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Formulation and Assessment of Delayed/Slow-Release Diclofenac Sodium Edible Organogel Utilizing Low Molecular Weight Organogelators

Zahraa Yahya Aziz[*], Masar Basim Mohsin Mohamed [*,1] and Marwa Hazim Jasim[*]

[*] Department of Pharmaceutics, College of Pharmacy, University of AL-Mustansiriyah, Baghdad, Iraq

Abstract

Organogel as a delayed and slow drug release dosage form was prepared and characterized various gelators, including 12HSA (12-hydroxystearic acid), span 60. span 40 were used; castor oil (CO) and anise oil (AO) were also used as a liquid phase. To achieve the aim of this work, diclofenac sodium (DS) was used as a model drug. Organogels specifications were characterized by estimating thermal attitude using tabletop rheology and differential scanning calorimetry (DSC). The organogel strength study was characterized by applying oscillatory rheology tests the amplitude sweep and the frequency sweep. The morphology of the organogel was observed using the optical microscope. CO and AO binding capacity was also measured. The transition temperatures for all organogels were reversible. Imaging demonstrated the existence of spherulites aggregates in organogels prepared using 12HSA and span 40 in CO and AO. However, span 60 containing organogels in both oils existed as fibers aggregates. Furthermore, 20 wt% 12HSA organogels exhibited viscoelastic characteristics with a linear frequency-independent elastic modulus (or G' and G''). The results revealed that the HPMC (hydroxyl propyl methyl cellulose) capsule containing the organogel resisted the dissolution in the acidic media for two hours. Moreover, organogels slowed the release of DS for 24 hours in an alkaline medium. Finally, all the selected organogel in CO exhibited a high oil binding capacity.

Keywords: 12HSA, Span 60 , Span 40, Sodium diclofenac, Slow release-organogel.

تصميم وتقييم الهلام العضوي البطئ والمتأخر التحرر باستخدام ١٢ هيدروكسي ستيارك اسد ،سبان ٦٠ وسبان ٤٠ كعناصر مكونة للهلام ذات وزن جزيئي منخفض في زيوت صالحة للأكل باستخدام دواء الدكلوفيناك صوديوم

زهراء يحيى عزيز [*،١]، مسار باسم محسن محمد [*] و مروة حازم جاسم[*]

[*] كلية الصيدلة ، فرع الصيدلانيات، الجامعة المستنصرية ، بغداد، العراق

الخلاصة

تقييم الهلام العضوي كنظام لتقدير أهليته على تأخير وابطاء تحرر الدواء في الاثنى عشري. تم استخدام ١٢ هيدروكسي ستيارك اسد ،سبان ٦٠ وسبان ٤٠ كعناصر مكونة للهلام وزيت الخروع وزيت اليانسون كطور سائل للهلام العضوي. لتحقيق اهداف هذا العمل، تم استعمال دواء الدكلوفيناك صوديوم. تم تحديد مواصفات الهلام العضوي بتقييم سلوكه الحراري باستخدام علم السيلان المنضدي والمسح التفاضلي المسعر. ايضا تم استخدام اختبارات علم السيلان التذبذبي التي تتضمن اختبار مدى السعة واختبار مدى التواتر. تم التحقق من شكل الهلام العضوي باستخدام المجهر البصري. اضافة الى ذلك تم ايضاح قدرة ربط زيت الخروع وزيت اليانسون. قد بينت النتائج أن كبسولة هيدروكسي بروبيل مثيل سيليولوز قاومت التحلل بالوسط الحامضي لمدة ساعتين. درجات الحراة الانتقالية للهلامات العضوية كانت قابلة للانعكاس. التصوير بالمجهر اظهر تجمعات كروية للهلامات العضوية المحتوية على ١٢ هيدروكسي ستيارك اسد وسبان ٤٠ في زيت الخروع. اما بالنسبة للهلامات العضوية الحاوية سبان ٦٠ فقد اظهرت تجمعات خيطية في كلا الزيتين. اضافة الى ذلك، فقد امتلكت بعض الهلامات العضوية صفات لزوجة مطاطية كما تبين في ٢٠ % وزن من ١٢ هيدروكسي ستيارك اسد في كلا الزيتين كان غير معتمد على التردد. الهلامات العضوية ابطأت تحرر الدواء لمدة ٢٤ ساعة بالوسط القاعدي. من ناحية اخرى، كل الهلامات العضوية المختارة بزيت الخروع اظهرت قوة ربط مرتفعة بالزيت.

الكلمات المفتاحية: ١٢ هيدروكسي ستيارك اسد- سبان ٦٠- سبان ٤٠- صوديوم دكلوفيناك- تحرر بطئ- هلام عضوي

Introduction

Organogels have obtained the interest of many researchers for their simple and inexpensive preparation. The organogel is neither non-crystalline nor glassy, consisting of an organic phase that is liquid engaged in a three-dimension tangled network of small molecular weight gelators (such as 12HSA, span 60, and span 40) or polymeric gelators (such as poloxamer and carbopol). Physical or chemical interactions occur amongst gelators, leading to fibrous self-assembled that engage with each other to cause the structure of the three-dimensionalnetwork[(1)]. Commonly seen gelators are sorbitan monostearate,lecithin and cholesteryl, 12HSA, anthraquinone derivates, and sterol. Organogel usages are various, including pharmaceuticals, chemistry, biotechnologies, cosmetics, and food technology[(2)]. Numerous organogel formulations were prepared to deliver the drugs by various administration routes.

In a previous study, 12HSA has been used to prepare organogels with soyabean oil to deliver ibuprofen. The release rates showed a reduction in the organogels release rate with the rise in the gelator quantity[(3)].

[1]Corresponding author E-mail: Zahraayahyaaziz@yahoo.com
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Cyclosporine A offered good effectiveness when taken orally in organogel of span 60[4]. Span 40 was formulated with various oils such as mustard oil and groundnut oil as organogels solid content was 20 wt% and used for the controlled delivery of metronidazole[5].

Organogel was also formulated to achieve gastroretentive characteristics using span 60, span 40, and stearic acid as gelators with olive and sesame oil to obtain a floating gastric system[6, 7].

This study aimed to investigate the organogel for the slow and delayed-release using the gelators (12- hydroxystearic acid (12HSA), span60, span 40) with oils (castor oil (CO) and anise oil (AO)). The drug model was diclofenac sodium (DS) as the delayed-release in the duodenum representing the site of absorption could be acquired using an HPMC acid-resistant enteric capsule to overcome DS gastric irritation. To our knowledge, the selected gelators and oils in this work were not formulated previously together except span 40, which was priorly gelled with CO and loaded with metronidazole to achieve controlled drug delivery for topical use[8].

Materials and Methods

Materials

DS was a kind gift from Safa pharma. 12HSA(purity 90%), span 60, and span 40 were purchased from Hangzhou Hyper Chemicals China and Sinopharm Chemical Reagent Co., Ltd, respectively. Also, CO and AO were bought from RS Spain and Hemani Herbal, respectively.

Methods

Formulation of organogel

In the beginning, the drug unloaded organogel was prepared by weighing out the particular quantity of each (span 40, span 60, and 12HSA) in the vials, then completed to 1 gm with CO and AO for each gelator as in the following concentrations (0.5, 1, 3, 5, 7, 10, 13, 15, 17, 20) wt% respectively (as clarified in Table 1). The vials incubation in the water bath was for 40 min at 85°C until a clear solution was obtained to confirm the solubility of gelators in oils. The vials were then brought out from the water bath and allowed to cool at room temperature (these gelators mechanisms of action are upon cooling make aggregates of fibers that constitute the three-dimension scaffold). After a period, an overturn to the vials was to examine the formulation of the organogel. A solid organogel is obtained when there is no flow in the preparation, but if flow occurs upon overturning, the result will be liquid formulation.

Finally, DS-loaded organogel was formulated as the above procedure. The 75mg of DS was weighed with the chosen quantity of the gelators and oil added to complete the weight to 1 gm, then solubilization of the contents in oils occurred at 85 ºC [9].

Table 1 . Organogel contents concentrations

Oil concentration (wt%)	Gelator concentration (wt%)
99.5	0.5
99	1
97	3
95	5
93	7
90	10
87	13
85	15
83	17
80	20

Tabletop rheology

Organogel vials were incubated in the water bath at 85 ºC. The reduction in the temperature then was allowed to be 2 ºC every 15 minutes until 32 ºC reached. The vials were tilted 45°C at the termination of each 15 minutes to check whether the organogel formulation was sol or gel. The transition temperatures from sol to gel for all organogels were revealed at this stage of the work. This portion of the study was pursued by adverse phase via raising the heating proportion (2°C/ 15 minutes) to 85°C for all organogels. The transition temperatures from gel to sol will be recorded. For each organogel, this procedure was performed in triplicate [10, 11]. The tabletop rheology test was done using the water bath by applying different temperatures from 85 ºC to 32 ºC as rheology in this test means the transfer of organogel status from sol to gel.

Differential scanning colorimetry (DSC)

Thermal analysis of the organogel was performed with a Setaram DSC Evo 131 differential scanning calorimeter (China). A weighing 10 mg of organogel and the gelators was in an aluminum pan and tightly sealed. The organogel was heated from room temperature to 110°C at 10°C/min [12].

Optical microscopy

The morphology of the organogels was examined by utilizing an optical microscope and slides to pick up the microscopic image. A drop of melting organogel withdrawn by micropipette, directly after taking the vial out of the water bath, added on the glass slide.

The liquid organogel was pressed softly using a glass coverslip placed over the drop for 15 minutes at 85ºC. Then the slide was transmitted into the microscope stage after cooling. Utilizing the software micro and the digital microscope camera MC500 to capture the images as the magnification was X40[13].

Oscillatory rheology study

The rheology was carried out utilizing Anton par mcr 302 rheometer using plate-plate configuration (PP 25/ SN 61895). All measurements were in triplicate at 37 ºC, and the acquired data estimation was by Rheoplus software[10]. These tests were carried out at the University of Petra/Pharmaceutical Center, Amman, Jordan, for DS-loaded organogel. The prepared organogel as shown in the organogel formulation section was scooped and placed between the two plates of (PP 25/ SN 61895).

Amplitude sweep

The amplitude sweep test was performed to determine storage modulus (G'), loss modulus (G''), flow point for each formulation, and the linear viscoelastic region (LVER). This study executed the oscillatory strain range from 0% to 100% at angular frequency 10 rad s^{-1}.

Frequency sweep

The second oscillatory test that followed the amplitude sweep was the frequency sweep. Picking the applied strain on the organogel was from the range of LVER data of the amplitude sweep test for each organogel (0.01-0.08 %). Then, different speeds were applied to the organogel sample via the angular frequency that transformed from 0.1 to 100 rad s^{-1}.

***In-vitro* release study**

The DS organogel-loaded HPMC capsule was first subjected to *in vitro* release in HCl solution pH 1.2 for 2 hours to examine the resistance of these capsules to the acidic media. Then, DS organogels release was for 24 hours to test the organogel slow release in sodium phosphate buffer (pH 6.8 containing 0.1 % w/v sodium lauryl sulfate) using USP apparatus the paddle type; where their jars were filled till 900 ml of HCl solution or alkaline media, that adjusted at 37±0.5°C and 75 rpm. The HPMC capsule that loaded with the organogel was put into the jars of the dissolution apparatus then the samples were withdrawn as the following time setting (0,1, 0,5, 1, and 2) hours for acidic media. Subsequently, the release of organogel in the alkaline media and the sample withdrawing was within this time frame (0.083, 0.25, 0.5, 1, 3, 6, 9, 12, 15, 18, 21, and 24 hours)[7, 14]. A withdrawal of 10 ml each time was replaced with a similar quantity of the media. After that, the withdrawn samples were filtered by utilizing a Millipore filter paper membrane (0.45 μm). After filtration, these samples were diluted and measured by a UV-visible spectrophotometer at its λmax in a phosphate buffer solution of pH 6.8 and 0.1 N HCl solution of PH 1.2 were 276 nm and 280 nm, respectively. Their calibration curve equations were y = 32.618x with a regression coefficient value R^2 = 0.9941 for pH 6.8 and y = 18.848x +0.0185 with a regression coefficient value R^2 = 0.997 for PH 1.2. This study was carried out three times.

Oil binding capacity

A certain amount of organogel was centrifuged to determine the oil binding capacity (OBC). One gm of organogel was prepared and left at room temperature for 24 hours. After that, the tube containing the organogel was centrifuged for 15 minutes at 6,000 rpm. A Whatman filter paper was weighed, and then the vial was inverted over it and stayed for 5 minutes to absorb the free liquid oil dripping from the organogel. After that, the filter paper was weighed to calculate the mass of expressed oil. OBC is determined by this equation:

Oil binding capacity (%) =

$$(1-\frac{\text{mass of expressed oil}}{initial\ sample\ mass}) \times 100$$

OBC was performed by calculating the average of 3 times of this study±SD[15]. This test reflects the organogels capacity for oil holding.

Statistical analysis

Statistical test the standard deviation was executed for release results using one way ANOVA with the aid of SPSS version 16.0 .

Results and Discussion

Organogel formulation

The organogel formulations in different gelator concentrations and oils lead to assessing the minimum gelation concentration for any gelator. Hence, the minimum gelation concentration (MGC) is essential to evaluate the least concentration of the gelators that gels oils, which, in turn, reflects the organogel strength[16]. As shown in Figure (1 A and, B), the formulations of 12HSA organogels at room temperature were gelled in AO, and CO and the MGC were 3 and 7 wt%, respectively. In addition, Figures (1 C and D) show the span 60 organogels, and the MGC was 10 wt% for the AO, and CO. Last, the span 40 organogels were shown in Figure 1 E and F, and their MGC were 7 and 20 wt% for AO, and CO.

The diversities in the solubility of gelators in oils cause variations in the MGC of different gelators [17]. At the elevated temperature (85°C), the gelators were soluble in oils, but they produced varied gelation concentrations when they were left to cool. This variation was imputed to the self-aggregation of the gelator when cooled, which was, at lower gelators concentration, not adequate to make a gel or the 3D structure. In conclusion, 12HSA and span 40 gave varied gelation concentrations in AO, and CO while span 60 showed a similar gelation concentration.

For the subsequent studies, the chosen organogels within the range of the selected concentrations were 20 wt% of each gelator. Since previous studies about organogels showed that the highest gelator concentration led to the slowest drug release, this represents the core of our aim. The attribution of the organogels to the slow release was due to the fiber density, which is a result of the aggregation's gelator molecules. This was shown in 12HSA/ PG (propylene glycol) organogel in which the highest concentration, the 14 wt% slowed the release of the N4-myristoyl gemcitabine in tumor pH media[18]. Furthermore, the 20 wt% of span 40 and 60 in sesame oil organogels slowed the release of cinnarizine in stomach media[7].

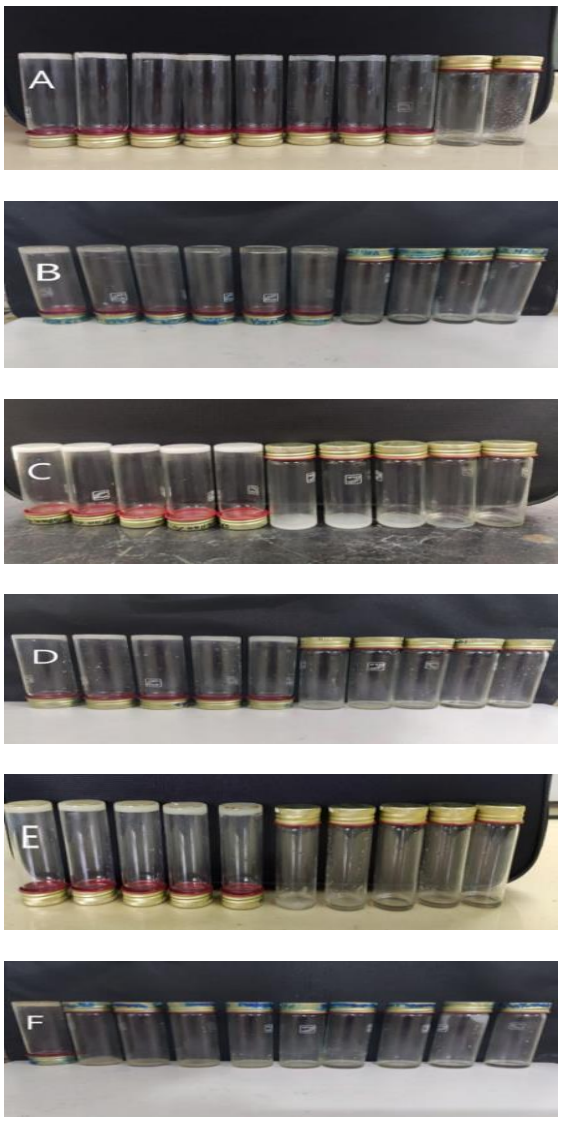


Figure 1. Organogels of 12HSA in AO and CO as in A and B, organogels of span 60 in AO and CO as in C and D while in E and F are span 40 in AO and CO organogel. The concentrations of gelators were from right to left (0.5, 1, 3, 5, 7, 10, 13, 15, 17, and 20) wt%.

Tabletop rheology

Tabletop rheology is an uncomplicated and suitable process that describes the phase transitions from gel to sol and from sol to gel[7]. Table (2) represents the temperatures at which the phase is transmitted from gel to sol and vice versa. The selected organogel showed the transition temperature from gel to sol (Tgel-sol) higher than body temperature, which indicated thermal stability. This thermal stability was ascertained via the reverse phase represented by the transition temperature from sol to gel (Tsol-gel). Previous work utilizing span 60 and span 40 in sesame oil has also shown convergent results[7]. All selected oraganogels needed a temperature higher than 37°C to solidify except the span 40 in CO as shown in Table (2) (Tsol-gel) ºC.

Table 2. Organogels phase transition temperatures

Gelator 20 wt%	Oil	(Tgel-sol) ºC	(Tsol-gel) ºC
12HSA	CO	58	48
	AO	68	54
Span 60	CO	56	42
	AO	54	40
Span 40	CO	64	34
	AO	64	40

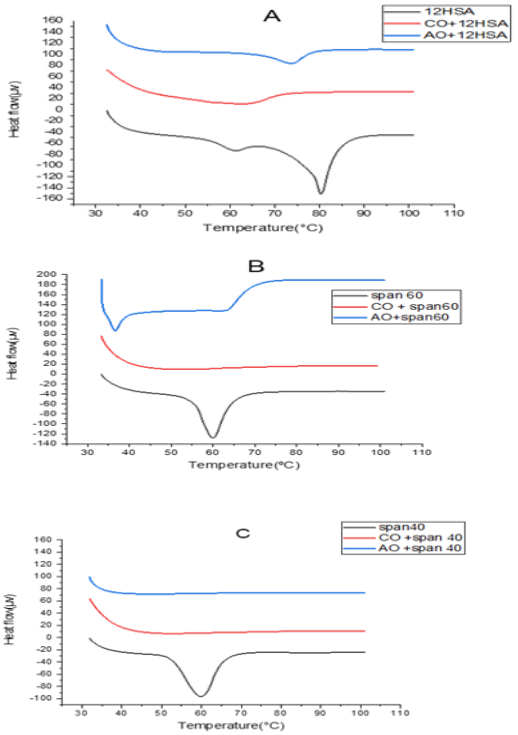


Figure 2. DSC characterization of the organogels. 12HSA pure powder, 20 wt% of 12HSA in CO and AO organogels (A), span 60 pure powder and the 20 wt% span 60 in CO and AO organogels (B), span 40 pure powder, and 20 wt% of span 40 in CO and AO organogels (C).

Differential scanning colorimetry (DSC)

DSC defines a precise thermal analysis to specify the organogel transition temperature [11, 19]. This is essential in our work as the aim is to have an intact organogel inside the body to achieve the slow release of the drug.

All the selected organogel's thermograms and the corresponding gelator powder were displayed in Figure (2 A, B, and C).

In the case of 12HSA, the temperature at which it was melted at 80 ºC and a minor peak was noticed at 60 ºC which might be caused by the impurities of 12HSA (12HSA purity 90%), an outcome that also was noticed in the previous research with 12HSA gel in toluene[20]. While for the organogels that contain CO and AO with 12HSA, the transition temperatures were 63 ºC. and 73 ºC, respectively.

Regarding span 60, the transition temperature was 59 ºC. However, the conversion temperature peak for the organogel of CO did not appear in the thermogram. This led to the conclusion that the fibers which form the organogel were amorphous. AO with span 60 organogel thermogram might also point to amorphous formation as this kind of figure is attributed to phase separation of the oil from gelators as both were amorphous and had different glass transition temperatures [21].

The thermogram of span 40 shows the peak of conversion at 59 ºC. Both organogels of CO and AO with span 40 did not produce peaks which can also be explained as that amorphization in the organogel fibers occurred.

Organogel amorphization can also be attributed to oil composition and this was also shown in a previous study of span 40 in CO organogel[8].

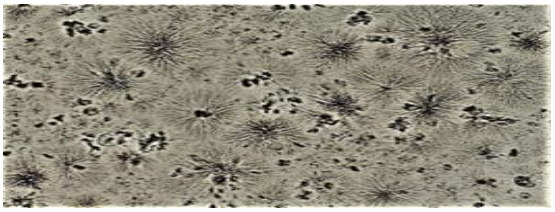
The 12HSA in both oils showed higher thermal transition than the span 40 and 60 organogels. Most of the transition temperatures were closed to the transition temperature of tabletop rheology results for all organogels**.**

Optical microscopy study

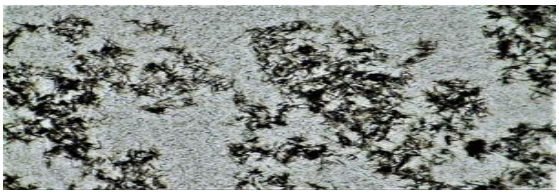
Optical microscopy was performed to study the morphology of the entangled network of the organogel with different gelators as this network is responsible for forming the 3-dimensional structure that held the oils and evidence of organogel formation. This study shows that different gelators give different microscopic shapes. As shown in Figure (3), the images revealed that all 12HSA organogels in AO and CO exhibited spherulite aggregates, and this outcome resembles a previous study that utilizes 12HSA with canola oil[22]. The spherulites appeared in the microscopic images of span 40 organogels formulated in AO and CO, similar to this result showed in former research that employed span 40 with sunflower oil[23]. Whereas the scaffold span 60 organogels in oils AO and CO present as fibers aggregates, another study of organogel prepared from span 60 and soya-bean oil showed the same fibers[24].

Different scaffold morphology could be attributed to the difference in the solubility of the gelators in oils that upon cooling led to the different molecular hierarchy assembly[25]. In conclusion, all images showed scaffolds; however, different underlying scaffold structures.

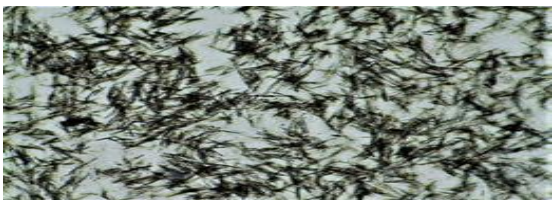
12HSA/AO



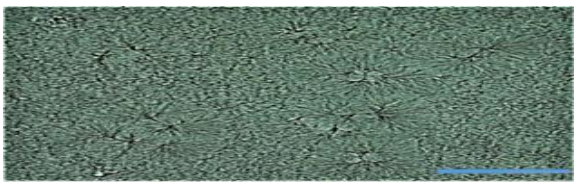
12HSA/CO



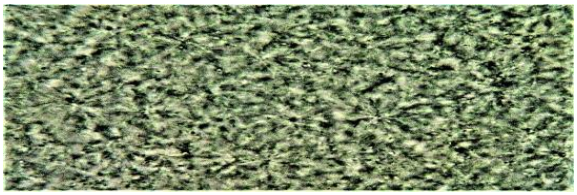
span 60/AO



span 60/CO



span 40/AO



span 40/CO

Figure 3. Microscopic images of organogels containing 12HSA, span 60 and span 40 in AO and CO, all images were captured using objective X40 and scaled against 50µm.

Oscillatory rheology studies

Rheology studies include amplitude sweep and frequency sweep, which are essential tests to investigate the strength of the organogel that is required to resist the motion of the gastrointestinal tract [26].

Amplitude sweep

In this study, the first portion examined DS-loaded organogels utilizing the amplitude sweep test for the selected organogel to determine storage modulus (G'), loose modulus (G"), LVER, and the flow point. The solid phase was represented by G', which reveals the organogels elasticity, whereas G" indicates the liquid phase. The amplitude sweep test was performed by putting the organogel to face a growing strain from zero to 100%. If the gel reveals good strength, the result of G' is higher than G" in parallel curves, and constant values of G' and G" until attaining a value of strain that the gel cannot keep the same G' value and begins weakening as before this point is the LVER. After that, with the continued rising strain, the gel attains a breaking point. At this point, the values of G' and G" are the same, defined as the flow point. All the organogel parameters are illustrated in Figure (4) and Table (3).

The values of G' of all organogels in this experiment appeared larger than G". This relation was also shown in the rheological study of bis-urea-based organogels in different primary alcohols [27]. The 12HSA in AO presented the highest G' value, and the lowest G' was detected by span 60 in AO organogel.

The LVER of 20 wt% 12HSA in both oils were approximate. The span 60 and 40 organogels appeared the same trend of the LVER as CO organogels were higher than AO organogels.

The flow point of 20 wt% 12HSA in CO organogel was the highest value compared with other organogels, whereas the lowest percentage was 20 wt% span 60 in AO. These different points for different organogels might pertain to different transient bonds which connect fibers that are responsible for the organogels structure[28].

To sum up, 12HSA organogels were the best to show the viscoelastic properties via presenting high G', LVER and, flow points at 37°C as this indicates the best resistance to the gastrointestinal motility.

Table 3. Amplitude sweep parameters G', G'', LVER, and flow points for the six selected organogels as each value is an average and standard deviation of 3 values. The study was set at a strain from 0% to 100%, angular frequency 10 rad.s$^{-1,}$ and temperature at 37°C.

Gelators	Oil	G' (pa)	G'' (pa)	LVER (%)	Flow point (%)
20 wt% 12HSA	CO	439000	46.8	0.04475	20.3
	AO	3230000	349	0.04335	6
20 wt% Span 60	CO	25100	2.66	0.0458	5
	AO	17545	1.9384	0.0293	0.65
20 wt% Span 40	CO	111000	117.15	0.175	4
	AO	74008	8.901185	0.0221	6.5

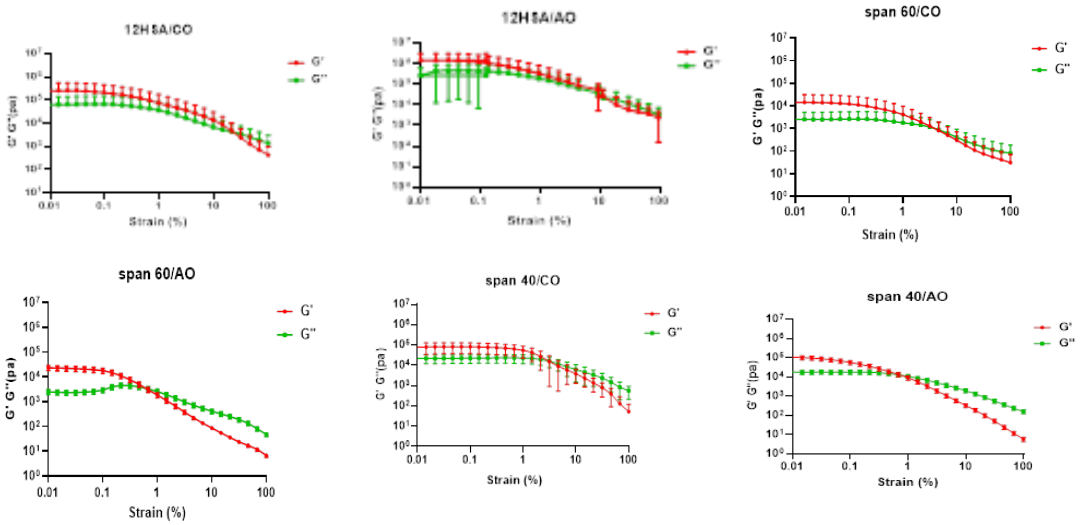


Figure 4.The amplitude sweep test for 12HSA in CO and AO organogels, span 60 in CO and AO organogels and last span 40 in CO and AO organogels.

Frequency sweep

This study was carried out to examine the ability of organogel to stay solid at different speeds or motions. The strong organogel usually shows non-intersecting G' and G" curves. As shown in Figure (5) the 20 wt% 12HSA in both oils have a similar pattern and were frequency-independent at high rate frequencies; nevertheless, at low frequencies, the organogels were highly affected by the low rate of frequency as the curves of G' and G" intersected.

The span 60 organogels in CO and AO showed the same pattern; but the G' and G" values were constant alongside the whole range of frequencies, indicating elastic organogels [7]. The last organogels, span 40 in both oils, showed almost similar attitudes as stable curves within the selected range of frequencies just the span 40 in AO curves of G' and G" were close at low frequency, this result is similar to a previous study in which organogelator molecules of amino-acid type was used[29].In summary, span 60 and 40 in CO and AO showed constant curves (G' and G'') at different frequencies, indicating frequency-independent organogels, while 12HSA organogels in both oils were impacted at low frequencies.

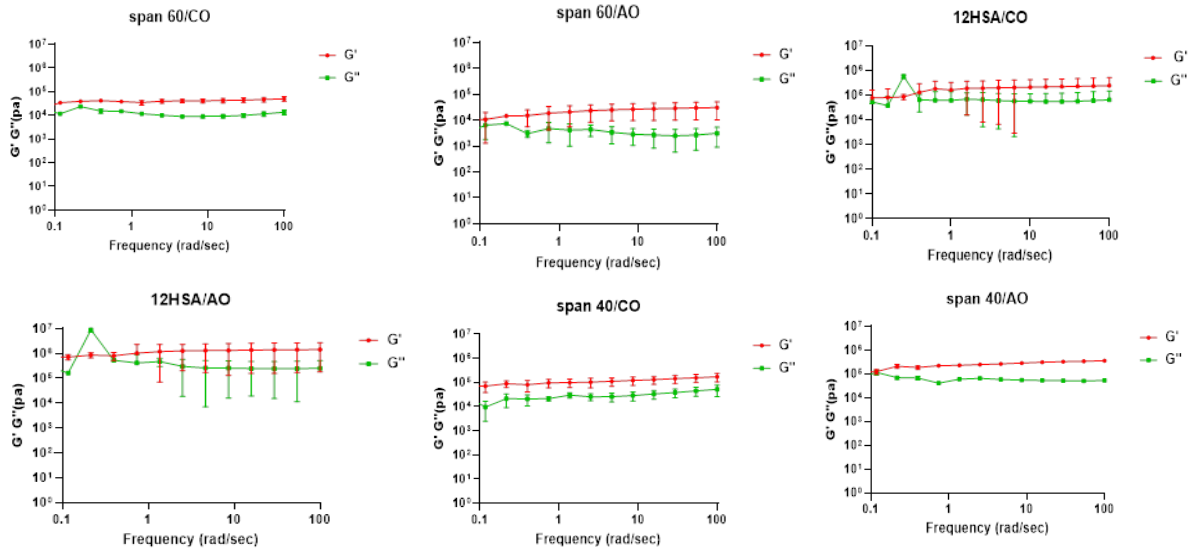


Figure 5. Frequency sweep test as the left column represents organogels of 12HSA, span 60 and span 40 in CO while the right column shows the same sequential organogels in AO. The angular frequency was set from 0 to 100 rad $s^{-1,}$ and the temperature was 37°C.

In-vitro release study

The *in vitro* release was executed to explore the organogels as formulations that can slow the release of DS. Firstly, the ultraviolet reads for the samples withdrawn from the acidic media revealed that DS did not release from the HPMC capsule in this media, which supports the concept that the enteric HPMC capsule resists dissolution in the acidic media [30]. Thus, the *in-vitro* release study for organogels was in small intestinal pH 6.8 for 24 hours to check the depot characteristic of organogels and the effect of different gelators on the DS release. With all the release examinations, a release for control formulation consisted of 75 mg DS mixed with CO and AO individually to understand the release of DS from the organogels as oily formulations are well-known as dosage forms with the depot property. Figure (6A) shows the release profiles of DS in CO of different organogels. As observed, 12HSA in CO shows the most depot release in this study; span 40 and 60 came sequentially. Statistically, the release profiles showed significant variation ($p \leq 0.05$) in the release percent amongst the three gelators in CO organogel. Figure (6B) shows the release profiles of DS in AO, which revealed that the organogel of 20 wt% 12HSA, span 60 and span 40, their release profile was close to each other within the frame time experiment.

The control of DS in CO and AO showed a higher difference ($p \leq 0.05$) in the DS release profile than the organogels, which is attributed to the organogel scaffold rather than oil property.In a nutshell, the 12HSA, span 60, and span 40 gave different release patterns in oils due to the different solubility of these gelators. A sodium alginate gel in another study was used as a carrier to sustain DS release. It showed a closed pattern to our organogel 12HSA/CO, as 73 wt% DS after 12 hours was released a promising matrix to slow the DS release [14]. The organogels 12HSA in CO was the closest to the aim of the current study via showing the slowest release, which was supported by the strength outcome of the amplitude sweep test presenting the best values of G' and flow point.

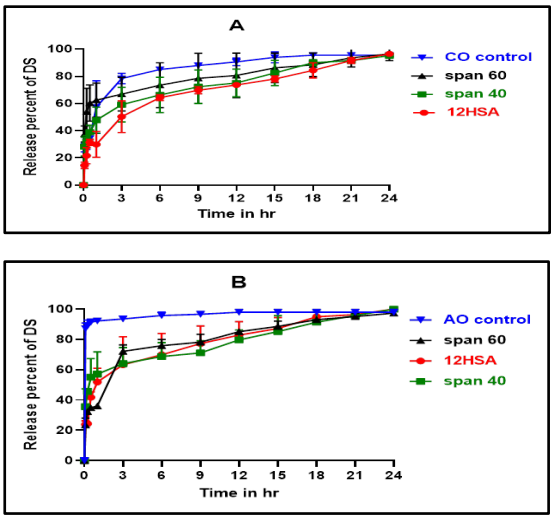


Figure 6. ***In-vitro*** **DS release in pH 6.8 phosphate buffer solution at 37°C as A and B represent 12HSA, span 60, and span 40 in CO and AO, respectively. Each release curve is an average of triplicate ± standard deviation.**

Oil binding capacity (OBC)

The binding capacity for oils to any organogel reflects the scaffold's strength that constructs the organogel and held the oil; hence, this test was carried out [31]. Table (4) reveals the OBC results as all the selected organogel in CO showed a high binding capacity. At the same time, the organogels in AO produce a noticeable low OBC compared with the CO organogels and this was supported by DSC results of span 60. These findings support the *in vitro* release as the organogels in CO; specifically, the 12HSA organogel showed slower DS release and the higher OBC, which means that these CO organogels were more capable of holding the DS and oil.

Table 4.OBC of 20 wt% 12HSA, span 60 and span 40 in CO and AO

20 wt% Gelators /Oil	OBC of CO (%) ±SD	OBC of AO (%) ±SD
12 HSA	99.9±0.06	89.61±0.1
span 60	95.6±0.1	72.61±0.17
Span 40	99.3±0.05	58.61±0.28

Conclusion

The target of this study was to fabricate organogel with the delayed and slow release of DS. This was achieved with the organogels formulated in CO compared to those organogels prepared in AO. Those organogels showed a slower release profile and presented good viscoelastic properties: higher G' and flow points. Furthermore, they were frequency independent in most applied frequency ranges. Also, they showed strong gelators binding toward CO.

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