JOURNAL OF MATERIALS SCIENCE 17 (1982) 1675–1682

The corrosion of pure cobalt in physiological media

D. F. WILLIAMS, G. C. F. CLARK
Department of Dental Sciences, University of Liverpool, P.O. Box 147, Liverpool, UK

The corrosion of cobalt in aqueous media with and without the presence of the protein serum albumin has been investigated using a number of techniques. The corrosion rate was found to increase significantly in the presence of albumin. Although the effect was related to albumin concentration to a certain extent, there is no equivalence between the metal ions released and the albumin present. It is believed that the effect is due to a catalytic process where the albumin reversibly binds cobalt during the corrosion process. The significance of this phenomenon in the context of the implantation of biomaterials in the human body is discussed.

1. Introduction

Metallic materials have been used for surgical implants and other biomedical applications for many years, as reviewed by Williams and Roaf [1] and Mears [2]. Numerous metals and alloys have been tested for such use, but most have been discarded because of their poor corrosion resistance in the physiological environment and the associated adverse response from the tissues. The result of this has been a rationalization in the use of metallic implant materials such that today the vast majority of surgical applications involve the alloys 316 stainless steel, titanium–aluminium–vanadium and a variety of cobalt–chromium based alloys such as cobalt–chromium–molybdenum and cobalt–nickel–chromium–tungsten–molybdenum.

Even with these alloys, however, the environmental conditions are so hostile (as a 0.9% NaCl solution containing numerous other ions and organic species) and the sensitivity of the tissues so great, that corrosion is still a problem [3]. Naturally, all three alloy systems rely on passivity for their corrosion resistance and we can distinguish two different types of corrosion behaviour under these conditions [4]. The first is associated with film breakdown and results in overt corrosion and the release of obvious corrosion products. As predicted by Hoar and Mears [5], this occurs most frequently with the 316 stainless steel, the breakdown potential of which is within the range for the isolated potential, resulting in many cases of crevice and pitting corrosion [6]. Such film breakdown rarely occurs with the cobalt based alloys and never in the titanium alloy. However, as electrochemical measurements will show, there is still a finite current density observed within the passive region of an anodic polarization curve and this will result in the second type of behaviour, slow release of metal ions into the surrounding tissue. This can be regarded as a slow diffusion of metal ions through the oxide layer or a slow dissolution of the oxide surface. While in many engineering situations such a metal ion loss would go unnoticed because there are no mechanical property implications, this is not the case in the human body and this type of corrosion is of some significance. Animal experiments and observations of human samples have shown that metal accumulates in the tissue around implants as a result of this phenomenon [7–9].

While overt corrosion, with voluminous corrosion products, provokes a readily identifiable response from the tissue [6], the slow release of metallic ions has less obvious clinical implications but may, nevertheless, be of great importance, especially when it is borne in mind that many of these elements, such as cobalt, chromium and nickel can be toxic. At a time when surgeons are favouring the use of some total joint replacement prostheses in very young people, where the

0022–2461/82/061675–08$03.46/0

lifetime of the prostheses may be expected to be up to 50 years, it is clearly desirable to study the precise characteristics and effects of this corrosion.

Although there is a certain amount of discussion in the literature concerning the clinical performance of the different alloys, no systematic study has been performed of the corrosion rates and their correlation with physiological activity. Such a study is being undertaken in the authors' laboratory in which both tissue response and corrosion behaviour are being studied. However, in a complex alloy such as 316 stainless steel, which contains iron, chromium, nickel and molybdenum, it is extremely difficult to correlate the observed response in the tissue with the corrosion behaviour since each constituent element behaves differently. Each will be released at a different rate and they will vary with respect to diffusion rates in tissue, ability to pass through cellular membranes, protein-binding capacity, enzyme-interference, and so on. It is, therefore, necessary to study each component element itself in order to gain an understanding of the biocompatibility of metallic materials. This is currently being undertaken with studies on the tissue response to pure metals [10, 11] and metal–protein interactions [12–14].

The present paper is concerned with corrosion studies on pure cobalt. This is the basis of the cobalt–chromium type alloys. It is known that cobalt may be found within the tissues surrounding an implant, and is also distributed systematically [15]. The response to particulate wear debris of these alloys may be intense [16] and can lead to hypersensitivity involving the immune system [17]. Metallic cobalt can induce tumours when implanted in rats [18] and it is cytotoxic in cell culture [19]. Cobalt salts can also lead to cardiomyopathy, a disease of the heart [20]. It is, therefore, appropriate to study the biocompatibility of this metal. One aspect of this is discussed in the present paper where particular emphasis is placed on the effects of different physiological species such as proteins on the corrosion behaviour.

2. Materials

Cobalt of both powder and rod form, of 99.999% purity and obtained from Metals Research Ltd, has been used in this study. The powder, which consisted of an aggregate of small particles, was sieved and the 30 to 75 μm fraction was used for part of the study. The rod, of 5 mm diameter, was sectioned into discs of 1 mm thickness for the anodic polarization studies.

Analar grade chemicals were used throughout. The protein studies were undertaken with bovine serum albumin and bovine fibrinogen, obtained from Miles Laboratories.

3. Methods

Corrosion rates were determined in two different ways, using anodic polarization and pH-stat methods. In both cases the effects of different components of physiological solution on corrosion were studied.

3.1. Anodic polarisation

The anodic polarization curves were determined using a PAR 174A polarographic recorder with a Bryans $X-Y$ plotter. The discs of cobalt were embedded in a thermosetting resin, polished to a 3 μm finish and placed in a rotating-electrode assembly. A platinum counter electrode and silver–silver chloride reference electrode were used. The salt bridge was filled with saturated potassium chloride with a porous plug junction. The reference electrode-working distance was maintained at less than 5 mm.

3.2. pH-stat experiments

Although electrochemical test methods are intrinsically very sensitive, they do suffer some disadvantages. Firstly, with anodic polarization the current includes a term due to other redox reactions which may be occurring in the solution, (e.g. conversion of Fe(II) to Fe(III) and, while this is generally negligible in simple solutions, it may be of importance for systems approximating *in vivo* conditions. Secondly, the surface area of a practical electrode is necessarily limited, which places a lower limit on the rates of reaction that can be measured. For an electrode of 1 cm^2 surface area, a current of 1 μA is equivalent to a rate of reaction of 10 nmol cm^{-2} sec^{-1}.

We have therefore used a different method, employing metal powders at the resting potential. Since each particle is isolated in the stirred solution, oxidation of the metal can only occur if a reduction occurs concurrently. These two reactions generally involve acid–base changes, causing a change in pH. If the system is operated in a pH-stat, the rate of reaction can be followed by recording the addition of acid or alkali necessary to maintain a constant pH. For a metal having

divalent ions which are not hydrolysed and which undergoes oxidation by oxygen, the following reactions occur

$$M \longrightarrow M^{2+} + 2e^- \quad (1)$$

and

$$2e^- + 2H^+ + 1/2\,O_2 \longrightarrow H_2O \quad (2)$$

or

$$M + 2H^+ + 1/2\,O_2 \longrightarrow M^{2+} + H_2O \quad (3)$$

If the metal forms a neutral hydroxide at the pH chosen for the reaction, there is no net acid or base consumption. Reactions of this type can only be followed if a ligand is added which will displace the metal from the complex:

$$M + 1/2\,O_2 + H_2O \longrightarrow M(OH)_2 \quad (4)$$

$$M(OH)_2 + 2L^- \longrightarrow ML_2 + 2OH^- \quad (5)$$

For those metals, such as molybdenum, which hydrolyse to anionic species, the system becomes more complex, but is still resolvable using these methods.

Fortunately for the present study, cobalt is simple in this respect and, within the pH range employed, no interfering mechanisms exist. The apparatus used was a Radiometer RTS 81 automatic titration system fitted with an REA 270 pH-stat unit and a 2.5 cm^3 burette filled with 0.05 M sulphuric acid. This system was able to follow a rate of acid addition of 1 mM at 0.01 $\mu l\,sec^{-1}$, with 0.1 g powder (and surface area 0.2 $m^2\,g^{-1}$); this represents a rate of reaction of 0.05 nmol $cm^{-2}\,sec^{-1}$, a 200 fold increase in sensitivity over electrochemical monitoring. The reaction vessel was blanketed either by oxygen or nitrogen. Both gases were passed through a soda-lime tube and were equilibrated with 0.1 M sodium chloride solution to prevent evaporation of the test solution. The nitrogen was also bubbled through ammonium metavanadate solution to remove oxygen.

3.3. Analyses

Titration curves for the albumin experiment were carried out with the same pH-stat apparatus, this time using 0.093 M sodium hydroxide in the burette. Optical spectra of the solution were also recorded, using a Pye Unicam SP1800 spectrophotometer with 1 cm quartz cells and water blank. These experiments were performed in order to see if there was any binding of cobalt to protein in solution.

4. Results

4.1. pH-stat

4.1.1. Hydrolysis

Hydrolysis of cobalt is not appreciable below pH 7.8 [21]. In this work, therefore, two moles of acid consumed are equivalent to one mole of metal oxidized.

4.1.2. The effect of pH

The rate of oxidation of cobalt as a function of pH is shown in Fig. 1. The results were obtained with 50 mg cobalt powder in 5 cm^3 0.1 M sodium chloride under oxygen cover with the pH adjusted by sulphuric acid. At pH 7.0 the standard deviation of the rate was 6.5%. There was no significant difference between these results and those obtained

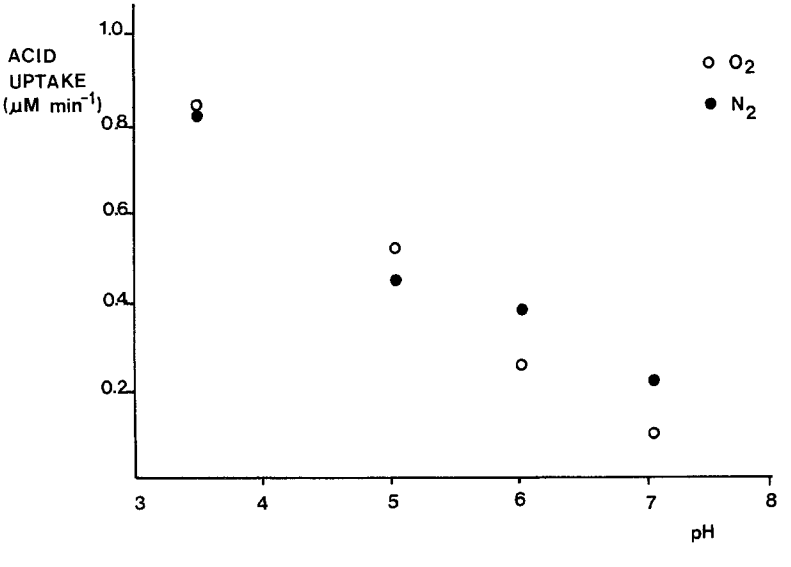

Figure 1 Rate of corrosion of cobalt powder in unbuffered saline, determined by the pH stat experiment, as a function of pH, using 50 mg cobalt in 5 mm^3 0.1 M NaCl.

with sodium sulphate. The effect of substituting nitrogen cover for oxygen is also shown in Fig. 1; the rate at neutral pH was reduced but corrosion was not entirely inhibited.

4.1.3. The effect of proteins

In the presence of 0.2 mM (1.3%) bovine serum albumin in 0.1 M sodium chloride, the rate of oxidation in an oxygen saturated solution at pH 7.0 was 10.1 μmol min^{-1}. This compares with the value of 0.21 μmol min^{-1} in an equivalent albumin-free solution. Within the conditions evaluated the rate was dependent upon the amount of protein present; with 0.02 mM albumin, the rate was 3.13 μmol min^{-1}. In an oxygen-free solution the 1.3% albumin gave a rate of 0.055 μmol min^{-1}. The effect of pH in the presence of albumin was not studied, since different groups of the protein would become active as the pH was changed. Fibrinogen was also found to have an effect, a 0.006 mM solution (0.5%) in 0.1 M sodium chloride giving a rate of 1.9 μmol min^{-1}.

4.1.4. The effect of non-protein chelating agents

Fig. 2 shows the results of cobalt oxidation in the presence of 2 mM potassium tartrate in 0.1 M sodium chloride, indicating that there is also enhanced oxidation with this chelating agent.

4.2. Potentiostat

The current density-potential curves obtained with the potentiostat are shown in Fig. 3. They were recorded in unbuffered solutions adjusted to the correct pH before each run and saturated with the appropriate gas. With the potential changing from positive to negative, the same current–potential path was followed for all solutions. The scan rate was varied between 10 mV sec^{-1} and 0.2 mV sec^{-1}, with no appreciable effect on the results.

The electrodes were freshly polished before each run. At the end of an anodic scan they were covered with an adherent film of brown material, presumably an oxide of cobalt. The presence of serum albumin had no effect upon the formation of this film. Microscopic examination of the metal surfaces revealed no noteworthy features although pitting could be seen on specimens repeatedly cycled without intermediate polishing. The curves recorded with sodium sulphate solution were not significantly different from those obtained with sodium chloride solution.

4.3. Optical spectra

The optical spectra for bovine serum albumin, cobalt chloride and mixtures of the two are shown in Figs 4 (u.v.) and 5 (visible). From the former, it appears that the tyrosine absorbance at 280 nm with albumin is unchanged in the presence of cobalt chloride, but the amount of light scattering has increased, implying some aggregation of the protein. There is no effect of albumin on the absorbance of cobalt even at a molar ratio of 1:4 albumin:cobalt. This implies that the electronic environment of cobalt in solution is not significantly altered by the presence of albumin.

4.4. Titration curves

The extent to which serum albumin can bind

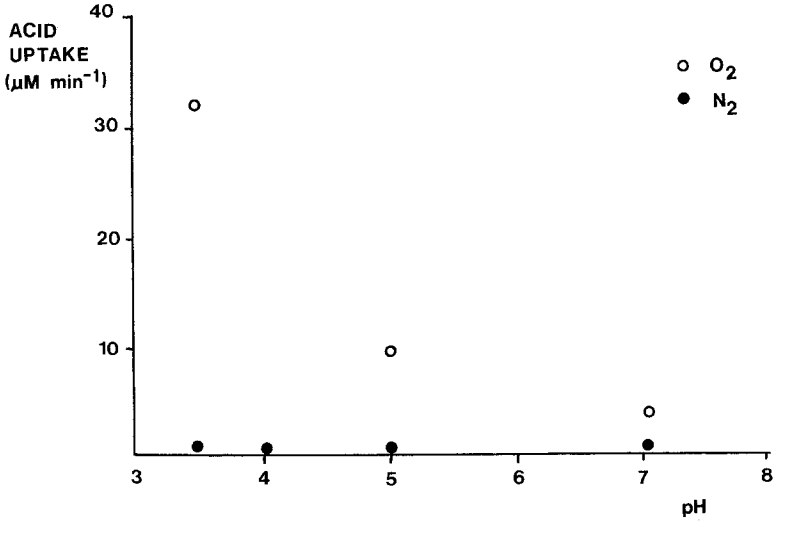

Figure 2 Rate of corrosion of cobalt powder in presence of potassium tartrate. Same conditions as in Fig. 1, but with 2 mM tartrate.

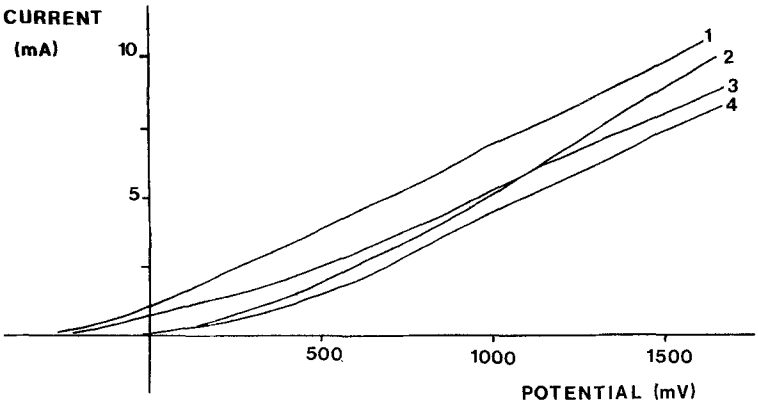

Figure 3 Anodic polarization curves for cobalt using scan rate of 0.1 mV sec^{-1}. (1) In saline, under nitrogen. (2) In saline, under oxygen. (3) In B.S.A. under nitrogen. (4) In B.S.A. under oxygen.

cobalt was also investigated by recording the titration curves of cobalt chloride, bovine serum and albumin and the two together. A solution of 0.1 M cobalt chloride was adjusted to pH 2.2 with hydrochloric acid and titrated with 0.093 M sodium hydroxide, the result being shown in Fig. 6. A green precipitate started to form at pH 7.7, which maintained the pH near this value until precipitation was complete. The colours of cobalt hydroxide are reported as either blue or pink [21] although the green precipitate here formed at the expected pH for the hydroxide. The titration curve for serum albumin was recorded under the same conditions, with 0.1 mM protein in 0.1 M sodium chloride, adjusted to pH 2.52. This protein is characterized by a large proportion of carboxyl groups titrating at pH 5 and amino acid chains titrating at pH 10, but much less histidine, the only amino acid titrating in the pH 6 to 8 range (Fig. 6).

The mixture of 0.1 mM albumin and 4 mM cobalt chloride in 0.1 M sodium chloride, starting at pH 2.52 shows a very small but significant difference from the albumin curve in the region of pH 2.5 to 4.5 (not easily discernable in Fig. 6). This would correspond to the binding of cobalt ions to the carboxylate groups of the albumin in a reversible manner. There is a marked divergence of the curves about pH 5.9, equivalent to 1.8 μmol of base. The separation of the two curves is constant up to pH 8.5, suggesting that it is not binding of hydroxide by metal ions, but rather the binding of the cobalt to four of the histidine residues of the protein that is responsible. At pH 8.9 there is a sharp break corresponding to the formation of cobalt hydroxide, although no precipitate was formed. At pH 11, the solution changes from green to yellow.

5. Discussion

The results clearly show that the corrosion of cobalt is influenced by the presence of the

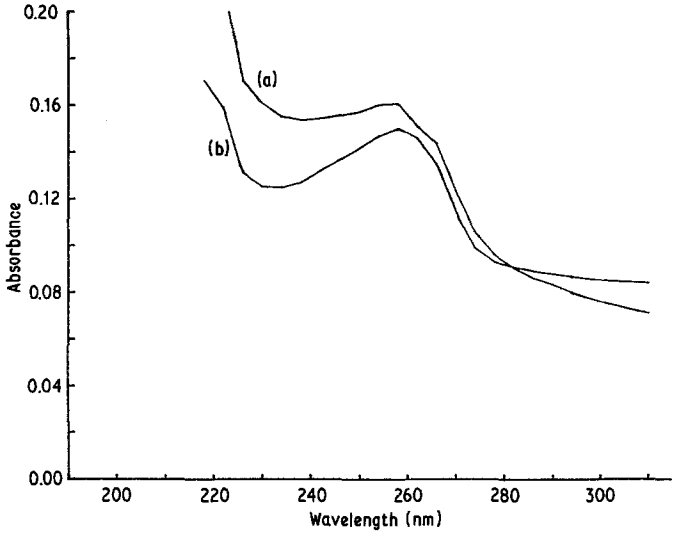

Figure 4 Spectrum of serum albumin plus cobalt (a) and serum albumin in the absence of cobalt (b) in pH 7.4, using 0.25 mM cobalt and 0.01 mM bovine serum albumin in 0.1 M NaCl.

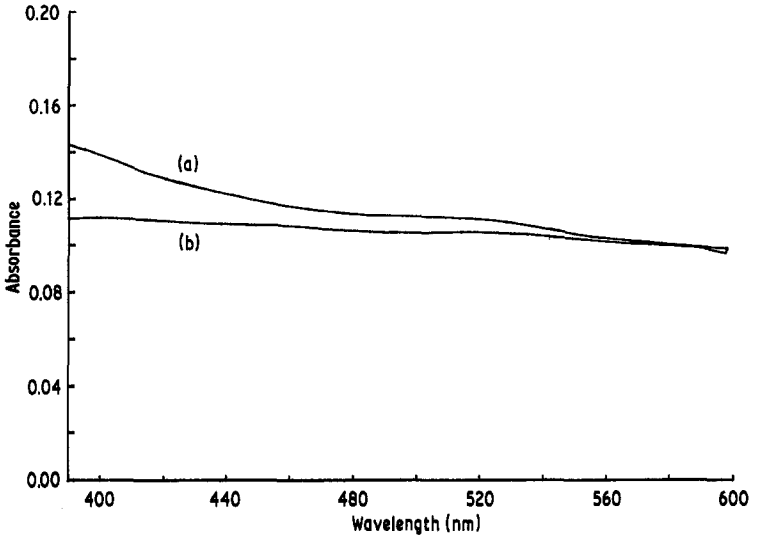

Figure 5 Spectrum of serum albumin plus cobalt (a) and cobalt alone (b) at the absorption maximum of hexa aquo-cobalt ions. The concentration of cobalt (1 mM) was kept to a minimum to maximize the contribution of any complexes.

proteins, serum albumin and fibrinogen and by a chelating agent such as potassium tartrate.

The pH-stat results indicate that in the absence of any chelating agents, cobalt is subject to oxidation by two processes. Under nitrogen cover, the reaction involves the formation of hydrogen:

$$Co + 2H^+ \longrightarrow Co^{2+} + H_2 \qquad (6)$$

whilst under oxygen, the reaction is

$$Co + \tfrac{1}{2}O_2 + 2H^+ \longrightarrow Co^{2+} + H_2O \qquad (7)$$

In the presence of tartrate, Reaction 6 shows little enhancement but Reaction 7 increases 18-fold at pH 7 and 39-fold at pH 3.5. This cannot be attributed to the stoichiometric formation of a cobalt tartrate complex, as the rate of reaction does not fall, even when the amount of metal dissolved is ten times the amount of tartrate present. The effect must therefore be attributed to a surface reaction in which the tartrate plays a catalytic role.

Serum albumin appears to have a similar effect. The molar concentration is very much smaller than the amount of metal dissolved and, as shown in the titration experiments, only a few cobalt ions are strongly bound to the protein, at most four per molecule. On a molar basis, serum albumin is thirty times as effective as tartrate in enhancing the corrosion of cobalt. The fact that this enhancement is dependent upon concentration to a certain extent, however, shows that the catalytic role of albumin is dependent on the proportion

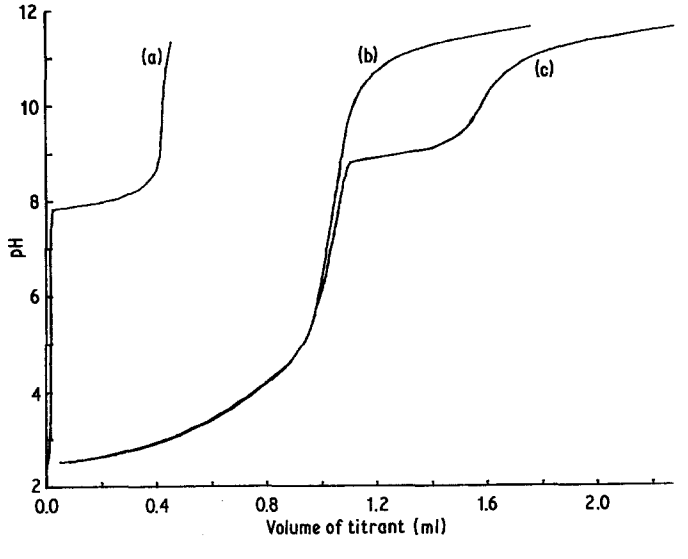

Figure 6 Titration curves of (a) cobalt, (b) serum albumin and (c) serum albumin plus cobalt, details as in text. The sharp discontinuity at pH 7.7 for Curve c corresponds to the onset of precipitation.

of albumin to the amount of metal particles, presumably being related to particle surface area.

In some early experiments in which the reaction was allowed to proceed for several days, the solutions became turbid, indicating that the protein was denatured. It is possible that the mechanism of corrosion enhancement involves the reduction of disulphide bonds by the metal and their subsequent re-oxidation by oxygen. This would, over a period of time, lead to polymer formation and precipitation [22].

The spectral results indicate that cobalt ions may cause some change in the aggregation of albumin, but the effect is very slight. There was no evidence that cobalt was bound to the protein in such a way as to change the spectrum of the metal which would be expected to occur if the cobalt ion were transferred from its normal high-spin octahedral complex with water to a nitrogen-bonded complex. It appears that, at neutral pH, whatever complexes may be formed, they are weak and probably of an electrostatic nature.

The titration results also show that although the binding of cobalt to serum albumin leads to no major changes in its structure, it does significantly modify the behaviour of the metal in solution. In the absence of protein, cobalt hydroxide precipitates at pH 7.7 while in its presence the hydroxide, which does not precipitate, does not start to form until the pH reaches 8.9. There is no sign in the titration curve that the cobalt is specifically bound to the protein except for the 10% possibly bound to histidine. However, the albumin has a net negative charge so the cobalt may be loosely associated with it, sufficiently closely to upset the metal hydroxide reaction. The lack of precipitate could be due to the stabilization of a colloid suspension. The colour change is the same as that for the formation of hydroxide in the absence of protein, implying that the co-ordination of the metal is the same.

The results, therefore, show that albumin, the major protein in serum, may greatly enhance the corrosion of cobalt. The mechanism by which it does this is not entirely clear, but it does not depend upon stoichiometric reactions. It is probably related more to the promotion of cathodic rather than anodic reactions and appears to be the result of a catalytic effect of the protein. It has been shown by Weinzierl and Webb [23] that serum can dissolve nickel and cobalt, but this implied the formation of stoichiometric complexes. It is possible that their results were due to a shift in pH as the metal dissolved giving a metal hydroxide–protein–complex. The carcinogenicity of the metal appeared to be closely related to the formation of this complex. The present results indicate that if the metal is slowly corroding and is not heavily encapsulated, then the ions released will be in full equilibrium with serum and to be distributed systematically around the body.

The extrapolation of these results to the more clinical situation where complex cobalt–chromium based alloys are used is not easy. Obviously the corrosion of these alloys will depend on the protection afforded by the chromium. If the oxide layer breaks down for any reason, we might expect cobalt to be released rapidly in the presence of serum. Dobbs and Minski [15] have shown that levels of chromium are raised locally while the systemic level of cobalt is increased. This is consistent with the present observations and the known ability of chromium to bind irreversibly to proteins.

The potentiostat results broadly support the early work on the electrochemistry of cobalt by Georgi [24] but, as Fig. 3 shows, little consistent difference was noted between the various conditions. As predicted, therefore, the potentiostat is less suited to monitor the changes in corrosion rates under these conditions than is the pH state. Since the effect of albumin is mainly upon the oxygen dependant oxidation, it is possible that the role is to facilitate the reduction of oxygen rather than the oxidation of the metal, in which case the potentiostat would not be expected to show any major effects since it monitors only the anodic process.

The implications of the enhancement of metallic corrosion by proteins are quite clear in the context of biomedical applications. It is also possible that such an effect is important in other areas where proteins contact metals, such as in the corrosion of off-shore structures through fouling by micro-organisms and in the reaction vessels used in current biotechnology processes.

6. Conclusions

It is clear that the corrosion of cobalt in aqueous saline solution is considerably enhanced by the presence of the protein serum albumin. The similarity between the effect with albumin and that found with another chelating agent, potassium tartrate, would suggest that binding of the cobalt to the protein is an important step in the process,

but the non-equivalence between the amount of metal dissolved and the amount of protein available indicate that the binding is reversible and that the protein is acting as a catalyst once adsorbed onto the metal surface.

Acknowledgements

The results reported in this paper represent part of a programme of work supported in parts by grants from both the Medical Research Council (G977/237/S) and the Science and Engineering Research Council (GRA63498), whose assistance we wish to acknowledge.

References

1. D. F. WILLIAMS and R. ROAF, "Implants in Surgery" (W. B. Saunders, London, 1973).
2. D. C. MEARS, *Int. Metall. Rev.* **22** (1977) 119.
3. D. F. WILLIAMS, *Ann. Rev. Mater. Sci.* **6** (1976) 237.
4. *Idem*, "Fundamental Aspects of Biocompatibility" Vol. I (CRC Press, Boca Raton, 1981) p. 11.
5. T. P. HOAR and D. C. MEARS, *Proc. Roy. Soc. London, A* **244** (1966) 486.
6. D. F. WILLIAMS and G. MEACHIM, *J. Biomed. Mater. Res. Symp.* **5** (1973) 1.
7. A. B. FERGUSON, Y. AKOHOSHI, P. G. LAING and E. S. HODGE, *J. Bone Jt. Surg.* **44A** (1962) 317.
8. G. MEACHIM and D. F. WILLIAMS, *J. Biomed. Mater. Res.* 7 (1973) 555.
9. D. F. WILLIAMS and D. ADAMS, *J. Clin. Path.* **29** (1976) 657.
10. A. McNAMARA and D. F. WILLIAMS, *Eng. Med.* **10** (1981) 17.
11. *Idem, Biomaterials* **2** (1981) 33.
12. G. C. F. CLARK, A. McNAMARA and D. F. WILLIAMS, Abstract of First World Biomaterials Congress, Vienna, April 1980.
13. C. P. SHARMA, G. C. F. CLARK and D. F. WILLIAMS, *Eng. Med.* **10** (1981) 11.
14. G. C. F. CLARK and D. F. WILLIAMS, *J. Biomed. Mater. Res.* **16** (1982), to be published.
15. H. DOBBS and M. J. MINSKI, *Biomaterials* **1** (1980) 193.
16. G. D. WINTER, in "Biocompatibility of Implant Materials", edited by D. F. Williams (Sector, London, 1976) p. 28.
17. E. M. EVANS, M. A. R. FREEMAN, A. J. MILLER and B. VERNON-ROBERTS, *J. Bone Jt. Surg.* **56B** (1974) 626.
18. J. C. HEATH, *Brit. J. Cancer* **14** (1960) 478.
19. T. RAE, in "Biocompatibility of Implant Materials", edited by D. F. Williams (Sector, London, 1976) p. 55.
20. Y. MORIN and P. DANIEL, *Canad. Med. Assoc. J.* **97** (1967) 926.
21. C. F. BEES and R. E. MESMER, "The Hydrolysis of Cations" (Wiley, New York, 1976) p. 238.
22. P. C. ALLEN, E. A. HILL and A. M. STOKES, "Plasma Proteins" (Blackwell, Oxford, 1973) p. 182.
23. S. M. WEINZIERL and M. WEBB, *Brit. J. Cancer* **26** (1972) 279.
24. K. GEORGI, *Z. Electrochem.* **39** (1933) 213.

Received 22 September
and accepted 4 November 1981