Universal Library of Business and Economics Research Article

ISSN: 3064-9951

Open Access | PP: 06-13

DOI: https://doi.org/10.70315/uloap.ulbec.2022.002

Stability and Product–Packaging Compatibility of ORS Formulations: A Comparative Study of Powder Barriers and the Case for Liquid Transition

Bekhzad Yuldashev

Strategic Operations Leader and Former CEO of Bayan Medical (Meros Pharm Group)", Windermere, Florida.

Abstract

This article examines the factors that determine the stability and product–packaging compatibility of pediatric oral rehydration salts (ORS) in both powder and ready-to-use liquid dosage forms. The relevance of the study is defined by the persistent burden of diarrheal disease in children and by the central role of oral rehydration therapy in preventing severe dehydration. Particular attention is given to the effects of package moisture permeability, seal integrity, and storage conditions on the physicochemical stability of ORS powder blends, as well as to the technological advantages of transition to pre-mixed oral solutions. The paper compares multilayer flexible packaging materials used for powders with bottle-based systems used for liquids. It is shown that, for hygroscopic ORS powders, the highest level of protection is provided by high-barrier laminates incorporating an aluminum layer, whereas for ready-to-use oral solutions the critical issue is the integrity of the primary container closure system rather than moisture transfer through flexible films. As an example of localization in Uzbekistan, the paper additionally considers Regidreyd (dextrose; sodium chloride; potassium chloride; sodium citrate dihydrate), an oral solution manufactured by Samarkand England Eco-Medical in 100 ml, 250 ml, and 500 ml bottles. The concluding argument is that the selection of packaging for pediatric ORS should be determined not only by economic considerations, but by the correspondence between dosage form and container system: high-barrier stick-packs for powders, and sealed bottle-based systems for liquid ready-to-use formulations.

Keywords: *Oral Rehydration Salts, Pediatrics, Pharmaceutical Packaging, Drug Stability, Vapor Permeability, Maillard Reaction, Pharmaceutical Market of Uzbekistan, Hygroscopicity, GMP, Stick Pack.*

INTRODUCTION

The problem of acute intestinal infections and the dehydration associated with them continues to carry substantial medical and social significance in pediatrics [7, 8]. Diarrheal diseases remain among the leading causes of mortality in young children, especially in low- and middle-income countries [9, 10, 12]. Oral rehydration therapy is regarded as the basic and most accessible method [16] for preventing severe complications of dehydration [14], while low-osmolarity oral rehydration salts are included among the essential medicines recognized by the World Health Organization [1–6].

For the Republic of Uzbekistan, this issue has not only a clinical dimension, but also an organizational and pharmaceutical one. According to WHO assessments, the country's health system in 2019 was undergoing an active phase of reform; at the same time, a significant share of healthcare expenditure was attributable to medical goods, primarily medicines, while the accessibility of therapy for the population depended to a considerable extent on the cost and actual availability of pharmaceutical products [29]. Under such conditions, questions related to the stability of dosage forms, shelf life, and the preservation of product quality during transportation and storage acquire particular practical importance [29].

In methodological terms, this means that pediatric ORS in Uzbekistan should be analyzed through at least two different packaging paradigms: moisture-protective flexible packaging for powders and container–closure systems for ready-to-use liquids.

Powdered ORS dosage forms are sensitive to moisture exposure, and for that reason their therapeutic reliability is determined to a large extent by the barrier properties of the package, the integrity of the seals, and compliance with storage conditions. This is especially important for countries with hot climates and a substantial logistical burden, since moisture uptake by the blend may lead to caking, impaired flowability, and deterioration of the product's consumer characteristics. Therefore, the selection of an optimal packaging system for pediatric ORS should be considered part of the broader task of ensuring both the quality and the accessibility of therapy [20–32].

The aim of the study is to provide a scientific rationale for selecting an optimal packaging system for pediatric ORS, taking into account barrier characteristics, seal integrity, and storage conditions, as well as to assess the economic efficiency of a modernized packaging process at a local pharmaceutical manufacturing site.

The scientific novelty of the study lies in the development of an authorial model for optimizing the packaging process of pediatric ORS formulations, a model that integrates requirements for microbiological purity, the barrier properties of multilayer films, and cost reduction through minimized material consumption during the transition to stick-pack packaging.

The author's hypothesis assumes that the use of high-barrier laminates with an aluminum layer in a stick-pack format ensures preservation of the stability of the standard ORS formulation for 24 months in climatic zones IVa and IVb, while at the same time making it possible to reduce production costs by 15–20% compared with traditional packaging formats.

MATERIALS AND METHODS

The methodological foundation of the study consisted of a systematic analysis of regulatory and scientific sources published between 2017 and 2019, supplemented by product-specific and technological data provided for the present work. The source base included WHO and UNICEF documents on ORS, publications addressing the clinical use of low-osmolarity rehydration solutions in children, studies on the hygroscopic behavior of powder blends, and research focused on the barrier properties of multilayer packaging materials.

The comparative technical analysis was conducted along two main packaging pathways. The first pathway concerned powdered ORS, for which the physicochemical and barrier characteristics of multilayer flexible packaging materials polyethylene terephthalate (PET), low-density polyethylene (LDPE), aluminum foil (Al), and metallized PET (VMPET) were evaluated using water vapor transmission rate (WVTR) and oxygen transmission rate (OTR) as the principal comparison parameters.

The second pathway concerned liquid ORS presentations, in which the central analytical focus was shifted from flexible-film permeability to the container–closure system. According to the supplied manufacturing data, the oral solution presentation was filled into an infusion-solution bottle without a rubber cap, whereas the infusion line used plastic bottles manufactured by blow-fill-seal (BFS) technology, with the bottle fitted with a rubber cap. These configurations were analyzed separately in order to avoid conflating the requirements applicable to powder sachets/stick-packs with those relevant to liquid bottle-based systems.

RESULTS AND DISCUSSION

Oral rehydration salts are complex multicomponent systems comprising anhydrous glucose, sodium chloride, potassium chloride, and sodium citrate. In accordance with WHO standards adopted in 2003 and still reflected in the 2019 essential medicines framework, preference is given to the low-osmolarity formulation with a total osmolarity of 245 mOsm/L, since this composition is associated with a reduction in the frequency of vomiting and a decrease in the need for intravenous therapy in children by approximately one third [1, 13, 17].

Below, Table 1 presents the composition of low-osmolarity oral rehydration salts according to the WHO and UNICEF.

Table 1. Composition of low-osmolarity oral rehydration salts according to the WHO and UNICEF (compiled by the author based on [1, 2]).

Component	Chemical formula	Concentration (g/L)	Role in the physiology of rehydration
Sodium chloride	NaCl	2.6	Replenishment of sodium and chloride ion deficits
Glucose (anhydrous)		13.5	Stimulation of sodium and water cotransport
Potassium chloride	KCl	1.5	Prevention of hypokalemia
Sodium citrate (dihydrate)		2.9	Correction of metabolic acidosis
Total osmolarity		245 mOsm/L	Optimal absorption gradient

The principal factor limiting the shelf life of oral rehydration salts is the high hygroscopicity of their components. Anhydrous glucose and the constituent salts, once brought into contact with atmospheric moisture, form microfilms of saturated solutions on the crystal surface, which leads to the phenomenon commonly described as caking. This process does not merely complicate the use of the product in practical terms; it also initiates chemical degradation [18, 19].

A key destructive mechanism in ORS is the Maillard reaction, that is, non-enzymatic browning caused by the interaction of the carbonyl group of glucose with amino groups of impurities or auxiliary substances, with the process becoming more pronounced in the presence of moisture. Powder darkening toward a yellow-brown shade may therefore be regarded as a direct visual indicator of declining product quality and loss of acceptable stability characteristics [20, 23]. In moisture-sensitive powder systems, even a modest increase in water activity can accelerate undesirable physicochemical transformations, which is precisely why protection from water vapor ingress becomes a decisive packaging function rather than a secondary technical consideration [20, 23, 24].

To ensure the stability of pediatric formulations that are sensitive to moisture, multilayer laminates with high barrier performance are required. In this setting, packaging efficiency is determined above all by the water vapor

transmission rate (WVTR), since that parameter directly affects the slowing of sorption processes and the prevention of component degradation. Oxygen barrier performance also remains important, although, for ORS powders, resistance to moisture transfer is typically the more critical variable in preserving the original state of the formulation during storage [21–25].

Table 2 presents the results of a comparative assessment of the barrier properties of flexible packaging materials.

Table 2. Comparative characteristics of the barrier properties of flexible packaging materials (compiled by the author based on [21, 22, 25, 27, 28]).

Type of laminate	Barrier layer	WVTR (g/m²/day)	Oxygen permeability (cc/m²/day)
PET/PE	None	1.0–10.0	45–65
PET/VMPET/PE	Metallized layer	0.5–5.0	0.1–1.0
PET/Al/PE	Aluminum foil	~0.01	~0.00
PET/AlOx/PE	Aluminum oxide	0.5–2.0	0.5–2.0

Aluminum foil with a thickness of 7–9 μm, when incorporated into a multilayer laminate structure, provides nearly complete protection against moisture and gases. Even so, during transportation and repeated flexing particularly under the conditions associated with delivery to rural areas of Uzbekistan microcracks may form in the foil layer, and these defects are capable of compromising the barrier performance of the package. Under such circumstances, metallized films (VMPET) tend to demonstrate greater mechanical resilience, although their permeability remains 50–100 times higher than that of aluminum foil [21, 25]. For pediatric ORS formulations, where long-term stability over a period of up to 2–3 years is critical, the PET/Al/PE combination still tends to be regarded as the "gold standard" [21–25].

Regional dynamics in ORS consumption reveal pronounced variation, and that variation directly shapes the requirements imposed on packaging systems and logistical solutions [26]. In the United States and Europe, the comparatively mature state of the market drives demand for ready-to-use and flavored dosage forms, with emphasis placed on convenience, patient acceptability, and the preservation of stability over extended storage periods. In Uzbekistan, by contrast, given the combination of harsh climatic conditions and the remoteness of part of the consumer base, the decisive consideration has traditionally been the resistance of the package to moisture, temperature fluctuations, and mechanical stress. That circumstance explains the priority assigned to high-barrier multilayer laminates in the case of locally relevant powder ORS formulations [20–32].

At the same time, the present analysis shows that the packaging discussion in Uzbekistan can no longer be limited to dry formulations alone. According to the product data supplied for this study, the local market also includes Regidreyd (dextrose; sodium chloride; potassium chloride; sodium citrate dihydrate), registered as an oral solution in 100 ml, 250 ml, and 500 ml bottles, manufactured by Samarkand England Eco-Medical, СП ООО. This fact is analytically important, because it requires a distinction between the packaging logic of powdered ORS in sachet or stick-pack format and that of ready-to-use oral solutions in bottles. The presence of a localized ready-to-use oral solution in the Uzbek pharmaceutical market changes the analytical scope of the present study.

The inclusion of this product in the present discussion is methodologically significant. Unlike dry ORS powders, which require protection from environmental moisture ingress, the oral solution is already in the hydrated state. Accordingly, the decisive issue in such a case is no longer the WVTR of a flexible laminate, but the integrity and compatibility of the primary bottle system throughout storage and distribution. Figure 1 will present a forecast of the global ORS market volume through 2034.

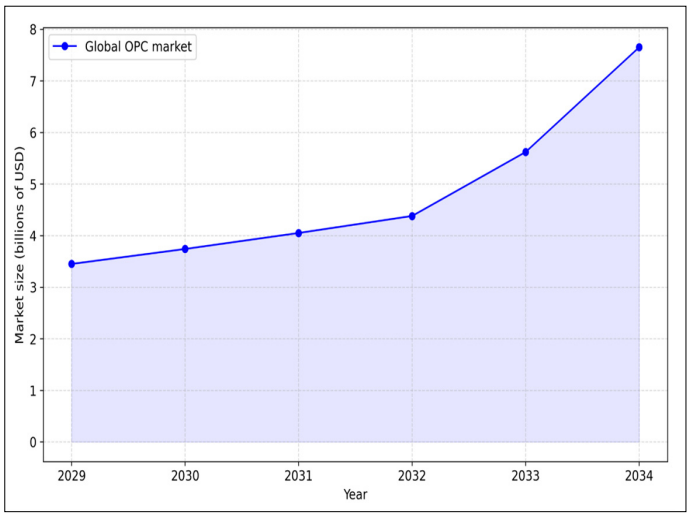

Figure 1. Forecast of the global ORS market volume through 2034 (compiled by the author based on [11, 23, 29]).

In the context of the late-2019 period, greater analytical value lies not in speculative commercial forecasts of the ORS market but in the practical task of ensuring the accessibility and quality of rehydration therapies used in pediatric care. For the Republic of Uzbekistan, this consideration appears especially relevant due to the large size of the child population.

Assessments published by the World Health Organization suggest that the health-care system of Uzbekistan in 2019

was undergoing a phase of active structural reform. Within this environment, a considerable share of health expenditure continued to be directed toward medical commodities, primarily pharmaceutical products, which in turn increased the importance of ensuring local access to stable and high-quality medicinal formulations [29, 30, 34].

Additional relevance arises from the government's policy aimed at strengthening the national pharmaceutical industry. The Presidential Decree of the Republic of Uzbekistan dated 10 April 2019 introduced a set of measures intended to accelerate the development of the pharmaceutical sector, including the expansion of domestic manufacturing capacity and the modernization of sectoral infrastructure [30, 34, 35]. In this context, the investigation of stability and compatibility within the "product–package" system for pediatric ORS in Uzbekistan may be viewed as part of a broader effort to improve the quality and reliability of pharmaceutical provision for the population [29–31].

The implementation of a production modernization project at the Samarkand pharmaceutical plant SEEM (Samarkand England Eco-Medical) emerged as a response to the market demand for locally manufactured, high-quality ORS products intended for children. The proposed engineering solution initially involved adapting the packaging line for the manufacture of stick-pack powder formats instead of conventional four-seal sachets. Such a configuration allowed a reduction in material consumption while improving dosing precision, while preserving the long-term stability of the powdered medicinal product (see Fig. 2).

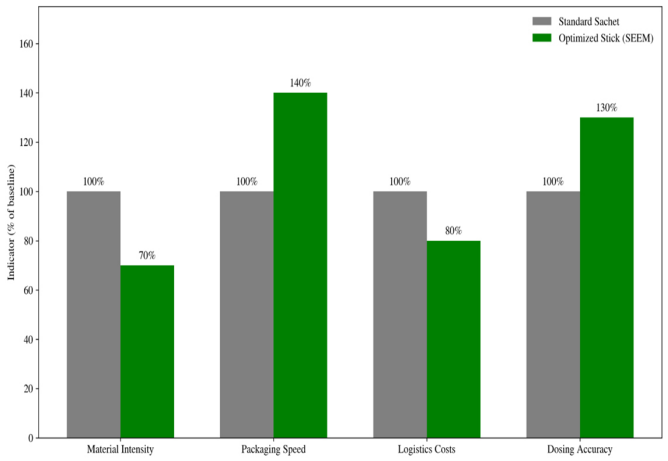

Figure 2. Efficiency of stick-pack implementation at the SEEM plant (compiled by the author based on [29-31]).

However, the technological relevance of the SEEM case is broader than powder packaging alone. The data supplied for the present work indicate that different dosage forms at the enterprise were associated with different primary packaging concepts. In particular, the infusion line used plastic bottles manufactured by blow-fill-seal (BFS) technology, with the bottle fitted with a rubber cap. By contrast, the oral solution presentation was filled into an infusion-solution bottle without a rubber cap. Since the article simultaneously discusses powder stick-pack production and liquid bottle-based presentations, these configurations must be clearly distinguished. In order to avoid conflating dry powder packaging with liquid bottle-based systems, the dosage forms and container configurations considered in the present study are differentiated in Table 3.

Table 3. Differentiation of dosage forms and primary packaging systems discussed in the study.

Product / line	Dosage form	Primary packaging format	Closure characteristic	Main packaging risk
Pediatric ORS powder	Powder for oral reconstitution	Sachet / stick-pack	Heat-sealed laminate	Moisture ingress, caking, browning
Oral solution (Regidreyd)	Ready-to-use oral solution	Bottle (infusion-solution type bottle)	Without rubber cap	Container integrity, physicochemical stability in liquid phase
Infusion line	Infusion solution	Plastic BFS bottle	With rubber cap	Closure integrity, hermeticity, suitability of BFS system

The distinction presented above is crucial for the correct interpretation of the results. The comparative analysis of WVTR, OTR, and laminate barrier performance applies primarily to powdered ORS, whereas the analysis of liquid oral and infusion presentations must be based on the characteristics of the container–closure system rather than flexible-film permeability.

The modernization of the packaging process at the SEEM plant made it possible to obtain substantial technological and economic gains. The decision to refuse from purchasing costly horizontal sachet machines in favor of vertical multilane form-fill-seal equipment (VFFS) designed for stick-pack production yielded investment savings of 15–20% per unit of installed capacity. At the same time, reducing the film area required per dose from 700 mm^2 to 550 mm^2 led to a 22% decrease in packaging cost [15, 22].

The transition to stick packs also had a favorable effect on ease of use and consumer acceptance. The geometry of the package makes it easier to pour the powder into the narrow neck of a child's bottle, thereby reducing the risk of product spillage by 30–40%, a point of more than minor importance in the case of relatively costly medicinal products [22].

Product quality, meanwhile, remained fully consistent with the WHO formula, and the high seal integrity achieved in the new format ensured preservation of compositional stability during storage under the elevated temperature conditions typical of the Samarkand region [1, 2, 23].

Nevertheless, the practical significance of the stick-pack solution should be interpreted within the limits of the powder dosage form. In the case of a ready-to-use oral solution, convenience is achieved not through improved pour control of a dry mixture, but through the elimination of the reconstitution step altogether. This shift reduces user-dependent preparation error and changes the hierarchy of packaging risks. For that reason, a direct comparison between powder stick-packs and bottled oral solution should be made not only in economic terms, but also in terms of their distinct quality determinants. Since the dominant mechanisms of instability differ between powders and ready-to-use liquids, the corresponding packaging requirements should be compared separately, as shown in Table 4.

Table 4. Comparison of critical packaging determinants for powdered and liquid ORS presentations.

Parameter	Powdered ORS in sachet/stick-pack	Ready-to-use oral solution in bottle
Physical state	Dry hygroscopic blend	Pre-mixed aqueous solution
Main cause of quality loss	Moisture uptake from environment	Loss of closure integrity / instability in liquid phase
Critical packaging function	High water-vapor barrier	Hermetic bottle–closure system
Main technical indicators	WVTR, OTR, seal integrity	Closure integrity, container compatibility, shelf-life stability
Typical visible defect	Caking, clumping, browning	Leakage, instability, contamination risk
User stage	Requires reconstitution before administration	Ready to use

As Table 4 demonstrates, the preferred packaging solution depends directly on the dosage form. High-barrier flexible laminates remain the rational option for powders, whereas bottle-based systems are more appropriate for ready-to-use liquid formulations.

A comparative analysis of the effectiveness of packaging systems should rest on an integrated approach that takes into account total cost of ownership (TCO) together with the potential risks of complaints and product claims. That approach makes it possible to evaluate not only the cost of materials and equipment as such, but also the long-term resistance of the product to degradation, the convenience of use for the end consumer, and conformity with regulatory requirements (see Table 5).

Table 5. Comparative analysis of ORS packaging formats (compiled by the author based on [22]).

Comparison factor	Conventional sachet	Modern stick pack
Material consumption (per 1,000 doses)	0.7–0.8 m^2	0.5–0.6 m^2
Material costs ($/1,000 units)	$30–$40	$25–$32
Child-use accessibility (pour control)	Low (wide cut)	High (narrow spout)
Packaging speed (line output)	40–60 units/min	60–100 units/min
Dosing error	±5–8%	±2–3%
Overall efficiency	Baseline	+20–25% profit

The obtained results suggest that the use of multilayer PET/Al/PE laminates in a stick-pack configuration can noticeably reduce the probability of moisture ingress by approximately 15–18% when compared with traditional sachets manufactured from comparable materials. The effect appears to arise primarily from the reduction in the overall length of heat-sealed seams per unit volume of product. Fewer and shorter seams, somewhat paradoxically, translate into fewer potential pathways through which water vapor may diffuse into the interior of the package, a factor repeatedly emphasized in studies dealing with barrier integrity and microdefects in flexible packaging structures [21, 25].

At the same time, the present study indicates that this conclusion should not be generalized to all pediatric ORS products irrespective of dosage form. For powdered formulations, minimizing moisture transfer remains the principal packaging objective. For liquid oral solutions, including the localized product Regidreyd, the decisive issue is the performance of the bottle-based primary package. Thus, the practical outcome of the analysis is not the identification of a single universal package, but the substantiation of a dosage-form-specific packaging strategy.

Such a reduction in moisture penetration carries particular importance for powdered ORS formulations. Maintaining the anhydrous state of glucose within the mixture remains essential, since even minor water uptake can initiate localized dissolution and subsequent recrystallization processes in contact with the surrounding salts. The resulting microstructural changes often manifest as caking and loss of powder flowability, and over longer storage periods may

accelerate chemical interactions between components. Consequently, improved seam geometry and enhanced barrier protection directly contribute to the long-term physicochemical stability of the formulation and, ultimately, to the preservation of the therapeutic effectiveness of oral rehydration salts [20, 23, 24].

CONCLUSION

The conducted study has shown that the stability of pediatric oral rehydration products is determined not only by the correctness of the pharmaceutical formulation, but also by the quality of the packaging system as an independent factor in ensuring therapeutic reliability. For powdered ORS mixtures containing glucose and mineral salts, critical importance attaches to protection against moisture, the integrity of heat-sealed seams, and compliance with regulated storage conditions. It is precisely the product–package system, taken as a whole, that shapes the actual shelf life of the preparation and its capacity to preserve its initial physicochemical properties throughout the circulation period.

At the same time, the results of the present study show that these requirements cannot be transferred without modification to ready-to-use liquid formulations. In the case of a bottled oral solution, the key quality determinants are associated not with the moisture permeability of a flexible laminate, but with the integrity and compatibility of the primary bottle–closure system.

The analysis of the scientific and regulatory literature published between 2017 and 2019 confirmed that the principal risk of ORS degradation is the absorption of atmospheric moisture, which leads to powder caking, deterioration of flowability, and the initiation of chemical changes, including non-enzymatic browning of the Maillard type. It was established that even where the nominal composition remains formally unchanged, moisture uptake reduces the technological suitability and consumer acceptability of the mixture and, consequently, its clinical reliability in pediatric practice. This makes it possible to conclude that the moisture-protective characteristics of packaging should be regarded as one of the key quality criteria for pediatric ORS formulations alongside pharmacopoeial indicators.

A comparison of the barrier properties of modern flexible packaging materials demonstrated that the most effective protection for hygroscopic powdered ORS mixtures is provided by multilayer laminates incorporating an aluminum layer, above all structures of the PET/Al/PE type. Taken together in terms of WVTR and OTR, such materials outperform both foil-free solutions and metallized analogues, providing what is, in practical terms, the highest barrier against the transfer of moisture and gases. At the same time, it was found that high material barrier performance alone is not sufficient in the absence of proper technological discipline: any loss of seal integrity, microdamage during transportation, or storage under conditions of elevated temperature and humidity may nullify the advantages of even a high-barrier package.

However, the present study also demonstrates that liquid ORS products require a different evaluative framework. The example of Regidreyd, an oral solution manufactured in Uzbekistan in 100 ml, 250 ml, and 500 ml bottles, confirms the practical relevance of bottle-based ready-to-use presentations in the local pharmaceutical context. In addition, the technological data analyzed in this article indicate the need to distinguish between oral solution bottles without a rubber cap and plastic BFS infusion bottles with a rubber cap, since these systems belong to different product categories and involve different packaging risks.

Under the conditions of Uzbekistan, the conclusions of the study carry particular practical significance. In a setting defined by health-system reform, the development of local pharmaceutical manufacturing, and the need to improve the accessibility of quality medicines for children, the selection of reliable packaging for ORS should be considered an element of the broader state task of pharmaceutical provision. Given the climatic features of the region, the logistical burdens involved, and the risk of prolonged storage under unstable conditions, it is specifically high-barrier packaging solutions that are capable of preserving product quality at every stage of the supply chain from manufacture to the final consumer.

Thus, the stated objective of the study has been achieved: it has been scientifically substantiated that the optimal packaging system for pediatric ORS should be determined according to dosage form. For powdered ORS, the preferred solution consists of individually sealed packets made of multilayer high-barrier laminates, primarily those based on aluminum foil, provided that strict control over seal quality and compliance with storage conditions are maintained. For ready-to-use liquid ORS, the more appropriate system is a sealed bottle-based primary package, in which the decisive parameters are closure integrity, material compatibility, and maintenance of product quality throughout the declared shelf life.

The practical conclusion of the work is that, in the development and localization of ORS production, priority should be given not merely to the minimization of initial packaging costs, but to the selection of a packaging concept appropriate to the formulation itself. For powders, this means maximizing moisture protection through high-barrier stick-pack or sachet structures; for liquids, it means selecting a bottle–closure system capable of maintaining hermeticity and stability under storage and distribution conditions. This position may serve as a methodological basis for the further standardization of packaging solutions in pediatric pharmacy and for the improvement of local production of rehydration products in Uzbekistan.

REFERENCES

1. World Health Organization. (2019). WHO model list of essential medicines (21st list). Geneva, Switzerland: World Health Organization. Retrieved from: https://iris.who.int/handle/10665/325771 (date accessed: November 12, 2019).
2. UNICEF Supply Division. (2019). ORS low osmolarity, powder for oral solution. Retrieved from: https://supply.unicef.org/s1561133.html (date accessed: October 21, 2019).
3. Global Health Supply Chain Program. (2019). Oral rehydration (MNCH commodities: Oral rehydration). Retrieved from: https://www.ghsupplychain.org/sites/default/files/2019-02/MNCH%20Commodities-OralRehydration.pdf (date accessed: September 18, 2019).
4. Troeger, C., Khalil, I. A., Rao, P. C., Cao, S., Blacker, B. F., Ahmed, T., ... Mokdad, A. H. (2017). Estimates of global, regional, and national morbidity, mortality, and aetiologies of diarrhoeal diseases: A systematic analysis for the Global Burden of Disease Study 2015. The Lancet Infectious Diseases, 17(9), 909–948. https://doi.org/10.1016/S1473-3099(17)30276-1
5. Billah, S. M., Sarker, A. R., Moinuddin, M., Rahman, M. M., Islam, Z., & Arifeen, S. E. (2019). Bangladesh: A success case in combating childhood diarrhoea. Journal of Global Health, 9(2), 020803. https://doi.org/10.7189/jogh.09.020803
6. Gregorio, G. V., Gonzales, M. L. A., Dans, L. F., & Martinez, E. G. (2016). Polymer-based oral rehydration solution for treating acute watery diarrhoea. Cochrane Database of Systematic Reviews, 12, CD006519. https://doi.org/10.1002/14651858.CD006519.pub3
7. Diallo, A. F., Cong, X., Henderson, W. A., & McGrath, J. M. (2017). Management of childhood diarrhea by healthcare professionals in low income countries: An integrative review. International Journal of Nursing Studies, 66, 82–92. https://doi.org/10.1016/j.ijnurstu.2016.08.014
8. Anigilaje, E. A. (2018). Management of diarrhoeal dehydration in childhood: A review for clinicians in developing countries. Frontiers in Pediatrics, 6, Article 28. https://doi.org/10.3389/fped.2018.00028
9. Santillanes, G., & Rose, E. (2018). Evaluation and management of dehydration in children. Emergency Medicine Clinics of North America, 36(2), 259–273. https://doi.org/10.1016/j.emc.2017.12.004
10. Brady, K. A. (2018). Acute gastroenteritis: Evidence-based management of pediatric patients. Pediatric Emergency Medicine Practice, 15(2), 1–24.
11. Guarino, A., Lo Vecchio, A., Dias, J. A., Berkley, J. A., Boey, C., Bruzzese, D., ... Szajewska, H. (2018). Universal recommendations for the management of acute diarrhea in nonmalnourished children. Journal of Pediatric Gastroenterology and Nutrition, 67(5), 586–593. https://doi.org/10.1097/MPG.0000000000002053
12. Freedman, S. B., Powell, E. C., Nava-Ocampo, A. A., & Finkelstein, Y. (2019). Oral ondansetron administration to nondehydrated children with diarrhea and associated vomiting in emergency departments in Pakistan: A randomized controlled trial. Annals of Emergency Medicine, 73(5), 519–526. https://doi.org/10.1016/j.annemergmed.2018.10.014
13. Freedman, S. B., Bhutta, Z. A., Xie, J., Parkin, P. C., Rennie, M., Nettel-Aguirre, A., ... Plint, A. C. (2019). Oral ondansetron administration to dehydrated children in Pakistan: A randomized clinical trial. Pediatrics, 144(6), e20192161. https://doi.org/10.1542/peds.2019-2161
14. Houston, K. A., Gibb, J. G., & Maitland, K. (2017). Oral rehydration of malnourished children with diarrhoea and dehydration: A systematic review. Wellcome Open Research, 2, Article 66. https://doi.org/10.12688/wellcomeopenres.12357.3
15. Rabaan, A. A. (2019). Cholera: An overview with reference to the Yemen epidemic. Frontiers in Medicine, 6, Article 319. https://doi.org/10.3389/fmed.2019.00319
16. Billah, S. M., Raihana, S., Ali, N. B., Iqbal, A., Rahman, M. M., Khan, A. N. S., ... Arifeen, S. E. (2019). Bangladesh: A success case in combating childhood diarrhoea. Journal of Global Health, 9(2), 020803. https://doi.org/10.7189/jogh.09.020803
17. Hanif, H., Ali, S. M., Sheikh, A. S., & Shah, S. A. (2019). Oral ondansetron versus domperidone for acute gastroenteritis associated vomiting in young children. Cureus, 11(9), e5639. https://doi.org/10.7759/cureus.5639
18. Freedman, S. B., Powell, E. C., Nava-Ocampo, A. A., & Finkelstein, Y. (2019). Oral ondansetron administration to nondehydrated children with diarrhea and associated vomiting in emergency departments in Pakistan: A randomized controlled trial. Annals of Emergency Medicine, 73(5), 519–526. https://doi.org/10.1016/j.annemergmed.2018.10.014
19. Harrell, J. E., Jr., & Brown, R. S. (2018). Inability to reduce morbidity of diarrhea by oral rehydration solutions: Can we design a better therapy? Pediatric Research, 84(4), 559–563. https://doi.org/10.1038/s41390-018-0136-2
20. Sollanek, K. J., Kenefick, R. W., & Cheuvront, S. N. (2019). Osmolality of commercially available oral rehydration solutions: Impact of brand, storage time, and temperature. Nutrients, 11(7), 1485. https://doi.org/10.3390/nu11071485

21. ASTM International. (2019). ASTM F1249-19: Standard test method for water vapor transmission rate through plastic film and sheeting using a modulated infrared sensor. Retrieved from: https://www.astm.org/f1249-20.html (date accessed: November 19, 2019).

22. ASTM International. (2017). ASTM D3985-17: Standard test method for oxygen gas transmission rate through plastic film and sheeting using a coulometric sensor. Retrieved from: https://www.astm.org/d3985-17.html (date accessed: October 14, 2019).

23. World Health Organization. (2018). WHO Expert Committee on Specifications for Pharmaceutical Preparations: Fifty-second report. Annex 10. Stability testing of active pharmaceutical ingredients and finished pharmaceutical products (WHO Technical Report Series No. 1010). Geneva, Switzerland: World Health Organization. Retrieved from: https://www.who.int/publications/m/item/trs1010-annex10 (date accessed: November 7, 2019).

24. United States Pharmacopeia. (2018). USP <671> Containers Performance testing (USP 41–NF 36). Retrieved from: https://doi.usp.org/USPNF/USPNF_M99430_03_01.html (date accessed: September 27, 2019).

25. Ibrahim, S., Hegazy, A., & El-Bisi, M. (2019). Multilayer flexible packaging materials. Egyptian Journal of Chemistry, 62(Special Issue), 311–326. https://doi.org/10.21608/ejchem.2019.9491.1643

26. Marsh, K., & Bugusu, B. (2017). Food packaging Roles, materials, and environmental issues. Journal of Food Science, 82(7), 1541–1547. https://doi.org/10.1111/1750-3841.13768

27. Siracusa, V. (2019). Packaging material properties and food shelf life. Food Engineering Reviews, 11(3), 109–128. https://doi.org/10.1007/s12393-019-09195-x

28. Gaikwad, K. K., Singh, S., & Lee, Y. S. (2018). Oxygen scavenging films in food packaging. Environmental Chemistry Letters, 16(2), 523-538.

29. World Health Organization. (2018). Prevention and control of noncommunicable diseases in Uzbekistan: The case for investment. Copenhagen, Denmark: WHO Regional Office for Europe. Retrieved from: https://iris.who.int/items/79d479d7-26ad-4a6e-8421-6af358c815f7 (date accessed: September 11, 2019).

30. President of the Republic of Uzbekistan. (2019). Decree No. DP-5707 of April 10, 2019: On further measures to accelerate the development of the pharmaceutical industry of the republic in 2019–2021. Retrieved from: https://lex.uz/en/docs/6968701?ONDATE=11.04.2019 (date accessed: November 4, 2019).

31. Cabinet of Ministers of the Republic of Uzbekistan. (2019). Resolution No. 641 of August 1, 2019: On approval of the regulations on the Fund for the support and development of the pharmaceutical industry under the Agency for the development of the pharmaceutical industry at the Ministry of Health of the Republic of Uzbekistan. Retrieved from: https://lex.uz/en/docs/7269131 (date accessed: November 22, 2019).

32. Cabinet of Ministers of the Republic of Uzbekistan. (2017). Resolution No. 284 of May 12, 2017: On measures for the further improvement of the licensing procedure for pharmaceutical activities. Retrieved from: https://lex.uz/en/docs/7258177?ONDATE=22.05.2017 (date accessed: October 3, 2019).

33. World Health Organization. (2017). WHO model list of essential medicines (20th list). Geneva, Switzerland: World Health Organization. Retrieved from: https://www.iccp-portal.org/resources/who-model-list-essential-medicines-20th-edition-2017 (date accessed: August 29, 2019).

34. State standard of the Republic of Uzbekistan. Good Storage Practice (GSP). Retrieved from: https://www.uzpharm-control.uz/en/documents/category/5 (date accessed: August 29, 2019).

35. Hammer, C. (2018). Digitisation & industry 4.0 in pharma production. ONdrugDelivery Mag, 83, 81-83.

Citation: Bekhzad Yuldashev, "Stability and Product–Packaging Compatibility of ORS Formulations: A Comparative Study of Powder Barriers and the Case for Liquid Transition", Universal Library of Business and Economics, 2022; 06-13. DOI: https://doi.org/10.70315/uloap.ulbec.2022.002.