ASTRA
ASTRA HÄSSLE

DRUG PRODUCT		**Synopsis**	(FOR NATIONAL AUTHORITY USE ONLY)
DRUG SUBSTANCE(S)	H 199/18	REFERRING TO PART OF THE DOSSIER	
DOCUMENT NO.	SH-QBE-0050		
VERSION NO.	01		
STUDY CODE	SH-QBE-0050		
DATE	7 May, 1999		

A food interaction study regarding effect on intragastric pH following treatment with H 199/18 tablets in healthy male and female subjects.

STUDY CENTRE(S)

Single centre study

STUDY PERIOD

- **DATE OF FIRST PATIENT ENROLLED** 5 October, 1998
- **DATE OF LAST PATIENT COMPLETED** 11 November, 1998

PHASE OF DEVELOPMENT

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OBJECTIVES

The primary objective was to compare the effect on 24-hour intragastric pH of H 199/18 MUPS tablet 40 mg when given together with food and under fasting conditions on day 1 and day 5.

The secondary objective was to assess the safety and tolerability of H 199/18.

STUDY DESIGN

Open, randomised, two-way cross-over study

MAIN CRITERIA FOR INCLUSION

Healthy male and female subjects

TEST PRODUCT, BATCH NUMBER, DOSAGE AND MODE OF ADMINISTRATION

H 199/18 MUPS tablet 40 mg, batch no. H 1365-01-01-01, oral dose of 40 mg o.m.

COMPARATOR PRODUCT, BATCH NUMBER, DOSAGE AND MODE OF ADMINISTRATION

None

DURATION OF TREATMENT

Two periods of 5 days separated by 14 days

MAIN VARIABLE:

The percentage of time with intragastric pH>4.

STATISTICAL METHODS

The percentage of time with intragastric pH>4 was analysed using a mixed model ANOVA (Analysis of Variance) with fixed effects for sequence, period and treatment and a random effect for subject within sequence. Comparisons of the treatments under fed and fasting conditions were made for day 1 as well as for day 5.

SUBJECTS

	Total
No. planned	24
No. randomised and treated	24
Males/Females	12/12
Mean age (range)	29.4 years (23-42)
No. analysed for clinical pharmacology	23
No. analysed for safety	24
No. completed	23

SUMMARY

- **CLINICAL PHARMACOLOGY RESULTS**

There were no statistically significant differences in effect on intragastric pH between fed and fasting conditions. On day 1 the estimated mean percentage of time with intragastric pH>4 was 38% under fed conditions and 33% under fasting conditions (Table 1). On day 5 the estimated mean percentage of time with intragastric pH>4 was 61% (fed) and 56% (fasting).

Table 1. Means of percentage time with pH>4 (%) and the difference of the means after food intake and under fasting conditions on day 1 (n=23) and day 5 (n=21) following daily oral doses of 40 mg H 199/18 MUPS tablets to healthy subjects. Estimates, limits for 95% CI and p-values for tests of equal means are presented.

	Estimated mean	95% confidence interval lower	upper	p-value
Day 1				
After food	38.2	30.6	45.8	
Fasting	33.3	25.7	40.9	
After food-Fasting	4.9	-0.9	10.8	0.096
Day 5				
After food	60.9	53.5	68.4	
Fasting	56.5	49.1	63.9	
After food-Fasting	4.4	-1.5	10.3	0.13

- **SAFETY RESULTS**

A total of 21 AEs was reported for 15 of the 24 subjects during the entire study (including wash-out periods). The adverse events reported were of mild to moderate intensity and mainly gastrointestinal in nature.

DATE OF THE REPORT

7 May, 1999