

of Galen to enter the dural wall of the straight venous sinus, where it runs in a subendothelial position.

In the human brain, the nerve passes through a remarkable formation of the arachnoid membrane. This resembles in some degree a greatly enlarged arachnoid granulation (Pacchionian body), measuring, in one specimen, 4.0 mm. in height and 2.5 mm. in width at its base. It projects up from the surface of the adjacent part of the cerebellum into the floor of the straight sinus at the point where this is joined by the vein of Galen, and is here attached to the dura mater. The structure of the granulation is peculiar in that it is filled with a sinusoidal plexus of blood-vessels and several large inter-connecting blood-sinuses. The pial matrix is unusually dense, and the general appearance bears a close resemblance to erectile tissue. The real nature and function of this arachnoid formation are still uncertain, but its structure and disposition suggest strongly that it may play an important part in regulating the venous return from the ventricles of the forebrain through the vein of Galen. In a distended condition, the granulation would bulge up conspicuously into the floor of the straight sinus at its anterior end, in a manner which must presumably impede the venous flow.

The nervus conarii, in traversing the granulation, actually passes through the cavity of one of the blood sinuses, ensheathed here in a fine covering of pial tissue. It then runs directly from the summit of the granulation into the dura mater and, as already noted, turns backwards in the floor of the straight sinus. Its further course has not yet been followed. The direction of conduction in the nerve is not known; the fact that in the monkey it can be traced to a core of neuropil in the centre of the pineal gland, in which are embedded numerous large ganglion cells of an autonomic type, suggests that it may be efferent with regard to the gland. On the other hand, most authorities are now agreed that true nerve cells are not a normal constituent of the human pineal gland. The nerve is accompanied by a small arteriole, but this vessel is considerably smaller than the nerve itself. Finally, it may be noted that neither the monkey nor the human material has provided confirmation for the existence of a ganglion at the tip of the pineal gland, as described by Pastori.

A detailed report of these observations will shortly be published.

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¹ Kolmer, W., and Loewy, R., *Pflügers Arch.*, **196**, 1 (1922).

² Pastori, G., *Zeitschr. d. ges. Neur. u. Psych.*, **117**, 202 (1928).

Cannabidiol and Cannabol, Constituents of *Cannabis indica* Resin

IN a previous publication, Work, Bergel and Todd¹ described a method for the separation of cannabiniol from *Cannabis indica* resin (hashish) of Indian origin as its crystalline *p*-nitrobenzoate. In the course of further work on hashish we have been able, through the co-operation of the Home Office (Drugs Branch), to examine a fresh specimen of the Egyptian drug.

Application of the *p*-nitrobenzoylation process to the distilled resin from this material yielded a less soluble fraction consisting of cannabiniol *p*-nitrobenzoate (in smaller amount than from the Indian drug) mixed with a second ester of much lower melting point. The latter was very difficult to separate and purify; the free phenol obtained from it by hydrolysis was a yellowish resin which, in contradistinction to cannabiniol, gave a positive Beam test (purple colour with alcoholic potassium hydroxide).

Adams, Hunt, and Clark² have recently described the isolation from American hemp resin of a substance, cannabidiol, yielding a *bis*-3:5-dinitrobenzoate, m.p. 106–107° ($[\alpha]_D^{27} = -76^\circ$). The similarity in colour reactions of cannabidiol and the above substance from the Egyptian resin was immediately evident, and conversion of the latter to its *bis*-3:5-dinitrobenzoate gave an ester m.p. 106–107° of which the analysis and optical rotation ($[\alpha]_D^{13} = -76.2^\circ$) also agreed with those of the cannabidiol derivative; there can be little doubt as to the identity of the two compounds. The molecular formulae of cannabiniol $C_{21}H_{32}O_2$ and cannabidiol $C_{21}H_{30-32}O_2$, together with their simultaneous occurrence in hemp resin, suggest a structural relationship between the two compounds, and preliminary chemical investigation seems to bear this out³. It would seem that, as regards these constituents, Egyptian hemp resin occupies a position intermediate between American resin, in which cannabiniol seems absent, and Indian resin, from which cannabidiol has not yet been isolated, although it may be present in small amount.

The physiological inactivity of cannabidiol lends further colour to the view that the Beam test is not a specific test for the active principle in hashish. We have noticed for some time that our most active fractions (Gayer test³) from the Indian drug give no coloration with alkali.

From certain fractions of Indian hashish we have recently, by acylation with azobenzene-4-carboxylic acid chloride, obtained a crystalline ester, m.p. 117–118° (Found: C, 78.0; H, 7.5; N, 6.1. $C_{21}H_{31}O_2 \cdot OCOC_6H_4N_2$ requires C, 77.9; H, 7.6; N, 5.4), apparently derived from a monohydric phenol. Alkaline hydrolysis of this ester gives a resinous phenol which reacts negative in the Beam test and gives, like cannabiniol and cannabidiol, a positive indophenol reaction. The constitution of this new substance, which we name *cannabol*, remains to be elucidated, but it seems probable that it is a partially hydrogenated cannabiniol isomeric with cannabidiol. This would accord with a possible view of the biogenesis of these substances. Cannabidiol may arise by condensation of a terpene with a dihydric phenol; cyclization would then yield cannabol, from which cannabiniol could be obtained by dehydrogenation.

Further details of this work will be published elsewhere.

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¹ *Biochem. J.*, **33**, 123 (1939).

² *J. Amer. Chem. Soc.*, **62**, 196 (1940).

³ *Arch. Exp. Path. Pharm.*, **129**, 312 (1928).