LETTERS TO THE EDITOR

Analgesic-Antipyretics

SIR,—A number of compounds with diverse chemical properties have been widely used for many years to relieve the discomfort of mild pain such as that caused by headache, toothache, and various rheumatic conditions.

These compounds can be divided into three main chemical groups: the salicylate derivatives, the *p*-aminophenol derivatives, and the pyrazole derivatives.

They have become known collectively as the Analgesic-Antipyretics, and are usually grouped together in most textbooks of pharmacology.

Over a number of years we have been investigating the activities of many pharmacological agents against an experimental inflammation, an erythema in the guinea pig, produced by ultra-violet irradiation. In the course of this work we have examined the inhibitory effects of the best known and most widely used representative members of the salicylates, pyrazoles, and *p*-aminophenols against this erythema, and the results are reported here. In addition, the effects of two isophthalic acids which have been shown experimentally to possess analgesic and antipyretic properties, have been examined.

For the determination of anti-inflammatory activity a modification[1] of the method first described by Wilhelmi[2] was used. A small area of the back of a depilated albino guinea pig was exposed to the ultra-violet radiation from a Hanovia Kromayer lamp for 20 seconds. Animals received test-substances or saline by mouth 30 minutes before irradiation, and the degree of erythema (0–4) was estimated 120 minutes later by a trained observer who was unaware of the dosage schedules. Saline-dosed animals invariably produced a degree 3 or degree 4 erythema. By using graded doses of active compounds it was possible to obtain an "Effective Dose" for erythema inhibition. This was defined as that dose of a compound which, in a group of animals, reduced the standard erythema to a mean response of 2. A compound which in a dose of 160 mg./kg. failed to reduce the mean erythema response below 3 was considered to be inactive.

Of eight of the clinically most important representative members of the Analgesic-Antipyretics, four had no anti-inflammatory activity (Table I). It is particularly significant that none of the *p*-aminophenol group was active. Salicylamide, a very old compound, re-introduced a few years ago because it was a form of salicylate which was well tolerated, lacked the anti-inflammatory activity which both aspirin and sodium salicylate exhibited. This compound was shown by Bavin and others[3] to be three times more active than aspirin as an analgesic in rats, although it was a weaker antipyretic.

Collier and Chesher[4] found that the two hydroxyisophthalic acids (Table I) showed antipyretic and analgesic activity at least as good as aspirin and placed them "in the group of analgesic-antipyretics of which aspirin is the most widely used". The results reported here indicate that this statement might now be considered inadequate, since neither of these compounds, unlike aspirin, produced any inhibition of guinea pig erythema.

It would appear therefore from our results that the group of compounds known collectively as Analgesic-Antipyretics can, experimentally at least, be further differentiated into those which have anti-inflammatory activity and those which have not. It is possible that this differentiation is also true clinically, and it is significant that only the active compounds in Table I have proved anti-rheumatic activity.

TABLE I

THE ANTI-INFLAMMATORY ACTIVITIES OF A NUMBER OF ANALGESIC-ANTIPYRETIC COMPOUNDS IN GUINEA PIGS WITH ULTRA-VIOLET LIGHT-INDUCED ERYTHEMA

Compound	Number of animals	Oral dose mg./kg.	Mean erythema response	Approximate "Effective Dose"* mg./kg.
Phenylbutazone	10	30	0·5	
	10	15	1·9	10
	10	7·5	3·1	
Amidopyrine	16	160	0·8	
	17	80	1·8	80
	14	40	3·0	
Aspirin	10	160	0·3	
	9	80	1·8	80
	10	40	3·5	
Sodium salicylate	9	320	0·4	
	9	160	1·6	120
	9	80	2·9	
Salicylamide	8	320	3·5	Not active at 320
Acetanilide	8	240	3·0	Not active at 240
Phenacetin	8	240	3·0	Not active at 240
N-Acetyl *p*-aminophenol	8	240	3·5	Not active at 240
4-Hydroxyisophthalic acid	6	320	4·0	Not active at 320
2-Hydroxyisophthalic acid	6	320	3·2	Not active at 320
Saline controls	20	—	3·8	

* As defined in text.

This may be an over-simplification of a complex problem, but the results recorded here suggest that there may no longer be any justification for classifying the so-called Analgesic-Antipyretics into a single pharmacological group.

S. S. ADAMS.

Biology Division,
Research Department,
Boots Pure Drug Co. Ltd.,
Nottingham.

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REFERENCES

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