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GLC Determination of Methaqualone in Plasma

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Abstract □ A simple GLC method was developed for the determination of methaqualone in plasma. The method is rapid and quantitative over the 0.1–1.0-mcg./ml. range.

Keyphrases □ Methaqualone—GLC determination in plasma □ GLC—determination of methaqualone in plasma

Methaqualone, 2-methyl-3-*o*-tolyl-4(3*H*)-quinazolinone, is a well-known compound which has been available for use as a hypnotic since 1960. Determination of this drug in biological fluids has been investigated using spectrophotometric (1) and GC (2, 3) procedures. The former technique is not suitable for precise measurement because of high blank values, while the latter procedure, which eliminates the blank problem, is tedious and time consuming. In addition, it requires 5.0 ml. of plasma. This report describes a GC method for the determination for methaqualone that is simple, rapid, and reliable.

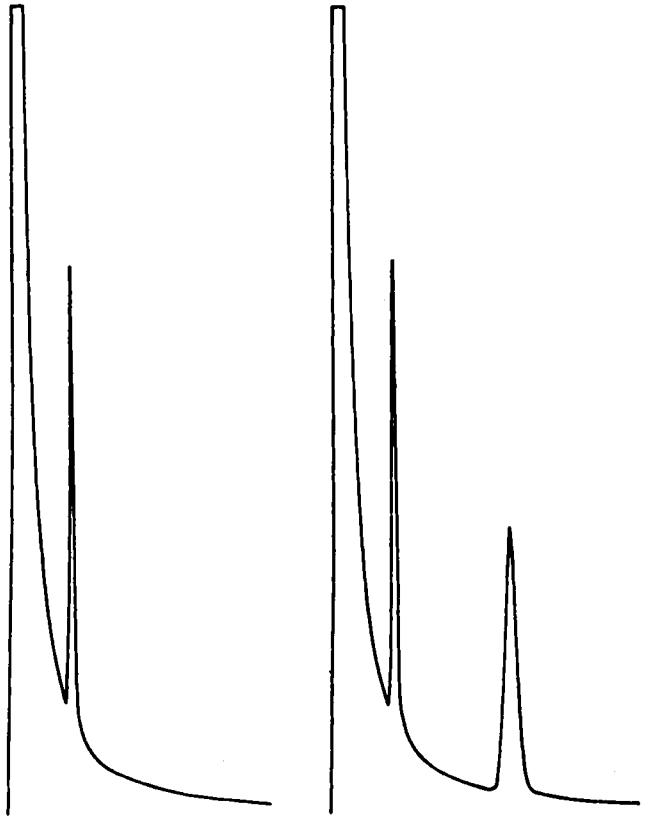

Figure 1—*Gas chromatograms of plasma treated as described. Left: chromatogram from normal plasma. Right: chromatogram from normal plasma with 0.5 mcg./ml. of methaqualone added.*

Table I—Recovery of Methaqualone from Plasma

Methaqualone Added, mcg./ml.	Methaqualone Recovered, mcg./ml.	Percent Recovery[a]
0.20	0.14	70
0.50	0.37	74
1.0	0.77	77
2.0	1.4	70
5.0	3.5	70
10.0	6.9	69
	Average	71.7 ± 1.3[b]

[a] Recoveries are based on a comparison to GC response to pure solutions of methaqualone. [b] Standard error.

Table II—Methaqualone Plasma Concentrations (Micrograms per Milliliter) in Human Subjects[a]

Methaqualone Dose, mg.	Hours						
	0	0.25	0.5	1	2	4	8
400	None detected	0.6	1.7	2.3	1.4	1.1	0.5
800	None detected	1.1	2.3	3.5	4.3	3.5	2.0

[a] Each value given is an average of three subjects.

EXPERIMENTAL

GC—A dual-column gas chromatograph[1] equipped with a hydrogen flame-ionization detector and a 1-mv. recorder[2] was employed. The chromatographic columns used were 0.6-m. (2-ft.) × 0.6-cm. (0.25-in.) glass tubes packed with 3% XE-60 on 100–120-mesh Gas Chrom Q[3]. The instrument settings were: column temperature, 180°; injection port temperature, 240°; and detector block temperature, 230°. Gas flow rates were: hydrogen, 25 ml./min.; and helium (carrier gas), 50 ml./min. Sensitivity settings were: range, 10; and attenuation factor, 2×. The retention times under these conditions were 1.6 min. for butyl stearate and 4.5 min. for methaqualone (Fig. 1).

Reagents—The reagents were redistilled chloroform[4] and butyl stearate[4].

Procedure—Plasma, 1.0 ml., was made alkaline with 0.05 ml. of 1 *N* NaOH, and 0.2 ml. of chloroform containing 0.5 mcg./ml. of

[1] F & M model 402.
[2] Minneapolis-Honeywell.
[3] Applied Science.
[4] Regis Chemical.

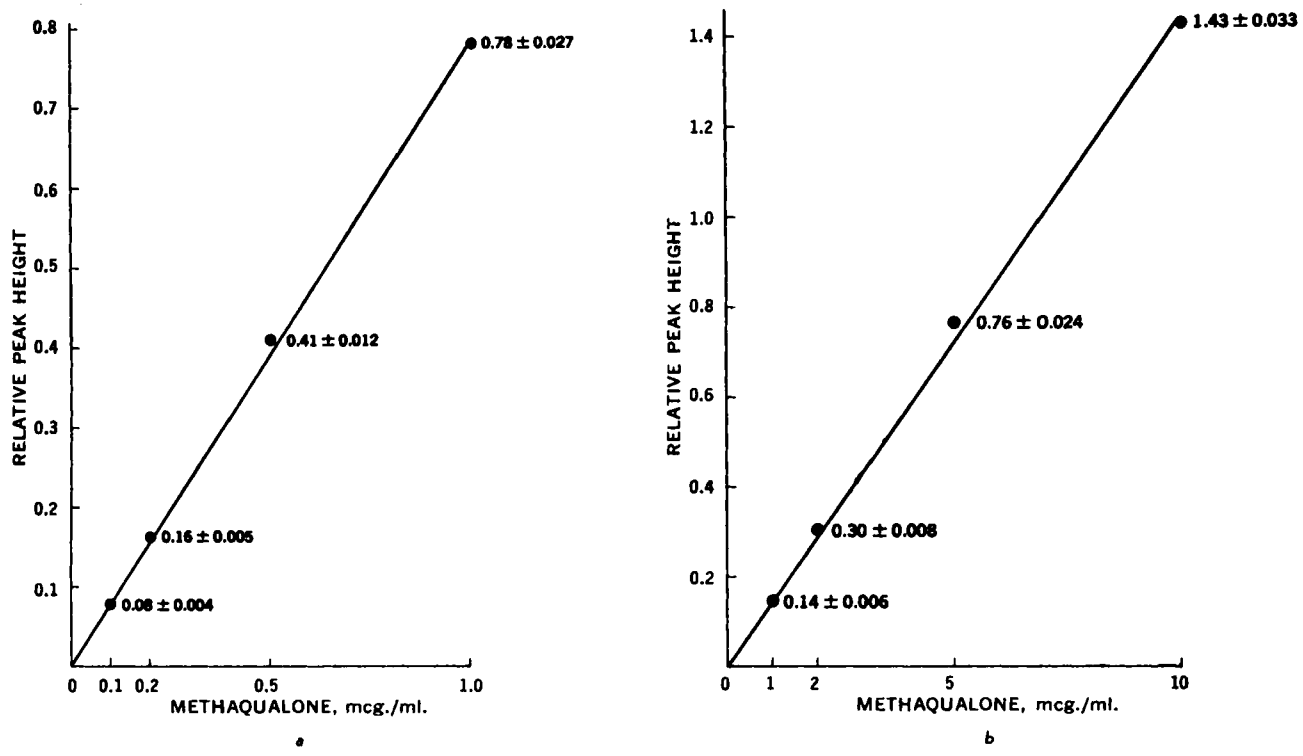

Figure 2—*Relationship between relative peak height and methaqualone concentration in plasma. Key:* a, *0.1–1.0 mcg./ml.; and* b, *1.0–10.0 mcg./ml.*

butyl stearate was added. The mixture was swirled using a Vortex mixer for 20 sec. and then was centrifuged for 10 min., and the aqueous layer was aspirated. One hundred microliters of the chloroform solution was transferred to a clean tube, and the solvent was removed under a stream of nitrogen. The residue was dissolved in distilled chloroform, 25 μl., and 2.6 μl. of this solution was injected into the gas chromatograph. The concentration of methaqualone was determined by the relative peak height method, using butyl stearate as internal standard.

RESULTS AND DISCUSSION

The relationship between relative peak height and methaqualone concentration in the range of 0.1–1.0 mcg./ml. of plasma is shown in Fig. 2*a*. The reproducibility of the procedure, as indicated by the standard error of quadruplicate determinations, is also shown. Concentrations of methaqualone greater than 1.0 mcg./ml. can readily be determined using the same extraction technique while omitting the chloroform concentration step. In this procedure, an aliquot of the chloroform solution was injected directly into the gas chromatograph after aspiration of the aqueous layer. The results obtained with plasma concentrations of 1.0–10.0 mcg./ml. are shown in Fig. 2*b*.

The extraction technique effectively separates methaqualone from normally interfering plasma constituents since determinations with normal plasma give little or no blank (Fig. 1). About 70% of the plasma methaqualone is reproducibly extracted regardless of drug concentration (Table I) over a range of 0.2–10.0 mcg./ml.

The blood-depletion pattern of methaqualone was studied by this procedure following oral administration of this drug to human subjects. The results obtained (Table II) are similar to those reported previously by Berry (2). The drug reached only low levels in the plasma, probably due to its rapid uptake by adipose tissue (4). A 400-mg. dose gave a peak plasma level at about 1 hr., while with a higher dose, 800 mg., the peak plasma level was obtained at 2 hr.

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