first 24 hours but there was no excretion of ^{14}C-CO_2 in expired air. These experiments establish that OMD is demethylated in rats *in vivo* and that the demethylation probably takes place in the gut.

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Comparison of effects exerted by isomers and analogues of (±)-2,3-dehydroemetine on protein synthesis in rat liver

J. D. DONAHUE, R. K. JOHNSON and W. R. JONDORF*† (introduced by T. C. MUIR)
Department of Pharmacology, George Washington University School of Medicine, Washington DC 20005, USA

(±)-2,3-Dehydroemetine (DHE), an amoebicidal drug (Johnson & Neal, 1968) with potential in anticancer chemotherapy (Abd-Rabbo, 1969; Jondorf, Abbott, Greenberg & Mead, 1971), has been compared with (−)-emetine for its effects on hepatic protein synthesis in the rat (Jondorf, Drassner, Johnson & Miller, 1969). It was of interest to extend the previous studies with racemic DHE to the individual optical isomers in view of the finding in some biological systems (Johnson & Neal, 1968; Jondorf *et al.*, 1971) but not in others (Brossi, Baumann, Burkhardt, Richle & Frey, 1962) that (−)-DHE was about twice as active as the racemic compound.

We have now been able to show that the intraperitoneal administration of (±)-DHE or (−)-DHE to 160 g female Sprague-Dawley rats (of the same age) stimulates the uptake of ^{14}C-labelled L-amino acid into protein in a liver microsomal incorporating system *in vitro* (Jondorf *et al.*, 1969) in the same dose-dependent way when the incubations are carried out with subcellular fractions prepared 24 h after pretreatment with the drugs. Maximal stimulation of incorporation occurs at a pretreatment level of 18 μmoles/kg. When (±)-DHE or (−)-DHE are added directly to the amino-acid incorporating system *in vitro*, there is a progressive concentration dependent inhibition of amino-acid incorporation, which appears to be very similar for the racemic compound and the (−)-isomer.

In a third type of experiment, the incorporation of L-leucine into liver protein *in vivo* is inhibited to the same extent at 2 h after pretreating rats with equimolar doses of (±)-DHE or (−)-DHE in the range 1·8–18 μmoles/kg.

None of these effects are observed with (+)-DHE which is as inactive in these respects as (−)-isoemetine or (+)-*O*-methylpsychotrine (Jondorf *et al.*, 1969). This is not altogether surprising, since (+)-DHE, in common with these other inactive compounds, lacks the correct stereospecific alignment at the C-1′ position in the molecule thought to be decisive for biological activity (Grollman, 1966). What is surprising is that the above effects observed with (±)-DHE are not seen when the corresponding experiments are performed at similar or greater dose levels with the analogues NSC-134754 and NSC-134756 each lacking one pair of adjacent OCH_3 substituents

†Present address: Department of Pharmacology, The University, Glasgow W.2.

(Schöpf, Gänshirt, Hutzler, Klug & Reinshagen, 1969). Although the (−)-isomers of these racemic compounds have the essential structure thought to be associated with biological potency, they are inactive in the rat liver protein synthesizing system *in vivo* and *in vitro*. This leads us to support the idea first put forward by Lietman (1971) that structural subtleties among emetine derivatives not originally envisaged by Grollman (1966) may emerge as different protein synthesizing systems are methodically studied.

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Vascular changes in tumours after treatment with ICRF 159

A. W. LE SERVE (introduced by K. HELLMANN)
Cancer Chemotherapy Department, Imperial Cancer Research Fund, London WC2A 3PX

Mice implanted subcutaneously with the Lewis lung (3LL) carcinoma regularly develop pulmonary metastases, which can be prevented by treatment with [(±)-1,2-bis (3,5-dioxopiperazin-1-yl) propane] (ICRF 159) (Hellman & Burrage, 1969). The poorly defined sinusoids which act as vascular channels in the periphery of control primary tumours are replaced by well formed discrete blood vessels in tumours treated with ICRF 159 (Burrage, Hellmann & Salsbury, 1970). These changes in the structure of the blood vessels are probably responsible for preventing the escape of malignant cells from the primary tumour into the circulation.

The distribution and character of these 3LL blood vessels has now been further investigated by means of X-ray angiography and by a colloidal carbon technique which specifically outlines damaged and inflamed blood vessels (Majno, Palade & Schoefl, 1961). A comparison has also been made of the effects of ICRF 159 treatment of rats inoculated with the Walker carcinosarcoma.

A polythene catheter was inserted into the inferior vena cava through the exposed right heart of animals anaesthetized with Avertin. Micropaque was introduced slowly by retrograde injection and care was taken that introduction of contrast medium was performed in exactly the same way each time.