

St. John Fisher University

Fisher Digital Publications

Pharmacy Faculty/Staff Publications

Wegmans School of Pharmacy

11-2018

Basics of Compounding: Vehicles for Compounded Oral Liquid Medications: A Review

Kara Cutaia

St. John Fisher University, kt03416@sjf.edu

Lipika Chablani

St. John Fisher University, lchablani@sjf.edu

Fang Zhao

St. John Fisher University, fzhao@sjf.edu

Follow this and additional works at: https://fisherpub.sjf.edu/pharmacy_facpub

 Part of the [Pharmacy and Pharmaceutical Sciences Commons](#)

Publication Information

Cutaia, Kara; Chablani, Lipika; and Zhao, Fang (2018). "Basics of Compounding: Vehicles for Compounded Oral Liquid Medications: A Review." *International Journal of Pharmaceutical Compounding* 22.6, 480-489. Please note that the Publication Information provides general citation information and may not be appropriate for your discipline. To receive help in creating a citation based on your discipline, please visit <http://libguides.sjfc.edu/citations>.

This document is posted at https://fisherpub.sjf.edu/pharmacy_facpub/187 and is brought to you for free and open access by Fisher Digital Publications at . For more information, please contact fisherpub@sjf.edu.

Basics of Compounding: Vehicles for Compounded Oral Liquid Medications: A Review

Abstract

Compounded oral liquid medications play an important role in addressing the unmet needs of special patient populations, including pediatric, geriatric, and tube fed patients. The use of manufactured vehicles can streamline the compounding activities for pharmacists. In recent years, there is an increase in the availability of manufactured vehicles with various promotional features. This article uses the general formulation principles as a guide to compare and contrast the manufactured vehicles regarding their physicochemical properties, presence of preservatives and dyes, organoleptic properties, and ease of use. A summary table is provided as a reference tool to assist pharmacists in selecting the optimal vehicles for their patient care.

Disciplines

Pharmacy and Pharmaceutical Sciences

Comments

This article was published in the *International Journal of Pharmaceutical Compounding* Nov/Dec 2018 - Volume 22, Number 6, Pages 480-489: <https://www.ijpc.com/Abstracts/Abstract.cfm?ABS=4536>

Reprinted with permission.



BASICS OF COMPOUNDING

Vehicles for Compounded Oral Liquid Medications: A Review



Kara Cutaia, PharmD, LPN
Lipika Chablani, PhD
Fang Zhao, PhD

Abstract

Compounded oral liquid medications play an important role in addressing the unmet needs of special patient populations, including pediatric, geriatric, and tube-fed patients. The use of manufactured vehicles can streamline the compounding activities for pharmacists. In recent years, there is an increase in the availability of manufactured vehicles with various promotional features. This article uses the general formulation principles as a guide to compare and contrast the manufactured vehicles regarding their physicochemical properties, presence of preservatives and dyes, organoleptic properties, and ease of use. A summary table is provided as a reference tool to assist pharmacists in selecting the optimal vehicles for their patient care.

*The authors' affiliations are: **Kara Cutaia**, Resident Pharmacist, Unity Hospital, Rochester Regional Health, Rochester, New York; **Lipika Chablani**, Associate Professor, and **Fang Zhao**, Professor, Department of Pharmaceutical Sciences, St. John Fisher College Wegmans School of Pharmacy, Rochester, New York.*

Unmedicated oral vehicles are used to prepare oral liquid medications. Compounding of oral liquid formulations expands treatment options for patients who have difficulty swallowing tablets or capsules, as extemporaneous preparation can provide dosage forms that are not commercially available. Specific populations who may benefit from the compounding of these dosage forms include pediatric patients, geriatric patients, and patients with enteral feeding tubes. Multiple oral vehicles are available, and these products differ in their physicochemical and organoleptic properties. These vehicles can be used to prepare a variety of oral liquid dosage forms including solutions, suspensions, and emulsions. This article provides a review of commercially available oral vehicles as well as a discussion of vehicle properties to consider when selecting a vehicle for a specific drug, route, and patient. This information may serve as a reference for compounding pharmacists as well as for persons involved in formulating oral-liquid dosage forms for commercial applications.

Discussion

We have reviewed 26 oral liquid vehicles, considering various aspects such as:

- Appearance
- Osmolality
- pH
- Presence of preservatives and dyes
- Viscosity
- Suspending agent used
- Taste

This information is summarized in Table 1 as a reference tool for compounding pharmacists. Additionally, we have examined published literature and reference books to provide context for this data.

Physicochemical Properties

Oral dosage forms should be palatable and well tolerated, provide accurate and consis-

tent dosing, and maintain physical integrity throughout their shelf life.¹ Physicochemical properties to consider when preparing oral liquid formulations include viscosity, suspending agent, pH, and osmolality.

VISCOSITY AND SUSPENDING AGENT

Oral liquid dosage forms include solutions, suspensions, and emulsions. In solutions, ingredients are solubilized in the solvent. Types of oral solutions include syrups, elixirs, spirits, and tinctures. Multiple syrups are commercially available as oral liquid vehicles. These do not contain suspending agents, and viscosity is essential primarily for pharmaceutical elegance and ease of use.²

Suspensions are dispersed systems which have physical-stability challenges. An ideal suspension settles slowly and readily re-disperses upon agitation.³ During storage, suspensions may undergo sedimentation and aggregation (including cake formation) leading to physical instability and variability in dosing. Inconsistent dosing can have severe consequences for patients including drug toxicity and, conversely, undertreatment. Increased viscosity of suspensions can slow the rate of particle setting. However, if viscosity is too high, the particles may be less readily re-dispersed upon agitation, and the product may be difficult to pour and measure.^{1,2} Suspensions are formulated with suspending agents that maintain the physical stability of the dispersion throughout the shelf life. Most of these suspending agents are pseudoplastic or shear-thinning systems, which leads to lowering of viscosity with respect to increased shear stress (i.e., shaking of the bottle or trituration of the ingredients to compound the suspension). Along with the pseudoplastic rheology, these systems are also thixotropic, a property which allows the system to regain its viscosity once the shear stress has been removed from the system. The thixotropic behavior of such commercial oral vehicles enhances the stability and shelf life of the compounded oral dispersions.

Like suspensions, emulsions are dispersed systems. Specifically, emulsions are dispersions of small globules of a substance in a vehicle in which it is immiscible. Because emulsions contain at least two phases, often an aqueous and an oleaginous phase, they provide a liquid dosage form more suitable for drugs that are unstable in aqueous formulations. Physical stability challenges for emulsions include creaming (weak associations between droplets of the internal phase) and cracking (irreversible coalescence of droplets of the internal phase). Viscosity regulators and thickening agents may be added to emulsions to slow the rate of particle settling and improve the stability of the dispersion.² An example of an oral liquid vehicle available as an emulsification system is Fagron's Unispand Anhydrous. This vehicle, available both sweetened and unsweetened, is formulated with triglycerides and provides an anhydrous system which is favorable for water unstable additives.⁴

As evident from Table 1, common suspending agents/viscosity enhancers include sodium carboxymethylcellulose, xanthan gum, and carrageenan. Each of these agents poses their own incompatibility issues that a compounding pharmacist must consider while using the commercial oral vehicles that contain them. A detailed description of incompatibility concerns for each of these agents is available in the *Handbook of Pharmaceutical Excipients*.⁵ This study provides a brief overview of some of these major incompatibilities with respect to each of these agents. Sodium carboxymethylcellulose solutions are most stable at pH 5 to 10, however, those solutions can tolerate a broader range of pH 2 to 10 for final preparations. These solutions are also incompatible with quaternary nitrogen-containing compounds, iron salts, and metals such as aluminum, mercury, and zinc. Similarly, due to the anionic chemical structure of xanthan gum, it is incompatible with large cationic drugs, surfactants, polymers, and preservatives. Xanthan gum is also incompatible with oxidizing agents, some tablet film-coatings, dried aluminum hydroxide gel, and some active ingredients such as

amitriptyline, tamoxifen, and verapamil. Lastly, carrageenan-containing solutions remain stable at pH 9 and can lead to its depolymerization if the pH of the solution is rendered acidic. Also, carrageenan may interact with cationic active pharmaceutical ingredients and is generally limited in its use in such cases.

A recent study by Visser et al⁶ compares the rheological and sedimentation behavior of some of the commercially available oral vehicles. The study describes the preparation of an oral suspension of paracetamol to evaluate the efficacy of the following oral vehicles:

- Base for Suspension
- Ora-Blend
- Ora-Blend SF
- Simple Syrup
- SuspendIt
- Syr-Spend SF PH4

The study concludes that SyrSpend SF PH4 and SuspendIt resulted in the best-compounded preparations due to their pronounced pseudoplastic rheological profile. Both the vehicles provided adequate sedimentation rates, even pourability, and good resuspendability. These results are promising. However, the study can further be expanded to include other commercially available vehicles.

pH

Because many drugs are weak electrolytes (weak acids or weak bases), the pH of the formulation affects drug ionization, solubility, and physicochemical stability. Vehicles and formulations may be prepared with buffers to prevent sudden changes in pH.⁷ When selecting a vehicle for the oral liquid formulation, consideration should be given to any data regarding the effect of pH on the solubility and stability of the drug being prepared in the formulation. Most of the oral liquid vehicles described in this review have an acidic pH. For drugs that are unstable in acidic pH, alkaline vehicles are available. An example of such a product is Fagron's SyrSpend SF Alka, which has a pH of >7.

OSMOLALITY

Oral vehicles with high osmolality have the potential to cause gastrointestinal (GI) upset and diarrhea.⁸⁻¹⁰ Some special patient populations are particularly prone to osmotic diarrhea. They include pediatric patients, geriatric patients, and patients with GI comorbidities such as irritable bowel syndrome. For instance, hypertonic solutions of >400 mOsm/kg were reported to injure GI tracts of neonates.³ Unfortunately, the osmolality data are not available for all vehicles from the manufacturers, and estimation is difficult for vehicles with proprietary formulas. The following discussion is based on the vehicles with reported values (Table 1) and general scientific knowledge of oral liquid formulations and excipients.¹¹

The osmolality of the normal GI fluids is between 100 mOsm/kg to 400 mOsm/kg.¹² Several sugar-based syrup vehicles contain high concentrations of sucrose which result in extremely high osmolality. For example, the osmolality is 4109 mOsm/kg for Ora-Sweet (Perrigo) and 2381 mOsm/kg for Oral Syrup (Medisca). The same issue exists for some sugar-free vehicles, depending on the sweeteners used. Generally, the natural polyol sweeteners (e.g., sorbitol) have much lower sweetness than the artificial sweeteners (e.g., sucralose)^{5,13,14} and thus require much higher concentrations in the formulation. For example, sorbitol is used in a number of commercial vehicles, and it is only about 50% to 70% as sweet as sucrose.¹³ Hence, a vehicle sweetened mainly by sorbitol still requires a high concentration of sorbitol, which again leads to hyperosmolality. Furthermore, sorbitol is only partially absorbed in the GI tract. The non-absorbed sorbitol is fermented by the colonic flora with gaseous byproducts, which exacerbate the GI disturbances.¹³ As a safe practice, the compounding pharmacist should make sure that the sorbitol consumption from the prescribed dosage is below 20 g/day for adults.^{5,13} On the other hand, the non-sweetened suspension vehicles tend to have low osmolality, which are suitable choices for patients who cannot tolerate hypertonic liquids. Two good vehicle examples are Ora-

Plus from Perrigo and Oral Suspend from Medisca at 157 mOsm/kg and 48 mOsm/kg, respectively. Finally, one notable product worth highlighting is SyrSpend SF from Fagron. It is the only all-in-one vehicle (sweetened, flavored, structured) with a low osmolality of <50 mOsm/kg. In addition, there are two similar SyrSpend SF powder products which are preservative-free but require reconstitution before use.

The concern of GI distress is heightened when the oral liquids are administered via enteral feeding tubes.^{9,15} Depending on the tubing types, the liquid medications are delivered directly to various GI regions without dilution. As expected, the adverse effects are most pronounced when the liquids are administered too rapidly into the stomach or delivered directly to the intestine. Since palatability is not a requirement for medications administered via enteral feeding tube, it is recommended to choose non-sweetened, non-flavored, and low-osmolality vehicles. If the viscosity of these vehicles presents a challenge for some narrow tubes, they should be diluted with purified water rather than another vehicle with high osmolality.

Preservatives and Dyes

Preservatives are often included in the formulations of oral liquid vehicles to provide microbial stability. Aqueous formulations are prone to microbial growth, and preservatives protect against bacterial, yeast, and mold infection. In addition to protecting the end user from pathogens, preservatives also provide a multiple year shelf life for products. Parabens are the most commonly-used class of preservatives which offer protection against a wide range of pathogens, even at low concentrations. Both methylparabens and propylparabens have low aqueous solubilities (1 g/400 mL of water and 1 g/2,500 mL of water, respectively) and are often solubilized with the aid of small amounts of a co-solvent such as alcohol or propylene glycol. Methylparaben is often used as a preferred preservative, as it can effectively preserve oral vehicles for a broader pH range of 4 to 8. Often, methylparaben is paired with propylpara-

TABLE 1. SUMMARY OF VEHICLES FOR COMPOUNDED ORAL LIQUID MEDICATIONS.

VEHICLE	MANUFACTURER NDC OR PRODUCT NUMBER	SUSPENDING AGENT	SWEET- ENER	pH	VISCOSITY (cPs)	OSMOLALITY (mOsm/ kg)	TASTE	PRESERVATIVE	APPEARANCE	DYE
Ora-Sweet ¹⁹	Perrigo 0574-0304-16	NA	• Sucrose	~ 4.3	NA	~ 4109	Sweet citrus- berry flavor	Methylparaben and potassium sorbate	Clear liquid with a slight tint	Red dye #40
Ora-Sweet SF ¹⁹	Perrigo 0574-0302-16	NA	• Saccharin	4.0 to 4.4	NA	~ 1979	Sweet citrus- berry flavor	Methylparaben (0.03%), propylparaben (0.008%), and potassium sor- bate (0.1%)	Clear liquid with a slight tint	Red dye #40
Ora-Plus ¹⁹	Perrigo 0574-0303-16	• Microcrystalline cellulose • Carboxymethyl- cellulose sodium	None	4.0 to 4.5	1300 to 6700 Thixotropic	~ 157	Bland (no sweeteners or flavors)	Methylparaben and potassium sorbate	Translucent, milky white	Dye-free
Ora-Blend ¹⁹	Perrigo 0574-0311-16	• Microcrystalline cellulose • Carboxymethyl- cellulose sodium	• Sucrose	~ 4.3	700	~ 1665	Sweet citrus- berry flavor	Methylparaben and potassium sorbate	Opaque, pinkish liquid	Red dye #40
Ora-Blend SF ¹⁹	Perrigo 0574-0312-16	• Microcrystalline cellulose • Carboxymethyl cellulose sodium	• Saccharin	~ 4.2	~ 1000	1027	Sweet citrus- berry flavor	Methylparaben, propylparaben, and potassium sorbate	Opaque, pinkish liquid	Red dye #40
Oral Suspend ²⁰	Medisca 38779-2510-08	• Cellulose	NA	4.0 to 5.0	Thixotropic 1600 to 2400	48	Bland, un- sweetened	Methylparaben	Viscous off-white aqueous liquid.	Dye-free
Oral Syrup ²⁰	Medisca 38779-2511-08	NA	• Sucrose	4.0 to 5.0	100 to 350	2381	Cherry	Methylparaben	Clear to slightly tinted liquid	Dye-free
Oral Mix ²⁰	Medisca 38779-2512-08	• Cellulose	• Sucrose	4.0 to 5.0	100 to 350	1231	Cherry	Methylparaben	Off-white aqueous liquid	Dye-free
Oral Syrup SF ²⁰	Medisca 38779-2599-08	NA	• Saccharin	4.0 to 5.0	250 to 450	1585	Cherry	Methylparaben Propylparaben	Clear to slightly tinted liquid	Dye-free
Oral Mix SF ²⁰	Medisca 38779-2600-08	• Cellulose	• Saccharin	4.0 to 5.0	300 to 550	795	Cherry	Methylparaben Propylparaben	Off-white aqueous liquid	Dye-free
Flavor Blend ²¹	Humco 00395-0089-16	• Microcrystalline cellulose • Carboxymethyl cellulose • Xanthan gum • Carrageenan	• Sugar • Sorbitol • Glycerin	4.0 to 5.5	NA	NA	Cherry flavor	Methylparaben Calcium Sulfate Potassium Sorbate Citric Acid	Viscous light pink opaque liquid	Red #3 FD&C #40
Flavor Sweet ²¹	Humco 00395-0090-16	NA	• Sugar • Sorbitol • Glycerin	4.0 to 4.5	NA	NA	Cherry flavor	Methylparaben Potassium Sorbate	Clear faint red slightly viscous liquid	Red #3 FD&C #40

TABLE 1. SUMMARY OF VEHICLES FOR COMPOUNDED ORAL LIQUID MEDICATIONS CONTINUED.

VEHICLE	MANUFACTURER NDC OR PRODUCT NUMBER	SUSPENDING AGENT	SWEETENER	pH	VISCOSITY (cPs)	OSMOLALITY (mOsm/kg)	TASTE	PRESERVATIVE	APPEARANCE	DYE
Flavor Plus ²¹	Humco 00395-0091-16	<ul style="list-style-type: none"> • Microcrystalline cellulose • Carboxymethyl cellulose • Xanthan gum • Carrageenan 	None	3.5 to 4.0	NA	NA	Unflavored	Methylparaben Citric Acid Sodium Phosphate Potassium Sorbate	Viscous white opaque liquid	Dye-free
Flavor Sweet SF ²¹	Humco 00395-0094-16	<ul style="list-style-type: none"> • Xanthan gum 	<ul style="list-style-type: none"> • Sodium saccharin • Sorbitol • Glycerin 	4.5 to 5.0	NA	NA	Cherry flavor	Propylparaben Methylparaben Potassium Sorbate Citric Acid Sodium Citrate	Pale pink clear liquid	Red#3 FD&C #40
Versa Free ²¹	Humco 00395-0125-16	<ul style="list-style-type: none"> • Xanthan gum 	<ul style="list-style-type: none"> • Sorbitol • Sorbitame • Glycerin 	4.3 to 5.0	750 to 1250	NA	Flavor-free	Sodium Benzoate Potassium Sorbate Citric Acid Sodium Citrate (Paraben-free)	Clear colorless liquid	Dye-free
Versa Plus ²¹	Humco 00395-0126-16	<ul style="list-style-type: none"> • Microcrystalline cellulose • Carboxymethyl cellulose • Xanthan gum • Carrageenan 	None	3.5 to 4.5	500 to 1600	NA	Flavor-free	Sodium Phosphate Citric Acid Potassium Sorbate (Paraben-free)	White liquid	Dye-free
Simple Syrup ²¹	Humco 0395-2661-16	NA	<ul style="list-style-type: none"> • Sucrose 	2.5 to 3.5	NA	NA	Unflavored	Methylparaben Citric Acid	Clear colorless liquid	Dye-free
Cherry Syrup ²¹	Humco 00395-2662-16	NA	<ul style="list-style-type: none"> • Sucrose 	2.5 to 3.5	NA	NA	Cherry flavor	Sodium Benzoate	Red viscous liquid	FD&C #40
SuspendIt ²²	PCCA 30-4825	NA	<ul style="list-style-type: none"> • Natural sweetener derived from Monk fruit • Sucrose 	NA	Thixotropic	NA	Vanilla	Paraben-free Sodium benzoate	Viscous white opaque liquid	Dye-free
SyrSpend SF ^{4,23}	Fagron 51552-1079-05	<ul style="list-style-type: none"> • Modified starch 	<ul style="list-style-type: none"> • Sucralose 	4 to 5	500 to 900	<50	Unflavored (also available as cherry, grape)	Sodium benzoate	Hazy, white, translucent syrup	Dye-free

TABLE 1. SUMMARY OF VEHICLES FOR COMPOUNDED ORAL LIQUID MEDICATIONS CONTINUED.

VEHICLE	MANUFACTURER NDC OR PRODUCT NUMBER	SUSPENDING AGENT	SWEETENER	pH	VISCOSITY (cPs)	OSMOLALITY (mOsm/kg)	TASTE	PRESERVATIVE	APPEARANCE	DYE
SyrSpend SF Powder ^{4,23}	Fagron 51552-1274-02	• Modified starch	• Sweeteners • Sugar-free	4 to 5	Unavailable	<50	Unflavored	Preservative-free	Coarse powder	Dye-free
SyrSpend SF PH4 (liquid) ^{4,23}	Fagron 51552-1434-06	• Starch	NA	4 to 5	500 to 900 (10 rpm), 1500-3000 (1 rpm)	<50	Unflavored (also available in cherry flavored)	sodium benzoate	Hazy, white, translucent syrup	NA
SyrSpend SF PH4 (dry, for reconstitution) ^{4,23}	Fagron 51552-1434-06	NA	NA	4 to 5	75 to 400 (10 rpm) 25 to 250 (1 rpm)	NA	Unflavored	Preservative-free	White, free-flowing powder. After reconstitution, hazy white translucent syrup	NA
SyrSpend SF Alka (dry, for reconstitution) ^{4,23}	Fagron 51552-1201-05	• Starch	NA	>7	NA	NA	Unflavored (also available as cherry flavored)	Preservative-free	White, free-flowing powder	NA
UniSpend Anhydrous (sweetened) ^{4,23}	Fagron 51552-1544-05	• Triglyceride emulsification system	• Naturally sweetened	NA	NA	NA	Unflavored	Preservative-free	White, opaque, slightly textured liquid	Dye-free
UniSpend Anhydrous (unsweetened) ^{4,23}	Fagron 51552-1545-05	• Triglyceride emulsification system	None	NA	NA	NA	Unflavored	Preservative-free	White, opaque, slightly textured liquid	Dye-free

ben to achieve a synergistic effect and allow the use of low concentrations. Due in part to consumer perceptions, many preservative-free or paraben-free products are currently being marketed. However, available evidence does not support a need to avoid parabens, and the safety and efficacy of parabens have repeatedly been reported. Many prestigious health organizations worldwide, including the U.S. Food and Drug Administration, continue to support the use of parabens.¹⁶ As evident from Table 1, other commonly used preservatives for oral vehicles include sodium benzoate and potassium sorbate. Sodium benzoate can be effectively used to preserve oral liquids with a pH <5. Several of the commercial oral vehicles, including syrups, satisfy this qualification and are effectively preserved with this water-soluble preservative. Sodium benzoate's pH-dependent efficacy should be considered with respect to the pH of the resulting compounded preparations using such oral vehicles. Similarly, potassium sorbate can be effectively used as a preservative for oral vehicles and formulations with a pH <6. Unlike the parabens, potassium sorbate is very soluble in aqueous systems (1 g/ 4.5 mL of water) and does not require any co-solvents. Additionally, Bruns et al also compares the stability of these common preservatives and concludes that potassium sorbate is the safest alternative for pediatric patients with respect to its efficacy for compounded oral preparations with a pH of 3.5 to 5.5.¹⁷

Dyes provide pharmaceutical elegance to liquid dosage forms. Multiple oral liquid vehicles contain dyes, often Red #3 and FD&C #40. For patients who are allergic or sensitive to dyes, many dye-free vehicles also are available. Because neonates have relatively limited metabolic activity, both preservative- and dye-free oral liquid vehicles are preferred for this population. Compounded oral preparations for this population are generally prepared in limited quantities, stored in refrigerators, and consumed immediately or within short durations from preparation to avoid the use of preservatives.

Organoleptic Properties

Organoleptic properties pertinent to oral liquid vehicles include taste, sweetness, and appearance. Patient adherence to therapy may

be enhanced when the dosage form is palatable and pharmaceutically elegant. Some oral vehicles are flavored, while others are unflavored, allowing the compounding pharmacist to add flavors that match patient preference. Syrups have a high degree of sweetness, which may be appealing to particular patient populations such as pediatric patients. Some vehicles contain sugar-free sweeteners (including sugar alcohols) with the advantage of the lower glycemic load for diabetic patients. As discussed previously under the topic of osmolality, sugar alcohols such as sorbitol can cause osmotic diarrhea, as can sugars.⁸

Practitioners should consider the effect of sweeteners, potentially avoiding those that cause diarrhea in certain patients, while recognizing that laxative effects may actually be beneficial for patients who are chronically constipated. The physical appearance of commercially available oral vehicles varies, ranging from clear to hazy and colorless to tinted (typically pink or red if colored). Multiple commercially available oral vehicles are also capable of taste-masking, which further enhances the palatability of compounded formulations, particularly when additives have an unpleasant taste.

In patients who are receiving medications through an enteral feeding tube, organoleptic properties are less important as the patient will not experience taste

Practitioners should consider the effect of sweeteners, potentially avoiding those that cause diarrhea in certain patients, while recognizing that laxative effects may actually be beneficial for patients who are chronically constipated.

and sweetness due to the route of drug delivery. However, physicochemical properties remain crucial as feeding tubes present unique drug-delivery challenges. When administration through an enteral tube is intended, the dosage form must neither be too viscous nor contain sizeable particulate matter which could occlude the tube.

should be maintained within a range high enough to maintain physical stability but low enough to permit these procedures. To further facilitate ease of use, the product should re-disperse readily upon simple agitation.² Prolonged or vigorous agitation may be time consuming or complicated for providers and patients alike. Additionally, patients, pharmacists, and caregivers may have different interpretations of the directions "Shake well before using."³ Dosage forms prepared with oral liquid vehicles should be able to provide uniform contents after simple manual agitation.

Additionally, most of these oral vehicles are available in conveniently packaged one-pint containers (473 mL), with a 24- to 36-month shelf life. This allows the pharmacist to easily stock and store these buffered, sweetened, flavored, and preserved oral vehicles in their inventory. Further, current published literature provides a plethora of information regarding the formulation and stability of several active pharmaceutical ingredients in these commercial vehicles. This strengthens the database for utilizing these vehicles to provide improved patient care. Due to the stability and versatile applications of these vehicles for compounded oral-liquid dosage forms, several pharmacies have phased out from preparing their in-house *United States Pharmacopeia*-compliant oral vehicles. The resulting increase in demand and competition by several manufacturers for these vehicles thereby feeds the cost-to-benefit ratio of purchasing these vehicles.

Ease of Use

For ease of use, oral vehicles ideally permit pouring, measuring, withdrawal into an oral syringe, and instillation through an enteral feeding tube. Viscosity

RS SOFTWARE

POWERFUL USER FRIENDLY
SOFTWARE THAT WORKS FOR YOU

Realizing that niche pharmacy is the key to success in this industry. We have continually added tools intended to help pharmacists perform their niche functions as efficiently as possible, thus creating the ultimate pharmacy solution.



OUR SYSTEMS THAT WORK FOR YOU

- Script Assist
- Compound Assist
- Prescription Assist
- HIPAA Bank



Norman, OK | (405)321-5356 | support@rssoftware.net

Cost Comparison

Standardized, current pricing information was not readily available for all the products. However, the average wholesale price (AWP) reported in *Red Book* ranged from approximately \$16 to \$63 (USD) per 473 mL.¹⁸ The actual cost of obtaining the vehicles can vary significantly from the AWP, depending on multiple factors such as bulk purchasing discounts and contract pricing between the manufacturer and buyer. For some of these products, multiple package sizes are available, which could impact pricing.

Limitations

This review is intended to describe common oral vehicles that may be seen in practice, and, as such, there may be additional oral vehicles on the market which have not been included. While multiple flavors and package sizes are available for some of the products described in this review, these parameters were simplified for the sake of summarization. In the case of multiple available package sizes, a representative package size is described in the Tables. The representative package size was selected as the closest size to 473 mL to facilitate comparison between products.

We identified four additional oral liquid vehicles, manufactured by Professional Compounding Centers of America (PCCA), which were not included in Table 1. These formulations are proprietary and, as such, we were not able to obtain data regarding specific ingredients and physicochemical properties. These products are PCCA-Plus Oral Suspending Vehicle, Syrup Vehicle, Sweet-SF Sugar-free Syrup Vehicle, and Acacia Syrup. The compounding pharmacist may be able to obtain guidance regarding these products from the manufacturer.

An additional limitation is the fact that product availability and formulations may change over time. This article does not replace the responsibility of the compounding pharmacist to check technical data sheets and ingredient lists for the oral vehicles that they use to prepare dosage forms.

Conclusion

In conclusion, multiple un-medicated oral vehicles are available for use in preparing oral formulations. By comparing physicochemical and organoleptic properties, the compounding pharmacist can select the oral vehicle best suited for the drug, route, and patient.

References

- Mobley WC. Dispersed systems. In: Amiji MM, Cook TJ, Mobley WC, eds. *Applied Physical Pharmacy*. 2nd ed. New York, NY: McGraw-Hill Education; 2013.
- Allen LV Jr., Popovich NG, Ansel HC. *Ansel's Pharmaceutical Dosage Forms and Drug Delivery Systems*. 9th ed. Baltimore, MD: Lippincott Williams & Wilkins; 2011.
- Helin-Tanninen M, Autio K, Keski-Rahkonen P et al. Comparison of six different suspension vehicles in compounding of oral extemporaneous nifedipine suspension for paediatric patients. *Eur J Hosp Pharm Sci Pract* 2012; 19(5): 432–437.
- Fagron. Documents (MSDS & CoA). [Fagron Website]. 2018. Available at: <https://fagron.com/en/knowledge/documents>. Accessed March 13, 2018.
- Sheskey PJ, Cook WG, Cable CG. *Handbook of Pharmaceutical Excipients*. Washington, DC: American Pharmacists Association (APhA); 2017.
- Visser JC, Seldam IE, van der Linden IJ et al. Comparison of rheological and sedimentation behavior of commercially available suspending vehicles for oral pharmaceutical preparations. *IJPC* 2018; 22(3): 247–251.
- Sandmann BJ, Dash AK, Al-Achi A et al. Ionic equilibria and buffers. In: Amiji MM, Cook TJ, Mobley WC, eds. *Applied Physical Pharmacy*. 2nd ed. New York, NY: McGraw-Hill Education; 2013.
- Makinen KK. Gastrointestinal disturbances associated with the consumption of sugar alcohols with special consideration of Xylitol: Scientific review and instructions for dentists and other health-care professionals. *Int J Dent* 2016; 2016: 1–16.
- Dickerson RN. Medication administration considerations for patients receiving enteral tube feedings. *Hosp Pharm* 2005; 40(12): 1081–1085.
- Edes TE, Walk BE, Austin JL. Diarrhea in Tube-fed patients: Feeding formula not necessarily the cause. *Am J Med* 1990; 88(2): 91–93.
- Elder DL. *A Practical Guide to Contemporary Pharmacy Practice and Compounding*. 4th ed. Philadelphia, PA: Wolters Kluwer; 2018.
- Dickerson RN, Melnik G. Osmolality of oral drug solutions and suspensions. *Am J Hosp Syst Pharm* 1988; 45(4): 832–834.
- Grembecka M. Sugar alcohols—their role in the modern world of sweeteners: A review. *Eur Food Res Technol* 2015; 241(1): 1–14.
- Thompson J. *A Practical Guide to Contemporary Pharmacy Practice*. 3rd ed. Lippincott Williams & Wilkins; 2009.
- Williams NT. Medication administration through enteral feeding tubes. *Am J Health Syst Pharm* 2008; 65(24): 2347–2357.
- [No author listed.] Parabens: The Importance and Safety of Preservatives. Medisca, Inc. Accessed January 16, 2018.
- Bruns C, Ober M. Development and Preparation of Oral Suspensions for Paediatric Patients – a Challenge for Pharmacists. *Pharm Technol Hosp Pharm* 2018; 3(2): 113–119.
- Truven Health Analytics LLC. *Red Book*. 2018. Accessed February 22, 2018 via MicroMedex.
- Ora-Sweet; Ora-Sweet SF; Ora-Plus; Ora-Blend; Ora-Blend SF. Perrigo Pharmaceuticals. [Perrigo Website.] 2018. Available at: www.perrigo.com/. Accessed March 7, 2018.
- Oral Suspend; Oral Syrup; Oral Mix; Oral Syrup SF; Oral Mix SF. Medisca. [Medisca Website.] 2018. Available at: www.medisca.com/products/compounding-bases/oral. Accessed March 7, 2018.
- Flavor Blend; Flavor Sweet; Flavor Plus; Flavor Sweet-SF; Versa Free; Versa Plus; Sinmple Syrup; Cherry Syrup. Humco. [Humco Website.] 2018. Available at: www.humco.com/store/pharmaceuticals/compounding-bases/oral-vehicles/. Accessed March 12, 2018.
- Professional Compounding Centers of America. *SuspendIt. PCCA 2016 Catalog*. [PCCA Website.] 2016.
- SyrSpend SF; SyrSpend SF Powder; SyrSpend SF PH4 (Liquid); SyrSpend SF PH4 (Dry for reconstitution); SyrSpend SF PH4 (Dry, for reconstitution); UniSpend Anhydrous (Sweetened); UniSpend Anhydrous (Unsweetened). Fagron. [Fagron Website.] 2018. Available at: <https://us.fagron.com/en-us/knowledge/product-innovations>. Accessed March 7, 2018.

Address correspondence to Kara Cutaia, PharmD, LPN, Resident Pharmacist, Unity Hospital, Rochester Regional Health, 1555 Long Pong Road, Rochester, NY 14626. Email: kt03416@sjfc.edu