J Diar Dis Res 1984 Sep;2(3):162-167
0253-8768/84 $1.00 + 0.10

PREPARATION AND QUALITY CONTROL OF HAND-PACKAGED ORAL REHYDRATION SALT SACHETS

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Received : 13 Mar 1983

Abstract

The feasibility of a simple method for preparation of oral rehydration salt (ORS) packets suitable for cottage industry-scale production over a 3-year period was tested. Each packet contained ingredients for making a liter of ORS solution, according to the WHO formula, except that glucose was replaced with sucrose. In each batch, ingredients for 200 packets were mixed thoroughly in a bowl, and a standardized scoop was used to measure the mixture for one liter. Then the ingredients were sealed in polyethylene bags. From each batch of 200 packets, 3 to 5 one liter bags were tested for weight and electrolyte content. The mean concentrations of sodium, potassium, chloride and bicarbonate in 3,359 packets were: 89.8, 19.8, 77.9 and 29.6 mmol/L, respectively. The shelf lives of the ORS packets were tested in different seasons, under various conditions of temperature and humidity. It was found that the ORS mixtures changed color from white to light brown, although the electrolyte concentrations remained almost unchanged up to 8 months storage. A simple quality control method suitable for rural Bangladesh was developed by titrimetric estimation of the chloride in an ORS solution.

Key words: Diarrhoea; Oral Rehydration Therapy; Oral Rehydration Solutions.

Introduction

The efficacy of oral rehydration solution (ORS) in management of diarrhoea is well-established (1-6). The main problem currently encountered is its availability and cost. These problems especially plague rural populations in developing countries. Industrially-produced packages require expensive machinery and high quality ingredients, both of which often must be imported. These industries usually are centrally located, making distribution of the packages to remote areas expensive and time-consuming.

Considering these difficulties, a simple method suitable for cottage industry-scale production of oral rehydration salt sachets was designed and evaluated at the ICDDR,B. The technique is so simple that it is suitable for the rural areas of non-industrialized countries.

The biggest obstacle to the preparation of home-made ORS is quality control. The concentration of Na^+ ions in ORS is considered to be critical to its safety and efficacy (10,11). Estimation of sodium requires a flame photometer, which is expensive and needs a high level of technical competence to operate and maintain. Thus, it is not suitable for operation and use in rural areas. To overcome this hurdle, we evaluated an indirect method for estimating sodium in an ORS solution, by titrating chloride against silver nitrate in the presence of an indicator.

Materials and methods

Preparation, quality control and shelf-life

To prepare ORS packets, the WHO-recommended formula was followed, except that 40 g of sucrose (table sugar) was substituted for the 20 g of glucose recommended. To prepare 200 ORS packets, sodium chloride, sodium bicarbonate, potassium chloride and sugar were weighed in a balance; and were mixed by hand thoroughly in a 15 kg bowl, until a homogenous mixture resulted. Large sodium chloride crystals and sodium bicarbonate lumps first were broken up, and then were sifted for proper mixing. For blending, ingredients were carefully kneaded, scraped and turned over by hand in the bowl. The process was repeated. To test the homogenicity, 47.5 g of the mixture (the amount required for 1 liter of ORS) was weighed out and assayed. When three different samples yielded results within the satisfactory range, the salt/sugar mixture was considered ready

for packaging. With a standardized scoop, 47.5 g was measured and was sealed in polyethylene bags, using an electric sealer or a wax candle. The measuring scoop was made in our laboratory, by cutting off a 50 ml plastic measuring cylinder (Nalge). It was standardized to contain by volume 47.5 g of a mixture containing some moisture at the high temperature and humidity normal for Bangladesh.

From each lot of 200 packets, 3 to 5 bags were tested again for quality control. The gross weight and electrolyte contents were measured. Electrolyte was estimated in the ICDDR,B's Biochemistry Laboratory, using an IL analyzer (Instrumentation Laboratories, models 446 and 443) (12, 13, 14).

Over 3 years, a total of 3,359 samples, 3-5 samples collected from each lot of ORS prepared, were analyzed and tabulated (Table I).

A method suitable for testing the quality of ORS in cottage industry settings was developed. The modified Mohr method was used to titrate chloride in oral solution (15). The chloride in a neutral or weak alkaline solution containing chromate is titrated with silver nitrate. Silver chloride precipitates, and at the end-point red silver chromate is formed. To 1 ml of oral therapy solution in a 100 ml Erlenmeyer flask, about 20 ml of water was added. The solution was warmed slightly on a heater or a spirit lamp; and 0.5 ml of K_2CrO_4 solution was added. The titration was carried out against a standard (0.01 N) $AgNO_3$ solution from burate, until the pure yellow color changed, and a pinkish-yellow precipitation appeared. The indicator blank was determined by titrating water in the same way. One standard (0.01 N NaCl) was run in each lot of analysis, following the procedure used to titrate an unknown. The color of the standard precipitation was used as a reference for observing the end-point of an unknown.

Calculation: $X = V \times S \times 1000 = Cl^-$ in mmol/L of ORS solution.
Where, X = chloride concentration in ORS in mmol/L.
V = Vol of $AgNO_3$ used to titrate the solution − Vol of $AgNO_3$ to titrate blank.
S = Actual strength in normality of $AgNO_3$

HCO_3^- was estimated by the titrimetric method with 0.1 N HCl, using a 1% aqueous methyl orange solution as an indicator. A 10 ml ORS solution was warmed slightly in a 100 ml Erlenmeyer flask, and was titrated against 0.1 N HCl with 3 drops of indicator.

Calculation: $X' = V' \times 10$ mmol/L
When, $X' = HCO_3^-$ concentration in ORS, mmol/L
V = Vol of 0.1 N HCl required to titrate 10 ml ORS solution.

Analyzed for sodium and chloride were 200 samples. Sodium was estimated by a flame photometer, and chloride by the titrimetric method and by an autotitrator (16), to verify the validity of the titrimetric method compared to instrumental analysis, and finally to establish the correlation between chloride and sodium ions in ORS solution. The raw materials, which were not supplied with proper labeling, were identified by some simple tests. Sodium and potassium were identified by a flame test. One match stick was carbonized in the candle flame, and was dipped quickly into concentrated HCl placed on a watch glass. The moistened carbonized stick adhering with salt then was placed on the flame: a yellow and brick red-colored flame indicated sodium and potassium salts, respectively. Sodium bicarbonate was identified from the observation of effervescence evolved when 1 N HCl was added in a test tube containing a pinch of the material.

To test the validity of the method in the field, four supervisors of two Bangladesh organizations, the Bangladesh Rural Advancement Committee (BRAC) and the National Oral Rehydration Programme (NORP), were trained in the ICDDR,B's Biochemistry Laboratory on ORS quality control using the titrimetric method. All were science graduates trained for a month, who then trained some field workers to check the quality of ORS solution prepared in the field. Most field workers lacked a science background, but had at least a higher secondary level education. Mothers or any other suitable family members were trained by BRAC workers to prepare "labon gur" solution (an oral solution containing one pinch sodium chloride and one fistful of molasses) (17). The field workers collected samples of home-made ORS solutions, and estimated chloride concentrations by the titrimetric method. One in every 10 samples tested was sent to the Biochemistry Laboratory for analysis, as part of quality control.

NORP set up the method in the central laboratory in Dhaka; and collected samples from their

district stations, where ORS packets are prepared by the method we advocated. After analyzing those samples in their laboratory using the titrimetric method, they too sent one in every 10 samples to the ICDDR,B laboratory, to check the validity of their method.

The shelf-life of ORS packets also was tested. Sixty ORS packets were kept in different atmospheric conditions for eight months; and were analyzed for electrolyte, sugar and moisture content at different time intervals. Sucrose was measured as glucose by the o-toludine method, hydrolyzing an ORS solution with 1 N HCl (18). The results were expressed as glucose. The pH was measured with a Corning pH meter. The moisture content was determined by keeping the ORS packets at 105°C in an oven, and taking the packets' weight every 12 h, until a constant weight was achieved. Water content percentage was calculated from the difference between the packets' initial and final weights.

Results

Continuous hand mixing for 30 min was required to make a homogeneous ORS mixture. Housewives who were taught to prepare the packets mastered the technique within three months. Use of plastic scoops to measure the mixture for one-liter ORS packets made the preparation method rapid, without considerable deviation of the results from expected values (Table I). The total expected weight of each packet with its polyethylene bag (size: 140 x 105 x 0.1 mm) and the observed mean weight were 48.9 g and 48.2 g, respectively. The calculated variation between observed and expected values of the concentration of Na^+, K^+, Cl^- and HCO_3^- was not significant.

The correlation coefficient between chloride values measured by the titrimetric method and by the autotitrator was found to be 0.98, while the correlation coefficient between chloride values measured by the titrimetric method and Na^+ values measured by a flame photometer was 0.8 (Fig.). The equation of the straight line in the Fig. was y=0.781 (x) + 6. The sodium ion concentration was calculated from x=(y-b)/a, where x=sodium ion concentration in ORS solution, y=chloride ion concentration obtained from titrimetric analysis, b=6, and a=0.781. The validity of the method also was tested in the field. The results were analyzed, and were compared with the results of instrumental analysis (Table II).

Initially, in higher chloride concentration ranges (more than 100 mmol/L), field workers reported low results. It was assumed that, lacking a scientific background, they failed to detect the titration end-point in the higher range. It then was suggested that they run two standards of the concentration 100 and 150 mmol chloride per

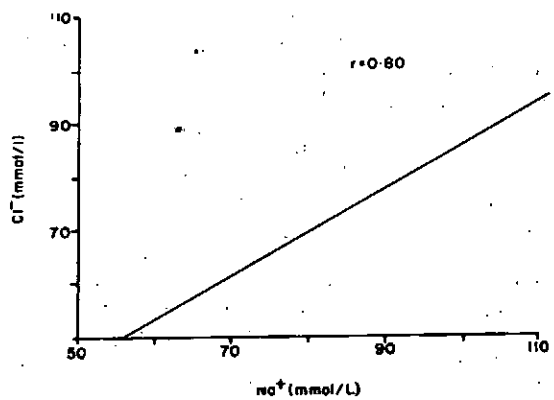

Fig. – Correlation between chloride concentration estimated by titrimetric method and sodium concentration estimated by flame photometer.

TABLE I –MEAN WEIGHT (±ISD) AND ELECTROLYTE CONCENTRATION (±ISD) OF 3,359 ORS PACKETS

		Electrolyte concentration (mmol/L)			
	Wt. (g)	Na^+	K^+	Cl^-	TCO_2^-
	48.2 ± 0.35	89.8 ± 3.6	19.8 ± 3.6	77.9 ± 4	29.6 ± 1.4
Range	46.5—49.1	85—101	17—22.5	70—90	25—34
Expected value	48.9	90	20	80	30

TABLE II — COMPARISON OF TWO METHODS OF CHLORIDE ESTIMATION IN ORS SOLUTION: TITRIMETRIC ESTIMATION IN THE FIELD (NORP* & BRAC†) AND INSTRUMENTAL ANALYSIS AT THE ICDDR,B

	N	Titrimetric analysis	Instrumental analysis	y	r	t
		Mean Cl^- Conc. in mmol/L	Mean Cl^- Conc. in mmol/L			
NORP	141	79.4 ± 10.5	76.1 ± 12.4	1.021X + 1.704	0.95	0.07
BRAC	621	79.7 ± 32.2	81.9 ± 35.4	1.099X + 1.456	0.98	0.01

* NORP (National Oral Rehydration Programme)
†BRAC (Bangladesh Rural Advancement Committee)

liter of solution (1 ml of each 0.1 M and 0.15 M NaCl solution were taken in 20 ml of water in separate conical flasks for titration), in order to use as a reference to detect the end-point in the higher range of chloride concentration.

When shelf-life was tested, it was found that glucose, HCO_3^- and pH varied during the 8-month storage period (Table 3). The color changed from white to brown, and the lump was formed.

TABLE III—CHANGES IN ORS PACKAGE COMPOSITION AFTER 8 MONTHS' STORAGE

	Initial	After 8 Months
CO_2 (mmol/L)	29.6 ± 1.5 (25.1 – 30.5)	23.7 ± 0.8 (22.6 – 24.9)
Glucose (mmol/L)	107 ± 6.0 (104 – 110)	100 ± 2.9 (95 – 103)
pH	8.4 ± 0.2 (8.2 – 8.5)	9.1 ± 0.1 (8.95 – 9.2)

However, the lump did not affect the mixture's solubility; HCO_3^- came down from 29.6 to 23.7 mmol/L, glucose dropped from 107 to 100 mmol/L, and pH increased from 8.4 to 9.1. The bicarbonate content of the salt mixture decreased gradually during storage. Packets stored from 3-5 months were safe, and still contained adequate concentrations (5) of bicarbonate to treat diarrhoea. The discoloration was due to the presence of sodium bicarbonate, indicating the decomposition of sucrose (19); but glucose concentration, even after decomposition during storage, remained satisfactory for maximal water and sodium absorption.

In the rainy season, the packets were analyzed after one month and 3 months. Except for moisture content, all other components remained stable. The mean moisture content was 5%, and varied from 2.6-10.5% during storage for 3 months (Table IV, column 3). During the rainy season in Bangladesh, humidity varies from 98-100% and temperature from 28°C - 30°C. When the rainy season was over, it seemed that absorbed water diffused out of the packets, and, at the end of eight months, the packets' moisture content was unchanged.

TABLE IV – MOISTURE CONTENT AND PHYSICAL APPEARANCE OF ORS PACKETS AT DIFFERENT TIME INTERVALS

Initial N = 80	After 1 month N = 20	After 3 months N = 20	After 8 months N = 20
1.3% ± 0.1	4.7% ± 2.2	5% ± 2.3	1.3% ± 0.2
(1.2—1.5%)	(2.4—10.1%)	(2.6—10.5%)	(1.2—1.6%)
White granular powder	Lump formed turned brown	Lump formed turned brown	Lump formed turned brown

Discussion

It may be concluded that, if centrally tested ingredients are supplied, a cottage industry for making ORS packets may be set up, using housewives to make ORS packets. The simple titrimetric method does not require sophisticated instruments, is adaptable to field situations, has been found satisfactory for estimation of chloride, and can be used to estimate sodium as well, thus ensuring the safety of ORS packets.

Since ORS solution is weakly alkaline, adjustment of pH for solution titration is unnecessary. This method is ideal for titrating chloride in ORS, because the interfering substances—iodine, bromide, phosphate, sulfide and cyanide—are not likely to be present in ORS in important amounts. Considering the value of y, r and t in Table II, it can be concluded that titrimetric analysis of chloride in the field, with minimum supervision, correlates well with instrumental analysis. Fifty samples were analyzed for CO_2 and HCO_3^-, using both a Vanslyke manometric apparatus and the titrimetric method. The mean HCO_3^- value in the titrimetric method was 31.53 ± 0.98, and the CO_2 on a Vanslyke manometric apparatus was 30.34 ± 1.26. The differences are not significant ($t=1.025$). It is possible also to calculate all 4 species of ions present in ORS solution, when HCO_3^- is titrated against 0.1 N HCl. Sodium concentration can be calculated from the equation $x=(y-b)/a$; HCO_3^- can be estimated by the titrimetric method; and the K^+ ion concentration is calculated as:

$x - C = D$, concentration of NaCl in mmol/L

When, C = concentration of HCO_3^- in mmol/L

and, $y - D$ = concentration of KCl in mmol/L,

when x and y, respectively, are the concentration of total sodium and chloride ions. However, the probable interchanges of quantity with one ingredient to another are 3!; and, in such cases, the above calculations are unsatisfactory for calculating separately the 4 species of ions. In such cases, the difference between calculated sodium and estimated HCO_3^- will indicate the satisfactory quality of ORS. The difference should be within the range of 50-65. If it is below or above this range, it is obvious that the ingredients were not proportionately weighed for mixing, and the salt mixture should be discarded. Another advantage of mixing ingredients for 200 packets at a time was that the large quantity was easier to measure, and reduced the margin of error incurred by using a rough balance.

Acknowledgements

This research was financed by the International Centre for Diarrhoeal Disease Research (ICDDR,B). The ICDDR,B is supported by countries and agencies which share its concern about the impact of diarrhoeal diseases on the developing world. Current ICDDR,B donors include: Aga Khan Foundation AGFUND Australia, Bangladesh, Belgium, Canadian CIDA, Ford Foundation, France, GTZ, IDRC Japan OPEC Fund, Population Council, SAREC, Saudi Arabia Sweden, Switzerland, UNDP, UNFPA UNICEF the United Kingdom and the United States.

The authors thank the Bangladesh Rural Advancement Committee and the National Oral Rehydration Programme, for allowing use of their field study data; and W.B. Greenough, III, M. Mujibur Rahaman and K.M.S. Aziz of the ICDDR,B for asking us to develop a simplified method for estimating ORS sodium concentration, and for their valuable suggestions.

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