European Journal of Clinical Pharmacy
Print ISSN: 2385-409X **Online ISSN**: Applied
Website: https://farmclin.es/

Original Research Article

Compounding, Stability Evaluation, Efficacy, And Safety of Vancomycin Syrup for the Treatment of Clostridioides Difficile Infection

Article History:

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How to cite this article:
Praveen K.S., *et al.* Compounding, Stability Evaluation, Efficacy, And Safety of Vancomycin Syrup for the Treatment of Clostridioides Difficile Infection. *Eur J Clin Pharm.* 2022;4(1);12-14

Received: 15-03-2022
Revised: 02-04-2022
Accepted: 28-04-2022
Published: 05-05-2022

Abstract: Vancomycin, delivered as an extemporaneously compounded oral syrup, is a mainstay for the treatment of Clostridioides difficile infection (CDI), especially in pediatric and adult populations unable to swallow capsules. This article reviews in depth the compounding protocols, stability testing, clinical efficacy, and safety profile of compounded vancomycin syrup for CDI. Evidence from recent literature and clinical studies is summarized alongside practical recommendations for pharmacists and providers.

Keywords: Vancomycin syrup, Clostridioides difficile infection (CDI), Extemporaneous compounding, Stability testing, Clinical efficacy.

INTRODUCTION

Clostridioides difficile infection (CDI) presents as a leading cause of healthcare-associated diarrhea. Oral vancomycin remains a key frontline therapy. Since commercial vancomycin syrups are often unavailable, extemporaneous compounding is required. Assessing the stability, efficacy, and safety of these preparations is critical to ensure successful clinical outcomes[1][2].

COMPOUNDING OF VANCOMYCIN SYRUP

Standard Compounding Procedure

The most common approach to prepare oral vancomycin syrup involves reconstituting the intravenous (IV) vancomycin hydrochloride powder or solution. A typical pharmacy-based recipe is as follows[3][4]:

- **Ingredients:**
  - Vancomycin hydrochloride powder for injection
  - Sterile Water for Injection (SWFI)
  - Flavored suspending and sweetening agents (e.g., Ora-Sweet, cherry syrup)
- **Method Example (25 mg/mL concentration):**

- Reconstitute each 500 mg vial of vancomycin with sterile water.
- Combine the reconstituted vancomycin with a mixture of sterile water and sweetened oral vehicle (1:1 water:Ora-Sweet).
- Mix thoroughly to a final volume (typically 100 mL for 25 mg/mL concentration).
- Transfer to an amber bottle to protect from light.
- Refrigerate; label for 30 days' expiry.

Note: Compounding instructions may vary, so local validated protocols and references should be followed[3][4][5].

STABILITY EVALUATION

Chemical and Physical Stability

- **Stability at 4°C (Refrigerated):**
  - Vancomycin oral suspensions (25–50 mg/mL) in water and commercial vehicles such as Ora-Sweet are stable for *at least 30 days* when stored in amber bottles in a refrigerator.
  - No significant decline in vancomycin potency was detected at 4°C over the evaluated period; visual and pH characteristics also remained within acceptable limits[2][1][3].
- **Stability at Room Temperature (25°C):**
  - While some commercial vehicles (e.g., Ora-Sweet) allow for room temperature storage, vancomycin concentration typically remains ≥90% for up to 14–26 days, depending on the formulation and container[4][2].
- **Effect of Vehicle and Preparation:**
  - Suspensions made from lyophilized vancomycin powder for injection tend to be more stable than those from commercial premixed IV solutions.
  - Addition of flavoring does not significantly affect chemical stability but may improve patient compliance[3][4][2].

Storage Condition	Maximum Stability*	Acceptable Vehicle	Container
Refrigerated (2–8°C)	30 days[3][1]	Water:Ora-Sweet 1:1	Amber bottle
Room Temperature (~25°C)	14–26 days[4][2]	Water:Ora-Sweet 1:1	Amber bottle

*Time until failure defined by >10% loss of original concentration or significant visual/pH change.

Efficacy in Clostridioides difficile Infection

Pharmacologic and Clinical Effectiveness

- **Mechanism:** Oral vancomycin is poorly absorbed systemically, acting locally in the GI tract—ideal for C. difficile colitis[6][7].
- **Clinical Outcomes:** In randomized and observational studies, vancomycin syrup demonstrated cure rates in initial CDI episodes ranging from 70% to more than 90%, often superior to metronidazole[6][8].
- **Strain Sensitivity:** Vancomycin is highly effective against epidemic strains including ribotype 027, rapidly reducing vegetative organism counts and cytotoxin titers[6].

Efficacy in Special Populations

- **Pediatrics:** Compounded syrups are critical for pediatric dosing and have shown high rates of symptom resolution.
- **Immunocompromised Patients:** High cure rates are observed, though recurrence risks may still apply.

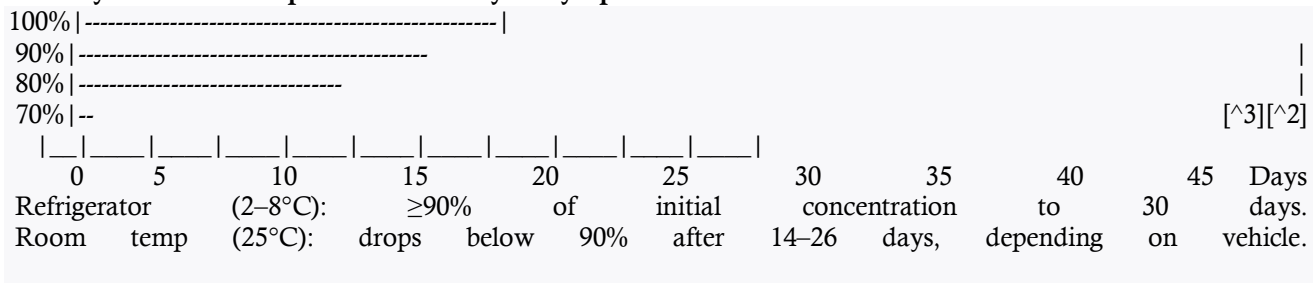
Safety and Tolerability

Adverse Effects

- **Local Action:** Minimal systemic absorption means vancomycin syrup is generally well tolerated, even at high oral doses[7].
- **Common Side Effects:** Nausea, abdominal discomfort, and rarely hypersensitivity reactions[7].
- **Superinfection Risk:** Prolonged or repeated courses can disrupt normal flora, rarely leading to candidiasis or emergence of vancomycin-resistant Enterococci (VRE)—though current studies indicate no increased risk compared to metronidazole[9][10].
- **Recurrence and Resistance:** Some studies highlight the possibility of CDI recurrence and VRE colonization, but population-level risks remain low for most patients[9][11].

Graphs & Figures

Stability Profile of Compounded Vancomycin Syrup



Clinical Cure and Recurrence Rates in CDI Treated with Vancomycin Syrup

Clinical Outcome	Range Reported
Initial cure rate	70–98%[8][6]
Recurrence rate	12–37%[8][12]
Severe adverse event	<5%[7][8]
VRE colonization	No higher than with metronidazole[9]

DISCUSSION

Compounded vancomycin syrup offers a practical and effective solution for CDI treatment, especially for patients who cannot swallow capsules. Ensuring chemical and microbiological stability of each batch is necessary for consistent dosing and efficacy. The risk of adverse effects and resistance remains low with short, guideline-concordant courses.

Limitations and Precautions

- Syrup should be refrigerated and discarded after 30 days or as per local protocol.
- Excipients such as sweeteners should be considered for patients with allergies or sensitivities.
- Pharmacist review of compounding protocols is advised prior to dispensing.

CONCLUSION

Extemporaneously prepared vancomycin oral suspensions have well-established protocols for compounding and storage. Their clinical efficacy in treating CDI, along with a favorable safety profile, is well-documented. Compounded syrup remains an essential formulation in both pediatric and adult cohorts, where commercial tablets or capsules are unsuitable.

Acknowledgements

No conflicts of interest. This review is for educational and research purposes.

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