A water in oil gelled emulsion as a topical release vehicle for curcumin

J. L. Pérez-Salas[1], L. Medina-Torres[2], N. E. Rocha-Guzmán[1], F. Calderas[3], R. F. González-Laredo[1], M. J. Bernad-Bernad[2], M. R. Moreno-Jiménez[1], J.A. Gallegos-Infante[1]*

[1]TecNM/Instituto Tecnológico de Durango, UPIDET. Blvd. Felipe Pescador 1830 Ote., Nueva Vizcaya, 34080 Victoria de Durango, Durango, México

[2]Universidad Nacional Autónoma de México, Facultad de Química, 04510 Ciudad de México, México

[3] Facultad de Estudios Superiores-Zaragoza, Universidad Nacional Autónoma de México, Batalla 5 de mayo s/n, Colonia Ejército de Oriente, Iztapalapa, 09230 Ciudad de México, México

Email: agallegos@itdurango.edu.mx

L. Medina-Torres: Universidad Nacional Autónoma de México, Facultad de Química, 04510 Ciudad de México, México.

J.A. Gallegos-Infante: TecNM/Instituto Tecnológico de Durango, UPIDET. Blvd. Felipe Pescador 1830 Ote., Nueva Vizcaya, 34080 Victoria de Durango, Durango, México.

This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as doi: 10.1111/star.202200006.

Abstract

The objective of this work was to assess the influence of the concentration of polyglycerol polyricinoleate (PGPR) (at 1, 1.5 and 2%) on the physical properties of water in oil gelled emulsions (W/O) and evaluate their efficiency as a delivery vehicle for curcumin. Emulsions were characterized by drop size, centrifugal test, texture, and rheology during 28 days of storage. When the surfactant concentration increased, smaller droplet sizes were obtained (< 5 μm) and the phase separation tested by centrifugal force decreased from around 6% to 4% with little or no variation at all with time. The mechanical properties of emulsions showed a tendency to decrease as time passed and concentration of PGPR increased. Regarding the rheological results, the emulsions become more viscous as the concentration increased, but upon the addition of curcumin, the viscosity was sharply reduced indicating that the curcumin was acting as a lubricant. The elasticity of emulsions also increased with the concentration evidenced by a reduction of the relaxation time, which denoted a higher interaction between the water droplets and the oily phase. In the controlled release profiles, a low concentration of PGPR showed an increase in the affinity between curcumin and the emulsion, following a pseudo-Fickian release behavior. In contrast, a higher concentration of PGPR denoted a decrease in the affinity between curcumin and the emulsion, displaying a Fickian release behavior. The obtained systems were shown to adequately encapsulate curcumin and were stable to flow and time, which seem to be appropriate for a possible application for the delivery of bioactive principles by the topical route.

Keywords

Emulsion, Topical Release Vehicle, Curcumin

Practical applications

The practical application of this research is the possibility to prepare functional cosmetic emulsions with curcumin, but since curcumin is a labile product and is not water soluble, we were able to prepare tailor made curcumin water in oil emulsion systems for the topical release of this compound that could be used in the pharmaceutical industry.

1. INTRODUCTION

Delivery of lipophilic bioactives is an important issue in the food and pharmaceutical industries. Natural bioactives can be susceptible to several degradation reactions that may diminish their efficiency (Calligaris, Mirolo, Da Pieve, Arrighetti, & Nicoli, 2014). Different non-aqueous systems have been developed for delivery of lipophilic molecules (Pinto, Martins, Pastrana, Pereira, Cerqueira, 2021). The main idea is that lipids offer a higher

loading capacity for lipophilic molecules compared to aqueous systems. Therefore, several authors have used organogels as a tool to deliver lipophilic bioactives (Wang, Chen, Liu, 2021; Zhao, Wei, Xue, 2021). Nevertheless, organogels might have several technical problems as the restricted diffusion of drugs, lack of a proper gelator molecules, and regarding topical drug delivery systems, a greasy sensation. An alternative to improve technological properties of organogels as delivery systems is the use of emulsions.

The definition of emulsions is complicated, however, Israelachvili, (1994) claimed that the most authoritative and least controversial definition of an emulsion was done by IUPAC in 1972 (Everett, 1972). An emulsion is a dispersion of droplets of one liquid into another one, which are incompletely miscible, and it can also be defined as biphasic systems consisting of a surfactant, oil, and water. Depending on the formulation, an emulsion may or may not contain a co-surfactant. Although, emulsions are also thermodynamically unstable. Organogelation is a promising alternative to stabilize and provide structure to (W/O) emulsions (Hughes, Marangoni, Wright, Rogers, & Rush, 2009). Those authors developed organogel-based emulsions using 12-hydroxystearic acid (12-HSA) as gelator, which were stable to coalescence and showed long-term stability. Several examples on the use of emulsions and organogels have been reported. For example, Sawalha et al. (2021) developed an emulsion based in organogels fusing several sterols. Zhang et al. (2021) developed a gelled emulsion with medium chain triacylglycerols, water and several surfactants (Span 20 (sorbitan monolaurate), Span 40 (sorbitan monopalmitate), Span 60 (sorbitan monostearate), Span 80 (sorbitan monooleate) and Tween 80 (polyoxyethylene sorbitan monooleate), Sugar ester (sucrose stearic acid ester, S370) in order to enhance the loading and bioaccessibility of 5-demethylnobiletin. Candelilla wax and monoglyceride have been used to produce safflower oil high in oleic acid and water (20%) emulsions (Toro-Vazquez et al. 2013). High oral accessibility and cell permeability has been reported for some oil emulsions (Ojeda-Serna et

al. 2019; Rocha-Guzmán et al. 2021). Regarding topical drug delivery systems, the delivery across the skin can offer many advantages, such as lower fluctuations in plasma drug levels, circumvent first-pass metabolism, improve patient compliance, and provide local (dermal) or systemic (transdermal) effects (Hua, 2015). Nonetheless, the topical route has several problems, in special related with skin, which represents a barrier for proper penetration and absorption of drugs (Bouwstra & Ponec, 2006).

The use of emulsions can enhance the efficacy of bioactive ingredients by the topical route. A large number of cosmetics (foundation creams, vanishing creams, sunscreen lotions and creams, hair creams, shaving creams, hand lotions and creams, cold creams, etc.) are sold in emulsion form. Both O/W and W/O emulsions are common, although a majority of the cosmetic emulsions marketed today are W/O emulsions (Mully, 1974; Davis et al. 1985; Bennet et al. 1968). An emulsion is better absorbed when it is processed to reduce droplet size (Chang, Hu, Huang, Hsieh, & Ting, 2020). Several factors may affect droplet size; one of them is the election of proper emulsifier to facilitate the uniform dispersion of two immiscible liquids (*i.e.*, water and oil). An interesting surfactant is polyglycerol polyricinoleate (**PGPR**), which has been reported to produce W/O emulsions with lower droplet size in comparison with glycerol-based emulsifiers (Tran, Green, Ghosh, & Rousseau, 2017). Moreover, the physical and release properties of the structured emulsions can be modulated by incorporating PGPR in various proportions (Behera et al. 2015; Contreras-Ramírez et al. 2021). On the other hand, curcumin is a well-known nutraceutical with many health benefits claims as antioxidant, anti-inflammatory, anticarcinogenic, antidepressant, antiarthritic, antidiabetic, hepatoprotective, and lipid-lowering properties (Panahi et al. 2017; Cicero et al. 2020; Alsharif & Almuhtadi, 2021). However, it has poor water solubility (Anand, Kunnumakkara, Newman, & Aggarwal, 2007). Several technologies have been used to increase absorption of curcumin by several delivery routes such as microencapsulation by

spray drying (Medina-Torres et al. 2019) and many other reposted elsewhere (Jiang, Liao, & Charcosset, 2020), including the use of organogel based emulsions (Sawalha et al. 2012; Yllmaz & Atc, 2014; Rocha-Guzmán et al. 2021; Dong et al. 2022, Palla et al. 2022). About the use of organogel based emulsions for topical bioactives delivery, Botega et al. (2021) have used high oleic sunflower oil and candelilla wax to obtain higher stability of emulsions. Vellido-Perez, Ochando-Pulido, La Fuente, and Martinez-Ferez. (2021) developed an organogel based emulsion for curcumin with high oil oxidation stability. Finally, to our best knowledge, there are not reports about the effect of PGPR content in Oil-Water emulsions for topical drug delivery of curcumin. In this regard, the main objective of the present study was to evaluate the influence of PGPR concentration on the stability of Oil-Water emulsions and their efficiency as a delivery vehicle for curcumin.

2. MATERIALS AND METHODS

2.1 Materials

Canola oil was purchased in a local market and manufactured by Aceites, Grasas y Derived, S.A. de C.V. (Zapopan, Jal, Mexico). Myverol 18-04 K, which is a mixture of monoglycerides (49% glycerol monostearate, 48% glycerol monopalmitate and 3% calcium silicate), was kindly provided by Kerry, SW FOOD TECHNOLOGY, S.A de C.V (Nuevo León, Mexico). The surfactant PGPR 4180 (E476) was provided by Palsgaard Industries (San Luis Potosí, Mexico). Curcumin (PubChem CID: 969516) with a purity of 65% was obtained from Sigma-Aldrich (St. Louis, Mo., USA).

2.2 Emulsion preparation

Emulsions (W/O) were produced at a concentration of 25 wt % aqueous phase and 75 wt % of oil phase by weight (including 10% Myverol), which resulted from the most stable emulsion of a preliminary study. Then the surfactant polyglycerol polyricinoleate (**PGPR**) was added at three different concentrations (1, 1.5 and 2 wt % in relation to the weight of

canola oil). The oily phase was obtained by heating at 80°C under magnetic stirring (100 rpm) for 10 min (Rocha-Amador et al. 2014) (**See Table 1**). Next, it was cooled down to 60°C and mixed with aqueous phase at the same temperature. The blend was homogenized with an ultra turrax at 7200 rpm for 5 min, and chilled to 4°C by means of a cold-water bath. A small amount of sodium azide (0.1 wt%) was added to the finished emulsions to retard microbial growth. W/O emulsions were kept in refrigeration at 5°C for 12 h, and stored at 25°C for 28 days.

2.3 Incorporation of curcumin

Curcumin was solubilized in the oily phase at a concentration of 0.4 mg/g according to previous reports (Ojeda-Serna et al. 2019). This oily phase was added to the water phase as described in the previous Section (2.2).

2.4 Drop size

Droplet size of emulsions was obtained by optical microscopy using an Axio-Lab A.1 microscope (Zeiss, Jena, Germany) at a total of 200 magnifications, with the use of ZEN lite software (Blue version, Zeiss, Jena, Germany). Images were taken and diameters of 100 drops measured for the creation of size distribution frequency graphics (Oh & Shah, 1993; Jimenez-Alvarado et al. 2009).

The average droplet diameter was calculated following the Equation:

$$d_n = \frac{\sum_i^N n_i * d_i}{\sum_i^N n_i} \quad (1)$$

where, d_i is the droplet diameter and n_i, the number of "i" measurements.

In a similar way, the ratio of the summation of the diameters to the fourth power and the sum of the diameters raised to the cube was calculated to obtain the $D(4,3)$, from:

$$D\ (4,3) = \frac{\sum_{i=1}^n d_i^4}{\sum_{i=1}^n d_i^3} \quad (2)$$

From the average diameter and $D(4,3)$, polydispersity index (PDI) was calculated according to the following equation (Lovell & El-Asser, 1997; Rawle et al. 2003):

$$PDI = \frac{D(4,3)}{d_n} \quad (3)$$

2.5 Centrifugation test

Centrifugation test is a form of evaluation of the accelerated stability of the emulsion in which two substances are separated under centrifugal force to predict the stability of the emulsion. (Mohsin et al. 2016). Emulsion samples (10 g) were centrifugated at 5500 rpm for 40 min, and the separation percentage was calculated as:

(Supernatant weight/sample weight) *100

2.6 Texture analysis

The texture analysis was performed with a TA texture analyzer, TX plus (Texture Technologies Corp, New York, USA) at room temperature; calibration was done with a probe of 5 kg. A penetration test was performed with the use of a cylindrical probe P20 (aluminum probe, 20 mm diameter). A sample (50 g) of the Oil-Water emulsion was placed in a bottle (35 mm diameter and 90 mm in height) up to a height of 35 mm. The probe penetrated 15 mm at 5 mm/s and returned to its initial position. Force *vs* time graphs were obtained, and four parameters were contemplated. Firmness was defined as the maximum value of force in a plot of force *vs* time. Consistency, as the area under the curve of the positive part of the curve in a plot of force vs time; Cohesiveness, as the maximum value of the force in the negative peak arising during the movement of the probe upwards, above the analyzed sample (See Figure 1b); and Work of Cohesion, as the area under the negative portion of the curve. All parameters were defined according to Tai, Bianchini, and Jachowicz, (2014).

2.7 Rheological characterization

Rheological measurements were carried out on a DHR-3 rheometer (TA Instruments, Wilmington, DE, USA) equipped with a Peltier system for temperature control. Parallel

plates geometries of rugged acrylic with diameter of 40 mm and a gap of 1 mm for all tests were used. The oscillatory shear tests were made in a frequency range of 1 to 300 rad/s, the linear viscoelastic range was previously found (the linear zone was determined following the evolution of the moduli *vs* % deformation, at different fixed frequencies of 1, 10 and 100 Hz). A 20% deformation for concentrations 1, and 1.5% was used, while for 2% concentration, a 10% deformation was used; all measurements were done at 25°C (Medina-Torres et al. 2019; Medina-Torres et al. 2009).

In the simple shear flow test, the sweep range was from 0.1 to 300 s^{-1}, at 25°C for all experimental samples, data were adjusted to the Cross model (Equation 4) (Cross, 1965):

$$\eta = \frac{\eta_0 - \eta_\infty}{1+\left(\frac{\dot{\gamma}}{\lambda_C}\right)^p} \quad (4)$$

where, η is the non-Newtonian viscosity of the material at steady shear (Pa*s), η_0 is the viscosity at low shear rate (Pa*s), η_∞ is the viscosity at high shear rate (Pa*s), λ_c is the characteristic time (s) of the Cross model, $\dot{\gamma}$ is the shear rate (1/s) and p is the dimensionless parameter related with the power law index.

2.8 Curcumin content

The content of curcumin in emulsions was determined by the method proposed by Kadam et al. (2018) with slight modifications. It was dissolved a fixed amount of formulation (50 mg) in 10 mL of ethanol, mixed with a vortex and transferred to centrifuge tubes 6000 rpm for 10 min, then a UV-Vis spectroscopy analysis of curcumin was performed at λ of 425 nm. The content of curcumin was calculated by the equation obtained in the linear regression of a calibration curve.

2.9 Controlled release profile

The release profiles were obtained using Franz cells (110 mL) with a nitrocellulose membrane of pore size 12--14 KDa. Two grams of formulation were placed in the donor compartment, while the surrounding solution was PBS/ethanol 50/50 v/v (pH 7.2).

Curcumin release was monitored for 24 h while maintaining a temperature of 37°C with a countercurrent bath and magnetic stirring of 100 rpm. Periodically, a sample of the surrounding solution was taken and replaced by fresh solution. Curcumin was analyzed by UV-Vis spectroscopy at a wavelength of 425 nm. The content of curcumin was calculated by the equation obtained from the calibration curve (Medina-Torres et al. 2019). The tests were conducted under sink conditions.

To understand the type of drug release from the structured emulsions, data were fitted to two different equations following the methodology described by Cháirez-Ramírez et al. (2015), first the Higuchi equation:

$$Mt/A = \sqrt{2}*C_{ini}*D*C_s*t \qquad (5)$$

where, Mt is the cumulative amount of compound released at the time t, A is the area of transport, C_{ini} is the initial drug concentration, D is the diffusivity constant, Cs is the drug solubility and t is the time. This equation can be simplified to:

$$Mt = k*\sqrt{t} \qquad (6)$$

where, k is a constant

And then, the Power law equation:

$$Mt/M\infty = k* t^n \qquad (7)$$

where, Mt and M∞ are the absolute cumulative amounts of active compound released at time t and at an infinite time, respectively; k is the release constant related to kinetic effects; the exponent n describes the release mechanism, which depends on the geometry of the system.

2.10 Statistical analysis

All tests, except for curcumin content test and controlled release profile, were performed at different storage times (1, 7, 14, 21 and 28 days). Data were analyzed using ANOVA and mean comparison tests ($p<0.05$, Tukey test), with 95% confidence with Statistica Software 12 (StatSoft, Tulsa, OK, USA). Controlled release data were fitted to the different proposed models by non-linear estimation using the algorithm of Levenberg -- Marquadt with Statistica software for Windows, version 12.5 (Stat Soft, Tulsa, OK, USA).

3. RESULTS AND DISCUSSIONS

3.1 Droplet size

None of the emulsions obtained in this study showed phase separation throughout the evaluation period (28 days). The average droplet diameter was found between 4.0 and 5.1 μm for all formulations (**Table 2**), with a slight tendency to increase over 28 days. Previous studies on formulation of similar emulsions, showed an average size of 37 μm (Ojeda-Serna et al. 2019). However, these authors employed only monoglycerides that functioned as gelator and surfactants at the same time, as reported in Toro-Vazquez et al. (2013). Thus, limiting the amount of monoglycerides in the interface by the addition of PGPR into gelled emulsions resulted in a decrease in droplet size. Also, according to Ushikubo and Cunha (2014), the presence of PGPR in emulsions lowered the interfacial tension, therefore, small droplets were formed (Elwell-Mark at al. 2004). Zembyla, Murray, and Sarkar, (2020) indicated that PGPR could form elastic interfaces that slow down the coalescence rate between droplets, diminishing their particle size. Non-significant statistical differences ($p<0.05$, Tukey test) in droplet size dependent on surfactant concentration (**Table 2**) were observed; this behavior was opposite to reported by Tcholakova, Denkov, and Danner (2004) with different types of surfactants. Poly-dispersity index (PDI) values (**Table 2**) indicate that emulsions are polydisperse, which is expected by the type of processing used (rotor/stator).

However, the theory points out that as time passes, droplet size increases, although this change was not observed during the evaluation period (28 days). This can be attributed to the stability given by the continuous phase being the oily phase, which increases the viscosity of the w/o gelled emulsion, improving the stability over prolonged storage periods (Rocha-Amador et al. 2014; Vintiloiu & Leroux, 2008; Yu & Huang, 2012).

3.2 Centrifugation test

The concentration of surfactant has significant influence in centrifugal force separation percentages ($p<0.05$, Tukey test). In **Figure 1**, the gelled emulsion with lower amount of surfactant (1%) showed higher degree of separation (around 6%), which is related to the PDI values reported on **Table 2.** Consequently, gelled emulsions with 1% of PGPR were the experimental samples with the highest value of PDI; the higher variation in particle size promotes the phenomena of instability in emulsions as droplets tend to coalesce easier and more rapidly. On the other hand, w/o gelled emulsions with 1.5 and 2% of PGPR showed lower degree of separation (*i.e*., around 4%). Márquez, Medrano, Panizzolo, and Wagner (2010) reported this phenomenon of stability as dependent on the concentration of PGPR and in synergism with the addition of electrolytes. Correspondingly, this was attributed to the decrease in droplet size in the formulation of emulsions (Contreras-Ramírez et al. 2021). This could also be directly related to the mechanical behavior, since lower concentrations of surfactant produced stiffer and less flexible emulsions that could promote syneresis. Recent works with gelled emulsions obtained with Myverol and PGPR showed that their presence contributed to reduce the droplet size in gelled emulsions. Myverol allows a closer interaction between gelator, other molecules, and PGPR forms elastic interfaces that slow down the coalescence rate between droplets (Contreras-Ramírez et al. 2021).

3.3 Texture

Results for texture test are shown in **Figure 2**. On the first day of evaluation, the gelled emulsions with 1.5% of PGPR showed the higher consistency (**Figure 2 upper right**) and work of cohesion (**Figure 2 lower right**); and gelled emulsions with 2% of PGPR showed higher firmness (**Figure 2 upper left**) and cohesiveness (**Figure 2 lower left**), but at the 7th day of evaluation, sample with 1% of PGPR exceeded them. This behavior could be attributed to the plasticizing effect of the PGPR, in physical gels, where Van der Waals interactions and hydrogen bonds occurred between polymer strands. According to the theory of plasticization, a plasticizing molecule interacts with the combinations of the gel, causing the polymer chains to slide on each other and thus causing these effects (Wypych, 2004).

From the 7th day of evaluation, there are no significant changes in the variation of texture parameters (storage temperature 25°C), which indicates a great potential for the use of these formulations.

3.4 Rheology

Figure 3 shows the results from the rheological assessment at day 28 of simple shear flow in the form of viscosity *versus* shear rate. In general, all curves show a shear thinning behavior and they overlap, this tendency was observed to be consistent with time. Parameters obtained from adjusting experimental data to the Cross model are shown in **Table 3** (*i.e.*, all parameters have shown an experimental error <5%). Results from **Table 3** indicate that the viscosity at zero shear rate and the viscosity at infinite rate, η_0 and η_∞, respectively, increased with the concentration as was expected. In the case for the sample with curcumin, the zero-shear rate viscosity was greatly reduced to 316 Pa∗s, which is a value between those of the 1% and 1.5% gelled emulsions. The viscosity of all samples increased with time, which

is related to the increase in particle diameter observed in **Table 2**. In particular, the 2% emulsion, is the most unstable as the viscosity values decrease more rapidly with time (see **Table 3**), this may be related with phase separation and is related to the lowest consistency shown for this emulsion in the texture tests. However, the 1.5% gelled emulsions with curcumin is the most stable up to day 21, whereas 1.5% emulsion without curcumin preserves its structure (*i.e.*, viscosity) until day 14, but in a lesser degree. From a storage point of view, low zero shear viscosity (η_0) is the most important parameter because, as mentioned earlier, it represents the viscosity of the unmodified structure of the material.

The addition of curcumin to the gelled emulsion generates a structure that in principle is very different compared to other concentrations without curcumin, since the viscosity is lower and more stable up to day 21. This was possibly caused by a decrease in the particle size, but it was not possible to measure it, since curcumin does not dissolve in water. Another possible reason is that the not-encapsulated curcumin is acting as a lubricant in the emulsion.

3.4.1 Small amplitude Oscillatory Shear (SAOS) flow test

Results from the linear viscoelastic (small amplitude oscillatory flow) test are disclosed in **Figure 4**, where both viscoelastic moduli (elastic, G' and viscous, G'') are plotted versus the oscillatory frequency. All samples show a predominant viscous behavior (G''>G') at low frequencies with a crossover point (G′ = G′′) at high frequencies. In the case of the sample at higher concentration (2%), the crossover time is observed at intermediate frequencies and at high frequencies the samples show a predominant elastic behavior, which is related to the higher content of droplet particles and the interaction of droplets (oil/water) with the continuous phase (oil). The inverse of the crossover frequency is called a relaxation time, therefore, to study the influence of time over the viscoelasticity of the emulsions, the relaxation time is plotted as a function of the storage time in **Figure 5**. In **Figure 5**, as the concentration in the gelled emulsion increases, the relaxation time of the material decreases

in general (Schramm, 2000). This is caused because the gelled emulsion becomes more elastic as the concentration increases, evidencing a higher interaction between the emulsified particles and the liquid matrix. Thus, the relaxation time increases, which is consistent with studies reported in the literature (Manca, Lapasin, Partal, & Gallegos, 2001). This is also true even for the sample with curcumin which justifies the assumption that the particle size in this sample is reduced. However, in the 1.5% gelled emulsion (1.5%) and in the 1.5% gelled emulsion with curcumin (1.5%+Cur), a minimum in the relaxation time was observed. This is thought to be caused by a reordering of the droplet particles in both samples, which recover their elastic properties after 28 days of storage. Finally, the rheological behavior of gelled emulsions is strongly influenced by the deformation and orientation of droplets caused by the flow field. When a droplet of one fluid is suspended in a continuum of a second fluid that is made to shear (**see Table 2**), the droplet will deform with respect to the flow direction (*i.e.*, shear rate or small amplitude oscillatory shear).

3.4.2 Activation energy

Activation energy was calculated by preparing master plots of viscoelastic moduli versus temperature (not shown here) and then, adjusting the shift factors to the Arrhenius equation (Partal et al. 1997). Results are shown in **Figure 6**. In the present experiment, activation energy can be considered as the mechanical energy required to disturb (*i.e.*, slightly modify) the intermolecular structure of the gelled emulsion. For samples: 1% and 2%, the activation energy remains constant until day 14, then decreases; this behavior implies a structural disruption after day 14th. The 1.5% gelled emulsion (1.5%) showed a higher stability of the activation energy with storage time, while the 2% gelled emulsion with curcumin showed the highest instability with a minimum on day 21th. However, more detailed analysis of data shown in **Figure 6** indicates that the 1.5% plus curcumin possesses the highest activation energy at day 1 in comparison to the 1.5%. This behavior indicates that the presence of

curcumin generates a more resistant intermolecular structure as noted in previous analyses, although subsequently decreases and recovers at day 28.

3.5 Controlled release profiles

The kinetics of curcumin release are shown in **Figure 7,** where the % curcumin delivered is plotted *versus* time. For this case all gelled emulsions were loaded with curcumin, and in all structured gelled emulsions, the initial curcumin load was the same. However, the cumulative drug release showed differences related with the PGPR content. The 1% gelled emulsion (1%+curcumin) reaches a plateau at around 3 h with a cumulative curcumin delivery of about 15%, whereas 1, 5 and 2% gelled emulsions (1.5% + curcumin and 2% + curcumin) reached the plateau at around 12 h with 22% of curcumin delivery for 1.5% and 25% for the 2% sample. These results suggested that the curcumin release from the structured emulsion was improved with the increase in the PGPR concentration at the end of the experiment. However, at shorter times (e.g., < 3 h), 1%+curcumin showed a higher release. The decrease in the drug release in the 1.5%+curcumin and 2%+curcumin could be attributed to the formation of highly viscous environments around the curcumin molecules (Yao, Liu, Chang, Hsu, & Chen, 2004). Also, the slow release of curcumin from 1.5%+curcumin and 2%+curcumin could be related to an increase in the overall hydrophobicity of gelled emulsions. Moreover, Behera et al. (2015) reported that a high concentration of PGPR increases the hydrophobic interactions into the gelled systems, and this type of interactions cause shrinkage of the structured gelled emulsions, diminishing the osmotic pressure (Peppas & Merril, 1977) and provoking the swelling of structured emulsions (Ofner III & Bubnis, 1996). Ngwabebhoh, Erdagi and Yildiz (2018) reported a 12% of curcumin release at 24 h fusing Pickering emulsion stabilized by nanocellulosic nanoparticles, in comparison with results obtained in the present experiment at the same time (24 h, 17 -- 25%). Similar results

were reported by Shah et al. (2016) after 24 h, by the use of Pickering emulsion stabilized by nanoparticles of chitosan-tripolyphosphate

Data obtained for parameter models from curcumin release are shown in **Table 4**. The Higuchi model fits well the experimental data, except the sample 1%+curcumin. However, power law model shows best fit of experimental data at all experimental concentrations. Regarding the "**n**" value, when it is equal to 0.5, indicates a Fickian behavior. However, if the geometry is a thin film, "n" needs to be equal to **0.43** to indicate such Fickian behavior (Siepmann & Siepmann, 2012). When the value of "n" is **<0.5**, pseudo-Fickian diffusion behavior occurs, in this case, the behavior resembles Fick´s law with a slower approach to equilibrium (Thakur et al. 2012). Thus, 1.5%+curcumin and 2%+curcumin show a release of curcumin by diffusion mechanism (*i.e.*, follows a Fickian behavior) similar to that observed in curcumin emulsions release, whereas 1%+curcumin shows a pseudo-Fickian behavior. Also, a progressive decrease in "k" value of power model was observed, as PGPR concentration increases, indicating that curcumin and emulsion affinity was decreased. It is interesting to compare this behavior with curcumin emulsion (*i.e.*, no PGPR), where its "k" value was similar to that of 1.5%+curcumin; thus, the use of PGPR in structured emulsions implies, at low concentrations, an increase in affinity between curcumin and emulsion, whereas a pseudo-Fickian release behavior at higher concentration of PGPR implies a decrease in affinity between curcumin and the gelled emulsion, with a Fickian release behavior.

3 CONCLUSIONS

An oil-water gelled emulsion at different PGPR concentrations was prepared to encapsulate curcumin. The most stable emulsion was found at a concentration of 1.5% PGRP. This emulsion was used to add curcumin. The presence of PGPR at concentrations of 1.5% in w/o gelled emulsions causes a decrease in the droplet size, as well as a greater stability regarding

phase separation as observed by centrifugal force. Mechanical properties are diminished (Hardness) at higher concentration (2%) of PGPR, due to the interactions between PGPR molecules and monoglycerides. Additionally, an increase of PGPR concentration, increases the viscosity of the w/o gelled emulsions. The elasticity of the emulsions is also increased by the PGPR concentration. The release profiles evidence that different concentrations of PGPR can modulate the curcumin release behavior of emulsions, reaching a release plateau and the total curcumin delivery. Due to the characteristics of the w/o gelled emulsions, they are suggested for the delivery of curcumin by the topical route.

Future work

The characterization and *in vitro* release profile are a starting point for subsequent biocompatibility analyzes and evaluation of local therapeutic effects. Further analysis such as controlled release under gastrointestinal simulated conditions may be necessary for pharmaceutical and other applications.

Acknowledgments

Author JLPS acknowledges graduate scholarship from the Mexican Council of Science and Technology (CONACyT). This project was partially funded by CONACyT-Ciencia-Basica (grant number 241241).

Conflict of interest

The authors declare no conflict of interest

Data Availability Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

REFERENCES

Alsharif, F. J., & Almuhtadi, Y. A. (2021). The Effect of Curcumin Supplementation on Anthropometric Measures among Overweight or Obese Adults. *Nutrients*, *13*, 680--689.

Anand, P., Kunnumakkara, A. B., Newman, R. A., & Aggarwal, B. B. (2007). Bioavailability of curcumin: problems and promises. *Pharmaceutics*, *4*, 807--818.

Behera, B., Biswal, D., Uvanesh, K., Srivastava, A. K., Bhattacharya, M. K., Paramanik, K., & Pal, K. (2015). Modulating the properties of sunflower oil based novel emulgels using castor oil fatty acid ester: Prospects for topical antimicrobial drug delivery. *Colloids and Surfaces B: Biointerfaces, 128*, 155--164.

Bennet H., Bishop J.L., Wulfinghoff M.F. (1968). Practical Emulsions-Applications, Vol. 2, Chemical Publishing Co., New York, Chap. 4.

Botega, D. C. Z., Nogueira, C., de Moura, N. M., Martinez, R. M., Rodrigues, C., & Barrera-Arellano, D. (2021). Influence of Aqueous Matrices into Candelilla Wax Organogels Emulsions for Topical Applications. *Journal of the American Oil Chemists' Society, 98*, 317--328.

Bouwstra, J. A., & Ponec, M. (2006). The skin barrier in healthy and diseased state. Biochimica et Biophysica Acta (BBA). *Biomembranes, 1758*, 2080--2095.

Calligaris, S., Mirolo, G., Da Pieve, S., Arrighetti, G., & Nicoli, M. C. (2014). Effect of oil type on formation, structure and thermal properties of γ-oryzanol and β-sitosterol-based organogels. *Food Biophysics, 9*, 69--75.

Cháirez-Ramírez, M.H., Sanchez-Burgos, J.A., Gomes, C., Moreno-Jiménez, M.R., González-Laredo, R.F., Bernad-Bernad, M.J., Gallegos-Infante, J.A. Rocha-Guzman, N.E. (2015). Morphological and release characterization of nanoparticles formulated with poly (dl-lactide-co-glycolide)(PLGA) and lupeol: In vitro permeability and modulator effect on NF-κB in Caco-2 cell system stimulated with TNF-α. *Food and Chemical Toxicology, 85*, 2--9.

Chang, W. C., Hu, Y. T., Huang, Q., Hsieh, S. C., & Ting, Y. (2020). Development of a topical applied functional food formulation: Adlay bran oil nanoemulgel. LWT-*Food Science and Technology, 117*, 1--8.

Cicero, A. F., Sahebkar, A., Fogacci, F., Bove, M., Giovannini, M., & Borghi, C. (2020). Effects of phytosomal curcumin on anthropometric parameters, insulin resistance, cortisolemia and non-alcoholic fatty liver disease indices: a double-blind, placebo-controlled clinical trial. *European journal of nutrition, 59*, 477--483.

Contreras-Ramírez, J. I., Villanueva-Fierro, I., González-Laredo, R. F., Toro-Vázquez, J. F., Pérez-Martínez, J. D., Rosas-Flores, W., & Gallegos-Infante, J. A. (2021). Study of the relationship of hydrogen bonding and hydrophobic interactions in W/O organogel emulsions by Raman microspectroscopy. *Colloid and Interface Science Communications*, *44*, 100486.

Contreras-Ramírez, J. I., Gallegos-Infante, J. A., Rosas-Flores, W., González-Laredo, R. F., Toro-Vázquez, J. F., & Pérez-Martínez, J. D. (2021). Relationship of rheological and thermal properties in organogel emulsions (W/O): Influence of temperature, time, and surfactant concentration on thermomechanical behavior. *Journal of Molecular Liquids*, *337*, 116403.

Cross, M. M. (1965). Rheology of non-newtonian fluids: a new flow equation for pseudoplastic system. *Journal of Colloid Science, 20*, 417--437.

Davis S.S., Hadgraft J., Palin K.J. (1985). Medical and pharmaceutical applications of emulsions, in Encyclopedia of Emulsion Technology, Vol. 2, P. Becher, Ed.,Marcel Dekker, New York, Chap. 6.

Dong, Y., Wei, Z., Wang, Y., Tang, Q., Xue, C., & Huang, Q. (2022). Oleogel-based Pickering emulsions stabilized by ovotransferrin--carboxymethyl chitosan nanoparticles for delivery of curcumin. *LWT-Food Science and Technology*, 113121.

Elwell Mark W., Roberts Robert F., Coupland John N. (2004). Effect of homogenization and surfactant type on the exchange of oil between emulsion droplets. *Food Hydrocolloids,* 18 413--418. https://doi.org/10.1016/j.foodhyd.2003.05.001.

Everett, D. H. (1972). Manual of symbols and terminology for physicochemical quantities and units, appendix II: Definitions, terminology and symbols in colloid and surface chemistry. *Pure and Applied Chemistry, 31*, 577--638.

Hua, S. (2015). Lipid-based nano-delivery systems for skin delivery of drugs and bioactives. *Frontiers in Pharmacology, 6*, 219.

Hughes, N. E., Marangoni, A. G., Wright, A. J., Rogers, M. A., & Rush, J. W. (2009). Potential food applications of edible oil organogels. *Trends & Food Science in Technology, 20*, 470--480.

Israelachvili, J. (1994). The science and applications of emulsions---an overview. *Colloids and Surfaces A: Physicochemical and Engineering Aspects, 91*, 1--8.

Jiang, T., Liao, W., & Charcosset, C. (2020). Recent advances in encapsulation of curcumin in nanoemulsions: A review of encapsulation technologies, bioaccessibility and applications. *Food Research International, 132*, 1--14.

Jimenez-Alvarado R., Beristain C.I., Medina-Torres L., Roman-Guerrero A., Vernon-Carter E.J. (2009). Ferrous bisglycinate content and release in W1/O/W2 multiple emulsions stabilized by protein--polysaccharide complexes. *Food Hydrocolloids*, 23 2425--2433.

Kadam, P. V., Yadav, K. N., Bhingare C. L., & Patil M. J. (2018). Standardization and quantification of curcumin from Curcuma longa extract using UV visible spectroscopy and HPLC. *Journal of Pharmacognosy and Phytochemistry*. 7(5): 1913--1918.

Lovell, P. A., & El-Asser, M. (1997) Emulsion Polymerization and Emulsion Polymers. John Wiley and Sons Ltd.

Manca, S., Lapasin, R., Partal, P., & Gallegos, C. (2001). Influence of surfactant addition on the rheological properties of aqueous Welan matrices. *Rheologica Acta, 40*, 128--134.

Márquez, A. L., Medrano, A., Panizzolo, L. A., & Wagner, J. R. (2010). Effect of calcium salts and surfactant concentration on the stability of water-in-oil (w/o) emulsions prepared with polyglycerol polyricinoleate. *Journal of Colloid and Interface Science, 341*, 101--108.

Medina-Torres L., Calderas F., Gallegos-Infante J. A., González-Laredo R.F., Rocha-Guzmán N.E. (2009). Stability of alcoholic emulsions containing different caseinates as a function of temperature and storage time. *Colloids and Surfaces A: Physicochem. Eng. Aspects*, 352 38--46. https://doi.org/10.1016/j.colsurfa.2009.09.046

Medina-Torres L., Núñez-Ramírez D. M., Calderas F., Bernad-Bernad M. J., Gracia-Mora J., Rodríguez-Ramírez J., González-Laredo R. F., Gallegos-Infante J. A., Manero O. (2019). Curcumin encapsulation by spray drying using Aloe vera mucilage as encapsulating agent. *Journal of Food Process Engineering, 42*, 1--12.

Mohsin, S., Akhtar, N., Mahmood, T., Khan, H., & Mustafa, R. (2016) Formulation and stability of topical water in oil emulsion containing corn silk extract. *Tropical Journal of Pharmaceutical Research*. 15 (6): 1115--1121.

Mully B.A. (1974). Medicinal emulsions, in Emulsions and Emulsion Technology, Part 1. K.J. Lissant, Ed., Marcel Dekker, New York, Chap. 6.

Ngwabebhoh, F. A., Erdagi, S. I., & Yildiz, U. (2018). Pickering emulsions stabilized nanocellulosic-based nanoparticles for coumarin and curcumin nanoencapsulations: In vitro release, anticancer and antimicrobial activities. *Carbohydrate polymers, 201*, 317--328.

Ofner III, C. M., & Bubnis, W. A. (1996). Chemical and swelling evaluations of amino group crosslinking in gelatin and modified gelatin matrices. *Pharmaceutical Research, 13*, 1821--1827.

Oh, S. G., & Shah D. O. (1993). Effect of counterions on the interfacial tension and emulsion droplet size in the oil/water/dodecyl sulfate system. *J. Phys. Chem.* 97(2), 284--286.

Ojeda-Serna, I.E., Rocha-Guzmán, N.E., Gallegos-Infante, J.A., Cháirez-Ramírez, M.H., Rosas-Flores, W., Pérez-Martínez, J.D., Moreno-Jiménez, M.R., González-Laredo, R.F. (2019). Water-in-oil organogel based emulsions as a tool for increasing bioaccessibility and cell permeability of poorly water-soluble nutraceuticals. *Food Research International, 120*, 415--424.

Palla, C. A., Aguilera-Garrido, A., Carrín, M. E., Galisteo-González, F., & Gálvez-Ruiz, M. J. (2022). Preparation of highly stable oleogel-based nanoemulsions for encapsulation and controlled release of curcumin. *Food Chemistry*, 132132.

Panahi, Y., Kianpour, P., Mohtashami, R., Jafari, R., Simental-Mendía, L. E., & Sahebkar, A. (2017). Efficacy and safety of phytosomal curcumin in non-alcoholic fatty liver disease: a randomized controlled trial. *Drug research*, *67*, 244--251.

Partal P., Guerrero, A., Berjano M., & Gallegos C. (1997). Influence of Concentration and Temperature on the Flow Behavior of Oil-in-Water Emulsions Stabilized by Sucrose Palmitate. *Journal of the American Oil Chemists' Society*. 74(10). 1203--1212.

Peppas, N. A., & Merril, E. W. (1977). Crosslinked poly (vinyl alcohol) hydrogels as swollen elastic networks. *Journal of Applied Polymer Science, 21*, 1763--1770.

Pinto, T. C., Martins, A. J., Pastrana, L., Pereira, M. C., & Cerqueira, M. A. (2021). Oleogel-based systems for the delivery of bioactive compounds in foods. Gels, 7(3), 86

Rawle, A., Limited, M.I., Park, E.B., & Road, G. (2003) Basics principles of particle size analysis. *Surf Coat Intl Part A Coatings J.* 44. 1--8.

Rocha-Amador, O. G., Gallegos-Infante, J. A., Huang, Q., Rocha-Guzmán, N. E., Moreno-Jiménez, M. R., & González-Laredo, R. F. (2014). Influence of commercial saturated monoglyceride, mono-/diglycerides mixtures, vegetable oil, stirring speed, and temperature on the physical properties of organogels. *International Journal of Food Science, 2014*, 1--8.

Rocha-Guzmán, N. E., Cháirez-Ramírez, M. H., Pérez-Martínez, J. D., Rosas-Flores, W., Ornelas-Paz, J. D. J., Moreno-Jiménez, M. R., … & Gallegos-Infante, J. A. (2021). Use of organogel-based emulsions (o/w) as a tool to increase the bioaccessibility of lupeol, curcumin, and quercetin. *Journal of the American Oil Chemists' Society, 98*, 1177--1188.

Sawalha, H., Venema, P., Bot, A., Flöter, E., Lan, Y., & van der Linden, E. (2021). Effects of oil type on sterol-based organogels and emulsions. *Food Biophysics, 16*, 109--118.

Sawalha, H., den Adel, R., Venema, P., Bot, A., Flöter, E., & van der Linden, E. (2012). Organogel-emulsions with mixtures of β-sitosterol and γ-oryzanol: influence of water activity and type of oil phase on gelling capability. *Journal of Agricultural and Food Chemistry, 60*, 3462--3470.

Schramm, G. (2000). *Practical Approach to Rheology and Rheometry*. Karlsruhe: Gebrüder Weiss GmbH: Thermo Haake.

Shah, B. R., Li, Y., Jin, W., An, Y., He, L., Li, Z., … & Li, B. (2016). Preparation and optimization of Pickering emulsion stabilized by chitosan-tripolyphosphate nanoparticles for curcumin encapsulation. *Food Hydrocolloids, 52*, 369--377.

Siepmann, J., & Siepmann, F. (2012). Modeling of diffusion controlled drug delivery. *Journal of Controlled Release, 161*, 351--362.

Tai, A., Bianchini, R., & Jachowicz, J. (2014). Texture analysis of cosmetic/pharmaceutical raw materials and formulations. *International journal of cosmetic science, 36*, 291--304.

Tcholakova, S., Denkov, N. D., & Danner, T. (2004). Role of surfactant type and concentration for the mean drop size during emulsification in turbulent flow. *Langmuir, 20*, 7444--7458.

Thakur, G., Naqvi, M. A., Rousseau, D., Pal, K., Mitra, A., & Basak, A. (2012). Gelatin-based emulsion gels for diffusion-controlled release applications. *Journal of Biomaterials Science, Polymer Edition, 23*, 645--661.

Toro-Vazquez, J. F., Mauricio-Pérez, R., González-Chávez, M. M., Sánchez-Becerril, M., Ornelas-Paz, J. d. J., & Pérez-Martínez, J. D. (2013). Physical properties of organogels and water in oil emulsions

structured by mixtures of candelilla wax and monoglycerides. *Food Research International, 54*, 1360--1368.

Tran, T., Green, N. L., Ghosh, S., & Rousseau, D. (2017). Encapsulation of water-in-oil emulsion droplets within crystal spheroids. *Colloids and Surfaces A: Physicochemical and Engineering Aspects, 524*, 1--7.

Ushikubo, F. Y., & Cunha, R. L. (2014). Stability mechanisms of liquid water-in-oil emulsions. *Food Hydrocolloids, 34*, 145--153.

Vellido-Perez, J. A., Ochando-Pulido, J. M., Brito-de la Fuente, E., & Martinez-Ferez, A. (2021). Effect of operating parameters on the physical and chemical stability of an oil gelled-in-water emulsified curcumin delivery system. *Journal of the Science of Food and Agriculture, 101*, 6395--6406.

Vintiloiu, A., & Leroux, J. C. (2008). Organogels and their use in drug delivery-A review. *Journal of Controlled Release, 125*, 179--192.

Wang, S., Chen, K., & Liu, G. (2021). Monoglyceride oleogels for lipophilic bioactive delivery--influence of self-assembled structures on stability and in vitro bioaccessibility of astaxanthin. *Food Chemistry*, 131880.

Wypych, G. (2004). *Handbook of Plasticizers*. Ontario: *ChemTech Publishing*.

Yao, C. H., Liu, B. S., Chang, C. J., Hsu, S. H., & Chen, Y. S. (2004). Preparation of networks of gelatin and genipin as degradable biomaterials. *Materials Chemistry and Physics, 83*, 204--208.

Yllmaz, E., & Atc, M. (2014). Properties and stability of hazelnut oil organogels with beeswax and monoglyceride. *Journal of the American Oil Chemists' Society, 91*, 1007--1017.

Yu, H., & Huang, Q. (2012). Improving the oral bioavailability of curcumin using novel organogel-based nanoemulsions. *Journal of Agricultural and Food Chemistry, 60*, 5373--5379.

Zembyla M, Murray M.S., Sarkar A. (2020). Water-in-oil emulsions stabilized by surfactants, biopolymers and/or particles: a review, *Trends in Food Science & Technology, 104*, 49--59.

Zhang, M., Pan, Y., Dong, Q., Tang, X., Xin, Y., Yin, B., … & Huang, Q. (2021). Development of organogel-based emulsions to enhance the loading and bioaccessibility of 5-demethylnobiletin. *Food Research International, 148*, 110592.

Zhao, W., Wei, Z., & Xue, C. (2021). Recent advances on food-grade oleogels: Fabrication, application and research trends. *Critical Reviews in Food Science and Nutrition*, 1--18.

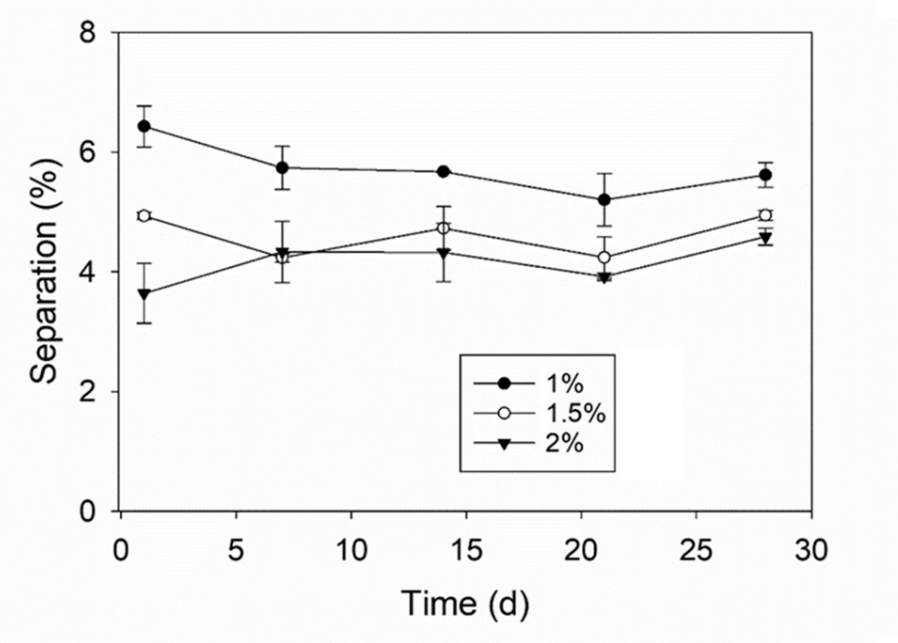

Figure 1. Influence of centrifugal force on the stability of emulsions with different amount of PGPR (1, 1.5 and 2%). (Data shown are the mean ± standard deviation).

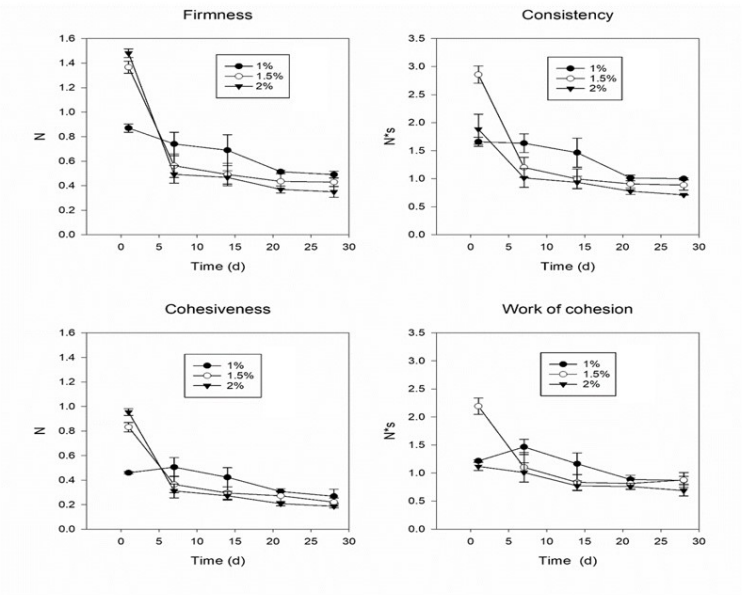

Figure 2. Influence of the storage time, PGPR amount on texture parameters (firmness, consistency, cohesiveness and cohesion work of emulsions. (Data shown are the mean ± standard deviation).

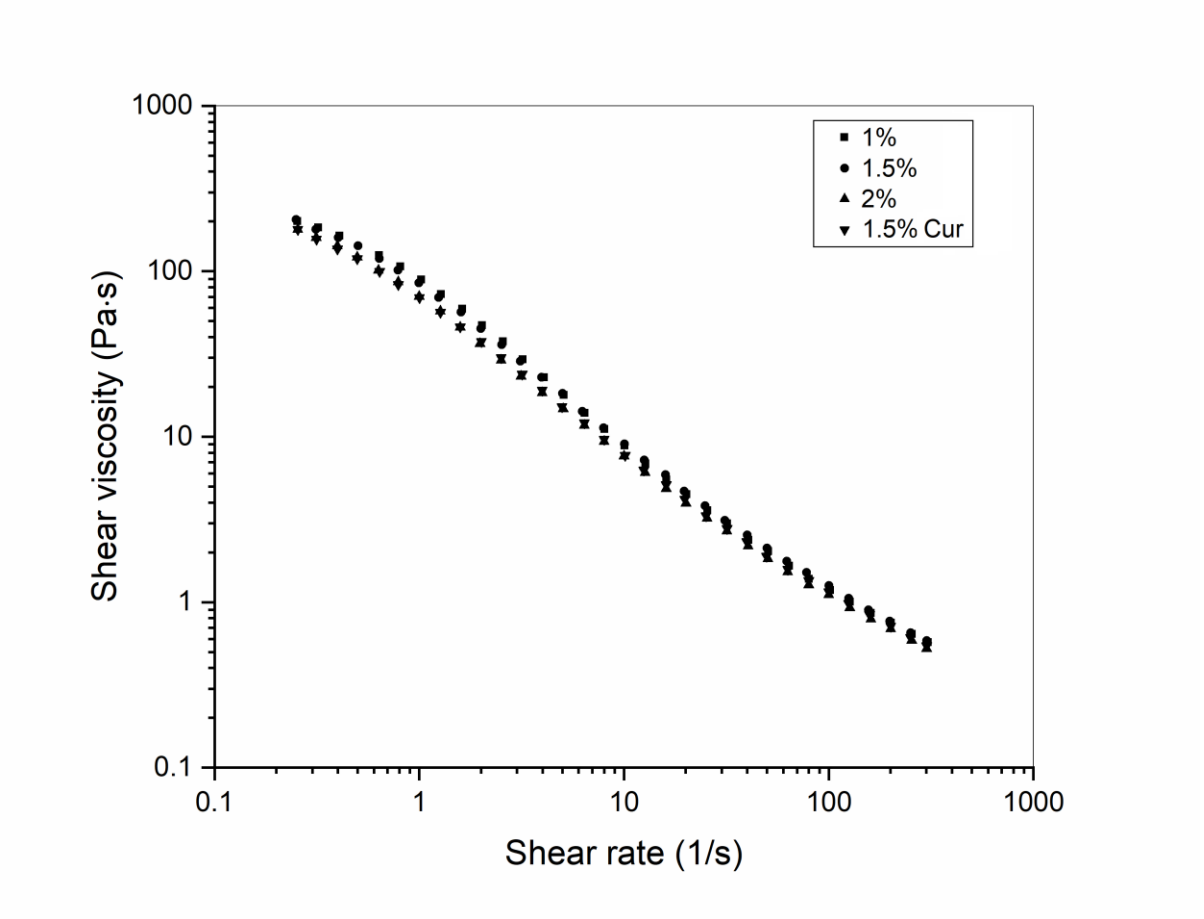

Figure 3. Influence of the concentration on the viscosity of simple shear flow test of the emulsions studied.

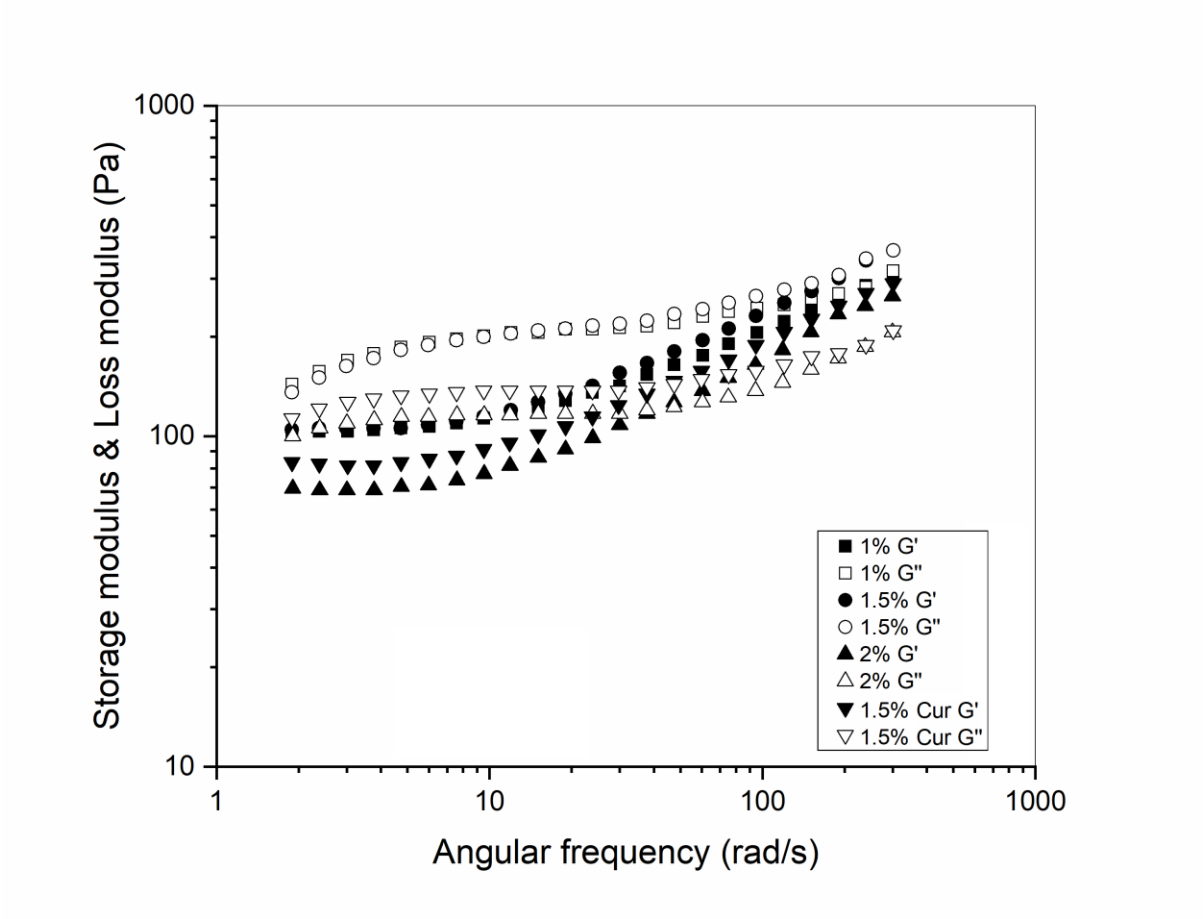

Figure 4. Influence of the concentration on the viscoelastic moduli of small amplitude oscillatory shear (SAOS) flow test of the emulsions studied.

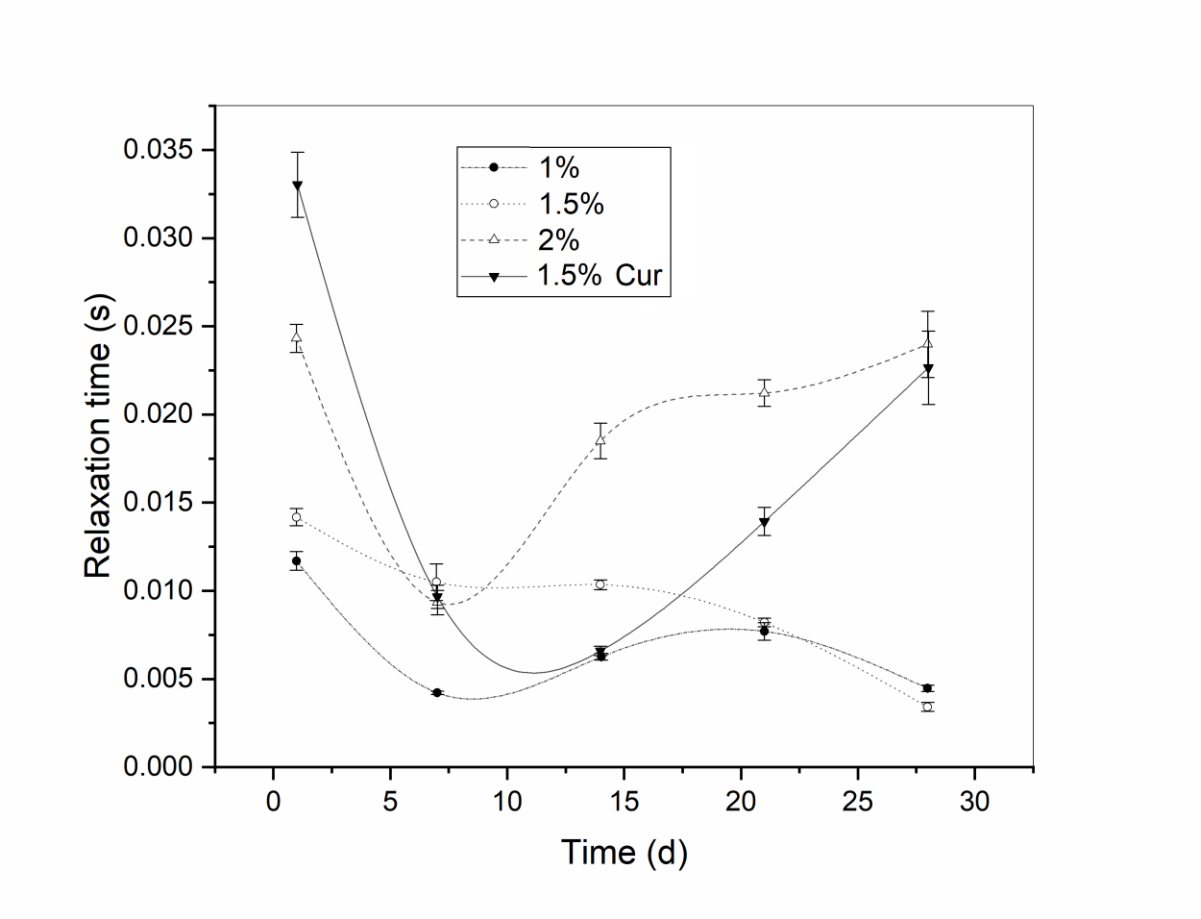

Figure 5. Influence of the storage time, PGPR amount on relaxation time of emulsions. (Data shown are the mean ± standard deviation).

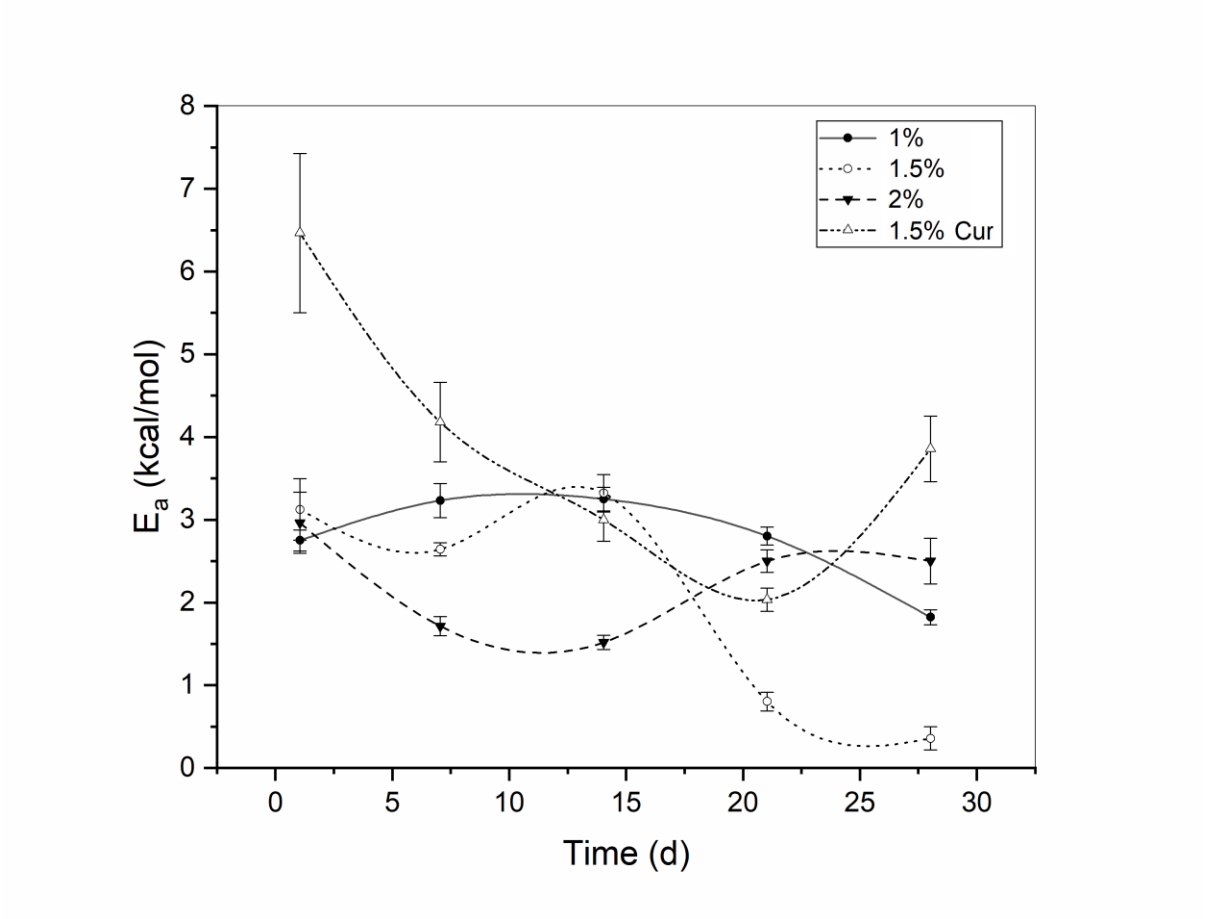

Figure 6. Influence of the storage time, PGPR amount on activation energy of emulsions. (Data shown are the mean ± standard deviation).

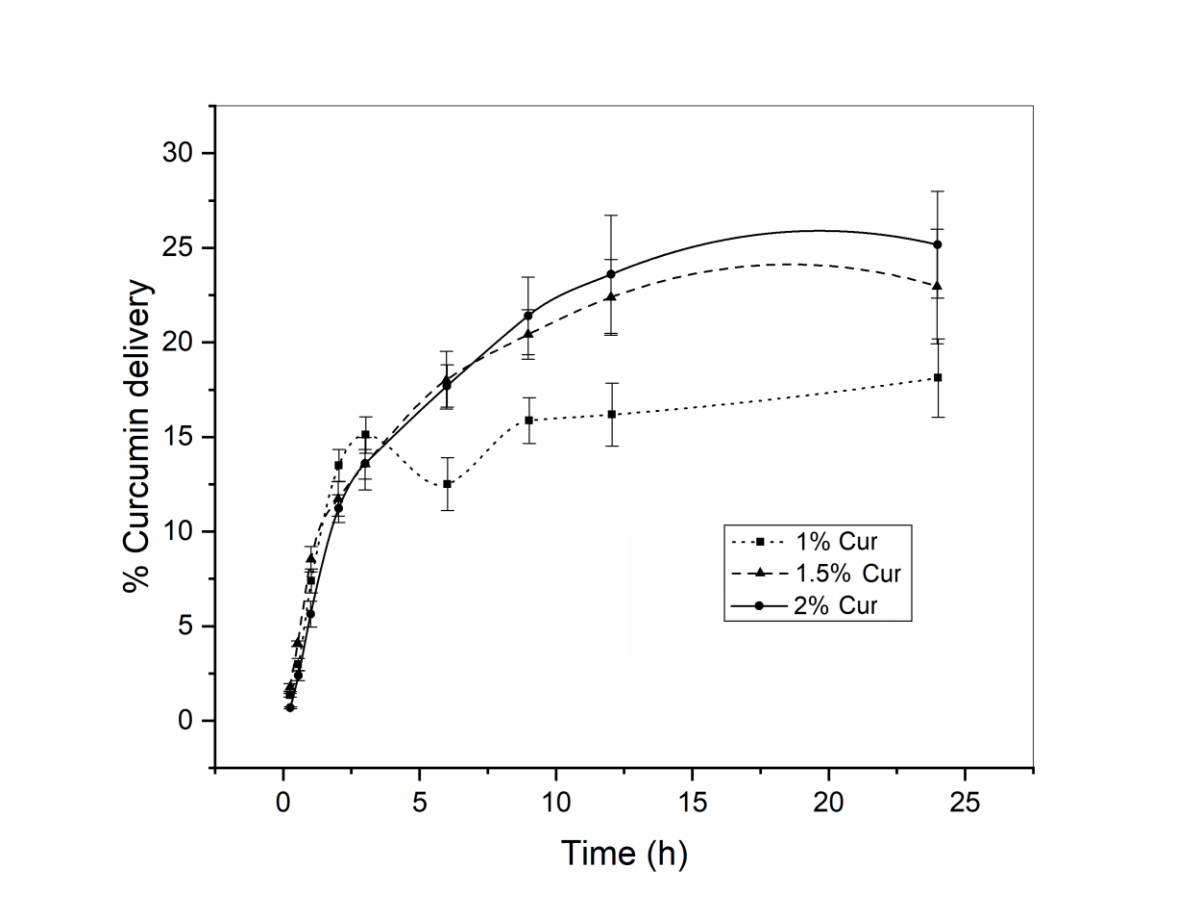

Figure 7. Behavior of curcumin release in emulsions with different amount of PGPR (1, 1.5, 2%). (Data shown are the mean ± standard deviation).

Table 1. Composition of the Oil-Water Emulsion Topical Release Vehicle for Curcumin.

Emulsion composition (W / O)	
Aqueous phase, (25%, wt)	Oil Phase, (75%, wt)
25% (wt), Aqueous phase	10% de Myverol, 1% Surfactant polyglycerol polyricinoleate, (PGPR)
25% (wt), Aqueous phase	10% de Myverol, 1.5% Surfactant polyglycerol polyricinoleate, (PGPR)
25% (wt), Aqueous phase	10% de Myverol, 2% Surfactant polyglycerol polyricinoleate, (PGPR)
25% (wt), Aqueous phase	10% de Myverol, 2% Surfactant polyglycerol polyricinoleate, (PGPR) plus (0.4 mg / g de emulsion) Curcumin

Table 2. Influence of time storage and PGPR amount on the particle size.

Time	Diameter	Polydispersity index,	Diameter		Diameter	
(days)	Average	(PDI)	Average	PDI	Average	PDI
	d_i(μm)		d_i(μm)		d_i(μm)	
	1%, Emulsion		**1.5%, Emulsion**		**2%, Emulsion**	
1	4.5±0.2^{a}	0.8±0.1^{a}	4.4±0.1^{ab}	0.4±0.1^{a}	4.1±0.1^{a}	0.4±0.1^{a}
7	4.8±0.2^{a}	0.7±0.1^{a}	4.0±0.1^{a}	0.6±0.1^{a}	4.5±0.2^{a}	0.7±0.1^{b}
14	5.0±0.3^{a}	0.4±0.1^{b}	4.3±0.2^{a}	0.7±0.1^{a}	4.6±0.2^{a}	0.5±0.1^{ab}
21	4.8±0.2^{a}	0.8±0.1^{a}	4.2±0.2^{a}	0.7±0.1^{a}	4.7±0.3^{a}	0.5±0.1^{ab}
28	5.1±0.3^{a}	0.6±0.1^{a}	4.6±0.3^{ab}	0.7±0.1^{a}	4.7±0.3^{a}	0.7±0.1^{b}

Data shown are means ± standard deviation. Different literal in the same column indicates statististically significant differences ($p<0.05$, Tukey test).

Table 3. Effect of storage time and emulsion PGPR amount (1, 1.5, 2 and 2% + Curcumin) on the

Time (d)	η_0, viscosity at low shear	η_∞, viscosity at high shear	η_0 (Pa*s)	η_∞ (Pa*s)	η_0 (Pa*s)	η_∞ (Pa*s)	η_0 (Pa*s)	η_∞ (Pa*s)

Cross-model parameters (low shear viscosity, η_0 and high shear viscosity, η_∞).

	rate (Pa*s)	rate (Pa*s)						
	1%		**1.5%**		**2%**		**1.5% + curcumin**	
1	252±9.10	0.35±0.03	270±9.10	0.368±0.02	282±8.91	0.305±0.02	260±8.10	0.36±0.01
14	274±8.06	0.37±0.03	289±8.10	0.38±0.01	290±8.20	0.300±0.02	278±8.10	0.36±0.01
21	295±7.10	0.36±0.03	299±6.10	0.39±0.01	307±7.10	0.287±0.02	290±8.91	0.370±0.02
28	**308±9.07**	**0.37±0.04**	**320±8.98**	**0.40±0.02**	**321±9.88**	**0.290±0.26**	**316±9.58**	**0.38±0.24**

Table 4. Models of curcumin release in emulsions with different amount of PGPR (1, 1.5 and 2%).

Emulsion	K	R^2	k	n	R^2
	Higuchi simplified model			**Power law model**	
1%	35.57±3.7	0.87	0.45±0.011	0.29±0.06	0.89
1.5%	51.04±1.6	0.97	0.40±0.013	0.40±0.04	0.99
2%	47.34±2.4	0.96	0.32±0.017	0.37±0.02	0.99

The water in oil gelled emulsions (W/O) showing good encapsulate curcumin properties, rheological analysis show that they are stable to the flow and time, also, release and particle size test results indicate that they are appropriate for a possible application for the delivery of bioactive principles by the topical route.

Organogel-Based Emulsion as a Topical Release Vehicle for Curcumin