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Rheological Investigation of Lipid Polymer Hybrid Nanocarriers for Oral Delivery of Felodipine (Conference Paper)[#]

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Abstract

The rheological behavior among the factors that are present in Stokes law can be used to control the stability of the colloidal dispersion system. Lipid/polymer hybrid nanocarriers (LPHNs) is an interesting colloidal dispersion system that is used for rheological characteristic analysis. The LPHNs are composed of polymeric components and lipids. This research aims to prepare oral felodipine LPHNs to investigate the effect of independent variables which are lipid content, surfactant mixture and distilled water, on the rheological behavior of the nanosystem. A microwave-based technique was successfully used to prepare felodipine LPHNs (H1-H9). The formulations were characterized for particle size and PDI to confirm the colloidal properties of the prepared nanosystem. Therefore, rheological evaluation study of described nanosystems was performed using the coaxial rotational digital rheometer. The outcomes showed that all felodipine LPHNs formulations (H1-H9) had a nanosize and homogenous structure which verified the colloidal features of the nanodispersion systems. The rheogram chart indicated that all felodipine LPHNs formulations (H1-H9) show pseudoplastic flow (non-Newtonian flow), suggesting a shear-thinning property. The microwave-based method successfully produced felodipine LPHNs with excellent physical texture that proves its ability as a nanoparticles preparation technique. The pseudoplastic flow behavior of felodipine LPHNs formulations (H1-H9) suggests that the described nanosystems in this study are physically stable

Keywords: Rheology, Felodipine, Lipid-polymer hybrid nanocarriers, Microwave-based method.

التحقيق الريولوجي للحاملات النانوية الهجينة للبوليمر الدهني للايصال الفموي لفيلوديبين (بحث مؤتمر)[#]

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الخلاصة

يمكن استخدام السلوك الريولوجي بين العوامل الموجودة في قانون ستوكس للتحكم في استقرار نظام التشتت الغروي. الناقلات النانوية الهجينة من البوليمر الشحمي فيلوديبين (LPHNs) هي نظام تشتت غرواني مثير للاهتمام يستخدم لتحليل الخصائص الريولوجية. تتكون LPHNs من مكونات بوليمرية ودهون. يهدف هذا البحث إلى إعداد فلوديبين LPHNs عن طريق الفم لاستقصاء تأثير المتغيرات المستقلة على السلوك الريولوجي للنظام النانوي. تم استخدام تقنية الميكروويف لتحضير فلوديبين(LPHNs H1-H9) بنجاح. تدخل جميع الصيغ في عملية التوصيف لحجم الجسيمات و PDI للتأكد من الخصائص الغروانية للنظام النانوي المحضر ثم استخدام مقياس الانسياب الرقمي الدوراني المحوري لتقييم الانسيابية. تظهر النتائج أن جميع تركيبات فلوديبين (LPHNs H1-H9) لها بنية نانوية ومتجانسة تؤكد السمات الغروانية لنظام التشتت النانوي. يشير مخطط الرسم البياني إلى أن جميع تركيبات فلوديبين (LPHNs H1-H9) تظهر تدفق البلاستيك الكاذب (التدفق غير النيوتوني) الذي له خاصية ترقق القص. تقوم الطريقة المعتمدة على الميكروويف بإعداد تركيبات فلوديبين (LPHNs H1-H9) التي تُظهر نسيجًا فيزيائيًا ممتازًا ، وهذا يؤكد قدرتها كأسلوب لتحضير الجسيمات النانوية. تُظهر جميع تركيبات الفلوديبين (LPHNs H1-H9) تدفق البلاستيك الكاذب الذي يدعم الاستقرار المادي للنظام النانوي.

الكلمات المفتاحية: الريولوجيا ، الفلوديبين ، الناقلات النانوية الهجينة للبوليمر الدهني ، طريقة الميكروويف.

Introduction

Rheology is an important physical characteristic in pharmaceutical design and manufacture. Creaming, flocculation, and coalescence are responsible for the instability of the colloidal dispersion system. The rheological behavior among factors that are present in Stokes law can be used to control the stability of the colloidal dispersion system[(1)]. Therefore, the viscosity of colloidal systems is of great importance in scientific pharmaceutical research [(1)]. The coaxial rotational rheometer, also known as Couette or concentric cylinder viscometers, is the most common machine used for measuring viscosity. A circular bob inserted concentrically inside a cup contains the tested colloidal dispersion. The process of measurement occurs when fluid will drag on the bob as a result of bob or cup rotation, and a sensor in the machine will record the viscosity at a specific shear rate and shear stress.

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Several readings can be obtained by changing revolutions per minute (RPM). These data can be analyzed to determine the rheological properties of pharmaceutical liquids[2-4].The felodipine lipid/polymer hybrid nanocarriers (LPHNs) is an interesting colloidal dispersion system that is used as an oral drug delivery system for rheological characteristic analysis[5-7]. The LPHNs compose of polymeric components and lipid matrices that constitute monolithic type colloidal nanocarriers. The felodipine LPHNs have properties of both polymer nanocarriers and lipid-based nanocarriers constructed from it[8]. The polymer content makes felodipine LPHNs provide more control on felodipine release. Whereas, the lipid content enhances felodipine solubility, the biological tissue penetration, and improve absorption in addition to felodipine entrapment efficiency will increase in comparison to lipid based nanoparticles and polymeric nanoparticles alone[9]. The process of hybridization between polymer and lipid gives nanoparticles that show: nanoscale particle size, higher drug payload, furiousness, provide sustained drug delivery and more stability in blood circulation and on long term storage of the formulation[10].

However, the methods to prepare the LPHNs in these studies were associated with several limitations such as cost, lower stability and time consuming. Recently, a microwave-based method has been used to prepare the LPHNs[11,12]. These reports indicated that the microwave-based method have many merits such as rapid processing, can achieve in both small and large scale, inexpensive, more stable, economical, and absence of impurities[11,12]. This research aims to prepare oral felodipine LPHNs to investigate the effect of independent variables which are lipid content, distilled water content, and surface-active agents:co-surfactant blend on the rheological behavior of the nanosystem.

Materials and Methods

Materials

The lauric acid, felodipine, polysorbate 80, propylene glycol were purchased from Nanjing Duly Biotech Co., Ltd . China. The PEG laurate was purchased from Beijing Yibai Biotechnology Co., Ltd. China. The cardamom oil was purchased from Hemani international KEPZ, Karachi, Pakistan.

Methods

Preparation of felodipine LPHNs

Nine felodipine LPHNs formulations (H1-H9) were prepared using the microwave-based method that was previously described by Drais H K and Hussein A A[11,12]. The hydrophobic mixture was prepared by dissolving chitosan polymer, felodipine, and lauric acid in a blend of cardamom oil and PEG-laurate using a magnetic stirrer device at 1000 rpm for 5 minutes. The hydrophilic mixture that contains distilled water, propylene glycol, and polyoxyethylene (20) sorbitan monooleate was prepared under a magnetic stirrer at 1000 rpm for 5 minutes. The final mixture that contains hydrophobic and hydrophilic phases according to the concentrations of each ingredient as shown in Table 1, was placed in microwave instrument for less than 15 seconds, then a mixture was subjected to magnetic stirring of 1000 rpm to form solution of the colloidal structure of felodipine LPHNs. The felodipine LPHNs formulations were stored in a tightly closed container at 25 ^{O}C temperature until the time of the rheological evaluation [11,12]. A coaxial rotational digital rheometer (Biobase Meihua Trading Co., Ltd, China) was used to measure the viscosity of the prepared nanodispersions. The spindle number (1) was used at 25°C. The felodipine LPHNs formulations were exposed to various rotational velocities (0.1, 0.3, 0.6,1.5, 3, 6, 12, 30, and 60 rpm). The experimental data were collected to analyze the rheological properties of the prepared nanosystems[2,11,12].

Table 1. The quantitative components of felodipine LPHNs formulations (H1-H9) for characterization and optimization

Formulation code	Felodipine % (w/w)	Cardamon oil % (w/w)	Lauric acid % (w/w)	Chitosan % (w/w)	PEG-(400) laurate :Polysorbate 80: Propylene glycol % (w/w)	Distilled water % (w/w) up to
H1	1	4	1	0.1	15:7.5:7.5	100
H2	1	4	1	0.1	17.5:8.75:8.75	100
H3	1	8	2	0.2	17.5:8.75:8.75	100
H4	1	4	1	0.2	20:10:10	100
H5	1	8	2	0.25	20:10:10	100
H6	1	12	3	0.35	20:10:10	100
H7	1	4	1	0.2	22.5:11.25:11.25	100
H8	1	8	2	0.35	22.5:11.25:11.25	100
H9	1	12	3	0.4	22.5:11.25:11.25	100

Characterization of the felodipine LPHNs

1. Measurement of particle size

The particle size was determined by the nanoparticle analyzer model SZ-100 - nanopartica series instruments (Horiba scientific company, Japan). Photon correlation spectroscopy (PCS) is a technique that has been used to determine the globular size of the nanosystem. The experiments were performed in triplicate [13,14].

2. Measurement of polydispersity index (PDI)

PDI is the uniformity parameter. PDI of the prepared nanosystems was measured by the DLS (dynamic light scattering) technique. PCS is a technique that has been used to determine PDI. The higher the PDI value indicates the lower particle size uniformity. The measurement was performed in three trials[13-15].

3. Atomic force microscopy (AFM)

The morphological attributes of felodipine LPHNs formulation can explain by AFM angstrom advanced inc. AA3000 USA. The AFM measurement was performed by using 1-3 drops of the felodipine LPHNs formulation onto a glass slide[13].

Statistical analysis

The investigation data was presented as the average of three trials and ± SD (n=3). The Microsoft Office Excel program was used to analyze the data. The analysis of variance (ANOVA) was used where the level at ($P<0.05$) was kept as significant while the level ($P>0.05$) was kept as not significant[16].

Results and Discussion

Particle size and PDI of felodipine LPHNs

The felodipine LPHNs formulations (H1-H9) were successfully prepared by the microwave-based technique according to specified component concentrations as shown in Table 1. All formulations were visually clear indicating colloidal properties of the hybrid dispersion system. The results of DLS revealed that the mean particle sizes of the felodipine LPHNs formulations were H1 (87 nm), H2 (70nm), H3 (146 nm), H4 (33 nm), H5 (94 nm), H6 (978 nm), H7 (49 nm), H8 (75 nm) and H9 (809nm).The outcomes show that all felodipine LPHNs formulations (H1-H9) had nanosize and ascertain colloidal features of the nanodispersion system[17]. According to the results, the analysis of variance show null hypothesis refusion that state the correlation between variables of investigation is no significant and accept the alternative hypothesis that state there is a significant correlation between variables of investigation [17]. Therefore, there is a significant relationship between surface-active agents: co-surfactant mixture, fat content, and distilled water as independent variables and particle size at level ($p<0.05$)[17]. The outcomes of the characterization process for PDI as shown in Table 2, were from 0.314 to 0.729. The PDI outcome indicated that felodipine LPHNs formulations (H1-H9) are the homogenous structure that ascertains the stability of felodipine LPHNs formulations (H1-H9) against physical instability processes of the dispersion system[17]. The ANOVA shows a significant correlation between independent variables and PDI at level ($p<0.05$) [17].

Table 2. The particle size and PDI results of felodipine LPHNs formulations (H1-H9)

Code	H1	H2	H3	H4	H5	H6	H7	H8	H9
Globule size (nm)*	87.6± 2.26	70.1± 3.38	146.2± 10.095	33.3± 1.216	94.21± 1.587	978.4± 3.004	49.6± 0.953	75± 2.816	809± 2.26
PDI*	0.538± 0.003	0.401± 0.001	0.547± 0.050	0.314± 0.002	0.54± 0.078	0.729± 0.011	0.374± 0.003	0.335± 0.005	0.798± 0.002

*Values are expressed as mean ± SD (n=3).

Rheological study

The rheological experiment was performed successfully at different rotational velocities and rheological data were collected which are viscosity, rate of shear, and shear stress. The rheogram chart is obtained by the plot of the rate of shear against shear stress as shown in Figure 1. The rheogram chart indicates that all of the felodipine LPHNs formulations (H1-H9) show pseudoplastic flow (non-Newtonian flow) that have shear-thinning property. The pseudoplastic rheological flow improves the stability of felodipine LPHNs formulations against creaming, flocculation, and coalescence which are responsible for the instability of hybrid dispersion system. Pseudoplastic flow behavior reduces the aggregation and settling rates of nanoparticles during a long period of pharmaceutical formulation storage also provide dose uniformity[1]. The felodipine LPHNs formulation (H4) was the selected formula due to has lower particle size and PDI in addition to pseudoplastic flow, in comparison with other present formulations. The AFM provides information for the size and shape of nanocarriers and apply for the felodipine LPHNs formulation (H4). The outcomes show that the morphology of

felodipine LPHNs (H4) was approached to spherical appearance with a smooth surface as shown in Figure 2, this ascertain the colloidal attributes of optimized felodipine LPHNs formulation (H4) .

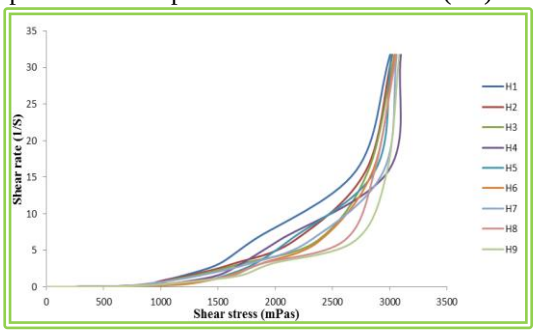

Figure 1. Shear stress against the shear rate of felodipine LPHNs formulations (H1-H9).

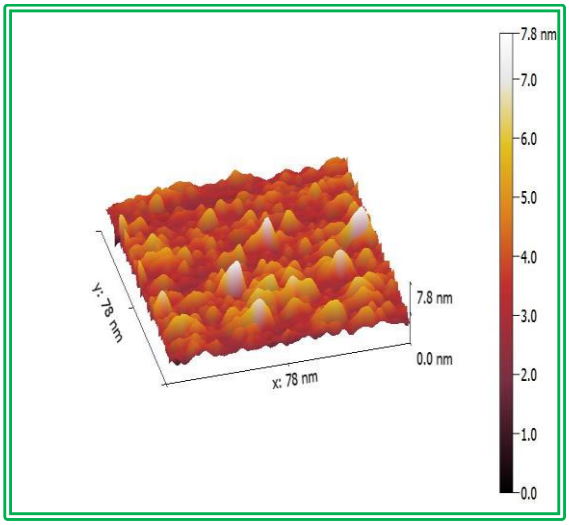

Figure 2. The AFM 3D image of felodipine LPHNs (H4) where the scanning area is 78 nm * 78 nm

Table 3. The shear stress results at different shear rates of felodipine LPHNs formulations (H1-H9)

Shear stress* / Shear rate	H1	H2	H3	H4	H5	H6	H7	H8	H9
0.0529	506± 0.177	601± 0.645	659± 0.473	521± 0.408	544± 0.296	576± 0.433	506± 0.257	514± 0.295	574± 0.492
0.158	755± 0.961	780± 1.214	810± 0.9	702± 0.816	854± 0.79	877± 1.77	755± 1.237	737± 0.711	789± 0.869
0.317	882± 1.565	933± 1.865	987± 4.972	989± 3.232	1121± 1.731	1178± 3.612	814± 2.215	930± 5.058	987± 1.771
0.793	995± 3.636	1002± 2.776	1046± 8.305	1240± 4.36	1377± 4.43	1386± 5.96	1057± 13.32	1289± 4.017	1320± 5.426
1.587	1205± 8.859	1257± 6.82	1302± 18.39	1499± 8.035	1569± 12.791	1601± 10.865	1347± 13.051	1632± 12.155	1703± 16.322
3.174	1511± 8.22	1634± 25.887	1704± 14.6	1703± 17.986	1820± 18.144	1873± 31.697	1770± 21.542	1877± 22.405	1966± 13.117
6.348	1804± 37.725	2166± 71.064	2369± 37.521	2030± 33.856	2120± 33.737	2389± 34.94	2303± 39.973	2602± 32.793	2698± 35.241
15.871	2703± 102.66	2789± 45.1	2810± 97.328	2987± 118.47	2870± 225.14	2850± 148.59	2945± 77.03	2866± 217.86	2975± 99.141
31.742	3001± 117.80	3020± 124.694	3040± 158.99	3095± 69.18	3012± 82.2	3044± 153.50	3058± 120.10	3055± 107.05	3081± 80.744

*****Values are expressed as mean ± SD (n=3).

Table 4. The viscosity results at different shear rates of felodipine LPHNs formulations (H1-H9)

Viscosity* / Shear rate	H1	H2	H3	H4	H5	H6	H7	H8	H9
0.0529	8733.45 ±3.347	11361.05 ±12.202	12457.46 ±8.947	9678.63 ±7.722	10283.55 ±5.595	10888.46 ±8.203	9565.21 ±4.863	9716.44 ±5.587	10850.66±9.303
0.158	4500 ±6.082	4936.7 ±7.692	5126.58 ±5.699	4443.03 ±5.17	5405.06 ±5	5550.63 ±11.212	4778.48 ±7.831	4664.55 ±4.5	4993.67 ±5.505
0.317	2782.33 ±4.936	2943.21 ±5.883	3113.56 ±15.6851	3119.87 ±10.195	3536.27 ±5.462	3716.08 ±11.397	2567.82 ±6.989	2933.75 ±15.958	3113.56 ±5.587

*Values are expressed as mean ± SD (n=3).

Continued table 4.

Viscosity* / Shear rate	H1	H2	H3	H4	H5	H6	H7	H8	H9
0.793	1254.72 ±4.586	1263.55 ±3.501	1319.04 ±10.473	1563.68± 5.497	1736.44 ±5.587	1747.79 ±7.516	1332.91± 16.797	1625.47 ±5.065	1664.56 ±6.842
1.587	759.29 ±5.582	792.06 ±4.297	820.41 ±11.588	944.54 ±5.063	988.65 ±8.06	1008.82 ±6.846	848.77 ±8.224	1028.35 ±7.659	1073.09 ±10.285
3.174	476.05± 2.589	514.8±8 .155	536.86± 4.599	536.54±5 .666	573.4±5. 716	590.1±9 .986	557.65±6 .787	591.36± 7.058	619.4±4 .132
6.348	284.18± 5.942	341.2±1 1.194	373.18± 5.91	319.78±5 .333	333.96±5 .314	376.33± 5.504	362.79±6 .297	409.89± 5.165	425.01± 5.551
15.871	170.31± 6.469	175.72± 2.841	177.05± 6.132	188.2±7. 464	180.83±1 4.186	179.57± 9.362	185.55±4 .853	180.58± 13.726	187.44± 6.246
31.742	94.54±3 .711	95.14±2 .408	95.77± 5.008	97.5± 2.179	94.89± 2.589	95.89± 4.835	96.33± 3.783	96.244± 3.372	97.06± 2.543

*Values are expressed as mean ± SD (n=3).

1. Effect of lipid content on the viscosity of felodipine LPHNs formulations (H1-H9)

It was found that the viscosity will increase as the concentration of lipid content (cardamom oil: lauric acid) increases at a constant concentration of PEG laurate: polysorbate 80: propylene glycol. The viscosity values have the following ascending order for H7 < H8 < H9 at 5%(w/w) of lipid content; up to 50%(w/w) of distilled water for H7, 10%(w/w) of lipid content, up to 45%(w/w) of distilled water for H8 and 15%(w/w) of lipid content, up to 40%(w/w) of distilled water for H9, at constant concentration of surface-active agents:co-surfactant blend which is 22.5%(w/w) of PEG-laurate and 11.25%(w/w) polysorbate 80 and 11.25%(w/w) of propylene glycol. The viscosity values have the following ascending order for H4 < H5 < H6 at 5%(w/w) of lipid content, up to 55%(w/w) of distilled water for H4, 10%(w/w) of lipid content, up to 50%(w/w) of distilled water for H5 and 15%(w/w) of lipid content, up to 45%(w/w) of distilled water for H6 , at constant concentration of surface-active agents:co-surfactant blend which is 20% (w/w) of PEG-laurate and 10%(w/w) polysorbate 80 and 10%(w/w) of propylene glycol. The viscosity values have the following ascending order for H2 < H3 at 5%(w/w) of lipid content, up to 60%(w/w) of distilled water for H2 and 10%(w/w) of lipid content; up to 55%(w/w) of distilled water for H3, at a constant concentration of surface-active agents:co-surfactant blend which is 17.5%(w/w) of PEG-laurate and 8.75%(w/w) polysorbate 80 and 8.75%(w/w) of propylene glycol. The H1 shows lower viscosity in comparison to other formulations due to low volume concentration of lipid content 5%(w/w) and higher concentration of continuous phase 65%(w/w) at lower concentration of surface-active agents:co-surfactant blend which is 15%(w/w) of PEG-laurate and 7.5%(w/w) polysorbate 80 and 7.5%(w/w) of propylene glycol. The increment in lipid content concentration which is cardamom oil: lauric acid (4:1) increases the viscosity of felodipine LPHNs formulations at a constant concentration of surface-active agents:co-surfactant blend is due to increase in volume concentration of nanocarriers that make colloidal dispersion system more resistant to flow and give pseudoplastic system[1,18].The analysis of variance indicates a significant correlation between the lipid content and viscosity at level $p < (0.05)$.

2. Effect of distilled water content on the viscosity of felodipine LPHNs formulations (H1-H9)

The distilled water constitutes the continuous or external phase of the colloidal dispersion systems (H1-H9). It was found that the viscosity will decrease as the distilled water increases at a constant concentration of PEG laurate: polysorbate 80: propylene glycol. The viscosity values have the following descending order for H9 > H8 > H7 at 15%(w/w) of lipid content, up to 40%(w/w) of distilled water for H9, 10%(w/w) of lipid content, up to 45%(w/w) of distilled water for H8 and 5%(w/w) of lipid content, up to 50%(w/w) of distilled water for H7 , at constant concentration of surface-active agents:co-surfactant blend which is 22.5%(w/w) of PEG-laurate and 11.25%(w/w) polysorbate 80 and 11.25%(w/w) of propylene glycol.

The viscosity values have the following descending order for H6 > H5 > H4 at15%(w/w) of lipid content; upto 45%(w/w) of distilled water for H6, 10%(w/w) of lipid content; upto 50%(w/w) of distilled water for H5 and 5%(w/w) of lipid content; upto 55%(w/w) of distilled water for H4 , at constant concentration of surface-active agents:co-surfactant blend which is 20% (w/w) of PEG-laurate and 10%(w/w) polysorbate 80 and 10%(w/w) of propylene glycol. The viscosity values have the following descending order for H3 > H2 at 10%(w/w) of lipid content; upto 55%(w/w) of distilled water for H3 and 5%(w/w) of lipid content; upto 60%(w/w) of distilled water for H2, at a constant concentration of surface-active agents:co-surfactant blend which is 17.5%(w/w) of PEG-laurate and 8.75%(w/w) polysorbate 80 and 8.75%(w/w) of propylene glycol.

The H1 shows lower viscosity in comparison with other formulations due to low volume concentration of lipid content 5%(w/w) and higher concentration of continuous phase 65%(w/w) at lower concentration of surface-active agents:co-surfactant blend which is 15%(w/w) of PEG-laurate and 7.5%(w/w) polysorbate 80 and 7.5%(w/w) of propylene glycol. The reason for increment in viscosity as distilled water decrease is due to reducing the continuous phase volume that makes felodipine LPHNs closer to each other that are stabilized by steric forces due to the presence of the outer coat of PEG[1,18]. The analysis of variance indicates a significant correlation between the continuous phase and viscosity at level $p < (0.05)$.

3. Effect of surface-active agents:co-surfactant blend on the viscosity of felodipine LPHNs formulations (H1-H9)

The surface-active agents:co-surfactant blend represent by PEG-laurate, polysorbate 80 and propylene glycol. It was found that the viscosity will increase as the concentration of surface-active agents:co-surfactant blend increases at a constant concentration of lipid content. The viscosity values have the following ascending order for H1 < H2 < H4< H7 at 15%(w/w):7.5%(w/w): 7.5%(w/w) of PEG-laurate:polysorbate 80 : propylene glycol respectively, upto 65%(w/w) of distilled water for H1. 17.5%(w/w):8.75%(w/w): 8.75%%(w/w) of PEG-laurate:polysorbate 80 : propylene glycol respectively, upto 60%(w/w) of distilled water for H2, 20%(w/w):10%(w/w): 10%(w/w) of PEG-laurate:polysorbate 80 : propylene glycol respectively, upto 55%(w/w) of distilled water for H4. 22.5%(w/w):11.25%(w/w): 11.25%(w/w) of PEG-laurate:polysorbate 80 : propylene glycol respectively, upto 50%(w/w) of distilled water for H4, at a constant concentration of lipid content which is 5%(w/w). The viscosity values have the following ascending order for H3 < H5 < H8 at 17.5%(w/w):8.75%(w/w): 8.75%%(w/w) of PEG-laurate:polysorbate 80 : propylene glycol respectively, upto 55%(w/w) of distilled water for H3, 20%(w/w):10%(w/w): 10%(w/w) of PEG-laurate:polysorbate 80 : propylene glycol respectively, upto 50%(w/w) of distilled water for H5. 22.5%(w/w):11.25%(w/w): 11.25%(w/w) of PEG-laurate:polysorbate 80 : propylene glycol respectively, upto 45%(w/w) of distilled water for H8, at a constant concentration of lipid content which is 10%(w/w). The viscosity values have the following ascending order for H6 < H9 at 20%(w/w):10%(w/w): 10%(w/w) of PEG-laurate:polysorbate 80 : propylene glycol respectively , upto 45%(w/w) of distilled water for H6, 22.5%(w/w):11.25%(w/w): 11.25%(w/w) of PEG-laurate:polysorbate 80 : propylene glycol respectively, upto 40%(w/w) of distilled water for H8, at a constant concentration of lipid content which is 15%(w/w). The increment in surface-active agents:co-surfactant blend concentration increases the viscosity of felodipine LPHNs formulations(H1-H9) at a constant lipid concentration is due to increase in volume concentration of nanoparticles that create dispersion medium more resistant to flow and improve medium viscosity[1,18]. The analysis of variance indicates a significant correlation between the continuous phase and viscosity at level $p < (0.05)$.

Conclusion

The microwave-based method was successful in producing the felodipine LPHNs (H1-H9) that show an excellent physical texture to reflect colloidal features of the hybrid nanosystem that make it the most advanced method for the preparation of nanoparticles. Rheological attributes are the main physical characteristics in the pharmaceutical liquid dosage form. From precise viscosity analysis, the type of flow can be determined. The rheogram chart indicates that all of the felodipine LPHNs formulations (H1-H9) show pseudoplastic flow. The pseudoplastic rheological flow enhances the felodipine LPHNs formulation's stability against physical instability and provides felodipine dose uniformity.

Ethical Approval

The present work does not include the use of human or animal subjects.

Conflict of Interest

The authors declare that there are no conflicts of interest.

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