EJAC
Eurasian Journal of Analytical Chemistry

Eurasian J Anal Chem 7(1): 43-48, 2012

Determination of diethylamine and triethylamine quantitatively using GC-headspace chromatography

Ashish R. Deshpande, Ganesh Ramachandran and Ramesh S. Yamgar [a*]

Chemistry Research Laboratory, Patkar-Varde College, Goregaon (W), Mumbai-400 062, Maharashtra, India.

Received: *30/03/2010****; Accepted:*** *17/07/2011*

Abstract

A Gas chromatographic-Head space (GC-HS) method was developed and validated for the determination of Diethylamine and Triethylamine. They were found well separated on the DB-624, 30m x 0.530 mm I.D. X 3 µ column with carrier gas nitrogen having pressure of 2.5 psi (Pound per square inch). Injector temperature was kept at 220°C and detector temperature was kept at 250°C. Detection was performed flame ionisation detector (FID). The method was validated for Specificity, LOD, LOQ, Linearity, Precision and Accuracy as per ICH guidelines [1, 2]. The method was found to be reliable for its intended purpose.

Keywords:

GC-HS, Diethylamine (DEA), Triethylamine (TEA), Dimethylsulfoxide (DMSO)

1. Introduction

Diethylamine (DEA) and Triethylamine (TEA) are used as reactants in the manufacturing process of many Active pharmaceutical ingredients (API) such as Oxybutynin hydrochloride, Trazadone hydrochloride, etc., are difficult to recover and analyze through GC – Head space when dissolved in water or other protic solvents.

When API such as Oxybutynin hydrochloride, Trazadone hydrochloride are dissolved in protic solvents such as water Diethyl amine and Triethylamine which may be entrapped in the molecule are not available for extraction due to the ionic interaction between H_3O^+ and OH^- ions of water molecule., and cannot be extracted & quantified accurately. Also, it was observed that when this API were dissolved in the DMSO, hydrochloride which is present as dot (. HCl) hydrochloride get freed and interacts with Diethylamine and Triethylamine to form salt because of it is not possible to recover.

Tried to search references on the determination of Diethylamine and Triethylamine from the API such as Oxybutynin hydrochloride, Trazadone hydrochloride, but found none and whatever references available did not mention from which API they have abstracted Diethylamine and triethylamine [6]. Also, some methods are available using derivatization of Diethylamine and Triethylamine contained in some less complex samples [7]. Another reference was found which involves direct injection of alkyl mine hydrochloride salt to gas chromatograph for the determination of alkyl amine [8], but none of the reference found for the determination of traces of Diethylamine and Triethylamine from API mentioned above.

* **Corresponding Author**
E-mail: rsy_chem@rediffmail.com
ISSN: 1306-3057,

Hence to determine DEA and TEA quantitatively from such a API, we add 1N Sodium hydroxide (NaOH) to neutralize the hydrochloride and make that API available in a free base, which can be dissolved easily in aprotic solvents such dimethylsulfoxide (DMSO). Since, no ionic bonding is possible DEA and TEA can easily be extracted and quantified using developed GC-headspace method. This method provide good separation and was validated as per ICH guidelines for specificity, Linearity, LOD, LOQ, Accuracy, and Precision [1,2].

2. Experimental

2.1. Instrumentation

Perkin Elmer Clarus 500 GC with Turbo matrix 40 headspace autosampler system (USA) consisted of Flame ionization detector (FID). The system control, data collection and processing was done by TOTALCHROM^{TM} WORKSTATION software. The weighing was done on Mettler Toledo AB204-S balance (Switzerland).

2.2. Solvents and Chemicals

Diethylamine (DEA) (GC grade), Triethylamine (TEA) (GC grade) and Sodium hydroxide (AR grade) was also obtained from Rankem. Dimethylsulphoxide (DMSO) (GC grade) was obtained from ACROS.

2.3. Chromatographic conditions

The column used was DB-624,30m x 0.53 mm I.D, 3µ film thickness from Agilent with nitrogen as carrier gas. It provided baseline separation for the Diethylamine, Triethylamine and Dimethylsulphoxide using Gas chromatograph - headspace condition given below in the Table 1.

Table 1. Gas headspace chromatographic condition

Gas chromatograph (GC) condition:	
Column	DB-624 ,30m x 0.53 mm I.D, 3µ film thickness
Oven temperature programming	45°C (hold for 5 mins) to 90°C @ 8°C min^{-1} to 200°C @ 20°C min^{-1}
Injection temperature	220°C
Detector	Flame Ionisation detector (FID)
Detector temperature	250°C
Detector Range	1
Detector Attenuation	2
Carrier Gas	Nitrogen
Carrier flow	2.5 psi (Pound per square inch)
Split ratio	1:5
Run time	18 min
Headspace sampler parameter	
Thermo stating temperature	85°C
Needle temperature	90°C
Transfer line temperature	100°C
Pressurization time	1.0 min.
Thermo stating time	15 min.
GC cycle time	25 min
Injection time	0.05 min.
Withdrawal time	0.20 in.

2.4. Test solution

Test solution was prepared by weighing 500 mg of the sample in a 20 mL of Headspace glass vial. To it added 1 mL of 0.1 mol L^{-1} Sodium hydroxide solution (NaOH), shake and then add 2 mL of Dimethylsulphoxide and seal airtight.

2.5. Standard solution preparation

The standard stock solutions were prepared by weighing accurately about 100 mg each of Diethylamine and Triethylamine in a separate 100 mL volumetric flask, dissolved and diluted up to the mark with dimethylsulphoxide. To prepare standard solution 5 mL of Diethylamine standard stock solution and 2 mL of Triethylamine standard stock solution was taken in a 100 mL volumetric flask and diluted up to the mark with dimethylsulphoxide. 2mL of this standard solution was then transferred to the headspace glass vial and seal airtight.

2.6. Blank solution preparation

To prepare blank solution 1 mL of 0.1M NaOH and 2 mL of dimethylsulphoxide was taken into a 20 mL headspace glass vial and seal airtight.

3. Result and Discussion

3.1. Chromatography

Different types of sample preparation and columns along with different oven ramp rates were tested [3, 4, 5], but sample preparation with 0.1 N NaoH and dimethylsulphoxide was found to be more suitable for extracting Diethylamine and Triethylamine from the API such as Oxybutanin hydrochloride, Trazadone hydrochloride, etc. The GC-HS method was validated for the following parameters.

3.2. Validation

3.2.1. Specificity

Specificity was established by injecting individually diluent (dimethylsulphoxide), standard solution of Diethylamine and Triethylamine individually and in combination into the chromatograph. Both Diethylamine and Triethylamine have different retention times and are well separated from each other. Diluent did not show any peak at these retention times. This indicates that both the solvents were properly resolved and there is no interference indicating that the method is specific for Diethylamine and Triethylamine. Chromatogram of mixture of solvents are shown in Fig 1.

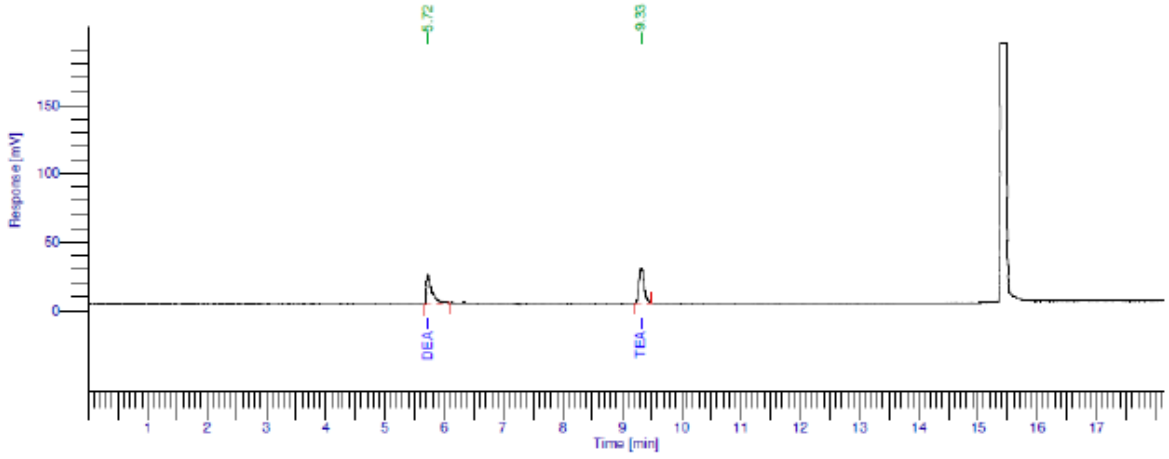

Fig 1. Chromatogram of mixture of Diethylamine and Triethylamine.

3.2.2. Limit of detection and limit of quantitation

For limit of detection (LOD) and limit of quantitation (LOQ) different concentrations of Diethylamine and Triethylamine were injected into the chromatograph up to their detectable concentration and quantitable concentration. The corresponding noise in blank injection was recorded and signal to noise ratio was calculated. Respective LOD and LOQ for diethylmine and Triethylamine were tabulated in Table 2.

Table 2: LOD and LOQ for Diethylamine and Triethylamine

Compound	LOD (mg L^{-1})	S/N Ratio for LOD	LOQ (mg L^{-1})	S/N Ratio for LOQ
Diethylamine	15	6.23	20	10.44
Triethylamine	0.3	5.11	0.5	9.42

For limit of detection signal to noise ratio must be at least 3: 1 and for limit of quantitation it must be at least 10:1 as given in ICH guidelines. The RSD of replicate injections at level of LOQ for Diethylamine and Triethylamine were 8.94% and 2.17% respectively, which shows excellent precision level at LOQ level.

3.2.4. Linearity

Linearities of Diethylamine and Triethylamine were carried out by injecting standard solutions of the components at different concentration levels starting from LOQ to 150% level into the chromatograph. A graph of Concentration (on X axis) vs Area (on Y axis) is plotted. A correlation coefficient, slope and intercept were calculated. For Diethylamine and Triethylamine the correlation coefficient was obtained as 0.996 and 0.999 respectively showing that response is linear.

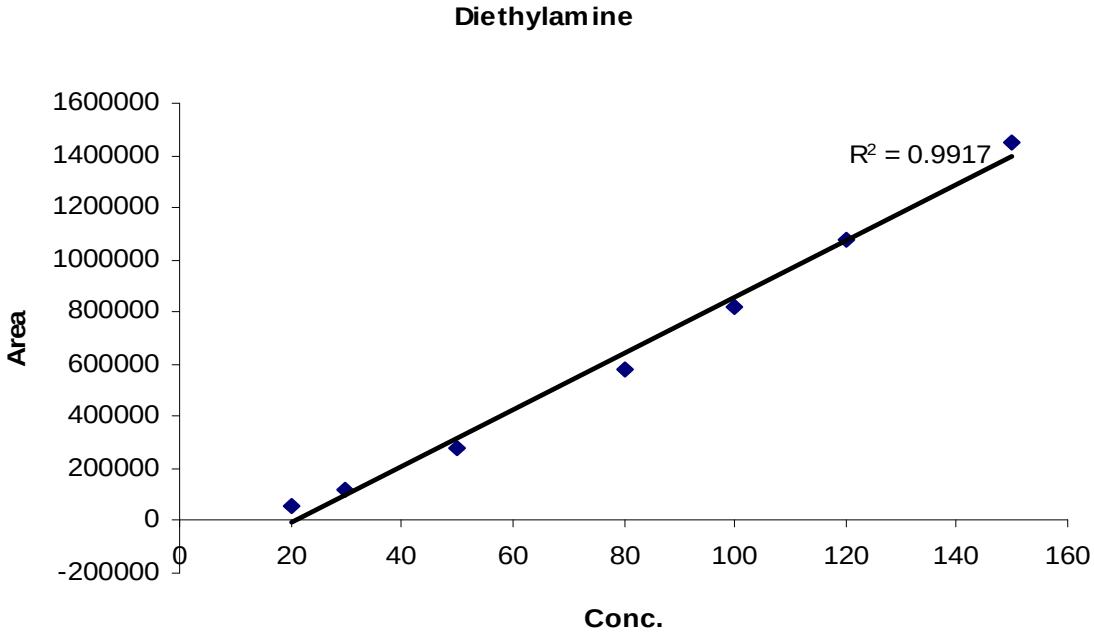

Fig 2. Linearity curve of Diethylamine

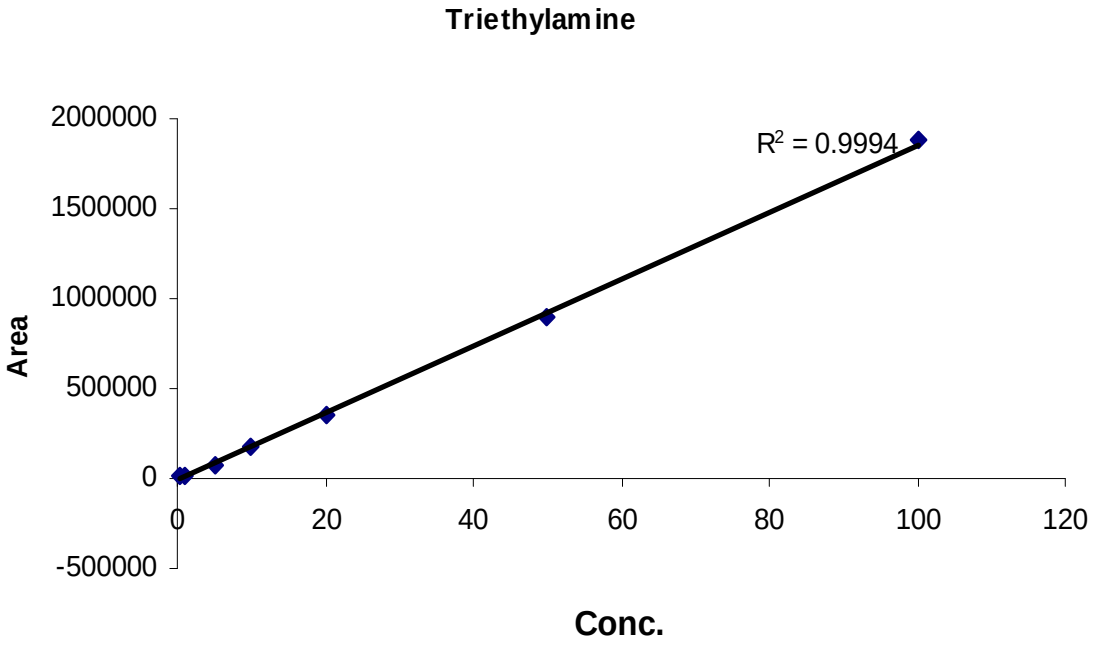

Fig 3. Linearity curve of Triethylamine

3.2.5. Precision (System Precision)

To ensure that analytical system is working satisfactory and giving precise results, standard solutions of Diethylamine and Triethylamine were injected into the chromatograph 6 times. The retention time and area is noted. Relative standard deviation (RSD) for Diethylamine and Triethylamine peak areas were found to be 6.14 and 4.65 respectively which indicates that the analytical system is precise.

3.5.6. Accuracy

The accuracy was carried out from 50% to 150% of the Diethylamine and Triethylamine limit. Both the solvents were spiked into the sample (Oxybutynin hydrochloride) at three levels, 50%, 100% and 150% of the limit. Three samples of each level were prepared and injected into the chromatograph. From the data obtained, % recovery at each level is calculated against added amount. The recovery for Diethylamine was found to be in the range of 93.4 % to 112.5% with %RSD 6.70. Similarly the recovery for Triethylamine was found to be in the range of 94.0% to 105.5% with %RSD 3.63. The mean recovery obtained for all components was well within the range of 80.0% to 120.0% and RSD calculated for all levels was less than 10% indicating accuracy of analytical method.

4. Conclusion

The developed method was found to be specific as proved by injecting known components into the chromatograph. Limit of detection and limit of quantitation has been established. The Analytical method was found to be linear in the specified range and also found to be Accurate and Precise. From the above data, it is concluded that, the analytical method can be used for quantitative analysis of Diethylamine and Triethylamine in salts like Oxybutynin hydrochloride, Trazadone hydrochloride, etc. and is capable of giving accurate and precise results.

Acknowledgements

We are grateful to the Management and Principal of Patkar-Varde College and Dr. A G Gadre, Head, Department of Chemistry for guidance, constant encouragement and support to carry out this research work.

References

1. International Conference On Harmonization (ICH), Q2 (R1) (2005) Validation of analytical procedures: Text and Methodology.
2. International Conference On Harmonization (ICH), Q3C(R3)(2006) Impurities: Guidelines for Residual solvents
3. European Pharmacopoeia 6.0 (2008) 1: 121.
4. British Pharmacopoeia (2008) IV: A568.
5. United state Pharmacopoeia 31 (2008) 1: 158
6. Raghuram P, Soma Raju I V and Sriramulu J (2010) GC Quantification of Cyclopropylamine, Diethylamine and Triethylamine in Active Pharmaceutical Ingredients: Chromatographia 71: 963.
7. Hiroyuki K (1996) Derivatization reactions for the determination of amines by gas chromatography and their applications in environmental analysis. J Chromatogr A 733: 19.
8. Umbreita G R, Nygrena R E and Testaa A J (1969) Determination of traces of amine salts in water by gas chromatography. J Chromatogr A 43: 25.