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THE NITROGEN–PHOSPHORUS DETECTOR AND ITS APPLICATIONS IN GAS CHROMATOGRAPHY

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SUMMARY

A new detector for gas chromatography is described. This stable detector is extremely sensitive to nitrogen- and phosphorus-containing compounds and is highly selective, having much less response to hydrocarbons, chlorine- and sulfur-containing compounds. The device uses an electrically heated novel alkali metal salt and a conventional flame ionization detector jet and block assembly. Ionization of the compounds occurs in a low-temperature plasma rather than a flame. The unique properties of this design allow detection of nitrogen-containing compounds without HCN bonding, such as underivatized barbiturates. The detector has a linear dynamic working range of greater than 10^4 for both nitrogen and phosphorus compounds. The minimum detectable level is improved by using 8% hydrogen-in-helium in place of hydrogen. The device has widespread application in drug screening and pesticide analysis, where many samples can be analyzed without prior clean-up.

INTRODUCTION

The emission of positive ions from heated metallic surfaces was described as early as 1904[1]. This emission was usually considered to result from alkali impurities in heated platinum wire. In addition, the emission was found to increase in the presence of halogen-containing vapors[2]. On the assumption that alkali metals were playing a key role in the thermionic phenomena, several studies on various alkali salts and glasses were initiated. In 1936, the emission of positive ions from alkali metal silicates was described by Blewett and Jones[3] and in 1951 a patent was granted to Rice[4] for an ion source consisting of a ceramic cylinder coated with alkali salts and glasses. The first detector utilizing the thermionic principle was a device described by Cremer and her coworkers for the detection of halogenated compounds[5]. Karmen and Giuffrida[6], Karmen[7,8], Giuffrida[9], and Giuffrida *et al.*[10,11] developed the first device for the detection of phosphorus and chlorinated hydrocarbons after elution from

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a gas chromatographic (GC) column, and Giuffrida was awarded a patent in 1968[12]. The first applications of an alkali flame detector for detection of organic nitrogen-containing compounds were described in 1966 by Wells[13] and Aue *et al.*[14]. Since that time, a number of detectors have been described and have found wide application in the determination of sulfur-, nitrogen-, phosphorus-, arsenic- and lead-containing compounds[15–22]. A complete review of thermionic detectors has been completed by Brazhnikov *et al.*[23] and a shorter presentation[24] describes alkali ionization detectors to 1970.

In general, these detectors have been construction modifications of the conventional flame ionization detector (FID). Unlike the FID, these devices have long been plagued with instabilities, which have made them unreliable for routine use. Many of the problems resulted from the use of alkali halides and the methods of heating used to generate the thermionic emission. Frequently, the flame was used both for combustion of the hydrocarbons and as the heating source. In 1966, Abel *et al.*[25] suggested electrically heating the ion source. This process was tried by Prager and Deblinger[26] in 1966 and later incorporated into a working detector[21]. Although the alkali metal salts did give satisfactory performance, other materials have also been used with success. Alkali-doped glass was described by Prager and Deblinger[26] and later used in a commercial detector[21]. Detectors of this type have improved stability but their performance is still markedly dependent on shape and temperature of the flame area and have been reported[21] to have little or no response to compounds which do not contain HCN chemical bonding.

The detector described in this paper uses an electrically heated novel alkali metal salt which allows rapid and reproducible detector turn-on, long-term stability, and high selectivity and sensitivity for both phosphorus- and nitrogen-containing organic compounds. Furthermore, the unique properties of the source and detector design allow detection of nitrogen-containing compounds without HCN bonding, such as underivatized barbiturates.

EXPERIMENTAL

A Hewlett-Packard Model 5700 gas chromatograph, equipped with a dual nitrogen–phosphorus flame ionization detector (N–P FID), was used for all chromatographic studies. All chromatograms were recorded on a Hewlett-Packard Model 7130 pen recorder. The columns and conditions used for the various studies are listed where appropriate. The plasma gases were hydrogen at a flow-rate of 3.7 ml/min or 8% hydrogen-in-helium at 30 ml/min and air at 100 ml/min for all studies. Typical operating parameters for the N–P FID are shown in Table I.

TABLE I

OPERATIONAL PARAMETERS FOR THE N–P FID

Carrier gas	Nitrogen or helium
Offset at zero suppression	$1.6 \cdot 10^{-11}$ A
Plasma gases (flow-rate)	Air (30–100 ml/min)
	Hydrogen (1.0–5.0 ml/min) or 8% hydrogen-in-helium (15–60 ml/min)

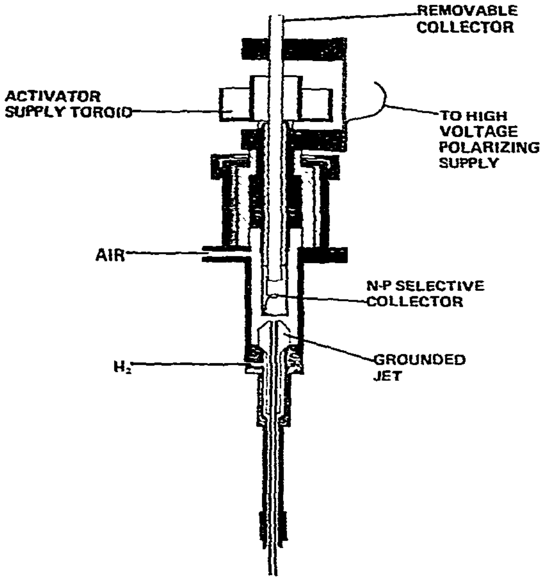


Fig. 1. Cross section view of the nitrogen-phosphorus detector. (Grounded jet = conventional FID-jet.)

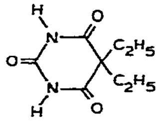
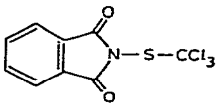
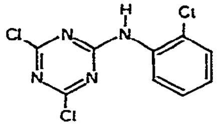
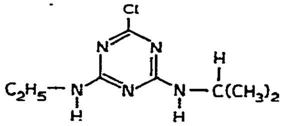
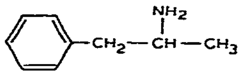
THEORY OF OPERATION

The Hewlett-Packard N-P FID operates using the conventional FID block. As shown in Fig. 1, the normal flame collector assembly is replaced with a collector that has a ceramic cylinder coated with an alkali salt activator similar to that described by Rice[4]. This cyclinder is suspended in the geometric center of the collector and is electrically heated by a step-down transformer to a dull red. A −240-V potential is applied to the collector for species collection and the thermionic emission is measured with the conventional FID electrometer. The flame is not ignited, but rather a low-temperature plasma is generated. In this way, the plasma is required only for ion formation and dissociation of the organic compounds and is not involved in the heating of the thermionic ion source. Once the collector height is set at approximately 0.05 in. above the jet and the hydrogen and air flows are established, the background current is adjusted by varying the potential applied to the cylinder. This current is determined by the extent of thermionic emission and is typically adjusted to 10% of full scale at 1×32, or $1.6 \cdot 10^{-11}$ A, with zero suppression.

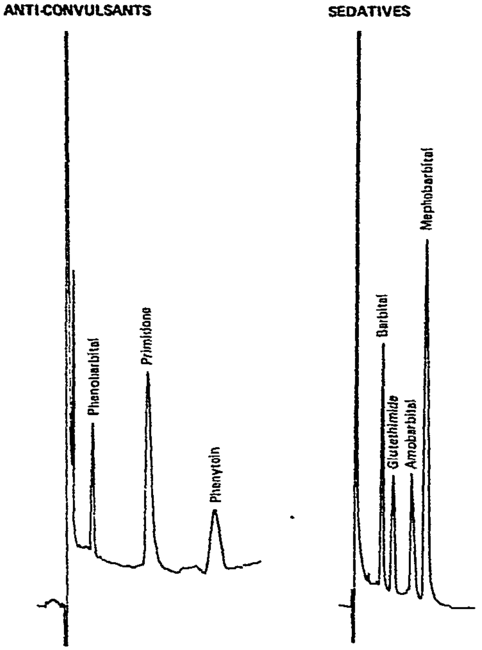
The exact nature of the response is not completely known. Several mechanisms have been proposed and are reviewed by Sevick[27] and Brazhnikov *et al.*[23]. In general, it is believed that the background current is a result of the ionization of the vaporized alkali atoms and the subsequent formation of M^+ (refs. 14, 23, 27, 28). The reactions which occur when nitrogen and phosphorus compounds enter the detector chamber are not understood. It has been suggested[14,21,22] that the organic molecules containing nitrogen are pyrolyzed to form cyano radicals which remove an electron from the vaporized alkali. These cyanide ions then combine at the collector to form hydrogen cyanide and thereby generate the output signal. The ionized alkali returns to the source surface to be re-vaporized. Proof for this mechanism has been offered in the fact that certain detectors do not have response to compounds in which HCN bonding does not exist: for example, underivatized barbiturates. The mechanism does not describe the response of the Hewlett-Packard detector because the collector potential is negative. In addition, it responds quite well to barbiturates and pesticides which contain vicinal carbonyl groups and no HCN bonding. By examining Table II, it is readily apparent that excellent response is achieved for a wide variety of chemical structures. Two compounds of particular note are barbital, which does show slightly reduced response, and Folpet®, which was selected as a model compound because of its interesting chemical structure. The nitrogen in Folpet, even though bonded to two vicinal carbonyl groups and a sulfur atom, apparently reacts to form an appropriate species for response. Thus, this detector is useful for the detection of a variety of nitrogenous compounds at low concentrations, as is illustrated by Figs. 2 and 3 for barbiturates and amphetamines.

TABLE II

RESPONSE OF MOLECULAR STRUCTURES STUDIED

Compound	*Structure*	*g Hetero atom per sec*
Barbital		$2.5 \cdot 10^{-13}$
Folpet		$7.5 \cdot 10^{-14}$
Dyrene		$6.9 \cdot 10^{-14}$
Atrazine		$5.4 \cdot 10^{-14}$
Amphetamine		$4.1 \cdot 10^{-14}$

Regardless of the mechanisms for response, the N–P FID is an extremely sensitive and selective detector. Fig. 4 demonstrates that even concentrations of 1.7·



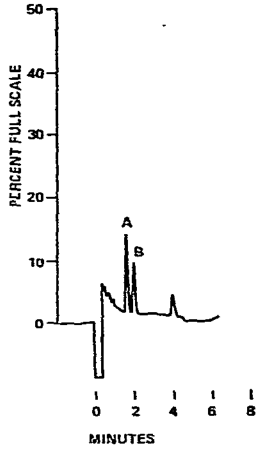


Fig. 2. Analysis of anti-convulsants and sedatives using the N–P FID. Concentration, approx. 1 ng of each; liquid phase, 0.25% NPGS + 0.025% H_3PO_4.

Fig. 3. Analysis of amphetamines, (A) 270 pg amphetamine and (B) 150 pg methamphetamine. Conditions: column, 6 ft. × 2 mm I.D. glass, 10% Apiezon L + 2% KOH on Chromosorb W AW DMCS HP (80–100 mesh); oven, 200°; N–P FID, 300°; carrier gas (helium) flow-rate, 30 ml/min; attenuation, 1 × 4.

10^{-4} g octadecane cause almost no response, while concentrations of $6.67 \cdot 10^{-12}$ g azobenzene can easily be detected. Selectivities of 35,000 g carbon per g nitrogen and 75,000 g carbon per g phosphorus are easily attainable with this detector. It is also interesting to note the negative solvent response and extremely low noise level. The noise level is actually lower than that of many conventional FIDs. The detector is linear for both phosphorus and nitrogen for a full 4 orders of magnitude. These linear ranges and sensitivities are achieved without adjustment of plasma gas flows or changes of source polarity when detecting phosphorus or nitrogen.

Operational specifications for this detector are given in Table III. As noted in this table, the performance of the detector is improved considerably by the use of a mixed plasma gas (8% hydrogen-in-helium) in place of 100% hydrogen. This property is a result of better flow stability at the higher flow-rate (30 ml/min) used with the mixed gas as compared with 3.7 ml/min with pure hydrogen.

The detector has an extremely long life time under conditions of normal operation. The rugged design permits rapid disassembly and cleaning with common solvents, except acids, should the collector assembly become fouled. After cleaning, the collector can be re-positioned in the detector housing and operation resumed immediately.

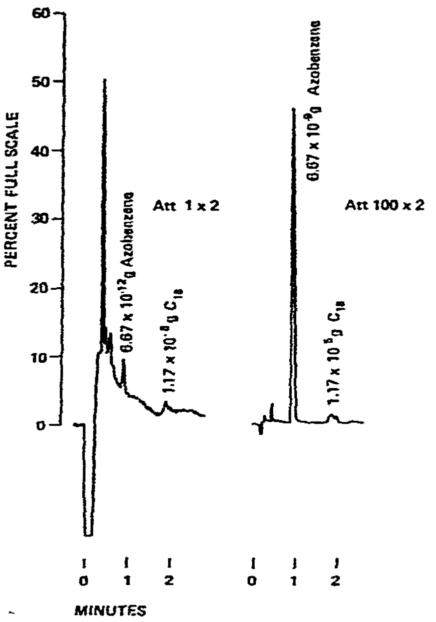


Fig. 4. Selectivity and sensitivity of N-P FID. Conditions: column, 4 ft. × 2 mm I.D., 3% OV-1 on Chromosorb W-HP (80–100 mesh); oven, 180°; N-P FID, 300°; helium flow-rate 30 ml/min.

TABLE III

SPECIFICATIONS OF THE N-P FID

Parameter	*Nitrogen*	*Phosphorus*
Minimum detectable level (2 noise*/signal)	$< 1\cdot10^{-13}$ g N per sec** (8% H_2/He support gas) $< 4\cdot10^{-13}$ g N per sec** (H_2 support gas)	$< 5\cdot10^{-14}$ g P per sec*** (8% H_2/He support gas) $< 2\cdot10^{-13}$ g P per sec*** (H_2 support gas)
Selectivity	$3.4\cdot10^4$ g C§ per g N**	$7.5\cdot10^4$ g C per g P***
Linearity	$> 10^4$**	$> 10^4$***

* Noise was measured peak-to-peak with 0.02 to 2 Hz bandwidth.
** As azobenzene.
*** As malathion.
§ As octadecane.

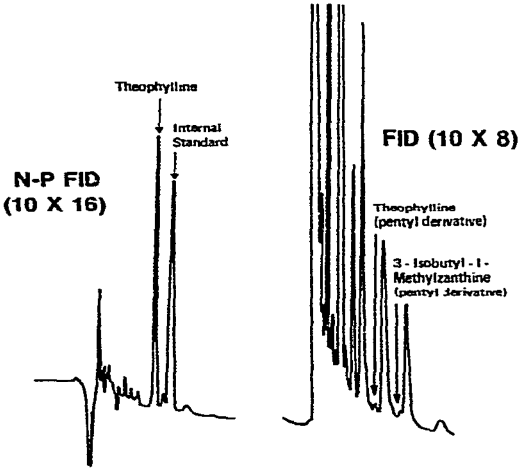
APPLICATIONS

Many types of columns have been used successfully with this detector. As shown in Fig. 2, a phosphoric acid-treated column has been used with great success for free barbiturates. The phosphoric acid caused no decrease in detector life time or stability, although the noise level is higher because of the response to the phosphorus column bleed. Columns of this type should not be used with solvents such as methanol since the solvent washes appreciable phosphoric acid from the column, which causes a detector response similar to a solvent tail. As shown in Fig. 3, columns treated with potassium hydroxide have also been used with the N-P FID with no adverse effects.

The sensitivity and selectivity of the N–P FID for nitrogen containing compounds make it very useful in the clinical laboratory. The analysis of theophylline in serum may be used as an example. A method was initially developed for use with the FID[29]. This method required 1 ml of serum and involved a back-extraction step. When a nitrogen-sensitive detector became available, the method was modified[30] to require only 20 μl of serum and the back-extraction step was eliminated. Fig. 5 shows chromatograms of serum containing theophylline which was extracted and derivatized by the second method[30]. The first chromatogram was run with the N–P FID and the second chromatogram was run with a standard FID. It is apparent that identification and quantitation of theophylline is easily accomplished with the N–P FID, but it would not be possible to quantitate the FID response without additional sample clean-up and concentration steps.

The stability of the detector is excellent. In one study, the Hewlett-Packard Model 7671 Automatic Liquid Sampler was used to inject 199 samples containing 1.4 ng each of amphetamine, methamphetamine, and diphenylamine. The Hewlett-Packard Model 3380 Reporting Integrator was used to record and calculate the results, using diphenylamine as the internal standard. The mean amounts calculated for the 199 runs were 1.47 ng and 1.41 ng for amphetamine and methamphetamine, respectively; the standard deviations were less than 5%.

The N–P FID has shown no response to sulfurous or chlorinated compounds. In fact, as shown in Fig. 6, methylene chloride may even be used as a solvent. Chlorinated solvents may cause a loss in sensitivity, but this is a reversible, non-destructive change and such solvents may be used with care. This allows use of the N–P FID for the analysis of many extracts without evaporation to dryness and reconstitution in another solvent. Because this is a trace detector, solvents must be extremely pure and



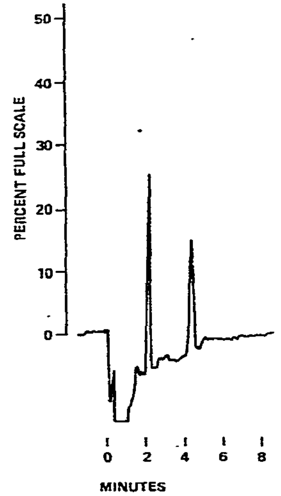


Fig. 5. Comparison of N–P FID and FID responses to theophylline in serum extract. Column 1.8 m × 2 mm I.D., 3% OV-17 on Chromosorb W-HP (80–100 mesh); Column temperature, 260°.

Fig. 6. Analysis of nor-acetyl and pivaloyl choline in methylene chloride (10 pmoles of each). Conditions: column, 6 ft. × 2 mm I.D., 5% OV-1 + 5% dodecyldiethylene triamine succinamide on Gas-chrom Q; N–P FID, 300°; helium flow-rate, 30 ml/min; attenuation, 1 × 4.

care must be used in cleaning glassware and syringes to prevent interferences and cross contamination. In addition, peaks are often observed from contaminants absorbed on syringe needles left exposed to lab air.

The N–P FID can rapidly be converted to conventional flame ionization operation by simply changing the collector and adjusting the combustion gas flow-rates. Furthermore, the FID can be rendered auto-igniting by simply using the special collector and applying current to the ignitor using the power supply which is used to heat the alkali source.

CONCLUSIONS

A novel nitrogen–phosphorus detector has been developed. This detector operates in both nitrogen and phosphorus modes without change in polarity or gas flows and shows outstanding selectivity over hydrocarbons, sulfurous and chlorinated compounds. The device shows high sensitivity to compounds such as underivatized barbiturates to which other alkali flame detectors have been reported to have little or no response, and is, therefore, suitable for use with a wider variety of nitrogenous compounds. In addition, the ease of operation and stability of this detector make it suitable for routine use.

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