& Snedden, 1968). There was a large variation in the changes produced but the significant fall in phenylephrine mydriasis after thymoxamine, 50 mg, compared with the placebo value indicates that sufficient drug or metabolite reached the pupillary tissue to produce some degree of receptor blockade.

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The stability of glyceryl trinitrate tablets

Tablets of glyceryl trinitrate based on mannitol may be expected to retain their potency for at least two years, as long as they are protected from light and stored in cool and dry conditions (British Pharmaceutical Codex, 1968). Nevertheless, it is sometimes implied that mannitol-based tablets deteriorate rapidly, and are of little use in the relief of anginal pain unless used within a year (Laurence, 1966) or even a few months (Mathews & Turck, 1969) of preparation. Any reduction in therapeutic effectiveness will be reflected in the hypotensive response to glyceryl trinitrate (Bernstein, Friesinger & others, 1966; Carson, Wilson & others, 1969). The effectiveness of mannitol-based glyceryl trinitrate tablets has been objectively assessed by measuring the hypotensive response of healthy young medical students to the same batch of tablets over three years.

Glyceryl trinitrate tablets (0·5 mg), prepared with a mannitol base, were stored in a capped brown glass bottle on an open shelf at room temperature. No special precautions were taken to protect the tablets from light. Placebo tablets, identical in appearance but containing only mannitol, were prepared at the same time (in 1967) and were similarly stored.

Each subject was given glyceryl trinitrate and the placebo at different times, and the effect on systolic blood pressure was measured with a sphygmomanometer by auscultation. The difference between the initial blood pressure and the value 6 min after sublingual administration of the drug or placebo was recorded; from these values, the hypotensive effect of glyceryl trinitrate in each subject was calculated.

The results (Table 1) are based on measurements in 133 sitting and standing subjects. In sitting subjects, the mean decrease in blood pressure produced by the drug declined from 10 mm Hg in 1967 to 7 mm Hg in 1969; differences between

these mean values were not statistically significant ($P > 0.05$). A similar response in normal subjects was observed by Besser, Curwen & Duncan (1966), on whose procedure the trial was based. In standing subjects, the mean response was greater (13–15 mm Hg). Throughout, there was a large variation in the hypotensive response in different individuals (Table 1). Approximately 70–80% of subjects complained

Table 1. *The hypotensive effect of glyceryl trinitrate during the three years of the study*

Year	Total number of subjects	Reduction in systolic blood pressure induced by 0·5 mg glyceryl trinitrate (mm Hg)					
		Standing			Sitting		
		Mean ± s.e.	Range	*P*	Mean ± s.e.	Range	*P*
1967	47	14 ± 3	7–22	—	10 ± 1	3–25	—
1968	46	15 ± 1	7–25	0·74	10 ± 2	0–24	0·90
1969	40	13 ± 3	4–21	0·81	7 ± 2	0–21	0·18

P represents the probability that the differences in the hypotensive response between 1967 and the two successive years are due to chance.

of headache of varying intensity, and in 5% of subjects the hypotensive response caused faintness. On chemical analysis two and a half years after their preparation, the tablets contained more than 85% of the stated amount of glyceryl trinitrate, and thus complied with the requirements of the British Pharmacopoeia (1968).

Although measurements were made by relatively inexperienced observers, the results suggest that the tablets retained their potency under ordinary conditions.

The hypotensive response probably reflects the efficacy of these tablets in the relief of ischaemic pain, it is therefore difficult to explain or account for any rapid deterioration in the clinical response to mannitol-based glyceryl trinitrate tablets in patients with coronary ischaemia. Since tolerance to organic nitrates develops and disappears rapidly, an apparent loss of potency might be due to this factor. Alternatively, the rapid deterioration of mannitol-based glyceryl trinitrate tablets may be illusory, and merely reflect the extension of views on chocolate-based tablets, whose limitations are well recognized (Bagnall & Stock, 1955).

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