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Predictive Modeling of Rheological Behavior in Semisolid Pharmaceutical Formulations Using Computational Tools.

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HIGHLIGHTS

- Gels-cream exhibited pseudoplasticity, viscosity decreased with speed.
- Python-based tool used to extract viscoelastic info of pharmaceutical formulations.
- Ostwald-de-Waele model best fits all formulations, validating pseudoplastic behavior.
- Open-source tools gain popularity for cost-effectiveness in diverse industries.

Abstract: Topical treatments for skin conditions offer significant benefits, yet understanding the rheological characteristics of semi-solid formulations is crucial, as they directly influence treatment adherence through their applicability. Ideally, these formulations should maintain their placement at the application site and facilitate easy spreading without requiring excessive force, particularly on painful lesions. In this study, a Python-based tool was developed to assess the rheological behavior of formulations, with a gel-cream

serving as a model to demonstrate its applicability. The model formulation was created by emulsifying an oily phase, including blackcurrant oil, with an aqueous phase containing xanthan gum as a gelling agent. Rheological parameters were determined using a rotational viscometer. The prepared gel-cream exhibited pseudoplastic behavior, with viscosity decreasing as rotation speed increased. The Python tool was utilized to extract information about the rheological properties of the samples. Upon applying the data to various mathematical models, it was confirmed that the formulations displayed pseudoplasticity, with the Ostwald-de-Waele model demonstrating the best fit for all evaluated formulations. This pseudoplastic behavior was further confirmed by calculating the flow index (n), which was found to be lower than 1. Open-source tools are gaining popularity across various industries due to their transparency, collaborative nature, and cost-effectiveness. They enable users to enhance product properties, explore therapeutic targets, facilitate efficient collaboration, develop customized software, create predictive models, and ensure regulatory compliance. Our study offers a precise solution for determining the rheological behavior of semi-solid formulations while mitigating human estimation errors. However, it's important to note that proficiency in programming is required to utilize this tool effectively.

Keywords: Mathematical modeling; hydrogels; pharmaceutic dosage form; rheology; non-Newtonian fluid.

INTRODUCTION

The delivery of bioactives to the skin offers numerous advantages; however, ensuring high patient compliance poses a significant challenge. New formulations can overcome this limitation [1–3]. Unlike conventional emulsions, gel-creams are pharmaceutical forms with a low oil content and high hydrophilic content, easily absorbed by the skin without leaving an oily residue, promoting a pleasant sensation of lightness and ease of spreading [4–6]. They can be stabilized by natural hydrophilic colloids, such as xanthan gum, which is biodegradable, non-toxic, and an efficient thickener and emulsifier in an aqueous medium. Thus, xanthan gum has potential applications in the cosmetic industry [5,7,8].

Skin formulations must have appropriate sensory characteristics to improve patient acceptance [2]. However, sensory evaluation presents challenges as it is subjective and requires extensive procedures with product-specific terminology [9]. Quantitative instrumental rheological methods can generate information about sensory attributes [10]. Rheology is the study of the flow and deformation behavior of liquids, solids, and semisolids, which includes both Newtonian and non-Newtonian behaviors [11]. Rheological parameters are important quality features of semisolid products because they influence formulation manufacture, stability, and drug release [12,13]. Semisolid pharmaceutic and cosmetic products should exhibit appropriate shear-thinning rheological properties for their specific application [13]. Knowing the rheological properties of skin care products is crucial to prevent adverse reactions like irritation and pain and to improve patient compliance with treatments. A formulation with adequate spreadability prevents accumulation on the skin, in addition to facilitating application and avoiding pain in places such as skin wounds [2].

Viscosity is a fundamental rheological property that influences the fluidity and ability of a material to pass through a nozzle or fill a mold. However, the flow behavior of materials is multifactorial, involving not only viscosity but also elasticity, plasticity, and thixotropy, in addition to being affected by conditions such as temperature, pressure, shear stress, and formulation constituents [14–16]. For example, thixotropy, the property of certain materials to decrease their viscosity under shear stress and recover it after it is relieved, is particularly valued in semi-solid formulations for therapeutic applications, facilitating smooth application and keeping the material in place application [17,18]. Additionally, elasticity and plasticity determine how a material deforms and flows in response to applied stress, which is essential for mold filling or extrusion in manufacturing processes [18–20]. Therefore, a comprehensive analysis of rheological properties is vital to choosing the appropriate components for formulations, ensuring therapeutic efficacy, ease of processing, and patient acceptance.

The viscoplastic behavior is observed for fluids with minimum shear stress required for deformation and the beginning of the flow [21]. Among the mathematical models that can describe this behavior are the models of Ostwald-de-Waele, Bingham, Casson, and Herschel-Bulkley [22]. The Bingham model is the one that, after reaching the minimum stress for the beginning of the flow, the deformation occurs proportionally to the shear stress, maintaining a linear relationship. This model is observed for formulations such as ointments and more consistent semisolids. The Casson model is characterized by a non-linear relationship between strain rate and shear stress, which is typically observed in less consistent and easily spreadable formulations, such as gels, lotions, and more fluid creams. Finally, the Herschel-Bulkley model describes preparations' pseudoplastic or viscoplastic behavior since the formulations need a minimum tension to start the flow. Still, after reaching this value, the viscosity decreases nonlinearly with the increase in shear stress, which

resembles pseudoplastic behavior [21,22]. This behavior is observed in formulations such as pastes, creams, and thicker gels with combined viscosity and plasticity properties. The Ostwald-de-Waele model simplifies this complex behavior by describing non-Newtonian fluids with an apparent viscosity that varies with shear rate. Ostwald-de-Waele proposed a power-law relationship between shear stress and shear rate [23]. Mathematically, the Ostwald-de-Waele model, also called the power law model, is the most used to describe pseudoplastic fluids [10,24].

Mathematical equations estimate the rheological behavior of topical formulations [8,25], which are usually fit to the data using Excel® or statistical software. Although is considered a valuable and accessible tool, Excel® can present challenges in large-scale analyses. Complexity or volume of data, where the accuracy of results depends on the benefit of the analyst's understanding and ability to enter formulas and data correctly. Furthermore, specialized software offers advanced features for rheological analysis, but the acquisition cost can be prohibitive for some institutions. Therefore, selecting a comprehensive tool based on the specific analysis needs is crucial, balancing accuracy, complexity, and resource availability. Mathematical models have gained attention in developing pharmaceutical forms and predicting behaviors such as permeability. These models can predict untested data based on preliminary experimental data [26–28]. They are a powerful tool that drives innovation and discovery across many fields. It combines the best of statistics, machine learning, pattern recognition, and other techniques to unlock new insights and easily solve complex problems [28].

Recognizing the complexity of the rheological behavior of semisolids and its direct influence on therapeutic efficacy and patient compliance, the main objective was to develop a computational tool based on specificity assessments to determine the rheological properties of skin formulations. The model, created using the Python programming language, stands out for its open-source approach, high accuracy, and ease of reproduction. This tool allows a description of the flow characteristics of the formulations, which can make the choice of therapeutic uses easier based on the specific behavior of the formulations.

MATERIAL AND METHODS

Materials

Xanthan gum (Xantural®; MW 241.115; CAS number: 11138-66-2) was obtained from CP Kelco (Limeira, Brazil). Propylene glycol (CAS number: 57-55-6) was obtained from Lambipex (São Paulo, Brazil). Olivem® 1000 (CAS number: 85116-80-9 / 92202-01-2), Spectrastat® (CAS Number: 56-81-5/ 1117-86-8/7377-03-9), and liquid vaseline (CAS number: 64742-55-8) were obtained from Engenharia das Essências (São Paulo, Brazil). Black current oil was obtained from Laszlo (Belo Horizonte, Brazil). The water used to prepare the formulations was distilled water.

Gel-cream preparation

The formulations were developed and characterized as previously demonstrated by Rudnicki and co-workers [29]. Table 1 depicts the qualitative and quantitative composition of the formulations. In brief, an aqueous phase containing xanthan gum, propylene glycol, and distilled water was heated and agitated until it reached a temperature of 60°C. At the same time, an oily phase containing Olivem® 1000 self-emulsifying wax and liquid vaseline was also made, agitated, and heated until it reached a temperature of 80°C. After both phases were thoroughly dispersed, the oily phase was poured over the aqueous phase and continuously homogenized until the system cooled, resulting in a gel-cream. Lastly, Spectrastat® preservative and black currant oil (1.5% and 3.0% w/w) were added to the formulation to obtain two gel-creams: Gel-Cream 1.5% (GC1.5) and Gel-Cream 3.0% (GC3.0) [29]. For comparison, a gel-cream base was also prepared without vegetable oil (Gel-cream base - GCB). Following preparation, semisolids underwent evaluation for organoleptic characteristics, pH, physical and physicochemical stability, spreadability, and occlusion potential [29].

Table 1. Quali-quantitative composition of the developed formulations.

	GCB	GC1.5	GC3.0
Oily phase			
Liquid Vaseline (% w/w)	2.0	2.0	2.0
Olivem® 1000 (% w/w)	5.0	5.0	5.0
Black currant oil (% w/w)	-	1.5	3.0
Aqueous phase			
Propylene glycol (% w/w)	2.0	2.0	2.0
Xanthan gum (% w/w)	0.4	0.4	0.4
Distilled water q.s.	100	100	100
Spectrastat® (% w/w)	0.7	0.7	0.7

Viscosity determination

A Brookfield rotational viscometer (RV-II Prime) coupled with an S03 spindle was applied to determine the formulations' viscosity. 30 g of each formulation was submitted to various rotation speeds (5, 10, 15, 20, and 30 rpm), which fitted in the ideal torque range of 10 to 90%. The amount of sample was selected to reach the groove in the spindle's shaft. The viscosity determinations were conducted at 24 ± 2 °C. The shear rate versus shear stress curves were fitted by the Bingham, Casson, Ostwald-de-Waele, and Herschel-Bulkley models (Table 2) [30,31].

Table 2. Flow equations for the different mathematical models utilized in this study.

Models	Equations
Bingham	$\sigma = \sigma_0 + \eta(\dot{\gamma})$
Casson	$\sigma^{0.5} = \sigma_0^{0.5} + K(\dot{\gamma})^{0.5}$
Ostwald-de-Waele	$\sigma = K(\dot{\gamma})^n$
Herschell-Bulkley	$\sigma = \sigma_0 + K(\dot{\gamma})^n$

Where σ is the shear stress, σ_0 is the initial shear stress of model, η is plastic viscosity, $\dot{\gamma}$ is the shear rate, and K is the consistency index.

Development and application of the computational tool for rheological profile determination

The computational tool was developed using Python programming language and implemented in the Spyder 4.0 software of the ANACONDA® package. The tool was developed on a notebook with an Intel Core i5 2.5 GHz processor, 8 GB of RAM, DDR 4 2133 MHz, GeForce MX 930 video card, and a Microsoft Windows 10 operating system.

The developed computational tool should be used to analyze data obtained from rotating viscometers, which provide measurements for viscosity (cP), torque (%), and speed (rpm). Figure 1 illustrates the different stages of the technique, as proposed in this study. Each formulation in the database included three batches of data for viscosity (η), torque (M), and speed (Ω). The data can be grouped by calculating the average, a simplified option for building the model, or by using more detailed batch-by-batch data. Regardless of the method used, the other stages of model development remain the same. Through the automated processing by our computational tool, the data for viscosity (η), torque (M), and speed (Ω) are utilized to calculate the constant K using Equation (1). This calculation is instrumental in indirectly obtaining the values for the shear rate (s^{-1}) and shear stress (cP), as outlined in Equations (2) and (3), respectively.

$$K = \frac{\ln(M_i)}{\ln(\Omega_i)} \quad (1)$$

$$\dot{\gamma}_i = \frac{4\pi\Omega_i}{60K} \quad (2)$$

$$\sigma_i = \eta_i \dot{\gamma}_i \quad (3)$$

Where K is a constant dependent on the geometry of the viscometer, $\dot{\gamma}_i$ is the shear rate, and σ_i is the shear stress.

To analyze the rheological models, data on shear rate, shear stress, and speed were collected and plotted on graphs (Table 3). The first model studied was Bingham, where the line equation was generated using speed data on the x-axis and shear stress data on the y-axis. The Casson model applied the square root of the shear rate on the x-axis and the square root of shear stress on the y-axis to derive the line equation. The Ostwald-de-Waele model used the Neperian logarithm of the shear rate on the x-axis and the Neperian logarithm of the shear stress on the y-axis to derive the line equation. For the Herschel-Bulkley model, the first point of both the x and y-axes was excluded, and the remaining data points were explored to derive the equation of the line. Finally, the consistency and flow indices are obtained from the equation of the straight line that presents the highest value of the coefficient of determination (r^2), where the flow index is given by the angular coefficient (a) and the consistency index is calculated as the exponential function of the linear coefficient (b) of this equation.

Table 3. Data used to plot the graphs to obtain the line equation for each mathematical model.

Mathematical model	x-axis	y-axis
Bingham	Ω_i	σ_i
Casson	$\sqrt{\dot{\gamma}_i}$	$\sqrt{\sigma_i}$
Ostwald-de-Waele	$\ln(\dot{\gamma}_i)$	$\ln(\sigma_i)$
Herschel-Bulkley	$\ln(\dot{\gamma}_i) \neq i = 1$	$\ln(\sigma_i) \neq i = 1$

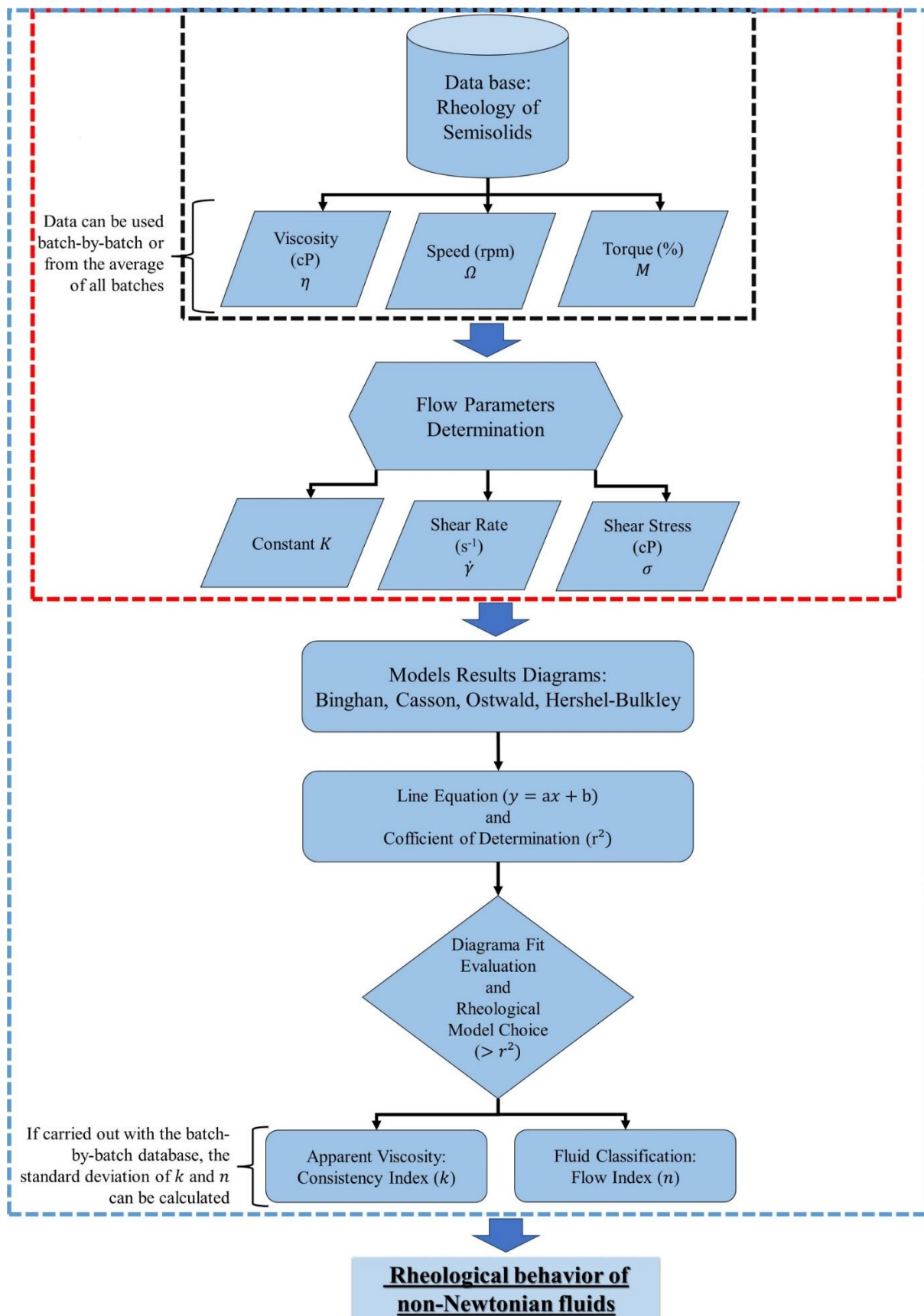


Figure 1. Flowchart of the computational process for evaluating the rheological behavior of non-Newtonian fluids. The black box represents inserting viscosity (cP), speed (rpm), and torque (%) data into the tool database. The red box demonstrates the next step, in which the tool calculates the constant K , rate and shear stress values. The blue box indicates the stage where the straight linear regression curves for the different mathematical models are plotted, obtaining the regression coefficient (r^2) and, subsequently, the flow index (η) and consistency index (K).

Statistical analysis

The results were expressed as the mean $\pm$ standard deviation. One-way or two-way analysis of variance (ANOVA) was conducted using the GraphPad Prism Program (version 8.0, GraphPad Software, San Diego, CA), with Tukey's post hoc test applied for multiple comparisons. Statistical significance was defined as $p < 0.05$.

RESULTS and DISCUSSION

Rheological measurements are widely used to develop semisolid formulations for viscosity behavior determination and spreadability profile estimation [32]. Herein, we describe the application of a computational tool based on Python to estimate the rheological behavior of xanthan gum gel-crems containing blackcurrant oil. Blackcurrant oil (*Ribes nigrum*) is an herbal-derived material obtained by cold-pressing fruit seeds and presents promising antioxidant potential [33]. The scientific literature assigned this property to the high content of fatty acids, such as gamma-linolenic acid (13 to 18%), alpha-linolenic acid, vitamin C, anthocyanins, and flavonoids. Remarkably, blackcurrant oil has already been applied for treating skin disorders, including dry skin, psoriasis, atopic dermatitis, and intense scaling, highlighting the potential uses of this material in developing novel semisolids formulations intending cutaneous pathologies [34].

Regardless of the composition of the formulations, our data showed that the viscosity decreases as the rotation speed increases (Figure 2A), indicating a pseudoplastic behavior (Figure 2B). The findings suggest that the gum exerts a significant impact on the rheological properties of the formulations, as previously reported in the other polysaccharides utilized for hydrogel formulations, such as gellan gum and locust bean gum [35][36]. This could indicate that the gum is responsible for the rheological properties of the gel-crems developed.

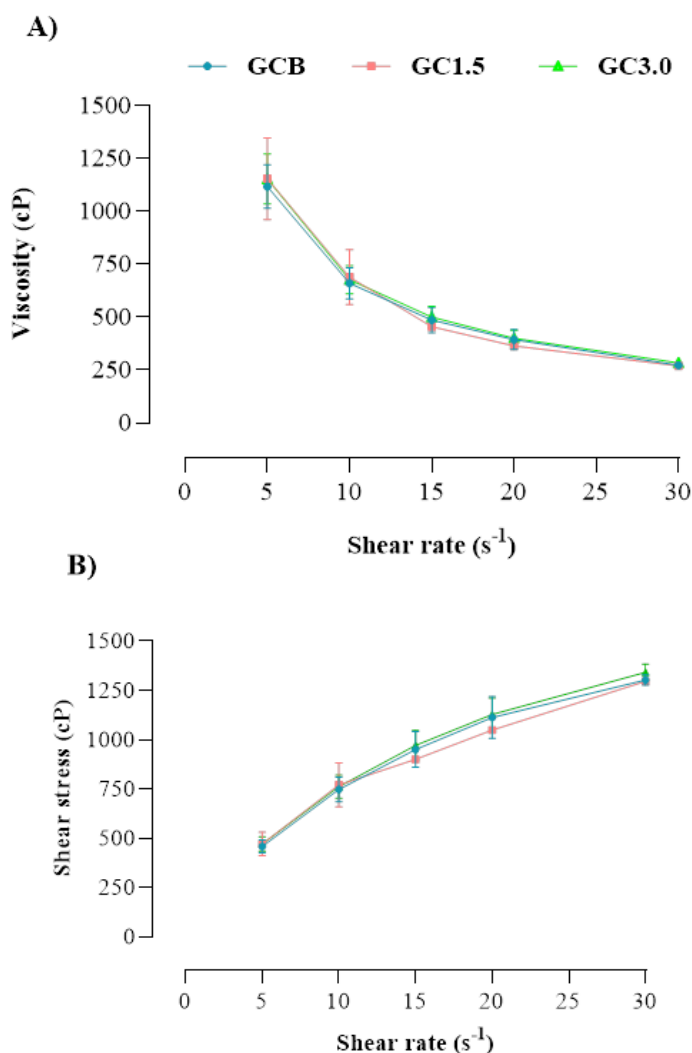


Figure 2. (A) Rheograms and (B) flow curves of gel-cream-based on xanthan gum containing blackcurrant oil. The analysis was realized at 24 ± 2 °C. Data were presented as mean $\pm$ standard deviation. Two-way ANOVA analysis indicated no significant difference among the samples ($p > 0.05$).

Non-Newtonian fluids are important in pharmaceutical formulations because they can have varying viscosity based on shear rate due to their non-linear relationship between shear stress and strain rate [37]. This behavior classifies them as dilatant, viscoplastic, or pseudoplastic, with the latter being most significant in product pharmaceutical development [38,39]. A decrease in viscosity as the shear rate increases characterizes pseudoplastic behavior. This behavior is desirable for pharmaceutical preparations because as soon as a force is applied, the formulation begins to flow more efficiently, which can favor the spreadability of a preparation over the skin, the dosing of a semi-solid from a package, or the dispersion and homogenization of a suspension [40,41]. In this sense, different mathematical models can describe pseudoplastic behavior, such as the Law of Tile, Cross Law, and Ostwald-de-Waele. In this study, we applied the Ostwald-de-Waele model given its wide use for characterizing pharmaceutical formulations [42].

Following, to estimate the mathematical model that best fits the data, we report the development of a computational tool applying the Python language for automated data processing to extract information about rheological properties of formulations with non-Newtonian behavior. After data mathematical modeling (**Table 3**), the pseudoplasticity of the formulations was confirmed, as the highest values of regression coefficients (r^2) were obtained for the Ostwald-de-Waele model, as depicted in Figures 3, 4, and 5, representing the mathematical model fit for GCB, GC1.5, and GC3.0, respectively.

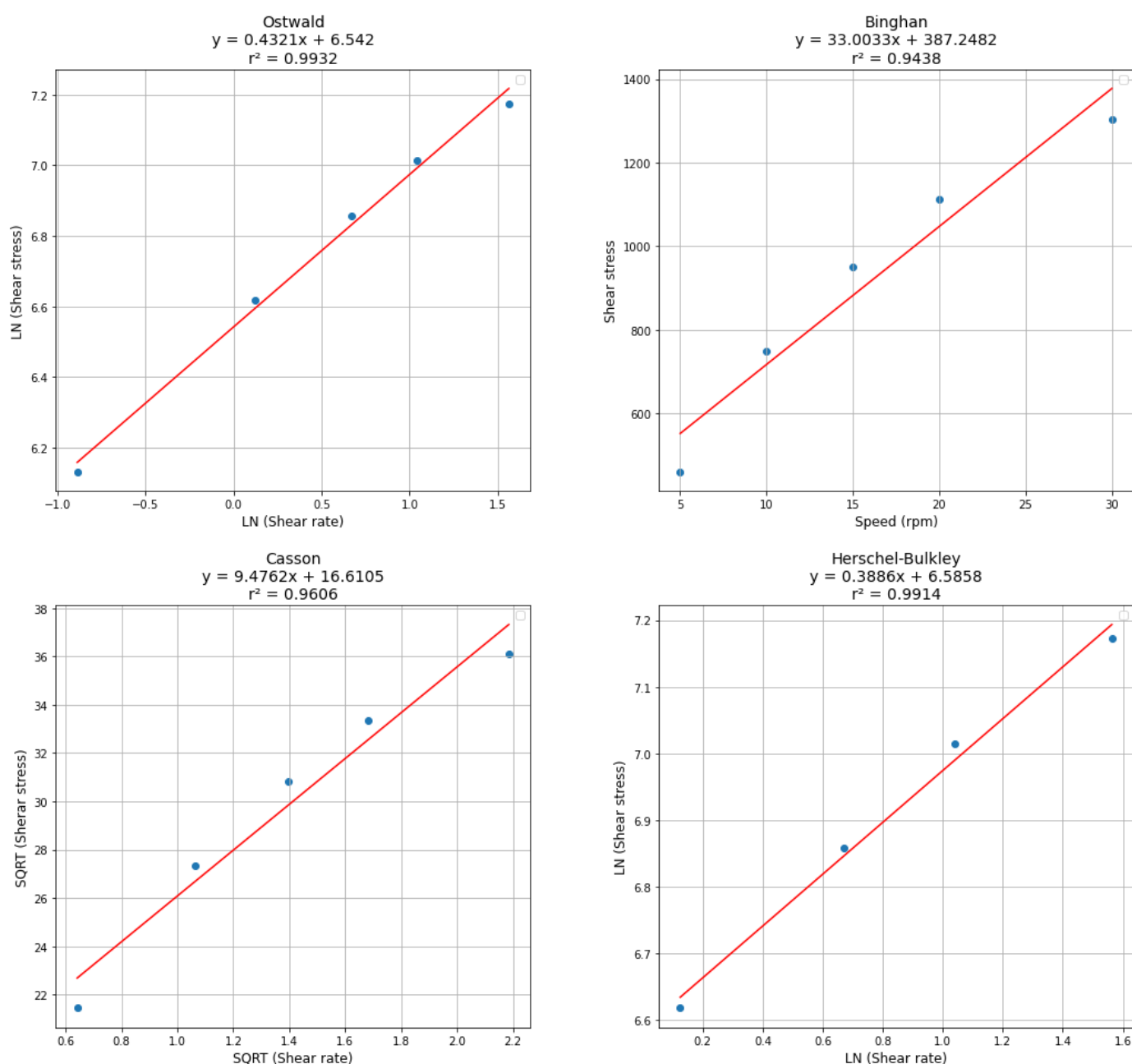


Figure 3. Linear regression of placebo formulations. The analysis was conducted at 24 ± 2 °C.

Considering Ostwald-de-Waele's mathematical model, the η and K indexes were calculated (Table 4). The values obtained for η were lower than 1, confirming the formulations' pseudoplastic behavior. Regarding the K index, which represents the apparent viscosity of the semisolds, it was observed that they have similar consistencies regardless of the incorporation of blackcurrant oil in different concentrations (One-way ANOVA $p>0.05$).

Table 4. Rheological parameters of the formulations.

Parameters	GCB	GC1.5	GC3.0
Consistency index (K) - cP	701.73 $\pm$ 44.11	704.49 $\pm$ 46.35	720.41 $\pm$ 42.15
Flow index (η)	0.4197 $\pm$ 0.0063	0.3907 $\pm$ 0.0386	0.4184 $\pm$ 0.0089
Mathematical model	Ostwald-de-Waele	Ostwald-de-Waele	Ostwald-de-Waele
r^2	0.9932	0.9946	0.9951

Data were presented as mean $\pm$ standard deviation. One-way ANOVA analysis revealed no significant differences among the samples ($p>0.05$).

Understanding and predicting rheological behaviors are crucial for the development and production of effective, safe, and high-quality pharmaceutical formulations. This knowledge enables optimization of performance concerning therapeutic purposes, manufacturing processes, and stability profiles [38,39,43]. In this context, numerous authors have included the evaluation of rheological measurements in their studies, aiming to determine the behavior of innovative pharmaceutical formulations [4,44,45].

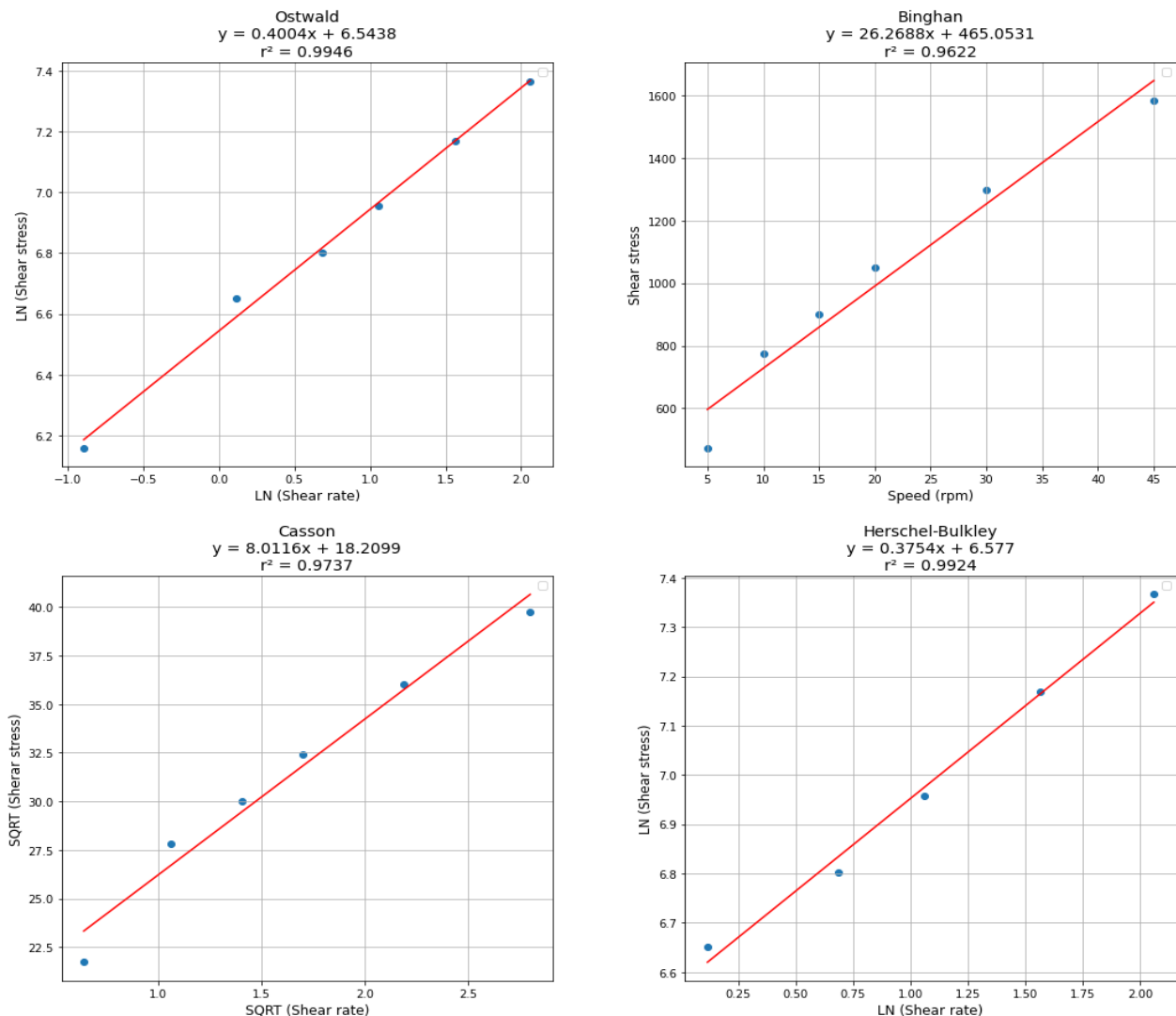


Figure 4. Linear regression of formulations containing 1.5% of blackcurrant oil. The analysis was conducted at 24 ± 2 °C.

The developed tool established the model that best describes the formulation flow according to the observed regression coefficient. The Ostwald-de-Waele model has the highest determination coefficient for the flow curve obtained graphically due to a decrease in viscosity with increasing shear rate [23]. In addition, the software confirmed the pseudoplastic behavior due to the obtained η values. Remarkably, similar η values were observed for cream gels evaluated for rheological behavior using the software coupled in the equipment manufacturer [4]. This behavior is especially interesting for pharmaceutical preparations for cutaneous use, especially for application to injured tissues. The Ostwald-de-Waele model is reported in the literature not to require a minimum tension to initiate the flow, thus minimizing the force needed for the application and, consequently, the painful stimulus [8,46,47].

Another essential aspect assessed using the developed software is the consistency index (K), which gives insights about the apparent viscosity of the preparation. In general, the higher the viscosity of a formulation, the greater its resistance to flow. This data can serve as a parameter to determine the necessary force for pumping and filling [48]. This insight enables rational selection regarding the most suitable packaging that facilitates the flow of the formulation and the force required to properly spread the preparation over the skin or mucous membranes. Formulations with greater consistency demand more force for filling, dosing, and application compared to those with lesser consistency. Moreover, formulations with higher consistency have garnered interest in treating disorders requiring an extended stay at the application site, such as pastes for veterinary use [49,50]. Furthermore, the high consistency can contribute to enhance both release and permeation of active substance on the skin [43]. On the other hand, formulations with lower K values, as the formulations evaluated in this study, may result in easier spread and more interesting precisely for injured tissues, where a minimum effort is required for application [51]. As a result, formulations can be easily and painlessly applied to burns, wounds, or other injuries, facilitating pronounced permeation into the tissue. The reduced consistency can enhance the permeation of the active substance through the skin.

The academic field faces many restrictions in accessing these methodologies in their research, such as limited budget and funding [52], factors that can hinder the acquisition of software necessary for achieving optimal performance in rheological modeling. Thus, many studies perform rheological modeling using easily accessible tools such as Excel®. However, these tools are not aimed at more complex modeling, such as rheological measurements, since the equations can be dispersed in several cells, making it difficult to trace the data and requiring more time and understanding of the analysis [53]. Therefore, in this study, we developed a free and easily accessible computational tool to meet the demands regarding the flow behavior of non-Newtonian fluids, which can be a more robust and faster tool for performing the rheological modeling of pharmaceutical formulations. In this tool, as no rounding is performed, the degree of precision increases, especially in formulations where the rheological behavior is very similar between the two models. The developed software offers a cost-effective solution for estimating rheological properties of semisolid formulations, presenting a distinct advantage over high-cost programs. By providing accurate predictions of rheological behavior, our software eliminates the need for expensive software licenses, making it accessible to a wider range of researchers and industries. Moreover, our user-friendly interface streamlines the analysis process, reducing the time and resources required for complex rheological studies. This accessibility and efficiency empower users to make informed decisions in formulation development, ultimately leading to more cost-effective and optimized products. Thus, our software presents a compelling alternative for researchers and industries seeking reliable rheological analysis without the financial burden associated with high-cost programs.

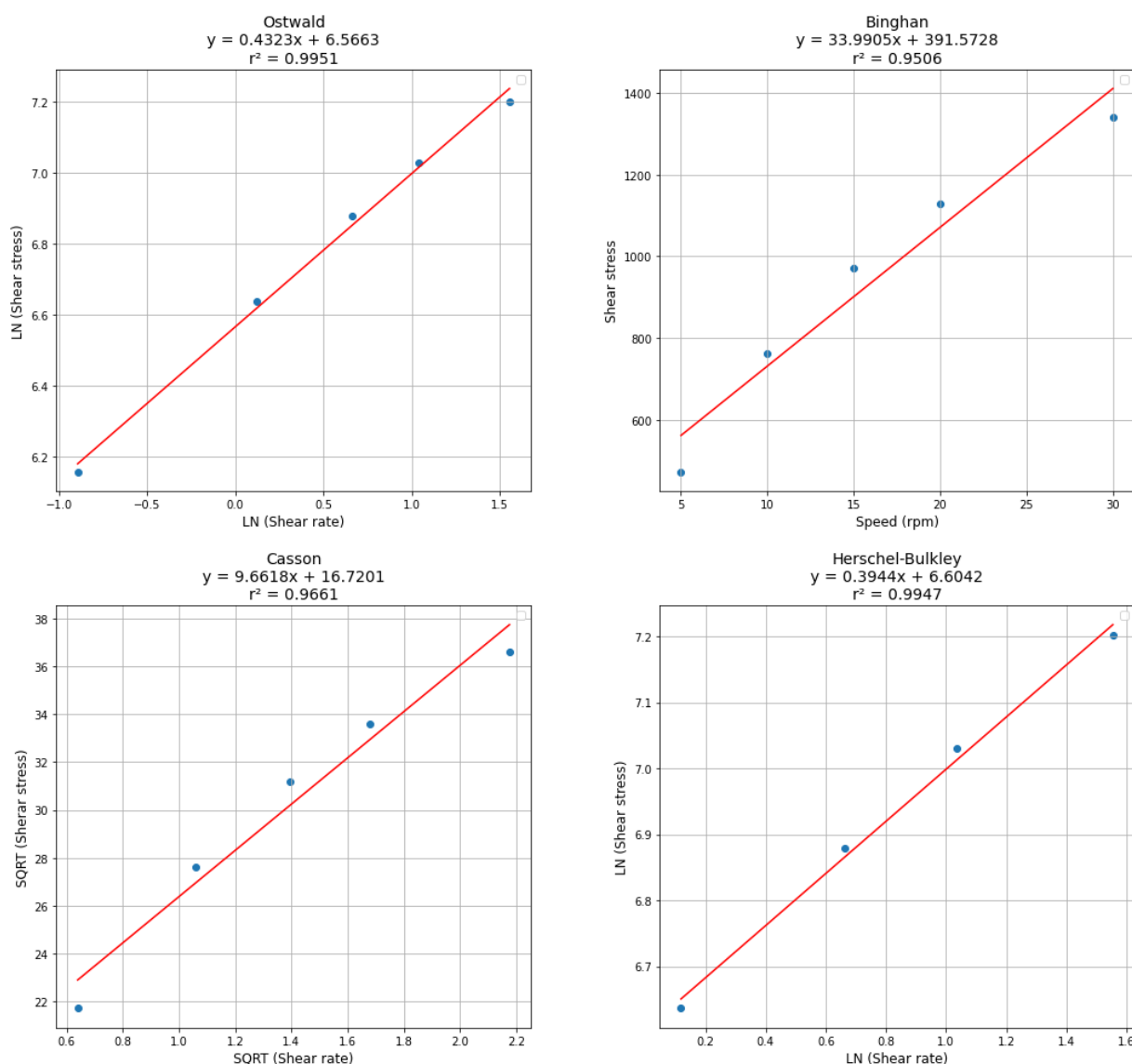


Figure 5. Linear regression of formulations containing 3.0% of blackcurrant oil. The analysis was conducted at $24 \pm 2^\circ\text{C}$.

Furthermore, it is imperative to highlight that traditional 'Materials and Methods' sections in scientific journals are frequently criticized for their brevity and lack of clarity. However, employing software-based experiment descriptions has the potential to enhance this situation by offering more comprehensive and detailed information about study methods. Through the use of software, researchers can furnish a more accurate and complete depiction of their work, facilitating others' ability to reproduce and build upon their findings. Consequently, software-based experiment descriptions can promote the reproducibility and reusability of published studies, ultimately benefiting the scientific community as a whole [54].

Utilizing a computational tool to ascertain the rheological behavior of fluids has proven invaluable, as evidenced by three distinct experiments. It is noteworthy that the mathematical model with the highest r^2 value, the Ostwald-de-Waele model, was identified only after meticulous analysis extending up to the third decimal place. The precision and accuracy of this tool are paramount, as it considers all decimal places to determine the correct representative model of the fluid's behavior, thereby leading to improved results.

Using all decimal places when performing calculations to determine the representative model is imperative. A lack of precision in calculations can result in inconsistencies in the results, causing a change in the representative model. Moreover, in some instances, the r^2 results of the Herschel-Bulkley model may be very similar to those of the Ostwald-de-Waele model. Therefore, it is essential to use computational tools to determine the rheological behavior accurately [53], which is provided by the model presented in this study, an open-source computational tool.

Open-source tools are gaining popularity in the pharmaceutical and cosmetic industries due to their transparency, collaborative nature, and cost-effectiveness [54]. They can be utilized in multiple areas, including molecular modeling and simulation, chemical compound databases, bioinformatics, virtual

laboratories, project management, data visualization, custom software development, artificial intelligence, and machine learning, and quality control and regulatory compliance [28,55,56]. These tools enable users to enhance product properties, identify ingredients, research therapeutic targets and product safety, train and experiment in virtual environments, collaborate effectively, interpret complex results, develop custom software, create predictive models, and ensure regulatory compliance [55,56]. Lastly, we acknowledge that our study has certain limitations that must be considered for proper data interpretation. While the software we developed demonstrated intriguing applicability in assessing the rheological behavior of the prepared formulation, it is imperative to verify its effectiveness for other pharmaceutical semisolids. Additionally, we intend to address accessibility concerns by developing a free app containing our software, thereby making it easily accessible to everyone.

CONCLUSION

Based on the results, it may be concluded that the developed computational tool successfully fulfilled its primary objective of characterizing semi-solid formulations regarding their rheological behavior, flow index, and consistency index. Confirming the pseudoplastic behavior of formulations through the tool highlights its applicability in pharmaceutical development, providing crucial data to select and optimize specific semi-solid formulations for skin application. Moreover, the open-source nature of the computational tool represents a significant contribution to the scientific community, especially for research groups with limited resources.

The availability of this resource as an accessible and affordable alternative to expensive commercial software highlights the potential to democratize access to advanced rheological modeling technologies. This initiative empowers the scientific community to explore and develop new semi-solid pharmaceutical formulations and promotes collaboration, innovation, and reproducibility in research. This work presents a novel solution for modeling medium to high-complexity data and precisely determining the rheological behavior of semisolid formulations, effectively mitigating errors attributable to human estimation. Ultimately, the developed computational tool offers a valuable contribution to advancing the understanding and control of the rheological properties of semi-solid formulations, opening new avenues for developing optimized pharmaceutical products.

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