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An overview of expired drugs as novel corrosion inhibitors for metals and alloys

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A B S T R A C T

The use of drugs as corrosion inhibitors for metals and alloys has emerged as an attractive replacement strategy to the otherwise toxic corrosion inhibitors. However, a major drawback is the financial constraints imposed on the method due to the high cost of pharmaceutical compounds. In the recent years, the use of outdated or expired medicines as corrosion inhibitors in a variety of aggressive media has provided an attractive alternative. In addition, this method addresses the issue of environmental contamination by the disposal of unused or expired drugs and also the costly degradation procedures. Although this area is still in the stage of early development, this review covers most of the contributions on the expired drugs as corrosion inhibitors as well as addresses some of the key parameters critical for evaluation of the corrosion inhibition efficacy of expired drugs in comparison to that of fresh drugs.

Keywords: Expired drugs, Corrosion inhibition, Electrochemical measurements, Density functional theory

A R T I C L E I N F O

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EIS = Electrochemical Impedance Spectroscopy; LPR = Linear Polarization Resistance, CV = Cyclic Voltammetry; XRD = X-ray Diffraction; EFM = Electrical Frequency Modulation; DFT = Density Functional Theory

1. Introduction

In order to control and mitigate the corrosion of metals and alloys in various industries, the use of organic compounds as corrosion inhibitors is a common strategy [1, 2]. Organic compounds containing N, O, S heteroatoms and π electrons in their molecules are considered as effective corrosion inhibitors [3, 4]. It is noteworthy that a vast majority of these organic compounds e.g. pyridines, furans, imidazoles, thiophenes, isoxazoles etc. have considerable similarity with the substructures of many of the commonly used drugs. This feature has prompted scientists across the globe to investigate the applicability of drugs as corrosion inhibitors. Bearing non-toxic characteristics and negligible negative environmental impact, drugs (chemical medicines) have emerged as ideally suited candidates to replace the conventionally used toxic corrosion inhibitors [5−13].

However, most of the commonly available drugs are far more expensive than the corrosion inhibitors currently being employed. Therefore, the notion of practical realization of drugs as corrosion inhibitors seems quite far-fetched. On the other hand, it has been established that in some cases the outdated drugs have retained potency for > 10 years after expiry [14−16].

A physician or a pharmaceutical company, however, would never recommend the administering of an expired drug due to concerns of legal action or such liabilities. People usually tend to dispose the leftover or expired drugs in the trash or toilet sink which directly exposes the drugs to the environment. The proper disposal of pharmaceutical compounds is generally performed by medium or high temperature incineration which in addition to being too expensive [17], can contaminate the atmosphere by releasing toxic organics comprising of N, P, S and halogens [17, 18]. Even the controlled degradation procedures are tedious and expensive [19].

Therefore, on one side, there is a growing interest in using drugs as corrosion inhibitors but the cost is creating the problem. On the other hand, an enormous stockpile of outdated drugs just sits there to unleash havoc on the environment. A convenient and promising resolution to the situation is the use of expired drugs as corrosion inhibitors which can create a cost effective and environmentally benign method to address the issue of corrosion mitigation (Fig. 1). It is noteworthy to mention that although there is a plethora of available articles describing the use of drugs as corrosion inhibitors as covered earlier [5], the literature survey reveals only a very few reports describing the use of expired drugs as corrosion inhibitors as shown vide infra. Hence, the goal of this study is to present a critical overview of the current state of research in the area to summarize the relevant research work as well as to understand various perspectives.

Entry of expired drugs in the environment

The accumulation of leftover or expired drugs in the environment poses a major concern for exposure of humans and wildlife [20]. In most of the cases, people dispose the unused drugs through waste basket or toilet flush through which the drug can be exposed to sunlight, oxygen, moisture or extreme temperature leading to an uncontrolled degradation which can potentially generate toxic waste products [20]. A detailed account on numerous ways of the entry of human pharmaceuticals in the aquatic environment and various natural degradation or modification mechanisms has been covered earlier [21]. Investigations of coroner records have shown that there are two major human controlled means by which drugs enter in the environment: indirect (via bathing and excretion) and direct (via disposal of leftover or expired medications) [22]. According to the Federal guidelines for proper disposal of unused drugs issued by the White House Office of National Drug Control Policy in 2007, the consumers are required to adulterate unwanted medicines by mixing with an unpalatable substance and then disposing into the household trash. The guidelines also recommend the return of leftover drugs to local “take-back” locations, whenever available.

The date of expiry is a typical reason for medicine disposal [20]. Other reasons include recovered health condition and a house-cleaning prompting the disposal of stored medications. The most common ways of disposal are the sink, toilet and trash. The results of a statistical and econometric analysis showed that ~43 % people are aware about the environmental concern created by discarded drugs [20]. Still there was a considerable non-compliance among people because some were aware of other environmental issues and consider pharmaceutical pollution a relatively low priority. Another possibility was that the aware respondents also believed that the indirect means i.e., the excretion of pharmaceutical compounds is the primary problem and were therefore skeptical about whether a proper disposal program would have an appreciable effect. Although, the survey of Kotchen et al [20] also revealed that when people are made aware about the environmental hazards of pharmaceutical compounds, they are even willing to spend some extra money over the prescription drugs in order to facilitate the safe disposal.

A major means through which the pharmaceuticals gain entry to the environment is due to the mismanagement of donated drugs [17]. During worldwide conflicts and natural disasters, often large quantities of pharmaceuticals are donated as humanitarian assistance. Although, a large part of this definitely does saves lives and relieves suffering, but still some of the donations especially those arriving past or nearing their date of expiry, may turn out inappropriate to meet the requirements. Also, such drugs may be unrecognizable because of language differences, or may be in excessive quantities than that required [23]. The poor management in such cases may also lead to entry of pharmaceuticals in the environment.

Mechanism of corrosion inhibition by drug/ organic inhibitor:

The drug molecules have plenty of heteroatoms (N, S, O) and phenyl rings which facilitate their interaction with the metal surface. A typical example of the protective action of an organic inhibitor on the corrosion of mild steel in acidic medium is given here. In acidic medium, an organic

inhibitor gets adsorbs on a metal surface and forms a protective film (Fig. 2) which retards the anodic/ cathodic corrosion reactions.

Figure 2: Typical action of a drug as a corrosion inhibitor in acidic medium

The inhibitor adsorption is influenced by the nature and the charge of the metal, chemical structure of the organic inhibitor and the nature of the aggressive electrolyte. The charge on the metal surface can be given by equation:

$$¤ = E_{corr} - E_{q=0} \quad (1)$$

Where, E_{corr} is corrosion potential and $E_{q=0}$ is the potential of zero charge (PZC) of the metal surface [24, 25].

In acidic solutions, the steel surface is positively charged with respect to its potential at zero charge [24]. The adsorption and corrosion inhibition process can proceed with following steps (Fig. 3):

3.1 Electrostatic attraction:

The acidic anions (e.g. Cl^-, SO_4^{2-}) are attracted towards the positively charge metal surface and form a negatively charged layer which attracts the protonated inhibitor molecules leading to the formation of the inhibitor film over metal surface (physical adsorption).

3.2 Chemical adsorption:

The protonated molecules of the inhibitor undergo a competition with the H^+ ions of the acid for the electrons that are being released from the metal surface. The cationic form of the inhibitor molecules, after accepting electrons from the metal surface returns to its neutral form. The heteroatoms of inhibitor molecule share their lone pair electrons with vacant d orbitals of Fe atom.

3.3 Back-donation:

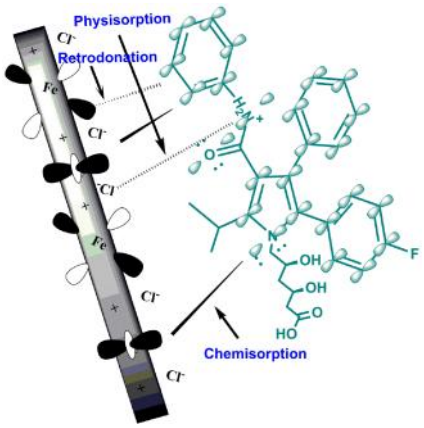


Fig 3:Adsorption of expired Atorvastatin drug on mild steel

Due to the continuous removal of electrons, there is an accumulation of negative charge on the metal surface. In order to relieve this excess negative charge, the d-orbital electrons of Fe can get transferred to vacant ®* (antibonding) orbital of inhibitor molecules (retro-donation). In addition to above, the drug molecules can also adsorb via interaction of the planar $p®$ orbitals of their aromatic rings with the vacant $d®$ orbitals of metal surface [25, 26].

2. Expired drugs as corrosion inhibitors

As mentioned above, the use of expired drugs for corrosion inhibition studies is still a field under developmental stage, hence there is a lack of research contributions in this area. Therefore, rather than providing a rigorous categorization of inhibitors into various drug classes as done earlier [5], we herein discuss the salient features of the corrosion inhibition studies conducted on expired drugs. The idea is to provide the reader an in-depth account of what has been done as well as the key features to look for when working in this area. The data on corrosion inhibition techniques used and the obtained results for various expired drugs is shown in Table 1. The molecular structures of the drugs are shown in Table 2.

Geethamani and Kasthuri performed a comparative study on corrosion inhibition effect of Asthalin (Table 1) on mild steel in 1 M HCl and 1 M H_2SO_4 using weight loss, potentiodynamic polarization and EIS [27]. The adsorption of drug followed Langmuir isotherm showing chemical adsorption. The weight loss study was performed from ½ h to 24 h immersion period and at 11 different sets of concentrations. Effect of temperature was studied from 303 to 343 K. Polarization curves showed a mixed mode of adsorption. The obtained inhibition efficiency was 94.76% and 95.48% in HCl and H_2SO_4 respectively. Earlier, the use of Asthalin expectorant was investigated in 1 M HCl in a wide concentration range and at different temperatures and it was found to efficiently mitigate the corrosion of mild steel specimens as observed from weight loss and electrochemical studies [28].

Earlier, the above group has reported the use of expired Lupicof (Table 1) for corrosion inhibition of mild steel in 1 M HCl using weight loss, potentiodynamic polarization and EIS [29]. The weight loss studies were conducted from 0.1 to 1.1 % v/v for ½ to 24 h and the highest efficiency was obtained at 8 h of immersion time. The effect of temperature was studied from 303 to 343 K and the ΔG values in each case were found to be less than 20 $kJmol^{-1}$ indicating physical adsorption. The maximum efficiency was obtained at 4 h immersion time and at 323 K. The adsorption curves were fitted to Langmuir, Freundlich and Temkin plots, among which the Temkin isotherm provided the best fit.

An investigation of expired Ambroxol (Table 1) drug was performed on mild steel in 1 M HCl and 1 M H_2SO_4 using

weight loss, potentiodynamic polarization and EIS [30]. The surface was examined using SEM. The study was carried out at different concentrations of inhibitor from 1.0% to 9.0% at different temperatures from 303 K to 343 K. Thermodynamic parameters such as energy of activation (E_a), free energy of adsorption (ΔG), enthalpy of adsorption (ΔH) and entropy of adsorption (ΔS) were evaluated in each case. The Langmuir isotherm showed the best fit for the adsorption of inhibitor. Earlier, the corrosion inhibition efficiency of expired Ambroxol was investigated on mild steel in 1 M H_2SO_4 alone and it showed that the inhibitor retards the corrosion process without affecting the mechanism [31]. The EDX spectra indicated the presence of C, N and S thereby confirming the presence of adsorbed inhibitor film on metal surface.

E.M. Attia has studied expired Farcolin (Table 1) for carbon steel in 1 M HCl at 293 and 303 K [32]. The weight loss studies were carried out at different immersion periods from 10 to 120 min at different concentrations from 0 to 20% v/v at both the temperatures. The inhibition efficiency increased with immersion period for all the studied concentrations. The Tafel plots showed that the drug acts as a mixed inhibitor with prominent influence on the anodic process. The adsorption of the inhibitor obeyed the Langmuir isotherm. The potentiostatic polarization was studied in a wide potential range from -200 to +100 mV vs SCE keeping the inhibitor concentration constant at 293 K and 303 K. The corrosion current density increased with increase in the applied potential and was in agreement with that of the Tafel data. The thickness of the oxide layer formed on the metal surface was evaluated according to Helmholtz model [33] and the trends were in agreement with those of the applied potential and varying concentration. The values of reciprocal capacitance ($1/C$) indicated a decrease in the stability of the oxide film for all the concentrations at 293 K and 303 K.

Vaszilcsin et al [18] carried out one of the most prominent investigations in this area. They used Paracetamol (active substance N-acetyl-4-aminophenol) and Carbamazepine (active substance 5H-dibenz[b,f]azepine-5-carboxamide) (Table 1) pills that were expired for 12 months. The corrosion testing was performed on carbon steel in 0.1 M H_2SO_4 and 0.25 M acetic acid/ 0.25 M sodium acetate. An interesting study on the stability of the inhibitors in the corrosive media was performed using cyclic voltammetry employing platinum as working electrode rather than the carbon steel electrode. This allowed the use of an increased potential window and also avoided the interferences with corrosion processes that occur at the steel-solution interface.

The above group has performed a thorough study using weight loss, cyclic voltammetry, LPR and Tafel on expired Zosyn (Table 1) drug as corrosion inhibitor for carbon steel in 3.5% NaCl [34]. The work is especially interesting because the drug Zosyn is made up of two components viz. Piperacillin and Tazobactam in a mass ratio of 2 g/0.25 g respectively. The cyclic voltammograms recorded in the absence and presence of Zosyn over a Pt electrode in the corrosive medium at the scan rates of 5 mV/s and 500 mV/s indicated a considerable suppression of hydrogen and oxygen evolution peaks. The influence of temperature was studied by recording Tafel curves in the absence and presence of 10^{-6} M Zosyn drug from 298 K to 338 K. The weight loss tests were conducted in the range of 10^{-6} M to 10^{-3} M concentration of the inhibitor. It was found that the inhibition efficiencies reached appreciable values in the presence of > 10^{-4} M concentration. Kurniawan et al [35] have investigated the influence of a phenol containing expired drug (Table 1) on API 5L Grade B Steel after 30 days immersion in 3.5 % NaCl pH 5 and 6

In presence of CO_2 at a pressure of 1 bar [35]. The corrosion testing was performed using electrochemical analyses i.e. Tafel and EIS. The experiments were conducted at different concentrations of inhibitors from 0 to 250 ppm from which 200 ppm was found out to be the optimum concentration. X-ray diffraction studies were carried out in the absence of inhibitor and a peak at $2\overline{\ }$ = ~33° appeared in both the samples at pH 5 and 6 indicating the presence of $FeCO_3$. In the presence of inhibitor, the above peak disappeared supporting the corrosion inhibition action.

El-Desoky et al [36] have performed a study on a series of expired pharmaceutical compounds namely Hydrochlorothiazide (HCT), Captopril (CAP) and Guaifenesin (GFN) (Table 1) for corrosion inhibition of carbon steel in 2 M HCl at 30°C [36]. The weight loss studies were conducted from 3 ×10^{-5} M to 15 ×10^{-5} M concentration and the adsorption of the inhibitors followed the Temkin isotherm. The kinetic parameters such as energy of activation, enthalpy of activation and entropy of activation were also determined. The values of ΔG^{o}_{ads} indicated chemical adsorption. A detailed EFM investigation was also carried out and the kinetic parameters including casualty factors were obtained. The results of EFM were found to be in good agreement with Tafel and EIS. In addition, different quantum chemical parameters such as energy of HOMO/ LUMO, electronegativity, global softness and dipole moment were evaluated and discussed. The results of E_{HOMO} and ΔE supported Hydrochlorothiazide as the best inhibitor among the studied ones. The results of global softness were in agreement with above observation although the values of E_{LUMO} did not follow this trend. The group of Abdel Hameed et al has contributed significantly in the application of expired drugs as corrosion inhibitors. They have used a number of expired drugs and conducted the corrosion inhibition studies in a variety of media. Expired Voltaren (Table 1) was used for aluminium in presence of 1 M HCl from 25 to 125 ppm concentration [37]. The influence of temperature was studied from 303 to 333 K. The adsorption of the inhibitor on aluminium surface followed the Langmuir isotherm. The group has also reported expired

Declophen i.e. 2-(2, 6-dichloranilino) phenylacetic acid (Table 1) ampoules as corrosion inhibitors for mild steel in 1 M HCl solution using weight loss and Tafel [38]. The inhibition efficiency increased with increase in concentration from 0.5% to 2.5% v/v and decreased with increase in temperature from 303 K to 333 K. The adsorption of the drug followed the Langmuir isotherm. From the potentiodynamic polarization studies, it was observed that the drug behaves as a mixed type inhibitor with predominant effect on the anodic process.

Earlier R.S. Abdel Hameed has used Ranitidine (Table 1) as corrosion inhibitor for mild steel in 1 M HCl using weight loss, potentiodynamic polarization and EIS studies in one of the earliest studies on expired drugs [39]. The corrosion inhibition efficiency increased with concentration from 50 to 400 ppm and decreased with rise in temperature from 303 K to 333 K. The adsorption of the inhibitor on metal surface obeyed the Langmuir isotherm. In the potentiodynamic polarization curves, the corrosion current densities showed a decrease along with a steady shift in corrosion potential towards anodic side with increase in inhibitor concentration indicating a prominent influence on the anodic reaction.

Al-Shafey et al have studied expired Phenytoin-sodium (Table 1) drug for carbon steel in 1 M HCl from 0 to 500 ppm concentration and at 25°C to 55°C [40]. The inhibitor exhibited physical as well as chemical mode of adsorption and followed the Langmuir isotherm. Various thermodynamic parameters were evaluated and they supported the adsorption and corrosion behavior of the inhibitor. The SEM images showed a considerably smoother surface of carbon steel in presence of inhibitor.

A detailed investigation was performed on the expired Amlodipine Besylate (Table 1) drug for corrosion inhibition of low-carbon steel in 1 M HCl using chemical, electrochemical and theoretical studies [41, 42]. The inhibition efficiency increased from 50 to 250 ppm and decreased from 84.0% to 69.0% when temperature was varied from 30°C to 45°C. The adsorption of the drug obeyed the Langmuir isotherm and mode of adsorption was physical in nature. A detailed evaluation of thermodynamic parameters was carried out. The results of weight loss, Tafel and EFM were found to be in good agreement. The EDX spectra showed the presence of C, N and O in the specimens thereby confirming the presence of adsorbed inhibitor on the metal substrate.

The corrosion inhibition of expired Fluconazole (2-(2,4-Difluorophenyl)-1,3-di(1H-1,2,4-triazol-1-yl)-2-propanol) (Table 1) was carried out on mild steel 1018 in a neutral chloride-sulphate solution [43]. The effect of concentration of inhibitor was studied by potentiodynamic polarization using different concentrations from 50 ppm to 200 ppm at different immersion periods up to 160 h. The highest inhibition efficiency was obtained for 24 h immersion period although the inhibitor was able to retain ~80% efficiency till 160 h.

Samide et al have studied expired Metronidazole (Table 1) drug from 0.2 mM to 1 mM as inhibitor for copper corrosion in 1 M HCl [44]. A significant cathodic shift in E_{corr} values > 200 mV towards cathodic direction indicated the cathodic behavior of inhibitor. In the presence of inhibitor, a decrease in the UV-vis maximum of corrosion products i.e. Cu^{+} and Cu^{2+} confirmed the inhibitor action. The results of cyclic voltammetry showed a considerable decrease in the anodic and cathodic current densities in the presence of inhibitor. DFT studies showed that the HOMO of Metronidazole are mainly centered on the heterocyclic ring whereas LUMO are focused on the $–NO_2$ group. The Mulliken charges showed a greater tendency of electron donation from the heteroatoms i.e. O and N.

Earlier our group has reported a series of contributions on the application of several fresh drugs for corrosion inhibition as mentioned above [7−13]. Recently, we have investigated the corrosion inhibition behavior of expired Atorvastatin (Table 1), a lipid-lowering drug, on the corrosion inhibition of mild steel in 1 M HCl (Manuscript Communicated). A comparative study was performed with fresh and expired Atorvastatin (FA and EA respectively) to validate the corrosion inhibition behavior of the expired drug (Fig. 3). It was found that the EA showed almost similar behavior as that of FA for the weight loss and electrochemical studies thereby justifying the use of the expired drug.

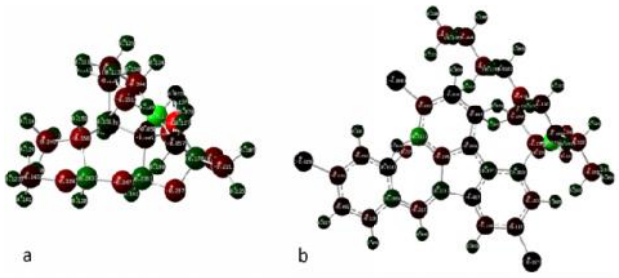


Figure 4: Optimized structures of Lumerax components (a) Artemether and (b) Lumefantrine

We have also studied Lumerax (Table 1), an antimalarial drug, for the corrosion inhibition of mild steel in 1 M HCl using gravimetric, electrochemical and DFT studies (Manuscript Communicated). The drug Lumerax is a combination of Artemether and Lumefantrine in the mass ratio of 1:6. It is expected that the Lumefantrine, which is present in a higher amount should govern the corrosion inhibition behavior, but a comprehensive analysis was performed. Using DFT to verify the relative efficacy of the two drug components in corrosion inhibition. It was observed that Lumefantrine exhibits a largely planar structure with a number of phenyl rings and a heterocyclic ring (Fig. 4). In addition, the results of DFT showed that above drug component has a higher E_{HOMO} value, smaller energy gap and is a softer compound as compared to Artemether. Hence, it was proposed that the Lumefantrine is the major active component of Lumerax for controlling the corrosion inhibition behavior.

3. Considerations in use of expired drugs as corrosion inhibitors

Preparation of a drug for corrosion inhibition: It is important to note that the tablets, capsules or such doses of drugs in addition to the pharmaceutically active component also contain certain additives (excipients) for maintaining stability and improving bioavailability of a drug. Such chemicals may either add to or hinder the corrosion inhibition behavior of the active component. Therefore, suitable separation techniques e.g. filtration, centrifugation etc. should be employed to isolate the active ingredient of a drug as far as possible.

Chemical reactivity of a drug in the corrosive environment: For studying the corrosion inhibition behavior of drugs it is necessary to consider the possible chemical reactions of the pharmaceutically active compound in the corrosive environment. For example, aspirin in corrosive medium hydrolyses into salicylic acid and acetic acid [18]. The corrosion inhibition in this case is given by the mixed effect of the hydrolysis products.

Determination of structural modification after expiry: Although as mentioned above, many drugs retain their potency even after expiry, but still the first and foremost parameter in the application of an expired drug is the identification of chemical change in a drug as a result of expiry. For this purpose, typical methods are spectroscopic techniques e.g. FTIR and NMR. In addition, this can also be determined electrochemically by cyclic voltammetry provided that there is a difference between the electrochemical oxidation-reduction behaviors of fresh and expired drug.

Application of DFT in predicting the corrosion inhibition efficacy of combination drugs:

The DFT is frequently used in case of corrosion inhibition for correlating the experimentally obtained inhibition efficiency with the structural properties such as optimized structure, Mulliken charges, energy gap, electronegativity, global softness, dipole moment etc. In addition to this, particularly in the case of combination drugs, an estimation of the most active component can be achieved by the calculated DFT parameters. The detailed account on the use of computational techniques for virtual screening and design of drugs is beyond the scope of this work and is provided elsewhere [45−47]. The detailed application of DFT in corrosion inhibition studies has been covered by others [48−50].

4. Issues in using expired drugs as corrosion inhibitors

Availability: Although the use of expired drugs for corrosion inhibition is a considerably more cost effective and greener alternative than the use of fresh drugs, but the continuous supply of expired drugs in desired amounts may not always be possible. The fresh drugs can be obtained at ease on demand from local drug stores while this is not the case for expired drugs. In order to address this issue, a previously tested mixture of expired/ outdated drugs could be used for corrosion inhibition. The development of various methods of collecting the unused drugs intended for reducing environmental pollution could well be used for collection of expired drugs for corrosion inhibition purpose. Also, awareness should be increased among people for returning the drugs to selected pharmacists rather than disposing them in the trash.

In some cases, it has been already observed that a drug containing two or more components can be useful in mitigation of corrosion. This suggests that a mixture of drugs could also be useful as a corrosion inhibitor. However, for this purpose, a systematically planned study on the available unused drug classes and their possible interactions (synergistic/ antagonistic) on the basis of theoretical investigation is required in order to obtain a complete picture of the possibilities for obtaining corrosion inhibitors to determine the most suitable inhibitor formulation approach.

Condition: whether active or extent of activity:

It is noteworthy to mention that a fresh drug is expected to have the exact chemical composition and structural integrity as promised from the manufacturer, while these properties of an expired drug will depend on storage condition to a great extent. Some people prefer to keep the drugs in kitchen while some store it in cupboards in bathrooms and others prefer living room. Hence, the same expired drug obtained from different sources may behave differently due to difference in storage conditions such as temperature, humidity etc. Also, the detection of expiry is sometimes not easy by conventional means [51].

Table 1A: Corrosion inhibition performance of some of the expired drugs

Drug	Substrate	Medium	Characterization of corrosion inhibition
Asthalin	Mild steel	1 M HCl 1 M H_2SO_4	a, b, d
Lupicof	Mild steel	1 M HCl	a, b, d
Ambroxol	Mild steel	1 M HCl 1 M H_2SO_4	a, b, d
Farcolin	Carbon steel	1 M HCl	a, d, PS
Carbamazepine	Carbon steel	0.1 M H_2SO_4	d, CV
Paracetamol	Carbon steel	0.25 mol L^{-1} CH_3COOH 0.25 mol L^{-1} CH_3COONa	d, CV
Zosyn	Carbon steel	3.5% NaCl	a, c, d, CV

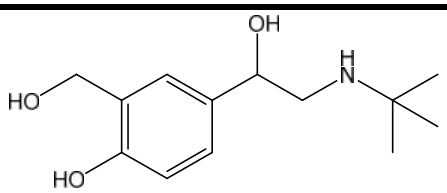
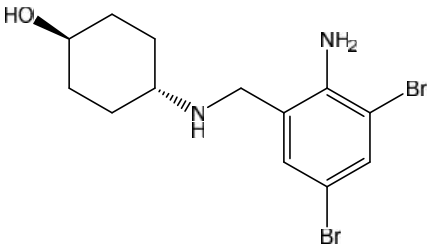
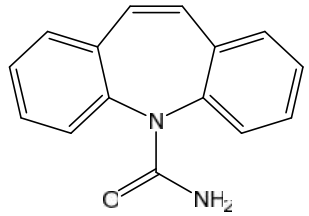
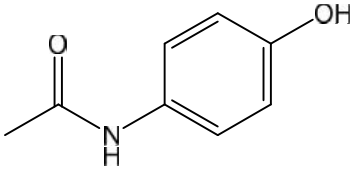
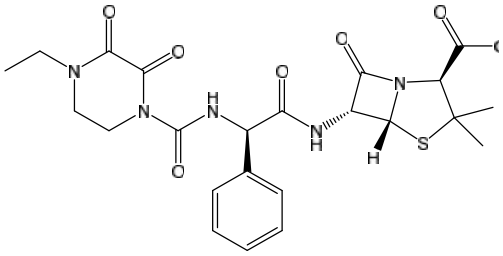
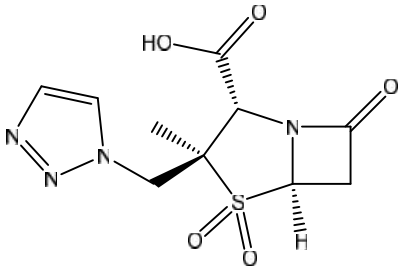
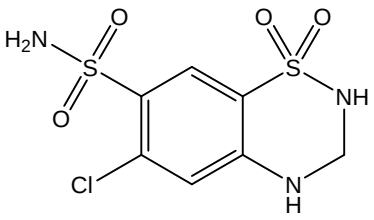
Phenol containing expired drug	Carbon steel	3.5% NaCl pH 5, pH 6 at CO_2 1 bar	b, d, XRD
Hydrochlorothiazide	Carbon steel	2 M HCl	a, b, d, e, f
Captopril	Carbon steel	2 M HCl	a, b, d, e, f
Guaifenesin	Carbon steel	2 M HCl	a, b, d, e, f
Voltaren	Aluminium	1 M HCl	a, d
Declophen	Mild steel	1 M HCl	a, d
Ranitidine	Mild steel	1 M HCl	a, b, d
Phenytoin sodium	Carbon steel	1 M HCl	a, b, d
Amlodipine Besylate	Low-carbon steel	1 M HCl	a, b, d, e, f
Fluconazole	Mild steel	2.% NaCl + 0.5% $(NH_4)_2SO_4$	b, d
Metronidazole	Copper	1 M HCl	c, d, f, CV, UV-vis
Atorvastatin	Mild steel	1 M HCl	a, b, d
Lumerax	Mild steel	1 M HCl	a, b, d, f

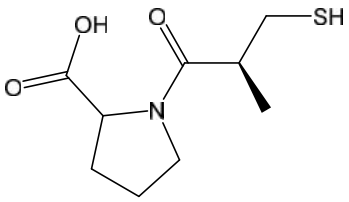
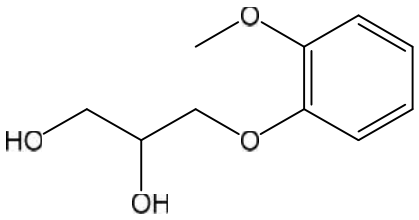
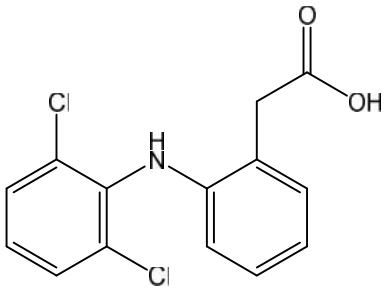
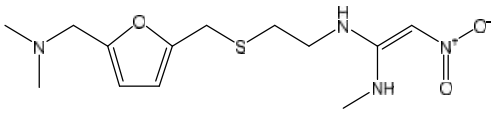
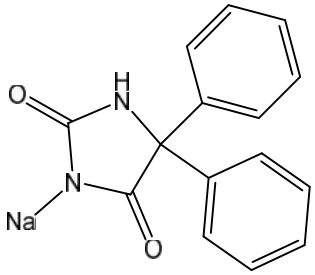
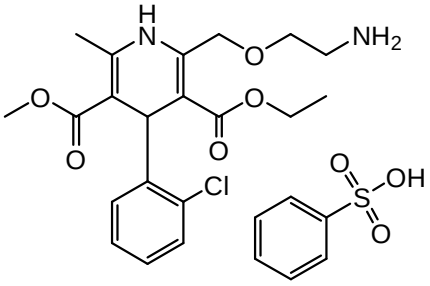
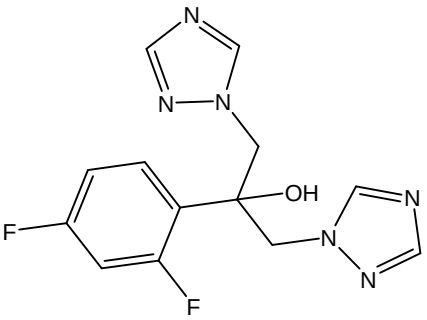
Table 1B: Corrosion inhibition performance of some of the expired drugs

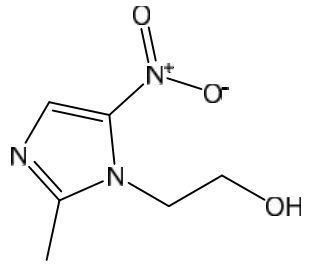
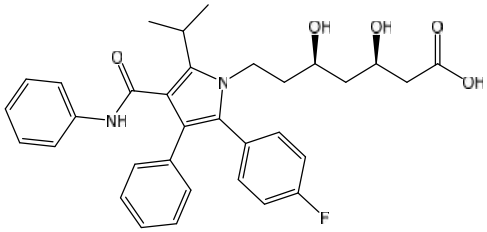
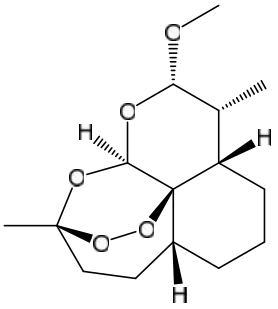
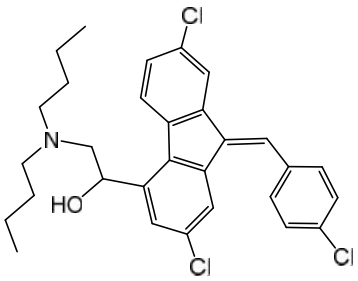
Drug	**¦ %; Concentration**	**Mode of Adsorption**	**Inhibitor type (from Tafel)**	**Reference**
Asthalin	94.76; 9.0% v/v 95.48; 9.0% v/v	Chemical	Mixed	27
Lupicof	70.86; 0.9% v/v	-	Mixed	29
Ambroxol	94.03; 9.0% v/v 95.54; 9.0% v/v	-	Mixed	30
Farcolin	98.0; 20% v/v	Physical	Mixed	32
Carbamazepine	90; 0.005 M	-	Mixed	18
Paracetamol	85	-	Anodic	18
Zosyn	91.08; 1×10^{-3} M	-	Mixed	34
Phenol containing expired drug	82.553; 200 ppm 80.980; 200 ppm	-	Cathodic Cathodic	35
Hydrochlorothiazide	81.8; 15×10^{-4} M	Chemical	Mixed	36
Captopril	77.9; 15×10^{-4} M	Chemical	Mixed	36
Guaifenesin	71.4; 15×10^{-4} M	Chemical	Mixed	36
Voltaren	91.7; 125 ppm	Physical and Chemical	Anodic	37
Declophen	87.5; 2.5 % v/v	Physical and Chemical	Mixed	38
Ranitidine	90; 400 ppm	Physical and Chemical	Mixed	39
Phenytoin sodium	79.1; 500 ppm	Physical and Chemical	Mixed	40
Amlodipine Besylate	84.0; 250 ppm	Physical	Anodic	42
Fluconazole	84.46; 150 ppm	-	Mixed	43
Metronidazole	90.0; 1 mmol L^{-1}	-	Cathodic	44
Atorvastatin	96.38; 150 ppm	Physical and Chemical	Mixed	Submitted
Lumerax	95.3; 100 ppm	Physical and Chemical	Mixed	Submitted

a = Weight loss, b = Electrochemical Impedance Spectroscopy, c = Linear Polarization Resistance, d = Potentiodynamic polarization (Tafel), e = Electrical Frequency Modulation, f = Density Functional Theory calculations; PS = Potentiostatic polarization, CV = Cyclic Voltammetry, XRD = X-ray diffraction, UV-VIS = UV-VIS spectroscopy

Table 2: Clinical use and molecular structures of some of the expired drugs that have been used as corrosion inhibitors

Drug	Clinical use	Molecular structure	Reference
Asthalin	Reversible bronchospasm linked with asthma and other pulmonary diseases		27
Ambroxol	Tracheobronchitis, emphysema with bronchitis pneumoconiosis, chronic inflammatory pulmonary conditions		30
Carbamazepine	Seizures and nerve pain e.g. trigeminal neuralgia and diabetic neuropathy; bipolar disorder		18
Paracetamol	Pain killer and fever reducer		18
Zosyn (Piperacillin)	Piperacillin and tazobactam are penicillin antibiotics; bacterial infections, e.g. infections of urinary tract, bone and joint, vagina, stomach, and skin		34
Zosyn (Tazobactam)	Same as above		34
Hydrochlorothiazide	Hypertension, liver cirrhosis, or kidney disorders		36

Captopril	Hypertension, congestive heart failure, kidney problems		36
Guaifenesin	Coughs and congestion caused by common cold, bronchitis, and other breathing illnesses		36
Voltaren	Mild to moderate pain, or signs and symptoms of osteoarthritis/ rheumatoid arthritis		37
Ranitidine	Stomach and intestinal ulcers; high acidity		39
Phenytoin sodium	Anticonvulsant		40
Amlodipine Besylate	Calcium channel blocker, hypertension or angina and other conditions caused by coronary artery disease.		42
Fluconazole	Vaginal, oral, and esophageal fungal infections caused by Candida; urinary tract infections, peritonitis, pneumonia and disseminated infections caused by Candida.		43

Metronidazole	Antibiotic; bacterial infections of the vagina, stomach, skin, joints, and respiratory tract		44
Atorvastatin	Hypercholesterolemia , Hyperlipidemia, Hypertriglyceridemia		Submitted
Lumerax (Artemether)	Combination of Artemether and Lumefantrine. Used to treat certain kinds of malaria		Submitted
Lumerax (Lumefantrine)	Same as above		Submitted

7. Conclusion

It is shown that a number of expired drugs have been used as corrosion inhibitors for protection of various metals in a variety of aggressive media. The use of expired drugs as corrosion inhibitors is an area still in its infancy. Therefore, this review is expected to provide a comprehensive reference guide to the researchers working in the area. Following are the major conclusions from this study: Currently, corrosion scientists on a global scale are focussing on the use of drugs for corrosion inhibition. But the high cost of fresh drugs is a major issue which can be addressed by the use of leftover or expired drugs for corrosion inhibition. However, the ease of availability of expired drugs in comparison to that of the fresh drugs is an issue that can be handled with proper disposal guidelines and awareness among people. There are a number of ways in which unused or expired drugs can enter in the environment and create contamination. The proper disposal of such pharmaceuticals is itself a costly and tedious enterprise. Hence, there is a need for alternative management of expired drugs. In this regard, the use of expired drugs as corrosion inhibitors presents an innovative solution. In comparison to different heterocyclic compounds that are used as corrosion inhibitors, the use of expired drugs is a more economic method and it considerably reduces the time and lengthy synthetic protocols. Systematic research is required on expired drugs for their application in corrosion inhibition. It is also necessary in order to predict the possible toxicity profiles and environmental concerns. Also a comparative analysis between the expired drugs should be made with that of the corresponding fresh drugs to verify the corrosion inhibition activity of due to breaking down/ degradation of constituents.

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