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**Short Communications**

# Sustained release tablet formulation of diethylcarbamazine

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Diethylcarbamazine citrate I.P. (DECC) is a drug of choice against human filariasis and is recommended at a dose of 50 mg t.i.d. for a period of 7–21 days. Filariasis is a major medical and social problem and affects about 250 million in the tropical zone of Africa, the Indian sub-continent, South East Asia, the Pacific Islands and South America (Lämmler, 1977). DECC has an average half-life (in man) of 8 h (Ree et al., 1977) and its therapeutic index is very high (Lämmler, 1977). Carnauba wax and stearyl alcohol were used for making sustained release (SR) DECC tablets (Kumar et al., 1975). But the release integrity on storage becomes unpredictable for wax formulations unless confirmed by stability studies. Eudragit RS and RL are the inert acrylic resins unaffected by GIT fluids and unchanged during storage (Lehmann, 1968). These resins were successfully employed to formulate SR tablets of DECC (I).

DECC was diluted with an equal amount of talc plus lactose (1 : 1). Eudragit RS (5% w/w) in acetone was incorporated with constant kneading into the above mixture and the resultant dough was passed through mesh 20. Tablets were compressed by placing weighed amounts of 20/30 mesh granules into 1/4 in. die of a single punch hand-operated machine so that the weight variation was negligible. Tablets were coated with 1% w/v acetonic solution of Eudragit RS/RL mixtures (100/0, 50/50, 60/40 and 75/25) using the miniature air-suspension coating apparatus of Baveja et al. (1983). While coating, tablets were withdrawn at different time intervals which represent different amounts of coating. In vitro release rates of all these matrix tablets were studied using USPXVIII dissolution rate apparatus with 0.2 M phosphate buffer, pH 7.4, as medium and rotated the basket at 100 rpm. The samples were assayed by the method of Baveja and Ranga Rao (1981).

It was observed that when Eudragit RS alone was used as coating material, a

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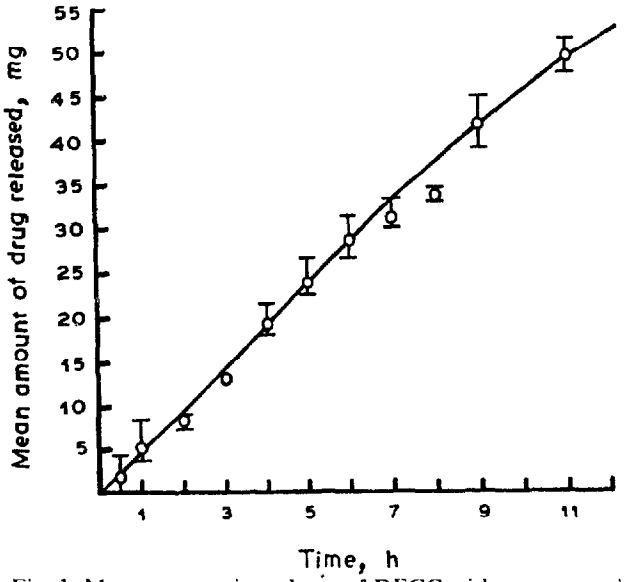


Fig. 1. Mean progressive release of DECC with respect to time from sustained release tablets coated with 3.7 mg/cm$^2$ of Eudragit RS/RL (75/25) resin mixture (n = 4). Vertical bars indicate S.D.

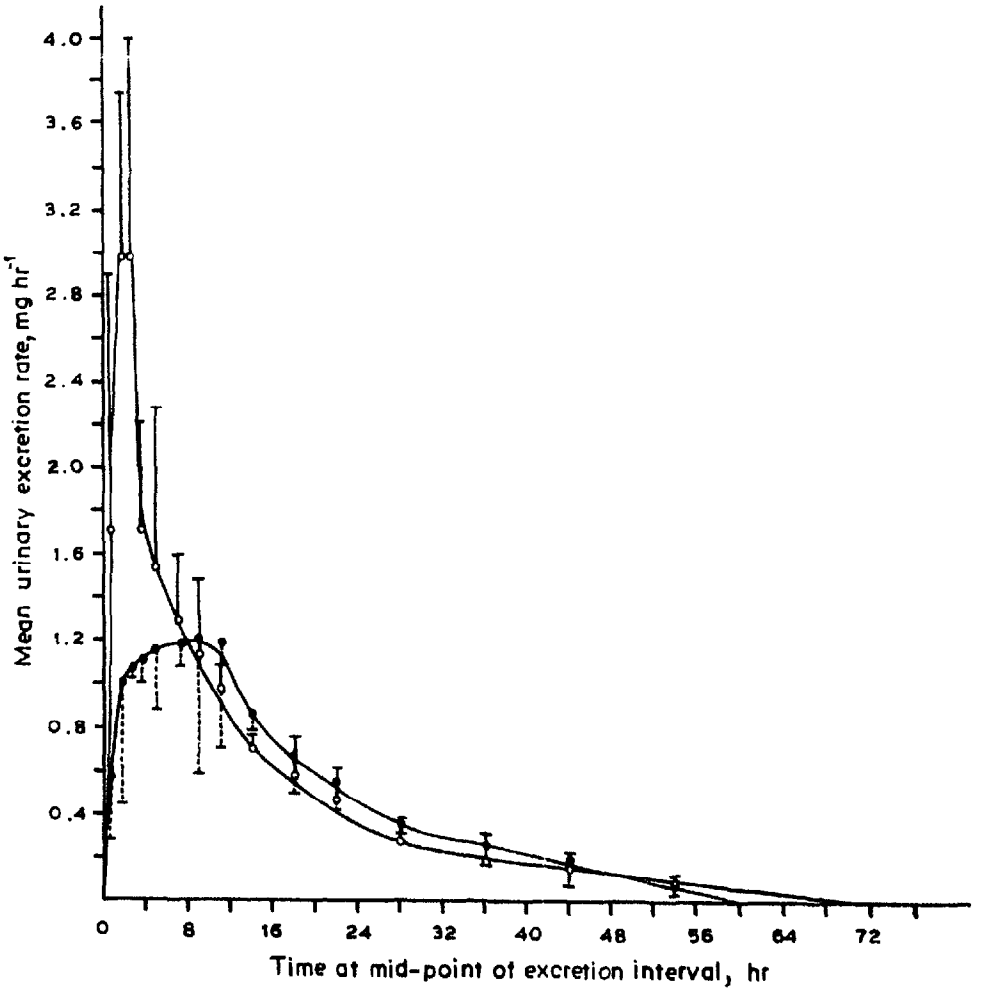


Fig. 2. Mean rate of excretion of DECC vs time after administration of (○) ordinary commercial tablet and (●) formulated sustained release tablet at same dose level (n = 4). Vertical bars indicate S.D.

small change in lacquer amount brought a large change in the release rate and also that the drug released in 12 h was far below 100%. When Eudragit RS/RL mixture (50/50) was used, the release rate deviated from the zero-order kinetics from the beginning, while with RS/RL (60/40) zero-order release was seen only up to 8 h. Eudragit RS/RL (75/25) was found to be the optimum ratio since zero-order kinetics was seen up to 12 h and, comparatively, release rate could be easily monitored. Also in this case, the release rate was in linear relationship with the film thickness (mg of coating lacquer per unit tablet surface area) calculated by the method of Dreher (1974). Tablets (110 mg) having a mean surface area of 1.22 $cm^2$, containing 52 mg DECC (maintenance dose for 12 h according to Nelson, 1957) with a mean coating film thickness of 3.7 mg/$cm^2$ (≡4.5 mg resin per tablet) released its contents uniformly for 11 h at a mean rate of 4.5 mg/h. Mean amount of drug released vs time for I is shown in Fig. 1.

In vivo performance of I was confirmed by comparing with ordinary commercial 50 mg DECC tablets (II). For this, urinary excretion studies were conducted in 4 normal male volunteers (age 22–27 years, weight 54–63 kg and height 163–175 cm.) according to the guide lines of Anthony (1979). Two volunteers were given two tablets of II and the other two were given one tablet each of I and II. Urine samples collected for 72 h were analyzed by the method of Baveja and Ranga Rao (1981). Later the formulations were crossed over after a washover period of one week. From the plots of mean rate of excretion vs time for I and II (Fig. 2.), it is evident that I maintained the steady-state levels for about 12 h.

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