Reduction of pollution by controlled disposal of hazardous pharmaceuticals

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Abstract. Human activities generate a series of waste increasingly more complex and difficult to manage (through the containment, inertization or destruction). Particular attention must be paid to hazardous waste with a high risk of environmental pollution but especially for infestation to the human generator.

In this context, we considered the possibility of integrated waste management resulted from the pharmaceutical industry, which is frequently mishandled and ends (reach) in the environment.

This paper proposes a method for neutralizing some hazardous pharmaceutical waste, using electrochemical methods for inactivation, respectively an electrochemical reactor with asymmetric current densities. The results obtained in the laboratory for four of these substances leads to the generation of viable solutions that can be used in practice.

1. Introduction

Medical activity, both the diagnostic and especially the treatment one, exposes day by day the atmosphere, water and soil, to the action of substances which, in small quantities, do not have an obvious polluting effect, but which can be accumulate in time and can lead to real environmental disasters.

The Romanian regulations that governing the pollutants loading limits are NTPA – 001/1997 and NTPA 002/2005 for water resources and WHO 645/1997 for the discharge of waste water into sewerage networks [1-3].

Electrochemical techniques for the treatment of waste from the pharmaceutical industry offer a number of distinct advantages compared to the usual ones such as incineration [4-9]:

- Environmental compatibility
- Versatility
- Energy efficiency
- Safety
- Selectivity
- Possibility of automation
- Low costs.
The electrochemical methods involve concomitant reactions to both at the anode and cathode. Organic substances can undergo electron transfer in a variety of circumstances and environments. The main factors that determine their electrochemical behavior are:

- Nature of the electroactive group in the organic molecule
- Nature of solvent and underlying electrolyte
- The material from which the electrode is made
- Potential applied
- Temperature.

The electrochemical methods can be achieved by:

a) Electrochemical reduction. The reduction process consists in the acceptance of electrons. The mechanism of achieving the electro reduction of an organic compound is relatively complicated, the transfer of electrons being often accompanied, preceded or followed by other homogeneous reactions.

b) Electrochemical oxidation.
   - Directly, by oxidation of the organic molecule absorbed on the surface of the electrode by an electron transfer
   - Indirectly, by oxidation of the molecule by atomic oxygen or hydroxyl radicals formed by water electrolysis.

2. Laboratory experiments

The laboratory experiments were carried out both in the laboratories of the Hunedoara Faculty of Engineering and in the Faculty of Industrial Chemistry and Environmental Engineering of UPT Timisoara; the aim was to approach a direction of inactivating dangerous substances used in the pharmaceutical industry. The objective of this theme was to identify a new approach to neutralizing hazardous chemical waste (such as expired medicines) [10-12].

The substances selected for the experiments were ephedrine, acetaminophen, caffeine and methylene blue. These substances are active in the composition of many commercial pharmaceutical preparations, used in the treatment of a wide range of conditions.

In the literature, as a way of inactivating dangerous substances from the pharmaceutical industry is mentioned incineration as the only method of controlled disposal. For these reasons, it was considered appropriate to find a new possibility of inactivation of this waste, with low energy consumption and significantly low impact on the environment.

Our method is based on two processes:

- Oxidation of hazardous waste considered in the study by reactive species of chlorine (sodium hypochlorite, hypo-chloric acid and physically dissolved chlorine);
- Direct anode electro-oxidation of these wastes.

The processes are carried out simultaneously, in an experimental laboratory installation consisting of an electrochemical micro-reactor with asymmetric current densities (which favorize anode oxidation reactions), magnetic agitator and a constant electrical current source which supplies powers to the micro-reactor – Figure 1.

In addition, a thermocouple was used to measure temperature in the reaction medium. Constructively, the micro reactor consists in a Berzelius glass with a volume of 100cm3, provided at the top with a cap which acts as a support for graphite anodes, lead cathode, which allows sampling for physico-chemical analysis and also allows temperature measurement during experiments.

For these purposes, all samples collected during and at the end of the electrolysis process were treated accordingly to neutralize residual free chlorine, so as to avoid any degradation of the substances from the time of sampling from the electrochemical micro-reactor until the time of analysis. This neutralization was done with a 20% sodium thiosulfate (Na$_2$S$_2$O$_3$) solution. It can neutralize large amounts of free chlorine according to the reaction:

$$4Cl_2 + Na_2S_2O_3 + 5H_2O = 8HCl + Na_2SO_4 + H_2SO_4$$ (1)
The samples were taken in Eppendorf tubes with a volume of 2ml. A volume of 0.5ml of sodium thiosulphate solution and 1.5ml of sample were introduced into each tube. The contents of the tube were homogenized immediately after sampling, in order to inactivate the effect of the reactive species of chlorine, thus to stop the further degradation of the analysed substances. Sampling was carried out at well-defined time points, as follows (where X is the number of compound):
- initial, i.e. minute 0, the sample being coded with X.0;
- 2.5 minute, the sample being coded with X.2.5;
- 5 minute, the sample being coded with X.5;
- 10 minute, the sample being coded with X.10;
- 15 minute, the sample being coded with X.15;
- 30 minute, the sample being coded with X.30;
- 60 minute, the sample being coded with X.60.

2.1. Synthetic waste water containing ephedrine
Ephedrine is a drug used to prevent hypotension during spinal anesthesia, but it also has a suppressive effect of appetite and nasal decongestant. In the past, it has been used to treat asthma, narcolepsy and obesity. The chemical formula of ephedrine is: C_{10}H_{15}NO.

Synthetic waste water containing ephedrine was prepared as follows: in 100ml sodium chloride solution 3% it was dissolved 500mg ephedrine for pharmaceutical use – Figure 2.

![Figure 1](image1.jpg)

**Figure 1.** The laboratory installation

![Figure 2](image2.jpg)

**Figure 2.** Aspects during electrochemical inactivation of ephedrine
2.2. Synthetic waste water containing acetaminophen
Acetaminophen belongs to the class of analgesic drugs (combats pain) and antipyretic (reduces fever). It is an analgesic and antipyretic drug that does not attack the stomach lining. This drug is used for symptomatic treatment of conditions that involving pain of low or moderate intensity such as: headache, dental neuralgia, surgical pain, sprains, fractures, arthritis, osteoarthritis, colds, flus, inflammation and muscle pain.

Synthetic waste water containing acetaminophen was prepared as follows: in 100ml sodium chloride solution 3% it was dissolved 500mg acetaminophen for pharmaceutical use – Figure 3.

![Figure 3. Aspects during electrochemical inactivation of acetaminophen](image)

2.3. Synthetic waste water containing caffeine
Caffeine is an alkaloid of the purine group, which is found in coffee, tea and cocoa. It is one of the oldest natural stimulants used by man. The chemical formula: C_{8}H_{10}N_{4}O_{2}.

Synthetic waste water containing caffeine was prepared as follows: in 100ml sodium chloride solution 3% it was dissolved 500mg caffeine for pharmaceutical use – Figure 4.

![Figure 4. Aspects during electrochemical inactivation of caffeine](image)

2.4. Synthetic waste water containing methylene blue
Methylene blue has an antiseptic and analgesic action on various damaged tissues (plagues, burns, redness, decubit, frostbite, etc.), favouring scarring. The chemical formula: C_{16}H_{18}ClN_{3}S.

Synthetic waste water containing methylene blue was prepared as follows: in 100ml sodium chloride solution 3% it was dissolved 5mg methylene blue for pharmaceutical use – Figure 5.
2.5. Synthetic waste water with mixture of ephedrine, acetaminophen, caffeine and methylene blue

Synthetic waste water containing ephedrine, acetaminophen, caffeine and methylene blue was prepared as follows: in 100ml sodium chloride solution 3% it was dissolved 500mg ephedrine, 500mg acetaminophen, 500mg caffeine and 5mg methylene blue for pharmaceutical use – Figure 6.

3. Discussions

All samples were processed in such a way that the substances of interest were quantitatively passed into an organic phase compatible with the gas chromatographic analysis method.

Was used the liquid-liquid extraction technique. The following were introduced in 7 polypropylene tubes with a volume of 10ml:

- 2ml dichloromethane (organic solvent);
- 5µl n-decan (internal standard);
- the contents (2 ml) of each Eppendorf tube, with the sample taken.

The extraction was done on a vortex system for 3 minutes for all samples - Figure 7.

After vortexing, tubes are left to rest for 15 minutes, to separate the organic phase (lower phase) from the aqueous phase (upper phase) - Figure 8.
A Varin GC-450 gas-chromatograph equipped with a flame ionization detector (FID) and computerized data acquisition was used - Figure 9. The analysis parameters were as follows:

- injector temperature: 300°C;
- detector temperature: 350°C;
- column type: non-polar, 15m, 5% phenyl-95% dimethyl polyoxyloxane;
- oven temperature program: initially 120°C - final 180°C, heating speed 15°C / min.

For the quantification of the chemical species from each analyzed sample, is used the method of the internal standard (n-decan), the normalization of the areas of the peaks of interest being done by referring to the area of the peak corresponding to the n-decan.

The samples taken and subsequently analyzed are summarized in Figure 10.

Figures 11, 12, 13, 14, 15 show synthetically the gas chromatograms obtained from the analysis of the 7 samples taken during the electrochemical treatment of ephedrine, acetaminophen, caffeine, methylene blue and the mixture of substances mentioned above. It should be mentioned that methylene blue was dosed by visible spectrophotometry, using a Jasco type device. From the literature data it is known the wavelength at which the absorbance is maximum for methylene blue, being 668nm.
In all cases, the treatment efficiency of the substance considered under the electrolysis conditions was calculated as the ratio between the normalized peak area of ephedrine at minute 60 of electrolysis (device detection limit) denoted by $A_f$ and the normalized peak area of the substance at minute 0, denoted by $A_i$. The results obtained are presented graphically (Figure 16), comparative, between the efficiencies of purify the individual compound and to purify in the mixture compound.
Figure 13. Efficiency of caffeine treatment

Figure 14. Efficiency of methylene blue treatment

Figure 15. Efficiency of mixed compounds treatment

Figure 16. Comparative analysis between individual compound treatment and mixture compounds

4. Conclusions
Following the bibliographical study and the experiments carried out, can be concluded the following:
- The need to implemented adequate waste management, in particular for hazardous waste, in order to improve and make more efficient collection, transport and neutralization of this wastes.
- Efficient information of the population related to the danger of uncontrolled removal of chemicals from expired medicinal products and a possible simplification of the papers to be completed when handing these substances over to accredited centers.
- The proposed electrochemical method can be applied to water-soluble substances or if is forming stable emulsions with water.
- It was concluded that: the combination of the 4 compounds has a favorable effect with regard to the purification of acetaminophen and methylene, but it is significantly unfavorable in the case of ephedrine and to a lesser extent in the case of caffeine.

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