MATERIALS SCIENCE AND CORONAVIRUS SERIES

ANTIMICROBIAL COPPER-CONTAINING STAINLESS STEELS SHOW PROMISE

Given the demonstrated antimicrobial properties of copper, it is incumbent upon materials scientists to design potent antimicrobial copper-containing stainless steels as an economical option.

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Transmission of bacteria and viruses through touched surfaces is an important public health concern, heightened recently by the COVID-19 pandemic. As discussed in a previous article in this series[1], it has long been known that copper and copper-rich alloys exhibit potent antimicrobial properties. However, instead of copper, stainless steels are in widespread use in hospitals, medical facilities, and public transportation, despite their lack of antimicrobial properties. One reason is the lower cost of stainless steels. Another reason is corrosion resistance and appearance. Stainless steel has a pleasing appearance and is more corrosion-resistant than Cu, which develops an unappealing green or dark brown tarnish when corroded. Finally, stainless steels have higher yield strength (e.g., 250 MPa for stainless steel 304) than annealed Cu and Cu-rich alloys (70-170 MPa) and are therefore more suitable for applications such as hospital beds and handholds used in public transportation.

KILLING BACTERIA AND VIRUSES

Bacteria range in size from 0.5 to 10 µm, whereas viruses are two orders of magnitude smaller, from about 5 to 300 nm. Bacteria come in many shapes such as spheres or rods depending on the species. All species have a cell membrane accompanied by an outer cell wall, which varies in sophistication. In contrast to bacteria, viruses are surrounded by a protein capsid and sometimes have an additional outer lipid envelope acquired from the host. Microorganisms including bacteria and viruses are often sorbed to particulates or contained within aerosolized droplets in the environment. When these droplets land on surfaces, rapid inactivation of the microorganisms contained therein would minimize transmission due to touch.

To test a surface for antimicrobial properties, microbes are first adhered to the surface by direct application or immersion of the surface into a solution containing a known concentration of microorganisms[2]. The microorganisms remain in contact with the sample at a given temperature (room temperature or 37°C) for a certain time period (incubation time), after which the remaining number of live microorganisms is determined. This number is...
compared with either the initial number or the number remaining after the same amount of time on another surface known not to possess antimicrobial properties. This is then stated in the literature as a measure of antimicrobial activity.

**REPORTS OF SUCCESS**

Over the past 20 years or so, there have been numerous efforts toward the development of antimicrobial stainless steels. For example, Bahmani-Oskooee et al. added 1 to 5 wt% Cu into 410 martensitic stainless steel. After solution treatment at 1100°C to dissolve all alloying elements followed by oil quenching, these steel samples were aged at 500°C for 0.25 to 4 hours. Transmission electron microscopy shows that precipitates of fcc Cu on the order of 10-30 nm in diameter formed after the aging treatment. It was discovered that the addition of 3 wt% Cu along with aging at 500°C for 2 hours was sufficient to deactivate all exposed bacteria (E. coli and S. aureus) in 24 hours. In another study, Xi et al. added 2.5 and 3.5 wt% Cu into 316L stainless steel. After solution treatment at 1100°C for 30 minutes and water quenching, the steel samples were aged at 700°C. The researchers found that after aging for 6 hours, 95% and 99% of E. coli in contact with the Cu-containing steel samples were inactivated within 24 hours.

In other research, Yang and Lu added 3.8 wt% Cu to 316L and explored its antimicrobial properties against four different types of bacteria after an aging treatment of 700°C for 6 hours. The team observed the formation of fcc Cu precipitates with diameters in the range of 10-20 nm. E. coli bacteria were deactivated the fastest, with complete inactivation in about 10 hours. In another study, Hong and Koo started with 304 stainless steel and added from 1.5 to 5.5 wt% Cu. After solution treatment at 1050°C, samples were aged at 700°C and 800°C for 0.5 to 4 hours. They observed formation of Cu precipitates with diameters on the order of 100 nm after aging at 800°C for 2 hours. Steel samples with 3.5 wt% Cu or higher and after aging at temperatures ≥ 700°C for 30 minutes were found to deactivate all bacteria (S. aureus) within 24 hours. Note that Cu-containing stainless steels exhibit only weak antimicrobial activity after solution treatment, indicating the importance of having Cu-rich precipitates. Several patents on antimicrobial stainless steels developed using similar strategies also exist.

**BUT IS IT REALLY SUCCESS?**

As noted earlier, most studies of antimicrobial stainless steel report results of bacteria inactivation on steel samples after 24 hours of incubation time. Such a measure is too imprecise to differentiate antimicrobial performance among different alloys and aging treatments and provides little information on inactivation kinetics. Yang and Lu measured E. coli inactivation as a function of time, giving 2.5 hours for the half-life of stainless steel 317L plus 3.8 wt% Cu. In other research, Chai et al. showed that the half-lives of E. coli and S. aureus on 317L plus 4.5 wt% Cu are both about 6 hours. In contrast, the half-life of SARS-CoV-2 (the virus causing COVID-19) is 0.77 hours on pure Cu, and the half-life of E. coli on pure Cu is 0.25 hours.

Based on the previous discussion of these results, the half-life of these microbes on Cu-containing stainless steels is significantly longer than that on pure Cu. One possibility can be inferred from studies of the antimicrobial activity of stainless steels and other samples with coatings containing different Cu concentrations. Zhang et al. found that the half-life of E. coli on 304 stainless steel coated with Cu-Ni alloy containing 90% Cu had a half-life of about 0.5 hours, increasing to about 2 hours when the coating contained 2.5% Cu. Efforts to increase the surface Cu concentration by increasing aging temperature to 800°C and aging time to 400 hours of 304 stainless steel plus 3.8 wt% Cu, followed by pickling, do not seem to yield antimicrobial properties any closer to Cu.

**PRELIMINARY STUDIES**

As noted in the previous discussion, it is not enough to just add Cu to stainless steels and expect things to work as well as Cu. The authors have been experimenting with Cu-precipitation-strengthened ferritic steels for the past 20 years as a new class of weathering steels for civil infrastructure applications, with markedly improved low-temperature toughness, weldability, and weathering resistance. These steels are approved as ASTM A710 Grade B bridge steels. They are low-carbon ferritic steels designed to maximize the number density of nanometer-size Cu precipitates. A typical alloy has the following composition in wt%: 0.06C-1.3Cu-0.9Ni-0.5Si-0.45Cu-0.1Ti, balance Fe, with 500 MPa yield strength, 30% elongation to failure, and Charpy impact fracture energy of 160 J at -80°C. This excellent combination of strength and toughness is primarily due to the precipitation of coherent bcc nanometer-size Cu precipitates.

Steels with improved strength based on ASTM A710 Grade B have since been developed, mainly by adding Ni and Al to promote the co-precipitation of Cu and NiAl, producing a new series of low-carbon ferritic steels (designated CF series) with yield strength up to 1600 MPa. It dawned on the authors that A710 Grade B and these CF steels may possess potent antimicrobial activity due to the high number density of nanometer-size Cu precipitates present in these alloys. As an example, Fig. 1 shows the atom probe tomography image obtained from one steel in this series after solution treatment at 950°C, followed by water quenching and aging at 500°C for 2 hours. Note the high density of Cu-containing precipitates, with an average radius of 2.0 nm and interprecipitate distance of ≈ 12 nm. Antimicrobial performance of two polished Cu-containing steel samples were explored using
MRSA bacteria, one with 2.5 wt% Cu (sample #2) and the other, sample #2 with 12 wt% Cr added (sample #2+Cr), both after heat treatment to form nanometer-size copper precipitates. Incubation at 37°C for 30 minutes is sufficient to inactivate 96% and 90%, respectively, on average for all MRSA bacteria exposed to these steel samples (Fig. 2).

The authors were curious about what might happen when Cu atoms on surfaces of these precipitates come into direct contact with microbes or active molecules in the vicinity. To explore this idea, molecular dynamics simulation using a large-scale atomic/molecular massively parallel simulator was conducted on the interaction between a bcc Cu (111) stepped surface and 150 hydrogen peroxide (H₂O₂) molecules at room temperature. H₂O₂ is produced by human cells and many bacteria species.

Figure 3 shows the evolution of the number of H₂O₂, hydroxyl radicals, molecular oxygen, and water molecules as a function of time. The fragmentation of H₂O₂ upon contact with Cu is almost immediate, producing hydroxyl radicals, oxygen, and water. These changes are accompanied by the oxidation of Cu to form Cu⁺, strongly suggestive of Fenton-like chemical reactions. The process appears to reach steady state after about 60 ps, which indicates the occurrence of a back-reaction, i.e., formation of H₂O₂ from initial reaction products. Both H₂O₂ and hydroxyl radicals are reactive oxygen species that play an important role in antimicrobial action.

**IS MORE COPPER BETTER?**

Cu is known to cause “hot shortness” in steels—embrittlement of steel due to formation of Cu-rich liquid and its penetration into grain boundaries during hot rolling or forging. Excessive Cu amplifies this problem. Also, how adding Cu affects the corrosion performance of stainless steels must also be considered. When Cu is in solid solution, it has no detrimental effect on the stability of passivation oxide films of ferritic or austenitic stainless steels[15]. However, when present as nanometer-size precipitates after aging, Cu...
reduces resistance against pitting corrosion in chloride environments\(^{16,17}\). This effect is related to localized galvanic corrosion, in which pits are formed in the vicinity of Cu precipitates. Therefore, one must limit the amount of Cu introduced into stainless steels to minimize pitting corrosion.

**CONCLUDING THOUGHTS**

Metallurgists rarely cross into the domain of biosciences and public health. The COVID-19 pandemic may serve as a trigger for those in the field to reflect on how to contribute. Given the demonstrated antimicrobial activity of Cu, it is incumbent upon materials scientists to design potent antimicrobial copper-containing stainless steels as an economical drop-in replacement for traditional stainless steels. To achieve antimicrobial potency comparable to pure Cu, one must design the alloy to contain the maximum volume fraction of nanometer-size Cu precipitates. Doing so with as little Cu as possible will not only minimize cost, but also avoid embrittlement and boost corrosion performance. Although these conflicting requirements are daunting, the challenge can be met by employing modern computational and simulation methods along with experimental validation.

As presented in this commentary, some of these methods were used to demonstrate the chemical reactivity of Cu step atoms on surfaces of nanometer-size precipitates in generating reactive oxygen species considered to be important in antimicrobial action. Equally important, Cu-precipitation-strengthened steels were fabricated with a high number density of nanometer-size Cu precipitates at modest Cu concentrations, with promising results regarding antibacterial activity and excellent potential in numerous applications. ~AM&P

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**References**

Lead image: 2019-nCoV spike protein, courtesy of Jason McLellan/University of Texas at Austin.