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# Use Of Oxidation Reactions For The Spectrophotometric Determination Of Acyclovir And Amantadine Hydrochloride In Their Dosage Forms

**Ibrahim A.Darwish**
**Department of Pharmaceutical Analytical Chemistry, Faculty of Pharmacy, Assiut University, Assiut 71526 (EGYPT)**
**Tel: +2 088-2411251; Fax: +2 088-2332776**
**E-mail: iadarwish@yahoo.com**

**Alaa S.Khedr[1], Hassan F.Askal[1], Ramadan M.Mahmoud[2]**
[1]Department of Pharmaceutical Analytical Chemistry, Faculty of Pharmacy, Assiut University, Assiut 71526 (EGYPT)
[2]Department of Pharmaceutical Analytical Chemistry, Faculty of Pharmacy, Al-Azhar University, Assiut, 71524 (EGYPT)

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## ABSTRACT

Five direct spectrophotometric methods for determination of acyclovir and amantadine hydrochloride has been developed and validated. These methods were based on the oxidation of the drugs by different inorganic oxidants: ceric ammonium sulphate, potassium permanganate, ammonium metavanidate, chromium trioxide, and potassium dichromate. Different variables affecting the reaction conditions were carefully studied and optimized. Under the optimum conditions, linear relationships with good correlation coefficients (0.9982–0.9999) were found between the reading and the corresponding concentration of the drug in the ranges of 2–1700 and 1-1100 μg/ml for acyclovir and amantadine HCl, respectively. The limits of detection ranged from 1.14-157.00 and 0.83-73.20 μg/ml for acyclovir and amantadine HCl, respectively. The precision of the methods was satisfactory; the values of relative standard deviations did not exceed 2%. The proposed methods were successfully applied to the analysis of acyclovir and amantadine HCl in their dosage forms with good accuracy and precisions; the label claim percentages ranged from 99.9–100.4 ± 0.62–1.05%. The results obtained by the proposed spectrophotometric methods were comparable with those obtained by the official methods.


## KEYWORDS

Acyclovir;
Amantadine HCl;
Oxidation;
Spectrophotometry;
Pharmaceutical analysis.

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## INTRODUCTION

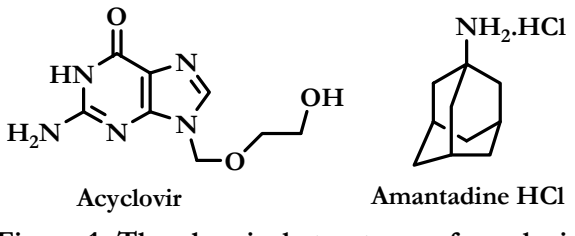
Acyclovir and amantadine hydrochloride (Figure 1) are the most widely used antiviral agents in our community. Acyclovir (9-[(2-hydroxyethoxy)-methyl]-guanine) is an acyclic guanosine derivative with clinical activity against HSV-1 and HSV-2 and against varicella-zoster virus[1,2]. It has been also used in the treatment of primary and recurrent genital herpes, herpes simplex encephalitis and neonatal HSV infection[1-3].

Amantadine (1-aminoadamantine) is used against infection with influenza type A virus and to ameliorate symptoms when administered during the early stages of infection[4], as well as in the management of herpes zoster[1]. Amantadine has mild antiparkinsonism activity and also has been used in the management parkinsonism of mainly in early disease stage when symptoms are mild. Amantadine is usually given by mouth as the hydrochloride salt[1].

The therapeutic importance of acyclovir and amantadine HCl has promoted the development of many analytical methods for their quantitative determination. These methods include high-performance liquid chromatography (HPLC)[5-18], micellar liquid chromatography[19], gas chromatography[20,21], capillary electrophoresis[22-23], radioimmunoassay[24], and potentiometry[25]. Most of these methods were devoted to biological fluids like plasma[5-7], serum[8], and/or urine[9]. Although some HPLC methods have been applied for the determination of acyclovir and amantadine HCl in their pharmaceutical dosage forms[15-18], however the procedures lack the sensitivity[15], besides being tedious and difficult to perform[16], or require selective and expensive detectors, which could not be available in many laboratories[17].

Spectrophotometric and fluorimetric analysis are considered more convenient alternative techniques because of their inherent simplicity and high sensitivity. Since acyclovir contains a weakly absorbing chromophore, and amantadine has no any light-absorbing chromophores in their molecules, few spectrophotometric methods[26-30] have been reported for their determination. These methods were laborious, time consuming, or/and require derivatization of the drug. Therefore, our laboratory involved to develop new simple spectrophotometric and fluorimetric methods that overcome these drawbacks. In our previous report[32], the development of a simple fluorimetric method for determination of acyclovir and amantadine HCl was described. The present study was dedicated to the development of new simple spectrophotometric methods for determination of both drugs in their pharmaceutical dosage forms.

Redox reactions have been used as the basis for the development of simple and sensitive spectrophotometric methods for the determination of many pharmaceutical compounds [33-46]. For these reasons, these reactions were attempted for use in the present study. This proposal was promoted by our previous report[32] that described the susceptibility of acyclovir and amantadine HCl for oxidation. In oxidimetric reactions, the most commonly used oxidizing agents are ceric ammonium sulphate[34-36], potassium permanganate[37-41], ammonium metavanidate[42-44], chromium trioxide, and potassium dichromate[45,46]. None of these reagents have not been previously used for the spectrophotmetric analysis of neither acyclovir nor amantadine HCl. For these reasons, the present study was dedicated to investigate the application of these reagents in the spectrophotometric analysis of both drugs in their pharmaceutical dosage forms.




Acyclovir Amantadine HCl

**Figure 1: The chemical structures of acyclovir and amantadine hydrochloride.**

## EXPERIMENTAL

### Apparatus

UV-1601 PC (Shimadzu, Kyoto, Japan) and Lambda-3 B (Perkin-Elmer Corporation, Norwalk, USA) ultraviolet-visible spectrophotometers with matched 1-cm quartz cells, were used for all measurements. MLW type thermostatically controlled water bath (Memmert GmbH, Co. Schwa bach, Ger-

many) was used.

### Materials and reagent solutions

Acyclovir (Misr Co. for Pharmaceutical Industries. S.A.E., Cairo, Egypt) and amantadine hydrochloride (Rameda Co. for Pharmaceutical Industries & Diagnostic Reagents, 6th October, Cairo, Egypt) were obtained and used as received. Both drugs were complying with various requirements recommended by the official methods[47]; purity percentages were 99.6 ± 0.64 and 100.02 ± 1.25% for acyclovir and amantadine HCl, respectively. Ceric ammonium sulphate (Sigma-Aldrich Co Ltd., Gillingham-Dorst, Germany) was 0.15% (w/v) in 0.25 M perchloric acid. Potassium permanganate (El-Nasr Pharmaceutical Chemical Co., Abo-Zaabal, Egypt) was 0.06% (w/v) in distilled water. Ammonium metavanidate (Veb Laborchemie Apolda, Germany) was 10% (w/v) in 20% (v/v) sulphuric acid. Chromium trioxide (Mallinckrodt Chemical Works Montreal, New York, USA) was 5% (w/v) in distilled water. Potassium dichromate (Cambrian Chemical Bedding Farm Road, Croydon, England) was 5% (w/v) in distilled water. All solvents, acids, and other chemicals used throughout this study were of analytical grade. Double distilled water was obtained through Nanopure II water purification system (Barnstead/Thermolyne, Dubuque, IA, USA), and used throughout the work.

### Pharmaceutical dosage forms

The following commercially available pharmaceutical dosage forms were subjected to the analysis. Novirus capsules (GlaxoWelcome Egypt S.A.E. Cairo, Egypt) are labeled to contain 200 mg of acyclovir per capsule. Lovir tablets (Global Napi Pharmaceuticals, Egypt) are labeled to contain 400 mg of acyclovir per tablet. Acyclovir eye ointment (Misr Co. for Pharmaceutical Industries S.A.E., Cairo, Egypt) is labeled to contain 3% of acyclovir. Acyclovir cream (Misr Co. for Pharmaceutical Industries S.A.E., Cairo, Egypt), and Zovirax cream (GlaxoWelcome Egypt S.A.E., Cairo, Egypt) are labeled to contain 5% of acyclovir. Adamin capsules (Rameda Co. for Pharmaceutical Industries & Diagnostic Reagents, 6th October, Cairo, Egypt.) are labeled to contain 100 mg of amantadine HCl per capsule.

### Preparation of standard solutions

An accurately weighed amount (1 g) of each of acyclovir and amantadine HCl was transferred into a 100-ml calibrated flask, and dissolved in about 40 ml of 0.1 N sulphuric acid for acyclovir, and in distilled water for amantadine HCl. The resulting solution were completed to the mark with water to provide a stock standard solution containing 10 mg/ml. Different volumes of this stock solution were then further diluted with water to obtain the working standard solutions of concentrations suitable for analysis by different oxidizing reagents.

### Preparation of pharmaceutical dosage forms

#### 1. Tablets and capsules

Twenty tablets or the contents of 20 capsules were weighed and finely powdered. An accurately weighed quantity of the powdered tablet or capsule contents equivalent to 1 g of the active ingredient was transferred into a 100-ml calibrated flask, and dissolved in about 40 ml of 0.1 N sulphuric acid for acyclovir, and in distilled water for amantadine HCl. The contents of the flask were swirled, sonicated for 5 min, and then completed to the volume with water. The mixtures were mixed well, filtered and the first portion of the filtrate was rejected. The prepared solution was diluted quantitatively with the distilled water to obtain a suitable concentration for analysis by each particular oxidant.

#### 2. Cream samples

An accurately weighed amount of the cream equivalent to 1 g of acyclovir was shaken with 50 ml of each of 0.5 M sulphuric acid and ethyl acetate. The mixture was then allowed to separate, and the clear lower aqueous layer was collected. The organic layer was washed two times with 20 ml of 0.5 M sulphuric acid. The combined washing and aqueous layer were quantitatively transferred to a 100 ml calibrated flask, and the volume was completed with 1 M sulphuric acid. The resulting solution was mixed well, filtered, and the first few milliliters of the filtrate were discarded. The working solution was pre-

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pared as described for preparation of stock standard solution.

**3. Eye ointment samples**

An accurately weighed amount of the eye ointment equivalent to 1 g of acyclovir was dispersed in 60 ml of hexane, and then extracted three times with 30 ml quantities of 0.1 M sodium hydroxide. The combined extracts were quantitatively transferred to a 100 ml calibrated flask, and the volume was completed with 1 M sulphuric acid. The resulting solution was filtered, and the first few milliliters of filtrate were discarded. The working solution was prepared as described for preparation of stock standard solution.

**General assay procedure**

One milliliter of the standard or sample solution was transferred into a 10 ml calibrated flask. One milliliter of the oxidizing analytical reagent was added. Different volumes (TABLE 1 - available as SUPPLEMENTARY INFORMATION) of an acid were added. The acids were perchloric for ceric ammonium sulphate, and sulphuric acid for the other reagents. The contents of the flasks were mixed and the reactions were allowed to proceed for different periods of time (TABLE 1 - available as SUPPLEMENTARY INFORMATION) at room temperature (25 ± 5 ºC), except in case of using ceric ammonium sulphate solution whereas the reaction mixture was heated in water bath adjusted to 80 ºC, and then cooled to room temperature. After completion of the reactions, the solutions were completed to volume with water. The absorbances of the resulting solutions were measured at their corresponding $\lambda_{max}$ (TABLE 1 - available as SUPPLEMENTARY INFORMATION) against reagent blanks treated similarly. In case of ceric ammonium sulphate and potassium permanganate, the positions of sample and blank cuvettes were exchanged for direct getting the difference in the absorbance values.

## RESULTS AND DISCUSSION

**Reactions involved and spectral characteristics**

**1. Reactions with ceric ammonium sulphate and potassium permanganate**

Ceric ammonium sulphate, Ce(IV) is a strong oxidizing agent having a yellow color of $\lambda_{max}$ 315 nm. The reduction of Ce(IV) to the colorless Ce(III) proceeds cleanly in acidic solution, and its potential is different according to the acid used. This reaction has been used for the spectrophotometric determination of many compounds either by direct measurement the decrease in its yellow color[34,35], or indirectly by measuring the excess Ce(IV) with oxidizable color-producing reagents[36].

Potassium permanganate is a strong oxidant, as well, with an intense violet color of $\lambda_{max}$ 525 nm. The oxidation of organic compounds with potassium permanganate was found to be a pH dependent. During the course of the reaction, the valance of manganese changes and the intermediate ions have been suggested as participating oxidants. The species that are considered as potential oxidants depend on the nature of the substrate and the pH of the medium. In strong acidic medium, potassium permanganate ($KMnO_4$) produces the $Mn^{2+}$ for a net transfer of five electrons[37]. In neutral or basic media, manganese dioxide ($MnO_2$) is formed with corresponding net transfer of three electrons[38]. In strongly alkaline solution, a green manganate ion ($MnO_4^{2-}$) is produced[39-41].

Both ceric ammonium sulphate and potassium permanganate were tested for their oxidizing effect on both acyclovir and amantadine HCl, and it was found that both drugs were vulnerable by both reagents in acidic solutions. This was evident from the decrease in the yellow color of ceric ammonium sulphate at 315 nm, and the violet color of potassium permanganate at 525 nm (Figure 2 - available as SUPPLEMENTARY INFORMATION). This decrease in color was used as a measure for the concentration of the drug. It is worth to note that both acyclovir and amantadine HCl have no absorption capabilities in region of measurements of both reagents (at 315 and 525 nm for ceric and potassium permanganate solutions, respectively.

**2. Reactions with ammonium metavanidate, chromium trioxide and potassium dichromate**

The reaction of acyclovir and amantadine HCl

with these reagents were studied, and it was found that the reaction proceeded by oxidation of both drugs and consequently the reduction of ammonium metavanidate, $VO_3^{-3}$ to the corresponding $VO_3^{-4}$ of $\lambda_{max}$ at 780 nm (Figure 3 - available as SUPPLEMENTARY INFORMATION). Both acyclovir and amantadine HCl were also found to be oxidizable by both chromium trioxide and potassium dichromate yielding the green Cr(III) ions of $\lambda_{max}$ 595 nm (Figure 3 - available as SUPPLEMENTARY INFORMATION).

**Optimization of reaction variables**

**1. Effect of oxidant concentration**

According to the above-mentioned reactions, ceric ammonium sulphate and potassium permanganate solutions should be added in excess to react with the drug. By measuring the excess reagent, the consumed reagent would correspond to the amount of the drug. The highest concentrations of either reagent which give the highest absorption value within the practical sensitivity range of absorption values (≈0.9) was found to be 0.15 and 0.06 % (w/v) for ceric ammonium sulphate and potassium permanganate, respectively (Figure 2 - available as SUPPLEMENTARY INFORMATION).

For the other oxidizing reagents, the effect of their concentrations on the reactions was studied by carrying out the reactions using 1 ml of different concentrations in the ranges cited in figure 4 (available as SUPPLEMENTARY INFORMATION). It was observed that the reactions increase by increasing the concentration until maximum absorbance is obtained. The optimum concentration selected for further experiments was considered as the concentration at which maximum absorption was obtained and in the plateau region of the concentration-absorption curve. These concentrations were 10% (w/v) for ammonium metavanidate, and 5% (w/v) for chromium trioxide and potassium dichromate.

**2. Effect of acid type and concentration**

The oxidation of acyclovir and amantadine HCl by different inorganic oxidants were performed in acid medium. In order to determine the most appropriate acid, different acids (sulphuric, hydrochloric, nitric, perchloric and acetic) were tested. As shown in TABLE 2 (available as SUPPLEMENTARY INFORMATION), sulphuric acid gave the highest readings with all oxidants, except with ceric ammonium sulphate whereas perchloric acid gave the highest readings. This was attributed to the fact that the potential of Ce(IV) in perchloric acid ($E^\circ$ =1.7 V) is higher than that of in sulphuric acid ($E^\circ$ =1.4 V)[48]. Therefore, sulphuric acid was selected for further testing with all reagents except ceric ammonium sulphate, whereas perchloric acid was selected.

Preliminary experiments indicated that for the oxidation of both drugs with the oxidants required high concentration of the acid. In order to determine the most appropriate concentration of the acid, the reactions were performed using varying volumes (0.5-6 ml) of the concentrated acids. It was found that all the reactions were dependent on the concentration of the acid. The absorption intensity increased as the concentration of the acid increased. After attaining the maximum readings, different behaviors were attained (Figure 5 - available as SUPPLEMENTARY INFORMATION). The optimum concentration of acid at which the maximum readings were obtained was 2 ml for potassium permanganate, 3 ml for ceric ammonium sulphate, and 4 ml for ammonium metavanidate, chromium trioxide, and potassium dichromate.

**3. Effect of temperature and reaction time**

The reactions between both drugs and the oxidants (except ceric ammonium sulphate) were performed in relatively high volumes of concentrated sulphuric acid. The generated heat was found to be sufficient for completion of the reaction. The reaction of both drugs with ceric ammonium sulphate that was performed in perchloric acid, required heating for its completion. The effect of heating temperature on the oxidation of acyclovir by ceric ammonium sulphate was studied by carrying out the reaction in a thermostatically controlled water bath at varying temperatures (25-100 °C). It was found that the reaction increased with increasing the temperature until reach optimum in the range of 70-100 °C (Figure 6 - available as SUPPLEMENTARY INFORMATION). Therefore, the further experiments

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were performed at 80 ºC.

The effect of time on the reaction was studied by carrying the reactions for different periods of time at 80 ºC for ceric ammonium sulphate and at room temperature for all other reagents. The reactions of acyclovir and amantadine HCl with ammonium metavanidate, chromium trioxide, and potassium dichromate were instantaneous, however for more precise readings, the reaction mixtures were allowed to stand for 5 min. For the reactions with ceric ammonium sulphate and potassium permanganate, the time required for completion of the reactions were 20 and 15 min for ceric ammonium sulphate and potassium permanganate, respectively (Figure 7 - available as SUPPLEMENTARY INFORMATION). After attaining the maximum readings, longer reaction time up to 60 min had no effects.

**4. Effect of diluting solvent**

The effect of diluting solvent on the absorption intensity of the oxidation reaction mixtures of both acyclovir and amantadine HCl with the different reagents were studied using various solvents for dilution (water, methanol, ethanol, acetonitrile, acetone, and isopropanol). It was found that water was the optimum diluting solvent, as it gave maximum readings, in all cases. Therefore water was selected for further work with all reagents

**5. Effect of time on stability of readings**

The effect of time on the stability of the readings after dilution was studied. It was found that the readings of the reaction mixtures were stable for at least 1 hour after diluting the reaction mixtures. This gaves the advantage of measuring comfortably at any time within that period without any changes in the reading values. This advantage is beneficial when processing of large number of samples is necessary.

**Validation of the proposed methods**

**1. Linearity, detection and quantitation limits**

Under the above mentioned optimum conditions (TABLE 1 - available as SUPPLEMENTARY INFORMATION), the calibration graphs correlating the absorption intensity with the corresponding concentration of both acyclovir and amantadine HCl were constructed for all the reagents used. Regression analysis for the results were as carried out using least-square method. In all cases, Beer's law plots (n = 5) were linear with very small intercepts (-0.0569-0.0520) and good correlation coefficients (0.9982-0.9999) in the general concentration ranges of 2–1700 and 1-1100 μg/ml for acyclovir and amantadine HCl, respectively (TABLE 3 - available as SUPPLEMENTARY INFORMATION). The limits of detection (LOD) and limits of quantitation (LOQ) were determined[47] using the formula: LOD or LOQ = $\kappa SD_a/b$, where $\kappa = 3$ for LOD and 10 for LOQ, $SD_a$ is the standard deviation of the intercept, and b is the slope. The LOD values ranged from 1.14-157.00 and 0.83-73.20 μg/ml for acyclovir and amantadine HCl, respectively. Results in TABLE 3 (available as SUPPLEMENTARY INFORMATION) indicated the the reagents that have the lowest oxidation potential, $E^0$ (chromium trioxide and potassium dichromate) gave the lowest sensitivities (lowest ε values), however reagents that have the highest oxidation potential (ceric ammonium sulphate and potassium permanganate) gave the highest sensitivities (highest ε values). These results indicated the correlation of the oxidation potential of the oxidants with the obtained ε values for each particular oxidant.

**2. Precision**

The precision of the proposed methods was determined[47] by replicate analysis of nine separate samples of the working standards at one concentration level. The relative standard deviations were less than 2% with all the tested reagents indicating the good reproducibility of the proposed methods (TABLE 4 - available as SUPPLEMENTARY INFORMATION). This precision level is adequate for the routine analysis of the investigated drugs in quality control laboratories.

**3. Interference liabilities**

Before proceeding with the analysis of acyclovir and amantadine HCl in their solid dosage forms, interference liabilities were carried out to explore the effect of common excipients that might be added during formulations. Samples were prepared by mixing known amounts (400 and 100 mg for acyclovir and amantadine HCl, respectively) with various

amounts of the common excipients: gum acacia (70 mg), sucrose (100 mg), glucose (90 mg), lactose (80 mg), starch (10 mg), citric acid (5 mg), and microcrystalline cellulose (6 mg), and the analysis was then performed. Good percentage recoveries (98.5-103.1 ± 0.12-1.37%, and 98.3-104.6 ± 0.12-1.31% for acyclovir and amantadine HCl, respectively) were obtained from the synthetic mixtures indicated the absence of interference liabilities from these excipients. Although the methods are not selective, being based on oxidation reactions; however the good recoveries ensured its suitability for the analysis of both acyclovir and amantadine HCl without interference from the common reducing excipients. This was attributed to the sensitivity of the methods, and the relatively high dosage of both drugs that necessitated the dilution of the sample, and consequently the excipients beyond their interference capabilities. In addition, the suspected interference from HCl moiety of amantadine HCl was studied by carrying out the oxidation reactions on the intact molecule, besides the free amantadine base. Similar results (molar absorbitivity values) were obtained in both cases. This indicated that the HCl moiety of amantadine HCl did not interference in the oxidation reactions of amantadine under the optimum recommended conditions.

**Robustness and ruggedness**

Robustness was examined by evaluating the influence of small variation of method variables including, concentration of oxidants, reaction time, volume of acid (perchloric for ceric ammonium sulphate and sulphuric for the other reagents) and temperature on the performance of the proposed methods. In these experiments, one parameter was changed where as the others were kept unchanged, and the recovery percentage was calculated each time. It was found that none of these variables significantly affected the method; the recovery values were 98.6-100.1 ± 0.45-0.96%, and 98.7-100.4 ± 0.45-0.95% for acyclovir and amantadine HCl, respectively. This provided an indication for the reliability of the proposed methods during routine application of the proposed methods in the analysis of both drugs.

Ruggedness was tested by applying the proposed methods to the assay of both antiviral drugs using the same operational conditions but using two different instruments at two different laboratories and different elapsed time. Results obtained from lab-to-lab and day-to-day variation were found to be reproducible, as RSD did not exceed 2%.

**Application of the proposed methods to analysis of dosage forms**

It is evident from the aforementioned results that the proposed methods gave satisfactory results with the drugs in bulk. Thus the dosage forms were subjected to the analysis for their contents of the active drug material by the proposed methods and the official method[47]. The label claim, as percentages, ranged from 97.5–101.4 ± 0.67-1.23% (TABLE 5 - available as SUPPLEMENTARY INFORMATION). These results were compared with those obtained from the official method by statistical analysis with respect to the accuracy (t-test) and precision (F-test). No significant differences were found between the calculated and theoretical values of t- and F-tests at 95% confidence level proving similar accuracy and precision in the analysis of both acyclovir and amantadine HCl in their dosage forms. It is evident from these results that all the proposed methods are applicable to the analysis of both drugs in their bulk and dosage forms with comparable analytical performance. The critical recommendations of some of these methods might be based on their relative sensitivities (that determines the amount of specimen available for analysis) and experimental conditions (reaction time, temperature, diluting solvent, etc.). For example, the methods involving ceric ammonium sulphate, and potassium permanganate gave more sensitive assays than the other reagents. However, the assay involving ceric solution needed an extra apparatus, water bath).

## CONCLUSIONS

The present study described oxidation-based simple and accurate spectrophotometric methods for the direct analysis of acyclovir and amantadine HCl. The methods are superior to the previously reported methods for determination of both drugs, in terms of simplicity, as they do not require pre-derivatization of the drugs prior to the analysis[29].

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The proposed methods involved measurements in the visible region which confer their selectivity and avoid the potential interferences from UV-absorbing excipients that are encountered in the methods that involve measurements in UV region[26-28]. The range of different sensitivities achieved with various reagents gives the opportunity for choosing from these methods, based on the amount of specimen available for analysis. The wide linear dynamic range that has been achieved in the proposed methods confers the ease in preparation of the samples for analysis. From the economical point of view, all the analytical reagents are inexpensive, have excellent shelf life, and are available in any analytical laboratory. Therefore, these methods can be recommended for the routine analysis of acyclovir and amantadine HCl in quality control laboratories.

## SUPPLEMENTARY INFORMATION AVAILABLE STATEMENT

Following information is available as SUPPLEMENTARY INFORMATION.

- TABLE 1: Experimental conditions for the spectrophotometric determination of acyclovir and amantadine HCl by the proposed oxidation-based methods using different oxidants
- TABLE 2: Effect of acid type on the oxidation of acyclovir and amantadine HCl with different oxidants.
- TABLE 3: Quantitative parameters and statistical data for the spectrophotometric determination of acyclovir and amantadine HCl with various oxidants
- TABLE 4: Precision of the spectrophotometric analysis of acyclovir and amantadine HCl by oxidation with different oxidants
- TABLE 5: Analysis of analysis of dosage forms containing acyclovir and amantadine HCl by the proposed and official methods
- Figure 2: Absorption spectra of 0.15 % (w/v) of ceric ammonium sulphate (1), 0.06% (w/v) of potassium permanganate (2), and their reaction mixtures (3, and 4, respectively) with acyclovir. The concentrations of acyclovir were 8 and 20 μg/ml for reaction with ceric ammonium sulphate and potassium permanganate, respectively.
- Figure 3: Absorption spectra of reaction mixtures of acyclovir with 10% (w/v) of ammonium metavanidate (1), 5% (w/v) of chromium trioxide (2), and 5% (w/v) of potassium dichromate (3). The concentrations of acyclovir were 600, 900, and 700 μg/ml for reaction with ammonium metavanidate, chromium trioxide, and potassium dichromate, respectively.
- Figure 4: Effect of reagent concentrations on the absorption intensity of the reaction mixtures of acyclovir (A) and amantadine HCl (B) with ammonium metavanidate (◆), chromium trioxide (•), and potassium dichromate (Δ). The concentrations of the drugs were 500, 600, and 900 μg/ml for reaction with ammonium metavanidate, chromium trioxide, and potassium dichromate, respectively.
- Figure 5: Effect of acid concentrations on the absorption intensity of the reaction mixtures of each of acyclovir (A) and amantadine HCl (B) with ceric ammonium sulphate (Δ), potassium permanganate (•), ammonium metavanidate (○), chromium trioxide (◆), and potassium dichromate (▼). The concentrations of the drugs were 8, 35, 700, 900, and 900 μg/ml for reaction with ceric ammonium sulphate, potassium permanganate, ammonium metavanidate, chromium trioxide, and potassium dichromate, respectively. Acids were perchloric with ceric ammonium sulphate and sulphuric for the other reagents.
- Figure 6: Effect of temperature on the absorption intensity of the oxidation product of 8 μg/ml of each of acyclovir (○) and amantadine HCl (•) with ceric ammonium sulphate (0.15%, w/v).
- Figure 7: Effect of reaction time on the absorption intensity of the reaction mixtures of each of acyclovir (A) and amantadine HCl (B) with ceric ammonium sulphate (○), potassium permanganate (▲), ammonium metavanidate (◆), chromium trioxide (•), and potassium dichromate (▽). The concentrations of the drugs were 8, 35, 600, 600, and 700 μg/ml for reaction with ceric ammonium sulphate, potassium permanganate, ammonium metavanidate, chromium trioxide, and potassium dichromate, respectively.

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