Aseel Musthaq Aljeboree et al /J. Pharm. Sci. & Res. Vol. 10(7), 2018, 1774-1779

ISSN:0975-1459
Journal of Pharmaceutical Sciences and Research
www.jpsr.pharmainfo.in

Colorimetric Determination of phenylephrine hydrochloride drug Using 4-Aminoantipyrine: Stability and higher sensitivity

Aseel Musthaq Aljeboree[1] Abbas Noor Alshirifi[2]
[1]*College of science for women-Chemistry Department/Babylon University*
[2]*College of science -Chemistry Department/Babylon University*

Abstract

A highly sensitive in the presence of optimum methods by using spectrophotometric to described for the determination of phenylephrine hydrochloride in aqueous solutions. The method is based on the oxidative coupling reaction of phenylephrine hydrochloride with 4-aminoantipyrine and potassium ferricyanide to form dirty ping water soluble stable product at λ 503 nm. Good linearity for both methods was obtained ranging from 5 to 100 µg mL^{-1}, respectively. This method is suitable for the analysis of phenylephrine in common tablet formulations without prior separation gives a color stable for over 3 hour. The developed methodology was applied in the spectrophotometric control of the drug in pharmaceutical formulations. In the present work, optimum conditions of the oxidative coupling Colorimetric methods for the quantitative determinations of phenylephrine hydrochloride can be assayed by coupling it with 4AAP as reagents in the presence of potassium ferricyanide Using 0.1N sodium hydroxyl as the basic medium, a sufficiently stable color is obtained.

Keywords : phenylephrine hydrochloride , 4- aminoantipyrine , Oxidative coupling, Colorimetric, highly sensitive method.

INTRODUCTION

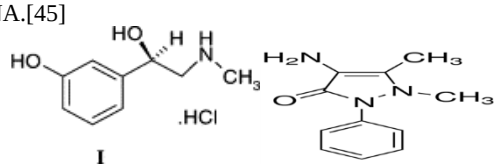
Pharmaceuticals and personal care products (PPCPs) are of scientific and public concern as newly recognized classes of environmental pollutants and they have received a growing concern for their pollutions [1].[2] As a result of frequent use, huge amounts of PPCPs have been released into aquatic environments [3], and the contamination of surface and ground water has emerged as a serious problem in recent years[3] Pharmaceuticals as emerging pollutants have become a major concern because of their low biodegradability, high persistence, and facile bioaccumulation[4]. These compounds include diverse groups, such as antibiotics, anti-inflammatory agents, blood-lipid regulators, and steroidal hormones [5]. Hospitals, households, and drug factories are the main sources of pharmaceuticals in wastewaters[6] .The continuous release of these pollutants into the environment significantly affects human health and aquatic systems[7] Thus, these pollutants must be eliminated from wastewater.[8]

Several methods, including biodegradation[9] ,electrocoagulation [10], ozonation [11], ultrafiltration membrane [12], and adsorption[13], have been used to treat pharmaceuticals. Among these methods, adsorption is the simplest, cheapest, and most versatile technique for holding these pollutants [14], Activated carbon [15, 16], biochar [17], mesoporous silica [18], zeolite [19], chitosan [20], carbon nanotubes (CNTs) [21]. clays [22], resin [23]. biomass wastes [23] . and graphene oxide [24] adsorbents have been effectively utilized to attract pharmaceutical pollutants from wastewaters. Numerous pharmaceuticals have been discovered in various surface and ground waters, and wastewaters globally, some of which have been linked to ecological impacts, even at trace concentrations[25-27] . Reports on pharmaceuticals for environmental risk and public health assessments have raised substantial concerns between both the public and regulatory agencies[28, 29] . Various conventional and advanced water and wastewater treatment processes have been investigated in terms of pharmaceutical removal from aqueous phase[30, 31] . It is worth mentioning that nanotechnology enabled remediation applications have captured enormous attention during the past years and gradually become the focus of research.[32].

Phenylephrine hydrochloride (Nec-synephrine) is (*R*)-1-(3-hydroxyphenyl)-2-methyl-aminoethanol hydrochloride .[33]. It is closely related chemically to epinephrine. It is a useful vasoconstrictor of sustained action with little effect on the myocardium or the central nervous system. It is used by topical application in nose drops. Sub-cutaneous injection has been employed extensively to prevent hypotension during spinal anaesthesia and for the treatment of orthostatic hypotension [34, 35]. The most recent methods for determination of phenylephrine hydrochloride included chromatographic electrochemical and spectrophotometric (Ahmed 2007)techniques.

Many procedures are known for the qualitative detection and for the quantitative determination of phenylephrine hydrochloride. Among the several analytical methods are titrimetric, [36] colorimetric,[37, 38]spectrophotometric, [39] fluorometry[40] and chromatographic[41]methods.

4-Aminoantipyrine(C11H13N3O) is known as the type of non-steroid anti-inflammatory drug. is a metabolite of aminopyrine with analgesic and anti-inflammatory properties [42, 43]. It is used as a reagent for biochemical reactions producing peroxides or phenols. [44] 4-Aminoantipyrine stimulates liver microsomes and is also used to measure extracellular water.[4] The derivatives derived from 4-aminoantipyrine have shown various pharmacological activities such as antipyretic, anti-inflammatory, analgesic, anti-oxidant, anti-fungal properties and anti-microbial. Moreover, in recent reports in the field of anticancer research, 4-aminoantipyrene exhibited promising antiproliferative activity against human carcinoma cell lines and as cleavage agents for DNA.[45]



I

Fig 1: chemical stretcher of a) Phenylephrine hydrochloride, b) 4-Aminoantipyrine

EXPERIMENTAL DETAILS

Preparation ***Reagents and samples***

4-Aminoantipyrine in different series was prepared by dissolving (0.02, 0.05, 0.1, 0.3, 0.5, 0.7 and 0.9) 100 mL of distilled water in a volumetric flask of 100 mL.

Phenylephrine hydrochloride standard solutions (100 µg mL^{-1}) were prepared by dissolving 0.1 g of **Phenylephrine hydrochloride** in distilled water the solution was made up to 1000 mL with distilled water.

Potassium Ferocyanide in different series was prepared by dissolving (0.02, 0.05, 0.1, 0.3, and 0.5) 100 mL of distilled water in a volumetric flask of 100 mL.

Preparation of Calibration Curve Phenylephrine hydrochloride

Aliquots of standard Samples containing different concentrations (5–100)mgL^{-1} of Phenylephrine hydrochloride drug were prepared by simple dilution with distilled water of the stock solution (100 mg l^{-1}). The following aqueous solutions were prepared fresh daily solution were transferred into a series of 10 mL calibrated volumetric flasks : A 2.0-ml quantity of standard solution Phenylephrine hydrochloride was mixed with 2 ml of potassium ferricyanide solution in a 10-ml volumetric flask. The volume was 1 ml sodium hydroxyl solution, and the solution was mixed. A 2-ml of 4-aminoantipyrine solution was then added, and the mixture was brought to volume and mixed. The absorbance were determined spectrophotometrically by using UV-Visible Spectrophotometer as shown in Fig.2 .

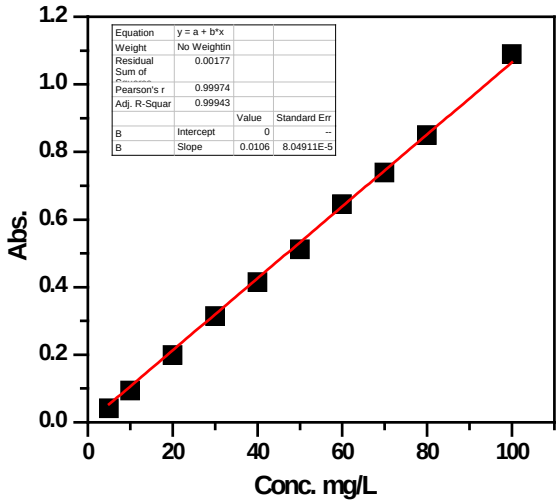


Fig. 2: Calibration curve of phenylephrine hydrochloride.

RESULTS AND DISCUSSION

3.1. Preliminary experiments and investigation

Throughout the preliminary investigation on the reaction of drug with 4-aminoantipyrine in the presence of potassium Ferocyanide. A ping color product was formed. It has a maximum absorption at λ_{max} 503 nm as shown in Fig. 3.

From the results obtained in Fig. 3, it appeared a possible to develop a new spectrophotometric method for the determination of Phenylephrine hydrochloride using the previous mentioned reaction.

Under the same conditions the reagent blank shows very small absorbance quantity (A = 0.0032) in the region of interest, so all the absorbance measurements were carried out against a reagent blank.[46]

From the results obtained, it appeared a possible to develop a new spectrophotometric method for the determination of Phenylephrine hydrochloride using the previous mentioned reaction. Initial studies were directed toward optimization of the experimental condition in order to obtain a more sensitive, stable and reproducible colored product. The influence of various reaction variables on the colored product was tested to establish the most favorable conditions for the determination of Phenylephrine hydrochloride. This study was started with the initial parameter given in Table 1.

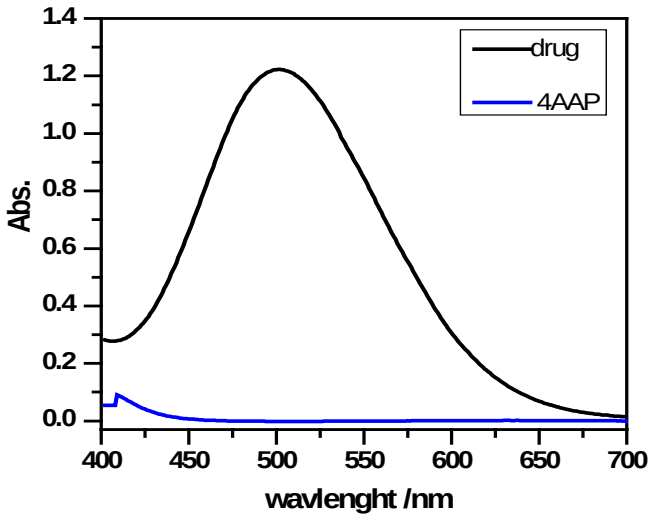


Fig. 3. Absorption spectra of A (100mgL^{-1}) of Phenylephrine hydrochloride treated as described under procedure and measured against reagent blank of B.

Table 1. Initial experimental chemical and physical conditions.

No.	Preliminary parameters	Value
1	Conc. of 4-aminoantipyrine	0.3 gm
2	Conc. of potassium ferricyanide	0.3 gm
3	Setting time	Immediately
4	Temperature	25 °C

3.2. Effect of time on the stability of complex

The effect of time on the reaction and stability of the colored dye were also studied. Fig. 4 shows that the high intensity can be obtained after 5 min from the beginning of the reaction and the complex color was stable up to 1 h, after that slowly decay between 2-4 hrs. Thus, 5 min was selected as a waiting time in this study

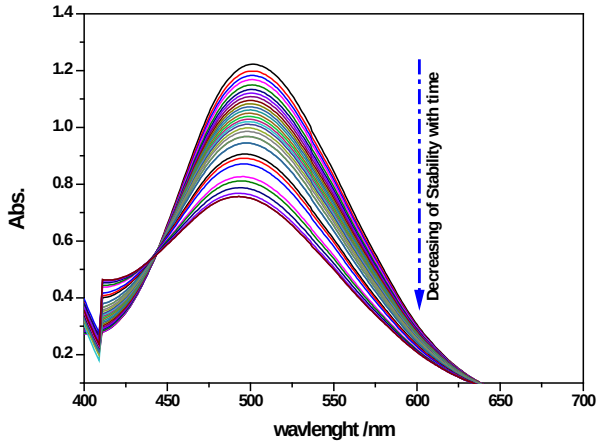


Fig. 4. Kinetic Absorption spectra of A (100 µgmL^{-1}) of Phenylephrine hydrochloride treated as described under procedure drug 3 hours

3.3 Concentration of 4-aminantipyrine

The effect of concentration of 4-aminoantipyrine was studied, results are shown in (Fig. 5 a & b). The absorbance increases with increasing concentration up till 0.3 gm/100 ml and started leveling off. The corresponding decrease in absorbance when the concentration increases above 0.5mg l^{-1}, therefore hence 0.3gm/100 ml was chosen for further investigations.[47]

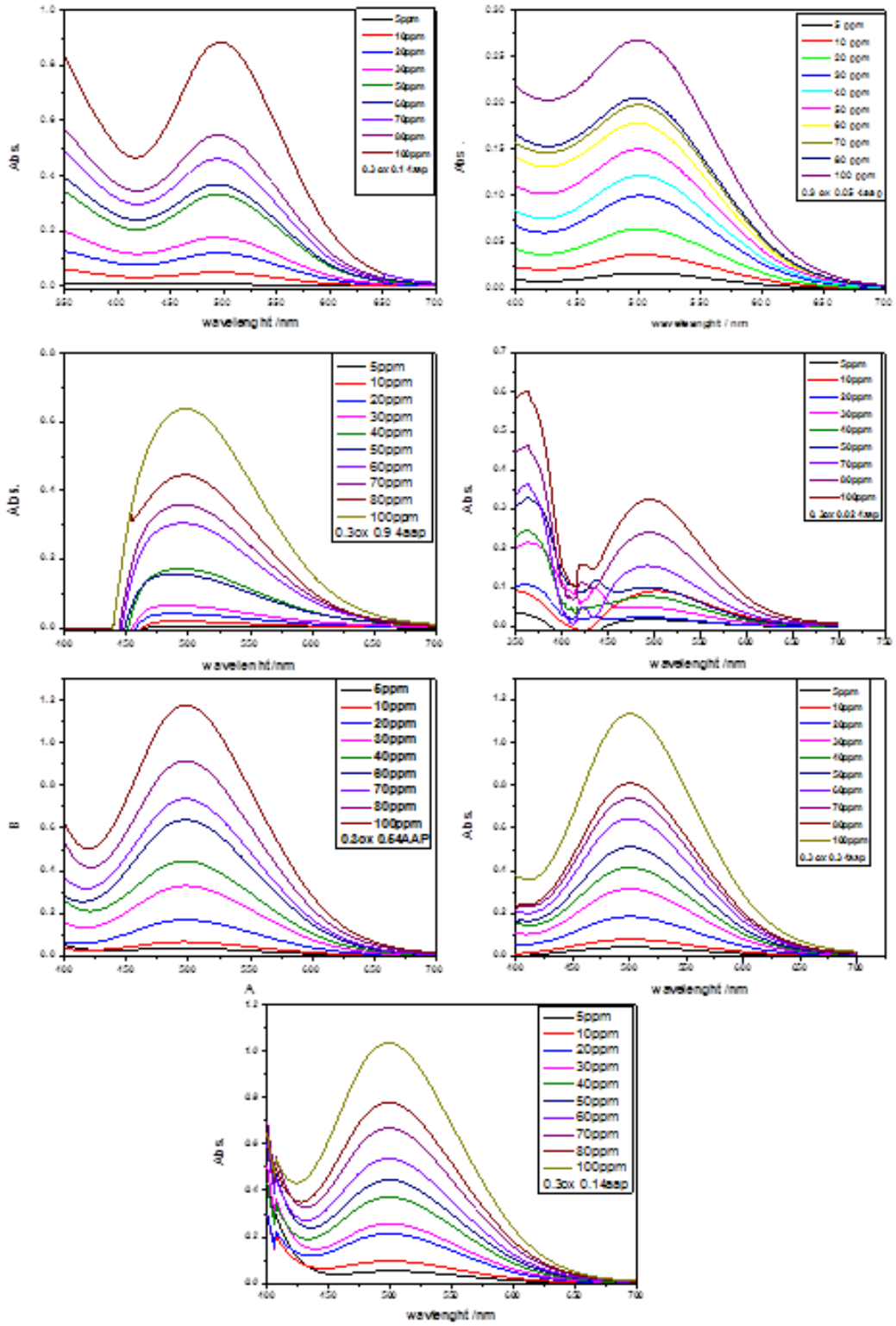


Fig.5a absorption Spectra of in the presence of difference concentrations of 4AAP

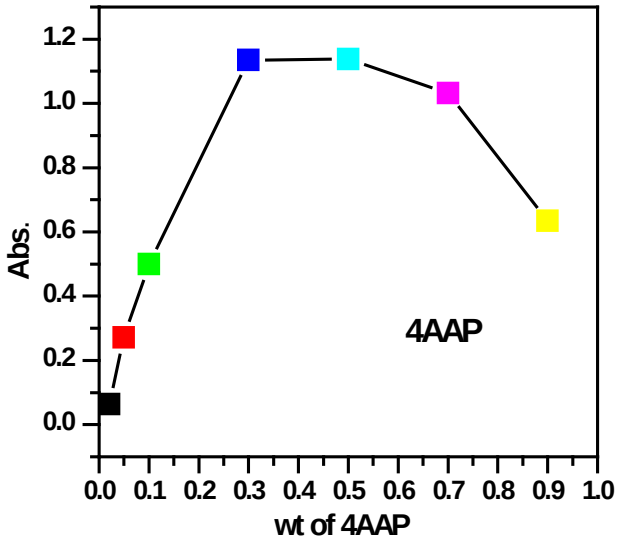


Fig. 5b. **Optimum absorption of complex in the presence of difference concentrations of 4APP**

3.4 Concentration of potassium ferricyanide

The measurements, it is vital to have sufficient reagent excess to have a better sensitivity. The effect of concentration of potassium ferricyanide was investigated from 0.02 to 0.5 mg l^{-1} (Fig. 5). The absorbance increases with increasing concentration, but as shown in Figure 4a after 0.3g/100 mL the absorbance have a negative behavior this may be attributed to the side reaction of complex in the presence of higher concentration of oxidant, therefore in our work the 0.3 g/100ml choose as the optimum conditions. [47]

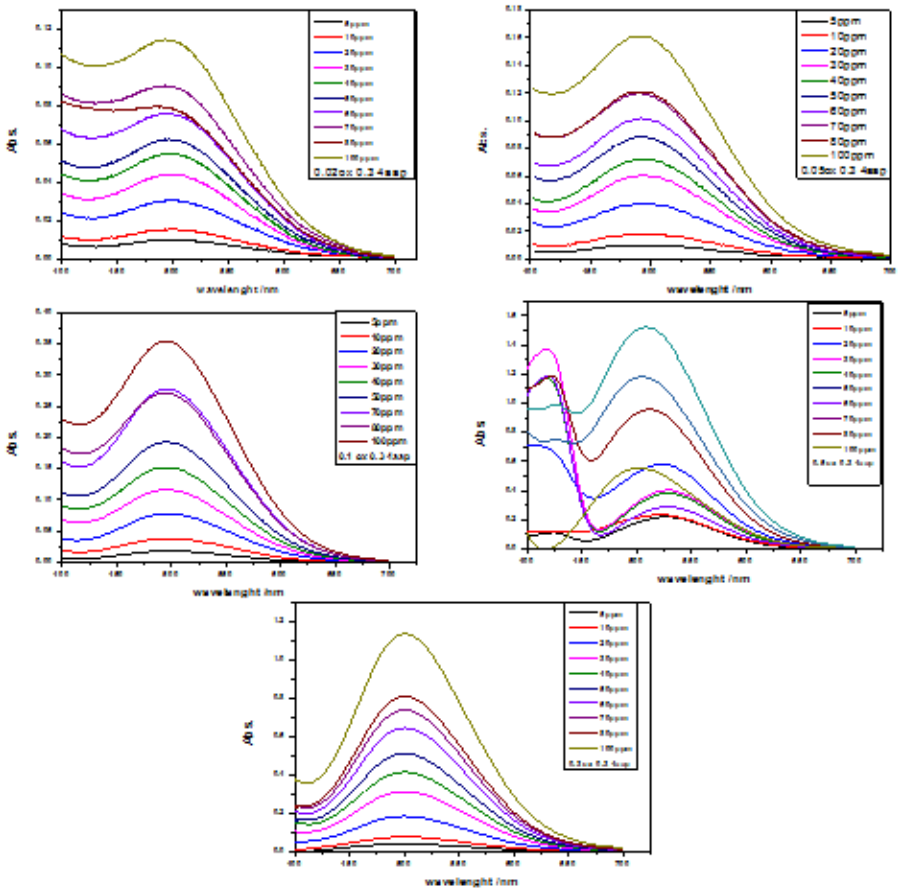


Fig.6a: Absorption spectra of oxidant in the presence of different concentrations

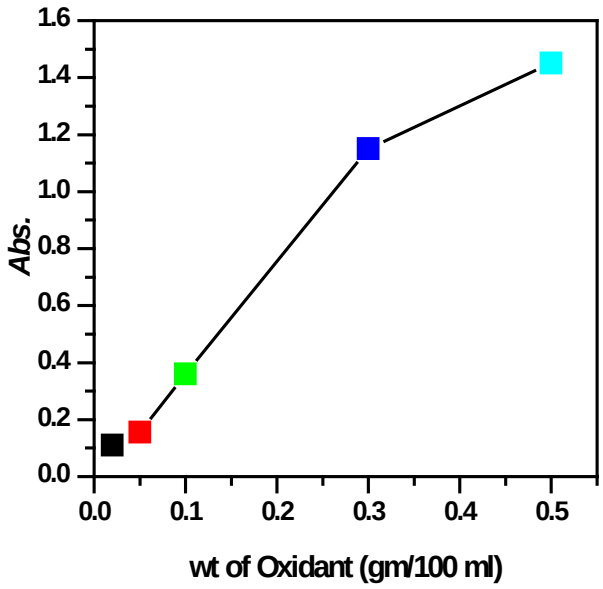


Fig.6b: absorptions value of oxidant in the presence of different concentrations

CONCLUSION:

1. Maximum absorbance attained at 503 nm by using UV-Vis spectrophotometer.
2. Coupling stability still at least 3 hrs.
3. The highest molar absorptivity attained when using 1:1 reagent /drug
4. 4AAP have a very important role on the stability and increasing the sensitivity until reach equilibrium, indeed of potassium ferricyanide solution.

REFERENCES

.1 Peng, G., et al., *Adsorption and catalytic oxidation of pharmaceuticals by nitrogen-doped reduced graphene oxide/Fe3O4 nanocomposite.* Chemical Engineering Journal. **341**: p. 361-370.

.2 Evgenidou, E.N., I.K. Konstantinou, and D.A. Lambropoulou, *Occurrence and removal of transformation products of PPCPs and illicit drugs in wastewaters: A review.* Science of The Total Environment. **505**: p. 905-926.

.3 Zhou, X., et al., *Enhanced adsorption of pharmaceuticals onto core-brush shaped aromatic rings-functionalized chitosan magnetic composite particles: Effects of structural characteristics of both pharmaceuticals and brushes.* Journal of Cleaner Production. **172**: p. 1025-1034.

.4 Zhang, S., et al., *Adsorption of pharmaceuticals on chitosan-based magnetic composite particles with core-brush topology.* Chemical Engineering Journal. **304**: p. 325-334.

.5 Sun, J., et al., *Occurrences of pharmaceuticals in drinking water sources of major river watersheds, China.* Ecotoxicology and Environmental Safety. **117**: p. 132-140.

.6 Nazari, G., H. Abolghasemi, and M. Esmaieli, *Batch adsorption of cephalexin antibiotic from aqueous solution by walnut shell-based activated carbon.* Journal of the Taiwan Institute of Chemical Engineers. **58**: p. 357-365.

.7 Lu, M.-C., et al., *Occurrence and treatment efficiency of pharmaceuticals in landfill leachates.* Waste Management. **55**: p. 257-264.

.8 Ahmed, M.J. and B.H. Hameed, *Removal of emerging pharmaceutical contaminants by adsorption in a fixed-bed column: A review.* Ecotoxicology and Environmental Safety. **149**: p. 257-266.

.9 Zhou, H., et al., *Enhancement with physicochemical and biological treatments in the removal of pharmaceutically active compounds during sewage sludge anaerobic digestion processes.* Chemical Engineering Journal. **316**: p. 361-3.69

.10 Nariyan, E., A. Aghababaei, and M. Sillanp ,ดl*Removal of pharmaceutical from water with an electrocoagulation process; effect of various parameters and studies of isotherm and kinetic.* Separation and Purification Technology. **188**: p. 266-281.

.11 Gomes, J.o., et al., *Application of ozonation for pharmaceuticals and personal care products removal from water.* Science of The Total Environment. **586**: p. 265-283.

.12 Sheng, C., et al., *Removal of Trace Pharmaceuticals from Water using coagulation and powdered activated carbon as pretreatment to ultrafiltration membrane system.* Science of The Total Environment. **550**: p. 1075-1083.

.13 Marques, S.C.R., et al., *Pharmaceuticals removal by activated carbons: Role of morphology on cyclic thermal regeneration* . Chemical Engineering Journal. **321**: p. 233-244.

.14 Moro, T.R., et al., *Adsorption of pharmaceuticals in water through lignocellulosic fibers synergism.* Chemosphere. **171**: p. 57-65.

.15 Calisto, V.n., et al., *Single and multi-component adsorption of psychiatric pharmaceuticals onto alternative and commercial carbons.* Journal of Environmental Management. **192**: p. 15-24.

.16 Aseel M. Aljeboree a, A.N.A.b., Ayad F. Alkaim a,, *Kinetics and equilibrium study for the adsorption of textile dyes on coconut shell activated carbon.* Arabian J. Chem,, 2013.

.17 Lin, L., W. Jiang, and P. Xu, *Comparative study on pharmaceuticals adsorption in reclaimed water desalination concentrate using biochar: Impact of salts and organic matter.* Science of The Total Environment. **601** :602-p. 857-864.

.18 Liang, Z., et al., *Adsorption of quinolone antibiotics in spherical mesoporous silica: Effects of the retained template and its alkyl chain length.* Journal of Hazardous Materials. **305**: p. 8-14.

.19 Sun, K., et al., *Sorption and retention of diclofenac on zeolite in the presence of cationic surfactant.* Journal of Hazardous Materials. **323**: p. 584-592.

.20 Kyzas, G.Z., D.N. Bikiaris, and D.A. Lambropoulou, *Effect of humic acid on pharmaceuticals adsorption using sulfonic acid grafted chitosan.* Journal of Molecular Liquids. **230**: p. 1-5.

.21 Zhao, H., et al., *Adsorption behavior and mechanism of chloramphenicols, sulfonamides, and non-antibiotic pharmaceuticals on multi-walled carbon nanotubes.* Journal of Hazardous Materials. **310**: p. 235-2.45

.22 Dordio, A.V., et al., *Mechanisms of removal of three widespread pharmaceuticals by two clay materials.* Journal of Hazardous Materials. **323**: p. 575-583.

.23 Zhou, Y., L. Zhang, and Z. Cheng, *Removal of organic pollutants from aqueous solution using agricultural wastes: A review.* Journal of Molecular Liquids. **212**: p. 739-762.

.24 Shan, D., et al., *Preparation of porous graphene oxide by chemically intercalating a rigid molecule for enhanced removal of typical pharmaceuticals.* Carbon. **119**: p. 101-109.

.25 M.J. Benotti, R.A.T., B.J. Vanderford, J.C. Holady, B.D. Stanford, S.A. Snyder, *Pharmaceuticals and endocrine disrupting compounds in US drinking water*
Environ. Sci. Technol., 2008. **43** p. 597-603.
.26 Q. Zhang, G.Y., C. Pan, Y. Liu, J. Zhao, *Comprehensive evaluation of antibiotics emission and fate in the river basins of China: source analysis, multimedia modeling, and linkage to bacterial resistance.* Environ. Sci. Technol.,, 2015. **49**: p. 6772-6782.
.27 J. Gao, J.H., W. Chen, B. Wang, Y. Wang, S. Deng, G. Yu, *Fate and removal of typical pharmaceutical and personal care products in a wastewater treatment plant from Beijing: a mass balance study Front.* Environ. Sci. Eng.,, 2016. **10**: p. 491-501.
.28 L.H. Santos, A.N.A., A. Fachini, A. Pena, C.D. Matos ,M.C.B.S.M. Montenegro, *Ecotoxicological aspects related to the presence of pharmaceuticals in the aquatic environment.* J. Hazard. Mater., 2010. **175**: p. 45-95.
.29 Cleuvers, M., *Aquatic ecotoxicity of pharmaceuticals including the assessment of combination effects.* Toxicol. Lett.,, 2003. **142** p. 185-194.
.30 Q. Liu, M.L., F. Zhang, H. Yu, Q. Zhang, X. Liu, *The removal of trimethoprim and sulfamethoxazole by a high infiltration rate artificial composite soil treatment system.* Front. Environ. Sci. Eng.,, 201 :11 .7p. 12.
.31 S. Khamparia, D.K.J., *Adsorption in combination with ozonation for the treatment of textile waste water: a critical review*
Front. Environ. Sci. Eng., , 2017. **11** p. 8.
.32 Shan, D., et al., *Intercalation of rigid molecules between carbon nanotubes for adsorption enhancement of typical pharmaceuticals.* Chemical Engineering Journal. **332**: p. 102-108.
.33 Al-Shaalan, N.H., *Determination of phenylephrine hydrochloride and chlorpheniramine maleate in binary mixture using chemometric-assisted spectrophotometric and high-performance liquid chromatographic-UV methods.* Journal of Saudi Chemical Society. **14**(1): p. 15-21.
.34 Ahmed, I.S. and A.S. Amin, *Spectrophotometric microdetermination of phenylephrine hydrochloride in pure and in pharmaceutical formulations using haematoxylin.* Journal of Molecular Liquids, 2007. **130**(1): p. 84-87.
.35 Goth, A., *Medical Pharmacology Principle and Concepts (10th Ed.),*. The Mosby C.V. Company 1981.
.36 Elsayed, M.A., Obiakara, A.C., Uzodinma, S.U., *Bromination methods for determination of phenylephrine hydrochloride in nose drops, salicylamide in tablets, and tetracycline hydrochloride in capsules.* Journal of the Association of Official Analytical Chemists, 1981. **64**(4): p. 860-863.
.37 Koshy, K.T., Mitchner, H.a ,*Colorimetric determination of phenylephrine using 4-aminoantipyrine.* Journal of Pharmaceutical Sciences
:(8)52 .1963p. 802-803.
.38 Sanghavi, N.M., Vyas, J.J., *Use of nitrating agent in the colorimetric estimation of drugs -Part II.* ndian Drugs, 1997. **3** :(8)4p. 463-466.
.39 Knochen, M.s. and J. Giglio, *Flow-injection determination of phenylephrine hydrochloride in pharmaceutical dosage forms with on-line solid-phase extraction and spectrophotometric detection.* Talanta, 2004. **64**(5): p. 1226-1232.
.40 Martin, M.A., B. del Castillo, and P. Prados, *13-Hydroxyacenaphato[1,2-b]quinolizinium bromide as a new flouorescence indicator.* Talanta, 1993. **40**(11): p. 1719-1723.
.41 De Beer, J.O., C.V. Vandenbroucke, and D.s.L. Massart, *Experimental design for the rapid selection of separation conditions for methyl and propyl parahydroxybenzoate, phenylephrine hydrochloride and chlorphenamine maleate by ion-pair liquid chromatography.* Journal of Pharmaceutical and Biomedical Analysis, 1994. **12**(11): p. 1379-1396.
.42 Elgemeie, G.H., M.A. Abu-Zaied, and S.A. Loutfy, *4-Aminoantipyrine in carbohydrate research: Design, synthesis and ¦anticancer activity of thioglycosides of a novel class of 4-aminoantipyrines and their corresponding pyrazolopyrimidine and ¦pyrazolopyridine thioglycosides.* Tetrahedron. **73**(40): p. 5853-5861.
.43 Costa, D., Vieira, A., Fernandes, E., *Dipyrone and aminopyrine are effective scavengers of reactive nitrogen species.* Redox Report. **11**(Issue): p. 136-142.
.44 Volume 33, I., 1999, Pages 191-193, *Synthesis and antiinflammatory activity of 4-aminoantipyrine derivatives of succinamides.* Pharmaceutical Chemistry Journal
)33 .1999Issue): p. 191-193.
.45 P©¦rez-Gilabert, M., A. S‹¦nchez-Ferrer, and F. Garc-¦a-Carmona, *Oxidation of Aminopyrine by the Hydroperoxidase Activity of Lipoxygenase: A New Proposed Mechanism of N-Demethylation.* Free Radical Biology and Medicine, 1997. **23**(4): p. 548-555.
.46 Hassan, M.J.M., W.S. Khayoon, and S. Abdul-Fatah Hasssan, *Batch and flow injection spectrophotometric methods for the determination of barbituric acid in aqueous samples via oxidative coupling with 4-aminoantipyrine.* Karbala International Journal of Modern Science. **1**(3): p. 135-141.
.47 Beyene, N.W. and J.F. Van Staden, *Sequential injection spectrophotometric determination of phenylephrine hydrochloride in pharmaceutical preparations.* Talanta, 2004. **63**(3): p. 599-604.