

CHAPTER

I

INTRODUCTION

Ayurveda is as old as mankind. The Indian system of medicine has been regarded by many scientists as a rich mine of knowledge. Much wisdom may well be hidden in this system of medicine, but it needs to be unveiled. Attempt must be made to confirm the truth of the statements made in 'Old Therapeutics' with scientific experimental models. During last decade, synthetic chemistry has made a remarkable

progress and new drugs have revolutionized the treatment of many disease. Medical care has graduated from empiricism to precision. The scientific study with indigenous drugs reminds one of the Editorial comments made in 'The Practitioner' (Dec. 1960), under the heading of 'Indigenous Herbs'. It says, 'The wise and experienced clinician never spurns an old wife's tale, until he has good evidence for doing so'. Although the modern western system itself is a product of various older systems of medicine, it has far outstripped its antecedents. In our country unfortunately, the practice of the indigenous system of medicine has remained static. However, there has been a tremendous upsurge of interest and research in the field of indigenous drugs in India.

TAMRA BHASMA (TABH) has been advocated for the treatment of acid pepsin disease termed as 'amlapitta', bronchial asthma, leucoderma, inflammatory diseases etc. in the Indian Ayurvedic Medicine.

ताम्रं सरं लघुस्वादु शीतं पित्तकफापहम् ।
 रोपणं पाण्डु कुष्ठार्शः श्वयथुश्वासकासजित् ॥
 पाण्डुराशौज्वरकुष्ठकासश्वासक्षयान्पीनसमम्लपित्तम् ।
 शोथं कृमिं शूलमपाकरोति प्राहुः परे वृंहणमल्पमेतत् ॥

While describing the therapeutic value, Madan and Bhavmishra advise to use copper for healing process and also in anaemia, skin diseases, piles, oedema, bronchitis and cough (Madanpal Nighantu, 1918; Bhavprakash Nighantu, 1931).

Peptic ulcer is an old and very common disease. Duodenal ulcer was a rare disease before 1900. By 1914 it had become common in Europe and north America. The sharp rise in duodenal ulcer was accompanied by modest increase in gastric ulcer. From 1914 to about 1955 they remained at a relatively constant level and then began to decrease. There is much variation in frequency of occurrence from time to time and from place to place. In almost all parts of the world morbidity from duodenal ulcer is reported as more common than from gastric ulcer, but deaths from gastric ulcer equal or exceed those from duodenal ulcer.

The pain which the ulcer causes, seriously impairs the working capacity of the important wealth making group of the population. It may also arise on prolonged use of steroidal and non steroidal anti-inflammatory drugs.

For 150 years it has been suggested that occurrence of gastric and duodenal ulcers are related to the production of excess acid. However, recent studies have shown that other factors such as antibody reaction, physiological make-up of patients and a role of endogenous histamine release, are known to be important in the genesis of ulcer formation (Piper and Heap, 1972). We don't know much that is certain about the aetiology of the ulcer. There is an interplay between environmental factors and individual susceptibility in ulcer disease. In general terms an ulcer is considered to be the outcome of the conflict between attack and defence, sometimes, violence of the former and sometimes the poverty of the latter may be the paramount factor in pathogenesis.

Recent advances in our understanding of this subject include particularly comments on the protective role of the mucus and the way this protection may be impaired or lost and also on the importance of the cellular processes of repair and regeneration and the factors which influence them. Mucosal epithelium remains intact so long as there is an equilibrium between the cell production and the rate of cell loss (Croft, 1977). Cell production is generally decreased due to stress and corticosteroids whereas irritants like aspirin, alcohol and phenylbutazone increase the cell loss. Croft et al. (1966) have shown that atrophic mucosa has an abnormal epithelial cell turnover. Once the mucosal integrity is lost, lesions such as gastric erosion may form. Satisfactory methods to promote the healing of the mucosal lesion and to increase the mucosal resistance to destruction have not yet become available.

The two most notable advances in the management of the ulcerative disease of the upper alimentary tract made in the last 30 years have been the introduction of fibre optic endoscope and synthesis of carbenoxolone sodium, the first therapeutic agent which has convincingly been shown to speed up greatly the rate of healing of gastric ulcers. However as with other important therapeutic drugs, carbenoxolone can cause a reversible hypertension which may or may not be associated with water retention and with hypokalemia. This is particularly important in older patients where increase in blood volume could precipitate cardiac embarrassment.

Another class of drugs, H₂ receptor blockers (Editorial, Medical journal of Australia, 1974) by suppressing the gastric secretion, represents the key for solving many problems of peptic ulceration. Although the mechanism of these drugs is not clear, it seems certain that this group of drugs exerts a direct action on acid and pepsin secreting cell (Wan et al., 1974). Antacids have been used in the treatment of peptic ulcer, mainly to relieve the symptoms associated with ulceration, particularly pain (Piper, 1973). Only carbenoxolone helps in healing of the ulcer. Recently omeprazole has been reported to be more powerful than cimetidine in inhibiting basal and pentagastrin stimulated acid output (Howden et al., 1984). Tripotassium dicitratobismuthate have been used clinically in duodenal ulcers, refractory to cimetidine. Anticholinergics are also used in combination with these potent drugs for the clinical management of ulceration.

Duodenal ulcer is a chronic relapsing disease. Although some ulcers are more resistant to treatment than others, the main problem today is not how to heal a duodenal ulcer, but how to keep it healed. Available evidences suggest that benefit of the maintenance treatment lasts only as long as the treatment itself.

Many traditional preparations including TABH (Sanyal et al., 1982; Pandey et al., 1983), vegetable banana (Sanyal et al., 1961, 1964, 1965; Elliot and Heward, 1976) and Narikelkhand (Pramanik and Debnath., 1980) have been reported to possess anti-ulcerogenic action in various experimental models in rats and guineapigs. All these traditional preparations have been shown to strengthen the mucosal barrier. Vegetable banana is reported to contain significant quantity of copper (Aykroyd et al., 1963). Nimbidin from MELIA AZADIRACHTA (Pillai et al., 1978), and Ayurvedic preparation Taramandur (Pillai et al., 1979), extract of OCIMUM SANCTUM (Bhargav and Singh, 1981), triterpenoids (ulsolic acid and lupeol) from a number of Indian plants belonging to Sapotaccae/Sapindaceae family (Gupta et al., 1981), alcoholic extract of TECTONA GRANDIS (Pandey et al., 1982) and WITHANIA SOMNIFERA (Singh et al., 1982) have been reported to cause significant inhibition of restraint and other experimental ulcer in rats and guineapigs.

Ulcerogenicity of the non-steroidal drugs is reduced when administered in the form of copper complex (Boyle et al., 1976; Rainsford and Whitehouse, 1976) suggesting that the copper can influence the incidence of ulceration.

Sanyal et al, (1982) have reported that TABH significantly reduced the volume of gastric juice, total acidity and total pepsin and significantly increased the

carbohydrate to protein ratio. Recently Pandey et al (1983) have shown that TABH preparation has significantly higher antiulcer activity (3 to 5 days) than either copper compound or the mixture of its known ingredients. It causes significant increase in mucosal thickness and carbohydrate to protein ratio. These authors also report that TABH has antiulcer effect against aspirin-induced ulcer without affecting its inflammatory activity. Nowhere the literature shows comparative study of any traditional remedy with the modern drugs used clinically in the management of peptic ulcer.

The availability of a wide range of experimental ulcer models are extremely useful, although extrapolation from the experimental model to human ulceration has obvious limitations. The present study was undertaken to confirm the antiulcerogenic action of TABH against gastric and duodenal ulcer in albino rats.

Gastric ulcers can be induced by widely used steroidal and non-steroidal drugs like dexamethasone and indomethacin respectively. Steroids have been reported to cause ulcer on prolonged treatment. It is well known that indomethacin causes gastrointestinal damage in human (Lorgreen and Allander, 1964; Katz et al., 1965; Beirne et al., 1974).

Cysteamine hydrochloride (β -mercaptoethylamine) was selected for inducing the duodenal ulcer in rats because the pathophysiological changes that occur in cysteamine-induced chronic ulcers are closely similar to human chronic ulceration (Szabo, 1978).

The major interest of the present study was to compare the effectiveness of TABH with clinically used drugs like cimetidine, carbenoxolone and combination thereof with TABH in the management of duodenal and gastric ulcers. After confirming the antiulcerogenic action of this traditional preparation, experiments were also designed to investigate its mode of action, specifically with reference to cell turnover. Chronic toxicity study was carried out for any deleterious effect of TABH on prolonged use. Antiulcerogenic action was confirmed in the study by change in ulcer index, as well as histopathological observation after hemotoxyline and Periodic acid Schiff reagent (PAS) stains.

Trace chemical analysis of the preparation used in the present study was also carried out by spectrophotometric method.