

# LETTERS TO THE EDITOR

## Binding of Quinidine to Myocardial Cellular Components

SIR,—The distribution of quinidine in tissues has been studied by Hiatt and Quinn (1945) and Kelsey, Oldham and Geiling (1945). We are concerned with the intracellular localisation of quinidine in the cardiac tissue of the dog.

Sixteen healthy mongrel dogs, of both sexes, weighing 7 to 15 kg. were used. Quinidine sulphate (Merck), dissolved in distilled water with a few drops of 0.1 N H<sub>2</sub>SO<sub>4</sub> and neutralised to pH 7.0, was administered intravenously in a dose of 15 mg./kg. weight. Fifteen min. after the injection, samples of tissue from the left ventricle were excised under ether anaesthesia (our preliminary experiments demonstrated that the left ventricle attained the highest quinidine concentration). After removing fibrous tags and blood and thoroughly mincing with scissors, the tissue was homogenised in a chilled Monel-metal Waring blender with cold isotonic sucrose solution for exactly 2 min., the homogenate was passed through muslin to remove connective tissue and cell debris and finally made to volume as a 10 per cent homogenate. Ten ml. of the homogenate was then differentially centrifuged at 4° in an International Refrigerated Centrifuge, Model PR-2, and various components of the cell (nuclei, sarcosomes and supernatant fraction) were isolated by adopting the technique of Schneider and Hogeboom (1950) for liver. Microsomes, however, could not be separated in this way. For *in vitro* studies, 10 ml. of the 10 per cent homogenate was incubated with 20 µg. quinidine for 15 min. at 37°, followed by separation into the different fractions. Quinidine was estimated in duplicate samples on a Klett Summerson fluorimeter by the method of Kelsey and Geiling (1942). Added quinidine gave 88–95 per cent recovery.

TABLE I  
INTRACELLULAR LOCALIZATION OF QUINIDINE IN LEFT VENTRICLE OF DOG

	Homogenate	Nuclei		Sarcosomes		Supernatant*	
	Units	Units	Per cent	Units	Per cent	Units	Per cent
<i>In vivo</i> (10) s.e.	24.91 ± 1.38	12.90 ± 0.93	52	1.87 ± 0.15	8	8.14 ± 0.26	33
<i>In vitro</i> (6) s.e.	18.30 ± 0.29	9.00 ± 0.26	49	0.83 ± 0.11	5	7.15 ± 0.63	39

Units = µg. quinidine per g. equivalent tissue. \* Fraction containing microsomes.  
Number of animals in parentheses.

The intracellular localization of quinidine in the left ventricle (Table I) was significantly higher in the nuclear fraction than in the sarcosomal and supernatant fractions. The percentage distribution of quinidine in nuclei, sarcosomes and supernatant in the *in vivo* studies was respectively 52, 8 and 33 and 49, 5 and 39 in the *in vitro* studies. Further investigations are in progress in this laboratory. Financial assistance from the Indian Council of Medical Research is gratefully acknowledged.

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December 4, 1962

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