UNIVERSIDAD DE INVESTIGACIÓN DE TECNOLOGÍA EXPERIMENTAL YACHAY

Escuela de Ciencias Químicas e Ingeniería

EXPIRED DRUGS FROM THE PHARMACEUTICAL INDUSTRY AS POSSIBLE CORROSION INHIBITORS

Trabajo de integración curricular presentado como requisito para la obtención del título de Ingeniero en Polímeros

Autor:

Marlon Guillermo Puma Torres

Tutor:

Ph.D Dario Alfredo Viloria Vera

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"How lucky to exist"

RESUMEN

Los altos costos que representa el mantenimiento, protección y control de la corrosión en las industrias; lleva a buscar nuevas alternativas que sean igual de efectivas y al mismo tiempo más económicas. Por tanto, este trabajo surge con el propósito de realizar una exploración bibliográfica, con el fin de plantear el posible potencial inhibidor de algunos residuos farmacéuticos provenientes de los procesos de fabricación o productos que ya han alcanzado su fecha de caducidad. Así, en la búsqueda de nuevas propuestas que actúen contra la corrosión, se ha seleccionado la aspirina, el ácido salicílico y el Alka Seltzer; para comprobar si cumplen las características necesarias para actuar como inhibidores de la corrosión. De esta forma, se encontró que su estructura química contiene los grupos funcionales que permiten inhibir la corrosión.

Sin embargo, es necesario demostrar su efecto inhibidor mediante pruebas de laboratorio para poder considerar a estos compuestos como inhibidores de la corrosión. De esta manera, se podrían aplicar técnicas electroquímicas, que permitan monitorear las reacciones electroquímicas que se están produciendo; y así analizar el potencial inhibidor de los compuestos frente al metal. Este trabajo propone realizar ensayos experimentales sobre los metales más utilizados en equipos industriales como: acero al carbono, acero inoxidable y cobre almirantazgo.

Palabras clave: Corrosión, inhibidores, residuos, aspirina, alka seltzer, electroquímica.

ABSTRACT

The high costs represented by the maintenance, protection, and control of the corrosion at industries; lead to looking for new alternatives that are just as effective and at the same time more economical. Hence, this job arises with the purpose to carry out a bibliographic exploration, to pose the possible inhibitory potential of some pharmaceutical wastes coming from the manufacturing process or products that have already reached their expiration date. Thus, in the search of new proposals that acts against corrosion, it has been selected aspirin, salicylic acid, and Alka seltzer; to check if these fit the necessary characteristics to act as corrosion inhibitors. In this way, it was found that their chemical structure contains the functional groups that allow inhibiting corrosion.

However, it is necessary to demonstrate their inhibitory effect through laboratory tests to consider these compounds as corrosion inhibitors. In this way, electrochemical techniques could be applied, which allow monitoring the electrochemical reactions that are taking place; and thus analyze the inhibitory potential of the compounds against the metal. This work proposes to carry out experimental tests on the most used metals in industrial equipment such as carbon steel, stainless steel, and admiralty brass.

Keywords: Corrosion, inhibitors, waste, aspirin, Alka seltzer, electrochemistry.

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CHAPTER I

1. INTRODUCTION

The pharmaceutical industry was born to synthesize, extract, purify, and encapsulate substances that help to develop treatments, cure diseases or alleviate discomforts in the body. Every year this industry is responsible for improving the health care systems and the quality of life of millions of people around the world, through medicines developed by organic, inorganic, and biological reactions (Gadipelly et al., 2014).

However, Ramos (2006), establishes that despite the benefits that medicines have brought for people, the inefficient waste management produced during the manufacturing of these medicines has arisen harmful effects on the environment. This is caused because industrial processes used to make up medicines, lead to producing chemical substances such as toxic and non-biodegradable organic compounds.

On the other hand, other of the industries that provides multiple benefits, is the petroleum industry. Which according to Ferrari (2013), this industry provides the largest sources of energy to people, because fossil fuels and its derivatives represent approximately 80% of energy consumption in the worldwide. Nevertheless, Lara & Torres (2016) mentions that, despite this industry generates sources of energy, the expenses of maintenance that comes from production operations; are very high.

This need for maintenance is because the multiple chemical processes that are carried out, can create conditions, as accumulation of some minerals; which affect physical and chemical characteristics of the metallic equipment. To treat this, one of the techniques more applied to give maintenance by the removing of these minerals, is the cleanings with inhibited acids such as hydrochloric acid. However, next will be seen that the use of acids produces corrosion conditions, which leads to use corrosion inhibitors.

In this way, based on the model of green corrosion inhibitors, this work raises with the purpose to use pharmaceutical products as inhibitors. For this, it will be focused on two categories of analysis, medicines that have reached expiration date and residues that can be recovered during the manufacturing. With this objective in mind, it seeks to do a bibliographic analysis that supports that the mechanism of action and chemical structure of some pharmaceutical fits perfectly to realize treatments against corrosion.

1.1. Problem Approach

There is no doubt that the industries, through the continuous development of products, have improved continuously our lifestyle over the years. However, as industries grow, at the same time the environmental impact increases; due to the large amount of wastes that are generated. But pollution does not only depends on industries, because people are also responsible of the environmental impact due to of the poor management that are realized to wastes.

Hence, to look for alternatives for these wastes and also with the objective to find new corrosion inhibitors proposals that could be applied in the petroleum industry. The present work seeks to investigate, the feasibility of using as inhibitors, medicines that have reached their expiration date, and also the medicine residues that are generated during their manufacture.

1.2. Objectives

1.2.1. General Objective

Carry out a bibliographic review about which drugs could be the best candidates to act as corrosion inhibitors

1.2.2. Specific Objectives

- To promote the investigation of new corrosion inhibitors that are more friendly with environment
- To determine in which area of the petroleum industry the proposed corrosion inhibitors could be applied.
- To analyze the industrial processes of the possible corrosion inhibitors, to establish where one can take advantage of the wastes.
- Provide necessary evidence about the inhibitory potential of compounds, to carry out future experimental tests.

CHAPTER II

2. BACKGROUND

2.1. Corrosion

Since years ago, corrosion is a problem that have affected all kind of industries, because corrosion can attack by decreasing the mechanical resistance of any metal, which can lead to fractures or other problems. This is why Syed (2008) mentions that because of the fact that metals are used in a lot of technology fields, corrosion must be studied to develop new alternatives for improving its control.

Therefore, this work will be focusing on studying for proposals to mitigate the effects of corrosion, but first it is important to understand what corrosion is? According to Shaw & Kelly (2006), corrosion is known as a process in which metallic materials suffer deterioration because, with time and the effects of the environment, the metal returns to its low energy oxide state through electrochemical reduction-oxidation reactions that affect the integrity of the material.

For instance, according to Husseing et al., (2018) a form of corrosion occurs when there is a direct clash between atmospheric gases as oxygen and metal; it leads to the formation of a metal oxide layer. Another way of corrosion occurs when it is produced by a liquid medium, where liquid acts as an electrolyte which serves as an electron transfer medium; in this way, the anode can oxidate and the cathode can reduce.

In general, Singh (1995) states that corrosion in metals and alloys takes place when electrochemical cells are formed at the metal-electrolyte interface. Hence, next reactions are produced during corrosion:

i. Anodic Reactions:

$$M \rightarrow M^{n+} + ne^- \quad (1)$$

ii. Cathodic Reactions:

$$2H^+ + 2e^- \rightarrow H_2^+ \ (Acidic) \quad (2)$$

$$O_2 + 4H + 4e^- \rightarrow 2H_2O \ (Acidic, in\ presence\ of\ O_2) \quad (3)$$

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

$$M^{n+} + e^- \rightarrow M^{(n-1)} \ (Acidic, neutral\ and\ alkaline) \quad (5)$$

Through the equations above described, it can be observed what kind of chemical reactions took place to produce corrosion, on the metal structure. On the one hand, equation 1 shows an anodic reaction, where practically the electrons are generated; this process is known as oxidation. On the other hand, equation 2, 3, 4 and 5 show cathodic reactions, where the electrons are consumed; this process is known as reduction (Singh, 1995).

As it can be seen, corrosion is produced by chemical reactions, but how these reactions interact to produce corrosion? To understand this, it is necessary to go deeper, and check some electrochemical concepts that are going to be useful to understand the corrosion behavior.

2.1.1 Electrochemistry

Electrochemical studies will be useful to understand what is behind the chemical reactions that produce corrosion. Firstly, it is necessary to look at the electric conductivity, which according to Suarez (2006), this parameter allows to measure the capacity that has a material or substance to conduct electric current through it. In this way, Gacitúa (2008) mention that, the electric current has the capability to flow through an electrical conductor, known as medium. Hence, there are two kinds of electrical conductor named as:

a) 1st class conductors: This kind of conductor allows the electricity to flow without alteration, for instance, copper and silver.

b) 2nd class conductors or electrolytes: these are ions that have been produced in a dissolution, these can conduct the electric current; for instance, aqueous solutions of acids, bases, and salts. However, it can be found a different kind of electrolytes as well.

i) Strong Electrolytes: Basically, these can be dissociated completely, which forms solutions highly conductive of electricity.

ii) Weak Electrolytes: These are partially dissociated, which forms solutions lowly conductive of electricity.

The electric conductivity depends on the behavior of ions, these ions can be influenced by their concentration, movement of positive and negative ions, valence, and also the temperature in which they are exposed (Suarez, 2006). Thereby, could exist solutions in which ions can interact in a better way, as in the case of inorganic compounds which can lead to forming ionic solutions; or where ions cannot interact as well, as in the case of organic molecules (Gacitúa, 2008). Hence, this is the way as electricity reacts through different media, but these interactions occurs under a certain velocity.

2.1.2 Kinetics of an electrochemical reaction

Thus, how will influence the electric conductivity in this study? Well to perform a quantitative study of chemical phenomena that are responsible for the corrosion process; it is necessary to use electrochemical techniques that allow to keep a track of the current and the time of the electrolysis (Suarez, 2006). Hence, a galvanic cell is a very didactic example, to explain how the electric current could influence the corrosion process. When a cell is connected to an electric source, flows through it a current, that according to Lara (2018), it lets to measure kinetic factors that allow knowing how fast the metal is being dissolved in a media.

Nevertheless, Gacitúa (2008), mentions that the electric flux is occurring through electrolytes and electrodes, which allows that current flows inside the chemical reaction. In this way, through the electrolyte and electrodes, are occurring electrochemical reactions, which are carried out at a certain velocity according to the next equation.

$$v=\frac{m}{At}=\frac{eq}{F}*\frac{I}{A}=\text{constant} * i \tag{6}$$

Where:

m = mass that reacts electrochemically (kg)

eq = equivalent kg

I = current intensity, A

A = constant, $kg^2 * m^2 / C$

t = time (s)

F = Faraday constant, 96500 C / eq

i = current density, A / m^2

Hence, this is the equation used to know the rate of a reaction, however there are both possible ways at which this velocity can be achieved; either by charge transfer (activation) or by mass transfer (diffusion). Any of these should occur to produce an electrochemical reaction (Gacitúa, 2008). The charge transfer or activation is the determining step of the reaction because this is the slowest; on this step, there is a contact between ion and electrode. This is possible because a charged particle is transferred, through the opposite layer of charges found on the electrode. On the other hand, in the case of the mass transfer, the ions of the reactants should move towards the electrode surface (Gacitúa, 2008). Next in Figure 1, is illustrated the behavior of both possible ways above described.

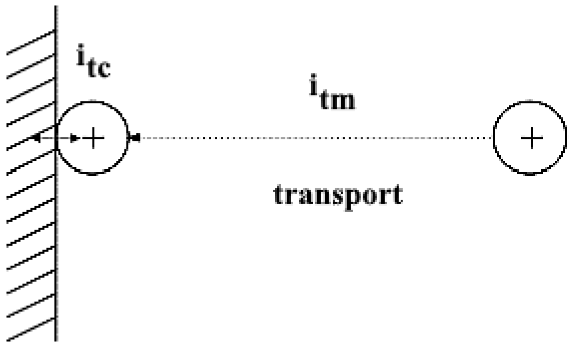


Figure 1, Movement of ions towards the electrode surface, adapted from (Gacitúa, 2008)

Where:

i_{tc} = current density under control by charge transfer

i_{tm} = current density under mass transfer control

Thereby, the rate of reaction could give data about which mechanism is taking place in a system metal-electrolyte. Anyway, next will be detailed some cases about under what conditions, the speed of reaction can benefit either activation or a diffusion process (Gacitúa, 2008).

Case a) If $i_{tm} >> i_{tc}$, it is a control by charge transfer (activation)

Case b) If $i_{tm} << i_{tc}$, it is a control by mass transfer (diffusion)

Case c) If $i_{tm} \approx i_{tc}$, it is a mixed control

2.1.3 Corrosion rate

Once analyzed that the electrochemical reactions are carried out at a certain speed, it is necessary to know what kind of information can be extracted from that. Thusly, as it was previously reviewed, the metals can suffer corrosion; but this phenomenon that affects the metal is due to an electrochemical reaction as well. Thus, these reactions involved in the degradation of the material can act under a certain rate of reaction, known as corrosion rate. According to Raigosa (2019), the studies of the corrosion rate, provide information about how is the corrosion behavior, when the material is exposed to an electric current. Then, it can help to determine values that allow knowing how fast or how slow a material corrodes (Raigosa, 2019)

According to Lara (2018), to get information about the corrosion rate, it is necessary to monitor the response that the electrode has in front of the excitation produced by the current; and thus plot a relationship between the current and the potential. In this way, one can obtain information about how fast or slow the corrosion occurs. According to the article "Basics of Corrosion Measurements" published on Princeton Applied Research, the measurements of the current vs potential can lead to getting information such as corrosion rates, coatings, films, pitting tendencies, and other important data.

2.1.4 Graphical methods to determine the rate of corrosion

For the main purposes of this job, it is necessary to check how corrosion acts on the material. Thereby, as it was previously mentioned, through the monitoring of the chemical reactions, it is possible to get useful information as the corrosion rate. Hence, it is important to look at which graphic methods, could be useful to monitore the electrochemical reactions. With the objective to get information about corrosion rate, and know how susceptible is a material to corrosion (Lara, 2018).

Aguilar (2012) established that, through the graphic method of the polarization curves, it can be studied the corrosion rate. Because this method allows to have a relation between the current-potential, which is useful to determine how susceptible is a material to corrosion (Lara, 2018). Also, according to Silva (2015), the polarization curves, mainly help to study the behavior of the oxidation or reduction processes that are occurring on the electrochemical reactions; when the metal is exposed to a corrosive medium in an electrochemical cell. This can be used for to determine the region where the metal-solution system, presents a state of activation or passivation.

This graphical method, according to Raigosa (2019), allows keeping a record about the response that has the electrode, in front of the excitation caused by the current. This stimulus causes the electrode moves away from the potential for corrosion, which makes the electrode becomes polarized. Thus, can be obtained a graph, where is related the change in potential with the current density in function of time. In Figure 2, can be observed a graph of polarization curves.

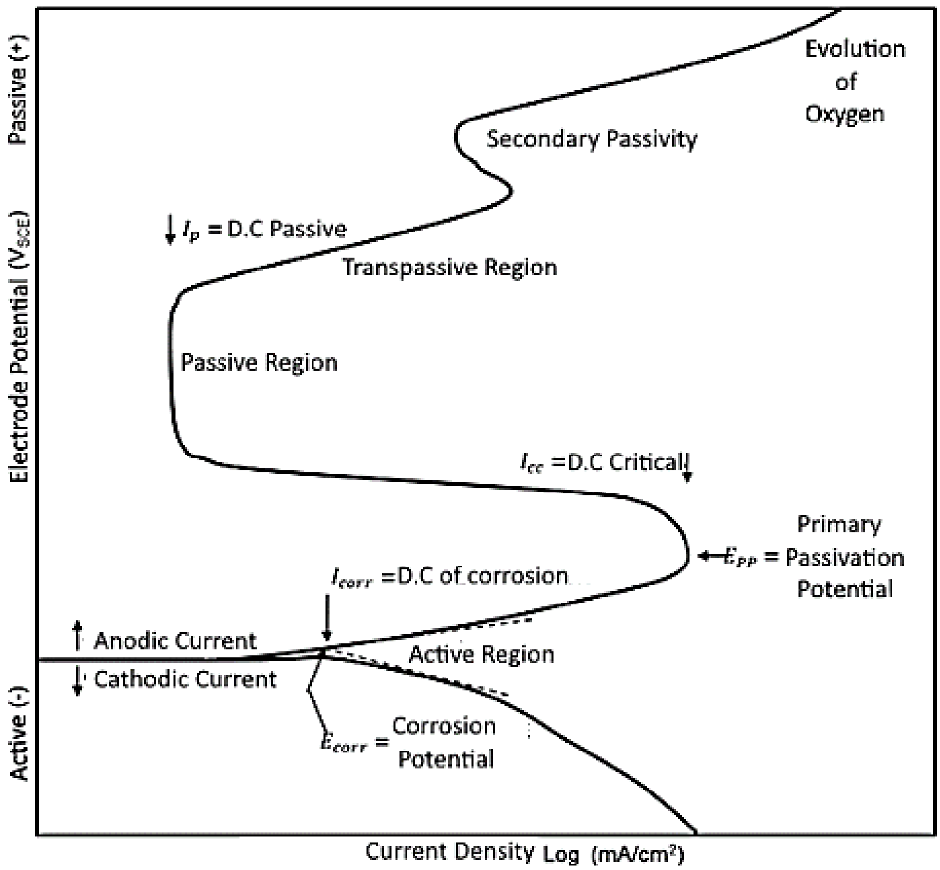


Figure 2, Anodic and Cathodic Polarization Diagram, adapted from (Lara, 2018)

Nonetheless, other useful parameters that can be obtained, and can be observed in Figure 2, are the next:

Corrosion Potential (E_{corr}): Potential present when the material is in contact with a corrosive liquid, but the material is not connected to any instrumentation.

Primary passivation potential (E_{pp}): Positive potential where the passive layer is formed

Critical current density (I_{∞}): Minimum current required before the formation of the passive layer

Potential breakout (E_b): Positive potential in which the surface of the passive layer is destroyed

Protection potential (E_{prot}): Potential in which the passive film is stable and protective

Passivation current (I_p): Electrode current in E_{prot}

To determine the polarization curves can be carried out electrochemical techniques such as tafel extrapolation, resistance to polarization, etc. These techniques put the materials under conductive electrolytes or corrosive media. With the purpose to observe the effects of reduction and oxidation, induced by an external current, on the surface of the material (Silva, 2015).

In this way, with a broader view about what corrosion is and how it works through chemical reactions. It is time to look at the effects that arise from corrosion in one of the biggest industries in the planet.

2.2. Corrosion on oil industry

As it was mentioned before, the fossil fuels, represents the major energy resources worldwide. According to the World Energy Council (2013), this is because from fossil resources, it can be obtained fuels of different types such as gasoline, diesel, etc. Which are highly demanded by people to do their daily activities. However, to obtain these fuels some chemical processes are needed, those are carried out at oil industries that transform gas and oil into fuels.

During the transformation of fossil resources to fuels, it should be considered that as a consequence of different substances interactions, environments, and processes involved inside these processes. The industrial metallic facilities, exposed to these conditions, can be involved and suffer the effects of corrosion. Ahmed et al., (2020), established that all metallic facilities can be affected, but the majority of time where it has been seen that the rate corrosion is higher, are in oil and gas pipelines; which are the heart for transportation of crude and refined petroleum.

According to Tamalmani & Husin (2020), the system of pipelines allows to transport oil and gas from the oil well to the processing facilities, in this way pipelines surfaces are directly exposed to sources of corrosion. In Figure 3, are presented some types of corrosion that could be present on pipelines.

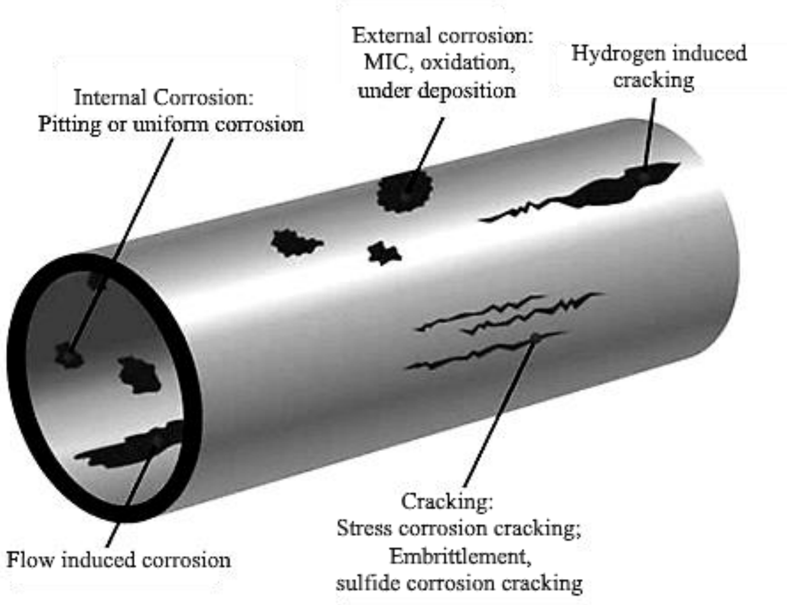


Figure 3, Corrosion in oil and gas pipeline, retrieved from (Ahmed et al., 2020)

Therefore, according to Figure 3, it can be observed some types of defects present on the surface of the metal caused by corrosion; but each of these defects is related to a rate of corrosion. This rate depends on several factors such as the quality and nature of crude oil, its acidic constituents, and the environment of the transport. Thereby these parameters should be studied for knowing the components or impurities that are causing the spread of corrosion and thus be able to find methods to act against this. Hence, below in Table 1 are listed some of the major sources of corrosion in the oil industries in accordance with Tamalmani & Husin (2020).

Table 1, Major sources of corrosion present in the oil industry, adapted from (Tamalmani & Husin, 2020).

Sources of Corrosion	
Hydrogen Sulfide	This compound is found in abundance in oil production processes, considering that it can be corrosive only when it is dissolved in water; also this one does not present visible signs of deterioration during the early phase of corrosion. However, with time it can produce iron sulfide and hydrogen, which leads to forming sulfide stress corrosion cracking, and might result in equipment loss.
Chloride	This substance has been detected on the mineralized water at the well bottom, it can produce intergranular corrosion and chloride stress corrosion cracking on the metal surface.

Carbon Dioxide	The corrosion product derived from this compound is known in industries as sweet corrosion, this happens when the carbon dioxide along with oil and gas dissolves in water to produce carbonic acid, in this way causing a decrease in pH. This type of corrosion can result in pittings on the metal surface.
Oxygen	This is responsible for causing pits in the drill pipe, where propagated fatigue cracks are due to the stress; moreover, byproducts of corrosion derived from oxygen can be seen as a problem to water injection equipment like pumps, piping, and water storage tanks.
Bacteria	This kind of corrosion is known as bacterial corrosion, these can be found in enhanced recovery processes and can cause more damaging corrosion on this type of process. The most common bacteria that promote corrosion are sulfate-reduction and iron bacteria.
Brines	These are formed of zinc chlorides or calcium bromides, and can regulate the well without damaging the formation; however they can be harmful to the downhole equipment since there is the presence of dissolved oxygen.
Strong Acids (Pickling)	To enhance production and remove unwanted fouling from industrial equipment, the acid cleaning method is the most efficient, this is performed through substances such as hydrofluoric acid, hydrochloric or acetic acids; to improve the formation permeability for sandstone and carbonates respectively. However, Obot et al., (2019) mention that to use this method it is necessary to apply inhibitors because, in the absence of these, this method can produce corrosion as well.

As can be seen in the Table 1, there are some sources that are responsible for causing corrosion in the oil industry. Many of these corrosive sources are unavoidable, since they are derived from industrial and environmental conditions. However, there is one corrosive source in particular, which is intentionally applied to industrial equipment for cleaning purposes. Therefore, for the interests of this work, it is necessary to perform a close look at how acids act to remove fouling.

2.2.1. Pickling

According to Villanueva (2008), the metal materials like carbon steel, stainless steel, and admiralty brass are used in many industrial units, because of their low cost and excellent mechanical properties. Nonetheless, those metallic materials are subjected to various environmental conditions during its manufacturing, storage, transportation, and use; that can produce fouling in the metal structure (Singh, 1995). Therefore, in accordance with Jafari, Akbarzade, & Danaee (2014), industries continuously are in the need to look for new techniques that helps to remove fouling to the equipment. Thus, to relieve metal surfaces, some techniques that help to clean and remove fouling, on metal surfaces such as sandblasting, shot blasting, and acid pickling (Singh, 1995).

Focusing on acid pickling, Chen & Yang (2019) mention that, pickling consists in pumped down HCl or any acid, in the tubing that is connected to the well, allowing that the acid enters in contact with the formation that will be removed. Formations such as oxides, that are formed by hot rolling of metal and alloys, are responsible for poor thermal conductivity and reduction of the material strength (Chen & Yang, 2019). In this way, formations of oxide can affect the efficiency of pipelines, some unit operations such as heat exchangers and cooling equipment.

To explain the most commonly way in which oxide scales can be formed, consider the case of iron. In which due to sudden temperature changes, can be formed thick and adherent layers of oxide scale, where could be found 80% of wustite (FeO), 18% of magnetite (Fe_3O_4), and 2% of hematite (Fe_2O_3) (Singh, 1995). As it can be observed, the wustite proportion is the highest, in this way due to wustite presents better solubility than magnetite and hematite in acid media. Many investigations have focused on the wustite, with the purpose to achieve more amenable conditions for applying pickling (Singh, 1995).

The pickling acts by penetrating the wustite cavities that have been formed, the acid solution get through these cavities and reaches the base metal surface, thus getting the dissolution of wustite and magnetite. Therefore, an electrochemical cell is formed in which the base metal behaves as the anode, and the wustite and magnetite behave as soluble cathodes; while hematite suffers a negligible dissolution, which has little effect on the cathodic process (Singh, 1995).

However, according to Sandianes et al., (2012), pickling treatment implemented in oil wells, is a very corrosive method for metal installations; because this method uses concentrated acids such as hydrochloric acid, which is used for acid cleaning at a concentration that varies from 10% to 30% (Sandianes et al., 2012). Therefore, with the purpose to avoid corrosion effects caused by hydrochloric acid during pickling, it is necessary to look for sources that helps to avoid this type corrosion.

Thusly, Syed (2008) establishes that, there are some methods to control corrosion such as metallic and organic protective coatings, alloys resistant to corrosion, coatings through plastics or polymers, cathodic protection, and corrosion inhibitors. According to Bammou et al., (2014), corrosion inhibitors are considered one of the most practical and simple application methods for industries to act against corrosion, especially when refers to acid media.

2.3. Corrosion inhibitors

According to Sandianes et al., (2012), corrosion inhibitors are the most appropriate and widespread protection methods in worldwide practice. These are chemical substances, that are added to metallic surface, to decrease the corrosion rate; since they form a barrier of one or several molecular layers to stop, protect and reduce the movement or diffusion of ions into the metallic surface (Ahmed et al., 2020). Thus, protecting the metallic surface from destructive surroundings that cause corrosion. This reducing of the corrosion rate is possible, because inhibitors can work under the following mechanism of action shown in Table 2.

Table 2, How inhibitors work, adapted from Ahmed et al., (2020)

MECHANISM OF ACTION OF INHIBITORS	
Adsorption	Ions or molecules coming from inhibitors are adsorbed onto the metal surface, in this way efficiency of the inhibitive process depends on the amount of inhibitor used to cover the metal area.
Existence of charge on the metal surface	The inhibitor is adsorbed on the metal surface, due to interactions of electrostatic forces between the charges, dipoles, or ions groups of the inhibitor.
Chemical Reaction	When the chemical structure of the inhibitor reacts with the metal surface, one electron could transfer from the inhibitor to the metal to form a coordinate bond. Thus, decreasing the diffusion rate of prejudicial reactants responsible for corrosion, to the surface of the metal.
Interaction between inhibitor and water molecules	The purpose of this is to eliminate water molecules from the metal surface, it is achieved through a replacement reaction between water and inhibitor; where the solubility of water is affected by the increase of the hydrocarbon size, which leads to the increase of adsorption process of inhibitor.

Electrochemical reaction of inhibitors	When the inhibitor is added to a metal surface (primary inhibitor) can interact with the metal surface through electrochemical reduction reaction, which leads to forming a compound with an inhibition effect (secondary inhibitor). However, the efficiency of the inhibitor might change, depending on what extend the primary inhibitor effectiveness is related to the secondary inhibitor
Diffusion wall	Through a barrier formed by the inhibitor, on the surface of the metal, it can be prevented that ions or molecules, be transferred from to the metal surface; in this way decreasing the electrical resistance and the corrosion rate

Once described the mechanism of action of inhibitors, one can remind that corrosion acts through to anodic or cathodic reactions. In this way, the main objective of an inhibitor is to interact with these anodic and cathodic reactions through the mechanisms detailed on Table 2, with the purpose to mitigate the effects of corrosion (Singh, 1995). Consequently, an inhibitor can be designed to work as anodic, cathodic, or mixing both behaviors; it depends on which reaction is better to work to control corrosion.

Therefore, the continuously investigation and improvements of inhibitors are important from the economic point of view. Because inhibitors can be the key to reduce the high expenses derived by corrosion such as expensive repairs, unnecessary plant closures, efficiency decreasing on materials, maintenance etc. (Singh, 1995). To relate the high economic cost derived from corrosion, the Report of Offshore Technology Conference (2008) mention that, the companies from The United States by the concept of corrosion, they spend approximately per year, an estimate $1.052 billion. Then, according to this data, it is highlighted that the costs derived from the damaging effects of corrosion on the facilities are very high.

Thus, once analyzed how the inhibitors can be useful to act against corrosion. It is also necessary to slightly review about what are the appropriate inhibitor concentrations to apply, in order that it performs efficiently.

2.3.1 Efficiency of an inhibitor

Firstly, it is important to consider that the effectiveness of the inhibitor, can be affected by conditions such as pH of the media, different components in the solution, the nature of the metal and high temperatures (Sandianes et al., 2012); this causes that:

- The amount of inhibitor absorbed decreases.
- The inhibitor can decompose, because of high temperatures.
- Weak interactions between the inhibitor and the metal

In regards to the efficiency of an inhibitor, it can be mentioned that this improves with an increase in the inhibitor concentration. The next equation 7 can be used to describe the efficiency of an inhibitor according its concentration (Singh, 1995).

$$\text{Inhibitor Efficiency } (\%) = 100\,\frac{(CR_{uninhinited} - CR_{inhibited})}{CR_{uninhinited}} \tag{7}$$

Where:

$CR_{uninhinited}$: Corrosion rate of the unhibited system

$CR_{inhibited}$: Corrosion rate of the inhibited system

Thus, as it was mentioned, although higher the concentration of the inhibitor, its effectiveness will be better. But it should be noted that corrosion inhibitors are chemical substances, which are already added at very low concentrations to the corrosive medium (Sandianes et al., 2012). To get an idea of the small concentrations that are used to cause an inhibitory effect, on Table 3 are shown some inhibitors have been efficiently used in corrosive environments, with their respective concentration.

Table 3, Inhibitors successfully used at industries, retrieved from (Corrosion Inhibitors, 2011)

System	Inhibitor	Metals	Concentration
	Acids		
HCl	Ethylaniline	Fe	0,50%
	MBT*	..	1%
	Pyridine + phenylhydrazine	..	0,5% +0,5%
	Rosin amine + ethylene oxide	..	0,20%
H_2SO_4	Phenylacridine	..	0,50%
H_3PO_4	NaI	..	200ppm
Others	Thiourea	..	1%
	Sulfonated castor oil	..	0,5-1,0%

	As_2O_3	..	0,50%
	Na_3AsO_4	..	0,50%
	Water		
Potable	$Ca(HCO_3)_2$	Steel, cast iron	10 ppm
	Polyphosphate	Fe, Zn, Cu, Al	5-10 ppm
	$Ca(OH)_2$	Fe, Zn, Cu	10 ppm
	Na_2SiO_3	..	10-20 ppm
Cooling	$Ca(HCO3)_2$	Steel, cast iron	10 ppm
	Na_2CrO_4	Fe, Zn, Cu	0,10%
	$NaNO_2$	Fe,	0,05%
	NaH_2PO_4	..	1%
	Morpholine	..	0,20%
Boilers	NaH_2PO_4	Fe, Zn, Cu	10 ppm
	Polyphosphate	..	10 ppm
	Morpholine	Fe	Variable
	Hydrazine	..	O_2 scavenger
	Ammonia	..	Neutralizer
	Octadecylamine	..	Variable
Engine coolants	Na_2CrO_4	Fe, Pb, Cu, Zn	0,1 - 1%
	$NaNO_2$	Fe	0,1 - 1%
	Borax	..	1%
Gycol/water	Borax + MBT*	All	1% + 0,1%
Oil field brines	Na_2SiO_3	Fe	0,01%
	Quaternary	..	10-25 ppm
	Imidazoline	..	10-25 ppm
Seawater	Na_2SiO_3	Zn	10 ppm
	$NaNO_2$	Fe	0,50%
	$Ca(HCO_3)_2$	All	pH-dependent
	$NaH_2PO_4 + NaNO_2$	Fe	10 ppm + 0,5%

MBT* = mercaptobenzotriazole

As it can be observed, the concentration at which inhibitors are added, is very small. However, at the moment to choose an inhibitor, it should be considered the costs, toxicity, availability, and it needs to have a great environmental friendliness. On the other hand, once analyzed how inhibitors work and its importance to treat corrosion, it is time to see how much useful these inhibitors are, to treat the corrosion caused by pickling.

2.4. Inhibitors for pickling

As already was mentioned, pickling is basically a technique used for cleaning processes, where can be removed rust or mill scale in order to obtain a better efficiency in the production of fuels derived from oil and gas (Tamalmani & Husin, 2020). However, due to pickling is a technique that uses acids solutions, this can cause corrosive environments that affects the metal integrity. In this way, to treat corrosion caused by pickling, inhibitors are a good option, that are already used at industries.

Inhibitors are used during the post service cleaning of metal surfaces, where acid solutions were applied. The primary step in the action of inhibitors in acid solution is the adsorption into the metal surface, which is usually oxide-free in acid solutions. In this way, the adsorbed inhibitor retards the cathodic and anodic electrochemical corrosion processes, which help to control and protect the material from pitting attack, uniform corrosion, and hydrogen attack. (Chen & Yang, 2019).

According to Hamadi et al., (2018), most efficient corrosion inhibitors that work better in acid media can be organic compounds that contain elements from Groups V and VI of the Periodic table such as N, S, P and O. From these can be found compounds such as halide ions, carbon monoxide, compounds that forms –OH, –COOH and NH_2 groups. Moreover, organic compounds that contain multiple bonds are effective inhibitors, especially triple bonds. Nevertheless, it should be considered that, inhibitors that contain compounds of high molecular weight, present serious handling problems because they are very toxic (Hamadi et al., 2018).

2.4.1. Inhibitors in acid medium

There are two principal ways on how acid solution acts. The first is the anodic process of corrosion, which is the passage of metal ions from the oxide-free metal surface into the solution; and the second is the cathodic process in which hydrogen ions are discharged to produce hydrogen gas (Singh, 1995). Therefore, the main function of an inhibitor is to act in these reactions, to decrease the reaction rate of anodic and cathodic processes. For this reason, a useful indicator to observe which process is retarded, is to analyze the change in the corrosion potential when an inhibitor is added. The corrosion potential of the metal, is a parameter that is useful to understand the tendency that has metals to corrode (Corrosion Inhibitors, 2011),.

To explain this, if the displacement of the corrosion potential is in the positive direction, it indicates mainly retardation of the anodic process; hence there is an anodic control. On the other hand, if the displacement of the corrosion potential is in the negative direction, it indicates mainly retardation of the cathodic process; hence there is a cathodic control (Corrosion Inhibitors, 2011). Another useful parameter to consider, to check the influence the inhibitor function, is the Zero charge potential; this is known as the potential of the metal at which the charge is equal to zero concerning to the solution.

Consider the next application example, in which will be analyzed which inhibitor is better to apply according to the parameters of corrosion potential and zero charge potentials. Consider iron, zinc, and cadmium submerged in 0.1N HCl; in Table 4 is described their corrosion potential (Ec), zero charge potentials (Eq=0), and corrosion potential expressed in zero charge potential scale (Eq) (Singh, 1995).

Table 4, Corrosion potential, zero charge potentials, and corrosion potential expressed in zero charge potential scale of iron, zinc, and cadmium. Retrieved from (Singh, 1995).

Metals	Ec (SHE)	Eq = 0	Eq= Ec-Eq = 0
Fe	-0.02	-0.02	-0.30
Zn	-0.75	-0.64	-0.11
Cd	-0.75	-0.72	+0.64

According to the above data when the iron surface is in contact with HCl acquires a negative charge in the acid solution be, use of chemisorption of Cl^{-}, and discharge of H^{+}on the surface, this means that during corrosion a cathodic reaction was produced. In this way, it is necessary to add a cationic type of inhibitor to replace H^{+} hence hindering the cathodic reaction. Thus, iron corrosion is controlled by amine, hexamine, acetylenic alcohols, quaternary ammonium salts, who provides cationic species due to the protonation of their molecule.

On the other hand, cadmium has a positive charge on the surface, hence the anionic type of inhibitor is needed. And for Zinc which presents a negative value near to zero, a mixed type of inhibitor or molecular form of inhibitor could work well (Singh, 1995)

Now, consider the following example retrieved from the article Corrosion Inhibitors (2011), which allows to observe how acts anodic and cathodic inhibitors for acid cleaning of industrial equipment. Hence, with the purpose to remove fouling, and restore the efficiency loss from industrial machines, will be used inhibited hydrochloric acid; which has been proven to be the most efficient method to remove fouling.

Firstly, to see the chemistry involved in fouling removal by inhibited hydrochloric acid, consider the next equations that are produced during this process of removal.

Cathodic Processes

$$Fe_2O_3 + 4Cl^- + 6H^+ + 2e^- \rightarrow 2FeCl_{2(aq)} + 3H_2O \tag{8}$$

$$Fe_3O_4 + 6Cl^- + 8H^+ + 2e^- \rightarrow 3FeCl_{2(aq)} + 4H_2O \tag{9}$$

$$2H^+ + 2e^- \rightarrow H_2 \tag{10}$$

Anodic Process

$$Fe + 2Cl^- \rightarrow FeCl_{2(aq)} + 2e^- \tag{11}$$

These equations show how iron works as a reducer, which allows the dissolution of magnetite (Fe_3O_4) and hematite (Fe_2O_3). In this way, once the iron oxides have been diluted, anodic or cathodic inhibitors can be added to retard metal corrosion. It has been observed that inhibitors in acid solutions can control the effects of corrosion due to the next behavior (Corrosion Inhibitors, 2011).

- Formation of a diffusion barrier: The inhibitor can form layers on the metal surface, which prevents the movement of ions or molecules. In this way, the rate of corrosion reactions can be retarded.
- Block reaction sites: This prevents that some atoms that cause corrosion, reacts on the metal surface.
- Reactions in the electrodes: During the corrosion process, can be formed some intermediate species that results harmful to the metal surface. Thusly, the function of the inhibitor will be to interfere or retard the formation of these intermediate species.

The next E-log i diagrams will be useful to observe how the inhibitor acts to dissolve the fouling caused by Fe_3O_4 and Fe_2O_3 on the iron, through the mechanism of action above described. For this, observe how equations 8, 9,10 and 11 are related in the next Figures 4 and 5, to illustrate the action that could be played by either an anodic inhibitor (Figure 4) or a cathodic inhibitor (Figure 5).

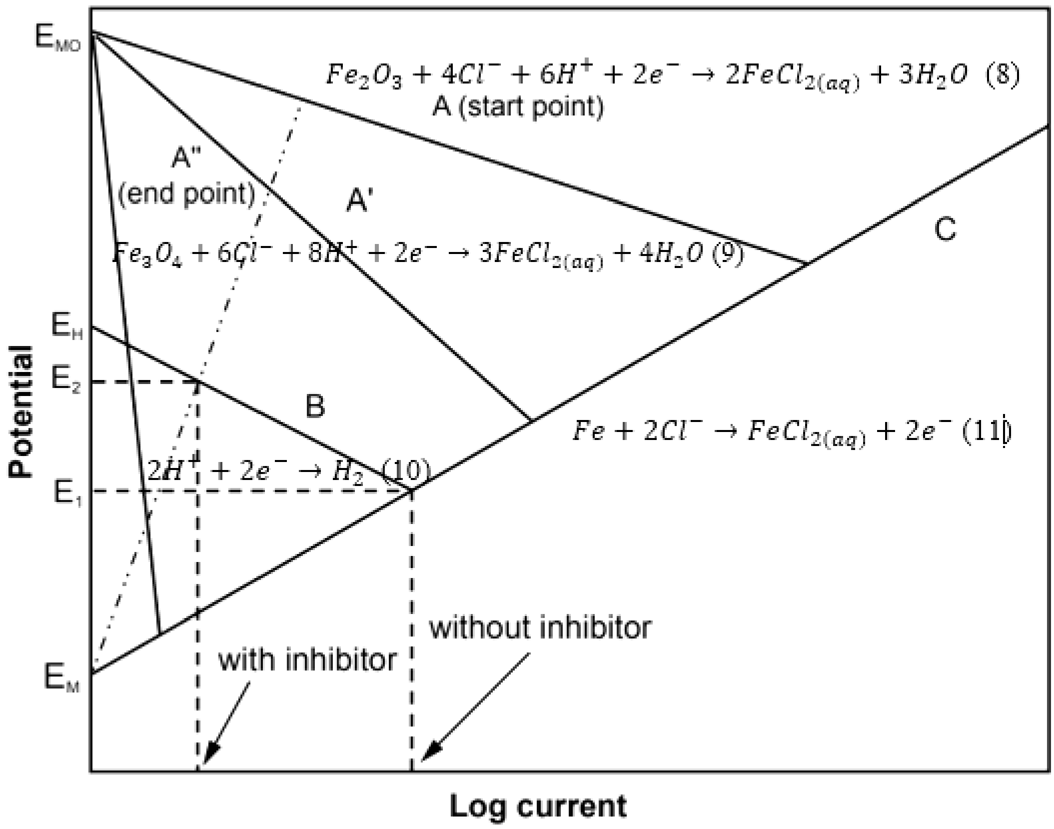


Figure 4, Effect of an anodic inhibitor on the dissolution rate of iron and iron oxide, adapted from (Corrosion Inhibitors, 2011).

Figure 4, shows the differences when inhibitor is applied and when it is not applied. But also, here can be observed how works the mechanism of action the inhibitor when it forms a diffusion barrier. Thereby, on this can be observed, how the anodic inhibitor retards the anodic dissolution of iron, but also decreases the rate of oxide dissolution. Next, proceed to observe the behavior of a cathodic inhibitor.

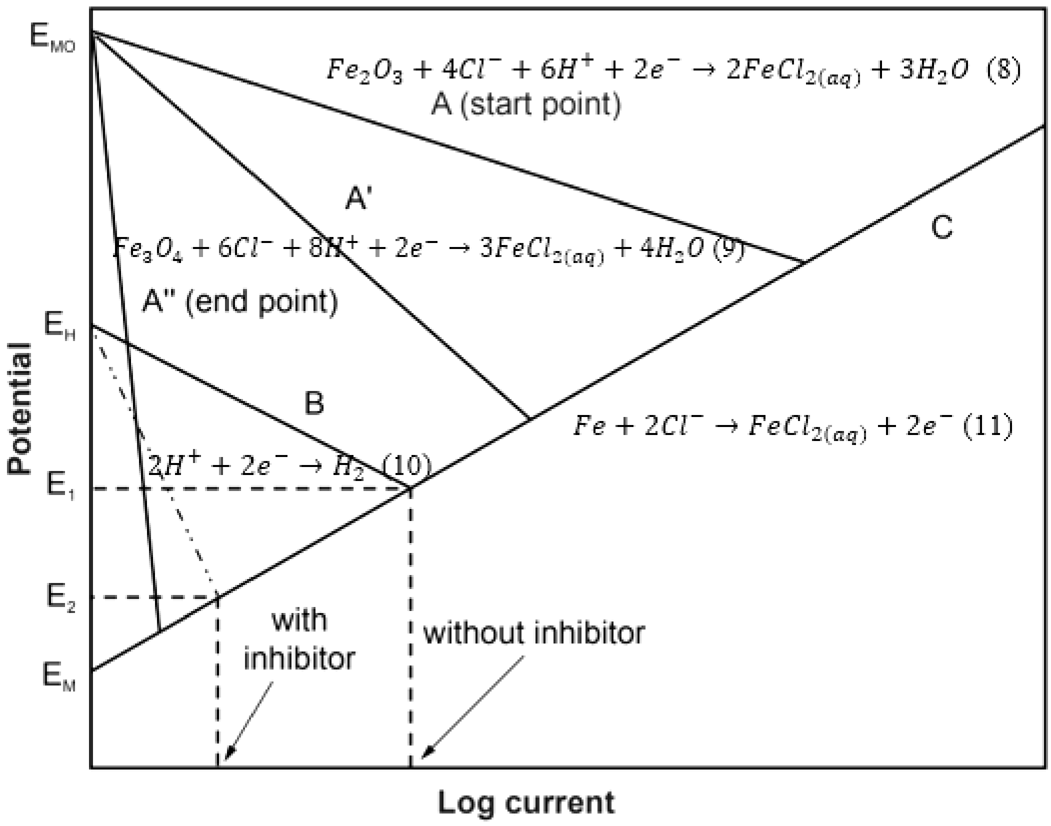


Figure 5, Effect of a cathodic inhibitor on the dissolution rate of iron and iron oxide, adapted from (Corrosion Inhibitors, 2011).

Figure 5, shows the influence that have the inhibitor in the electrode reactions. On this can be observed how the cathodic inhibitor retards dissolution of iron, also retards the reduction of protons, that could be responsible to form intermediate species. But additionally, it can be observed that with this cathodic inhibitor, the reduction of oxides is not affected.

During this chapter, pickling has been analyzed as one of the most implemented techniques to remove fouling caused by the different conditions and processes that are carried out in oil industry. However, it has been observed how this technique can cause corrosive environments, due to the implementation of acids. Therefore, in order to reduce the impacts of corrosion derived from pickling, can be implemented the use of inhibitors as control treatment. Which has been proven to be a very effective technique for treating corrosion in acid media. In this way, next it will be reviewed the inhibitors types that this work seeks to apply during the acid cleaning or pickling.

2.5. Green Corrosion Inhibitors

As it was reviewed, the metal facilities from oil production industries, can be easily exposed to corrosion problems. To treat this, inhibitors are applyed, but some of them result toxic and can cause damage to the environment. In this way, Agraje et al., (2019), establish that, in response to this problem, the concept of "green inhibitors" was born, which are presented as an option that generates low levels of pollution, fewer environmental risks, and good protection efficiency.

According to Anastas & Beach (2007), recently the emergence of the concept of green chemistry in the fields of science, technology, and engineering is restricting the application of commercial corrosion inhibitors, through the implementation of environmentally friendly chemicals that help to reduce pollution. Hence, as a movement to support this concept, the use of green-based corrosion inhibitors such as plant extracts, chemical drugs, and ionic liquids is being practiced.

Next Table 5, includes a comparative table with indicators related to the environment, pollution, economic value, and effectiveness between commonly used green inhibitors and industrial inhibitors.

Table 5, Comparative table between industrial inhibitors and green inhibitors, adapted from Chávez et al., (2019) and Agraje et al., (2019)

	Industrial Inhibitors	**Green Inhibitors**
Damage to the environment	High	Low
Effectiveness	High	Good
Toxicity	High	Low
Pollution	High	Low
Based on	Toxic chemicals	Plant extracts, chemical drugs
Price	High	Economic

Table 5 shows the negative impact of industrial inhibitors, due to the chemical and toxic products that they contain; and also they result very expensive. However, as it can be seen, the effectiveness is the only indicator in the comparison Table 5 that shows a difference between industrial inhibitors and green inhibitors. By this, Agraje et al., (2019) mention that, despite that industrial inhibitor can be more effective, since they have been designed for that; the studies of green corrosion inhibitors continue being improved, to find better alternatives.

To see how investigation of corrosion inhibitors have gained importance. According to Rodriguez et al., (2020), recently has been investigated the use of powders, essential oils, aqueous infusions, and natural extracts obtained from plant leaves, peels, fruits, seeds, and roots, as ecological corrosion inhibitors. This is because they are of safe effect, practical use, low cost, and for being renewable materials. Next, some successful case studies of green corrosion inhibitors are cited.

Esquivel et al., (2020) in their study called "Study of corrosion inhibition of copper in synthetic seawater by Equisetum arvense as green corrosion inhibitor" studied the extract of the stems of Equisetum arvense (horsetail) as a green corrosion inhibitor in copper samples immersed in synthetic seawater. Thereby, to determine the protective effect of the inhibitor, electrochemical tests were performed using: potentiodynamic polarization curves, electrochemical impedance spectroscopy, and resistance to linear polarization.

Research results from the studies from (Esquivel et al., 2020) indicate that Equisetum arvense acts as a mixed-type green corrosion inhibitor with an inhibition efficiency ranging from 53.78% -87.43%. Also, through Fourier transformed infrared spectroscopy, it was determined that the methanolic extract of Equisetum arvense is constituted by functional groups of -OH, C-H, C = O, and C-O.

Another green corrosion inhibitor is presented by Ramos et al., (2021), who obtained an alternative corrosion inhibitor from Apricot Juice. The study was carried out on carbon steel, which was exposed to a corrosive medium composed of H_3PO_4 solution, the results show that this green inhibitor has an efficiency of 70.6%. to act against corrosion.

It can be seen how green corrosion inhibitors result to be a cheap and ecological option in benefit of industries. In this way, as this job pretends to use drugs as corrosion inhibitors, it is observed that these fits perfectly as a green corrosion inhibitor; since it seeks to use chemical drugs. In fact, the time to know the type of drugs that are intended to be used as corrosion inhibitors has come.

CHAPTER III

3. PHARMACEUTICAL PRODUCTS

3.1. Digestive System and pH

According to the most recent demographic data from the United Nations published in 2019, around the world, there are 7700 million people, all these people are in the need to consume daily a set of nutrients, acquire through food, for energetic and health purposes. Thereby, all that food ends up in the digestive system, where are developed different functions, so that the body obtains energy through food. Hence, according to Faris et al., (2021), the digestive system performs a process known as digestion, where food or large molecules are broken down into simple and soluble molecules; consequently, nutrients can be absorbed into blood for transport to the cells that utilize them.

Throughout the digestive tract, one will find substances that are of great help to break down food such as saliva, gastric fluids, mucous membranes, among others. Food can be assimilated, because these substances have different physical and chemical characteristics, which influence the assimilation of nutrients by the body (Faris et al., 2021). Among its main chemical characteristics, could be found pH, which is a logarithmic unit of measurement used to measure the concentration of protons in an aqueous solution; thus, the higher the concentration of protons in a solution, the lower the pH value.

In accordance with Siemens (2016), within the scale to measure pH, acids are characterized by having a value between 0-7 and bases between 7-14; considering 7 as a neutral pH value. Thereby, throughout the digestive system, there are different pH levels, these levels are very important since they provide to internal organs the conditions for proper functioning (Siemens, 2016). Therefore, the pH levels in the digestive system are responsible for some symptoms of different diseases, such as hyperacidity, acid indigestion, or gastroesophageal reflux; these are some diseases that occur when there is a lack of balance between acids and bases in the digestive system (Cienfuegos, 2010). In Figure 6, can be observed the different pH levels throughout the digestive system.

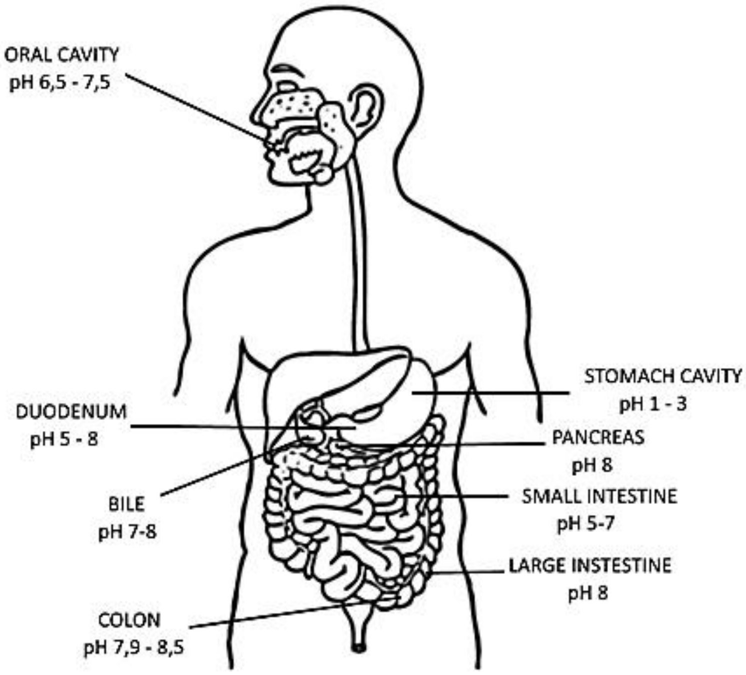


Figure 6, pH in the Digestive System, adapted from (Armijo & Briceño, 2020)

It is observed clearly, the different pH environments presented in each organ belonging to the digestive system. As it can be seen the more acidic one, is presented in the stomach; this is due to gastric acid produced on it.

3.2. Gastric acid production

All food that enters the body is processed in the digestive system by the stomach, where can be found receivers that stimulate the production of hydrochloric acid or commonly known as gastric acid. In this way, in accordance with Rodríguez & Alfaro (2010), from all the stimulus coming from stomach receivers, the most principal stimulus that allows segregating acid, is the one coming from histamine. This one allows parietal cells to regulate and produce hydrochloric acid; thanks to this, food can be converted in useful molecules for the body. For this reason, according to Comas et al., (2020), histamine has become research of big interest in recent years, because this could help to define, diagnose and perform good clinical management of medicines for stomach problems.

In accordance with Mondal (2017), to produce hydrochloric acid in the stomach, some previous reactions are carried out. In which inside parietal cells reacts CO_2 and H_2O to form HCO_3^- and H^+. Consequently, H^+ and Cl^- secreted from parietal cells, are pumped into the lumen of the stomach, which in combination with water forms HCl; and the rest of HCO_3^- produced goes to the bloodstream.

Hydrochloric acid is really important for the organism because it kills harmful organisms, aid digestion, and activates digestive enzymes. However, according to Ruiz (2019), sometimes this substance can act against the organism since from malfunction of the stomach cavities, bad eating habits, and unfavorable conditions caused by imbalances in substances of the stomach; hydrochloric acid can produce several nuisance and illnesses.

3.3. Importance of antacids

Owing to acids could produce some problems that have affected the entire population, in accordance with Al-Lami (2017), to find methods to treat gastric problems as heartburn, since 1910 the scientific use of antacids began to be implemented; onwards research on antacids products grew further and have had a great reception by consumers that suffer various gastric and duodenal disorders. Consequently, according to Bosch (2014), antacids are prescribed to produce rapid and transitory relief of the next symptoms:

- Heartburn
- Duodenal and gastric ulcers
- Gastritis
- Pancreatic insufficiency
- Reflux esophagitis
- Non-ulcer dyspepsia
- Irritable stomach
- Diarrhea caused by bile acids
- Constipation
- Osteoporosis
- Urinary alkalinization
- Phosphate binding in chronic kidney failure

The majority of gastric problems are caused when the stomach presents very acid pH levels due to the presence of HCl. Thus, to alleviate the discomfort produced by the acid in the stomach, antacids are prescribed for this purpose. According to Mondal (2017), antacids are weak alkaline compounds, which reduce hydrogen ion concentration to neutralize or control the excessive secretion of hydrochloric acid. Additionally, antacids can absorb bile acids and stimulate the synthesis of bicarbonates to relieve symptoms of heartburn.

However, what makes those antacids become so effective in neutralizing stomach acids? Well, antacids are developed based on carbonates, hydroxides from the group II and III of metals, and bicarbonates of the alkali metals. Next, thanks to the article written by Dr. Luis Malgor and Dr. Mabel Valsecia in Medical Pharmacology (2016), below can be observed how these antacids acts against hydrochloric acid.

Sodium Bicarbonate

$$HCl\ (aq) + NaHCO_3\ (aq) \rightarrow NaCl\ (aq) + H_2O + CO_2 \quad (12)$$

One of the most efficient antacids due to its fast and powerful action, it is very soluble and reacts immediately with hydrochloric acid (Al-Lami, 2017). Equation 12 shows how the hydrochloric acid is neutralized, when the sodium bicarbonate reacts with gastric acid, which forms sodium chloride, water, and carbon dioxide.

Calcium Carbonate

$$2HCl\ (aq) + CaCO_3\ (aq) \rightarrow CaCl_2\ (aq) + H_2O + CO_2 \quad (13)$$

According to Mondal (2017), it is a very reactive antacid, which has a crystalline structure and it is found in different forms such as Argonite and Calcite. Calcium salts neutralize gastric acid because it increases the pH of the gastric and duodenal bulb; however, it causes constipation. Thereby, when calcium carbonate reacts with the acid, it forms calcium chloride, water, and carbon dioxide as can be observed in equation 13.

Magnesium Compounds

$$MgO + H_2O \rightarrow Mg\ (OH)_2 \quad (14)$$

$$2HCl\ (aq) + Mg\ (OH)_2 \rightarrow MgCl_2 + 2H_2O \quad (15)$$

These salts, in the same way, are less powerful but their effect is longer, they are formulated together with the aluminum and calcium salts; to better counteract the effects on the small intestine, which is why they tend to have a laxative effect (Mondal, 2017). When antacids that contain magnesium react with stomach acid, magnesium chloride and water are formed as one can observe in equation 15.

Aluminum Compounds

$$Al(OH)_3 + 3HCl \rightarrow AlCl_3 + 3H_2O \quad (16)$$

Less powerful, but with longer action than the antacids mentioned above, these salts are capable to produce fewer side effects for organism (Mondal, 2017). As it can be observed on equation 16, when aluminum salts come into contact with gastric acid, aluminum trichloride and water are produced.

According to these reactions, it can be observed that antacid structure performs correctly to treat acids, since as result of these interactions is produced salt and water. However, the mechanism and rate of acid neutralization of these salts can vary, and each salt has a different mechanism of acid neutralization; Below in Table 6, are listed the most common antacids and their rate of neutralization.

Table 6, Reaction speed of some antacids, retrieved from (Bosch, 2004)

Substance	**Speed of Reaction**
Magnesium hydroxide	Very fast
Sodium bicarbonate	Very fast
Magnesium carbonate	Moderate
Aluminum hydroxide	Slow
Calcium carbonate	Slow
Bismuth carbonate	Fast

Furthermore, there are two types of antacids, systematic and non-systematic antacids; these act in different ways inside the stomach. In the case of systematic antacids, can be highlighted that these have a cationic group, which does not react with HCO_3^-; hence, these are absorbed into the bloodstream (Mondal, 2017).

On the other hand, in non-systematic antacids there are anionic groups that neutralize H^+ ions, thus cationic groups are released, and these combine with HCO_3^- to form a basic compound that is released through feces; therefore non-systematic antacids do not produce metabolic alkalosis (Mondal, 2017). Figure 7 is presented how systematic antacids and non-systematic antacids act inside the stomach.

Adsorbable (systematic) **Nonabsorbable (nonsystematic)**

$CaCO_3$
$Mg(OH)_2$
$NaHCO_3$ $Al(OH)_3$

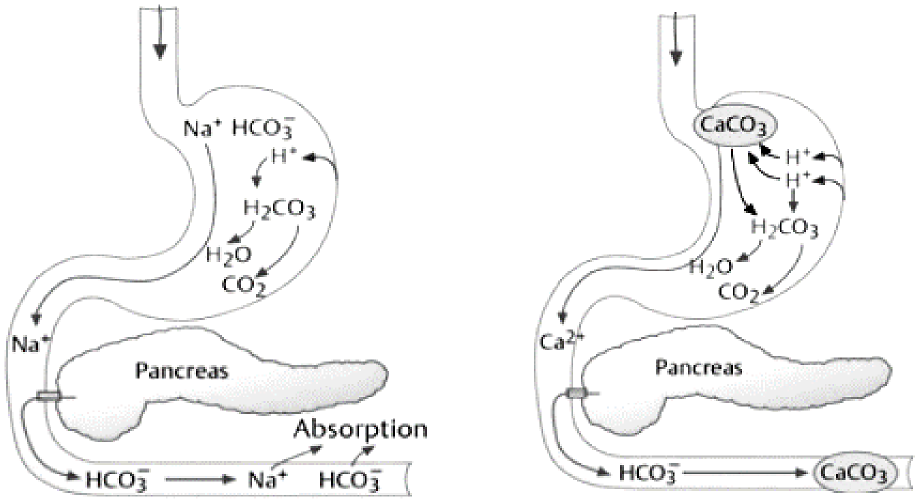


Figure 7, Working of Systematic antacids and non-systematic antacids inside the stomach, retrieved from (Mondal, 2017)

It should be considered that antacids have to be carefully designed to not cause any damage to the body when they are inside the organism. Therefore, some considerations that have to be taken into account when designing them, can be the next:

- They should not cause systemic alkalosis (excess of base)
- Antacid should buffer in the pH 4-6 range
- They must act quickly on stomach
- They have to increase the gastric pH

3.4. Antacid Tablets

It has been mentioned some general considerations about the mechanism on how antacids should act, but physically, an antacid is subject to some design parameters as well to give a good performance. Therefore, because antacids have to work inside the stomach, these are developed through different layers; where each layer contains specific compounds that allow releasing the antacids on the right media where it must work (Al-Lami, 2017).

Antacids are prepared in such way that form a wet or dry gel, known as layer lattice antacids (Al-Lami, 2017). These layers must be pH-responsive, since antacids have to react inside the stomach, to release the active principles and performs the neutralization of acid. Also, these layers have to be insoluble in water, but soluble in dilute acids, where can be generated ion sources and gas due to CO2 release.

Table 7, shows the compounds and quantities used in the study of two formulas of antacids tablets, where was used calcium and magnesium carbonate as sources of acid-neutralizing, and also sodium carboxymethylcellulose as coating and binder of those tablets.

Table 7, Compounds and quantities used in Antacids Formulas 1 and 2, retrieved from (Al-Lami, 2019)

Materials	Formula (1)	Formula (2)
Calcium Carbonate	400 mg	490 mg
Magnesium Carbonate	50 mg	60 mg
Sodium Carboxymethyl Cellulose	200 mg	100 mg
Cross Carmelose Sodium	50 mg	50 mg
Total Weight	700 mg	700 mg

As it can be observed, to correctly achieve the antacid's performance, they should have a coating or layer that allows them to be released at different pH. Thus, together with sources of acid-neutralizing, the antacid can perform efficiently its functions inside stomach.

Consequently, once analyzed the mechanism of action of the antacids, it can be observed how they act by neutralizing the negative effects of hydrochloric acid inside the stomach. Go back quickly on Chapter II, to remember how the hydrochloric acid from the pickling technique, was the main responsible to provoke corrosion problems. This leads to consider the next question, could these types of drugs be used to control the corrosive effects of hydrochloric acid in pickling? Thus, next will be analyzed the possible drugs that could be considered to be applied as corrosion inhibitors at pickling

3.5. Aspirin

For years, medicine has evolved to treat diseases that people suffer, therefore according to Mesa (2017), this evolved is possible because plants and vegetables have become the principal sources to develop new technologies. Thanks to their pharmacological activities, medicines, and treatments useful for society have been developed. For instance, Egyptians used plants to make remedies, and among them, they used the leaves of the willow to treat pain and fever (Mesa, 2017). This discovery led to converting the bark and leaf of the willow into a medicine, actually known as aspirin; therefore willow is proof that shows how medicinal properties of plants can be optimized and led to medicaments.

Acetylsalicylic acid or Aspirin is an analgesic that took years to be developed industrially. According to González (2002) in the summer of 1758, the properties of willow leaves were verified by chance, since these when were chewed, certain discomforts. In 1835, one acid was elaborated from the willow leaves, called “spisaure”, later known as salicylic acid. But salicylic acid showed limitations because it irritated the gastric membrane. In this way, in 1895 was synthesized from salicylic acid, the acetylsalicylic acid, which showed the same medicinal properties as salicylic acid, but with a lower degree of side effects for the gastric membranes (Mesa, 2017). Finally, according to Martínez et al., (2016), at 1900 Félix Hoffman describes the pure and stable form of acetylsalicylic acid, which nowadays is commercialized by the Bayer Company with the name of Aspirin. Figure 8 shows the chemical structure of aspirin.

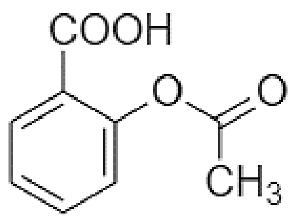


Figure 8, The chemical structure of aspirin, retrieved from (Aparici, 2018)

According to Gonzáles (2002), aspirin is considered one of the most used drugs worldwide since Bayer company launched it for sale. This due to the effectiveness of its results in treatments to alleviate discomforts. Furthermore, aspirin is also very commercial, since 1915, it has been sold without a medical prescription; in this way becoming to aspirin as one of the drugs of easier access for people (Martinez et al., 2016).

3.5.1. Aspirin within the body

Aspirin is a drug that belongs to the family of salicylates, this can be found as a white dust or in form of a colorless crystal (Martinez et al., 2016). This medicine will act inside the organism to treat some annoyances, however it should be considered that the way as aspirin will act, is influenced by the amounts or doses that will be used; for instance, Sepúlveda et al., (2018), mentions that according to doses, the most important ways of action of aspirin are antithrombotic, analgesic, anti-inflammatory.

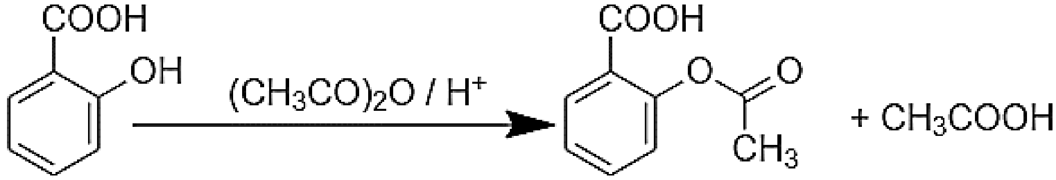
These are the most characteristic uses of aspirin, however how does this compound act inside the body? According to Santos (2016), the action of this compound begins when it is consumed orally, where around 75% of aspirin will be absorbed in the duodenum, stomach, blood, and liver. Therefore, after ingestion of aspirin, this is hydrolyzed and transformed into salicylic acid which is the main responsible of the healing properties (Martinéz et al., 2016).

However, according to Vargas et al., (2017), hydrolysis of acetylsalicylic acid is faster as the pH levels increase, on the contrary at low levels of pH, the hydrolysis occurs slowly and causes the increase of acidity in the stomach. Thereby, it should be important to consider that acetylsalicylic and salicylic acids are strong acids with pKa = 3, 5 and pKa = 3 respectively; hence the absorption speed will be influenced by gastric mucosa's pH (Santos, 2016).

Finally, the wastes derived from the biotransformation of acetylsalicylic, they become inactive and more water-soluble metabolites, which facilitates their elimination by renal route (Sepúlveda et al., 2018). In this way, aspirin can develop its different functions throughout the body, however even though its use and sale is free. Lanas (2005) mentions that, its consumption should be controlled since high doses can cause intoxication and problems in the organism.

3.5.2. Synthesis of acetylsalicylic acid

According to Tamez (2012), acetylsalicylic acid could be synthesized through an esterification process, from salicylic acid and acetic anhydride in presence of sulfuric acid. The esterification consists of the reaction that is carried out when a carboxyl group (-COOH) and a hydroxyl group (-OH) interact to form an ester group (-COOR). Next is shown how these reactions occur.



(17)

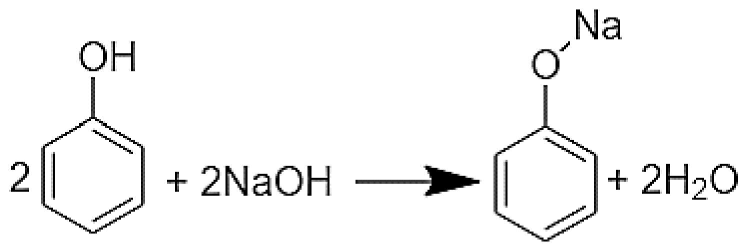
As a result, acetylsalicylic acid and a small amount of polymerized product are obtained, this is caused by the presence of a carboxyl group and a hydroxyl group in the same molecule. However, once the acetylsalicylic acid has been synthesized, this comes with impurities that should be removed; thus it is necessary to carry out a process of crystallization in presence of sodium bicarbonate ($NaHCO_3$), to purify the acetylsalicylic acid (Tamez, 2012).

This is the process of how aspirin could be prepared at a laboratory scale, where low amounts of aspirin can be obtained. But according to Machuca et al., (2009) around the world, aspirin is the highest consumption product, used to alleviate pain. Therefore, to produce big amounts of aspirin, it is necessary to lead the process to an industrial scale.

3.5.3. Synthesis of acetylsalicylic acid at industrial scale

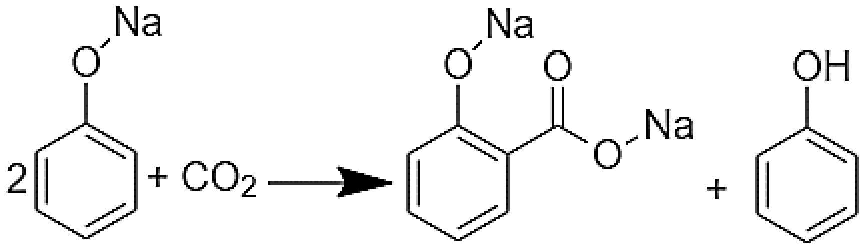
In this way, the industrial process to obtain aspirin is not so different from the one obtained at the laboratory. Thus, the next process about how aspirin is obtained at industries scale is retrieved from the thesis elaborated by Tamez (2012), and from the project about, aspirin production plant elaborated by Aleu et al., (2019). In these works, are described some of the most important equipment, reactive required, products obtained; and the main reactions that take place to develop aspirin.

Thereby, the process begins from phenol and sodium hydroxide as raw materials; these have a high reaction rate and lead to form the sodium felonate according to the next.



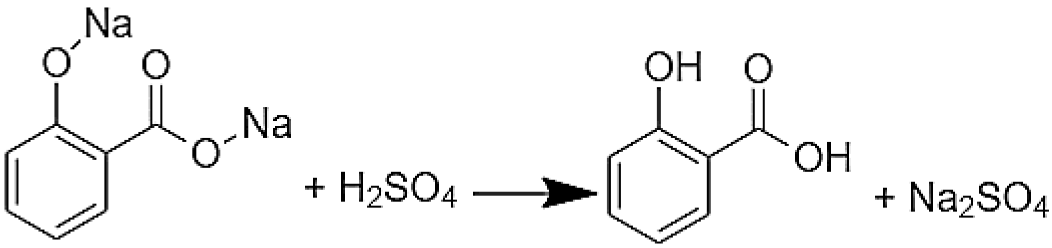
(18)

Once obtained the sodium felonate, this is placed in a reactor where it is exposed to the action of carbon dioxide under controlled conditions of pressure and temperature. Inside the reactor, a carboxylation reaction is carried out, to form sodium phenyl carbonate; which is isomerized to produce sodium salicylate according to the next.



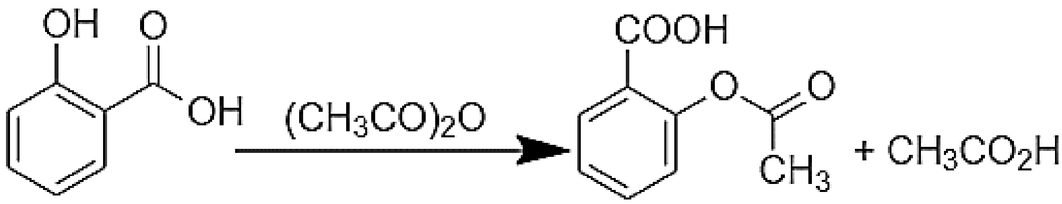
(19)

With the obtaining of sodium salicylate, this is exposed to the action of activated carbon and sulfuric acid; to form a precipitate of salicylic acid, which is separated and purified by sublimation.



(20)

At this point of the process, it is necessary to have prepared a mother liquor composed from a solution of acetic anhydride, which is very corrosive to most metals, and toluene (Martinez et al., 2016). In this way, the salicylic acid obtained will react with acetic anhydride prepared; to produce an acetylation reaction and obtain the acetylsalicylic acid. This process is carried out under controlled conditions of temperature where an increase in the volume of the product occurs, this reaction takes place according to the next.



(21)

Subsequently, this reaction must be cooled down so that the acetylsalicylic acid precipitates in the form of long crystals, those crystals are taken to a funnel crystallizer where the major amount of mother liquor (acetic anhydride and toluene) is removed.

Finally, to purify the acetylsalicylic acid crystals, drying and washing processes with distilled water are applied to remove acetic acid excesses.

In this way, the excesses that have been obtained of acetic acid, are retrieved and stored in a tank, where with sufficient agitation and diffusion of an acetylating agent known as ketene (CH_2CO); it can be obtained more acetic anhydride to reuse in the process. The reaction between ketene and acetic acid to obtain acetic anhydride is shown in the following.

$$CH_2CO + CH_3COOH \rightarrow (CH_3CO)_2 \quad (22)$$

Once studied the process of synthesis of acetylsalicylic acid or aspirin on industrial and laboratory scale. It is important to review the aspirin manufacturing process, to identify which parts of the process can be recovered a certain amount of product; for the purposes of this investigation.

3.5.4. Process description

Next will be described some of the equipment and the process involved in the production of aspirin, this process is retrieved from the project about an Aspirin Production Plant elaborated by Aleu et al., (2018) in Figures 9a and 9b. This process begins in the mixer (M-201), where the reaction between the sodium hydroxide and phenol is carried out at temperatures of 100 ^oC; to evaporate water formed during the reaction. From this process, excess of phenol is obtained, and it is recirculated to the mixer (M-201), as well as a mass is dried in a rotary vacuum band filter (F-202); in this way sodium phenolate is obtained in powder form which is stored in a tank (T-203).

It should be considered that the dried process must be rigorous because the presence of water decreases the process performance. On the other hand, with sodium phenolate obtained, this is taken to the carboxylation process in the reactor (R-204), where sodium phenolate is exposed to CO_2. From this, sodium salicylate is obtained, which is cooled and taken to a homogenization tank (M-205); in this tank, sodium salicylate dissolves with water, and also it is bleached with activated carbon. Then sodium salicylate is taken to a precipitation tank (T-207), where sulfuric acid is added to have salicylic acid; this is precipitated, centrifuged, dried, and stored in a tank (T-210).

Once obtained the salicylic acid of high purity, this is fed to a reactor of stainless steel (R-301), where calcium oxide and acetic anhydride are added; to have an acetylation reaction. Then, the temperature must be controlled with the purpose that the reaction cools down; in this way, amounts of aspirin, calcium acetate, and water are obtained and taken to be taken to the homogenizer (M-302). In this homogenizer calcium acetate dissolves in cold water, then to remove out the moisture percentage, this is taken to an evaporator (E-308); to separate calcium salt and aspirin crystals. Finally, aspirin passes into the processes of dried, milled, and sieved to be packed. Thus, next is shown the diagrams of the process described above.

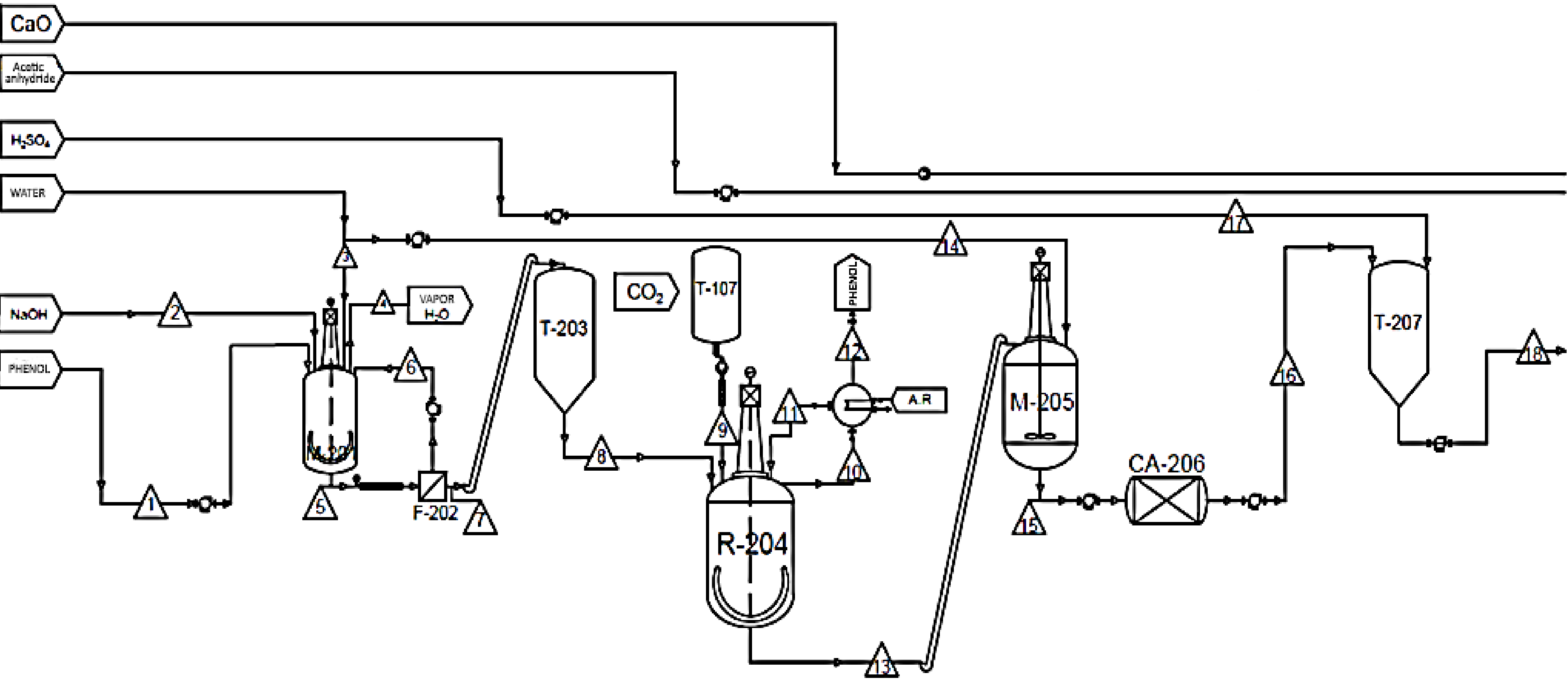


Figure 9a, Process diagram 1/2, adapted from (Aleu et al., 2018)

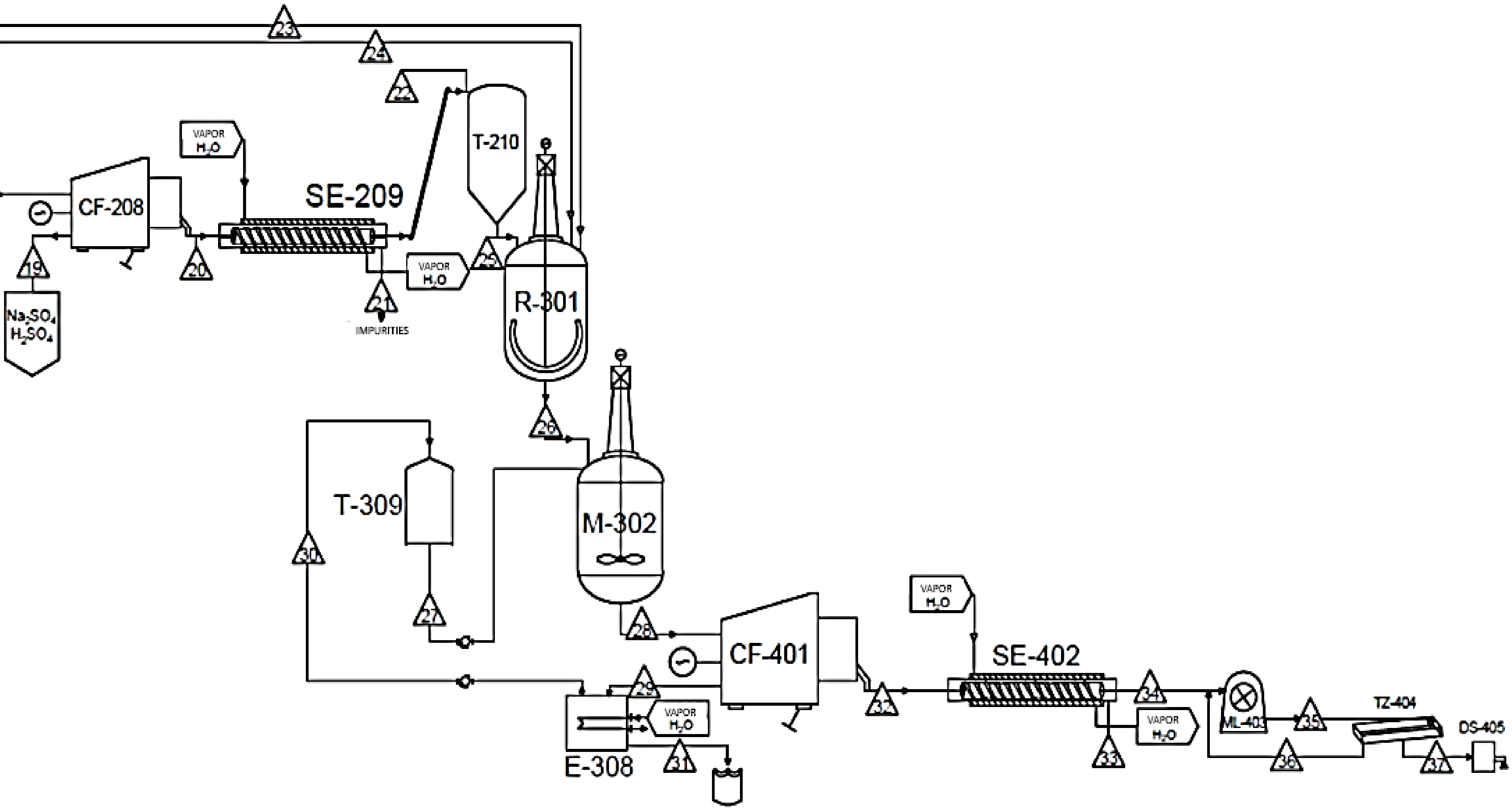


Figure 9b, Process diagram 2/2, adapted from (Aleu et al., 2018)

Therefore, this is how aspirin is obtained at an industrial scale, as it can be observed there are several steps that are carried out under controlled conditions. All this is to have a good quality of aspirin and take it to the main consumers. Next tables shows the mass balances of the work made by Aleu et al., (2018). The input and output currents in the different unit operations in units of kmol are described.

Table 8, Mass Balance 1 / 4, adapted from (Aleu et al., 2018)

Units (Kmol)	1	2	3	4	5	6	7	8	9	10	11
Salicylic acid	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
H_2O	0.00	0.00	37.33	54.13	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Na_2SO_4	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Phenol	16.80	0.00	0.00	0.00	5.04	5.04	0.00	0.00	0.00	2.18	0.00
NaOH 50%	0.00	16.80	000	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
CO_2	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	16.80	2.18	2.18
H_2SO_4	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Sodium salicylate	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Sodium Felonate	0.00	0.00	0.00	0.00	16.80	0.00	16.80	16.80	0.00	0.00	0.00
T (ºC)	45.00	25.00	25.00	100.00	100.00	95.00	200.00	192.00	192.00	192.01	175.02
P (atm)	2.24	1.00	2.90	1.00	1.00	2.45	1.00	1.00	6.00	6.00	6.00

Table 9, Mass Balance 2 / 4, adapted from (Aleu et al., 2018)

Units (Kmol)	12	13	14	15	16	17	18	19	20	21	22
Salicylic acid	0.00	0.00	0.00	0.00	0.00	0.00	14.62	0.73	13.89	0.00	13.89
H_2O	0.00	0.00	130.01	130.01	130.01	29.20	159.21	157.62	1.59	1.59	0.00
Na_2SO_4	0.00	0.00	0.00	0.00	0.00	0.00	7.31	7.31	0.00	0.00	0.00
Phenol	2.18	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
NaOH 50%	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
CO_2	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
H_2SO_4	0.00	0.00	0.00	0.00	0.00	8.04	0.73	0.73	0.00	0.00	0.00
Sodium salicylate	0.00	14.62	0.00	14.62	14.62	0.00	0.00	0.00	0.00	0.00	0.00
Sodium Felonate	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
T (ºC)	175.00	192.00	25.00	52.97	52.97	25.00	47.84	47.84	47.84	47.84	47.84
P (atm)	1.00	1.00	1.93	4.22	1.82	2.88	1.00	1.00	1.00	1.00	1.00

Table 10, Mass Balance 3 / 4, adapted from (Aleu et al., 2018)

Units (Kmol)	23	24	25	26	27	28	29	30	31	32	33
Aspirin	0.00	0.00	0.00	1389	0.00	13.89	0.00	0.00	0.00	13.89	0.00
Calcium Acetate	0.00	0.00	0.00	6.94	0.00	6.94	6.94	0.00	6.94	0.00	0.00
CaO	6.94	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Salicylic acid	0.00	0.00	13.89	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Acetic Anhydride	0.00	13.89	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
H_2O	0.00	0.00	0.00	6.94	183.02	189.96	189.01	189.01	0.00	0.95	0.95
T (ºC)	25.00	25.00	47.84	85.00	5.00	20.56	20.56	100.00	100.00	20.56	40.00
P (atm)	1.85	1.74	1.00	1.00	1.95	1.00	1.00	1.00	1.00	1.00	1.00

Table 11, Mass Balance 4 / 4, adapted from (Aleu et al., 2018)

Units (Kmol)	34	35	36	37
Aspirin	13.89	13.89	0.01	13.88
Calcium Acetate	0.00	0.00	0.00	0.00
CaO	0.00	0.00	0.00	0.00
Salicylic acid	0.00	0.00	0.00	0.00
Acetic Anhydride	0.00	0.00	0.00	0.00
H2O	0.00	0.00	0.00	0.00
T (oC)	40.00	40.00	40.00	40.00
P (atm)	1.00	1.00	1.00	1.00

Thus, as it can be observed from Table 11 at the exit of the production line 37, the reaching of this industrial process leads to obtaining 13.88 kmol of aspirin theoretically. Therefore, with the purpose to know the amount of aspirin that one can obtain from this process, it is necessary to carry out a simple conversion based on the molecular weight of aspirin; which is 180.158 g / mol. The molecular weight of aspirin will be used in units of kg / kmol according to the next math operation:

$$13.88 \text{ kmol (Asp)} * 180.158 \frac{\text{kg}}{\text{kmol}} (\text{MW}_{\text{Asp}}) = 2500.59 \text{ Kg Asp} \qquad (23)$$

As can be expected from an industrial process, the amounts of production are very high. This can be clearly observed in the industrial process proposed by Aleu et al., (2018), whose process leads to obtaining 2,500.59 kg or 2.5 tons of aspirin.

The high demand for the production of this medicine, according to Wiser & Weigmann (2019) and the World Health Organization's (2021), is due to the fact that analgesics such as aspirin are considered one of the most essential medicines worldwide to treat pain. This can be seen reflected in the study carried out by the Statista Research Department (2021), where it is observed that in 2020, the Bayer company, through its flagship product, managed to invoice around 41,400 million euros. Which shows the immense consumption of this medicine worldwide. Therefore, it is not surprising that Coba (2020) establishes that, due to the discomfort caused by Covid, the drugs with the most demand in Ecuador are of the analgesic type. But how does aspirin relate to the purposes of this paper?

3.6. Alka Seltzer

As it was mentioned from the beginning, the main objective of this project is the use of drugs as a corrosion inhibitor. For this purpose, drugs of antacids type have been chosen to analyze its inhibitory potential. Probably this leads to wonder why it was important to do an aspirin review? Well According to de Abajo & Garcia (2009), aspirin is one of the most important components of the most famous antacid worldwide, known as Alka Seltzer. Therefore, next will be analyzed the characteristics of Alka Seltzer.

Since the 1930s Alka Seltzer has been recognized, as one of the most successful and influential medicines of all time, because this medicine has helped to treat pains caused by indigestion, stomach upset and heartburn (de Abajo & Garcia, 2009). In this way, Alka Seltzer is a tablet that is made up of aspirin (0.325 g), sodium bicarbonate (1.9 g), and citric acid (1 g); each one of these components fulfills a specific function, to carry out their activities within the body (de Abajo & Garcia, 2009).

Thereby Alka Seltzer tablets are composed of acidic substances and bicarbonates, which are released thanks to their effervescent action in presence of water that will act as a catalyst of the reaction. This chemical reaction occurs quickly, allowing to increase the absorption speed and also facilitating the assimilation of the drug too (de Abajo & Garcia, 2009). In this way, Alka Seltzer can act rapidly by neutralizing the stomach acid.

3.6.1. Mechanism of action in the body

One of the most important advantages in drinking Alka Seltzer instead of Aspirin according to Gutierrez (2002), is because acetylsalicylic acid by itself can irritate the stomach because of the acidity that causes. On the other hand, the Alka Seltzer tablet is less aggressive for the stomach, because this is formulated with an antacid that helps to control the levels of acidity. Thus, this tablet can act rapidly by its effervescent action, but what is happening inside the organism?

As it was previously mentioned, Alka Seltzer is made up of aspirin, sodium bicarbonate, and citric acid; these compounds are administered in a single tablet by mouth and react to relieve stomach discomfort. In this way, it will be analyzed the behavior of each one of these components. The first to be analyzed will be sodium bicarbonate, which has a great influence on the acid neutralization process, and also according to Delli (2017), the amount of sodium bicarbonate in an effervescent tablet is quite high. Therefore, this compound has an important role in the acid neutralization process. With this objective in mind, let's take a look at the state Alka Seltzer tablet before it is ingested inside the organism.

So that the active principles from Alka Seltzer act in the body, firstly this should be dissolved in water, where an effervescent reaction begins in form of gas bubbles (Delli, 2017). According to Avendaño & Vásquez (2014), this is caused when the sodium bicarbonate comes into contact with water, which produces a dissociation of the ions; these ions react with the acid component of the tablet to produce carbon dioxide gas. Hence, this effervescent reaction allows a better dosage, since the CO_2 generated improves the permeability and solubility of the active principles (Delli, 2017). Moreover, Santos (2016) mentions that effervescent formulations produce protection of the gastric mucosa, which minimizes its irritation.

According to the technical paper developed by the Spanish agency CIMA in 2019, in this effervescent reaction, a buffered reaction is formed; resulting carbon dioxide and sodium dihydrogen citrate. Next is shown the reaction that occurs.

$$C_6H_80_7 + NaHCO_3 \rightarrow NaH_2(C_3H_5O(\mathrm{COO})_3) + C0_2 + H_2O \qquad (25)$$

These compounds, together with the remaining sodium bicarbonate prevent the dissociation of HCl; which is responsible to provoke stomach heartburn (CIMA, 2019). Thus, on the one hand it is achieved that the pH increases, until reaching alkaline levels of 5.5-6.5 (Santos, 2016); and by the other hand, this buffered reaction neutralizes the secretions of hydrochloric acid in the esophagus and stomach (CIMA, 2019). Consider equation (6) reviewed in Chapter III, to see how the HCl neutralization process occurs by sodium bicarbonate.

$$HCl\ (aq) + NaHCO_3\ (aq) \rightarrow NaCl\ (aq) + H_2O + CO_2 \qquad (26)$$

However, where aspirin is involved during this process? Well, the acetylsalicylic acid as it was previously studied, acts to treat pain and discomforts; in this case acts in the same way to treat the same symptoms of pain caused by heartburn. The acetylsalicylic acid reacts rapidly and it is converted into salicylic acid, then it is metabolized in conjugation with glycine and glucuronic acid (CIMA, 2019). Thereby, it is necessary to mention, that the reaction kinetics and therefore the effectiveness of Alka Seltzer's tablet, during the process of neutralizing the acid action of HCl; it depends a lot on the acid-base state of each individual (CIMA, 2019)

Finally, all the reactions that took place during the absorption process between the sodium bicarbonate, citric acid, and aspirin generate some products wastes. Thus, concerning the products of the reactions that took place during the absorption of Alka seltzer, it has been observed that ions and other wastes are generated; these are excreted through urine by the renal system (CECMED, 2017).

3.6.2. Alka Seltzer Production

As detailed above, the Alka Seltzer tablet is made up of three main ingredients: sodium bicarbonate, citric acid, and aspirin. In this way, the manufacturing process recovered from Delli (2017) is detailed a process in which it is not necessary to synthesize any compound since the raw materials must already be available for obtaining Alka Seltzer. Thus, what remains to be done to obtain the tablet, is to homogenize these compounds, in Figure 10 is shown a diagram of the process for the manufacture of Alka Seltzer.

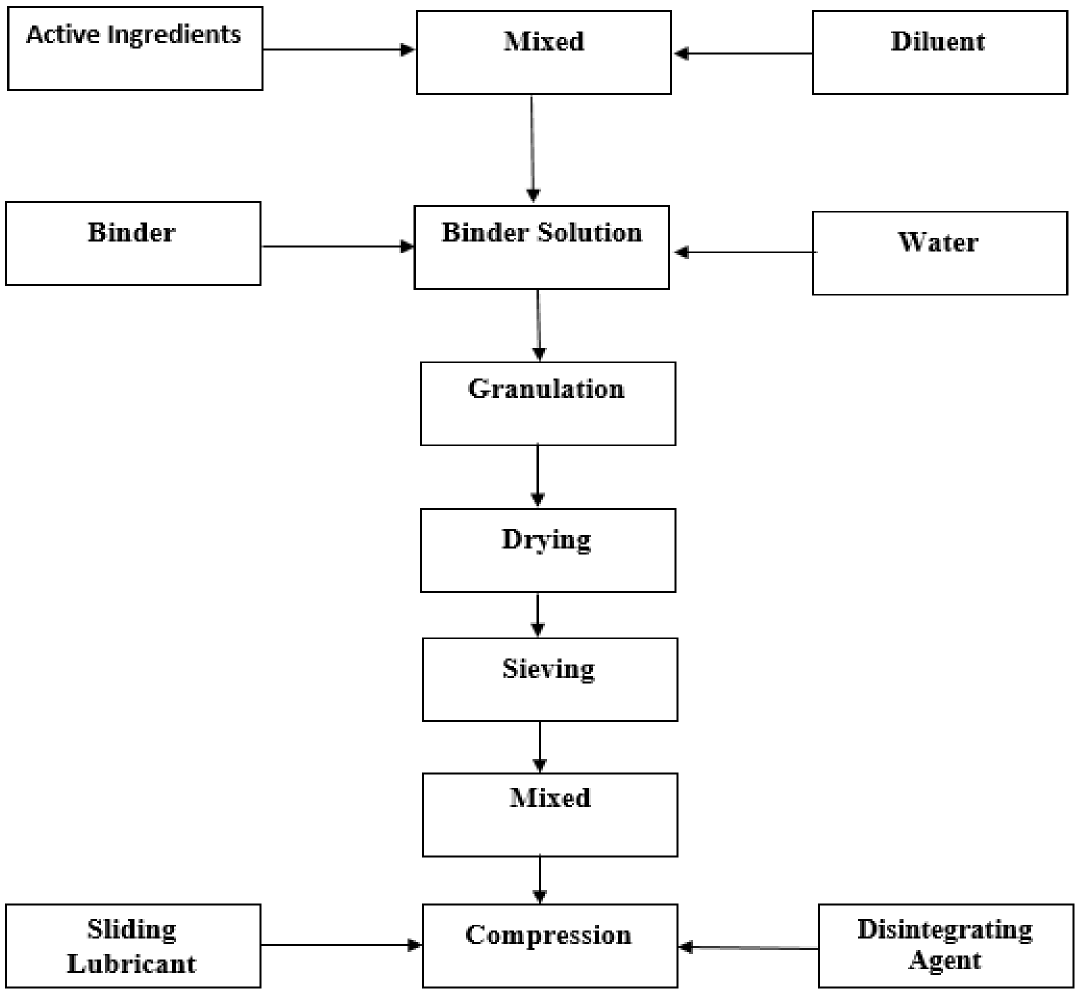


Figure 10, Process diagram for obtaining Alka Seltzer, adapted from Delli (2017)

First of all, as it will be worked with a tablet that reacts instantly in presence of water, it is necessary to control the environment from the humidity; to avoid any reaction with the Alka Seltzer tablet or possible degradation of the raw materials. Thereby, the machinery needed for the process includes mixers, granulators, roller compactors, drying equipment, and mills.

In this way, the manufacturing will start with a mixing process, where the active ingredients will be added. Hence, to homogenize the mixture and also to prevent a rapid dissolution of effervescent tablets, binder liquids are commonly used; in this case could be used water or organic solvents. Then, using organic solvents has some advantages, since as mentioned the effervescent reaction only takes place when the materials come in contact with water. Thereby, the use of organic solvents could be a good option to avoid effervescence, and also because these allow the drying process to be carried out at lower temperatures; as they have a lower evaporation point.

On the other hand, if you choose to use water as a binder liquid, it must be considered to add water in small amounts; this causes a pre-effervescence reaction. Therefore, from this reaction, CO_2 and water are produced, these will act as a binder liquid; however using water has the disadvantage that the process conditions must be carried out very carefully to obtain the desired product. Regardless, if water or an organic solvent has been used, a binder solution is formed; which goes to a granulation process where larger structures are formed, called granules. Once the granules are obtained, these are taken to a drying process with the purpose to remove the humidity caused by any binder liquid; this is because humidity conditions must be below 0.3%.

Continuing with the process, once the mixture is dry, this is taken to a sieving process to obtain particles of smaller size. Then, these are homogenized again on a mixing process and then take the mixture to the compression procedure. In this process, the materials are transformed into tablets, but own to the fact that rotary valves are used on compression procedures, it must be used a lubricant that prevents the product sticks to walls. Thereby, so that the least amount of product adheres to the walls of the machinery, the perfect candidates to be used in these effervescent tablets are sodium chloride, sodium acetate, L-leucine, and paraffin because they are soluble in water.

In this way, in the compression process, the Alka Seltzer tablets are obtained, which are directed to a packaging process, where correct preservation of the product must be ensured. Thus, the packages commonly used for being hermetically sealed, are aluminum blisters, because these have low permeability to water.

Consequently, once the processes to obtain aspirin and Alka Seltzer are known, it will be analyzed if some wastes can be generated during the processes of manufacturing. With the purpose of carrying out a good management of these wastes and taking advantage of them for the aims of this work.

3.7. Waste management

According to data from the World Health Organization published in 2018, there is approximately 85% of common waste, and the other 15% is considered dangerous waste that can be infectious, toxic, and radioactive. For instance, along the Elbe and Saale rivers in Germany, the presence of drugs that are polluting water has been evidenced; in the same way in samples of wastewater in effluents from the hospital in Tromsø, Norway; drugs, analgesics, antidepressants, caffeine, triclosan, and insect repellent were identified. (Wiegel et al., 2004). Another case is located in Spain, where emerging pollutants of different classes such as cosmetic ingredients, drugs, hormones, caffeine, and ibuprofen have been detected in raw wastewater (Rodil et al., 2011). Therefore, the pharmaceutical industry has been aware for several years of the waste that is produced and its presence in the environment.

According to Mutaseim et al., (2019), the lack of information about the management of pharmaceutical wastes; makes these easily become part of the environment. For instance, according to Incerox (2020), the antibiotics that end up in aquatic environments have caused an increase in toxicity and antibiotic resistance of aquatic organisms; which already represents a serious health issue. To support this, Serra (2017), also considers that the bad handling of the pharmaceutical wastes, is responsible for the majority of problems of the environment; since these residues have chemical, biological and microbiological procedures that could impact directly to the ecosystem.

It can clearly observe the detrimental impact that the environment receives, due to inefficient management of pharmaceutical waste, that industries and consumers performs. In this way, looking for alternatives that help reduce the impact on the environment, with measures that are in accordance with the nature of the products manufactured, the use of technologies in production and the type of waste generated. It is proposed to take advantage of the waste generated from aspirin and Alka seltzer in two categories. Through the collection of products that can be generated during the process, and products that have already reached their expiration date; since according to Zuñiga et al., (2016), expired drugs are also a source of environmental contamination.

Consequently, through a better management of waste in these two categories, could be generated a positive impact for the environment and the economy. Since according to the article written by Mella (2020), it mentions that in the year 2020, the Ecuadorian Institute of Social Security (IESS) allowed to expire medicines in 101 Ecuadorian Hospitals; that was valued at $1,622,117.72. Thus, it can be seen that, through the implementation of new alternatives to take advantage of these expired drugs, a better management of economic resources could be carried out as well.

3.7.1. Aspirin Waste

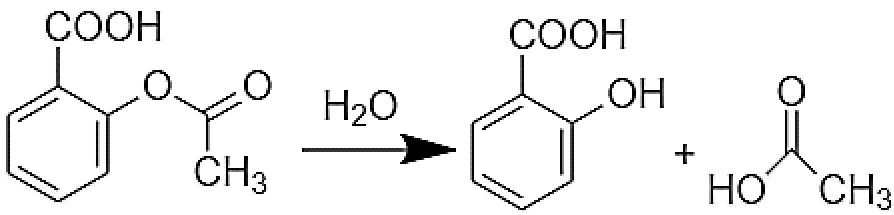
As it could be seen in the description of the process, the production of aspirin involves some steps, where some quantity of aspirin can be lost. But also, this is not the only way how aspirin can be wasted, because like any product, it has a useful life period. According to Sinche (2018), the shelf life is considered the period in which the product no longer meets the specifications, so that the consumer cannot use the product; this can be influenced by the conditions under which the product is stored.

As was mentioned, one of the approaches is to analyze the waste generated during the process, thus it proceeds to locate in which part of the manufacturing process can be generated residues to be reused. The granular and dust residues of aspirin can be lost in their majority through closed processes of acetylation, sieving, filtration, and granulation; where exists small particles that can escape to the environment (Martinez et al., 2016). But what do industries do with these residues?

According to Navarrete (2010), granular and dust residues are common elements that are generated in industrial process production, in this way these residues are collected by systems of air filtration, and in the case of residues that falls to the floor, are collected in holsters. Thus, at industries, these aspirin residues that are collected from the floor and systems of air filtration, are treated in incinerators that generate ash, slag, and smoke; which is a problem because it causes atmospheric pollution (Martinez et al., 2016).

Another approach to be analyzed, was to take advantage of the expired aspirin. Aspirin ceases to be effective when the raw materials and pharmaceutical formulations have lost their activity over time (Martinez et al., 2016). But what causes aspirin to lose its effective? Well, the quality and condition of a medicine like this, can be seen affected by environmental factors, temperature, light, and humidity in which is stored (Sinche, 2018). Thusly, according to Mamani (2016), the expiration date for aspirin is three years.

But in the case of aspirin, the principal way that causes degradation and instability is caused by the humidity; because this leads aspirin to hydrolyze with water. Hydrolysis can be produced by either the hydroxide ion or the hydrogen ion, this causes acetylsalicylic acid to be degraded into salicylic acid and acetic acid (Sinche, 2018). Figure 11, shows how hydrolysis is carried out in aspirin.



(17)

Figure 11, Hydrolysis of acetylsalicylic acid, adapted from (Sinche, 2018)

As it can be observed, when aspirin has expired, there is a high probability that it will be found as salicylic acid and acetic acid. Thereby, according to the article written by Rodriguez (2016) in "Myths and realities of the expiration dates of medicines and creams", it mentions that after 6 months after the expiration date of aspirin, its consumption is not recommended, since there may be toxic compounds harmful to the organism. Therefore, what is done with these expired aspirin, as well as the aspirin residues coming from manufacturing process, these are recovered and incinerated (Martinez et al., 2016).

In fact, with the purpose to prevent that those expired medicines, affects the health and the environment. According to the Ecuadorian Ministry of Public Health (2020), exists procedures and regulations, directed by the National Agency for Regulation, Control and Health Surveillance (ARCSA), which focuses on supervising the incineration of expired medicines from businesses, homes, etc.

3.7.2 Alka Seltzer wastes

As in the case of aspirin reviewed above, it proceeds to analyze the wastes that can be generated during its manufacturing, and also its expiration date. Thusly, according to the process of manufacturing of Alka Seltzer, it can be observed that it involves stages of mixing, drying, granulation, and sieving where some solid residues of the product can be generated. First of all, the place where the Alka seltzer tablet can be found already formed is from the granulation process. Then, this is taken to a process of dry which leads to the sieving process, where the main purpose of this; is to obtain particles of smaller size.

During this process, the particles of Alka Seltzer can either escape to the environment and fall to the floor, or also a certain amount of Alka Seltzer can remain in the machine of sieving. Thus, the next step where can be found residues are during the compression procedure, here the effervescent tablet is obtained; this is achieved due to rotary valves. However, the walls of these rotary valves can keep amounts of product that could be recovered. Consequently, in the same way as in the case of aspirin, these residues can be collected either by air filtration systems or stored in covers.

Finally, with respect to manufacturing process, can be find Alka Seltzer residues during the quality control process that according to Tait (2012) these processes are carried out in the pharmaceutical industry to ensure the quality and the state of the products. During this procedure, may be found tablets of Alka Seltzer that have not been properly packaged can be detected. In this way, as previously reviewed, this tablet is very sensitive to humidity. Hence, these Alka seltzer tablets poorly packed, can be discarded and not sent to the market.

Respecting to the Alka Seltzer expiration date, according to the report made by Bunce (2017) and to the technical sheet of CIMA (2019), on these are detailed that the expiration date of Alka Seltzer is 3 years. However, this expiry time could be influenced by some factors, for instance due to this tablet reacts instantaneously with water; if bad packaging is done or is exposed to humidity conditions. It can cause that the tablet reacts and degrade it at the same time.

4. Discussion

All this literature review leads to the following question. Can the drugs presented in this work fulfill the function of corrosion inhibitors for acid cleaning? Well, to answer this, first it is important to identify what are the pharmaceutical products that are proposed to be used as corrosion inhibitors. These are aspirin and Alka seltzer, however, salicylic acid, as a product of expired aspirin, can also be included as another candidate to inhibit corrosion.

Once aspirin, salicylic acid and Alka seltzer have been identified as possible corrosion inhibitors, it proceeds to analyze the reasons why they could function as inhibitors. In chapter II, it was studied how the most effective inhibitors that work efficiently in an acid medium contain elements of Groups V and VI of the periodic table such as N, S, P and O. Which resulted to be excellent inhibitors, those that are conformed by functional groups such as –OH, –COOH, NH2, and they were even better if they had double and triple bonds within their structure. Additionally, a green corrosion inhibitor was analyzed, which with an efficiency of 87.43%, was capable of inhibiting corrosion. This green corrosion inhibitor was made up of the following functional groups -OH, C-H, C = O, and C-O. Therefore, it is important to go back and check the structures of the possible corrosion inhibitors.

It can be seen in Figure 8 and Figure 11, the chemical structures of aspirin and salicylic acid, respectively. In the case of Alka Seltzer, it should be remembered that this is a tablet made up of different compounds, including aspirin. Therefore, within these chemical structures, it can be identified that they comply with the elements and functional groups to act as inhibitors, according to the examples cited above. In this way, aspirin and salicylic acid could function as pickling inhibitors, since they have elements such as oxygen, functional groups such as –COOH, CH, OH. But in addition, these chemical structures present double bonds, which contribute to the metal interactions.

In the case of Alka Seltzer, as previously reviewed, the amount of aspirin present is not very high compared to the amount of antacid present. Therefore, principally this tablet acts by neutralizing hydrochloric acid, by reducing the concentration of hydrogen ions. This behavior against hydrochloric acid must be considered, since it can affect the mechanism of action of acid cleaning during pickling.

This leads to consider the different modes of application that the drugs proposed as inhibitors in acid cleaning could have. Thus, aspirin and salicylic acid could be applied together with pickling, however, Alka seltzer, due to its antacid character, could not be applied together with acid to treat pickling. Since it could considerably affect the effectiveness of acid cleaning. However, one could think of Alka seltzer, for treatments prior to acid cleaning, where once the fouling has been removed, the Alka Seltzer could be applied.

Consequently, to verify the anticorrosive efficacy of these drugs, it is necessary to carry out electrochemical studies, in order to analyze their rate of corrosion against metals in acid conditions. Thus, if the inhibitory potential of these drugs is verified, the waste generated during the manufacturing process could be used, as well as the waste that comes from expired drugs. In order to better manage waste for the benefit of the environment and the economy.

5. Conclusion

To develop methods that allow better management of both, wastes from the pharmaceutical industry and products that sooner or later expire. This work has been developed, to carry out an exploratory bibliographic review, which allows to supports the idea, that the aspirin, salicylic acid, and Alka seltzer; can be used as corrosion inhibitors. These drugs have been presented as possible corrosion inhibitors since they meet the necessary characteristics to test their inhibitory potential within acid cleaning in oil wells.

The application of these drugs is proposed, because, its chemical structure assemble the main characteristics of the corrosion inhibitors that act in the most effective way in acid medium. Thus, as its chemical structure is conformed by functional groups such as –OH, –COOH, and doble bonds that allow to generate interactions with the metal in order to treat corrosion. In this way, the aspirin, salicylic acid, and Alka seltzer could be considerate as candidates to treat corrosion in pickling.

However, it should be considered that the way of application, in the case of aspirin or salicylic acid, if the expired drug is applied, may be different from the Alka Seltzer application mode. Since in Alka Seltzer, due to the presence of antacid, this could affect the effectiveness in the action mechanism of the acid applied in the pickling. Thus, it is proposed to apply aspirin or salicylic acid, in conjunction with the acid during pickling. On the other hand, in the case of Alka Seltzer, it could be applied prior to acid cleaning, once it has already removed the fouling on the metal surface.

However, it should be considered must be taken into account that this work has been carried out to search for new alternatives of corrosion inhibitors. So, apart addition to the information presented in this work, these drugs require electrochemical tests that allow to monitor the corrosion rate during the exposure of these drugs on acid media. This with the purpose to verify and sustaining the inhibitory potential of the drugs proposed.

6. Recommendations

- Because the drugs have good characteristics to behave as efficient corrosion inhibitors. It is recommended to expand the search and investigation of more drugs that can be applied as corrosion inhibitors.
- It is recommended that for no reason the drugs mentioned in this work are used for anticorrosive purposes, without first having carried out experimental studies that prove their effectiveness as corrosion inhibitors.
- It is recommended to carefully review the mechanisms of action of the different compounds that make up a drug. Since in the search for applications, the compounds can react in a way that is not suitable for the main purposes.
- It is recommended to continue with research based on green corrosion inhibitors, since they result to be a good ecological option and also economically viable.

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