INTRODUCTION

INTRODUCTION

Peptic ulcer represents a major health problem, both in terms of morbidity and mortality. Because of its frequency and worldwide distribution, peptic ulcer continues to be a subject of numerous investigation, both experimental and clinico pathological. In this respect peptic ulcer occupies a place secondary to carcinoma in the field of gastroenterology. Quineke (1) was probably the first to use the term "Peptic ulcer" which is an excoriated area of gastroduodenal mucosa caused by digestive action of gastric juice.

STRESS AND STRESS INDUCED ULCER

Stress, as Selye (2) described, is a state manifested by a specific syndrome which consists of all the non-specifically induced changes in a biologic system. Essentially, stress is the consequences of the rate of wear and tear in a biologic system.

Several studies in human subjects have demonstrated that emotion can cause increase in gastric acidity. On this basis "emotional stress" has been considered as an important factor in the etiology of peptic ulcer. James (3) discussed the work of Wolf and Wolf on fistulous patient. He showed that when the patient was subjected to acute or chronic periods of emotional stress there was an increase in gastric acidity. Shay and co-workers (4) demonstrated that the emotional stress increased the total acid output to over four times the basal levels. Eichhorn and Trackfier (5) observed alteration in acid

secretion in patients with hypnotically-induced emotions. Thus, it appears that emotional stress can be a factor in the etiology of peptic ulcer.

EXPERIMENTAL STRESS ULCER

Seyle (6) was probably the first to report the experimental peptic ulcer in rats subjected to different types of noxious stimuli such as immobilization, injection of drugs, exposure to cold or surgical trauma. Since then many other workers reported the restraint ulcers in rats by immobilization (7, 8). These stimuli were classified as nonspecific stresses. It was postulated that nonspecific stresses produced certain emotional disturbances in the animals, which increase adrenal function and resulted into the appearance of "neurogenic" ulcer in 85 – 100% animals. Behavioral techniques for the production of neurogenic ulcers have been described in rats by Weisz (9) and in monkey by Porter *et al.* (10). They used conflict situation in the animals by electrical shock, anxiety, punishment and condition avoidance situation.

Parmar and Desai in their review (11) mentioned that experimental ulcers, induced by stress, appear to be the experimental counterpart of Curling's ulcers or human stress ulcers. They were of the opinion that these ulcers, located in the glandular region of the stomach of animals, are of several types viz.

1. Restraint ulcers
2. Water immersion – induced restraint ulcers
3. Cold and restraint ulcers
4. Gastric erosions following short – term stress and concurrent administration of non steroidal anti-inflammatory drugs (NSAIDs)
5. Restraint + aspirin ulcers
6. Swimming stress ulcers
7. Activity stress ulcers
8. Haemorrhagic shock induced ulcers.

Experimental stress ulcer due to burn (12), hepatectomy(13), adrenaline (14), thermal injury (15), lateral hypothalamic lesions (16), disseminated intra vascular coagulation (17) etc. are also known in the literature.

MECHANISM OF EXPERIMENTAL STRESS ULCER

Numerous studies have been undertaken to investigate the mechanism underlying the stress induced experimental gastric ulceration . Various factors have been Identified. These are :

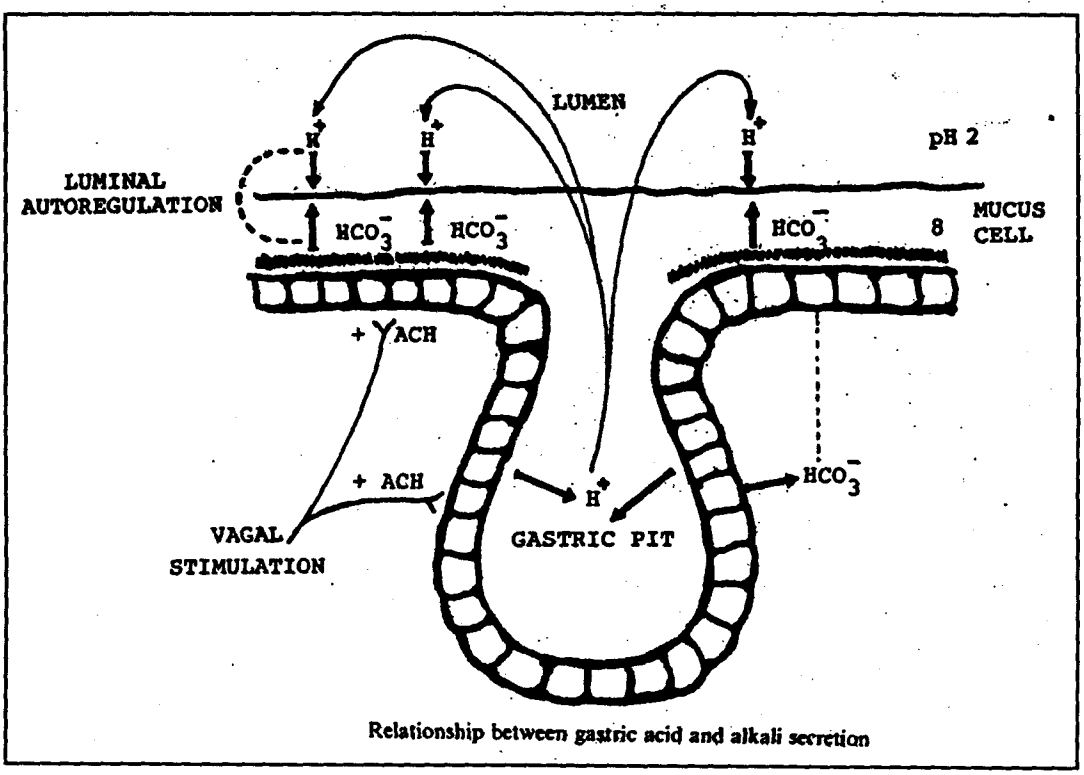
ACID - PEPSIN

The stomach has a pivotal role in the digestive process, functioning both as a reservoir and a mill by virtue of gastric glands secreting hydrochloric acid and pepsin. Acidification of ingested food initiated the process of digestion by creating optimal conditions for peptic digestions of proteins. Parietal cells of stomach secrete hydrochloric acid while chief cells formed pepsinogen which is activated into pepsin in the acid medium of gastric juice. Both acid and pepsin have proteolytic actions on living tissue and are capable of autodigestion of gastroduodenal mucosa (18).

For several decades, the dictim "no acid – no ulcer" has dominated the pharmacological basis of ulcer therapy, and the drugs used, reduced acid secretion. However, it was observed that in 45-75% patients of duodenal ulcer acid secretion was within normal limits, whereas in gastric ulcer patients acid secretion was either normal or subnormal (19). Patients of Zollinger-Ellison syndrome, characterized by abnormally high acid secretion, show minimal incidence of peptic ulceration (20). It was, therefore, apparent that peptic ulcer was not solely induced by the offensive factors of the acid and pepsin . In experimental studies also same picture was found out . Reports (21 - 23) showed that ulcerogenic effect of immobilization stress in albino rats did not seem to be related to acid- pepsin hypersecretion. Zherev (24) ,rather, observed reduction in the number of pepsinogen fraction in rats with experimental stress ulcer induced by immobilization and cooling. On the other hand, Yamazaki (25) and Sakai (26) reported an increase in gastric secretion and acidity during restraint and water immersion stress ulceration in rats. Brodie *et al.* (27, 28) studied the effects of restraint on gastric secretion in the chronic fistulated rat. They found increase in the concentration of free and total acid of gastric juice. Menguy (29), however, demonstrated that restraint significantly decreased free acid output in the pyloric-ligated rats. He, thus, concluded that acid-pepsin digestion was not the basic mechanism in the production of restraint ulcers in the animals.

MUCUS SECRETION

Mucus is one of nature's perfections, protecting the gastrointestinal tract from infective, chemical and physical insults. It has been commented that it encloses the gastric juice in the stomach as if it was an impermeable porcelain vase. Mucus is secreted into the gastroduodenal lumen by surface epithelial cells and mucus neck cells (goblet cells) and submucosal Brunner's glands. The secretion has two components, a water insoluble gel adherent to the mucosal surface and soluble mucus in the lumen. The latter can either be secreted directly into the lumen or may be derived from the mucus gel by proteolytic

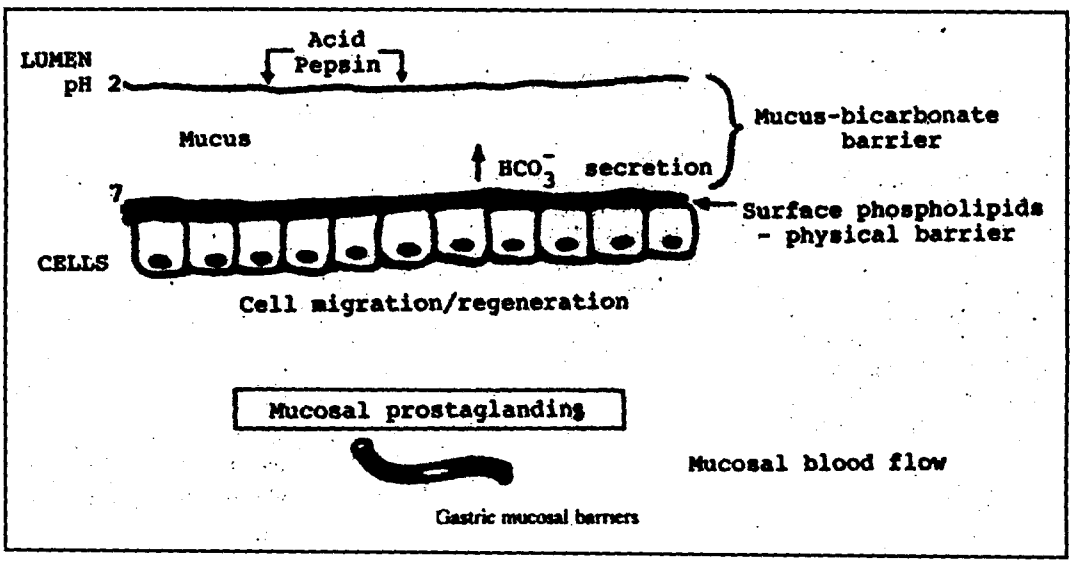


Relationship between gastric acid and alkali secretion

degradation or mechanical shearing during digestion (30).

Mucus consists of about 1% by weight of salts and other diaiyzable components, 0.5 – 1% of free proteins and a similar quantum of carbohydrate rich glycoproteins and 95% or more of water. The glycoprotein component of mucus is responsible for the characteristic viscous gel forming property, believed to be important for the functional role of mucus. Native human mucus glycoprotein has a high molecular weight of about two million daltons and is formed by polymerization of four glycoprotein subunits, joined by disulphide bridges. Each subunit consists of a protein core with about 150 side chains, studded along the length of the protein core, projecting out like bristles of a test tube brush. About 25% of the protein core, which is bereft of these carbohydrate side chains, is non-glycosylated, and the disulphide bridges, 78 per molecule, are located in this region. Disulphide bond splitting reagents, like mercaptoethanol and proteolytic enzymes, break the native glycoprotein molecule into its four component subunits which are water soluble and do not have the viscous gel forming characteristics of the parent glycoprotein molecule. The linkage between carbohydrate and protein in the mucus glycoprotein is 0-glycosidic and the monosaccharide involved is N-acetyl galactosamine, which is attached to either serine or threonine. Apart from these two, the other predominant amino acid in the protein core is proline which does not permit alpha-helix conformation within the peptide chain, providing the requisite close packing of the carbohydrate chains found in these glycoproteins. The carbohydrate side chains comprise over 80% by weight of the glycoprotein molecule and their presence is compatible with the high degree of hydration essential for the special rheological properties of the molecule. There are approximately 600 carbohydrate side chains per molecule of native glcoprotein and each branched side chain consists of about 15 oligosaccharide units composed of galactose, fucose (methyl pentose), N-acetyl glucosamine, N-acetyl galactosamine and sialic acid, with traces, if any, of mannose and no uronic acid , which distinguish them from serum glycoproteins and proteo glycans, respectively. The carbohydrate chains are often negatively charged due to the presence of ester sulphate and sialic acid, the latter being located in the terminal position. The most important sialic acid is N-acetyl neuraminic acid. Rejection of the neighbourly negatively charged group of glycoproteins results in molecular expansion and increase in viscosity. An interesting feature of mucus glycoprotein is that the structure of the terminal parts of the sugar chain is similar to that determining the specificity of ABO blood groups on the erythrocyte surface (31 - 33) .

Mucus has several functions which contribute significantly to cytoprotection.



Gastric mucosal barriers

a) Lubrication and mechanical protection :

The mucus gel covers the entire surface of the gastroduodenal mucosa with a variable thickness of less that 500 μm, lubricating the mucosa and forming the first line of defense against noxious gastric contents. It exists in a dynamic balance between production on one hand and degradation by pepsin and shear forces on the other (34).

b) Mixing barrier :

Mucus is readily permeable to hydrogen ions and provides a mixing barrier at the mucosal surface , preventing the relatively small amounts of bicarbonate ions from mixing with the bulk of hydrogen ions in the lumen, thus confining the neutralization at the mucosal surface, ensuring a pH gradient across the mucus layer . The glycoprotein molecules appear to retard the diffusion of hydrogen ions, the rate of diffusion being four times slower than that in unstirred water. However, this retardation of hydrogen ion diffusion across the mucus layer is unlikely to be the sole factor protecting the mucosa from acid since this would require the renewal of a mucus layer of at lease 0.4 mm thickness , ten times each second, in order to maintain epithelial surface neutrality (35).

c) Unidirectional flux of hydrogen ions :

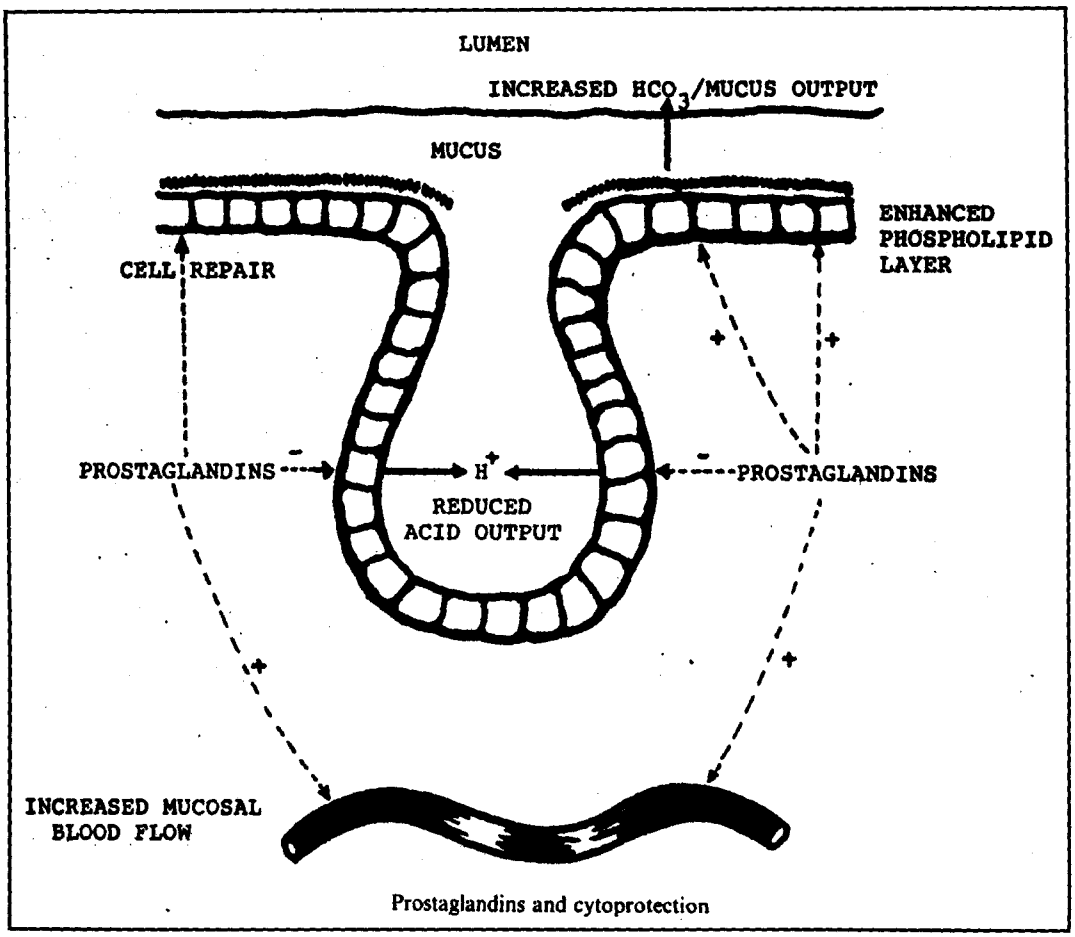
The mucus facilitates unidirectional flux of hydrogen ions from the gastric glands into the lumen. The passage of acid secreted by the parietal cells appears to occur through mucus channels which are highly sulphated. These channels, with high negative charge, contributed by sulphate and sialic acid radicals, produced predominantly by the neck mucus cells, behave as cation exchangers. Periodically, instead of an increasing pH gradient across mucus, there is a sudden drop in pH. A concentration gradient of sodium ions appear to be generated across the mucus layer by the continuous activity of Na/K-ATPase at the baso-lateral membrane of mucus cells. Sodium diffusing across this gradient will generate a diffusion potential positive at the cell facing surface of the mucus gel. It is postulated that this potential moves hydrogen ions into the lumen and retards back diffusion (36).

d) Prevention of back diffusion of pepsin and pepsinogen activation :

Since mucus exploits the phenomenon of phase separation, it attenuates back diffusion of macromolecules like pepsin from gastric juice. Mucus also has a function in transporting pepsinogen and preventing its activation into pepsin (37).

e) Repair of superficial mucosal damage :

Following damage of surface cells, there is rapid release of large amounts of mucus and plasma proteins which, together with the cellular debris, form a coating over the destroyed area, providing a favourable micro-environment for repair and



Prostaglandins and cytoprotection

restitution (38).

f) Antibacterial activity :

Identification of bacteria in human stomach in gastritis indicates that normal gastric mucus may have antibacterial activity (39).

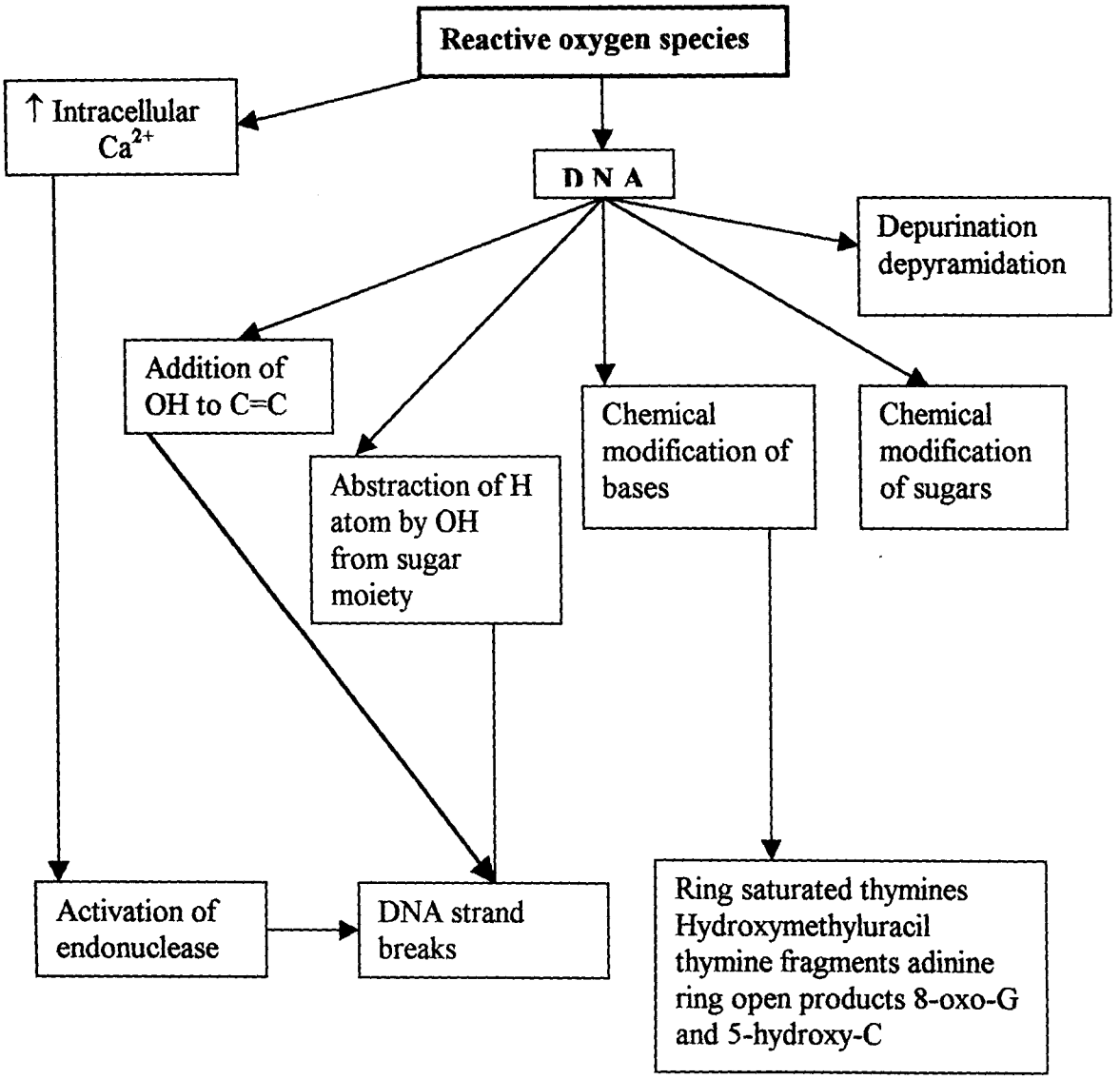
The ability of mucus to afford mucosal protection appears to depend upon its thickness commonly known as mucus gel thickness. It has been reported that the gel is resistant to hypertonic saline, bile, ethanol and nonsteroidal anti-inflammatory drugs and its secretion is augmented by chemical irritants, carbachol, carbenoxolone, prostaglandins and secretin (40). It has also been suggested that bicarbonate secretion (41), intrinsic barrier properties of epithelial cells (42), mucosal blood flow (43), acid-base balance and acid secretion (44), endogenous prostaglandins (45), *Helicobacter pylori* (46), dietary factors (47), nonsteroidal anti-inflammatory drugs (48) etc. are somehow related with the mucus gel thickness.

Role of gastric mucus both in clinical and experiment ulcers has been studied by several workers. Patients of gastric ulcer have an abnormal mucus gel structure containing less polymeric glycoproteins (49) and certain pepsins, more prevalent in duodenal ulcer patients induce marked digestion of the glycoprotein matrix (50). In experimental system, Goel et al. (23) observed reduction in gastric mucus secretion during immobilization stress induced gastric ulcer in albino rats. Grijalva *et al.* in their series of experiments (51 – 56) showed that following lateral hypothalamic lesions in rat there was the decrease in the amount of gastric mucosubstances with simultaneous production of gastric ulcers in the animals. Reduction in the rate of synthesis and secretion of mucus was also noted by various workers in their experimental stress ulcer models (57 – 63).It seems possible, as Menguy suggested (64), that it is the loss of mucus 'barrier' that permits the back diffusion of hydrochloric acid into the stress-damaged gastric mucosa causing ulcer.

LIPID PEROXIDATION

Role of lipid peroxidation in gastric mucosa has been extensively studied in the pathogenesis of peptic ulcer. It has been found out that lipid peroxidation mediated by active oxygen species plays an important role in the pathogenesis of peptic ulcer (65 – 70). Antioxidants, however, act as anti-ulcer agents by inhibiting lipid peroxidation through decrease of reactive oxygen metabolites (71 – 73).

Chemical agents like quercetin, rebamipide, zinc acexamate etc. also exert their anti-ulcer activity by inhibiting lipid peroxidation (74 – 79). Guth (80 – 81) explained that oxygen derived free radicals, specially the superoxide radical, play an



Mechanism of oxidative damage to DNA

important role in ischaemic gastric mucosal lesions, particularly in presence of hydrochloric acid. Ischaemia is followed by utilization of high energy compounds like adenosine tri phosphate (ATP), resulting in accumulation of adenosine mono phosphate (AMP) in the presence of reduced oxidative phosphorylation. AMP is further catalyzed to hypoxanthine, which tends to accumulate. Ischaemia also converts the enzyme xanthine dehydrogenase to xanthine oxidase form. The latter requires the presence of oxygen for its activity, and when oxygen is available after rapid reperfusion, the enzyme acts on hypoxanthine to produce superoxide radicals, hydrogen peroxide and hydroxyl radicals. These free radicals, each containing an unpaired electron in their outer shell, are highly reactive and are potent oxidizing and/or reducing agents, including cell wall damage and the release of intracellular lysosomal enzymes.

In an experimental study Ohara *et al.* (82) measured the level of lipid peroxides of the gastric mucosa of guinea pigs before and serially after stress. Water-immersion, ethanol and burn were used as experimental stress. They observed that stress increased the level of lipid peroxides which was inhibited after giving injection of heparin.In another experiment these workers noted (83) that during stress superoxide dismutase like plasma substance increased in plasma. Upon chromatography on heparin sepharose, this substance was separated into three fractions :

A – without affinity for heparin

B – with intermediate affinity for heparin

C – with relatively strong affinity for heparin.

The fraction "C" was specially increased during stress. Analysis by a polyacrylamide gel electrophoresis of the fraction revealed superoxide dismutase activity and seemed to be the same as extra cellular superoxide dismutase .

To evaluate whether pre-treatment with vitamin – E can minimize gastric ulceration induced by pyloric ligation, George *et al.* (84) observed that vitamin – E protected the gastric mucosa from the development of stress ulcer through its anti-oxidant effect. They thus concluded that stress - condition increased the rate of lipid peroxidation which, in turn, damaged gastric mucosa caused ulceration.

Pandit *et al.* (85) noted that when rats were subjected under the influence of cold restraint stress, rate of lipid peroxidation was increased in the gastric mucosa of the animals. They also noted that formation of stress ulcer in the stomach of rats had a distinct relation with increased rate of lipid peroxidation. These workers used *Shankha Bhasma* as anti-ulcer agent and observed that *Shankha Bhasma* reduced ulcer index by reducing the amount of gastric "thiobarbituric acid reacting substances" which were the index of lipid peroxidation.

Apart from acid-pepsin, mucus secretion and lipid peroxidation, other factors related with experimental stress ulcer were also identified. These are :

1. **Catecholamines** (86 - 88) :

   Intraperitoneal injection of adrenaline in single, double or triple doses of 0.6 mg/kg produced gastric mucus haemorrhages and ulcers in rats. Lesions were produced in 2 or 3 hours without ligation of pylorus. Severe mucosal changes were associated with a fall in gastric mucosal histamine concentration. Mucosal serotonin did not change. Rises in mucosal adrenaline were accompanied by a fall in noradrenaline, total catecholamine levels being unchanged.

2. **Mucosal blood flow; mast cell degranulation** (89 - 91) :

   When dogs were subjected to haemorrhagic shock, a decline of 46% cardiac output was observed while celiac artery blood flow decreased by 40% and gastric artery blood flow by 60%. In addition, pronounced degranulation of mast cells preceding major tissue damage was observed. Based on the findings, a cascade of events was thought to be present resulting in the development of stress ulcer.

3. **Hepatic failure** (92, 93) :

   Experimental studies confirm the clinical results of a correlation between jaundice dependent hepatic failure and an incidence of stress ulcer. Stress ulcer appeared much more frequently in stress exposed rats with ligation of the choledochus and in animals with operative restitution of the bile flow after ligation of the choledochus than they appeared in controls.

4. **Energy metabolism** (94 – 96) :

   A progressive decrease of glucose levels and an increase of ATP and Atkinson's index were observed following 4 hours of restraint in albino rats. This finding referred to ATP not being used in HCl synthesis, and to activation of protein kinase in the parietal cells due to an increase of histamine in the gastric mucosa. The increase in free fatty acids and a marked decrease of cholesterol in glandular mucosa suggested an alteration in the membrane phospholipid composition as a resut of local phospholipases activated by histamine. A decrease in oxidative metabolism also explained the susceptibility to stress ulcer.

5. **Reflux of bile salts** (97 – 99) :

   Studies on animals implicating reflux of bile salts in formation of stress ulcer often are suspect because of the inordinately high intra gastric concentrations of bile salts used to induce experimental acute gastric mucosal damage. It has been demonstrated that bile salts aggravate stress ulcers during haemorrhagic shock.

6. **Thyrotropin releasing hormone** (100, 101) :

   When administered intracerebroventricularly thyrotropin releasing hormone (TRH) alone induced, in a dose-dependent fashion, the formation of gastric ulcers. TRH antiserum infused intracerebroventricularly inhibited ulcer formation induced by cold-restraint stress. TRH, thus, played a role in stress ulcer formation, possibly by a cholinergic mediated mechanism.

7. **Gastrin, endothelin, nitric oxide** (102) :

   In noise induced stress ulcer models of rats, levels of gastrin and endothelin were found higher and serum nitric oxide level was conspicuously lower than those in the control ground – suggesting that gastrin, endothelin and nitric oxide played an important role in stress ulcer.

8. **Diabetes** (103) :

   Low susceptibility of stress ulcer in diabetic rats : role of cholinergic gastric motility was studied. It is indicated that colinergic gastric motility was lowered in diabetic rats in a manner can decrease mucosal lesion induced by cold restraint stress.

9. **Gender difference** (104) :

   Studies indicated that female rats were more vulnerable to chronic stress than male rats.

10. **Age difference** (105, 106) :

    Severity of gastric corpus ulceration due to water immersion increased linearly with age. An insufficiency of gastric mucosal microvascular networks and the preserved gastric acid response in the vulnerable mucosa may be involved in the mechanism underlying aggravation of stress ulcer formation in aged rats. In another study, however, it was noted that older rats were not more susceptible to stress ulcer induced by restraint.

EXPERIMENTAL STRESS ULCER : ANTI – ULCER AGENTS

Numerous chemical agents, surgical techniques, natural products have been identified possessing anti-ulcer effect in experimental stress ulceration. These are :

CHEMICAL AGENTS

1. **Cimetidine** (107 – 109)

   Cimetidine was found efficacious in preventing stress ulcers after hepatectomy, and adrenaline as well as restraint induced gastric lesions.

2. **Neurotensin** (110)

   Neurotensin prevented development of gastric ulcer in rats induced by forced immersion stress.

3. **Vitamin – A** (111)

   Vitamine – A could prevent formation of stress ulcers in rat. Ulcers were induced by restraint stress.

4. **D – Penicillamine** (112)

   D – penicillamine showed a dose dependent antiulcerogenic effect in experimental gastric ulcer model induced by restraint stress.

5. **Female sex hormones** (113)

   Progesterone, estrogen and a combination of both were found to have significant anti-ulcer activity in stress ulcer models (Restraint, Shay rat etc.)

6. **Prostaglandin E2** (114 – 116)

   Prostaglandin E2 was found efficacious to prevent formation of stress ulcer in rats induced by haemorrhagic shock, water immersion, hepatectomy etc.

7. **Clonidine** (117)

   Clonidine showed an inhibitory effect on stress ulcer.

8. **AI-77-C2** (118)

   Chemically AI-77-C2 is 6- { 1s-(3s, 4 – Dihydro-8 hydroxy-1H-2-benzo-pyran-1-one-3-yl)-methylbutylamino}-4s, 5s-dihydroxy-6-oxo-3s-ammoniohexanoate (AI-77B)-gamma-lactone-N-ethyl derivative. It was examined in several experimental stress ulcer models (water immersion, Shay rat etc.) and showed marked inhibition of all the models employed.

9. **BTM – 1086** (119)

   BTM – 1086 is chemically (-)-cis-2, 3-dihydro-3-(4-methylpiperazinylmethyl)-2-phenyl-1, 5-benzothiazepin-4-(5H)-One-hydrochloride. It was found out that in the pylorus-ligated ulcer, restraint and water immersion stress ulcer BTM – 1086 prevented the development of ulcer at a dose of 0.1 mg/kg p.o.

10. **Lysolecithin** (120)

    Incidence of stress ulcer in rats induced by immobilization was significantly reduced by lysolecithin.

11. **Pivagabine** (121)

    Pivagabine determined a significant reduction in the number of animals with gastric lesions induced by immobilization in cold, in the linear extension of ulcers, percent protection and in the linear extension of haemorrhages. This

protective effect of pivagabine was likely to be mediated by the inhibition of corticotropin releasing factor released from hypothalamus, as also suggested by behavioral studies.

12. **Glucose** (122)

In order to prevent stress ulcers, experimental administration of intra gastric glucose has been tested. A 30% dextrose solution given intragastrically decreased both luminal acidity and mean ulcer index.

13. **AG 629** (123)

Chemically AG 629 is, 5-acetylspiro[benzofuran-2 (3H), 1'-cyclopropan]-3-one. It was found out that AG 629 has both prophylactic and curative effects on various ulcers. The anti-ulcer effect of this agent seems to be mediated primarily by increasing mucosal resistance and secondarily by an antisecretory activity.

14. **Succinic acid mono-3-guaiazulenamide** (124)

In various stress ulcer models like Shay's ulcer, restraint ulcer, water immersion in rats succiunic acid mono-3-guaiazulenamide (TPH – 3) showed a statistically significant inhibition.

15. **Metiamide** (125)

Metiamide was effective in preventing stress ulcer in dogs during haemorrhagic shock. The protective effect of metiamide is probably due to its inhibitory effect of hydrogen ion secretion.

SURGICAL TECHNIQUES

1. **Vagotomy** (126 – 132) :

Both truncal vagotomy alone and truncalk vagotomy + pyloroplasty were effective in maintaining the blood flow during stress and preventing the development of stress ulcer in rats induced by forced immersion.

2. **An operation model** (133) :

The duodenum is divided distally from the pylorus and a pyloro-jejunostomy performed combined with a Roux-en-Y anastomosis. Rats operated this way and submitted to restraint stress developed significantly less stress lesions than operated control under same conditions.

NATURAL PRODUCTS

1. **Chilli powder** (134)

It was found out that capsaicin and long-term chilli protected rats against haemorrhagic shock induced gastric mucosal injury and the protection may be

mediated by capsaicin –sensitive afferent neurons.

2. **Other natural products :**

The use of some plant and mineral drugs, including vegetable banana, narikelkhand (coconut) and tamrabhasma (copper preparation), has been advocated in Ayurveda for the therapy of a symptom complex akin to the modern version of peptic ulcer syndrome. Some of these have been subjected to experimental evaluation.

Vegetable banana (*Musa paradisiaca*) has been extensively investigated by Sanyal and his coworkers for nearly three decades. The antiulcerogenic activity of unripe green banana was first reported in 1961 (135) and later confirmed on a variety of experimental models (136 – 137). Though it was initially postulated that the anti-ulcer effect was due to the high serotonin content of green banana (135), it was later realized that the effective dose of banana did not contain sufficient serotonin to justify this postulate (138). Further studies not only confirmed the anti-ulcer activity of banana but also showed that this effect was not due inhibition of acid-pepsin output but was associated with augmentation of gastroduodenal mucosal protective factors (139 – 142). Some of the active principles likely to be responsible for the anti-ulcer action of banana have been identified (143 – 146).

Tamrabhasma inhibits acid-pepsin secretion and also exerts significant mucosal protection in experimental ulcer (147 – 149). Narikelkhand also exert significant anti-ulcer effect due to mucosal protection (150). Anti-ulcer activity of amlaki (*Emblica officinalis* Linn.) (151 -154), black tea extract (155), *Piper longum* Linn. (156), UI-409, Cauvery-100 and PK-2001 (multiconstituent herbal preparations) (157 – 159), *Symplocos racemosa* (160), *Synclisia scabrida* (161), Shankha Bhasma (162), *Rhamnus triquerta* (163) etc. were also studied and reported in the literature.

From pilot experiments we came to know (151 – 154) that Amlaki (*Emblica officinalis* Linn.) exerted anti-ulcer effect on experimental ulcers in rats induced by

1. swimming stress
2. cold and restraint stress.

Since two experimental models are not sufficient to evaluate the anti-ulcer property of a fruit, it was thought worthwhile to study the same in more experimental ulcer models. The present work, thus, was an attempt to evaluate the anti-ulcer activity of Amlaki (*Emblica officinalis* Linn.) and its effect on various biochemical parameters in stress induced experimental ulcer models. ##