The distal ends of some of the electrodes were surrounded by a small 3 × 3 mm whitish-grey tissue nodule. On sectioning, these nodules were found to be composed of granulation tissue with a small central cavity surrounded by a variable degree of fibrous tissue. The reaction was characterized by central polymorphonuclear infiltrates, epithelial cells, fibroblasts and histiocytes.

Figure 2 shows a blood pressure and ECG tracing obtained in this way and the response to 2 μg/kg adrenaline before and after administration of atropine. The reflex bradycardia produced by adrenaline before atropine and the tachycardia after atropine emphasizes the differences in cardiovascular response in the conscious animal compared with the anaesthetized animal where tachycardia predominates. This type of phenomenon has been described previously in other species (Whitty & Shepard, 1967; van Miert, 1969).

In a series of 6 animals prepared to determine how long satisfactory ECG recordings could be obtained, excellent recordings showing all components of the ECG were obtained 5 months after surgery in 4 animals. Electrode failure occurred in 2 animals after 3 weeks. Thus, this method has been found useful for the long-term assessment of cardiotoxic effects of chemicals (Grice, Heggtveit & others, 1970) and for the study of the cardiac effects of drugs in the conscious rat.

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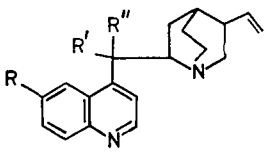
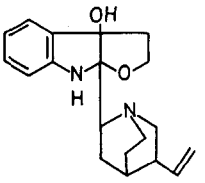
The isolation and identification of quininone from *Cinchona ledgeriana*

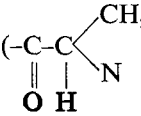
We have isolated and identified an alkaloid from the bark of a variation of *C. ledgeriana* collected in Guatamala. To the mother liquors remaining after the industrial isolation of quinine (I, R=OMe, R′=H, R″=OH) from this bark (these were supplied, as the residual bases in the form of their thiocyanate salts in aqueous solution, by Lake & Cruickshank Ltd.) (1 litre) was added excess sodium carbonate. The liberated bases were extracted with ether, the total ethereal extract was reduced to small volume under reduced pressure and the residue was subjected to column chromatography on alumina. Elution with ether–chloroform (2:1 v/v) afforded quinamine (II) (0·21 g) (Henry, 1949; Turner & Woodward, 1953), and subsequently with ether–chloroform (1:1 v/v) a white crystalline solid (0·04 g) (initial eluate) and cinchonine (I, R=H, R′=H, R″=OH) (1·24 g) (Henry, 1949; Turner & Woodward, 1953) (latter eluate). Both quinamine and cinchonine, along with quinine, have been isolated previously (Henry, Kirby & Shaw, 1945) from *C. ledgeriana*. The above white crystalline solid was recrystallized from ether–light petroleum (b.p. 40°–60°) to afford prisms, m.p. 98–101°. Elemental analysis gave an empirical formula $C_{20}H_{22}N_2O_2$ which was confirmed and shown to be the molecular formula by mass spectrometry. The ultraviolet spectrum in absolute ethanol showed λ_{max} 361–364 nm



I



II

(log ϵ = 3·77), λ_{infl} 242–245 nm (log ϵ = 4·18) and λ_{infl} 252–257 nm (log ϵ = 3·99) and in ethanolic hydrochloric acid showed λ_{max} 342–344 nm (log ϵ = 3·79) and λ_{sh} 250–261 nm (log ϵ = 3·96) and the infrared spectrum in Nujol showed a strong band at 1685 ± 3 cm^{-1} (C=O) but was devoid of absorption between 3100–4000 cm^{-1} (N–H and O–H groups absent). The proton magnetic resonance spectrum in $CDCl_3$ included a 3-proton singlet at 6·14 τ (OMe), a 5-proton signal between 1·20–2·65 τ (5 aromatic protons), a 1-proton multiplet between 3·85–4·29 τ and a 2-proton multiplet between 4·81–5·18 τ (CH_2=CH–) and a 1-proton triplet centred at 5·88 τ (J = 9Hz) (). The mass spectrum was similar to that of quinine (Budzikiewicz, Djerrasi & Williams, 1964) and indicated a molecular ion at m/e 322, a base peak at m/e 136 and other significant peaks at m/e 307, 292, 186, 172, 159, 158, 137 and 81.

These above data suggest the alkaloid is quininone (I, R=OMe, R′+R″=O). This was verified by its synthesis by oxidation of quinine (I, R=OMe, R′=H, R″=OH) using potassium t-butoxide–fluorenone mixture (Warnhoff & Reynolds-Warnhoff, 1963) (see also Doering, Cortes & Knox, 1947; Turner & Woodward, 1953), the natural and synthetic compounds having identical melting points and mixed melting point and infrared, ultraviolet, proton magnetic resonance and mass spectra.

Quininone has previously been detected by thin-layer and paper chromatography and by ultraviolet spectroscopy in several *Cinchona* species although it was only isolated in an amorphous state (Vácha, Cŭba & others, 1964). The above studies further establish quininone as a natural product and represent its first isolation in a crystalline form from a natural source.

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