Studies on the Stability of Atenolol During the Heating Programme of Thermoanalytical Methods

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During a running research programme dedicated to the polymorphism of the atenolol, cardioselective â$_1$ adrenergic blocker, questions concerning the stability of this substance at high temperatures arose. The DSC fusion curves performed under common procedure are wider than those expected for a single pure substance and moreover on re-heating a sample obtained by cooling the melt a significant decrease in the fusion enthalpy is observed. A crucial point to assume reliability to the data obtained for fusion is to investigate the stability of the atenolol at high temperatures.

Samples of atenolol encapsulated in aluminium pans sealed in contact with air were mantained at 145ºC (7ºC below the melting point) for a certain time. The samples were analysed by HPLC-MS. Identical experiments were undertaken at 165ºC (13ºC above the melting point). In order to see the effect of the oxygen an identical plan to that described was carried out with samples handled and encapsulated in a nitrogen atmosphere. The analytical results show in all the experiments the existence of a species with 516.4 molecular weight and a decrease of the peak corresponding to atenolol. The decomposition is favoured by the presence of oxygen.

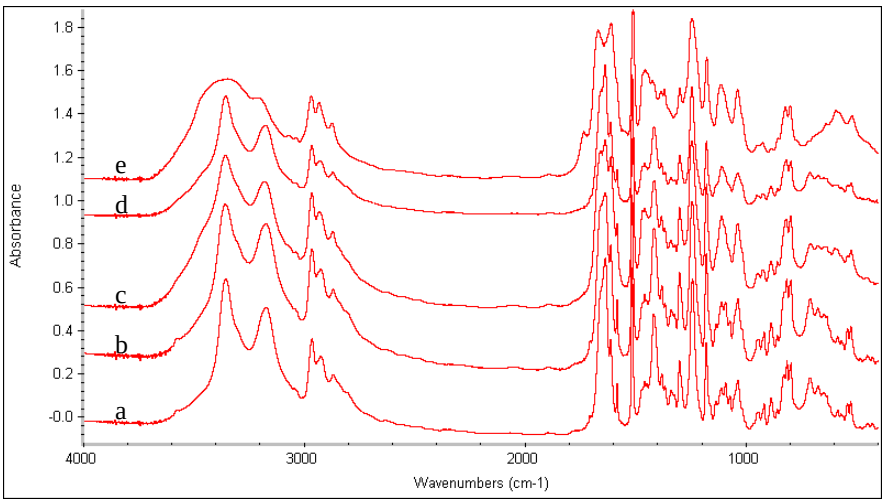

Fig. 1: FTIR spectra of atenolol **a)** original substance **b)** sample at 165ºC for 30 min. in nitrogen atmosphere **c)** sample at 165ºC for 12 hr. in nitrogen atmosphere **d)** sample at 165ºC for 30 min. in air atmosphere **e)** sample at 165ºC for 12 hr. in air atmosphere

Infrared spectra of atenolol after thermal treatments differ from that of the original substance. The spectral regions 4000-2000, 1800-1500, and 800-600 cm^{-1} are decomposed into individual vibration bands by peak fitting analysis and the effect of heat on the atenolol is shown. The spectral data combined with the chromatographic information indicates a thermal decomposition of acetamide group of the atenolol giving rise by molecular condensation to a higher molecular weight species.