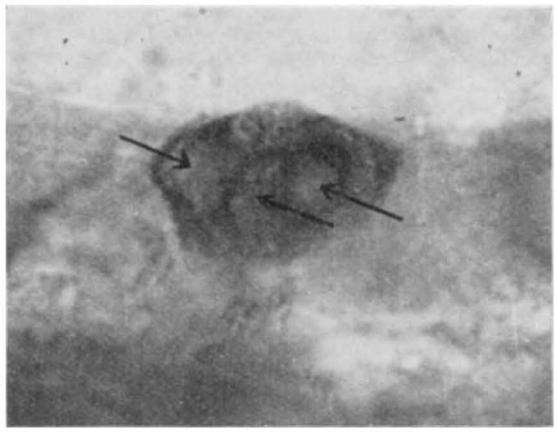

Fig. 2. Cytochemical localization of liberated calcium in a motor end-plate of the rat diaphragm after intraperitoneal 'Prostigmine'. Arrows point to fundamental nuclei of the sole plate. Note the fine granular appearance of the reaction in the cytoplasm of the sole plate (× 1,000)

Roche) results in the appearance of free (histochemically detectable) calcium in the sole plates, that is, in the post-synaptic cytoplasm underlying the motor end plates. Release of calcium could also be demonstrated in the sole plates of the deep plantar muscle (m. quadratus) after a 30-min stimulation of the sciatic nerve (50 hz, 1·2 V). The liberated calcium is confined to 1–2μ granules in the sole plate, localized under the terminal arborization of the motor nerve fibre. The histochemical pattern obtained closely resembles the so-called 'telosomes'[4]. However, telosomes are present in resting muscles, too, while liberated calcium can only be demonstrated after activity. Localization of calcium is different from that of acetyl-cholinesterase, which is confined to the post-synaptic membrane of the end-plate[5–7].

The histochemical technique used for the demonstration of liberated calcium is as follows: fresh samples of the muscle were fixed in acetone or other lipid solvents, as benzene, xylene, chloroform, carbon tetrachloride, ether, methyl or ethylalcohol (30 min), and floated afterwards in distilled water adjusted to *p*H 8 with sodium barbital (5 min). Frozen sections 20–30μ thick were cut on the freezing microtome and stained immediately with a 1 per cent aqueous solution of alizarin red. It should be stressed that no similar reaction could be found in muscle fixed in formalin or in osmic acid.

These histochemical observations suggest that the cytoplasm of the sole plate is the most sensitive part of the muscle calcium system, correlated in all probability with the calcium-binding sites localized in the sarcoplasmic reticulum. Presumably depolarization of the post-synaptic membrane by pre-synaptic stimuli affects first of all the calcium-stores in the sole plate which results in a general membrane depolarization. This in turn activates the sarcoplasmic system, giving rise to myofibrillar contraction.

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PATHOLOGY

An Early Test for Possible Skin Carcinogens in the Mouse : Effects of a Benzacridine and of some Tricycloquinazolines

An early test for possible skin carcinogens in the mouse has been reported[1]. The test is based on a tetrazolium reduction method. It was demonstrated that the test could reveal the carcinogens in a blind test of 21 substances of which seven were carcinogens[2], and that a complete correlation existed between the results of the test and the yield of tumour after a single application of different doses of 3-methylcholanthrene[3].

It was found of interest to study the possible specificity of the test with other types of skin carcinogens differing from those used in the first blind test. The 7,9-dimethyl-benz-(*c*)-acridine has a strong carcinogenic potency on mouse skin, but a very faint effect as measured with the sebaceous gland suppression test[4]. A sample of this compound was obtained from Dr. F. G. Bock[4], and the tetrazolium test performed. The result was 1·310, which, according to the criteria, is characteristic for carcinogenicity.

Table 1. Tetrazolium Blind Test of Different Tricycloquinazolines (TCQ)

Compound labelled	Test result	Test prediction	Compound	Skin carcinogenic potency *
1	0·874	non-carcinogenic	2-methyl-TCQ	non-carcinogenic
2	1·887	carcinogenic	TCQ	carcinogenic (3+)
3	1·303	carcinogenic	3-methyl-TCQ	carcinogenic (2+)

* Skin carcinogenic activity refers to the measurements by Baldwin *et al.* (ref. 6).

The carcinogenic potency for mouse skin of tricyclo-quinazoline was demonstrated in 1959[5]. Further research[6] showed that different derivatives of this compound revealed very different results, varying from strong carcinogenic potency to non-carcinogenicity. Three substances of this type were sent me by Dr. R. W. Baldwin[6]. The substances were labelled 1, 2 and 3 respectively, and were unknown to me until all the experiments were finished. Table 1 demonstrates the results. There is a complete correlation between the carcinogenicity of the compounds and the test results.

The possible specificity of the tetrazolium test is thus given a strong further support.

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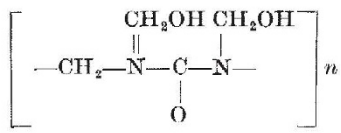
Polynoxylin

Polynoxylin is polynoxymethyleneurea, a condensation product of formaldehyde and urea which has interesting antibacterial and antifungal properties[1]. It is a white, stable powder, soluble in water to an extent of less than 0·3 per cent, and probably having the following type of formula:



In view of the evidence indicating that the compound has a low acute and chronic toxicity and is effective and