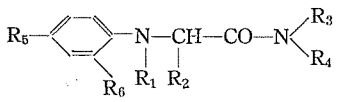
algesic action, on numerous 2-anilinoacetamide derivatives, prepared for the purpose of decreasing the toxicity and increasing solubility of acetanilide and acetophenetidine with increase or retention of their pharmacological effect.

Two compounds were found to satisfy these obiectives: GB-105 and GB-302.



GB-105: R_1=$COCH_3$, R_3, R_4=CH_3, R_2, R_5, R_6=H

GB-302: R_1=COCH, R_3, R_4=CH_3, R_2, R_6=H, R_5=OC_2H_5

A Phrmacological Study of 6-Hydroxy-4a, 10-Trimethylene-1, 2, 3, 4, 4a, 9, 10, 10a-Octahydrophenanthridine

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Japanese Journal of Pharmacology, **11**, 101-113 (1962)

The structure-activity relationship of various chemical compounds, which resembled to morphine in their structures and which were synthesized by Sugimoto *et al.*, has been reported. Among those compounds a reacemic 6-hydroxy-4a, 10-trimethylene-1, 2, 3, 4, 4a, 10, 10a-octahydrophenanthridine hydrochloride (DH-7), which have a nitrogen atom at 9-position of the morphinan ring, showed almost the same strong analgesic activities as morphine hydrochloride in a series of screening test.

Further studies of the analgesic activity of DH-7 and the comparative pharmacological studies of the drug with morphine hydrochloride and levorphanol tartrate are described in this report.

1. The pharmacological effects of DH-7 which resembled to that of morphine were as follows: the analgesic effect which was not inferior to that of morphine was antagonized by nalorphine. The same effect of DH-7 by the intraperitoneal injection was potentiated by beta-glucuronidase. The same effect was decreased and at last disappeared by its chronic daily administration. Among these effects, the hypothermic effect in mice and the hyperthermic effect in rats, miosis in rabbits and mydriasis in dog by the subcutaneous injection, the depressive effects on the spontaneous respiration and blood pressure of the anesthetized dog and rabbit, hyperglycemia in rabbits, inhibition of the transfer movement of intestine of mice, DH-7 was usually less active except the analgesic effect. Besides the stronger analgesic effect, DH-7 showed a powerful tendency toward the analgesic tolerance in mice.

2. The chronic administration of 4, 8 and 16 mg/kg of DH-7 to rats for 90 days did not reveal any effect on the body weight, blood picture and viscera.

Addenda

1) The abstinence symptoms of morphine addicted monkies were not suppressed by administration of 1-16 mg/kg of DH-7. Therefore, it seems that DH-7 has not physical dependence capacity.

2) From the result of clinical trials analgesic effect of 10 mg of DH-7 was

as potent as that of 50 mg of meperidine in post partum and post-operative pain, while such side effects as nausea, vomiting, drowsiness, *etc*, were not observable.