TABLE II.—COMPUTATION OF CALCULATED VALUE OF THE Me_{50} 9.25 MCG./KG. FOR DONNA (CBA)

Alkaloid	Concentration in Donna	Actual Me_{50} 9.25 mcg./Kg.
Hyoscyamine sulfate	1037 × 0.01316	= 13.6469
Atropine sulfate	194 × 0.03000	= 5.8200
Hyoscine hydrobromide	65 × 0.00685	= 0.4453
	1296	19.9122[a]

[a] $\frac{19.9122}{1296}$ = 0.01536 mg./Kg. of Donna is the calculated value of the Me_{50} 9.25 mcg./Kg.

TABLE III.—ANTISPASMODIC ACTIVITY IN COMPARISON WITH ATROPINE SULFATE

Drug	Me_{50} 9.25 mcg./Kg.	Potency Compared to Atropine Sulfate
Atropine sulfate	0.0300	1.0
Hyoscyamine sulfate	0.01316	2.28
Hyoscine hydrobromide	0.00685	4.38
CBA	0.01120	2.68

cholinergic agents generally. The potency of such agents may be assessed in the procedure on the basis of comparison with an established standard. The advantage claimed for the method is that it is carried out in the intact dog without the necessity for surgical intervention in the placement of the sensing element. Thus, the same group of animals can be used repeatedly and without lengthy preparation in the determination involved.

The method developed has made possible a comparison of the relative effectiveness of the individual components of the combination CBA with the relative effectiveness of the combination. The results obtained have indicated potentiation of action in the combination.

Although atropine, hyoscyamine, and hyoscine were administered intravenously, it is very likely that similar results would be produced by oral administration, since these alkaloids are well absorbed from the gastrointestinal tract. Synthetic blockers should be studied, to be sure, by several routes of administration, since an agent which shows considerable cholinergic blocking activity parenterally could fail to achieve clinical usefulness because of poor absorption from the gastrointestinal tract.

Another possibility for further application of the method involves the direction of the alteration of the concentrations of the various alkaloids in such combinations as CBA in order to achieve an optimum combination of the component alkaloids, *i.e.*, one providing the greatest potentiation of the therapeutic benefits of the components consistent with the lowest incidence and least severity of untoward side effects.

SUMMARY

A biological assay employing the surgically intact dog is used to determine the relative activity of atropine sulfate, hyoscyamine sulfate, and hyoscine hydrobromide both alone and in combination on the gastrointestinal tract.

Indication of potentiation in the antispasmodic activity of CBA is provided by a comparison of the experimentally determined activity with the activity calculated from the activities of the components.

REFERENCES

(1) Luduena, F. P., and Lands, A. M., *J. Pharmacol. Exptl. Therap.*, **282**, 110(1954).
(2) Seevers, M. H., and Gray, G. W., *ibid.*, **113**, 319(1955).
(3) Quigley, J. P., *Proc. Soc. Expll. Biol. Med.*, **36**, 450 (1937).

ERRATUM

In the paper titled "Effects of Ionizing Radiation on Two Gelatin Fractions I. Material Preparation, Dosimetry, and Acid-Base Behavior" (1), the caption for Fig. 3 should be revised to read: ". . . after 5% dispersions of each were subjected to an irradiation dose of 2.0 Mrads."

(1) Prusak, L. P., and Sciarrone, B. J., THIS JOURNAL, **51**, 1046(1962).