

## MAKING THE MEDICINES EASIER FOR PEDIATRIC DIARRHEA PATIENTS

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### DIARRHEA: A BABY KILLER

Diarrhea is the second leading cause of death in children under the age of five. It accounts for approximately one in every six deaths amongst this age group worldwide. Though the global under-five mortality from acute diarrhea has decreased, acute and persistent diarrhea continues to take a huge toll on children's health in developing countries (WHO 2006).

Diarrhea can lead to dehydration, loss of electrolytes, and malnutrition which represents a significant burden on the health system, the household, and the nutritional status of children. The most common sources of diarrhea are related to unclean water, dirty hands at mealtime, and spoiled food. The means to prevent diarrhea through water supply treatment, sanitation, and hygiene have been well documented. Yet, each year, roughly 1.5 billion episodes of acute and persistent diarrhea still occur among children under the age of five and most of them live in developing and emerging countries.

Prevention is always the best treatment for any disease and diarrhea is not an exception to that rule. Despite the hard and dedicated work of so many; infants and toddlers still get sick. The treatment for diarrhea in children is well documented and relatively inexpensive. However, getting the treatments to the child is a problem but getting the child and caregiver to complete a 10 day treatment is often the larger challenge.

### FINISHING THE COURSE IS A HURDLE

Patient compliance is a substantial health issue which is significantly magnified when dealing with children. Compliance is especially challenging when treating diarrhea. The

**"Diarrhea is the world's most effective weapon of mass destruction."**

-- Rose George  
in *"The Big Necessity: The Unmentionable World of Human Waste and Why it Matters"*

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WHO now recommends the use of Zinc supplements as part of an oral rehydration therapy as the most cost effective and safe treatment for diarrhea. However, effective treatment with Zinc supplements means taking the medication daily for one to two weeks. It becomes increasingly more difficult to maintain treatment regiment with each passing day, as the child appears to be no longer “sick”. Caregivers forget to give the medicine. The children forget to ask for the medicine. Also, many of the Zinc treatments involve mixing a powder with food or drink. That means multiple steps for the care provider and sometimes it’s a hassle to get the child to finish the food or drink. Using an oral thin film (often referred to as a “strip”) simplifies the process; the strip is removed from the packaging, placed on the inner cheek in the mouth and it quickly dissolves while releasing the active ingredient. Furthermore, using a strip as a vehicle for delivery, the medicine can be made palatable and quick dissolving; therefore it is more likely to actually be consumed. Additionally, the risk of having a child refuse or even spit out the medicine is greatly decreased when using a strip as an alternative to other delivery forms such as liquids or tablets.

## Historical Standards for Dealing with Diarrhea

### Prevention

The best way to deal with diarrhea, like any disease, is to prevent it in the first place. There has been considerable effort put into providing safer water and foods through better hygiene practices especially in regions with high diarrhea incident rates. This helps reduce the problem but not eliminate it completely. Prevention does not help the person once they contract diarrhea.

### Oral Rehydration Therapy

For most adults, diarrhea will usually resolve itself in 1-3 days with no treatment other than drinking plenty of clean water to avoid dehydration. Unlike adults, dehydration in children can occur quickly and with dire consequences. Dehydration in children or anyone with a compromised immune system must be treated promptly to avoid serious health problems, such as organ damage, shock, coma or even death. Oral Rehydration Therapy (ORT) is a combination of water, glucose and electrolytes (sodium, potassium, chloride ions) taken as a drink to replace the ones lost during the diarrhea bout.

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## Anti-diarrhea Medications

Over-the-counter medicines such as Imodium (loperamide) or Pepto-Bismol and Kaopectate (bismuth subsalicylate) may help stop diarrhea in adults. However, if diarrhea is caused by bacteria or parasites, over-the-counter medicines may prolong the problem. Furthermore, medications to treat diarrhea in adults can be dangerous for infants and children and should only be given with a doctor's guidance.

## Zinc Supplements

Studies have shown that Zinc treatment results in a 25- percent reduction in duration of acute diarrhea and a 40- percent reduction in treatment failure or death in persistent diarrhea (Bhutta, AJCN, **2000**). The studies determined that a 10-day therapy of Zinc treatment can considerably reduce the duration and severity of diarrheal episodes, decrease stool output, and lessen the need for hospitalization. Zinc may also prevent future diarrhea episodes for up to three months. (Bhandari, Paediatrics, **2008**)

Zinc treatment is a critical new tool for treating diarrheal episodes among children in the developing world. This safe, effective, and inexpensive treatment option can lead to significantly less severe diarrhea in children and may help prevent future episodes.

WHO and UNICEF specifically recommend the use of Zinc treatment, as well as a new formulation of oral rehydration solution (ORS), as a two-pronged approach to treatment of acute diarrhea in children. This involves a 10 day treatment of 10 mg Zinc per day for 10 days for infants less than six months of age and 20 mg dosing for older children.

## OAK Pediatric Electrolytes, Pediatric Micronutrient Formulation (PMF) and a Proposed OAK Rehydration Supplement (ORS).

The OAK Electrolyte product (sodium, potassium, and chloride ions) is currently sold in Japan. <http://global.rakuten.com/en/store/yellow1/item/10004485/>

The OAK PMF product is new and has undergone market acceptability testing in El Salvador and Uganda. The children found the strips more enjoyable than chewable tablets and they liked the taste too. The caregivers also found that this dissolvable strip delivery method was easy to administer and they enjoyed not having the children complain. This strip contains Vitamins A, C, D, and E as well as a Vitamin B complex and Zinc.

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Experience developing these two products can be combined to develop an easy, convenient, oral dissolvable product that could be used as an integral part of an oral rehydration therapy.

An added benefit of oral thin film is its potential as a means to deliver active ingredients using oral absorption (oral trans-mucosal). This allows the active ingredients to get to where they are needed without relying on being absorbed in the stomach or intestines. This is a benefit, especially with a disease like diarrhea.

## State of Research

### Development of an OAK ORS product

A new OAK ORS product has been created by reformulation of the existing Electrolyte product by adjusting the dosing of electrolytes for pediatric patients and adding a blend of encapsulated and non-encapsulated Zinc to the formulation. Low dosing per strip can be used to gain maximum flexibility for adjusting for the weight of the child.

Further research into buccal and other trans-mucosal deliver can improve the efficiency of this product.

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