is thus little or no substrate for kinin-forming agents in BN plasma. The same procedure, this time using BN plasma as a source of kinin-forming agents, does not produce kinins.

7. Dextran sulfate (mol.wt 500,000) activates the Hageman factor which in turn accelerates the conversion of prekallikrein into kallikrein[27,28]. These processes can be estimated by the method of Amundsen and Svenden[29] which measures the amidolytic potency of the kallikrein formed. In W plasma this activity is 0.449 ± 0.047 units/ml, whereas it is nil in BN plasma.

Discussion. BN plasma is characterized by its low content of kininogens. This has been demonstrated directly, and confirmed by the fact that salivary gland kallikreins possess only a weak hypotensive activity in BN rats. Moreover if kallikrein is activated by carrageenan in W plasma and then transferred to BN plasma, little or no kinin is formed in the latter, indicating that HMW kininogens are practically absent from BN plasma.

BN plasma is also devoid of kallikrein. This conclusion is supported by 3 pieces of evidence: a) ellagic acid has no hypotensive activity in BN rats in vivo; b) ellagic acid and carrageenan iota fail to produce kinins from BN plasma in vitro; c) no amidolytic activity can be demonstrated in BN plasma when prekallikrein is activated by means of dextran sulfate. As ellagic acid, carrageenan and dextran sulfate activate prekallikrein through the activation of the Hageman factor[16,28,29] and as this factor is present in W and BN plasma[30], it seems most probable that the lack of kallikrein in BN plasma is responsible for the inactivity of these 3 compounds.

On the other hand, kallikreins are found in the salivary glands of both BN and W rats. Homogenates of the glands in BN rats exert a hypotensive activity in W rats and cross tachyphylaxis can be demonstrated on the vascular effects of BN and W homogenates.

These results provide a logical explanation for the fact that inflammatory processes caused by 3 different carrageenans are less marked in BN than in W rats[30]. It is thus hoped that the use of the BN strain may throw some light on the role of the kinin system in other physiological or pathological processes.

Conclusion. The plasma of the brown Norway rat is devoid of kallikrein and poor in kininogens, but in the salivary glands of this breed, glandular kallikreins are present.

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Candida utilis as a convenient and safe substitute for the pathogenic yeast *C. albicans* in Daniels' phototoxicity test

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Summary. Candida utilis is a safe and convenient substitute for the pathogenic yeast *C. albicans* in phototoxicity tests. With both organisms 8-methoxypsoralen and α-terthienyl give positive results while photodynamic compounds give negative results.

Since Daniels introduced *Candida albicans* as a test organism for determining whether plant materials or isolated chemicals displayed an antibiotic activity in the presence of long wavelength UV-light[2], the use of this phototoxicity test has grown, especially since the phototoxic psoralens have been applied in medicine[3]. For example, Towers and his coworkers have tested extensively for the presence of phototoxic compounds in several plant families, with emphasis on the Compositae[4–6].

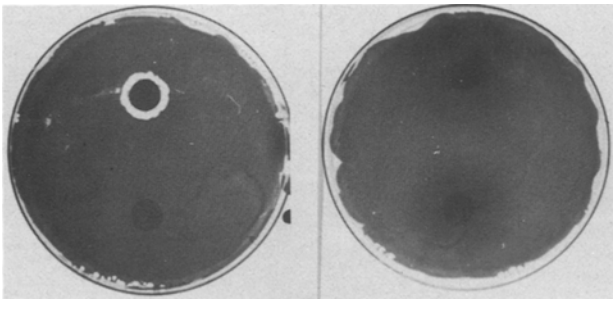
It is appropriate to stress that *C. albicans* is a pathogenic organism which has been implicated in many different types of infections[7]. A superficial candidiasis may be either cutaneous, affecting for example the skin or the nails, or it may be mucosal, affecting the digestive, genital, urinary or

respiratory tracts. Even more serious, a systemic infection may affect the circulatory, respiratory, digestive, urinary, or central nervous systems, as well as other organs such as liver, spleen, or pancreas. The use of *C. albicans* should therefore not be undertaken casually by anyone, and it should be strongly discouraged in the absence of overriding justification, a fact which was not mentioned by the above workers in this field.

We wish to demonstrate that *C. utilis,* a common food yeast, is an excellent substitute for *C. albicans.* As shown in the pictures (figure) a clear positive test was obtained with a classical phototoxic compound such as 8-methoxypsoralen. A positive response was also obtained with α-terthienyl. The phototoxicity of the latter had been discovered through a test performed with *C. albicans*[5], and it would certainly not have been missed had *C. utilis* been used instead. Typical photodynamic compounds such as rose Bengal (figure), hypericin, and methylene blue were found to give a negative test for phototoxicity with *C. utilis.* Negative results had also been obtained for the first 2 compounds with *C. albicans,* but the 3rd had given variable results with this organism.

In conclusion, *C. utilis* appears to be in every respect as good as *C. albicans* for the phototoxicity tests, with the added advantage of not being pathogenic. Therefore, there does not seem to be any justification for using the latter organism in investigating the phototoxicity of either chemicals or plant samples.

Experimental. Candida utilis was grown on a TGY medium, consisting of 1% tryptone, 2% glucose, and 0.5% yeast extract. TGY agar plates were inoculated evenly with *C. utilis* from a 48-h slant, and the chemical to be examined was applied to a piece of Whatmann No. 1 filter paper, about 1 cm in diameter, which had been previously sterilized with 95% ethanol. The paper was placed on the plate, which was irradiated from a distance of 10 cm with a 19.5-W UVL-22 'Black-Ray' UV-lamp, with an emission at 320–390 nm. A blank similarly prepared was kept in the dark for the length of the irradiation (12–24 h). A positive response could be observed with 10^{-7} g of 8-methoxypsoralen, or 10^{-6} g of α-terthienyl.



Phototoxicity test with *C. utilis.* Left: 8-methoxypsoralen, right: rose Bengal. In each case the lower half of the plate was shielded from the light with an aluminium foil.

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The effects of β-sympathomimetic amines and phosphodiesterase inhibitors on electrophysiological parameters in Purkinje fibres[1]

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Summary. Dose-dependent responses to L-isoprenaline of spontaneous activity and plateau height in Purkinje fibres can be mimicked closely by the PDE-inhibitor IBMX. Simultaneous applications of sympathomimetic amines and IBMX result in potentiated responses. The results support the hypothesis that cyclic-AMP is the common mediator of positive chronotropic and inotropic effects induced by β-sympathomimetic amines.

Catecholamines act in a characteristic way upon heart preparations: the effect on the pacemaker potassium current (ik_2) starts at relatively low concentrations and can be described by a 1:1 binding curve[3]. The increase in slow inward current (i_{si}) becomes visible at higher concentrations and the dose response curve suggests a 2:1 relation[4]. Both effects have been proposed to be mediated by the intracellular 'second messenger', cyclic-AMP (adenosine 3′,5′-monophosphate)[5]. In spontaneously active fibres the attempt to correlate the catecholamine effects with an increase in the intracellular level of cyclic-AMP has only been partly successful[6,7]. High doses of catecholamines produce a distinct elevation of adenyl cyclase activity, whereas with low but still efficacious doses, which mainly effect the pacemaker current, a significant increase is not detected. This observation might be explained either by assuming that part of the positive chronotropic effect is not mediated by cyclic-AMP, or that the change in the functionally relevant fraction of cyclic-AMP is too small to be detected, e.g. because a large background level of cyclic-AMP might be present. In order to avoid the difficulties of cyclic-AMP determinations the following approach seems to be applicable: if, as suggested, both effects are mediated by cyclic-AMP, similar characteristic dose-response relations for both effects should be obtained by an inhibition of the phosphodiesterase (PDE) which converts cyclic-AMP into inactive 5′-AMP. In addition an inhibition of the PDE together with a simultaneous stimulation of the β-receptor