of the presumed ancestral chromosome number i.e. all acrocentrics have fused to form biarmed chromosomes. Unlike the muntjacs[7,8] the number of major chromosome arms of 64, however, is not very different from those of most Bovidae, Suidae and Cervidae. This fits well into the evolutionary history of these artiodactyls.

Whether complete Robertsonian fusion is a characteristic feature of all tragulids remains to be confirmed. To this end, attempts are being made to secure specimens of the larger mouse deer, *T. napu*[9].

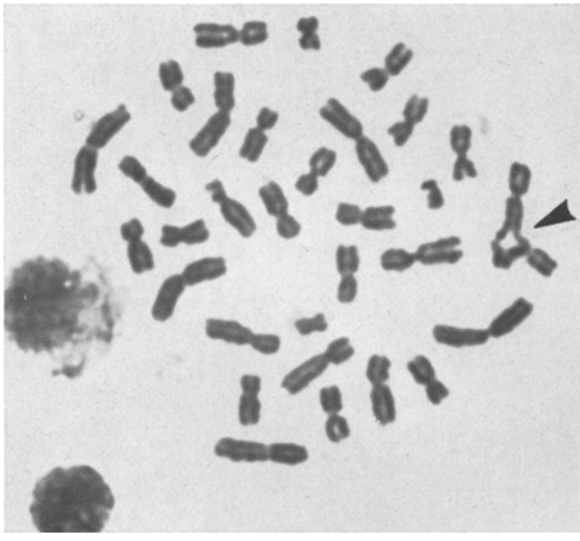

Fig. 3. c-Metaphase of male *T. javanicus* showing chromatid exchange (arrowed).

Zusammenfassung. Der malayische Tragulid (*Tragulus javanicus*) besitzt $2n = 32$. Alle Chromosomen sind entweder metazentrisch oder submetazentrisch, wobei die metazentrischen *Y*-Chromosomen am kleinsten sind. Die Sex-Chromosomen sind vom gewöhnlichen Typ, während ein Autosomenpaar durch das Vorhandensein einer sekundären Konstriktion charakterisiert ist.

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Antimalarial Activity of Racemic 3-*Epi*dihydroquinine, 3-*Epi*dihydroquinidine and their Various Racemic Analogs in Mice Infected with *Plasmodium berghei*

Reduction of the vinyl substituent has only a minimal effect on the antimalarial activities of quinine and related alkaloids[1,2]. Natural, unnatural and racemic dihydroquinine and the corresponding dihydroquinidines are equally active as antimalarials in mice infected with *Plasmodium berghei*[2]. In order to determine the importance of the stereochemistry at C-3 in these dihydro compounds, (±)-3-*epi*dihydroquinine, (±)-3-*epi*dihydroquinidine and 3 of their respective analogs were prepared and tested. The toxicities and activities of the 2 dihydro series are summarized in Tables I and II respectively.

These compounds were synthesized by the method previously described for the preparation of quinine and quinidine[3] using the appropriate intermediate with the requisite stereochemistry at the centers of asymmetry.

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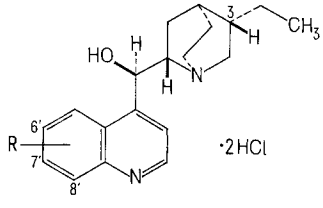
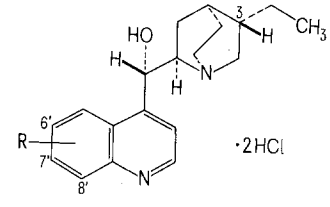
3 J. Gutzwiller and M. Uskoković, J. Am. chem. Soc. *92*, 204 (1970).

Table I. (±)-3-*Epi*dihydroquinine analogs



$R_{6'}$	$R_{7'}$	$R_{8'}$	LD_{50}, i.p. in mice (mg/kg)	Activity in mice vs. *Plasmodium berghei* MED (mg/kg)
CH_3O			285 ± 11	> 200
CH_3O		CH_3O	230	> 200
	Cl		150 ± 10	100
–O–CH_2–O–			275 ± 14	200

Table II. (±)-3-*Epi*dihydroquinidine analogs



$R_{6'}$	$R_{7'}$	$R_{8'}$	LD_{50}, i.p. in mice (mg/kg)	Activity in mice vs. *Plasmodium berghei* MED (mg/kg)
CH_3O			130 ± 6	100
CH_3O		CH_3O	205 ± 0	100
	Cl		187 ± 9	100
–O–CH_2–O–			150 ± 6	100

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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