Metabolism of Bismuth Subsalicylate and Intracellular Accumulation of Bismuth by *Fusarium* sp. Strain BI

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Enrichment cultures were conducted using bismuth subsalicylate as the sole source of carbon and activated sludge as the inoculum. A pure culture was obtained and identified as a *Fusarium* sp. based on spore morphology and partial sequences of 18S rRNA, translation elongation factor 1-α, and β-tubulin genes. The isolate, named *Fusarium* sp. strain BI, grew to equivalent densities when using salicylate or bismuth subsalicylate as carbon sources. Bismuth nitrate at concentrations of up to 200 μM did not limit growth of this organism on glucose. The concentration of soluble bismuth in suspensions of bismuth subsalicylate decreased during growth of *Fusarium* sp. strain BI. Transmission electron microscopy and energy-dispersive spectroscopy revealed that the accumulated bismuth was localized in phosphorus-rich granules distributed in the cytoplasm and vacuoles. Long-chain polyphosphates were extracted from fresh biomass grown on bismuth subsalicylate, and inductively coupled plasma optical emission spectrometry showed that these fractions also contained high concentrations of bismuth. Enzyme activity assays of crude extracts of *Fusarium* sp. strain BI showed that salicylate hydroxylase and catechol 1,2-dioxygenase were induced during growth on salicylate, indicating that this organism degrades salicylate by conversion of salicylate to catechol, followed by ortho cleavage of the aromatic ring. Catechol 2,3-dioxygenase activity was not detected. *Fusarium* sp. strain BI grew with several other aromatic acids as carbon sources: benzoate, 3-hydroxybenzoate, 4-hydroxybenzoate, gentisate, o-mandelate, l-phenylalanine, l-tyrosine, phenylacetate, 3-hydroxyphenylacetate, 4-hydroxyphenylacetate, and phenylpropionate.

Bismuth subsalicylate is the active ingredient in Pepto-Bismol. It is one of a class of bismuth-containing medicinals used to treat ulcers and other gastrointestinal disorders. The use of bismuth compounds for this purpose dates back to the 18th century (38). The mechanism of action of bismuth subsalicylate and related compounds was not understood for most of the duration of their medicinal usage.

In general, microbial interactions with bismuth salts and organobismuth compounds are not well known, but there are insights largely derived from studies on sensitivity and resistance to bismuth. Bismuth sulfite has been used in growth medium for the selective isolation of *Salmonella* strains from foods by inhibiting other bacteria (46). Organobismuth compounds and salts have been shown to inhibit growth of *Helicobacter pylori* (28), other bacteria implicated in gastrointestinal disorders (27), and some fungi (8, 32).

Even less is known about the metabolic disposition of inorganic bismuth by microbes. Putative bismuth resistance genes were mapped on penicillin resistance plasmids in *Staphylococcus aureus* to regions containing the cadmium/zinc and mercury resistance genes, but no specific genes were correlated with bismuth resistance (35). Bismuth ions induce bacterial cadmium and arsenical/antimonial resistance operons (12, 19) and synthesis of metal binding peptides in yeast (16), but these phenomena have not been specifically linked to a bismuth resistance phenotype. Bacteria exposed to bismuth salts and organobismuth compounds have been shown to accumulate bismuth by unknown mechanisms onto cell surfaces, in cell walls, and in the cytoplasm (26, 33, 42). In anaerobic ecosystems, trimethylbismuth gas effluent has been detected and attributed to microbial action (4). Several bacterial species have been reported to form reflective “bismuth mirrors” when growing around filter disks soaked with bismuth salts on solid media (28, 33). Although bismuth mirrors have been suggested to arise from bismuth reduction, the lack of analytical procedures has left this issue unresolved.

To better understand resistance and metabolic responses to bismuth by microbes, an enrichment culture approach was used to isolate microbes that could grow using bismuth subsalicylate as the sole carbon source. A filamentous fungus identified as a *Fusarium* species was isolated. *Fusarium* sp. strain BI accumulated bismuth intracellularly during growth on bismuth subsalicylate, and the accumulated bismuth was concentrated in phosphorus-rich inclusions in specimens prepared for electron microscopy. The metabolic pathway through which *Fusarium* sp. strain BI degraded bismuth subsalicylate was determined by assaying the activities of known enzymes involved in salicylate catabolism in crude extracts of biomass grown on salicylate and glucose. The ability of *Fusarium* sp. strain BI to grow using a variety of other organic acids as carbon sources was also evaluated.

**MATERIALS AND METHODS**

**Enrichment culture.** The minimal medium used for the enrichment culture consisted of a 0.015 M potassium phosphate buffer (pH 7.0) with salts of essential metals and trace elements added to give the following final concentrations: 5 mM NH$_4$Cl, 80 μM MgSO$_4$, 1.8 μM CaCl$_2$, 80 nM Na$_2$MoO$_4$, 50 nM MnSO$_4$, 20 nM...
Fe(II)SO₄, 10 mM CoSO₄, 10 mM ZnSO₄, 10 mM Fe(III)SO₄, 10 mM Al₂(SO₄)₃, 10 mM NiSO₄, 10 mM CuSO₄, 10 mM H₂BO₃. Vitamins were added to the following final concentrations: 0.15 μM thiamine, 82 mM biontin, 45 mM folic acid, 0.49 μM pyridoxine, and 0.82 μM nicotinamide. A 15 mM suspension of bismuth subsalicylate (Sigma-Aldrich, St. Louis, Mo.) was prepared in 50 ml of minimal medium, inoculated with 1 ml of activated sewage sludge (Morto Waste-water Treatment Plant, St. Paul, Minn.), and incubated at room temperature on a rotary shaker. After 14 days, 5 ml of the initial enrichment culture was transferred to a fresh 15 mM suspension of bismuth subsalicylate. After incubation for 6 days, the final subculture was streaked by adding 5 ml of this culture to another fresh 15 mM suspension of bismuth subsalicylate. After incubation for 6 days, the final subculture was streaked for isolation onto a 0.25× Luria-Bertani (LB) agar plate and incubated at 30°C for 72 h. Different colony types were then isolated as pure cultures on additional 0.25× LB agar plates.

Strain identification. Wet mounts of spores from a 14-day plate culture were examined by light microscopy. To obtain template DNA for PCR amplification and sequencing, a loop of aerial hyphae from a plate culture was added to 50 μl of sterile distilled H₂O (dH₂O) in a 1.7-ml microcentrifuge tube. The tube was placed in a boiling water bath for 10 min and then centrifuged. The supernatant (template DNA) was decanted into a sterile microcentrifuge tube. PCR amplification reaction mixtures had 10 μl of 10X PCR buffer, 10 mM each of deoxyribonucleoside triphosphate, 50 mM MgCl₂, 2 μl of template DNA, 5 μl of Taq DNA polymerase, and MilliQ dH₂O to 100 μl. The same cycling regime was used for each of the primers (21). Amplification was verified by agarose gel electrophoresis. PCR product was purified for sequencing using a QiAquick gel extraction kit (QIAGEN, Valencia, Calif.). Primers S1 and S3 (21) and FF1 and FF0 (45) were used to amplify sections of the 18S rRNA gene, and primers 51F, 511F, and FF700 (45) were used for sequencing. Primers EF-1 and EF-2 (21) were used to amplify a section of the translation elongation factor 1-α gene, and EF-1 was used for sequencing (36). Primers Bt2a and Bt2b (14) were used to amplify and sequence a section of the β-tubulin gene. Sequences were aligned against all DNA sequences deposited in GenBank using BLAST (1).

Photomicroscopy. Photomicrographs were taken with Porra 100T tungsten film (Kodak, Rochester, N.Y.) and an FX-35 (Nikon, Melville, N.Y.) camera mounted on a Zeiss (Thornwood, N.Y.) standard universal microscope.

Assay for total soluble bismuth. Total soluble bismuth in cultures and extracts was determined with an Optima 3000 DV inductively coupled plasma optical emission spectrometer (Perkin Elmer, Boston, Mass.). Suspensions of 1.5 mM bismuth subsalicylate were prepared in 250 ml of minimal medium and incubated on a shaker at 30°C. After 24 h, 10 ml aliquots were removed using a sterile pipette and filtered with sterile 25-mm-diameter mesh 47-mm-diameter nylon membranes (Millipore, Milw., Wisc., U.S.A.) and an FX-35 (Nikon, Melville, N.Y.) camera mounted on a Zeiss (Thornwood, N. Y.) standard universal microscope.

RESULTS AND DISCUSSION

Enrichment culture and strain identification. Growth was evident in the initial enrichment culture after 14 days. After subcultureing the enrichment culture to verify growth on bis-
muth subsalicylate, a filamentous fungus was isolated that was identified as *Fusarium* sp. based on spore type and morphology (Fig. 1). Microconidia, macroconidia, and chlamydospores were all present (Fig. 1A and B). To confirm the genus of the isolate was most similar (1,048 of 1,051 nucleotides [nt]) to corresponding *Fusarium culmorum* strain UPSC 1981 (GenBank accession number AF48073) and an un-cultured ascomycete (GenBank accession number AB074659). Translation elongation factor 1-α gene sequence from the isolate was aligned against sequences in GenBank. 18S rRNA gene sequence from *Fusarium* strain were all present (Fig. 1A and B). To confirm the genus of the isolate, partial sequences of 18S rRNA, translation elongation factor 1-α, and β-tubulin genes from the isolate were aligned against sequences in GenBank. 18S rRNA gene sequence from the isolate was most similar (1,048 of 1,051 nucleotides [nt]) to 18S rRNA gene sequences from *Fusarium culmorum* strain UPSC 1981 (GenBank accession number AF48073) and an un-cultured ascomycete (GenBank accession number AB074659).

Translation elongation factor 1-α gene sequence from the isolate had the highest similarity (656 of 673 nt) to corresponding sequences from *Fusarium solani f. sp. batatas* strains NRRL22402 and NRRL22400 (GenBank accession numbers AF178344 and AF178343, respectively). Sequence from the β-tubulin gene of the isolate was most similar (267 of 290 nt) to β-tubulin gene sequence from *Gibberella zeae* PH-1 (teleomorph of *Fusarium graminearum*) (GenBank accession number XM389706). Due to the varied results from the sequence alignments and lack of a globally accepted *Fusarium* taxonomy (34), identification of the isolate to the species level was not considered possible. The isolate was designated *Fusarium* sp. strain BI.

**Depletion of bismuth from the culture medium and bismuth tolerance.** While organobismuth compounds have been shown to inhibit growth of fusaria (8, 29), mechanisms of bismuth tolerance and toxicity in fusaria and other fungi have not previously been explored in depth. Evaluation of bismuth reduction by *Fusarium* sp. strain BI was hampered by the lack of both a commercially available stable bismuth isotope and a practical assay to distinguish bismuth oxidation states. However, changes in bismuth concentration in the culture medium and cellular localization of bismuth were determined in the present study. ICP-OES was used to monitor the concentration of soluble bismuth during growth of *Fusarium* sp. strain BI in a 1.5 mM bismuth subsalicylate suspension in minimal medium (Fig. 2). Total soluble bismuth in inoculated suspensions decreased by ~0.4 mg/liter (~75% of initial concentration) after 6 days, while total soluble bismuth in the uninoculated control increased by ~0.2 mg/liter (Fig. 2) during the same period. The increase in soluble bismuth in the control is likely due to slow solubilization of bismuth subsalicylate, which is relatively insoluble in aqueous media. Therefore, the net decrease in soluble bismuth during growth of the culture was closer to 0.6 mg/liter.

Independent experiments were conducted to test bismuth tolerance of *Fusarium* sp. strain BI. No discernible difference in biomass production was observed in cultures grown in the presence of 0 to 200 μM bismuth nitrate in minimal medium with glucose as the sole carbon source. Optical density data showed that cultures grown on salicylate reached stationary phase ~24 h sooner than cultures grown on bismuth subsalicylate. However, the cultures achieved equivalent optical densities at stationary phase (data not shown).

Bismuth ions have a high affinity for thiolate ligands and are proposed to be a hazard in the cytoplasmic environment (38). Regulating cytoplasmic levels of free essential and nonessential metal ions is central to fungal metal tolerance (13). Because intracellular bismuth accumulation did not reduce the growth yield of *Fusarium* sp. strain BI, this organism appears to have a mechanism that either maintains low levels of intracellular bismuth or renders bismuth nontoxic inside the cell.

**Localization of accumulated bismuth.** TEM-EDS analysis of ultrathin (60 nm) sections of *Fusarium* sp. strain BI was used to investigate if soluble bismuth depleted from the medium during growth was accumulated by the organism. In cross-sections of hyphal filaments grown on bismuth subsalicylate as a sole carbon source, discrete electron-dense regions were observed in the cytoplasm and central vacuole (Fig. 3A and B). Electron-transparent regions of similar size and shape to the electron-dense regions (Fig. 3A and B) likely represent the locations of bismuth.
electron-dense granules that were torn from or fell out of the sections. EDS analysis of the electron-dense regions revealed the presence of bismuth, phosphorus, calcium, and sometimes also magnesium and/or aluminum (Fig. 3C). Uranium was present (Fig. 3C) because the sections were stained with uranyl acetate; aluminum is a component of the culture medium and could have been accumulated by the organism during growth. The spot size of the beam used for EDS analysis was slightly larger than the diameter of the granules, and material surrounding the granule is included in the spectrum (Fig. 3C). Separate EDS analysis of areas surrounding the electron-dense granules showed that no phosphorus, bismuth, or other metals were present in these regions (data not shown). No electron-dense granules were found located in the cell walls. EDS analysis of electron-dense regions outside the cell wall showed that bismuth was present in higher concentrations and that phosphorus was present in lower concentrations in these regions than in the intracellular granules (Fig. 3A, spectrum not shown). These regions are assumed to be undissolved bismuth subsalicylate crystals, and the presence of phosphorus can be attributed to phosphate in the growth medium. In control samples grown on salicylate, intracellular electron-dense regions were also present (data not shown). EDS analysis (data not shown) of these regions revealed the presence of phosphorus and low levels of calcium and aluminum (bismuth was not detected).

**Polyphosphate isolation and association with bismuth.** Inorganic polyphosphate has been identified in a wide range of organisms (23), including several species of *Fusarium* (11, 15, 31). Among other functions, polyphosphate is known to chelate metal ions in some biological systems (22). Polyphosphate was extracted from cells grown on bismuth subsalicylate or salicylate and was fractionated into three separate fractions: (i) short-chain soluble, (ii) long-chain soluble, and (iii) granular (10). Polyphosphate content of each fraction was determined as orthophosphate after acid hydrolysis via a colorimetric assay (39, 25).

Short-chain polyphosphates were present in low concentrations, and long-chain polyphosphates were present in relatively high concentrations, which is in accordance with previous studies of fusaria (31). Each fraction was analyzed for bismuth content by ICP-OES, and the ratio of bismuth to phosphate from polyphosphate was calculated (Fig. 4). The negative control culture grown on salicylate showed only background levels of bismuth in all fractions, but polyphosphate levels were equivalent to those in fractions from biomass grown on bismuth subsalicylate. The long-chain-soluble and granular fractions from bismuth subsalicylate-grown biomass had the highest bismuth:phosphate ratios (Fig. 4). Average bismuth concentrations in these fractions were ~50 times higher than the average bismuth concentrations in the short-chain fractions. In biomass grown on bismuth subsalicylate, the bismuth concentrations in the short-chain polyphosphate fractions ranged from 0.01 to 0.03 mM (average, 0.02 mM), bismuth concentrations in the long-chain-soluble polyphosphate fractions ranged from 0.91 to 1.15 mM (average, 1.03 mM), and bismuth concentrations in the granular polyphosphate fractions ranged from 0.77 to 1.31 mM (average, 1.04 mM).

The TEM-EDS analysis showed that accumulated bismuth was localized in phosphate-rich granules located primarily in the cytoplasm (Fig. 3). This result, coupled with the high con-

![Figure 3](image-url)
centrations of bismuth found in the long-chain and granular polyphosphate fractions from biomass grown on bismuth subsalicylate, suggests that at least some of the bismuth ions accumulated by *Fusarium* sp. strain BI during degradation of bismuth subsalicylate are complexed with polyphosphate. This interaction may have a role in bismuth tolerance in this organism. Experiments conducted in vitro have shown that Bi^{3+} can complex with polyphosphate (43). To our knowledge, no previous reports of bismuth accumulation in polyphosphate granules in a biological system have been published.

![Graph](image1.png)

**FIG. 4.** Ratio of bismuth to polyphosphate in extracts of *Fusarium* sp. strain BI biomass grown on salicylate and bismuth subsalicylate. Biomass was ground and extracted to yield fractions containing polyphosphate of different chain lengths (10). Bismuth concentrations were determined in each fraction by ICP-OES. Polyphosphate concentrations were determined colorimetrically (39) as orthophosphate released after acid hydrolysis of polyphosphate in each fraction (25). Error bars represent the standard deviations of three replicates.

Degradation of the salicylate moiety. Bismuth subsalicylate is composed of a Bi^{3+} ion chelated by a salicylate molecule (Fig. 5). An organism utilizing this compound as a carbon source would be expected to degrade it through one or more of the known salicylate catabolic pathways (Fig. 5). *Fusarium* sp. strain BI grew with salicylate, gentisate, or catechol as a sole carbon source (Fig. 6). During growth of *Fusarium* sp. strain BI on bismuth subsalicylate or salicylate, no degradative intermediates accumulated in the culture medium as detected by UV/visible light spectrophotometry. Crude extracts of *Fusarium* sp. strain BI grown on salicylate and glucose were assayed for specific activities of the enzymes in the predicted pathways, with hexokinase activity assayed as a control (Table 1). Catechol 1,2-dioxygenase activity was induced eightfold in cultures grown on salicylate compared to cultures grown on glucose (Table 1). Gentisate 1,2-dioxygenase activity was equivalent in extracts from cultures grown on salicylate or glucose (Table 1). These results suggest that *Fusarium* sp. strain BI degrades salicylate primarily through a catechol intermediate, with ring cleavage catalyzed by a catechol 1,2-dioxygenase (Fig. 5). By extension, this is proposed as the pathway through which *Fusarium* sp. strain BI degrades bismuth subsalicylate (Fig. 5).

The pathway for salicylate degradation by *Fusarium* sp. strain BI described above follows previously described pathways of salicylate degradation by yeasts and filamentous fungi: conversion of salicylate to catechol by salicylate hydroxylase and cleavage of the aromatic ring by catechol 1,2-dioxygenase (Fig. 5) (2, 40). This pathway links to the Krebs cycle via β-ketoadipate (2, 40). Catechol 2,3-dioxygenase activity is well documented in bacteria (24), but we found only one report of

![Diagram](image2.png)

**FIG. 5.** Known pathways for salicylate catabolism in fungi and/or bacteria. Intermediates in the proposed primary pathway of bismuth subsalicylate degradation by *Fusarium* sp. strain BI are shown in boldface.
this activity in a fungus (37). Conversion of salicylate to gentisate by salicylate 5-hydroxylase has been described for bacteria (17), but to our knowledge it has not been described for fungi. We did not find previously published descriptions of salicylate degradation by fusaria. Cain et al. reported a Fusarium oxysporum strain that did not grow on salicylate but grew well on catechol (9). Catechol and gentisate are intermediates in other catabolic pathways that do not include salicylate (18), and catechol 1,2-dioxygenase activity and gentisate 1,2-dioxygenase activity have been detected in fusaria grown on other aromatic substrates (6).

Growth on other aromatic compounds. Fusarium sp. strain BI could grow using a variety of aromatic compounds, primarily aromatic acids, as sole carbon sources. Measurable growth was detected on 12 of 14 compounds tested (in addition to bismuth subsalicylate, salicylate, catechol, and gentisate), with negative results only on L-mandelate and cyanuric acid (Fig. 6). Fusaria have previously been reported to grow on benzoic acid, 3-hydroxybenzoic acid, 4-hydroxybenzoic acid, phenol, phenylalanine, bismuth subsalicylate, salicylate, catechol, and gentisate), with measurable growth in other catabolic pathways that do not include salicylate (18), but to our knowledge it has not been described for fungi.

FIG. 6. Total dry biomass of Fusarium sp. strain BI grown for 96 h on 0.25 mmol of various substrates as sole carbon sources. Error bars represent the standard deviation of three replicates.

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### References

1. Altschul, S. F., W. Gish, W. Miller, E. W. Myers, and D. J. Lipman. 1990. Basic local alignment search tool. J. Mol. Biol. 215:403–410.
2. Anderson, J. J., and S. Bagley. 1980. Catabolism of aromatic acids in Trichophyton cutaneum. J. Bacteriol. 141:534–543.
3. Barz, W. 1971. Über den abbau aromatischer verbindungen durch Fusarium oxysporum schlecht. Arch. Mikrobiol. 78:341–352.
4. Bentley, R., and T. G. Chasten. 2002. Microbial methylation of metalloids: arsenic, antimony, and bismuth. Microbiol. Mol. Biol. Rev. 66:250–271.
5. Bergmeyer, H. U., M. Grassl, and H. E. Walter. 1983. Reagents for enzymatic analysis, p. 222–223. In H. U. Bergmeyer, J. Bergmeyer, and M. Grassl (ed.). Methods of enzymatic analysis, 3rd ed., vol. 2. Verlag Chemie, Weinheim, Germany.
6. Boonminathan, K., and A. Mahadevan. 1989. Dissimilation of aromatic substances by fungi. Zentralbl. Mikrobiol. 144:37–45.
7. Bradford, M. M. 1976. A rapid and sensitive method for the quantitation of microgram quantities of protein utilizing the principle of protein-dye binding. Anal. Biochem. 72:248–254.
8. Burrell, R. E., C. T. Corke, and R. G. Goel. 1983. Fungitoxicity of organo-antimony and organobismuth compounds. J. Agri. Food Chem. 31:85–88.
9. Cain, R. B., R. F. Hilton, and J. A. Darragh. 1968. The metabolism of aromatic acids by micro-organisms. Metabolic pathways in the fungi. Biochem. J. 108:797–828.
10. Clark, J. E., H. Beechen, and H. G. Wood. 1986. Isolation of intact chains of polyphosphate from "Propionibacterium shermanii" grown on glucose or lactate. J. Bacteriol. 168:1212–1219.
11. Ebel, J. P., and S. Muller. 1958. Cytochemical investigations of the inorganic polyphosphates present in living organisms. III. Presence of polyphosphates in some lower organisms. Exp. Cell Res. Suppl. 15:36–42.
12. Endo, G., and S. Silver. 1995. CadC, the transcriptional regulatory protein of the cadmium resistance system of Staphylococcus aureus plasmid pC258. J. Bacteriol. 177:4374–4441.
13. Gadd, G. M. 1993. Tansley review No. 47. Interactions of fungi with toxic metals. New Phyto1. 124:25–60.
14. Glass, N. L., and G. C. Donaldson. 1995. Development of primer sets...
designed for use with the PCR to amplify conserved genes from filamentous ascomycetes. Appl. Environ. Microbiol. 61:1323–1330.
15. Gorbik, L. T., and I. A. Ellanskaya. 1981. Metachromatin inclusions in conidia and hyphae cells of Fusarium I. K. ex. fr. species. Mikrobiol. Zh. 45:342–346.
16. Grilli, E., E.-L. Winnacker, and M. H. Zenk. 1986. Synthesis of seven different homologous phytocelatins in metal-exposed Schizophyllum commune cells. FEBS Lett. 197:115–120.
17. Grund, E., B. Denecke, and R. Eichenlaub. 1992. Naphthalene degradation via salicylate and gentisate by Rhodococcus sp. strain B4. Appl. Environ. Microbiol. 58:1874–1877.
18. Harper, D. B. 1977. Fungal degradation of aromatic nitriles. Enzymology of C-N cleavage by Fusarium solani. Biochem. J. 167:685–692.
19. Ji, G., and S. Silver. 1990. In vitro antimicrobial activity of bismuth subsalicylate against the yeast Saccharomyces cerevisiae: structure-activity relationship. J. Inorg. Biochem. 39:4–13.
20. Wilson, J. W., and E. M. M. Blair. 1992. In vitro antimicrobial activity of organobismuth compounds against the yeast Saccharomyces cerevisiae: structure-activity relationship. In: J. T. N. M. Blair. 1982. Degradation of benzoate and salicylate by Aspergillus niger. Ind. J. Exp. Biol. 20:166–168.
21. Kornberg, A. 1958. Study of condensed phosphates contained in 185 rDNA. Mycoses 39:25–30.
22. Kornberg, A. 1995. Inorganic polyphosphate: toward making a forgotten polymer unforgettable. J. Bacteriol. 177:58–66.
23. Kulaev, I. S. 1997. The biochemistry of inorganic polyphosphates, p. 17–21. In: J. van der Nat. Acad. Sci. USA 95:2044–2049.
24. Kacchy, A. N., and V. V. Modi. 1976. Catechol metabolism in Pseudomonas aeruginosa: regulation of meta-fission pathway, Ind. J. Exp. Biol. 14:163–165.
25. Lorenz, B., and H. C. Schröder. 1999. Methods for investigation of inorganic polyphosphates and polyphosphate-metabolizing enzymes. Prog. Mol. Subcell. Biol. 23:217–239.
26. Mahoney, D. E., S. Lim-Morrison, L. Bryden, G. Faulkner, P. S. Hoffman, L. Agocs, G. G. Briand, N. Hameed, and H. Maguire. 1999. Antimicrobial activities of synthetic bismuth compounds against Clostridium difficile. Antimicrob. Agents Chemother. 43:582–588.
27. Manhart, M. D. 1990. In vitro antimicrobial activity of bismuth subsalicylate and other bismuth salts. Rev. Infect. Dis. 12(Suppl. 1):S11–S15.
28. Marshall, B. J., J. A. Armstrong, G. J. Francis, N. T. Nokes, and S. H. Wee. 1987. Antibacterial action of bismuth in relation to Campylobacter pyloridis colonization and gastritis. Digestion 37(Suppl. 2):16–30.
29. McClellan, W. D. 1947. Response of Gladiolus to corm treatments. N. Am. Gladiolus Coun. Bull. 41:20.
30. Middelhoven, W. J. 1993. Catabolism of benzoate compounds by ascomycetes and basidiomycetous yeasts and yeastlike fungi. Antonie Leeuwenhoek 63:125–144.
31. Muller, S., and J. P. Ebel. 1958. Study of condensed phosphates contained in various fungi. Bull. Soc. Chim. Biol. 40:1153–1161.
32. Murafuji, T., Y. Miyoshi, M. Ishibashi, A. F. Mustafizur Rahman, Y. Sugihara, I. Miyakawa, and H. Uno. 2004. Antifungal activity of organobismuth compounds against the yeast Saccharomyces cerevisiae: structure-activity relationship. J. Inorg. Biochem. 98:547–552.
33. Nadeau, O. W., D. W. Gump, G. M. Hendricks, and D. H. Meyer. 1992. Deposition of bismuth by Yersinia enterocolitica. Med. Microbiol. Immunol. 181:145–152.
34. Nelson, P. E., M. C. Dignani, and E. J. A. Anaissie. 1994. Taxonomy, biology, and clinical aspects of Fusarium species. Clin. Microbiol. Rev. 7:479–504.
35. Novick, R. P., and C. Roth. 1968. Plasmid-linked resistance to inorganic salts in Staphylococcus aureus. J. Bacteriol. 95:1335–1342.
36. O’Donnell, K., H. C. Kistler, E. Cigelnik, and R. C. Plotz. 1998. Multiple evolutionary origins of the fungus causing Panama disease of banana: concordant evidence from nuclear and mitochondrial gene genealogies. Proc. Natl. Acad. Sci. USA 95:2044–2049.
37. Patel, T. R., N. Hameed, and A. M. Martin. 1990. Initial steps of phloroglucin metabolism in Penicillium simplicissimum. Arch. Microbiol. 153:338–343.
38. Sadler, P. J., H. Li, and H. Sun. 1999. Coordination chemistry of metals in medicine: target sites for bismuth. Coord. Chem. Rev. 186:689–709.
39. Sahs, S. H. 1979. Antimicrobial activity of bismuth subsalicylate. Antimicrob. Agents Chemother. 33:1016–1017.
40. Shalihbhai, K., N. N. Rao, and V. V. Modi. 1982. Degradation of benzoate and salicylate by Aspergillus niger. Ind. J. Exp. Biol. 20:166–168.
41. Sox, T. E., and C. A. Olson. 1989. Binding and killing of bacteria by bismuth subsalicylate. Antimicrob. Agents Chemother. 33:2075–2082.
42. Stoltenberg, M., M. Martini, K. Sorensen, J. Runghy, and K. A. Krogfelt. 2001. Histochemical tracing of bismuth in Helicobacter pylori after in vitro exposure to bismuth citrate. Scand. J. Gastroenterol. 36:144–148.
43. Thito, E. 1962. Condensed phosphates and arsenates. Adv. Inorg. Chem. Radiochem. 4:1–75.
44. Tousson, T. A., and P. E. Nelson. 1976. Fusarium: a pictorial guide to the identification of Fusarium species, 2nd ed. The Pennsylvania State University Press, University Park, Pa.
45. Vainio, E. J., and J. Haultu. 2000. Direct analysis of wood-inhabiting fungi using denaturing gradient gel electrophoresis of amplified ribosomal DNA. Mycol. Res. 104:927–936.
46. Wilson, J. W., and E. M. M. Blair. 1926. A combination of bismuth and sodium sulphide affording an enrichment and selective medium for the typhoid-paratyphoid groups of bacteria. J. Pathol. Bacteriol. 28:310–311.
47. Yamamoto, S., M. Katagiri, H. Maeno, and O. Hayashi. 1965. Salicylate hydroxylase, a monoxygenase requiring flavin adenine dinucleotide. J. Biol. Chem. 240:3408–3413.