The second phases which separate from solutions containing amines, nucleotides and bivalent cations are highly viscous, transparent and located at the bottom of the tube[11]. They contain all 3 components in concentrations several times higher than in the supernatant.

The results of analytical ultracentrifugation as well as the composition of the second phases indicate that addition of amines to nucleotide-metal aggregates enhances their average apparent molecular weight and that the new aggregates consist of nucleotides, amines and bivalent cations. Therefore, nucleotide-metal aggregates seem to be able to incorporate added monoamines.

Based on these experimental results and on the previous findings that amines in contrast to the nucleotides do not aggregate in the presence of Ca^{++} and Mg^{++} a tentative hypothesis for the uptake of biogenic monoamines by storage organelles may be presented. Accordingly the organelles which have a high concentration of bivalent cations would primarily accumulate nucleotides in the form of aggregates. These aggregates can probably not leave the organelles, as they are too large to pass through the surrounding membrane. The amines, e.g. the 5HT of blood platelets, have been shown to enter the cells by an active transport at the level of the cytoplasmic membrane[17] and also to be able to penetrate into the organelles[18]. Here, they are probably incorporated into the preexisting nucleotide-metal aggregates. As a consequence, the concentration gradient of the free amine between exterior and interior of the organelles would be maintained, enabling more of the amine to penetrate and to be incorporated into nucleotide-metal aggregates. This may result in an accumulation of amines in the organelles without the anticipation of an active transport mechanism for amines at the level of the membrane of the organelles[14,18].

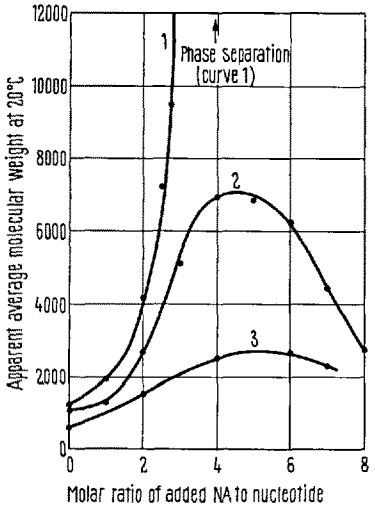

Fig. 2. Effect of added noradrenaline (NA) on the apparent average molecular weight at 20 °C of 12% w/v solutions of different nucleotides, containing $CaCl_2$ in a molar ratio to the nucleotide of 0.23; pH adjusted to 6. Curve 1: Guanosine-5′-triphosphate (GTP). Curve 2: Adenosine-5′-triphosphate (ATP). Curve 3: Uridine-5′-triphosphate (UTP).

This hypothesis is supported by the finding that in platelets of guinea-pig, which normally are poor in 5HT, the isolated storage organelles contain nucleotides and bivalent metals in high concentrations but only little 5HT[19]. On exposure of these platelets to exogenous 5HT the organelles take up and store considerable amounts of the amine[4].

In conclusion, preexisting aggregates between ATP or GTP and bivalent cations seem to be able to incorporate biogenic monoamines, resulting in a further increase in the apparent molecular weight. This may be an essential mechanism for the uptake and storage of amines in the subcellular organelles, e.g. of blood platelets, adrenal medulla and possibly sympathetic nerve endings.

Zusammenfassung. Analytische Ultrazentrifugation ergibt, dass Adenosin-5′-triphosphat und Guanosin-5′-triphosphat in Gegenwart von Ca und Mg hochmolekulare Aggregate bilden. Die scheinbaren mittleren Molekulargewichte dieser Aggregate nehmen nach Zusatz von 5-Hydroxytryptamin oder Noradrenalin stark zu. Es wird daraus geschlossen, dass Nucleotidaggregate biogene Amine inkorporieren, wobei Nucleotid-Aminaggregate entstehen. Dies erklärt möglicherweise die Aufnahme und Speicherung von biogenen Aminen in nucleotidhaltigen subzellulären Organellen, z.B. von Blutplättchen, Nebennierenmark und noradrenergen Nerven.

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Relationship Between Rm Values and Biological Activity of Steroid Esters

A reversed-phase TLC method was previously used in order to determine the Rm values of antibiotics and testosterone derivatives as an expression of their lipophilic character[1–3]. A significant relationship was observed between the Rm values, which were also shown to be very well correlated with the Hansch' π values[3], and the hemolytic activity of testosterone compounds[3]. The purpose of the present paper was to show that the Rm values are also correlated with the in vivo activity of long-acting testosterone esters.

The Rm values of testosterone esters were previously determined in the presence of acetone or methanol in the mobile phase[3]. It was shown that, because of a linear relationship, both series of Rm values were equally correlated with biological activity[3]. The Rm values at 54% acetone in the mobile phase were used in the present work (Table). Higher and/or positive Rm values indicate compounds more lipophilic than those characterized by lower and/or negative Rm values.

Some activity data were taken from the literature[4]; the biological response (BR) was represented by the time (days) of maximum effect of testosterone esters in the capon's comb test[5] (Table).

The relationship between lipophilic character (Rm values) and logarithm of the biological response (log BR values) was analyzed by means of regression analysis. A

significant linear relationship was shown between Rm and log BR values. The standard deviation and the multiple correlation coefficient are indicated by s and r.

	n	s	r
$\log BR = 0.295 + 0.416\ Rm$	7	0.085	0.934

The positive sign associated with the Rm term shows that the activity of testosterone derivatives is longer in compounds with higher lipophilic character.

The above results could be explained on the basis of a slower absorption from the site of administration as the lipophilic character increases. A classical concept has been that esterification delays absorption and therefore prevents the rapid destruction of the compounds[4,7,8]. A higher lipophilic character could also protect testosterone from metabolism until it reaches the site of action[9]. The mechanism by which the testosterone esters evoke their increased duration of action remains to be fully elucidated. However the present data show the importance of the lipophilic character. In particular the relationship beween Rm values and biological activity point out the usefulness of the chromatographic method in this kind of structure/activity studies.

Riassunto. I valori Rm di una serie di esteri del testosterone sono stati determinati con un metodo cromatografico su strato sottile a fasi invertite. Si è dimostrata una relazione lineare fra i valori Rm, espressione del carattere lipofilo delle molecole, e il protrarsi dell'attività degli stessi esteri del testosterone. Si conclude che i valori cromatografici Rm possono essere utili nello studio delle relazioni fra struttura e attività.

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Lipophilic character and biological activity of androgenic compounds

Compound	Rm values	Time of maximum effect	
		Obs. log BR	Calc. log BR
Testosterone	−0.60	0.00	0.04
−17-acetate	−0.22	0.12	0.20
−17-propionate	−0.05	0.25	0.27
−17-butyrate	0.09	0.39	0.33
−17-isobutyrate	0.09	0.43	0.33
−17-valerate	0.25	0.48	0.40
−17-caprinate	0.96	0.61	0.69

The data regarding the time of maximum effect are expressed on a molar basis and calculated on a relative scale with testosterone.

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Effets inhibiteurs de l'acide tellurique sur le développement des tumeurs de Crown-gall chez la tomate

Nous nous proposons d'étudier sur des plantes de Tomate saines ou inoculées par *Agrobacterium tumefaciens* l'effet de l'acide tellurique dont le pouvoir «rééquilibrant» chez des malades avait été mis en évidence par l'un de nous[1,2].

Matériel et techniques. Nous avons choisi comme matériel *Lycopersicum esculentum* var. Stalingrad que nous cultivons en serres entre 15 et 25 °C, chaque lot expérimental comprenant une centaine de sujets. Les bactéries (souche B_6 de l'institut Pasteur, Paris) sont inoculées au moyen d'une seringue à tuberculine traversant la tige de part en part au niveau du 2e ou du 3e entrenœud. Les solutions à tester sont appliquées quotidiennement pendant 71 jours au moyen d'un compte-gouttes à l'endroit de l'inoculation, ou au même niveau de la tige pour les sujets de contrôle, non infectés, le premier traitement étant appliqué, sauf pour des témoins exempts de tout traitement, 120 h après l'inoculation bactérienne. Par des essais préliminaires, nous avons déterminé la teneur en acide tellurique (10^{-4} et 10^{-3} g/ml) des solutions à tester qui permette une croissance subnormale des plantes et qui inhibe néanmoins le développement des tumeurs.

Résultats. Nous avons suivi la croissance des plantes, et éventuellement la formation et le développement des tumeurs, pour les quatre catégories de sujets: plantes saines ni inoculées ni traitées, plantes saines mais traitées par l'acide tellurique, plantes inoculées non traitées et enfin plantes inoculées et traitées.

Le traitement est arrêté 76 jours après le moment de l'inoculation. Dans chaque catégorie la moitié – soit une cinquantaine de sujets – est alors mesurée, pesée, ainsi que les tumeurs de Crown-gall (colonne 76 jours, Tableau), l'autre moitié étant encore maintenue en culture pendant 33 jours, sans nouvelle application d'acide tellurique (colonne 109 jours, Tableau).

A la fin de l'expérience (109 jours) nous constatons aucune différence significative entre les plantes saines qu'elles soient traitées ou non, l'acide tellurique aux concentrations employées n'ayant aucun effet nocif sur leur développement.

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