D I S C U S S I O N

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Amlaki-tree is common in the mixed deciduous forests of India ascending to 4,500 ft on the hills. It is often cultivated in gardens and honeyards. Fruit amlaki (Emblica officinalis Linn.) in different Indian languages is called as under[139] :

In bengali and uriya : Amlaki

In hindi and punjabi : Amla

In malayalam and tamil : Nelli

In sanscrit and kanada : Amalaka

In telegu : Amalakamu

In santal : Meral

In assam : Amluki

Fruit 'Amlaki'(Emblica officinalis Linn.) has a sour, astringent taste riches in tanin and vitamin C. It has both diuretic and laxative property. When dried, the fruit is useful in haemorrhage, diarrhoea and dysentery. In combination with iron [redacted]

the fruit is used in jaundice, dyspepsia and cough. Sherbet of the fruit with lemon juice is taken to arrest acute bacillary dysentery. Exudation from incisions on the fruit is used as external application for the inflammation of the eye. As a good source of vitamin C the fruit is successfully used in the treatment of human scurvy. Considering all these medicinal properties, the fruit is being used as a common medicine in Indian households.

In addition to these medicinal properties of amlaki (Emblica officinalis Linn.) , it has been recently demonstrated by Verma et al.[123] that the fruit is beneficial for peptic ulcer patients. Radiologically proved peptic ulcer patients when took 'Amlaki Rasayana' | an indigenous medicine main ingredient of which is amlaki (Emblica officinalis Linn.) | for a period of three months got relief at least symptometically. In certain cases healing of ulcer was evident in X-ray plate. Experimental work demonstrating antiulcerogenic property of amlaki (Emblica officinalis Linn.), however, was not observed in the available literature.

It was thus thought worthwhile to study the antiulcerogenic effect of amlaki (Emblica officinalis Linn.) in experimental animals. In a pilot experiment we studied this on aspirin induced peptic ulcers in albino rats. We observed a significant reduction in the incidence of gastric ulcers when the animals were treated with amlaki (Emblica officinalis Linn.) . This pilot study tempted us to undertake this project in detail where we studied the role of amlaki (Emblica officinalis Linn.) on various experimental ulcer models as induced by :

1. Aspirin

2. Salicylic acid
3. Paracetamol
4. Indomethacin
5. Prednisolone
6. Hydrocortisone
7. Phenyl butazone
8. Histamine
9. Restraint stress
10. Shay technique

ASPIRIN INDUCED ULCER : ROLE OF AMLAKI (Emblica officinalis Linn.)

It appears from the result (Table 1) that in albino rats aspirin in the dose of 100 mg/kg induced ulcers in the glandular portion of stomach and the stomach was invariably accompanied by frank intragastric haemorrhage - an earlier observation made by Brodie and Chase[34] , Djahanguiri[35] using different doses of aspirin.Our study also confirmed that amlaki (Emblica officinalis Linn.) diet significantly reduced the incidence of aspirin induced gastric ulcers.

While studing the effect of aspirin on the rate of gastric secretion, gastric acidity and peptic activity Paul et al.[37] observed that aspirin causes a decrease in volume and acidity of gastric secretion while Lynch et al.[36] observed an increase, no change or a decrease in gastric secretion and gastric acidity by aspirin depending on the dose and species studied. We, however, observed no significant change in volume, acidity and peptic activity of gastric secretion by the dose of aspirin (100 mg/kg, intraperitonially once in a day for consecutive three days) we used in albino rats. Effect of

amleki (Emblica officinalis Linn.) diet on the said parameters was also not significant although a decreasing trend in the volume, acidity and peptic activity of the gastric secretion in comparison to that of aspirin treated group was observed.

That aspirin reduces the secretion of gastric mucus was an earlier observation made by Menguy and his group of workers[41]. We also found that aspirin reduced the amount of dissolved gastric mucin as well as gastric mucosal mucose. The constituent carbohydrate components of dissolved gastric mucin and mucosal mucus viz. total hexose, hexosamine, methyl pentose, sialic acid etc. showed a significant ($p < .01$ to $p < .001$) decrease in levels. The amount of dissolved mucin and mucosal mucus as represented by total carbohydrate[41] also showed significant decrease ($p < .001$) by aspirin. Amleki (Emblica officinalis Linn.) treatment, on the other hand, increased the levels of all these constituent carbohydrate components and thus the total carbohydrate of dissolved gastric mucin and gastric mucosal mucus.

SALICYLIC ACID INDUCED ULCER : ROLE OF AMLAKI (Emblica officinalis Linn.)

Brodie and Chase[34], while working on the ulcerogenic role of salicylic acid in rat, observed a dose dependent response of salicylic acid in the production of gastric ulcer. We in our study noticed (Table 2) that salicylic acid in the dose 100 mg/kg when given to rats intraperitonially once in a day for consecutive three days produced profuse ulcers in the glandular part of stomach. Ulcers were associated with frank intragastric haemorrhage. Dodd et al.[48] also found the intragastric haemorrhage associated with ulcers induced by salicylic acid.

Reports on the effect of salicylic acid on gastric volume, acidity and peptic activity are conflicting. Lish et al.[38] reported, salicylic acid causes a decrease in volume and acidity of the gastric secretion while Winkelman and Summerskill[39] found that salicylic acid has no effect on rate of gastric secretion and gastric acidity. We in this study also observed that salicylic acid had no significant effect on rate of gastric secretion, gastric acidity and peptic activity. Treatment with amlaki (Emblica officinalis Linn.) had also no effect on the said parameters.(Table 12)

With the aforesaid dose of salicylic acid we observed a significant decrease in the levels of gastric dissolved mucin and gastric mucosal mucus when measured the constituent carbohydrate components like total hexose, hexosamine, methyl pentose and sialic acid (Table :22, Table :32). Kent and Allen[42] also observed a reduction in the rate of synthesis and secretion of mucus by salicylic acid. They thus said, 'It is the loss of mucus barrier that permits the toxic effects of salicylic acid to produce ulcers in stomach'. These decreased levels of gastric dissolved mucin and gastric mucosal mucus during salicylic acid induced ulcers were increased significantly (Table:22, Table:32) when the rats were treated with amlaki (Emblica officinalis Linn.).

PARACETAMOL INDUCED ULCERS : ROLE OF AMLAKI (Emblica officinali Linn.)

Studies on paracetamol for its ulcerogenic potency are few in the available literature. Proudfoot and Wright[51] when studied the cases of acute paracetamol poisoning noticed

gastrointestinal haemorrhage. We found the presence of massive ulcers at the glandular part of the stomach of rats when the animals were treated by paracetamol (100 mg/kg) intraperitonially once in a day for consecutive three days. Ulcers were associated with frank intragastric haemorrhage. When amlaki (Emblica officinalis Linn.) was given to the rats orally in the dose of 1 g/kg once in a day for consecutive three days in addition to the scheduled doses of paracetamol, we observed a significant decrease in the incidence of ulcers and its severity (Table : 3). This antiulcerogenic property was not related to acid-peptic digestion as we did not observe any significant changes in gastric volume, acidity and peptic activity after amlaki (Emblica officinalis Linn.) treatment |Table : 13 |. Rather, this antiulcerogenic property of amlaki (Emblica officinalis Linn.) was found related to mucus secretion as levels of gastric dissolved mucin and gastric mucosal mucus increased significantly when the rats received amlaki (Emblica officinalis Linn.) diet. Considering the mucus 'barrier' hypothesis of Menguy[41] it can thus be stated that amlaki (Emblica officinalis Linn.) increases the level of mucus which resists the toxic effects of paracetamol to induce ulcers in the stomach.

INDOMETHACIN INDUCED ULCER : EFFECT OF AMLAKI (Emblica officinali Linn.)

In animal experiments, Djahanguiri[74] and Lee et [7] showed that indomethacin caused gastric, duodenal, antral and jejunal ulcerations, haemorrhage and perforation. On studing this ulcerogenic property, Nicolff[76] showed that ulcerogenic effect of indomethacin did not seem to be related to acid hypersecretion.

On the other hand, Menguy[41] observed that ulcerogenic effect of indomethacin was related to mucus secretion as it lowered the rate of mucus secretion and diminished the amount of carbohydrate incorporation into the mucosubstance, which helped the drug to exert its toxic effect to damage the mucosa.

In our experiment we observed that indomethacin in the dose of 25 mg/kg when given to rats intraperitonially once in a day for consecutive three days formed several ulcers at the glandular region of stomach (Table : 4). This ulcer formation was not related with acid-peptic digestion since in the aforesaid dose indomethacin had no effect on rate of gastric secretion, gastric acidity and peptic activity. (Table : 18)

On the other hand, we observed, indomethacin had a relation with gastric mucus secretion since it decreased the levels of total hexose, hexosamine, methyl pentose and sialic acid (the constituent carbohydrate components of mucin) and thus the levels of dissolved gastric mucin and gastric mucosal mucus (Table:24 & 34). Our study thus confirmed the earlier observation of Menguy[41].

When amlaki (Emblica officinalis Linn.) was given to rats orally in the dose of 1 g/kg once in a day for consecutive three days, we found a significant reduction in the incidence of ulceration by indomethacin (Table : 4). We observed that there was no change in the acid-peptic value by amlaki (Emblica officinalis Linn.) but significant increase was found in the levels of dissolved gastric mucin and gastric mucosal mucose. Thus, antiulcerogenic effec of amlaki (Emblica officinalis Linn.) in indomethacin induced gastric ulcers can be explained in terms of mucus secretion (Defensive factor

PREDNISOLONE INDUCED ULCER : ROLE OF AMLAKI (Emblica officinalis Linn.)

Several reports[54-57] are available in literature showing the ulcerogenic potency of prednisolone in experimental animals. In rats, it is stated, prednisolone induced profuse gastric ulcers. We also observed the presence of ulcers at glandular part of stomach of rats when the animals received prednisolone (30 mg/kg) intraperitonially once in a day for consecutive three days(Table:5). 4 rats out of 33, died during experiment, showed the extension and perforation of ulcers . This finding was in agreement with the earlier reported observation of Kaham et al.[61]

When studied the effect of prednisolone on acid-peptic as well as mucus factor, we found that this drug had no effect on rate of gastric secretion, gastric acidity and peptic activity. But the mucus factor represented by the levels of dissolved gastric mucin and gastric mucosal mucosa was found significantly decreased by prednisolne. Earlier, this was observed by Seyle[64] who stressed on the fact that diminution of tissue resistance is related to the anti-inflammatory action of corticosteroids in the genesis of ulceration.

We noticed the antiulcerogenic effect of amlaki (Emblica officinalis Linn.) in this experimental ulcer model as amlaki-diet in the dose of 1 g/kg, orally, once in a day for consecutive three days significantly reduced the incidence of prednisolone induced ulcer in rats. (Table :5). Sanyal et al. observed the same effect for vegetable banana[28]. This antiulcerogenic

property of amlaki (Emblica officinalis Linn.) had a relation with mucus factor and not with acid-peptic factor since we found that this indigenous fruit increased the mucus secretion in ulcerated stomach (Table : 25 and 35) but had no effect on gastric acidity and peptic activity (Table : 15).

HYDROCORTISONE INDUCED ULCER : ROLE OF AMLAKI (Emblica officinali Linn.)

Table 06, showing the effect of amlaki (Emblica officinalis Linn.) on hydrocortisone induced ulcers in albino rats reveals that hydrocortisone acetate in the dose of 50 mg/kg/day when given to rats intraperitonially once in a day for consecutive three days produced massive ulcers of different size at the glandular region of stomach. Ulcerogenic potency of hydrocortisone in man as well as in experimental animals has been stated earlier elsewhere[58-60]. We observed that this ulcerogenic dose of hydrocortisone had no effect on the rate of gastric secretion, gastric acidity and peptic activity (Table : 16) but decreased the levels of dissolved gastric mucin and gastric mucosal mucus (Table : 26, 36). All the carbohydrate components like total hexose, hexosamine, methyl pentose and sialic acid were found in less amount in gastric juice and gastric mucosa after the administration of hydrocortisone. Importance of mucus secretion during hydrocortisone induced ulcers was noted by Seyle[64].

Antiulcerogenic effect of amlaki (Emblica officinalis Linn.) on hydrocortisone induced ulcers was evident from our study. We observed a significant reduction in the incidence of gastric ulcers in albino rats as induced by hydrocortisone, when amlaki diet was given to rats in a specific dose (1 g/kg, once in a day for consecutive three days orally). (Table : 6). This

antiulcerogenic effect of amlaki (Emblica officinalis Linn.) , we observed, had a relation with mucus secretion since the levels of dissolved gastric mucin and gastric mucosal mucosa in ulcerated stomach were increased significantly by amlaki (Emblica officinalis Linn.) (Teble : 26,36).

PHENYLBUTAZONE INDUCED ULCER : ROLE OF AMLAKI (Emblica officinal Linn.)

Phenylbutazone in the dose of 100 mg/kg when given to guinea-pigs orally once in a day for consecutive three days produced profuse ulcers at the glandular part of stomach (Figure:1). Ulcers were associated with pathologies like frank intragastric haemorrhage, adhesion and acute dilatation of the blood vessels, (Teble : 7). Animals, died during experiment, showed the presence of big penetrating ulcers as well as perforation of ulcer. All these observations are in confirmatory with the earlier reported findings.[82-84]

On studing the cause of phenylbutazone induced ulcers, Schimid et al.[85] reported that phenyl butazone stimulated both gastric acid secretion and peptic activity of the gastric juice, while Bonfils[86] did not observe any significent change in gastric acid secretion after oral or parenteral administration of the drug. We also did not observe any significant effect of phenyl butazone on rate of gastric secretion, gastric acidity and peptic activity (Teble :17), rather this drug decreased the levels of all the constituent carbohydrates (Total hexose, hexosamine, methyl pentose and sialic acid) of dissolved gastric mucin and gastric

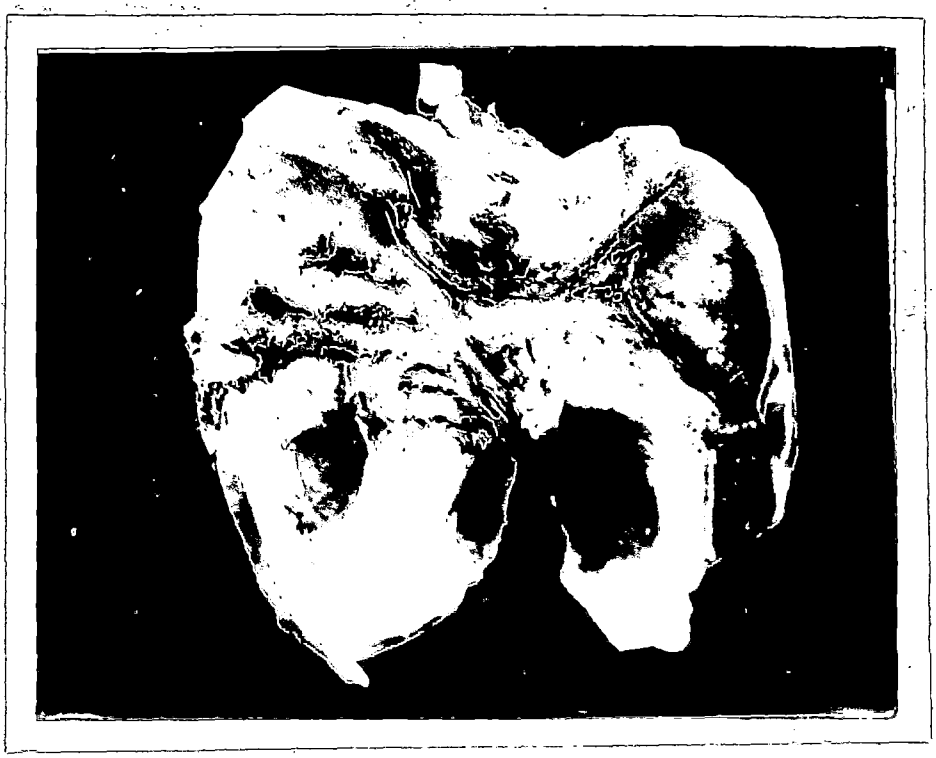

FIGURE-1 : Showing phenylbutazone induced ulcers in the stomach of guinea-pig.

FIGURE-2 : Showing the effect of amlaki (*Emblica officinalis* Linn.) on phenylbutazone induced ulcers in the stomach of guinea-pig.

mucosal mucus (Table : 27 and 37). Zaidi et al.[91] also observed a steady decreese of mucin in the gastric juice after 30 days of phenylbutazone treatment in guineapigs.

Antiulcerogenic effect of amlaki (Emblica officinalis Linn.) on phenylbutazone induced ulcer in guinea-pigs can be noted from Figure : 2. It was found out that amlaki-diet (1 g/kg, orally once in a day for consecutive three days) significan-tly reduced the incidence of phenylbutazone induced ulceration and its severity (Table : 7). It was also observed that this antiulcero-genic property had no relation with gastric acidity and peptic activity (Table : 17) but had a relation with gastric mucus (Table : 27, 37). It was found out that amlaki (Emblica officinalis Linn.) in the aforesaid dose had no effect on gastric secretion and acidity but increased significantly the levels of dissolved gastric mucin as well as gastric mucosal mucus during ulceration.

HISTAMINE INDUCED ULCERS : EFFECT OF AMLAKI (Emblica officinalis Linn.)

There are reports that histamine in specific dose when administered through specific route caused gastric and duodenal ulcers in man and animals[63,122]. Ulcerogenic potency of the drug was related to gastric hypersecretion. In our experiment when histamine (33 µg/mouse) was given to the mice intraperitonially once in a day for consecutive three days, severe ulcers were noted at the glandular part of the stomach . Ulcers were associated with haemorrhage and other pathologies like adhesion and acute dilatation of the blood vessels (Table : 8). We, however, did not observe any

change in the rate of gastric secretion, gastric acidity and peptic activity by the aforesaid dose of histamine indicating thereby the probable dose dependent response on these parameters by the drug. On the other hand, we found a significant decrease in the levels of dissolved gastric mucin and gastric mucosal mucus in ulcerated stomach caused by histamine. (Table : 18, 28, 38).

Effect of banana-diet on histamine induced gastric ulcers in mice was studied by Elliott and Heward[122]. These workers noted that pretreatment of mice with banana diet caused a significant reduction in the incidence of histamine induced ulcers. We also noted the same thing. We gave amleki (Emblica officinalis Linn.) diet (1 g/kg, orally once in a day for consecutive three days alongwith histamine) to the mice and observed a significant reduction (70%) in the incidence of ulceration induced by histamine. We found that this antiulcerogenic effect of amleki (Emblica officinalis Linn.) was not related with acid-peptic factor since amleki-diet could not exert any significant change in the rate of gastric secretion, gastri acidity and peptic activity during ulceration (Table : 18). Rather, amleki (Emblica officinalis Linn.) exerted a significant increase in the levels of hexosamine, methyl pentose and sialic acid of dissloved gastric mucin and gastric mucosal mucus. This increased mucus levels during ulceration might give a protective barrier to the stomach wall which resisted the toxic effect of histamine for forming ulcer as reported elsewhere[41].

RESTRAINT ULCER : ROLE OF AMLAKI (Emblica officinalis Linn.)

Table : 9 clearly shows the effect of restreint

stress and the effect of amlaki (Emblica officinalis Linn.) towards the production of gastric ulcer. We found that restraint stress induced gastric ulcers (at the glandular part of stomach) in rats. Incidence of ulceration was 100%. Most of the ulcers were associated with intragastric haemorrhage, perforation, adhesion and acute dilatation of the blood vessels. Earlier Brodie and Hanson as well as Rossi et al. developed restraint ulcers in experimental animals[24,95]. On studing the mechanism of restraint ulcers, Menguy[27] did not found any change in the acid-peptic output by restraint stress. Thus, he concluded that acid-peptic digestion was not the basic mechanism in the production of restraint ulcers. Brodie et al.[24,98], on the other hand, found an increase in the concentration of gastric acid during restraint ulcers. In our study, we however did not notice any change in the rate of gastric secretion, gastric acidity and peptic activity during restraint ulceration (Table : 19). Working on gastric mucosa in restraint ulcer, Hase and Moss[103] noted the microvascular changes in gastric mucosa in the development of restraint ulcer in rats. We observed that restraint stress decreased the levels of dissolved gastric mucin and gastric mucosal mucus which helped to develop the ulcers in the stomach (Table : 29, 39).

Effect of indigenous fruit on restraint ulcers was ,for the first time, studied by Sanyal et al.[28] They worked on unripe vegetable banana and found that banana could prevent the incidence of restraint ulcers. In the present study we, when given amlaki (Emblica officinalis Linn.) to the rats orally in the dose of 1 g/kg once in a day for consecutive three days prior to give the restraint stress, observed that amlaki (Emblica officinalis Linn.)

reduced the incidence and severity of restraint ulcers by about 80%. This antiulcerogenic effect was not found related with gastric acidity or peptic activity since amlaki (Emblica officinalis Linn.) could not exert any significant effect on rate of gastric secretion, gastric acidity and peptic activity. On the other hand, we observed * amlaki-diet could increase the levels of constituent carbohydrate components viz. total hexose, hexosamine, methyl pentose, sialic acid etc. of dissolved gastric mucin and gastric mucosal mucus during ulceration ($p < .025$ to $p < .001$). This increased level of gastric mucosubstances (Table : 29, 39) might give a protective layer to the stomach-wall which reduced the incidence of restraint ulcers.

SHAY ULCERS : EFFECT OF AMLAKI (Emblica officinalis Linn.)

As early as 1945, Shay and his group of workers developed a methodology by which ulcers can be induced in stomach of experimental animals.[128] They noted the presence of ulcers in the stomach of rat when the animal was kept in a cage for 16 hours under pylorous ligation. We adopted the same methodology and found severe ulcers in the glandular part of stomach of rats. Some ulcers were large, penetrating associated with haemorrhage. Shay et al. did not study the reason behind this ulceration. We observed that Shay technique did not exert any effect of gastric acidity and peptic activity (Table :20), but decreases the levels of gastric dissolved mucin and gastric mucosal mucose (Table 30, 40).

When studing the role of amlaki (Emblica officinalis Linn.) on Shay ulcers, we found that amlaki-diet could

prevent the incidence of Shay ulcers by about 60%. We gave amlaki (Emblica officinalis Linn.) to the rats orally in the dose of 1 g/kg once in a day for consecutive three days before giving Shay stress. (Table :10)

It was found out that amlaki (Emblica officinalis Linn.) had no effect on the rate of gastric secretion, gastric acidity and peptic activity during Shay ulceration (Table :20)but could increase the levels of total hexose, hexosamine, methyl pentose and sialic acid (Table :30, 40) - the constituent carbohydrates of gastric mucin as well as gastric mucosal mucus. Antiulcerogenic effect of amlaki (Emblica officinalis Linn.) in Shay ulcer can thus be explained in terms of defensive mucosubstances.

Concept of antiulcerogenic property of indigenous plants and fruits was not new. Sanyal and his group of workers observed the antiulcerogenic effect of vegetable banana in restraint ulcers in rat and phenylbutazone induced peptic ulcers in guinea-pig.[28,122] Sinha et al.[140] advocated the use of banana (Musa sapientum), tomato (Lycopersicum esculentum), brinjal (Solenum melongena), etc. in peptic ulcer as these vegetables could decrease the rate of gastric secretion.

Present study also confirms the antiulcerogenic property of amlaki (Emblica officinalis Linn.) in experimental ulcers as we observed :

* Amlaki (Emblica officinalis Linn.) could decrease the incidence and severity of gastric ulcers in ten different experimental ulcer models.

** Antiulcerogenic property of amlaki (Emblica officinalis Linn.) could not be explained by offensive (acid-peptic) factors since amlaki-diet had no effect on rate of gastric secretion, gastric acidity and peptic activity during ulceration.

*** Antiulcerogenic property of amlaki (Emblica officinalis Linn.) could be explained by defen--sive (mucus) factor since amlaki-diet increased the levels of gastric dissolved mucin and gastric mucosal mucus during ulceration. This increased level of gastric mucosubstances might render a 'protective barrier' on the stomach-wall which could resist the toxic effect of ulcerogenic drugs / methods for forming ulcer.