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Peroxotitanate- and monosodium metal-titanate compounds as inhibitors of bacterial growth

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Abstract: Sodium titanates are ion-exchange materials that effectively bind a variety of metal ions over a wide pH range. Sodium titanates alone have no known adverse biological effects but metal-exchanged titanates (or metal titanates) can deliver metal ions to mammalian cells to alter cell processes *in vitro*. In this work, we test a hypothesis that metal-titanate compounds inhibit bacterial growth; demonstration of this principle is one prerequisite to developing metal-based, titanate-delivered antibacterial agents. Focusing initially on oral diseases, we exposed five species of oral bacteria to titanates for 24 h, with or without loading of Au(III), Pd(II), Pt(II), and Pt(IV), and measuring bacterial growth in planktonic assays through increases in optical density. In each experiment, bacterial growth was compared with control cultures of titanates or bacteria alone. We observed no suppression of bacterial growth by the sodium titanates alone, but significant ($p < 0.05$, two-sided *t*-tests) suppression was observed with metal-titanate compounds, particularly Au(III)-titanates, but with other metal titanates as well. Growth inhibition ranged from 15 to 100% depending on the metal ion and bacterial species involved. Furthermore, in specific cases, the titanates inhibited bacterial growth 5- to 375-fold *versus* metal ions alone, suggesting that titanates enhanced metal–bacteria interactions. This work supports further development of metal titanates as a novel class of antibacterials. © 2011 Wiley Periodicals, Inc.* J Biomed Mater Res Part A: 97A: 348–354, 2011.

Key Words: metal ions, titanate, periodontal disease, caries, biodelivery, metal-based drugs, antibiotics

INTRODUCTION

Sodium titanates are inorganic ion-exchangers with affinity for a variety of metal ions including strontium, actinides, and noble metals such as gold, palladium, and platinum.[1,2] One of the titanate family of materials, monosodium titanate (MST), was developed as a sorbent for removing radioactive components from high-level waste solutions produced during the reprocessing of nuclear materials.[3] A peroxo derivative, referred to as amorphous peroxotitanate (APT), also exhibits high affinity for metal ions in aqueous solutions.[3] Recent literature has reported that metal-titanate compounds deliver ions of gold, palladium, or platinum to mammalian cells; these studies suggest that metal-based drugs for the treatment of inflammatory or neoplastic diseases might be plausible.[2,3] In these applications, the solid-phase titanate could retain a toxic metal-based drug within a tissue or compartment, thereby limiting systemic toxicity and sustaining drug delivery at the treatment site.

Both MST and APT form occur as spherically shaped particles 1–10 μm in diameter.[4] MST solids exhibit a bright white color, whereas the APT solids are bright yellow indicative of the presence of the peroxotitanate species. Both materials appear to deliver metal ions to mammalian cells, and by themselves, both have no published adverse effects on monocyte or fibroblast metabolism.[1,2,5] The APT material has been reported to have some ability to alter secretion of cytokines from activated monocytes.[5]

In this study, we sought to extend previous work to bacteria, first evaluating the effect of MST or APT alone on the growth of oral bacteria, then assessing the effects of metal-titanate compounds. Our initial focus on oral bacteria was based on potential utility of a solid-phase antibacterial agent to treat caries, periodontal disease, or endodontic infection. For example, titanates could be incorporated into dental restorative materials to limit bacterially mediated occurrence or recurrence of oral disease. A solid phase antibacterial would be useful beyond dentistry however, on the skin or in tissue compartments with poor perfusion. As with mammalian cells, the use of the metal-titanate compound has a potential advantage that by limiting systemic distribution, the relatively toxic nature of metal ions might be avoided, and therapeutic effects might be focused and sustained in a particular tissue. Thus, our purpose in this work was to test a hypothesis that metal-titanate compounds inhibit bacterial growth.

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TABLE I. Bacteria Used in This Study

Bacteria (Code)	Full Name	Source (ATCC)[a]	Gram Staining	Role in Oral Disease	Culture Condition
Aa	*Aggregatibacter actinomycetemcomitans*	25586	negative	aggressive periodontal pathogen	anaerobic (85%N_2, 10%H_2, 5% CO_2)
An	*Actinomyces naeslundii*	19039	positive	root caries, early childhood caries	N_2-free, O_2 depleted
Fn	*Fusobacterium nucleatum*	43718	negative	bridging organism between pathogens and nonpathogens	anaerobic (85%N_2, 10%H_2, 5% CO_2)
Pg	*Porphyromonas gingivalis*	33277	negative	periodontal pathogen	anaerobic (85%N_2, 10%H_2, 5% CO_2)
Pi	*Prevotella intermedia*	25611	negative	gingival and periodontal pathogen	anaerobic (85%N_2, 10%H_2, 5% CO_2)

[a] American Type Culture Collection number.

METHODS AND MATERIALS

Bacterial cultures

Oral bacteria were the focus of this study; these species are etiologic agents in periodontal disease, gingivitis, or caries that might be treated with a solid-phase metal-titanate compound (Table I). *Porphyromonas gingivalis* (*Pg*, American Type Culture Collection no. 33277) was cultured under anaerobic conditions (85% N_2, 10% H_2, 5% CO_2) at 37°C in trypticase soy broth (BBL, Sparks MD) supplemented with 1 g of yeast extract, 5 mg of hemin, and 1 mg of menadione per liter. *Fusobacterium nucleatum* (*Fn*, ATCC no. 43718) and *Aggregatibacter actinomycetemcomitans* (*Aa*, ATCC no. 25586) were cultured in Todd-Hewitt broth supplemented with 10 g of yeast extract/L at 37°C under the same anaerobic conditions. *Prevotella intermedia* (*Pi*, ATCC no. 25611) was cultured under anaerobic conditions in trypticase soy broth supplemented wit 0.5% yeast extract, 0.05% cysteine, 0.5 mg/mL hemin, and 2 μg/mL menadione, and *Actinomyces naeslundii* (*An*, ATCC no. 19039) was cultured in an oxygen-depleted, N_2-free atmosphere at 37°C in BBL Actinomyces broth. All bacteria were cultured from frozen stocks expanded from ATCC cultures; the absence of contamination was verified at each thaw via Gram stain. All bacteria were grown 24 h to mid-log phase before inoculating experimental cultures.

Preparation of metal-titanate compounds

Gold, palladium, or platinum were the focus of this study because they have a history of successful use in dentistry and medicine,[6–8] and previous studies have shown that they bind the titanates.[9] APT and MST particles were loaded with Au(III), Pd(II), Pt(II), or Pt(IV) by combining 0.25 g of the sodium titanate (APT or MST) suspended in 1.4 g of water (pH = 6.9) with 10 mL of phosphate-buffered saline (PBS, pH 7.4) containing the desired metal ion. Because we wanted to maximize metal loading to the particles, the concentrations of metals in the loading solutions were maximized (limited by solubility in PBS, Table II) to provide the greatest loading driving force. After mixing at ambient temperature for 48 h, the metal-exchanged titanates were separated from the parent solutions by centrifugation (RCF = 1200×*g*, 3 min), after which the solid phases were rinsed quickly with six portions of chilled PBS (4°C; pH = 7.4), then stored as moist solids with water contents of ~75 wt % (but determined to 0.1 wt % accuracy for each preparation). Maintaining moist solids greatly increased the ability to resuspend the particles in solution during bacteria-culture experiments.

The amount of metal loaded onto the titanates was determined by quantitatively measuring the difference in metal concentrations of the metal loading solutions before and after contact with the titanate solids using inductively coupled plasma emission spectroscopy. Metal loading was calculated as the number of grams of metal per gram of MST or APT (Table II).

Exposure of bacteria to metal ions, titanates, and metal-titanate compounds

One hundred microliters of the initial culture was plated in 96-well plate format, and the number of bacterial cells present in a given volume of culture was determined by correlating OD reading of bacterial culture at 595 nm to the number of cells present. This method is based on a previously established system of how OD reading converts to colony forming units for each bacterial species.[10,11] Before exposing bacteria to metal-titanate compounds, appropriate dilutions of each bacterial species were made so that metal-titanate compounds are consistently exposed to 3.56E9 bacteria for all species tested. This strategy assured the same cell to titanate particle ratio, allowed repeatability, and allowed log growth phase throughout the 24 h time when bacteria were exposed to the titanates. A 24 h-incubation time with titanates was chosen to maximize the exposure to the titanates without risking culture deterioration from overgrowth. Typical initial OD readings were 0.05; typical final OD readings were 0.4 or higher.

For metal ions alone, 5 μL of a concentrated stock solution of the respective metal salt were added to 95 μL of the bacterial cultures (n = 8 per condition). For MST and APT experiments, 5 μL/well of a stock titanate solution was added to provide a final titanate concentration of 0–25 μg/mL (n = 8). The cultures were mixed to ensure contact between the titanates and the bacteria. MST and APT suspensions were thoroughly mixed before addition to ensure

TABLE II. Metal Compounds and Titanate Loading

Metal Ion	Source Compound	Supplier	Titanate Loading Concentration (μ*M*)	Loaded Concentration (g metal/g APT)	Loaded Concentration (g metal/g MST)
Au(III)	$HAuCl_4 \cdot 3H_20$	Sigma-Aldrich	13,251	0.0852	0.0789
Pd(II)	$PdCl_2$	Johnson Mathey, Inc.	13,240	0.0539	0.0557
Pt(II)	$PtCl_2$	Johnson Mathey, Inc.	114	0.00086	0.00084
Pt(IV)	$PtCl_4$	Johnson Mathey, Inc.	14,912	0.0155	0.0686

accurate transfer of the particles. Concentrations of titanate greater than 25 μg/mL were avoided to prevent OD from the titanate particles from masking bacterial growth (also assessed by changes in OD). Titanate-bacterial cultures were incubated for 24 h under the conditions appropriate for each type of bacterium. After 24 h, the cultures were thoroughly mixed before reading the OD. Control cultures for experiments included cultures of media alone (no titanates or bacteria), titanates in media (no bacteria), and bacteria alone (no titanates). Additional controls for bacterial growth inhibition included bacteria with erythromycin (100 μg/mL, no titanates), which was an effective antibiotic against all oral pathogens used in this study. Although all the anaerobic species tested remain viable for up to 24 h in aerobic environments, exposure of anaerobes to aerobic conditions was minimized and experiments were carried out under anaerobic conditions. Bacteria-only controls verified the growth potential under these experimental conditions. All experiments were repeated in triplicate to assure reproducibility.

The initial and final mean and standard deviation OD readings were calculated and plotted as a function of concentration. The titanate-only controls were also plotted as a baseline. Conditions with titanates alone were compared (two-sided Student's *t*-tests, $\alpha = 0.05$) with cultures without added titanates. Conditions with titanates with or without loaded metal were compared to determine significant effects of added metal on bacterial growth.

The delivery potential of metal ion from the metal-titanate compounds to bacteria was determined by calculating the total metal mass complexed with the titanates at each titanate particle concentration (Table II), then calculating the maximum concentration of metal ion that could be delivered by the metal-titanate compound into the culture. This potential concentration was compared with concentrations of metal ions alone that inhibited growth. In this manner, we were able to estimate if the metal-titanate compounds enhanced the ability of metal ions to inhibit growth.

RESULTS

Antibacterial effects of metal ions alone

Metal ions differed in their ability to suppress planktonic bacterial growth of the species in Table I. For example, *An* growth (Fig. 1) was not suppressed by Pt(IV) concentrations $\leq$ 750 μ*M*, was suppressed ~30% by Pd(II) > 1000 μ*M*, and was completely suppressed by Au(III) > 10 μ*M*. We could not measure the effects of Pt(II) alone because of limited aqueous solubility of the chloride salt (Table II); maximum concentrations of the other metal ions were limited by the aqueous solubility of their salts as well. The maximum concentrations achievable in the bacterial cultures were 5–10% of the stock metal ion solutions in Table I to maintain the osmolarity, pH, and nutrition of the culture medium when the metal ions were added. A summary of the effects of metal ions alone is listed in Table III.

In general, the bacteria in Table I were equally susceptible to the metal ions alone. Among the metal ions (excepting Pt(II)), Au(III) was the most potent, inhibiting growth of *Aa*, *An*, *Fn*, and *Pg* by at least 50% above 10–50 μ*M* (Table III). Yet concentrations of Au(III) $\leq$ 1500 μ*M* had no observable effect on *Pi*, which demonstrated the specificity of these effects on bacterial species.

Antibacterial effects of titanates (MST and APT) alone

MST and APT in their sodium forms did not inhibit growth of any of the bacterial species as shown in Table I and Figures 2 and 3. Growth of the bacterial control cultures varied somewhat by species although approximately equal starting numbers were used (Figs. 2 and 3); *Pg* was the slowest growing of the bacteria tested (Table I). For all species, the OD values of bacteria alone at 24 h were sufficient (0.3–1.2) to detect any inhibition by the titanates. Controls for medium alone (Med) and bacterial with erythromycin (Bac-

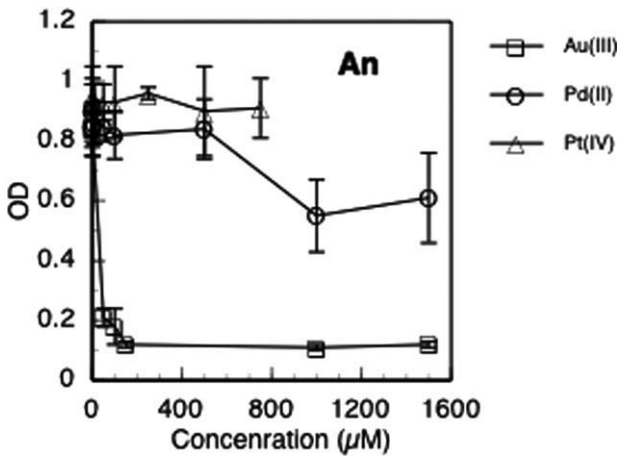

FIGURE 1. Example of a dose response curve of bacterial growth to metals alone, using An *Actinomyces naeslundii* (*An*) as an example. The inoculum of *An* with an optical density (OD) of ~ 0.05 was plated into 96 well format, after which 5 μL of the metal ion solution was added. After 24 h of incubation, the OD was assessed to estimate bacterial growth. From plots such as this one, concentrations of metal ions were identified that suppressed bacterial growth by 50%; these values appear in Table III. Maximum concentrations for each metal ion were limited by solubility of the chloride salt (Table I). Note that Pt(II) was not tested because aqueous solutions of adequate concentration were not possible because of limited solubility of $PtCl_2$. Error bars indicate one standard deviation ($n = 8$).

TABLE III. Suppression of Bacterial Growth by Metal Ions and Metal-Titanate Compounds [Color table can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

			MST-Metal Compound				APT-Metal Compound			
Bacteria	Metal Ion	TC50 Conc., Metal Ion Alone (μ*M*)[a]	Max. Bacterial Growth Suppression (%)	Inhibitory Conc. (μg/mL)[b]	Max. Metal Ion Delivery (μ*M*)[c]	Titanate Enhancement of Metal Suppression (fold)[d]	Max. Bacterial Growth Suppression (%)	Inhibitory Conc. (μg/mL)[b]	Max. Metal Ion Delivery (μ*M*)[c]	Titanate Enhancement of Metal Suppression (fold)[d]
Aa										
	Au(III)	10	100[e]	5[e]	2	5	10	25	–	–
	Pd(II)	1500	0	–	–	–	25	10	–	–
	Pt(II)	ND[f]	0	–	–	–	60[e]	25[e]	0.11	–
	Pt(IV)	>1500	20	25	–	–	30[e]	25[e]	–	–
An										
	Au(III)	50	80[e]	20[e]	8	6	0	–	–	–
	Pd(II)	>1500	10	25	–	–	10[e]	10[e]	–	–
	Pt(II)	ND	0	–	–	–	0	–	–	–
	Pt(IV)	>750	0	–	–	–	0	–	–	–
Fn										
	Au(III)	10	100[e]	5[e]	2	5	40	25	–	–
	Pd(II)	1000	0	–	–	–	30	10	–	–
	Pt(II)	ND	0	–	–	–	25	25	–	–
	Pt(IV)	750	0	–	–	–	35	10	–	–
Pg										
	Au(III)	1	100[e]	1[e]	0.4	25	100[e]	25[e]	11	0.9
	Pd(II)	>1500	45[e]	25[e]	–	–	100[e]	25[e]	13	>190
	Pt(II)	ND	20	25	–	–	100[e]	25[e]	–	–
	Pt(IV)	>750	40[e]	25[e]	–	–	100[e]	25[e]	2	>375
Pi										
	Au(III)	>1500	30[e]	25[e]	–	–	30[e]	25[e]		–
	Pd(II)	1500	60[e]	25[e]	13	115	15[e]	25[e]		–
	Pt(II)	ND	30[e]	25[e]	–	–	30[e]	10[e]		–
	Pt(IV)	>750	60[e]	10[e]	3.5	>210	60[e]	25[e]	2	>375

Red cells indicate that bacterial growth suppression was ≥50% *versus* titanate controls. Green indicates that titanates enhanced metal interactions with bacteria.
[a] Concentration that suppressed bacterial growth by ≥50% *versus* control.
[b] Concentration of loaded metal-titanate compound that suppressed bacterial growth maximally relative to titanate-only controls.
[c] Assuming that all of the loaded metal was delivered to the bacteria from the inhibitory metal-titanate concentration.
[d] TC50 concentration of ion alone to divided by the maximal delivered concentration when titanate compound suppressed bacterial growth by ≥50% *versus* controls.
[e] Statistical significance *versus* titanate-only controls (paired *t*-test, $\alpha = 0.05$).
[f] Not determined. Concentration of Pt(II) solution not high enough for cell-culture experiments at high Pt(II) concentrations. –Not calculated because conditions for accurate calculations not met or data not available.

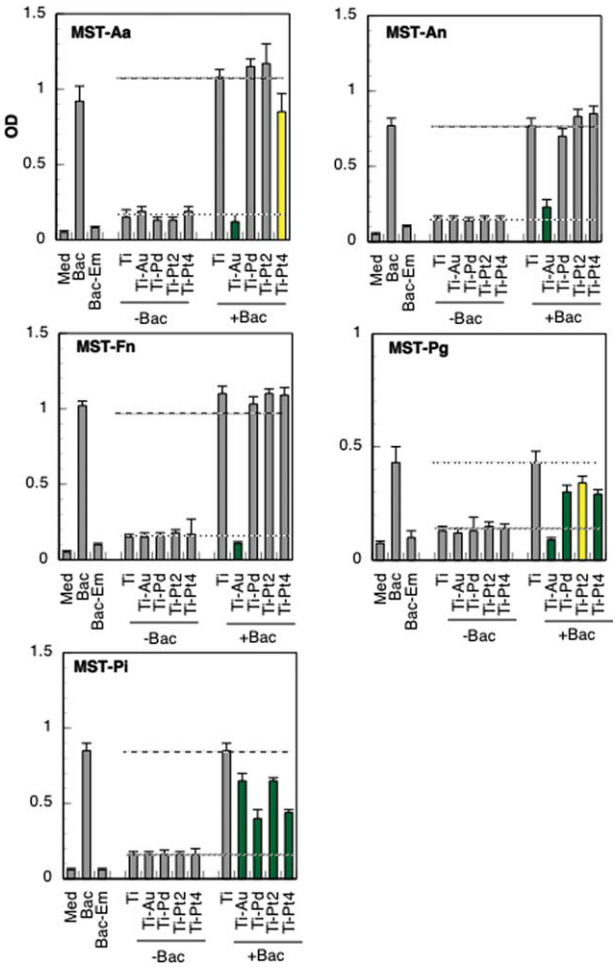

FIGURE 2. Effect of MST loaded with Au(III), Pd(II), Pt(II), or Pt(IV) on growth of the bacteria listed in Table II. In each plot, the controls for medium alone (Med), bacteria alone (Bac), or bacteria treated with erythromycin as a growth-inhibiting control (100 μg/mL, Bac-Em) are shown. Controls without bacteria for titanates alone (Ti) or titanates loaded with the metal ions (Ti-Au, Ti-Pd, Ti-Pt2, Ti-Pt4) are shown, and the horizontal dashed line indicates the average background optical density (OD) from the native titanate solution at 20 μg/mL. At the right of each plot, the titanate control with bacteria (Ti) and other metal-loaded titanates are shown. The upper horizontal dashed line is the OD of bacterial growth with native titanate. Error bars indicate one standard deviation ($n = 9$). Bars in green were significantly lower than titanate-only controls (two-sided Student's *t*-tests, $\alpha = 0.05$). Yellow bars show had effect on bacterial growth, but were not significantly different from the titanate controls. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

Em) behaved as expected (Figs. 2 and 3). Controls with titanates (no bacteria) had ODs of 0.1–0.15; thus, the OD of the titanates did not obscure growth in experiments measuring the effects of loaded or unloaded titanates on bacterial growth.

Antibacterial effects of metal-MST or metal-APT compounds

The APT or MST loaded with Au(III), Pd(II), Pt(IV), or Pt(II) inhibited growth of some, but not all bacterial species. Bacterial growth suppression varied by the metal ion, the type of titanate, and the species (Figs. 2 and 3). In general, *Pi* and *Pg* growth was most susceptible to the metal titanates, and *An* was the least susceptible. Among the metal ions tested, Au(III)-titanates most often inhibited growth. However, there were many exceptions and variations. The degree of growth inhibition also varied significantly. As with the titanates alone, control cultures with the metal-titanate compounds added (without bacteria) had OD values of 0.1–0.2. OD among the different metal-titanate compounds and titanates alone did not vary, and the window of OD between maximal bacterial growth and the OD of the metal-titanate compounds ranged from 0.3 to 0.9, providing a sufficient

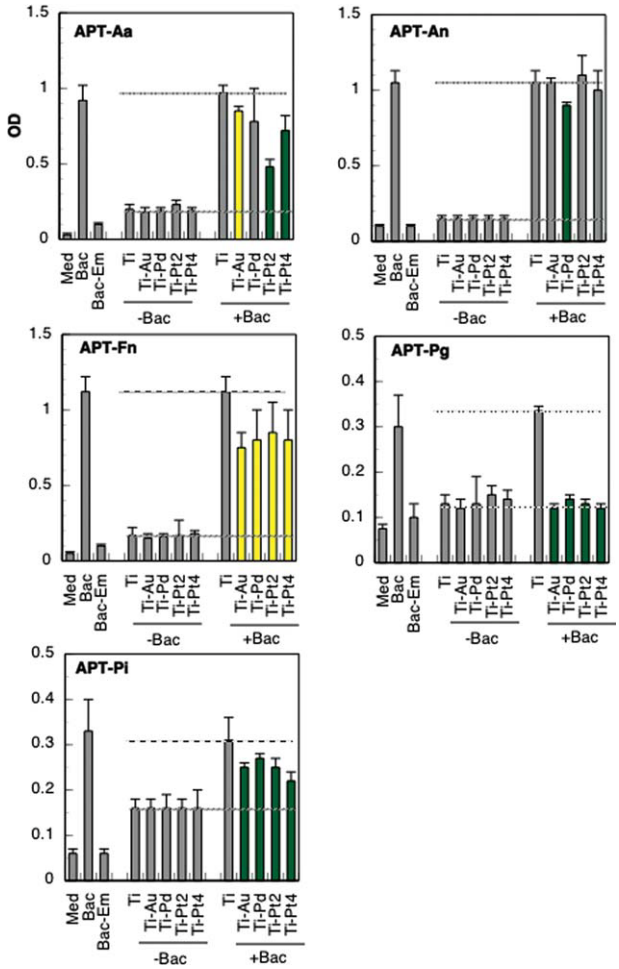

FIGURE 3. Effect of APT loaded with Au(III), Pd(II), Pt(II), or Pt(IV) on growth of the bacteria listed in Table II. In each plot, the controls for medium alone (Med), bacteria alone (Bac), or bacteria treated with erythromycin as a growth-inhibiting control (100 μg/mL, Bac-Em) are shown. Controls without bacteria for titanates alone (Ti) or titanates loaded with the metal ions (Ti-Au, Ti-Pd, Ti-Pt2, Ti-Pt4) are shown, and the horizontal dashed line indicates the average background optical density (OD) from the native titanate solution at 20 μg/mL. At the right of each plot, the titanate control with bacteria (Ti) and other metal-loaded titanates are shown. The upper horizontal dashed line is the OD of bacterial growth with native titanate. Error bars indicate one standard deviation ($n = 9$). Bars in green were significantly lower than titanate-only controls (two-sided Student's *t*-tests, $\alpha = 0.05$). Yellow bars show had effect on bacterial growth, but were not significantly different from the titanate controls. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

signal range to see any growth inhibition caused by the metal-titanate compounds. Variation among replicates in these tests were generally 10–15%, but sometimes greater (e.g., APT-*Fn*, Fig. 3).

We were interested in assessing if titanates could enhance inhibition of bacterial growth by metal ions. Analysis of this enhancement was restricted to conditions where the metal-titanate compounds inhibited bacterial growth by $\geq$50% (Table III). For example, 750 μ*M* of Pt(IV) alone did not inhibit *Pi* growth by 50%, yet the Pt(IV)-APT compound, with a maximum potential delivery of only 2 μ*M*, inhibited *Pi* growth by 60%. Because APT by itself did not suppress *Pi* growth, APT appeared to have increased the ability of Pt(IV) to inhibit growth by over 375-fold. Such "enhancement" was most common with *Pg* and *Pi*. Enhanced effects of Au(III) was common but less (0.9- to 25-fold). Pt(II) was excluded from this analysis because Pt(II) could not be tested by itself in bacterial culture (see previous discussion).

DISCUSSION

The current results show unequivocally that metal-titanate compounds inhibit planktonic bacterial growth and that titanates enhance the ability of metal ions to inhibit growth, depending on specific experimental conditions. In spite of these findings, there were few patterns to these effects. Au(III)-MST was the most effective inhibitor of the metal titanates, perhaps reflecting the potency of Au(III) alone (Fig. 1, Table III) and the ability to load more Au(III) onto the MST (Table II). On the other hand, the enhancement of Au(III)-induced inhibition by MST was not as large (5- to 25-fold) as for other elements such as Pt(IV) (over 375-fold in some cases). Given the current data, which are relatively limited, it appears that further development of this area will need to focus on specific bacteria and specific metal ions. Such specificity may ultimately be a therapeutic asset.

How metal-titanate compounds inhibit bacterial growth is not known. However, given the relative size of the titanates (1–10 μm, Ref. 1) and most bacteria ($<$0.2 μm), it seems unlikely that bacteria ingest the titanates. The relatively large size of the titanates, current data, and previous research suggest that inhibition is more likely to occur via some direct contact mechanism; many bacteria might bind with one titanate particle.[2,5] Inhibition by release of metal ions into the medium seems a remote possibility because the metal-titanate compounds are relatively stable and do not release appreciable metal ions over the 24-h test.[5] Furthermore, the maximum potential concentrations of metal ions from the metal-titanate compounds, even if all metal mass was released, were far below inhibitory doses (Table III). The direct contact mechanism therefore seems likely, even more so than with mammalian cells, where cellular "ingestion" of the titanate particles is plausible.[2,5] The direct contact inhibition hypothesis, if true, suggests that the metal-titanate compounds could be used in solid-phase disinfection schemes.

Pd(II) and Pt(IV) ions are more potent inhibitors of mammalian cells than bacteria. The TC50 concentrations for these ions against the bacteria in Table I were $>$750–1500 μ*M* (Table III), yet Pd(II) inhibits mammalian cells at 100–300 μ*M* and Pt(IV) at 25 μ*M* based on previous reports.[2,12] This differential is not encouraging for metal ions for systemic treatment of bacterial infections in human tissues. Yet the metal-titanate compounds inhibited bacterial growth (e.g., *Pi* and *Pg*) with far lower metal ion loads (2–13 μ*M*; Table III). Coupled with the solid phase nature of the titanates to limit systemic distribution, the titanates may provide a favorable shift of the therapeutic index for these metal ions as antibacterials. For Au(III), these factors were more favorable because the inhibitory concentration for bacteria (often 10–50 μ*M*, Table III) was below that for several types of mammalian cells (60–115 μ*M*, Ref. 10), and titanates inhibited bacteria at effective doses of 0.4–11 μ*M* (Table III). For Pt(II), the solubility of the ion alone was so low that its toxicity could not even be tested, yet Pt(II)-APT was an effective inhibitor of *Aa* and *Pg* growth at doses of only 0.11 μ*M* (Table III). All of these data suggest a therapeutic advantage of the metal-titanate compounds as antibacterials.

If safe and effective metal-titanate bacterial inhibitors could be developed, several therapeutic roles come to mind. Intraorally, metal titanates could be used as an adjunct treatment at the base of carious lesions, in residual canals postendodontic therapy, or incorporated into restorative materials to limit recurrent caries at the margins of restorations. Titanates could be used in any poorly perfused area to inhibit bacterial growth where the solid phase would be advantageous; one example would be in osteomyelitis. On the skin, titanates might be used in bandages to limit bacterial growth in wounds or ingress into wounds.

In spite of potential for therapy, significant barriers remain to clinical utility. The current results do not reveal if bacterial growth inhibition results from bacterial killing. The compounds may only suppress growth. Current results are limited to planktonic assays, yet most tissue infections occur in an organized biofilm. Current results are limited by relatively low loading levels of the titanates (Table I); other particle sizes or loading strategies might boost the potential to deliver metal ions or change mechanisms of inhibition.

In conclusion, the current results show that by themselves, sodium titanates (MST or APT) have no effect on planktonic growth of several oral bacterial species but that inhibition of growth is possible when Au(III), Pd(II), Pt(II), or Pt(IV) are loaded onto the MST or APT. Furthermore, the current results support a facilitative role for the titanates in metal-mediated inhibition of bacterial growth in some cases.

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