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*NOTE*

# Gas Chromatographic Determination of Methyl-isonicotinate in Methyl-isonipecotinate

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A simple, fast and accurate gas chromatographic method has been developed for the determination of isonicotinic acid as an impurity in isonipicotic acid. The analysis was carried out on Perkin-Elmer GC and the column used was DB-5 (30 metres, 0.53 mm ID and 2.65 μ film thickness). The plot area of isonicotinic acid *vs.* respective concentration of isonicotinic acid is found linear in the range 0.1–1.0% with correlation coefficient 0.9997.

**Key Words: Gas chromatography, Isonicotinic acid, Isonipecotic acid.**

Literature surveys show that no methods nave been reported towards the determination of methyl isonicotinate. Siegmund *et al.*[1] have reported the development of a simple sample preparation technique for gas chromatographic-mass spectrometric determination of nicotine. As isonicotinic acid and isonipecotic acid have very high melting points, these could not be analyzed on gas chromatography. It is also difficult to analyze these acids on high performance liquid chromatography because both the acids do not show ideal spectrum. Thus it is necessary to monitor isonicotinic acid while synthesizing isonipecotic acid using modern chromatographic technique by which it can be detected up to ppm level. On account of the above points it was essential to derivatise isonicotinic acid and isonipecotic acid into their methyl esters by esterification reaction. Then both the esters were monitored using gas chromatographic technique. Methanol HPLC grade supplied by E. Merck India Ltd. and working reference standards of isonicotinate and isonipicotinate were used.

**Chromatographic condition:** Instrument: Perkin-Elmer GC coupled with Turbochem Navigator software; Column: DB-5, 30 m × 0.53 mm internal diameter × 2.65 μ film thickness; Detector: flame ionization detector; Carrier gas: nitrogen; Injector temperature: 230°C; Detector temperature: 250°C; Oven temperature: 100°C (0 min) @ 10°C to 270°C (5 min); Column flow: 5.0 mL/min; Split ratio: 1 : 20; Injection volume: 1 μL.

The response for both the acids was found good. The retention time for isonicotinate was found at 5.60 min while for nipicotate 6.20 min. The response factor was checked for isonicotinate at 0.10, 0.20, 0.50, 0.75 and 1% levels by spiking the solution of isonicotinate in isonipecotinate and the values obtained with respect to isonipecotinate were 0.12, 0.24, 0.62, 0.90 and 1.25% respectively, which shows that isonicotinate has more response as compared to isonipecotinate and the value is about 1.25 times more.

**Preparation of solution:** Isonicotinate stock solution: 10 mg of isonicotinate dissolved in 100 mL methanol (100 ppm). Isonipecotinate stock solution: 1000 mg of isonipecotinate dissolved in 100 mL methanol (10,000 ppm).

**Preparation of solutions for linearity:** 1, 2, 5, 7.5 and 10 mL of isonicotinate stock solution was transferred into 100 mL volumetric flask and 10 mL of isonipecotinate stock solution was transferred and volume made up with methanol. Five linearity levels were prepared by diluting standard stock solution as given above, area obtained for each concentration is given in Table-1 and linearity graph was plotted as shown in Fig. 1.

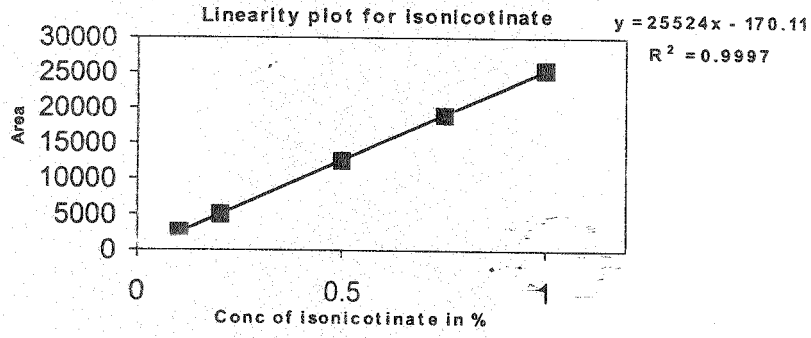


Fig. 1. Linearity plot for isonicotinate

TABLE-1
AREA ATTRIBUTED TO CONCENTRATION OF ISONICOTINATE

| S.No. | Concentration of isonicotinate (%) | Area counts |
|---|---|---|
| 1. | 0.10 | 2505 |
| 2. | 0.20 | 4891 |
| 3. | 0.50 | 12546 |
| 4. | 0.75 | 18762 |
| 5. | 1.00 | 25531 |

**Recovery:** To study the accuracy, reproducibility and the precision of the proposed method, recovery experiment was carried out by adding standard Isonicotinate at three different levels in presence of isonicotinic acid and isonipicotic acid at 1% level to check the interference of isonicotinic acid and isonipicotic acid. The values obtained in the recovery study are given in Table-2.

TABLE-2
RECOVERY STUDY OF ISONICOTINATE

| S.No. | Concentration of isonicotinate (%) | Standard area for 1% solution free from raw materials | Standard area after adding known quantity of standard area | Recovery (%) |
|---|---|---|---|---|
| Level-1 | 2 | 25531 | 51699 | 101.24% |
| Level-2 | 5 | 25531 | 129550 | 101.48% |
| Level-3 | 10 | 25531 | 510661 | 100.00% |

The $r^2$ value found, 0.9997, which shows the response, is linear from 0.1% level to 1.0%. High percentage of recovery shows that the method is free from interference of raw material. The recovery values prove that the method is accurate and reproducible.

## REFERENCES

1. B. Siegmond, E. Leitner and W. Pfannhauser, *J. Chromatogr. A.*, 840, 249 (1999).

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