from chalcomycin in that it lacks the C-6 methyl group which the latter contains. Both neutramycin and chalcomycin fit in with the generally accepted biogenesis of the lactone ring from a polyketide precursor, itself formed from acetate and propionate units. Thus an acetate unit is apparently incorporated into the C-5, C-6 portion of neutramycin whereas a propionate unit is incorporated in chalcomycin[5].

Zusammenfassung. Für das Antibiotikum Neutramycin wird die Strukturformel I abgeleitet.

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Polarographic Behaviour of Polycytidylic Acid and its Double-Stranded Complex with Polyinosinic Acid

Our previous results have shown that denatured deoxyribonucleic acid (DNA) is polarographically reducible in a neutral medium, while native double-helical DNA is non-reducible under the same conditions[1,2]. We have explained the polarographic reducibility of denatured DNA by the availability of the potentially reducible bases contained in DNA for the electrode process. It has been presumed that the residues of cytosine, which yields in a monomeric form a direct current (d-c) polarographic reduction step at pH 7, take part in the process[3-5]. Provided the above-mentioned presumptions are correct, it can be expected that polycytidylic acid (poly C), which is at neutral pH a random coil with fluctuating regions of helicity[6], will behave similarly to denatured DNA, while its double-helical complex with polyinosinic acid poly (I) · poly (C) will be polarographically non-reducible. Our experiments confirmed this expectation in principle.

Polarographic measurements were carried out in ammonium formate with sodium phosphate background electrolyte, which had been used earlier for DNA analysis. The instruments used were described in our previous papers[1,2]. Poly C was prepared by using a polynucleotide phosphorylase (2.7.7.8) obtained from *Micrococcus lysodeikticus*[7]. Commercial preparation of poly I (California Corporation for Biochemical Research) was kindly donated by Dr. V. KLEINWÄCHTER. All chemicals used for background electrolyte solutions were of analytical grade.

In 0.5 M ammonium formate with 0.1 M sodium phosphate (pH 7) $2 \times 10^{-4} M$ poly C (related to phosphorus content) produced a d-c polarographic reduction step whose height corresponded to c. 0.6 μA and the half-step potential ($E_{1/2}$) was about -1.34 V, i.e. slightly more positive than $E_{1/2}$ of denatured DNA in the same medium[2]. Poly I was, in agreement with the polarographic non-reducibility of monomeric hypoxanthine at neutral pH[8], inactive. The d-c polarographic step of poly C almost disappeared after the addition of the equivalent amount of poly I (formation of the 1:1 complex was controlled spectrophotometrically).

The oscillopolarographic behaviour of poly C, poly I and poly (I) · poly (C) agreed in principle with their d-c polarographic behaviour, the sensitivity of the estimation of poly C by means of the oscillopolarographic 'first curve technique'[1] was, however, much higher, as compared with d-c polarographic analysis (Figure 1). For the oscillopolarographic analysis only a few tenths of μg of poly C were necessary. The depth of the indentation of poly C depended on the ammonium formate concentration (Figure 2) like the depth of the indentation of denatured DNA. Mixing of poly C with poly I caused a decrease in the depth of the indentation of poly C; however, this indentation did not disappear completely even in the presence of an excess of poly I (Figure 3). It is possible that the presence of a small indentation or a step on the curves of poly (I) · poly (C) may be con-

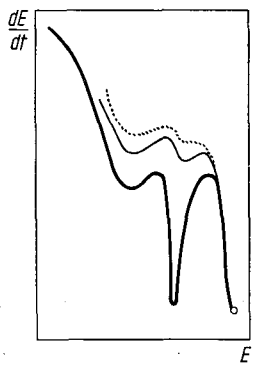

Fig. 1. Right section of the cathodic part of the oscillopolarogram dE/dt against E. $1.7 \times 10^{-5} M$ poly C in 1.0 M ammonium formate with 0.1 M sodium phosphate (pH 7). ——— first curve, ——— second curve, ····· third curve.

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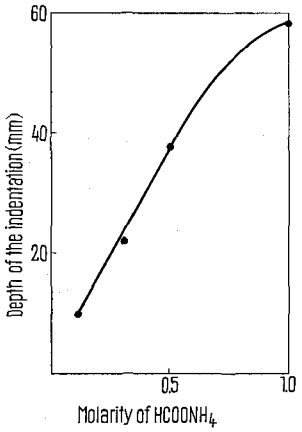

Fig. 2. Dependence of the depth of the indentation of poly C on the concentration of ammonium formate. $1.7 \times 10^{-5} M$ poly C in $0.1 M$ sodium phosphate with ammonium formate in the concentration given in the graph (pH 7).

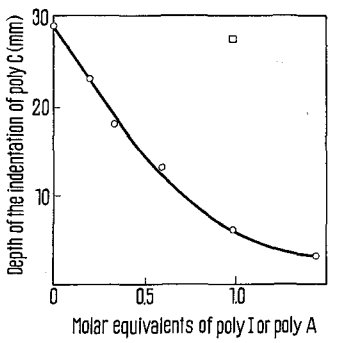

Fig. 3. Formation of the 1:1 complex of poly (C) × poly (I) followed by oscillopolarographic technique. Homopolymers were mixed in $0.1 M$ NaCl with $0.01 M$ sodium phosphate (pH 7). After 2 h of incubation at room temperature, the supporting background electrolyte was added. The oscillopolarographic measurements were carried out in $0.3 M$ ammonium formate with $0.1 M$ sodium phosphate pH 7. The depth of the indentation of poly C was measured on the first curve. Concentration of poly C ($7.5 \times 10^{-5} M$) was held constant in all samples, while the amount of poly I (○——○) or poly A (□) varied as indicated in the Figure.

nected with single-strand breaks and/or other irregularities present in the double-helical structure of poly (I) · poly (C), as is the case with DNA[9]. The mixing of poly C with polyadenylic acid (poly A) had almost no influence on the depth of the indentation of poly C (Figure 3) (poly A does not form a complex with poly C under the given conditions[6]).

Our preliminary results[10] show that polarographic techniques may become useful in the study of the structure of synthetic polynucleotides. A paper concerning the character of processes to which poly C and other polynucleotides are subject on the electrode will be published elsewhere.

Zusammenfassung. Es ergibt sich, dass die Polyzytidylsäure unter dem neutralen pH eine polarographische Reduktionswelle ähnlich der Welle der denaturierten Desoxyribonukleinsäure gewährt. Zur Bestimmung der Polyzytidylsäure mit der «ersten Kurve» genügt bereits 1/10 μg des Stoffes. Im Komplex der Polyzytidylsäure mit Polyinosinsäure ist die Reduzierbarkeit der Polyzytidylsäure eliminiert.

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Anti-Tumour Activity of Carbobenzoxy-L-Asparagine

Various neoplasms in different animal species are inhibited by treatment with L-asparaginase derived from either guinea-pig serum or *Escherichia coli*[1-5]. Certain human leukemias were also found to be sensitive to treatment with the bacterial enzyme[6]. This effect was ascribed to the enzymatic deamidation of L-asparagine, an amino acid essential for the growth of the susceptible tumours[7]. Since it is possible to prevent utilization of nutrilites by structural analogues, it was felt that compounds structurally related to L-asparagine might also inhibit the growth of L-asparaginase-sensitive tumours. Various L-asparagine analogues were found to inhibit L-asparaginase activity of *Mycobacterium phlei*[8] and of rat liver[9]. The L-asparaginase activity of *Saccharomyces cerevisiae* was previously found to be competitively inhibited by carbobenzoxy-L-asparagine[10]. The present communication describes the effect of the latter compound on the growth of an L-asparaginase-sensitive murine lymphoma.

Carbobenzoxy-L-asparagine (CBZ-asparagine) was purchased from Fluka AG, Buchs, Switzerland. A fine suspension was obtained by homogenizing it in normal saline with mortar and pestle. A single injection of CBZ-asparagine at doses up to 120 mg per mouse did not show any noticeable toxic effects. For treatment of

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