





Research Article

Preparation and Characterization of Bilastine Solid Self-Nanoemulsion using Lquisolid Technique

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Abstract

Background: Supersaturable self-nanoemulsion (S-SNE) is an approach for dealing with low oral bioavailability problems. Bilastine (BL) is a selective H1-antihistamine with a bioavailability of 59%. **Objective:** To use a liquisolid technique to transform liquid BL S-SNE into powder so that both the S-SNE and liquisolid procedures could be used. **Methods:** Oleic acid, tween 60, transcutool, and soluplus were used to make the liquid BL-loaded S-SNE that was adsorbed onto the Avicel PH101 and Aerosil 200 admixtures. In vitro dissolving and powder flow characteristics were tested. SEM, DSC, X-ray diffraction, FT-IR analysis, and the average droplet size after dispersion in 0.1N HCl were also utilized to define the best formula's solid state. **Results:** The best liquid-solid composition, SS-F2, is composed of oleic acid, tween 60, transcutool, soluplus, Avicel 101, and Aerosil 200, with a liquid SNE to Avicel 101 ratio of 1.5:1 and an Avicel 200 to Aerosil 200 ratio of 10:1. SS-F2 displayed good flowability and a significant improvement in drug dissolution, with 100% of the medication released after 60 min compared to 62.27% of the marketed BL tablets. According to the solid-state investigation of formula (SS-F2), BL was shown to be in a solvated state in the solidified nanosystem, with no interactions with the excipient used. It also formed a nanoemulsion with mean droplet sizes of 77.57 nm and a PDI of 0.4178, which was similar to liquid S-SNE. **Conclusion:** The liquisolid technique is a potential method for solidifying a liquid self-emulsifying system while preserving self-nanoemulsion characteristics and increasing dissolving rate.

Keywords: Liquisolid powder, Bilastine, SNEDDS, Dissolution efficiency.

تحضير وتوصيف مستحلب البيلاستين الذاتي الصلب باستخدام تقنية ليكويوسوليد

الخلاصة

الخلفية: المستحلب النانوي الذاتي فائق التشبع (S-SNE) هو نهج للتعامل مع مشاكل التوافر البيولوجي الفموي المنخفضة. بيلاستين (BL) هو مضاد أنتقائي للهستامين H1 مع توافر البيولوجي بنسبة 59%. **الهدف:** استخدام تقنية liquisolid لتحويل السائل BL S-SNE إلى مسحوق بحيث يمكن استخدام كل من إجراءات S-SNE و liquisolid. **الطرائق:** تم استخدام حمض الأوليك، توين 60، ترانسكوتول، وسولوبلس لصنع السائل المحمل ب BL S-SNE الذي تم امتصاصه على مضافات Avicel PH101 و Aerosil 200. تم اختبار خصائص الذوبان في المختبر وتدفق المسحوق. كما تم استخدام SEM و DSC وحيود الأشعة السينية وتحليل FT-IR ومتوسط حجم القطرة بعد التشتت في 0.1N HCl لتحديد الحالة الصلبة لأفضل صيغة. **النتائج:** يتكون أفضل سائل صلب، SS-F2، من حمض الأوليك، توين 60، ترانسكوتول، وسولوبلس، أفيسيل 101، وأيروسيل 200 مع نسبة SNE سائلة إلى Avicel 101 تبلغ 1.5 : 1 ونسبة Avicel 200 إلى Aerosil 200 تبلغ 10 : 1. أظهر SS-F2 قابلية تدفق جيدة وتحسنا كبيرا في إذابة الدواء، تم إطلاق 100% من الدواء بعد 60 دقيقة مقارنة ب 62.27% من أقراص BL التجارية. وفقا لفحص الحالة الصلبة للصيغة، تبين أن BL في حالة مذابة في النظام النانوي المتصلب، مع عدم وجود تفاعلات مع السواغ المستخدم. كما شكل مستحلبا نانويا بمتوسط أحجام قطرات يبلغ 77.57 نانومتر و PDI يبلغ 0.4178، والذي كان مشابها للسائل. **الاستنتاج:** تقنية liquisolid هي طريقة محتملة لترسيخ نظام الاستحلاب الذاتي السائل مع الحفاظ على خصائص مستحلب التانو الذاتي وزيادة معدل الذوبان.

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INTRODUCTION

Poor water solubility is an issue prevalent in many new drug candidates, which frequently results in low oral bioavailability [1]. In particular, self-nanoemulsifying drug delivery systems (SNEDDS) are a new way to improve the oral bioavailability of medications that don't dissolve well in water but can be absorbed well through the intestinal wall. SNEDDS are typically liquid formulations and are superior to conventional emulsions in some ways. For instance, SNEDDS formulations have greater physical stability, are simpler to scale up and manufacture on a large scale, and can be transformed into unit dosage forms to increase patient compliance [2]. Liquid Supersaturable self-nanoemulsion (LS-SNE) refers to a pre-concentrate or anhydrous mixture made from a variety of excipients, including oils, surfactants, and co-surfactants with precipitation inhibitors, in which the drug candidates are dissolved [1,3]. When SNEDDS are administered orally, they are intended to create a transparent emulsion with average droplet sizes of about 100 nm when they come into contact with gastrointestinal fluids under normal gastrointestinal motility conditions [4]. The poorly soluble drugs are typically kept dissolved in the inner phase of the resulting SNEDDS and are thus solubilized in this manner [5]. The majority of the ingredients used in SNEDDS as drug vehicles are intestinal lymphatic absorption promoters and permeability bioenhancers, which improve bioavailability. While liquid SNEDDS have some other advantages, like simple preparation methods and low cost, they also have some drawbacks [6]. Some of these drawbacks arise from the higher cost of the necessary processes for the conversion of SNEDDS into suitable dosage forms, like the filing of soft capsules or sealed hard capsules (7). In addition to the low storage stability of liquid SNEDDS and short shelf life [8]. Also, they are hardly suitable for the development of controlled release dosage forms, and they pose the risk of interactions with the material of the capsule shell and leakage from the capsule [1]. So the conversion of liquid to solid SNEDDS could overcome these drawbacks. Solid carrier materials have generally been assigned up to this moment for the solidification of lipid-based drug delivery systems based on their potential to enable high oil loading efficiency, good redispersibility, and adequate product properties [9]. The adsorption technique was selected for this study as the simplest, most inexpensive, and most accessible process control method with a high level of stability [10,11]. Bilastine, also called 2-[4-[2-[1-(2-ethoxyethyl) benzimidazole-2-yl] piperidine-1-yl] ethyl] phenyl]-2-methylpropane acid, has the chemical formula C₂₈H₃₇N₃O₃. It is a second-generation non-sedating H₁-antihistamine that was approved for the symptomatic management of seasonal or chronic allergic urticaria and rhinoconjunctivitis [12]. The goal of this study was to create a solid, supersaturable, self-

nanoemulsion that would serve as a lipid nanocarrier for bilastine. It is a BCS class II drug with high permeability and low solubility [13]. The prepared liquidsolid powders were evaluated in order to select the most optimal formula, which was then tested for solid-state characteristics and re-dispersion properties to determine whether the method for solidification was practical.

METHODS

Materials

The following components were used to develop solid supersaturable SNE (SS-SNE): bilastine (HyperChem LTD Co., China); pharmaceutical-grade oleic acid oil (Hunan ER-KANG Pharmaceutical Co., Ltd., China); tween 60 (Xi'an Sonwu Biotech Co., Ltd., China); transcutol® HP (Energy Chemical Company, China); soluplus (BASF Co., Germany); avicel PH101 (Safa Pharmaceutical Industries Co., Iraq); Aerosil (Al-Mansour Pharmaceutical Industries Co., Iraq).

Selection of proper solid adsorbent

The selected liquid supersaturable self-nanoemulsion (LS-SNE) formula that could be prepared with a lower liquid volume was converted into dry solid powder using different porous hydrophilic or hydrophobic adsorbents, including mannitol, starch® 1500, Avicel PH101, Avicel PH 102, and Aerosil 200. Utilizing the levigation method, the liquid loading capacity of each solid adsorbent was calculated. In a mortar, a fixed weight of the chosen LS-SNE formula was poured. Once the carrier had been added gradually, it was mixed with a pestle until a uniform powder was obtained [14]. The weight of all the carriers needed to completely adsorb a unit dose of LS-SNE was then calculated. The LS-SNE formula adsorbed by one gram of the tested solid carrier was used to represent the adsorption capacity [14].

Formulation of bilastine loaded supersaturable self-nanoemulsion liquisolid powder

The bilastine-loaded self-nanoemulsion LS-SNE was made by dissolving the exact amount of BL in 20% w/w oleic acid, 40% w/w tween 60, 40% w/w transcutol, and 5% w/w soluplus, which were used as oil, surfactant, cosurfactant, and precipitation inhibitor, respectively. A clear liquid was then obtained by stirring and sonicating the mixture with a Sonicator (Qsonica, LLC, Q500, USA) using 50% amplitude at 2 seconds on and 2 seconds off for 5 minutes. Then, for the purpose of solidifying the prepared LS-SuSNE, a combination of Avicel PH101 and Aerosil 200 was chosen as the carrier and coating materials, respectively. For the preparation of liquisolid powder, three different carriers: LS-SNE ratios (1:1, 1.5:1, and 2:1) and carrier-coating materials ratios (R = 10, 15, and 20) were tested, as shown in Table 1.

Table 1: Composition of the solidified bilastine supersaturable self-nanoemulsion

Formula code	Carrier:LS-SNE ratio	Avicel PH101: aerosol 200 ratio	LS-SNE dose (mg)	Avicel PH101 (mg)	Aerosol 200 (mg)	Formula weight (g)
SS-F1	1:1		548	548	54.8	1.151
SS-F2	1.5:1	10	548	822	82.2	1.45
SS-F3	2:1		548	1096	109.6	1.754
SS-F4	1:1		548	548	36.53	1.133
SS-F5	1.5:1	15	548	822	54.8	1.425
SS-F6	2:1		548	1096	73.06	1.72
SS-F7	1:1		548	548	27.4	1.123
SS-F8	1.5:1	20	548	822	41.1	1.41
SS-F9	2:1		548	1096	54.8	1.7

A mortar and pestle was used to pour the liquid oily formulation onto the surface of porous carriers (avicel PH101 and Aerosil 200), which were then thoroughly mixed and put through a sieve number 30 sieve to produce a homogeneous powder and left for 48 h at room temperature [15]. Following this, the prepared powder was evaluated for its flow characteristics in order to optimize the carrier:LS-SNE ratio before being put into 0-size capsules.

Evaluation of micrometric properties of SS-SNE

Estimating the powder flow properties before the capsule filling process is one of the crucial steps for controlling the uniformity of a powder mixture of SS-SNE. As inadequate powder flows have a negative impact on the consistency of blending, this results in incorrect filling and dosage and ultimately defective end products. The laboratory tests for flow property assessment are angle of repose (θ°). Carr's compressibility Index (CI%) and Hausner's Ratio (HR) were calculated by measuring bulk density and tapped density [16]. The obtained values were compared to the United States Pharmacopeia's flowability range [17]. The powder mixture was packed into hard gelatin capsules and subjected to more study.

Disintegration time measurement

In each of the six tubes of the disintegration apparatus basket, one capsule was placed. The disintegration medium was 0.1 N HCl, which was maintained at $37 \pm 0.5^\circ\text{C}$. After that, the disintegration apparatus was operated. The test was carried out to record the disintegration time when the capsule shell and its contents pass entirely through the basket mesh. The accepted value for capsule disintegration is up to 30 minutes [18].

Drug content of bilastine loaded SS-SNE

In order to ensure that each capsule contains the necessary amount of drug substance, the drug content was determined. A known, accurately weighed amount was added to ethanol and stirred for about 15 minutes for all SS-SNE formulas. The sample was then

centrifuged for 15 minutes at 3500 rpm to separate the undissolved excipients. The supernatant had been appropriately diluted. Then, its drug content was measured spectrophotometrically at 283 nm [16,19].

In-vitro bilastine dissolution from SS-SNE

With the help of a USP type II (RC-6 Dissolution Tester, Germany) dissolution device, you could figure out how BL is released from solid self-nanoemulsion capsules. 300 ml of 0.1 N HCl were used as the dissolution medium, and the paddle rotated at a speed of 100 rpm at 37°C . A 5 ml sample was collected and replaced with an equal volume of a fresh dissolution medium at periodic intervals. To filter the withdrawn samples, a 0.22-mm filter syringe was used. The UV spectrophotometer (UV-1900i Shimadzu Spectrophotometer, Delhi) was used to measure the amount of BL in the filtrate at 278 nm. Additionally, the *in vitro* dissolution of marketed BL tablets (Alerbix) was also determined. For comparing a single value, the model-independent approach was applied to evaluate the dissolution profiles of prepared SS-SNE capsules and alerbix tablets. The percent dissolution efficiency (% DE_{10min}), the mean dissolution time at 60 minutes (MDT_{60 min}), and the similarity factor (f₂) were computed [20]. The dissolution data were analyzed using the DDSolver software program. According to the data collected from the flow parameter evaluation, drug content, and *in-vitro* dissolution tests, the selection of the best BL-loaded SS-SNE formula was made for further investigation.

Morphological analysis

The external particle shape and surface morphology were investigated through using the following test:

Field emission-scanning electron microscopy (Fe-SEM) – energy dispersive spectroscopy (EDS)

The external particle shape and surface morphology were investigated using the Fe-SEM (FESEM EDS). It was carried out for the optimal formula of BL-loaded SS-SNE (formula SS-F2) and pure BL. With the help of double-sided adhesive tape, each powder sample was sprinkled onto the specimen stub. Each sample had a 20

μm gold layer applied to it for electrical conduction at room temperature [21].

Differential scanning calorimetry (DSC) thermal analysis

DSC (DSC 60, Shimadzu, Japan) was used for assessing the thermal behavior of BL and the physical mixture of equal amounts of BL, as well as the optimized formula. Each sample had a weight of around 2 mg and was put into a typical aluminum pan. Under the flow of nitrogen gas, the samples were heated at a rate of 10°C per minute from 25°C up to 300°C [22].

Analysis of X-ray diffraction

For the best formula, the physical mixture of BL with Avicel PH 101 and aerosol 200 at a 1:1:1 ratio and pure BL powder was analyzed by X-ray diffraction. Using the copper-target X-ray tube, the diffractometer (Xrd Phillips Xpert PA Analytical, Holland) was operated to scan over a 2θ at an angle of 2–80 degrees. The measurement was performed at a 40 kV voltage, a 30 mA current, and an 8 degree/min scan speed.

Reconstitution characteristics of the selected BL solid self-nanoemulsion capsule

By mixing and stirring on a magnetic stirrer for 30 minutes, the selected formula was reconstituted after a 100-fold dilution of liquisolid powder with 0.1 N HCl and compared to LS-SuSNE. After that, it enabled settling for the measurement of supernatant droplet size. A particle size analyzer (Malvern Zetasizer, USA) was used to measure the average droplet size and PDI.

Statistical analysis

The experiment's findings were presented as the mean and standard deviation (SD) of samples taken in triplicate. by using one-way analysis of variance (ANOVA) to find significant differences between the relevant data. The results of dissolution were represented by the similarity factor (f_2). When using Microsoft Excel 2016, at a p-value less than 0.05, the outcome was deemed significantly different.

RESULTS AND DISCUSSION

Based on our preliminary research, we were able to successfully prepare BL LS-SNE that quickly emulsified as an o/w emulsion upon dilution within 34 ± 2.48 seconds. The polydispersity index (PDI) was 0.33 and the droplet size was 73.59 nm. The amount of LS-SNE adsorbed by one gram of the tested solid carrier was used to represent the adsorption capacity. Levigation was used to calculate each solid adsorbent's capacity to hold liquid. According to the results of our pre-formulation study, the diluent Avicel PH101 had a lower adsorbing capacity 0.86 ± 0.08 g of LS-SNE/1g of Avicel PH101 than the adsorbent Aerosil 200, which

had a capacity of 2.8 ± 0.13 g of LS-SNE/1g of Aerosol 200 (Figure 1).

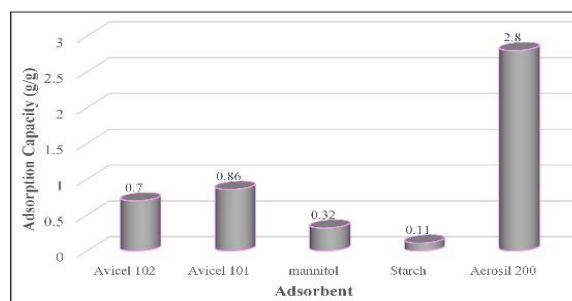


Figure 1: The ability of various pharmaceutical carriers to adsorb 1 g of liquid SNEDDS.

The blending uniformity has been negatively impacted by insufficient powder flow, which has led to inaccurate filling doses and, ultimately, defective end products [23]. Various micrometric properties of SS-SNE formulations were determined to evaluate the flowability characteristics of the powder that was produced, as shown in Table 2. The angles of repose of more than 50, 25–40, and less than 25, respectively, correspond to poor, moderate, or excellent powder flow properties [24]. The Cars compatibility index (IR) and Hausner ratio (HR) were calculated for each formula using equations that are dependent on the bulk and tapped densities (p -bulk and p -tap). Powders with an HI of less than 1.25 are expected to have acceptable flowability, and those with CI in the range of 5–18% are considered appropriate for the production of solid dosage forms [25]. There was no significant difference ($p > 0.05$) concerning all micrometric properties between formulas within the same group that have the ratio 10, 15, or 20 of Avicel PH101: aerosol 200 ratio, except for Cars' Index between F1 and F2, where there was a significant difference ($p < 0.05$). Table 2 illustrates the flowability results, showing that angle and repose, Cars' Inde and Hausner ratios ranged between 24.99 and 37.4560, 9.01 and 18.33%, and 1.1 and 1.19, respectively. The variation in flowability may be related to the concentration of aerosol 200 in each formula, since it is well known that aerosol can impact the flowability of powders [10]. Higher concentrations of aerosol 200 generally enhance the flow properties by reducing friction between particles and promoting better dispersion [26]. Similar results had been investigated by Jabbar and Hussein [27]. Table 3 presents the findings of the drug content analysis. The drug content percentages of all the prepared formulations fell within the acceptable limits (85%–115%) defined by the USP pharmacopoeia [28]. The highest drug contents were 99.62 and 99.7 in SS-F2 and SS-F8, respectively, indicating successful entrapment without any precipitation or degradation.

Table 2: The flowability parameters of solid self-nanoemulsion formulations at various avicel: aerosil ratio R=10, R=15, and R=20

Formula code	Angle of repose	Cars' Index	Hausner Ratio	Flow Type
SS-F1	31.64±0.70	14.65±1.43	1.17±0.02	Good
SS-F2	24.99±1.30	9.01±0.015	1.1±0.01	Excellent
SS-F3	26.31±0.68	12.02±0.88	1.136±0.01	Excellent
SS-F4	28.75±0.18	10.14±1.03	1.11±0.017	Excellent
SS-F5	32.01±0.1	14.05±0.89	1.16±0.012	Good
SS-F6	31.33±0.5	13.01±0.023	1.15±0.0	Good
SS-F7	35.54±1.3	16.44±1.19	1.19±0.015	Fair
SS-F8	33.47±0.22	13.66±1.19	1.155±0.018	Good
SS-F9	37.456±0.27	18.33±2.28	1.185±0.008	Fair

Table 3: Drug content percent and disintegration time of solid bilastine-loaded self-nanoemulsion

Formula code	Drug content (%)	Disintegration time (min)
SS-F1	93.83±1.15	2.07±0.06
SS-F2	99.62±0.33	2.05±0.02
SS-F3	94.95±1.56	2.48±0.09
SS-F4	97.83±2.73	2.26± 0.4
SS-F5	98.5±1.55	2.43±0.33
SS-F6	94.8±1.153	2.3±0.186
SS-F7	96.±2.0	3.14±0.72
SS-F8	99.7±0.3	2.07±0.03
SS-F9	92.3±3.2	3.46±0.25

The disintegration time of the prepared hard gelatin capsules ranged from 2.05±0.02 to 3.46±0.25 min, as shown in Table 3. No significant difference ($p>0.05$) was obtained among the various formulations tested. Notably, all solidified self-nanoemulsion capsules did not exceed 4 minutes for disintegration. Avicel PH101 may have contributed to that outcome. It is well known as an excipient that is insoluble, swellable, and has excellent disintegrating properties [29]. As a result, the capillary action of the porous fibrous structure can quickly draw up or wicked the disintegrated media, swelling and rupturing the inter-particulate bonds of the solid powder [30]. Aerosil 200 may also be related to acceptable disintegration times of formulas related to its hydrophilic nature [31]. All prepared formulas were subjected to an in vitro release study as they showed acceptable flowability properties and appropriate drug content and disintegration time, in addition to "Alerbix," the marketed bilastine tablet, for comparison using 0.1 N HCl. Figure 1 shows that at a fixed carrier to liquid formula (carrier:LS-SNE) ratio (1:1), the percent of BL released from the prepared capsule was 92.535 %, 94.164%, and 75.132 % of formulas SS-F1, SS-F4, and SS-F7, respectively. Figures 2 and 3 also show the release of BL from SS-F2, SS-F5, and SS-F8 with a constant ratio of (1.5:1) carrier:LS-SNE, which was 96.716%, 75.109%, and 94.189%, and from SS-F3, SS-F6, and SS-F9 with a 2:1 ratio of carrier:LS-SNE, which was 80.69%, 87.477%, and 68. According to the results of in vitro drug release, the percent of a drug that dissolves was found to be directly correlated with the excipients ratio (R-value), and all prepared formulas

significantly ($p<0.05$) improved dissolution more than reference tablets. These results may be attributed to the effect of Aerosil 200, as it adsorbs water in relatively small quantities and retains it in large pores [32]. This effect may enhance the dissolution of formulas that have a larger amount of aerosol 200. Albertini et al. also observed the enhancement effect of aerosil 200 on the release of Theophylline from theophylline loaded microparticles of lipid carriers [33].

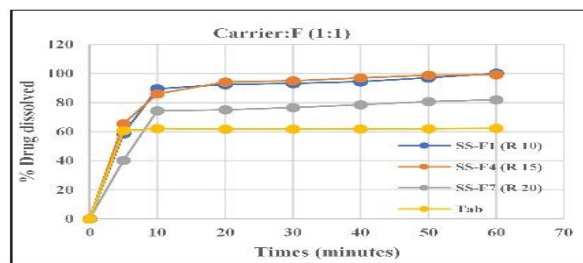


Figure 2: Bilastine-loaded solid self-nanoemulsion dissolution profiles at various (R= carrier: coating) and constant carriers LS-SNE (1:1) in 0.1N HCl with alerbix.

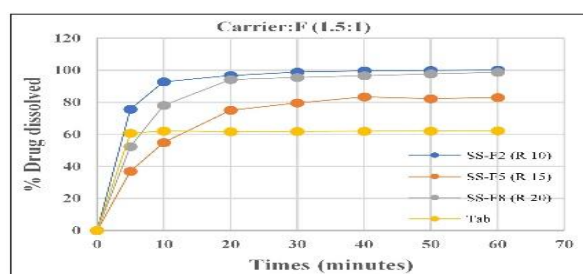


Figure 3: Bilastine-loaded solid self-nanoemulsion dissolution profiles at various (R= carrier: coating) and constant carriers LS-SNE (1.5:1) in 0.1N HCl with alerbix.

Table 4 illustrates the dissolution parameters of the SS-DNE formulas. The percent of drug dissolved in 10 minutes ranged from 54.88 to 92.8%; the mean dissolution time was 4.81–10.21 minutes; and the dissolution efficiency was 64.1–92.11%. SS-F2 was selected according to its high dissolution test, low disintegration time, and acceptable drug content and flowability.

Table 4: Dissolution parameters of SS-SNE formulas

Formula code	Q _{10min} (%)	MDT _{60min} (%)	DE (%)	F2
SS-F1	89.49	7.68	87.316	27.40
SS-F2	92.8	4.81	92.11	24.92
SS-F3	71.01	10.21	79.4	31.80
SS-F4	86.1	6.38	88.68	26.90
SS-F5	54.88	9.23	70.2	37.98
SS-F6	68.45	9.65	81	28.21
SS-F7	74.39	7.48	71.32	40.13
SS-F8	78.1	7.56	86.35	27.56
SS-F9	60.195	8.33	64.1	48.64

As shown in Figure 4, the BL photomicrograph revealed rectangular crystals with smooth surfaces of varying sizes, indicating a crystalline nature, which would be further confirmed by the DSC and XRD.

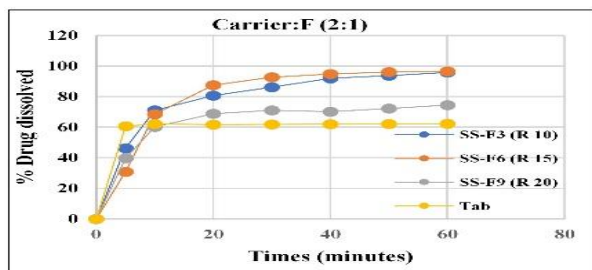


Figure 4: Bilastine-loaded solid self-nanoemulsion dissolution profiles at various (R= carrier: coating) and constant carriers LS-SNE (2:1) in 0.1N HCl with alibrix.

Additionally, the optimum formula SS-F2 demonstrated that the morphology had completely changed, as seen in Figure 5, and a bar-like shape was not observed. There was a complete absence of the rectangular crystalline nature of raw BL, proving that the liquid SNEDDS adsorption process was successful and that the BL crystals converted into molecular dispersion within oily components.

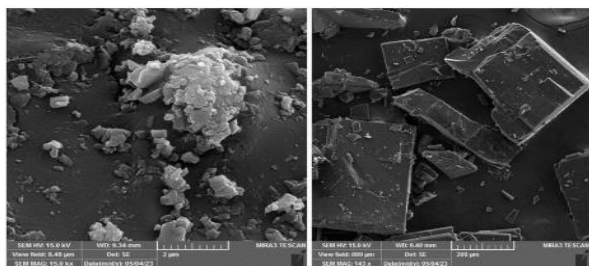


Figure 5: The photomicrographs of bilastine pure powder at two magnification power of Fe-SEM.

As shown in Figure 6, the DSC thermogram of pure BL powder showed a single sharp peak at 203.4 oC in the endothermic heat flow direction, which corresponds to its melting point in accordance with previously published data [34]. Such a sharp peak demonstrated BL's highly pure crystal nature.

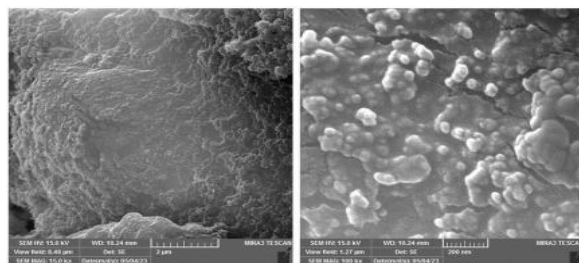


Figure 6: The photomicrographs of optimum formula (SS-F2) at two magnification power of Fe-SEM

The physical mixture thermogram (Figure 7) also showed an endothermic peak for BL at 205 °C, which is its original melting point, indicating that solid adsorbents and BL were compatible. In other words, the BL was still in its pure crystalline form and had not been impacted by its mixing with Avicel or Aerosil 200.

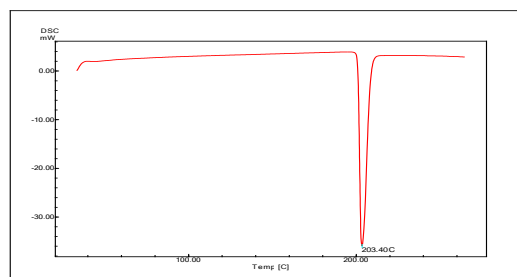


Figure 7: DSC thermogram of pure bilastine powder.

Figure 8 shows that the solid SS-F2 did not show any signs of crystallization, which means that the BL and the formula's components mixed perfectly and dissolved completely. It has been demonstrated that BL was molecularly dispersed in the solid formula.

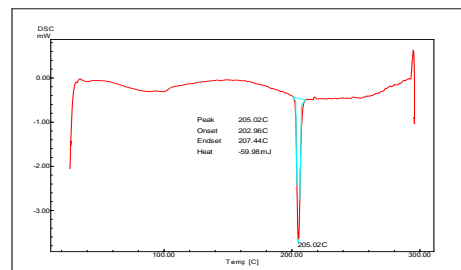


Figure 8: DSC thermogram of physical mixture of 1:1:1 of bilastine, Avicel PH 101 and aerosil 200.

Figures 9, 10, and 11 showed the X-ray diffraction profiles of pure BL, a physical mix of 1:1:1 bilastine, Avicel PH 101, and Aerosil 200, and the solid formula SS-F2. The diffractogram X-ray of pure BL powder displayed sharp, intense characteristic peaks at diffraction angles of 11.6, 14, 17.7, 18.8, and 20.1. This pattern indicated the crystallinity of BL and agreed with that reported previously in the literature [35].

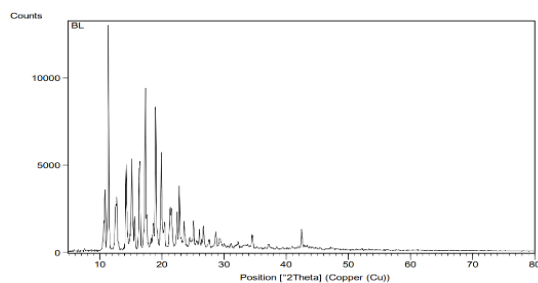


Figure 9: The X-ray diffractogram of pure bilastine powder.

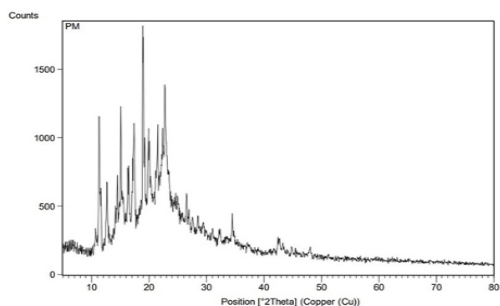


Figure 10: The X-ray diffractogram of physical mixture of 1:1:1 of bilastine, Avicel PH 101 and aerosil 200.

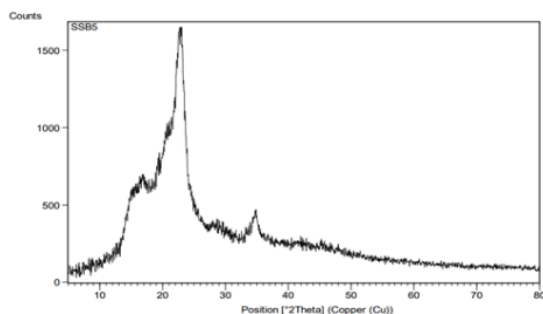


Figure 11: The X-ray diffractogram of optimum formula (SS-F2).

Similarly, the diffractogram of the physical mixture revealed that all characteristic peaks of BL were retained but with different intensities, indicating that the crystallinity of BL remained unchanged after the mixing process. On the other hand, the characteristic peaks of BL completely disappeared in the solid formula SS-F2, and instead there were diffused broader peaks, suggesting that BL was present in a solubilized state in oily excipients and at the same time retained in the solidifying agents with no drug precipitation. There were only diffused peaks at 15.23 and 22.32 that were associated with Avicel pH 101 [36]. The results of DSC and X-ray diffraction clearly revealed the full transformation of crystalline BL into a molecular dispersion state. In other words, these findings indicated that BL is incorporated in solubilized form within its formula even though the dosage form is solid, which explains the enhancement in the dissolution rates. Such

results concurred with previous studies [37,38]. The self-nanoemulsifying properties of LS-SNE must be preserved for effective conversion into solid dosage forms. In other words, similar to LS-SNE performance, the solidified SS-SNE is anticipated to quickly form nanoemulsion upon contact with aqueous medium and agitation in GIT. This would indicate that the solidification techniques and/or carriers used had no impact on the globule size. The capsule formula (SS-F2) had mean droplets of about 77.57 ± 1.45 nm with PDI 0.42 ± 0.04 and was similar to LS-SNE, which had mean droplets of 73.59 ± 1.22 nm with PDI 0.33 ± 0.008 without significant difference ($p > 0.05$). It was clear that the SS-SNE retained the ability of the LS-SNE components to emulsify their components and that the system was capable of maintaining system qualities and properties suitable for large-scale capsule production or may compress into tablets.

Conclusion

With a cheap adsorption method based on the idea of liquid solids, Bilastine LS-SNE could be solidified while the droplets kept their nanoscale size after being spread out. The final liquid solid powder showed excellent flowability and a notable improvement in dissolution rate compared to marketed tablets. A promising method for solidifying a liquid self-emulsifying system is the liquid solid technique.

Conflicts of interest

There are no conflicts of interest.

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Data sharing statement

Supplementary data can be shared with the corresponding author upon reasonable request.

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