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Corrosive effect of the uterine mucosa on the copper IUD

Efecto corrosivo de la mucosa uterina sobre el DIU de cobre

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RESUMEN

El DIU de cobre es un dispositivo intrauterino que actúa mecánica y químicamente para evitar la fertilización del óvulo en el útero materno. En este trabajo se usaron métodos electroquímicos para estudiar la corrosión acelerada de la T de Cu 380A en mucosa uterina en una celda de película delgada, se analizó el ataque corrosivo con microscopía electrónica de barrido, los productos de corrosión por EDS, y se calculó la vida media de la T Cu-380A en el útero materno simulado, encontrándose que la vida media del DIU de cobre es 10 años aproximadamente y los productos de corrosión formados son CuO, Cu_2O, fosfatos, Cu_2S, $CaCO_3$ e hidróxido de cobre ($Cu(OH)_2$) entre otros.

Palabras clave: Corrosión, DIU de Cobre, mucosa uterina, inflamación, productos de corrosión.

ABSTRACT

The copper IUD is an intrauterine device that acts mechanically and chemically to prevent fertilization of the ovum in the mother's womb. In this work, electrochemical methods were used to study the accelerated corrosion of the Cu 380A T in uterine mucosa in a thin film cell, the corrosive attack was analyzed with scanning electron microscopy, the corrosion products by EDS, and the half-life of T Cu-380A in the simulated maternal uterus was calculated, finding that the half-life of the copper IUD is approximately 10 years and the corrosion products formed are CuO, Cu_2O, phosphates, Cu_2 S, $CaCO_3$ and copper hydroxide ($Cu(OH)_2$) among others.

Keywords: Corrosion, Copper IUD, uterine mucosa, inflammation, corrosion products.

1. INTRODUCTION

Reproductive health implies the ability to enjoy a satisfactory sex life, without risks of procreating when the couple decides to do so. For this reason, various contraceptive methods have been used to regulate births. In ancient times concoctions were used, objects placed in the womb, prayers and talismans. For example, the Kahun papyrus made around 1800 BC, discovered by Flinders Petrie in 1889, is considered to be the oldest writing related to contraceptive techniques, in which one of his recipes advised the preparation of pessaries to insert it into the vagina based on crocodile droppings or caps fermented with honey, vegetable gum and acacia branches; Another recipe recommended an irrigation with honey and natural sodium bicarbonate. In the Ebers Papyrus written probably in Thebes found in 1835 BC, a medicated yarn plug moistened with honey was recommended to place it on the woman's vulva [1-4].

Nowadays contraceptive methods are classified as traditional, natural, modern and surgical. Among the modern we have, the barrier, systemic hormonal contraception and intrauterine devices (IUDs) [5]. Richter described the first IUD in 1909 consisting of a silkworm gut ring. Subsequently the silver and gold rings

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were known but their use was discontinued for technical and medical reasons. In the 50s and 60s of the last century, plastic devices were produced that had a certain advantage such as flexibility, safety, less bleeding and pain for the user. These devices were used in the United States and internationally. The plastic IUD that appeared was the Handle of Lippes. Subsequently, attachments such as copper, silver and hormones were added to increase the effectiveness of the IUD [6-8].

In recent decades, several investigations have been carried out related to the behavior of copper IUD ions in simulated uterine fluids [9-17]. At present it is not known with certainty officially why the IUD prevents pregnancy. There are two hypotheses, the first suggests that the dissolution of copper in uterine secretions leads to the inactivation of sperm and the suppression of myometrial contractions; the second establishes that the IUD acts as a foreign body in the uterus and produces an inflammatory reaction similar to the body's response to an infection causing the endometrial lining to become inhospitable for egg implantation [18, 19]. In this work we will study the corrosive effect of the uterine mucosa on the T of Cu 380A using electrochemical methods, we will analyze the type of corrosion by scanning electron microscopy, the corrosion products by EDS and also calculate the dissolution rate that the IUD would have of copper in the womb.

2. MATERIALS AND METHODS

2.1 Materials

Three T Cu model 380A whose chemical composition is 99.99% copper according to ISO 7439 and the Population Council NDA were used. The IUD consists of a T-shaped frame made of low density polyethylene with barium sulfate added for opacity to X-rays (Fig. 1), with a plastic ball at the bottom of the vertical stem to prevent penetration cervical. The device has solid copper rings on each of its two horizontal arms with a surface area of 35 mm^2. The copper wire with a surface of 310 mm^2 is wrapped tightly around the vertical rod, giving a total surface of 380 mm^2 of copper. It also has two small strands of pigmented polyethylene knotted in a small hole in the ball of the stem of the T to provide a means to locate and remove the device [9, 20].

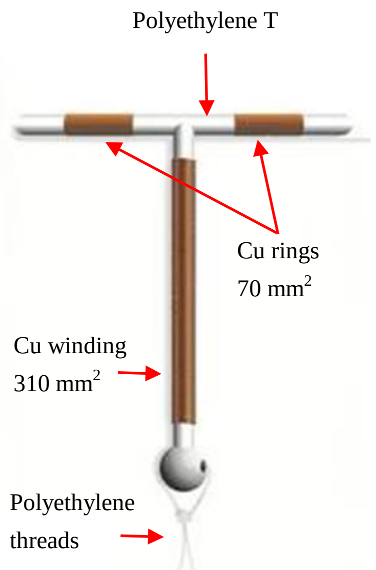

Figure 1. T Cu model 380A, made of a flexible polyethylene body opaque to X-rays.

2.2. Electrolyte

The electrolyte was obtained by manual vacuum aspiration of 10 donor women between 35 and 40 years of age, extracted 3 hours before being used in the electrochemical test. The chemical composition should be similar to that of cervical mucus composed of two phases [21]:

- Aqueous phase, formed by water in a proportion of 90 to 95% and 1% of inorganic salts such as KCl, $CaCl_2$ and NaCl.

• Gel phase, made up of glycoproteins called mucins and high molecular mass biomolecules.

2.3. Electrochemical cell

It is made up of a platinum ring 20 mm in diameter and 1 mm thick connected to the reference electrode through a salt bridge. The counter electrode was a platinum wire 2 mm in diameter and 5 mm in length; the working electrodes were two square copper lamellae made from the rings of the T arms of 25 mm^2 each, attached to a conductive wire [22]. All these elements were encapsulated in epoxy resin as shown in figure 2. The surface of each working specimen was prepared metallographically by polishing with silicon carbide papers of different granulometry up to 1200. Then it was cleaned with acetone and dried with hot air. The uterine mucosa, used as the electrolyte, was placed on the surface of the electrochemical cell as a thin flat layer of fluid.

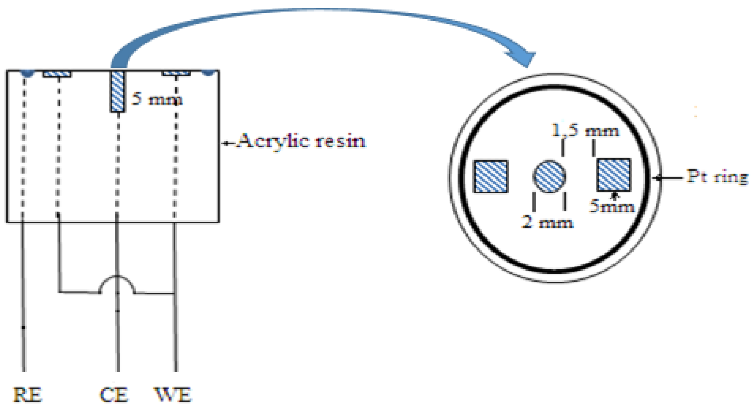

Figure 2. Electrochemical cell diagram showing vertical section and cell surface.

2.4. Copper corrosion

The corrosion of the T Cu 380A inserted in the maternal uterus releases Cu2 + ions, which are responsible for the contraceptive action and the adverse effects that may occur. As an electrochemical phenomenon, it is the consequence of two concurrent half-reactions in different areas of the surface under minimal asymmetries [23]:

- Oxidation or anodic semi-reaction, in which the metal atoms are oxidized generating soluble positive ions, and the metal surface is degraded by loss of material

$$Cu \rightarrow Cu^{2+} + 2e^{-} \quad (1)$$

- Reduction or cathodic semi-reaction, in which the electrons released at the anode are transferred through the material and captured by oxidants, usually dissolved oxygen:

$$O_2 + 2H_2O + 4e^{-} \rightarrow 4OH^{-} \quad (2)$$

Copper from the IUD in contact with the endometrium oxidizes in endometrial solutions that are oxidizing and strongly alkaline.

2.5. Electrochemical tests

Potentiodynamic polarization curves were plotted in triplicate, with a PJT 35-2 Tacussel Potentiostat-Galvanostat, at a temperature of 25 °C using the electrochemical cell described above at a scanning speed of 12 mV / min controlled by a universal processor PAR 175. The curves were recorded with an XT PAR plotter model REO 151 from -600 mV$_{sce}$ to 100 mV$_{sce}$; V$_{sce}$ refers to the potential with respect to the saturated calomel electrode.

According to ASTM G102-89 [24], the corrosion rate in terms of penetration rate is calculated using the equation:

$$v_{corr}(mm/year) = \frac{3.27\times10^{-3} i_{corr}(\mu A/cm^2) W_{eq}}{\rho(g/cm^3)} \quad (3)$$

where W_{eq} is the equivalent weight of the alloy and ρ the density of the material; for copper the equivalent weight is 31.77 and the density 6.39 g / cm^3. The corrosion current density, i_{corr}, is determined by the method of extrapolation of the Tafel slopes [25].

3. RESULTS AND DISCUSSION

3.1. Polarization curves

The polarization curve of the copper T rings in uterine mucosa is shown in Figure 3. The corrosion potential (E_{corr}) of that material in said medium is -502 mV_{sce} and the corrosion current density (i_{corr}) is of 3.20 µA / cm^2. It has an active zone that extends from the corrosion potential to -380 mV_{sce} and a passive zone from -360 mV_{sce} to more than 200 mV_{sce}. The average passivation current density is approximately 172.50 µA / cm^2. The passivation process is due to the layers of cuprous oxide (Cu_2O, cuprite), cupric oxide (CuO, tenorite) and calcium carbonates that are formed on the surface giving rise to corrosion products in accordance with the studies of BASTIDAS *et al.* [26].

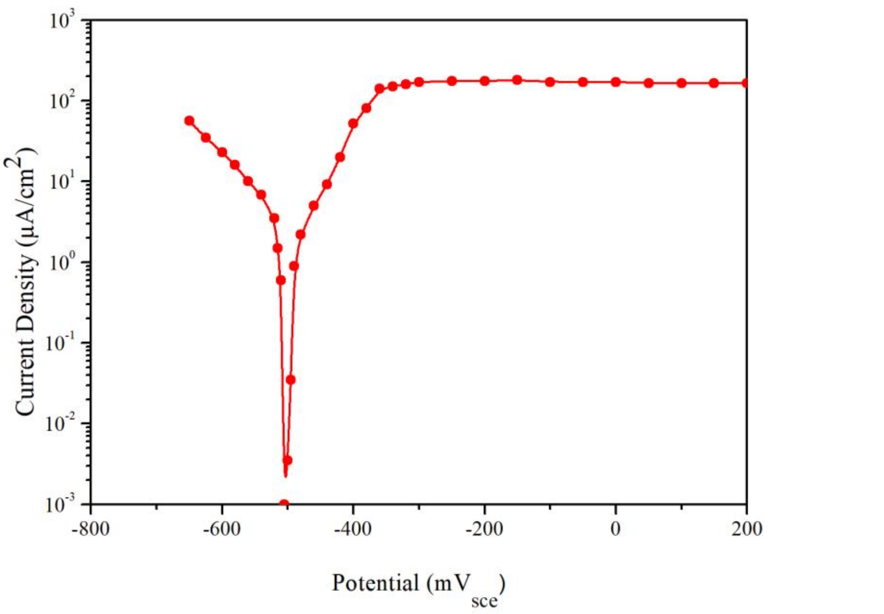

Figure 3. Polarization curve of T Cu380A in uterine mucosa

3.2. Analysis of the surface of the copper T 380 A

Figure 4 shows SEM photomicrographs of the corrosive attack of the uterine mucosa on the surface of the Cu T rings removed after three years of the maternal uterus. In (A) the layer of corrosion products is observed which, when removed by mechanical means, shows the presence of cavities or holes that reveal a corrosion process located by pitting on the bare metal (B and C), probably due to the chlorides and sulfides that the electrolyte contains. The photomicrograph (D) is a magnification of a cut from the photograph on the left, indicated by a yellow arrow.

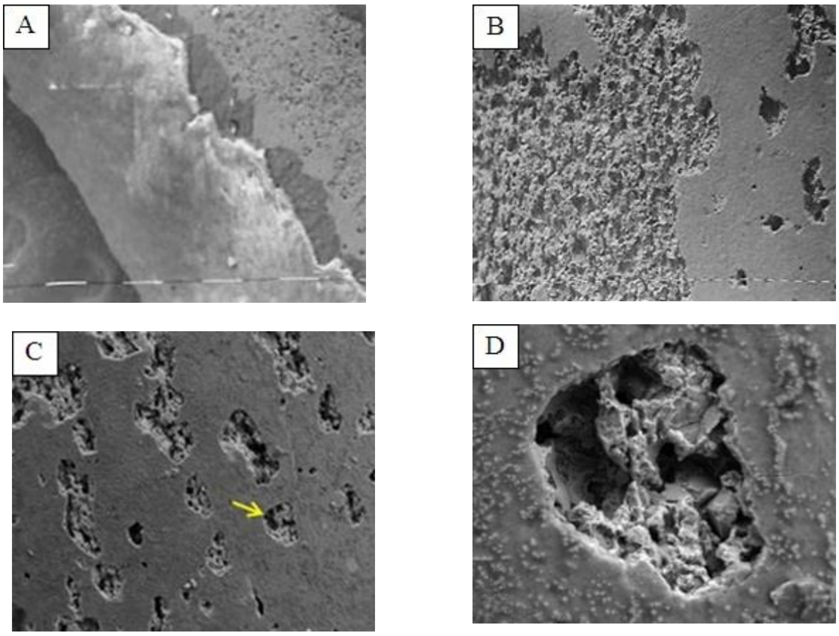

Figure 4. SEM micrographs of the surface of the cooper T rings after 3 years in the womb: (A) x80, (B) x150, (C) x391 and (D) x2520

3.3. Corrosion products

The thick layer of corrosion products presented in Figure 5B can apparently obstruct the diffusion of copper ions from the surface of the IUD. However, the morphology of corrosion products and deposits is not a uniform layer, it shows some routes, paths and porosities (Fig. 5 C and D) through which the ions released from the copper T fulfills its contraceptive function in accordance with the studies carried out by Bastidas, CANO and MORA [27]. The 5E and 5F micrographs show the corrosion products on the surface of the copper coil, which is damaged by twisting the wire around the polyethylene rod of the T when suffering stress and cracking damage resulting in corrosion processes due to fatigue and under tension, a phenomenon that could be related to the "burst release" of copper ions in the first months of implantation of the copper IUD [13, 28].

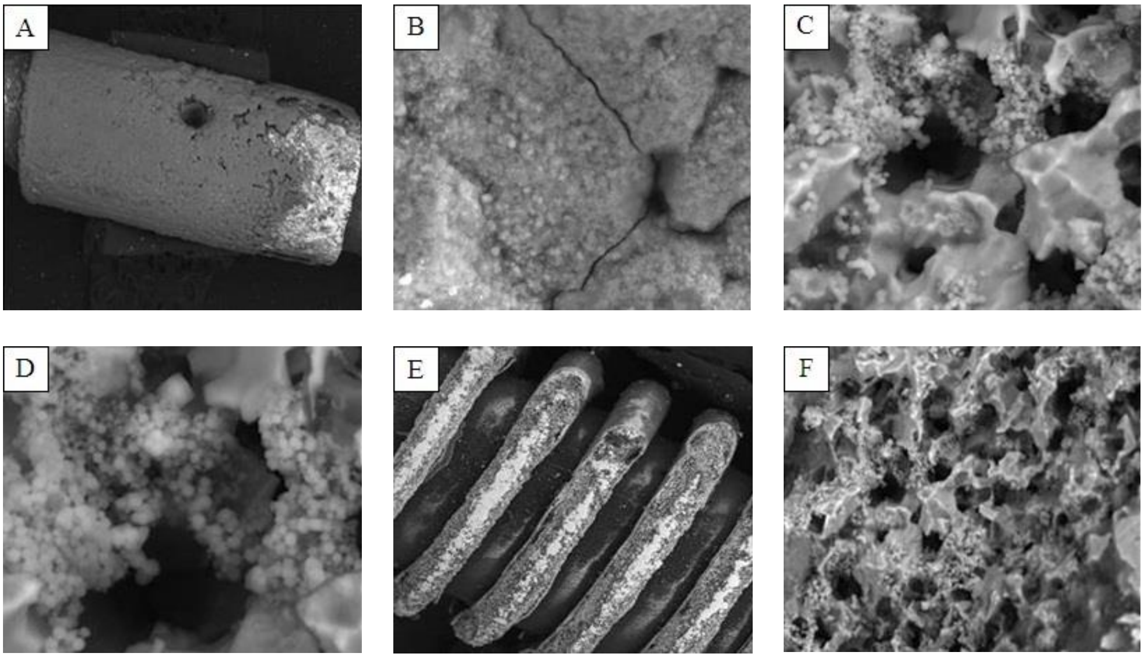

Figure 5. SEM micrographs of the copper T spiral after 5 years in the womb: (A) ×40, B) ×2000, (C) ×5000, (D) ×10000, (E) ×100 and (F) ×2000.

Figure 6 shows the EDS of a general scan of the corrosion products on the T Cu (left side of the photomicrograph 4 (A) extracted from the mother's womb after three years. In the spectrum, prominent peaks of Cu corresponding to the material are observed of the IUD, medium peaks C, O, S and small peaks of Cl, Ca, K and Mg belonging to the electrolyte (uterine fluid) which leads us to assume that copper oxides, chlorides and sulphides are formed. P has been detected does not exclude its presence, indicating that P compounds are found in deeper layers.

Figure 7 shows the EDS of a general scan of the corrosion products of the T Cu extracted from the mother's womb after 5 years, observing high peaks of C, Cu and O; minor peaks Ca and S, and small peaks of P, Mg, Si and Cl. The high C content is probably due to the presence of organic components that would correspond to extracellular polymeric substances (EPS) secreted by microorganisms such as bacteria[29]. Table 1 shows in w% the corrosion products found in copper IUDs after 3 and 5 years of permanence in the maternal uterus according to the EDS.

The predominant compounds in the process of corrosion in the womb would be cuprite (Cu_2O) and tenorite (CuO); Calcite ($CaCO_3$), phosphates, copper hydroxide ($Cu(OH)_2$) and chalcosine (Cu_2S) would also be found in accordance with the results obtained in solutions simulated by several researchers who used X-ray photoelectron spectroscopy techniques (XPS) and X-ray dispersive energy spectrum (EDX) to identify them [18, 30-33].

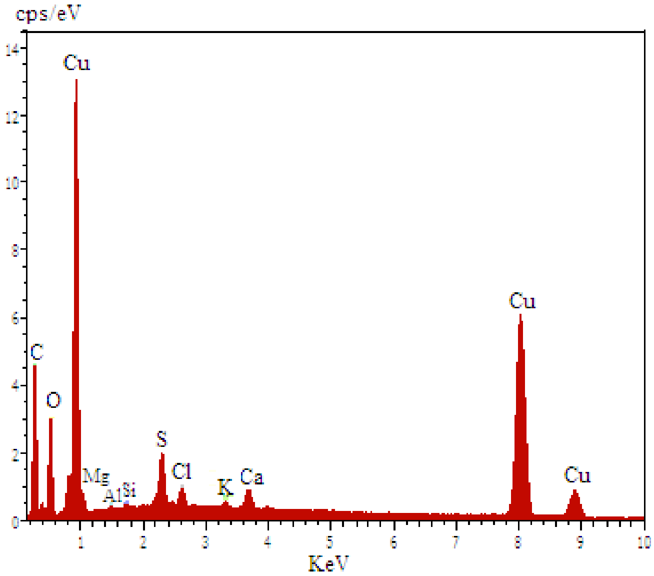

Figure 6. EDS of corrosion products of the T Cu 380A extracted from the mother's womb after 3 years.

Table 1. Elements in wt.% of corrosion products found in copper IUDs of 3 and 5 years of use in the womb.

Time in the womb	C	O	Ca	Cu	Si	S	P	Cl	Mg
3 year	21.88	19.58	1.54	52.28	2.98	0.41	0.00	1.20	0.00
5 year	42.24	23.75	8.92	23.77	0.20	0.26	0.22	0.13	0.29

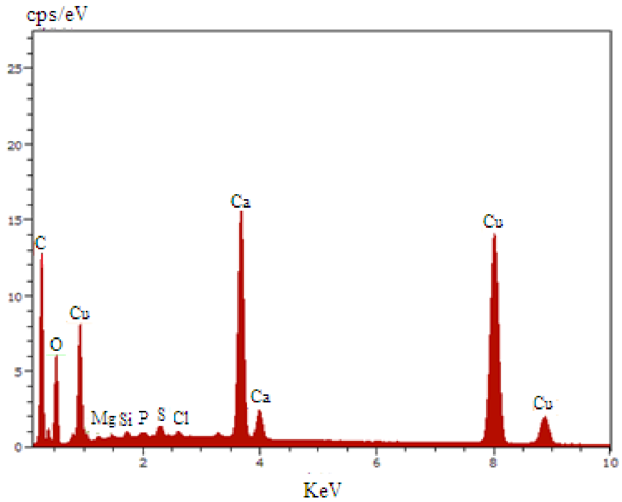

Figure 7. EDS of corrosion products of the T Cu 380A extracted from the mother's womb after 5 years.

The pitting produced by the uterine mucosa on the surface of the copper IUD according to BASTIDAS *et al.* [26], consists of a central area that acts as an anode with restricted oxygen access, surrounded by a peripheral area that acts as a cathode with access oxygen free; pitting corrosion is caused by corrosion products deposited on the surface of the copper IUD and precipitates of calcite (CaCO3) and calcium chloride ($CaCl_2$) made by calcium and chloride from the uterine mucosa.

3.4. IUD half-life in the womb

The corrosion current density was determined from the global polarization curve of the TCu-380A, i_{corr} = 3.20 μA / cm^2 and the corrosion rate was calculated by replacing data in equation (3), obtaining: v_{corr} = 0.052 mm/year

Therefore, the rings of the arms of the T of 0.5 mm thick will remain approximately 10 years in the maternal uterus before dissolving completely, a result consistent with those obtained by other researchers who ensure a duration between 10 and 12 years of the T Cu-380A [16, 33-36].

3.5. Effect of copper ions in the womb

When the Cu dissolves, the ions of the metallic network pass to the electrolytic medium according to the reaction

$$Cu \rightarrow Cu^+ + e^- \tag{4}$$

where the corrosion current is the manifestation of the released electrons that are transferred to the cathode.

These ions released from the copper IUD increase the inflammatory reaction and reach concentrations in the luminal fluids of the genital tract, which are toxic to sperm and embryos. In women who use the IUD, the entire genital tract is affected, at least partially, by the luminal transmission of accumulated fluids in the uterine environment. This affects the function or viability of gametes, decreasing the fertilization rate and decreasing the chances of survival of an embryo that may have formed, even before reaching the uterus [37].

The cells attached to the surface of the IUD have the ability to produce prostaglandins PGF2 and PGE2 that will make it difficult for gametes to meet by decreasing the motility of the uterus and tubes. The most commonly accepted mechanism of action of IUDs involves alteration of the uterine environment as a result of action on a foreign body. This biological response could cause a contraceptive effect by interfering with several of the stages leading to successful implantation. Fluids from the uterus and tubes when you have a copper IUD are likely to alter gamete viability [38, 39].

The effect of the copper IUD at the uterine level has several hypotheses: the first assumes that the release of cupric ions in the uterine mucosa leads to the inactivation of sperm and the suppression of contractions of the myometrium; the second proposes a sterile inflamed mucosa reinforced with copper ions in which the blastocyst has no chance of implanting; the third assumes that it accelerates the transport of the fertilized ovum through the tube, so when it reaches the uterus it is not able to receive it and aborts it; the fourth that the IUD mechanically displaces from the endometrium to the blastocyst already implanted in it and prevents its evolution due to the inflammatory response of the foreign body that occurs in this organ [28, 40, 41].

Copper can also cause biochemical alterations in the endometrial lining by inhibiting the normal functioning of cellular enzymes, thus preventing egg implantation. In addition, copper ions released into the uterine cavity by the device modify the secretion of endometrial cells, reducing the viscosity of the endometrial surface and thus making implantation difficult [42]. Comparative studies with other simple T-shaped devices demonstrate greater contraceptive effectiveness with the addition of copper, which is why they are used worldwide, particularly in China, India and Latin America [26]; This is corroborated by the worldwide acceptance of the T Cu 380A as the most commonly used IUD according to the World Health Organization (WHO) and the Pan American Health Organization (PAHO) [5]. The actual effectiveness rate of this copper IUD is 98%.

3.6. The IUD as a barrier to cervical cancer

According to the WHO, cervical cancer produces more than 380,000 deaths per year, mainly affecting women in low-income countries. To thoroughly analyze the relationship between cervical cancer and the use of copper IUDs, a group of researchers identified 16 high-quality studies conducted worldwide in which more than 12,000 women participated. The results showed that in women who used copper IUDs, the incidence of cervical cancer decreased by one third [43, 44]. This is probably due to the fact that the insertion of the copper IUD in the mother's womb is associated with metabolic changes in the endometrium leading to the decrease in enzymes, a possible interruption of carbohydrate metabolism, gluconeogenesis and mucopolysaccharide metabolism [45].

The results of several investigations showed that the use of the copper IUD seems to inhibit the development of precancerous lesions in women infected with the Human Papillomavirus (HPV), considering it as safe by women at risk of infection as carriers [46]. In addition, studies conducted by Mónica Sánchez [47] argue that the biological mechanisms of IUDs can exert a protective effect on precancerous or cervical lesions in women infected with HPV or with established precancerous lesions.

4. CONCLUSIONS

The potentiodynamic polarization curves of the T Cu-380A in uterine mucosa were plotted with a thin film cell, the corrosion current density was determined by the Tafel extrapolation method and the IUD corrosion rate was calculated with the Standard ASTM 102 being found to be approximately 10 years old in the womb.

The corrosive attack of the uterine mucosa characterized by scanning electron microscopy is by pitting. The analysis by EDS of the corrosion products accumulated in the metal parts of the copper IUD removed from the uterus after 3 and 5 years of use, allowed to infer the existence of the following products: CuO, Cu_2O, phosphates, Cu_2S, $CaCO_3$ and hydroxide of copper ($Cu(OH)_2$) among others.

Copper IUDs benefit users not only as a contraceptive method but also as a probable protector against endometrial cancer, cervical cancer, and an HPV inhibitor.

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