

ORIGINAL ARTICLE

SENSITIVE SPECTROPHOTOMETRIC METHODS FOR QUANTITATIVE DETERMINATION OF CHLORPROTHIXENE IN PHARMACEUTICAL DOSAGE FORM

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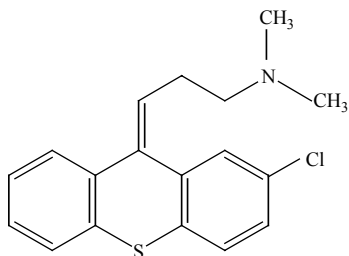
ABSTRACT

Simple and sensitive UV-VIS spectrophotometric methods for the determination of chlorprothixene hydrochloride have been developed. One of them is based on the oxidation of chlorprothixene (CPT) by ammonium metavanadate with the formation of colourless product. The second method involves the formation of ion-pair between the drug under investigation and inorganic complexes of titanium (IV) thiocyanate followed by its extraction with mixture of butanol-chloroform (1:9, v/v). The optimum conditions for the oxidation of CPT or ion-pair formation are established. The studies are examined by UV-VIS, IR or NMR spectroscopy. The methods permit the determination of CPT over the concentration range of 2.5-25 µg/ml and 4-35 µg/ml using ammonium metavanadate or the titanium (IV) thiocyanate complex, respectively. The methods are rapid, highly reproducible and accurate with $\pm 0.8\%$. The methods are applicable to the assay of the drug under investigation in different dosage forms and the results are in good agreement with those obtained by the official methods. Common excipients used as additives to active ingredient in pharmaceutical preparations do not interfere in the proposed methods. The extractive spectrophotometric method can be applied to the determination of chlorprothixene hydrochloride in tablets after solid phase extraction (SPE).

Keywords: Chlorprothixene hydrochloride; oxidation; ammonium metavanadate; UV-VIS spectrophotometry; ion-pair formation; titanium (IV) ions; solid phase extraction; pharmaceutical preparations.

INTRODUCTION

Chlorprothixene (CPT) belongs to the important group of bioactive organic compounds - thioxanthene derivatives, which have been introduced into medicine as tricyclic aromatic neuroleptics. Chlorprothixene is known for its therapeutic activities. Owing to its relatively low toxicity and wide pharmacological action it is frequently used in treatment of depression and phobic diseases. It is also prescribed for the treatment of schizophrenia, neurosis, alcoholic psychosis and personality disorders.



Structure 1

Due to chemical structure (presence of atoms of sulphur and nitrogen, tricyclic aromatic ring to which the side chain is

linked by C = C double bond), chlorprothixene displays interesting analytical properties. It is reacted with halide and thiocyanate complexes of metals, e.g. Co(II), Fe(III), Cd(II), Cr(III), Mo(V), W(V), and some organic compounds such as dipicrylamine or methyl orange forming ion- association type complexes easily extracted in some organic solvents. This property can be used as a base of some extractive spectrophotometric methods for the chlorprothixene determination (Popelkova-Mala & Malat, 1985 and Hopkala *et al.*, 1996). Reactions with 2,3-dichloro-5,6-dicyano-p-benzoquinone (DDQ) and chloranil (El-Sebai *et al.*, 1983 and Salam *et al.*, 1985) are also applied for CPT determinations.

CPT is easily oxidised with generation of colourless products: sulfoxide, sulphone or thioxanones (Aly, 1990; El-Brashy, 1990; Walash *et al.*, 1988 and Tammilehto, 1980). The reactions depend on type and concentration of oxidizing agents applied. The properties of the oxidation products formed can be applied for the determination of chlorprothixene in pharmaceuticals.

The frequent application of CPT in the treatment of psychiatric disorders demands fast, simple, accurate and sensitive methods for its determination and monitoring in body liquids. Based on scientific literature various procedures and techniques have been reported for CPT

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determinations in pure form, pharmaceuticals and biological media. This compound and its main metabolites have been determined in urine and blood by thin layer chromatography method (Christensen, 1974). HPLC methods with various detection techniques are applied for its determinations in serum, blood and pharmaceutical preparations (Misztal, 1991; Kontourelis *et al.*, 1993 and Belal *et al.*, 1997). Spectrophotometric, fluorimetric or titrimetric methods are frequently used for CPT determinations in commercial products (Hassan *et al.*, 1989 and Walash *et al.*, 1988). The sensitive and fast spectrofluorimetric method based on the reaction of CPT with 85% orthophosphoric (V) acid was proposed for its determination in pharmaceuticals (Belal *et al.*, 1991). The reaction product of CPT with hexamine-cobalt (III) tricarbonatocobaltate (III) (HCTC) in sulphuric (VI) acid medium (Belal *et al.*, 1988) has also fluorescent properties. In scientific literature are also known indirect iodometric method, polarographic and immune methods (Walash *et al.*, 1988 and Masaon *et al.*, 1984).

In continuation of our studies on the determination of some organic compounds of biological interest and pharmaceutical importance (Misiuk *et al.*, 2001; Misiuk, 2000 and 2005), the present paper reports sensitive and simple spectrophotometric methods for the determination of chlorprothixene hydrochloride. In the methods developed, chlorprothixene hydrochloride was oxidised with ammonium metavanadate or formed ion association compound with the thiocyanate complex of titanium (IV). Using ammonium metavanadate, chlorprothixene was oxidized to 2-chlorthioxanthone (scheme 1). The proposed methods offer the advantages of sensitivity and stability. The methods have been allowed for the determination of the mentioned drug in pharmaceutical preparations. Common additives used as excipients in pharmaceutical preparations do not interfere in the determination of chlorprothixene hydrochloride by the proposed methods. The extractive spectrophotometric method can be also developed to determination of chlorprothixene hydrochloride after its isolation from tablets by solid phase extraction (SPE).

EXPERIMENTAL

Chemical and reagents

Chlorprothixene (CPT) hydrochloride aqueous stock solution (10^{-2} mol/l) prepared from a commercial product (SIGMA Chemical Co., purity 99.9 %) by dissolving an appropriate weight in 1 l of double distilled water and was stored in a refrigerator at + 4°C. CPT was assayed by EP 4 (European Pharmacopoeia, 2002) method and found to contain (99.9±0.24)% for chlorprothixene hydrochloride. Working solutions of lower concentrations were prepared freshly every day.

Chlorprothixene tablets. Solutions of concentrations of 1000 µg/ml were prepared by dissolving an amount of crushed

and powdered tablets equivalent the required amount of chlorprothixene in double distilled water. The mixture was filtered, brought to volume in a 50 ml calibrated flask by double distilled water. Working solutions were prepared by appropriate dilution.

NH₄VO₃ stock solution (10^{-2} mol/l) was prepared by dissolving an appropriate weight of the pure product (POCH, Poland) in 0.5 mol/l sulphuric (VI) acid. The working solutions were prepared by dilution of stock solution in double distilled water.

Standard titanium (IV) solution (10^{-1} mol/l) was prepared from commercial product (MERCK) by dissolving TiCl₄ in 1 mol/l hydrochloric acid. The working solution was prepared by dissolving the stock solution. Ammonium thiocyanate solution (10 mol/l) was prepared by dissolving an appropriate amount in distilled deionized water. Solutions of hydrochloric, sulphuric (VI), orthophosphoric and acetic acids were prepared by dilution of concentrated acids (POCH, Poland). All substances and solvents were of analytical and spectroscopic grade.

Apparatus

CECIL CE 8020 UV-VIS spectrophotometer, Spekol 11 (Carl Zeiss Jena), FTIR – spectrometer Magna 550, II serie, Nicolet and Bruker AC 200F spectrometer were used. The chemical shifts were measured in DMSO-d₆ with tetramethylsilane as the internal standard. There were also used J.T. Baker 3 ml solid phase extraction columns packed with reversed phase cyclohexylsilane (C₆H₁₁) bonded to silica gel (40 µm APD, 60 Å). Extraction was done by SPE – 12G, System J.T. Baker.

The chromatographic system (Thermo Separation) consisted of the 3D detector spectra system UV 3000, the low gradient pump P2000, the vacuum membrane degasser SCM Thermo Separation and the Rheodyne loop injector (20 µl) was used. ChromQuest Chromatography Data System software version for Windows NT was used for the acquisition of data. The measurements at 252 nm were carried out using the reversed-phase analytical column, Lichrospher 100 RP-18 250x4 mm (5 µm) with a guard column 4x4 mm (5 µm) (Merck, Germany) and mobile phase included acetonitrile and 0.01 M aqueous solution of triethylamine in proportion 1:1 adjusted to pH 2.7 by drop addition of concentrated phosphoric acid. The flow rate was set at 0.9 ml/min.

Procedures of chlorprothixene determination

Ammonium metavanadate method

Into 10 ml calibrated test tubes were placed 1 ml of 3×10^{-4} mol/l NH₄VO₃ solution, 1 ml of 10 mol/l H₂SO₄ solution and variable volumes of 3×10^{-4} mol/l aqueous solution of CPT. The total volume was diluted to the mark with distilled water and mixed well. The absorbance was measured at 268 nm against reagent blank as reference.

Titanium (IV) thiocyanate method

Into 25 separatory funnel were placed 1 ml of 3×10^{-3} mol/l Ti(IV) aqueous solution, 4 ml of 10 mol/l H_2SO_4 , 0.8 ml of 10 mol/l NH_4SCN and variable volumes of 3×10^{-4} mol/l of CPT hydrochloride. The total volume of water phase was adjusted to 10 ml with distilled water. Next 10 ml of butyl alcohol-chloroform (1:9) mixture was added and shaken vigorously for 2 min. The two phases were allowed to separate and the organic layer was transferred into 10 ml calibrated test tubes. The absorbance was measured at 390 nm against a reagent blank as reference.

Sample preparation: assay in dosage forms by HPLC method

Tablets of chlorprothixene (Chlorprothixen) (included 15 mg of CPT). 20 tablets, each included 15 mg of chlorprothixene, were finely powdered. An accurately weighed portion, equivalent to about 15 mg of chlorprothixene was transferred into 100 ml calibrated flask and diluted to the volume with methanol (HPLC-grade). The powder was completely disintegrated by using a mechanical shaker and solution was filtered. The filtrate was transferred into a 100 ml and fulfilled to the mark with methanol. The working solution was prepared by an appropriate dilution with methanol.

Solid phase extraction (SPE)

Before use, the SPE column was properly conditioned as follows: CH extraction column was conditioned subsequently by 2.0 ml of methanol, 2.0 ml of water, 0.5 ml of 15% CH_3OH in 0.2 mol/l HCl and 1.0 ml of water. For this purpose the 1 ml cartridges CH column was used. A 2 ml aliquot of the sample solution was applied to the SPE column.

Sample preparation for SPE

A sample of chlorprothixene hydrochloride, equivalent to about 1.5 mg of the drug was dissolved in 100 ml of methanol and a 1.0 ml of aliquot of the sample solution was mixed with 1.0 ml 12% CH_3OH in 0.2 mol/l HCl. After loaded the whole spiked sample onto the activated column, the cartridge was then washed with 1.0 ml of acetonitrile. Afterwards, the column was dried completely before eluting step. Elution was done with three 1.0 ml portions of chloroform – n-butanol mixture (5:1, v/v) to a glass tube and then transferred to a 50 ml separatory funnel. Finally, the extract was subjected to an extractive spectrophotometric determination according to the proposed procedure described in the section 2.3.2.

RESULTS AND DISCUSSION**Oxidation of chlorprothixene hydrochloride**

It was found, that chlorprothixene reacts with ammonium metavanadate with the formation of oxidation product. As the reaction is dependent on the kind of acid used and its

concentration, the time and temperature of the reaction and the concentration of the oxidant, we have selected the optimal conditions based on a series of tests. The optimisation of experimental conditions was led spectrophotometrically using 3×10^{-4} mol/l solution of chlorprothixene hydrochloride at 268 nm wavelength. The optimization of these studies were established by altering each variable in turn while keeping the others constant and observing the resulting effect on the absorbance of the oxidation species.

Maximum absorption of chlorprothixene and its colourless oxidation product with ammonium metavanadate shows maximum absorption in UV region. The UV spectrum of chlorprothixene exhibits maximum absorption at 195 nm, 225 nm, 268 nm and 324 nm. The colourless oxidation product of chlorprothixene shows maxima absorption at 195 nm and 268 nm in UV region. The peaks at 225 nm and 324 nm disappear in the spectrum of oxidation product.

The IR spectra of chlorprothixene and its oxidation product show several differences, of which the most significant is the appearance of a band at 1670 cm^{-1} in the spectrum of the reaction product. This band is thought to be produced by a carbonyl group formed by metavanadate oxidation of the olefinic carbon- to – carbon bond in the parent compound.

The disappearance of absorption by the product in the $2430\text{--}2620\text{ cm}^{-1}$ band area implies that the dimethylamino-propylidene group is removed during the oxidation process.

Based on UV, IR results it can be concluded that in the examined conditions chlorprothixene is oxidized to 2-chlorthioxanthone (scheme 1).

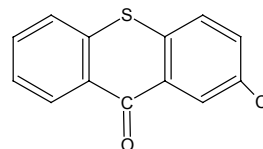


Fig. 1: Structural formulae of 2-chlorthioxanthone.

The homogeneity of produced oxidative product of chlorprothixene has been studied by thin-layer chromatography on silica gel GF₂₅₄. The TLC plates were developed with ethanol:toluene:water (20:20:1). The obtained results of separation of chlorprothixene and its oxidation product were good, the R_f values were found to be of 0.52 and 0.73, respectively.

The influence of ammonium metavanadate on the stable absorbance of the reaction solution was obtained with 1-5 fold excess of the oxidant over CPT used. The concentration of 3×10^{-4} mol/l of ammonium metavanadate was selected as optimal. Further, the effect of acidification by hydrochloric, orthophosphoric (V) and sulphuric (VI) acids and their concentrations were tested. Sulphuric (VI) acid significantly

increased the absorbance of the solution. In our further studies of 1 mol/l sulphuric (VI) acid was applied.

The influence of temperature and time of heating on the values of absorbance was also examined. For this purpose the reaction mixtures were thermostated from 25 up to 70°C for different times of heating ranging from 5, 10 to 20 min. Room temperature (25°C) was found the best. The absorbance measurements were done immediately after mixing the reagents. The optimal conditions of reaction were used for chlorprothixene hydrochloride quantification. Beer's law was obeyed between 2.5 and 25 µg/ml with a molar absorption coefficient of $\epsilon = 1.44 \cdot 10^4 \text{ l mol}^{-1} \text{ cm}^{-1}$. The equation of calibration curve is $y = 0.0411x - 0.003$ with the correlation coefficient of 0.9998. The results are shown in table 1. The characteristic detection limit is found to be 0.2 µg/ml. The reproducibility of the measurements expressed as RSD varied to 0.8% for the concentration of the drug at the studied level. The proposed method is sensitive and can be applied for determination of chlorprothixene in pharmaceutical preparations.

Table 1: Analytical features of the proposed methods

Parameter	NH ₄ VO ₃ method	CPT-Ti-SCN method
Beer's law range (µg/ml)	2.5- 25	4-35
Molar absorptivity ($\text{l mol}^{-1} \text{ cm}^{-1}$)	1.44×10^4	4.29×10^3
Regression equation*		
Intercept, a	0.003	0.004
Slope, b	0.0411	0.0136
Correlation coefficient	0.9998	0.9993
Reproducibility (%RSD)	0.8 ^a	0.7 ^b
Limit of quantification LQ (µg/ml)	0.54	0.80
Limit of detection LD (µg/ml)	0.2	0.3

* $Y = a + bx$, where x is the concentration in µg/ml

^a For six replicates samples (8 µg/ml)

^b for six replicates samples (10 µg/ml).

Chlorprothixene- titanium (IV) thiocyanate

The second study was concerned with the reaction of CPT with titanium (IV) thiocyanate complex during which precipitates insoluble in water were formed. The generated product is well extracted from the aqueous phase by organic solvents among which the mixture of butanol-chloroform (1:9) appeared to be the most efficient. Single extraction is sufficient to transfer the compound into organic layer. Extraction was carried at room temperature. The visible spectrum of the coloured extract showed a maximum at 390 nm and the wavelength was used for the analytical measurements. The compound formation and the efficiency of its extraction being strongly dependent on the acidic

medium. The influence of sulphuric (VI), orthophosphoric (V), hydrochloric and acetic acids on the absorbance of the extracts were studied. The best results were obtained with the concentration of sulphuric (VI) acid varied from 3.5 to 5 mol/l in the aqueous phase.

The influences of excess of Ti(IV) and NH₄SCN to chlorprothixene were also studied. It was found that 3-10 fold excess of Ti (IV) to CPT and the concentration of NH₄SCN in the range 0.6 to 1.0 mol/l are sufficient to obtain stable absorbance of extracts. A concentration of 0.8 mol/l NH₄SCN was selected for further measurements.

The composition of the ion associate was studied by Job's method of continuous variation and spectrophotometric titration. The obtained results exhibited that the molar ratio of CPT:Ti(IV) was equal 2:1 in the associate. Coloured extracts were stable for about 4 h.

It is known that titanium (IV) thiocyanate complex, at the used conditions, exists as an anion $[\text{Ti}(\text{CNS})_6]^{2-}$, while CPT forms in aqueous solution a large CPTH^+ cation. They react to produce an ion association complex. The proposed character of the studied compound was confirmed by UV-VIS, IR and ¹³CNMR spectroscopy.

In UV-VIS region the absorption spectrum of the examined compound exhibited maxima at 209 nm, 229 nm, 270 nm, 329 nm and 390 nm. The obtained spectrum was compared with the UV spectrum of chlorprothixene hydrochloride and UV-VIS spectrum of titanium (IV) thiocyanate complex. It was found that the characteristic for Ti(IV) thiocyanate complex band at 217 nm, 270 nm, 390 nm and the CPT hydrochloride bands at 195 nm, 229 nm, 268 nm and 324 nm preserved in the ion associate spectrum. These obtained results suggested that the examined compound is formed by electrostatic interaction between chlorprothixene cations and the anions of titanium (IV) thiocyanate complex.

In the IR spectrum of the investigated compound the absorption bands at 2430-2620 cm^{-1} attributed to ternary amines N-H group disappear. At 2065 cm^{-1} a strong band, characteristic of $\text{C}\equiv\text{N}$ group of Ti(IV) thiocyanate complex, appears in the IR spectrum of the examined compound. These observations seemed that the compound was formed by participation of nitrogen atom from the aliphatic chain of chlorprothixene. Some IR results are presented in fig. 2.

For the purpose of confirmation the ¹³C NMR spectrum was studied in DMSO-d₆. The results for the system CPT-Ti-SCN are given in table 2.

Analytical data

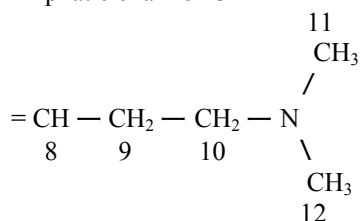
A new extractive spectrophotometric method for CPT determination has been developed. The analytical appraisals of the method are presented in the table 1. The elaborated

method allowed determining chlorprothixene in the range of 4-35 µg/ml. The extractive spectrophotometric method was characterized by the molar absorption coefficient of $4.29 \times 10^3 \text{ l mol}^{-1} \text{ cm}^{-1}$ and the correlation coefficient of 0.9993. The calibration curve is described by the equation $y = 0.0136x - 0.004$. Detection limit was found to be 0.3 µg/ml. RSD is less than 0.7% for the concentration of CPT in the studied range.

Table 2: Values of the chemical shift (^{13}C NMR) in aliphatic chain of CPT hydrochloride and its compound with thiocyanate complex of titanium (IV) in DMSO-d_6

Investigated compound	Chemical shift ^{13}C , ppm			
	C 9	C 11, 12	C 10	C 8
CPT	27,00	45,03	59,05	131,04
CPT-Ti-SCN	30,45	18,72 13,79	69,58	145,07

Aliphatic chain of CPT



Impurities

In order to establish the selectivity of the proposed extractive spectrophotometric method for the analysis of pharmaceutical formulations, the effect of the presence of several species which can occur in the real samples with chlorprothixene were investigated. The influence of foreign compounds that can commonly accompany CPT in pharmaceutical preparations was investigated by preparing solutions containing 10 µg/ml of the drug and increasing concentration of potential interferent. The tolerance concentration of each interferent was considered to be acceptable if the error was not longer than 2% in the analytical signal of CPT. The results obtained for different interfering compounds were as follows (concentration in µg/ml): sodium chloride, 500; magnesium nitrate, 500; sodium citrate, 200; starch, 250; ascorbic acid, 100; glucose, 900; lactose, 1000; sodium saccharin 1000. The proposed method was successfully applied to the determination of CPM hydrochloride in pharmaceutical preparations.

Solid phase extraction (SPE) of CPT

The proposed extractive spectrophotometric method was applied to the determination of CPT after its SPE isolation from tablets. The solid phase extraction (SPE) procedure allow the selective isolation of CPT from the complex matrix by adsorption onto an appropriate sorbent, the removal of interfering impurities by washing with a suitable solvent system and then the selective recovery of the

retained analyte with a modified solvent system of suitable elution strength. If necessary, this process can be modified by selection of sorbent and solvent system, so that interfering components are retained by the sorbent and the analyte is then recovered in the filtrate eluate. The SPE reported here is simple and rapid to carry out and do not require deproteinisation and evaporation steps. In order to select appropriate solvents to elute interferences from CH columns, the following solvents were checked: acetonitrile, water, acetone, chloromethane, acetate buffer and different mixtures of these solvents. The correct selection of the washing solvent was the most important for obtaining the good recoveries of studied drug by SPE procedure. The best results were achieved when 1.0 ml of acetonitrile for CPT was used.

In order to obtain a new SPE procedure for isolation of studied drug from tablets the spiked samples were used. The preparation procedures of the samples usually includes the deproteinisation step with organic solvents (e.g. methanol or ethanol alcohols) or inorganic salts. It was observed that the deproteinisation operation is the source of serious error, probably due to co-precipitation and/or adsorption of studied compounds on protein precipitate. The introduction of this step into elaborated SPE procedures resulted in very poor recoveries (about 27%), therefore, this operation was abandoned. The use of mixture of chloroform-acetone mixture (1:1, v/v) and organic solvents: acetonitrile, dichloro-methane to elution of interferences has removed effectively almost all excipients of tablets and for this reason, the sorbent materials were not plugged. It caused that the SPE columns may be used for a long time.

The simplification of the procedure by elimination of evaporation step of eluent was studied. Thus for this purpose different volumes of organic solvents (chloroform – n-butanol) used for the spectrophotometric determination of CPT were checked. The optimal volume of solvent found was dependent on the type of sorbent materials and kind of researched drug. For elution of CPT, 3 ml of chloroform – n-butanol mixture in proportion 5:1 v/v was used. In every instance, the selected elution solvents provided the cleanest samples which could be directly be analysed by the proposed extractive spectrophotometric method. The accuracy of the proposed methods was determined by analyzing commercial samples spiked with a known quantity of drug. In every instance, the recoveries of drug from CH bonded silica columns (Baker) were surprisingly high, uniform and stable in range 99-101%. Above mentioned values of recoveries were obtained for samples investigated directly and within 24 h. The results are shown in table 3. The precision of the method was good, as indicated by the RSD.

The connection of solid phase extraction procedures of sample preparations with spectrophotometric methods of

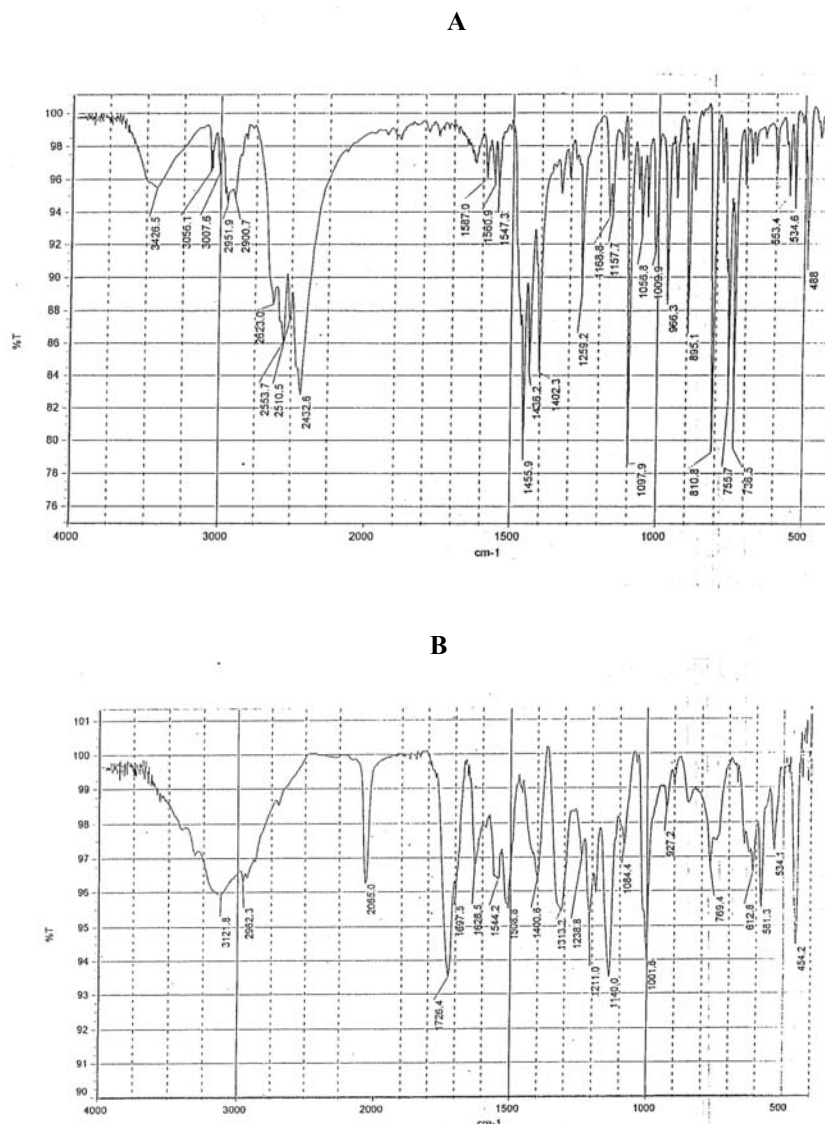


Fig. 2: IR spectra of CPT (A) and the compound formed in CPT – Ti - SCN system (B)

determination of drug caused high analyte recovery, reduced time of analysis and use of toxic organic solvents and neglected multi-step procedures (evaporation, deprotonisation) that are prone to losing analytes.

Application to a commercial product

The methods were applied to the analysis of pharmaceutical preparations of chlorprothixene hydrochloride presented in commercial injections and tablets (Chlorprothixen, Leciva, Czech Republic). The results were compared with those obtained by official methods (Polish Pharmacopoeia, 2002 and European Pharmacopoeia, 2002) and reported HPLC method (Karpińska and Starczewska, 2002) and showed no significant differences (table 4). The relative error of determination does not exceed $\pm 1\%$.

CONCLUSIONS

We have presented two procedures for the chlorprothixene determination based on its analytical properties. The methods are useful for the assay of the active compound in bulk and pharmaceutical preparations. The method based on the oxidation reaction seems more helpful in fast determination of CPT in bulk and in pharmaceutical samples. The extractive spectrophotometric method is better recommended for analysis of commercial product, as it allows separation of CPT from other auxiliary substances. The method can be also used for chlorprothixene determination after its isolation from tablets by solid phase extraction (SPE). Both methods are characterized by good precision, reproducibility of determination and high

Table 3: Results of the extractive spectrophotometric determination of CPT after SPE isolation from tablets (*Chlorprothixen*, Leciva)

Drug	Found by described Method (µg)	Recovery (%)	S	RSD (%)
CPT	16.87	100.30	0.12	0.71
	16.76	99.64		
	16.79	99.82		
	16.94	100.71		
	16.89	100.42		
	16.74	99.52		
CPT	20.80	100.58	0.09	0.43
	20.6	100.05		
	20.60	99.61		
	20.74	100.29		
	20.81	100.63		
	20.58	99.52		

Table 4: Results of determination of studied active substance in commercial formulations

Determination Substance	Pharmaceutical formulation	Labelled amount (mg)	Determination amount					
			by described method*		by PP ^a (mg) (n=6)	by HPLC method ^b (mg) (n=6)	Error**	
			A	B			A	B
			(mg)	(n=6)				
Chlorprothixene Hydrochloride	Tablets Chlorprothixen (Leciva, Czech Republic)	15	14.92	15.14	15.04	14.88	- 0.53	+ 0.93
Chlorprothixene Hydrochloride	Injection Chlorprothixen (Leciva, Czech Republic)	50	50.20	49.86	50.10	50.18	+ 0.40	- 0.28

*Described spectrophotometric (A) and extractive spectrophotometric (B) methods

**Error (%) vs. labeled amount, ^aPolish Pharmacopoeia (2002), ^bKarpińska *et al.* (2002).

sensitivity. The main advantages of these procedures are short time of analysis, low cost of reagents and apparatus used.

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