DISSOLUTION METHOD

FOR

DURACOR TABLETS

METHOD APPROVALS

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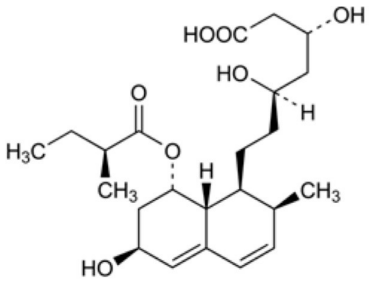
INTRODUCTION

Dissolution testing is routinely used by pharmaceutical companies in developing drug formulations (combinations of ingredients in tablets/capsules), identifying critical manufacturing variables, monitoring

batch-to-batch variations and stability, and to predict the performance of the drug in the body. The dissolution profile of Duracor will be determined using a specialized instrument called USP Dissolution Apparatus I. It consists of a basket rotating at 30 rpm in 500 mL of dissolution media (which is supposed to behave like stomach fluid) at a constant temperature bath of 37 ˚C (which is the temperature of the human body). Samples will be withdrawn at 10, 20, and 30 minutes and diluted prior to analysis by UV spectroscopy. This method is designed to verify that Duracor Tablets will meet the manufacturers requirements for dissolution rate.

The samples will be analyzed using a UV spectrophotometer based on the following principles. The active ingredient in Duracor is propactaline, which is an organic molecule that can absorb UV light.



Note that this molecule has a system of alternating double bonds that is called aromatic system. These types of bonds absorb UV light strongly. The wavelength range that the molecules absorb is called its UV absorption spectrum. You will measure the absorption spectrum of this molecule with an instrument called a UV spectrophotometer. This instrument measures the amount of UV light absorbed by a solution of the molecules over individual wavelengths from 400 nm to 200 nm. The amount of light absorbed by the molecule at a specific wavelength is called the Absorbance, A. The instrument records the absorbance at each wavelength. In addition, the absorbance is also directly related to the concentration (the number of molecules in a given volume) and the path length that light must pass through. Thus, the higher the concentration of molecules, the higher is the absorbance. We will take advantage of this property to measure the amount of drug dissolved at the different sampling time points.

TEST METHOD

Dissolution method in Norvin Pharma monograph “Duracor” current version.

Dissolution Medium:

0.05 M acetate buffer, prepared by mixing 2.99 g of sodium acetate trihydrate and 1.66 mL of glacial acetic acid with water to obtain 1000 mL of solution having a pH of 4.50.

Quantity of Dissolution Medium in Dissolution Vessel:

500 mL

Apparatus:

USP Apparatus I (rotating basket) – 30 rpm

Number of Tablets to be Tested:

3 tablets

Requirement:

For each of the 3 tablets tested:
Not less than 25% of the labeled amount released after 10 minutes
Not less than 50% of the labeled amount released after 20 minutes
Not less than 80% of the labeled amount released after 30 minutes

Sampling Times and Amount:

At 10, 20, and 30 minutes, withdraw 2 mL

Dilution of Samples:

1:5 dilution. Place 2 mL of sample into graduated vial, dilute to 10 mL with pH 4.5 acetate buffer, and mix.

Preparation of a Standard:

1. Place 1 tablet of Duracor NDA Reference Batch into a 500 mL volumetric flask and add 300 mL of pH 4.5 acetate buffer and place on a wrist action shaker for 20 min.
2. Dilute to volume with pH 4.5 acetate buffer and mix well.
3. Filter a 10 mL portion through a 0.45 micron filter.
4. Place 2 mL of this solution into graduated vial, dilute to 10 mL with pH 4.5 acetate buffer, and mix well.

Experimental Procedure:

5. Place 500 mL of 0.05 M pH 4.5 acetate buffer into a dissolution vessel and equilibrate to 37 ˚C
6. Place 1 tablet into each basket and fasten the basket onto the end of the shaft.
7. Start the baskets rotating at 30 rpm.
8. Lower the first basket into the dissolution medium and start the stopwatch. Lower baskets 2 then 3 at 2-minute intervals.
9. Withdraw a 2 mL sample from each dissolution vessel at 10, 20, and 30 minutes using a sampling syringe, cannula, and 10 micron filter. Remove the filter/cannula assembly and transfer the 2 mL sample into a graduated vial.
10. Dilute each sample with 0.05 M pH 4.5 acetate buffer to 10 mL.

PROCEDURE FOR UV ANALYSIS

1. Clean the quartz cells by rinsing them with pH 4.5 acetate buffer
2. Fill both cells with pH 4.5 acetate buffer and dry the outsides with a Kimwipe
3. Place the cells in the reference and sample cell holders within the spectrometer with the clear sides of each cell facing the open slots of the cell holder
4. Click the grey start button on the computer monitor
5. When the dialog box comes up for the blank, click OK. A background correction is carried out from the maximum to the minimum wavelength range (400 nm – 200 nm).
6. Wait for the next dialog box to come up

7. Take out the sample cell (front cell) and place its contents into the waste beaker
8. Fill the sample cell until approximately ¾ full with the first 10 minute dissolution sample and wipe the outside of the cell with a Kimwipe. Place the sample cell back into the spectrometer and click OK to record the 10 minute sample spectrum
9. Repeat this process for the 20 minute and 30 minute dissolution samples and the standard solution (theoretical 100% release).

EVALUATION OF RESULTS

Compare the results of the dissolution profile against the specification requirements.