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Research Article

ANALYTICAL METHOD DEVELOPMENT AND VALIDATION OF RESIDUAL SOLVENT METHOD FOR BENZONATATE CAPSULES USP [100/200mg] BY GAS CHROMATOGRAPHY

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ABSTRACT

A simple, fast and precise Gas chromatographic method developed for Residual solvent method for Benzonatate capsules USP. HP-1, capillary column (30mx0.53mmx3.0µm) with carrier gas Hydrogen were used. The flow rate was 5.0ml/min. The relative standard deviation for six replicate injections of standard solution for Area response was 0.7%,for retention time response was 0.1%.The peak of diluent and sample solution were not interfered with solvent peak. The RSD of calculated results of Residual solvent in sample solution from six set was Isopropyl alcohol: Not Detected. The response was linear between 0.1% to 200% levels. The correlation coefficient was 1.00. LOD was 16.9 ppm and LOQ was 51.2 ppm. The proposed method is accurate, precise, selective and rapid for the residual solvent of Benzonatate capsules USP.

Keywords: GC, Validation, Isopropyl alcohol

INTRODUCTION

Benzonatate is a non narcotic oral anti tussive last for approximately 3 hours.

Chemically the drug is 2,5,8,11,14,17,20,23,26-nonaoxaoctacosan-28-yl para-butylaminobenzoate. Several methods such as GC[1], TD-GC/MS[2], have been reported in the literature.

MATERIALS AND METHODS

Gas chromatography with flame ionization detector, carrier gas Hydrogen, Reference standard of Isopropyl alcohol, Benzonatate capsules(100/200mg)were procured from market. Stationary phase HP-1, capillary column(30mX0.53mmX3.0µm) were used.

Preparation of standard stock solution

Weigh accurately about 0.34 grams of Isopropyl alcohol in to a 100ml volumetric flask and dilute with water to volume and mix well. Transfer 5ml of the above solution in to a 50 ml volumetric flask, dilute with water to volume and mix well.

Preparation of sample solution

Weigh and Transfer about 1.7grams of capsules directly in to a 25ml volumetric flask containing 10ml of water,shake it for 5minutes to dissolve the capsules and make up to volume with water.

RESULTS AND DISCUSSION

System suitability

System suitability tests were carried out on freshly prepared standard solution of Isopropyl alcohol and the area responses with 1µl injection volume and standard stock solution (n=6) were 286.10379,287.56036,290.68539,285.08398,286.42117,285.48398.

The RSD for area response was 0.7%.

Specificity

The blank, standard solution, sample solution, standard spiked in sample solution were injected separately in to a GC system. Typical chromatogram were obtained as shown in fig(1).The retention time of IPA standard and standarad spiked in sample were 3.523 and 3.526 respectively. The peaks of diluent and sample solution were not interfered with solvent peak.

System Precision

System precision tests were carried out on freshly prepared standard solution of Isopropyl alcohol and the retention time obtained with 1µl injection volume and standard stock solutions(n=6) were 3.519,3.525,3.528,3.528,3.525,3.531.The RSD for retention time was 0.1%.The area responses obtained with 1µl injection volume and standard stock solution (n=6) were 286.10379,287.56036,290.68539,285.08398,286.42117,285.48398.
The RSD for area response was 0.7%.

Method Precision

The sample set 1 of 1, 2 of 1, 1 of 2, 2 of 2, 1 of 3, 2 of 3, 1 of 4, 2of 4, 1 of 5, 2 of 5, 1 of 6, 2 of 6.contains sample weight 1.65564,1.65564,1.65213,1.65213, 1.66084, 1.66084,1.64900,1.64900,1.65467,1.65467, 1.66012,1.66012 respectively. The sample area and concentration in ppm for the above sample sets were ND,ND,ND,ND,ND ND, ND,ND,ND,ND,ND,ND and NA,NA,NA,NA,NA,NA,NA,NA,NA,NA,NA,NA respectively. The RSD of calculated results of Residual solvent in sample solution from six sets was Not Detected.

Linearity

Preparation of standard stock solution

Weigh about 0.3382gram of IPA in to a 100ml volumetric flask containing 10ml of water. Dissolved and diluted to volume with water. In to a series of 18 standard measuring flask, varying amount of standard stock solution of IPA was taken and made up to varies concentration of 2.5,5,10,15,20,25,35,50,100, 249,497,995,1989,2487,3979, 4974,7460,9947 ppm of IPA,1µl was injected from each flask. The peak area responses of each solutions were recorded. The plot of peak area versus the concentration of IPA was linear between 0.1% to 200% levels with coefficient of correlation (r=1.00) as shown in fig (2).

Limit of Detection/Limit of Qualification

For LOD and LOQ calculations first 7 levels of linearity were considered. The slope was 0.0555 and residual standard deviation was 0.2840.The LOD and LOQ were 16.9 and 51.2 ppm respectively. A distinct visible peak was observed at LOD level concentration and the RSD of the area obtained from six injections(LOQ level) was 2.5%.

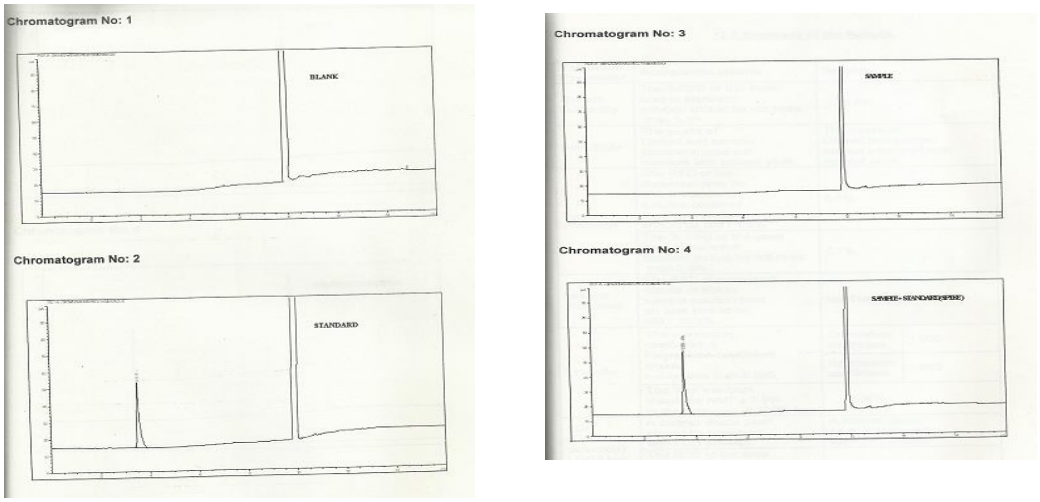

Fig.1: Typical Chromatogram of blank, standard solution, sample solution, sample+100% standard.

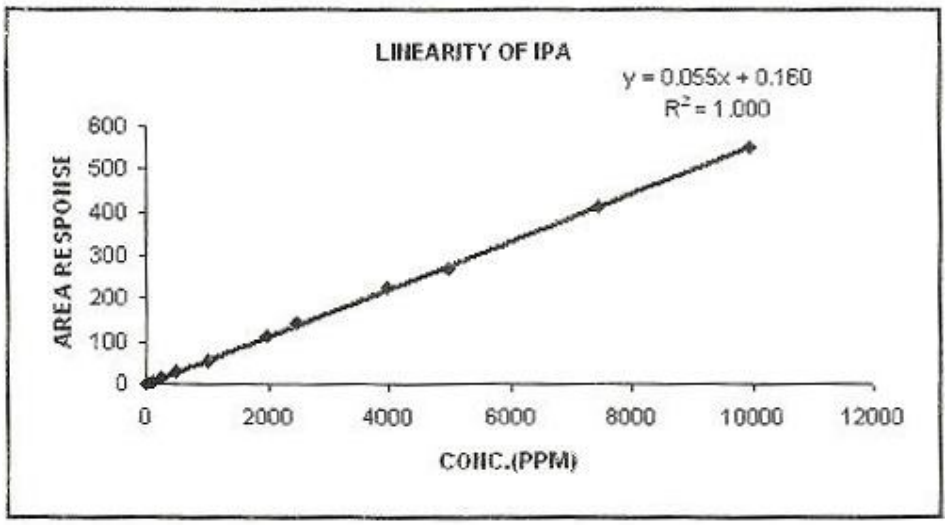

Fig. 2: Typical Linearity curve of IPA

CONCLUSION

The proposed GC method validation for residual solvent of Benzonatate capsules usp was carried out as per ICH and USP Guidelines. The system suitability test was established and recorded. The method was found to be specific for residual solvent of Benzonatate Capsules USP. The method was found to be linear in the specified range. The LOD and LOQ for the method was established and recorded.Hence this method stands validated and can be used for routine sample analysis.

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