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RESEARCH PROJECT INITIATION

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Date: 18 April 1973

Project Title: **"In Vitro Study of the Corrosion Release of Metallic Ions
from Medical Implant Materials"**

Project No: **E-19-614**

Principal Investigators: **Dr. R. F. Hochman and Dr. M. Marek**

Sponsor: **Public Health Service**

Agreement Period: From April 1, 1973 Until May 31, 1973

Type Agreement: **Internal Grant**

Amount: **\$4,210**

Reports Required: **Summary Report to be submitted to the Biomedical Sciences
Support Grant Committee by 8/1/73.**

Sponsor Contact Person (s):

**Dr. J. W. Crenshaw, Jr.
Chairman, Biomedical Sciences
Support Grant Committee
School of Biology
Campus**

Assigned to: Chemical Engineering

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GEORGIA INSTITUTE OF TECHNOLOGY

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RESEARCH PROJECT TERMINATION

Date: September 21, 1973

Project Title: In Vitro Study of the Corrosion Release of Metallic Ions from Medical Implant Materials

Project No: E-19-614

Principal Investigator: Dr. R. F. Hochman & Dr. M. Marek

Sponsor: Public Health Service - Biomedical Sciences Support Grant

Effective Termination Date: 5/31/73

Clearance of Accounting Charges: N/A - all funds expended

Grant/Contract Closeout Actions Remaining: Annual Expenditure Report

See G-32-604 (PRIME)

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In Vitro Study of the Corrosion Release of Metallic Ions
from Medical Implant Materials

By

Robert F. Hochman and Miroslav Marek
School of Chemical Engineering

FINAL REPORT

Project E-19-614

July 31, 1973

Georgia Institute of Technology
Atlanta, Georgia

TITLE:

In Vitro Study of the Corrosion Release of Metallic Ions from Medical Implant Materials.

CO-INVESTIGATORS:

Dr. Robert F. Hochman, Professor, Associate Director for Metallurgy, School of Chemical Engineering

Dr. Miroslav Marek, Postdoctoral Research Fellow, School of Chemical Engineering

PURPOSE:

The purpose of the proposed research was to study the identity of the metallic ions released from medical implants when exposed to simulated body fluids, and to measure the rate of the release. This was a preliminary study which is expected to be followed by a combined in vivo - in vitro investigation of the relationship between corrosion of metallic implants and tissue reactions.

BACKGROUND:

Materials commonly used for orthopedic implants - stainless steel, cobalt-chromium alloys, and titanium - are generally resistant to corrosion attack in the environment of the body. However, interactions occur which result in a release of metallic ions into the surrounding tissues. This may cause adverse reactions such as inflammation and pain, which may necessitate a premature surgical removal of the implant. It was suggested that the toxicity of heavy metals might be associated with inhibition of enzymes, prevention of diffusion through cell membranes, and the breakdown of lysozymes (1). The presence of corrosion products in tissues surrounding an implant may be responsible for persistent infection and pain that sometimes follow metallic

implantation. There is also evidence that a relationship exists between the presence of metallic ions in the tissues and lowering of the amount of antibodies, resulting in a lowering of the defensive potential of the body or organs.

The corrosion resistance of the implant materials is related to the formation of a passive layer on the metal surface. A release of metallic ions into the environment is due to two types of a corrosion interaction:

- (a) The passive corrosion rate, which is essentially the rate of dissolution and re-formation of the passive film. Although the rate is usually quite low, the amount of metallic ions released over a long period of time may become significant. The process may become accelerated due to galvanic effects if dissimilar materials are present, and is affected by environment variables.
- (b) Localized corrosion attack. This phenomenon results in high corrosion rates in localized areas and a significant local accumulation and release of corrosion products, which often leads to severe tissue reactions. Several forms of localized corrosion have been observed on orthopedic implants removed from patients, such as crevice corrosion, pitting, and fretting corrosion.

Ferguson et al (2) reported the concentration of trace metals in animal muscle adjacent to metal implants. Laing et al (3) made a comprehensive study of the histology of the rabbit muscle adjacent to implants of a wide variety of metals and alloys and its relationship to the concentration of trace elements in the muscle. They stated that the tissue reaction was in general proportional to the amounts of metallic ions released; it was also strongly dependent on the identity of the ions, ranging from violently inflammatory reaction caused by nickel and cobalt to little reaction to titanium and aluminum.

EXPERIMENTAL PROCEDURES:

In this work tests were made on type 316L implant-grade stainless steel and a cobalt-chromium-molybdenum implant alloy (Zimaloy). Two types of experiments were performed: (A) Exposure of the implant materials to a 3.5% saline solution under free-corrosion conditions. (B) Exposure of electrodes of implant material to a 3.5% saline solution at an impressed current of constant intensity.

The solutions were analyzed for the presence of metallic ions both qualitatively and quantitatively before and following the exposures. Atomic absorption spectrophotometry and differential pulse stripping polarography were used as analytical methods.

Experiment A.

To obtain a high amount of released ions in a short time it was necessary to use a large metal surface/solution volume ratio. This was achieved by using shavings of the implant material (obtained by cutting on a lathe), which was covered with the solution during the exposure. The experimental set-up is illustrated in Figure 1. The solution was continuously aerated by bubbling wet air through it; a reflux condenser prevented loss of the solution. The temperature was kept at 37°C (body temperature) by a constant-temperature bath. Acidity of the solution was determined at the beginning and at the end of the exposure. Both stainless steel and a cobalt-chromium alloy were tested. Test parameters are summarized in Table 1.

Experiment B.

For this experiment a cell illustrated in Figure 2 was built. It was made of methyl-methacrylate and has two electrode compartments which are separated by a membrane of porous glass. The membrane prevents mixing

of the species in the two compartments. Identical material was used for both electrodes. The edges and back sides of the electrodes were covered with epoxy. The surface area of the uncovered front side was 25 cm². The solution in both compartments was continuously aerated by bubbling wet air through it. The cell was partly submerged in a constant-temperature bath kept at 37° C. The electrodes were connected to a constant current source and to an electrometer, as shown schematically in Figure 3.

At the beginning of the experiment the open circuit potential difference between the electrodes was measured. The current was then applied and held constant. The potential difference between the electrodes was measured periodically. Following the exposure both the anolyte and the catholyte were analyzed by atomic absorption spectrophotometry and by differential pulse stripping polarography. The solution was then replaced with a fresh one and the experiment was continued.

Only stainless steel electrodes were used in this experiment because cobalt-chromium material in suitable form was not available at this time. Test parameters for this experiment are also summarized in Table 1.

RESULTS:

The results of solution analyses are summarized in Table 2. Determination of the following elements was made: Fe, Cr, Ni, Mn, Co. Tests for molybdenum were unsuccessful because of technical difficulties which were not resolved in the short time available.

The potential-difference vs. time data for experiment B are presented in Figure 4. As indicated on the graph there was an open-circuit potential difference of 120 millivolts between the two stainless steel electrodes. In the first two tests the current was applied in such a direction that the

potential difference decreased or even changed sign. In the third test the applied current increased the potential difference.

The reason for the high open-circuit potential difference was not found. Both electrodes were machined from the same plate and were identically prepared. Inhomogeneity is suspected but has not been positively identified.

The evaluation of the release of ions into the solutions was hampered by the presence of impurities in the original solution. Although a high purity sodium chloride was used, the amount of metallic impurities in the solution was high enough to prevent detection of small amounts of released ions (see results of the analysis of the unused solution in Table 2).

The results presented in Table 2 are for clear solutions without visible precipitates only. There was a substantial amount of corrosion products precipitated in the solutions of experiment A. These were rich in iron in case of the solution on stainless steel, and in cobalt in case of the cobalt-chromium alloy. A quantitative analysis was not attempted. Solid corrosion products were also observed in the third test of the experiment B which involved higher impressed current and a large potential difference.

DISCUSSION:

The set-up in experiment A represents a rather severe corrosion test; the use of metallic shavings creates numerous differential cells so that the test probably closely simulates localized attack rather than uniform corrosion of the implant. Formation of differential cells involves localized changes of pH and concentration which greatly affect the corrosion processes.

The experiment B, in which an external current was impressed on the electrodes, simulated a condition under which the potential of the implant is changed from the natural value. This may be due to a contact with another metal of different nobility; however, the observed potential difference between the two stainless steel electrodes indicates that inhomogeneity of the material can result in a significant acceleration of the corrosion attack even on a single implant.

The results of the analyses of the solutions can be best evaluated in comparison with the composition of the alloy. Such a comparison, on a percentual basis, is presented graphically in Figure 5 for the stainless steel and in Figure 6 for the cobalt-chromium alloy.

The comparison in Figure 5 shows that the relative amounts of ions released into the solution from stainless steel in the experiment A were generally consistent with the composition of the alloy. The difference is in a somewhat larger proportion of iron and a smaller one of chromium in the solution. This difference might have been substantially higher if the precipitates were taken into account, since the indication was that they were rich in iron. These results are in general agreement with the potential-pH diagrams of the elements involved (4). When acidity increases locally as a result of hydrolysis of the corrosion products conditions for active dissolution of iron may be reached; chromium, on the other hand, has a more limited active region and is thus more resistant to the attack.

Substantially different results were obtained in the experiment B, when the solution was found to be much richer in nickel than in any other element, especially in tests with smaller applied current (tests B1 and B2). The evaluation is difficult because the potential was not measured with respect to any standard. The potential-pH diagrams of iron, nickel and

chromium show, however, that at the pH of the solution a potential change in the anodic direction results in passivation of iron while nickel is still partly active; at the same time chromium is quite passive and forms an oxide layer on the surface of the alloy, which limits the corrosion rate. At a higher impressed current (test B3) the electrode potential might have reached the value of the pitting potential and iron was attacked.

The results on the cobalt-chromium alloy (Fig. 6) show the corrosion release to be in general accord with the proportion of the elements in the alloy. The amount of chromium is, however, again somewhat lower, and those of nickel and iron are higher, in agreement with the arguments presented above for stainless steel.

It is interesting to compare these results with the data reported by Laing et al (3) on the analysis of tissues around implants in rabbits. For stainless steel Laing et al reported about equal amounts of iron and chromium, which were about twice that of nickel. For the cobalt-chromium-molybdenum alloy the amount of chromium was again comparable to that of cobalt. These results are at variance with the in vitro results presented here, and the high amounts of chromium are difficult to explain. However, the data spread in the results of Laing et al is so large that a quantitative comparison is difficult. Still, the high concentration of chromium found in tissues is worth attention, because it may be due to complexing in the tissues which does not occur in the simple saline solution.

CONCLUSIONS:

Corrosion release of metallic ions from implant-grade stainless steel and a cobalt-chromium-molybdenum alloy into a sodium chloride solution was

determined by analyses of the saline solutions to which the metals were exposed. In the experiment in which metallic shavings were exposed to a small amount of solution the proportion of the ions in the solution was found to be comparable to that in the alloys, except for a lower chromium content. It is suggested that this is due to a higher resistance of chromium to a localized attack because of a smaller active region in the potential-pH diagram compared to the other elements.

In the case of stainless steel electrodes, polarized by an impressed current, the solutions were consistently rich in nickel. This might be explained by the difference in passivation characteristics between iron and nickel. More precise potential data are necessary for a closer evaluation.

RECOMMENDATIONS:

The work reported here was an exploratory study under conditions of severely limited experimental time. A more systematic study of the corrosion release of ions from metallic and ceramic implant materials should be initiated with experiments simulating free corrosion, galvanic corrosion, and localized corrosion. Electrolytic purification of the solutions is necessary to make possible detection of small amounts of released ions. Further steps should include variations of the environment and animal studies with implants under controlled corrosion conditions.

REFERENCES:

1. D. C. Mears. J. Bone Joint Surg., 48B, 567 (1966).
2. A. B. Ferguson, P. G. Laing, and E. S. Hodge. J. Bone Joint Surg., 42A, 77 (1960).
3. P. G. Laing, A. B. Ferguson, and E. S. Hodge. J. Biomed. Mater. Res., 1, 135 (1967).
4. M. Pourbaix: "Atlas of Electrochemical Equilibria". Pergamon Press, N. Y. (1966).

TABLE 1

Test Parameters

All Tests:

Solution: 3.5 % NaCl aqueous solution
Temperature: 37° C

Test A1:

Material: 316L stainless steel (Intramedullary pin)
Nominal composition Cr 17.0-20.0%, Ni 10.0-14.0%
Mo 2.0-4.0%, C 0.08% max., Mn 2.0% max., Si 0.75% max.,
balance Fe
Weight of Metal: 132 grams
Volume of Solution: 52 milliliters
Exposure: 400 hours
Initial pH: 6.4
Final pH: 6.85

Test A2:

Material: Zimaloy (hip joint prosthesis)
Nominal composition Cr 27.0-30.0%, Mo 5.0-7.0%,
Ni 2.5 % max., Fe 0.75 % max., C 0.35% max., Si 1.0% max.,
Mn 1.0% max., balance Co
Weight of Metal: 30 grams
Volume of Solution: 100 milliliters
Exposure: 260 hours
Initial pH: 6.4
Final pH: 6.8

Tests B1, B2, B3:

Material: 316 stainless steel (0.25" plate)
Nominal composition Cr 16-18 %, Ni 10-14%, Mo 2.0-3.0%,
C 0.10% max., Mn 2.0% max., Si 1.0% max.,
balance Fe
Electrode Surface: 25 cm² (each electrode)
Volume of Solution: 35 milliliters (each compartment)
Impressed Current: B1 & B2 : 5 x 10⁻⁶ amps
B3: 5 x 10⁻⁵ amps
Exposure: B1 : 100 hours
B2 : 150 hours
B3 : 50 hours

TABLE 2

Results of Solution Analyses
(all values in ppm)

<u>Test</u>	<u>Fe</u>	<u>Cr</u>	<u>Ni</u>	<u>Mn</u>	<u>Co</u>
Unused solution	0.10	0.02*	1.6	0.01*	0.12
Test A1	12.90	1.08	1.6	0.72	N.D.
Test A2	0.17	0.32	0.2	0.07	1.04
Test B1 - anolyte	0.12	0.25	11.8	0.22	N.D.
Test B1 - catholyte	0.11	0.14	0.4	0.10	N.D.
Test B2 - anolyte	<0.01	0.57	13.2	0.04*	N.D.
Test B2 - catholyte	<0.01	0.43	5.8	0.05*	N.D.
Test B3 - anolyte	5.70	1.30	8.6	0.62	N.D.
Test B3 - catholyte	0.01	0.06*	1.4	0.02*	N.D.

N. D. means not determined.

Note: All results obtained by atomic absorption spectrophotometry except those marked * which were obtained by differential pulse stripping polarography. Results of the tests have been corrected for the amount of ions in the unused solution.

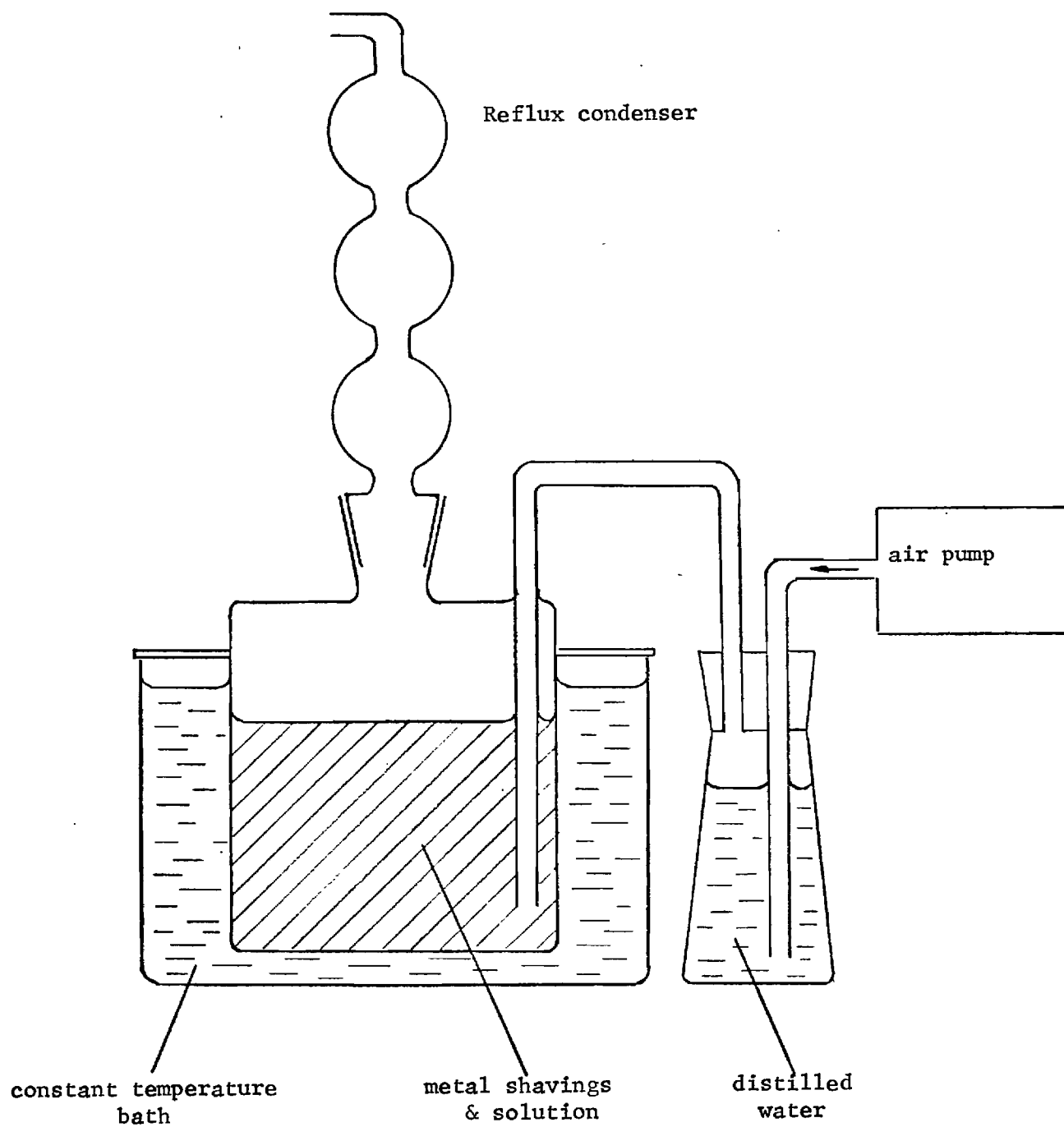


Figure 1. Set-up for Experiment A.

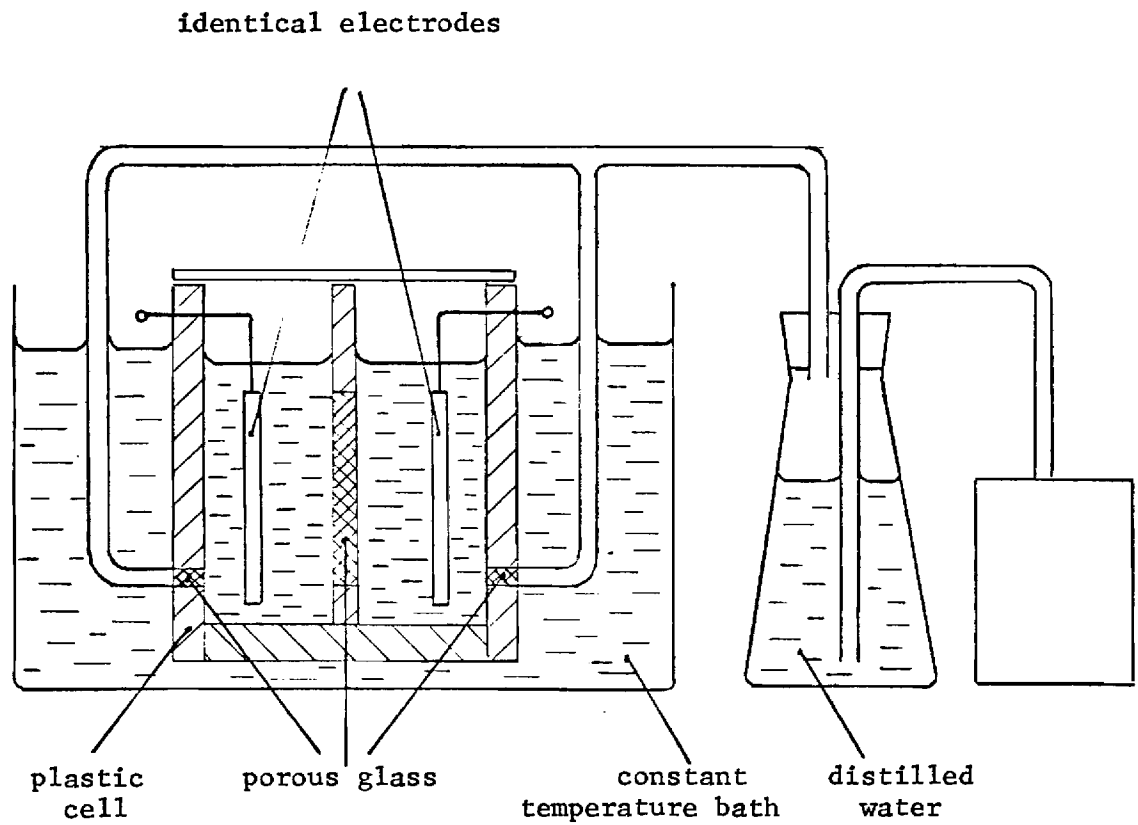


Figure 2. Corrosion Cell for Experiment B.

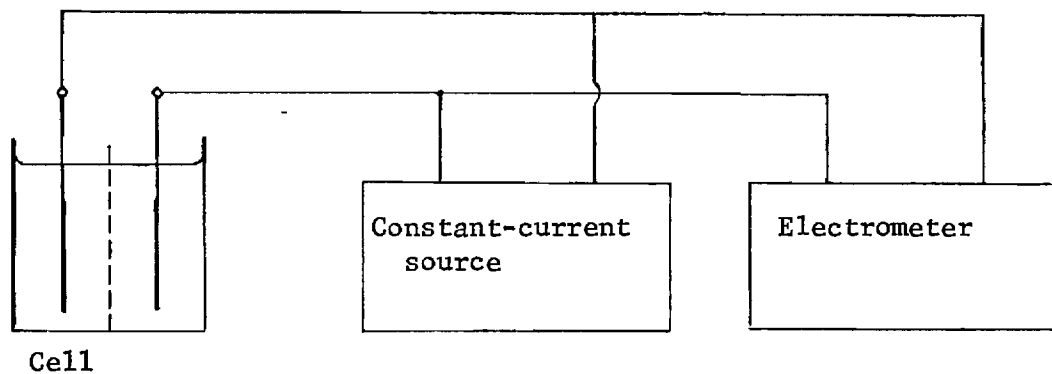


Figure 3. Schematic of the Experiment B Set-up.

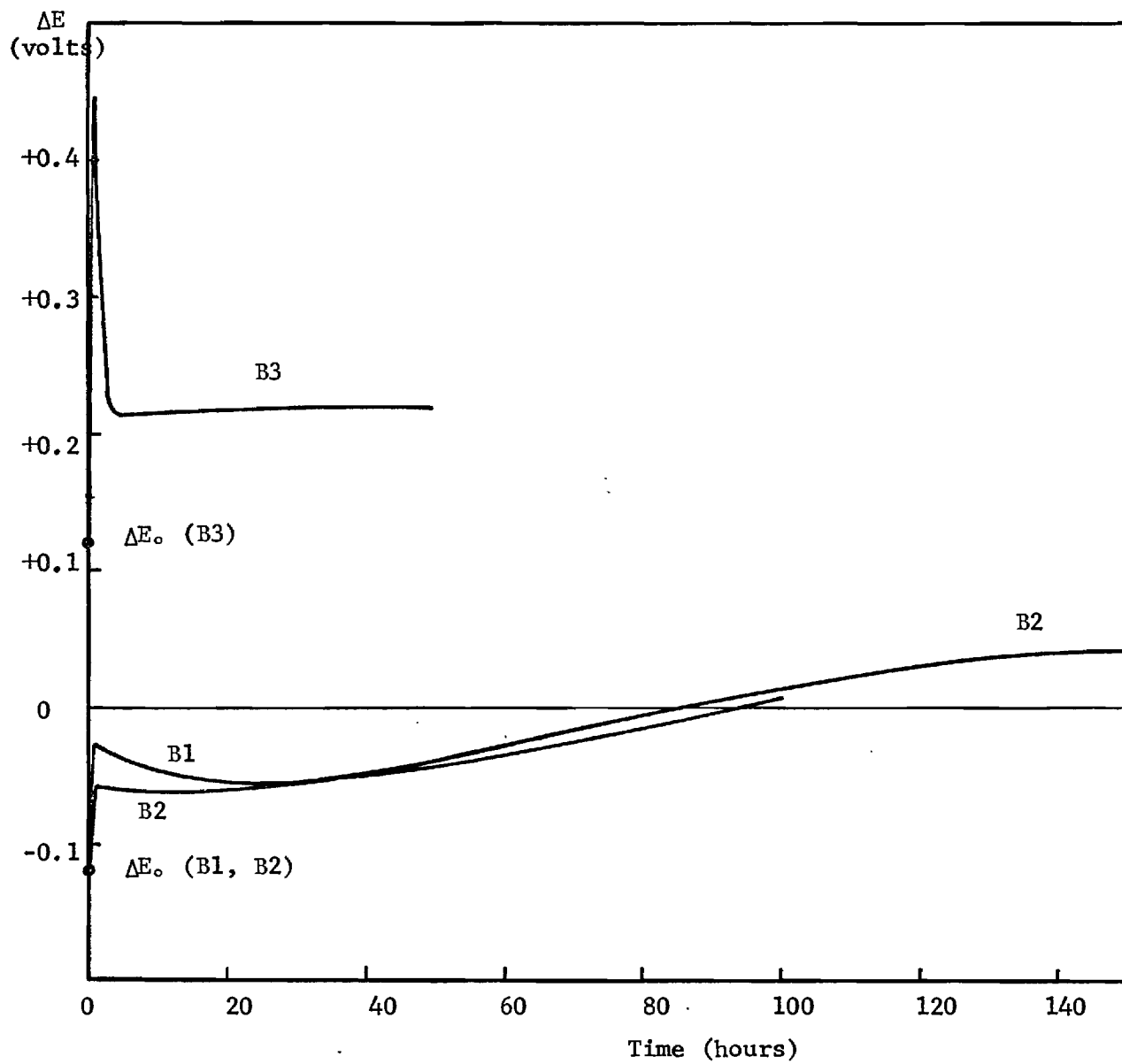


Figure 4. Potential Difference vs. Time Data in Experiment B.

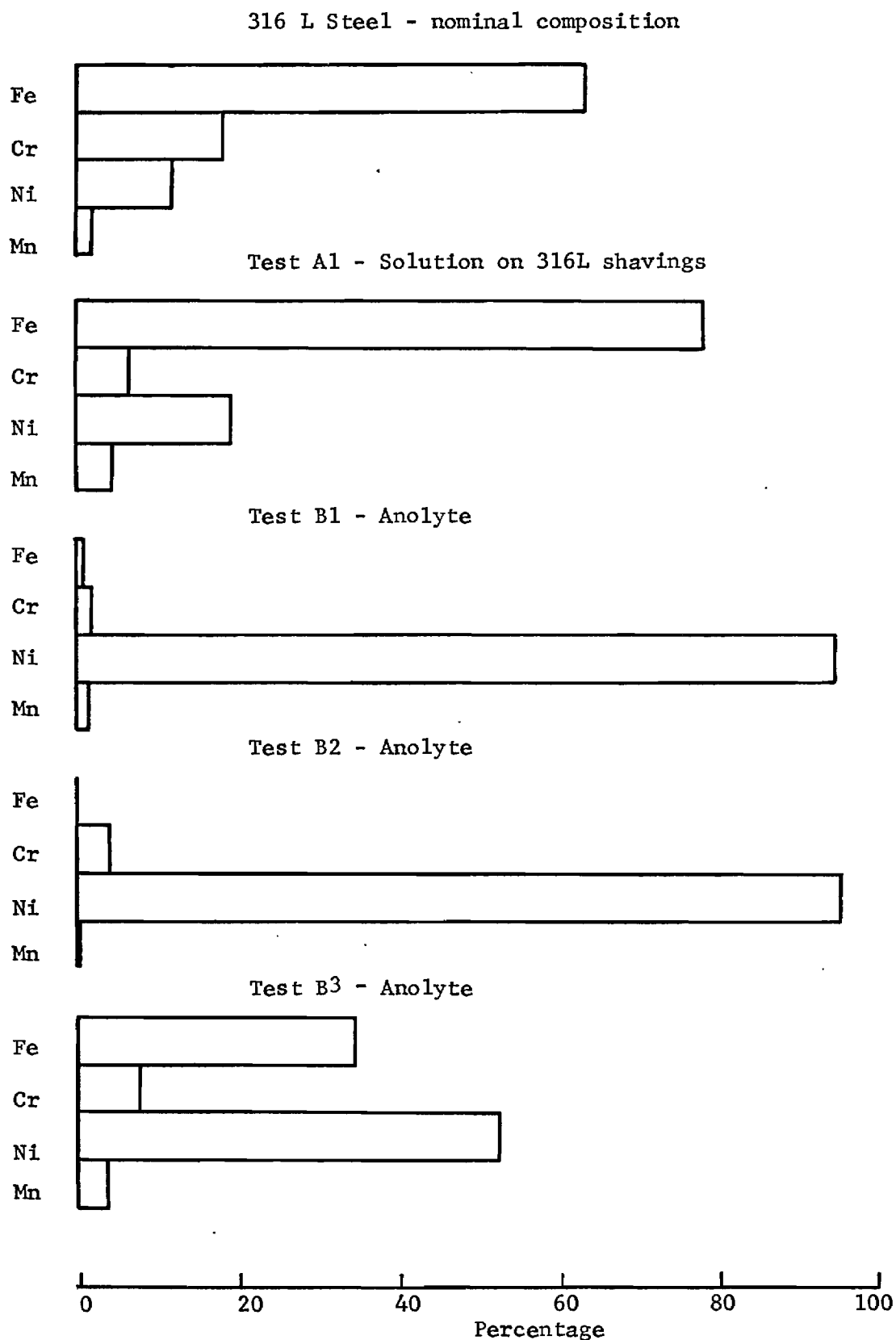


Figure 5. Proportion of Elements Fe, Cr, Ni, and Mn in the Alloy and in the Solution. Alloy: Type 316 Stainless Steel

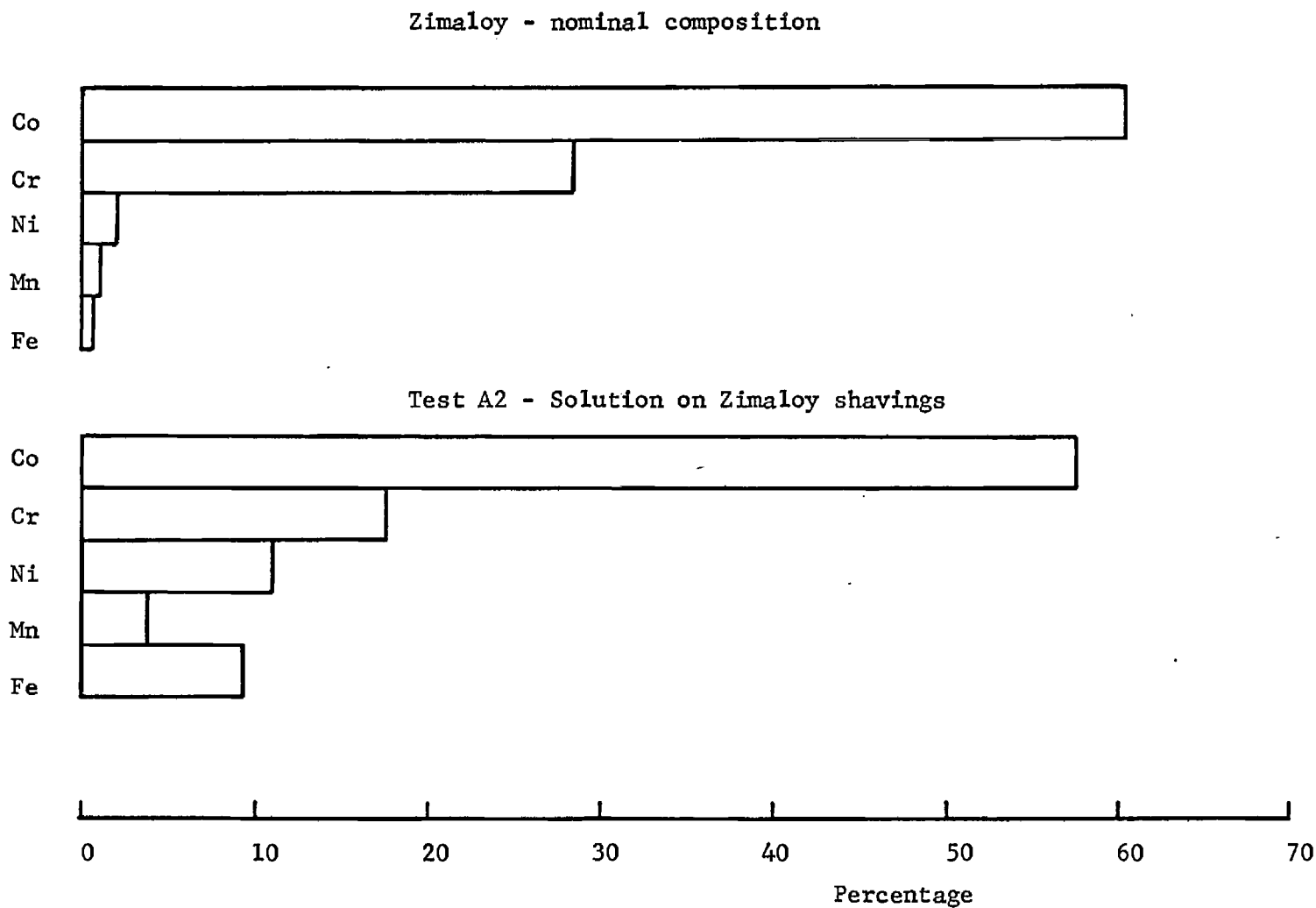


Figure 6. Proportion of Elements Co, Cr, Ni, Fe, and Mn in the Alloy and in the Solution. Alloy: Cast Cobalt-Chromium-Molybdenum (Zimaloy).