The Analgesic Action of Teropterin[1]

Donald Slaughter

Department of Physiology and Pharmacology, University of South Dakota School of Medicine, Vermillion

In 1947 Farber and his associates (*1*) indicated that teropterin, when administered to patients suffering from various forms of cancer, made it possible in some instances to reduce the amount of analgesia required. This indicated that teropterin possessed a certain amount of pain-relieving activity. Lehv, *et al* (*2*) stated categorically that "Our clinical observations indicate that the drug is nontoxic in the dosage given. Pain was relieved in most instances, if not all, by the use of teropterin. This obviated, in the main, the necessity for further use for opiates with their concomitant depressive effect."

These clinical observations on the analgesic property of teropterin were of interest in our laboratory, and we decided to prove or disprove the pure pain-relieving activity of this drug.

Twelve experiments on premedical students were performed, using a modified Wolff-Hardy-Goodell technique. Each one of the subjects received a 20-mg dose of teropterin injected intramuscularly. Neither the operator of the pain threshold apparatus nor the subject was cognizant of the nature of the drug that was injected, since all doses were administered by a third individual.

A definite rise in the pain threshold response was observed 15 min following the injection of 20 mg of teropterin. On an average, the peak of the effects were reached in 70 min and lasted for 155 min. Teropterin produced a 6.6% rise in pain threshold when the peak of the effects were reached. In each instance the experimental data showed that the effects were always in the same direction. This fact made it clear to us that teropterin was actually producing a true analgesic effect.

The results on 12 subjects definitely indicate that teropterin causes analgesia as interpreted by a rise in pain threshold in man. This confirms the clinical observations thus far reported. Contrary to the sense of well-being and some slight euphoria as was noted in those patients with cancer who received teropterin, we did not observe any of these effects. Nausea and other subjective symptoms were also lacking.

Teropterin possesses true analgesic action when tested on the normal human subject. This activity should be of value in reducing the amount of sedation needed when teropterin is used clinically.

References

1. Farber, Sidney, Cutler, Elliott C., Hawkins, James W., Harrison, J. Hartwell, Pierce, E. Converse, II, and Lenz, Gilbert G. *Science*, 1947, **106**, 619.
2. Lehv, S. P., Wright, L. T., Weintraub, S., and Arons, I. *N. Y. Acad. Sci.*, 1948, **10**, 75.

[1] Teropterin was kindly furnished by the Lederle Company, Pearl River, New York.

Flow in a Thin Glass Capillary as Affected by Wetting the Exterior of the Capillary[1]

J. C. Henniker and J. W. McBain

Stanford Research Institute, California

A review of pertinent literature has revealed widespread evidence that the outermost monolayer of molecules at the phase boundary of a liquid induces an orientation extending into the body of the liquid for many molecular lengths (*1*). The most reliable examples involve a range of orientation from a few tens of Angstrom units to a few thousand. The experiments of Nutting (*3*), however, pointed to an immobile layer of much greater depth.

Nutting found that the flow of crude petroleum oil through a narrow thin-walled glass capillary was appreciably slowed (6.8%) when the *outside* of the capillary was surrounded with water. He accounted for this by postulating an immobile layer of oil on the inside of the tube no less than 65,000 A thick. Kaminski, working in these laboratories and following the method outlined by Nutting, obtained comparable results (*2*).

It was apparent, however, that the effect could have been due to variations in temperature, since the temperature coefficient of viscosity of the medicinal paraffin oil used by Kaminski was such that the flow would have

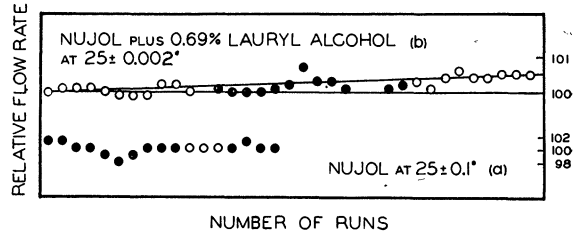

FIG. 1. Relative flow rate plotted against the number of passes through the capillary in (a) Series 1, and (b) Series 3. Open circles refer to passes when the outside of the capillary was dry; solid circles when the capillary was surrounded by water.

increased 7%/°C. Nutting's effect could be accounted for by the oil's being a degree warmer when not surrounded by water, and Kaminski's could be accounted for similarly by variations of a degree or two. This might well have occurred if the apparatus or the oil had been exposed to radiant energy during a measurement, or if the room temperature had risen just before a measurement. The particularly marked retardation in the flow of crude petroleum reported by Nutting and confirmed by Kaminski might thus be explained by the strong absorption this oil shows in the near infrared. Either of these variations would have warmed the dry capillary or reservoir of oil more rapidly than the capillary surrounded by a relatively large mass of water, and would then have led to a faster flow in the dry tube than in the wet.

[1] This work was done under contract between the Office of Naval Research and Stanford Research Institute.