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Toxicity of "Eucupin" in Local Analgesia.

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A group study for the evaluation of local analgesics by clinical trial was organized at the University of California Hospital in December, 1927. Prolongation of analgesia was especially desired. The analgesics first studied were 0.5% and 1.0% procaine and "tutocaine" to which 0.1% "eucupin" had been added, as suggested by De Takats.[1] These solutions gave extremely satisfactory analgesia, lasting in some cases as long as 24 to 36 hours. Local reactions, such as erythema, induration, and delayed healing occurred, however, in the majority of cases. Extensive sloughs of the skin and subcutaneous structures that greatly prolonged the post-operative course, developed in 2 out of 15 patients. Four others suffered minor sloughing.

These reactions suggested excessive toxicity for the infiltrated structures and made the abandonment of the "eucupin" containing solutions advisable. As a further check, a series of controlled intradermal wheals were made, using 10 medical students as subjects. The solutions used were 1% procaine and 1% "tutocaine" to which 0.1% "eucupin" had been added, and solutions of 1% procaine and 1% "tutocaine" for controls. The results checked the clinical observations. The average duration of analgesia for the 1% procaine and the 1% "tutocaine" was 2 hours. The average duration of analgesia for the 1% procaine-0.1% "eucupin" mixture was 20 hours; for the 1% "tutocaine"-0.1% "eucupin," 24 hours. There was no evidence of local tissue damage at the site of either the procaine or "tutocaine" injections. Local reactions occurred in 6 cases (60%) with each of the "eucupin" solutions. These varied in intensity from a persistent erythema to definite sloughing. There were 2 small sloughs from the procaine-"eucupin" and 3 sloughs from the "tutocaine"-"eucupin". Of the latter, 2 were quite small, but the third was nearly 2 cm. in diameter and accompanied by marked vesication and erythema. All were non-painful. Pigmentation and partial analgesia were still present 8 months later at the sites of 4 of the procaine-"eucupin" and 5 of the "tutocaine"-"eucupin" wheals.

[1] Takats, G. De, *Surg., Gynec. and Obst.*, 1926, xliii, 100.

Further tests were carried out using 0.05% and 0.01% "eucupin" with both procaine and "tutocaine". These weaker solutions gave no definite prolongation of analgesia beyond that of the controls and gave no local reactions.

All of the solutions were prepared by the Pharmacy of the University of California Hospital. "Eucupin base" was used throughout. It was dissolved by the addition of 0.1 N HCl and the solution was then neutralized with 0.1 N NaOH until the mixture remained persistently cloudy. The addition of 2 or 3 drops of 0.1 N HCl then sufficed to clear the solution by redissolving the precipitated "eucupin base".

Our conclusion is that, although solutions containing "eucupin" give satisfactorily prolonged analgesia, the local toxicity is too great for clinical use. Solutions made directly from "eucupin dihydrochloride" might possibly prove less toxic and tests are now in progress to determine this.

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X-Ray Diffraction Spectra of Glycine.

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There still remains some uncertainty[1] as to whether the needle-like crystals of glycine (produced by precipitation with alcohol from aqueous solution) are identical with the plate form of the crystals (produced by crystallization from water).

This investigation attempts to throw some light on the problem by making use of X-ray diffraction patterns; the powder method was employed.

Glycine from 4 different sources, as follows, was used. A—Prepared by Pfanstiehl. B—Prepared by Eastman Kodak Company. C—Prepared at the Biochemistry Department of this University by the formaldehyde method.[2] D—"Dunn No. 1, 1927," prepared by the reaction of monochloracetic acid and ammonia. The samples,

[1] Falk and Sugiura, PROC. SOC. EXP. BIOL. AND MED., 1917, xv, 25. Falk and Sugiura, *J. Biol. Chem.*, 1918, xxxiv, 29. Biltz and Paetzold, *Ber. deutsch. chem. Ges.*, 1922, xvi, 1066. Brautlecht and Eberman, *J. Am. Chem. Soc.*, 1923, xlv, 1934. Ley and Arends, *Ber. deutsch. chem. Ges.*, 1928, 618, 212.

[2] Ling and Nanji, *Biochem. J.*, 1922, xvi, 707.