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ORIGINAL RESEARCH

Tuber-Based Oral Rehydration Solution Enhanced the Activity of Alkaline Phosphatase and Repaired Damage in The Intestinal Compartments of Rats Induced with Diarrhoea

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Abstract:

Introduction: Diarrhoea remains a disease of global health concern. Less is known about the functional effects of tuber-based oral rehydration solution (ORS) in diarrhoea pathophysiology.

Aims: This study was designed to investigate the effects of tuber-based ORS on intestinal alkaline phosphatase (IAP) activity and serum albumin concentration in diarrhoeic animals.

Materials and Methods: Forty Wistar rats were randomly divided into six groups (n=6). Group A received food and water only; Group B was induced with osmotic diarrhoea; Group C, D, E and F received standard World Health Organization (WHO)-ORS, *Colocasia esculenta*-ORS, *Pachyrhizus erosus*-ORS, and *Ipomoea batatas*-ORS respectively, after diarrhoea induction. After the experimental period, the animals were sacrificed, and IAP activity was evaluated using spectrophotometry. Blood collected was assessed for serum albumin concentration. Sections of the small intestine were subjected to histopathological examination.

Results: Diarrhoeic animals administered tuber-based ORS had higher IAP activities, compared to animals treated with WHO-ORS (P=.05). All animals induced with osmotic diarrhoea had decreased levels of serum albumin (regardless of ORS treatment), which did not vary significantly compared to the control (P=.05). Micrographs of small intestinal tissues revealed that untreated diarrhoeic animals had depleted Brunner's gland and cellular components, while animals administered with WHO-ORS and tuber-based ORS showed improved intestinal mucosa features, similar to the control.

Conclusion*:* The results revealed that tuber-based ORS had a higher enhancing effect on IAP activity than WHO-ORS. Tuber-based ORS and WHO ORS showed the potential to repair intestinal mucosa damage and restore normal serum albumin concentration in animals with diarrhoea.

Keywords*:* Diarrhoea, oral rehydration solution*, Ipomoea batatas, Colocasia esculenta and Pachyrhizus erosus.*

All co-authors agreed to have their names listed as authors.

1. INTRODUCTION

Diarrhoea is characterized by an abrupt discharge of abnormally watery stools at a frequency of more than two times per day [1]. Diarrhoea is transmitted by infectious organisms, such as viruses, bacteria, protozoa, and helminths through fecal-oral routes [2, 3]. Non-infectious etiologies of diarrhea include food poisoning, lactose intolerance, intestinal inflammatory and autoimmune conditions (Chron's disease, ulcerative colitis, celiac disease) and adverse effects of antibiotics as well as some cancer and HIV medications [4, 5]. Diarrhoea can be classified from a clinical perspective as acute watery diarrhoea (lasts for several hours to few days), acute bloody diarrhea (referred to as dysentery) and persistent diarrhea (lasts for 14 days or more) [6]. From a pathophysiological viewpoint, diarrhoeal disease may occur from malabsorption/maldigestion of osmotically active substrates with subsequent passage of fat in the stool (osmotic mechanism) or aberrantly high secretion and/or diminished absorption of fluid and electrolyte in the small bowel lumen (secretory mechanism) [7, 8].

Although diarrhea is preventable and treatable, it remains a disease of global health concern. The burden of diarrhoea is higher in developing countries, especially for children under five years [9]. In 2016, diarrhea resulted in an estimated 446,000 deaths worldwide, among children under the age of 5 [10]. The prevalence of diarrhoea in developing countries is associated with environmental and socio-economic factors, such as unsanitary fecal waste disposal, inadequate access to clean water, poor housing and overcrowding, and cohabitation with domestic animals that may harbor human pathogens [11-13].

Diarrhoea may result in marked alteration in the architecture as well as composition of enzymes and microbiota of the intestinal mucosa [14]. Intestinal alkaline phosphatase (IAP), a resident enzyme of the brush-border that catalyzes the hydrolyses of monophosphate ester, belongs to the family of Alkaline Phosphatase (AP) which are ubiquitously distributed in human tissues [15]. In addition to the vital role IAP plays in gut mucosal defense against pathogens, they are also required for the maintenance of intestinal homeostasis [16]. IAP is expressed exclusively in villus-associated enterocyte and considered an excellent biomarker for assessing intestinal epithelial damage in diarrhoeic condition [16, 17].

The prevention and treatment of diarrhoea has evolved over the years, since the approval of oral rehydration therapy (ORT) by the world health organization (WHO) in 1978 [18, 19]. ORT is a simple fluid replacement treatment for dehydration associated with diarrhea resulting from any etiology (including cholera) in all age groups around the world [20]. Standard oral rehydration solution (ORS) is a glucose electrolyte solution (GES) with osmolarity of 311 mmol/l [21, 22].

ORS has significantly reduced the number of deaths. caused by diarrhea globally [23, 24]. Despite the therapeutic and cost benefits of ORS, several studies established that they are less effective in reducing purging and duration of diarrhea illness [19].

ORS has undergone several modifications to improve their safety and effectiveness in diarrhea management, including reduced osmolarity formulations lower than the standard ORS [25]. ORS modifications have also extended to the incorporation of common food such as cereals (rice, wheat, maize, millet) and legumes [18]. Food-based ORS are better substitutes to standard ORS due to their accessibility, affordability, effectiveness, and higher nutritional benefits [18]. Starch in staples (such as rice, wheat, and millet) used as ORS is slowly degraded to glucose in the presence of amylase, which is abundant in the small intestine, including during diarrhoea. The resulting glucose released is involved in the co-transport of sodium and water across the intestinal epithelium, thereby circumventing the problem of increased osmolarity that may result when the concentration of glucose is further increased from the use of ORS≥310 [26]. Rice-ORS was reported to improve water and sodium absorption, reduce stool volumes, and provide shorter duration of diarrheal illness than standard glucose ORS in a rat model of osmotic diarrhoea [27]. Another study demonstrated that children receiving ORS prepared from cereals (maize, millet, wheat, sorghum, or rice) had substantially reduced stool outputs compared to those that were administered standard glucose ORS [28]. However, less is known about the functional effects of tuber-based oral ORS in diarrhoea pathophysiology despite their common use as traditional remedies for diarrhoea in many tropical and subtropical countries [29, 30]. Traditionally, the edible tuberous roots of plants including *Ipomea batatas* [31], *Colocasia esculenta* [32], and *Pachyrhizus erosus* [33]—commonly known as potato, cocoyam, and yam bean, respectively—have been used as remedies for diarrhoea. The aim of this study is to investigate the effect of ORS derived from tubers, including *Ipomea batatas, Colocasia esculenta, and Pachyrhizus erosus* on the activity of IAP and thus evaluate their potential to repair intestinal mucosa damage.

2. MATERIAL AND METHODS

2.1. Chemicals and Reagents

All reagents used for this study were of analytical grade. Glucose, sodium chloride, formalin, D-mannitol, and sodium hydrogencarbonate were obtained from the Department of Biochemistry, Lagos State University, Lagos, Nigeria. Alkaline phosphatase kit was acquired from Randox Laboratories Limited (Great Britain).

2.2. Collection and Authentication of Plant Materials

Ipomea batatas, Colocasia esculenta, and Pachyrhizus erosus tubers were obtained from Iyana-Iba market, Ojo, Lagos, Nigeria and authenticated at the Herbarium

of the Department of Botany, Lagos State University, Lagos, Nigeria.

2.3. Experimental Animals

Forty (40) weaning Wistar rats were obtained from the Lagos University Teaching Hospital (LUTH), Idi-Araba, Lagos, Nigeria. The rats were randomly grouped and placed in plastic cages, allowed to acclimatize for two weeks, and given free access to food and water for the entire period of the experiment.

2.4. Preparation of ORS

This was performed according to the procedure described by Vettorazzi *et al*; [34] with few modifications. 200 g portion of sweet potato, cocoyam, and jicama each were properly washed and cooked separately in 1000 ml of water for 30 min, dried for several days to remove all moisture present and then ground to powder. Afterward, 100 g of the respective sweet potato, cocoyam and jicama powder were used in place of glucose in standard ORS (comprising of the following in mmol/L: sodium, 90; chloride, 80; potassium, 20; glucose, 111; and a base, such as citrate tribasic or bicarbonate, 30) [35]. The powder was boiled in 1000 ml of water for 10 min and stirred continuously. The solution was brought to room temperature and then 300 ml of orange juice, 2.5 g of baking powder and 1.75 g of cooking salt respectively were added to provide the ions, chloride bicarbonate, sodium, and potassium. The resulting solution was allowed to cool and stored in a refrigerator.

2.5. Induction and Treatment of Diarrhoea

Following two weeks of acclimatization period, rats weighing between 150 g and 200 g were separated into six groups (n=6); the remaining 4 rats weighed below 120 g and were excluded. Group A (control) received food and water only; Group B was induced with osmotic diarrhoea and left untreated; Group C, D, E and F received WHO-, *Colocasia esculenta* -, *Pachyrhizus erosus*- and *Ipomea batatas*-ORS respectively, following osmotic diarrhoea induction. Osmotic diarrhoea was induced according to the procedure described by Elemo and Akinwande [36]. Briefly, animals were given doses of 5 ml/100 g body weight of 20% solution of D-mannitol daily between 9 am and 10 am for three days using an oral canular. Diarrhoea manifestation was ascertained in rats when they produced watery, soft, yellowish stools differing from the normal, pliable, soft, well-formed pellets as previously described by Boakye *et al*; [37]. Other signs that were monitored include the rate of food consumption, body weight, ruffled fur, hunched back and hair loss. Animals that showed no symptoms of diarrhoea were immunocompromised by oral administration of erythromycin (25 mg/kg body weight daily) for two days, and then administered double the initial dose of D-mannitol (5 ml/100 g body weight of 40% solution of D-mannitol).

2.6. Preparation of Mucosa Homogenates

At the end of the experimental period, the animals were weighed and sacrificed under ketamine anesthesia. Thereafter, the small intestine was immediately harvested and then homogenized. The nuclei and large cell fragments were removed by centrifugation at low speed, while the supernatant was placed in labelled Eppendorf tubes and stored in a refrigerator.

2.7. Histology

Sections of the small intestine (duodenum, ileum, and ileum) were excised and preserved in 10% formol-saline. The already fixed tissues in 10% formol-saline, after whole body perfusions, were transferred to a graded series of ethanol. They were placed in 70% and 90% alcohol for 1 hour respectively, and then transferred to three changes of absolute alcohol for another 1 hour each. The tissues were then cleared in xylene. Once cleared, the tissues were infiltrated in molten paraffin wax in the oven at 58°C. Two changes of molten paraffin wax at one-hour interval were made, after which the tissues were embedded in wax and blocked out. Prior to embedding, it was ensured that the mounted sections to be cut by the rotary microtome were oriented perpendicular to the long axes of the tissues. These sections were designated 'vertical sections'. Serial sections of 5 µm thick were obtained from a solid block of tissue; the sections were then floated out on warm water bath, picked by a clean slide which Mayer's egg albumin had been coated to cement the sections to the slides properly. Afterwards, they were passed through a mixture of equal concentration of xylene and alcohol and subsequently stained with hematoxylin and eosin following clearance in xylene. The sections were dried between 35°C and 40°C. The slides were viewed under a research microscope connected to a computer monitor for qualitative and quantitative evaluation.

2.8. Biochemical Analysis

2.8.1. Determination of Total Protein

Serum total protein was estimated by the Biuret method according to Doumas *et al*; [38], using Randox reagent kits.

2.8.2. Alkaline Phosphatase Activity

Alkaline phosphatase activity was assayed according to the method described in the Randox kit. Alkaline phosphatase activity was expressed as the amount of substrate (P-nitrophenylphosphate) in units per liter (U/l) hydrolyzed to p-nitrophenol and phosphate. Absorbance of samples were measured at 405 nm and 37°C using a spectrophotometer.

2.9. Statistical Analyses

Data were analyzed using GraphPad Prism. Values were expressed as mean ± standard error of mean (SEM). Variations within groups were assessed using

one way analysis of Variance (ANOVA) and Tukey's honest significant difference post hoc test.

3. RESULTS AND DISCUSSION

3.1 Intestinal alkaline phosphatase activity

The result of intestinal alkaline phosphatase activity in the control and treatment groups is presented in Fig. 1. Diarrhoea induction resulted in 46% decrease in IAP activity (Group B), compared to the control. However, animals that received WHO-ORS (Group C) and tuber-based ORS (Group D, E and F) had elevated IAP activity, compared to the control. The highest increase (48%) in IAP activity was observed in animals that were administered Ipomoea batatas-ORS (Group F). All changes recorded in the treatment groups were statistically not different from the control group (*P*=.05).

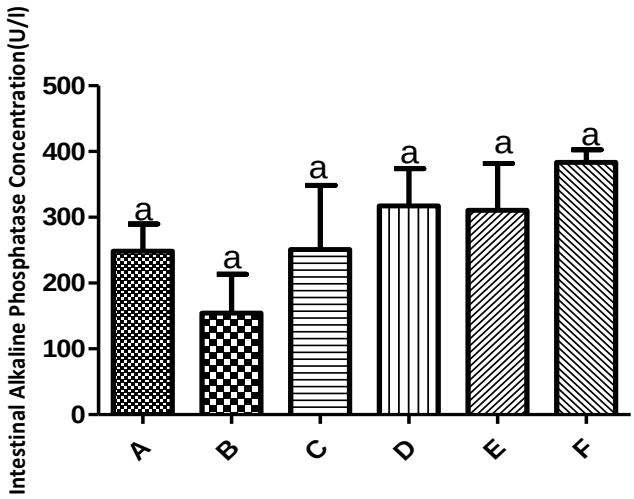

Figure 1: Intestinal alkaline phosphatase activity in experimental animals. Groups with the same superscript do not vary significantly at *P*=.05. Group A (control) received food and water only; Group B was induced with osmotic diarrhoea and left untreated; Group C, D, E and F received WHO-, *Colocasia esculenta* -, *Pachyrhizus erosus*- and *Ipomea batatas*-ORS respectively.

3.2. Serum albumin concentration

The concentration of serum albumin in experimental animals is shown in Fig. 2. All animal groups that were induced with diarrhoea had reduced serum albumin concentrations irrespective of WHO-ORS or tuber-based ORS treatment. The variations in serum albumin concentration among the experimental groups were not statistically significant compared to the control (*p*=.05).

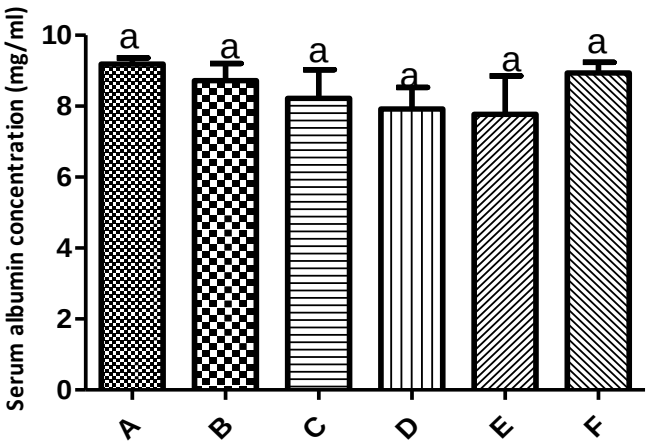

Figure 2: Serum albumin concentration in experiment animals. Groups with the same superscript do not vary significantly at *P*=.05.

3.3 Mean body weights of experimental animals

Figure 3 shows the effects of diarrhoea induction and oral rehydration therapy on mean body weights of animals during the experimental 3period. The body weights of animals that were induced with diarrhoea and left untreated (Group B) fluctuated during the entire period but showed a marked decrease after 3 days of diarrhoea induction, compared to the control. However, animals in other groups (Group C, D, E and F) exhibited an increase in body weights from the first to third day of ORS treatment, compared to the control. Animals administered *Colocasia esculenta*-ORS showed the highest increase in body weight after the last day of treatment.

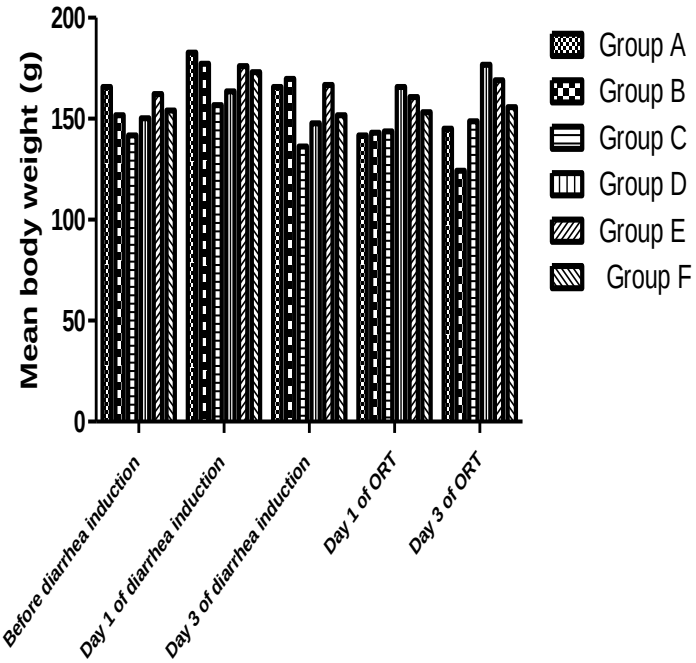

Figure 3: Effects of diarrhoea induction and Oral Rehydration Therapy on mean body weights of animals during the experimental period. Group A (control)

received food and water only; Group B was induced with osmotic diarrhoea and left untreated; Group C, D, E and F received WHO-, *Colocasia esculenta* -, *Pachyrhizus erosus*- and *Ipomea batatas*-ORS respectively.

3.4 Histographs of intestinal tissue sections of experimental rats

Group A: normal tissue pattern with well-preserved villi and sub-mucosal gland of Brunner were observed in the duodenum. Well-kept villi were also seen in the Jejunum. Ileum had well preserved villi, intact layers, normal cyto-architecture, and many Payer's patches are visible; **Group B:** duodenum showed disrupted cells in some villi and fewer submucosal glands. Jejunum possessed good villi with some cell loss; **Group C**: duodenum/duodenum-Jejunum (DJ) junction appeared well-kept with thick brush border and numerous Brunner's gland. Villi and mucosal cell are adequately preserved in some parts of jejunum with cryptic glands showing normal cellularity and architecture. Ileum had poor cellularity in villi, but a few Payer's patches are seen which appeared dislodged in position probably by processing; **Group D:** duodenum/DJ junction had normal appearances. Ileum displayed normal features, though villi are sectioned transversely. In the jejunum, villi showed considerable loss of cells along their borders in wide areas, while muscle layers appeared intact. **Group E**: duodenum appeared with shattered cells in some villi and shredded cells in the lumen. The presence of normal tissue architecture and villi as well as intact gland cells were observed at the DJ junction. In the Jejunum, many villi were denuded in significant features of mucosal cell and epithelial cell atrophy; **Group F:** duodenum appeared largely intact with a few areas of cell loss in the villi. Ileum had shattered villi in many areas with massive cell loss but possessed normal tissue architecture in muscle layers. Jejunum showed good tissue architecture with only minor cell loss seen in some villi.

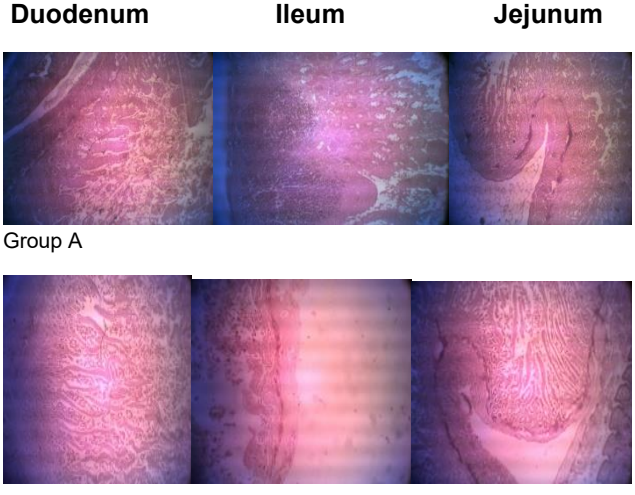

Figure 4: Micrographs of the small intestinal tissue sections (duodenum, Ileum and Jejunum) of experimental rats. Group A (control) received food and water only; Group B was induced with osmotic diarrhoea and left untreated; Group C, D, E and F received WHO-, *Colocasia esculenta* -, *Pachyrhizus erosus*- and *Ipomea batatas*-ORS respectively.

DISCUSSION

The use of staple food as ORS in the treatment of diarrhoea can offer numerous advantages, ranging from affordability to widespread accessibility [39]. Tubers, including sweet potato and cocoyam are among the most commonly consumed staples worldwide, especially in sub-Saharan Africa [40]. Yam bean, however, is a legume mainly cultivated for its large tuberous root. It has been reported to be underutilized globally, despite its suitability for wider food uses due to the paucity of information on its physicochemical, functional, nutritional, and rheological properties [41].

Results from this study showed that diarrhoeic animals administered tuber-based ORS had higher IAP concentrations compared to animals treated with WHO-ORS (**Fig.1**), suggesting that the tuber-based ORS possess a greater capacity to restore normal intestinal physiology following diarrhoea disease, compared to the WHO-ORS. Numerous studies have reported the efficacy of cereal- (including rice, maize, wheat, sorghum, and millet) as well as legume-(mainly bean (lentil)) derived ORS in diarrhoea treatment [26, 28, 41,

42]. Depleted IAP concentration (as observed in animals induced with diarrhoea but left untreated) is associated with increased intestinal pathophysiology [15]. Moreover, among all the animals that received tuber-based ORS, those administered sweet potato-ORS had the most elevated level of IAP. Sweet potato has an ample store of phytochemical compounds such as carotenoids, tocopherols, phenolic compounds, tannins, flavonoids, saponins, and anthocyanins, which have been reported to possess antioxidant, anti-inflammatory and bowel regulatory properties [43]. The presence of these phytoconstituents in sweet potato could be responsible for its most pronounced elevating effect on IAP, compared to the other tubers.

All animals induced with osmotic diarrhoea had reduced levels of serum albumin, compared to the control, which did not vary significantly (**Fig. 2**). This is in correlation with the study of Brinson and Kolts [44] that demonstrated a relationship between reduced serum albumin and diarrhoea. Similarly, Emejuo *et al;* [45] reported that decreased serum albumin level is linked with gastrointestinal disease. However, animals administered sweet potato ORS had their serum albumin level decrease only slightly compared to the control, thereby suggesting that sweet potato have the highest capacity to protect against rapid reduction in serum albumin levels that may accompany diarrhoea. This could be as a result of the broader range of micronutrients inherent in sweet potato, including manganese, copper, potassium, iron, vitamin B complex, vitamin C, vitamin E, and carotenoids, which may have promoted the metabolism of protein [43].

Assessment of body weights revealed that animals that were induced with diarrhoea and left untreated had a marked reduction in their body weights after about a week, compared to all other groups of animals (**Fig.3**). This suggests that ORS could play vital roles in the rejuvenation of muscle mass, prevention of rapid body fluid loss, replacement of volume lost in stools, and restoration of normal metabolic activities in animals with diarrhoea disease [28]. EMurugaiah *et al;* [18] demonstrated that food-based ORS reduced the duration and volume of purging and promoted early diarrhoea recovery. Moreover, Greenough [46] reported that cereal-based ORS produced significant reductions in stool volumes, compared to glucose-based ORS. In contrast, the study of Meyers *et a*l; [47] showed that cereal-based ORS did not offer significant advantage over glucose-based ORS in relation to the effects on stool volume and duration as well as weight gain.

Micrographs of small intestinal sections (duodenum, ileum, and jejunum) of experimental animals are shown in **Fig.4**. Diarrhoeic animals that received no treatment (Group B) had depleted Brunner's gland and cellular components which are suggestive of intestinal damage [48] while animals administered with WHO-ORS and tuber-based ORS after diarrhoea induction had improved intestinal mucosa features, similar to the control. The improvement in the intestinal histoarchitecture of animals that received tuber-based ORS, compared to animals induced with diarrhoea without ORS treatment revealed that tuber-based ORS has the potential to repair intestinal mucosa damage and restore normal intestinal cellularity.

4. CONCLUSION

The results revealed that tuber-based ORS had a higher enhancing effect on IAP activity than WHO-ORS. Tuber-based ORS and WHO-ORS showed the potential to repair intestinal mucosa damage and restore normal serum albumin concentration in animals with diarrhoea. There is a need to further investigate the nutritional and physiochemical properties responsible for the activity of the tuber-derived ORS in restoring normal gut homeostasis and repairing intestinal mucosa damage that accompany diarrhoea.

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COMPETING INTERESTS

The authors declare no competing interests.

AUTHORS' CONTRIBUTIONS

BE was involved in the conceptualization; BE and OF were involved in the methodology; RK, OA, SR and AZ carried out the experiment; OF and RK were involved in the analysis of data and review of the manuscript; OO supervised the experiment. All authors have read and approved the manuscript.

REFERENCES

1. Schiller LR. Evaluation of chronic diarrhea and irritable bowel syndrome with diarrhea in adults in the era of precision medicine. Am College Gastroenterol. 2018; 113(5): 660-669.
2. Kotloff KL. The burden and etiology of diarrheal illness in developing countries. Pediatr Clin North Am. 2017; 64(4): 799-814.
3. Kotloff KL, Nataro JP, Blackwelder WC, Nasrin D, Farag TH, Panchalingam S, et al. Burden and aetiology of diarrhoeal disease in infants and young children in developing countries (the Global Enteric Multicenter Study, GEMS): a prospective, case-control study. The Lancet. 2013; 382(9888): 209-222.
4. Cobo F. Imported infectious diseases: the impact in developed countries. 2014: Elsevier.
5. Clay PG and Crutchley RD. Noninfectious diarrhea in HIV seropositive individuals: a review of prevalence rates, etiology, and management in the era of combination

antiretroviral therapy. Infect Dis Ther. 2014; 3(2): 103-122.
6. Bawankule R, Shetye S, Singh A, Singh A, Kumar K. Epidemiological investigation and management of bloody diarrhea among children in India. PloS one. 2019; 14(9): e0222208.
7. Thiagarajah JR, Donowitz M, Verkman AS. Secretory diarrhoea: mechanisms and emerging therapies. Nat Rev Gastroenterol Hepatol. 2015; 12(8): 446-457.
8. Philip NA, Ahmed N, Pitchumoni CS. Spectrum of drug-induced chronic diarrhea. J Clin Gastroenterol. 2017; 51(2): 111-117.
9. Ugboko HU, Nwinyi OC, Oranusi SU, Oyewale JO. Childhood diarrhoeal diseases in developing countries. Heliyon. 2020; 6(4): e03690.
10. Niyibitegeka F, Riewpaiboon A, Youngkong S, Thavorncharoensap M. Economic burden of childhood diarrhea in Burundi. Glob Health Res Policy. 2021; 6(1): 1-12.
11. Mallick R, Mandal S, Chouhan P. Impact of sanitation and clean drinking water on the prevalence of diarrhea among the under-five children in India. Child Youth Serv Rev. 2020; 118: 105478.
12. Keusch GT, Fontaine O, Bhargava A, Boschi-Pinto C, Bhutta ZA, Gotuzzo E, et al. Diarrheal diseases. Disease Control Priorities in Developing Countries. 2006; 2: 371-388.
13. Zedie, F and Kassa D. Socio-economic, behavioral and environmental factors associated with diarrhea among under five children in health development and non-health development army member mothers in Wondogenet, south Ethiopia. Health Educ Care. 2018; 3(3): 1-8.
14. Gorkiewicz G, Thallinger GG, Trajanoski S, Lackner S, Stocker G, Hinterleitner T, et al. Alterations in the colonic microbiota in response to osmotic diarrhea. PloS one. 2013; 8(2): e55817.
15. Fawley J and Gourlay DM. Intestinal alkaline phosphatase: a summary of its role in clinical disease. J Surg Res. 2016; 202(1): 225-234.
16. Goldberg R, Austen WG Jr, Zhang X, Munene G, Mostafa G, Biswas S, et al. Intestinal alkaline phosphatase is a gut mucosal defense factor maintained by enteral nutrition. Proc Natl Acad Sci USA. 2008; 105: 3551-3556.
17. Ok M, Yildiz R, Hatipoglu F, Baspinar N, Ider M, Üney K, et al. Use of intestine-related biomarkers for detecting intestinal epithelial damage in neonatal calves with diarrhea. Am J Vet Res. 2020; 81(2): 139-146.
18. EMurugaiah C, Palasuberniam P, Falah M, Al-Talib H. Food based Oral Rehydration Therapy: Towards a Better Cholera Treatment. J Prob Health. 2016; 4(151): 2.
19. Harrell JE and Cheng SX. Inability to reduce morbidity of diarrhea by ORS: can we design a better therapy? Pediatr Res. 2018; 83(3): 559-563.
20. Wiens KE, Schaeffer LE, Sow SO, Ndoye B, Cain CL, Baunn MM, et al. Oral rehydration therapies in Senegal, Mali, and Sierra Leone: a spatial analysis of changes over time and implications for policy. BMC Med. 2020; 18(1): 1-13.
21. Ko W, Kwan E, Leung S, Poon K, Sin W, Wong Y, et al. Clinical Guideline. HK J Paediatr (new series). 2003; 8: 203-236.
22. Hartling L, Bellemare S, Wiebe N, Russell K, Klassen T, and Craig W. Cochrane review: Oral versus intravenous rehydration for treating dehydration due to gastroenteritis in children. Evidence-Based Child Health: Cochrane Rev J. 2007; 2(1): 163-218.
23. Nalin DR and Cash RA. 50 years of oral rehydration therapy: the solution is still simple. The Lancet. 2018; 392(10147): 536-538.
24. Bennett JE, Dolin R, Blaser MJ. Mandell, Douglas, and Bennett's Principles and Practice of Infectious Diseases E-Book. 2019: Elsevier Health Sci.
25. Mohanty N, Thapa BR, Mathai U Pai J, Mohanty N, Biradar V, et al. Low Osmolarity Oral Rehydration Salt Solution (LORS) in Management of Dehydration in Children. Indian Pediatr. 2021; 58(3): 266.
26. Gregorio GV, Gonzales ML, Dans LF, Martinez EG. Polymer-based oral rehydration solution for treating acute watery diarrhoea. Cochrane Database of Syst Rev. 2016; (12).
27. Wapnir RA, Litov RE, Zdanowicz MM, Lifshitz F. Improved water and sodium absorption from oral rehydration solutions based on rice syrup in a rat model of osmotic diarrhea. J Pediatr. 1991; 118(4): S53-S61.
28. Molla AM, Nath S, Molla A, Khatun M. Food-based oral rehydration salt solution for acute childhood diarrhoea. The Lancet. 1989; 334(8660): 429-431.
29. Das PR, Akter S, Islam MT, Kabir MH, Haque M, Khatun Z, et al. A selection of medicinal plants used for treatment of diarrhea by folk medicinal practitioners of Bangladesh. Am Eurasian J Sustain Agric. 2012; 6(3): 153-161.
30. Asnaashari S, Dastmalchi S, Javadzadeh Y. Gastroprotective effects of herbal medicines (roots). Int J Food Prop. 2018; 21(1): 902-920.
31. Panda V and Sonkamble M. Phytochemical constituents and pharmacological activities of Ipomoea batatas l.(Lam)–A review. Int J Res Phytochem Pharmacol. 2012; 2(1): 25-34.
32. Prajapati R, Kalariya M, Umbarkar R, Parmar S, Sheth N. *Colocasia esculenta*: A potent indigenous plant. Int J Nutr Pharmacol Neurol Dis. 2011; 1(2): 90-96.
33. Rawat M and Vimal V. Production Technology of Underutilized Vegetable Crops. 2023: Springer Nature.
34. Vettorazzi C, Mazariegos M, Molina S, Ramirez I, Solomons NW. Amylase-treated rice flour oral rehydration solution with enhanced energy density. II. In vivo studies of tolerance, energy intake, and rehydration efficacy in the

initial treatment of dehydrated diarrhoeic children. Food Nutr Bull. 1996; 17(2): 1-6.
35. Council NR. Nutritional management of acute diarrhea in infants and children. 1985.
36. Elemo B and Akinwande A. Effect of osmotic diarrhoea on the protein nutritional status of rat. Nigerian Q J Hosp Med. 2000; 10(2): 113-117.
37. Boakye PA, Brierley SM, Pasilis SP, Balemba OB. *Garcinia buchananii* bark extract is an effective anti-diarrheal remedy for lactose-induced diarrhea. J Ethnopharmacol. 2012; 142(2): 539-547.
38. Doumas BT, Watson WA, Biggs HG. Albumin standards and the measurement of serum albumin with bromcresol green. Clin Chim Acta. 1971; 31(1): 87-96.
39. Onyechi UA and Agu-Udemba MO. Nutrient Composition Of Cereal Based Oral Rehydration Solutions For Management Of Diarrhoea In Infants. Animal Research International. 2009; 6(1).
40. Rinaldo D. Carbohydrate and bioactive compounds composition of starchy tropical fruits and tubers, in relation to pre and postharvest conditions: A review. J Food Sci. 2020; 85(2): 249-259.
41. Buckman ES, Oduro I, Plahar WA, Tortoe C. Determination of the chemical and functional properties of yam bean (Pachyrhizus erosus (L.) Urban) flour for food systems. Food Sci Nutr. 2018; 6(2): 457-463.
42. Fontaine O, Gore S, Pierce NF. Rice-based oral rehydration solution for treating diarrhoea. Cochrane Database Syst Rev. 1998; (4).
43. Amagloh FC, Yada B, Tumuhimbise GA, Amagloh FK, Kaaya AN. The Potential of Sweetpotato as a Functional Food in Sub-Saharan Africa and Its Implications for Health: A Review. Molecules. 2021; 26(10): 2971.
44. Brinson RR and Kolts BE. Hypoalbuminemia as an indicator of diarrheal incidence in critically ill patients. Crit Care Med. 1987; 15(5): 506-509.
45. Emejuo, NT, OA Agina, IJ Udeani, UU Eze. Electrolytes, Serum biochemical and Acid-Base Disturbances in Dogs with Foul-Smelling Bloody Diarrhoea. Alex J Vet Sci. 2020; 66(1).
46. Greenough III WB. Cereal-based oral rehydration therapy. I. Clinical studies. The Journal of pediatrics. 1991; 118(4): S72-S79.
47. Meyers A, Sampson A, Saladino R, Dixit S, Adams W, Mondolfi A. Safety and effectiveness of homemade and reconstituted packet cereal-based oral rehydration solutions: a randomized clinical trial. Pediatr. 1997; 100(5): e3-e3.
48. Wang Y, Tan J, Sutton-Smith M, Ditto D, Panico M, Campbell RM, et al. Modeling human congenital disorder of glycosylation type IIa in the mouse: conservation of asparagine-linked glycan-dependent functions in mammalian physiology and insights into disease pathogenesis. Glycobiol. 2001; 11(12): 1051-1070.