Effect of Some Anti-Inflammatory Drugs on The Corrosion Behavior of Implant Biomaterials in Human Body Fluid

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ABSTRACT

The aim of this research is to compare the electrochemical behavior of two surgical implant biomaterials alloys, SS 316L and Co–Cr–Mo alloy in simulated body fluid. This comparison is focused on the influence of presence of three anti-inflammatory drugs, aspirin ($C_9H_8O_4$), paracetamol ($C_8H_9NO_2$), and mefenamic acid ($C_{15}H_{15}NO_2$) with three concentrations of each drug (0.00303, 0.00606, and 0.01212), (0.0086, 0.0172, and 0.0344), and (0.00111, 0.00156, and 0.00201) g/300ml respectively at pH=7.4 and 37^{o}C using electrochemical techniques, potentiodynamic curves and potentiostatic tests.

Influence of these drugs on both biomaterials depends on the formation of organometallic complexes between released metals ions from implant alloys and drugs molecules. The study shows that the drugs behave as inhibitors for SS 316L through the measured corrosion parameters, while gives irregular behavior in the case of Co – Cr – Mo alloy. However, difference between two alloys appear with different affinity of released metal ions to binding with other molecules inside human body.

Keywords: corrosion, SS 316L, Co-Cr-Mo alloy, $C_9H_7O_4$, $C_8H_9NO_2$, $C_{15}H_{15}NO_2$, Ringer's solution.

تأثير بعض الادوية المضادة للالتهاب على سلوك تاكل المواد الحيوية المزروعة في محيط جسم الانسان

الخلاصة

ان الهدف من هذا البحث هو مقارنة السلوك الكهروكيميائي لسبيكتين من المواد الحيوية المزروعة وهي الحديد المقاوم للصدأ (SS 316L) وسبيكة (Co-Cr-Mo) في محلول شبيه بمحلول جسم الانسان. هذه المقارنة تسلط الضوء على تأثير وجود بعض الادوية المضادة للالتهاب وهي الاسبرين والباراسيتول و حامض الميفيناميك (البونستان) وبثلاث تراكيز من كل دواء (0.00303 و0.00606 و0.1212) و(0.0086 و0.0172 و0.0344) و(0.00111 و0.00156 و0.00201) غرام لكل 300 مللتر على التوالي وعند اس هيدروجيني 7.4 درجة حرارة 37 ^{0}م باستخدام التقنيات الكهروكيمائية ومنحنيات تافل واختبارات المجهاد الساكن.

تأثير هذه الادوية على كلا السبيكتين اعتمد على قابلية تكوين المعقدات العضوية المعدنية بين ايونات المعادن المتحررة وجزيئات الدواء. بينت هذه الدراسة بان الادوية المضادة للالتهابات سلكت

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كمثبطات للـــ (SS 316L) ،في حين اعطت سلوكاً غير منتظم لسبيكة (Co-Cr-Mo)، وان الاختلاف بين السبيكتين يظهر من خلال اختلاف ميل ايونات المعدن المتحررة للتأصر مع الجزيئـــات الاخـــرى داخل جسم الانسان.

INTRODUCTION

Anti-inflammatory refers to the property of a substance or treatment that reduces inflammation. Anti-inflammatory drugs make up about half of analgesics, remedying pain by reducing inflammation as opposed to opioids which affect the central nervous system. Many steroids, specifically glucocorticoids, reduce inflammation or swelling by binding to glucocorticoid receptors. These drugs are often referred to as corticosteroids.

Non-steroidal anti-inflammatory drugs NSAIDs), alleviate pain by counteracting the cyclooxygenase (COX) enzyme. On its own COX enzyme synthesizes prostaglandins, creating inflammation. In whole the NSAIDs prevent the prostaglandins from ever being synthesized, reducing or eliminating the pain [1].

Some common examples of NSAIDs are: aspirin, ibuprofen, and naproxen. The newer specific COX-inhibitors, although probably sharing a similar mode of action, are not classified together with the traditional NSAIDs. On the other hand, there are analgesics that are commonly associated with anti-inflammatory drugs but that have no anti-inflammatory effects.

An example is paracetamol, called acetaminophen in the U.S. and sold under the brand name of Tylenol. As opposed to NSAIDS, which reduce pain and inflammation by inhibiting COX enzymes, paracetamol has recently been shown to block the reuptake of endocannabinoids, which only reduces pain, likely explaining why it has minimal effect on inflammation [1].

This study concerned with effect of these drugs on the corrosion of surgical implant biomaterials. The metallic biomaterials are generally used for orthopedic applications, since high-strength components are needed for bone repair and replacement. These materials may be corroded, and they were removed because of tissue irritation or infection produced by the products of corrosion. Compatibility, or the absence of body reaction, is one of the major problems associated with metal implants. Qualitative estimates suggest that implants must corrode at rates of 0.01 mpy or less to avoid the possibility of tissue reaction [2].

In this study some anti-inflammatory drugs were used, the first is aspirin ($C_9H_8O_4$) also known as acetylsalicylic acid is a salicylate drug, often used as an analgesic to relieve minor aches and pains, as an antipyretic to reduce fever, and as an anti-inflammatory medication.

The chemical structure of this drug is shown in Fig. (1a) [3]. The second drug was paracetamol or acetaminophen which is a widely used over-the-counter analgesic (pain reliever) and antipyretic (fever reducer). It is commonly used for the relief of fever, headaches, and other minor aches and pains, and is a major ingredient in numerous cold and flu remedies [4]. The chemical structure of paracetamol is shown in Fig. (1b). The third drug was mefenamic acid is a non-steroidal anti-inflammatory drug used to treat pain, including menstrual pain. It is typically prescribed for oral administration. Mefenamic acid is marketed in the USA as ponstel, and the chemical structure was shown in Fig. (1c)[5].

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There are many studies about the corrosion of alloys as biomaterial in human body fluid by using electrochemical methods include potentiostatic measuring, auger spectroscopy, and impedance spectroscopy in addition to use scanning electron microscope and X-ray spectroscopy to identification the protective and type of corrosion that can be occur [6-12].

On other hand, LeeAnn O. Bailey et. al. studied the quantification of cellular viability and inflammatory response to stainless steel alloys[13].

The establishment of quantitative tests of biocompatibility is an important issue for biomaterials development. Therefore, LeeAnn O. Bailey and co-worker developed an in vitro model to measure the pro-inflammatory cytokine production and in this study investigated the cellular responses induced by nitrogenated and 316L stainless steel alloys in both particulate and solid form. Fluorescence microscopy and flow cytometry were used to probe the viability of the population[13].

THE AIM OF THE PRESENT WORK

The goals of this work were to develop improved measurement methods for the quantification of cellular inflammatory responses to biomaterials and to obtain data that leads to an enhanced understanding of the ways in which the body responds to biomaterials. The aim of the current work was to know effect of anti-inflammatory drugs on the corrosion behavior of SS 316L and Co-Cr-Mo alloy in human body fluid at pH=7.4 and Temp.=37^{o}C during measuring the corrosion parameters to calculate polarization resistance (R_p) and corrosion rate (C_R).

EXPERIMENTAL PART

Materials and Chemicals

The used materials in this study were SS 316L and Co–Cr–Mo alloy and the chemical composition are shown in Table (1) and (2) respectively which obtained by Bruker advanced X-ray solutions D8-advance. The human body fluid (HBF) prepared by dissolved tables of Ringer's solution, which obtained from (Germany), in 300 ml of distilled water and then heated until adjusted the pH at 7.4 value. This solution used after cooling at room temperature and then heated to 37^{o}C for corrosion test.

The anti-inflammatory drugs used in this work were aspirin, paracetamol, and mefenamic acid with three concentration of each drug prepared by dissolved certain weight of drugs in 300ml HBF.

To perform corrosion test, SS 316L was cutting to cylinder shape with dimensions of (1.266×10 mm), while Co-Cr-Mo alloy was cutting to cubic shape with dimensions of (1×1 mm), mounting by using 2X-QB hot mounting using phenolic resin in mold and heated up to 140^{o}C under pressure of 3500 – 4000 psi. for 5 – 10 minutes. Suitable provision was made on one side for electrical contact.

The mounted specimens were ground with SiC emery papers in sequence on 120, 180, 220, 320, 500, 800, 1000, and 1200 grit to get flat and scratch- free surface. The specimens were polished using polish cloth and alpha alumina 0.05µm and 0.1 µm then washed with distilled water.

The polished specimens were degreased with acetone trichloroethylene and cleaned in the same solution. The degreased specimens were washed with deionized water, dried and kept in a dissector over a silica gel pad and used for electrochemical investigation. Kroll's reagent containing 45ml of Glycerol, 15 ml of HNO_3 and 30 ml of HCl was used

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for etching the surface of stainless steel 316L for optical observation. While etching solution for Co–Cr–Mo alloys contained 60 ml HCl, 15 ml Water, 15 ml acetic acid, and 15 ml HNO_3 with time of exposure was 30 seconds for the two alloys.

Electrochemical Measurements

Polarization experiments were performed on autolab potentiostat provided with Nova software which allows performing a wide variety of electrochemical techniques as well as sophisticated data analysis and fit and simulation software. Electrochemical standard cell with three electrodes was used, the first was working which represents the SS 316L or Co-Cr-Mo alloys, the second was auxiliary electrode (Pt electrode), and the third was saturated calomel electrode (SCE) as a reference electrode which was connected with electrochemical cell by Luggin capillary. All experiences perform in science of Malaysia University.

Metallographic Examination

In order to obtain useful information about effect of anti-inflammatory drugs on the corrosion behavior of implant biomaterials as well as to show the type of corrosion, the alloy surface was micrographed by using optical microscopy Olympus BX2M, magnification used was 50X.

RESULTS AND DISCUSSION

Potentiodynamic methods were used to evaluate the in vitro corrosion characteristics of SS 316L and Co–Cr–Mo alloys in simulated body fluid (HBF).

Figures (2) to (4) show the polarization behavior of SS 316L in human body fluid in presence of aspirin, paracetamol and mefenamic acid respectively with three concentrations of each drug at simulated human body environment (pH=7.4 and Temp.=37^{o}C).

The cathodic curve corresponding to the lower section of the polarization curve and represents the reduction of oxygen according to the following reaction:

$$O_2 + 2H_2O + 4\bar{e} \rightarrow 4OH^- \ (E=+0.401V) \qquad \ldots(1)$$

Where the main cathodic reaction in neutral (pH=7.4) and basic solution is reduction of oxygen to produce hydroxide ions (OH^-), while in acidic medium the cathodic reactions are reduction of hydrogen:

$$(2H^+ + 2\bar{e} \rightarrow H_2 \ E=0.00V) \qquad \ldots(2)$$

and reduction of oxygen:

$$(O_2 + 4H^+ + 4\bar{e} \rightarrow 2H_2O \ E=+1.229V) \qquad \ldots(3)$$

The anodic curve corresponding to the upper section of the curve which represents the oxidation of metals in SS 316L.

Generally, the presence of drugs shifts the corrosion potential (E_{corr}) to the active direction, where the corrosion potential (E_{corr}) of a material in a certain medium at a constant temperature is a thermodynamic parameter. When (E_{corr}) becomes more negative, the potential of the galvanic cell becomes more positive and hence the Gibbs free energy change (ΔG) for the corrosion process becomes more negative. The corrosion reaction is then expected to be more spontaneous on pure thermodynamic ground and vice versa. It is thus shown that (E_{corr}) value is a measure for the extent of the feasibility of the corrosion reaction on purely thermodynamic basis.

While the corrosion current density (i_{corr}) is a kinetic parameter and represents the rate of corrosion under specified equilibrium condition. Any factor that enhances the

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value of (i_{corr}) results in an enhanced value of the corrosion rate on pure kinetic ground. The rate ($C_{Rmm/y}$) of corrosion in a given environment is directly proportional with its corrosion current density (i_{corr}) in accordance with the relation [14]:

$$C_R\,(mm\ /\ y) = 3.271\ \frac{e}{r} i_{corr}\ .....(4)$$

where $C_R(mm/y)$: corrosion rate in millimeter per year, e: equivalent weight of alloy (g), and ρ: density of alloy (gm/cm^3).

The data listed in Table (3) show that corrosion current density (i_{corr}) shift to the lower value in the presence of drugs than that obtained without addition of drugs. Therefore the values of corrosion rate were also lower in the presence of drugs.

The polarization resistance, R_p, of according electrode is defined as the slope of a potential (E) – current density (i) plot of the corrosion potential (E_{corr}) as [15-16]:

$$R_p = \left(\frac{\partial h}{\partial i}\right)_{T,C} at\ h \to 0 \qquad .....(5)$$

Where $\eta = E - E_{corr}$, is the extent of polarization of the corrosion potential and (i) is the current density corresponding to a particular value of (η). From the polarization resistance, R_p the corrosion current density (i_{corr}) can be calculated as:

$$i_{corr} = \frac{b}{R_p} \qquad ...(6)$$

Where β is a combination of the anodic and cathodic Tafel slopes (b_a, b_c) as:

$$b = \frac{b_a b_c}{2.303(b_a + b_c)} \qquad ...(7)$$

For the general case, by inserting equation (3) into equation (4) one obtains the so – called the Stern – Geary equation [17-18]:

$$R_p = \frac{b_a b_c}{2.303(b_a + b_c) i_{corr}} \qquad ....(8)$$

The data of polarization resistance for SS 316L which listed in the Table (3) indicate that the resistance in presence the three anti-inflammation drugs higher than the resistance in the absence of them.

These results refer to the inhibition action of drugs for corrosion of SS 316L in human body fluid because of producing organometallic complexes between metal ions and drug molecules. Where in the metal ions – mechanisms, biological risks of metal ions include wear debris, colloidal organometallic complexes, free metal ions, and inorganic metal salts or oxides formed.

Organometallic complexes are formed by metal ions binding to proteins. Since proteins are Zwitter ions, most are negatively charged in the body's pH of 7.4. The first successful application of an organometallic compound as a drug is the anti-syphilis drug Salvarsan in 1910.

Some successful examples of organometallic based drugs include the anti-tumor properties of the cisplatin, ferroquine for the treatment of malaria, and the use of

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radioactive Tc compounds as radiopharmaceuticals. The action of metalloantibiotics mimics in the whole living organisms are expected to differ in general from the action of non-metal containing agents and may offer unique research, diagnostic, or therapeutic opportunities. Mixed antibiotics metal complexes possessed better physical properties and are much more effective as chemotherapy agents than their parent antibiotics. Metal ions can be administered in polymeric microparticles, deformable films or microparticles embedded within deformable films [19].

Positively charged metal ions, including iron, cobalt, chromium, and nickel bind to proteins, changing the pH of solutions. Proteins increase corrosion rate of an implant by increasing the dissolution of metals, especially cobalt and chromium. Cobalt and chromium have the same affinity for proteins, but nickel significantly competes for cobalt and chromium binding areas [20]. This mean that the released metal ions from SS 316L stay at electrode surface to form organometallic complexes and then covered the surface and act as protective layer.

This result is in agreement with the results observed by Von et al. [21] who indicated that oxytetracycline at addition levels of 0.01-1.0 mg/ml acts as an anodic corrosion inhibitor when they studied the antibiotic- metal interactions in saline medium. In the other research, Von et al. [22] studied the effect of fused- ring antibiotics on metallic corrosion, where he observed that the variable depended upon the nature of the metal and its surface condition.

Figures (5) to (7) shows the polarization curves of Co-Cr-Mo alloy in human body fluid in presence of aspirin, paracetamol, and mefenamic acid respectively. The lower cathodic section of curves represents the reduction of oxygen to produce hydroxide ions because of neutralization of medium (pH=7.4), while the upper section represents the oxidation of metals in alloy.

Generally, the presence of drugs gives irregular behavior for corrosion potential values (E_{corr}), but shifts the corrosion current density to higher values, therefore the values of corrosion rate were also higher than that obtained before addition of drugs.

The data were listed in Table (4) indicates that the effect of presence three drugs gives irregular behavior of polarization resistance. Depending on the corrosion rate values, we can say that the presence of three anti-inflammatory drugs increases the rate of dissolution of metals in Co-Cr-Mo alloy.

The data of corrosion parameters indicates that the SS 316L has more resistance to corrosion in human body fluid than Co-Cr-Mo alloy in the presence of anti-inflammatory drugs. The causes of this behavior can be interpret by the interactions (affinity) between released metal ions from Co-Cr-Mo alloy and drugs molecules more than that observed from SS 316L.

Also, in Co based alloy, cobalt is transported from tissue to the blood and eliminated in the urine within 48h, while chromium builds up in the tissues and red blood cells [23]. The only ion taken up intracellular by red blood cells following corrosion of alloy is Cr^{6+}, which is then rapidly converted to Cr^{3+}. This phenomenon decreases the concentration of chromium ions at surface and then increases the dissolution of metal atoms.

Morais et al. [24] found that chromium and nickel are retained in bone marrow. Nickel is very small and has a low affinity for blood cells. Cobalt binds to both red blood cells and white blood cells. Although only very small quantities of Cr^{3+} bind to cells, Cr^{6+} binds very strongly to red blood cells and white blood cells [25].

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Fig. (8) shows the microstructure of SS 316L and Co-Cr-Mo alloy in human body fluid before addition of drugs (as received). Figs. (9) to (12) show the microstructure of SS 316L in human body fluid after addition of drugs with and without etching. These figures show the presence of uneven shaped pits and the inhibition action of drugs.

While Figs. (13) to (16) show the microstructure of Co-Cr-Mo alloy in human body fluid after addition of drugs with and without etching. These figures show the presence of uneven shaped pits and the corrosive action of drugs by refining the surface after addition the drugs.

CONCLUSIONS

In presence of anti- inflammatory drugs (aspirin, paracetamol and mefenamic acid) using SS 316L in the surgical implants is more favorite than Co-Cr-Mo alloy because of corrosive action of anti-inflammatory drugs on the Co-Cr-Mo alloy. While these drugs act as inhibitors for corrosion of SS 316L in human body fluid through producing the organometallic complexes at surface and act as protective layer, also in Co-Cr-Mo alloy the rate of transport of ions from tissue to blood increases the rate of oxidation. Therefore the failure in Co-Cr-Mo alloy can occur more than in SS 316L as implant biomaterials.

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Table (1): Chemical composition of Stainless Steel 316L Obtained by XRF.

Element	*C*	*N*	*Mo*	*Ni*	*Mn*	*Cr*	*S*	*P*	*Si*	*Fe*
Wt%	*0.03*	*0.05*	*3.00*	*12.0*	*1.50*	*16.0*	*0.01*	*0.03*	*0.75*	*66.33*

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Table (2): Chemical composition of Co – Cr – Mo alloy obtained by XRF.

Element	*Cr*	*Mo*	*C*	*Si*	*Co*
Wt%	*28.0*	*6.00*	*0.35*	*1.00*	*Remained*

Table (3): Corrosion parameters of SS 316L in Ringer's solution (HBF), corrosion potential (E_{corr}), corrosion current density (i_{corr}), cathodic & anodic Tafel slopes (b_c&b_a), polarization resistance (R_p), and corrosion rate (C_R) in the absence and presence of three anti-inflammatory drugs at pH=7.4 and temperature 37°C.

Drugs	***Conc. (g/300ml)***	***$-E_{corr}$ (mV)***	***i_{corr} ($A.cm^{-2}$)***	***$-b_c$ ($mV.dec^{-1}$)***	***b_a ($mV.dec^{-1}$)***	***R_p (Ωcm^{-2})***	***C_R (mm/y)***
HBF		437	$1.693\ e^{-5}$	075	333	$5.229e^{2}$	$1.752e^{-1}$
Aspirin	0.00303	677	$1.413e^{-8}$	618	162	$2.508e^{6}$	$1.461e^{-4}$
	0.00606	576	$9.021\ e^{-6}$	134	238	$1.251e^{3}$	$9.331e^{-2}$
	0.01212	632	$1.789\ e^{-5}$	137	397	$1.081e^{3}$	$1.851e^{-1}$
Paracetamol	0.0086	632	$6.414\ e^{-6}$	09	222	$1.063e^{3}$	$6.634e^{-2}$
	0.0172	224	$1.022\ e^{-6}$	175	359	$2.112e^{4}$	$1.057e^{-2}$
	0.0344	667	$1.524\ e^{-5}$	189	256	$1.091e^{3}$	$1.558e^{-1}$
Mefenamic Acid	0.00111	671	$4.397\ e^{-6}$	063	102	$5.219e^{2}$	$4.548e^{-2}$
	0.00156	606	$1.11\ e^{-5}$	143	294	$1.341e^{3}$	$1.148e^{-1}$
	0.00201	630	$8.134\ e^{-6}$	157	248	$1.643e^{3}$	$8.414e^{-2}$

Table (4): Corrosion parameters of Co-Cr-Mo alloy in Ringer's solution (HBF), corrosion potential (E_{corr}), corrosion current density (i_{corr}), cathodic & anodic Tafel slopes (b_c&b_a), polarization resistance (R_p), and corrosion rate (C_R) in the absence and presence of three anti- inflammatory drugs at pH=7.4 and temperature 37°C.

Drugs	***Conc. (g/300ml)***	***$-E_{corr}$ (mV)***	***i_{corr} ($A.cm^{-2}$)***	***$-b_c$ ($mV.dec^{-1}$)***	***b_a ($mV.dec^{-1}$)***	***R_p (Ωcm^{-2})***	***C_R (mm/y)***
HBF		677	$6.311e^{-7}$	101	07	$4.859\ e^{3}$	$6.946\ e^{-3}$
Aspirin	0.00303	870	$2.785e^{-5}$	229	079	$2.839\ e^{2}$	$3.065\ e^{-1}$
	0.00606	829	$3.234e^{-5}$	301	131	$5.28\ e^{2}$	$3.522\ e^{-1}$
	0.01212	592	$1.369e^{-6}$	149	137	$6.471\ e^{3}$	$1.491\ e^{-2}$
Paracetamol	0.0086	808	$1.333e^{-5}$	178	084	$4.848\ e^{2}$	$1.467\ e^{-1}$
	0.0172	458	$8.287e^{-6}$	119	395	$2.46\ e^{3}$	$9.121\ e^{-2}$
	0.0344	775	$7.949e^{-6}$	158	094	$8.152\ e^{2}$	$8.748\ e^{-2}$
Mefenamic Acid	0.00111	827	$1.554e^{-5}$	22	115	$7.076\ e^{2}$	$1.71\ e^{-1}$
	0.00156	776	$1.307e^{-6}$	17	107	$6.028\ e^{3}$	$1.438\ e^{-2}$
	0.00201	779	$5.507e^{-6}$	181	096	$1.366\ e^{3}$	$5.998e^{-2}$

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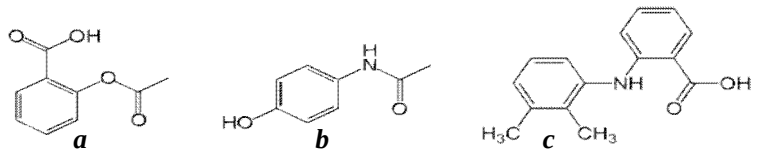

Figure (1): Chemical structure of anti-inflammatory drugs; (a): Aspirin, (b): Paracetamol, and (c): Mefenamic acid.

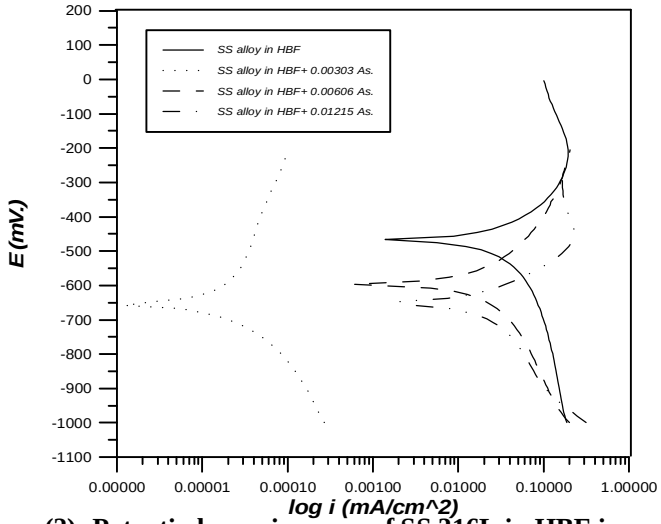

Figure (2): Potentiodynamic curve of SS 316L in HBF in presence of Aspirin with three concentrations at pH=7.4 and Temp. 37°C.

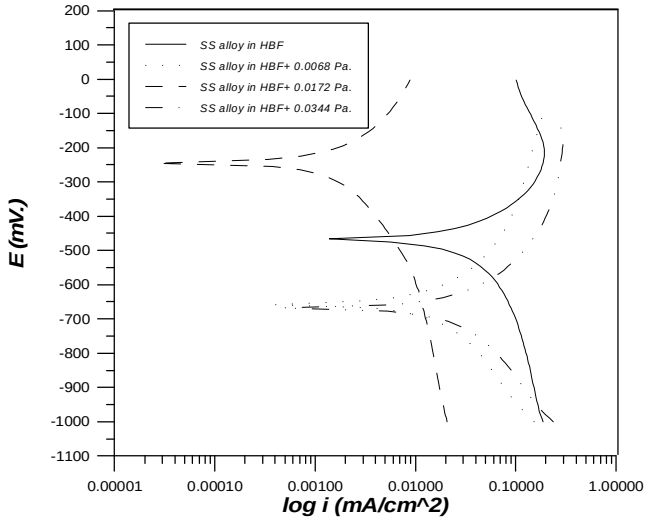

Figure (3): Potentiodynamic curve of SS 316L in HBF in presence of Paracetamol with three concentrations at pH=7.4 and Temp. 37°C.

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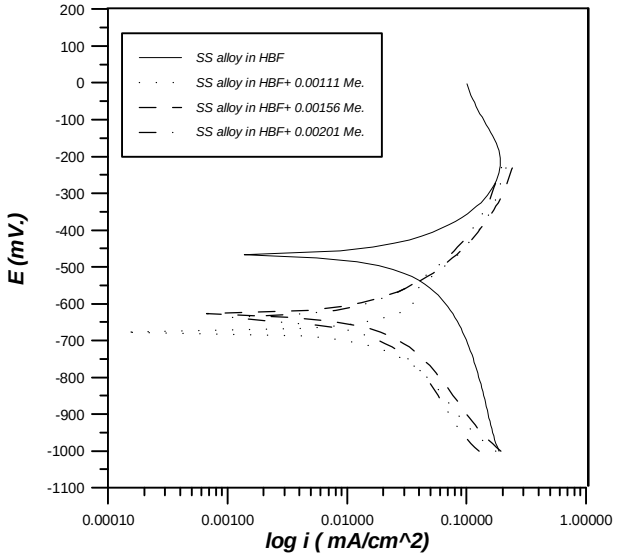

Figure (4): Potentiodynamic curve of SS 316L in HBF in presence of Mefenamic acid with three concentrations at pH=7.4 and Temp. 37^{o}C.

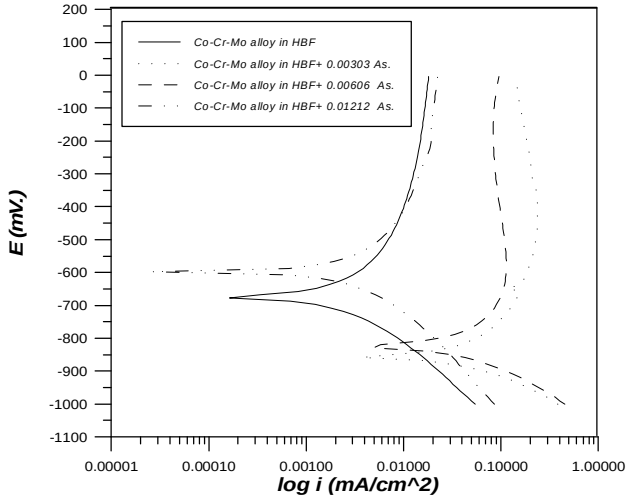

Figure (5): Potentiodynamic curve of Co-Cr-Mo alloy in HBF in presence of Aspirin with three concentrations at pH=7.4 and Temp. 37^{o}C.

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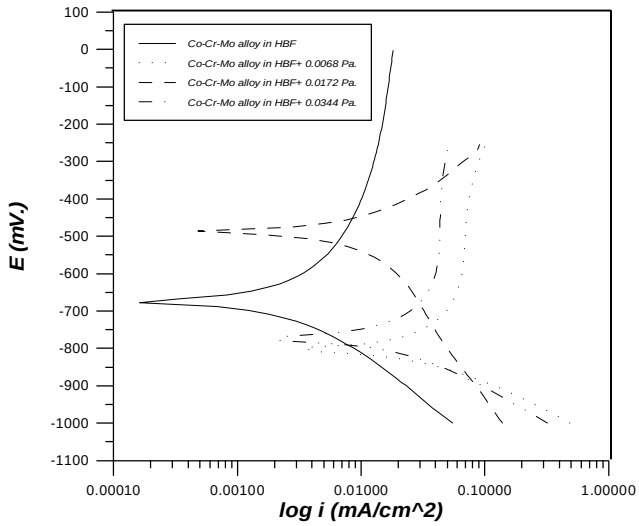

Figure (6): Potentiodynamic curve of Co-Cr-Mo alloy in HBF in presence of Paracetamol with three concentrations at pH=7.4 and Temp. 37°C.

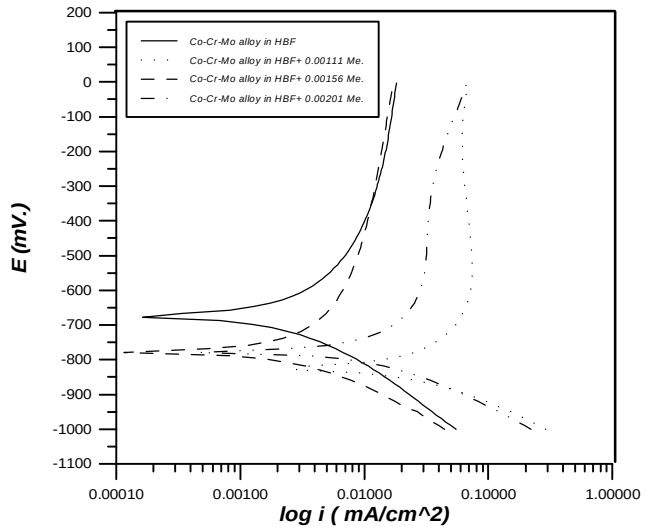

Figure (7): Potentiodynamic curve of Co-Cr-Mo alloy in HBF in presence of Mefenamic acid with three concentrations at pH=7.4 and Temp. 37°C.

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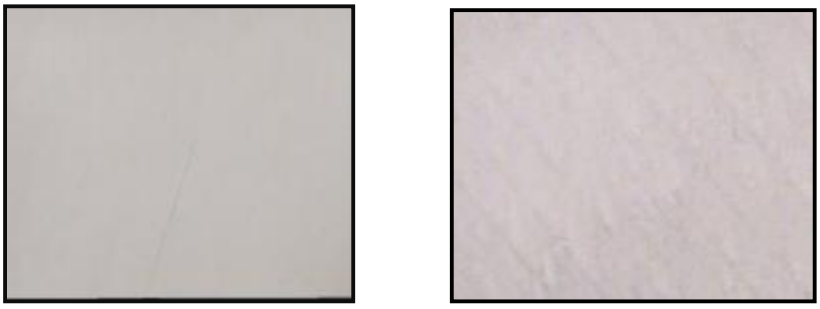
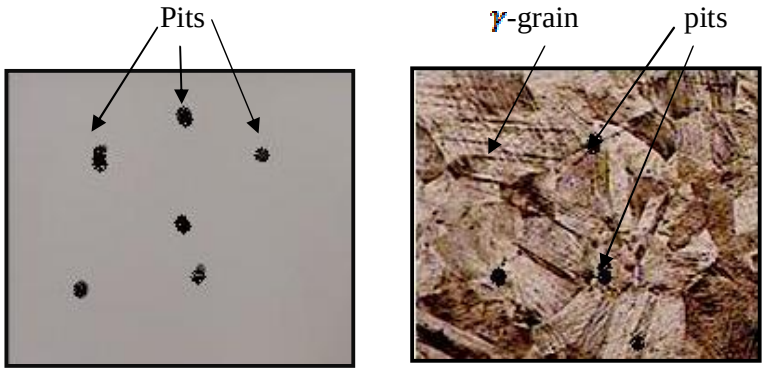


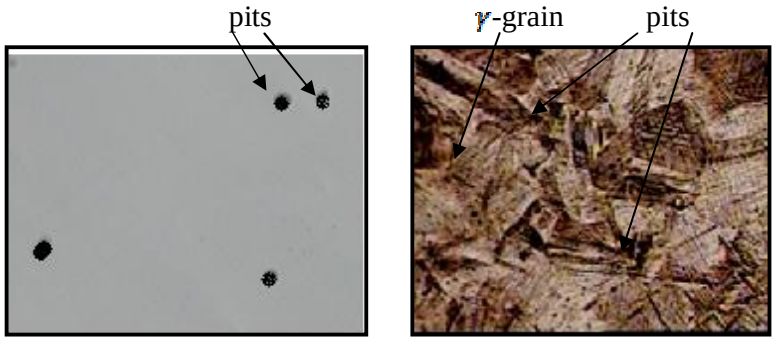
SS 316L **Co-Cr-Mo alloy**

Figure (8): Microstructure of as received implants in HBF (X=50).



(a) **(b)**

Figure (9): Microstructure of SS 316L in HBF (X=50),
(a) after immersion in HBF, and (b) after etching (as polished).



(a) **(b)**

Figure (10): Microstructure of SS 316L in HBF with Aspirin (X=50),
(a) after immersion in HBF, and (b) after etching (as polished).

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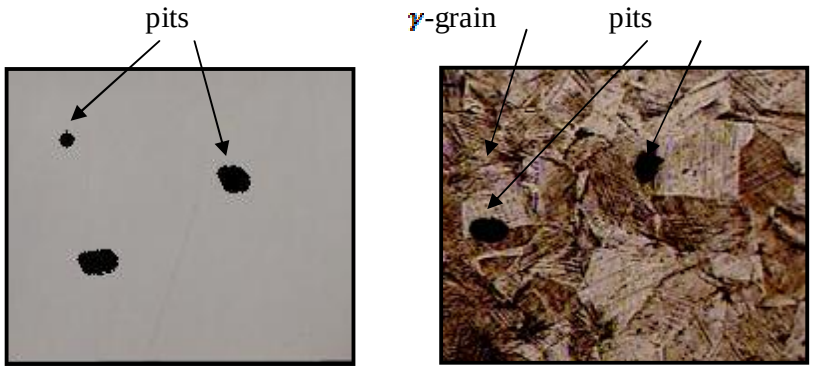
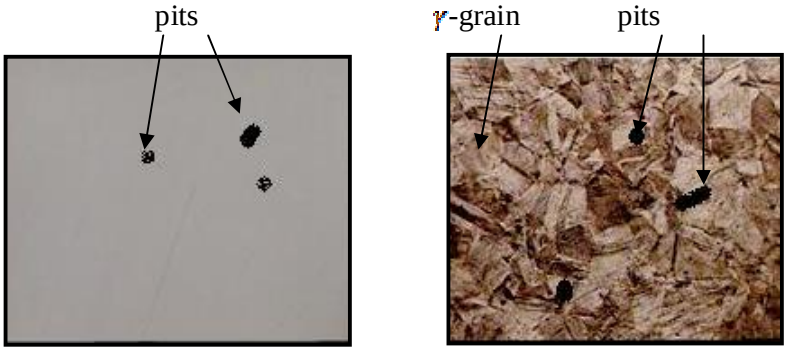


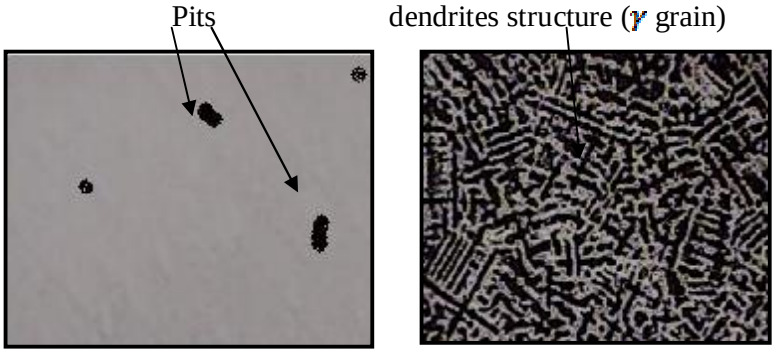
(a) (b)

Figure (11): Microstructure of SS 316L inHBF with Paracetamol (X=50), (a) after immersion in HBF, and (b) after etching (as polished).



(a) (b)

Figure (12) : Microstructure of SS 316L in HBFwith Mefenamic acid (X=50), (a) after immersion in HBF, and (b) after etching (as polished).



(a) (b)

Figure (13): Microstructure of Co-Cr-Mo alloy in HBF (X=50), (a) after immersion in HBF, and (b) after etching (as polished).

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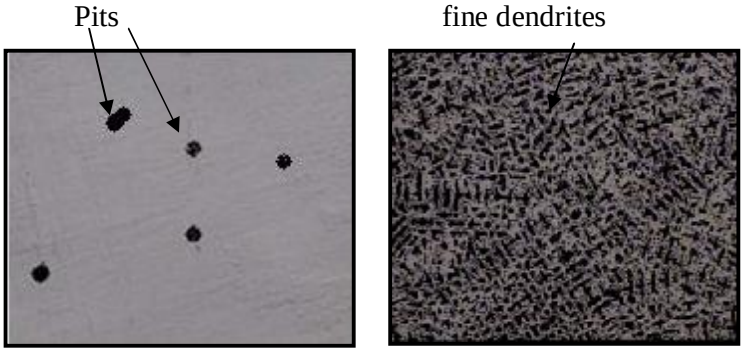
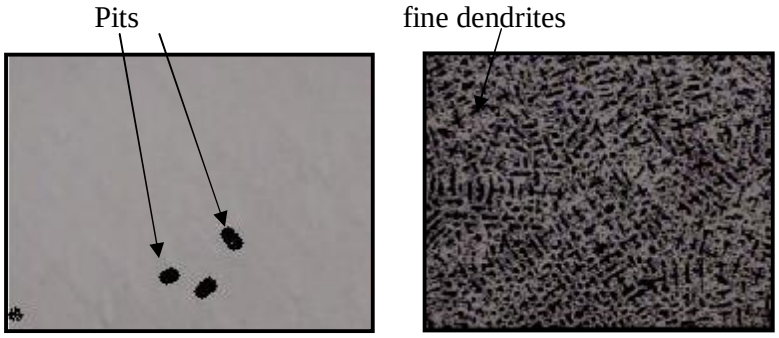


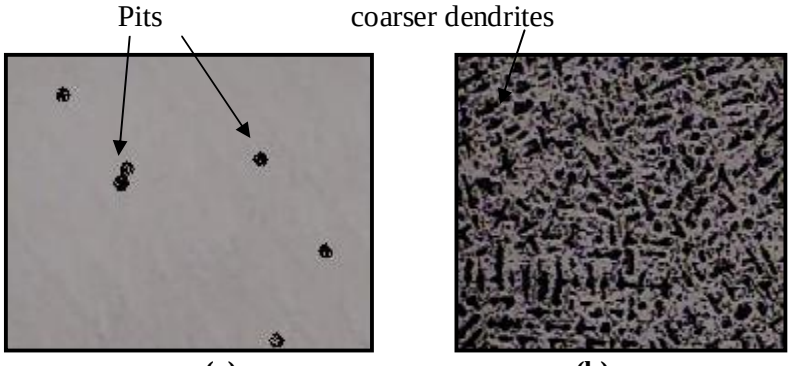
(a) (b)

Figure (14): Microstructure of Co-Cr-Mo alloy inHBF with Aspirin (X=50), (a) after immersion in HBF, and (b) after etching (as polished).



(a) (b)

Figure (15) : Microstructure of Co-Cr-Mo alloy inHBFwith Paracetamol (X=50), (a) after immersion in HBF, and (b) after etching (as polished).



(a) (b)

Figure (16): Microstructure of Co-Cr-Mo alloy inHBF with Mefenamic acid (X=50), (a) after immersion in HBF, and (b) after etching (as polished).

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