On the Reactions of Amino Acids, Including D-penicillamine, with some Metals and Alloys

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In a recent communication Brown and Smith [1] concluded that care should be taken in the use of metal-stabilising drugs, such as D-penicillamine, with patients who have had metal hip-replacement operations. Their conclusion was based on their observation that 0.01 mol l^{-1} D-penicillamine attacked metal alloys leading to dissolution of some of the metals. They also noted that the naturally occurring amino acid L-cysteine behaved similarly.

However, the conditions and concentrations used by these authors were far from those of physiological fluids, and the amounts of metal dissolved were not given. Questions then arise as to whether the corrosive action of penicillamine is significant under physiological conditions and whether physiological fluids themselves could act in a like manner? It has been known for some time that copper metal can be dissolved by saline solution [2, 3], human sweat [3] and uterine fluid [4].

We have examined the ability of the amino acids to dissolve Cu metal (foil) and Fe (steel) by treating the metals at 37 °C with our amino acid 'plasma model' solution as developed earlier [5]. The 'plasma model' solution comprised 3×10^{-3} mol l^{-1} L-alanine (to represent the total bidentate amino acids), 8.5×10^{-5} mol l^{-1} L-histidine, 2.3×10^{-5} mol l^{-1} L-cysteine, 0.15 mol l^{-1} NaCl and 0.1 mol dm^{-3} pH 7.4 phosphate buffer. We found that under aerobic conditions the dissolution of both metals reached *ca.* 10^{-4} mol l^{-1} concentrations, mainly as dissolved Cu(II) and Fe(III) complexes together with some metal hydroxide suspension. These concentration levels were achieved after 1–2 days for Cu but required 4–6 days for Fe. L-histidine had the largest solubilising effect on Cu But not with Fe. Addition of D-penicillamine (2×10^{-5} mol l^{-1}) to the aerobic solutions produced no observable increase in metal dissolution. However, under anaerobic conditions both L-cysteine and D-penicillamine were similarly active in dissolving the metals. In their absence the amounts of dissolved metal were of the order 10^{-5}–10^{-6} mol dm^{-3}, this increased to *ca.* 10^{-4} mol l^{-1} on addition of 2×10^{-5} mol dm^{-3} L-cysteine or D-penicillamine.

From these results the driving force for the dissolution of the metals would appear to be the formation of metal–amino acid complexes, the presence of an oxidant (air) favouring the formation of the Cu(II) and Fe(III) states. In the absence of an oxidant, ligands which stabilise lower oxidation states (as with thiols) are required for effective dissolution. The levels of D-penicillamine in the bloodstream of long-term Wilson's disease patients has been shown to be low ($<10^{-4}$ mol l^{-1}) [6], similar levels are likely to be encountered in penicillamine-treated rheumatoid arthritis patients. Since much of the thiol is also likely to be oxidised to the disulphide form then the corrosive action of this drug on metal prostheses, contrary to the earlier claim [1], is likely to be insignificant. However, quite clearly blood plasma itself could have a long-term corrosive effect and, just as importantly, could lead to toxic levels of metal ions in the bloodstream.

References

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