INDOCIN®
(Indomethacin)

not obtained with 200 mg. a day, larger doses probably will not be effective.

If adverse reactions develop as the dosage is increased, decrease to a tolerated level and maintain at that dosage for 3 to 4 weeks. If an adequate response has not then been obtained, gradually increase the daily dosage by 25 mg. at about weekly intervals to 150 to 200 mg. a day.

For patients with *acute* rheumatoid arthritis or with *acute flares* of chronic rheumatoid arthritis, increase the dosage *daily* by 25 mg. until a satisfactory response is obtained or a total daily dosage of 150 to 200 mg. is reached. If adverse effects develop as the dosage is increased, it should be reduced to a tolerated level for 2 or 3 days and then gradually increased by 25 mg. every few days as tolerated. After the acute phase is under control, it is often possible to reduce the daily dosage of INDOCIN gradually to 75 to 100 mg.

Reduction of steroid dosage: Use of INDOCIN often will permit a gradual reduction of steroid dosage by 25 to 50 per cent. In some patients steroids can be slowly discontinued over a period of several weeks or months. The usual precautions should be observed in withdrawing steroids.

2. *Degenerative Joint Disease (Osteoarthritis) of the Hip*

Initial dosage: 25 mg. two or three times a day. If the response is not adequate, increase the daily dosage by 25 mg. at about *weekly* intervals until a satisfactory response is obtained or a dosage of 150 to 200 mg. a day is reached. If a satisfactory response is not obtained with 200 mg. a day, larger doses will probably not be effective.

If adverse reactions develop as the dosage is increased, decrease to a tolerated level and maintain at that dosage for 3 to 4 weeks. If an adequate response has not then been obtained, gradually increase the daily dosage by 25 mg. at about weekly intervals to 150 to 200 mg. a day.

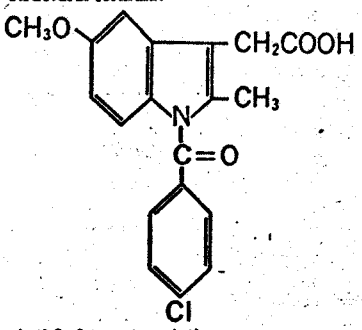
3. *Gout*

To control acute attacks: 50 mg. three times a day until all signs and symptoms subside. Definite relief of pain has been reported within 2 to 4 hours. Tenderness and heat usually subside in 24 to 36 hours, and swelling gradually disappears in 3 to 5 days.

To prevent acute attacks: During the interval phase of gouty arthritis the dosage may be reduced to as little as 25 mg. twice a day, given with an adequate dose of a uricosuric agent such as probenecid.

CHEMISTRY AND PHARMACOLOGY

The chemical name for indomethacin is 1-(*p*-chlorobenzoyl) -5-methoxy -2-methyl-indole-3-acetic acid. It has the following structural formula:



Anti-Inflammatory Action

In laboratory animals, INDOCIN is a potent anti-inflammatory compound. Results of granuloma inhibition tests in rats receiving the compound either orally or by local application indicated activity about 85 times that of phenylbutazone. Given orally, the compound was about 4 times as active as hydrocortisone. When given in effective doses to intact rats, indomethacin, unlike anti-inflammatory steroids, did not affect the size of the adrenals or thymus, or retard gain in body weight. Its anti-inflammatory activity does not depend upon activation of the adrenals, since it was fully active in adrenalectomized rats.

The anti-inflammatory activity of INDOCIN was also demonstrated by its ability to inhibit edema formation induced by subplantar injection of carrageenin in rats. By this test, the relative potency of indomethacin was: 30 times aspirin, 20 times phenylbutazone, and 2 times hydrocortisone. INDOCIN does not possess antihistaminic or antiserotonin activity, since it did not affect edema induced by injection of egg white, serotonin, or yeast. Combinations of indomethacin and a steroid were more effective than comparable doses of either drug alone in inhibiting granuloma growth or edema formation.

Antipyretic Activity

INDOCIN is an antipyretic in laboratory animals. In rabbits it was about 20 times as potent as phenylbutazone and 10 times as potent as aminopyrine. Its duration of action was much longer than that of aminopyrine and comparable to that of phenylbutazone. In rats indomethacin appeared to be about 10 times as potent as phenylbutazone.

The antipyretic activity of INDOCIN has been confirmed clinically by observations in patients with Hodgkin's disease, acute rheumatic fever, and a variety of other acute febrile conditions.

Analgesic Activity

Laboratory tests designed to detect mild analgesic activity indicate that indomethacin is more potent than aspirin or aminopyrine.