How to Cite:
Al-Bayatie, Y. K., Muhamad, Y. H., Kareem, Z. M., & Khathi, M. T. (2022). Determination of dutasteride in pure and tablet by flow injection system. *International Journal of Health Sciences*, *6*(S3), 201–208. https://doi.org/10.53730/ijhs.v6nS3.5260

Determination of Dutasteride in Pure and Tablet by Flow Injection System

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***Abstract*---**A new Spectrophotometric flaw injection method has been established for the determination of Dutasteride (DS) in Pure and pharmaceutical tablets preparations. The method was based on the interaction of Dutasteride, as an n-electron donor with Chloranil as a π-acceptor, in acetonitrile to give reddish orange colored Chloranil radical anion with absorption maxima at 525 nm. The linearity of this method was in the range of (0.9948-8.932) ug.ml' with a correlation coefficient of 0.9969, a relative standard deviation (RSD) 0.422 %, with detection limit of (0.420) ug.ml".

***Keywords*---**determination, dutasteride (DS), flaw injection, injection system, linearity.

Introduction

Dutasteride is a synthetic 4-azasteroid compound, chemically it is (5a, 178)-N- (2, 5 bis (trifluoromethyl) phenyl}-3- oxo-4-azaandrost-1-ene-17-carboxamide is a 5-alpha -reductase inhibitor that inhibits the conversion of testosterone into dihydrotestosterone (DHT). Dutasteride belongs to a class of drugs called 5-alpha-reductase inhibitors, which block the action of the 5-alpha-reductase enzymes that convert testosterone into dihydrotestosterone (DHT) and is used treat benign prostatic hyperplasia (BPH). Dutasteride inhibits both isoforms of 5-alpha reductase (1).

International Journal of Health Sciences ISSN 2550-6978 E-ISSN 2550-696X © 2022.
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Manuscript submitted: 18 Nov 2021, Manuscript revised: 09 Feb 2022, Accepted for publication: 27 March 2022

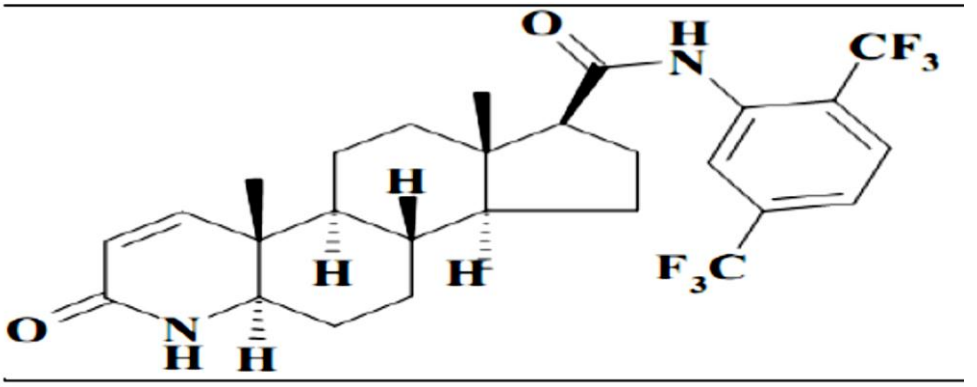

Figure1. Chemical structure of Dutasteride

Many methods have been developed for the determination of (DS) in various matrices such as pharmaceutical formulations, blood, urine and aqueous solutions. A survey of literature has not revealed any FI-Spectrophotometric method for the determination of the drug in bulk or pharmaceutical formulation. The other analytical methods that have been reported for its determination in bulk and pharmaceutical formulation as LC (2), HPTLC Method (3). TLC (4), LC-MS (5.6,7) and Spectrophotometric method (8) have also been reported for quantification of the drug According to our knowledge, no Fl-visible Spectrophotometric methods have been reported for the quantitation of the DSE in tablet dosage forms. Kumar et al. has reported Spectrophotometric method for the quantification of DSE in pharmaceutical formulations based on Charge-transfer complex results from a donor-acceptor mechanism of Lewis acid-base reaction between two or more different chemical constituents (8), The formation of charge transfer complex can be rapidly assessed for its validity as a simple quantitative analytical method for many drug substances which can act as electron donors. Chloranil (s acceptor) has been investigated spectrophotometrically and has been successfully utilized in the determination of a variety of electron-donating basic compounds (9,10,11). Describes Fl-Spectrophotometric developed above method for the determination of (D.S) in the pharmaceutical preparation samples.

Experimental

- **Apparatus** A UV-Visible double beam spectrophotometer (UV-1601 SHIMADZU Limited, Japan) supplied with a 100 µl flow cell was used. The response was recorded at recorder (Semins, Germany).
- **Reagents** 2.033 x 10-2 M Chloranil (CRL): Prepared by dissolving 500 mg of chloranil (Merck, Mumbai, India) in 100 mL of acetonitrile (Merck, Mumbai, India).
- **Standard solutions of Dutasteride**
- Pharmaceutical grade DSE was supplied by ministry of science and technology Iraq. A stock standard solution containing I mg/ ml. of DS was prepared in methanol. Working standard solution equivalent 200 ug/ ml.

- **Tablet dosage forms of Dutasteride**
- Tablet dosage forms of DS such as Duprost (0.5 mg/tablet, SDI, Iraq) and Dutas (0.5mg/tablet, Lad., India) were purchased from local pharmacy market.
- **Reference method**
  (Charge-transfer complexation with CRL) Aliquots of (0.1-2.0 mL) standard drug solution (200 ug/ml.) of DS were pipetted into a series of 10 ml. standard volumetric flasks and the volume in each flask was brought to 2 ml by adding acetonitrile. Then, 2 ml of 2.033 x 10-2 M Chloranil was added to each flask. The contents of each flask was mixed well and allowed to stand at room temperature (25 =/ 1loC) for 10 min. The volume was made up to the mark with acetonitrile. The absorbance of the reddish orange colored species was measured at 525 nm against the reagent blank prepared similarly omitting the drug (8).
- **General procedure for the determination of dutasteride drug**
  The flow manifold is show in Fig. 2 a two-channel manifold were used for the (F1) Spectrophotometric determination of drug. Four channel peristaltic pump [Ismatec, labortechnik-Analytic CH-8152 Glatbrugg-Zurich, Switzerland] minipuls (2) peristaltic pump was employed to transport the carrier stream. Local injector 88 valve was used for injection of the drug sample. Flexible vinyl tubing of 0.8 mm internal diameter was used for the peristaltic pump. The reaction coil (RC) was made from glass with an internal diameter of 0.5 mm. In Fig. 1, the channel 1 was used to transport Chloranil and channel 2 to introduce methanol. The drug sample was injected through the injection valve into the resulting stream of the mixture of 2.033 x 10-2 M Chloranil with methanol and were propelled by the peristaltic pump with an individual flow rate of (1.2, 1.5, 1.5) ml.min-1 and The absorbance of the reddish orange colored species was measured at γmax 525 nm against the reagent blank prepared similarly omitting the drug.

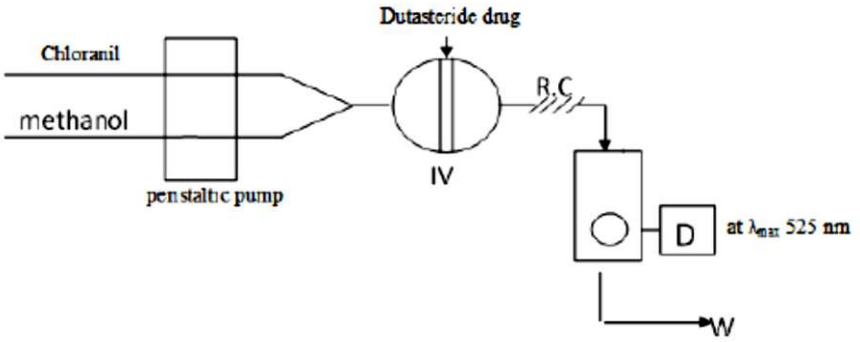

Figure 2. Manifold employed for FI-Spectrophotometric determination of Dutasteride drug with Chloranil

Where: IV: injection valve. R.C: reaction coil. SX: drugs sample (Dutasteride). P: peristaltic pump. D: detector, W: waste.

Result and Discussion

The Dutasteride drug reacted with Chloranil in the presence of acetonitrile to form an intense reddish orange product that can be measured at 525nm. Fig.3 showed the spectrum of the drug and product. It was found that the sensitivity of the color products depends on the reaction conditions and was optimized as follow:

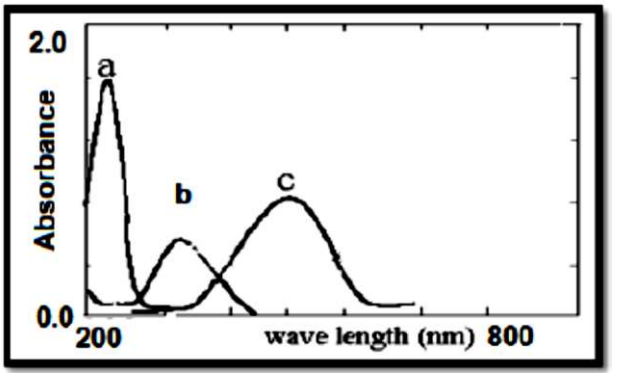

Figure 3. a. Spectrum of the drug only h. spectrum of the reagent e. spectrum of the product

Effect of the Chloranil concentration

The effect of various concentration of Chloranil was investigated. A concentration of (150µL) gave the highest absorbance and were used for further experiments. The results obtained are shown in Table1.

Table1
Effect of the Chloranil concentration

Volume of Chloranil (2.033 x 10^{-2} M)	10 µl	20 µl	50 µl	80 µl	100 µl	150 µl
Peak height (cm)	3.2	4.5	6.9	8.6	9.5	10.0

Effect of flow rate

Flow rate is an essential parameter in FIA. The results obtained showed that a flow rate of (2.5 ml.min^{-1}) gave the highest response for dutasteride as shown in Table.2 and was used in all subsequent experiments.

Table 2
Flow rate of a reagent and carrier

Time (min)	Flow rate (ml/min)	Time of response (sec)	Peak height (cm)
2.30	2	20	8.3
2.00	2.5	16	8.8
1.40	3.0	12	6.4
1.30	3.3	10	6.2
1.20	3.8	6	4.6
50	6.0	2	4.2

Effect of reaction coil length

The coil length is an essential parameter that affected on the sensitivity of the color reaction product and was investigated in the range of 50-200 cm. The results obtained showed that a coil length of (50 cm) gave the highest absorbance for dutasteride as shown in Table J and were used in all subsequent experiments.

Table 3
The effect of reaction coil length on the product

Length of coil (cm)	Absorbance (mV)		
50	452	436	496
100	426	428	426
150	436	432	440
200	440	436	432

Effect of injected sample volume

The effect of sample volume was investigated by injection of a volume of difference length of sample loop. The results obtained showed that an injection sample of 100 (ul) gave the best absorbance for dutasteride drug as shown in Table.4 and were used in the general recommended procedure.

Table 4
Volume of sample injected (ul)

Volume of Sample injected (µl)	1	5	10	20	50	100
Peak height (cm)	0.8	3.7	6.4	9.9	11.5	12.5

Calibration graph for the determination of dutasteride drug

Under the optimum condition a linear calibration graph. Fig. 10 was obtained over the concentration range of (10-70 pg.ml ') for dutasteride. The limit of detections (signal/noise 3) were (0.57 pg.ml "). The correlation coefficients was 0.9998. The relative standard deviation of the method was better than 1.47% (Fig. 4).

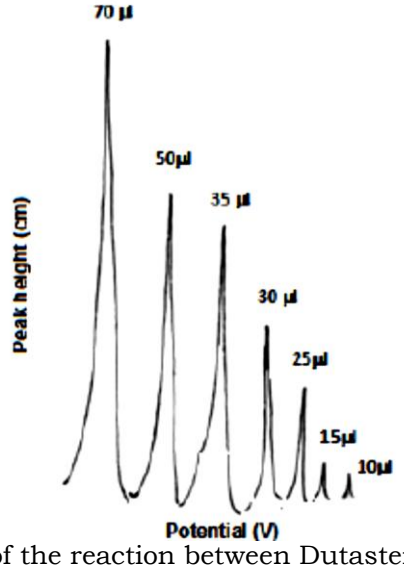

Figure 4. Stoichiometry of the reaction between Dutasteride and Chloranil

The stoichiometry of the reaction between dutasteride and Chloranil was investigated using the mole ratio method under the optimized conditions. The results obtained (Fig.5) show a 1:1 drug to reagent product was formed.

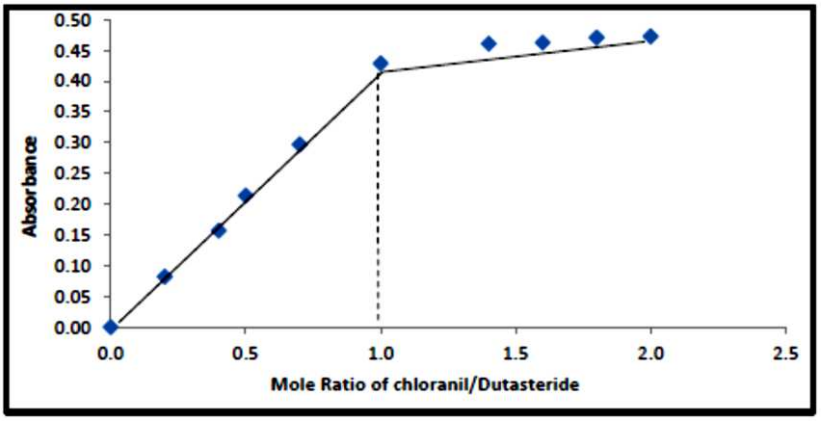

Figure 5. Mole ratio 1:1 Drug to reagent product

Analytical applications

The proposed method was applied for the determination of dutasteride drug in pharmaceutical preparations. Good accuracy and precision were obtained for the studied drugs. The results obtained were given in Table 5 which confirms the applicability of the method. Finally, the proposed method was compared successfully with the standard method (Table 5).

Table 5
The application of the proposed method for the determination of dutasteride drug in pharmaceutical preparations

Sample	Amount of drugs taken µg.ml^{-1}	RSD % *	Recovery %	
			Proposed method	Standard method*
Pure dutasteride	50	0.38	100.20	100.00
Duprost	50	0.86	99.8	
Dutas	100	0.16	100.10	

* average of three determination. * U.S.P standard method.

Conclusions

A simple accurate and sensitive FI- Spectrophotometric method for the determination dutasteride drug in pharmaceutical preparation has been developed. The method needs neither temperature nor pH control. The method was applied successfully to different pharmaceutical samples.

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