

C H A P T E R

I V

R E S U L T S

EFFECT OF TABH ON DEXAMETHASONE-INDUCED GASTRIC ULCER

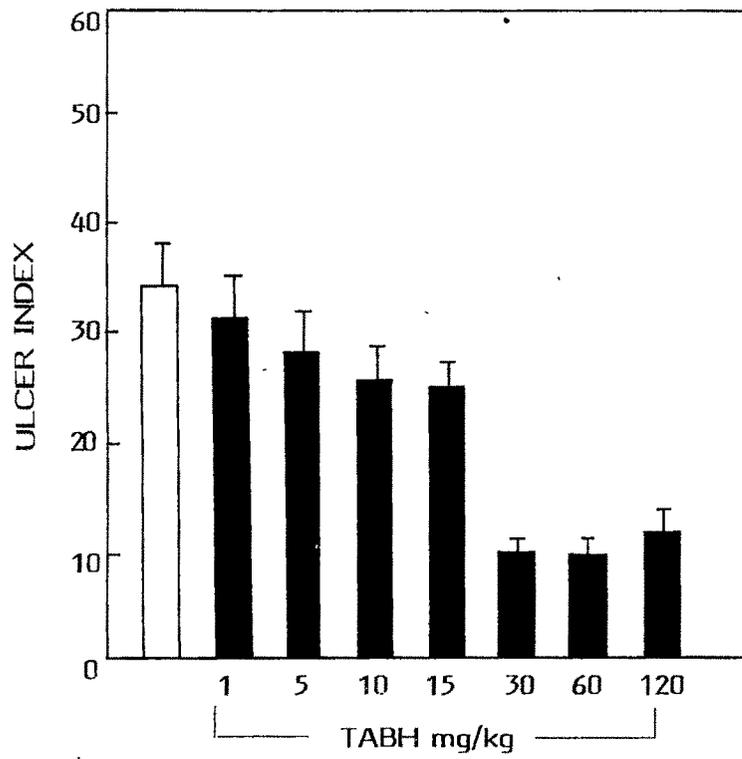
Preliminary experiments were carried out to select the maximum effective anti-ulcerogenic dose of TABH in dexamethasone induced gastric ulcer. TABH in all doses (1 mg/kg to 120 mg/kg p.o., 4 days) had significant protective effect compared

to vehicle treated control (Fig.5 a,b). The ulcer index was significantly reduced and percentage protection was increased after TABH treatment. The effect was dose-related between doses of 1 and 30 mg/kg. No significant difference was observed between the effects produced by 30 mg/kg, 60 mg/kg and 120 mg/kg of TABH and hence 60 mg/kg was considered as producing maximum protective effect.

PREVENTIVE EFFECT OF TABH IN DEXAMETHASONE-INDUCED GASTRIC ULCER

TABH (60 mg/kg p.o.) treatment for 4 days after dexamethasone induced gastric ulcer caused significant reduction in ulcer index and increase in the percentage protection compared to control values (Fig. 6). However, TABH for 4 days administered before and simultaneously along with dexamethasone had no significant protective effect compared to TABH administered after dexamethasone.

Fig. 5a

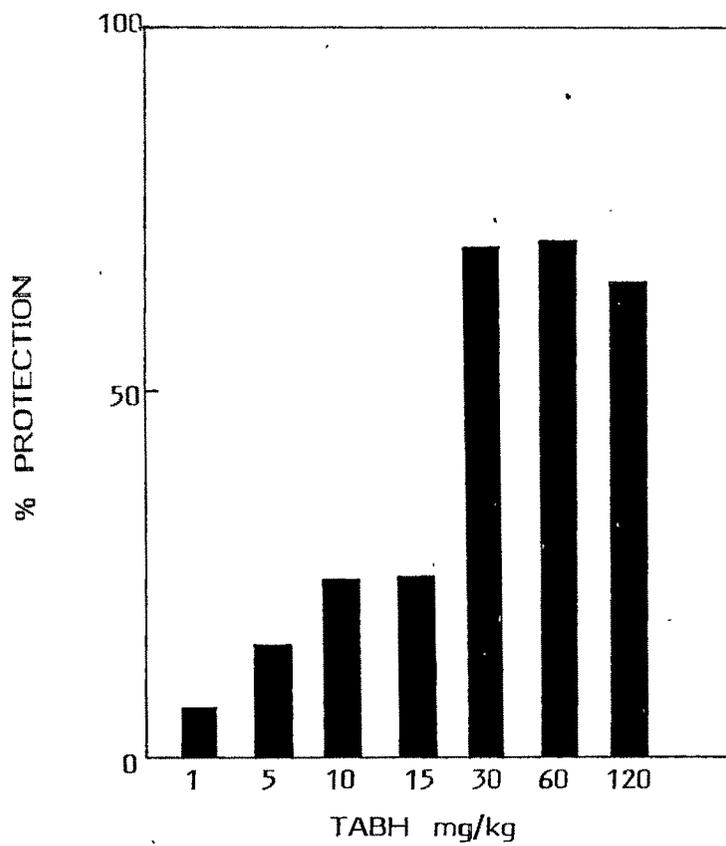


□ CONTROL

■ TABH TREATED

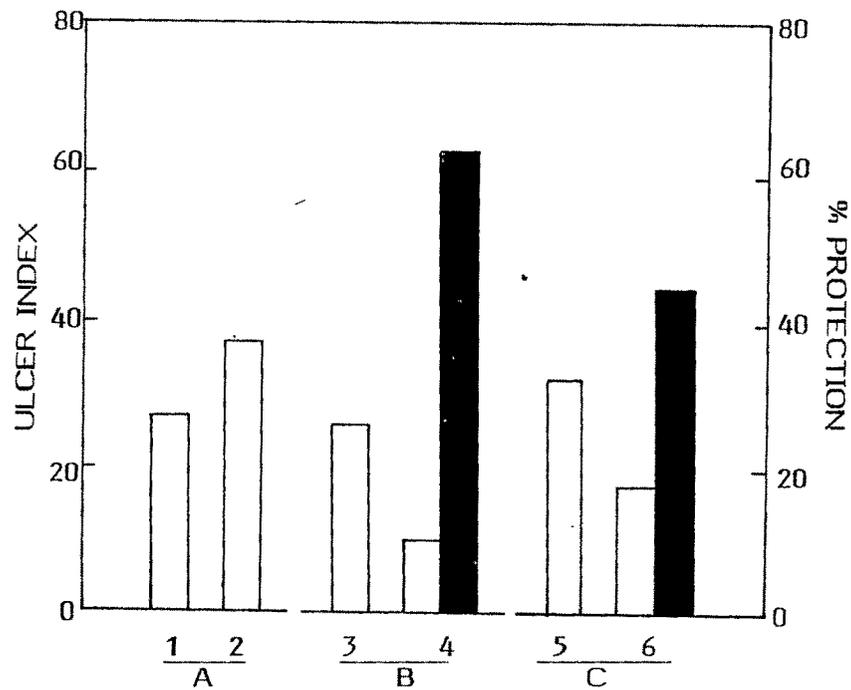
Histogram showing effect of TABH on ulcer index after dexamethasone treatment.

Fig. 5b



Histogram showing effect of TABH on % protection after dexamethasone treatment.

Fig. 6



Histogram showing effect of TABH 60 mg/kg, on ulcer index; (A) before, (B) simultaneously and (C) after dexamethasone treatment.

- (1) Vehicle in equivalent volume (p.o.) for four days followed by dexamethasone 8 mg/kg. s.c.
- (2) TABH 60 mg/kg. p.o. for four days followed by dexamethasone.
- (3) Dexamethasone followed by vehicle
- (4) Dexamethasone followed by TABH
- (5) Simultaneous administration of Dexamethasone and vehicle
- (6) Simultaneous administration of Dexamethasone and TABH.

□ ULCER INDEX

■ % PROTECTION

EFFECT OF TABH PERSE ON THE CONTENTS OF GASTRIC JUICE

Treatment with TABH (60 mg/kg p.o.) for 4 days or 10 days produced no significant change of any parameter (Table 2).

INDUCTION OF ULCER

DEXAMETHASONE-INDUCED GASTRIC ULCER

Dexamethasone (8 mg/kg s.c.) administered to fasting rats for 4 days produced severe lesions in the stomach with deep haemorrhagic spots (Fig.7a) and sometimes perforation.

INDOMETHACIN-INDUCED GASTRIC ULCER

Indomethacin administered in a single dose (20 mg/kg s.c. suspended in a trace of Tween 80) produced severe lesions in the stomach within 18 hours of administration (Fig. 7b).

CYSTEAMINE-INDUCED DUODENAL ULCER

Cysteamine single dose (300 mg/kg s.c.) produced severe duodenal ulcers within 18 hours of administration (Fig. 7c).

ANTIULCEROGENIC EFFECT OF TABH

EFFECT OF TABH, CARBENOXOLONE, CIMETIDINE AND VARIOUS COMBINATIONS THEREOF ON DEXAMETHASONE-INDUCED GASTRIC ULCERS.

Dexamethasone (8 mg/kg s.c.) administered to fasted rats for 4 days produced severe gastric ulcers with mean ulcer index of $12.63 \pm 2.36 \text{ mm}^2$ (Table 3). TABH 60 mg/kg treatment for 4 days and 10 days after dexamethasone administration significantly reduced the ulcer index affording 60 and 80% protection respectively. Carbenoxolone 30 mg/kg p.o. for 4 days produced effect equivalent to TABH treatment for 10 days.

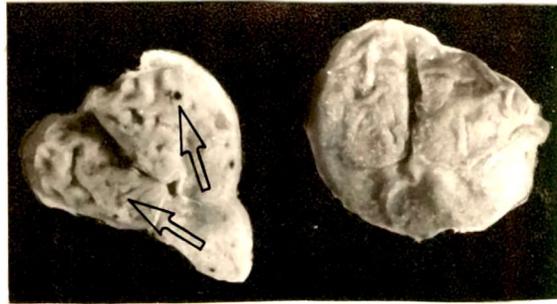
Table 2

EFFECT OF TABH PERSE ON VOLUME, TOTAL ACIDITY, PEPSIN
ACTIVITY AND COMPOSITION OF GASTRIC JUICE IN PYLORUS LIGATED
ALBINO RATS.

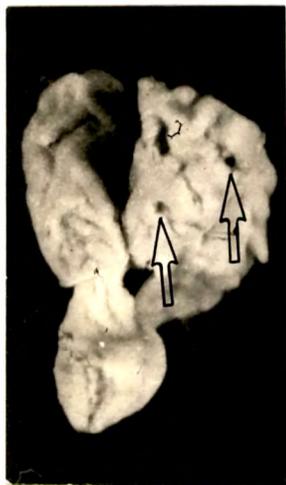
Parameter (Mean \pm S.E.M.)	Vehicle treated control	TABH 60 mg/kg p.o. 4 days	TABH 60 mg/kg p.o. 10 days
Volume ml/4 hours	4.49 \pm 0.22	4.12 \pm 0.26	3.98 \pm 0.14
Total acidity μ Eq/4 hours	730.8 \pm 31.9	707.2 \pm 27.1	702.5 \pm 28.9
Pepsin activity mmol/4 hours.	1.35 \pm 0.1	1.33 \pm 0.1	1.43 \pm 0.1
Hexoses μ g/ml	598.31 \pm 45.97	618.2 \pm 25.4	642.1 \pm 20.2
Hexosamine μ g/ml	233.8 \pm 16.3	218.4 \pm 20.3	231.5 \pm 24.3
Fucose μ g/ml	40.37 \pm 2.6	38.2 \pm 2.4	44.0 \pm 10.6
Sialic acid μ g/ml	44.8 \pm 3.1	48.5 \pm 3.6	46.7 \pm 13.4
Total carbohydrates μ g/ml	920.5 \pm 51.5	935.2 \pm 3.6	993.1 \pm 23.1
Total protein μ g/ml	262.8 \pm 22.5	318.8 \pm 22.2	232.1 \pm 20.2
C/P Ratio	3.03 \pm 0.2	3.25 \pm 0.2	3.47 \pm 0.6

n = 10

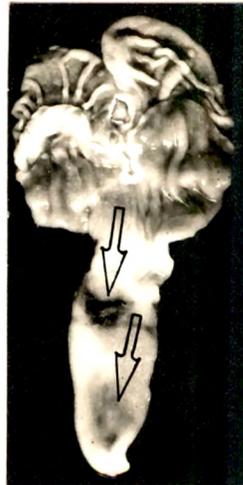
Fig. 7 Gross appearance of gastric and duodenal ulcers.



(a) Gastric ulcers after dexamethasone administration (left) and normal stomach of the rat (right).



(b) Gastric ulcers after indomethacin administration.



(c) Cysteamine-induced duodenal ulcers.

Table - 3

EFFECT OF TABH, CARBENOXOLONE, CIMETIDINE AND VARIOUS COMBINATIONS THEREOF ON DEXAMETHASONE INDUCED GASTRIC ULCER IN ALBINO RATS.

Group	Mean no of ulcers ± S.E.M.	Mean ulcer index mm ² ± S.E.M.	% Protection
1. Dexamethasone (8 mg/kg s.c.) treated control	2.26 ± 0.21	12.63 ± 2.36	-
2. TABH 60 mg/kg p.o. 4 days	0.86 ± 0.26 [*]	4.66 ± 1.36 ⁺	63.10
3. TABH 60 mg/kg p.o. 10 days	0.50 ± 0.33 [*]	2.53 ± 1.70 ⁺	79.96
4. Carbenoxolone 30 mg/kg p.o. 4 days	0.50 ± 0.40 ⁺	2.55 ± 0.90 [*]	79.80
5. Cimetidine 20 mg/kg p.o. 4 days	1.00 ± 0.45 ^x	5.16 ± 0.85 ⁺	59.14
6. Carbenoxolone 15 mg/kg p.o. + TABH 60 mg/kg p.o. 4 days	0.40 ± 0.25 [*]	2.45 ± 0.93 [*]	80.60
7. Cimetidine 10 mg/kg p.o. 4 days + TABH 60 mg/kg p.o. 4 days	0.75 ± 0.26 [*]	3.12 ± 1.13 ⁺	75.29

n = 10 compared to dexamethasone

x, P < .05

+, P < .01

*, P < .001

Cimetidine 20 mg/kg p.o. for 4 days also caused a significant decrease in ulcer index compared to the control group; affording 55% protection. The number of ulcers was also less in the groups treated with TABH or carbenoxolone, or cimetidine.

Combination of the same dose of TABH (60 mg/kg) together with 50% dose of carbenoxolone (15 mg/kg) produced maximum 80% protection which is equivalent to that afforded by carbenoxolone (30 mg/kg) for 4 days or TABH 60 mg/kg for 10 days. Similar combination of TABH with 50% dose of cimetidine (10 mg/kg p.o.) treatment produced better effect than cimetidine alone. The number of ulcers was reduced corresponding to decrease in the ulcer index and increase in the percentage protection.

EFFECT OF TABH, CARBENOXOLONE, CIMETIDINE AND VARIOUS COMBINATIONS THEREOF ON VOLUME, TOTAL ACIDITY AND PEPSIN ACTIVITY OF THE GASTRIC JUICE IN DEXAMETHASONE TREATED ALBINO RATS.

Administration of dexamethasone (8 mg/kg s.c., 4 days) caused insignificant increase in volume, total acidity and pepsin activity compared to that in vehicle treated control rats (Table 4). TABH (60 mg/kg p.o.) for 4 days caused 42% decrease in the gastric juice volume and significant decrease in the total acidity and pepsin activity compared to that in dexamethasone-treated control and vehicle treated control. Long term treatment with TABH (60 mg/kg p.o. for 10 days) after dexamethasone administration caused further decrease in the gastric juice volume i.e. 55% which was significantly less when compared to that observed with TABH treatment administered for 4 days. There was also significant decrease in the total acidity and pepsin activity. Carbenoxolone (30 mg/kg p.o. for 4 days) treatment after dexamethasone administration had no effect on gastric juice volume. It caused significant decrease in total acidity and pepsin activity, which is less than that observed with TABH (60 mg/kg, treatment for 4 and 10 days).

Cimetidine (20 mg/kg p.o. 4 days) caused maximum decrease in the gastric juice volume, total acidity and pepsin activity.

Combination of TABH (60 mg/kg) with 50% of carbenoxolone (15 mg/kg p.o.) produced significant decrease in the gastric juice volume compared to that with carbenoxolone (30 mg/kg) alone, and also significantly reduced total acidity and

Table - 4

EFFECT OF TABH, CARBENOXOLONE, CIMETIDINE AND VARIOUS COMBINATIONS THEREOF ON GASTRIC JUICE VOLUME, TOTAL ACIDITY AND PEPSIN ACTIVITY OF THE GASTRIC JUICE IN DEXAMETHASONE TREATED ALBINO RATS.

Group	Mean volume ml \pm S.E.M.	Mean total acidity μ Eq./4 hours \pm S.E.M.	Mean pepsin activity mmol/4 hours \pm S.E.M.
Vehicle treated	4.61 \pm 0.16	796.30 \pm 27.04	1.57 \pm 0.13
Dexamethasone 8 mg/kg s.c. 4 days	4.69 \pm 0.16	834.82 \pm 22.26	1.74 \pm 0.14
TABH 60 mg/kg p.o. 4 days	2.71 \pm 0.17 ^{b*}	644.20 \pm 63.68 ^{bx}	1.04 \pm 0.02 ^{b*}
TABH 60 mg/kg p.o. 10 days	2.11 \pm 0.09 ^{bx}	648.00 \pm 44.63 ^{b+}	0.83 \pm 0.04 ^{b*}
Carbenoxolone 30 mg/kg p.o. 4 days	4.50 \pm 0.20	754.24 \pm 28.32 ^{bx}	1.20 \pm 0.12 ^{b+}
Cimetidine 20 mg/kg p.o. 4 days	2.10 \pm 0.15 ^{b*}	405.15 \pm 13.42 ^{b*}	0.70 \pm 0.06 ^{b*}
Carbenoxolone 15 mg/kg p.o. + TABH 60 mg/kg p.o. 4 days	3.15 \pm 0.29 ^{b* c+}	604.10 \pm 38.50 ^{b+ c+}	0.74 \pm 0.06 ^{b* c+}
Cimetidine 10 mg/kg p.o. + TABH 60 mg/kg p.o. 4 days	2.50 \pm 0.18 ^{b*}	450.10 \pm 15.20 ^{b* cx}	0.72 \pm 0.04 ^{b* b*}

n = 10

x, P < .05
+, P < .01
*, P < .001

b - compared to dexamethasone
c - compared to carbenoxolone or Cimetidine

pepsin activity. Combination of TABH (60 mg/kg) with the 50% dose of cimetidine (10 mg/kg) produced better effect than TABH (60mg/kg) administered for 4 days or carbenoxolone 30 mg/kg or the combination of TABH with carbenoxolone treatment for 4 days.

EFFECT OF TABH, CARBENOXLONE, CIMETIDINE AND VARIOUS COMBINATIONS THEREOF ON CARBOHYDRATES AND PROTEIN CONTENT OF THE GASTRIC JUICE IN DEXAMETHASONE-TREATED ALBINO RATS.

Dexamethasone (8 mg/kg s.c. 4 days) caused decrease in total carbohydrates and significant increase in protein leading to altered carbohydrate to protein ratio compared to that in vehicle-treated control group (Table 5).

TABH (60 mg/kg p.o.) administered for 4 days in dexamethasone treated rats significantly altered the carbohydrate to protein ratio by increasing other carbohydrates like hexoses, hexosamine, fucose and sialic acid.

TABH (60 mg/kg p.o.) caused 2-fold and 3-fold increase in fucose and sialic acid contents of gastric juice respectively.

TABH (60 mg/kg p.o.) administered for 10 days produced significant increase in the hexoses, hexosamine, fucose and sialic acid concentration and 55% decrease in protein. However, no significant change was observed between the effects of TABH administered for 4 or 10 days.

Carbenoxolone (30 mg/kg p.o.) administered for 4 days produced more effect than TABH administered for 4 or 10 days; there was 4-fold increase in fucose and sialic acid contents and significant decrease in protein, leading to increase in carbohydrate to protein ratio.

Cimetidine (20 mg/kg p.o.) administered for 4 days had no significant effect on hexoses, hexosamine, fucose and sialic acid in dexamethasone treated rats but there was decrease in protein content of the gastric juice which altered the carbohydrate to protein ratio. TABH administered for 4 or 10 days had better effect compared to cimetidine.

EFFECT OF TABH, CARBENOXOLONE, CIMETIDINE AND VARIOUS COMBINATIONS THEREOF ON DIFFERENT CARBOHYDRATES AND PROTEIN OF GASTRIC JUICE IN DEXAMETHASONE TREATED ALBINO RATS.

Group	Hexoses $\mu\text{g/ml}$	Hexosamine $\mu\text{g/ml}$	Fucose $\mu\text{g/ml}$	Sialic acid $\mu\text{g/ml}$	Total carbohydrate $\mu\text{g/ml}$	Total protein $\mu\text{g/ml}$	C/P ratio
Vehicle treated control	590.5 \pm 50.77	210.1 \pm 19.9	45.3 \pm 3.9	46.9 \pm 4.4	892.8 \pm 59.3	319.3 \pm 16.7	2.6 \pm 0.2
Dexamethasone 8 mg/kg s.c. 4 days	411.5 \pm 50.8 ^{ax}	156.5 \pm 10.8 ^{ax}	34.4 \pm 2.8 ^{ax}	31.8 \pm 2.1 ^{ax}	634.2 \pm 28.9 ^{ax}	437.9 \pm 30.3 ^{ax}	1.36 \pm 0.2 ^{a*}
TABH 60 mg/kg p.o.4 days	527.8 \pm 36.3	205.9 \pm 20.3 ^{b*}	83.3 \pm 3.2 ^{b*}	93.5 \pm 5.1 ^{b*}	910.4 \pm 38.1 ^{b*}	193.7 \pm 19.7 ^{b*}	4.9 \pm 0.4 ^{b*}
TABH 60 mg/kg p.o.10 days	535.9 \pm 35.9	211.3 \pm 10.6 ^{b+}	88.9 \pm 3.5 ^{b*}	96.2 \pm 5.5 ^{b*}	932.3 \pm 37.6 ^{b*}	186.9 \pm 22.3 ^{b*}	4.5 \pm 0.3 ^{b*}
Carbenoxolone 30 mg/kg p.o.4 days	626.5 \pm 44.7 ^{b+}	215.4 \pm 11.8 ^{b+}	155.7 \pm 13.1 ^{b*}	130.5 \pm 8.34 ^{b*}	1128.1 \pm 57.6 ^{b*}	163.1 \pm 11.4 ^{b*}	6.9 \pm 0.5 ^{b*}
Cimetidine 20 mg/kg p.o.4 days	440.9 \pm 35.9	181.4 \pm 12.4	41.68 \pm 2.9	35.2 \pm 2.8	699.2 \pm 37.2	188.3 \pm 26.9 ^{b*}	4.3 \pm 0.5 ^{b*}
Carbenoxolone 15 mg/kg + TABH 60 mg/kg p.o.4 days	597.0 \pm 15.8	253.9 \pm 11.9 ^{cx}	178.2 \pm 14.6 ^{b*}	112.1 \pm 8.0 ^{b*}	1141.2 \pm 18.2 ^{b*}	215.3 \pm 10.6 ^{b+}	5.2 \pm 0.3 ^{c+}
Cimetidine 10 mg/kg + TABH 60 mg/kg p.o.4 days	511.6 \pm 18.5	245.9 \pm 20.2 ^{cx}	82.9 \pm 4.9	102.3 \pm 3.4 ^{c*}	942.7 \pm 21.7 ^{c*}	211.1 \pm 13.3 ^{b*}	4.7 \pm 0.5 ^{b*}

n = 10, All values are mean \pm S.E.M.

x, p < .05

+, p < .01

*, p < .001

a - compared to vehicle

b - compared to dexamethasone

c - compared to carbenoxolone or cimetidine

Combination of TABH (60 mg/kg) with 50% dose of carbenoxolone (15 mg/kg) was more effective than TABH administered for 4 or 10 days or cimetidine. Similarly combination of TABH with 50% dose of cimetidine (10 mg/kg) produced effect equivalent to TABH administered for 4 or 10 days or cimetidine alone.

HISTOPATHOLOGICAL STUDY

DEXAMETHASONE INDUCED GASTRIC ULCER

Administration of dexamethasone (8 mg/kg s.c. for 4 days) produced varying grades of damage to the gastric mucosa. It produced frank ulcers involving partial or whole thickness of the mucosa (Fig.9). In some cases it produced only micro abscesses in the basal portion of the mucosa (Fig.9c). These histopathological changes were interpreted as early developing ulcer. Fig.8 shows normal gastric mucosa for comparison.

ANTIULCEROGENIC ACTION OF TABH

Histopathological study of the gastric mucosa with 4 days TABH (60 mg/kg) treatment was carried out after inducing gastric ulcers by dexamethasone. Early healing of the ulcer in the form of Congested blood vessels, early fibrosis at the base of mucosa and few inflammatory cells in the submucosal region can be seen (Fig.10). After 10 days treatment with TABH (60 mg/kg) there was marked healing of the ulcer with fibrosis, presence of inflammatory cells at the base of mucosa, dilated blood vessel (Fig. 11a, 11b) and regeneration of the gastric mucosa (Fig.11c). Staining of the same histopathological section by PAS shows increased PAS activity and regeneration of the gastric mucosa (Fig.12a, 12b).

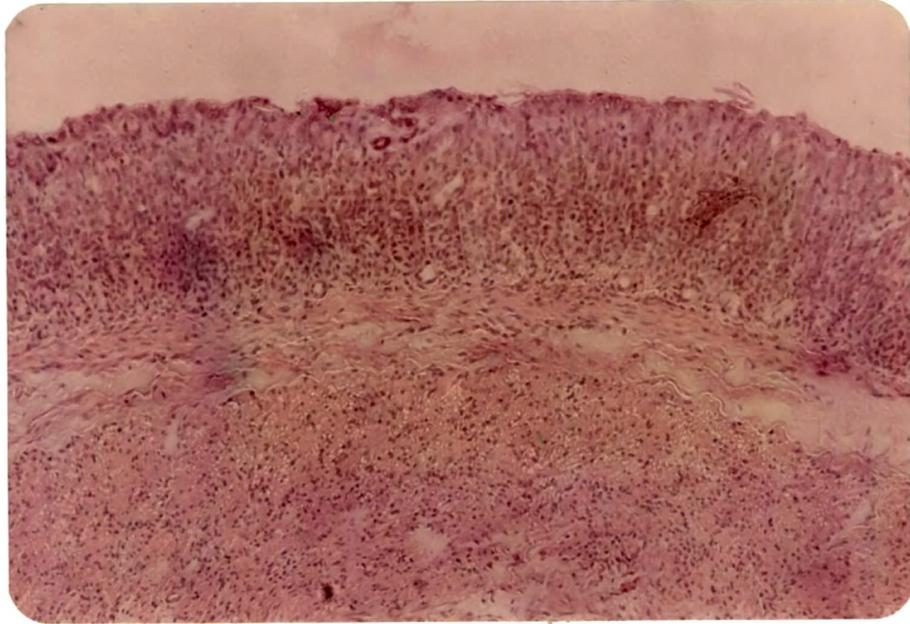


Fig.8

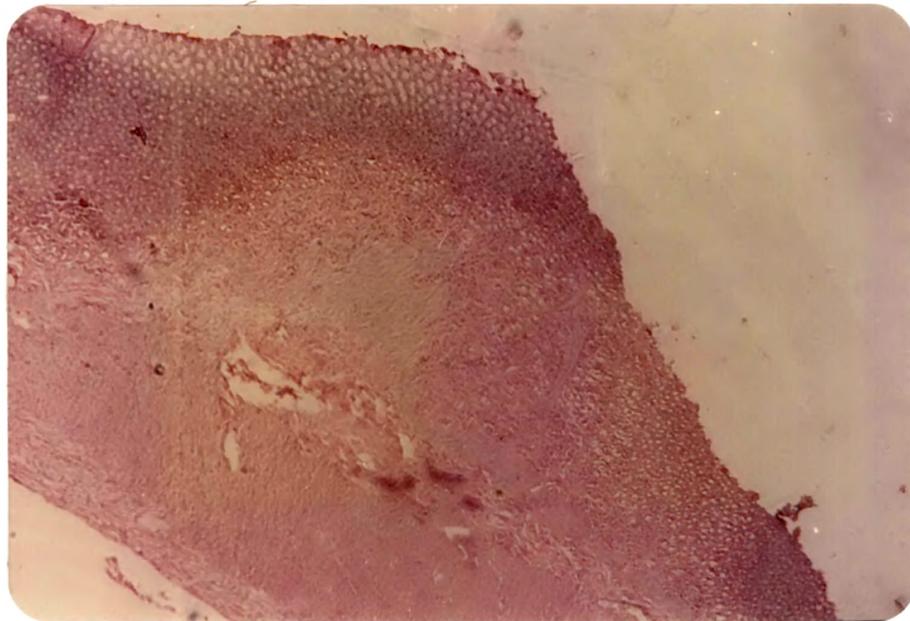


Fig.9a

(b) Section shows fully developed ulcer with partial necrosis of the gastric mucosa (10 X)

(c) Section shows gastric ulcer with mucosal necrosis and micro abscesses at the base of the mucosa (10 X)

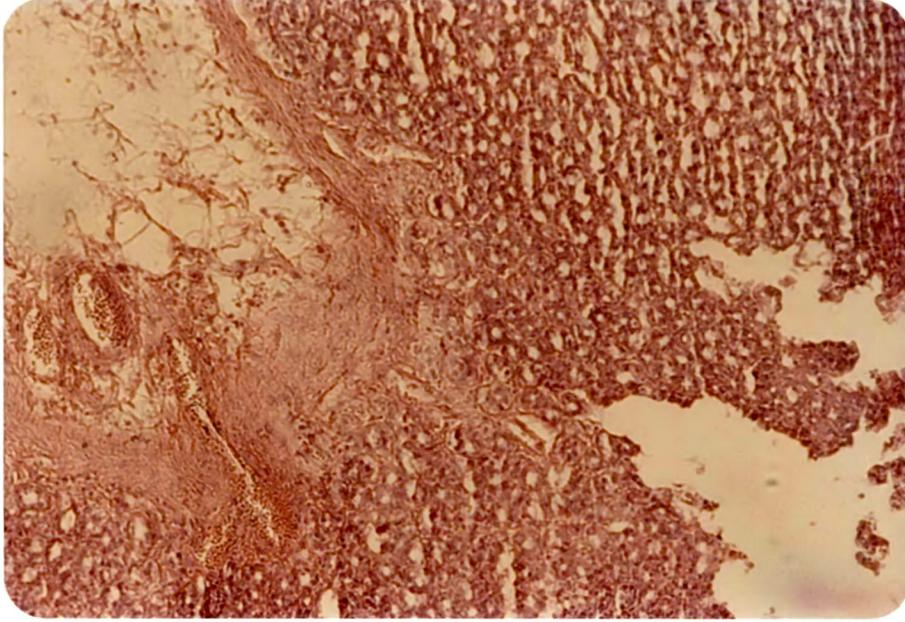


Fig.9b

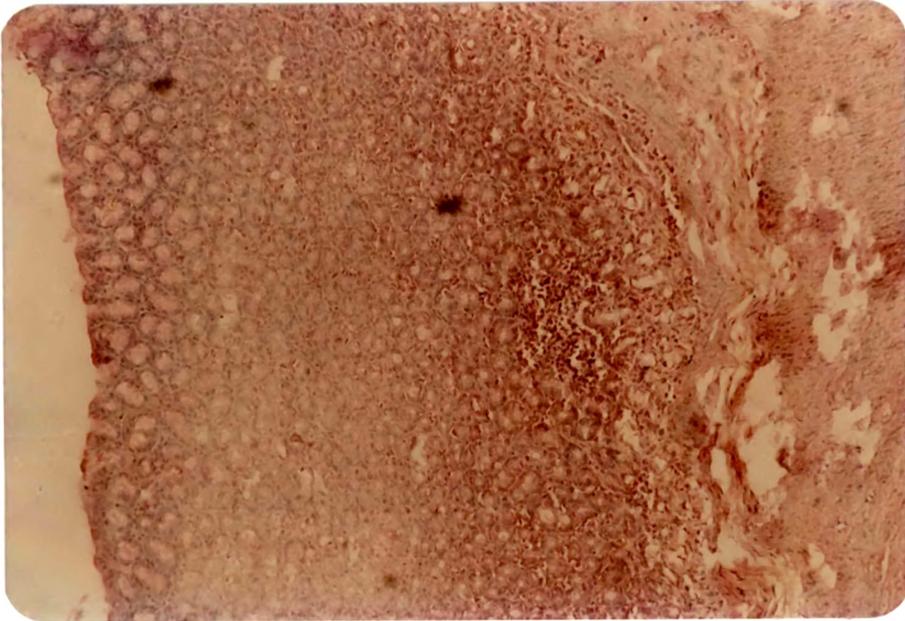


Fig.9c

Fig.10.

Section of gastric mucosa with 4 days TABH treatment after inducing ulcer by dexamethasone. There is early healing of the ulcer, showing congestion of blood vessel, early fibrosis and inflammatory cells in the submucosal region (4 X).

Fig.11.

Section of the gastric mucosa with 10 **days** TABH treatment after inducing ulcer by dexamethasone.

(a) Healing of the ulcer in the form of **fibrosis**, dilated blood vessels and few inflammatory cells at the **base** of mucosa can be seen (10 X).

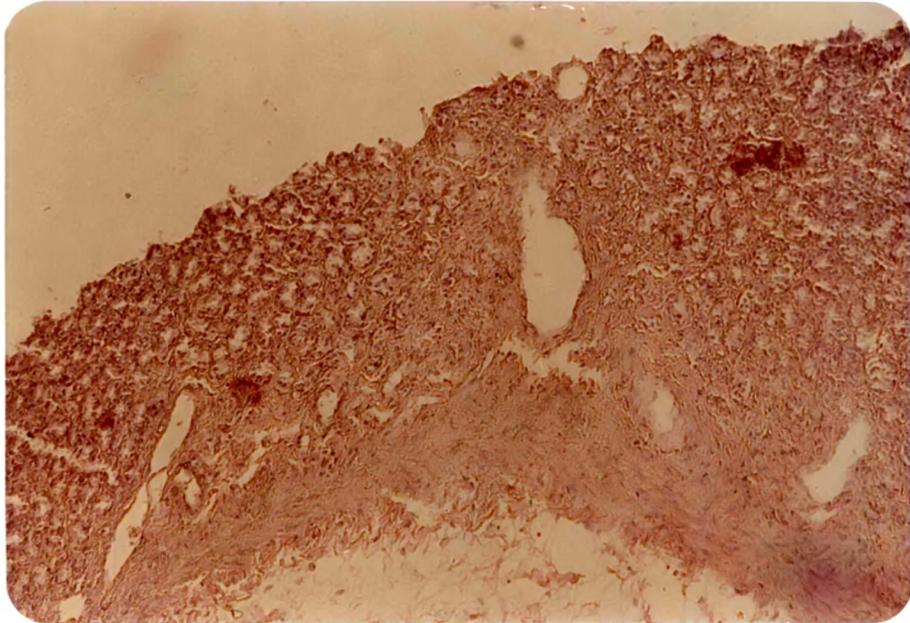


Fig.10

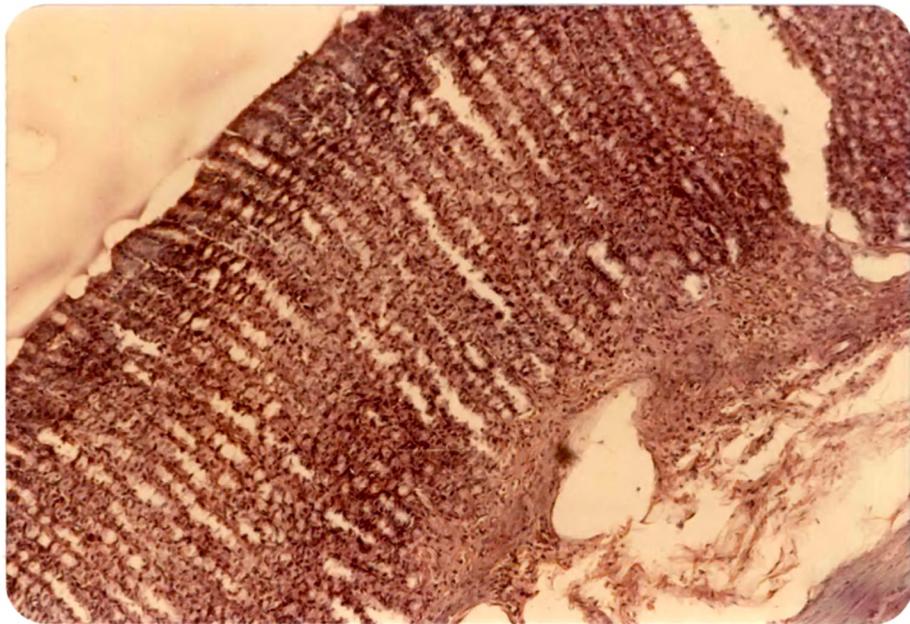


Fig.11 a

(b) A completely healed ulcer can be seen (10 X)

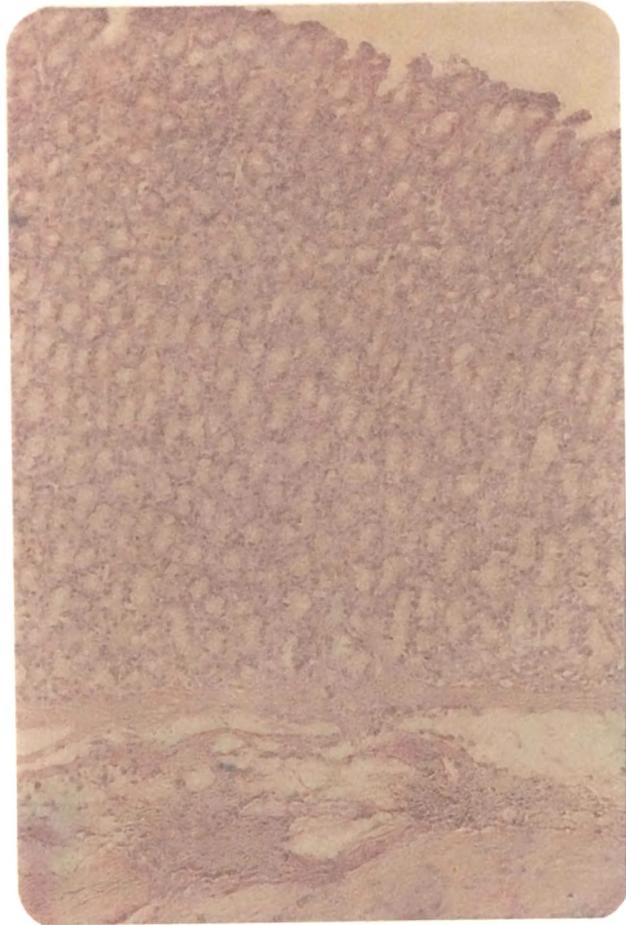


Fig.11 b

- (c) Healing of the ulcer in the form of creeping fibrosis, congested blood vessel and complete regeneration of the mucosa can be seen (10 X)

Fig.12.

Section of the gastric mucosa with 10 days TABH treatment after inducing ulcer by dexamethasone and stained by Periodic acid Schiff reagent.

- (a) Same section (11c) showing increased PAS activity and regeneration (10 X).

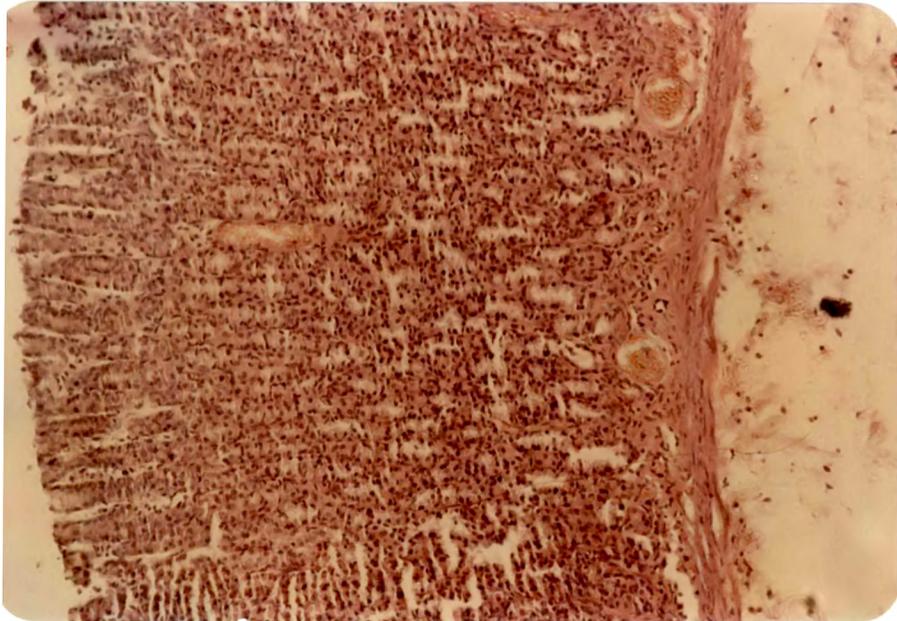


Fig.11 c

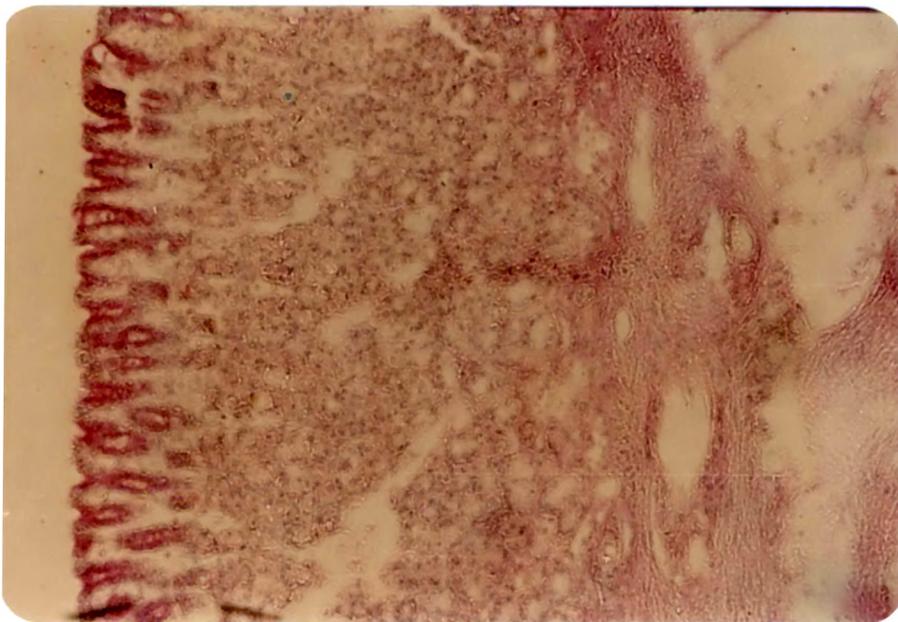


Fig.12 a

(b) Section of gastric mucosa showing increased PAS activity and regeneration (10 X).

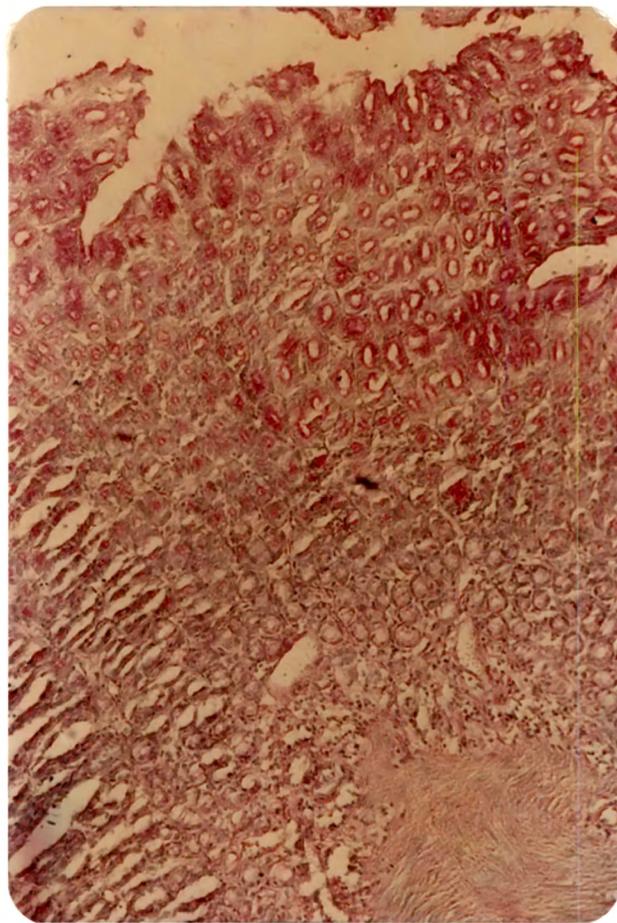


Fig .12 b

EFFECT OF TABH, CARBENOXOLONE, CIMETIDINE AND VARIOUS COMBINATIONS THEREOF ON INDOMETHACIN-INDUCED GASTRIC ULCERS

A single dose of indomethacin (20 mg/kg s.c.) administered to fasted rats produced gastric ulcers with mean ulcer index of $16.30 \pm 1.00 \text{ mm}^2$ (Table 6). TABH 60 mg/kg for 4 days and 10 days caused a significant decrease in ulcer index with 55 and 80% protection respectively. Carbenoxolone 30 mg/kg p.o. for 4 days produced effect equivalent to TABH administered for 10 days. Cimetidine (20 mg/kg p.o.) treatment produced 61% protection.

Combination of TABH (60 mg/kg) with the 50% dose of carbenoxolone (15 mg/kg) administered for 4 days produced 81% protection which is equivalent to the effect obtained with carbenoxolone 30 mg/kg administered alone for 4 days or TABH administered alone for 10 days.

A similar combination of TABH with 50% dose of cimetidine (10 mg/kg) produced more protection than cimetidine administered alone. The number of ulcers was reduced more than that with cimetidine administered alone.

EFFECT OF TABH, CARBONEXOLONE, CIMETIDINE AND VARIOUS COMBINATIONS THEREOF ON VOLUME, TOTAL ACIDITY AND PEPSIN ACTIVITY OF THE GASTRIC JUICE IN INDOMETHACIN TREATED ALBINO RATS.

Indomethacin (20 mg/kg s.c., single dose) administered to fasted rats caused no increase in volume and pepsin activity. However, there was significant increase in total acidity of the gastric juice secreted within 4 hours of pylorus ligation (Table 7).

TABH (60 mg/kg p.o.) treatment for 4 days after indomethacin administration caused significant decrease in volume, total acidity and pepsin activity. TABH (60 mg/kg p.o.) treatment for 10 days produced more effect than TABH treatment for 4 days; furthermore, there was significant decrease in total acidity compared to that observed with TABH administered for 4 days or carbenoxolone (30 mg/kg p.o.) administered for 4 days.

Table - 6

EFFECT OF TABH, CARBENOXOLONE, CIMETIDINE AND VARIOUS COMBINATIONS THEREOF ON INDOMETHACIN INDUCED GASTRIC ULCER IN ALBINO RATS.

Group	Mean no. of ulcers ± S.E.M.	Mean ulcer index mm ² ± S.E.M.	% protection
1. Indomethacin (20 mg/kg s.c.) treated control	4.60 ± 0.43	16.30 ± 1.00	-
2. TABH 60 mg/kg p.o. 4 days	1.30 ± 0.54 [*]	6.80 ± 2.85 ⁺	58.28
3. TABH 60 mg/kg p.o. 10 days	0.75 ± 0.49 [*]	3.03 ± 1.99 [*]	81.41
4. Carbenoxolone 30 mg/kg p.o. 4 days	0.78 ± 0.46 [*]	3.06 ± 1.02 [*]	81.22
5. Cimetidine 20 mg/kg p.o. 4 days	1.25 ± 0.45 [*]	6.30 ± 2.15 [*]	61.35
6. Carbenoxolone 15 mg/kg p.o. + TABH 60 mg/kg p.o. 4 days	0.72 ± 0.39 [*]	3.01 ± 1.05 [*]	81.73
7. Cimetidine 10 mg/kg p.o. 4 days + TABH 60 mg/kg p.o. 4 days	0.95 ± 0.45 [*]	4.74 ± 1.62 [*]	70.92

n = 10

+, P < .01

*, P < .001

compared to indomethacin

Table - 7

EFFECT OF TABH, CARBENOXOLONE, CIMETIDINE AND VARIOUS COMBINATIONS THEREOF ON GASTRIC JUICE VOLUME, TOTAL ACIDITY AND PEPSIN ACTIVITY OF THE GASTRIC JUICE IN INDOMETHACIN TREATED ALBINO RATS.

Group	Mean volume ml \pm S.E.M.	Mean total acidity μ Eq./4 hours \pm S.E.M.	Mean pepsin activity mmol/4 hours \pm S.E.M.
Vehicle treated	4.01 \pm 0.28	618.50 \pm 45.80	1.07 \pm 0.08
Indomethacin 20 mg/kg s.c. single dose	4.44 \pm 0.17	782.20 \pm 11.85 ^{a+}	1.22 \pm 0.08
TABH 60 mg/kg p.o. 4 days	2.45 \pm 0.15 ^{b*}	558.30 \pm 30.55 ^{b*}	0.70 \pm 0.02 ^{b*}
TABH 60 mg/kg p.o. 10 days	2.49 \pm 0.11 ^{b*}	455.30 \pm 22.43 ^{b*}	0.72 \pm 0.05 ^{b*}
Carbenoxolone 30 mg/kg p.o. 4 days	3.50 \pm 0.38 ^{bx}	625.05 \pm 21.60 ^{b*}	1.03 \pm 0.09
Cimetidine 20 mg/kg p.o. 4 days	2.10 \pm 0.13 ^{b*}	355.20 \pm 21.32 ^{b*}	0.65 \pm 0.03 ^{b*}
Carbenoxolone 15 mg/kg p.o. + TABH 60 mg/kg p.o. 4 days	3.20 \pm 0.31 ^{b*}	590.50 \pm 23.10 ^{b*}	0.84 \pm 0.05 ^{b*}
Cimetidine 10 mg/kg p.o. + TABH 60 mg/kg p.o. 4 days	2.75 \pm 0.17 ^{b* c+}	342.10 \pm 15.20 ^{b*}	0.72 \pm 0.04 ^{b*}

n = 15

x, P < .05
+, P < .01
*, P < .001

a - compared to vehicle
b - compared to indomethacin
c - compared to carbenoxolone or cimetidine

Carbenoxolone (30 mg/kg p.o.) treatment for 4 days after indomethacin caused significant decrease in total acidity of the gastric juice. It had no effect on peptic activity.

Cimetidine (20 mg/kg p.o.) treatment for 4 days produced maximum decrease in the volume, total acidity and pepsin activity compared with TABH administered for 4 or 10 days or all modalities of all combinations of TABH.

Combination of TABH (60 mg/kg p.o. 4 days) with the 50% dose of carbenoxolone (15 mg/kg p.o.) produced significant decrease in volume, total acidity and pepsin activity. This combination caused significant decrease in pepsin activity whereas carbenoxolone alone did not produce significant decrease in pepsin activity. Combination of TABH (60 mg/kg) with the 50% dose of cimetidine (10 mg/kg p.o.) caused significant decrease in volume, total acidity and pepsin activity of the gastric juice which was more than observed with carbenoxolone administered alone.

EFFECT OF TABH, CARBENOXOLONE, CIMETIDINE AND VARIOUS COMBINATIONS THEREOF ON CARBOHYDRATES AND PROTEIN OF GASTRIC JUICE IN INDOMETHACIN TREATED ALBINO RATS.

Indomethacin (20 mg/kg s.c.) caused 40% decrease in the total carbohydrates and 85% increase in the protein contents of gastric juice (Table 8). TABH (60 mg/kg p.o.) treatment for 4 days produced significant increase in all carbohydrates and significant decrease in total protein contents with an increase in the carbohydrate to protein ratio. Treatment with TABH (60 mg/kg p.o.) for 10 days produced the same effect as obtained with 4 days treatment.

Carbenoxolone (30 mg/kg p.o. 4 days) caused 3-fold and 4-fold increase in fucose and Sialic after indomethacin administration. Protein reduction by carbenoxolone was similar as with TABH treatment.

Cimetidine (20 mg/kg p.o. 4 days) caused significant increase in total hexoses and significant decrease in protein only. No significant change was observed in hexosamine, fucose and sialic acid with cimetidine. Carbohydrate to protein ratio increased by cimetidine was because of the decrease in protein.

EFFECT OF TABH, CARBENOXOLONE, CIMETIDINE AND VARIOUS COMBINATIONS THEREOF ON DIFFERENT CARBOHYDRATES AND PROTEIN OF GASTRIC JUICE IN INDOMETHACIN TREATED ALBINO RATS.

Group	Hexoses µg/ml	Hexamine µg/ml	Fucose µg/ml	Sialic acid µg/ml	Total carbohydrate µg/ml	Total protein µg/ml	C/P ratio
Vehicle treated control	642.0 ± 37.6 ^{a*}	248.9 ± 11.2	50.6 ± 2.2	41.32 ± 2.5	982.8 ± 40.6	242.5 ± 31.6	3.06 ± 0.6 ^{a*}
Indomethacin 20 mg/kg s.c. single dose	363.8 ± 11.4	152.9 ± 9.9	39.5 ± 3.0	32.2 ± 2.2	588.7 ± 19.8	448.4 ± 22.1	1.34 ± 0.1
TABH 60 mg/kg p.o.4 days	461.4 ± 27.0	237.7 ± 9.1	96.46 ± 2.9	84.7 ± 4.6	880.3 ± 34.8 ^{b*}	207.4 ± 21.3	4.59 ± 0.4
TABH 60 mg/kg p.o.10 days	481.5 ± 29.7	240.8 ± 16.4	91.6 ± 3.9	93.9 ± 6.4	907.8 ± 19.8 ^{b*}	227.8 ± 19.7	4.19 ± 0.4
Carbenoxolone 30 mg/kg p.o.4 days	606.1 ± 25.0	298.3 ± 25.8	134.4 ± 21.9	148.4 ± 25.3	1187.2 ± 39.7	202.7 ± 21.3	6.36 ± 0.6
Cimetidine p.o.4 days	439.8 ± 28.6	185.1 ± 14.3	51.1 ± 16.1	37.7 ± 3.1	712.7 ± 41.5	182.1 ± 23.1	4.47 ± 0.4 ^{b*}
Carbenoxolone 15 mg/kg + TABH 60 mg/kg p.o.4 days	512.8 ± 22.3	256.6 ± 21.4	111.9 ± 10.6	114.6 ± 4.0	995.9 ± 33.3	191.0 ± 18.7	5.72 ± 0.6
Cimetidine 10 mg/kg + TABH 60 mg/kg p.o.4 days	454.7 ± 29.7	201.0 ± 20.2	93.1 ± 4.4	96.0 ± 1.9	844.8 ± 27.9	167.8 ± 8.2	5.13 ± 0.5

n = 10 All values are mean ± S.E.M.
 x p < 0.05
 + p < .01
 * p < .001
 a - compared to vehicle
 b - compared to indomethacin
 c - compared to carbenoxolone or cimetidine

Combination of TABH (60 mg/kg) with the 50% dose of carbenoxolone (15 mg/kg) caused better effect than with TABH treatment alone for 4 days or 10 days. Combination of TABH (60 mg/kg) with cimetidine (10/kg) caused significant increase in hexoses, hexosamine, fucose and sialic acid and significant decrease in total protein. Combination of TABH with cimetidine caused insignificant increase in carbohydrates and decrease in protein.

HISTOPATHOLOGICAL STUDY

INDOMETHACIN INDUCED GASTRIC ULCER

Administration of indomethacin (20 mg/kg s.c.) produced varying grades of damage to the gastric mucosa. Histopathological sections showed partial necrosis of the gastric mucosa and the presence of inflammatory cells in the submucosa (Fig. 13 a, b). These histopathological changes were interpreted as early developing ulcer.

ANTIULCEROGENIC EFFECT OF TABH

Histopathological section of the gastric mucosa with 4 days TABH (60 mg/kg) treatment after inducing ulcers by indomethacin showed creeping fibrosis at the base of mucosa, presence of inflammatory cells in the submucosa and healing of the gastric ulcer (Fig.14). However, section of tissue from animals treated for 10 days with TABH (60 mg/kg) showed complete healing of the ulcer in the form of presence of thick-walled congested blood vessels at the base of mucosa and submucosa, regeneration of mucosa and the presence of few fibroblasts at the base of mucosa (Fig.15 a, b.). Staining of the same sections by PAS showed increased PAS activity and mucosal regeneration (Fig. 16).

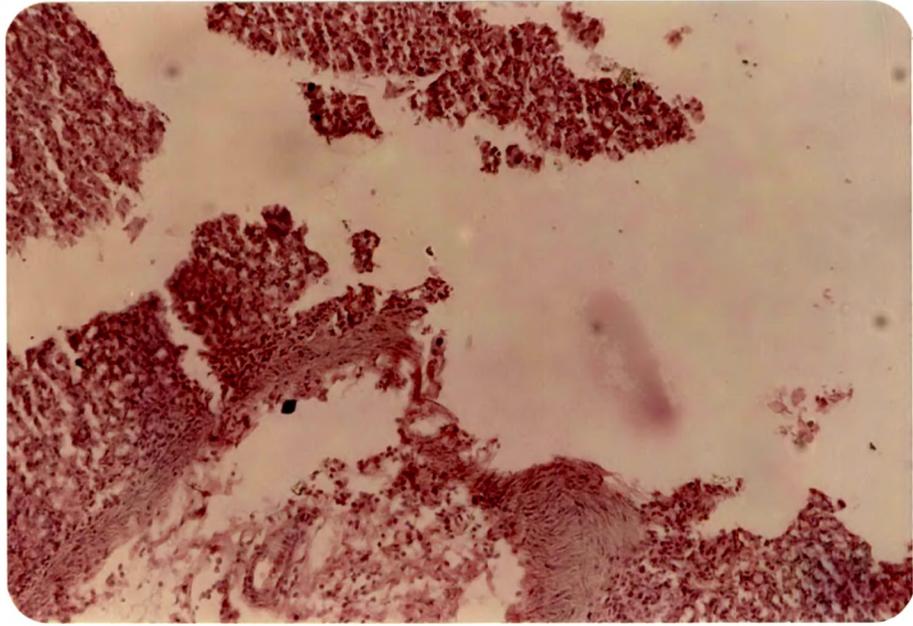


Fig.13 a

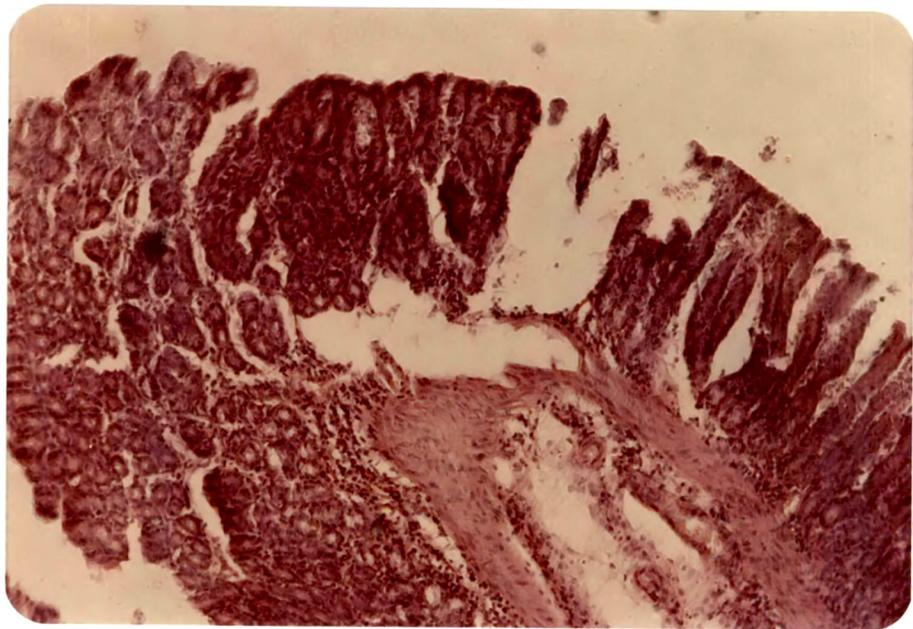


Fig.13 b

Fig. 14

Section of the gastric mucosa with 4 days TABH treatment after inducing the ulcer by indomethacin. Note the early healing of ulcer with creeping fibrosis and the presence of inflammatory cells (10 X)

Fig. 15

Sections of the gastric mucosa with 10 days TABH treatment after inducing gastric ulcer by indomethacin.

- (a) Note the healing of ulcer in the form of thick walled congested blood vessels and inflammatory cells in the submucosa (10 X).

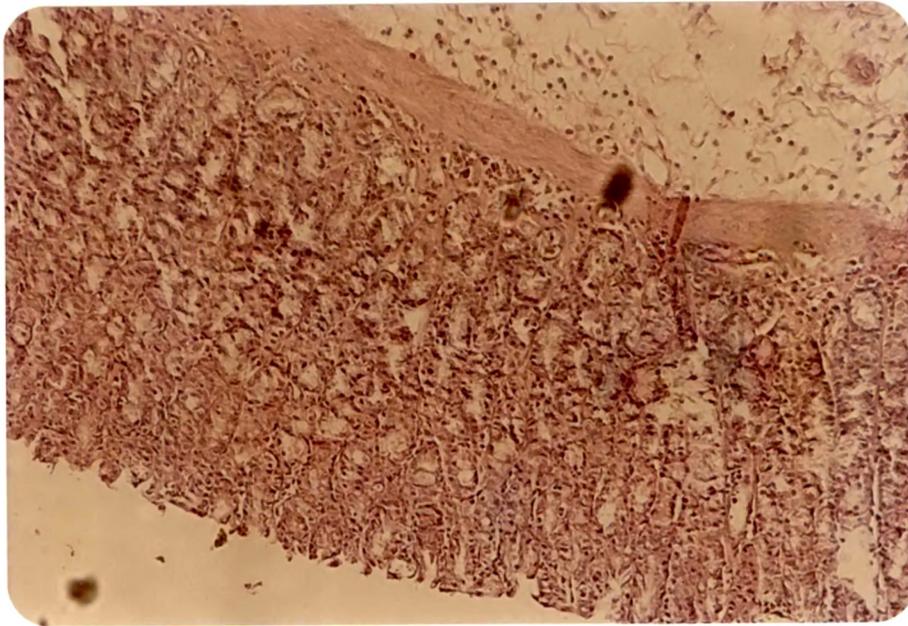


Fig .14

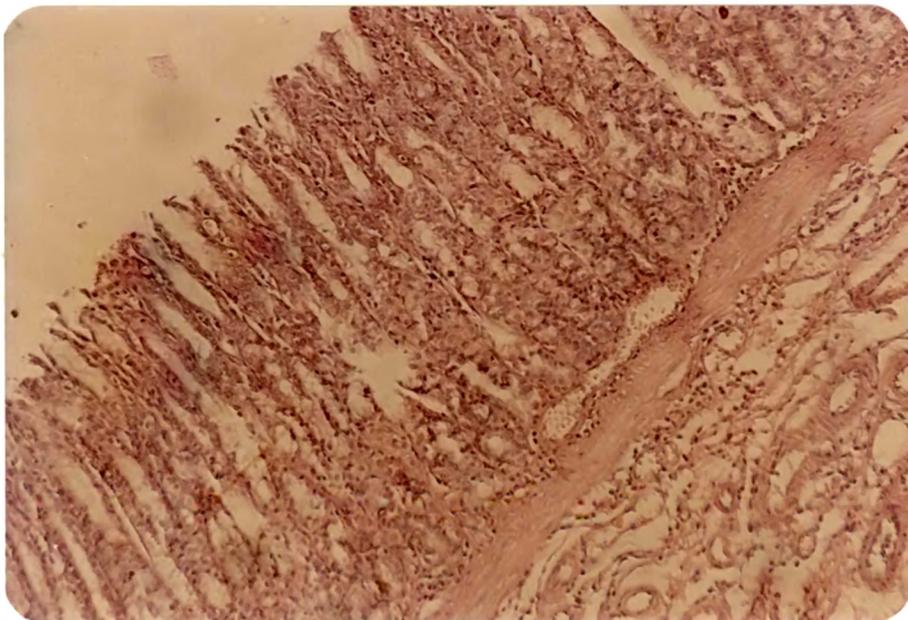


Fig.15 a

- (b) Note completely healed ulcer with complete regeneration of the mucosa, few fibroblasts at the base of mucosa and congested blood vessels in the submucosa (10 X).

Fig. 16

Section of gastric mucosa with 10 days TABH treatment after inducing ulcer by indomethacin and stained by Periodic Acid Schiff reagent (PAS). Same (15 b). Section shows increased PAS activity and regeneration of mucosa (10 X).

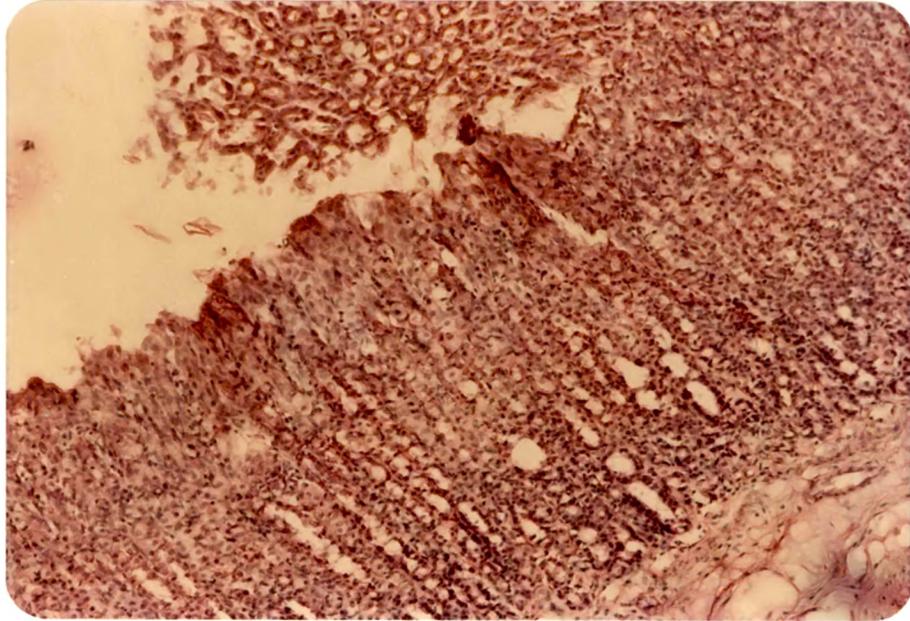


Fig.15 b

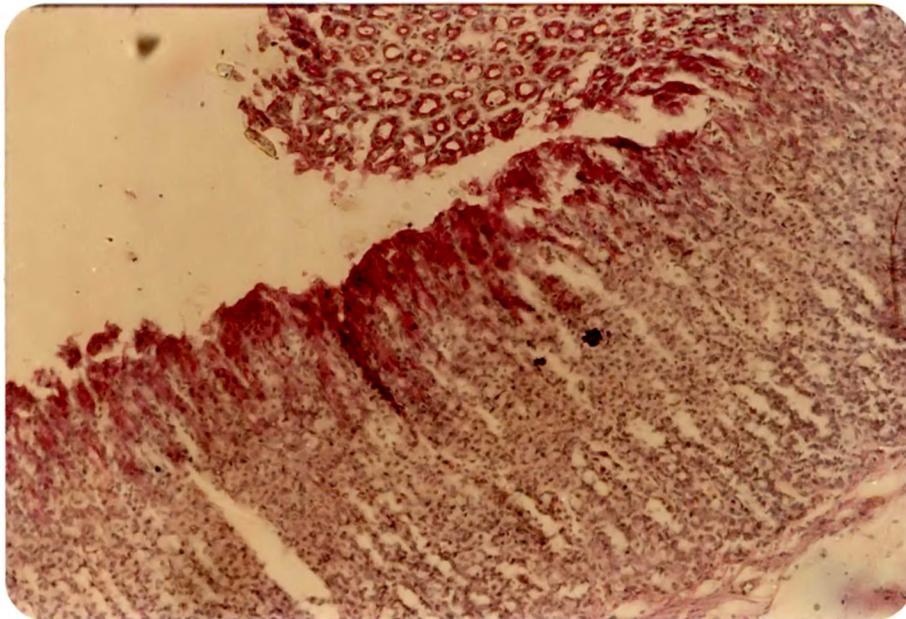


Fig .16

EFFECT OF TABH, CARBENOXOLONE, CIMETIDINE AND VARIOUS COMBINATIONS THEREOF ON CYSTEAMINE-INDUCED GASTRIC ULCERS.

A single dose of cysteamine (300 mg/kg s.c.) produced severe duodenal ulcers with mean ulcer index of $18.30 \pm 0.84 \text{ mm}^2$ (Table 9). TABH 60 mg/kg for 4 days and 10 days after cysteamine administration caused significant decrease in the ulcer index with 57% and 83% protection respectively. Carbenoxolone 30 mg/kg p.o. for 4 days produced maximum protective effect equivalent to that with TABH administered for 10 days. Cimetidine (20 mg/kg p.o.) administered for 4 days also caused significant decrease in the ulcer index. Cimetidine 20 mg/kg caused 60% protection which is equivalent to that by TABH administered for 4 days.

Combination of TABH with the 50% dose of carbenoxolone (15 mg/kg) produced effect equivalent to carbenoxolone (30 mg/kg) or TABH (60 mg/kg) administered for 10 days. Similar combination with the 50% dose of cimetidine (10 mg/kg p.o.) for 4 days produced better effect than that with cimetidine alone. The number of ulcers was reduced corresponding to decrease in the ulcer index and increase in the percentage protection.

EFFECT OF TABH, CARBENOXOLONE, CIMETIDINE AND VARIOUS COMBINATIONS THEREOF ON VOLUME, TOTAL ACIDITY AND PEPSIN ACTIVITY OF THE GASTRIC JUICE IN CYSTEAMINE-TREATED ALBINO RATS.

Administration of cysteamine (300 mg/kg s.c.) caused significant decrease in the volume and increase in the total acidity without affecting pepsin activity of the gastric juice secreted within four hours of pylorus ligation (Table 10). TABH (60 mg/kg p.o.) treatment for 4 days after cysteamine administration caused 26% decrease in the volume and significant decrease in the total acidity and pepsin activity of the gastric juice. Furthermore, 10 days treatment with TABH (60 mg/kg p.o.) produced more effect than 4 days treatment.

Carbenoxolone (30 mg/kg p.o.) administration for 4 days after cysteamine produced no significant change in the volume and total acidity of the gastric juice; however, pepsin activity was significantly reduced. Administration of cimetidine (20 mg/kg p.o.) for 4 days after cysteamine caused 55% decrease in the volume and significant decrease in the total acidity and pepsin activity of the gastric juice.

Table - 9

EFFECT OF TABH, CARBENOXOLONE, CIMETIDINE AND VARIOUS COMBINATIONS THEREOF ON CYSTEAMINE - INDUCED DUODENAL ULCER IN ALBINO RATS.

Group	Mean no. of ulcers ± S.E.M.	Mean ulcer index mm ² ± S.E.M.	% protection
1. Cysteamine treated control (300 mg/kg s.c.)	6.00 ± 0.49	18.30 ± 0.84	-
2. TABH 60 mg/kg p.o. 4 days	2.20 ± 0.77 *	7.80 ± 2.70 *	57.37
3. TABH 60 mg/kg p.o. 10 days	1.25 ± 0.66 *	3.06 ± 1.54 *	83.27
4. Carbenoxolone 30 mg/kg p.o. 4 days	1.15 ± 0.67 *	3.06 ± 0.93 *	83.27
5. Cimetidine 20 mg/kg p.o. 4 days	2.30 ± 0.67 *	7.15 ± 1.26 *	60.93
6. Carbenoxolone 15 mg/kg p.o. + TABH 60 mg/kg p.o. 4 days	1.00 ± 0.47 *	2.80 ± 1.03 *	84.69
7. Cimetidine 10 mg/kg p.o. 4 days + TABH 60 mg/kg p.o. 4 days	2.15 ± 0.58 *	5.01 ± 1.16 *	72.62

n = 15

*, P < .001 compared to cysteamine

Table - 10

EFFECT OF TABH, CARBENOXOLONE, CIMETIDINE AND VARIOUS COMBINATIONS THEREOF ON GASTRIC JUICE VOLUME, TOTAL ACIDITY AND PEPSIN ACTIVITY OF THE GASTRIC JUICE IN CYSTEAMINE TREATED ALBINO RATS.

Group	Mean volume ml ± S.E.M.	Mean total acidity μEq./4 hours ± S.E.M.	Mean pepsin activity mmol/4 hours ± S.E.M.
Vehicle treated	4.85 ± 0.23	777.60 ± 23.14	1.42 ± 0.07
Cysteamine 300 mg/kg p.o. single dose	4.1 ± 0.09 ^{a+}	956.05 ± 18.34 ^{a*}	1.47 ± 0.07
TABH 60 mg/kg p.o. 4 days	3.6 ± 0.20 ^{bx}	561.05 ± 19.48 ^{b*}	0.97 ± 0.07 ^{b*}
TABH 60 mg/kg p.o. 10 days	2.36 ± 0.15 ^{b*}	443.84 ± 14.70 ^{b*}	0.94 ± 0.07 ^{b*}
Carbenoxolone 30 mg/kg p.o. 4 days	4.0 ± 0.21	910.18 ± 21.45	1.16 ± 0.09 ^{b+}
Cimetidine 20 mg/kg p.o. 4 days	2.80 ± 0.19 ^{b*}	401.50 ± 15.34 ^{b*}	0.70 ± 0.03 ^{b*}
Carbenoxolone 15 mg/kg p.o. + TABH 60 mg/kg p.o. 4 days	2.50 ± 0.34 ^{b+ c+}	578.00 ± 21.60 ^{b* c*}	0.90 ± 0.05 ^{b* Cx}
Cimetidine 10 mg/kg p.o. + TABH 60 mg/kg p.o. 4 days	2.10 ± 0.12 ^{b* c+}	390.50 ± 13.20 ^{b*}	0.74 ± 0.05 ^{b*}

n = 15

x, P < .05
+, P < .01
*, P < .001

a - compared to vehicle
b - compared to cysteamine
c - compared to carbenoxolone or cimetidine

Combination of the same dose of TABH (60mg/kg) with 50% dose of carbenoxolone (15 mg/kg) produced better effect than that with carbenoxolone alone. Similar combination of TABH (60/kg) with cimetidine (10 mg/kg) produced better effect than that with cimetidine alone.

EFFECT OF TABH, CARBENOXOLONE, CIMETIDINE AND VARIOUS COMBINATIONS THEREOF ON CARBOHYDRATES AND PROTEIN OF THE GASTRIC JUICE IN CYSTEAMINE TREATED ALBINO RATS:

Cysteamine (300 mg/kg s.c.) caused decrease in the total carbohydrates and significant increase in the protein content of the gastric juice leading to decrease in the carbohydrates to protein ratio (Table 11). Amongst various carbohydrates, hexosamine concentration was significantly increased whereas total hexoses fucose and sialic acid were significantly reduced.

Administration of TABH (60 mg/kg p.o.) for 4 days caused significant increase in total carbohydrates and significant decrease in the protein leading to increased carbohydrate to protein ratio. TABH caused two fold increase in the formation of fucose and sialic acid, significant decrease was observed in the hexosamine. TABH (60 mg/kg p.o.) administered for 10 days produced significant change in carbohydrates, protein and carbohydrate to protein ratio.

Carbenoxolone (30 mg/kg p.o.) treatment for 4 days produced maximum increase in the total carbohydrates and decrease in the protein leading to maximum rise in the carbohydrate to protein ratio. Carbenoxolone caused 3-fold increase in the formation of sialic acid, fucose and significant decrease in hexosamine.

Cimetidine (20 mg/kg p.o.) treatment for 4 days did not affect any carbohydrates; hence no significant change was observed in total carbohydrates. However, because of the significant decrease in the protein, the carbohydrate to protein ratio was significantly increased after cysteamine which was less than with 4 days TABH treatment.

Combination of TABH with 50% dose of carbenoxolone produced more effect than TABH alone for 4 days or 10 days or cimetidine. However, similar combination of TABH with cimetidine was less effective.

Table - 11

EFFECT OF TABH, CARBENOXOLONE, CIMETIDINE AND VARIOUS COMBINATIONS THEREOF ON DIFFERENT CARBOHYDRATES AND PROTEIN OF GASTRIC JUICE IN CYSTEAMINE TREATED ALBINO RATS.

Group	Hexoses $\mu\text{g/ml}$	Hexosamine $\mu\text{g/ml}$	Fucose $\mu\text{g/ml}$	Sialic acid $\mu\text{g/ml}$	Total carbohydrate $\mu\text{g/ml}$	Total protein $\mu\text{g/ml}$	C/P
Vehicle treated control	628.2 \pm 49.6	212.2 \pm 17.4	52.2 \pm 1.5	37.8 \pm 2.3	930.4 \pm 54.8	358.7 \pm 19.2	2.79 \pm 0.2
Cysteamine 30 mg/kg s.c. single dose	a* 294.7 \pm 27.8	a* 302.3 \pm 18.8	a* 30.7 \pm 1.1	a* 24.2 \pm 2.2	a* 651.9 \pm 25.9	a* 454.9 \pm 31.9	a* 1.53 \pm 0.1
TABH 60 mg/kg p.o. 4 days	b+ 432.3 \pm 29.9	b* 231.3 \pm 21.8	b* 85.1 \pm 1.9	b* 69.6 \pm 4.5	b* 818.3 \pm 35.2	b* 204.2 \pm 17.7	b* 4.23 \pm 0.4
TABH 60 mg/kg p.o. 10 days	b+ 455.3 \pm 38.2	b+ 223.3 \pm 11.8	b+ 82.2 \pm 3.1	b* 76.6 \pm 6.0	b+ 847.4 \pm 59.2	b* 207.2 \pm 13.9	b* 4.11 \pm 0.2
Carbenoxolone 30 mg/kg p.o. 4 days	b+ 540.3 \pm 64.9	b+ 225.7 \pm 19.2	b* 131.6 \pm 1.5	b* 115.2 \pm 6.6	b* 1012.8 \pm 70.56	b* 171.3 \pm 6.0	b* 6.58 \pm 1.1
Cimetidine 20 mg/kg p.o. 4 days	391.4 \pm 25.5	258.8 \pm 21.8	39.7 \pm 5.8	37.2 \pm 7.0	687.1 \pm 17.9	171.2 \pm 15.4	b* 4.43 \pm 0.4
Carbenoxolone 15 mg/kg + TABH 60 mg/kg p.o. 4 days	b+ 496.6 \pm 36.9	b* 208.8 \pm 16.1	b* 117.8 \pm 11.4	b* 90.7 \pm 8.8	b* 913.9 \pm 59.3	b* 190.1 \pm 15.0	b* 5.12 \pm 0.5
Cimetidine 10 mg/kg + TABH 60 mg/kg p.o. 4 days	b+ 458.6 \pm 33.9	236.1 \pm 26.8	b* 96.0 \pm 1.5	b* 84.5 \pm 4.7	b* 875.3 \pm 35.6	b* 181.4 \pm 11.0	b* 4.06 \pm 0.6

n = 15, All values are mean \pm S.E.M.

x, p < 0.05

+, p < .01

*, p < .001

a - compared to vehicle

b - compared to Cysteamine

c - compared to carbenoxolone or cimetidine

HISTOPATHOLOGICAL STUDY

CYSTEAMINE-INDUCED DUODENAL ULCERS

Cysteamine (300 mg/kg s.c.) produced full fledged ulcer in the first part of the duodenum. Histopathological section showed necrosis of the mucosa and submucosa. The wall of the intestine in the vicinity showed inflammatory cells and congestion (Fig.18 a, b). These histopathological changes were interpreted as early developing ulcer. Fig.17 shows normal pyloroduodenal mucosa for comparison.

ANTIULCEROGENIC EFFECT OF TABH

Histopathological section of duodenal mucosa with 4 days of TABH (60 mg/kg) treatment after inducing ulcer by cysteamine showed early healing of the duodenal ulcer in the form of inflammatory cells in the lamina propria and normal Brunner's gland (Fig. 19). However, sections of duodenum after 10 days TABH (60 mg/kg) treatment showed creeping fibrosis, mucosal regeneration, presence of fibroblastic cell and inflammatory cells at the base of mucosa and complete healing of the duodenal ulcer (Fig.20 a, b).

Fig.17

Section of the normal pyloroduodenal mucosa. Section shows the presence of normal Brunner's glands and duodenal mucosa (4 X).

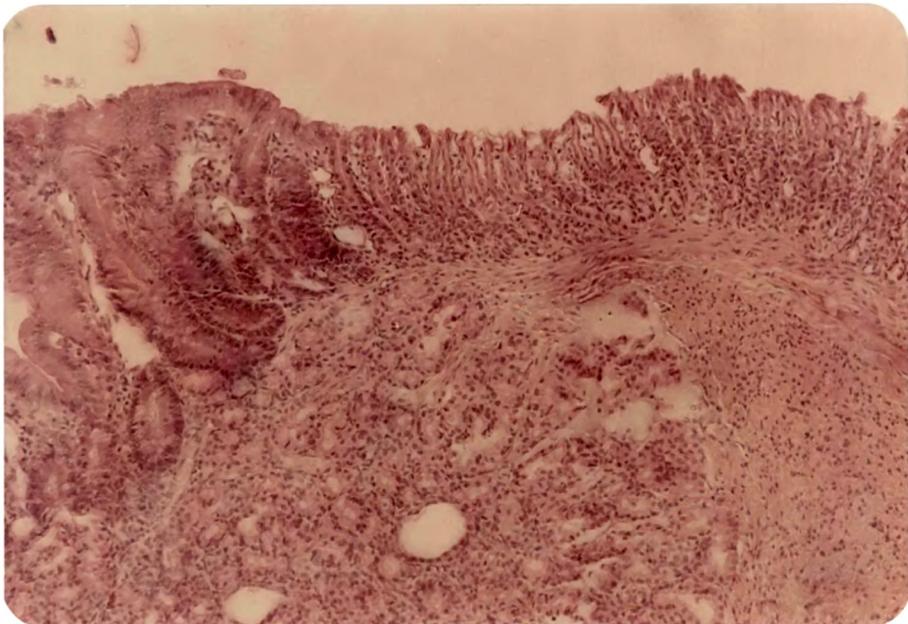


Fig.17

Fig.18

Sections of the duodenal mucosa after cysteamine administration.

- (a) Full-fledged ulcer in the first part of duodenum with necrosis of mucosa and submucosa are seen. The wall of the intestine in the vicinity shows inflammatory cells and congestion (4 X).

- (b) Same section (18a) with higher magnification shows full-fledged ulcer in the first part of the duodenum (10 X).



Fig.18a

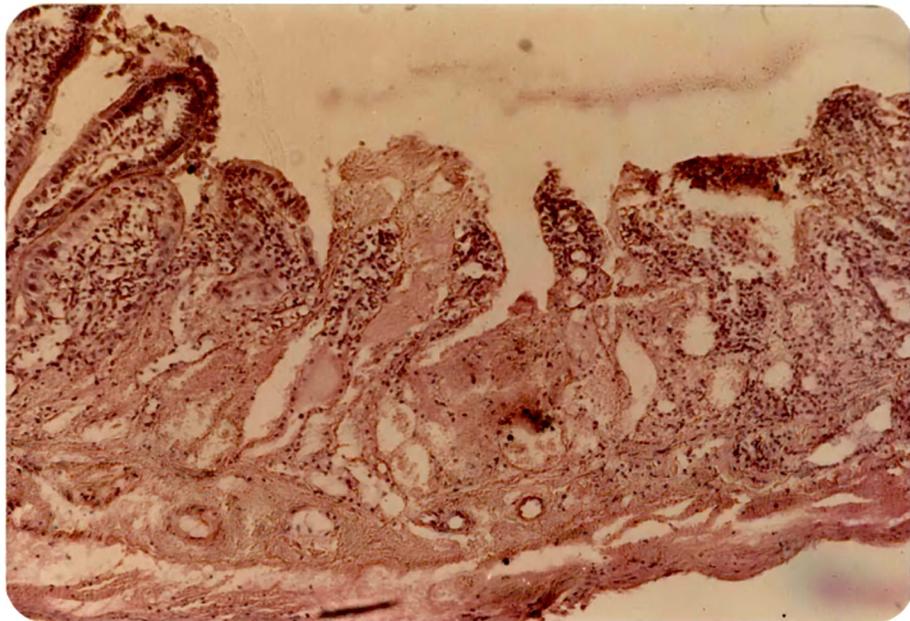


Fig . 18b

Fig.19

Section of the duodenal mucosa with 4 days TABH treatment after inducing ulcers by cysteamine. Early healing in the first part of the duodenum with the presence of intact mucosa and inflammatory cells in the lamina propria and normal Brunner's gland are seen (10 X).

Fig. 20

Sections of the duodenal mucosa with 10 days TABH treatment after inducing ulcer by cysteamine showing healing of the duodenal ulcer

- (a) Regeneration of the mucosa, inflammatory cells and fibroblastic cells at the base of mucosa. (10 X).

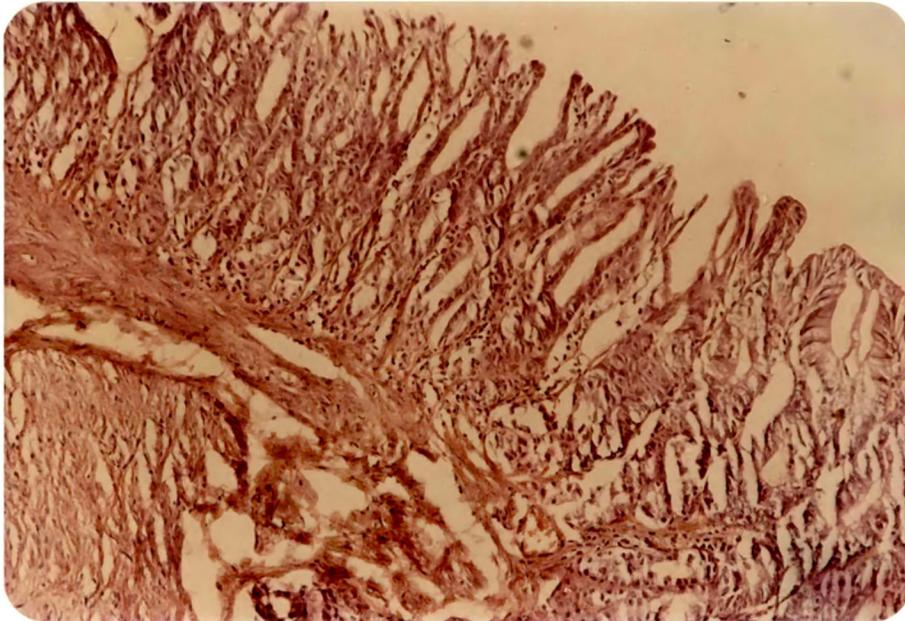


Fig. 20 b

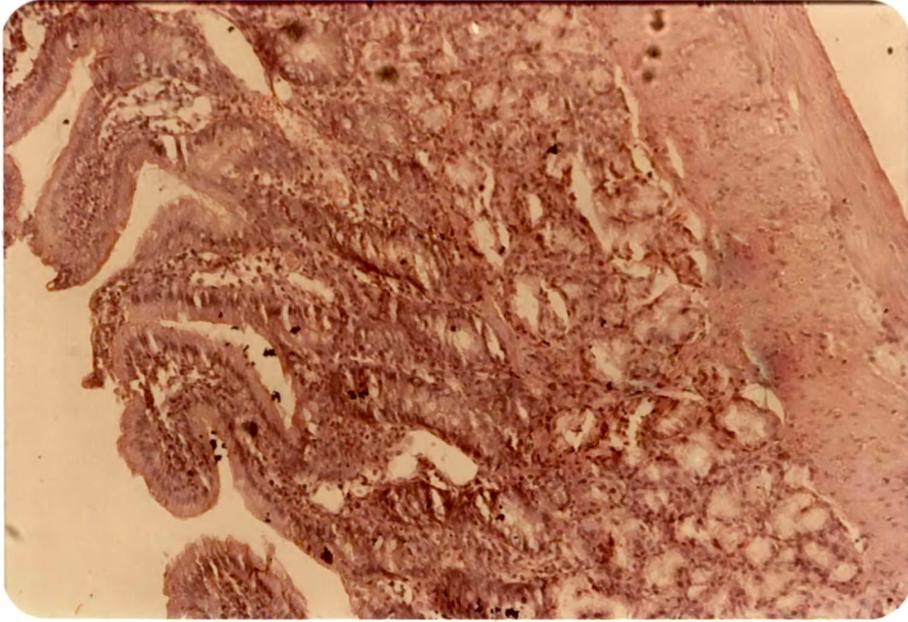


Fig.19

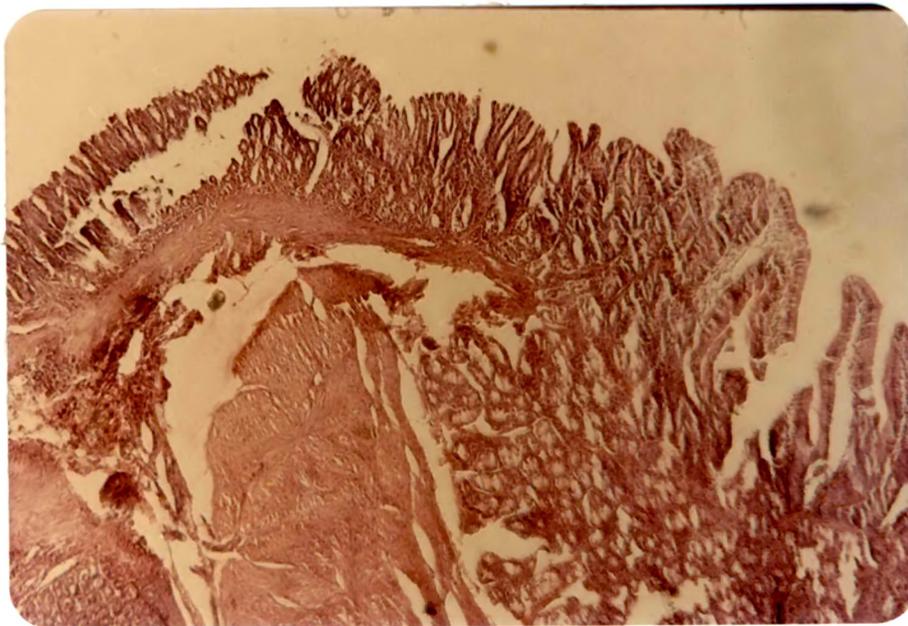


Fig. 20a

(b) Healing in the form of creeping fibrosis and inflammatory cells at the base of the mucosa and complete mucosal regeneration are seen (10 X).

EFFECT OF TABH, DEXAMETHASONE AND INDOMETHACIN ON EPITHELIAL CELL TURNOVER IN PYLORUS LIGATED ALBINO RATS.

Epithelial cells are desquamated into the stomach and lumen of the small intestine with their nuclei, and it is therefore reasonable to assume that the estimation of DNA in the perfusions or stomach wash is a measure of cell loss.

Dexamethasone and indomethacin caused four to five fold increase in the total DNA of the stomach wash collected after 4 hours of pylorus ligation compared to vehicle treated control, suggesting that epithelial cell loss is increased during ulceration (Table 12). TABH (60 mg/kg p.o. for 10 days) treatment caused significant decrease in the total DNA of the stomach wash; however it was still significantly higher than vehicle treated control value.

CHRONIC TOXICITY OF TABH

Chronic administration of TABH (120 mg/kg p.o. for 30 days) did not produce any significant change in general behaviour of rat and did not cause any death. TABH caused significant change only in few parameters whereas others remained unaltered (Table 13). The drug caused significant increase (control 11.9 ± 0.28 gm% and treated 14.30 ± 0.30 gm%) in Hb content and total RBC (control 5.01 ± 0.09 and treated 5.40 ± 0.09 million/mm²) count of the blood. TABH caused insignificant rise in body weight and total WBC count after 30 days of treatment.

Differential WBC count showed significant rise only in lymphocytes (control 37.90 ± 1.74 and treated $46.27 \pm 3.1\%$) without affecting neutrophil, eosinophil and monocyte count. Total wet weight of both adrenal glands (control 48.00 ± 2.25 and treated 47.13 ± 2.81 mg), S.G.P.T. (control 37.40 ± 1.91 and treated 33.13 ± 2.04 i.u/ml) and S.G.P.T. (control 27.60 ± 1.23 and treated 27.80 ± 2.83 i.u/ml) also remained unaltered. No abnormal changes grossly or histopathologically were observed in liver, kidney, heart and spleen.

Table - 12

EFFECT OF TABH, DEXAMETHASONE AND INDOMETHACIN ON TOTAL DNA
(μ g/4 HOURS OF STOMACH WASH) IN PYLORUS LIGATED ALBINO RATS.

Group	Mean total DNA (μ /g) + S.E.M.	
	Dexamethasone	Indomethacin
Vehicle treated	126.50 \pm 14.20	135.00 \pm 18.91
Ulcerated	a* 675.00 \pm 40.40	a* 624.69 \pm 49.14
TABH 60 mg/kg p.o. for 4 days.	b* 241.56 \pm 22.48	b* 280.00 \pm 26.21

n = 6

*, P < .01

a - compared to vehicle

b - compared to dexamethasone or indomethacin

Table - 13

CHRONIC TOXICITY STUDY OF TABH 120 MG/KG P.O. FOR 30 DAYS IN RATS.

Parameters	Control	Treated
1. Body weight	220.00 ± 6.79	227.33 ± 4.57*
2. Haemoglobin gm%	11.9 ± 0.28*	14.30 ± 0.30*
3. Total RBC count million/mm ³	5.01 ± 0.09	5.40 ± 0.09
4. Total WBC count million/mm ³	6390.0 ± 225.02	6535.0 ± 302.4
<u>DIFFERENTIAL W.B.C. COUNT:</u>		
1. Neutrophil	59.10 ± 1.78	55.20 ± 2.95*
2. Lymphocyte	37.90 ± 1.74	46.27 ± 3.11
3. Eosinophil	1.70 ± 0.34	1.20 ± 0.22
4. Monocyte	1.30 ± 0.44	1.33 ± 0.39
Total wet weight of both adrenal glands in mg	48.00 ± 2.25	47.13 ± 2.81
S.G.O.T. i.u/ml	37.40 ± 1.91	33.13 ± 2.04
S.G.P.T. i.u/ml	27.60 ± 1.23	27.80 ± 2.83
	(n=10)	(n=15)

* P < .05

TRACE CHEMICAL ANALYSIS

Spectrophotometric analysis of TABH used in the present study showed maximum quantity of Cu (680 ppm) followed by Fe, Ni and other metals (Table.14).

Table - 14

TRACE CHEMICAL ANALYSIS OF TAMRABHASMA (TABH)

Cu	680 μ g
Fe	100 ppm
Ni	80 ppm
Zn	60 ppm
Mn	40 ppm
Bi	10 ppm
Mg	5 ppm
Na	5 ppm
Sb	5 ppm
Sr	5 ppm
Pb	10 ppm