

# Stability-indicating method for the analysis of salbutamol and its pharmaceutical dosage forms by HPLC

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## الخلاصة

في هذا البحث تم وضع ظروف فصل جديدة لطريقة الكروماتوغرافيا السائلة ذات التقنية العكسية والتزاوج الايوني والتي ام استخدامها في تحليل مادة السالبيتامول في الحبوب والشراب وكذلك كشف المشتقات التالفة للمادة. لقد انجز فصل مادة السالبيوتامول بهذه الطريقة خلال 16 دقيقة وبكفاءة عالية وذلك باستعمال عمود الفصل نوع اوكتادسيل سيلان بطول 25 سم وكانت الطبقة المتحركة مؤلفة من 30% ميثانول مع 0.02 بالمائة مادة صوديوم لوريل سلفيت وتضبيب الحموضة بواسطة حامض الخليك الى 3.5. ان دقة وانضباط التحليل لهذه الطريقة قد اثبتت من خلال علاقة الخط المستقيم بين مساحات المنحني التابع للمادة ودرجات تركيزها في المستوى بين 0.1 الى 0.8 ملغم بالمائة من مادة السالبيوتامول بالماء وكانت حدود الثقة للخط المستقيم هي 0.998 ومقدار التذبذب القياسي النسبي اقل من 1.1 بالمائة. بالاضافة الى ذلك فان هذه الطريقة قد اثبتت قابلية لاستعمالها في دراسة ثبوتية السالبيوتامول وذلك لعدم تداخل مشتقات التلف للمادة مع نتائج تحليل المادة الاصلية.

## **Abstract**

In this work ,an ion-pair reversed phase HPLC method was developed for the determination of salbutamol sulphate and its degradation products which can be applied for the assay of tablet, injection and syrup .The separation of salbutamol was performed in 16minutes with high efficiency using ODS column 25cm and a mobile phase consists of methanol 30 % and SLS 0.02% ,adjusted with acetic acid to pH3.5 . The accuracy and precision of this HPLC method was proved since a straight line relationship was obtained between the peak areas and the different concentrations of salbutamol sulphate standard in the range ( 0.1 – 0.8 )mg/100ml water with confidence limit 0.998 and the RSD is not more than 1.1% . In addition, this method was found to be quiet suitable for stability work on salbutamol since, there is no interference between the peaks of degradation products and the peak of the parent compound.

## **Introduction**

Salbutamol is Beta-adrenoreceptor agonist and used as bronchodilator as its sulphate salt in preparation of the dosage forms including ; tablet , injection ,and syrup .

The spectrophotometric determination of salbutamol sulphate is appeared to be rather difficult,due to the low intensity of its absorbance maxima ,and its doses in various pharmaceutical products are so small. Attempts to get suitable colorimetric method for assay of salbutamol sulphate in dosage forms lake the accuracy and precision . In addition, the spectrophotometric methods are invalid for stability work, since the degradation products can interfere with the detection of the parent substance (Ref.1- 4 ).

other method as thin-layer chromatography and electrophoresis were also applied for determination of salbutamol but ,rather tedious and unreliable (5-6 ) .Therefore, and recently the HPLC method of analysis was applied for determination of salbutamol ,particularly in body fluid due its high sensitivity ( 7-14).Analysis of salbutamol in its dosage forms as tablet,injection and syrup was also carried by different modes of HPLC techniques ( 15-20).

The latest edition of USP and B.P reported a specific methods for the assay of salbutamol sulphate in dosage forms ,in combination with TLC method for the related substances or degradation products .

Therefore , the aim of this study is to develop an HPLC method of analysis that can be applied for the assay of salbutamol in its dosage forms and to detect its degradation products simultaneously .

## **Materials and methods**

Salbutamol sulphate USP standard is obtained from Al-Haditha Co. for drug manufacturing , Ventolin tablets and ventolin syrups (Avenzor Co. Syria), Sodium lauryl sulfate (SLS), (Reagent grade) (supplied by al-furat pharm.Ind.), Acetic acid (BDH, Reagent grade ). Methanol (BDH, HPLC grade).

Apparatus; HPLC instrument with UV-detector ( Shimadzo Co. japan ).

Tablet Dissolution tester apparatus USP with 6 vessels

### **Chromatographic conditions**

Column : ODS type, 5 µm particle size , 250 x 4.6 mm dimension.

Mobile phase : methanol, water ( 30:70) which contains 0.02% SLS

and the pH is adjusted to 3.5 with acetic acid solution .the solvent is degassed and ultrasonic .

Detection: by UV at 276 nm.

Flow rate: 1 ml per minute.

## **Quantitative determination;**

Preparation of standard solution ;

Accurately weigh an amount of standard salbutamol sulphate equivalent to 2mg of salbutamol and dissolve it in 100 ml of 0.1N HCL solution. This solution is filtered through 0.45 µ membrane filter and 20µL is injected in the HPLC chromatogram .The mean value of the peaks areas for five injections of salbutamol sulphate standard solution is measured .

## **Preparation of test solution;**

Tablet : 20 Ventolin tablets were weighed for average weight calculation and then grinded . Amount of powder equivalent to 2 mg of salbutamol was taken and dissolved in 100 ml of 0.1N HCL solution. The solution was filtered through membrane filter size 0 .45 $\mu$  and then injected in the chromatogram as 20  $\mu$ l .

Syrup: 5 ml of Ventolin syrup was diluted to 100 ml with 0.1N HCL solution which yield a concentration of 2mg salbutamol/100ml according to the labeled amount of the syrup.

Calculation;

Percent of salbutamol in sample = ( peak area of test solution / peak area of standard solution)

X 100

## **Validation ;**

Accuracy ; different concentrations of standard solution in the range between 0.1mg – 2.0mg of salbutamol in 100 ml 0.1N HCL solution were prepared. The resulted solutions were filtered through membrane filter and assayed by HPLC method which recorded the peaks areas of these different dilutions successively.

Precision; a definite concentration ( 0.4mg/100ml ) of standard solution were injected ( 20 $\mu$ L ,injection volume) in the chromatogram by six successive applications and the peaks areas were recorded for determination of standard deviation.

## **Dissolution Profile:**

By using the USP dissolution system consists of ; paddle type apparatus, medium water 500ml

Procedure;one table in each of 6 vessels is inserted and the operated system is last for 30 minutes,during that sample (about 10ml)is withdrawn each 10 minutes and filtered ,then determined by the HPLC method for the dissolved amount of salbutamol .

## **Degradation products;**

Sample of standard solution of salbutamol sulphated in alkaline medium is subjected for accelerated degradation test by heating at 70C<sup>o</sup> for 1 hour. The solution is cooled and analyzed by HPLC method for detection of the resulted degradation products.

## **Results and discussion**

Quantitative analysis ; salbutamol is well separated by ion-pair reversed phase chromatography and the retention time was about 16 minutes (fig.-1-).

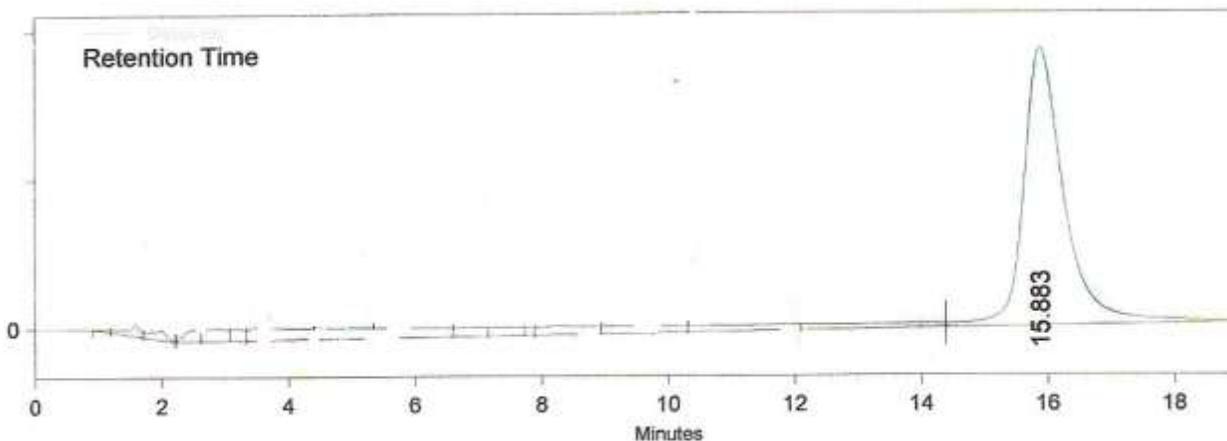


Figure 1- the HPLC chromatogram of salbutamol sulphate

Assay of salbutamol sulphate of a definite concentration showed a percent of recovery of 99.9% .

validation; the accuracy of this HPLC method was revealed by its constructed straight-line relationship between the peaks areas and the different concentrations of standard solution which has a confidence limit value of 0.998(Fig . -2- ).

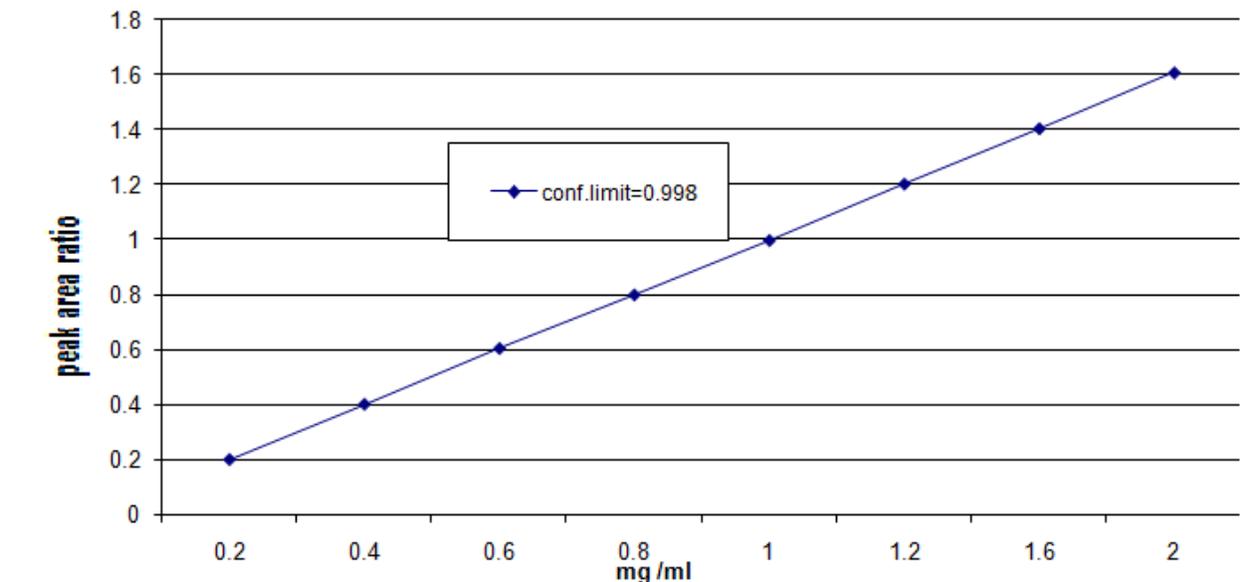


Figure-2- the relation of peak area ratio of standard salbutamol solution and its different concentrations

On other hand, precision of the method was also proved and the value of six repeated injections of a sample showed that the RSD value is not more than 1.1 %.For at least detection limit , a concentration of 0.05mg salbutamol/100ml was well detected and accurately measured .

The chromatogram of the assay of salbutamol tablet and syrup showed that all the excipients used in manufacturing of these dosage forms have no interference with the assay ,since they eluted in the first few minute (Fig.4and 5).

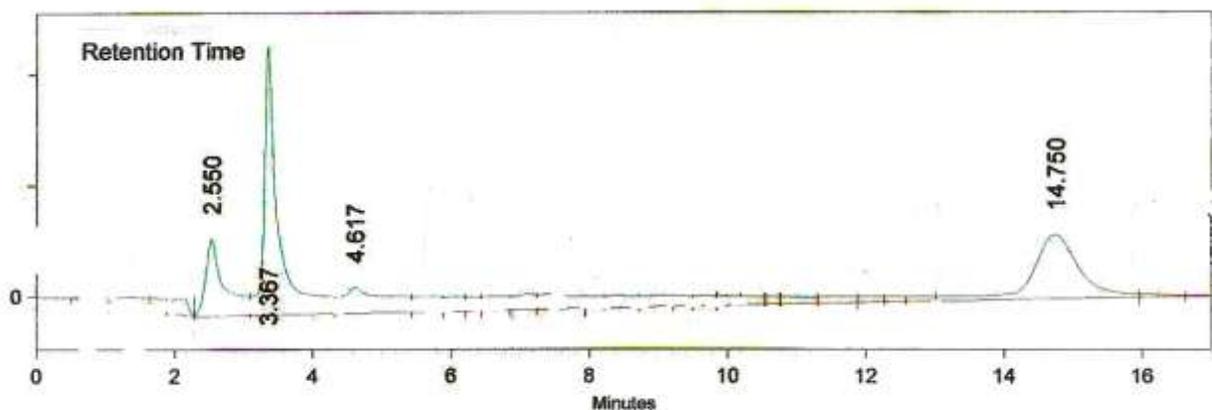


Figure-4- the chromatogram of salbutamol tablet ;all the excipients peaks are eluted at first few minutes.

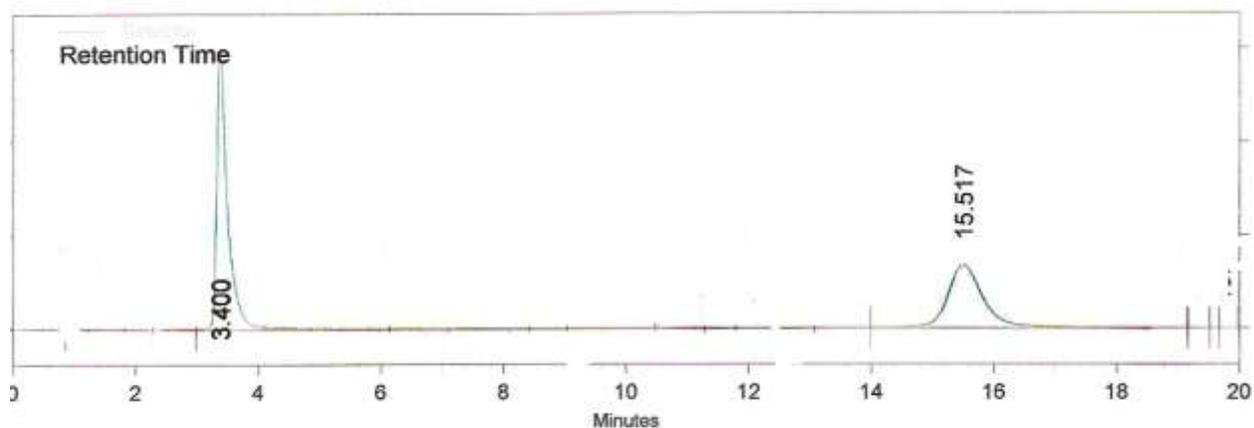


Figure-5- the chromatogram of salbutamol syrup in which ;saccharin sodium peak appeared at 3.4 minutes ,and salbutamol at 15.5 minutes .

Dissolution of salbutamol tablet;due to the high sensitivity of this HPLC method ,the determination of salbutamol 2mg per tablet in dissolution medium (500 ml) become more feasible (Fig.-6-).

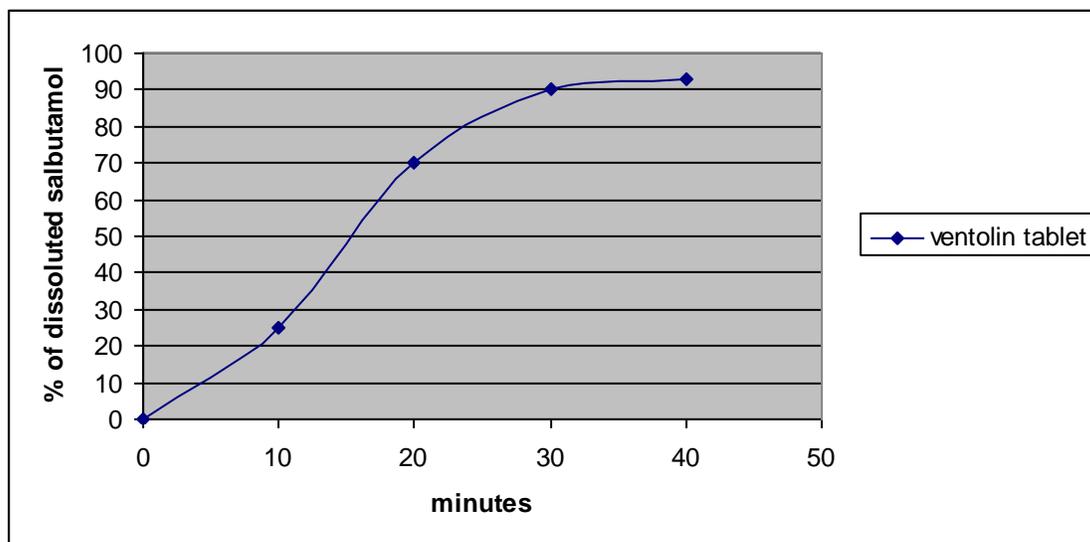


Figure-6- dissolution profile of ventolin tablet containing 2 mg of salbutamol in 500 ml water.

Detection of degradation product ;other peak rather than the peak of parent compound was appeared at about 10 minutes of retention time on the assay of degraded sample which indicated that method of analysis is quite suitable for stability study ,since the degradation products have on interference with the peak of salbutamol ( Fig.-7- ) .

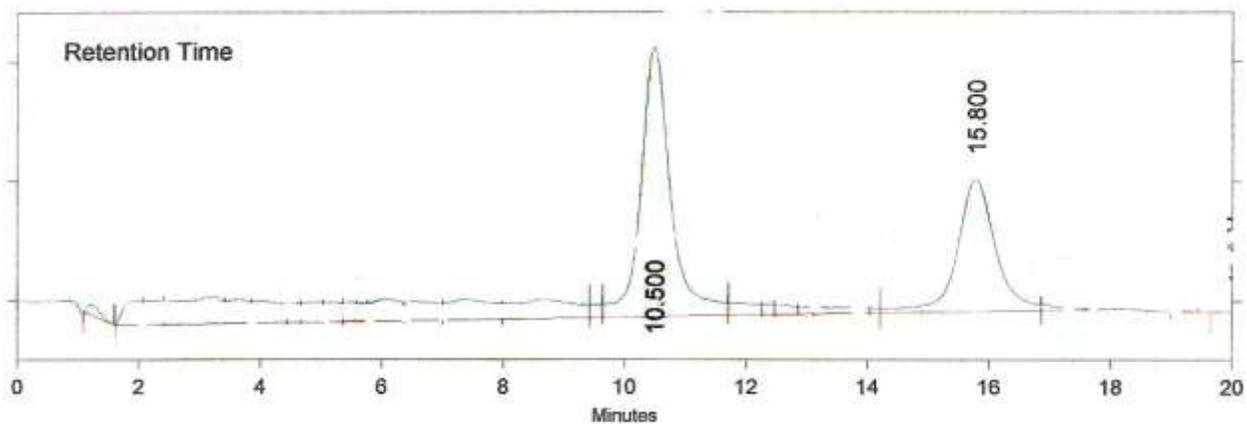


Figure-7- the chromatogram of salbutamol (15.8 minutes) and its degradation product (peak at 10.5 minutes ) .

## **Conclusion**

The results of this work indicated that the developed HPLC method using ion-pair reversed phase liquid chromatography mode showed good efficiency in separation of salbutamol with high accuracy and precision in quantitative analysis of salbutamol in its dosage forms including tablet and syrup. The high sensitivity of detection of this method permits the carrying of dissolution test for salbutamol tablet. Eventually, this HPLC method is considered as a stability –indicating method of analysis for salbutamol and its degradation products.

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