	-	100	100	-
	Bacitracin	-	0	-	0	-	16	-	88	-	88	-	-	100
	TAO	24	-	24	-	32	-	80	-	100	-	100	100	-
2001 (26)	Neomycin	27	-	27	-	54	-	77	-	85	-	89	96	-
	Polymyxin B	0	-	0	-	0	-	0	-	62	-	96	100	-
	Bacitracin	-	0	-	4	-	15	-	77	-	85	-	-	100
	TAO	27	-	27	-	31	-	65	-	100	-	100	100	-
2002 (22)	Neomycin	32	-	55	-	55	-	73	-	91	-	100	100	-
	Polymyxin B	0	-	0	-	0	-	0	-	9	-	82	100	-
	Bacitracin	-	9	-	9	-	18	-	68	-	73	-	-	100
	TAO	32	-	46	-	46	-	68	-	100	-	100	100	-
All years (159)	Neomycin	28	-	36	-	52	-	79	-	93	-	95	98	-
	Polymyxin B	0	-	51	-	1	-	2	-	48	-	95	100	-
	Bacitracin	-	3	-	6	-	18	-	81	-	88	-	-	100
	TAO	27	-	29	-	35	-	73	-	99	-	100	100	-

a. Neomycin MIC results in µg/ml, polymyxin B and bacitracin in units/ml.
b. - = dilution concentration not tested.
c. TAO (triple antibiotic ointment), neomycin, polymyxin B and bacitracin in a mixture of 5,000 mg neomycin sulfate (3.5 mg of neomycin base), 5,000 Iunits of polymyxin B and 400 Iunits of bacitracin/gm shown as MIC of the neomycin component.

- In Phase III (Table 5), 300 clinical strains from medical centers in Australia (year 2002 - 2003) were tested by *S. aureus* strains resistant to oxacillin (MIC, > 2 µg/ml and/or *mecA*-positive) were observed to be slightly less susceptible to TAO than oxacillin-susceptible strains. The best single TAO component versus *S. aureus* was neomycin (85.0 - 96.0% susceptible), but TAO showed enhanced inhibition and complete coverage at the 1:100 dilution breakpoint (≤ 39 µg/ml). Mupirocin resistance including high-level patterns were detected and the susceptibility rates ranged from 95.0% for oxacillin-resistant strains to 99.0% for oxacillin-susceptible *S. aureus*.
- Across all 300 strains isolated from the Australian AGARS Program, TAO exhibited excellent potency and spectrum with enhanced (synergy) activity in combination. When using the proposed 1:100 dilution of the formulation concentration as the breakpoint for susceptibility (≤ 39 µg/ml; 27 µg/ml neomycin base), we observed that only two oxacillin-resistant *S. aureus* from Australia were not killed (0.7% of tested isolates).

Table 4. Distribution of gentamicin resistance rates among four (4) major pathogen groups as monitored by the SENTRY Antimicrobial Surveillance Program (USA, 1997-2003).

Year	% resistance by year *S. aureus*	CoNS	*E. coli*	*P. aeruginosa*
1997	11.1	32.8	2.9	11.8
1998	11.7	30.6	2.4	8.8
1999	11.1	27.1	2.9	9.1
2000	9.8	27.8	2.7	11.3
2001	8.6	27.8	3.2	9.6
2002	6.4	22.6	4.2	8.9
2003	4.4	18.7	4.7	7.1
All (no.)	9.2 (20,319)	27.6 (6,061)	3.2 (12,797)	9.8 (6,632)

Table 5. Antimicrobial activity of triple antibiotic ointment (TAO), its components and seven comparison agents tested against endemic Gram-positive and -negative pathogens isolated from patients in Australia (300 strains).

Organism (no. tested)	Antimicrobial agent	MIC (µg/ml or Iu/ml) 50%	MIC (µg/ml or Iu/ml) 90%	% Susceptible[a]
S. aureus				
oxacillin-susceptible (100)	TAO[b]	2.4	2.4	100.0(100.0)
	Neomycin	≤1.2	≤1.2	96.0
	Polymyxin B	157	157	-
	Bacitracin	25	50	0.0
	Mupirocin	≤0.5	≤0.5	99.0
	Fusidic Acid	≤1	8	88.0
	Gentamicin	≤0.5	≤0.5	96.0
oxacillin-resistant (100)	TAO	≤1.2	9.8	94.0(98.0)
	Neomycin	≤1.2	39	85.0
	Polymyxin B	157	157	-
	Bacitracin	25	50	1.0
	Mupirocin	≤0.5	≤0.5	95.0
	Fusidic Acid	≤1	8	81.0
	Gentamicin	≤0.5	>8	83.0
Coagulase-neg. staphylococci				
oxacillin-susceptible (10)	TAO	≤1.2	≤1.2	100.0(100.0)
	Neomycin	≤1.2	≤1.2	100.0
	Polymyxin B	39	78	-
	Bacitracin	50	50	0.0
	Mupirocin	≤0.5	≤0.5	100.0
	Fusidic Acid	≤1	≤1	100.0
	Gentamicin	≤0.5	≤0.5	90.0
oxacillin-resistant (30)	TAO	≤1.2	9.8	100.0(100.0)
	Neomycin	≤1.2	4.9	100.0
	Polymyxin B	39	157	-
	Bacitracin	50	50	0.0
	Mupirocin	≤0.5	≤0.5	93.3
	Fusidic Acid	≤1	32	66.7
	Gentamicin	8	>8	33.3
Enterobacteriaceae (40)	TAO	≤1.2	2.4	97.5(100.0)
	Neomycin	≤1.2	2.4	97.5
	Polymyxin B	≤1.2	2.4	94.4
	Bacitracin	>400	>400	-
	Mupirocin	128	256	-
	Fusidic Acid	>32	>32	-
	Gentamicin	≤0.5	1	100.0
P. aeruginosa (20)	TAO	2.4	4.9	100.0(100.0)
	Neomycin	9.8	9.8	95.0
	Polymyxin B	2.4	2.4	90.0
	Bacitracin	>400	>400	-
	Mupirocin	>1024	>1024	-
	Fusidic Acid	>32	>32	-
	Gentamicin	1	2	95.0

a. Susceptibility criteria of the NCCLS, where available. Breakpoints for TAO (breakpoint of the most active component; ≤ 1:100 dilution in parenthesis), neomycin (≤ 10 µg/ml), polymyxin (≤ 2 Iu/ml), bacitracin (≤ 2 Iu/ml), and fusidic acid (≤ 2 µg/ml) were applied for comparison purposes only.
b. TAO = triple antibiotic ointment diluted (6oz.) from the commercial product mixture of 5000/5000/400 µg/ml or international units/ml. Only the neomycin sulfate component is listed as the MIC.

CONCLUSIONS

- The Phase I USA results indicated that aminoglycoside resistance patterns differ significantly and commonly tested drugs in this class (amikacin, gentamicin, tobramycin) can not act as surrogate markers to assess increasing resistance to the TAO component, neomycin.
- Phase II results again illustrated that TAO resistance was rare in the USA, most common among gentamicin-resistant isolates. Current trends in the frequency of the at-risk gentamicin-resistant populations of *S. aureus*, CoNS, Enterobacteriaceae and *P. aeruginosa* indicate a decline of significance in the USA. This illustrates that TAO resistance remains low or possibly decreasing and that its use has not adversely selected for resistance to parenteral aminoglycosides. In contrast, mupirocin-resistant staphylococci continue to evolve.
- The Australian organism sample from a pan-Australia surveillance effort showed high levels of TAO susceptibility among staphylococci (98.0 - 100.0%), Enterobacteriaceae (100.0%) and *P. aeruginosa* (100.0%). These rates were comparable to those in the USA.
- No evidence of advancing TAO resistance or its components could be detected, nor adverse interactions between TAO components (antagonism) that would compromise the spectrum of activity. After several decades of OTC use in the USA and worldwide, this commonly used topical agent had sustained activity and spectrum against those pathogens associated with community-acquired, as well as, nosocomial cutaneous infections.

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