Rheological Studies on Different Oily Vehicles for Pharmaceutical Preparations

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Abstract

Aims: The rheological properties of oily vehicles based on patents of non-aqueous vehicles for pharmaceutical suspensions were studied. The effects of different concentrations of suspending agents and different excipients on the flow curves were also investigated.

Methods: A Rotovisko viscometer (Haake) fitted with concentric cylinder sensors, NV measuring head–500 and a temperature controlled water jacket at 37 ^{0}C was used.

Results: The results showed that Fractionated Coconut Oil (FCO) alone and with 0.7% w/v lecithin exhibited Newtonian behavior. Dispersions of aluminium stearate, hydrogenated castor oil, Cab-o-sil and sucrose in FCO exhibited pseudoplastic behavior. Aluminium stearate 1% w/v and above and the oily vehicle containing aluminium stearate, hydrogenated castor oil, lecithin and sucrose exhibited thixotropic pseudoplastic properties. The omission of lecithin from the later vehicle resulted in a decrease in the apparent viscosity and the loss of thixotropy.

Conclusion: The thixotropic pseudoplastic behavior of oily vehicles is a desirable property in liquid pharmaceutical systems that ideally should have a high consistency in the container, yet pour or spread easily after they had been stirred vigorously. Possible reasoning and suggestions were discussed.

Keywords: Fractionated Coconut Oil (FCO), rheology, thixotropy, pseudoplastic behavior, Newtonian behavior.

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Introduction

Several reports indicated that the bioavailability of drugs is enhanced by the co-administration of fatty meals [1, 2] or oils.[3-9] In addition, in many cases the physiologically active agent is not chemically stable in either a water-based oral pharmaceutical suspension or an oral pharmaceutical solution. In such cases it is impossible to prepare a satisfactory liquid pharmaceutical dosage form utilizing water as the base for the preparation. Even when the drugs are supplied as a powder where water can be added immediately before use, drug degradation may still occur during daily use by patients. Consequently, the use of non-aqueous vehicles, e.g. oily vehicles, would seem reasonable in these cases.

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Rheological studies on these non-aqueous vehicles are important. Its application has been suggested in the formulation and analysis of such pharmaceutical products as emulsion, suspension, pastes, suppositories and tablet coatings. The manufacturer must be capable of producing a product with an acceptable consistency and smoothness and must be able to reproduce these qualities each time a new batch is prepared.

Whilst the rheological aspects of aqueous suspension media have received considerable attention with respect to drug release and dissolution in vitro [10-13] and drug release and bioavailability in vivo,[14-18] little attention has been paid to these aspects in the case of non-aqueous vehicles. In addition, the limited publications concerning the effects of the rheological properties of such vehicles have been restricted to dermatological products [19-21] or to injectables.[22] Thus, there is inadequate information available concerning the effects of the rheological properties of non-aqueous vehicles on the bioavailabilities of orally administered drugs. In fact, there is even little information on the rheological properties of such vehicles.[23-26]

Some oily vehicles for pharmaceutical formulations have been the subject of various patents.[27,28] These patents were concentrated with the physical and chemical stability of given suspensions and only a few aspects regarding rheological behaviors were mentioned.[28] In spite of the importance of the rheological properties of vehicles gelled with either aluminium stearate or colloidal silica, these properties were not specified for the oils and gels in the above studies, except for the systems investigated.[29] Previous work on the flow properties of aluminium soap-hydrocarbon systems has been reported [23,24] but these studies were limited to systems containing liquid paraffin and many aspects of the rheological behaviors of these systems were not fully explained.

In view of such deficiency, the present work was undertaken in order to study the flow curves of the oily vehicles mentioned in the above patents with different concentrations of suspending agents and the effects of the different excipients on the flow curves. Thixotropic behavior exhibited by some oily vehicles was also studied and discussed.

Materials and Methods

Materials

Fractionated Coconut Oil (FCO) was obtained from Alembic Product Ltd. (Chester, Chestershire, England). Colloidal silica (Cab-o-sil) and lecithin 90% (refined grade) were obtained from B.D.H. Chemicals Ltd. (Leicester, England). Aluminium mono-and di-stearates were obtained from Witco Chemical Ltd. (USA). Hydrogenated castor oil was obtained from Akzo Chemie UK Ltd. Sucrose (icing sugar) was obtained from the British Sugar Corporation Ltd.(UK).

Methods

Preparation of the Dispersion Media. In addition to the FCO alone, the following two types of systems were investigated in the assessment of the rheological behaviors of 22 different oily vehicles.

Type 1 Vehicles

Vehicles of this type relate to that described by Stephens and Su.[27]

(a) 0.5 w/v, 1% w/v, 1.5% w/v, 2% w/v, 2.5% w/v, 3% w/v, 3.5% w/v, 4% w/v or 5% w/v of a 50:50 mixture of aluminium mono-and di-stearates in FCO
(b) Solution of 0.7% w/v lecithin in FCO
(c) Dispersion of 0.35% w/v of hydrogenated castor oil in FCO
(d) Dispersion of 0.5% w/v aluminium stearate + 0.7 w/v lecithin + 0.35% w/v hydrogenated castor oil + 20% w/v sucrose in FCO
(e) Dispersion of 0.5% w/v aluminium stearate + 0.35% w/v hydrogenated castor oil + 20% w/v sucrose in FCO

(f) Dispersion of 0.5% w/v aluminium stearate + 0.7% w/v lecithin + 0.35% hydrogenated castor oil + 30% w/v sucrose in FCO.

Vehicles (d) and (f) were prepared according to the patent of Stephens and Su [27] by dissolving the lecithin in a portion of the FCO. Dissolution was facilitated by heating the FCO to about 90-100 ^{0}C and agitating the mixture thoroughly until all the solids were dissolved. To this solution, with the heat maintained, the aluminium stearate and hydrogenated castor oil were added and the resulting mixture was mixed well until the latter two ingredients were thoroughly dispersed. Then the sucrose, previously sieved to a mesh size of 63-75 μm, was added and the resulting dispersion was mixed thoroughly with the temperature at 90-100 ^{0}C for 3 hrs.

The resulting dispersion was cooled to room temperature with mixing. The remainder of the FCO was then added to bring the dispersion up to the required volume. Care was taken to avoid the entry of any moisture into the container, since preliminary studies showed that water affects the structure of the gel. The remaining vehicles (a), (b), (c), and (e) were prepared in accordance with the appropriate stages in the above method. For example, vehicles of type 1(a) were prepared simply by adding the required amounts of aluminium stearate to a portion of the FCO in a flask and heating in a water bath (90-100 ^{0}C) for 3 hrs with thorough agitation. For vehicles (b) and (c) the required amount of the ingredient was added to a portion of the oil and mixed thoroughly at a temperature of 90-100 ^{0}C until the solid was dissolved in the case of (b) or thoroughly dispersed in (c). Vehicles (a), (b) and (c) were then cooled to room temperature and the remainder of the oil was added as mentioned above.

Type 2 Vehicles

Vehicles of this type relate to that described by Lin and Pramoda.[28]

(a) dispersion of (i) 20% w/v or (ii) 30% w/v of sucrose in FCO

(b) (i) 0.3% w/v, (ii) 0.5% w/v or (iii) 1% w/v of Cab-o-sil in a 20% w/v dispersion of sucrose in FCO.

(c) 1.25% w/v Cab-o-sil + 30% w/v sucrose in FCO.

(d) 1% w/v Cab-o-sil in FCO.

Vehicles (b) and (c) were prepared according to the patent of Lin and Pramoda [28] by adding the sugar in successive portions to a portion of the FCO in a suitable container and stirring until the system was suitably dispersed and suspended. The Cab-o-sil was then added and stirred until dispersed. Sufficient additional oil was added and stirred to obtain a uniform dispersion. Although it was not specified in this patent, the sucrose was sieved and the portion corresponding to a mesh size of 63-75 μm was used in the preparation of the vehicle. Precautions were taken to avoid the entry of moisture into the container for the same reason mentioned above.

The vehicles that contain only dispersions of sucrose in the oil (a) or Cab-o-sil in the oil (d) were also prepared according to this patent simply by adding the sucrose or Cab-o-sil to the oil and stirring until complete dispersion was obtained.

Rheological Measurements

A Rotovisko viscometer (Haake) fitted with concentric cylinder sensors and a temperature controlled water jacket at 37 ^{0}C was used. The NV measuring cup and bob with measuring head 500 were selected; this combination was suitable for the viscosity range studied.

The measuring cup was filled with dispersion, previously warmed to 37 ^{0}C, and the bob immersed. The dispersion was allowed to remain undisturbed for 2 min to allow temperature equilibrium to be re-established. The bob was set in motion at the lowest shear rate, and a reading was taken at the end of 30 seconds. The rotational speed of the bob was then increased to the next setting at 30 second intervals until the highest shear rate was reached, then decreased at the same rate to the lowest shear rate and scale

readings were recorded at the end of each 30 second period. The total time for each measuring cycle was therefore 5 minutes.

The rate of shear (D) that was applied to the system being tested at a given speed of rotation of the bob in the Rotovisko viscometer is given by Eq. 1.

$$D = \frac{B}{U} \quad s^{-1} \qquad \text{Eq. 1}$$

where B is a constant that depends on the dimensions of the concentric cylinders and U is a speed factor. The scale readings (S) observed on the instrument can be converted into shear stress (Υ) values by Eq. 2.

$\Upsilon = AS \quad Nm^{-2} \qquad$ Eq. 2

where A is a constant (the stress factor) that depends on the dimensions of the sensor system that is used and on the torsional constant of the instrument.

Results

Tables of the results that listed the values of the instrument parameters, observed scale readings and derived shear rates and stresses were prepared for each system that was studied. Table (1) is an example of such a table and shows the results obtained for FCO.

Rheograms or flow curves, i.e. plots of shear rate versus shear stress, for all the systems studied are shown in Fig. (1) – Fig. (5). These figures describe the "up curves" only and extend to a maximum shear rate of 436 s^{-1} for the sake of clarity at the lower shear rates. With the exception of the linear (i.e. Newtonian) flow curves that were obtained for FCO alone (Fig. 1), 0.7% w/v lecithin in oil (curve 1(b) in Fig. 2) and the remaining rheograms indicated varying degrees of pseudoplastic behavior for the oily dispersions referred to in Fig.(1)– Fig. (3). In addition to pseudoplastic behavior, systems containing concentrations of aluminium stearate greater than 1% w/v in FCO also exhibited a slight thixotropy. The complete rheograms (i.e. up curves and down curves) for 1% w/v and 5% w/v aluminium stearate in FCO over the complete range of shear rates that were used and that for vehicle type 1(f), which corresponds to the vehicle described in Stephens and Su`s patent,[27] are shown in Fig. (4) and Fig. (5), respectively, in order to illustrate the hysteresis loops that denote thixotropic behavior in these systems.

The apparent viscosities at an arbitrarily chosen low shear rate of 100 s^{-1} of a series of aqueous vehicles have been correlated with the bioavailabilities and the in vitro release rates of a series of drugs.[13,17] The apparent viscosities of the systems used in the present work were calculated at the same shear rate and their values are listed in Table (2).

Table (1): Rheological parameters for FCO at 37 ^{0}C.

	Sensor – NV, Measuring head - 500		
U	***S***	***D (s^{-1})***	***Υ (Nm^{-2})***
162	*-*	*-*	*-*
81	*0.31*	*32*	*0.6*
54	*0.50*	*49*	*0.9*
27	*1.00*	*97*	*1.75*
18	*1.38*	*146*	*2.5*
9	*2.75*	*291*	*5.0*
6	*4.25*	*436*	*7.8*
3	*8.38*	*873*	*15.3*
2	*12.75*	*1310*	*23.3*
1	*25.00*	*2620*	*45.8*

Table (2): Apparent viscosities (η_{app}) of the vehicles at a shear rate of 100 s^{-1} and temperature of 37 ^{0}C.

The Vehicle	*Vehicle Code*	*η_{app} ($mN\ s\ m^{-2}$)*
Fractionated Coconut Oil (FCO)	*-*	*17.5*
0.7% w/v lecithin solution in FCO	*(1b)*	*23*
0.5% w/v aluminium stearate in FCO	*(1a)*	*37*
0.35% w/v hydrogenated castor oil in FCO	*(1c)*	*40*
1% w/v aluminium stearate in FCO	*(1a)*	*50*
20% w/v sucrose in FCO	*(2ai)*	*51*
1% w/v Cab-o-sil in FCO	*(2d)*	*58*

1.5% w/v aluminium stearate in FCO	*(1a)*	*59*
30% w/v sucrose in FCO	*(2aii)*	*64*
2% w/v aluminium stearate in FCO	*(1a)*	*69*
2.5 % w/v aluminium stearate in FCO	*(1a)*	*81*
0.3% w/v Cab-o-sil + 20% w/v sucrose in FCO	*(2bi)*	*83*
3% w/v aluminium stearate in FCO	*(1a)*	*92*
0.5% w/v Cab-o-sil + 20% w/v sucrose in FCO	*(2bii)*	*98*
3.5% w/v aluminium stearate in FCO	*(1a)*	*104*
0.5% w/v aluminium stearate + 0.35 w/v hydrogenated castor oil + 20% w/v sucrose in FCO,	*type1(e) vehicle*	*105*
Vehicle 1(e) + 0.7% w/v lecithin,	*type1(d) vehicle*	*120*
1% w/v Cab-o-sil + 20% w/v sucrose in FCO	*(2biii)*	*131*
Vehicle 1(d) using 30% w/v sucrose,	*type 1(f) vehicle*	*140*
4% w/v aluminium stearate in FCO	*(1a)*	*144*
1.25% w/v Cab-o-sil + 30% w/v sucrose in FCO	*(2c)*	*150*
5% w/v aluminium stearate in FCO	*(1a)*	*176*

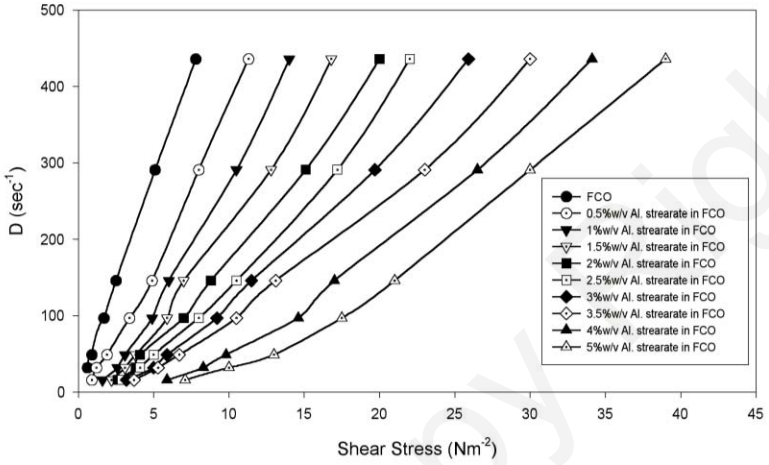

Fig. (1): Rheograms of FCO and the dispersions of aluminium stearate in FCO (type 1a vehicles) at 37°C.

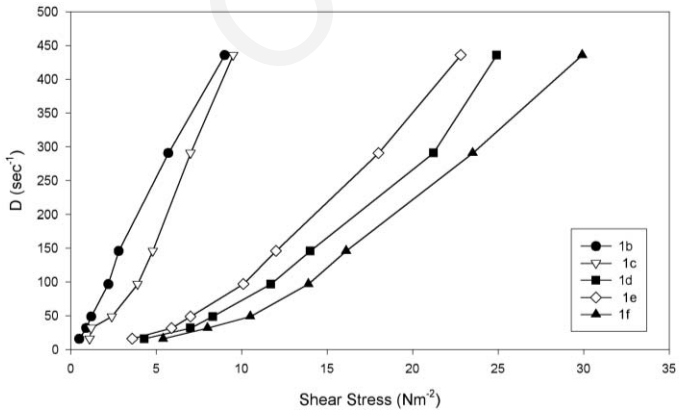

Fig. (2): Rheograms of oily vehicles type 1b-1f at 37 °C (See table (2) for vehicle code).

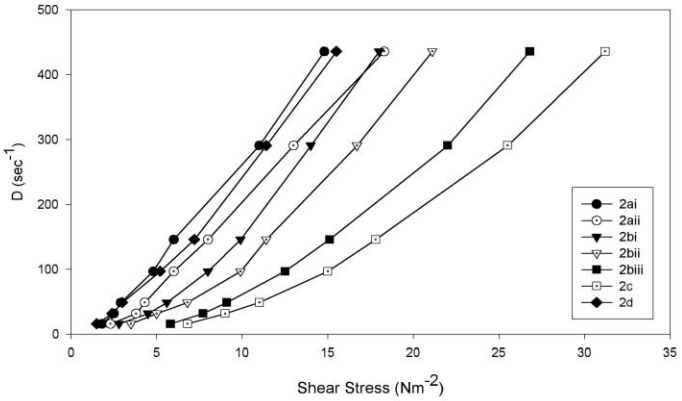

Fig. (3): Rheograms of oily vehicles type 2 at 37 °C. (See table 2 for vehicle code).

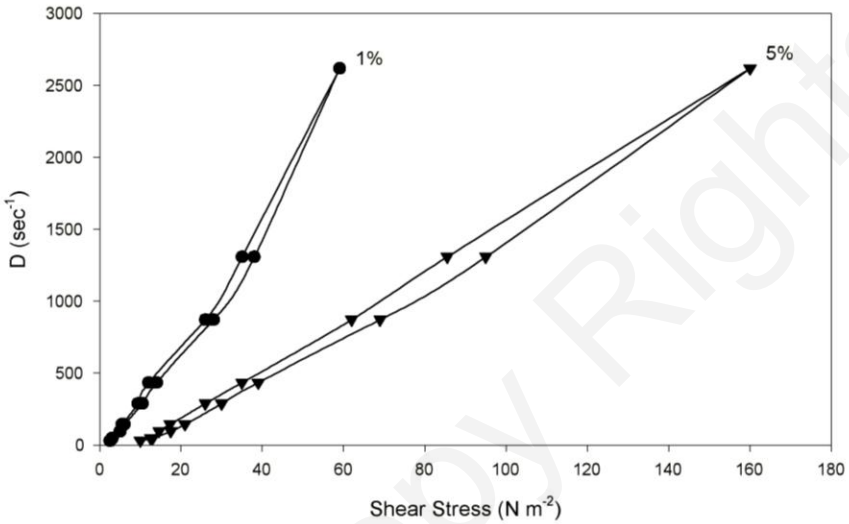

Fig. (4): Rheograms of oily vehicles 1% w/v and 5%w/v aluminium stearate in FCO showing hysteresis loop.

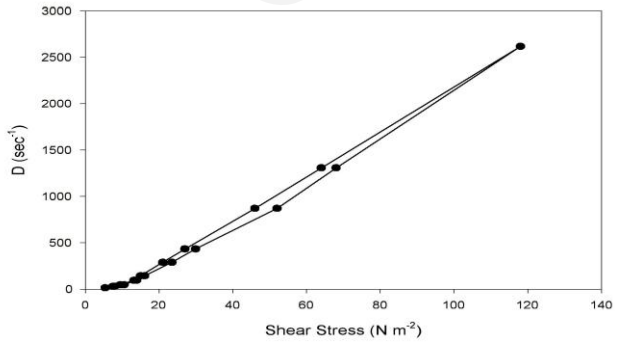

Fig. (5): Rheograms of oily vehicles type - 1f showing hysteresis loop.

Discussion

The Newtonian behavior exhibited by FCO and 0.7 w/v lecithin solution in the oil is as expected for simple liquids and true solutions.[26] Dispersions of aluminium stearate, hydrogenated castor oil, Cab-o-sil and sucrose in FCO, together with those oily vehicles specified by the patents of Stephens and Su [27] (type 1 vehicles, d and f) and Lin and Pramoda [28] (type 2 vehicles, b and c), exhibited pseudoplastic behavior. These findings are in agreement with those reported in the literature concerning Cab-o-sil [28] and sucrose.[26] Furthermore, aluminium stearate, 1% w/v and above, and the oily vehicle type 1 (d and f) exhibited thixotropic pseudoplastic behaviors. The thixotropic property of oily gels of aluminium stearate has been reported previously.[22]

The addition of dispersed particles and/or suspending agents to a Newtonian vehicle often produces non-Newtonian properties. For example, the addition of the aluminium stearate (Fig. 1), hydrogenated castor oil (curve 1(c) in Fig. 2), sucrose and Cab-o-sil (Fig. 3) to the oil produced non-Newtonian systems. Only pseudoplasticity and thixotropic pseudoplasticity will be discussed here since other non-Newtonian properties (plastic and dilatant behaviors) are not encountered in this study.

Since the viscosity of a pseudoplastic substance decreases with an increasing rate of shear, an apparent viscosity (η_{app}) is commonly used to denote the viscosity of the system at a particular shear stress or shear rate. It can be expressed as either the reciprocal slope of a line joining the appropriate point on the flow curve with the origin of the graph or as cotangent to the flow curve at the specified point.[26] The former method has been used to express the apparent viscosity of the vehicle dispersions at a shear rate of 100 s^{-1} throughout this study.

The decrease in the η_{app} with an increasing shear results from the breakdown, under the influence of a shearing force, of structures within the system. The structural features of these systems involve gel formation, e.g. aluminium stearate[23,24] and Cab-o-sil in the oil.[29] Breakdown of these structures occurs under the influence of shear, i.e. gel networks are disrupted. The viscosity of the system, consequently, decreases with an increase in the rate of shear. For this reason pseudoplastic materials are sometimes called "shear thinning systems". When structural breakdown is complete the η_{app} becomes constant, i.e. a further increase in the shear rate will not cause any additional decrease in viscosity. On removal or reduction of the shear force, reformation of the structural units occurs under the influence of Brownian motion. If this reformation occurs immediately, the flow curve obtained at decreasing shear rates (the down curve) is therefore super imposable on that obtained from measurements made at increasing shear rates (the up curve). This is the case with the oily dispersions of sucrose (curves 2(a) in Fig. 3), Cab-o-sil alone (curve 2(d)) and sucrose (curves 2(b) and 2(c)) in Fig. 3. This type of pseudoplastic behavior is called time independent pseudoplastic behavior.

However, there are instances where the down curve is not super imposable on the up curve, i.e. the reformation of structure is not immediate when the stress is removed or reduced, and the down curve is therefore displaced to the left with regard to the up curve. For this reason, such flow behavior is called time dependent or thixotropic pseudoplasticity.[26]

The extreme behavior is an isothermal, reversible sol ↔ gel transformation produced by shear and by rest, respectively. For example, higher concentrations of aluminium stearate (e.g. 4% w/v and 5% w/v, Fig. 4) and the oily vehicle (type 1 vehicles (d) and (f), Fig. 5) form gels after preparation when unstirred, but can be poured more easily after they had been stirred vigorously. After a period of about 1 hour, they revert to gels as the Brownian motion rebuilds their gel structure.

It has been suggested that the area enclosed by the hysteresis loop in the rheogram of a thixotropic system can be used as a relative

measure of the degree of thixotropic breakdown. In addition, thixotropy can be represented quantitatively by the decay of shear stress or apparent viscosity as a function of time at a constant rate of shear or by a coefficient of thixotropic breakdown, i.e. the loss in shearing stress per unit increase in shear rate.[26] Using the trapezoidal rule that is commonly used in bioavailability studies, the areas of the hysteresis loops of the oily vehicles (type 1 vehicles (d) and (f)) and the oily dispersions of aluminium stearate systems were calculated by subtracting the smaller area under the curve from the larger one. These areas (thixotropic indices) are shown in Table (3).

Fig. (4) illustrates the thixotropic nature of oily dispersions of 1% w/v and 5% w/v aluminium stearate. The hysteresis loops obtained for other intermediate concentrations lie between these two curves but have been omitted from the figure for the sake of clarity. Fig. 5 shows that the type 1(f) vehicle and type 1(d) vehicle were omitted for the same reason. However, their thixotropic indices are given in Table 3. Fig. 4 and Table 3 show that the degree of thixotropy increased with an increase in the aluminium stearate concentration. The apparent viscosity at a given shear rate also increased in an approximately linear manner as indicated by Fig. (6).

There is a disagreement in the literature concerning the time dependency of the flow behaviors of aluminium soap-hydrocarbon systems. Complete recovery was reported by Goldberg and Sandvick.[30] However, Shiba [23] stated that the change caused by the applied shearing stress was not thixotropic but appeared to be a permanent change in the structure of the gel. Although no evidence of recovery was observed with a 9% w/w gel, gradual recovery did occur with a 3% w/w and this latter system was, therefore, thixotropic.[24] The author suggested that recovery might, in fact, occur with the 9% w/w gel but at an extremely slow rate due to the viscosity of the system.

However, the discrepancies between the results obtained by different researchers can be ascribed mainly to differences in the experimental conditions; [23] for example, the rate of shear, temperature, concentration and the properties of aluminium stearate are not always pure substances. Although the above discrepancies have been reported, Shiba [23] thought that the paraffin gels were thixotropic at high temperature or under low rates of shear.

On the basis of differences in experimental conditions and the nature of the oily phase, it is possible, therefore, to explain why aluminium stearate exhibited pseudoplastic flow behavior in the FCO in this study, whereas plastic behavior in liquid paraffin was reported previously.[23,24] Furthermore, these differences are also likely to be responsible for the fact that 0.5% w/v aluminium stearate produced a gel in FCO (Fig. 1) and 1% w/v produced a gel with thixotropic properties (Fig. 4) whereas 1.5% w/w aluminium stearate appeared to be required in liquid paraffin to produce the same sort of effects.[24]

Thixotropic pseudoplastic behavior is a desirable property in liquid pharmaceutical systems that ideally should have a high consistency in the container, yet pour or spread easily after they had been stirred vigorously. For example, a well-formulated thixotropic suspension will not settle readily in the container, will become fluid on shaking, and will remain long enough for a dose to be dispensed. Finally, it will regain consistency rapidly enough so as to maintain the particles in a suspended state. The thixotropic pseudoplastic behavior is also applicable and desirable in parenteral suspensions. Martin et al [26] stated that the "breakdown of the structure occurred when the suspension was caused to pass through the hypodermic needle. The consistency was then recovered as the rheological structure reformed. This led to the formation of a depot of drug at the site of injection in the muscle, from which drug was slowly removed and made available to the body."

The dispersion of sucrose (20% w/v and 30% w/v) in FCO also exhibited non-Newtonian properties, but these were limited to pseudoplastic behavior since no evidence of

thixotropy was observed. In systems containing 20% w/v sucrose plus different concentrations of Cab-o-sil, the pseudoplastic viscosity increased with increasing concentrations of Cab-o-sil (curves 2(b) in Fig. 3). Pseudoplasticity was also exhibited by 1.25% w/v Cab-o-sil plus 30% w/v sucrose as well as by 1% w/v Cab-o-sil in the oil alone (curves 2(c) and 2 (d) in Fig. 3, respectively). The effects of Cab-o-sil have been reported by Lin and Pramoda.[28] The action of Cab-o-sil as a viscosity enhancing agent may be largely attributed to the ability of the very small silica particles to form a network structure throughout the medium by interparticular hydrogen bonding via the silanol groups on the silica surface. In addition to these particle interactions, there is a possible bonding between the silanol groups and other components that are also capable of hydrogen bond formation.[25] No thixotropic properties were detected in the Cab-o-sil systems and it is suggested that the recovery and reformation of the structural units, on removal or reduction of shear force, occurs immediately under the influence of Brownian motion.

The effects of the other pharmaceutical additives that are included in type 1 vehicles on the rheological properties of the oil are shown in Fig. (2) (curves 1(b), 1(c), 1(d), 1(e), and 1(f)). A 0.7% w/v solution of lecithin in FCO was still Newtonian although the viscosity was increased slightly as indicated in Table (2).

The omission of 0.7% w/v lecithin from type 1 vehicles d and f (i.e. type 1 vehicle (e)) resulted in a decrease in the apparent viscosity as shown by Table (2) and the loss of the thixotropy that is exhibited by vehicles of type 1(d) and 1(f). Thus, the thixotropic structure in these latter vehicles depended on the presence of lecithin, although on its own in FCO this compound appeared to act as a simple Newtonian solution. The tendency for lecithin to form reasonably stable complexes with other substances, especially other lipids, proteins and carbohydrates, provides a probable explanation for the formation of a thixotropic system.[31] Thus type 1 vehicles (d) and (f), that are described by the patent of Stephens and Su,[27] probably consist of the dispersion of sucrose and hydrogenated castor oil particles that are coated with adsorbed aluminium stearate and lecithin molecules and the thixotropic structure results from interparticular bridges formed by the combined effects of lecithin and aluminium stearate when their concentrations are adequate. Alternatively, or additionally, the lecithin and stearate may, if their combined concentrations are sufficient, form a gel network through the system and the insoluble sucrose and hydrogenated castor oil particles are simply suspended in this network.

Table (3): Thixotropic indices of the oily vehicles that formed hysteresis loops.

Vehicle Type	*Concentration of aluminium stearate*	*Thixotropic index* $N\,s^{-1}\,m^{-2}\,1 \times 10^{3}$
1a	*1%*	*1.433*
	1.5%	*2.224*
	2%	*2.662*
	2.5%	*5.697*
	3%	*7.141*
	3.5%	*10.632*
	4%	*11.705*
	5%	*13.840*
1d		*4.549*
1f		*4.826*

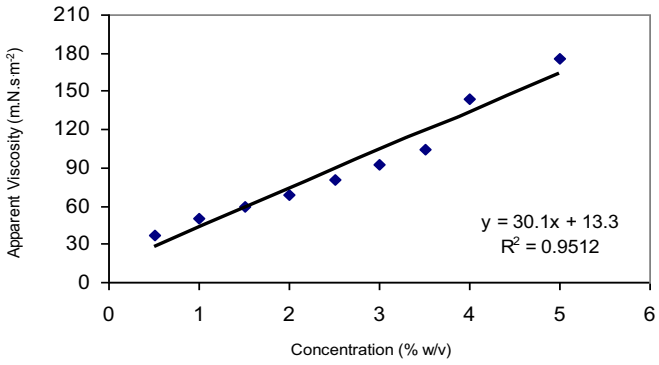

Fig. (6) : Apparent viscosity of aluminium stearate in FCO systems at 100 s^{-1} and 37 °C versus concentration of the stearate

Conclusion

Thixotropic pseudoplastic behavior is a desirable property in liquid pharmaceutical systems that ideally should have a high consistency in the container, yet pour or spread easily after they have been stirred vigorously. The suspension will then regain consistency rapidly enough, as the structure reforms, so as to maintain the particles in a suspended state. This property can lead to the formation of a depot of a drug (in the case of a parenteral suspension) when the suspension is passed through a hypodermic needle, at the site of injection in the muscle, from which the drug is slowly removed and made available to the body.

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دراسات اللزوجية على محاليل زيتية مختلفة لمستحضرات صيدلانية

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الملخص

تمّت دراسة خواص اللزوجية لمحاليل زيتية مبتكرة في براعة اختراع لمحاليل غير مائية لمعلقات صيدلانية. كذلك تم استقصاء تأثيرات التراكيز المختلفة لمختلف المواد الصيدلانية المضافة في سير المنحني البياني، وكذلك تم استخدام جهاز الروتوفزكو لقياس اللزوجة مثبت بسلندر حساس، ورأس قياس 500 تحت درجة حرارة 37 درجة مئوية باستخدام الحمام المائي. دلّت النتائج على أن زيت الذرة وحده أو مع 0.7% لسيثين يسلك سلوك نيوتن. وعند إضافة ستياريت الألمنيوم، وزيت الخروع الهيدروجيني، وكاب أو سيل وسكروز إلى زيت الذرة سلكت المحاليل سلوك البسيدوبلاستك. بينما سلكت المحاليل سلوك ثكسوتروبك بسيدوبلاستك عند إضافة ستياريت الألمنيوم 1% فما فوق أو المحاليل الزيتية المحتوية ستياريت الألمنيوم، زيت الخروع الهيدروجيني، كاب او سيل وسكروز. عند حذف الليسيثين من المحلول الأخير نتج نقصان اللزوجة الظاهرية وفقدان ظاهرة الثكسوتروبي.

نستنتج من هذه الدراسة أنه يمكن الإفادة من ظاهرة سلوك المحاليل الزيتية سلوك ثكسوتروبك بسيدوبلاستك في تحضير واستخدام المستحضرات الصيدلانية السائلة وغير المائية، والتي يجب أن تكون محافظة على قوامها في قنانيها وفي نفس الوقت سهلة الانسكاب عند الاستخدام. وقد تمّت مناقشة الاقتراحات والتعليلات بإسهاب.