



Research Note



Rheological Measurements of Compounded Emulsions and Suspensions: A Laboratory Exercise to Support Theoretical Learning

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Abstract

Laboratory exercises often emphasize the theoretical knowledge gained in the classroom and make concepts easier to understand. To that end, in a class of physical pharmacy (Campbell University College of Pharmacy & Health Sciences; master level graduate students), the students prepared two compounded dosage forms in order to establish their flow properties. The compounded formulations were a mineral oil emulsion and an aspirin suspension. The mineral oil emulsion was prepared by the dry gum method, while the suspension was prepared in a vehicle containing suspending agents. A Brookfield viscometer was used in the determination of the flow characteristic of the formulations. The emulsion showed a pseudoplastic flow whereas the suspension exhibited a plastic profile. During the laboratory exercise, students learned the proper use of a viscometer, how to obtain data from the viscometer using compounded dosage forms, and how to analyze the empirical results by matching them with the expected theoretical profiles. The overall informal feedback from the students on this exercise was positive.

Introduction

Rheological measurements are often done on the final product as well on intermediate forms of the product during development. These measurements aim to characterize the flow profile of the formulated mass as they collectively influence the handling of the formulation. The flow characteristics of a formulation may be described to be either Newtonian or non-Newtonian [1,2]. The Newtonian system follows Newton's law of flow, and it describes the linear relationship existing between the shearing stress (i.e., the applied stress on the material) and the rate of shear [1-3]. (Shear is a term used to describe the actual movement produced by the shearing force). Examples of pharmaceutical dosage forms and vehicles that exhibit a Newtonian flow are oral solutions, syrups, elixirs, glycerin, mineral oil, and water [4]. Systems that do not obey Newton's law of flow are known as non-Newtonian. There are three types of non-Newtonian systems, plastic (e.g., concentrated flocculated suspensions; Ketchup), pseudo-plastic (e.g., emulsions; aqueous solutions of carboxymethylcellulose; paints), and dilatant (e.g., starch in water; concentrated deflocculated suspensions) [4]. In addition to these classifications, certain dosage forms do not conform to either type of flow. These systems exhibit both viscous and solid characteristics, and thus, are known as viscoelastic materials. Examples of pharmaceutical dosage forms that have viscoelastic properties are creams, pastes, and ointments [2,4].

In this study, we examined the flow characteristics of two commonly used dosage forms in pharmacy, a suspension and an emulsion. The project aimed to demonstrate to graduate students in pharmaceutical sciences enrolled in a physical pharmacy course the use of a viscometer, the type of data that might be generated from the instrument, and how to analyze the empirical results. Physical pharmacy subject is intended to deliver to students the necessary information related to the physical and chemical characteristics of drugs and how these characteristics influence the preparation of the dosage forms [2,4]. Among the physical properties of the formulation is its flow characteristics (i.e., its rheological profile). This type of laboratory demonstrations may also be suited to student-pharmacists while taking their compounding courses or to undergraduate students in a pharmaceutical sciences program. In general, suspensions exhibit plastic flow, whereas emulsions exhibit pseudo-plastic one [1-3]. Both preparations were made following the art and science of compounding pharmaceuticals.

Materials and Methods

Materials

Campbell University's USP water system supplied USP water (the diluent). Aspirin tablets were a generic immediate-release brand by Walmart Corporation. All other items used in the preparation of the emulsions (mineral oil; acacia; sucrose; alcohol) and suspensions (tragacanth) were obtained from Thermo Fisher Scientific (Philadelphia, PA). In addition to the chemicals, basic compounding laboratory glassware such as mortars and pestles (glass and porcelain types), graduate and conical cylinders, and various glass beakers and stirring rods were also available to students in the pharmaceuticals laboratory at the college.

Methods

Students prepared the formulations and tested them for their rheological properties with the help of the instructor. Immediately following the preparation, students recorded the data obtained from the viscometer as the instructor operated the instrument. Following the laboratory exercise, students analyzed the data that were obtained from the viscometer and plotted the rheograms for both formulations. The instructor evaluated students' work based on the quality of the compounded dosage forms, the analysis of the rheological results, and their participation during the exercises.

Preparation of suspension: The preparation of the suspension and the emulsion followed the art and science of compounding dosage forms in pharmacy [1,5]. A suspension is a coarse dispersion of solid particles in a liquid medium [2,4]. Eight

immediate-release aspirin tablets (Walmart), each containing 325 mg of aspirin were reduced to a powder with the help of a porcelain mortar and pestle. The resulting powder was dispersed in 20 mL of purified water. In a glass mortar, the suspending agents, acacia (1.5 g) and tragacanth (0.3 g), were mixed with 20 mL of purified water. The suspending agents' mixture was then gradually added to the aspirin dispersion with continuous mixing. The mixture was transferred to a 100-mL graduated cylinder and brought to its final volume (60 mL) with the aqueous washings of the mortar and pestle.

Preparation of emulsion: An emulsion is a two-phase system where one immiscible liquid is dispersed in the form of small droplets throughout another liquid [1,5]. The emulsion was prepared in a dry porcelain mortar and pestle using the "dry gum method" of making emulsions [5]. A portion of mineral oil (4 parts; 50 mL) was mixed with acacia (1 part; 12.5 g) to form a slurry. Then, and all at once, two parts of purified water (25 mL) were added to the content of the mortar, and the mixture was triturated rapidly, but lightly until a primary emulsion was formed. The syrup was then added (10 mL), diluted with 5-mL of purified water (a total of 15 mL). Alcohol (6 mL) was then added, and the mixture was transferred to a 100-mL graduated cylinder for a final dilution with the aqueous washings of the mortar and pestle to its desired volume (100 mL).

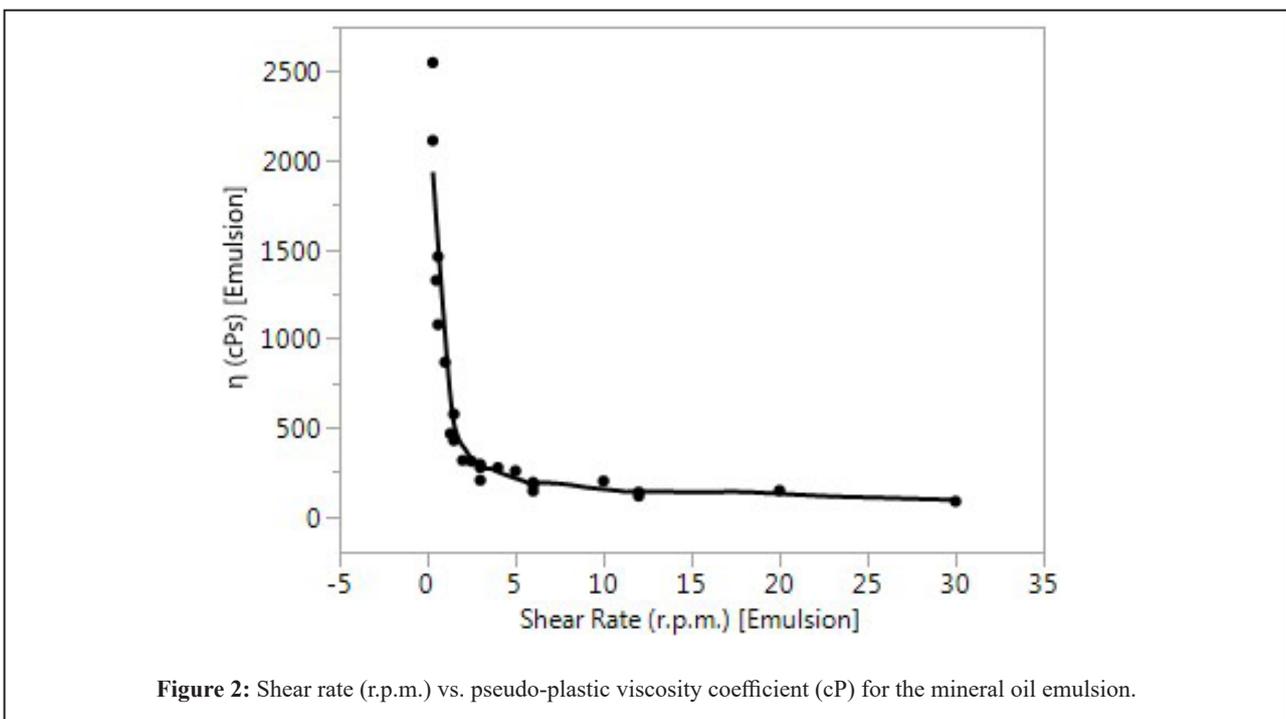
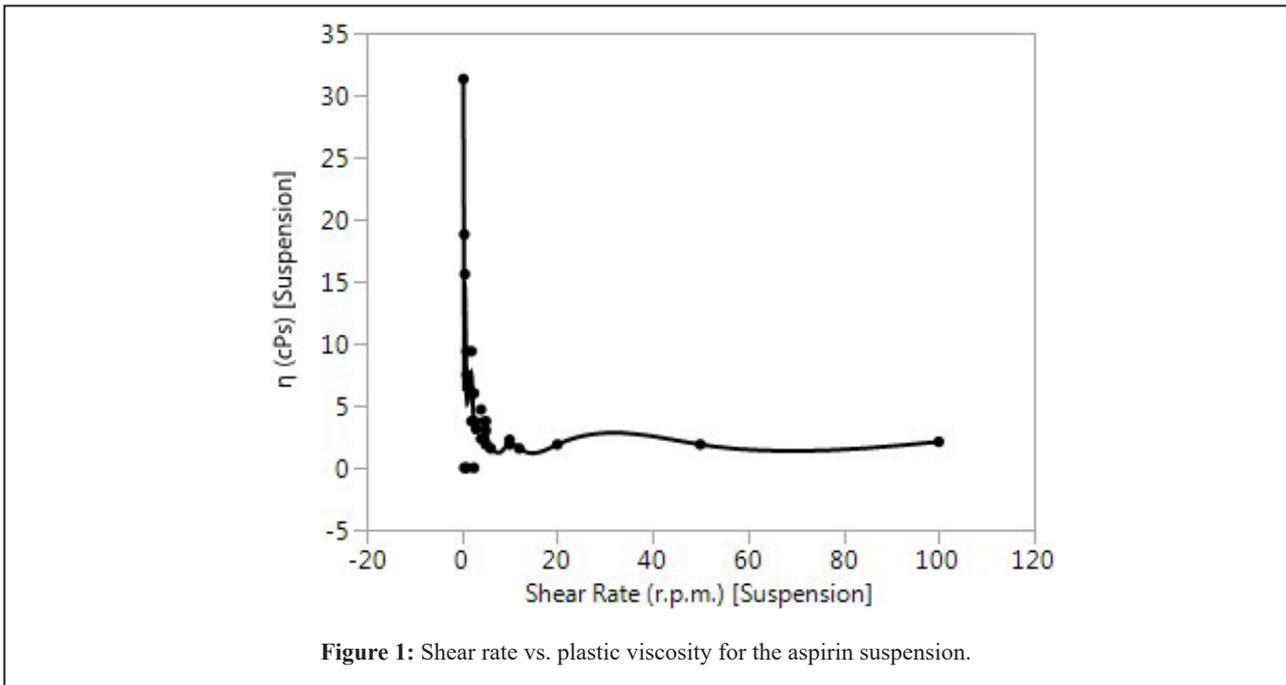
Rheological testing: The compounded preparations (three formulations of each dosage forms) were then subjected to rheological testing using a Brookfield viscometer (Middleboro, MA) [6]. The test preparation was placed in a tall glass container, and the spindle was immersed in the liquid to a level where a predetermined marking was found on the spindle. The spindle was set in motion at different shearing rates (r.p.m.), and readings for the shearing force (%F) and viscosity (cP) were displayed on the screen of the instrument for each of the shearing rates used. Purified water was used as the control liquid.

Results

The results from the rheological profiles of the suspension and the emulsion showed that both dosage forms exhibited a shear-thinning property. Figure 1 shows the decrease in the viscosity of the aspirin suspension as the shear rate increased. The curve reached a minimum plateau corresponding to the plastic viscosity value obtained from the graph on the y-axis. Similarly, for the compounded emulsion, the line declined rapidly with the increase in the shear rate, however, within the limit of our experiment it did not reach a constant, minimum value (Figure 2). The rheograms for the compounded emulsion and suspension are shown in figures 3 and 4, respectively. By

definition, a rheogram is the graph obtained by plotting the shearing rate versus the rate of shear on a rectangular type graph paper [2]. For Newtonian systems, the rheogram shows a positive linear relationship between (%F) and shearing rate with a slope equals to fluidity which is the inverse of Newtonian viscosity [2,5]. Plastic flow rheogram shows an initial portion parallel to the x-axis followed by a curvilinear portion, and after that the graph becomes linear. The slope of the linear portion of the graph is known as mobility which

is the inverse of the plastic viscosity [5]. The rheogram for a pseudo-plastic flow is expected to be curvilinear increasing in its slope value as %F and rate of shear increase [5]. The viscosity of a pseudo-plastic material decreases as the material is being sheared at increasing rates, and thus the name shear-thinning property is given to these types of agents. The shear-thinning property is also assigned to plastic materials as the viscosity of the material decreases with increasing the rate of shear and reaches a constant value at the linear portion of the graph [2,5].



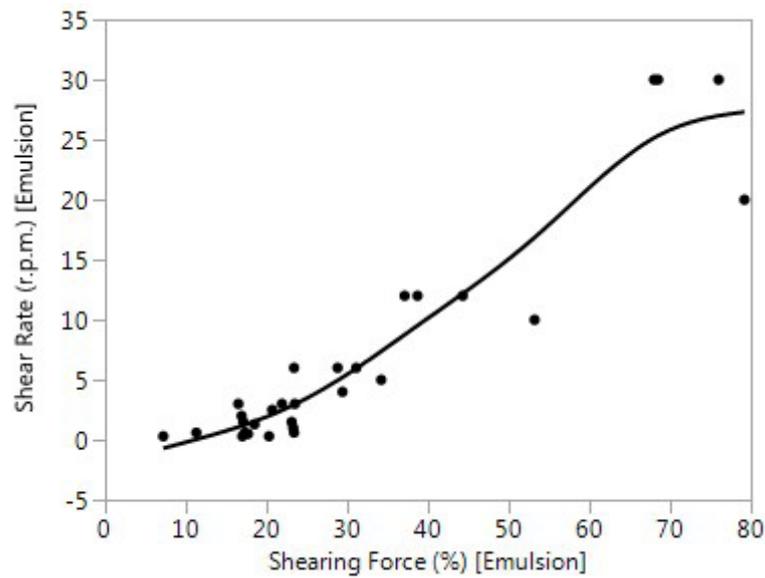


Figure 3: A rheogram for the compounded emulsion (pseudo-plastic flow).

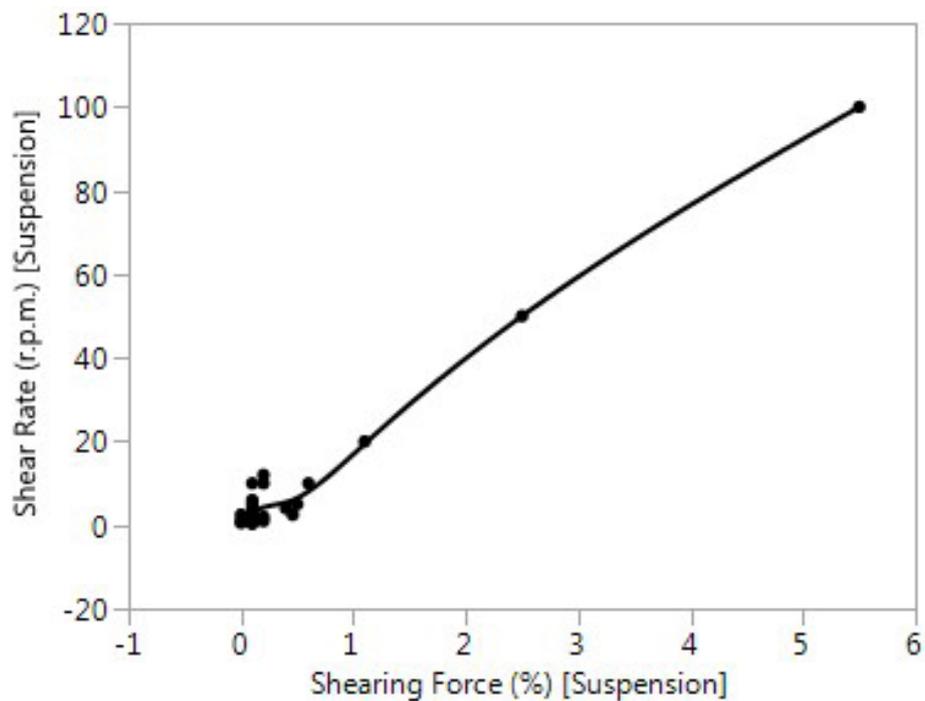


Figure 4: A rheogram for the compounded suspension (plastic flow).

Discussion

Non-Newtonian rheological profiles of the compounded preparations were evident by a change in their viscosity as the preparations were continuously sheared. The change in the viscosity of these systems may be a “mechanical proposition” and related to the undergoing re-arrangement of the suspended

particles (solid or liquid) as the preparation is being sheared [2]. The newly formed arrangements result with either a more facilitated movement between the particles (shear-thinning properties) or a more restricted one (shear-thickening properties; such as the case with slurries like starch dispersed in water) [2]. In the latter case, the viscosity of the preparation increases as the product undergoes an increase in shearing

rate. Dilatant flow is the name given to systems that behave in this fashion (i.e., an increase in the viscosity as the rate of shear increases) [2,5].

As noted in figures 1 and 2, the initial viscosity of the emulsion was much higher (> 2500 cP) in value than that of the suspension (approximately 30 cP). (The unit of viscosity “cP” signifies centipoises.) The lower plateau in figure 1 corresponds to the actual plastic viscosity value of the suspension. The final viscosity was about 2 cP for the suspension (in comparison, the viscosity of water at room temperature 1 cP) (Figure 1). The emulsion did not reach its actual ultimate final minimal value within the experimental range tested. However, the lowest recorded value for its viscosity was approximately 85 cP (Figure 2). The high initial viscosity of the emulsion was probably due to the presence of mineral oil and syrup in the formulation.

On the other hand, the suspension contained, in addition to aspirin, a structured vehicle type which was made of acacia and tragacanth, the suspending agents. Structured vehicles are pseudo-plastic or plastic materials that exhibit thixotropy (i.e., high viscosity upon standing and low viscosity when sheared) [1-5]. As expected, the rheogram describing the emulsion exhibited a pseudo-plastic flow, and that of the suspension was plastic (Figure 3,4) [7-10].

Students learned how to differentiate among the types of flow by recognizing their general flow behavior. The main feature that distinguishes a pseudo-plastic flow from a plastic one is that with the pseudo-plastic profile the material begins immediately to flow when it is subjected to stress, whereas the plastic material initially demonstrates an elastic behavior (i.e., it expands and contracts), and then it begins to flow when subjected to sufficient stress [5]. The shearing stress at which the plastic material begins to flow is known as the “yield value” [2]. For the compounded aspirin suspension, its yield value was approximately (%F = 0.5%) (Figure 4). No yield value is recognized for the pseudo-plastic flow because the material begins its shear immediately upon applying the stress on it.

With the availability of computer graphing software and some basic laboratory instruments such as the ones described in this report, student learning objectives may be better achieved by applying similar techniques [11,12]. An informal survey of students following the laboratory exercise showed that their overall feedback on this laboratory exercise was positive as they perceived the exercise to be informative and complementary to the theoretical knowledge they gained from textbooks. This informal survey was done at the end of the laboratory period, and students expressed their opinion verbally rather than by writing.

Conclusion

Graduate students in a physical pharmacy class prepared two compounded preparations and studied their rheological flow characteristics. Data collected was then analyzed and plotted to demonstrate how the empirical data fit into the actual theoretical profiles. As expected, the compounded suspension and emulsion showed a plastic and a pseudo-plastic flow, respectively. Laboratory exercises such as these are valuable tools to enhance the student’s traditional didactic classroom learning experience.

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