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Preparation and Characterization of Atenolol Base from Hydrochloric Salt

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Abstract: -Atenolol is a beta-blocker. Beta-blockers affect the heart and circulation (blood flow through arteries and veins).Atenolol is a nonselective beta-adrenergic receptor blocker (beta-blocker) that is widely used for the therapy of hypertension, cardiac arrhythmias, angina pectoris and hyperthyroidism. Atenolol has yet to be convincingly associated with clinically apparent liver injury and is often used in patients with liver disease and cirrhosis. The present study of preparation of Atenolol base from hydrochloric salt, which results white amorphous powder of Atenolol base and characterization of different parameters is done for its physiochemical properties.

Keywords: Atenolol, Solubility, Spectroscopic analysis, DSC study.

I. INTRODUCTION

Atenolol is used to treat tremors, angina (chest pain), hypertension (high blood pressure), heart rhythm disorders, and other heart or circulatory conditions. It is also used to treat or prevent heart attack, and to reduce the severity and frequency of migraine headaches.

Atenolol is almost completely absorbed from the GI tract; however, plasma concentrations attained are quite variable among individuals. There is no difference in the rate of absorption of the 2 isomers of Atenolol. Atenolol appears in the plasma within 45 min, and peak plasma concentrations are reached about 90-120 min after oral administration of the conventional tablets.

Atenolol Hydrochloride is the hydrochloride form of Atenolol, a synthetic beta-adrenergic receptor blocker with antianginal, antiarrhythmic, and antihypertensive properties. Atenolol competitively antagonizes beta-adrenergic receptors, thereby inhibiting beta-adrenergic reactions, such as vasodilation, and negative chronotropic and inotropic effects.

Atenolol hydrochloride is slowly absorbed following administration of the drug as extended release capsules, and peak blood concentrations are reached about 8hr after administration.

II. EXPERIMENTAL WORK

Preparation of Atenolol free base from official salt form:-

Firstly we prepared Atenolol base from hydrochloric salt. In 25 ml of distilled water, 1 gm of Atenolol hydrochloride was dissolved. Addition of Strong ammonia solution and pH was adjusted up to 9.5, and then Atenolol free base was precipitated out. Extraction and purification of base using solvent ether. Four times, the Extraction process was carried out using 25 ml ether. Ethereal phase was collected and evaporated at 60^{o}C.White amorphous powder of Atenolol base was obtained.

A. Characterization Parameters:-

The physiochemical properties of Atenolol free base were determined using following Parameters

- **Determination of Melting point:-**

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Determination of melting point of drug was done by taking small amount of drug in a capillary tube closed at one end and placed in a melting point apparatus and the temperature at which drug melts was recorded. This was performed in triplicates and average value was noted.

- **Determination of partition co-efficient:-**

Using n-octanol as oily phase and phosphate buffer, pH 7.4, as aqueous phase, the partition co-efficient study was performed. The two phases were mixed in an equal quantity and were saturated with each other on a mechanical water bath shaker NSW-133 at 34ºC for 18 hr. The saturated phases were separated by centrifugation at 2000 rpm on a REMI R-23 centrifuge. Standard plots of drug were prepared for both, the phosphate buffer and octanol. Equal volumes (12.5ml each) of the two phases were taken in conical flasks and, to each; 100mg of weighed amount of drug was added. The flasks were shaken at 34ºC for 6hr to achieve a complete partitioning at 100rpm. The two phases were separated by centrifugation at 1000 rpm for 5min and they were then analyzed for respective drug contents by UV/VIS spectroscopy method. The partition co- efficient of drug K o/w was calculated using the following formula:
K o/w = (Concentration in octanol/ Concentration in phosphate buffer pH 7.4)

- **Solubility studies:-**

In phosphate buffer solution, pH 7.4, the solubility study of Atenolol base was performed in distilled water, methanol, chloroform, ether, alcohol (95%), acetone, toluene, glycerol, liquid paraffin, triethanol amine and silicone oil separately by adding excess amounts of drug in each case and keeping the excess drug containing flasks on a water bath shaker NSW-133 for 18hr at 34ºC.

- **UV /VIS Spectroscopic Analysis:-**

UV spectrum of Atenolol base was recorded on UV/VIS Spectrophotometer by scanning 5 µg/ml solution of Atenolol base in 0.01N hydrochloric acid and scanned between 200-400nm using UV/VIS Spectrophotometer.

- **Infrared (IR) Spectroscopic Analysis:-**

Using potassium bromide (KBr) pellet method, Fourier Infrared (FTIR) spectrums of moisture free samples of Atenolol base was recorded on IR spectrophotometer. The scanning range was 4000 – 400 $cm^{-1}$and the resolution was 1 cm^{-1}.

- **Differential Scanning Calorimetry (DSC) Analysis:-**

DSC scans of the powered samples were recorded using DSC- Shimadzu 60 with TDA trend line software. Drug was weighed (7-10 mg) and heated at a scanning rate of 10ºC/min under dry nitrogen flow (100 ml/min) between 50-350ºC. Aluminium pans and lids were used for drug sample. Pure water and indium were used to calibrate the DSC temperature scale and enthalpy response.

III. RESULTS

Atenolol base prepared form hydrochloric salt was white amorphous powder, which showed following characteristics:

- **Melting point:-**

Melting point of Atenolol base was determined by capillary tube method and it was found to be 158º C±1.502 (average of three readings). This value is same as that of the literature citation.

- **Partition co-efficient:-**

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Octanol and in vitro study fluid (here phosphate buffer, pH 7.4) are considered to be the standard system to determine drug partition coefficient between skin and in vitro study fluid. The logarithmic value of partition coefficient (log P) value was experimentally found to be 2.186. The results obtained also indicate that the drug possess sufficient lipophilicity, which fulfills the requirements of formulating it into a transdermal patch. Partition coefficient should be in the range of 1 to 4.

- **Solubility study:-**

Solubility of Atenolol base was evaluated in different solvent.

Table: Solubility of Atenolol base in different solvents

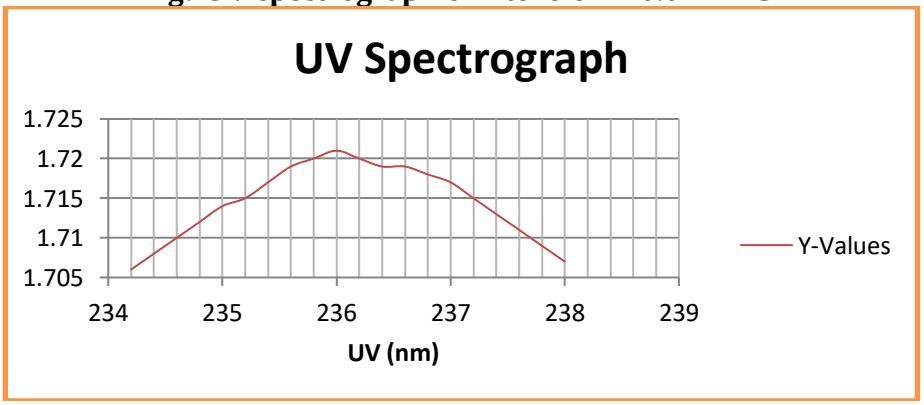
Solvent	Solubility
Phosphate buffer (pH 7.4)	Insoluble
Methanol	Freely soluble
Chloroform	Freely soluble
Alcohol (95%)	Freely soluble
Acetone	Freely soluble
Silicone oil	Insoluble
0.01N Hydrochloric acid	Soluble
Distilled water	Insoluble
Liquid paraffin	Soluble
Triethanolamine	Soluble
Ether	Freely soluble
Toluene	Freely soluble
Glycerol	Insoluble

An attempt was made at this point to learn whether the media phosphate buffer, pH 7.4, was able to maintain sink condition in diffusion as well as in permeation studies. Here form solubility studied data it was found that solubility of drug was poor in phosphate buffer, pH 7.4. Therefore it becomes difficult to maintain sink condition during diffusion study. Atenolol base was soluble in 0.01 N HCl and it was selected as a diffusion medium.

- **UV/VIS Spectroscopic analysis:-**

The UV maxima of resultant solution were measured with Shimadzu, Japan UV/VIS Spectrophotometer. The UV maxima of Atenolol base in the solution was found to be 236.0 nm, which was suitable for the preparation of standard curve and estimation of Atenolol base from various formulations. Figure shows the UV spectrograph of Atenolol base in 0.01N HCL.

Fig: UV spectrograph of Atenolol in 0.01N HCl



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Sr. No.	UV (nm)	Concentration	Sr. No.	UV (nm)	Concentration
1	238	1.704	11	236	1.722
2	237.7	1.708	12	235.8	1.72
3	237.8	1.710	13	235.6	1.718
4	237.3	1.712	14	235.4	1.716
5	237.1	1.714	15	235.2	1.715
6	236	1.717	16	235	1.714
7	236.9	1.718	17	234.8	1.713
8	236.6	1.718	18	234.6	1.71
9	236.3	1.719	19	234.4	1.709
10	236.1	1.72	20	234.2	1.707

- **Infrared (IR) Spectroscopic Analysis**

Atenolol was subjected for FTIR spectroscopic analysis, to characterize drug. The FTIR spectra obtained for pure drug is given in Figure. The characteristic peak of the pure drug and group was mentioned in Table. FTIR Spectra for base was compared with that given for FTIR spectra of official salt form. Diagnostic peaks and finger print regions were identical. These characteristics peaks are useful in drug excipients compatibility study**.**

Fig: FT-IR Spectra of pure drug (Atenolol)

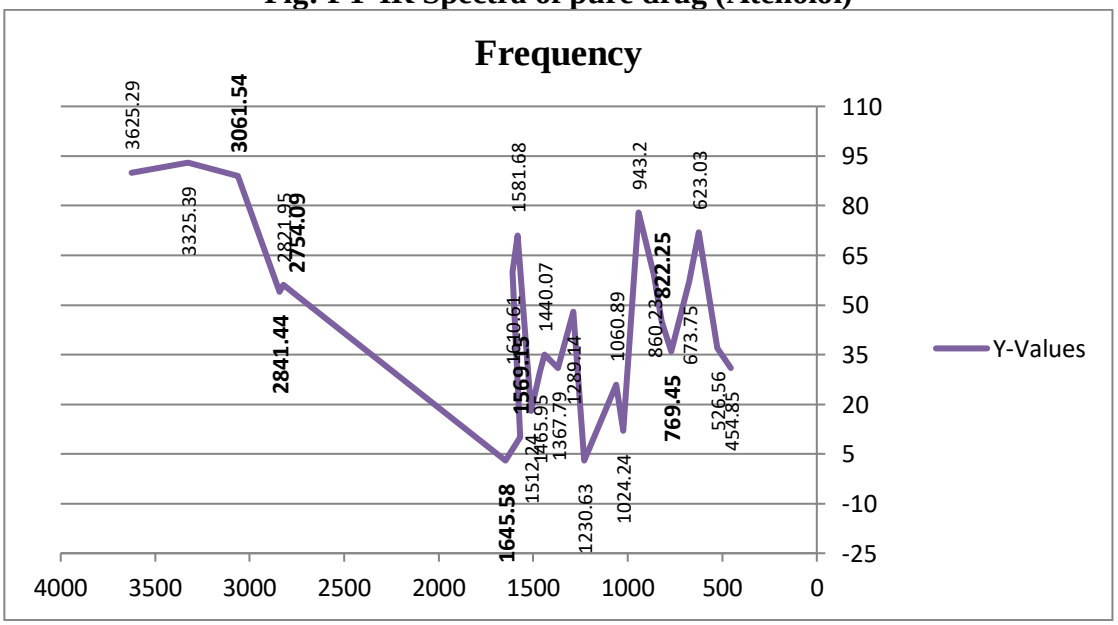

Table: FT-IR Spectral data of Atenolol

Frequency (cm^{-1})	Assignment
3061.54	Aromatic C-H stretch
2841.44	Aliphatic C-H stretch
2754.09	O-CH_3 C-H stretch
1645.58	Acetate C = O stretch
1569.15	Lactam C = O stretch
822.25	o-substituted aromatic C-H outof-plane deformation
769.45	p-substituted aromatic C-H outof-plane deformation

- **Differential Scanning calorimetry (DSC) analysis**

Differential Scanning Calorimetry enables the quantitative detection of all processes in which

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energy is required or produced (endothermic or exothermic phase transformation). DSC curves obtained for pure drug is shown in figure pure powered Atenolol showed a melting endotherm at 158ºC.

DSC study is useful for further drug excipients interaction study to check suitability of polymer.

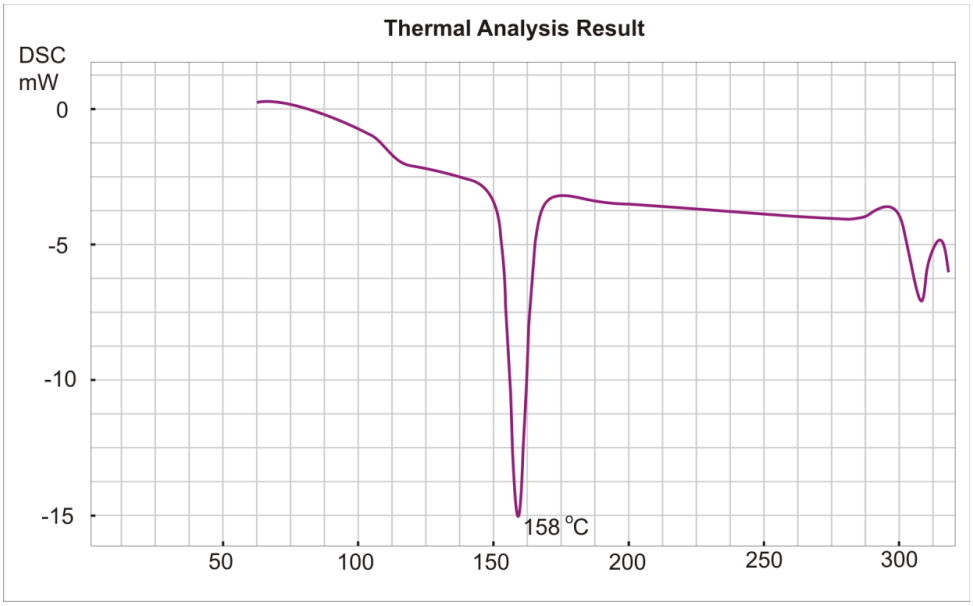

Figure: DSC thermogram of Atenolol

IV. CONCLUSION

Atenolol base was prepared from its official hydrochloride salt and characterized using different parameters. Melting point was determined to check purity of drug. From solubility study it was found that 0.01N HCl was able to maintain sink condition, so it was suitable as a diffusion medium. The results obtained from Partition co-efficient study revealed that the drug possessed sufficient lipophilicity, which fulfills the requirements of formulating it into a transdermal patch. Differential scanning calorimetry and Fourier transform infrared spectroscopy gave idea regarding chemical structure of pure drug. UV/VIS Spectroscopic data are useful for the preparation of standard curve and estimation of Atenolol base released from various formulations.

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