THE ALIMENTARY ABSORPTION OF SOME ENTERIC-COATED SODIUM AND POTASSIUM CHLORIDE TABLETS

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The alimentary absorption of sodium chloride and potassium chloride tablets covered with a new enteric coating, has shown their absorption to be satisfactory. Of three other brands, one has been found to be only poorly absorbed, producing diarrhoea in some subjects; a second brand was poorly absorbed in 1 out of 5 patients, while the third proved moderately satisfactory. Samples of all the brands of enteric-coated tablets passed the *in vitro* tests for disintegration specified by the British Pharmacopoeia (1958, Appendix 21B).

An enteric coating is useful when the material to be absorbed may cause gastric irritation. Sodium, potassium and ammonium chloride are often prescribed as enteric-coated tablets, as are salicylates and some glucocorticoids. Enteric-coated tablets should comply with the test for disintegration described in Appendix 21B of the British Pharmacopoeia, 1958. However, tablets which conform to this specification are sometimes excreted intact, or only partially digested, in the stools. Pirnie and Staffurth (1961) drew attention to this problem and suggested a revision of the British Pharmacopoeia specification.

We have examined in man the absorption of sodium and potassium chloride "nuseals"* enteric-coated tablets. Three other commercially available enteric-coated potassium chloride tablets have also been investigated, but less extensively.

Methods

Various enteric-coated tablets† were given to 28 patients suffering from a variety of illnesses. In only 2 patients, cases 2 and 11, was there any known bowel disorder, and in both the disorder was mild. Twenty patients were studied in the metabolic ward and they had a constant food intake. Eight patients were studied in an orthopaedic ward, their diet was kept as constant as possible.

Faeces were collected for consecutive 3-day periods, and each collection was homogenised with distilled water in a blender and analysed for sodium and potassium by flame photometry. The average daily faecal sodium and potassium for 3 or 6 days before administration of the test tablets was subtracted from the average daily excretion during the administration of the tablets to estimate the amount of administered salt

* The "nuseal" is of commercial manufacture; the coating contains the following ingredients according to the manufacturers: cellulose acetate phthalate, acacia, sucrose, gelatin, calcium sulphate and talc (hydrated magnesium silicate). The red dye is ponceaux S.X.

† The symbols A, B, C and D are used to describe the four brands of tablets. A are "nuseals." The remaining tablets will be identified on application to the authors.

TABLE I

ABSORPTION OF POTASSIUM CHLORIDE TABLETS (A)

Case	Diagnosis	Duration of therapy (days)	Faecal K before therapy, m-equiv./3 days	Mean, m-equiv./day	Faecal K during therapy, m-equiv./3 days	Mean, m-equiv./day	Loss of K supplement in faeces, per cent
1	Malnutrition K depletion	39	30	10·0	27, 21, 24, 30, 42, 30, 27, 27, 27, 24, 45, 18, 28	9·5	0
2	Mild steatorrhoea	36	42	14·0	87, 81, 108, 51, 33, 12, 51, 63, 33, 72, 21, 27	18·0	3
3	Cushing's Syndrome	21	54, 62, 48	18·0	45, 66, 39, 33, 81, 39, 63	17·0	0
4	Malnutrition K depletion	18	42, 54, 51	16·0	39, 54, 39, 39, 42, 45	14·0	0
5	Hirsutes	12	27, 31	9·5	30, 37, 15, 30	9·0	0

* Each patient received 134 m-equiv./day (10 g.).

TABLE II

ABSORPTION OF SODIUM AND POTASSIUM CHLORIDE TABLETS (A) ADMINISTERED CONCURRENTLY

Case	Diagnosis	Duration of therapy (days)	Dose of NaCl m-equiv./day (g./day)	Faecal Na				Loss of Na supplement in faeces per cent	Dose of KCl m-equiv./day (g./day)	Faecal K				Loss of K supplement in faeces per cent
				Before therapy m-equiv./3 days	Mean m-equiv./day	During therapy m-equiv./3 days	Mean m-equiv./day			Before therapy m-equiv./3 days	Mean m-equiv./day	During therapy m-equiv./3 days	Mean m-equiv./day	
6	Salt-losing pyelonephritis	36	171(10)	9, 10	3	9, 15, 9, 6, 3, 9, 6, 50, 27, 75, 48, 26	8	3	54(4)	39, 45	14	39, 93, 65, 42, 30, 45, 27, 108, 98, 90, 78, 56	19	9
7	Salt-losing pyelonephritis	30	203(12)	4, 5	2	5, 2, 28, 21, 15, 4, 6, 3, 5, 3	3	0	108(8)	9, 33	7	18, 9, 90, 78, 63, 24, 66, 24, 48, 15	16	8
8	Salt-losing pyelonephritis	9	342(20)	30	10	81, 66, 93	27	5	54(4)	36	12	54, 60, 78	21	17
9	Malnutrition	12	171(10)	9, 11	3	15, 15, 30, 25	7	2	67(5)	24, 45	12	36, 32, 23, 45	11	0

excreted. This value was then expressed as a percentage of the dose given.

In all the tests 0·5 g. tablets were used.

Results

Table I shows the results of the study of the absorption of potassium chloride tablets A given to 5 patients. The daily dose was 10 g. (20 × 0·5 g. tablets) and the longest duration of the administration was 39 days. In these 5 patients absorption of the tablets was complete.

Table II reports a study of 4 patients to whom it was necessary to give both sodium chloride and potassium chloride tablets A, each 0·5 g., in large doses. The longest duration of study was 36 days. Despite the large number of tablets taken the absorption of sodium chloride was virtually complete and the faecal loss of potassium was small. No whole tablet or recognisable fragment appeared in any of the stools.

The only symptoms noticed during the administration of these tablets occurred in Case 1 who complained of a "colicy" abdominal pain on several occasions during the first two days. The pain disappeared despite the continued administration of the tablets.

Table III shows the results from three other brands of enteric-coated potassium chloride tablets given to patients. In the patients given tablets B (Cases 10–15) absorption was fair in cases 10 and 11 and poor in the remaining four. In these 4 patients the tablets produced diarrhoea and the stools contained many whole tablets and fragments of tablets.

Five patients, 16–20, were given enteric-coated potassium chloride tablets C and these were absorbed satisfactorily, except in one patient, 16, in whom the tablets produced increased frequency of defaecation. His stools contained fragments of undigested tablets and the faecal loss of potassium increased progressively, exceeding 40 per cent of the supplementary potassium for the last 3 days of the test. Five patients, 21–25, were given enteric-coated potassium chloride tablets D. Absorption was good in two patients, 22 and 23, and fair in three, 21, 24 and 25. In two patients, 21 and 25, two whole tablets appeared in the stools during the test period.

Table IV reports the study of a cross-over experiment designed to compare the absorption of potassium chloride tablets A with tablets B. The patients were given tablets A first and then, after a suitable interval, they were given the equivalent dose of tablets B. As before, tablets A were well absorbed and tablets B were poorly absorbed.

Table V reports the results of disintegration tests made on samples of the tablets used. All the enteric-coated tablets conformed to the B.P. standards for disintegration.

Discussion

High doses of sodium chloride and potassium chloride are frequently indicated in medicine. Disintegration of tablets containing sodium or potassium chloride in the stomach may lead to gastric irritation and

TABLE III

ABSORPTION OF OTHER BRANDS OF ENTERIC-COATED POTASSIUM CHLORIDE TABLETS

Tablet	Case	Diagnosis	Duration of therapy (days)	Faecal K			Mean m-equiv./day	Loss of K supplement in faeces, per cent	Total no. of KCl tablets in faeces
				Before therapy m-equiv./3 days	Mean m-equiv./day	During therapy m-equiv./3 days			
B	10	Asthma	9	24	8	54, 84, 97	26	22	3
	11	Crohn's disease	12	27, 23	8	42, 62, 115, 45	22	17	6
81 m-equiv./day	12	Idiopathic osteoporosis	12	25, 36	10	141, 186, 116, 229	56	57	9
(6 g./day)	13	Orthopaedic	9	12	4	78, 129, 117	32	35	9
	14	Orthopaedic	9	19, 21	7	93, 87, 134	35	35	25
	15	Orthopaedic	9	31, 24	9	165, 240, 276	76	83	33
	16	Chronic bronchitis	9	40, 39	13	90, 122, 136	39	32	Many fragments
C	17	Cushing's Syndrome (iatrogenic)	9	36, 31	11	37, 34, 39	12	0	0
81 m-equiv./day	18	Idiopathic hypercalcuria	9	15	5	29, 20, 30	9	5	0
(6 g./day)	19	Anorexia nervosa	9	30, 46	13	37, 25, 46	12	0	0
	20	Chronic nephritis	9	8	3	12, 11, 11	4	0	0
D	21	Orthopaedic	9	33, 35	11	75, 63, 69	23	15	2
	22	Orthopaedic	9	27	9	0, 42, 42	9	0	0
81 m-equiv./day	23	Orthopaedic	9	62, 34	16	63, 42, 40	16	0	0
(6 g./day)	24	Orthopaedic	9	15	5	81, 27, 25	15	12	0
	25	Orthopaedic	9	12, 18	5	51, 42, 59	17	15	2

TABLE IV

CROSS-OVER EXPERIMENTS TO COMPARE ABSORPTION OF TWO BRANDS OF POTASSIUM CHLORIDE TABLETS, A AND B

Case	Diagnosis	Faecal K				Loss of supplement in faeces, per cent	Faecal K				Loss of supplement in faeces, per cent
		Before tablet A therapy m-equiv./ 3 days	Mean m-equiv./ day	During tablet A therapy m-equiv./ 3 days	Mean m-equiv./ day		Before tablet B therapy m-equiv./ 3 days	Mean m-equiv./ day	During tablet B therapy m-equiv./ 3 days	Mean m-equiv./ day	
26	Anorexia nervosa	40, 20	10	27, 19, 24	8	0	15, 25	8	81, 181, 221	54	57*
27	Anorexia nervosa	27	9	27, 72, 57	17	10	33, 35	11	108, 95, 119	36	31*
28	Obesity	65, 54	20	64, 67, 44	19	0	50, 58	18	102, 130, 162	44	32*

In each case the dose of KCl was 6 g./day (81 m-equiv.) as 0·5 g. tablets.

* Analysis of the 3 day stool from the 9th–12th day contained higher amounts of K than was to be expected from the control excretion level because of the continued excretion of unabsorbed KCl. If this additional loss is included, the corrected figures for the loss of KCl supplement becomes 63, 38 and 35 per cent, respectively.

dyspeptic symptoms. To avoid this, enteric coatings have been devised to resist disintegration in the stomach, while rapidly disintegrating in the small intestine, so allowing absorption of their contents. A risk of such coatings is that they may resist disintegration in the small intestine, the contents being wholly or partially lost in the faeces.

TABLE V

STUDY OF DISINTEGRATION OF FOUR TYPES OF ENTERIC-COATED POTASSIUM CHLORIDE TABLETS

Sample*	Results of immersion in acid-pepsin solution for 3 hr.	Results of immersion in alkaline-pancreatin solution
A	Red coating dissolved within 5 min. All 5 intact after 3 hr.	1 disintegrated in 22 min. 2 ,, ,, 22 min. 3 ,, ,, 30 min. 4 ,, ,, 32 min. 5 ,, ,, 35 min.
B_1	All 5 tablets intact at the end of 3 hr. Brown coating intact.	1 disintegrated in 20 min. 2 ,, ,, 35 min. 3 ,, ,, 40 min. 4 and 5 ,, ,, 45 min.
B_2	All 5 tablets still intact at the end of 3 hr.	All coating gone,, 47 min. 1 ,, ,, 25 min. 2 ,, ,, 27 min. 3 ,, ,, 32 min. 4 ,, ,, 34 min. 5 ,, ,, 36 min. All coating gone,, 45 min.
C	Brown sugar coating dissolved within 10 min. of immersion. Tablets intact after 3 hr.	1 tablet disintegrated in 20 min. Coating cracked on all others within 23 min. 2 disintegrated in 25 min. 3 ,, ,, 30 min. 4 ,, ,, 35 min. 5 ,, ,, 40 min.
D	Sugar coating dissolved within 10 min. All 5 intact after 3 hr.	Coating split after 8 min. 1 disintegrated in 13 min. 2 ,, ,, 16 min. 3 ,, ,, 26 min. 4 ,, ,, 26 min. 5 ,, ,, 35 min. Coating still visible after 60 min.

* Five tablets were used for each test.

The tablets most intensively investigated in this study (A) have proved satisfactory for prolonged administration. Indeed, one patient (6) has been on continuous treatment with 10 g. of sodium chloride and 4 g. potassium chloride for 18 months with satisfactory results, while another (8) was treated with 20 g. of sodium chloride and 4 g. potassium chloride for 13 months with satisfactory results. She died suddenly of uraemic heart failure and at autopsy the gut was free from undissolved tablets. These two patients have demonstrated the feasibility of using large doses of enteric-coated sodium and potassium chloride tablets for prolonged periods without undesirable effects. The results of the short-term studies reported here confirm the favourable clinical impression we have formed of the use of tablets A in a variety of patients.

It was not possible to subject the other enteric-coated tablets mentioned to the same extensive test as has been applied to tablet A so that a comparison cannot be attempted. It is clear, however, that one brand of tablets used in this study is quite unsuitable for clinical use despite the

fact that it successfully passes the *in vitro* test specified by the British Pharmacopoeia.

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REFERENCE

Pirnie, J. S., and Staffurth, J. S. (1961). *Lancet*, **1**, 48–49.