removal of virtually all penicillin G by extensive dialysis or by treatment with 1 N NH_2OH for 1 h at pH 7.0. Since penicillin is potentially an acylating agent of protein[12], the irreversible inactivation by penicillin G may result from the acylation of the essential functional group of the enzyme molecule. It is considered that N-acyl linkage, rather than S-acyl linkage or O-acyl linkage, might have been formed since the latter would be expected to be reversed by NH_2OH[13]. We recently observed that yeast glucose-6-P dehydrogenase was extremely sensitive to inactivation by pyridoxal-P[5]. Since pyridoxal-P is highly specific for modifying ϵ-amino group of lysine in proteins[6], it is considered that this enzyme contains reactive lysyl residues at its active site. The reaction of pyridoxal-P with amino groups is well known to result in the formation of Schiff base which is reversible upon dilution or dialysis[10]. The data presented in the table show that inactivation of this enzyme by pyridoxal-P was reversed by dialysis. These data also show that in the presence of pyridoxal-P the irreversible inactivation of the enzyme by penicillin G was largely prevented. This suggests that pyridoxal-P and penicillin G may react with the enzyme at the same site, namely by acylating the ϵ-amino group of a lysyl residue essential for catalytic activity. The enhanced rate of inactivation with increasing pH appears to be consistent with the proposed mechanism, since according to this mechanism the unprotonated form of the amino group should react with penicillin G.

Although it is generally regarded that penicillenic acid is probably the molecular form that acylates proteins[4,12], it is still considered possible that penicillin may directly acylate protein without molecular rearrangement. This is based on the assumption that beta-lactam carbonyl is reactive and susceptible to nucleophilic attack as originally suggested by Woodward[14] who recognized that inhibition of amide resonance by ring strain could account for this.

1 This work was supported by grant RR-8006 from the General Research Branch, Division of Research Resources, NIH (USA).
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Acetaldehyde metabolism in *Drosophila melanogaster*[1]

M.C. Lietaert, M. Libion-Mannaert and A. Elens

Unité de Génétique et Physiologie Cellulaire, Facultés N.D. de la Paix, 61, rue de Bruxelles, B-5000 Namur (Belgium), 24 September 1980

Summary. A quantitative study on in vitro acetaldehyde degradation in homogenates from *Drosophila melanogaster* flies shows that aldehyde oxidase plays the major part in acetaldehyde detoxification. However, in a strain, called 'AO null', because its *Aldox* locus produces no aldehyde-oxidase, acetaldehyde is also degradated by a still unknown mechanism. Alcoholdehydrogenase which is responsible for the dehydrogenation of ethanol in acetaldehyde, appears to catalyze the reversed reaction as well, regenerating ethanol from acetaldehyde.

In *Drosophila melanogaster* alcohol dehydrogenase (ADH) seems to play an essential part in the ethanol tolerance[2-6], the physiological and ecological importance of which is no longer questioned[7-10]. It has generally been accepted[6] that *Drosophila* ADH converts ethanol into acetaldehyde, a highly toxic substance[11], which therefore must be transformed immediately into non toxic and even useful products. As a matter of fact, it has been shown that ethanol is used as a food in metabolism[12-14].

Our purpose is to question the part played by the enzyme aldehyde oxidase (AO) in the detoxification of acetaldehyde. Experiences in vivo have shown that a mutant strain 'AO null' which does not produce any active AO is nevertheless tolerant of alcohol[15], although it is not very tolerant of acetaldehyde[11]. According to David[15] such a physiological paradox could probably be explained by the discovery of another locus which produces a small amount of AO even when the *Aldox* locus (3-56.7) does not give active AO. This small amount of enzyme should be sufficient for the detoxification of the metabolic acetaldehyde produced by ADH, although unable to cope with greater quantities of acetaldehyde in food and environment.

The same problem is here approached by another way. One measures the degradation in vitro of small quantities of acetaldehyde by homogenates of flies from three strains, one of which is 'AO null' whereas another is 'ADH null' but with normally active AO. The third strain, having highly active ADH and AO enzymes, is used as a control[11].

The flies were grown on axenic medium, according to David and Clavel[16] and 'deyeasted' before the test, according to Day et al.[17]. Immediately before homogenization, they were immobilized by cooling. For each experiment, 500 mg of adult flies were homogenized with a Potter homogenizer in 1.1 ml of 0.25 M sucrose Tris buffer at pH 7.5. The homogenate was centrifugated at 15,000 rpm for 20 min, at 0 °C.

60-µl aliquots of supernatant were then placed in 5-ml vials, with 20 µl 20 mM acetaldehyde, 10 µl 0.05 M Tris buffer (pH 7.5) and, when indicated, the following compound: pyrazole 20 mM + sodium azide 1 mM Tris buffer. The vials were then sealed hermetically and incubated for 1 h at 15 °C.

5-ml vials were also incubated containing 60 µl 0.25 M sucrose Tris buffer, 20 µl acetaldehyde 20 mM and 10 µl

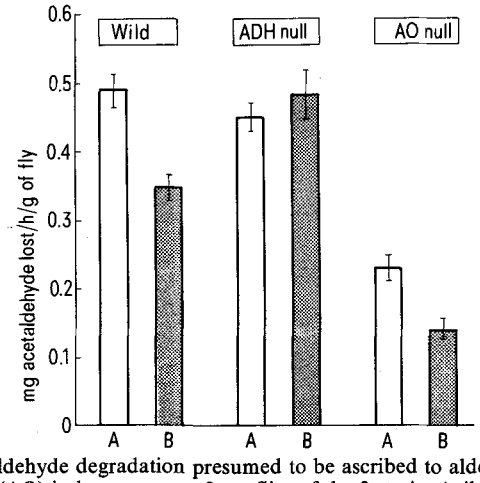
0.05 M Tris buffer (pH 7.5). The values thus obtained were used as control.

After incubation, the aliquots received 10 µl of 40 mM isopropanol, which is used as a reference standard in the gas-liquid chromatography test, as its retention time is slightly superior to the retention time of acetaldehyde or ethanol. 1 µl of this mixture was injected into the gas-liquid chromatography column.

Quantitative assessment of both acetaldehyde and ethanol in the incubation medium, following the 1 h incubation, was achieved by use of a Perkin-Elmer gas-liquid chromatograph.

In the absence of pyrazole, which is a specific inhibitor of ADH activity[11], the acetaldehyde concentration decrease observed can be partially ascribed to a reverse reaction restoring some ethanol back from the initially present acetaldehyde. Such a 'return to ethanol' is lacking in homogenates from the 'ADH null' strain flies, which do not have any active ADH enzyme. For these 'ADH null' flies, addition of pyrazole changes nothing. But the results are quite different for the 'AO null' and the wild flies (fig.). For the wild ones, pyrazole suppresses any restoration of ethanol; the acetaldehyde concentration loss observed in these conditions seems to be attributable almost exclusively to AO. A slight but significant restoration of ethanol subsists in the case of the 'AO null' flies (could it be due to some enzyme other than ADH?). Even if one takes into account this slight 'return to ethanol', an important degradation of acetaldehyde is evident.

These last results are in good agreement with David's and our own previous observations in vivo. For David the strains which do not produce an active AO enzyme show about the same tolerance to alcohol as do wild strains[15]. In our experiments the 'AO null' flies are relatively tolerant of ethanol (although to a lower degree than our wild ones) and they can even tolerate some acetaldehyde in their environment, whereas the 'ADH null' flies are much less tolerant of both ethanol and acetaldehyde[11]. In our present state of knowledge it is, however, impossible to conclude that this acetaldehyde degradation by the 'AO null' flies is, without any doubt, due to the action of an AO produced by some gene other than *Aldox;* the action of some other enzyme cannot be excluded.



Acetaldehyde degradation presumed to be ascribed to aldehydeoxidase (AO) in homogenates from flies of the 3 strains 'wild', 'ADH null', 'AO null'. It is the difference between the total acetaldehyde concentration loss observed and the part of this concentration diminution which is probably due to the retransformation of acetaldehyde into ethanol, as estimated from the ethanol concentration increase observed at the same time. This reversed reaction seems to be catalyzed by alcoholdehydrogenase (ADH) which is known to be responsible for the dehydrogenation of ethanol into acetaldehyde; indeed, it is almost completely suppressed by pyrazole, which is a specific inhibitor of ADH (however, not in homogenates from the 'AO null' strain flies). The mean values are given with confidence intervals (95%). A. Incubation with pyrazole. B. Incubation without any inhibitor.

1 This work was supported in part by a grant from the FNRS of Belgium.

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Asymmetric distribution of male and female foetuses in the pregnant rabbit uterus

E.V. YoungLai, C.-C. Pan and B.R. Bhavnani

Department of Obstetrics and Gynecology, Faculty of Health Sciences, McMaster University, 1200 Main St. West, Hamilton (Ontario, Canada L8N 3Z5), 25 August 1980

Summary. The sex distribution of foetuses in the uterine horn of the pregnant rabbit was found to be asymmetrical, with more males being present in the left uterine horn and more females in the right ($p < 0.05$).

It has been suggested that in general more males than females are born in the rabbit[1-5], but no statistical data were presented. Brambell[6] recorded 506 males to 534 females from 226 litters of wild rabbits. In a study of the biological effects of active immunization of female rabbits against testosterone, it was observed that when pregnancy ensued more male foetuses were present in the left uterine horn than in the right[7]. It was therefore of interest to