Devil's Claw was given to one group of animals at 100 mg/kg (about five times the recommended human dose) and to another at 1 g/kg (about 1/15th of the amount shown to be without effect in acute toxicity studies). Other groups received either tap water (controls) or indomethacin (3 mg/kg). Indomethacin inhibited both the primary reaction (−17% on Day 5, $P<0.01$) and the secondary reaction (−30% on Day 18, $P<0.001$). Devil's Claw (100 mg/kg) produced no significant effect on either the primary or secondary reaction, but at 1 g/kg the reaction was consistently greater than the controls in both the injected and uninjected feet. Only on Day 7 was this statistically significant (+16% $P<0.05$).

If these tests can be regarded as predictive of efficacy in humans, Devil's Claw when used at the recommended dose would not be expected to show anti-arthritic activity. The possibility that high doses of Devil's Claw potentiate adjuvant arthritis in a manner similar to that seen with levamisole and penicillamine (Trabert, Rosenthal & Muller, 1976; Arrigoni-Martelli & Bramm, 1975) requires further investigation.

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Inhibitory effects of gold salts in adjuvant arthritis and on lysosomal enzyme activity

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We recently reported that oral but not parenteral forms of gold possess potent acute anti-inflammatory effects, but that none of the gold salts possessed marked activity in adjuvant arthritis produced in Wistar rats (Brown, Bruin, Lewis, McNeillie & Smith, 1978). This latter observation was in contrast to the reports of others (Walz, DiMartino & Sutton, 1974) and consequently we have re-examined the effects of several gold salts in the inbred Lewis rat, a strain previously reported to be susceptible to the anti-arthritic effects of gold (Walz, DiMartino, Sutton & Misher, 1972). In addition to measuring the progression of the disease we have examined the effect of these treatments on serum hydrolases known to be elevated during adjuvant arthritis (Collins & Lewis, 1971). Indeed, it has been suggested that gold salts may exhibit inhibitory effects on lysosomal enzyme activity or release from inflammatory cells, and that this is a major mechanism for their anti-rheumatic activity (Walz, DiMartino & Sutton, 1974). The effects of gold salts on β-N-acetylglucosaminidase (β-NAG), β-glucuronidase, cathepsin B_1 and cathepsin D, all extracted from mouse peritoneal macrophages have also been examined *in vitro* for comparison with the *in vivo* studies.

Adjuvant arthritis was induced in male Lewis rats (180–200 g) by injection of 0.05 ml *Mycobacterium butyricum* in liquid paraffin (10 mg/ml) into the left hind paw only.

Aurothiomalate (s.c.), triethyl phosphine gold chloride (S K & F 36914, oral) and S-triethyl phosphine gold 2, 3, 4, 6-tetra-O-acetyl-1-thio-β-D-glucopyranoside (S K & F D-39162 oral) significantly suppressed the symptoms of adjuvant arthritis when administered at a dose of 5 mg Au kg^{-1} d^{-1} for 20 days from the day of adjuvant administration. Serum cathepsin D was elevated (33%) in the arthritic control animals when measured on day 21. None of the orally active gold salts significantly influenced this level.

The effect of aurothiomalate, S K & F 36914, S K & F D-39162 and sodium gold chloride dihydrate was studied on β-NAG, β-glucuronidase, cathepsin B_1, cathepsin D, and the cytoplasmic enzyme lactate dehydrogenase (LDH) from purified mouse macrophages, *in vitro*. Aurothiomalate significantly inhibited β-glucuronidase ($ED_{20} = 1 \times 10^{-2}$M) and cathepsin B_1 ($ED_{50} = 6 \times 10^{-3}$M) but not β-NAG, cathepsin D or LDH. S K & F D-39162, a compound reported to inhibit the release of lysosomal enzymes from rat leucocytes but not their activity (DiMartino & Walz, 1977) only inhibited cathepsin B_1 ($ED_{50} = 8 \times 10^{-3}$M), but both S K & F 36914 and sodium gold chloride dihydrate strongly inhibited all the hydrolytic enzymes and LDH.

In conclusion, we have confirmed the activity of gold salts in adjuvant induced arthritis in the Lewis strain of rat, a result markedly different from our previous findings with the Wistar strain of rat (Brown *et al.*, 1978). We have also demonstrated that gold salts have little influence on elevated serum hydrolase

levels produced during adjuvant arthritis. However, gold salts are capable of inhibiting these enzymes *in vitro* although each salt displayed a different profile of enzyme inhibition.

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Mediation by adrenaline of lung surfactant secretion induced by oxotremorine in neonatal rabbits

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Thirty min after oxotremorine (0.2 mg/kg i.p.) the total content of phosphatidylcholines (PC) of 6 lung washes obtained from neonatal rabbits via the trachea was double that of saline controls (Abdellatif & Hollingsworth, 1977). However, oxotremorine infused via the pulmonary artery into isolated, perfused and ventilated lungs of neonatal rabbits failed to alter the PC content of lung washes. We have now further examined this action of oxotremorine and suggest that an indirect mechanism is involved.

Atropine or (±)-propranolol were given at 40 min and oxotremorine at 30 min before killing. The antagonists had no effect themselves on the lung wash PC content but abolished the rise induced by oxotremorine. Adrenaline given 30 min before killing significantly raised the PC content of lung washes and this was antagonized by (±)-propranolol. The PC content of washes was not altered 45 min after bilateral adrenalectomy but the action of oxotremorine was abolished. The PC contents of the residual lung tissues were similar in all groups.

The surfactant activity in lung washes from further groups of rabbits was measured using a Wilhelmy surface tension balance against a standard curve with dipalmitoylphosphatidylcholine. Oxotremorine and adrenaline significantly ($2P<0.05$; analysis of variance) increased the surfactant in washes to 73.8 and

Table 1 Total mean phosphatidylcholine (PC) content of lung washes from neonatal rabbits.

Drug or treatment and dose	*PC content (mg/g dry wt)*	*n*
Saline	25.7[a, b]	5
Oxotremorine (0.2 mg/kg)	50.5[a, c, d, f]	7
Atropine (2 mg/kg)	20.8	5
Oxotremorine (0.2 mg/kg) + Atropine (2 mg/kg)	21.5[c]	5
(±)-Propranolol (1 mg/kg)	32.9	5
(±)-Propranolol (1 mg/kg) + Oxotremorine (0.2 mg/kg)	20.4[d]	5
Adrenaline (50 μg/kg)	78.0[b, e]	5
Adrenaline (50 μg/kg) + (±)-Propranolol (1 mg/kg)	20.4[e]	5
Adrenalectomized	29.5	4
Adrenalectomized + Oxotremorine (0.2 mg/kg)	26.9[f]	4

Values with same superscripts were compared and are significantly different (Analysis of variance; a, $2P<0.01$; b–f, $2P<0.001$).