Greenlee et al (1978) have reported baclofen to significantly displace ^{3}H-GABA binding at 100 μM though the IC50 was rather higher. In human post-mortem brain tissue, Iversen (1978) has reported baclofen to displace ^{3}H-GABA binding with an IC50 of 80 μM.

Baclofen has been shown to induce an increase in Cl^- influx in crayfish muscle, competition studies with GABA suggesting an action on the same receptor (Olsen et al 1978). Similarly, recent electrophysiological studies have shown baclofen to produce GABA-like, bicuculline sensitive effects (Fox et al 1978). Our own behavioural studies have indicated that baclofen may be a partial agonist or dualist at the GABA receptor, and that these effects are weakly sensitive to antagonism by picrotoxin (Waddington & Cross 1979). These studies suggest that baclofen can weakly interact directly with GABA receptors and that this effect occurs at concentrations considerably below those active on GABA release mechanisms.

However, the GABAergic activity of baclofen is substantially less than that of potent and specific GABA agonists such as muscimol. It should not be overlooked that the most potent action of baclofen may be to inhibit release of excitatory amino acid neurotransmitters (Potashner 1978; Fox et al 1978), in a manner stereospecific for the (—)-isomer (Ault & Evans 1978). At much higher concentrations of baclofen, GABA receptors may be stimulated directly and this effect does not show stereospecificity (Cross & Waddington 1978).

In discussing the therapeutic potential of baclofen, particularly in schizophrenia, Kerwin & Pycock (1978) have failed to note both that reduced activity of the GABA-synthesizing enzyme glutamic acid decarboxylase in postmortem brain tissue from schizophrenic patients is not a replicable finding (McGeer & McGeer 1977; Crow et al 1978) and that placebo-controlled trials of baclofen in schizophrenia have clearly indicated its lack of antipsychotic effect (Gulmann et al 1976; Bigelow et al 1977).

In the light of its duplicity of action and low potency, baclofen would seem to be a poor pharmacological tool for the study of GABAergic mechanisms in experimental animals and in the clinic.

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An observation on the determination of thiomersol at preservative concentration by flameless atomic absorption spectroscopy

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The determination of organomercurial compounds by flameless atomic absorption spectroscopy is a well established technique involving oxidative digestion of the compound to inorganic mercury and subsequent reduction to atomic mercury with stannous chloride (Thompson & Hoffman 1975; Ure 1975).

In a study of the organomercurial preservative content of eye drops, Calder & Miller (1976) reported a rapid (5–10 min) cold sulphuric acid-perchloric acid digestion procedure which was claimed to give complete recovery of mercury from solutions containing phenylmercuric nitrate and acetate and thiomersal. During investigations into the stability of thiomersal (Meakin & Khammas 1978) we have been unable to repeat this finding, even after prolonged treatment with the cold digestion mixture. Fig. 1 shows plots of absorbance against concentration (ppm of mercury) in the sample to be treated for solutions of thiomersal (B.P. quality recrystallized from 95% ethanol, M.P. 229 °C, acidimetric assay 101·8%) subjected to the cold sulphuric acid-perchloric acid process (A) and a more conventional hot permanganate-sulphuric acid digestion process (B). The absorbance obtained for solutions of mercuric chloride ($HgCl_2$ content 99·8%) is shown for comparison. Absorbances were measured on a Hilger-Watts H1170 Atomspek fitted with a mercury cold

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Table 1. Linear regression data for the effect of cold (A) and hot (B) digestion procedures on the atomic absorbance-concentration plots for thiomersal.

Conc. (% × 10^4)[1]	Concentration mercury (ppm)[1]	Digestion process	Slope	s.d. slope	Intercept	s.d. intercept	Correlation coefficient
Thiomersal 5–20	2·5–10	A	0·0629	0·0044	−0·005	0·030	0·9951
Thiomersal 1–3	0·5–1·5	B	0·338[2]	0·0096[2]	−0·004	0·009	0·9984
Mercuric chloride 0·5–3·0	0·4–2·3	—	0·337[2]	0·0034[2]	−0·003	0·005	0·9998

[1] Concentration in the 1 ml sample subjected to digestion.
[2] $t_{calc} = 0·098$, $t_{tab} = 2·31$, $p = 0·05$.

vapour analyser kit similar to that described in the Pye-Unicam Product News, No. 72, September 1971.

A. *Cold digestion process (Calder & Miller 1976).* 1 ml of thiomersal solution (0·0005–0·002%) was added to 2 ml 72% AR perchloric acid and 5 ml AR sulphuric acid. After standing 10 min the mixture was diluted to 50 ml with double distilled water, transferred to the atomization apparatus and 2 ml of stannous chloride solution (10% AR, low in mercury stannous chloride in AR hydrochloric acid) added before aerating into the absorption cell.

B. *Hot digestion process.* 1 ml of thiomersal solution (0·00009–0·0003%) was refluxed with 10 ml of 10% AR potassium permanganate and 2 ml AR sulphuric acid for 45 min and after cooling, 4 ml of 20% AR hydroxylamine hydrochloride added. After dilution to 50 ml with double distilled water the mixture was transferred to the atomization apparatus and 2 ml stannous chloride reagent added.

Table 1 shows the results obtained from least squares linear regression analysis of the data plotted in Fig. 1, the *t*-test indicating the data for mercuric chloride and thiomersal subjected to hot digestion (A) are not significantly different, and that there is a quantitative conversion of thiomersal to mercury by this process. Replicate experiments showed the same result. The cold treatment (B) of Calder & Miller (1976) however, only gives an 18·6% conversion, and the slope to standard deviation ratio of the calibration plot is greater than that for process A. No significant change in the degree of conversion was noted when the 10 min digestion time reported by Calder & Miller (1976) was increased to 24 h. Two other analytical laboratories have also observed similar problems with the cold digestion method, obtaining similar levels of recovery to that reported here (Dr A. Fell 1978 personal communication; Mr G. F. Phillips, 1979 personal communication).

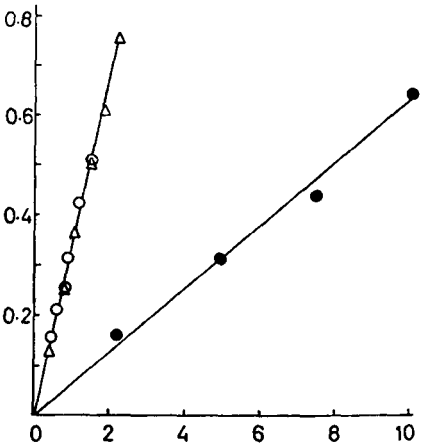

FIG. 1. Absorbance-concentration plots for thiomersal, subjected to cold (A) and hot (B) digestion processes, and mercuric chloride. Ordinate: absorbance. Abscissa: mercury concentration of sample (ppm). Open triangle, mercuric chloride; open circle, thiomersal, process B; closed circle, thiomersal process A.

These results would indicate that the cold digestion process, which is attractive because of its relative simplicity is a questionable technique in the determination of thiomersal.

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