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Cyanide ion release from disinfection of pharmaceutical wastewater

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Abstract

The reaction of some pharmaceuticals containing nitrogen with sodium hypochlorite was investigated under conditions simulates wastewater disinfection. Initially, the reaction was studied in pure pharmaceuticals at concentration of $1x10^{-3}$ molar and molar excess of sodium hypochlorite ($5x10^{-3}$M), this reaction was monitored using spectrophotometric method for ten different compounds. The cyanide ion was detected in chlorhexidine –gluconate, metronidazole, frusemide, diphenoxylate.HCl , chloramphenicol and metformin. The largest formation was observed in chlorhexidine gluconate, the amount of cyanide ion formed increased to maximum at 10-30 minute. The formation of cyanide ion was attributed to the formation of dichloramine product by oxidizing action of sodium hypochlorite, which decomposition to cyanide .The reaction studied in industrial waste water sample from the state company for drug industries and medical appliances Mosul-Iraq ,was similar to reactive noted.

Keywords: Cyanide ion, Pharmaceuticals, Sodium hypochlorite, Wastewater.

ايون السيانيد المتكون من تعقيم المياه المطروحة من صناعة الادوية

الخلاصة

تمت دراسة تفاعل بَعْض المواد الصيدلانيةِ التي تَحتوي النتروجينَ مع هايبوكلورات الصوديومِ تحت نفس ظروف تعقيم المياه الصناعيةِ المطروحة. وقد تمت الدراسة الأولية على بعض المواد الصيدلانيةِ النقية بتركيزِ(1×10^{-3}) مولاري مع زيادة من الهايبوكلورات بتركيز 5×10^{-3} مولاري وقد تم قياس السيانيد المتحرر باستعمال طريقةِ طيفيةِ لعشرة مركّباتِ دوائية مختلفةِ.وقد لوحظ تحرر أيون السيانيدَ من كلورهكسدين كلوكونيت وميترونادازول وفريزيمايد وداي فينوكسليت هيدروكلورايد و الكلورفينكول كذالك من المتفورمين.وان اكبر كمية كانت من كلورهكسدين كلوكونيت وان الوقت اللازم لظهور أعلى كمية من السيانيد كانت بين ١٠-٣٠ دقيقة، وان تكوين أيون السيانيدِ يعزى إلى تكوين داي كلورامين من عملية أكسدة المركبات الدوائية بواسطة هايبوكلورات الصوديوم والذي بدورة يتفكك إلى السيانيد وقد تمت دراسة تكوين ايون السيانيد على عيّنةِ من المياه الصناعيةِ المطروحة مِنْ الشركةِ العامة لصناعةِ الأدوية والمستلزماتِ الطبيةِ (الموصل –العراق).

Introduction

Cyanides, are highly toxic to all forms of life .The lethal dose for an adult human being is in the range 100-150 mg and lethal dose for humans (LD50) is approximately 1 mg/kg per orally [1-3].Cyanides enter in to the environment through synthesis of fertilizers , electroplating , metal cleaning , chemicals , plastics, resins, agriculture ,cigarette smoke and combustion of coal [4-6] .If the environment is protected from pollution , the cyanide content of natural waters does not exceed 0.025 ppm [7].The maximum recommended amount of cyanide in water by WHO as CN^- (0.01mg/l) for human being and 0.03 mg/l for fishes .Cyanides act directly on the nervous system and readily absorbed through intact skin and by inhalation. The origin of blood cyanide concentrations may be from hydrocyanic acid inhalation from the combustion fumes of plastics [8, 9].Anoxia, headache, enlargement of the thyroid glands and convulsions with the paralysis of the respiratory center in brain are some of symptoms associated with cyanide poisoning. The maximum tolerable concentration of cyanide is $5mg/m^3$ in air and the maximum contaminant level goal and the maximum contaminant level in drinking water are both 200 μg/L as FCN, a limit set by the US Environmental Protection Agency (USEPA). [4,10]. Sodium hypochlorite has been widely used as a disinfectant for water and wastewater treatment [11, 12]. The versatility of sodium hypochlorite as an analytical reagent can be gauged by its applications in the spectrophotometric determination of many organic compounds of therapeutic importance [13,14]. Literature survey revealed that cyanides formation from the oxidation of amino-acids by hypochlorite[15,16],and also formation from oxidation of glycine by a pseudomonas species[17],for these researches I predict that cyanide ion is formed by the reaction of some pharmaceuticals containing nitrogen with sodium hypochlorite,. Pharmaceuticals are chemicals used for diagnosis, cure, mitigation or prevention of disease. Such drugs are used in large quantities in human. Many studies have now been conducted which show that drugs and their metabolites are widely distributed in surface waters [18,19].The aim of this work is present the formation of cyanide ion by the reaction of some pharmaceuticals containing nitrogen with sodium hypochlorite on the laboratory scale and the reaction studied in industrial waste water sample from the state company for drug industries and medical appliances Mosul-Iraq was similar to reactive noted.

Experimental

Apparatus

A spectra scan 50 UV- visible spectrophotometer with 1.0 cm quartz cells was used.

Reagents

All chemical used were of analytical grade or pharmaceutical grade and the metformin hydrochloride, chlorhexidine gluconate, metronidazol, frusemide, trimethoprime, theophylline, diphenhydramine hydrochloride ,diphenoxylate hydrochloride ,naphazoline nitrate and chloramphenicol standard materials were provided from state company of drug industries and medical appliance (NDI) and Al-Hokama (HPI) for pharmaceutical industry(Nineveh – Iraq.) .

Metformin hydrochloride solution ($1x10^{-3}$M)

This solution was prepared by dissolving 0.016 gm of metformin hydrochloride in 100 ml distilled water in a volumetric flask.

Chlorhexidine gluconate solution ($1x10^{-3}$M)

This solution was prepared by diluting 0.45ml of 20% chlorhexidine gluconate solution to 100 ml by distilled water in a volumetric flask.

Metronidazol solution ($1x10^{-3}$M)

This solution was prepared by dissolving 0.017 gm of metronidazol in 100 ml distilled water in a volumetric flask .

Frusemide solution ($1x10^{-3}$M)

This solution was prepared by dissolving 0.033 gm of frusemide in 100 ml of 0.01 N NaOH solution in a volumetric flask.

Trimethoprime solution ($1x10^{-3}$M)

This solution was prepared by dissolving 0.029 gm of trimethoprime in100 ml of 0.01 N NaOH solution in a volumetric flask.

Theophylline solution ($1x10^{-3}$M)

This solution was prepared by dissolving 0.018 gm of theophylline in 100 ml distilled water in a volumetric flask.

Chloramphenicol solution ($1x10^{-3}$M)

This solution was prepared by dissolving 0.032 gm of chloramphenicol in 100 ml distilled water in a volumetric flask.

Diphenhydramine hydrochloride solution ($1x10^{-3}$M)

This solution was prepared by dissolving 0.029 gm of Diphenhydramine hydrochloride in 100 ml distilled water in a volumetric flask.

Diphenoxylate hydrochloride solution ($1x10^{-3}$M)

This solution was prepared by dissolving 0.0489 gm of Diphenoxylate hydrochloride in 100 ml of 0.001 N HCl solution in a volumetric flask.

Naphazoline nitrate solution ($1x10^{-3}$M)

This solution was prepared by dissolving 0.0273 gm of Naphazoline nitrate in 100 ml distilled water in a volumetric flask.

Cyanide stock solution (100ppm)

This solution was prepared by dissolving 0.025 gm of KCN (BDH) in 100 ml distilled water in a volumetric flask.

Cyanide working standard solution (1ppm) ($3.8x10^{-3}$M)

This solution was prepared by diluting 1ml of cyanide stock solution to 100 ml by distilled water in a volumetric flask.

Ninhydrine solution (1%)

Sodium carbonate solution (5%).

Sodium hypochlorite solution ($5x10^{-3}$M):

This solution was prepared by dilution 1ml of 4% sodium hypochlorite to 100 ml by distilled water, standardized every 4-5 days. This solution stored in a dark bottle [20,21]

Sodium hydroxide solution (2.5N) .

Recommended procedure [22] **:**

An aliquot of cyanide standard solution containing (1.0-6.0 µg) of cyanide was transferred into a series of 25 ml volumetric flasks, to which 4ml of 1% ninhydrin and 4ml of 5% sodium carbonate were added, the solution was kept aside with occasional shaking for about 20 min for completion of the reaction to give a deep red color , and diluted to the mark with 2.5 N sodium hydroxide. The deep-blue color, which developed instantaneously, was stable for 30 min. The absorbance was measured at 590 nm against a reagent blank prepared in the same manner without cyanide, and a calibration graph was constructed.

Analysis of pharmaceuticals

To aliquot (50 ml) of each sample solution including pharmaceuticals added 50 ml of sodium hypochlorite solution. The solutions were kept aside for 20 min. Treat 2 ml of each solution as mentioned under recommended procedure. The reagent blank prepared in the same manner but containing no pharmaceuticals.

Analysis of wastewater sample

The sample was collected from the effluents of the state company for drug industries and medical appliances, Mosul-Iraq , the sample was tested and found to be free of cyanide. An aliquot (50ml) of wastewater sample was treated as mentioned under analysis of pharmaceuticals.

Result and discussion

The formation of cyanide ions by the reaction of pharmaceuticals containing nitrogen with sodium hypochlorite was examined using seven different compounds. These compounds were provided from the state company of drug industries and medical appliance (NDI) and al-hokamaa for pharmaceutical industry (HPI) (Nineveh – Iraq.).The formation of cyanide ion was observed in chlorhexidine gluconate, metronidazol ,frusemide, diphenoxylate.HCl , chloramphenicol and metformin. HCl .The largest formation was observed in chlorhexidine gluconate and the lowest formation was observed in metformin. .

Table[1]: Formation of cyanide ions from pharmaceuticals by NaOCl.

Pharmaceuticals($1x10^{-3}$M)	Cyanide ions formed(mg/l)*
Chlorhexidine gluconate	0.18
Metronidazol	0.15
Frusemide	0.14
Chloramphenicol	0.088
diphenoxylate.HCl	0.075
Metformine.HCl	0.049
Trimethoprim	undetectable
Di phenhydramine hydrochloride	undetectable
Naphazoline nitrate	undetectable
Theophylline	undetectable

* Average of ten determinations.

The reaction variable were optimized by varying each variable while keeping others constant for obtaining maximum absorbance .The effect of pharmaceuticals concentration ($1x10^{-3}$M) at a reaction time of 20 min. The amount of cyanide ion formed to a maximum when the concentration of sodium hypochlorite at 4-$6x10^{-3}$M and $5x10^{-3}$M have been used for subsequent experiment. Table 2show the effect of sodium hypochlorite on the formation of cyanide ion from chlorhexidine gluconate ($1x10^{-3}$M).

Table[2]:Effect of NaOCl on the concentration of cyanide from chlorhexidine gluconate $1x10^{-3}$M.

Concentration of sodium hypochlorite	Cyanide ions formed(mg/l)⋆
$1x10^{-3}$M	0.036
$2X10^{-3}$M	0.097
$3X10^{-3}$M	0.15
$4X10^{-3}$M	0.18
$5X10^{-3}$M	0.18
$6X10^{-3}$M	0.18

⋆ Average of ten determinations.

The effect of time on the formation of cyanide ion by the reaction of chlorhexidine gluconate ($1x10^{-3}$M) with $5x10^{-3}$M sodium hypochlorite , increased to maximum at 10-30 mint before decreasing , and 20 mint have been selected for subsequent experiment Table(3). .

Table[3]:effect of reaction time on the formation of cyanide ion.

Reaction time (min)	Cyanide ions formed(mg/l)
١	0.058
٥	0.14
١٠	0.18
١٥	0.18
٢٠	0.18
٣٠	0.18
٤٥	0.14
٦٠	0.10

The mechanism of the formation of cyanide ion was attributed to Norman-and Dakin [17,18].The first step mono chloramines formed which in excess of hypochlorite converted to di chloramines as unstable and subsequently decomposed to cyanide as shown below.

$$\mathbf{R\text{-}CH_2NH_2 + NaOCl \rightarrow R\text{-}CH_2NHCl + NaOCl \rightarrow R\text{-}CH_2NCl_2 \rightarrow HCN + RCl_2}$$

Analytical application of the proposed method

The proposed method has been successfully applied for the formation and determination of cyanide ion in environmental wastewater sample which

collected from the effluent of the state company of drug industries and medical appliance (NDI) (Nineveh – Iraq.) .The results are given in Table 4.

Table[4]: Formation of cyanide ions from wastewater by NaOCl .

Wastewater samples	Cyanide ions formed(mg/L)
١	0.174
2	0.170
3	0.172
4	0.164
5	0.170
6	0.168
7	0.170
8	0.172
9	0.166
10	0.164
Mean	0.169

Conclusions

The proposed method described the formation of cyanide ion by the reaction of some pharmaceuticals containing nitrogen with sodium hypochlorite on the laboratory scale and the reaction studied in industrial waste water sample from the state company for drug industries and medical appliances Mosul-Iraq was similar to reactive noted.

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