Table 4. Various constants obtained for water vapour sorption by wheat and by maize starch from the Young & Nelson model. In all cases regression correlation was no less than 0·999.

Solid	A_{ADS}	A_{DES}	B_{ADS}	B_{DES}	E_{ADS}	E_{DES}	Reference
Wheat	0·080	0·060	−0·42	0·41	0·12	0·05	Young & Nelson 1976b
Maize starch	0·059	0·0074	−0·038	0·15	0·10	0·30	York 1981
Maize starch	0·022	0·024	0·18	0·15	10^{-7}	0·14	Wurster et al 1982
Maize starch	0·047	0·050	0·086	0·086	10^{-4}	0·12	Hellman et al 1952
Maize starch	0·054	0·043	0·071	0·10	0·015	0·11	Sair & Fetzer 1944
Wheat starch	0·022	0·014	0·23	0·25	2×10^{-5}	0·47	Van den Berg 1981

be open to some question. In view of these uncertainties, and the very complex nature of this process, it would appear that methods independent of sorption isotherm analysis will have to be developed before we can gain a more thorough understanding of the thermodynamic state of water in such biological materials.

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Comparison of the effects of nabumetone, a new anti-inflammatory drug, and indomethacin on arachidonic acid-induced hypotension in the rat

T. C. HAMILTON, SUSAN D. LONGMAN*, *Beecham Pharmaceuticals, Medicinal Research Centre, Coldharbour Road, The Pinnacles, Harlow, Essex, CM19 5AD, U.K.*

Endogenous vasodilator prostaglandins, such as prostacyclin, may play an important role in the regulation of vascular tone such that impairment of their synthesis leads to an unwanted increase in vascular resistance in specific beds (Dusting et al 1981). The recent report that a high intravenous dose of indomethacin, an acidic non-steroidal anti-inflammatory drug that inhibits prostaglandin synthesis, caused coronary vasoconstriction in patients with coronary artery disease, has highlighted this problem (Friedman et al 1981).

Nabumetone is a novel non-acidic anti-inflammatory drug which only weakly inhibits prostaglandin synthesis in-vitro (Boyle et al 1982). As such, nabumetone may cause less interference with the cardiovascular action of endogenous vascular prostaglandins than indomethacin and so we undertook a comparison of the effects of these anti-inflammatory drugs on the hypotensive response to the prostaglandin precursor, arachidonic acid, in spontaneously hypertensive rats (SHR). This model was chosen since Dusting et al (1981) have recently shown that the secondary phase of the hypotensive response to arachidonic acid is dependent on its conversion to vasodilator prostaglandins.

* Correspondence.

Method

Groups of 6 male spontaneously hypertensive rats (SHR) (300–400 g), derived from the Japanese strain (Okamoto & Aoki 1963), were pretreated orally with nabumetone (20 or 50 mg kg^{-1}), indomethacin (1·5 mg kg^{-1}) or vehicle and anaesthetized 2–2½ h later with pentobarbitone sodium (60 mg kg^{-1} intraperitoneally). The choice of pretreatment period and doses of drug was based on the time course and relative ability

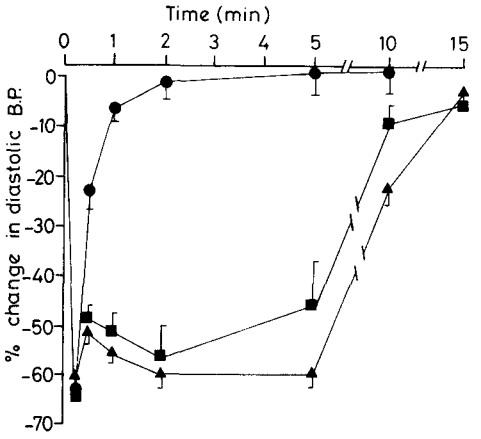

FIG. 1. Percentage change in diastolic blood pressure with time (min) in groups of anaesthetized SHR receiving arachidonic acid (5 mg kg^{-1} i.v.) 2½–3 h after oral pretreatment with methylcellulose (▲——▲), indomethacin (1·5 mg kg^{-1}) (●——●) or nabumetone (50 mg kg^{-1}) (■——■). Six rats were used per group and the vertical bars show s.e. mean. No significant difference in resting DBP was observed between methylcellulose, indomethacin or nabumetone pretreated groups.

of these drugs to reduce carrageenan-induced inflammation in the rat (Boyle et al 1982). Under anaesthesia, a carotid artery and a jugular vein were cannulated. Systemic blood pressure was monitored using a Bell & Howell physiological pressure transducer and heart rate was obtained from the pulse in the blood pressure signal; both parameters were displayed on an Ormed MX4 chart recorder. After the attainment of stable levels of blood pressure and heart rate, animals in each treatment group received a sub-maximal dose of arachidonic acid, 5 mg kg^{-1} intravenously, and the percentage fall in diastolic blood pressure (DBP) was measured at intervals over the 15 min period post-dose.

Nabumetone (4-[6-methoxy-2-naphthyl]-butan-2-one) (Beecham) and indomethacin (MSD) were administered orally as a suspension in 1% methylcellulose. Arachidonic acid (Sigma) was dissolved, immediately before use, in 30 mmol sodium carbonate gassed with nitrogen, and kept in the dark.

Results

In vehicle pretreated SHR, arachidonic acid (5 mg kg^{-1} i.v.) caused a characteristic biphasic fall in diastolic blood pressure (DBP) (Fig. 1), an initial rapid fall being followed by slight recovery and a subsequent secondary decrease in DBP.

The secondary depressor response produced by arachidonic acid was slightly reduced by pretreatment of SHR with nabumetone, 20 or 50 mg kg^{-1}, and abolished in SHR pretreated with indomethacin, 1·5 mg kg^{-1} (Fig. 1). As found in animals receiving vehicle, arachidonic acid did not affect heart rate in SHR given nabumetone or indomethacin.

Discussion

In the present investigation the new non-acidic anti-inflammatory drug, nabumetone, had little effect on the hypotensive response to arachidonic acid in SHR whilst indomethacin abolished the secondary phase of this response. The latter finding confirms that of Dusting et al (1981) who used intravenous indomethacin in SHR. The difference in the actions of nabumetone and indomethacin on the hypotensive response to arachidonic acid reflects the weaker potency of nabumetone, in comparison with that of indomethacin, as an inhibitor of prostaglandin synthesis (Boyle et al 1982).

Our findings extend those of Nunn & Chamberlain (1982) who reported that in man naproxen, but not nabumetone, markedly inhibited arachidonic acid induced platelet aggregation ex-vivo. Taken together these results demonstrate that nabumetone has less propensity than the acidic anti-flammatory drugs to interfere with the actions of endogenous prostaglandins involved in the modulation of vascular tone and in haemostasis. These findings, as well as the absence of gastric irritation after nabumetone (Boyle et al 1982), are related to the weak activity of nabumetone as an inhibitor of prostaglandin synthesis and, in conjunction with good anti-inflammatory activitiy of this drug in the clinic (Fostiropoulos & Croydon 1982), confer a potentially more favourable profile of activity on nabumetone compared with that of the acidic anti-inflammatory drugs.

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