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Visible spectrophotometric methods for the determination of duloxitine hydrochloride in bulk and dosage forms

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ABSTRACT

Two simple and sensitive visible spectrophotometric methods (method A and method B) have been reported for the determination of Duloxetiine hydrochloride (DXT) in bulk and dosage forms. Method A involves oxidation of DXT with Brucine in presence of Sodium meta periodate (IO_4^-),λ max 530 nm. Method B involves charge-transfer complex formation of DXT with in situ oxidized form obtained from Haematoxylin with Chloramine-T (CAT).The absorption Maximum were obtained at λmax (Method-A,530nm and 550nm for Method-B) . These methods are simple sensitive and reproducible with a recovery percent of 98.79±1.29(Method-A)and 99.17±0.69(Meth od-B) respectively and can be applied for the determination of (DXT) Both in bulk and Dosage Forms.

Key Words: Brucine,Haematoxylin,Chloramine-T,charge transfer complex.

INRODUCTION

Duloxetine Hydrochloride(**Fig.1**) is a selective serotonin and norepinephrine reuptake inhibitor (SSNRI) for oral administration. Its chemical designation is (+)-(S)-N-methyl-γ-(1-naphthyloxy)-2-thiophenepropyl aminehydrochloride. Duloxetine hydrochloride (DXT) is an antidepressent and is Chemically (+)-(s)-(gamma)-(1-naphthyloxy)-2-thiophene propylamine hydrochloride.A very few physico-chemical methods appeared in the literature for the determination of DXT in pharmaceutical formulations (less). The methods so far reported include HPLC[1-5] and UV-visible spectrophotometry [6-7] and flurometry methods[8]·It is clear from the literature that no one has attempted the reagents used by the author to determine the selected drug by the author· This paper describes two simple and sensitive methods (A-B) using the reagents Brucine[9]-[$IO4^-$],Haematoxylin[10]·CAT respectively for the assay of DXT is bulk and pharmaceutical formulations. Each capsule contains enteric-coated pellets of 22.4, 33.7, or 67.3 mg of DXT equivalent to 20, 30, or 60 mg of, DXT respectively. These enteric-coated pellets are designed to prevent degradation of the drug in the acidic environment of the stomach. Inactive ingredients include FD&C Blue No. 2, gelatin, hypromellose, hydroxypropyl methylcellulose acetate succinate, Sodium Lauryl Sulfate, sucrose, sugar spheres, talc, titanium dioxide, and triethyl citrate. The 20 and 60 mg capsules also contains Iron oxide yellow.

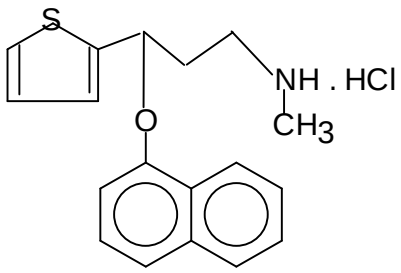


Fig.1.Chemical structure of DXT

MATERIALS AND METHODS

INSTRUMENT: A Systronics UV-Visible spectrophotometer 117 and A Systronics 106 visible spectrophotometer with 1 cm matched quartz cells were used for the absorbance measurements . Elico LI-120 digital pH meter was used for pH measurements.

Reagents :
All the chemicals used were of analytical grade and the solutions were prepared in triply distilled water.
Method A
1.Brucine Aqueous solution of (5.0x10-3M in 0.16 M sulphuric acid)
2.Sodium meta periodate ($9.35x10^{-3}$M)
3.Sulphuric acid (2.3M)
Method B
4.Haematoxylin ($6.62x10^{-3}$ M in Methanol)
5. CAT aqueous solution (1.412×10^{-2} M)
6.Buffer solution (pH 7, by mixing 390 ml of 0.067 M Potassium dihydrogen phosphate and 10 ml of 0.067 M disodium hydrogen phosphate)

A Standard Drug Solution: The stock solution (1 mg/ml) of duloxetine (DXT) was prepared by dissolving 100mg of it in 3 ml of 0.1 N HCl and made up to 100ml with distilled water.A portion of this stock solution was diluted stepwise with distilled water to obtain the working standard DXT solution of concentrations of 200 µg/ml for Methods A & B.

Sample solution: An accurately weighed portion of capsule content equivalent to 100 mg of drug was extracted with chloroform (3 x 15 ml) and filtered. The combined filtrate was evaporated to dryness and the residue was dissolved in 20 ml of 0.1N HCl, shaken well and diluted to 100ml with 0.1N HCl .Then ten ml of the above solution was further diluted to 100ml with 0.1N HCl. The above solutions were used as under working standard solutions for Methods A &B.

Assay Procedures:
Method A:
Aliquots of standard solution (0.5 – 2.5 ml, 200 µg/ml) were placed separately in series of 10 ml calibrated tubes. Then 3.0 ml of Brucine solution, 1.5 ml of $NaIO_4$ solution and 2.0 ml of 2.3 M H_2SO_4 were added successively. The total volume in each tube was made to 9.0 ml with distilled water and heated for 15 min in a boiling water bath. All the tubes were cooled rapidly to room temperature and made up to 10 ml with distilled water, mixed thoroughly and the absorbances were measured at 530nm(**Fig.4**) against a reagent blank. The amount of DXT in a sample solution was obtained from the Beer-Lambert's plot **(Fig.6)**.

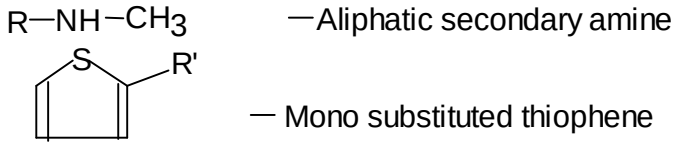
Method B:
To a series of 25 ml graduated tubes, 1.0 ml each of haematoxylin and Chloramine –T and 15 ml of buffer (pH 7.0) solutions were added successively. The mixture was set aside for 20 min.Then added aliquots of DXT with in Beer-Lambert's limits (0.5 - 2.5 ml, 200 µg/ml) and kept in a water bath at 70^0C for 20 min. The tubes were removed from the water bath, cooled to the room temp. The contents in tube were diluted to 25 ml with distilled water and the absorbance read at 550nm (**Fig.5**) with in the stability period.The amount of DXT was deduced from its standard calibration curve **(Fig.7)**.

Recovery studies: As an additional demonstration of accuracy, recovery experiments were carried out by adding known amounts of drug to the already analysed formulation. The results are presented in Table 2.

RESULTS AND DISCUSSION

The optical characteristics such as absorption maxima. Beer's law limits, molar absorptivity and sandell's sensitivity for these methods are given in Table 1.The percent relative standard deviation and percentage of error (0.05 level confidence limit) calculated from six measurements containing ¾ amount of upper Beer's law limit of DXT are also given in Table.1. Commercial formulations were successfully analysed by the proposed Methods.The values obtained by the proposed and reference method (UV) for pharmaceutical formulations were compared statistically by the t-and F- test were given in Table.2 and found not to differ significantly.

CHEMISTRY OF COLORED SPECIES: The structre and partial structures of DXT earmarking the analytically useful functional groups are presented here.



Method A :
The dimethoxy benzene nucleus of brucine is attacked by IO_4^- with the formation of o-quinone (Bruciquinone), which in turn undergoes nucleophillic attack on the most electron rich portion of the coupler (i.e. imino group in DXT) to give 1- mono substituted Bruciquinone derivative. The nature of colored species formed for DXT with brucine in presence of IO_4^- is described in (**Fig.2)**

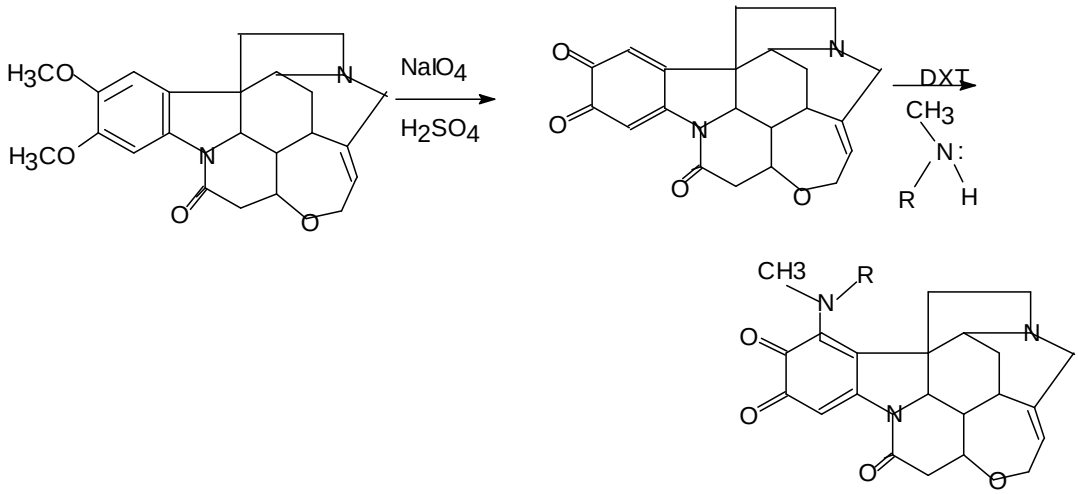


Fig.2.Colored complex of DXT-BCN-IO_4^-

Method B :
The method appears to be due to formation of charge transfer complex involving in situ formed haematin (oxidation product of hematoxylin with CAT , electron acceptor due to the presence of enolic form of o-quinone moiety) and DXT due to presence of hetero sulphur with lone pair of electrons as in the case of quinone and organo sulphur compound (eg. chloranil and pencillin G). The nature of colored species formed for DXT with brucine in presence of IO_4^- is described in **Fig.3**

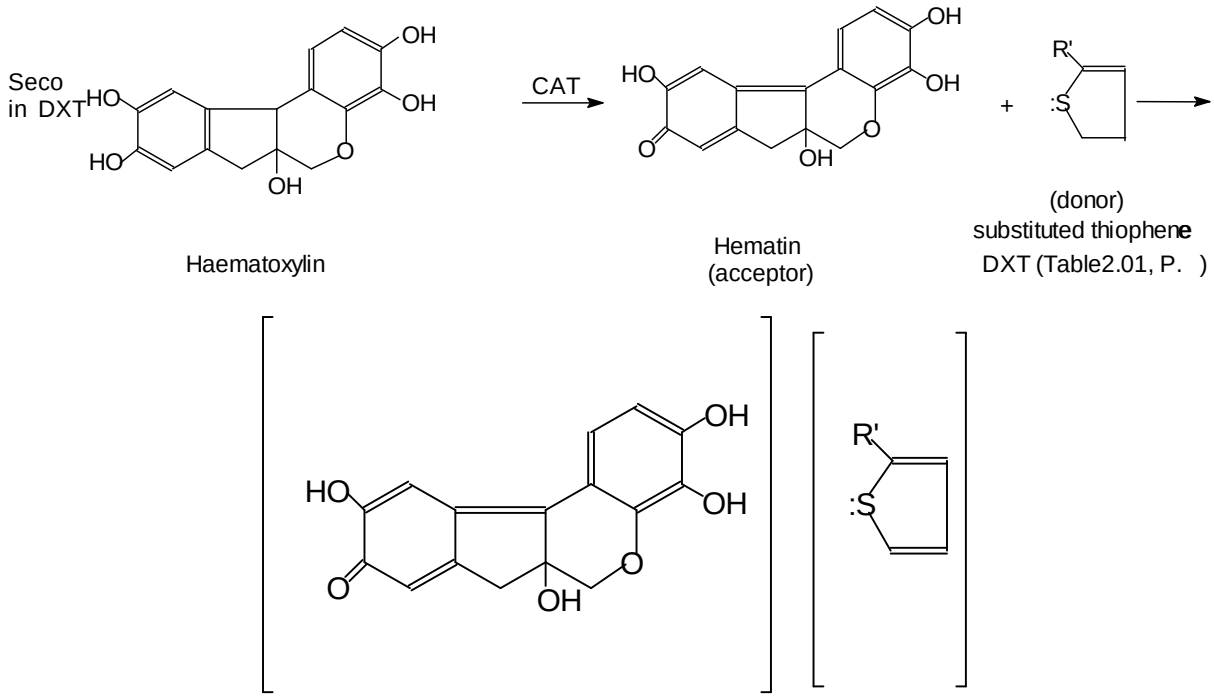


Fig.3.Colored complex of DXT-BCN-IO_4^-

Table.1. Optical characteristics, precision, accuracy of the methodsproposed in the determination of DXT

Parameter	Method A	Method B
λ_{max} (nm)	530	550
Beer's law limits (µg ml^{-1})	10 –50	4-20
Molar absorptivity (1 $mole^{-1}$ cm^{-1})	4.17x 10^3	1.08 x 10^4
Sandell's sensitivity (µg cm^{-2}/0.001 absorbance unit)	0.08	0.030
Correlation coefficient (r)	0.9998	0.9999
Relative standard deviation (%)*	1.115	1.075
% Range of error (Confidence limits)* 0.05 level(95%)	1.170	1.128

Recovery experiments indicated the absence of interference from the commonly encountered pharmaceutical excipients present in pharmaceutical formulations. The proposed methods are found to be simple, sentsitive and accurate and can be used for the routine quality control analysis of DXT in bulk and samples and pharmaceutical formulations.

Table .2. Determination of DXT in pharmaceutical formulations

Method	Pharmaceutical Formulations	Labeled Amount (mg)	Proposed Methods			Found by Reference method ± S.D.	% Recovery by proposed methods** ±S.D.
			Amount found* (mg) ± S.D.	F	t		
A	Capsules I	20	19.80 ± 0.16	1.88	0.40	19.84 ± 0.18	98.79±1.29
	Capsules II	30	29.57 ± 0.28	0.09	0.32	29.61 ± 0.40	98.65±0.93
	Capsules III	40	39.68 ± 0.37	2.22	1.83	39.84 ± 0.25	98.79±1.29
	Capsules IV	60	59.18 ± 0.87	1.89	1.84	60.03 ± 0.56	98.65±0.93
							98.59±0.96
B	Capsules I	20	19.80 ± 0.16	1.86	0.03	19.84 ± 0.18	99.17±0.69
	Capsules II	30	29.63 ± 0.22	2.27	0.09	29.61 ± 0.40	98.70±0.89
	Capsules III	40	39.44 ± 0.46	3.06	1.44	39.84 ± 0.25	98.99±1.12
	Capsules IV	60	59.43 ± 0.61	1.68	1.05	60.03 ± 0.56	98.94±1.23

** Average ±standard deviation of eight determinati ons, the t and F – values refer to comparison of the proposed method with reference method. Theoretical values at 95% confidence limits t = 2.365 and F = 4.88*

*** Average of five determinations.*

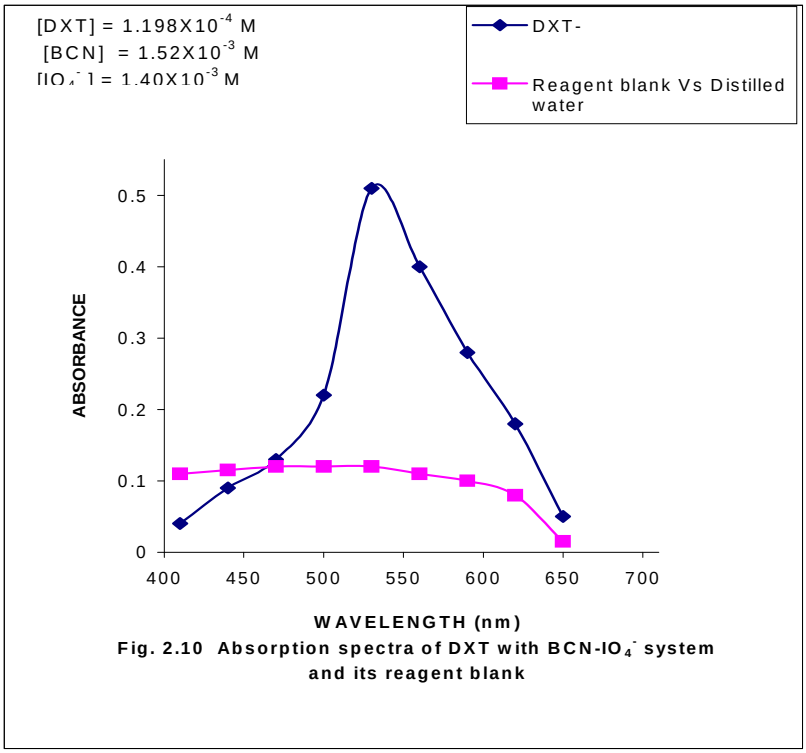


Fig. 2.10 Absorption spectra of DXT with BCN-IO_4^- system and its reagent blank

Fig.4. Absorption spectra of DXT-BCN

Fig.5. Absorption spectra of Haet-CAT

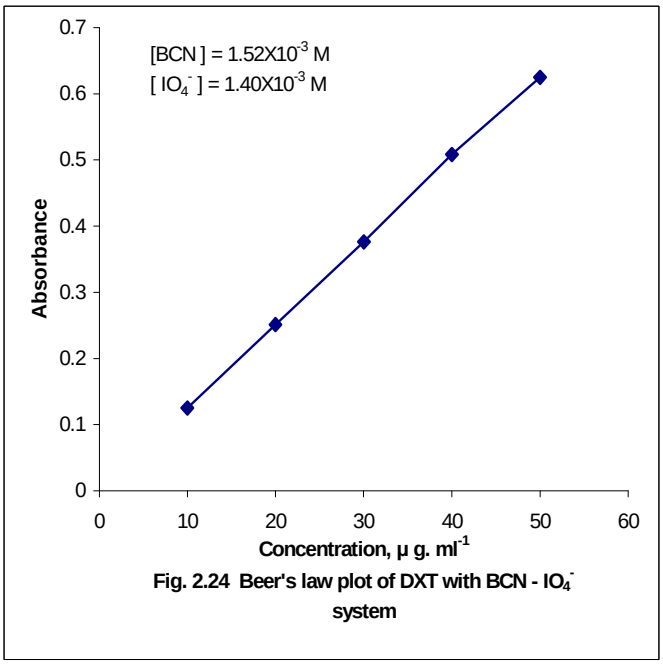


Fig.7. Beer"s plot of BCN-IO_4^-

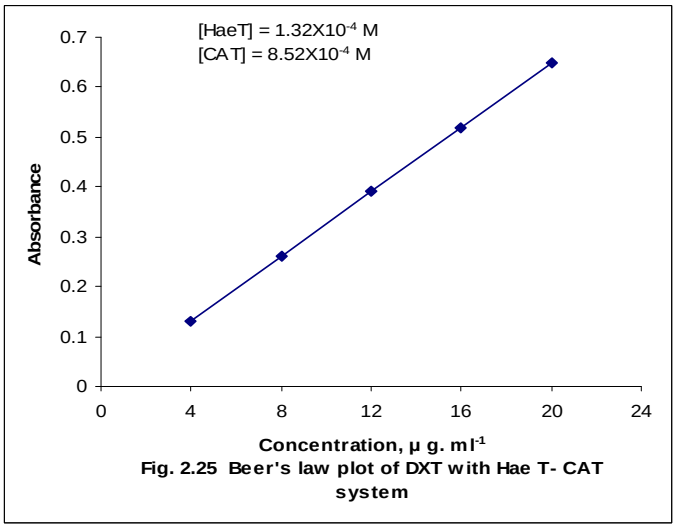


Fig.7. Beer"s plot of Haet-CAT

CONCLUSION

The proposed methods are simple, sensitive, accurate and economical for routine analysis of DXT in bulk and its pharmaceutical formulations. Based on molar absorptivity data and Beer's law range, it may be concluded that among the proposed methods, method B is more sensitive than method A

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