



FORMALDEHYD CONTENT DETERMINATION BY GC AS DERIVATIZATION WITH PTSA

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Article Received on
01 Jan. 2019,

Revised on 22 Jan. 2019,
Accepted on 12 Feb. 2019

DOI: 10.20959/wjpps20193-13279

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ABSTRACT

This GCHS method describes, developed and validated method for the quantification of formaldehyde in residual solvents. Method was developed on AT-WAX- 30mx 0.53mm id, 1.0µm column, with a flame ionization detector. Split ratio as 1:1 and oven program as initially held at 40°C for 5 min then increased to 230°C at the rate of 35°C per min and held at 230°C for 15 min. Method is identified as linear in the range 0.4 ppm to 3.0 ppm. Minimum quantification level for this method achieved as 0.4 ppm, whereas the minimum detection level for the formaldehyde was 0.2 ppm. Method is validated as per the ICH guidelines.

KEYWORDS: Formaldehyde, Para toluene sulphonic acid, GCHSS, FID detector, Validation.

INTRODUCTION

Formaldehyde is the first series of aliphatic aldehydes. Formaldehyde was discovered by Mikhailovich Butlerov in 1859 and also it has been manufactured since the beginning of the twentieth century. At room temperatures formaldehyde is a colorless gas with a pungent odor. Because of high purity, low cost and variety of chemical reactions, formaldehyde has become one of the most used industrial chemicals. In general it has been manufactured from methanol. Formaldehyde is a basic building block for production of variety of chemicals as well as organic solvents, which are usually used in synthesis of drug substances, hence it is very essential to control the formaldehyde in several solvents. For the quantification of formaldehyde in different solvents, derivatized GC method was developed. Derivative may have similar or closely related structure to the target analyte. The advantage of derivatization

methods compare to the regular methods was low level detection and less interference from the sample matrix. Formaldehyde will reacts with PTSA and produce a derivative, which is quantified in GCHS by using derivatization method.^[1,2] This method is suitable for the quantification of residual formaldehyde in several regularly used solvents, which are using in the regular manufacturing process. This method has greatly quantified the formaldehyde in several solvents as around 16 solvents with different make. Formaldehyde content results are tabulated in Table 1. And recovery shown in one of the solvent which is methanol.

MATERILAS AND METHODS

Derivatization: Derivatization is the process by which a compound is chemically changed, producing a new compound that has properties more amenable to a particular analytical method. Some samples analyzed by GC require derivatization in order to make them suitable for analysis. Compounds that have poor volatility, poor thermal stability, or that can be adsorbed in the injector will exhibit nonreproducible peak areas, heights, and shapes. Other compounds that respond poorly on a specific detector may need to be “tagged” with a different functional group to improve detection.

Need of derivatization

- ❖ To permit analysis of compounds not readily responsible to analyze due to inadequate volatility or stability.
- ❖ To improve chromatographic behavior or detectability.

Properties of derivatization reagent

- ❖ The reagent should produce more than 95% complete derivatives.
- ❖ It should not cause any rearrangements or structural alterations of compounds during formation of the derivative.
- ❖ It should not contribute to loss of the sample during the reaction.
- ❖ It should produce a derivative that will not interact with the GC column.
- ❖ It should produce a derivative that is stable with respect to time.

Reaction

P-Toluene sulfonic acid (PTSA or pTsOH) or tosylic acid (TsOH) is an organic compound with the formula $\text{CH}_3\text{C}_6\text{H}_4\text{SO}_3\text{H}$.

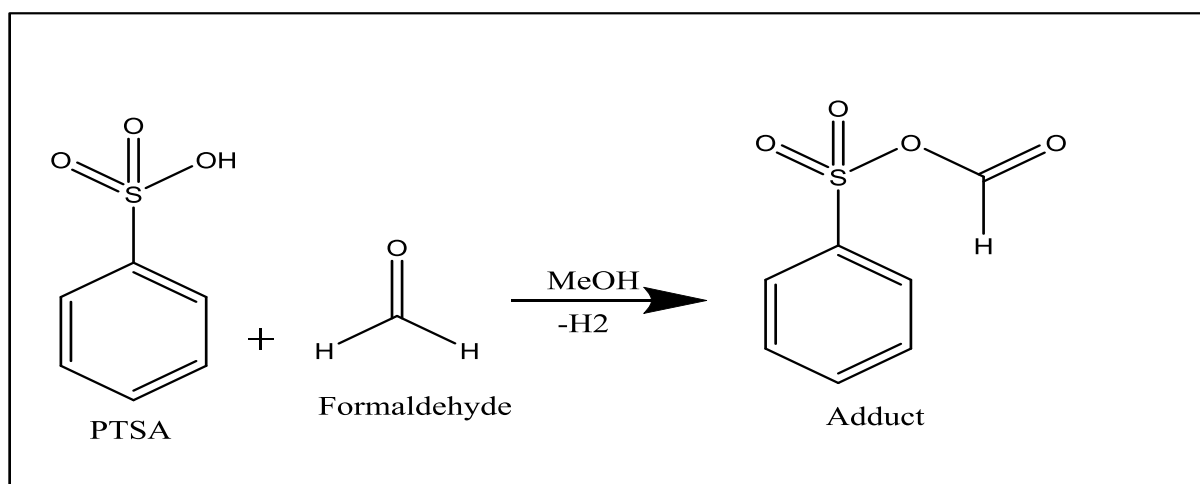


Fig. 1: Reaction between Para toluene sulfonic acid and Formaldehyde.

Chemicals: Formaldehyde was procured as Merck grade (Mumbai, India); PTSA was procured as TCI chemicals (Mumbai, India); Methanol was purchased with rankem grade.

Instrumentation and chromatographic conditions: GC instrument with make Agilent Infinity 7890A series and Head space system with make Agilent G1888. Sample and standard weights are taken by using analytical balance with make Sartorius and model MSA 225S-100-DA.^[3] For processing the chromatographic data Empower -3 software was used. Chromatographic conditions for quantification of formaldehyde content in the residual solvents were, HS Oven temperature is 80°C, Loop temperature is 110°C, Transfer line temperature is 120°C, Vial pressure is 10 psi, Vial equilibration time is 10 min, Pressurization time is 0.01 min, Loop fill time is 0.20 min, injection time 1.0 min, Split ratio is 1:1, Carrier gas is 8.0 mL/min (helium), Flow mode is Constant flow, Injector temperature is 180°C, Detector temperature is 260°C, Run time is 25.43 min. Sample concentration 100.0 mg/mL, diluent was 1% PTSA in Methanol.

Sample preparation: Test samples were prepared with concentration of 100 mg/mL by dissolving in the diluent (Diluent is 1% PTSA methanol).^[4,5] Spiked solutions of formaldehyde at different concentration were prepared by adding the adequate amount of formaldehyde standard stock solution in the residual solvents.^[6,7]

RESULTS AND DISCUSSION

To develop the quantitative GC method for formaldehyde content in the residual solvents, several development trial were taken up by changing the oven temperature program, different columns and also different techniques. Upon the several development trails, consistent and

robust method was achieved on AT-WAX- 30mx 0.53mm id, 1.0 μ m, with FID detector by GCHS.^[8]

Method Validation: The described formaldehyde content in the residual solvents samples was validated as per the ICH guidelines.

Limit of detection and Limit of quantification: LOD and LOQ of formaldehyde were established by preparing the solution from the known concentration of stock solution to achieve the signal-to-noise ratio as 3:1 and 10:1. Carried out the LOQ precision by preparing six individual solutions of residual solvents with LOQ concentration of formaldehyde. Accuracy at LOQ was also carried out by preparing the solutions with formaldehyde at LOQ level concentration. The results for the precision at LOQ and accuracy at LOQ are tabulated in the Table 2.

Method precision: Method precision was carried out by preparing the six individual solutions with spiking of 20 ppm formaldehyde in each preparation.

Linearity: Linearity was carried out by preparing the formaldehyde solutions at different concentration levels (i.e. LOQ, 50%, 75%, 100%, 125% and 150%) in the diluent. Calculated the values of correlation coefficient and %Y-intercept. Results are tabulated in Table 2. Linearity graph was shown in Figure1.

Accuracy: The accuracy of the method was carried out by triplicate preparation at three different concentration levels of formaldehyde in residual solvents (i.e. 10 ppm, 20 ppm and 30 ppm). Calculated the recovery of formaldehyde in all the preparations and tabulated in Table 2.

Table 1: Formaldehyde content in different solvents.

S.No	Name of the solvent	Batch number	Formaldehyde content(ppm)
1	Ethanol(Hayman)	F202871	0.5
2	Acetonitrile(Merck)	DK7DF71255	0.5
3	(IPA)Merck	DI7P672319	0.4
4	IPE(Rankem)	R044A16	Not detected
5	n-Hexane(Finar)	544650307GQ	Not detected
6	Acetone(Rankem)	R069J16	103
7	EA(Finar)	550310227BR	0.6
8	DCM(Finar)	549531028KQ	0.7
9	THF(Merck)	I803710545	2.3
10	Toluene(Rankem)	R282G16	27

11	n-Propanol(Finar)	225800212GQ	0.5
12	DMA(Finar)	R028M16	0.5
13	DMSO(Finar)	546380222KQ	1.7
14	DMSO(Bio solve)	1210271	0.28
15	NMP(Merck)	SK6S660865	7.8
16	Benzyl alcohol(Merck)	DI7P671903	2.1

Table 2: Validation results of Formaldehyde.

S.No	Validation parameter	Criteria	Result
1	LOD	formaldehyde (ppm)	0.2
2	LOQ	formaldehyde (ppm)	0.4
3	Method precision(n=6)	%RSD for area	0.8
4	System precision(n=6)	%RSD for area	1.2
7	LOQ Precision(n=6)	%RSD for area	2.3
8	Accuracy at LOQ	%Recovery	101.4
9	Accuracy	%Recovery at 50%	101.1
		%Recovery at 100%	95.9
		%Recovery at 150%	98.5
10	Linearity	Correlation coefficient	0.9992
		% Y-intercept	2.7

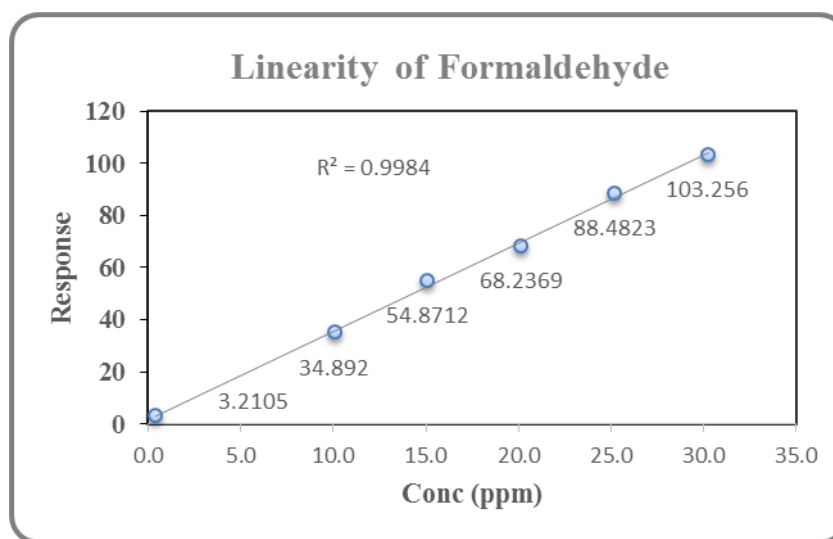


Fig. 2: Linearity Graph of formaldehyde.

CONCLUSION

The developed rapid GCHS method for the determination of formaldehyde in residual solvents is precise, accurate, linear and specific. The method was validated as per the requirements of ICH guidelines, hence it can be used for the routine analysis of production residual solvents samples to check the formaldehyde content.

ACKNOWLEDGEMENTS: Author thanks the management of Dr.Reddys's laboratories Ltd., for permitting this work to be published. Cooperation extended by all the colleagues of Analytical R&D, and CTO-VI QC is gratefully acknowledged.

REFERENCE CHROMATOGRAMS

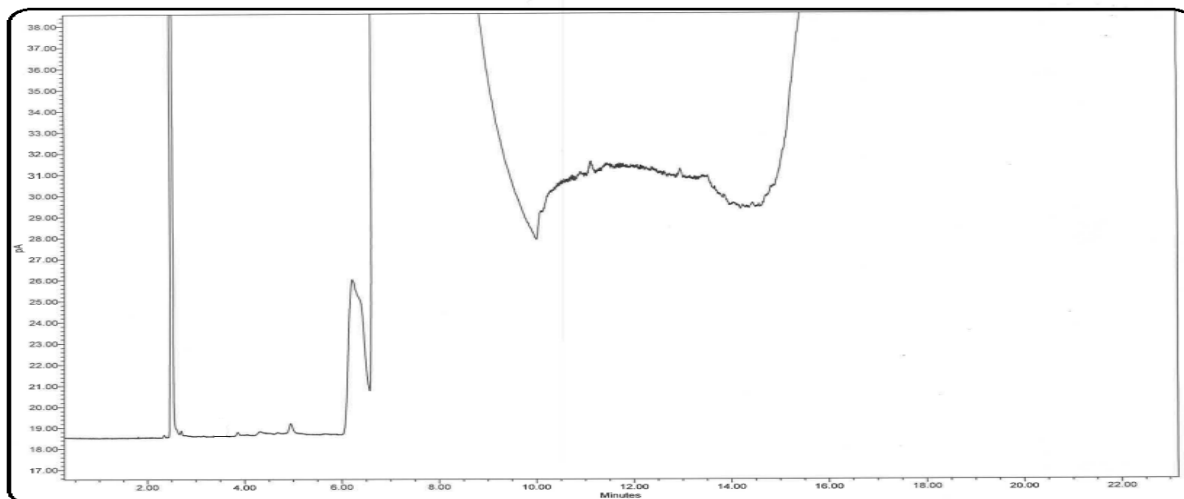


Fig-3: Blank Chromatogram.

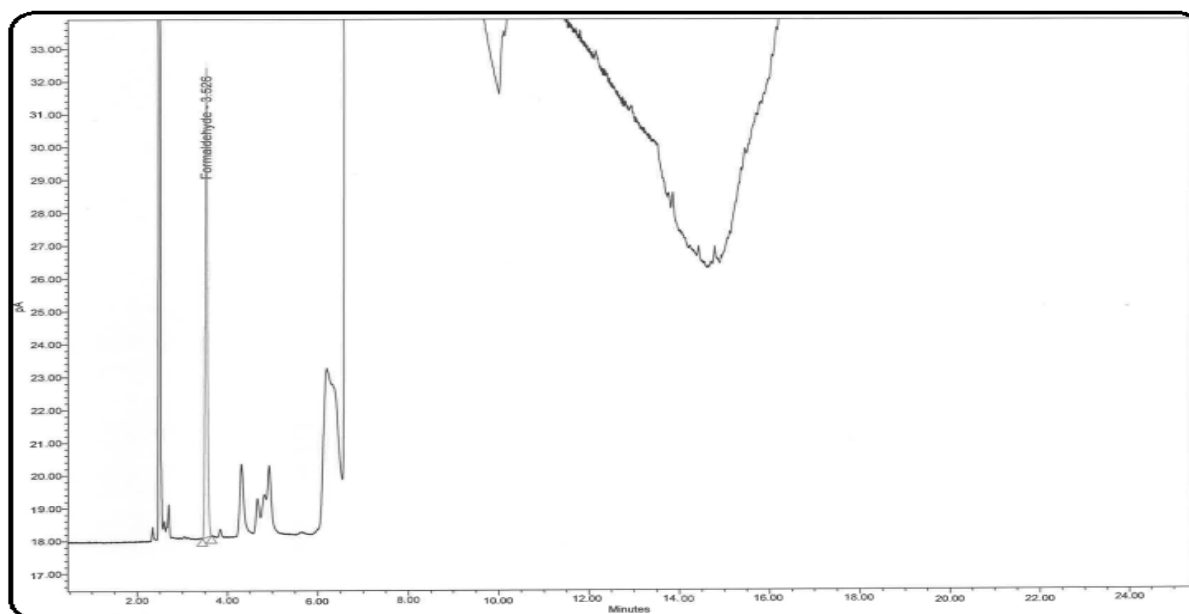


Fig-4: Standard chromatogram.

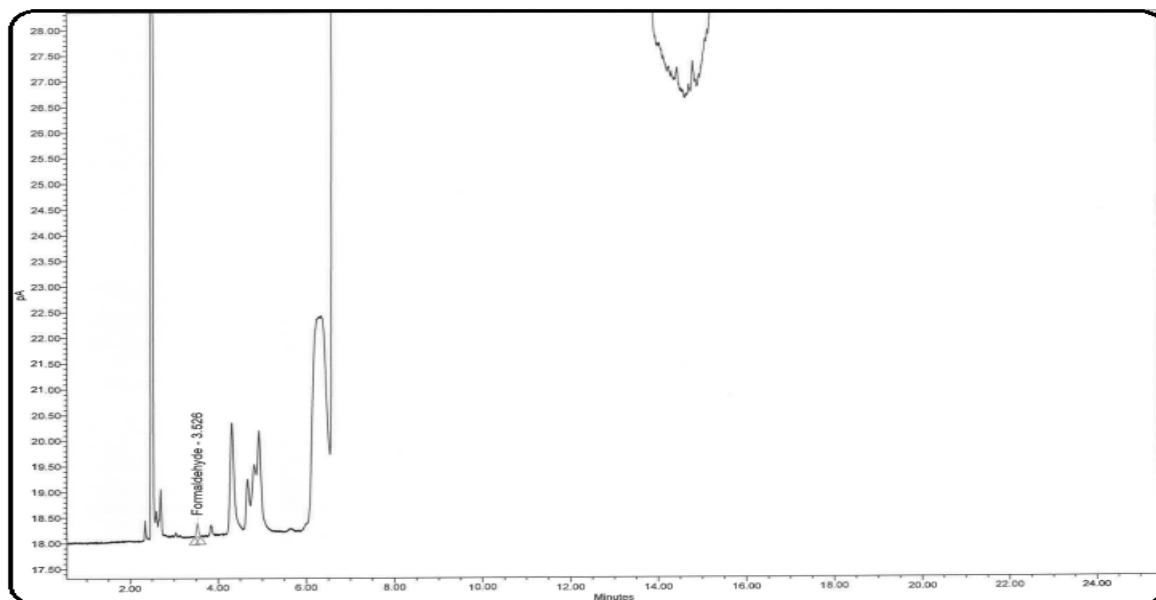


Fig-5: Limit of Detection Chromatogram.

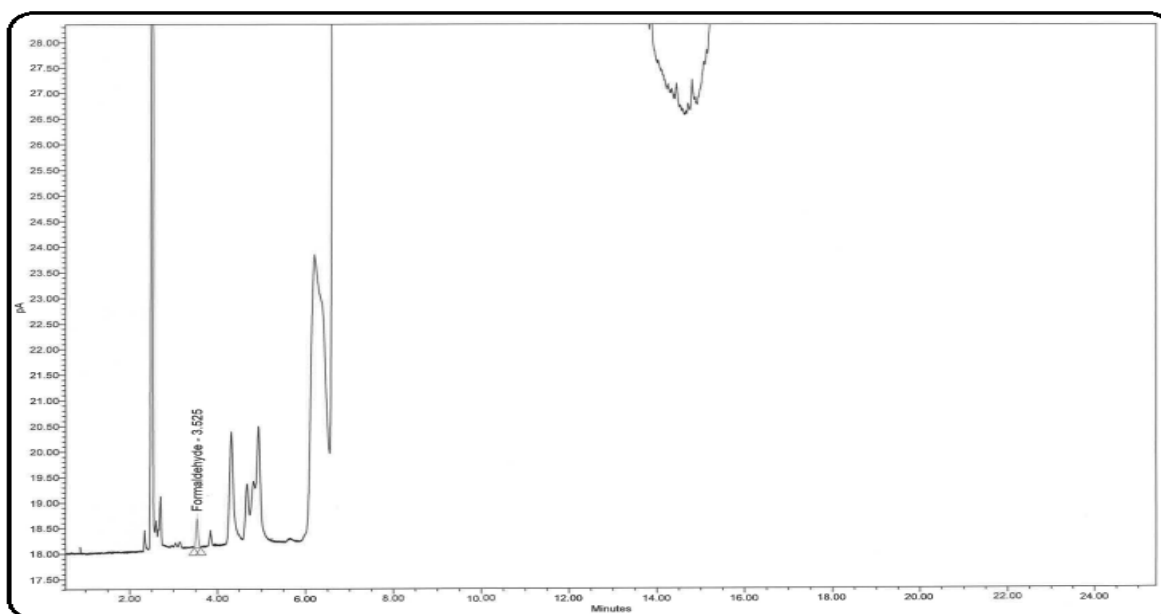


Fig-6: Limit of Quantification Chromatogram.

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