In Vitro Total Potassium-Binding Capacity of Patiromer When Mixed With Apple or Cranberry Juice

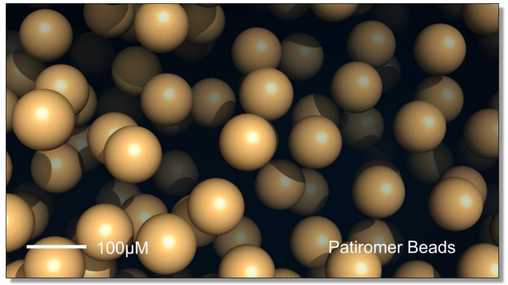
Jeanene Fogli, Martha R. Mayo, John Miyawa, Reyn Ono, Coleman Gross
Relypsa, Inc., a Vifor Pharma Group Company, Redwood City, CA

#19

BACKGROUND ON PATIROMER

- Nonabsorbed potassium (K^+)-binding polymer[1,2] consisting of uniform, spherical beads of approximately 100 µm **(Figure 1)**, which maintain their structure during passage through the gastrointestinal system.
- Uses calcium (Ca^{2+}) as the counterion for exchange with K^+.[1,2]
- Approved for treatment of hyperkalemia in the United States,[1] the European Union,[3] Switzerland,[4] and Australia.[5]
- In clinical trials[6-8] patiromer has been shown to:
  - Reduce elevated serum K^+ with equivalent efficacy when taken without or with food.
  - Facilitate continued use of renin-angiotensin-aldosterone system (RAAS) inhibitors.
  - Maintain mean serum K^+ in the normal range for up to 52 weeks.
- Supplied as a powder for oral suspension **(Figure 2)**.
- United States prescribing information recommends mixing patiromer (8.4–25.2 g once daily) with ⅓ cup water (~80 mL).[1]
- European Union prescribing information indicates that apple juice or cranberry juice can be used instead of water to prepare the suspension.[3]

Figure 1. Patiromer's uniform sphere shape and size



Spherical particles with an average particle size of 100 µM.

Figure 2. Patiromer single-use (8.4 g) packet (A)* and example of drug suspended in water (B)

*8.4 g once daily is the recommended starting dose of patiromer; 16.8 g and 25.2 g packets are also available.

OBJECTIVES

- In a palatability study in healthy volunteers, 90% of subjects reported positive palatability experiences with patiromer in terms of odor or taste.[9]
- However, palatability of patiromer may be a more important factor in clinical practice, as patients with chronic kidney disease (CKD) have altered taste function. CKD patients are at higher risk of hyperkalemia, and may require chronic use of patiromer.[10–12]
- In addition, patients and healthcare providers commonly request information on the use of alternatives to water for mixing patiromer.
- We evaluated the compatibility of patiromer with apple and cranberry juices, as alternatives to water.

METHODS

- The *in vitro* K^+-binding effects of mixing patiromer with apple juice and cranberry juice cocktail were assessed at two dilution ratios to evaluate a range of concentrations at clinically relevant patiromer doses:
  - 2.1 g patiromer suspended in 40 mL of juice (high dilution, low concentration).
  - 6.3 g patiromer suspended in 20 mL of juice (low dilution, high concentration).

Disclosures
J. Fogli, M. Mayo, J. Miyawa, R. Ono, and C. Gross are employees of Relypsa, Inc., a Vifor Pharma Group Company.

Acknowledgements
Editorial support was provided by Impact Communication Partners, Inc., and funded by Relypsa, Inc., a Vifor Pharma Group Company.

METHODS (CONT'D)

- We selected apple juice and cranberry juice cocktail for evaluation because they are relatively low in K^+ compared with other juices **(Table 1)**.[13]
- After suspension of patiromer in juice, samples were vortexed for 5 minutes before and after a 45-minute waiting period; samples were then centrifuged for 5 minutes to separate the supernatant from the polymer.
- The polymer was then vacuum filtered, washed, dried, and analyzed for total K^+-binding capacity (mEq/g).
- Samples were prepared in triplicate for both juices at each dilution. Results for each juice were averaged and compared with the total K^+-binding capacity of patiromer when mixed with deionized water.

Table 1. K^+ content of commonly available juices[13]

Type of juice	USDA standard (Release 28) reference number	K^+ content mg (mEq) per 1 cup (approximately 240 mL)
Examples with relatively high K^+ content		
Orange	09206	496 (12.7)
Tomato-vegetable, low sodium	43365	467 (11.9)
Examples with relatively low K^+ content		
Apple	09016	250 (6.4)
Cranberry cocktail	14242	35 (0.9)

RESULTS

- The mean total K^+-binding capacity (potency) of patiromer suspended in apple juice was 8.8 mEq/g at both high and low dilutions. For cranberry juice cocktail, the values were 8.8 and 8.6 mEq/g, respectively. The mean result for control (water) was 9.1 mEq/g **(Table 2)**.
- The differences are not considered clinically relevant.

RESULTS (CONT'D)

Table 2. Total K^+-binding capacity (potency) of patiromer suspended in apple or cranberry juice vs water

Type of juice	K^+-binding capacity (mEq/g)	
	High dilution, low concentration	Low dilution, high concentration
Apple (mean)	**8.8**	**8.8**
Test 1	8.9	8.7
Test 2	8.8	8.9
Test 3	8.8	8.8
Cranberry cocktail (mean)	**8.8**	**8.6**
Test 1	8.9	8.6
Test 2	8.9	8.6
Test 3	8.7	8.7
Water	**9.1**	

CLINICAL IMPLICATIONS AND CONCLUSIONS

- Patiromer is a once-daily K^+ binder for the treatment of hyperkalemia, a chronic medical condition that commonly affects patients with CKD.
- Patiromer (8.4–25.2 g once daily) is supplied as a powder, and the United States prescribing information recommends mixing patiromer with ⅓ cup water (~80 mL).[1]
- Adherence to prescribed therapies may be a challenge for some patients with CKD, owing to multi-pharmacological treatment and high pill burden.[14,15]
- Providing alternatives to water for patients to mix patiromer may increase palatability and reduce the risk of nonadherence.
- In conclusion, there was no adverse impact on *in vitro* total K^+-binding capacity when patiromer was mixed with apple juice or cranberry juice cocktail.

References
1. Veltassa® (patiromer) for oral suspension [package insert]. Redwood City, CA: Relypsa, Inc. 2016. 2. Li L, et al. *J Cardiovasc Pharmacol Ther*. 2016;21(5):456-465. 3. Veltassa® (patiromer): European public assessment report. European medicines agency. 4. Swissmedic. https://www.swissmedic.ch/swissmedic/en/home/humanarzneimittel/authorisations/authorised-medicinal-products-with-new-active-substances/veltassa_pulver_fuer_orale_suspension_patiromer.html. Accessed March 28, 2018. 5. Australian Government Department of Health: Therapeutic Goods Administration. https://www.tga.gov.au/sites/default/files/delegates-final-decisions-jan-2018.pdf. Accessed March 28, 2018. 6. Weir MR, et al. *N Engl J Med*. 2015;372(3):211-221. 7. Bakris GL, et al. *JAMA*. 2015;314(2):151-161. 8. Pergola PE, et al. *Am J Nephrol*. 2017;46(4):323-332. 9. Brenner M, et al. Presented at: American Society of Health-System Pharmacists 2016 Mid-Year Meeting, Dec 4-8, 2016, Las Vegas, NV. 10. Armstrong JE, et al. *Pediatr Nephrol*. 2010;25(8):1497-1504. 11. van der Eijk I, et al. *J Ren Nutr*. 1997;7(1):3-9. 12. Konstantinova D, et al. *G Ital Nefrol*. 2018;34(3):1-7. 13. United States Department of Agriculture. USDA National Nutrient Database for Standard Reference (Release 28, released Sept 2015, slightly revised May 2016). Available at: https://ndb.nal.usda.gov/ndb/. Accessed March 18, 2018. 14. Burnier M, et al. *Nephrol Dial Transplant*. 2015;30(1):39-44. 15. Nielsen TM, et al. *Clin Kidney J*. 2017, sfx140, https://doi.org/10.1093/ckj/sfx140.

Presented at the American Nephrology Nurses Association 2018 National Symposium, April 15–18, 2018, Las Vegas, Nevada.

Supported by Relypsa, Inc., a Vifor Pharma Group Company