Influence of L-glutamine on aspirin-induced gastrointestinal microbleeding in dogs

J. L. LEELING*, N. JOHNSON, Jnr, R. J. HELMS, *Toxicology Department, Miles Laboratories, Inc., P.O. Box 40, Elkhart, Indiana 46515, U.S.A.*

The results of Okabe et al (1974a,b) and of Tanaka et al (1974) clearly suggest that L-glutamine administration can, probably by inhibition of back diffusion of acid, prevent the formation of gastric lesions produced by aspirin in the rat. Rats are, however, highly susceptible to the gastric effects of aspirin and other organic acids (Menassé-Gdynia & Krupp 1974) and, thus, not a suitable species in which to obtain preclinical data on the potential value of L-glutamine. Following ingestion of plain aspirin tablets an increase in gastrointestinal (GI) microbleeding, a widely recognized side effect, may occur resulting in increased occult blood loss in faeces. Phillips (1973) showed the dog to be a relevant species, responding to ingestion of plain aspirin with an increase in GI microbleeding in a manner similar to that of man. The study described here was designed to determine the effect of concurrent oral administration of L-glutamine on aspirin-induced GI microbleeding in dogs.

Ten male beagle dogs, 9·6–11·5 kg, never before used in a faecal blood loss study, were caged individually with free access to food and water. On study day minus 17, 1·0 ml of isotonic saline containing 50 μCi of $^{59}FeSO_4$ was administered intravenously to each dog. The dogs were assigned at random (Snedecor & Cochran 1969) to the columns of two 5 × 5 latin squares so that the lighter 5 and the heavier 5 were in separate squares. Five treatments were assigned at random to rows within squares. These treatments, administered in gelatin capsules (by gavage, twice daily in complete crossover fashion), were: 2 lactose placebo tablets, 650 mg of aspirin, and 650 mg of aspirin plus 264, 528, or 1056 mg of L-glutamine. Starting on day one alternating 5-day control (no dosing) and 7-day treatment periods were initiated which continued through day 59 when the 5th treatment period was terminated. Significant residual effects of treatments were not evidenced during control periods.

Gastrointestinal microbleeding was determined by measurement, and comparison, of the ^{59}Fe content of daily 24 h stool collections and of weekly whole blood samples essentially as described by Phillips (1973). In the present study ^{59}Fe counted (Armac, Packard Instrument Co., Downers Grove, Ill., U.S.A.) with about 11·3% efficiency and the blank count rate was about 570 counts min^{-1}.

After evaluation of the data summarized in Table 1 by analysis of variance and the Student-Newman-Keuls test (Sokal & Rohlf 1969), it was determined that faecal blood loss elicited by all aspirin-containing treatments was statistically greater than that produced by the placebo. Administration of L-glutamine did not influence the degree of aspirin-induced GI microbleeding in dogs.

Table 1. Summary of average daily aspirin-induced microbleeding in L-glutamine treated dogs.

Treatment*	Daily faecal blood volume (ml)**
Placebo	0·50 ± 0·02
Aspirin 650 mg	4·13 ± 0·35
Aspirin 650 mg and L-glutamine 264 mg	4·10 ± 0·36
Aspirin 650 mg and L-glutamine 528 mg	3·67 ± 0·34
Aspirin 650 mg and L-glutamine 1056 mg	4·33 ± 0·45

* By gavage, twice daily.
** Each value is the mean ± s.e. of 70 (7 treatment days × 10 dogs) determinations.

The presently reported study was conducted in a manner differently from that of Okabe et al (1974a,b) and Tanaka et al (1974) who administered aspirin in suspension acutely to fasted rats (in some cases with pyloric ligatures) and assessed gastric damage directly. Nevertheless, the total lack of protection from aspirin-induced GI microbleeding provided by L-glutamine in the present study does not support the suggestion of Okabe et al (1974b) and Tanaka et al (1974) that L-glutamine may be useful in preventing aspirin-induced gastric irritation in man.

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* Correspondence.

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