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Preparation and Optimization of a Basic Pickering Emulsion Using Factorial Experimental Design and Experimental Evidence

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ABSTRACT

Pickering emulsion is a surfactant-free emulsion that is stabilized by solid particles. While Pickering emulsion is also utilized as a drug-releasing control system, these solid particles help reduce the usage of synthetic surfactants, which may have toxicological implications. Therefore, the objective is to create and assess W/O Pickering emulsions stabilized by solid particles of magnesium oxide. In order to emulsify an oil-dispersing phase, we gradually add an aqueous phase and use a stator mixer to disperse it. The results of our investigation into the stability of emulsions (physical, conductivity, pH, droplet size, and rheology, including viscosity) indicate that the type of Pickering emulsion is W/O by dye test. The goal of this work is to prepare a basic Pickering emulsion utilizing a factorial experimental design, along with other tests like pH, rheology (including viscosity and droplet size), and PDI. The factorial experimental design will be used to examine the impact of several parameters on the general emulsion features and the interactions between these factors as they relate to the created Pickering emulsion. Increasing the concentration of MgO from 2 gm to 3 gm led to a decrease in the Pickering emulsion droplet size from 2005 nm to 727.4 nm and an increase in the Pickering emulsion formulation stability. An increase in the yield values is in agreement with the logical concept that increasing the solid particle concentration requires more shear stress to move, with a viscosity of 23,068 Pa. An optimized basic Pickering emulsion formulation for a variety of applications is obtained by applying the factorial experimental design, confirming that the stability of the emulsion may be improved by adding more magnesium oxide particles. This indicates the effective formulation of the W/O Pickering emulsion, which includes magnesium oxide particles for stabilization.

1. INTRODUCTION

A mixture of two liquids that are either completely or partially immiscible, one of which is distributed as tiny droplets within the other, is called an emulsion. The surrounding liquid is known as the continuous phase, whereas the dispersed liquid is known as the dispersed phase. Water-in-oil (w/o) emulsions have water droplets suspended in oil, while oil-in-water (o/w) emulsions have oil droplets suspended in water. Unless stabilized by emulsifying agents, emulsions have a tendency to separate over time due to their thermodynamic instability [1, 2] (Loi *et al.*, 2019; McClements, 2007).

Various emulsification theories exist. A few will be summarized as the article's topic. According to the oriented-wedge theory, a droplet of the emulsion's internal phase is surrounded by monomolecular layers of the emulsifying agent. The idea behind the notion is that different emulsifying agents have different solubility in different liquids, and that these solubilities affect how they arrange themselves around and inside the liquid. It is likely that the emulsifying agent is more strongly bound to one phase and has a preference for solubilizing in that phase when two immiscible liquids are present in a system. Many molecules of the compounds that support this idea (such as soaps) have a water-loving and a water-hating part, but they typically have a lipophilic and an oil-loving part, so the molecules naturally position or orient themselves into each phase [3] (Jr & Ansel, 2014).

In oral preparations, hydrophilic colloids such as polysaccharides, including gums like acacia, tragacanth, and cellulose and alginate derivatives, are employed as emulsifying agents. Such hydrophilic colloids have the disadvantage of being easily broken down by depolymerization. Preservatives should be applied because they also provide an excellent medium for bacterial growth. By creating thick, multilayered films with strong resistance to rupture, hydrophilic colloids stabilize o/w emulsions. They primarily function as viscosity modifiers by making the external phase more consistent, which prevents creaming and coalescence.

Fine solid particles are another type of emulsifying agent. By partially wetting emulsions with both the water and oil phases, they can be stabilized by solid particles—finely divided solid particles. They are sufficiently bonded to each other to create a cohesive interfacial layer that prevents droplet coalescence by acting as a mechanical barrier. For o/w emulsions, the aqueous phase preferentially wets the particles, while for w/o emulsions, the solid is preferentially wetted by oil.

The size of the particles must be less than that of the droplets. Shape, wettability, inter-particle interactions, and the emulsion media all affect how effective the fine solid particles are. Pickering emulsions and surfactant-free emulsions are terms used to refer to emulsions stabilized by solid particles [4] (Ortiz *et al.*, 2020).

Pickering emulsions are emulsions in which two immiscible phases (W/O or O/W) are stabilized by dispersions using solid particles acting as surfactants. In 1903, Ramsden was the first investigator to make the discovery of Pickering emulsions [4, 5] (Ortiz *et al.*, 2020) (Chevalier & Bolzinger, 2013).

Currently, the solid particles used as surfactants in Pickering emulsions are free from the adverse effects of regular surfactants. They are appealing for several applications where surfactants frequently exhibit negative effects (hemolytic, environmental issues, behavioral issues, irritation, etc.) due to their "surfactant-free" nature [6] (Sy *et al.*, 2018). Furthermore, the Pickering emulsion is the most stable kind of emulsion. This results from solid particles adhering to the oil-water interface. This adsorption is irreversible, powerful, and strongly resists coalescence by the creation of a barrier around droplets in dense film formulation. The energy of adsorbed solid particles [$\Delta E = \gamma_{HE}\pi r2\left(1\pm\cos\theta\right)2$] is indicated by the partial wetting ability of the two emulsion phases [7-9] (Sy *et al.*, 2019) (Arditty *et al.*, 2004) (Fouilloux, 2011).

The contact angle on the aqueous phase side between the solid particles and the two Pickering emulsion dispersion phases was determined. If solid particles are hydrophilic, their O/W stability will be improved. Since the Pickering emulsion contact angle is smaller than 90˚ and those solid particles are hydrophilic, the O/W stability is improved. When the contact angle is more than 90˚, the emulsion is W/O [6] (Sy *et al.*, 2018). Pickering emulsions may be stabilized by silica, clays, laponite, and other metal hydroxides and oxides [10-13] (Aveyard *et al.*, 2003) (Levine & Sanford, 1985) (Abend & Legaly, 2001) (Ashby& Binks, 2000).

Magnesium Oxide can be used in many specialties like food additives, and heartburn as an antacid and antimicrobial [14, 15] (Sharma & S., 2017) (Sy *et al.*, 2018).

This system may also serve as a means of protecting and encapsulating active principles in therapy, as a reservoir system and/or a sustained, controlled, or retarded release system for the active substances. As an exemplary application, a Pickering emulsion using MgO, olive oil, and water for medical treatment is given, involving the preparation of a stable W/O system to co-encapsulate drugs. Utilizing MgO particles to stabilize droplets enables enhanced solubility, protection, and targeted release of compounds such as Paracetamol (hydrophilic) and Griseofulvin (hydrophobic), potentially for topical or oral administration, while masking taste and improving bioavailability by maintaining the separation of drugs within a robust delivery vehicle. Utilizing MgO particles to stabilize droplets for enhanced solubility, protection, and targeted release of compounds such as Paracetamol (hydrophilic) and Griseofulvin (hydrophobic), potentially for topical or oral administration, while masking taste and improving bioavailability by maintaining the separation of drugs within a robust delivery vehicle [15] (Sy *et al.*, 2018).

The goal of this work is to prepare a basic Pickering emulsion using a factorial experimental design, based on the irreversible adsorption of solid particles at the oil-water interface, which results in the high stability of the emulsion. To investigate how various factors affect the overall emulsion characteristics, the factorial experimental design will be used to study the interactions between these factors concerning the prepared Pickering emulsion. The application of the factorial experimental design will lead to an optimized basic Pickering emulsion formulation for different applications.

2. MATERIALS AND METHODS

2.1. Materials

Virgin olive oil Nile Garden premium quality was purchased from Nile Garden company-Alex Egypt and Vaseline from El Gomhouria Co. Egypt, Magnesium Oxide (MgO) Heavy 98% extra pure batch number L339032007 was purchased from Loba Chemie PVT LTD India. Used exactly as received, all of the chemicals were of analytical grade.

2.2. Methods

2.2.1. Experimental Design

By using the software MINITAB, version 17, an experimental design for the formulation of a basic Pickering system was carried out. A multilevel factorial design was applied, and the dependent and independent variables are represented in Table 1. The selected independent variables are the weight of Vaseline, the weight of magnesium oxide, and the volume of olive oil, each with two levels.

Table 1. Coded units of variables and their respective levels for the application of (2^3) multi-level factorial design.

Factors	Coded levels condition	
(A) Magnesium oxide	2	3
(B) Vaseline	10	15
(C) Olive oil	10	13
Dependent variables	**Constraints**	
Y1 = Particle size	Minimum	
Y2 = PDI	Maximum	
Y3 = Zeta potential (21)	−10	+10
Y4 = viscosity	Maximum	

The ability to wrap droplets using varying concentrations of MgO in Pickering emulsions offers opportunities to tune droplet size, viscosity, and long-term stability by maximizing (or minimizing) particle coverage at the oil-water interface; a deficiency produces instability, while an excess forms a rigid network with impacts on properties such as apparent viscosity or viscoelasticity, or the capacity of the emulsion to stabilize functionalized active ingredients, a crucial factor for applications like drug delivery and catalyst experimental design. This demonstrates the impact of particle density on structure, and how scientists can design emulsions that display a host of different types of structure to meet specific needs for any particular application.

Viscosity of the prepared system, system zeta potential, mean particle size, and particle size index (PDI) are the tested dependent variables; all experimental trials were conducted for all eight possible combinations (Table 2) [16] (Clogston & Patri, 2011).

Table 2. The pickering formulations' prepared design systems.

Formula Code	Coded levels			Magnesium Oxide	Vaseline	Olive Oil
	A	B	C			
F1	2	10	10	2	10	10
F2	3	10	10	3	10	10
F3	2	15	10	2	15	10
F4	3	15	10	3	15	10
F5	2	10	13	2	10	13
F6	3	10	13	3	10	13
F7	2	15	13	2	15	13
F8	3	15	13	3	15	13

2.2.2. Formulation of Basic Pickering Emulsions

One Among the main aspects of Pickering emulsion is the direction of the emulsion formulation, W/O or O/W, based on the Bancroft rule, which indicates the emulsion type depends on the phases in which the solid particles are incorporated.

Oil Dispersing Phase Preparation:

Different Pickering systems were prepared according to Table 2. The required amount of magnesium oxide was added gradually to the amount of Vaseline with progressive trituration until the formation of a homogeneous product. Then, the required amount of olive oil was added to the previously prepared product gradually with continuous trituration until the oil phase (olive oil) was dispersed in the mixture. The produced mixture was continuously stirred using a Velpscientifica Dls overhead mechanical stirrer at a stirring rate of 1250 rpm for 3 minutes.

Addition of the dispersed aqueous phase:

The previously prepared mixture was mixed with a fixed volume of distilled water (15 ml) dropwise while stirring using a Velpscientifica Dls overhead mechanical stirrer at 1250 rpm. The emulsions were kept at room temperature for future research once they were completed.

2.2.3. Characterization of the Prepared Basic Pickering Systems

Visual inspection of the prepared systems (bottle method):

The visual inspection of the prepared emulsions for their instability was studied using the bottle method (Ortiz *et al.*, 2020).

The prepared systems were placed at room temperature and in the absence of light, which may enhance the instability of the emulsion. The studied visual instability tests were the systems' flocculation, sedimentation, and coalescence.

2.3. Emulsion Orientation

The emulsion type was determined using a light microscopy dye method, employing Sudan III as the staining agent. A few drops of the dye were added to 2 ml of the formulated emulsion and thoroughly mixed. The emulsion type was then examined using a Reichert light microscope (Germany).

2.4. Particle Size (PS), Zeta Potential, and Particle Distribution index (PDI) Measurements

Particle size index, mean particle size distribution (represented as average particle diameter), and zeta potential were measured for the prepared plain Pickering systems. Photon correlation spectroscopy was used to perform these measurements at a constant temperature of 25˚C and a fixed angle of 173˚ using a Dynamic Light Scattering (DLS) particle size analyzer (Zetasizer Nano ZN, Malvern Panalytical Ltd, UK). To guarantee accuracy, each sample was examined three times.

2.5. Measurements of the Rheology and Viscosity of the Prepared Systems

An Anton Paar rheometer (Anton Paar MCR 301, Anton Paar GmbH, Austria) was used to measure the rheological characteristics of the Pickering emulsion at 25˚C. A 25 mm diameter plate-plate arrangement with a 0.5 mm gap spacing was used for the rotational mode measurement. Over the course of 150 s, the shear rate was increased linearly from 1 to 100 min^{-1}.

2.6. Observations of the Systems' pH

The pH of the prepared plain Pickering systems was measured using a pH meter (Hanna Instruments pH 211 Microprocessor pH meter). The pH meter electrode was immersed in the system. After the insertion of the electrode into a prepared Pickering system for three minutes, the reading of the digital pH meter was recorded. The experiment was carried out in triplicate.

2.7. Statistical Analysis

The properties of the created Pickering emulsions are allocated for all formulas as indicated in the table in order to examine the impact of each factor at the chosen levels on the desired responses (Jr & Ansel, 2014). Minitab version 17 was used for optimization and selection of the most suitable optimized formula to be used as a base for preparing a plain Pickering system. A statistical model incorporating the interactive and polynomial terms was used to evaluate the response according to Equation (1):

$$Y = b_0 + b_1A + b_2B + b_3C + b_{12}AB + b_{13}AC + b_{23}BC + b_{123}ABC \quad (1)$$

Where Y (Y_1 is particle size, Y_2 is particle distribution index, Y_3 is Zeta potential, and Y_4 is viscosity). Particle size is regarded as a dependent variable; the estimated coefficients for the components MGO (A), Vaseline (B), and Olive oil (C) are denoted by b_1, b_2, and b_3, whereas b_0 is the arithmetic mean response of the eight runs. The average outcomes of adjusting one element at a time from its low to its high level are shown by the mean effects (A, B, and C). When two or three factors change at the same time, the interaction terms (AB, AC, BC, ABC) indicate how the responses change. The significance level ($p < 0.05$) was used to assess the importance, validation of the chosen formula and each factor's contribution using different response levels [17] (Mady *et al.*, 2021).

3. RESULTS AND DISCUSSION

The prepared basic Pickering systems were stored for additional investigations at room temperature and in a dark location. Visual inspection represents the first step for controlling any product. The visual

inspection of the prepared plain Pickering systems showed a homogeneous color ranging from yellow to beige (Figure 1). The origin of the color of the system may be attributed to the color of the olive oil. The volume of oil used was at two levels, and it is expected that magnesium oxide can also reflect the color of the oil used. Therefore, the color range of the systems is due to the volume of oil used and the concentration of magnesium oxide. Increasing the olive oil and the concentration of magnesium oxide led to a more intensive system color. The visual observation may indicate the type of prepared emulsion, which is a W/O type.

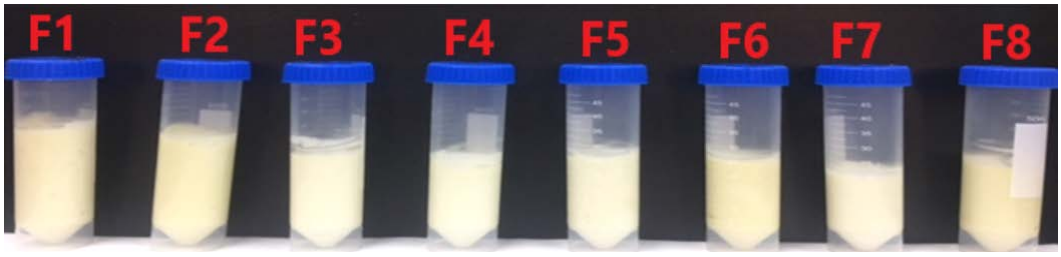
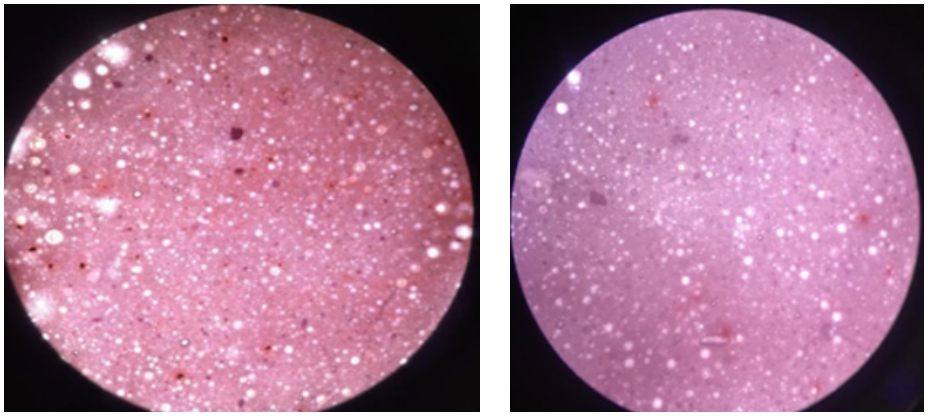


Figure 1. A photograph of the prepared Pickering system according to Table 2.

Confirming the type of emulsion was carried out using the dye test. The prepared emulsion systems consist of two phases, the oil phase and the aqueous phase. Sudan III is a lipophilic dye with a red color. Therefore, it can be used for the determination of the emulsion type. Figure 2 A&B showed the light microscope photo of two emulsions prepared with different concentrations of magnesium oxide. From the figure, it can be noticed that the colored phase of the emulsion is the external phase. Accordingly, it can be concluded that the emulsion system is a W/O emulsion, which is in line with the goal of the Pickering emulsion base preparation. In addition, the effect of increasing the concentration of magnesium oxide could be noticed concerning the particle size and particle size homogeneity of the water's internal phase.



(2 g of magnesium oxide) (3 g of magnesium oxide)

Figure 2. A light microscope photo of two Pickering emulsion systems prepared with two different concentrations of magnesium oxide.

***In-vitro* Characterization of all prepared basic Pickering systems:**

The size of the droplets has an inverse relationship with an emulsion's stability, which is related to describing the rate of sedimentation and the system's zeta potential value, in addition to the viscosity of the prepared system, which retards the particle sedimentation process [15] (Sy *et al.*, 2018).

Therefore, a factorial experimental design was carried out including these factors with two different levels to study not only the impact of these elements on the emulsion's stability but also their effect on their interactions. The results are summarized in Table 3.

Table 3. *In vitro* characterization of the plain prepared pickering systems.

Formula	Physical characteristic parameters			
Code	Particle size (nm)	PDI	Zeta potential (mV)	Viscosity (poise)
F1	1300 ± 99.80	0.197 ± 0.148	(−) 0.694	8159.5
F2	727.4 ± 23.39	1.0 ± 0	(+) 0.047	11,670
F3	1395 ± 206.7	0.1437 ± 0.151	(−) 0.0702	8695.6
F4	745.1 ± 78.56	1.0 ± 0	(−) 0.28	32,262
F5	1187 ± 541.8	1.0 ± 0	(−) 0.027	16,206
F6	974.2 ± 47.04	1.0 ± 0	(−) 0.003	78,004
F7	2005 ± 631.4	0.807 ± 0.167	(−) 0.058	1820.7
F8	877.7 ± 146.8	1.0 ± 0	(−) 0.0408	23,068

Particle size as the dependent response versus the amount of MgO (A), Vaseline (B), and the volume of olive oil (C) as independent factors:

The prepared basic Pickering emulsion's particle size was examined, and Figure 3 and Table 3 provide a summary of the findings. The concept of particle size was developed to compare the sizes of gaseous (bubbles), liquid (droplets), and solid (flecks) particles. The amount of particles present is determined by their size distribution, which is known as the particle size distribution. The normal curve is divided into two identical halves by the peak frequency value, also referred to as the mode. In this instance, the data are normally distributed, meaning that the size distribution is completely symmetrical [4] (Ortiz *et al.*, 2020).

Figure 3 represents the particle size distribution curves of the different basic Pickering emulsions. From the figures, it can be noticed that, in each case, there is a symmetrical distribution of prepared emulsion particles around the mode. Increasing the mode value, which is represented by the equipment as intensity and combined with a narrow size distribution, agrees with the logical concept of distribution. According to the equipment, the prepared Pickering emulsion's particle size ranges from 727.4 nm to 2005 nm (Table 3), indicating the particle size of all prepared runs ranges from small to large particles [15, 18] (Sy *et al.*, 2018) (El-gizawy *et al.*, 2019).

From Table 3, it can be noticed that the mode of Pickering emulsion size is in the nano range for the odd-numbered F formulae and in the micro range for the even-numbered F formulae. Regarding Table 2, which represents the design systems of the prepared Pickering formulations, the odd-numbered Pickering emulsion formulations are prepared using a lower amount of MGO, and the even-numbered ones are prepared using a high MGO concentration. These findings might suggest the reverse impact of the MGO concentrations in decreasing the Pickering emulsion size from microns to nanometers. The mode of the particle size in the nano range can be arranged as follows: F5 < F1 < F3 > F7. For the same formula composition concerning the amount of Vaseline and olive oil, the mode of the particle size in microns can be arranged as follows: F2 < F4 < F8 < F6.

While Vaseline (petrolatum), a lipophilic base, affects oil-phase properties and can increase droplet size or create larger, less stable systems if not combined with proper emulsifiers, frequently requiring surfactants to create stable nanoemulsions with fine droplets, magnesium oxide (MgO) nanoparticles act as a Pickering stabilizer in emulsion systems, reducing droplet size by increasing the interfacial area. More MgO typically results in smaller, more stable droplets.

Effects of Magnesium Oxide (MgO)

• Stabilizer: MgO particles function as solid emulsifiers (Pickering emulsions) to stabilize water-in-oil (W/O) or oil-in-water (O/W) emulsions.

• Size Reduction: Because the particles efficiently cover the droplet surfaces and prevent coalescence, adding more MgO particles usually results in smaller droplet sizes.

• Improved Stability: MgO frequently produces smaller droplets, which increase the surface area available for emulsifier action and improve emulsion stability.

Effects of Vaseline (Petrolatum)

• Increased Droplet Size: Higher concentrations of oil (like Vaseline) in nanoemulsions frequently result in larger droplet sizes, especially if the surfactant concentration is low, as it can overwhelm the emulsifier's ability to coat the droplets effectively.

• Stability Challenge: Large droplets formed with high oil content are less stable, making them prone to creaming or breaking.

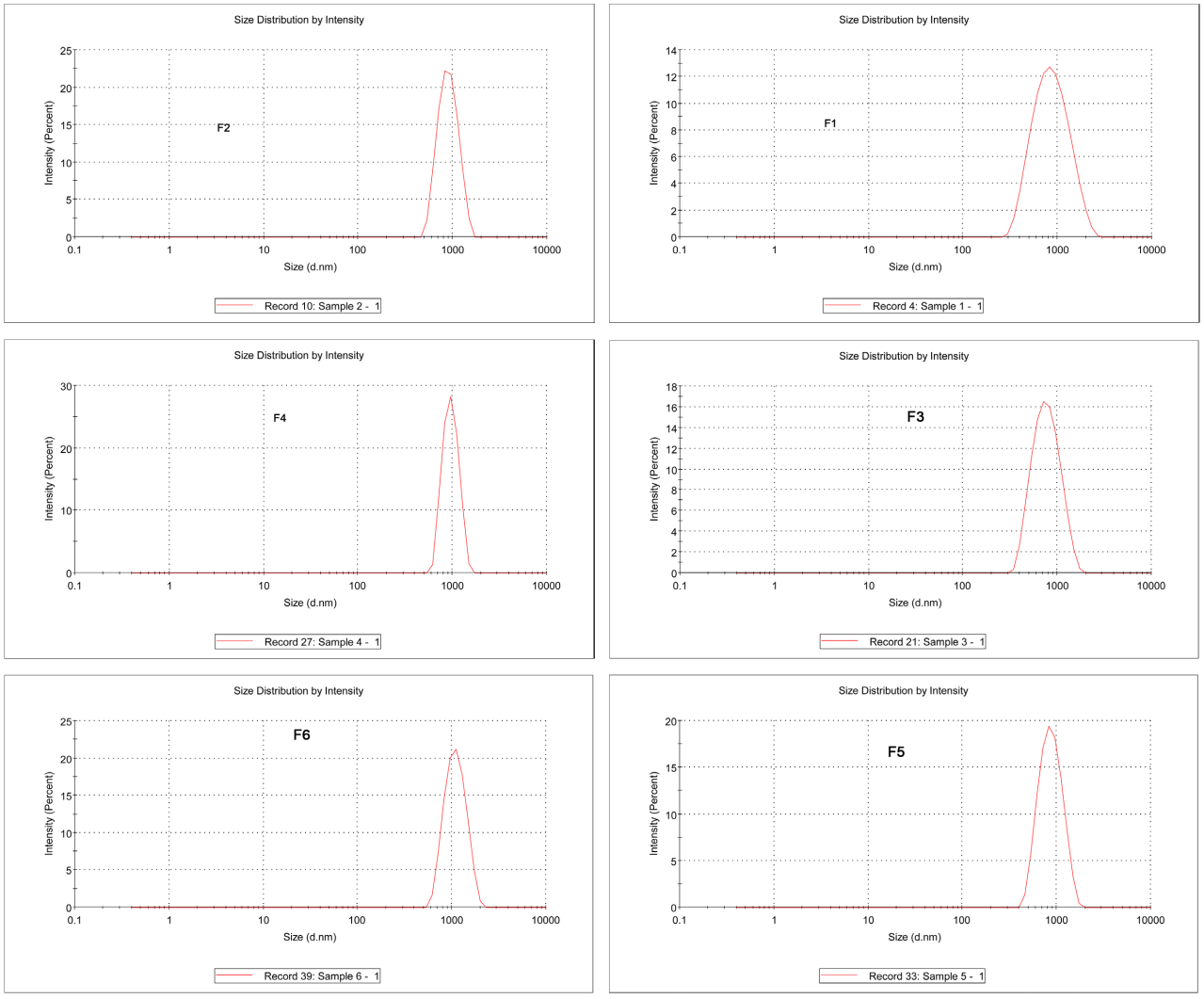
• Lipophilic Base: Vaseline is an oil-based substance that provides the oil phase in emulsions.

Combined Effect (Vaseline + MgO)

• The objective is to use MgO's stabilizing power to counteract Vaseline's propensity to form huge droplets when formulating with MgO (solid stabilizer) and Vaseline (oil phase).

• This aims to create small, stable nanoemulsions for uses like drug delivery, where precise droplet size (nanometer scale) is essential for efficacy, by optimizing the ratio of MgO to Vaseline.

MgO counteracts the coarsening effect of the oil phase to generate fine, stable systems, while Vaseline supplies the oil bulk. The interaction and concentrations define the final droplet size [15] (Sy *et al.*, 2018).



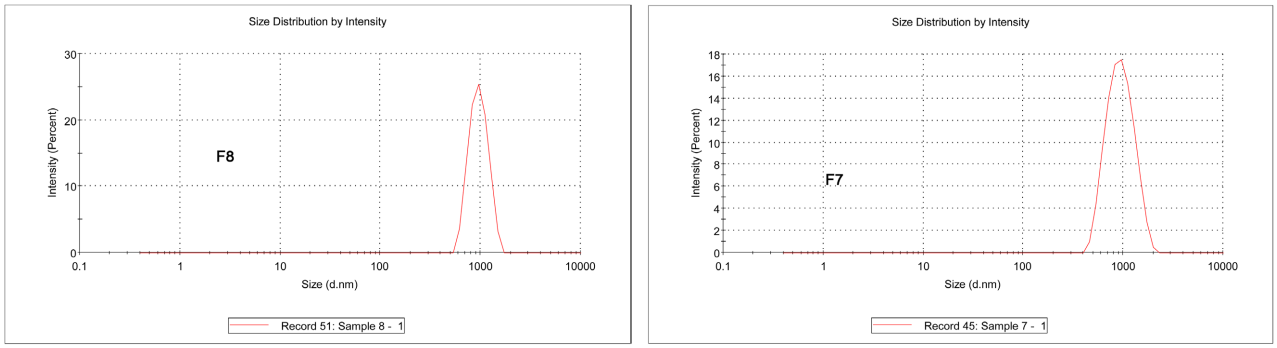


Figure 3. Particle size distribution and mean size intensity of the prepared basic Pickering emulsion.

MGO is a fine solid particle. It stabilizes the emulsions by partially wetting both the oil and water phases. They have enough adherence to provide a cohesive interfacial layer that provides a mechanical barrier to prevent droplet coalescence. It was found that the nano-size mode is produced using a high MGO concentration. Therefore, it can be suggested that increasing the concentration of MGO led to the formation of a fine layer of a coherent interfacial film around the emulsified droplet. A sufficient concentration of MGO hindered the emulsified droplets' coalescence and the formation of nano-size droplets.

The relationship between the response Y1 (particle size) and the independent variables MGO, Vaseline, and Olive Oil and their interactions A, B, C, AB, AC, BC, and ABC, respectively, was assessed using a multivariate linear regression stepwise. The equation reports the outcome. 2.

$$\begin{aligned}\text{Particle Size} = {} & 20704 - 7199\,\text{MGO} - 1548\,\text{Vaseline} - 1876\,\text{Olive Oil} + 542.7\,\text{MGO}\times\text{Vaseline} \\ & + 678.1\,\text{MGO}\times\text{Olive Oil} + 159.8\,\text{Vaseline}\times\text{Olive Oil} - 55.81\,\text{MGO}\times\text{Vaseline}\times\text{Olive Oil}\end{aligned} \quad (2)$$

Regression analyses reveal no significant effect of factors A, B, and C or their interactions AB, AC, BC, and ABC on the particle size values ($p < 0.05$). The most effective factor is A, with a positive coefficient value indicating that a high concentration of MGO decreases the droplet size [15] (Sy *et al.*, 2018).

Particle size index (PDI) versus the amount of MGO (A) and Vaseline (B) and the volume of Olive Oil (C):

The polydispersibility index (PDI) is calculated by dividing the mean particle diameter by the standard deviation (σ) of the particle diameter distribution. It shows how different population sizes are distributed within a sample. A fully uniform sample with respect to particle size has a PDI of 0.0, while a highly different particle size population in a polydisperse sample has a PDI of 1.0. A narrow distribution of particle sizes is indicated by PDI values less than 0.5.

The values of the PDIs are between 0.1437 and 1.0 (**Table 3**), indicating that the PDI of all prepared runs has a low to high distribution [19] (Kawano *et al.*, 2015). From **Table 2**, it can be noted that the even-numbered F formulae had a PDI equal to one, indicating a polydisperse sample with multiple particle size populations. At the same time, F1 and F3 had low PDI values, indicating that both had a narrow particle size distribution. The difference between these two formulations is the increasing amount of Vaseline, which may cancel the effect of increasing Vaseline concentration on the PDI. The PDI value of F5 is one for a formula with a lower concentration of Vaseline and a higher concentration of olive oil. Therefore, it can be concluded that the higher olive oil concentration is responsible for the high polydispersity in the sample, especially since the PDI of F7 is lower than one with a high concentration of both Vaseline and olive oil, because both substances are greasy. On the other side, for all even-numbered formulae, the value of PDI is one, although they were prepared using higher or lower concentrations of greasy substances. Regarding the Pickering emulsion preparation method, Vaseline would first be homogenized with MGO to form, to some extent, a hard mass, which would be softened by stepwise adding olive oil while mixing. A high Polydispersity Index (PDI) up to 1.0 indicates a wide distribution of particle/molecule sizes, denoting significant heterogeneity; it frequently indicates multimodal distributions (multiple distinct size populations) or extreme

polydispersity where conventional analysis struggles, rather than just instability or greasy substances. It indicates that you have both very small and very large components, affecting material properties and serving as a measure of size heterogeneity; values close to 1.0 suggest a wide, diverse range that may indicate instability or poor control in synthesis, which could result in complex interactions and possibly aggregation.

Therefore, it could be expected that the MGO would be completely oriented around the Vaseline, which led to the cancellation of its effect on the PDI of the emulsion and the shifting of the disturbance effect to the method of olive oil addition. This could be a technical reason during Pickering emulsion preparation. In addition, this conclusion may support the suggested mechanism of particle size decrease by using a high concentration of MGO.

The relationship between the response Y2 (PDI) and the independent variables and their interactions—A, B, C, AB, AC, BC, and ABC, respectively—was assessed using a multivariate linear regression stepwise equation, which reports the outcome (Jr & Ansel, 2014).

$$\begin{aligned}\text{PDI} = &-19.54 + 6.846\ \text{MGO} + 1.010\ \text{Vaseline} + 1.669\ \text{Olive Oil} - 0.3367\ \text{MGO} \times \text{Vaseline} \\ &- 0.5563\ \text{MGO} \times \text{Olive Oil} - 0.08660\ \text{Vaseline} \times \text{Olive Oil} + 0.02887\text{MGO} \times \text{Vaseline} \times \text{Olive Oil}\end{aligned} \quad (3)$$

Regression analyses reveal that there is no significant effect of factors A, B, and C or their interactions AB, AC, BC, and ABC on the PDI values ($p < 0.05$). The most effective factor is A, with a positive coefficient value indicating that a high concentration of MGO increases the PDI by decreasing the particle size.

Zeta Potential versus the amount of MGO (A) and Vaseline (B) and the volume of Olive Oil (C):

The potential difference between the electroneutral area of the solution and the firmly bonded layer's (shear plane) surface is known as the zeta potential. Since this potential controls the strength of repulsion between nearby, similarly charged, scattered particles, it can be used practically to ensure the stability of systems with dispersed particles. The particles come together when the attractive forces outweigh the repulsive forces when the zeta potential is lowered below a specific value, which varies depending on the specific system being used [20] (Sinko & Singh, 2011).

Pickering emulsion is a dispersed system. Therefore, it was essential to measure the zeta potential value for all Pickering emulsions. The equipment used for measuring the system's zeta potential provides a zeta potential distribution for all prepared basic Pickering emulsions, represented in **Figure 4**. The zeta potential distribution is an interpretation of potential contributions from differently charged particles that could have contributed to the result [18] (El-Gizawy *et al.*, 2019). From **Figure 4**, it can be noticed that in each case the system's zeta potential distribution has a symmetrical form. In addition, the curves for F3, F5, F6, F7, and F8 have a small peak behind the major one. The appearance of the second peak may represent two peaks in the zeta potential analysis corresponding to two different populations found in the size distribution analysis. It is also possible that multiple scattering or particle-particle interactions could be the cause of the second peak. Regarding the composition of the system, from **Table 2**, it can be noticed that the second peak appeared when using olive oil at a high concentration, regardless of using Vaseline or MGO at high or lower amounts, except in F3. Therefore, it can be suggested that olive oil may be responsible for the formation of the second peak. This explanation is based on the method of olive oil addition to the mixture of Vaseline and MGO. Concerning the formation of the second peak in the F3 system, from the same table, it can be noticed that the amount of Vaseline is high but the amount of MGO is low. Therefore, it could be expected that the second peak is due to the olive oil [18] (El-Gizawy *et al.*, 2019).

The values of the Zeta Potential are between −0.694 mV and 0.047 mV (**Table 3**), indicating that the Zeta potential of all prepared runs ranges from negative to positive values, which indicates the stability of the prepared Pickering systems [18] (El-gizawy *et al.*, 2019).

The relationship between the response Y3 (Zeta Potential) and the independent variables A, B, and C and their interactions AB, AC, BC, and ABC, respectively, was evaluated by using stepwise multivariate linear regression. The result is reported in Equation (4).

$$\begin{aligned}\text{Zeta Potential} = &-31.18 + 11.33\ \text{MGO} + 2.200\ \text{Vaseline} + 2.396\ \text{Olive Oil} - 0.8195\ \text{MGO} \times \text{Vaseline} \\ &- 0.8683\ \text{MGO} \times \text{Olive Oil} - 0.1695\ \text{Vaseline} \times \text{Olive Oil} + 0.06293\ \text{MGO} \\ &\times \text{Vaseline} \times \text{Olive Oil}\end{aligned} \quad (4)$$

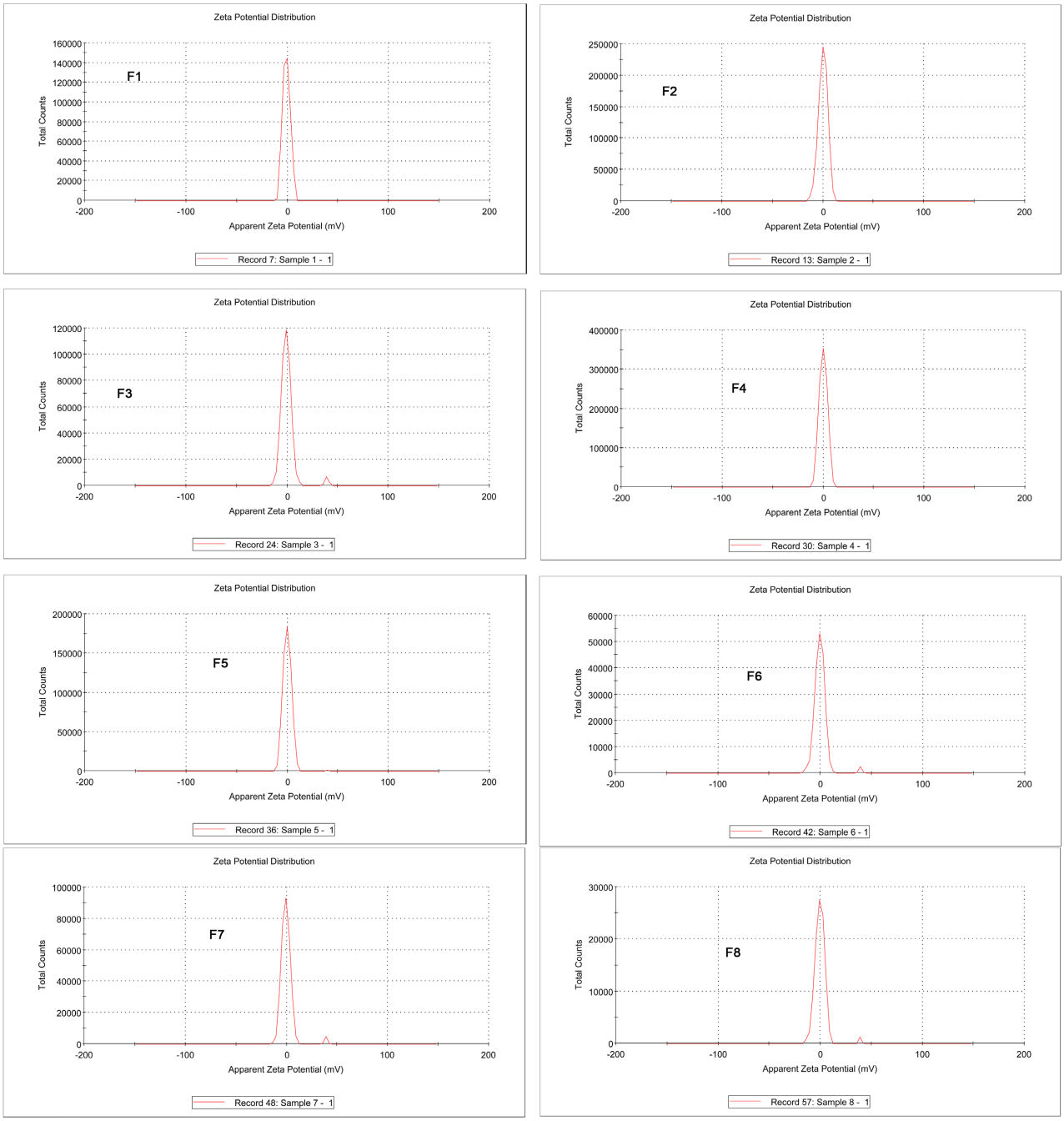


Figure 4. Zeta potential distribution of the prepared basic Pickering emulsion.

- High-molecular-weight stabilizers form thicker, more effective barriers against coalescence even with lower electrostatic repulsion; solid particles (Pickering emulsions) create a strong mechanical barrier that prevents droplet fusion; and steric stabilization, in which adsorbed polymer layers physically push droplets apart, keeps emulsions with low zeta potential stable.

Regression analyses reveal that there is no significant effect of factors A, B, and C and their interactions AB, AC, BC, and ABC on the zeta potential of the emulsion ($p < 0.05$). The most effective factor is A, with a positive coefficient value indicating that a high concentration increases the zeta potential positively and negatively [18] (El-gizawy *et al.*, 2019).

Viscosity versus the amount of MGO (A) and Vaseline (B) and the volume of olive oil:

The rheological behavior of all prepared Pickering emulsions was studied, and the rheograms of each formula are represented in Figure 5 using the software Rheology Lite for Windows (an app for rheological analysis of the flow behavior of materials). The figure shows that increasing the shear stress led to an increase in the shear rate after a yield value, indicating the non-Newtonian flow behavior of all systems. Different flow models (Power Law, Bingham, Herschel-Bulkley, and Casson) were applied to the rheometer data. Based on the values of the correlation coefficient, the Herschel-Bulkley model was selected. The flow model equation is:

$$\tau = \tau_{0+K}\dot{\gamma}_n$$

where τ is the shear stress, γ is the shear rate, τ_0 is the yield stress, K is the consistency index, and n is the shear-thinning index. It is a flow model for solid-containing, system-like material. The system flows only if the applied stress (τ) is higher than the yield stress (τ_0). Once the flow starts, the viscosity decreases with the shear rate. The results of the model application are summarized in Table 4.

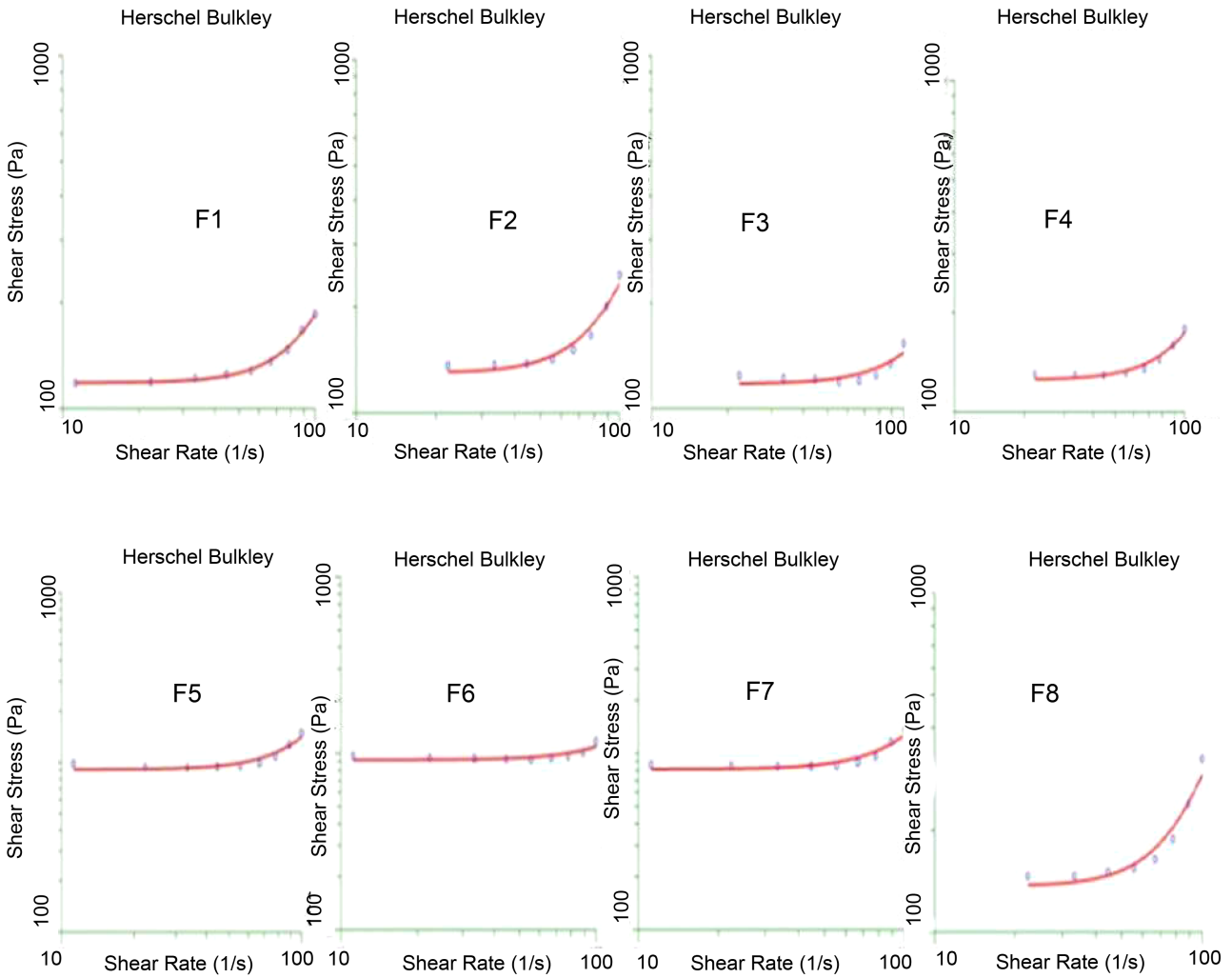


Figure 5. Rheological behavior of all prepared Pickering systems.

It is evident from the table that the values of R^2 are sufficiently high to conclude the correlation between shearing stress and shearing rate, except for F3 and F6. In each case, the values of the shear thinning index

(n) are more than one, indicating all systems are non-Newtonian pseudoplastic (shear thinning systems). In addition, the values of yield stress depend on the concentration of MGO used. Increasing the concentration of MGO led to an increase in the yield values, which is in agreement with the logical concept that increasing the solid particle concentration needs more shear stress to move.

Table 4. Rheological parameters of the fitting data to the Herschel-Bulkley and viscosity to Carreau models.

	F1	F2	F3	F4	F5	F6	F7	F8
τ_0	129.67	118.31	124.98	117.37	91.766	90.772	136.36	81.241
k	3.93E−05	4.46E−05	4.88E−05	3.59E−05	4.19E−05	4.73E−05	3.64E−05	4.53E−05
n	3.21	3.09	3	2.93	2.81	3.01	3.31	3
R^2	0.965	0.996	0.962	0.763	0.721	0.925	0.94	0.926
η (Pa)	11670	8159.5	8695.6	32,262	16,206	78,004	1820.7	23,068

τ_0 = the yield stress; k = the consistency; n = the shear-thinning index; R^2 = correlation coefficient; η = viscosity.

Figure 6 represents the viscosity flow behavior of different systems. From the figure, it can be concluded that the exponential decrease of the different systems' viscosity with increasing shear stress indicates the shear-thinning character of the systems, which is in agreement with the calculated value of the shear-thinning index. Different viscosity models (Cross, Carreau, Carreau Yasuda) were applied, and based on the value of R^2, the Carreau viscosity model was selected for determination of the viscosity of the systems. It is a model for shear-thinning materials where the viscosity decreases with increasing shear rate. According to the model, the zero-shear viscosity is reported in Table 4 for comparison.

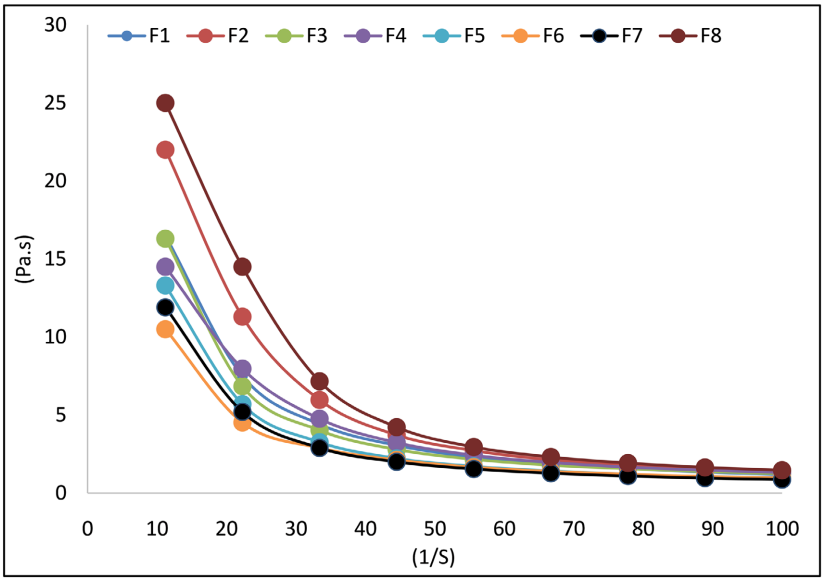


Figure 6. Viscous flow behavior of the different Pickering systems.

PH measurements of the prepared Pickering systems:

MgO is a basic solid mineral that dissociates into magnesium cations and water in pH media lower than

5, with the rate dependent upon the concentration of H^+ and Mg^{2+} already present in the solution. Increasing the media pH between 7 and 8.5 leads to the dissociation of MgO into magnesium cations and hydroxyl anions [15] (Sy *et al.*, 2018). Therefore, it would be expected to increase the pH value of the Pickering emulsion as a result of the presence of MgO as an emulsifying agent and water as part of the emulsion composition [21] (Wetteland *et al.*, 2018).

The pH values of different basic Pickering systems were measured, and the results are tabulated in Table 5. From the table, a change in the system pH values could be noticed. The pH changes of the emulsions based on the quantity of magnesium oxide used coincide with the reported principle stated previously. The higher system pH value is due to the higher amount of MgO used. It was reported that increasing the emulsion basicity leads to better stability, and a basic pH makes W/O Pickering emulsions more stable [15] [22] (Sy *et al.*, 2018; Hwang *et al.*, 2004).

Table 5. pH measurements of the prepared basic Pickering systems.

Formula	PH
F1	7.83
F2	8.40
F3	7.72
F4	8.32
F5	8.61
F6	8.68
F7	8.10
F8	8.47

Increasing the pH value of the Pickering emulsion could be considered a disadvantage for the incorporation of some drugs whose stability is affected by increasing the pH.

The optimization response:

The optimum Pickering formulation is achieved by using 3 g of MgO solid particles (high level), Vaseline & olive oil (high level), and a 1250 rpm stirring rate at ambient temperature. These outcomes can be regarded as adhering to the Pickering emulsion formulation procedure because raising the concentration of MgO leads to an increase in Pickering emulsion stability, as shown in Table 4 and Table 6 (Torres *et al.*, 2008).

Table 6. Summary of optimization responses.

Parameters	Goal	Values		
Response		Lower	Target	Upper
Particle Size	Minimum	727.4	727.4	2005
PDI	Maximum	0.1437	1	1
Zeta potential	Target	−0.694	0.047	0.047
Viscosity	Maximum	1820.7	1820.7	78,004

In run number 8, the optimized multiple response prediction yields the following parameter settings: MGO: 3; Vaseline: 15; Olive Oil: 13.

4. CONCLUSION

Pickering emulsions can solve the problems facing normal emulsion formulations regarding stability, cost, and production procedures. Therefore, an attempt was made to formulate a general basic Pickering emulsion for different applications. Not only that, but different factors affecting the formulation procedures and their interactions were also studied using a factorial experimental design. Studying the factors and their interactions provides a guiding light for the formulation of Pickering emulsions in the pharmaceutical, chemical, or biological fields.

The optimum Pickering formulation is achieved by using 3 g of MgO solid particles (high level), 15 g of Vaseline (high level), and 13 mL of olive oil (high level); raising the concentration of MgO leads to a decrease in droplet size and an increase in Pickering emulsion formulation stability (**Table 4**) [23] (Torres *et al*., 2008).

Pickering emulsion's new applications include strong stability, shear-thinning rheological qualities for simple processing, and good biocompatibility for broad use. It offers good adherence to moist tissues for tissue engineering, a broad temperature range, and carefully regulated sustained release under intestinal circumstances.

Pickering emulsion is a strategy for achieving more material design improvements and a promising delivery platform [24] (Zhang *et al*., 2024).

CONFLICTS OF INTEREST

The authors declare no conflicts of interest regarding the publication of this paper.

REFERENCES

1. Loi, C.C., Eyres, G.T. and Birch, E.J. (2019) Effect of Mono- and Diglycerides on Physical Properties and Stability of a Protein-Stabilised Oil-in-Water Emulsion. *Journal of Food Engineering*, **240**, 56-64. https://doi.org/10.1016/j.jfoodeng.2018.07.016
2. Mcclements, D.J. (2007) Critical Review of Techniques and Methodologies for Characterization of Emulsion Stability. *Critical Reviews in Food Science and Nutrition*, **47**, 611-649. https://doi.org/10.1080/10408390701289292
3. Allen, L.V. and Ansel, H.C. (2014) Ansel's Pharmaceutical Dosage Forms and Drug Delivery Systems. Wolters Kluwer Health.
4. Gonzalez Ortiz, D., Pochat-Bohatier, C., Cambedouzou, J., Bechelany, M. and Miele, P. (2020) Current Trends in Pickering Emulsions: Particle Morphology and Applications. *Engineering*, **6**, 468-482. https://doi.org/10.1016/j.eng.2019.08.017
5. Chevalier, Y. and Bolzinger, M. (2013) Emulsions Stabilized with Solid Nanoparticles: Pickering Emulsions. *Colloids and Surfaces A*: *Physicochemical and Engineering Aspects*, **439**, 23-34. https://doi.org/10.1016/j.colsurfa.2013.02.054
6. Mady Sy, P., Dieng, S.M., Diouf, L.A.D., Djiboune, A.R., Soumboundou, M., Ndong, B., *et al*. (2018) Tramadol Encapsulation in Aqueous Phase of Water/Oil Pickering Emulsion Stabilized by Magnesium Oxide Particles. *International Journal of Biochemistry and Biophysics*, **6**, 37-43. https://doi.org/10.13189/ijbb.2018.060202
7. Sy, P.M., Dieng, S.M. and Diarra, M. (2019) Formulation, Stability and Physicochemical Properties of Pickering Emulsions: An Overview. *Applied Physics Research*, **11**, 41-51. https://doi.org/10.5539/apr.v11n1p41
8. Arditty, S., Schmitt, V., Giermanska-Kahn, J. and Leal-Calderon, F. (2004) Materials Based on Solid-Stabilized Emulsions. *Journal of Colloid and Interface Science*, **275**, 659-664. https://doi.org/10.1016/j.jcis.2004.03.001

9. Fouilloux, S. (2011) Nanoparticules et microfluides pour un système modèle d'émulsions de Pickering. Etude des mécanismes de stabilisation et destabilisation. Pierre et Marie Curie University.

10. Aveyard, R., Binks, B.P. and Clint, J.H. (2003) Emulsions Stabilised Solely by Colloidal Particles. *Advances in Colloid and Interface Science*, **100**, 503-546. https://doi.org/10.1016/s0001-8686(02)00069-6

11. Levine, S. and Sanford, E. (1985) Stabilisation of Emulsion Droplets by Fine Powders. *The Canadian Journal of Chemical Engineering*, **63**, 258-268. https://doi.org/10.1002/cjce.5450630211

12. Abend, S. and Lagaly, G. (2001) Bentonite and Double Hydroxides as Emulsifying Agents. *Clay Minerals*, **36**, 557-570. https://doi.org/10.1180/0009855013640009

13. Ashby, N.P. and Binks, B.P. (2000) Pickering Emulsions Stabilised by Laponite Clay Particles. *Physical Chemistry Chemical Physics*, **2**, 5640-5646. https://doi.org/10.1039/b007098j

14. Sharma, G., Soni, R. and Jasuja, N.D. (2017) Phytoassisted Synthesis of Magnesium Oxide Nanoparticles with *Swertia chirayaita*. *Journal of Taibah University for Science*, **11**, 471-477. https://doi.org/10.1016/j.jtusci.2016.09.004

15. Sy, P.M., Djiboune, A.R., Diouf, L.A.D., Soumboundou, M., Ndong, B., Ndiaye, A., *et al.* (2018) Water/Oil Pickering Emulsion Stabilized by Magnesium Oxide Particles: A Potential System with Two Active Substances (Paracetamol and Griseofulvin). *Open Journal of Biophysics*, **8**, 68-84. https://doi.org/10.4236/ojbiphy.2018.82006

16. Clogston, J.D. and Patri, A.K. (2010) Zeta Potential Measurement. In: McNeil, S.E., Ed., *Characterization of Nanoparticles Intended for Drug Delivery*, Humana Press, 63-70. https://doi.org/10.1007/978-1-60327-198-1_6

17. Mady, O.Y., Al-Shoubki, A.A. and Donia, A. (2021) An Industrial Procedure for Pharmacodynamic Improvement of Metformin HCl via Granulation with Its Paracellular Pathway Enhancer Using Factorial Experimental Design. *Drug Design, Development and Therapy*, **15**, 4469-4487. https://doi.org/10.2147/dddt.s328262

18. El-Gizawy, S.A., El-Maghraby, G.M. and Hedaya, A.A. (2019) Formulation of Acyclovir-Loaded Solid Lipid Nanoparticles: Design, Optimization, and *In- Vitro* Characterization. *Pharmaceutical Development and Technology*, **24**, 1287-1298. https://doi.org/10.1080/10837450.2019.1667385

19. Kawano, S., Kida, T., Akashi, M., Sato, H., Shizuma, M. and Ono, D. (2015) Preparation of Pickering Emulsions through Interfacial Adsorption by Soft Cyclodextrin Nanogels. *Beilstein Journal of Organic Chemistry*, **11**, 2355-2364. https://doi.org/10.3762/bjoc.11.257

20. Sinko, P. and Singh, Y. (2011) Martin's Physical Pharmacy and Pharmaceutical Sciences. 6th Edition, Lippincott Williams and Wilkins, 384.

21. Wetteland, C.L., de Jesus Sanchez, J., Silken, C.A., Nguyen, N.T., Mahmood, O. and Liu, H. (2018) Dissociation of Magnesium Oxide and Magnesium Hydroxide Nanoparticles in Physiologically Relevant Fluids. *Journal of Nanoparticle Research*, **20**, Article No. 215. https://doi.org/10.1007/s11051-018-4314-3

22. Hwang, K., Song-I, K., Kee-Yeol, K., Eun-Joo, L. and Moung-Seok, Y. (2004) Effect of Aqueous Phase Composition on the Stability of a Silica-Stabilized Water-in-Oil Emulsion. LG Household and Healthcare Research Park, 343-350. *Journal of the Society of Cosmetic Scientists of Korea*, **30**, 353-359.

23. Torres, L., Iturbe, R., Snowden, M.J., Chowdhry, B. and Leharne, S. (2008) Can Pickering Emulsion Formation Aid the Removal of Creosote DNAPL from Porous Media? *Chemosphere*, **71**, 123-132. https://doi.org/10.1016/j.chemosphere.2007.09.053

24. Zhang, J., Zheng, Y., Guo, B., Sun, D., Xiao, Y., Yang, Z., *et al.* (2024) Jammed Pickering Emulsion Gels. *Advanced Science*, **11**, Article ID: 2409678. https://doi.org/10.1002/advs.202409678