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Anti-inflammatory Effect of Piroxicam with Different Crystal Modifications

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Many organic medicinal compounds are capable of existing in more than one crystalline form having different physicochemical properties. The resulting variation in thermodynamic properties associated with difference in crystal form may be of considerable pharmaceutical importance as pointed out previously by Higuch [1]. The importance of cystalline modification of relatively insoluble drugs in regard of their biological availability and drug stability has been discussed [2-6]. The different crystalline forms exhibited by one substance may result from a variation in the crystallization temperature, a change of solvent or rate of cooling [7].

Piroxicam [4-hydroxy-2-methyl-N-(2-pyridyl)-2H-1, 2-benzothiazine-3-carboxamide -1,1-dioxide], nonsteroidal anti-inflammatory agent, is an example of water-insoluble drugs [8, 9]. The authors have reported previously the formation of polymorphs(Form a,b,c,d) of piroxicam as well as the basic properties such as crystal shape, solubilizy and disolution rate [10].

In the pressent study, the anti-inflammatory effect of these polymorphs was examined according to Winter's paw edema method [11]. Rats (Sprague-Dawley, male, 200-330g) were kept on standard diet and made to fast for about 24 hours prior to experiments. The drugs were administered orally as 0.2% CMC Na suspension containing 0.66 mg/kg, 3.3 mg/kg and 16.5 mg/kg of four crystalline modifications, respectively. And then 0.1m*l* of 1.0% carragenin saline solution as an edema inducer was administered subcutaneously 60 minutes after drug administration.

The anti-inflammatory effect of four crystalline modifications by oral administration in rats are given in Table I. As shown in Table I, the reducing effect of inflammation by four crystal forms was similar to one another. This might indicate that there was no direct relationship between the solubility in water and the absorption of piroxicam polymorphs in oral administartion.

Table I –*Effect of Piroxicam Polymorphism on Inhibition of Carrageenan-Induced Foot Edema of the Rat Four Hours after Oral Administration.*

Sample	Percent inhibition of edema* Dase (mg/kg)		
	0.66	3.3	16.5
Piroxicam	25.0± 7.5	77.5± 7.3	66.2±10.4
Form a	24.6± 5.0	72.8± 5.7	68.7± 7.8
Form b	30.3±12.0	76.2± 7.0	82.5± 3.4
Form c	44.4± 6.5	66.3±11.6	78.1± 7.3
Form d	47.5± 3.5	67.7±11.5	73.3± 7.4

Form a, piroxicam monohydrate; Form b, piroxicam, MeOH reflux; Form c, piroxicam, toluene fast cooling; Form d, piroxicam, MeOH slow cooling. * Each value represents the mean±S.E. of 5 rats.

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