Protective dietary factors in experimental ulceration—study of some Nigerian cereals and tubers

R. A. ELEGBE

M.B., B.S., Cert. Immunology

S. O. A. BAMGBOSE

B.Sc., Ph.D.

Departments of Physiology and Pharmacology, University of Ibadan, Ibadan, Nigeria

Summary

Rats fed on a supplement of millet, Guinea-corn, rice or maize given in addition to laboratory stock diet showed a high degree of protection against experimental ulceration following indomethacin administration. A higher degree of protection was shown when the rats were fed with the mixture of the four cereals and laboratory stock diet. The tubers did not offer protection, while a mixture of beans and millet, Guinea-corn, unpolished rice, and maize offered no protection. The significance of such findings with regard to the geographical distribution of duodenal ulcer in Nigeria is discussed.

Introduction

The work of Cheney (1940, 1948, 1949, 1950a, b, c), Singh, Zaidi and Bajpal (1962), Adami (1955, 1964), Wissmer and Adami (1965), Tovey (1972, 1974a, 1975), Tovey, Jayaraj and Clark (1975), and Tovey and Tunstall (1975) on experimental ulcers in animals suggested that a factor in the aetiology of peptic ulcer might be the absence or presence of protective substances, either as a result of refining the staple carbohydrate diet or as a result of an associated low intake of supplementary foods containing such factors. The protective factor against experimental ulceration was shown to be thermolabile by Cheney (1950a, b, c) and Tovey *et al.* (1975). It has been shown that any possible protective action of wheat and rice bran or certain unrefined grains against peptic ulceration is unlikely to be due to any acid or pepsin-lowering effect (Tovey, 1974b). Although these substances contain a significant amount of buffer, they also act as antral stimulants resulting in increased acid output and have no inhibitory effect on pepsin activity (Tovey, 1974b). It was further suggested that any protective compound might be similar to carbenoxolone or gefarnate, and that such a protective factor may or may not be present in the supplementary foods which are consumed with the staple carbohydrate diet (Tovey *et al.*, 1975). The latter possibility, Tovey stated (1974a, 1975), would provide an explanation for those rural areas on the west coast of Africa (apart

from Southern Nigeria), in Ethiopia, in Burundi and Rwanda, and in Northern Tanzania around Mount Kilimanjaro where there is a high incidence of duodenal ulcer not apparently associated with a refined carbohydrate diet, and also such areas as those of Zaire where cassava is the main carbohydrate food; but duodenal ulcer is rare.

Nigeria is divided geographically into three parts by the rivers Niger and Benue. The part of the Niger which runs in an easterly direction divides the country roughly into northern and southern parts. Proceeding northward from the Guinea coast, mangrove and rain forest is succeeded by deciduous forest (Guinea savannah) and lastly a semi-arid Sudan savannah which merges into the Saharan desert. Duodenal ulcer is said to be common in most of the coastal, rain forest areas and rare in the northern savannah region. Konstam (1966) stated that the staple diet in the south of Nigeria is cassava, yam and maize, whereas in the northern parts, millet and ground-nut are eaten, and milk can be obtained so that more protein is available than in the south. According to Omololu (1974), however, it is impossible to talk about the Nigerian diet or a diet of the Nigerians. This is because the foods eaten by the average Nigerian are still dictated by his cultural upbringing and origin. While the Igun Yorubas take a lot of beans, the northerners (Zaria) take very little and the mid-westerners a little more. The Ibos and Oba Yorubas take half as much as the Igun Yorubas. Vegetable intake is highest amongst the Ibos, while the Oba group of Yorubas take very little if any at all. The Ibos take a lot of roots and tubers, the Igun Yorubas take less while the northerners take very little if any at all. The northerners, on the other hand, take a lot of cereals (millet, Guinea-corn, rice), the Igun Yorubas take less and the Ibos take very little (Table 1).

It was therefore interesting, in the light of the foregoing suggestions, to investigate some of the local food substances to find out if they offer any protective effects against experimentally produced ulceration. In this study, results on the common Nigerian cereals and tubers are reported.

TABLE 1.* Average daily intake of some foods from the dietary of Nigerians

	(g/head/day)				
	Yoruba Igun	Yoruba Oba	North Zaria	Midwest Eguare	Ibo Etiti
Cereals	362	90	960	76	43
Maize	259	45	—	63	8
Rice	95	42	19	13	32
Wheat	2	3	1	—	3
Sorghum and millet	—	—	940	—	—
Roots and tubers	413	132	1	272	695
Yam	146	16	—	172	138
Cassava	145	116	1	90	378
Cocoyam	52	11	—	—	115
Plantain	70	8	—	10	39
Breadfruit	—	—	—	—	25
Fish	9	12	—	12	28
Dry fish	4	7	—	7	14
Fresh fish	5	5	—	2	2
Stockfish	—	—	—	—	9
Shrimps	—	—	—	—	3
Vegetables	13	1	5	6	273
Palm oil	21	24	15	28	45
Pal wine and local beer	48	—	—	2	243
Beans	100	42	4	19	38

* Taken from Omololu (1974).

TABLE 2.

(a) Composition of the reference diet (on dry matter basis)

Components	Percentages
Corn starch	53.2
Egg	38.3
Ground-nut oil	5.0
Rice bran	1.0
Mineral/vitamin mixture*	2.5

(b) * Composition of the mineral/vitamin mixture from I.C.I., Lagos

Component	Amount	Component	Amount (U.S.P. units)
Calcium	31.7%	Vitamin A	10×10^6
Phosphorus	2.45%	Vitamin D ₃	1.4×10^6
Iron	0.51%	Vitamin E	5000
Sodium chloride	14.8%	Vitamin E	2000
Magnesium oxide	1.25 p.p.m.	Riboflavin	4500
Potassium iodide	100 p.p.m.	Pantothenic acid	1000
Cobalt	25 p.p.m.	Vitamin B ₁₂	8
Copper	500 p.p.m.		
Manganese	600 p.p.m.	Anti-oxidant	125,000

Methods

Male and female albino rats of the Wistar strain weighing between 130 and 160 g were fed the standard cube diet to determine the daily intake. In subsequent experiments, so as not to make conditions unphysiological, the rats were given a daily feed comprising 50% of the required intake of cubes (standard diet, Table 2) and 50% of the pure

food substance the effect of which was being investigated. In some experiments, there was a proportional addition of the standard stock diet to the various food items mixed together. During a period of 1 week before the start of the experiment the rats were put into their cages, and fed freely on the standard diet. After this 1 week of acclimatization, the animals were then given the experimental diet.

The food and standard cubes were ground into fine powder and mixed thoroughly so that there would be no preference for any component of the mixture. A control group fed on ground standard diet was also included. Throughout these experiments, the feed was given twice daily, and water *ad libitum*. The weights of the animals were checked weekly. After the second week on the prescribed diet, the twenty-four experimental rats were starved for 16 hr before sixteen of them were given i.p. 40 mg/kg body-weight of indomethacin dissolved in *N*-methyl acetamide; the remaining eight served as controls—four had 0.4 ml of 0.15 M saline i.p., and four had 0.4 ml of *N*-methyl acetamide 80% v/v. Four hours later, all the animals were killed with a blow on the head, their stomachs were removed and opened along the lesser curvature. Both macroscopic and microscopic examinations were performed on the stomach to assess the degree of ulceration using the scoring method of Alphin and Ward (1967).

Results

The results obtained include:—

(i) The effect of the different diets on weight-gain in two weeks. Figures 1–3 show the percentage weight-gain in 2 weeks of the rats in each dietary group.

(ii) The effect of the diet on indomethacin-induced ulceration. Figures 4–6 show the 'mean ulcer score', calculated by dividing the total score from the scoring system by the number of rats in each dietary group.

Ground standard cubes gave the rats a weight-gain of about 25% in 2 weeks. From Figs. 1–3 it is apparent that gari (grated and fried cassava), maize, cassava flour, fresh water yam (*Dioscorea alata*) and fresh cassava (*Manihot utilisima*) produce less gain in weight compared with the standard cubes when mixed in a 1 : 1 ratio with the cubes (Fig. 1). However when the cube was mixed in a 1 : 1 ratio with unpolished rice (*Oryza sativa*), beans, millet (*Pennisetum typhoides*), Guinea-corn (*Sorghum*) and maize (*Zea mays*) the weight-gain in 2 weeks was higher than that obtained with the cubes. However, Guinea-corn and maize gave less gain in weight (Fig. 2). In a mixture of all the components (millet, beans, rice, Guinea-corn, maize and cubes in equal proportion) the weight-gain in 2 weeks was the highest (Fig. 2). A mixture of Guinea-corn and millet with cubes in equal proportion gave a little less weight-gain than did millet alone with cubes, while other mixtures (beans, gari, and cubes; maize, rice, Guinea-corn and cubes; maize, rice, Guinea-corn, millet and cubes) gave a lower weight-gain (Fig. 3) than with cubes alone. From these results it

FIGS 1–3. There were sixteen test rats in each group. Each of them was pre-fed with standard ground cubes and the appropriate test diet for 2 weeks and later had 40 mg/kg body-weight indomethacin dissolved in *N*-methyl acetamide 80% v/v i.p. for 4 hr.

Mean % weight-gain = $\frac{\text{Total \% weight-gain in 2 weeks}}{\text{no. of rats}} \times \text{in each group}$

FIG. 1. Effect of tubers and processed tubers on weight-gain in 2 weeks in laboratory rats. Number of rats in each group in parentheses.

(a) Cubes only (16); (b) yam flour + cubes (16); (c) yam (*Dioscorea dumetorum*) + cubes (16); (d) cassava flour + cubes (16); (e) fresh cassava + cubes (16); (f) cassava flour + yam flour + cubes (16); (g) gari + cubes (16); (h) yam (*D. alata*) + cubes (16).

FIG. 2. Effect of some cereals on weight-gain in 2 weeks in rats. Number of rats in each group in parentheses. (a) All components in equal proportions (16); (b) millet + cubes (16); (c) beans + cubes (16); (d) unpolished rice + cubes (16); (e) cubes only (16); (f) Guinea-corn + cubes (16); (g) maize + cubes (16).

would appear that millet, Guinea-corn and beans mixed with the standard cubes would go a long way to enhancing the growth of laboratory rats. These items are, however, expensive so that they cannot be

FIG. 3. Effect of combination of cereals on weight-gain in 2 weeks in laboratory rats. Number of rats in each group in parentheses.

(a) Millet + Guinea-corn + cubes (16); (b) cubes only (16); (c) beans + gari + cubes (16); (d) maize + rice + Guinea-corn + millet + cubes (16); (e) maize + rice + Guinea-corn + cubes (16).

FIGS. 4-6. There were sixteen test rats in each group. Each was pre-fed with standard ground cubes and the appropriate test diet for 2 weeks and later was given 40 mg/kg indomethacin dissolved in *N*-methyl acetamide 80% v/v i.p. for 4 hr.

Mean ulcer score = $\frac{\text{Total score}}{\text{no. of rats}}$ in each group.

FIG. 4. Effect of tubers and processed tubers on indomethacin-induced ulceration. A score of < 1.0 is taken as offer of protection. Number of rats in each group in parentheses.

(a) Cubes only (16); (b) gari (cassava, grated and fried) + cubes (16); (c) cassava flour + cubes (16); (d) fresh cassava + cubes (16); (e) water yam (*D. alata*) + cubes (16); (f) normal yam (*D. dumentorum*) + cubes (16); (g) cassava flour + yam flour + cubes (16); (h) yam flour + cubes (16).

used for animal feeds, whereas they form the staple diet of the population in parts of Nigeria.

Throughout all the experiments, using 320 rats, indomethacin produced ulceration only in the glandular (mucosal) part of the stomach, there was no ulceration in the duodenum or in the rumen. This confirms former findings (Elegbe and Bamgbose,

FIG. 5. Effect of some cereals on indomethacin-induced ulceration. A score of < 1.0 is taken as offer of protection. Number of rats in each group in parentheses.

(a) All components in equal proportions (16); (b) cubes only (16); (c) beans + cubes (16); (d) Guinea-corn + cubes (16); (e) maize + cubes (16); (f) unpolished rice + cubes (16); (g) millet + cubes (16).

FIG. 6. Effect of combination of cereals on indomethacin-induced ulceration. A score of < 1.0 is taken as an offer of protection. Number of rats in each group in parentheses.

(a) Cubes only (16); (b) beans + gari (grated and fried cassava) + cubes (16); (c) millet + Guinea-corn + cubes (16); (d) maize + unpolished rice + Guinea-corn + millet + cubes (16); (e) maize + unpolished rice + Guinea-corn + cubes (16).

1974; Djahanguiri, 1969). Using the method of Alphin and Ward (1967), for ulcer scoring, score 0—normal stomach; 0.5—punctate haemorrhage or pinpoint ulcers; 1.0—two or more small haemorrhagic ulcers; 2.0—ulcers > 3 mm in diameter; the results of ulceration are as shown in Figs. 4-6.

The standard cube diet offered no protection to indomethacin-induced ulceration. The same could be said of the following diets taking a score of > 1.0 as no offer of protection:

(1) All tubers in all their different forms (gari, cassava flour, cassava, water yam, yam flour, and trifoliate yam—*D. dumentorum*) (Fig. 4).

(2) Beans; beans plus gari; and mixture of beans, Guinea-corn, maize, rice and millet (Figs. 5 and 6).

Protection was offered against musocal ulceration produced by indomethacin with maize, Guinea-corn, unpolished rice and millet (Fig. 5); while a mixture of these four cereals offered most protection (Fig. 6).

From these results it is apparent that maize, rice, Guinea-corn and millet all contain some protective factor against indomethacin-induced gastric mucosal ulceration.

Discussion

Until now there had been no carefully conducted and documented record on the incidence of peptic ulceration in the different parts of Nigeria. Clinical observations by Amure (1965, 1967), Konstam (1966), Tovey (1974a, 1975) and Tovey and Tunstall (1975), however, give the impression that the incidence of peptic ulceration is lower in the northern compared with the southern part of Nigeria. In one of the studies over a 3-year period in the University of Ibadan Teaching Hospital, Amure (1967) found that the 300 patients who were treated for peptic ulceration included westerners, mid-westerners, easterners and those from the southern parts of the northern region of Nigeria. Although there are northerners in Ibadan and other parts of the western region of Nigeria, there were no Hausa, Fulani, or Kanuri patients (northern tribes). This general statement, if it is true, could be linked with social or dietary factors. If, according to Amure (1967), Tovey (1972, 1974a, 1975) and Tovey and Tunstall (1975), it could be linked to diet, then the findings might be easy to explain.

In Nigeria, according to Omololu (1974), the northerners take a lot of cereals with little consumption of beans, vegetables and tubers while the reverse is true of the southerners. Konstam (1966) also stated that northerners take a lot of fresh milk very freely compared with the inhabitants of the southern part. In the south however, the easterners take a lot of vegetables and tubers while westerners depend on beans, some tubers and vegetables with some cereals. Looking at the results, it thus seems that the northerners should have a good protection from peptic ulceration since they take cereals in the crude form as well as in the locally refined form. For instance, maize, millet, rice and Guinea-corn are milled and cooked as common diets (tuwo dawa; tuwo shinkafa; kamu; dabu; koko; kunu zaki; alele, tibani, etc.) in every home in the northern part of the country. This protection might not be due to cereals alone since milk which is freely taken in the north (Konstam, 1966) may offer some protection (Tovey *et al.*, 1975).

Tovey *et al.* (1975), using pylorus-ligated rats as a model, found that pre-feeding with unrefined cereals

gave no protection against rumenal ulceration, whereas cabbage, brinjal, dhal (a lentil) and dried milk powder gave marked protection. They did, however, find that maize gave some protection against mucosal ulceration although not against ulceration of the rumen.

In the eastern part of southern Nigeria, pounded yam mixed with gari (grated and fried cassava) as well as fresh cooked yam and cassava form the staple diet always mixed with vegetables. These mixtures, according to the experiments, offer very little protection. In the western part of southern Nigeria, yam, yam flour, cassava, cassava flour, beans and some vegetables (apart from those of the easterners) form the staple diet. All the tubers and beans tested in this section gave no protection. If there is a lower incidence of peptic ulceration in the west, as compared with the east, it may be due to the higher consumption of cereals in the west. These suggestions are made on the assumption of the general belief that the incidence of peptic ulceration is less in the north than in the south of Nigeria. Epidemiological studies will be necessary to substantiate this belief. Moreover, work is in progress to include more foodstuffs and to find out whether the protective factors in Nigerian food are heat labile such as are those in Indian food, as observed by Tovey *et al.* (1975). Attempts will be made in future experiments to test food preparations from cooked whole food as consumed by man.

Acknowledgment

We wish to thank Dr F. I. Tovey of Basingstoke District Hospital for his support and interest in this study.

References

- ADAMI, E. (1955) Experimental studies on the anti-ulcer factor. *Atti della Società lombarda di scienze mediche e biologiche*, **10**, 60.
- ADAMI, E. (1964) A new class of drugs active in gastroduodenal ulcers. *Clinica Europa*, **3**, (typescript only).
- ALPHIN, R.S. & WARD, J.W. (1967) Actions of hexopyrronium bromide on gastric secretion in dogs and ulceration in rats. *Archives internationales de pharmacodynamie et de thérapie*, **168**, 82.
- AMURE, B.O. (1965) Anticholinergic drugs in the management of duodenal ulcer. *Practitioner*, **195**, 335.
- AMURE, B.O. (1967) Aspects of duodenal ulcer disease in Nigeria. *Practitioner*, **199**, 330.
- CHENEY, G. (1940) Effect of diet and cinchophen on production of experimental gastric ulcers in chicks. *Proceedings of the Society for Experimental Biology and Medicine*, **45**, 190.
- CHENEY, G. (1948) Prevention of histamine induced peptic ulcers by diet. *Stanford Medical Bulletin*, **6**, 334.
- CHENEY, G. (1949) Rapid healing of peptic ulcers in patients receiving fresh cabbage juice. *California Medicine*, **70**, 10.
- CHENEY, G. (1950a) Anti-peptic ulcer dietary factor. *Journal of the American Dietetic Association*, **26**, 668.
- CHENEY, G. (1950b) Vitamin U therapy of peptic ulcer. *California Medicine*, **77**, 248.

- CHENEY, G. (1950c) The nature of the anti-peptic ulcer dietary factor. *Stanford Medical Bulletin*, **8**, 144.
- DJAHANGUIRI, B. (1969) The production of acute gastric ulceration by indomethacin in the rat. *Scandinavian Journal of Gastroenterology*, **4**, 256.
- ELEGBE, R.A. & BAMGBOSE, S.O.A. (1974) (Unpublished observation).
- KONSTAM, P.G. (1966) Surgical problems in West Africa. *American Journal of Surgery*, **112**, 864.
- OMOLOLU, A. (1974) *Food, Famine and Health*. 'Inaugural lectures' 1973-74, University of Ibadan Press.
- SINGH, G.B., ZAIDI, S.H. & BAJPAL, B.P. (1962) Effect of *Brassica oleracea* in the prevention and healing of experimental peptic ulceration. *Indian Journal of Medical Research*, **50**, 741.
- TOVEY, F.I. (1972) Duodenal ulcer in Mysore. *Tropical Geographical Medicine*, **24**, 107.
- TOVEY, F.I. (1974a) Geographical distribution and possible factors in the aetiology of peptic ulcer. *Tropical Doctor*, **4**, 17.
- TOVEY, F.I. (1974b) Aetiology of duodenal ulcer: an investigation into the buffering action and effect on pepsin of bran and unrefined carbohydrate foods. *Postgraduate Medical Journal*, **50**, 683.
- TOVEY, F.I. (1975) Peptic ulcer. In: *Refined Carbohydrate Foods and Disease* (Ed. by D. Burkitt & H. Trowell). Academic Press Inc., London.
- TOVEY, F.I., JAYARAJ, A.P. & CLARK, C.G. (1975) The possibility of dietary protective factors in duodenal ulcer. *Postgraduate Medical Journal*, **51**, 366.
- TOVEY, F.I., TUNSTALL, M. (1975) Progress Report. Duodenal ulcer in Africa South of the Sahara. *Gut* (In press).
- WISSMER, B.A.L. & ADAMI, E. (1965) A new way in ulcer therapy? *Current Therapeutic Research, Clinical and Experimental*, **7**, 444.