sulphate solution, and then converted into base chlorides with barium chloride. The residue obtained on evaporation of the solution to dryness was dissolved in absolute alcohol, and the alcoholic solution was passed through a column of aluminium oxide for chromatography. The first few fractions of the eluant yielded hygroscopic crystalline needles, identified as choline chloride by comparison with an authentic specimen. The later fractions of the alcoholic eluant yielded crystalline needles of a new quaternary base chloride named as Pluchine, m.p. 243–244 °C (decomposition and volatalization with evolution of gas), $[\alpha]_D^{20}$ – 29.51 (H_2O). Analysis found: C, 38.74, 38.59, 39.12, 39.09; H, 7.79, 7.67, 7.78, 7.81; N, 8.64, 8.30, 7.49, 7.68; cl, 23.55, 23.80, 22.85, 22.80. With alcoholic picric acid Pluchine gave a picrate, m.p. 181–182 °C. Analysis found: C, 38.46, 38.58; H, 3.87, 4.08; N, 16.09, 15.86; mol. wt. (Rast), 690, 674. Pluchine has no UV-absorption peaks between 220–340 nm, but has IR-absorption peaks (Nujol) at 3.75, 3.85, 3.95, 4.06, 4.17, 4.25, 4.8, 5.0, 5.36, 5.67, 5.8 (S), 6.75 (S), 7.05, 7.15 (S), 7.46, 7.75, 8.02 (S), 8.3 (S), 8.82 (S), 9.33, 10.1 (S), 10.54 (S), 10.75 (S), 11.1 (S), 11.35 (S) and 12.88 (S) μ (Figure 3, sample V-29-6). The NMR-spectrum[9] of Pluchine determined in D_2O solvent with TMS as external reference is given in Figure 4, sample V-33-2. When heated Pluchine decomposes with evolution of a volatile gas having amine-like smell and turning red litmus blue. The evolved gas was dissolved in alcohol and the alcoholic solution yielded with picric acid a picrate, needles, m.p. 219–222 °C, identified as trimethylamine picrate. Under identical conditions of heating acetylcholine chloride also yielded trimethylamine as the volatile component. As Pluchine has no UV-absorption, and as both Pluchine and acetylcholine chloride decompose on heating with evolution of trimethylamine, Pluchine has possibly an open chain structure with the trimethylammonium moiety at one end, similar to acetylcholine chloride.

On preliminary pharmacological investigations on rat's isolated intestine, SANYAL[10] found Pluchine to be a non-specific relaxant. It antagonises both acetylcholine and barium chloride induced spasms. It thus resembles Papaverine in its action. It was further observed by SANYAL[10] that Pluchine potentiates barbiturate-induced hypnosis in albino rats. Pluchine has also been found by PRASAD[8] to have antiinflammatory action in reducing carrageenin-induced inflammation in hind paw of albino rats when compared with cortisone taken as standard.

Thus, the cholinergic activity of the water-soluble portion of the alcoholic extract of *P. lanceolata*, as observed by PRASAD et al.[2] can be accounted for as due to the presence of choline in the drug. The smooth muscle relaxant spasmolytic action, central nervous system activity as evidenced by potentiation of barbiturate-induced hypnosis and the antiinflammatory activity of the water-soluble portion of the alcoholic extract as found by PRASAD et al.[2,3] are all due to the presence of a new quaternary base chloride, Pluchine, in *P. lanceolata*.

Further studies to elucidate the chemical structure of Pluchine are in progress. Detailed pharmacological investigations on Pluchine will be published shortly elsewhere.

Zusammenfassung. Es wird über die aktiven Prinzipien einer Pflanze, die in Indien zu Medizinalzwecken verwendet wird (*Pluchea lanceolata* I.), berichtet.

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[9] The author is indebted to Dr. J. MARKI, Varian AG, Switzerland, for determining the NMR-spectrum.
[10] A. K. SANYAL, unpublished report.

β-Ergokryptine, a New Alkaloid of the Ergotoxine Group[1]

Paper chromatographic analysis with the help of a special system (dimethyl phthalate impregnated paper as stationary phase, 20% formamide plus 80% citrate buffer pH 3.2 as mobile phase) has shown that certain ergokryptine preparations are not single substances but an isomorphically crystallizing mixture of 2 very closely related isomers which we would like to designate as α- and β-ergokryptine respectively. α-Ergokryptine corresponds to the alkaloid which at one time was described together with ergocristine and ergocornine as a component of the isomorphically crystallizing alkaloidal complex ergotoxine[2].

The separation of β-ergokryptine from α-ergokryptine in preparative quantities was achieved in the form of the salt with di-(*p*-toluyl)-L-tartaric acid. In ergokryptine preparations from Portuguese ergot an isomeric proportion α-: β-ergokryptine of 4:1 was established whilst Swiss cultivated ergot gave the proportion 2:1.

β-Ergokryptine $C_{32}H_{41}N_5O_5$ crystallized from benzene in rectangular plates m.p. 173° (decomp.) $[\alpha]_D^{20} = -174°$ (c = 1.5 in $CHCl_3$); – 91° (c = 2.0 in pyridine).

Epimerisation in alkaline or acid solution gave β-ergokryptinine $C_{32}H_{41}N_5O_5$. From methanol long needles, m.p. 220° (decomp.) $[\alpha]_D^{20} = +424°$ (c = 1.0 in $CHCl_3$); +492° (c = 1.0 in pyridine).

Catalytic hydrogenation of β-ergokryptine under the usual conditions for ergot alkaloids[3] led to 9,10-dihydro-β-ergokryptine, $C_{32}H_{43}N_5O_5$. From methanol or ethanol rhombic leaves, m.p. 194–195° (decomp.) $[\alpha]_D^{20} = -31°$ (c = 1.5 in pyridine).

On hydrolysis of β-ergokryptine under various conditions one equivalent of each D-lysergic acid, NH_3, dimethylpyruvic acid, rac. proline and L-isoleucine (natural *threo* form) were obtained. From these results and from the comparison of additional chemical, physical and spectroscopic data it follows that β-ergokryptine is differentiated from α-ergokryptine (earlier designated without

[1] 66. Mitteilung über Mutterkornalkaloide (65. Mitteilung: H. OTT, A. HOFMANN and A. J. FREY, J. Am. chem. Soc. *88*, 1251 (1966)).
[2] A. STOLL and A. HOFMANN, Helv. Chim. Acta *26*, 1570 (1943).
[3] A. STOLL and A. HOFMANN, Helv. Chim. Acta *26*, 2070 (1943).

the prefix as ergokryptine[4]) only through the substitution of the L-leucine residue by the L-isoleucine residue.

As would be expected from the trivial difference in chemical structure α- and β-ergokryptine and dihydro-α- and dihydro-β-ergokryptine respectively correspond with one another extensively in their pharmacological activity. The pharmacological comparison covered the main actions of the ergot alkaloids namely the adrenolytic activity[5], the action on uterus motility[6], serotonin antagonism[7] and the influence on vascular tone[8]. β-Ergokryptine is somewhat more active than α-ergokryptine.

No statistically significant difference was established in the pharmacological activity of dihydro-α-ergokryptine and dihydro-β-ergokryptine.

A detailed account of the experimental results will be given elsewhere.

Zusammenfassung. Es wird die Isolierung eines neuen Isomeren des Ergokryptins beschrieben, das sich von diesem nur durch den Ersatz des Leucin-Restes durch den Isoleucin-Rest im Peptidteil des Moleküls unterscheidet. Das neue Isomere soll als β-Ergokryptin und das früher beschriebene Alkaloid als α-Ergokryptin bezeichnet werden. Die beiden Isomeren, ebenso ihre Dihydro-Derivate, unterscheiden sich pharmakologisch nur ganz unwesentlich.

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Pharmaceutical Chemical Laboratories and Biological and Medical Research Division, Sandoz Ltd., Basel (Switzerland), 22 September 1967.

[4] Chemical Structure and Other Data of Ergokryptine, see A. HOFMANN: *Die Mutterkorn-Alkaloide* (F. Enke Verlag, Stuttgart, 1964), p. 25.

[5] J. BRÜGGER, Helv. physiol. Acta *3*, 117 (1945).

[6] B. BERDE and K. SAAMELI, in *Methods in Drug Evaluation*, Proc. of the Internat. Symposium, Milano 20–23 September 1965 (Eds P. MANTEGAZZA and F. PICCININI; North-Holland Publishing Co., Amsterdam 1966), p. 481.

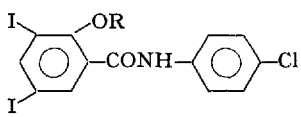
[7] A. CERLETTI and W. DOEPFNER, J. Pharmac. exp. Ther. *122*, 124 (1958).

[8] G. BARGER and H. H. DALE, J. Physiol. *41*, 19 (1910).

A New Compound Effective Against Acute Fascioliasis in Sheep

Although adult *Fasciola hepatica* infections in sheep can be treated by available products, acute fascioliasis continues to be a costly problem. Some fasciolicides are ineffective against the immature flukes. Most require the administration of high dose levels to produce even a moderate response. Unfortunately a very narrow therapeutic index at these levels makes their use hazardous to the sheep under field conditions.

In our search for a new fasciolicide, efficacy against immature worms and a high therapeutic index under field conditions were major objectives. From a series of 70 candidates, 2-acetoxy-4′-chloro-3,5-di-iodobenzanilide, SYD-230 (I, R = $COCH_3$), was chosen because it fulfilled these requirements. The compound was prepared by condensing 3,5-di-iodosalicylic acid with *p*-chloroaniline to give 4′-chloro-3,5-di-iodosalicylanilide (I, R = H). Subsequent acetylation gave SYD-230 which crystallized from aqueous dimethylformamide or acetone as white needles, m.p. 215–216 °C. 2-Acetoxy-4′-chloro-3,5:di-iodobenzanilide has a theoretical elementary composition for $C_{15}H_{10}ClI_2NO_3$ of C, 33.27; H, 1.86; N, 2.59; Cl, 6.55; I, 46.87. Found: C, 33.30; H, 1.94; N, 2.48; Cl, 6.52; I, 46.83. It has strong IR-absorption peaks (KBr disc) at 3290, 1770, 1657, 1535, 1575, 1600, 1490, 1190, 830 cm^{-1}. Its UV-spectrum exhibits a maximum at 262 nm (methanol).



(I)

The activity of SYD-230 against immature and mature *F. hepatica* was assessed in approximately 1000 grazing sheep. In a number of experiments, infections were induced by the administration of metacercariae in gelatin capsules. Drug effectiveness was measured by quantitative fecal egg counts made before 2–8 weeks after dosing, or by live fluke counts at autopsy. Effectiveness is expressed as percentage reduction in egg output or live flukes, when compared with untreated controls.

The Table shows results from a typical slaughter experiment to determine the activity of SYD-230 against immature *F. hepatica* in sheep dosed with 300 metacercariae.

Infections with adult *F. hepatica* were reduced 98–100% by a single oral dose of SYD-230 at 25 mg/kg.

In sheep carrying natural *Haemonchus contortus* infections, activity greater than 95% was found against adult worms after a single oral dose at 25 mg/kg. There was no significant activity against *Ostertagia* spp., *Trichostrongylus colubriformis* or *Nematodirus* spp.

The LD_{50} of SYD-230 in sheep was approximately 420 mg/kg by the rumenal route; 1600 mg/kg by the abomasal route. When administered orally as a 4% aqueous suspension, by conventional drenching equipment, to normal or stressed (heavily parasitized, advanced pregnancy,

Drug	Dose level mg/kg	Age of fluke (weeks)	% effectiveness
SYD-230	60	4	31
	90	4	83
	32	6	67
	48	6	97
CCl_4	120	4	35
	180	4	35
	64	6	0
	96	6	6