Available online at www.ijpsdronline.com
International Journal of Pharmaceutical Sciences and Drug Research 2011; 3(2): 127-129

Research Article ISSN 0975-248X

UV Spectrophotometric Method for the Estimation of Norethindrone in Immediate Release Tablet

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ABSTRACT

A modification of the U.S.P. dissolution method for the quantitative determination of Norethindrone in solid oral tablet is proposed. This modification consists of the use of varying concentration of sodium lauryl sulfate in dissolution media (0.1 N Hydrochloric acid) and use of UV spectroscopy instead of HPLC for analysis of samples. The rate and extent of dissolution of Norethindrone was much greater when high concentration of sodium lauryl sulfate 1.0% w/v was used. Different dissolution trials were conducted on a pre-optimized formulation. The proposed method has been applied successfully for the analysis of the drug in the tablet dosage form. The percentage assay of Norethindrone in tablet was 99.95%. This method has the advantage of quicker turnaround time of sample analysis and less cost involved. It can serve as a surrogate for HPLC method for the routine use in quality control laboratories of pharmaceutical industry.

Keywords: *In-vitro* dissolution, Norethindrone, sodium lauryl sulfate, UV spectrophotometry.

INTRODUCTION

Norethisterone or Norethindrone, 19-nor-17α-ethynyltestosterone, Fig. 1, is a progestogen used to treat premenstrual syndrome, painful periods, abnormal heavy bleeding, irregular periods, menopausal syndrome (in combination with estrogen), or to postpone a period. [1] The objective of this study is to present and propose a simple dissolution method for Norethindrone Tablet 5 mg. A dissolution analysis method of Norethindrone Tablet by States
Pharmacopeia in their 32nd edition. Before this development, pharmaceutical industry was performing the test using In-House developed method. In this study, one such In-House method for dissolution of Norethindrone Tablet is discussed which is a simple, sensitive and highly accurate UV spectrophotometric method. Direct UV/VIS spectrophotometric determination of absorbance has been the traditional analytical method for dissolution testing. A compound will exhibit absorption in the UV region if it contains one or more chromophores, such as aromatic nitro, azoxy, nitroso, carbonyl, or azo groups. The dynamic range of UV/VIS absorption is typically from 0.1 to 2 absorbance units for commercially available instruments. [3] Ultraviolet spectrophotometric methods are the instrumental methods of choice commonly used in industrial laboratories because of their simplicity, selectivity, and sensitivity. Norethindrone and ethinylestradiol tablets have been studied using UV spectroscopy. [4] Reported method as per USP 32 refers to a HPLC method and a modified method thereof has been investigated here with UV spectrophotometer. The aim of the present work was to develop simple and rapid UV spectrophotometric method for routine quality control use in the determination of Norethindrone in tablet dosage form.

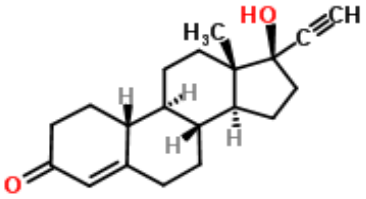

Fig. I: Structure of Norethindrone

MATERIALS AND METHODS

Pharmaceutical grade of Norethindrone was procured from Indo Phyto Chemicals Pvt. Ltd, India. All the chemicals were of analytical reagent grade, procured from Merck (Germany), unless otherwise specified. Purified Water was used to prepare all solutions. Freshly prepared solutions were always employed.

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FORMULATION OF NORETHINDRONE TABLET

Tablets of Norethindrone drug was prepared using a pre-optimized formula (Table 1) using Lactose monohydrate, Maize starch as diluent, Povidone as binder, Crospovidone as disintegrant, Talc as glidant and Magnesium stearate as lubricant to make a 100 mg tablet containing 5 mg Norethindrone (Table 2). Norethindrone, Lactose Monohydrate, Maize Starch and Crospovidone were passed through sieve #30. Dry mixing was done in rapid mixer granulator (Ganson, Mumbai) for 7 minutes keeping impeller at slow speed. Povidone binder solution was added over a time of 1 minute at impeller slow speed. Kneading (Wet mixing) was done at impeller fast and chopper slow speed for 3 minutes. Drying of granules was done using a table top fluidized bed dryer (Retsch GmbH, Germany) at 50±5ºC inlet temperature for 45 minutes. Dried granules were milled in Multimill (Ganson, Mumbai) at Medium Speed Knife Forward using 1.0 mm screen and blending was done in Octagonal blender (Ganson, Mumbai) for 15 minutes with addition of Talc. Thereafter added magnesium stearate into Octagonal blender (Ganson, Mumbai) and carried out blending for 5 minutes. Compression of blend was done on 12-station single rotary compression machine (Labpress model by CIP, Ahmedabad) using 6.00 mm diameter, round flat faced beveled edged punches. Compressed tablets of formulations F1 was subjected to evaluation viz. average weight, thickness, hardness, friability and disintegration time (Table 2). Dissolution studies of the tablets using different concentration of sodium lauryl sulfate is compiled in Table 3.

INSTRUMENTATION

Dissolution test was performed in Dissolution Test Apparatus by Electrolab, India, Model TDT-08L, as per USP. [5] The dissolution media was degassed using vacuum and maintained at 37±0.5°C by using a thermostatic bath. A double-beam UV-Vis spectrophotometer (Shimadzu, Japan) model UV-1800, with a fixed slit width (2 nm) using 1.0 cm quartz cells was used for all absorbance measurements.

DISSOLUTION STUDY

In vitro dissolution studies was carried out using a modified USP 32 method which includes USP Apparatus II at 37±0.5ºC and Paddle speed 75 rpm using 500 ml of hydrochloric acid with varying concentration of sodium lauryl sulfate. Sampling aliquots of 5.0 ml were withdrawn at 30 and 45 minutes, and replaced with an equal volume of the fresh medium to maintain a constant total volume. After the end of each test time, samples aliquots were filtered and diluted in dissolution medium and quantified using UV spectrophotometer.

RESULTS AND DISCUSSION

The absorption spectrum of Norethindrone was measured in the range 200-400 nm against the blank solution 0.1N HCl similarly prepared. The amount of Norethindrone dissolved was determined by UV absorbance at the wavelength of maximum absorbance at about 248 nm. Two dissolution methods, called Test 1 and Test 2, have been recommended by USP 32. The tolerance limit (also called Q point) given as not less than 80% of the labeled amount of $C_{20}H_{26}O_2$ is dissolved in 30 minutes (Test 1) and not less than 80% of the labeled amount of $C_{20}H_{26}O_2$ is dissolved in 45 minutes (Test 2). [5] Sampling of dissolution samples were done in compliance with USP 32.

Result of percentage recovery and placebo interference shows that the method was not affected by the presence of common excipients. As the concentration of sodium lauryl sulfate increased in the dissolution media, the percentage release of drug increased up to sodium lauryl sulfate level 1.0% (Table 3). This concentration of sodium lauryl sulfate is pharmaceutically acceptable for use in dissolution media. Dissolution method containing 0.1 N hydrochloric acid with 1.0% sodium lauryl sulfate, volume 500 ml, USP apparatus II, and speed 75 rpm and analysis using UV spectrophotometer was found to be a good quality control tool for the determination of Norethindrone.

Table 1: Batch formula

S. No.	Ingredients	Qty./Unit (mg)
1.	Norethindrone	5.0
2.	Lactose monohydrate	70.00
3.	Maize Starch	20.00
3.	Crospovidone	1.00
4.	Povidone	1.00
5.	Purified Water	q.s.
5.	Talc	2.00
7.	Magnesium Stearate	1.00
	Total weight	100.00

Table 2: Tablet Quality Parameters for Norethindrone Tablet 5 mg

S. No.	Parameters	Results
1.	Average Weight (mg)	100.0
2.	Thickness (mm)	3.25± 0.20
3.	Diameter (mm)	6.00 ± 0.03
4.	Hardness (N)	55 ± 5
5.	Friability (%w/w)	0.25
6.	Disintegration Time (minutes)	3-5
7.	Drug Content (%)	99.85±0.05

Table 3: Comparative of dissolution profile of formulation with varying concentration of Sodium Lauryl Sulfate

Time (Minutes)	Cumulative Percent Drug Release (%) in Media – 0.1 N Hydrochloric Acid with Sodium Lauryl Sulfate , Volume 500 ml, USP Apparatus II, Speed – 75 rpm						
	Concentration of Sodium Lauryl Sulfate (w/v)						
	0.09 %	0.15 %	0.30 %	0.40 %	0.50 %	0.75 %	1.00 %
30	29±2.8	32±3.2	51±1.7	55±2.5	74±2.3	83±3.6	90±2.8
45	40±2.4	41±4.5	59±3.2	62±2.9	82±3.8	89±2.3	93±1.6

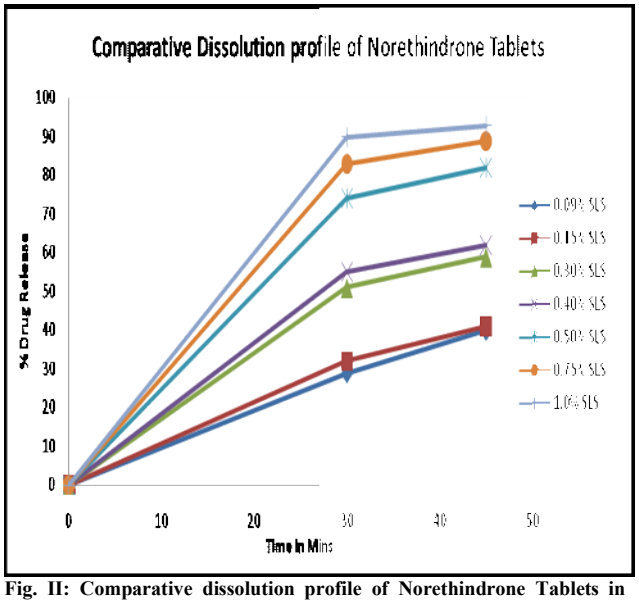

Fig. II: Comparative dissolution profile of Norethindrone Tablets in dissolution media containing different concentrations of Sodium Lauryl Sulphate (SLS)

Long before the dissolution method included in USP, the pharmaceutical industry was performing the test using In-House methods. We have developed one such In-House method for dissolution of Norethindrone Tablet. The assay of Norethindrone tablet was found to be 99.95%. The high percentage recovery indicates the high accuracy of the method. Thus the developed method can be easily used for the routine analysis of Norethindrone in tablet dosage form. The proposed UV method has advantage over official USP method [5] (by HPLC) for quicker turnaround time of sample analysis and less cost involved. This novel UV method for Norethindrone Tablets is likely to be well received by quality control professionals in pharmaceutical industry as a surrogate for HPLC method [5] for India and semi-regulated market where USP dissolution test is not mandatory. Though full fledged analytical method validation as per ICH guideline [2] need to be performed to demonstrate ruggedness and reproducibility of the proposed method.

ACKNOWLEDGMENT

The authors are thankful to M/s Indo Phyto Chemicals Pvt. Ltd., Nainital for providing generous gift sample of Norethindrone.

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