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Research Article

Preparation and Characterization of Isradipine as Surfactant-Free Dry Emulsion

Zahraa M. Naji[1]*, Fatima J. Jawad[2]

[1] *Ministry of Health and Environment, Al-Najaf Health Directorate, Al-Najaf, Iraq.*
[2]*Department of Pharmaceutics, College of Pharmacy, University of Baghdad, Baghdad, Iraq.*

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Abstract:

Background: The prevalence of hypertension in Iraqi children is increasing, and most drugs are not suitable for children, leading to unsafe off-label use. Liquid dosage forms are favorable for pediatric patients due to their dose flexibility. Isradipine, the preferred oral therapy for severe hypertension in pediatrics, belongs to the biopharmaceutical classification system class II. Its oral bioavailability is approximately 15 to 24 %, so it needs to be made as a surfactant-free emulsion for improved oral bioavailability and pediatric safety, but it lacks physicochemical stability. Surfactant-free dry emulsion is a promising solution to all these challenges.

Objectives: The study aims to create a stable, eco-friendly, and surfactant-free oral oil in water emulsion of Isradipine for pediatric patients, protecting it from hydrolysis, oxidation, and photosensitivity and increasing its solubility and absorption.

Methods: The study used Corn oil for solubilizing Isradipine, and then the surfactant free emulsion was stabilized by different percentages of β-cyclodextrin. Eight formulas were prepared using a homogenizer and mixed for 5 minutes at 10,000 rpm and 25ºC. The surfactant free emulsion (SFE) formulas were evaluated for organoleptic attributes, thermodynamic stability, viscosity, pH, drug content, droplet size distribution, and in-vitro dissolution. Then, the selected formula was lyophilized with 15gm Mannitol using a freeze-drying system. The experimental results were expressed as a mean triplicate sample ± standard deviation (SD) and were analyzed according to a one-way analysis of variance (ANOVA).

Results: Among all the prepared surfactant-free emulsion formulas, F4 containing 8g of beta-cyclodextrin (β-CD) and 15g of Corn oil was chosen as the optimum SFE formula due to its small particle size range of 1451±0.01 nm, respectable pH, good organoleptic attributes, excellent thermodynamic stability, acceptable viscosity 1869.5±1.54 mg/ml, acceptable drug content percentage, and drug release in 90minuets. F4 was freeze-dried and then further evaluated for Flow and compressibility Properties.

Conclusion: The study found that surfactant-free emulsion provided an important pediatric dosage form for the oral water-insoluble drug. It improves the dissolution rate and solubility of Isradipine.

Keywords: Beta-cyclodextrin; Corn oil; Pickering emulsion**;** Surfactant-free dry emulsion; Surfactant-free emulsion.

Introduction:

Hypertension is the third most common chronic pediatric disease, with a prevalence in Iraqi children increasing from 1.7% (1) in 2006 to 19.6% in recent years (2). Factors contributing to this increase include family history, low birth weight, high body mass index, insulin resistance, and sympathetic nervous system activation (3, 2). Hypertension is also common in Iraqi children with type 1 diabetes (4) and dyslipidemia among Iraqi teenagers (5).

Pediatric patients have unique pharmacokinetics, pharmacodynamics, administration routes, toxicity, and taste preferences compared to adults. This necessitates the development of convenient formulations for children of all age groups due to their varying responses to active substances and excipients (6, 7).

The majority of drugs in the market are not suitable for children, leading to unsafe off-label or extemporaneous compounding practices. Thereby, crushing hard tablets containing the active pharmaceutical ingredient can alter the rate of drug dissolution and absorption, increasing risks of inaccurate dosing, hospitalization, elevated healthcare costs, contamination, and death would be increased. Therefore, it is necessary to have convenient formulations for children in all age groups (8, 9). The optimal pediatric formulations should have low dosing frequency, appropriate dosage forms for

*Corresponding Author: zahraazmnm23@gmail.com

different age groups, convenient administration, minimal impact on ifestyle, use of
non-toxic, well-tolerated excipients, taste masking, easy production, elegant, stable, and cost-efficient manufacturing (7).

Liquid dosage forms are advantageous for pediatric patients and infants due to their dose flexibility and ease of swallowing (9). Emulsions are dispersions of two immiscible liquids that are thermodynamically unstable and need to be stabilized by surfactants (10) However, synthetic emulsifiers in these systems can cause health problems and toxic symptoms with prolonged use. Clinical tests show that anionic emulsifiers may bind to proteins, enzymes, and phospholipid membranes, leading to adverse effects such as enzyme dysfunction, protein structure modification, and phospholipid changes in the cell membrane (11).

Pickering emulsion is a surfactant-free emulsion (SFE) stabilized by solid particles (12). These non-toxic, biocompatible, and biodegradable stabilizers are edible, natural substances, readily available and inexpensive. This unique structure for SFE endows them with good stability, excellent biocompatibility, and environmental friendliness (13).

Liquid emulsion offers several advantages over other dosage forms, including improved oral bioavailability, but it exhibits a lack of physicochemical stability. Dry emulsion formulations are a promising solution to these challenges (14).

Dry emulsions are prepared using lyophilization, this process prolongs shelf-life by shielding the drug from oxygen, light, and water. Dry emulsions are also easier to handle and storage than liquid emulsions (15).

Isradipine is a calcium channel blocker drug. It is the drug of choice for oral therapy of hypertensive crisis. The usual dose of Isradipine for pediatrics is 0.05–0.1mg/kg/dose/8hr up to 5 mg/dose (16). Isradipine is a class II drug according to the biopharmaceutical classification system (17).

The study aims to create a stable, eco-friendly, and oral oil in water surfactant-free dry emulsion (SFDE) of Isradipine for pediatric patients, protecting it from hydrolysis, oxidation, and photosensitivity and increasing its solubility and absorption.

Materials and Methods:

Isradipine and Native β-CD were purchased from Hyper Chem Company, China. Olive oil supplied by Pomace Olive oil Oilex ,S.A. Spain. Avocado oil and almond oil were obtained from Now (USA). Corn, grape, sesame, sunflower, soybean, canola, and cottonseed were bought from Shaanxi Guanjie Technology CO, LTD ,China. HCl was purchased from Avantor Performance Materials. Sodium Dodecyl Sulfate (SDS) was purchased from Panreac Barcelona, Spain. Methanol was obtained from Sigma-Aldrich, Germany. Janeen supplied deionized water for chemical and laboratory materials in Baghdad, Iraq.

Methods

Solubility Study of Isradipine

Isradipine's saturated solubility was tested in various oils: Sesame oil, Olive, Sunflower, Almond oil, Soybean oil, Canola oil, Grape seed, Cotton seed, Avocado oil, and Corn oil. An excess amount of Isradipine powder was added to 5 grams of each oil in small plain tubes to measure the solubility. These tubes were tightly closed and placed in an isothermal shaker water bath at 25 ± 0.5 °C for 48 hours (18). After 48 hours, the samples were centrifuged at 3000 rpm for 20 minutes. The supernatant layer of each sample was then filtered using a 0.45 µm filter membrane. Once filtered, the samples were diluted with methanol, and the solubility was evaluated at λ max at 326nm using a UV-visible spectrophotometer (19).

Formulations of surfactant-free emulsions of Isradipine

Isradipine SFE was prepared by using β-CD in different weights as stabilizers instead of surfactants with a selected oil based on a solubility study as the oil phase, as seen in Table 1. The drug dose incorporated in each of these formulations was 2.5 mg of Isradipine/5 mg of SFE. The method of preparation is the mechanical method, where the specified Weight of the drug is dissolved in the oil (as the oil phase), while in another beaker, the specialized amount of β-CD with deionized water (as the aqueous phase), then while continuously mixing the aqueous phase by using a homogenizer (Witeg HG-15D), dropped the oil phase containing drug slowly on it then the homogenizer still mixed for 5 minutes at 10,000 rpm at 25ºC to obtain surfactant free o/w emulsion. The percent of each component is based on a ternary phase diagram and references (20, 21). As shown in the Table 1.

The selected formula was lyophilized with 15gm of Mannitol by using a drying system (Labconco, USA) to obtain SFDE (20).

Table 1. Components of surfactant-free emulsion for Isradipine

F. NO.	β-CD (g)	Corn oil(g)	Water (g)	drug(mg)
F1	2	15	83	50
F2	4	15	81	50
F3	6	15	79	50
F4	8	15	77	50
F5	2	20	78	50
F6	4	20	76	50
F7	6	20	74	50
F8	8	20	72	50

Evaluation of the prepared surfactant-free emulsion

Evaluation of organoleptic attributes

The study evaluated the organoleptic attributes of formulations, including color and odor, through visual and olfactory evaluation. The texture of emulsions was assessed by pressing a small amount between the thumb and index finger. At the same

time, consistency was evaluated based on homogeneity. The ease of removal of emulsions was also assessed after washing the body part with tap water (22).

Thermodynamic stability studies: Due to their different densities between oil and aqueous phases, emulsions rapidly separate into oil and water layers, making them thermodynamically unstable systems. The stability of emulsions means their ability to maintain their properties. Their strength depends on phenomena like flocculation, sedimentation, creaming, phase inversion, Ostwald ripening, and coalescence, which contribute to their destabilization (10)**.**

a) Observation of phase separation: Ten ml of the prepared emulsions were stored in tubes fixed vertically at room temperature (25 ± 2 °C) and evaluated for instability phenomena after 1, 2, 4, 6, and 24 h of preparation (23).

b) Heating-cooling cycle: Six cycles of temperature changes (4 ºC to 45 ºC) were conducted in a refrigerator, then storage at each temperature for 48 hours, and the stability of the formulations was examined at temperatures (24).

c) Freeze-thaw cycle: By this test, the emulsion was stored at -5 ºC (in a fridge) for 24 hrs. Then, at 27 ºC (at room temperature) for 24 hrs. Then, in an oven at 40 ºC for 24 hrs. The results were recorded for further studies (25).

Viscosity determination: The viscosity of a prepared SFE sample was determined without dilution using a digital viscometer and spindle number 4, which was inserted into a glass beaker at different speeds: 6, 12, 30, and 60 rpm (26).

Particle size distribution determination: The SFE's mean particle size distribution was measured using a laser particle size analyzer instrument (Malvern Instruments Ltd Great Britain) by taking the angle of detection at 90º and 25 ºC after being diluted fivefold with double-deionized water before measurements (20).

pH measurement: The pH measurement was done using a pH meter. A glass electrode was dipped in SFE emulsion, and the reading was noted (27). The measurement was repeated three times for each sample, and the result was presented as mean ±SD.

Drug content estimation: Accurately, 5gm of each SFE formula which contains 2.5mg of Isradipine was dissolved in 100 ml Methanol, then filtered using a 0.45 µm filter syringe and suitably diluted. The contents of Isradipine were determined using a UV/Vis spectrophotometer at the selected λ max 328 nm (17).

The in-vitro dissolution profile of Isradipine SFE: The in-vitro dissolution test of Isradipine SFE was conducted using a paddle assembly type II dissolution test apparatus. Each formula equivalent to 2.5 mg of Isradipine was placed in a dialysis bag. The paddle rotated at 50 rpm at 50 rpm at 37 ± 0.5°C in 250ml of dissolution medium, 0.1N HCl with SDS 1%w/v, to ensure sink condition. An aliquot of 5 ml samples was drawn at predetermined time intervals, and compensated by an equal volume of fresh dissolution medium then, samples were assayed spectrophotometrically using a UV-spectrophotometer at 328 nm. The same procedure was made for the pure drug

Selection optimum Isradipine surfactant-free emulsion: The best formula of Isradipine SFE was selected according to the results that are obtained from the evaluation tests that included intrinsic stability, drug content, pH, particle size, viscosity, accelerated stability, and in vitro release study. Then this formula will be dried by lyophilization to form surfactant free dry emulsion (SFDE).

Evaluation of selected optimum Isradipine lyophilized surfactant free dry emulsion

Flow Properties

These properties were determined in terms of angle of repose, Bulk density, Tapped density, Carr's index, and Hausner's ratio for the SFDE formula (29).

Determination angle of repose

It is a method for assessing the flow properties of powder. It was determined using the fixed funnel method, by permitting a powder to flow throughout a funnel and pass freely onto a surface. The height and diameter of the resultant cone were measured and the angle of repose was calculated from this equation:

$$\text{Tan}(\theta) = h/r$$

Where: h is the height of the powder cone and r is the radius of the powder cone (29).

Bulk density: It is a ratio of the powder mass to bulk volume. The bulk density depends on particle size distribution, shape, and cohesiveness of particles. The weighted amount of the powder was carefully poured into the graduated measuring cylinder through the large funnel and volume was measured, which is the initial bulk volume. Then it was expressed in g/ml. Bulk density was calculated by the following equation (30).

$$\text{Bulk Density} = \text{Weight of powder} / \text{Bulk volume}$$

Tapped density: The graduated cylinder containing a known mass of mixture was tapped for a permanent time. The volume was measured, and the tapped density was calculated by the following equation (30).

$$\text{Tapped Density} = \text{Weight of powder} / \text{Tapped volume}$$

Carr's index (compressibility index)

Carr's index indicates the flow properties of the powder. It was expressed in percentage and was calculated by the following equation (31):

$$\text{Carr's index} = [(\text{Tapped density} - \text{Bulk})/ (\text{Tapped density})] \times 100$$

Hausner's ratio: Hausner's ratio is an indirect index of powder flow. It was calculated by the following equation (31):

$$\text{Hausner's ratio} = (\text{Tapped density})/(\text{Bulk density})$$

Scanning electron microscopy (SEM): By Scanning electron microscope, the morphological

features, including (shape and surface characteristics) of SFE, were evaluated (19).

Statistical analysis

The experimental results were expressed as the mean of triplicate samples ± standard deviation (SD) and were analyzed using one-way analysis of variance (ANOVA) in SPSS software. Results were considered significant if $p < 0.05$ and non-significant if $p > 0.05$.

Results

Solubility study

Isradipine solubility was indicated to be highest in Corn oil (4.9 mg/ml) in comparison to other oils in Table 2, so it was selected as an oil phase for preparing SFE for Isradipine.

Table 2. Saturation solubility of Isradipine in different oils.

Oil	Solubility (mg/ml)*
Sesame oil	1.4±0.01
Olive market	1.41±0.02
Sunflower	1.4±0.13
Almond oil	2.2±0.12
Soybean oil	2±0.06
Canola oil	2.4±0.06
Grape seed	4.7±0.03
Cotton seed	4.6±0.10
Avocado	4.4 ±0.04
Corn oil	4.9±0.017

***Data are presented as mean ± SD of n= 3.**

Evaluation of the prepared surfactant-free emulsion

Evaluation of organoleptic attributes: All formulations freshly prepared have a yellowish-white color. Their appearance is homogenous, with a smooth texture, and no lumps were detected after 24 and 48 hrs, and odorless. They offer smoothness to the touch. After applying all twelve samples to the hand, they were readily removed by washing the body part with running water.

Thermodynamic stability studies

a) Observation of phase separation: The study found that F1 exhibits phase separation after 24 hours, indicating they cannot be further investigated. However, other formulas remained thermodynamically stable during this time, maintaining emulsion stability without phase separation, flocculation, sedimentation, creaming, or phase inversion.

b) Heating-cooling cycle: All formulas pass this test except F2 and F6 so only the formulations that remained stable at these temperatures were exposed to further studies.

c) Freeze-thaw test

F2 and F6 showed oiling-off after 2 cycles of freeze-thaw provided that evidence of coalescence was already evident so that all formulations passed this test except F2 and F6. So there are no further studies for F2 and F6

Viscosity determination: The viscosity range of the investigated formulas is 1665.9-311 mP, as shown in Table 3.

Particle size distribution determination: The particle size range of the investigated formulas is 1451-4112 nm, as shown in Table 3.

Table 3. Viscosity (mP) and Mean droplet size of Isradipine SFE

F. NO.	Viscosity (mP) *	Mean droplet size (nm) *
F3	1665.9±1.62	1825±0.1
F4	1869.5±1.54	1451±0.01
F7	2621±1.38	4121±0.3
F8	3115 ± 1.64	3109±0.02

***Data are presented as mean ± SD of n= 3.**

Determination of pH: The pH related to all the formulations has been determined via pH meter in triplicate at 25 ± 1 °C and indicated to be in the range of 6.2-6.7.

Drug content: The drug content related to all prepared Isradipine SFE was more than 95% and there has been no considerable difference between different formulations ($p > 0.05$),

In vitro drug release: The study reveals a flexible duration time for Isradipine release from each formula, with F4 completely releasing Isradipine after 90 minutes, while F3, F7, and F8 took more than 120 minutes without completing the release. Pure Isradipine showed 15.4% drug release at the end of 120 minutes, as shown in Figure 1.

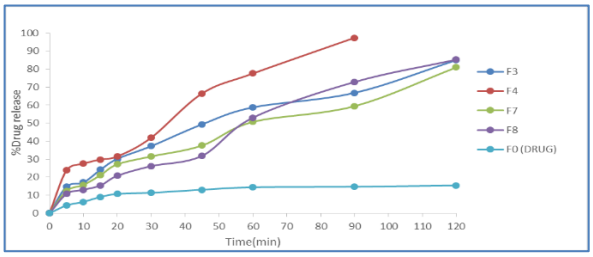

Figure 1. A comparative dissolution profile of Isradipine SFE (F3, F4, F7, F8, and pure Isradipine) in 250ml of 0.1 N HCl (containing 1% SDS) dissolution medium at 37°C.

Selection optimum Isradipine surfactant-free emulsion: Based on previous results, F4 was chosen as the best Isradipine SFE formula since it had a globule size range of 1451±0.01 nm, respectable pH, good organoleptic attributes, excellent thermodynamic stability, acceptable viscosity of 1869.5±1.54 mP, great % drug content and In vitro release 100% in 90 minutes. The selected formula was subjected to further studies.

Evaluation of selected optimum Isradipine lyophilized surfactant-free emulsion

Flow Properties

The flow properties of the selected surfactant-free dry emulsion formula were evaluated. The results are shown in Table 4.

Table (4): The Flow Properties of a surfactant-free dry emulsion of Isradipine.

Parameter	Result*
Angle of repose	34.01 ± 0.015
Bulk density(g/cm3)	0.39 ± 0.024
Tapped density(g/cm3)	0.54 ± 0.014
Carr's index %	27.074 ± 0.163
Hausner's ratio	1.37 ±0.005

***Data are presented as mean ± SD of n= 3.**

Scanning electron microscopy (SEM): The SEM shows the spherical shape of spherical droplets of Corn oil that are surrounded by β-CD as shown in Figure 2.

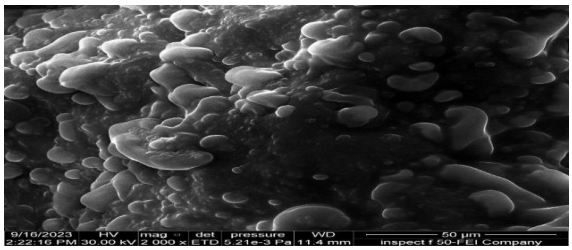

Figure 2. SEM of the selected formula (F4).

Discussion:

According to the solubility result, the choice of corn oil as the oil phase for surfactant-free emulsion of Isradipine based on the highest Isradipine solubility in corn oil to obtain stable formulas with high drug miscibility and superior drug loading (32)**.** Moreover, all prepared formulations were accepted in color, odor, and texture so can be passed to the next evaluation (22).

Thermodynamic stability studies: The results of this study demonstrated that all the prepared SFE formulations were stable except for (F1). The reason for this was the irreversible adsorption of β-CD on oil droplets causes β-CD in the continuous phase to cover the oil droplets' surface, preventing aggregation and improving emulsion stability (33). F1 has an insufficient concentration of solid particles enough to form a robust, dense layer surrounding the oil particles, leading to phase separation (34). Regarding the stability, the formulations that are stable against storage in extreme conditions and ensure the system remains dispersed with no separation (35). All formulas pass this test except F2 and F6. According to Freeze-thaw which is commonly used parameter to evaluate the stability of emulsions, a higher oil phase volume or higher particle concentration has better freeze-thaw stability than that of a lower particle concentration and lower oil phase volume (36). F2 and F6 showed oiling-off after 2 cycles of freeze-thaw, providing that evidence of coalescence was already evident (37), so all formulations passed this test except F2 and F6. The viscosity study found that formulas F4 and F8 had more viscous emulsions than formulas F3 and F7, respectively, due to F4 and F8 having higher amounts of β-CD. This is because excess particles form a network structure around each droplet, improving emulsion stability and increasing emulsion viscosity (33). Systems with a higher volume fraction of dispersed phase have the viscosity of SFE increased by increasing the number of particles (34). Formulas F7 and F8 had more viscous emulsions than the group of formulas F3 and F4, respectively, due to higher oil content (32). This is because as oil content increased, the number of emulsified oil droplets increased, which caused a decrease in the aggregation of oil droplets and resulted in smaller droplet sizes, leading to increased interfacial area, allowing more interactions between one particle and another and increased emulsion viscosity (38).

Particle size distribution determination: The particle size range of the investigated formulas is 1451-4112nm, with variations attributed to the amount of β-CD and oil. The formulas F3 and F7 had larger particle sizes than formulas F4 and F8, respectively, with the same amount of oil due to having a lower amount of β-CD. The increase in particle size by decreasing surfactant concentration can be explained by the partial coverage of oil droplets by solid particles, leading to coalescence and large droplets (39, 40).

Formulas F7 and F8 had larger particle sizes than F3 and F4, respectively, with the same amount of β-CD due to higher oil content and increased oil volume, leading to droplet coalescence and droplet size increase (41, 42).

The pH range of all formulations (6.2-6.7). The acceptable range of pH for oral solutions is (2-9); therefore, all formulations have accepted pH values (43).

Drug content: The drug content of all prepared Isradipine SFE formulas was within an acceptable range (95.0%- 105.0%), which meets British pharmacopeia requirements and indicates that the drug has not precipitated in any of the prepared formulations (44).

In vitro drug release: The percentage of drugs released from SFE of Isradipine formulation increased with the increase in the percentage of β-CD. This was observed in F4 and F8, which have smaller particle sizes than F3 and F7, respectively. Decreased particle size results in an increased surface area for drug transfer, which enhances drug release absorption and overall promotes drug bioavailability (45). As the percentage of oils increased in the SFE of Isradipine formulation, there was a decrease in the percentage of drugs released. Specifically, F3 and F4 had higher drug release compared to F7 and F8. The findings suggest that Isradipine released more from formulas with lower oil content because these formulations had a lower viscosity (32). Pure

Isradipine showed the lowest release at the end of 120 minutes due to its practically insoluble (17).

Flow Properties and SEM analysis: The flow properties of the selected formula indicate that the surfactant free dry emulsion of Isradipine has passable flowability and poor compressibility (46). These flow properties are typical for powder with lipophilic core material and have previously been observed in dried oil-based powders.

SEM analysis revealed the absence of drug crystals, indicating complete solubilization of the drug within the emulsion (20).

Conclusions

The study found that SFDE provided an important pediatric dosage form for the oral water-insoluble drug. SFDE, which was prepared from Corn oil, β-CD was an encouraging method for improving the dissolution rate and solubility of Isradipine and could serve as a prototype for developing other hydrophobic drug formulations using surfactant-free emulsion drug delivery systems.

Authors' declaration

We confirm that all the Figures and Tables in the manuscript are ours. Besides, the figures and images, which are not ours, have been given permission for re-publication attached to the manuscript.

Conflicts of Interest: None

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Authors' Contributions

Study conception & design: (Zahraa M. Naji & Fatima J. Jawad). Literature search: (Zahraa M. Naji). Data acquisition: (Zahraa M. Naji). Data analysis & interpretation: (Zahraa M. Naji). Manuscript preparation: (Zahraa M. Naji). Manuscript editing & review: (All Authors).

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تحضير وتوصيف الأسرادبين كمستحلب جاف خال من المادة المستحلبة

زهراء محمد ناجي[1]* / وزارة الصحة والبيئة، دائرة صحة النجف، النجف، العراق.
فاطمة جلال جواد[2] / فرع الصيدلانيات، كلية الصيدلة جامعة بغداد ، بغداد، العراق

الخلاصة:
خلفية البحث: يتزايد انتشار ارتفاع ضغط الدم بين الأطفال العراقيين، ومعظم الأدوية المتوفرة ليست مناسبة للأطفال، مما يؤدي إلى استخدام غير مصرح به وغير آمن .تعد أشكال الجرعات السائلة مفيدة للمرضى الأطفال والرضع بسبب مرونتها في الجرعة وسهولة بلعها .إسراديبين، العلاج الفموي المفضل لارتفاع ضغط الدم الشديد في للأطفال ينتمي الدواء للأدويه المصنفه من الدرجة الثانية حسب نظام تصنيف الصيدلانيات البيولوجي. التوافر البيولوجي له منخفض بحوالي15-24٪. ويحتاج إلى أن يكون مستحلبًا خاليًا من المادة المستحلبه (SFE) لتحسين التوافر البيولوجي الفموي ,وسلامة الأطفال ولكنه يفتقر إلى الاستقرار الكيمياء الفيزيائية .يعتبر SFE الجاف حلاً واعدًا لجميع هذه التحديات.
الاهداف : تهدف الدراسة إلى إنشاء مستحلب دهني مائي فموي للأسرادبين فموي مستقر وصديق للبيئة وخالي من المادة المستحلبة للأطفال، وحمايته من التحلل المائي والأكسدة والحساسية للضوء، وزيادة قابليته للذوبان وامتصاصه.
المواد وطرق العمل: استخدمت الدراسة زيت الذرة لتذويب الإسراديبين. حضر SFE بنسب مختلفة من البيتا-سيكلودكسترين. تم تحضير ثمان صيغ باستخدام جهاز التجانس وخلطها لمدة 5 دقائق عند 10000 دورة في الدقيقة و 25° م. تم تقييم صيغ SFE للصفات الحسية، ودراسة الاستقرار الديناميكي الحراري، وتحديد اللزوجة، وقياس الأس الهيدروجيني، ومحتوى الدواء، وتوزيع حجم القطرات، ودراسة تحرر الدواء. ثم تم تجميد الصيغة المختارة باستخدام المانيتول وذلك باستخدام نظام التجفيف بالتجميد.
النتائج: من بين جميع صيغ SFE المحضرة، تم اختيار F4 التي تحتوي على 8 غم من β-CD و 15 غم من زيت الذرة، كأفضل صيغة SFE بسبب نطاق حجم الجسيمات الصغيرة 1451 ± 0.01 نم، والدرجة الحمضية المحترمة، والصفات الحسية الجيدة، والاستقرار الديناميكي الحراري الممتاز، واللزوجة المقبولة 1869.5 ± 1.54 ملغم/مل، ونسبة محتوى الدواء المقبولة، وأعلى تحرردواء. تم تجفيف F4 بالتجميد ثم تم تقييمها لاحقًا لتدفقها وقابليتها للضغط.
الاستنتاجات: وجدت الدراسة أن SFE الجاف قدم شكل جرعة دوائيه فموية مهمة للأطفال للدواء الغير القابل للذوبان في الماء.
مفتاح الكلمات: مستحلب بيكرنك,المستحلب الخال من المادة المستحلبة,المستحلب الجاف الخال من المادة المستحلبة,بيتاسايكلودكسترين, زيت الذرة.