Research Papers

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A SIMPLE HEAD-SPACE GAS CHROMATOGRAPHY METHOD TO QUANTIFY THE FORMALDEHYDE CONTENT IN COSMETIC PRODUCTS.

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Abstract

The method developed   based on derivatization of formaldehyde with O-(2, 3, 4, 5, 6-pentafluorobenzyl) hydroxylamine   to formaldehyde oxime. The final derivative was quantified by using capillary GC column with the help of flame ionisation detection in Head-space gas chromatography. The finalised method was validated and found method is simple, accurate, robust, precise and linear. The method can detect even in the lower concentration around 0.006 ppm and quantification range from 0.02 ppm to 600 ppm levels.

KEYWORDS :

Formaldehyde, Head-space gas chromatography, O-(2, 3, 4, 5, 6-pentafluorobenzyl) hydroxylamine, Tetrahydrofuran

INTRODUCTION:

Based on toxicity of formaldehyde, required to measure the formaldehyde content in cosmetic and pharma formulations. If preservatives used in cosmetic formulations, some of preservatives are released the formaldehyde [1].The regulation of formaldehyde donor (or formaldehyde releasing preservative) in cosmetics also differs from country to country [2, 3, 4]. Since FDA in USA has no regulation on content of formaldehyde and formaldehyde donor in cosmetics. As per country regulations different countries are having different specifications [2, 3, 5].

Different methods like polarography [6], thin layer chromatography [7], colorimetry, HPLC [8, 9, 10], GC and GCMS methods are developed in early days. Direct determination of formaldehyde by GC or HPLC is difficult, because it has low boiling point (-19 ˚C). So, it should be converted to other forms by using derivatising agents. Using 2, 4-dinitrophenyl hydrazene, formaldehyde should be converted to its oxime and analysed by HPLC-UV detection at 360nm. Formaldehyde derivatization by ethanol in the presence of p- toluenesulfonic acid catalyst and form diethoxymethane and detect by using GCMS. Formaldehyde derivatization by O-(2,3,4,5,6-pentafluorobenzyl)hydroxyl amine and form oxime. This derivative detect by using GC-MS [11]. As per best of my knowledge there is no autosampler method for formaldehyde analysis using GC and HPLC for sequence running the samples, because of instability of solution. The aim of new developed Head-space GC method was to develop a simple, selective, sensitive and stable method with autosampler injections for analyze the cosmetic products with huge range of formaldehyde content.

EXPERIMENTAL

Apparatus: Gas Chromatography with FID and AOC-20i Auto injector (model: GC-2010 Plus, make: Shimadzu), Column-ZB-624 (Length-30m, Diam-0.32mm, Film-1.80µm, Make: phenomenex), Head-Space Gas Chromatography (Model: Versa, Make: Teledyne Tekmar), 20 mL crimp cap Head-Space GC vials, Crimper, Sonicator (model: Soltec, Make: Sonica).

Chemicals and Reagents: Formaldehyde solution (37%)(Make: Sigma-Aldrich), Tetrahydrofuran (ARgrade) (Make: SD-fine-chem.-limited),   O-(2,3,4,5,6-Pentafluorobenzyl) Hydroxylaminehydrochloride(Analyticalgrade)(Alfa-Aesar),

SodiumChloride (AR-grade) (Make : Rankem) and water (HPLC Grade).

INSTRUMENTATION

GC Conditions:

Initial temperature	:	80^0C
Hold time-1	:	5 minutes
Rate	:	12^0C per minute
Final temperature	:	150^0C
Hold time-2	:	4.0minutes
Rate	:	30^0C per minute
Final temperature	:	220^0C
Hold time-3	:	12.0 minutes
Injector temperature	:	180^0C
Detector temperature	:	240^0C
Nitrogen gas flow rate	:	1.3 ml/ min
Split ratio	:	1:10
Detector	:	FID
Total run time	:	29.17 Minutes
Injection Volume	:	1 μl

Head Space Condition:

GC Cycle time	:	40.0min
Volume oven temperature	:	110^0C
Transfer line temperature	:	140^0C
Platen/Sample temperature	:	80^0C
Platen temp Equil.time	:	0.5min
Sample equil.time	:	3.0minutes
Mixer	:	On
Mixing level	:	Medium
Mixing time	:	20 minutes
Mixer stabilize time	:	0.5 minutes
Pressurize	:	10psig
Pressurize time	:	2 minutes
Pressurize equil.time	:	0.25 minutes
Loop fill pressure	:	7 minutes
Loop fill time	:	2 minutes
Inject time	:	1 minute

METHODS

Standard Solution Preparation:

Stock Solution: Weighed accurately 550mg of Formaldehyde solution (37%) in   100mL volumetric flask and   dissolved in water and made up to mark with water.

Standard Solution-A :(20ppm Formaldehyde): Transferred the 1mL of the stock solution in to a 100mL volumetric flask and made up to the mark with water.

Standard Solution-B: (1ppm Formaldehyde): Transferred the 5mL of the standard solution-A in to a 100mL volumetric flask and made up to the mark with water.

Internal Standard Preparation:

Solution-1: Transferred 1mL of Tetrahydrofuran into 100mL volumetric flask dissolved in water and made up to the mark with water.

Solution-2: Transferred 1mL of solution-1 into 100mL volumetric flask and made up to the mark with water.

Reagent and Internal standard solution: Weighed accurately 100mg of O-(2,3,4,5,6-pentafluorobenzyl)hydroxylamine hydrochloride in 50mL volumetric flask , dissolved in water and added 2ml of Internal standard solution-2 and made up to

the mark with water.

Sample Preparation: Weighed accurately 1g of the sample, which is required to analyze in 100mL volumetric flask and dissolved in water and made up to the mark with water.

Sample analysis:

       0.5mL of water was taken in to a dry 20mL crimp cap Headspace GC vial and added 2ml of reagent and internal standard solution and 1.5g of Sodium chloride then crimp the cap with crimper with tightly. Inject this vial for blank in head space GC and repeat it.
       0.5mL of standard solution-B was taken in to a dry 20mL crimp cap Headspace GC vial and added 2mL of reagent and internal standard solution and 1.5g of Sodium chloride then crimp the cap with crimper with tightly. Inject this vial for standard analysis. Inject the standard 6times and calculate the average ratio of standard and internal standard.
       0.5mL of sample solution was taken in to a dry 20mL crimp cap Headspace GC vial and added 2ml of reagent and internal standard solution and 1.5g of Sodium chloride then crimp the cap with crimper with tightly. Inject this vial for sample analysis in head space GC and repeat it. Calculate the ratio of Sample and internal standard.

CALCULATION:

$$\text{Sample ratio} = \frac{(\text{Formaldehyde derivative area in sample})}{(\text{Internal standard area})}$$

$$\text{Standard ratio} = \frac{(\text{Formaldehyde derivative area in standard})}{(\text{Internal standard area})}$$

$$\% \text{ of Formaldehyde} = \frac{(\text{Sample ratio})}{(\text{Standard ratio})} \times \frac{(\text{Standard weight})}{(\text{Sample weight})} \times \frac{5}{10000} \times (\text{Standard purity})$$
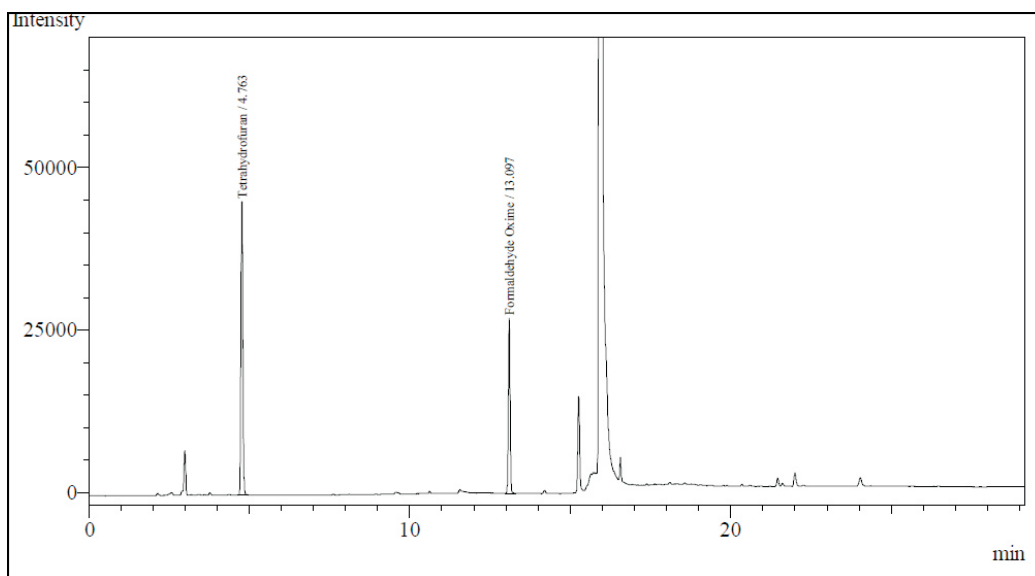

Figure 1: Chromatogram of Formaldehyde analysis by Head-Space GC.

Method Validation:

Specificity and Selectivity: The specificity of the method was checked by injecting blank solution and sample solution. There was no interference from blank and excipients at the retention time of analyte peak.

Linearity: The method showed linear in the concentration range of 0.5ppm to 1.5ppm, the correlation coefficient was 0.9986. The results are shown in table1. The method showed linear in the concentration range of 1ppm to 600ppm, the correlation coefficient was 0.9979.The results are shown in table2.

Accuracy: The accuracy of the method was determined by adding known amount of formaldehyde content corresponding to following concentration levels of 50%(0.5ppm), 100%(1.0ppm), 150%(1.5ppm), 200ppm, 400ppm, 600ppm of target analyte concentration(1ppm) along with the excipients in triplicate. The accuracy was calculated by the percentage of analyte recovered by the assay method. The accuracy results are shown in table3.

Precision: The method precession, system precession and intermediate precession were calculated. The results were within the limits.

Robustness of the method: Changing with the flow rate (±0.2mL/min), and temperature program, no change in area of fluoride and RSD was within limits. It indicates robustness of the method.

Ruggedness of the method: Changing with different column (ZB-624 and DB-624), different analyst and different instruments (Shimadzu and Agilent systems) the results are within limits.

LOD and LOQ: Method limit of detection is 0.006ppm and limit of quantification is 0.02ppm.

EXPERIMENTAL RESULTS

The method was optimized based on using ZB-624 capillary column in gas chromatography. The deravatization process was simplified with optimization of deravatizing reagent. This method was validated as per ICH guidelines for specificity, linearity, accuracy, precession, robustness and ruggedness. The results were within limits.

Table 1: Linearity1

Parameter	Value
Concentration range(ppm)	0.5ppm-1.5ppm
Slope of regression	0.7747
Intercept	-0.0301
Correlation coefficient	0.9986

Table 2: Linearity2

Parameter	Value
Concentration range(ppm)	1ppm-600ppm
Slope of regression	1.0267
Intercept	7.4245
Correlation coefficient	0.9979

Table 3: Accuracy

Added amount(ppm)	Recovery (%)
0.5	106.58
1.0	98.60
1.5	98.15
200	108.25
400	108.41
600	101.97

CONCLUSION

This developed and validated Head-Space gas chromatography method was very simple, good efficient and stable method for the analysis of formaldehyde content in cosmetic products. This method developed with auto sampler injections. Prepared the solutions and kept the sequence and run the continuously. The sample solution was stable up to 3days. Solution preparation was very simple on this method. In this method, first time tetrahydrofuran was used as an internal standard, based on that we got good repeatable results. The formaldehyde derivative is very stable in solution form, prepared the samples and keep the sequence. This method is first time developed for auto sampler analysis, based on that reduced the manpower for the analysis. Using this same method we were analysed the samples in large range of formaldehyde from 0.02ppm to 600ppm. This method was specific, selective, linear, precise, accurate and robust. So as per best of my knowledge this method is very good suitable for analysis of formaldehyde in cosmetic products and its raw materials.

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