ler als kleinere, so dass z. B. bei einem Chromatogramm von *D*-, *L*- und *DL*-Histidin je nach den Umständen bei Besprühen mit Pauly-Reagenz zu Unrecht der Eindruck einer Trennung in die Antipoden entstehen kann. Auf diese Weise kann man beliebige Effekte erzielen. Für das Chromatogramm in Figur 2 wurden die Mengen so gewählt, dass eine Verteilung von *R_f*-Werten zustandekam, wie sie in keinem Fall bei einer Trennung in Antipoden zu erwarten ist. Am schnellsten laufen hier 30 γ *DL*-Histidin, dann folgen 20 γ *D*- und 15 γ *L*-Histidin. «Gewichtsloser» Tracer allein bleibt am weitesten zurück. Auf einer anderen Papiersorte, Whatman Nr. 4, die diesen Konzentrationseffekt nicht zeigt, erfolgt dagegen mit Sicherheit eine Antipodentrennung (Figur 3). Ein einwandfreier Nachweis der tatsächlichen Vorgänge wird also besonders für eine gleichzeitige und unabhängige Identifizierung von optischen Antipoden (als Substanzen

gleicher skalarer Grössen ergeben diese ähnliche Probleme wie Untersuchungen über Selbstdiffusion) nur durch die Simultanauftragung radioaktiver Tracer ermöglicht.

Summary. Weightless amounts of radioactive test-mixtures are run from the same starting point as the compounds to investigate while checked independently. It is shown that this allows a dependable identification even in cases where the technique of inactive parallel running test-mixtures fails completely.

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New Centrally Acting Drugs: Coumarin Derivatives

According to JONGEBREUR¹, there seems to be no pharmacological difference in coronary-dilator potency between chromone and coumarin derivatives. As a number of *N*-substituted 8-amino-methyl-7-methoxy and 7-hydroxychromones and flavones with central nervous system (C.N.S.) stimulating activity have recently been described^{2,3}, we thought it interesting to test whether this activity was retained in the corresponding coumarin derivatives. These are represented by the general formula:

in which the positions of the hydroxy or methoxy group and the basic chain were 7,8 – 7,6 – 6,5 – and 8,5 respectively. These compounds were prepared via the Mannich reaction on hydroxycoumarins or by means of the chloromethylation procedure applied to methoxy analogues, followed by amination. In both cases, secondary amines such as dimethyl and diethylamine, piperidine and morpholine were employed.

The pharmacological screening of fifty coumarin derivatives has shown that the C.N.S. stimulating activity is retained, though to a lower degree than in the corresponding chromone and flavone compounds. No difference is noticeable between hydroxy and methoxy derivatives, although the latter seem to furnish the most active compounds. The optimal position for the methoxy group and the basic chain is the *ortho* position, and, of the locations

tried, the 6:5 positions were found to be the best for C.N.S. stimulating activity. When the oxygen function and the basic chain are *para* to one another, a considerable loss of activity is observed, e.g. in the *N*-substituted 5-aminomethyl-8-methoxy (and 8-hydroxy) derivatives, with the sole exception of 3-methyl-8-methoxy-5-dimethylaminomethylcoumarin.

Of the basic chains, the dimethylaminomethyl is the most efficient, as in the corresponding chromone and flavone compounds. 6-Methoxy-5-dimethylaminomethyl-3-phenylcoumarin (Rec 14-0073) seems to be the most active compound in the series. Its activity expressed as the reciprocal of the intraperitoneal LD₅₀ of metrazol (71 mg/kg) was 17,8, on a molar basis, i.e. half that of the most active compound in the chromone series.

Riassunto. Si descrive una nuova classe di farmaci stimolanti il sistema nervoso centrale, rappresentata dalle aminometilidrossi- e dalle aminometilmetossicumarine *N*-sostituite.

L'attività di questi nuovi composti è inferiore a quella dei corrispondenti isomeri derivati dal cromone e dal flavone.

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¹ G. JONGEBREUR, *Arch. int. Pharmacodyn.* **90**, 384 (1952).

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