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Compounding Protocol

Compounding Lidocaine Topical Gel: An Exhibit of a "Master Formulation and Compounding Records" for 503A pharmacies

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A B S T R A C T

Master Formulation Record (MFR) and Compounding Record (CR) must be created for each single formulation of a compounded nonsterile preparation (CNSP). Documentation is one of the most important components of quality assurance to prevent errors and ensure accuracy and safety in the compounding process. The MFR can be duplicated, leaving blank spaces to fill in the details needed to finish the CR. In this article, the MFR and CR for lidocaine topical gel preparation are combined for 503A pharmacies. Most of the information that is required as per the current USP <795> Standard is included. The manual compounding method was validated and characterized using HPLC. The study results indicated that the compounding method produced a uniform, reproducible (%Assay ± SD; 101.6% ± 2.2) and elegant (clear hydro-alcoholic) gel preparation with an excellent yield (~99.0%). This compounding protocol may serve as a valuable resource for compounding professionals to minimize errors and to ensure accuracy, consistency, quality, and safety in the compounding process.

Keywords: Lidocaine Topical Gel, Master Formulation and Compounding Records, 503A pharmacies, USP <795>

Introduction

Lidocaine is frequently used as a local anesthetic drug. It is a weak base with a pKa of 7.9 and falls under the BCS class II drug (high permeability and low solubility) category.[1] The molecular weight is 234.34 g/mol. Lidocaine Hydrochloride monohydrate (LHM) is the salt form of the Lidocaine and it is a white powder freely soluble in water. The molecular weight of the salt is 288.82.[2] LHM salt contains ~81% of the base (Lidocaine). This percentage can be used to calculate the active drug moiety of the drug (to convert the base to salt or salt to the base form of the Lidocaine) during compounding. Patients undergoing specific medical procedures can manage pain by applying lidocaine topical preparations.[3,4]

Pharmaceutical compounding involves creating specialized drugs to address individual patient requirements. A thorough document that provides detailed directions for compounding a particular medication is called a “Master Formulation and Compounding Records”. USP General Chapter <795> Pharmaceutical compounding—nonsterile preparation defined Master Formulation Record and

Compounding Records as "A master formulation record (MFR) is a detailed record of procedures that describes how the CNSP is to be prepared" and "A compounding record (CR) documents the compounding of each CNSP."[5] To ensure accuracy and uniformity in the compounding process, this record is used as a guide for compounders. In this protocol, the master formulation and compounding records are combined to make one protocol. This protocol is developed for topical lidocaine gel (TLG) compounded preparation.

Materials

Pharmaceutical grade drug and excipients, and ACS/HPLC grade chemicals were used to compound and analyze the formulation to evaluate the quality. The items were purchased from commercial suppliers: Lidocaine Hydrochloride, Carbomer 940, Propylene Glycol, Ethyl alcohol, Acetonitrile, Phosphoric acid, Monobasic potassium phosphate, Trifluoroacetic acid. Distilled water was obtained through the in-house water distillation system located at ACP Faculty Lab.

Compounding Methods

The Master Formula was originally developed by the author and published in IJPC.[6] In this article, the master formula and compounding method were optimized for manual compounding. According to this method, all formulation materials were to be placed directly into the dispensing container in the proper order while being weighed on the weighing scale. The ingredients were mixed with a glass rod to complete the formulation. The master formula and the detailed compounding procedure are described in Table 1.

HPLC Analysis

The following chromatographic conditions were used to calculate the content of lidocaine present in the gel. The active ingredient (lidocaine) was extracted using a solution of acetonitrile and 0.1% phosphoric acid (1:1) with sonication for 10 minutes and shaking intermittently. The standard curve of lidocaine was used to calculate the content (Figure 1). The chromatographic separation was achieved by the use of a Shimadzu Prominence HPLC system with a Waters XBridge C-18 (4.6 mm x 100 mm, 10 µm) column using isocratic elution mode with a flow rate of 1 mL/min. The detection wavelength was 220 nm. The mobile phase consisted of acetonitrile and a buffer (25 mM KH2PO4; pH adjusted to 3.6 with trifluoroacetic acid) at a ratio of 20:80 (v/v). The pH of CLG was determined by using the pH test paper.

Results and Discussion

In the formulation, propylene glycol and ethanol are employed as co-solvents to improve medication penetration through the skin from the gel matrix. To decrease potency errors and prevent cross-contamination which produces a decrease in the amount of mass to clean up, a direct compounding process with a cumulative weighing approach was used. Following process and formulation optimization, TLGs were analyzed. The study's findings show that it is uniform and reproducible (%Assay ± SD; 101.6% ± 2.2). The gel preparation can be made in less than ten minutes by taking advantage of this user-friendly compounding method. The pH is between 5 -6. An approximate loss of 1g of gel on the glass rod may occur, thus the process loss is very minimal.

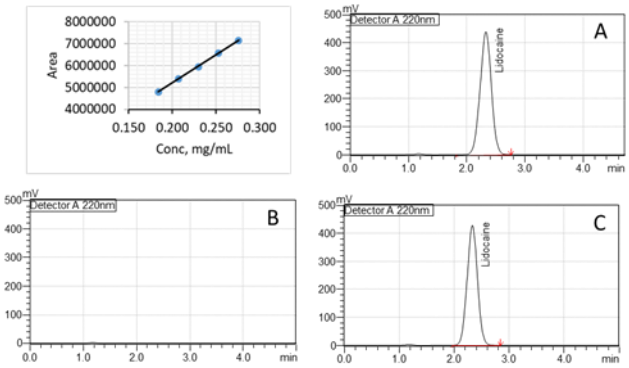

Fig. 1. Linear curve (0.184 mg/mL to 0.276 mg/mL) of lidocaine; B: Representative high-performance liquid chromatogram of the A: Diluent, B: Lidocaine Standard and C: Lidocaine Gel sample (RT of lidocaine is 2.5 minutes).

When the pharmacy receives an Active Drug Substance (API) from a supplier or manufacturer they must verify the test results such as purity (% Assay), Impurities, water content, etc reported on

the Certificate of Analysis (CoA) with the specifications published in the USP Monograph for that specific API. They also need to verify the type, whether it is a base (Lidocaine) or the Salt (Lidocaine Hydrochloride). If the pharmacy has the salt form of the lidocaine in stock, then they need to adjust the weight of the API by calculating the conversion factor (CF) using their Molecular Weights (CF=MW of the Lidocaine/MW of the lidocaine Salt = 0.81) to get the equivalent amount of Active drug. For instance, 2 g of Lidocaine is equivalent to 2.5 g of Lidocaine Hydrochloride Monohydrate. Before compounding any preparation, the responsible personnel must check and verify all ingredients' expiration dates, and the purity (% Assay) of API and write on the MFR & CR. Based on the purity, the compounder may need to adjust the amount of the API required to compound the preparation. For example: as per USP Monograph, Lidocaine should contain NLT 97.5% and NMT 102.5% of lidocaine. So if the purity of the API available in the pharmacy is 97.5% then it may be necessary to adjust the weight using the purity factor. In this situation, the compound should use 2.05 g of Lidocaine instead of 2 g of Lidocaine to compound the gel preparation.

Calculation:
Purity Factor = 97.5/100 = 0.975

Amount of API required to get the correct dose = 2 g/0.975= 2 g/0.975= 2.05 g

The author believes that the inclusion of calculation formulas with appropriate instruction in the compounding protocol will significantly minimize compounding errors. All of the important findings and information obtained from USP, CoA, and Literature Review for every compounded preparation should be included in the MFR and CR.

Conclusions

Simplified compounding approaches and the application of QA and QC in compounding have a significant impact on minimizing errors and improving preparation quality and patient safety. This compounding protocol will serve as a valuable resource for student pharmacists, practicing pharmacists, and compounding professionals to ensure accuracy, consistency, and safety in the compounding process.

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Conflict of interest

The authors declare no Conflict of interest.

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- Added "ISSN" on February 07, 2024.

Table 1
The Master Formulation and Compounding Records for Lidocaine Topical Gel. *Next Page

MASTER FORMULATION AND COMPOUNDING RECORDS Protocol# ACP10001

JPCTs, Oakwood, VA, USA

Lidocaine 2%Topical Compounded Gel Preparation

Strength: *2% Lidocaine as Lidocaine Hydrochloride* LOT Number# *ACPKG240101*

Date and time of preparation of the CNSP: *January 10, 2024* Time: *11 AM*

Patient's Name: *Ms. Begum, Grundy, VA, USA* Sex: *Female* Age: *18 years*

Prescriber's Info# *Dr. Afraz, Hossain, Grundy, VA, USA* Prescription/order# *6333125*

Prepared By: *Dr. Hossain* Checked By: *Dr. Jeff* Approved By: *Dr. Mullins*

Supplier/Manufacturer Certificate of Analysis (CoA) verification
Specification: As per USP Monograph: Lidocaine contains NLT 97.5% and NMT 102.5% of lidocaine.
Results: % Assay: *99.7%*

Master Formula (MF)

Sl. No	Name of the ingredients	Weight of the ingredients
1.	Lidocaine, USP	2 g
2.	Propylene glycol, USP	10 g
3.	Ethyl Alcohol, USP	35 g
4.	Carbomer 940, USP	0.6 g
5.	Purified Water, q.s. to make	100 g

*Reference: In house

Calculation

1) Amount of Gel needs to be dispensed as per the prescription: *50 g*

2) Total Amount of the Gel that needs to be **COMPOUNDED**: *50* g + 1g (Process loss) = *51 g*

3) **Calculation Formula:**
Amount of each ingredients required = (Weight of the ingredient from MF, g) × (Total Amount, g) / 100 g

4) Note:
2 g of Lidocaine is equivalent to 2.5 g of Lidocaine Hydrochloride Monohydrate. So, if you need to use Lidocaine Hydrochloride Monohydrate instead of Lidocaine, please use 2.5 g.

*Base to Salt Conversion: 2 g/0.81 = 2.5 g of Lidocaine Hydrochloride Monohydrate.

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Manufacturer, lot number, and expiration date of each component

Name of the ingredients	Manufacturer	Lot Number	Expiration Date (M/D/Y)	**Amount required, g	Cumulative Reading (Calculated), g
Lidocaine	*XXXX*	*A1234*	*10/11/2024*	*1.02 g*	*1.02 g*
Propylene glycol	*XXXX*	*F1234*	*01/12/2024*	*5.1 g*	*6.12 g*
Ethyl Alcohol	*XXXX*	*R1234*	*08/23/2025*	*17.85 g*	*23.97 g*
Carbomer 940	*XXXX*	*A1234*	*01/19/2026*	*0.306 g*	*24.276 g*
Purified Water, q.s	*XXXX*	*Z1234*	*09/01/2024*	*q.s.*	*51 g*

a) Training is required for new employee to understand Cumulative Reading (increasing by successive additions)

Compounding Direction and Procedure:

1) To begin, measure the weight of the carbomer 940 using a weighing boat and set it aside. Weight: *0.310* g

2) Place a suitable dispensing container on the scale and record the weight of the empty container. Reset the scale to zero. *0*

3) According to the calculated value, weigh the following ingredients directly into the dispensing container and confirm the weight:

   a. Lidocaine (Record the Cumulative Balance Reading: *1.023* g
   b. Propylene glycol (Record the Cumulative Balance Reading: *6.233* g
   c. Alcohol (Record the Cumulative Balance Reading: *24.105* g

4) Gently swirl the mixture for 2 minutes to dissolve the drug.

5) Then, add the carbomer 940 to the mixture by sifting it through a small stainless-steel powder sieve. Swirl the mixture again for 2 minutes to evenly disperse the carbomer.

6) Record the cumulative weight reading after adding the carbomer. *24.415* g

7) Finally, place the dispensing container back on the scale and add enough purified water to reach the total quantity required for compounding. (Record the Cumulative Balance Reading: *51.016* g).

8) Mixed for 5 minutes using a glass rod and check the final weight of the CNSP *50.023* g

Quality Control (QC) procedures (e.g., pH testing, visual inspection) and expected results

Specification:
Visual inspection: Should be a clear hydroalcoholic gel
pH: approx. 6 *Using a pH paper

Test Results:

- Physical description of the final CNSP: *Clear gel*
- pH: ~ *6*
- Amount Dispensed: *50.023* g

Beyond-use date (BUD and storage requirements:

Not more than 35 Days at Controlled room temperature

Reference: USP General Chapter <795> pharmaceutical compounding—nonsterile preparation.

Labeling information	JPCTs Pharmacy 1234, VA, USA, Phone# 123456789 Pharmacy lot number#ACP001, 01/01/2024 #6200589, Dr. R. Patel Afraz Hossain, Lidocaine 2% w/w Compounded Topical Gel Preparation Instruction: #as per the Prescription Quantity: 50 g Store at Room Temperature Beyond-use date: 01/30/2024 For External use only

Note: *This protocol is created by Dr. Hossain, Assistant Professor, Department of Pharmaceutical Sciences, Appalachian College of Pharmacy for educational purposes only.*