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TEACHERS TOPICS

Introduction to Pharmaceutical Calculations

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This manuscript describes material presented in the first lecture of a pharmaceutical calculations lecture series. The first lecture focuses primarily on the key concepts needed to approach pharmaceutical calculations systematically and in a manner that will develop good calculation habits and ultimately lead to optimal patient care. Much of the content of subsequent lectures is specific to the respective topics covered (calculations related to dosing, parenteral preparation, isotonicity, milliequivalents, concentrated acids, etc). Concepts covered in the first lecture are emphasized through application in subsequent lectures in the series.

Keywords: Pharmaceutical calculations

INTRODUCTION

Accurately performing pharmaceutical calculations is a critical component in providing patient care in every pharmacy practice environment. Consequently, pharmaceutical calculations are a vital part of any pharmacy curriculum. Although most pharmaceutical calculations are not 'difficult,' it is a topic that deserves attention because it requires flawless accuracy. Before students are able to become optimally proficient at performing pharmaceutical calculations and using them to contribute to optimal patient care, they must understand approaches to pharmaceutical calculations that help minimize error and maximize accuracy. The objectives of this introduction to pharmaceutical calculations are:

1. Openly address common student perceptions so that these perceptions do not hinder students' focus on pharmaceutical calculations.
2. Review the two main approaches to pharmaceutical calculations, proportion and dimensional analysis, and describe advantages and shortcomings of each.
3. Provide recommendations for improving efficiency and accuracy while avoiding errors and misinterpretations when completing pharmaceutical calculations.
4. Describe methods for double-checking calculations.

Frequent Perceptions

Like any class, students come to a pharmaceutical calculations class with perceptions and expectations. Some of these are accurate and some require refinement or explanation. The following issues often come up when students first come to the calculations course.

"I already know how to do this — it is just simple math."—Although some pharmaceutical calculations require basic science knowledge, such as interpreting a chemical formula to determine the number of equivalents per mole or knowing that 1ml of water weighs 1g, a large part of performing pharmaceutical calculations requires math skills learned prior to high school. Students quickly recognize this fact and some may perceive that pharmaceutical calculations should be easy. The fact of the matter is that pharmaceutical calculations are NOT easy. No student in 8th grade was expected to be correct 100% of the time. The major difficulty in pharmaceutical calculations is not the math, it is the fact that the margin for error is non-existent.

Some of the content of the remaining discussion will provide mathematical reviews that will be quite basic to some students. This level of detail is purposely provided

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so that ALL students fully understand these basic mathematical concepts, as their future patients' doses, dosage forms, and lives will depend on it.

"I can do this in my head."—As students and later as practitioners, there are occasions when calculations are done without a paper and pen. Most students and pharmacists do not need a paper and pen to determine that if 1 tsp contains 250 mg of amoxicillin, one half tsp will contain 125 mg. Students need to show their work for even the simplest calculations, however. The obvious reason for this (grading) is not the most important. Showing their work allows a student to visualize the problem and slow down their thought process, making it less likely for errors to occur. It also develops good habits for practice, when documentation allows other practitioners to double-check work and easily see the method of calculation used.

"It is boring — let's get to the exciting stuff."—Pharmaceutical calculations are not glamorous. In fact, one could argue that they are somewhat mundane. This can be particularly true early in a lecture series on pharmaceutical calculations, when the topic focuses on understanding the basic concepts of proportions and dimensional analysis (before diving into the slightly more glamorous calculations themselves). The challenge lies in the fact that many students (and instructors alike) would rather spend time discussing new and innovative therapies for a condition than basic concepts in pharmaceutical calculations, and consequently, it is tempting to rush through introductory material. Calculations can be occasionally mundane, particularly the repetition necessary to develop confidence as well as accuracy. Nevertheless, deliberate and undivided attention to detail is required to clearly understand the basic concepts that will serve as building blocks during later coursework. There can be no misunderstanding of the basic concepts among students. Correct calculations contribute just as much to patient outcomes as the newest methods and guidelines for diagnosis, treatment, and prevention. Furthermore, errors in calculations can make the otherwise best attempts at optimal patient care catastrophic.

With these perceptions and their implications discussed, the focus will shift to the basic concepts of pharmaceutical calculations themselves.

CALCULATION METHODS

One of the common difficulties students have related to pharmaceutical calculations is setting up the calculation. There are three basic ways to approach most pharmaceutical calculations: proportion, dimensional analysis, and empiric formulas.

Proportion

Ratios define the relationship between 2 amounts, and they are the building blocks of proportions. Examples of ratios include the number of milliequivalents of drug per tablet (eg, 10 mEq potassium per tablet) and the number of milligrams of drug per volume of product (eg, 80 mg acetaminophen per 0.8 mL suspension). One might think of a ratio as a concentration, such as grams of steroid per pound of ointment, but ratios can express any relationship between 2 amounts, such as 1 kg per 2.2 lbs, whether or not they reflect a concentration.

The use of proportions in pharmaceutical calculations can be shown through the following example. A suspension is labeled to contain 250 mg of amoxicillin per 5 mL of product. If a patient's dose is 125 mg, what volume of suspension should the patient receive? Given the known ratio of 250 mg of amoxicllin per 5 mL of product, the volume needed can be calculated as shown in Figure 1a. The proportion is set up with the known ratio on the left side. Because the numerator of the ratio on the left side contains mg of amoxicillin, the desired dose of 125 mg amoxicillin must go in the numerator of the ratio on the right side. The units in both numerators of the proportion must be the same, as must be the denominators' units. The denominator of the ratio on the right side is entered as unknown. One can then cross-multiply (Step 1) and divide (Step 2) to determine the unknown (Figure 1b), multiplying the known value in the numerator on the right side (125 mg) by the known value in the denominator on the left side (5 mL) and then dividing this product (625 mg·mL) by the value in the numerator on the left side (250 mg), giving the unknown value (2.5 mL).

Where the unknown is located does not matter (numerator versus denominator); the principles still apply. Consider a situation where the suspension above has been taken home and the child is inadvertently administered 12.5 mL of suspension rather than 2.5 mL. How many milligrams of amoxicillin did the patient receive when administered the 12.5 mL? The set up and solution is shown in Figure 1c. As above, the known ratio is on the left side of the proportion. The known volume administered (12.5 mL) is entered in the denominator on the right side — the denominator is the correct location because the units of 12.5 mL match the units of the left side proportion (5 mL). The numerator (the number of milligrams of amoxicillin) is the unknown. Cross-multiplying 12.5 mL times 250 mg gives a product of

1a.

$$\frac{250 \text{ mg amoxicillin}}{5 \text{ mL suspension}} = \frac{125 \text{ mg amoxicillin}}{x \text{ mL suspension}}$$

1b.

Step 1. Cross-multiply:

$$5 \text{ mL suspension} \times 125 \text{ mg amoxicillin} = 625 \text{ mg amoxicillin} \cdot \text{mL suspension}$$

Step 2. Divide product by unused known:

$$\frac{625 \text{ mg amoxicillin} \cdot \text{mL suspension}}{250 \text{ mg amoxicillin}} = 2.5 \text{ mL suspension}$$

1c.

$$\frac{250 \text{ mg amoxicillin}}{5 \text{ mL suspension}} = \frac{x \text{ mg amoxicillin}}{12.5 \text{ mL suspension}} \qquad x = 625 \text{ mg amoxicillin}$$

Figure 1. Example of Calculation Using Proportion.

3125 mL·mg, which when divided by 5 mL gives an answer of 625 mg amoxicillin.

The use of proportions to solve calculations has an important consideration. A single proportion can only solve 1 step of the calculation. In the example above, this was not a problem because the entire question only required 1 step. In more complex calculations, it takes multiple steps to reach an answer, each requiring a separate proportion. This is good and bad. It is bad because it is inefficient. It is good because it allows the student or practitioner to see their intermediate answers throughout the steps of the calculation and more easily identify mistakes if they occur.

Dimensional Analysis

Similar to proportions, dimensional analysis is heavily dependent on the use of ratios. It has 2 main differences compared to proportions: the ability to "cancel units" to help verify the setup of the problem and the ability to handle multiple steps of a calculation at once. The first of these differences is the most important. The units of all numbers involved in the calculation should algebraically cancel so that the only units remaining are those desired for the calculated answer.

As was done with proportions, the use of dimensional analysis can be shown through an example. A patient weighs 32 pounds and is prescribed 5 mg/kg/day of diphenhydramine HCl. The daily dose is to be divided into 4 doses, each administered 6 hours apart. The practical information a parent will need to know is how much diphenhydramine HCl solution needs to be administered to the child every 6 hours. The solution comes in a concentration of 12.5 mg diphenhydramine HCl per 5 mL solution. This problem requires 4 proportion calculations: (1) convert pounds to kilograms, (2) convert mg/kg/day to mg/day, (3) convert mg/day to mg/dose, and (4) convert mg/dose to mL solution/dose. With dimensional analysis it requires one setup, as shown in Figure 2a. The setup begins by placing the units and description of the desired answer at the right of an equal sign, mL diphenhydramine HCl solution per dose. The pertinent ratios are then placed on the left side of the equal sign with multiplication signs between them. Ratios often need to be inverted to place the units in the correct orientation (numerator versus denominator) so that they cancel each other out and leave only the desired final units. The ratios are then multiplied together and the units canceled to give the final answer of 7.3 mL diphenhydramine HCl solution (Figure 2b). (For students struggling with this concept it may be necessary to give a stepwise approach to picking each individual ratio on the left side of the equal sign. That discussion is not provided here.)

As stated earlier, dimensional analysis provides a method of verifying the setup of the calculation through canceling units that proportion does not. Like proportions, however, dimensional analysis is NOT fool-proof. It is still dependent on the student or practitioner properly identifying relationships between the patient and general data that should be used as ratios in the calculation.

Empiric Formulas

Empiric formulas, such as those for calculating ideal body weight and estimated creatinine clearance, are not covered in detail in this discussion. They are mentioned, however, because an important point related to units needs to be made. In proportion, the units on either

2a.

$$\frac{32\ \text{pounds}}{\ } \times \frac{1\ \text{kilogram}}{2.2\ \text{pounds}} \times \frac{1\ \text{day}}{4\ \text{doses}} \times \frac{5\ \text{mg diphenhydramine}}{\text{kg} \cdot \text{day}} \times \frac{5\ \text{mL diphenhydramine solution}}{12.5\ \text{mg diphenhydramine}} = \frac{\text{mL diphenhydramine solution}}{\text{dose}}$$

2b.

$$\frac{32\ \cancel{\text{pounds}}}{\ } \times \frac{1\ \cancel{\text{kilogram}}}{2.2\ \cancel{\text{pounds}}} \times \frac{1\ \cancel{\text{day}}}{4\ \text{doses}} \times \frac{5\ \cancel{\text{mg diphenhydramine}}}{\cancel{\text{kg} \cdot \text{day}}} \times \frac{5\ \text{mL diphenhydramine solution}}{12.5\ \cancel{\text{mg diphenhydramine}}} = \frac{7.3\ \text{mL diphenhydramine solution}}{\text{dose}}$$

Figure 2. Example of Calculation Using Dimensional Analysis.

side of the equal sign need to be equal. In dimensional analysis, the units on the left side of the equal sign need to cancel to leave only the desired units on the right. In empiric formulas, neither of these is true. Using ideal body weight for a woman as an example (IBW = 45.5 kg + 2.3 kg times height in inches over 5 feet), the units are important, but they do not mathematically cancel. The calculation relies on the height over 5 feet being entered in inches and no other units of measurement. Similarly, calculations for estimating creatinine clearance rely on the values expressed in defined units to give the correct result.

CALCULATION RECOMMENDATIONS

While performing pharmaceutical calculations with the methods outlined above, there are several recommendations that can improve proficiency and foster good habits that can be carried forward into practice.

The 'Number' Should Always Have Three Parts

In Figures 1 and 2, all examples of numbers expressed in the calculations have included 3 essential components: the numerical value (ie, 12.5, 250, 5), the units of measure (ie, mg, mL), and a descriptive name of the substance (ie, diphenhydramine solution, amoxicillin). It is critical that all numbers in a calculation or series of calculations include all 3 components in order to minimize the likelihood that mistakes occur due to confusion between similar ingredients. It is unfortunate that the entire health care system does not follow a single convention when writing units. Consequently, the abbreviations chosen for units should be common, and once in practice, one should follow conventions established at a given practice site. Realizing that not all practitioners within a single practice site or between practice sites will adopt a common set of abbreviations, care should be taken to avoid errors by diligently watching for other practitioners' use of non-conventional abbreviations.

To illustrate the importance of units and the descriptive name, consider another example. A pharmacist is compounding 60 mL of a topical solution. The order is written so that the final solution is 40%(v/v) isopropyl alcohol. The pharmacist's source of isopropyl alcohol is a 70%(v/v) solution. Figure 3a shows the calculations for this problem with numbers written with their numerical value, units, and descriptive name. Notice from this figure that a distinction is made in calculations involving 'isopropyl alcohol (pure)' and 'isopropyl alcohol 70% solution'. The calculations in Figure 3a can be clearly followed and the pharmacist's work double-checked. Compare this with Figure 3b. Figure 3b shows the same calculation, but because of the failure to use discriminating descriptive names, it is not immediately clear which volumes correspond to isopropyl alcohol (pure) and which to isopropyl alcohol 70% solution. The ability to follow the logic in the series of calculations shown in Figure 3b and double-check the work is severely hampered. This would be further hampered if the isopropyl alcohol descriptions were omitted completely and/or if the units of volume (milliliters) were omitted.

The Numerical Value Should NEVER Contain a Naked Decimal Point or Trailing Zero

This is an example of a trailing zero: **1.0**. This is an example of a naked decimal point: **.1**. Students and practitioners should NEVER write numbers this way! Students have a difficult time with this concept, especially when they want to use trailing zeros to convey precision with "significant figures." For clinical purposes, the importance of showing all significant figures is outweighed by the occasional disastrous consequences of including them. Students should still calculate to the desired number of significant digits, but not show them on paper when they result in a trailing zero. It is amazing and unfortunate that something so simple can lead to medica-

3a.

A 40% v/v isopropyl alcohol product is, by definition, 40 mL isopropyl alcohol (pure) in every 100 mL of product

$$\frac{\text{40 mL isopropyl alcohol (pure)}}{\text{100 mL product}} = \frac{\text{x mL isopropyl alcohol (pure)}}{\text{60 mL product}} \quad \text{x = 24 mL isopropyl alcohol (pure)}$$

$$\frac{\text{70 mL isopropyl alcohol (pure)}}{\text{100 mL isopropyl alcohol 70\% solution}} = \frac{\text{24 mL isopropyl alcohol (pure)}}{\text{x mL isopropyl alcohol 70\% solution}} \quad \text{x = 34.3 mL isopropyl alcohol 70\% solution}$$

3b.

$$\frac{\text{40 mL isopropyl}}{\text{100 mL}} = \frac{\text{x}}{\text{60 mL}} \quad \text{x = 24 mL isopropyl}$$

$$\frac{\text{70 mL isopropyl}}{\text{100 mL isopropyl}} = \frac{\text{24 mL isopropyl}}{\text{x}} \quad \text{x = 34.3 mL isopropyl}$$

Figure 3. Example of Good and Poor Use of Descriptive Names When Writing Numbers

tion errors, but trailing zeros have led to errors when the decimal point is not noticed (1.0 interpreted as 10, for example).[1-3] Similarly, naked decimal points cause errors.[2,3] The number .1 can and has been interpreted as a 1, leading to medication errors. It is critical that students begin writing numbers without naked decimal points or trailing zeros early so that doing so is second nature to them by the time they are in practice.

Memorize the Definitions of Standardized Expressions of Concentration

Flawless precision in pharmaceutical calculations is completely dependent on a flawless understanding of the terminology of standardized concentrations. Concentrations can be expressed in many standardized ways. Five of the most frequently encountered standardized expressions of concentration include %w/w, %w/v, %v/v, ratio strength, and molarity. In order to use these standardized expressions of concentration in proportion and dimensional analysis calculations, they need to be expressed as ratios. Table 1 provides the definition of these 5 standardized expressions of concentration along with examples and their respective ratios. The definitions of each should be memorized. The ratio expression should be reproducible from the definition.

Memorize Common Conversions

There are some common conversions that students and practitioner will use so frequently that they need to be committed to memory. These are shown in Table 2. (There are many more conversions one may choose to memorize. It is not the purpose of Table 2 to exhaustively list them all.) On occasion, either because of a memory lapse or a lack of use, conversions are not remembered. In such a case a practitioner should have a favorite calculations textbook or electronic database of conversions handy.

THE FINAL CHECK

Double-checking

There are 3 ways to check the answer: (1) estimate before the calculation and then compare the estimation to the answer, (2) verify the answer by a different method, and (3) have 2 people independently perform the calculation and compare answers. Estimation is a good approach because it provides a ballpark in which one can expect the answer to fall. Many students and hopefully most practitioners could look at the amoxicillin 250mg/5 mL example above and estimate that the dose of 125 mg will be contained in 2.5 mL. Estimation is more difficult when the numbers are more complex. It then relies on rounding numbers to the nearest number that can be calculated in one's head or quickly on paper. Estimation is a good practice.

"Verifying the answer by a different method" can have multiple meanings. In the first, the student calculates the answer both with proportion and with dimensional analysis and then checks that the answers match. While in concept this is a very good idea, often the proportion and dimensional analysis calculations will be dependent on the same ratios. If the ratio is incorrect in one calculation, it is likely incorrect (and therefore causing the same error) in both. If care is taken to set up ratios with the known values properly, this method of double-checking is reasonable.

"Verifying the answer by a different method" can take on a second meaning in some situations. Consider isotonicity. The amount of solute required to make a solution isotonic can be calculated using 3 methods:

Table 1. Definitions of Standardized Expressions of Concentration

Expression	Definition	Example(s) Written as Ratio
% w/w	Grams of substance contained in 100 grams of product	2.5%(w/w) hydrocortisone cream = $\frac{\text{2.5 grams hydrocortisone}}{\text{100 grams cream}}$
% w/v	Grams of substance contained in 100 mL of solution	5%(w/v) dextrose = $\frac{\text{5 grams dextrose}}{\text{100 mL solution}}$
% v/v	Milliliters of substance contained in 100 mL of solution	95%(v/v) ethanol = $\frac{\text{95 mL ethanol}}{\text{100 mL solution}}$
Molarity (M)	Moles of substance contained in 1 L of solution	3 M NaOH solution = $\frac{\text{3 moles NaOH}}{\text{1 L solution}}$
Ratio Strength	Grams (solids) or milliliters (liquids) of substance in a specified weight (in grams) or volume (in mL) of product	Benzalkonium chloride 1:5000 solution = $\frac{\text{1 gram benzalkonium chloride}}{\text{5000 mL solution}}$ Hydrocortisone 1:20 cream = $\frac{\text{1 gram hydrocortisone}}{\text{20 grams cream}}$ Isopropyl alcohol 1:2 solution = $\frac{\text{1 mL isopropyl alcohol}}{\text{2 mL solution}}$

(1) the sodium chloride equivalents method, (2) the USP method, and (3) the freezing point depression method.[6] If a student or practitioner is reasonably comfortable with 2 of these 3 methods, they can calculate the answer with both methods and verify that the answers match.

Finally, in a practice setting and in some learning activities, accuracy can be verified when 2 individuals independently perform the calculation and the resulting answers are compared. This is ideal, as the probability of 2 individuals independently making the same mistake is low. Double-checking with 2 independent persons performing the calculation should always be done when possible.

Ask Oneself: Does This Answer Make Sense?

Despite best efforts to use care when performing and double-checking calculations, it can still happen: the 10 pound baby that weighs 22 kilograms, the 50 mL piggyback bag with 3 mL of additive ordered to run over 30 minutes with a flow rate of 0.1 mL/min, the IM injection volume calculated to administer 25 mL. All people make mistakes, including students and practitioners, but there has to be a last step that requires the student or practitioner to ask, "Does this make sense?" This is an absolutely critical step. Certainly a person's weight in kilograms should not be more than it is in pounds, and the flow rate of a 50 mL bag set to run over one half hour should be greater than 1 mL/min, and the volume

Table 2. Conversions to Memorize

Length
100 centimeters = 1 meter
1,000 millimeters = 1 meter
2.54 centimeters = 1 inch
12 inches = 1 foot
Volume
1 liter = 1,000 milliliters
1 pint = 473 milliliters (480 milliliters)
1 fluid ounce = 29.57 milliliters (30 milliliters)
1 teaspoonful = 5 milliliters
1 tablespoonful = 3 teaspoonsful
Weight
1 gram = 1,000 milligrams
1,000 grams = 1 kilogram
1 kilogram = 2.2 pounds*
16 ounces = 1 pound*
1 grain = 65 milligrams

*All pounds are avoirdupois pounds, not apothecary pounds

calculated to administer by the IM route should not be bigger than a volume that could be safely administered. Early in their pharmacy education this is a difficult question for students to answer because they might not always recognize the 'impossible' or 'improbable' answers. Nevertheless, students need to be constantly driven to verify the sensibility of the answer so that calculation mistakes that manage to make it through the rest of the calculations process can still be caught. It is, after all, the non-sensible answers that have the highest potential for negative patient outcomes.

CLOSING

This first discussion of calculations is necessary to raise students' awareness of common perceptions and introduce the critical concepts in pharmaceutical calculations. The success of this presentation lies in its application in subsequent course and curricular material. Only through the combination of presentation content, practice, occasional error, more practice, timely feedback, application, and assessment will pharmacy students develop the confidence and accuracy in pharmaceutical calculations that their profession demands and their future patients deserve.

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