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STRESS DEGRADATION STUDY OF PACLITAXEL IN BULK BY UV SPECTROSCOPIC METHOD

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ABSTRACT

A simple, sensitive, precise, accurate, economic and rapid UV spectroscopic method has been developed for estimation of paclitaxel. Paclitaxel was a subjected to different stress condition as per ICH guideline Q1A (R2). A stability- indicating UV Spectroscopic method has been developed for analysis of the drug in the presence of the degradation products. Detection carry out at wavelength 223 nm. Degradation of paclitaxel was studied in acid, alkaline, hydrogen peroxide, photolytic and thermal conditions. The amount of degraded drug was calculated by taking absorbance at 223 nm. The drug was found to be more liable to decompositions in acidic, oxidative medium than in alkaline conditions.

KEYWORDS: Paclitaxel, UV- Spectroscopy, API, International Conference on Harmonization.

INTRODUCTION[3]

Paclitaxel is a mitotic inhibitor used to treat different types of cancer. This includes ovarian cancer, breast cancer, lung cancer, Kaposi sarcoma, cervical cancer and pancreatic cancer. Paclitaxel is also used for the prevention of restenosis. Paclitaxel is approved in the UK for ovarian, breast and lung, bladder, prostate, melanoma, esophageal, and other types of solid tumor cancers as well as Kaposi's sarcoma. It is use in the United States for the treatment of breast, pancreatic, and non-small cell lung cancers was approved by the FDA. In India the drug is sold under various brands. It is given by injection into a vein. A newer formulation, in which Paclitaxel is bound to albumin, is sold under the trademark Abraxane. To analyze the Paclitaxel, various analytical methods have been reported. Analytical methods for Paclitaxel includes, Stability indicating HPLC method, Assay method, Bioanalytical method ,bio-analytical with other drug, UV-Spectrophotometer , UV- derivative Spectrophotomete. The structure of Paclitaxel shown.
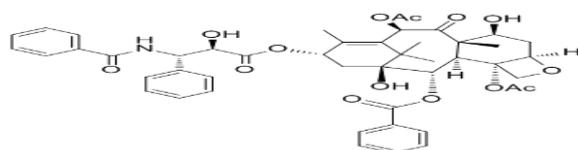
Fig. Chemical structure of paclitaxel.

MATERIAL AND METHODS
Materials & Reagents

- Pharmaceutical grade paclitaxel standard was obtained as from Samyang biopharmaceutical corporation.

- The solution of 0.1 N Naoh, 0.1 N HCL, 5% hydrogen peroxide was prepared in double distilled water as per IP 1996 procedure.

- Methanol and other chemicals used which were of analytical grade and were procured from local market.

Instruments

- Shimadzu UV-1800, double beam spectrophotometer with matching pair of 1cm quartz cuvettes with a fixed slit width 2 nm was used for all spectral measurements.

- Analytical balance (Acculab ALC-2014, Huntigdon Valley, PA)

Preparation of standard stock solution

A 10 mg of paclitaxel standard was weighed and transferred to a 100 ml volumetric flask. 50 mL of methanol was transferred to this volumetric flask. The flask was shaken and volume was made up to the mark with same solvent to give a solution containing 100μg/mL paclitaxel.

Preparation of working standard stock solution

In this method, 10µg/ml working standard solution was prepared by appropriate dilution of standard stock solution in methanol and methanol was used as blank solution.

Detection of absorption maxima (λmax)

The working standard solution was scanned in the spectrum mode from 400nm to200 nm wavelength ranges and the UV spectra of bulk were obtained. From this study sharp peak obtained at 225 nm.
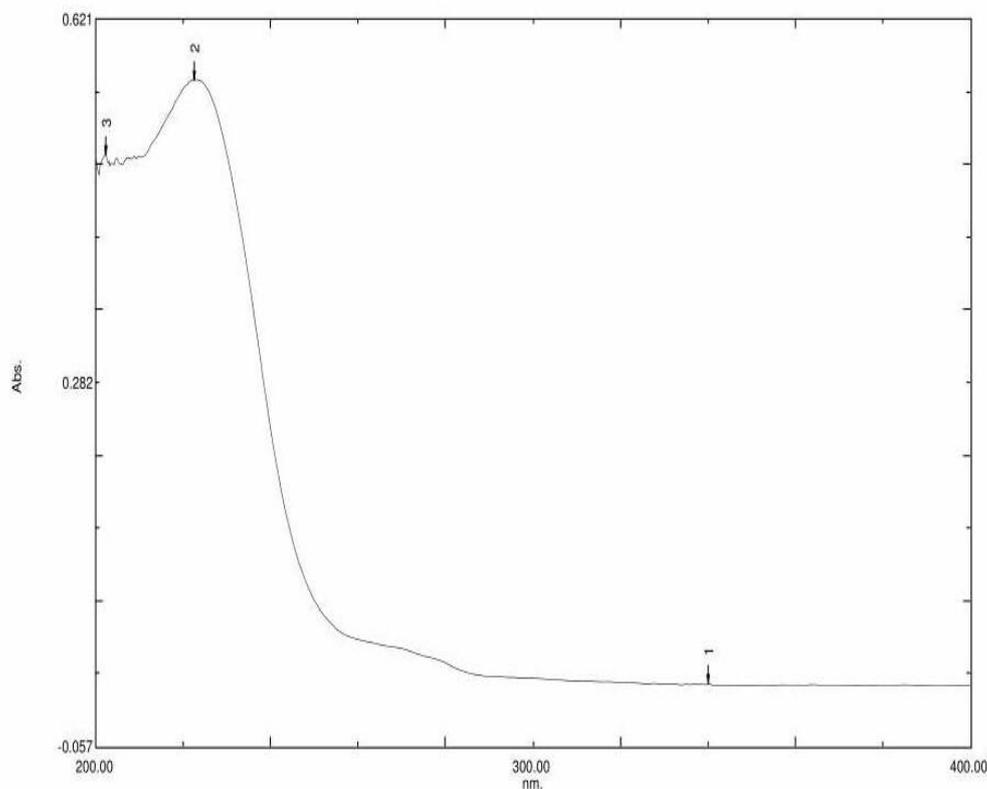

Fig.1 UV spectrum of Standard paclitaxel.

Forced degradation studies

The forced degradation studies were carried out on bulk drug substance in order to prove the stability-indicating property and selectivity of the developed method. The API was subjected to hydrolysis under different pH, oxidative, thermal and photolytic conditions. Optimization of conditions was done by changing strength of reagent and duration of exposure to achieve degradation in 10 to 30% range as per ICH Q1A (R2) guideline. For each study, working standard solution of paclitaxel was subjected to stress condition except thermal & photolytic study where in solid form of API is exposed to stress.

Fig 2: Degradation in acidic condition.

Acidic Degradation

1 mg of drug sample was transferred to 10 mL volumetric flask. To this sufficient quantity of methanol (2 mL) was added to dissolve the drug. To this 2 mL of 0.1 N HCL was added and was kept at room temperature, and further diluted with methanol to get concentration of 10 µg/mL. solution and were scanned over a range of 400 to 200 nm by placing respective solvents as blank. Note down the absorbance at absorption maxima.(fig 2)
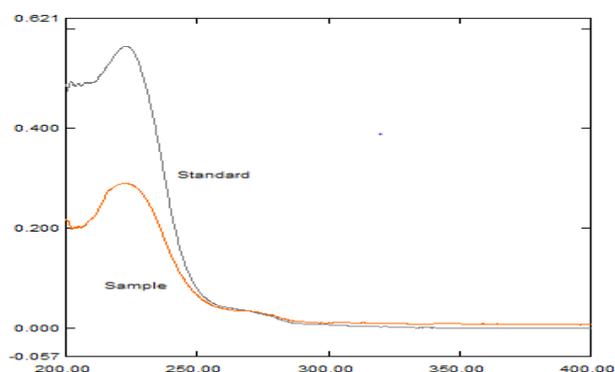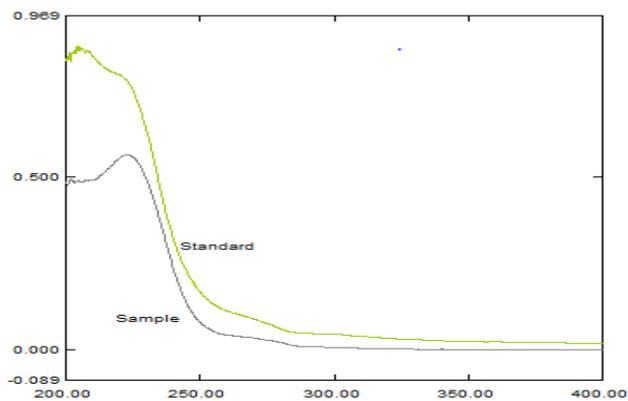
Alkali Degradation

1 mg of drug sample was transferred to 10 mL volumetric flask. To this sufficient quantity of methanol (2mL) was added to dissolve the drug. To this 2 mL of 0.1 N NAOH was added and kept at room temperature, and further diluted with water to get concentration of 10 µg/mL. solution and were scanned over a range of 400 to 200 nm by placing respective solvents as blank. Note down the absorbance at absorption maxima. (fig:3)

Fig 3: Degradation in alkaline condition.

Oxidative Degradation
1.mg of drug sample was transferred to 10 mL volumetric flask. To this sufficient quantity of methanol (2 mL) was added to dissolve the drug. To this 2 mL of 3 % H2O2 was added and was kept at room temperature for 1hr, and further diluted with water to get a concentration of 10 mL. solution and were scanned over a range of 400 to 200 nm by placing respective solvents as blank. Note down the absorbance absorption maxima..(fig:4)
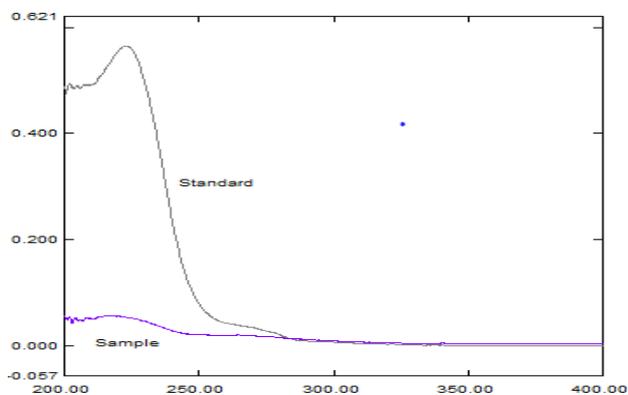

Fig 4: Degradation in oxidative condition.

Photolytic Degradation
1 mg of drug sample was placed in closed petri dish and was exposed to sunlight for 2 hrs.and
further the solution was dissolved in methanol to get a concentration of 10 μg/mL. solution and were scanned

over a range of 400 to 200 nm by placing respective solvents as blank. Note down the absorbance at absorption maxima.(fig 5)
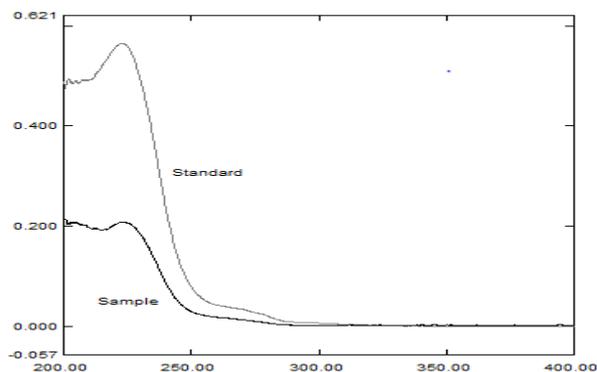
Fig 5: Degradation in photolytic condition.

Thermal degradation
The bulk sample was exposed to dry heat 40^0C. inoven at for 1 hrs. by placing 1 mg of paclitaxel in closed petri dish. All the stress conditions samples were appropriately diluted to get a final concentration of 10 μg/mL solution and were scanned over a range of 400 to 200 nm by placing respective solvents as blank. Note down the absorbance absorption maxima.(fig 6)
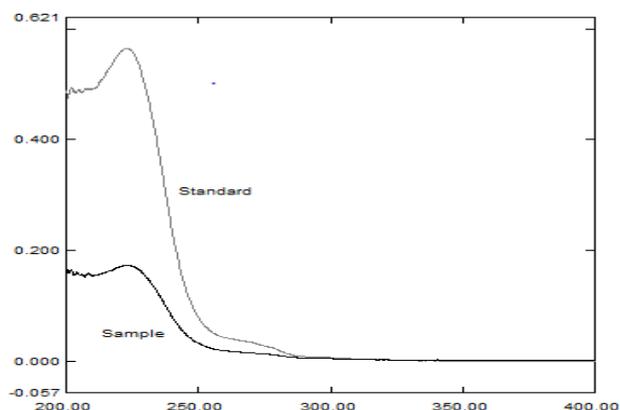
Fig 6: Degradation in Thermal Condition.

RESULT

Condition	Concentration Standard (μg/ml)	Absorbance	Absorbance after treatment (μg/ml)	% degradation
Acid hydrolysis	10	0.598	0.289	51.68
Alkaline hydrolysis	10	0.598	0.565	5.52
Oxidation	10	0.598	0.052	91.31
Photolytic	10	0.598	0.206	65.56
Thermal	10	0.598	0.173	71.08

CONCLUSION
From the above study it concluded that the stability indicating UV spectrophotometry method describe in this paper is simple and inexpensive for paclitaxel. This method can be use for routine analysis of paclitaxel.

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