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Spectrophotometric Method for the Determination of Paracetamol and Levodopa in Pharmaceutical Preparation

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Abstract

An indirect method for the determination of paracetamol and levodopa in described. The method based on the extraction of iodine. Beer's law obeyed over the concentration range 0.1-0.6 $mg.ml^{-1}$ and 0.1-0.2 $mg.ml^{-1}$ at 520 nm, with apparent molar absorptivity of $0.88x10^5$ $Lcm^{-1}mol^{-1}$ and $0.85x10^5$ Lcm^{-1} mol^{-1} for paracetamol and levodopa, respectively. The precision and accuracy of the proposed method and the effect of various diverse ions have been studied and the analysis of paracetamol and levodopa in pharmaceutical preparations have been carried out. The results obtained were compared with those of the reference method.

Key words: Extraction spectrophotometry; determination; paracetamol and levodopa; pharmaceutical preparation

Introduction

Paracetamol has been widely used as an analgesic and antipyretic drug alone or in combination with other components, thus several methods for its determination have been used. The majority of these methods were based on the use of oxidizing agents such as potassium dichromate (Sultan, 1987), hexacyanoferrate (III) in alkaline medium and subsequent coupling with m-cresol (Qureshi *et al.*, 1992), cerium IV (Sultan *et al.*, 1986). Where as the same interest extend to levodopa determination with some other oxidizig agents, which include the use of p-aminophenol in the presence of KIO_4 (Hasan *et al.*, 1987), molybdatophosphoric acid (Issopoulos, 1989), phosphotungstic acid (Scott *et al.*, 1988), ammonium vanadate (Sane *et al.*, 1987), sodium tungstate (Rao *et al.*, 1986) and hydrogen peroxide (Cudina *et al.*, 1985). Moreover, the literature survey reported many other methods including HPLC (Gilpin *et al.*, 1982). Ultraviolet spectrophotometric official method for paracetamol (BP, 1973) and official BP method and USP method for the levodopa (BP, 1973-USPXXII).

In the present study the reaction between the drug which act as a reduction agent and potassium iodate, which then extracted with carbon tetrachloride. The absorbance measured at 520 nm in both cases. The aim of this study is to provide a simple, accurate and precise method in compare to other methods and could overcome the influences of various interferences which may alter the spectrophotometric determination.

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Experimental

Apparatus: Absorbance measurements were recorded with a Bausch and Lomb Spectronic-20 Spectrophotometer.
Reagents: 1 $mg.ml^{-1}$ paracetamol and levodopa solutions, 0.1 M potassium iodate and 1M HCl were prepared with double distilled water. The apparent purity of paracetamol was checked by nitrosation method (Qureshi *et al.*, 1991), and the purity of levodopa was also confirmed by 1, 10-phenanthroline method (Grime *et al.*, 1979).
Procedure: To a known volume of solution containing 0.1-0.6 mg of paracetamol and 0.1-2.0 mg of levodoap. 2.5 ml and 0.4 ml of 0.1 M potassium iodate was added respectively followed by 0.4 ml of 0.1 M hydrochloric acid. The content was transferred to a separating funnel after shaking with 5 ml of CCl_4 for a few minutes. The organic layer was separated and dried over anhydrous Na_2SO_4 and the absorbance was measured at 520 nm against a reagent blank.
Assay of formulations: Tablets to be analysed were powdered and dissolved in distilled water and filtered through a Whatman No.1 filter paper and the filtrate was adjusted to the final concentration of 1 $mg.ml^{-1}$. Syrups or drops were diluted to volume with water to obtain a concentration suitable for use in the general procedure.

Results and Discussion

Iodate is a powerful oxidizing agent and the most commonly quoted chemical assay for many types of drugs such as ascorbic acid (Belal *et al.*, 1979) and penicillin group of antibiotics (Issopoulos, 1990). This fact has been described by Hurka, that the organic compounds can be determined by oxidation with potassium iodate. Thus, iodate oxidizes paracetamol and levodopa in moderately acidic medium and if present in excess
it is reduced to iodine, which can be extracted by CCl_4. The reaction may be regarded as the composite result of reduction to iodine followed by the well known iodide/idodate reaction to yield iodine.

Paracetamol:

$$IO^-_3 + 3\ C_8H_9NO_6 \text{ ---------} \rightarrow I^- + 3\ C_8H_9NO_6 + 3H_2O$$
$$5I^- + IO^-_3 + 6H^+ \text{ ----------} \rightarrow 3I_2 + 3H_2O$$

Levodopa:

$$IO^-_3 + 3\ C_7H_{11}NO_4 \text{ ---------} \rightarrow I^- + 3\ C_9H_9NO_4 + 3H_2O$$
$$5I^- + IO^-_3 + 6H^+ \text{ ----------} \rightarrow 3I_2 + 3H_2O$$

Analytical appraisal: The absorption spectrum for the yellow extract in the organic layer (CCl_4) gave a maximum at 520 nm. Beer's law was valid at 20-120 $\mu g.ml^{-1}$ and 20-400 $\mu g.ml^{-1}$ for paracetamol and levodopa respectively, with apparent molar absorptivies as $8.8x10^4$ Lcm^{-1} mol^{-1} and $8.5x10^4$ Lcm^{-1} mol^{-1}.
The effects of variables were extended in order to optimize the conditions. It was found that 2.5 ml and 0.4 ml of 0.1 M potassium iodate and 0.4 ml of 0.1 M hydrochloric acid are suitable for the determination of paracetamol and levodopa, respectively.
Precision: The precision and accuracy of the methods were checked by running 15 replicate samples for paracetamol and levodopa using different concentrations, each containing 20, 40, 50 $\mu g.ml^{-1}$ paracetamol and 40, 90 and 120 $\mu g.ml^{-1}$ levodopa. The results are summarized in Tables 1 and 2 for paracetamol and levodopa, respectively.

Table 1. Test on precision and accuracy of the proposed method for the determination of paracetamol.

S. No.	Amount ($\mu g.ml^{-1}$)		SD*	RSD*	Error	% recovery***
	Taken	found				
1	20.00	20.00 20.50 20.00 20.50 19.50	0.42	2.10	0.5	100.5
2	40.00	40.00 39.50 40.00 40.00 40.00	0.55	1.30	0.25	100.25
3	50.00	50.00 50.50 50.00 50.00 51.00	0.45	0.89	0.6	100.6

*Mean standard deviation= 0.47 **Mean relative standard deviation=1.43 *** Mean % recovery= 100.45

Table 2. Test on precision and accuracy of the proposed method for the determination of levodopa.

S. No.	Amount ($\mu g.ml^{-1}$)		SD*	RSD*	Error	% recovery***
	Taken	found				
1	40.00	40.00 40.50 39.50 41.00 40.00	0.59	1.48	-0.25	99.75
2	90.00	90.00 90.50 90.50 90.00 89.50	0.42	0.47	0.10	100.10
3	120.00	120.00 120.50 121.00 120.00 119.00	0.55	0.46	0.083	100.08

*Mean standard deviation= 0.52 ** Mean relative deviation= 0.8 *** Mean % recovery= 99.98

The proposed method has been successfully applied to the determination of paracetamol and levodopa in their pure forms and in proprietary drugs, supplied by different manufactures and

containing other active ingredients as listed in Table 3 and 4. The results of comparison are presented in Table 5 and 6.

Table 3. Paracetamol amounts in proprietory drugs by the proposed method

Drug name and suplier.	Nominal composition (mg)	Amount taken (mg)	Amount found* (mg)	Error**
Crocin tab. (Duphar)	500 Paracetamol	500.0	501.70	0.34
Calpol tab. (Dulphar)	500 Paracetamol	500.0	499.00	-0.20
Crocin syrup (Dulphar)	500 Paracetamol	500.0	498.33	-0.33
Paramet tab. (Wallace)	500 Paracetamol 5 metachlopramide	500.0	500.0	0.00
Saridon (Roche)	250 Paracetamol 150 Propylphenazon 50 Cafiene	500.0	500.63	0.13
Corflam (Core)	500 Paracetamol 400 Ibuprofen	500.0	500.03	0.66
Spontral (America Remed)	300 Paracetamol 250 Chlorzpxazone 400 Ibuprofen	500.0	499.20	-0.16

*Mean of five determinations. ** Error calculated with reference to amount taken.

Table 4. Levodopa amounts in Pharmaceutical preparation by the proposed method

Drug name and supplier	Amount (mg)		SD*	RSD	Error**	Recovery %
	Taken	Found				
Levodopa (Wallace)	500.0	500.5	0.49	0.71	0.09	100.1

*Average of eight determinations. ** Error calculated with reference to nominal content.

Table 5. Composition of the results for the determination of paracetamol by the proposed and nitrosation methods

Drug name	% recovery		t**
	Proposed method	Nitrosation method	
Crocin tablet	100.30	100.00	0.41
Calpol Tablet	99.80	100.25	0.43
Crocin syrup	99.70	100.40	1.66
Paramet tablet	100.00	102.00	0.00
Saridon	100.10	100.88	0.18
Corflam	100.06	100.20	1.49
Spontral	99.83	99.90	1.72

*Average of five determinations.
** Theoretical value= 2.78 as 95% confidence level.

Table 6. Comparison of the results for the determination of levodopa by the proposed and 1,10 phenanthroline methods

Drug name	% recovery*		t**
	Proposed method	1,10 phenanthroline method	
Levopa (Wallace)	100.1	99.96	0.35

*Average of five determinations.
**Theoretical values= 2.365 at 95% probability levels.

Common excipients such as lactose, fructose, glucose, starch and sucrose did not interfere. Furthermore, the presence of different components in paracetamol dosage forms did not interfere with the determinations.
The calculated *t* test values indicated no significant difference between the two methods for paracetamol and levodopa, respectively.
In conclusion, the new method is simple, rapid, accurate and suitable for routine analysis.

References

Belal, S.F., El-Sayed, M.A.H., El-Walily, A. and Abdine, H. (1979). Spectrophotometric determination of acetaminophen [paracetamol] and salicylamide through nitrosation and subsequent chelation. *Analyst* 104: 919-927.

British pharmacopoeia (1973) p.340, HMSO, London.

British Pharmacopoeia (1973), p. 254, HMSO, London.

Cudina, I. and Joksimovic, L.R. (1985). Spectrophotometric determination of tyrosine and dopa in the presence of hydrogen peroxide. *J. Serb. Chem. Soc.* 50 : 457-461.

Gilpin, R.K. and Gaudet, M.H. (1982). Rapid high performance liquid-chromatographic determination of acetoaminophen [paracetamol] in dosage form using a totally aqueous mobile phase. *J. Chromatogr.* 248 (1): 160-164.

Grime, J.K. and Lockhart, K.R. (1979). Determination of selected penicillins by enzymic enthalpimetry. *Anal. Chem. Acta* 107: 319-326.

Hasan, B.A., Khalaf, K.D. and Dela, G.M. (1995). Flow analysis spectrophotometric determination of L-dopa in pharmaceutical formulations by reaction with p-aminophenol. *Talanta* 42 (4): 627-633.

Issopoulos, P.B. (1989) Spectrophotometric determination of microquantities of carbidopa and alpha-methyldopa using molybdophosphoric acid. *Pharm. Acta Helv.* 64 (3): 82-85.

Issopoulos, P.B. (1990). High sensitivity spectrophotometric determination of trace amounts of levodopa, carbidopa and methyldopa. *Freseniu's J. Anal. Chem.* 336(2): 124-128.

Qureshi, S.Z., Saeed, A. and Rahman, N. (1992). Spectrophotometric method for the determination of acetaminophen in drug formulations by oxidative coupling with m-cresol. *Chem. Anal.* 37 (2): 227-229.

Qureshi, S.Z., Saeed, A., Haque, S. and Khan, M.A. (1991). Spectrophotometric method for the determination of ascorbic acid in pharmaceutical preparation using urine and fruit juices with potassium iodate. *Talanta* 38 (6): 637-639.

Rao, G.R. and Avadhanulu, A.B. (1986). Spectrophotometric determination of 1,2-diphenolic drugs and formulations: sodium tungstate as reagent. *Indian Drugs* 23(12): 699-701.

Sane, R.T., Bhounsula, G. J. and Sawant, S.V. (1987). Colorimetric determination of levodopa and methyldopa from formulations. *Indian Drugs* 24(4): 207-209.

Scott, S. and Behrman, E.J. (1988) simple colorimetric assay for L-dopa in presence of tyrosine using tungstophosphoric acid reagent. *Anal. Lett.* 21(2): 183-191.

Sultan, M.S. (1987). Spectrophotometric determination of paracetamol in drug formulations by oxidation with potassium dichromate. *Talanta* 34(7): 605-608.

Sultan, M.S., Al-Zamil, I.Z., Al-Rahman, A.M.A., Al-Tamrah, S.A. and Asha, Y. (1986) Use of cerium (IV) sulphate in the spectrophotometric determination of paracetamol in pharmaceutical preparations. *Analyst* 111(8): 919-921.

USP XX II, p. 757.

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