All compounds were tested in form of their water-soluble hydrochlorides by procedures already reported[2].

Results. The (±)-3-*epi*dihydroquinines bearing a chloro or a methylenedioxy substituent on the aromatic ring A showed appreciable antimalarial activity. In the 3-*epi*-dihydroquinidine series, all the analogs tested were active at 100 mg/kg. All the compounds had comparable i.p. toxicities in mice.

Conclusions. In comparison with our data reported for (±)-dihydroquinines and (±)-dihydroquinidines[2], these results support the findings of other investigators[4] that inversion at C-3 causes only insignificant reduction in antimalarial activity. The following order of activity in the *Plasmodium berghei* test in mice[2] has been established: dihydroquinidine > dihydroquinine ≅ 3-*epi*dihydroquinidine > 3-*epi*dihydroquinine. Replacement of the 6′-methoxy group with a 6′,7′-methylenedioxy or a 7′-chloro group is an effective modification; the 7′-chloro analogs appear, thus far, to be the most active compounds in the 3-*epi*- as well as in the *normal* series[2].

Zusammenfassung. Ein Vergleich dieser Resultate mit denjenigen, die wir für (±)-Dihydrochinin und (±)-Dihydrochinidin berichtet haben[2], bestätigt die Ergebnisse anderer Arbeiten[4], dass Inversion am C-3 nur eine geringe Abnahme der Aktivität zur Folge hat. Die folgenden Aktivitäten gegen *Plasmodium berghei* in Mäusen[2] wurden in abnehmender Ordnung festgestellt: Dihydrochinidin > Dihydrochinin ≅ 3-*Epi*dihydrochinidin > 3-*Epi*dihydrochinin. Die Ersetzung der 6′-Methoxygruppe mit einer 6′,7′-Methylendioxy- oder 7′-Chlorgruppe ist eine wirksame Abwandlung; die 7′-Chlorderivate scheinen bisher die wirksamsten Verbindungen sowohl in der 3-*Epi*- als auch in der *normalen* Serie zu sein[2].

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The Effect of Bacterial Host Strains on the Inactivation of Polyvalent *Staphylococcus aureus* Bacteriophages

Recent investigations have indicated that the DNA molecule damaged by physical agents (UV- or ionizing radiation resp.) might be repaired by means of enzymes and in this way provide again the correct genetic information[1–5].

In the present work we tried to find out whether it would be possible to repair in the same way lesions induced by chemical agents such as hydroxylamine (HA). The polyvalent phages of *Staphylococcus aureus* have been chosen for these studies. Their wide host spectrum enabled us to use a large number of various host strains to study the relationship between the inactivated phage and host cell, which might influence the potential repair processes.

Material and methods. Experiments were carried out using following polyvalent *St. aureus* phages: PK, φ200, φ131, X, PA, P66, A/5 and 812.

Bacterial *Staphylococcus aureus* host strains were: Sta K (host for phage PK); 6409 (host for phages A/5, φ200 and φ131); 812 (host for phage 812); 809š (host for phages X and P66). Sta 66 (host for phage PA) and strains 53, 55, 42E, 3B and 879. All host and phage strains were obtained from the collection of bacteriophages and bacteria from Institute of Biophysics, Brno. Bacteria were cultivated on tryptone medium (15 g of tryptone Oxoid, 2 g of yeast extract, 7 g NaCl, 1000 ml of dist. H_2O; pH 7.5 was adjusted before autoclaving).

Preparation of phage stocks: each phage stock was prepared on its host strain in tryptone medium enriched by yeast extract. The titer of the lysates was usually about 5×10^{10} plaque forming units/ml. Inactivation of phages by hydroxylamine: 0.1 *M* aqueus solution of HA adjusted to pH 7 by 10% NaOH before the experiment was used for the inactivation of phages. Inactivation proceeded at the temperature 37 °C. Oxygen was bubbled through the suspension during the experiment. At the beginning and at given time intervals, samples were taken and in appropriate dilution plated by the double layer agar technique with the host strain and incubated overnight at 37 °C.

Results and discussion. When studying the inactivating effect of HA on polyvalent phages of *Staphylococcus aureus*, we have observed that these phages were more sensitive to the aciton of HA as compared with the phages of *E. coli*. It is apparent from Figure 1 that the treatment of *Staphylococcus* phages with 0.1 *M* HA decreased the titer of phages to 0.1% within 5–10 min, whereas *E. coli* phages containing double stranded DNA and treated by HA under the same conditions were inactivated to the same extent within 50–60 min[6]. We have observed differences between the *Staphylococcus* phages with respect to the HA treatment even between the phages with the same antigenic structure, belonging to the same serological group (for example φ131, 812, A/5 and PA – serological group D).

We have furthermore investigated the possibility of repair of lesions induced in phages by HA treatment by means of host strain. In these experiments the polyvalence of *Staphylococcus* phages has been exploited. The phages PA and φ131 were chosen, as they differed in their sensitivity to HA and simultaneously lysed most of the bacterial strains used. For our purposes we have used those host strains which revealed at normal titration the same sensitivity: strain 53, 55, 42E, 3B, 812 and 879. In this way the possibility of the influence of external factors on the inactivation, like different ability of phage growth on the host strain used or resistance of a certain part of the population of the strains employed to the phage investigated, has been eliminated.

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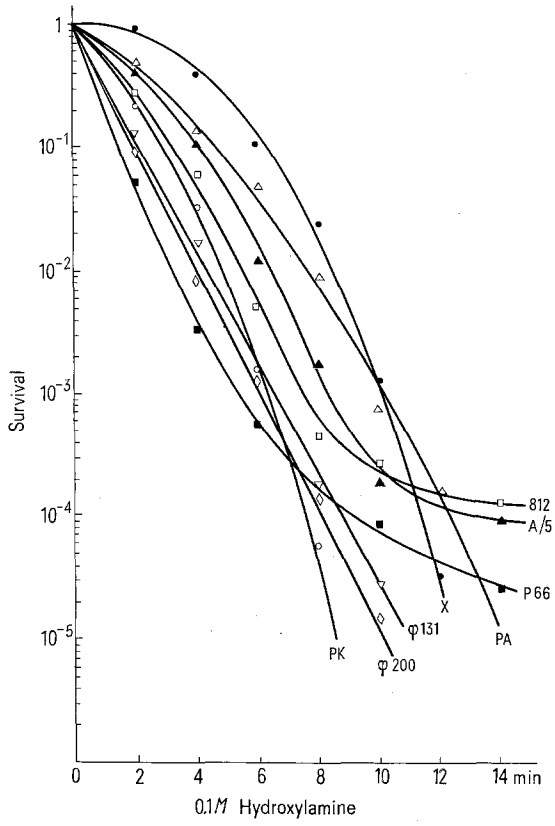

Fig. 1. Inactivation of polyvalent phages of *Staphylococcus aureus* by 0.1 *M* hydroxylamine. The phages were plated on the respective host strains.

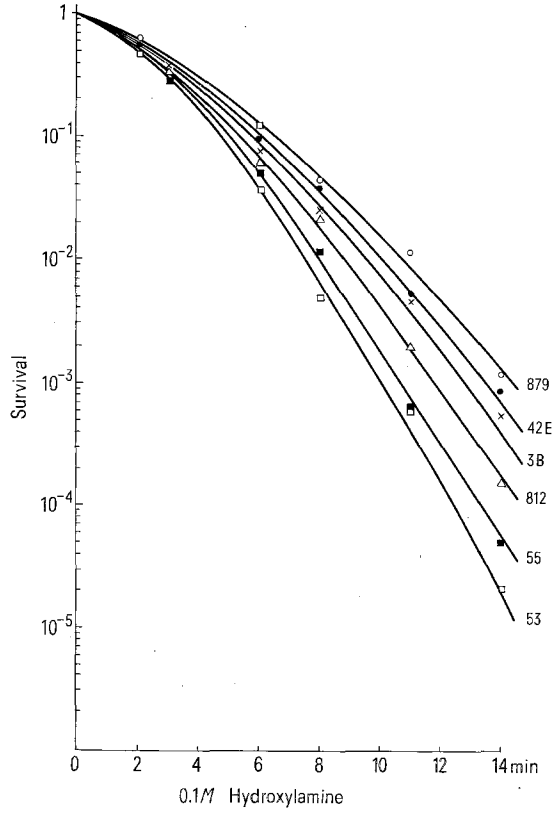

Fig. 2. Inactivation of polyvalent phage PA by 0.1*M* hydroxylamine after plating on 6 different host strains: 53, 55, 812, 42 E, 3 B and 879.

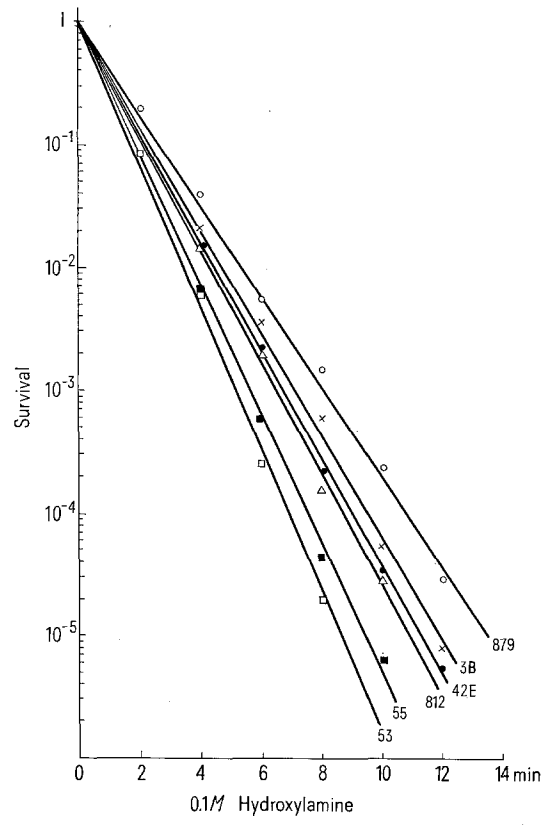

Fig. 3. Inactivation of polyvalent *Staphylococcus* phage φ131 by 0.1*M* hydroxylamine after plating on 6 different host strains. The strains were those shown in Figure 2.

From Figures 2 and 3 it is evident that the extent of inactivation depends to same extent on the bacterial strain used. In both phages the lethal damage induced by HA was maximum on the strain 53; while on the contrary, after plating on the strain 879 the lethal (DRF) effect was minimum. The corresponding dose reduction factor in phage φ131 was 1.54 and 1.42 in phage PA; both values are high compared with the value 1.12 obtained after the host cell reactivation (HCR) of hydroxylamine inactivated *E. coli* phage λcb_2[7]. Inactivation curves obtained after plating the phages on the other host strains (55, 812, 3B and 42E) were between the two extremes mentioned above (Figures 2 and 3).

These results support the assumption that there are a number of host strains of *Staphylococcus aureus* which may influence the surviral of hydroxylamine treated phages by host cell reactivation. The extent of the lethal damage induced in phage by HA is apparently dependent on the state of the repair mechanism controlling the enzymatic excision. These problems are now being studied in more detail in our laboratory.

Zusammenfassung. Versuche über Inaktivierung von Staphylokokkenphagen durch Hydroxylamin. Das Resultat wird auch durch die Wahl des Wirtsorganismus bestimmt.

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