Original Article

Study of effect of mixed Tween 20 and Span with different HLBs on the properties of spironolactone-loaded solid lipid nanoparticles (SLNs)

Atefeh Naimifar*, S. S Ale_Nabi, M. Saeedi, J. Akbari, K. Morteza-Semnani

Faculty of Pharmacy, Mazandaran University of Medical Sciences, Sari, Iran.

Correspondence: Atefeh Naimifar, Faculty of Pharmacy, Mazandaran University of Medical Sciences, Sari, Iran.

ABSTRACT

Introduction: following oral administration, spironolactone may cause stomach inflammation and ulcer. One of the new and promising methods to avoid gastrointestinal irritations, minimize systemic toxicity, and achieve optimal therapeutic effects is administration of this drug through the skin. Studies have shown that SLNs can be used in the treatment of skin diseases such as atopic dermatitis, psoriasis, acne, skin fungus (dermatophytosis) and inflammation. Methodology: Spironolactone-loaded SLNs were prepared as carriers by solvent evaporation method and using palmitic acid. Different weight ratios of carrier to drug and different ratios of Tween and Span were tested with the effect of HLB examined on nanoparticle properties. Optimum formulation was selected to examine the properties of nanoparticles by DSC (Differential scanning calorimetry) and FT-IR (Fourier Transform Infrared) spectroscopy according to the studies conducted. Discussion and conclusion: The results showed that the increase in the lipid and decrease in the drug in formulations F_9 - F_{15} significantly reduced the average particle size. Thus, in F_{11}, the particle size reduced to 150.8 ± 7.6. Moreover, the highest zeta potential was seen in F_4=-31.73 ± 4.92 and F_{11}=28.36 ± 2.36 with HLB 10.5. By decreasing HLB to 4.3 in F_{15}, zeta potential reduced to -9.6 ± 0.45. The maximum loading rate (4.17 ± 81.3) was observed in F_{13} formulation with HLB 16.7 and reduced by distancing from this HLB. In this study, the value of the drug released in the dissolution medium increased compared to the standard drug sample.

Keywords: SLNs, spironolactone, solvent evaporation, Tween 20.

Introduction

Drugs might be used in one of the variety of dosage forms available for administration [1]. Drugs might be used in parental, oral, inhalation, transdermal and intranasal routes [2]. The main problem in oral formulation is that the drug undergoes liver First Pass Metabolism after absorption. During this process, the liver may metabolize some or all of the drug and the bioavailability of the drug may decrease. Pharmaceutical industries may use other ways of administration, like intravenous, intramuscular, or sublingual ways to compensate for this effect [1]. Skin is one of the most important organs in the body and the main agent for the protection of other organs and internal fluids and tissues of the body. The skin is composed of three layers: epidermis, dermis and hypodermis [3].

Colloidal particles are recognized as nanoparticles at the range of 1 to 1000 nanometers [4]. SLNs are colloidal structures with less than 1 µm in size, able to be prepared by emulsion, and make their size sub-micrometer using mechanical forces such as ultrasound and a homogenizer. These structures can carry drugs and active ingredients in their lipid part, which brings about protection of the drug from environmental damage. Thus, this spectrum of nanoparticles can be used in carrying drugs and prolonging their efficacy [5]. SLNs have a coating effect that comes from the formation of film layer on the surface of the skin, which reduces transepidermal water loss. It improves skin drug delivery and increases the specific surface area above SLNs, increasing the contact of the trapped drug with the stratum corneum layer. Moreover, lipid nanoparticles can

Access this article online	
Website: www.japer.in	**E-ISSN:** 2249-3379

How to cite this article: Atefeh Naimifar, S. S Ale_Nabi, M. Saeedi, J. Akbari, K. Morteza-Semnani. Study of effect of mixed Tween 20 and Span with different HLBs on the properties of spironolactone-loaded solid lipid nanoparticles (SLNs). J Adv Pharm Edu Res 2019;9(S2):190-198.
Source of Support: Nil, Conflict of Interest: None declared.

enhance the chemical stability of light sensitive, sensitive to oxidation and hydrolysis drugs.

In the drug delivery by nanoparticles, drug molecules are trapped in or absorbed in the matrix of dissolved nanoparticles. Nanotechnology is a good tool for delivering low molecular weight drugs and macromolecules such as proteins or genes to cells and tissues. Due to their small size, they can pass through small capillaries, be picked up by cells, and allow the release of drug at target site and for a specific period to facilitate the correct delivery of the drug in the body. This can increase the therapeutic effects or reduce the side effects [6].

There are several methods for the preparation of nanoparticles, the most important of which are using high-pressure homogenizers and ultrasonication. In the preparation of these particles, biodegradable compounds such as biolipids are used, which results in the biocompatibility of SLNs. These structures can be used in pharmaceutical formulations, such as transdermal dosage forms [5, 7]. The advantages of SLNs are targeted drug delivery, suitable biocompatibility, increased stability of pharmaceutical formulations, increase in drug content, easy sterilization of prepared formulations, chemical protection of the drug contained in solid lipid nanoparticles, preparation by common methods, emulsion preparations, and long lasting [7, 8]. Factors such as the type of lipid and emulsifier effect on the lipid nanoparticles quality [7].

Drug delivery by SLNs depends on various factors such as the administration rout, the type of lipid, the active ingredient, and the type of body-to-particle interaction. The most important enzyme that affects these structures in the body is lipid. Topical treatment though the skin has some advantages like the possibility of reaching a high dose of drug to the target site and reduction in systemic adverse effect compared with oral or injectable administration routs. Topical administration of drug is among the pharmaceutical problems due to the difficulty in controlling and determining the exact value of the drug that reaches different layers of the skin. Topical drug delivery has many advantages compared to other routs, such as the possibility of using high concentrations of the drug on the skin, reduction in the systemic use of the drug and subsequently reduction in the side effects, the possibility of long-term drug exposure to the surface and reduction in use times, especially for medications with short half-life, having easy and painless use, and increased patient compliance. Recently, the preparation of nanoparticles is being studied as a new treatment for skin diseases such as acne vulgaris, recurrent genital warts, atopic dermatitis, and hyperpigmented lesions of the skin [9]. Spironolactone has a slight solubility in water and it is possible to increase its solubility by nanoparticles.

The study examined the production of Spironolactone-loaded SLNs and the effect of HLB changes on its physicochemical properties.

Materials and Methods

In this study, 15 different formulations with different HLBs were made to create SLNs and to examine the effect of HLB changes. The effect of lipid content and HLB changes on particle size, drug loading and polydispersity index were examined.

First, 100 milligrams of spironolactone was dissolved in 100 cc of 30 g alcohol and 0.5, 1, 1.5, 2 and 2.5 milliliters of stock solution, respectively, poured into separate balloon jogege and was volume to draw the calibration curve for spironolactone. Their absorption was then recorded using UV spectrophotometer at 238 nm. Absorption of these stoke solutions was read at intervals of two hours, and it was triplicated. Various ratios of Spironolactone and Palmitic acid were poured into beakers and Span 80 and Dichloromethane were added to them to make SLNs. Parailm was used to cover the beaker and shook slowly to be completely solved. In another beaker, 80 cc of deionized water was homogenized with Tween 20 at 13,000 rpm. Then, the organic phase was added with a droplet syringe to the water phase that was coexisting at about 13,000 rpm of homogenizer units. Then it was sonicated for 5 minutes and placed on a stirrer for 24 hours. The size, zeta potential and polydispersity index of Spironolactone-loaded SLNs were measured by Dynamic Light Scattering (DLS) (Pyris 6), using Zetasizer Nano ZS (Malvern Instruments, UK at 25°C and 90 degrees' angle). Sample concentration was such that in all the samples, 20-400 kilo counts per second was obtained to measure the zeta potential and to measure the severity of the dispersion 100,000 counts per second was obtained in all samples. To evaluate the drug loading, SLNs were centrifuges for 30 minutes at 25,000 rpm at 4 ° C in three eppendorf 2 ml and the supernatants were collected separately. They read absorbtion of solution after 50 times dilution at 238 nm using a spectrophotometer. Then, by inserting the absorption number into the standard curve and calculating the concentration in microg/ml concentration at dilution factor (50) was multiplied to a true concentration. The actual concentration was multiplied in supernatant volume and the amount of unloaded drug was calculated in micrograms per eppendorf. The unloaded drug was calculated from the amount of microgram of the drug in each eppendorf and the amount of drug loaded. The percentage of Entrapment Efficiency was calculated.

$$\text{Entrapment Efficiency} = W_{total} - W_{free} / W_{total} \times 100\%$$

The Pekrin-Elmer Spectrum One was used to obtain the FTIR spectrum. Each specimen was mixed with potassium bromide at a ratio of 1:5 and pressurized for 15 seconds under 3- 6 tons' pressure to prepare the 10 mm discs needed for testing. The force needed to apply this pressure was provided by a hydraulic jack mounted on the press. The scan accuracy was 0.5 cm^{-1} and the scan range was 4000-400 cm^{-1}. Pekrin-Elmer Pyris 6 was used to obtain the thermograms of the specimens. To do this test, 5 mg of each specimen was removed and placed inside the aluminum pan of the device. The device was examined at a temperature of 10°C/min at a temperature range of 30-300°C. The dissolution of spironolactone from SLNs was tested

according to the Paddle method. The dissolution medium was 900 ml of intestinal fluid simulated with pH 6.8 at 37 ° C and a rotary paddle of 60 rpm and 5 milliliter was removed at different intervals (0.5, 1, 2, 4, 6, 8 and 24 hours), filtered and its concentration was measured using UV device at a wavelength of 238 nm. The dissolution information was compared with pure spironolactone dissolution.

The results were analyzed using one-way ANOVA and then Tukey test was used to examine zero tests to compare the mean of available data in each section. The difference with $P<0.05$ was considered statistically significant at each point.

Results

Table 1 shows the data related to drawing the standard spironolactone curve in 30-degree alcohol at a wavelength of 239.8 nm on the first, second, third, and three consecutive days.

Table 1: Data related to drawing spironolactone standard curve data in 30-degree alcohols at the wavelength of 239.8 nm in the first, second, third, and three consecutive days

Day	Mg/L concentration	Absorption			Mean	SD±	CV%
		First specimen	Second specimen	Third specimen			
First	5×10^{-3}	0.2493	0.2388	0.2391	0.2424	0.0059	0.4632
	10×10^{-3}	0.4929	0.4936	0.5001	0.4955	0.0039	0.8012
	15×10^{-3}	0.7204	0.7094	0.6970	0.7089	0.0117	1.6513
	20×10^{-3}	0.9334	0.9501	0.9266	0.9367	0.0120	1.2909
	25×10^{-3}	1.1712	1.1693	1.1603	1.1669	0.0058	0.4989
Second	5×10^{-3}	0.2553	0.2502	0.2579	0.2544	0.0039	1.5393
	10×10^{-3}	0.5465	0.5381	0.5563	0.5469	0.0091	1.6653
	15×10^{-3}	0.7196	0.7086	0.7217	0.7166	0.0070	0.9811
	20×10^{-3}	0.9429	0.9721	0.9949	0.9699	0.0260	2.6872
	25×10^{-3}	1.1927	1.2730	1.2471	1.2376	0.0409	3.3111
Third	5×10^{-3}	0.2555	0.2435	0.2451	0.2480	0.0065	2.6203
	10×10^{-3}	0.5413	0.5612	0.5407	0.5477	0.0116	2.1299
	15×10^{-3}	0.7036	0.7116	0.7173	0.7108	0.0068	0.9681
	20×10^{-3}	0.9851	0.9384	0.9338	0.9524	0.0283	2.9801
	25×10^{-3}	1.2251	1.1766	1.1883	1.1966	0.253	2.1149
Three consecutive days	5×10^{-3}	0.2424	0.2544	0.2480	0.2483	0.0060	2.4298
	10×10^{-3}	0.4955	0.5469	0.5477	0.5300	0.0299	5.6442
	15×10^{-3}	0.7089	0.7166	0.7108	0.7121	0.0040	0.5432
	20×10^{-3}	0.9368	0.9699	0.9524	0.9530	0.0166	1.7461
	25×10^{-3}	1.1669	1.2376	1.1966	1.2004	0.0345	2.9559

Table 2 shows the value of drug, carrier and surfactant used in formulations in milligrams.

Table 2: The value of drug, carrier and surfactant used in the formulation in milligrams

Formulation	Drug value	The value of palmitic acid	Tween 20	Span 80	HLB
F1	160	640	1017.2	352.8	13.6
F2	160	640	960	480	12.56
F3	160	640	840	600	7.17
F4	160	640	720	720	10.5
F5	160	640	612	828	9.57
F6	160	640	480	960	8.43
F7	160	320	1328.7	431.2	16.69
F8	160	320	1179.2	580.8	15.40
F9	50	640	1017.2	352.8	13.5
F10	50	640	960	480	12.56
F11	50	640	720	720	10.5
F12	50	640	480	960	8.42
F13	50	640	1440	_	16.7
F14	50	640	228	1152	6.5
F15	50	640	_	1440	4.3

Table 3 shows the size of SLNs.

Table 3: The particle Size of SLNs

Formulation	Particle Size of SLNs in nanometer			Mean	SD±	CV%
	First specimen	Second specimen	Third specimen			
	333.5	571	561.1	488.53	134.35	27.50
F1	407	953.1	850.1	736.73	290.16	39.38
F2	1943.1	2096	2051	2030.03	78.57	3.87
F3	354	428	523	435	84.71	19.47
F4	675.2	890.1	760	775.1	108.24	13.96
F5	906	407.9	940	751.3	297.87	39.64
F6	5743	3525	4232	4500	1133.02	25.17
F7	4032	4523	5321	4625.33	650.56	14.065
F8	556	109.7	172.1	279.26	241.68	86.54
F9	158	143.5	210.5	170.6	35.25	20.65
F10	136.7	153.6	162.1	150.8	12.92	8.57
F11	129.9	250.9	197.8	192.86	60.65	31.44
F12	641.8	218.4	605.1	488.43	234.57	48.02
F13	296.9	291	217.2	268.5	44.17	16.45
F14	279	284.2	273.7	278.96	5.25	1.88

Table 4 shows PDI of SLNs.

Table 4: PDI of SLNs

Formulation	Dispersion			Mean	SD±	CV%
	First specimen	Second specimen	Third specimen			
F1	0.78	0.89	0.81	0.826	0.056	6.878
F2	0.76	0.96	0.7	0.806	0.136	16.876
F3	0.96	1	0.92	0.96	0.04	4.16
F4	0.7	1	0.8	0.83	0.152	18.33
F5	1	0.91	1	0.97	0.052	5.35
F6	1	0.76	0.91	0.89	0.121	13.62
F7	0.1	0.31	0.43	0.28	0.167	59.65
F8	0.69	0.7	0.72	0.703	0.0152	2.171
F9	0.57	0.35	0.42	0.44	0.112	25.16
F10	0.33	0.41	0.43	0.39	0.0529	13.56
F11	0.2	0.21	0.18	0.19	0.015	7.76
F12	0.23	0.21	0.29	0.24	0.041	17.10
F13	0.36	0.38	0.34	0.36	0.02	5.55
F14	v35	0.32	0.46	0.37	0.073	19.56
F15	0.43	0.39	0.35	0.39	0.04	10.25

Table 5 shows the zeta potential of SLNs.

Table 5: Zeta potential of SLNs

Formulation	Zeta Potential Value in MW			Mean	SD±	CV%
	First specimen	Second specimen	Third specimen			
F1	-25	-18.2	- 16.2	- 19.8	4.61	23.29
F2	18 years	- 20.1	- 19.3	- 19.13	1.05	5.53
F3	-20	-18.6	- 15.2	-17.93	2.46	13.76
F4	-33	-26.1	-26	- 28.36	4.0112	14.14
F5	-12.3	-16	-10.5	-12.93	2.80	21.68
F6	-16	-18	- 17.1	- 17.03	1	5.88
F7	-27	26.1	-29	- 27.36	1.48	5.42
F8	-25	- 29.2	-26	- 26.73	2.19	8.20
F9	-26	-28	- 30.6	-28.2	2.30	8.17
F10	-14	-16	-26	- 18.66	6.42	34.4
F11	-33	-39.4	- 22.8	- 31.73	8.37	26.38
F12	-9.21	- 25.2	- 28.9	- 21.10	10.46	49.58
F13	-14.8	-16.2	-18	- 16.33	1.6	9.82
F14	-21.2	-14	-15	- 16.73	3.9	23.30
F15	-8.5	-10	-9.6	-9.36	77	8.29

Table 6 shows the average percentage of drug loaded in SLNs in 15 formulations.

Table 6: Average percentage of drug loaded in SLNs

Formulation	Average drug loaded in SLNs			Mean	SD±	CV%
	First specimen	Second specimen	Third specimen			
F1	80.53	64	72	72.17	8.26	11.45
F2	75.10	75	66	72.03	5.22	7.25
F3	66.31	74	67.2	69.40	4.05	5.84
F4	75.28	85	77	79.09	5.18	6.55
F5	72.42	67	68.9	69.44	2.75	3.96
F6	70.18	71	73.2	71.42	1.50	2.10
F7	57.83	71	56.2	61.72	8.11	13.15
F8	70.7	69	68.4	69.36	1.19	1.71
F9	63	61	56	60	3.60	6.00
F10	63.5	65	61	63.16	2.02	3.19
F11	71	69	70	70	1	1.42
F12	64	71	65	66.6	3.78	5.67
F13	89	80	75	81.3	7.09	8.72
F14	88	77	76	80.3	6.65	8.28
F15	53.6	56	54	54.53	1.28	2.35

Table 7 shows the drug release data for Formulation 11.

Table 7: The drug release data for Formulation 11

Time in hours	The percentage of the drug released			Mean	SD±	CV%
	First specimen	Second specimen	Third specimen			
5	6.84	5.32	4.18	5.44	1.33	24.5
1	10.36	11.77	14.43	12.27	1.95	15.88
2	15.95	14.81	17.85	16.2	1.53	9.47
4	19.63	19.41	22.82	20.62	1.90	9.23
6	22.82	30.80	26.2	26.6	4.00	15.05
8	23.96	30.38	37.56	30.64	6.81	22.25
24	79.7	44.81	81.27	68.59	20.6	30.04

Figure 1 shows the mean diameter of SLNs.

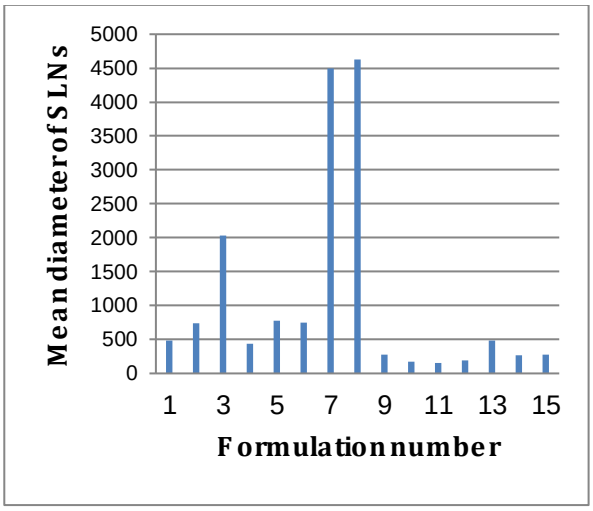

Figure 1: Average diameter of solid lipid nanoparticles

Figure 2 shows the percentage of the drug released for Formulation 11 during 24 hours compared to the pure spironolactone sample.

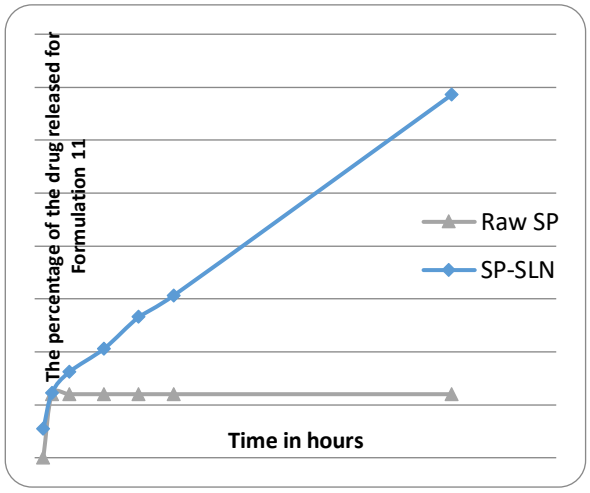

Figure 2: The percentage of the drug released for Formulation 11 during 24 hours compared to the pure spironolactone sample.

Figure 3 shows the spectrum of FT-IR spironolactone.

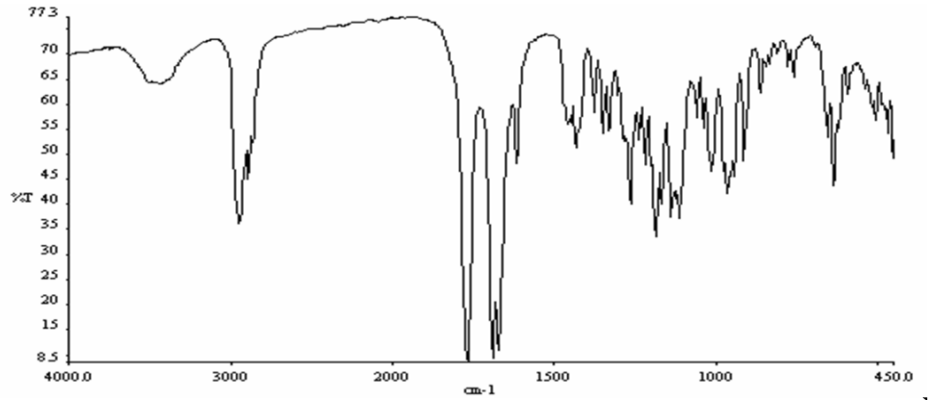

Figure 3: FT-IR Spironolactone Spectrum

Figure 4 shows the FT-IR spectrum of palmitic acid.

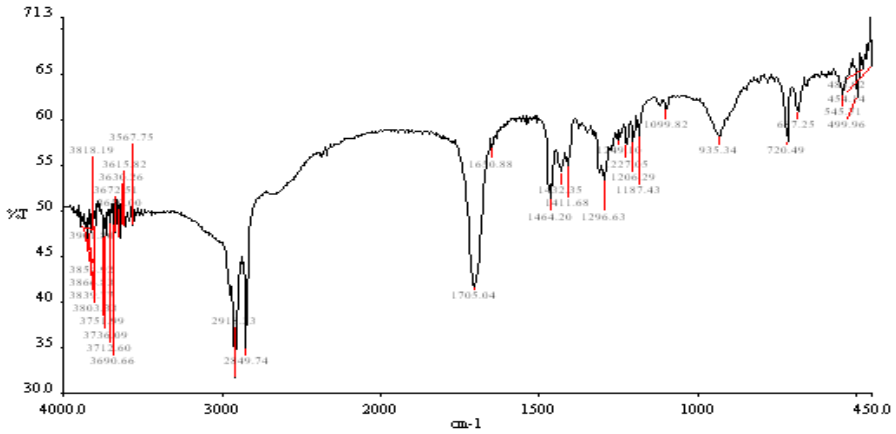

Figure 4: FT-IR spectrum of palmitic acid

Figure 5 shows the FT-IR spectrum of span 80.

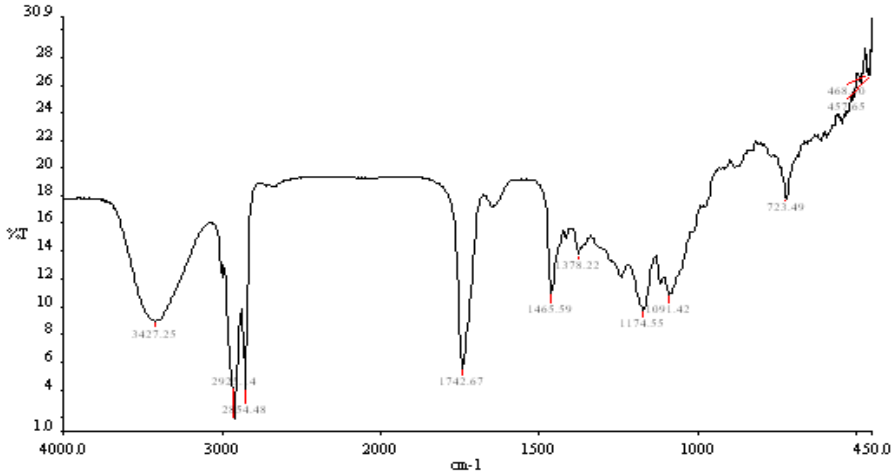

Figure 5: FT-IR spectrum of span 80

Figure 6 shows FT-IR spectrum of the Tween 20.

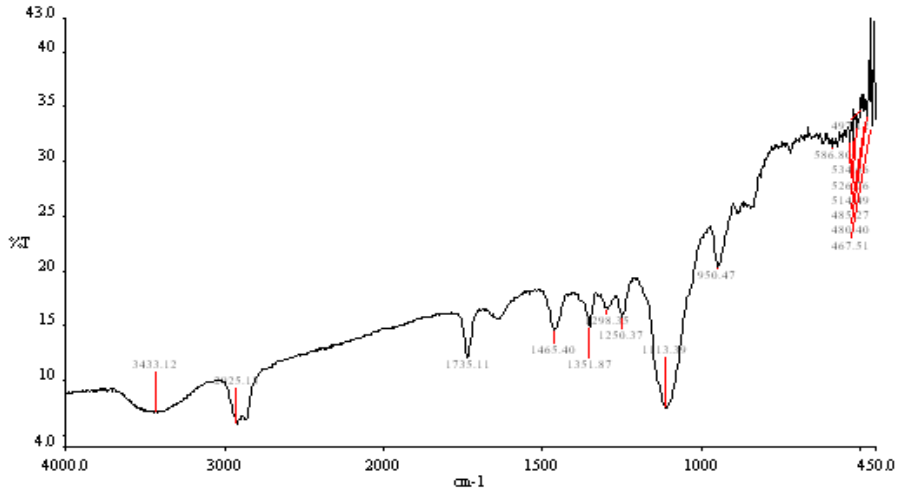

Figure 6: FT-IR Spectrum Tween 20

Figure 7 shows the FT-IR spectrum of the physical mixture of palmitic acid, spironolactone, tween 20 and span 80 with a ratio of 2: 1.

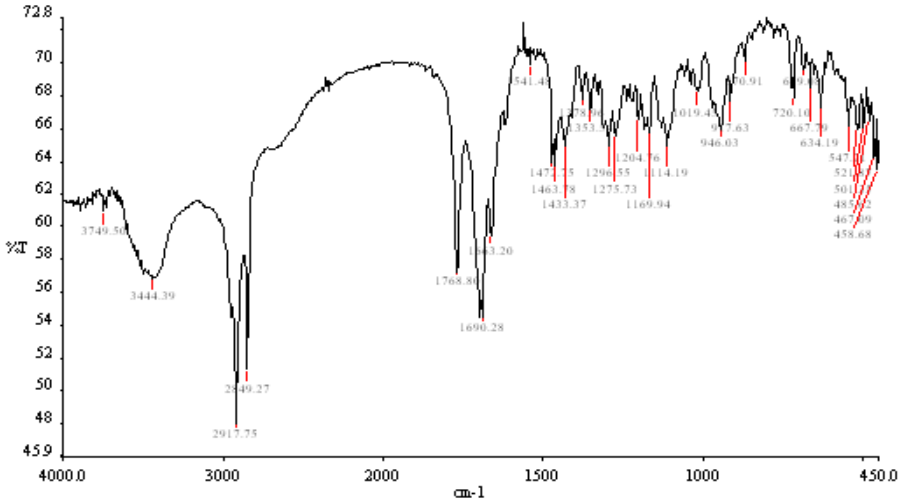

Figure 7: FT-IR spectrum of the physical mixture of palmitic acid, spironolactone, tween 20 and span 80 with a ratio of 2: 1

Figure 8 shows DSC thermograms of pure spironolactone.

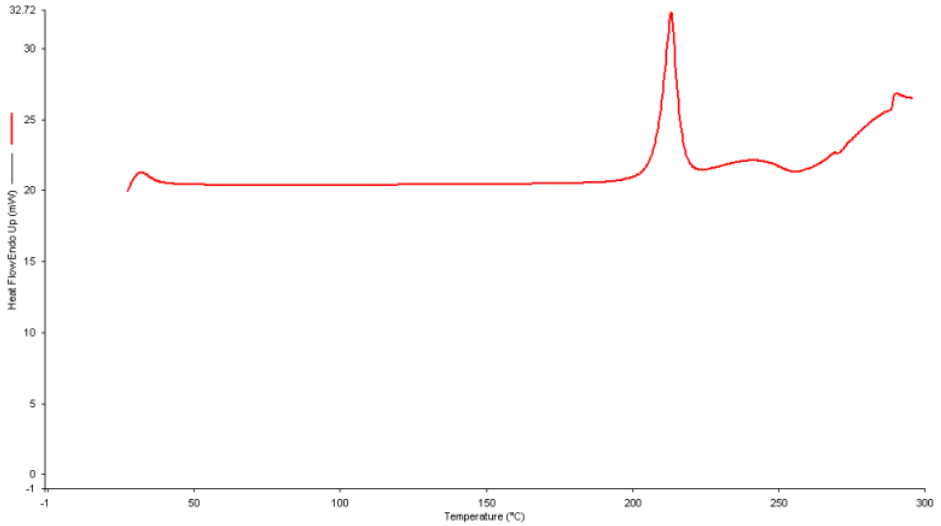

Figure 8: DSC thermogram of pure spironolactone

Figure 9 shows the DSC thermogram of palmictic acid.

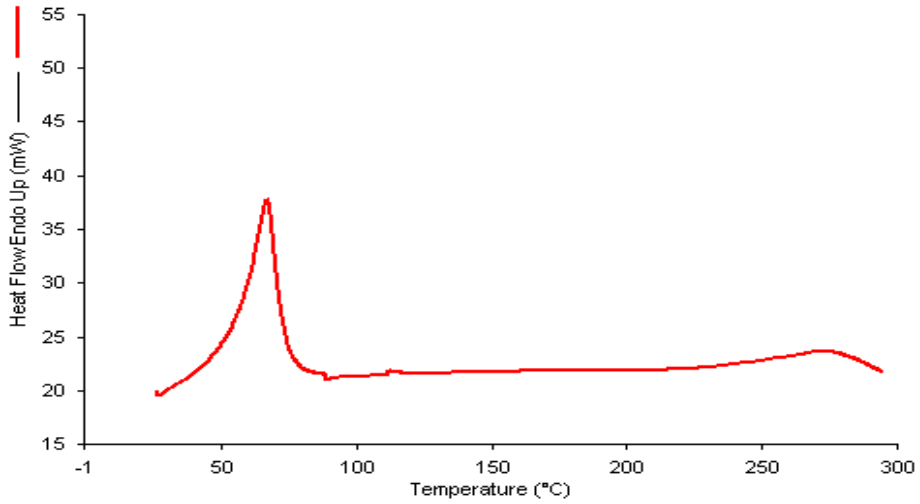

Figure 9: DSC thermogram of palmictic acid

Figure 10 shows the DSC thermograms of Spironolactone-loaded SLNs obtained from the rinsed and dried precipitation in a 24-hour cycle by a freeze-dryer device.

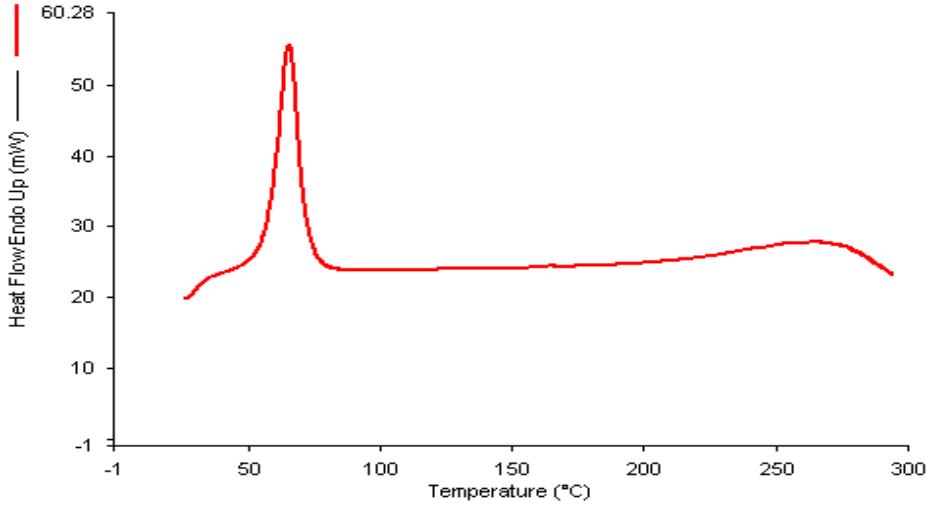

Figure 10: DSC thermograms of Spironolactone-loaded SLNs obtained from the rinsed and dried precipitation in a 24-hour cycle by a freeze-dryer device

Discussion and Conclusion

Microvesicles, like liposomes and nanoparticles, carry the drug molecules to deeper places of the hair follicles compared to old formulations such as cream and ointment. Some other studies have mentioned titanium dioxide particles penetration into hair follicles [10]. Lipid nanoparticles are capable of increasing the chemical stability of light-sensitive drugs, oxidation and hydrolysis [11].

The results indicated that in the formulations F7 and F8, where the ratio of lipid to drug is 1: 2, the percentage of drug loading decreased, but in F13 and F14, the ratio of lipid to the drug increased to 1:13. The percentage of drug loading reached 81%. The results were in line with the results of other studies in this regard. In a study on the formulation and in Vitro characterization of domperidone SLNs, Lakshmi et al. showed that by reducing the lipid concentration, drug loading decreases [12]. In a study conducted on meloxicam SLNs, Rawia et al. showed that when the concentration of lipid increases from 5% to 7.5%, drug loading increases [13]. In a study on formulation and in Vitro characterization of atorvastatin SLNs, Pankanti et al. showed that drug loading decreases with decreasing lipid concentrations [14].

Concerning particle size, the size of the nanoparticles increased with increasing lipid content, which is consistent with the results of previous experiments carried out by other researchers. In their study, Trotta et al. showed that in formulations containing benzyl alcohol and butyl alcohol with glyceryl monostearate, when the lipid phase content reaches 10% from 2.5, the size of the nanoparticles in the formulation with benzyl alcohol reached 695 from 205 and in the formulation containing butyl alcohol reached 368 from 320 [15]. In a study done on meloxicam SLNs, Rawia et al. showed that when the concentration of lipid increases, the size of nanoparticles increases effectively [13].

Concerning zeta potential, with an increase in the lipid-drug ratio from 1:5 to 1:20, zeta potential becomes slightly more negative, but this change is insignificant. In a study conducted

on meloxicam SLNs, Rawia et al. indicated that when lipid concentration increases, zeta potential is negatively affected [13].

The results showed that the reduction in HLB in Formulations F10 - F15 from 12.56 to 4.3, the nanoparticle size increased, so that the average diameter of the nanoparticles increased to 278.96±3.08 from 170.6 ± 20.73. The results were in line with the scientific evidence showing that HLBs 8-16 are suitable for making oil emulsions. In addition, the increase in the concentration of Tween 20 by decreasing the tension between the surface between the maison phase and the lipid leads to the formation of droplets of a smaller size, which effectively increase the stability of the particles by forming a space barrier on the surface of the nanoparticles and protecting them from coagulation. In a study on the preparation and evaluation of nicotine SLNs using glyceryl menatearate, Tween 80 and span 60 for topical delivery using Box Behnken design, Samein showed that the increase in the concentration of span 60 decreased nanoparticle sizes [16].

The results show that all formulations have zeta potential in an acceptable range and zeta potential decreases with decrease in HLB. In Formulation F15, zeta potential reaches -9.6 ± 0.45. Observations were in line with the scientific evidence that HLBs 8-16 are suitable for making oil-in-water emulsions. Observations showed that PDI levels are within the acceptable limits, and with the decrease of HLB, PDI levels reduced as well. A significant value of drug was loaded in the lipid component in HLB range of 16.7- 6.5, so that in Formulation F13, the maximum drug was loaded as much as 81.3 ± 4.17%. Nevertheless, F15 had the lowest drug loading with HLB 4.3 (54.53±3.08). It is likely that in low HLBs due to improper HLB to build an oil-in-water emulsion in the water, after sonication and applying energy to the initial emulsion and increasing instability, lipid droplets are attached and the drug is released into the environment. With increase in the concentration of spa in the HLBs that can keep emulsions in water, copper can increase the solubility of spironolactone in the lipid. Moghimipour et al. showed that each gram of span 80 could dissolve 15.033 ± 208 mg of naproxen, whereas for Tween it is much lower [17]. In a study on the preparation and evaluation of nicotine SLNs using glyceryl monostearates, tween 80 and spin 60 for topical delivery using Box Behnken design, Samein showed that the drug loading increases in nanoparticles with increase in span concentration [16]. In a study using Tween 80 and span 80 to prepare Spironolactone-loaded SLNs with palmitic, Kelidari et al. showed that with increase in concentration of span 80, the drug loading increased and the particle size decreased. Moreover, they obtained good results by studying the dermal absorption effect of Spironolactone-loaded SLNs [17].

According to the results, compared with the standard specimen (pure spironolactone), it was seen that rapid release of spironolactone from the surface of lipid nanoparticles at initial times (30-60 minutes) and gradually increased within 24 hours of release. The slow release of spironolactone can be due to the slow penetration of the dissolution medium into the nucleus of nanoparticles, following the slow release of spironolactone from the nucleus.

FT-IR spectra obtained from Spironolactone-loaded SLNs with a pure spectronulactone spectrum, pure palmitic acid, tween 20 and pure span 80 were compared for possible interactions. In studying FT-IR spectrum of Spironolactone-loaded SLNs, it was concluded that the peaks on the functional groups of spiernolactone were observed. Due to the lack of displacement of drug categories (such as carbonyls) in the product, there was no chemical interaction between the drug and the components of the product.

DSC thermogram of pure spinolactone showed a sharp endothermic peak at about 212 ° C. The existance of this sharp peak in the thermogram indicates that spironolactone is in crystalline form in its drug powder. In addition, SLNs thermogram showed a peak of about 70 degrees. DSC thermocouple of spironolactone SLNs and the physical mixture showed an endothermic peak around the melting point of palmitic acid and the endothermic peak of the crystalline form of drug disappeared. Probably, lipid inhibits the formation of spironolactone crystals during the formation of nanoparticles. The more probable cause of the disappearance of spironolactone peak in the physical mixture may be due to the dissolution of spironolactone in the lipid, showing the effective loading of the drug by the carrier. Concerning the thermogram of spironolactone SLNs, it has been reported that when the drug does not show its endothermic peak, it is in amorphous state [17].

Solid lipid nanoparticles have been prepared in different ways in different studies. In this study, an economical, easier, and repeatable way of preparing SLNs was selected [13]. According to the results of DSC thermogram and FT-IR spectrum, proper loading was done by the carrier, and there were no interaction or chemical bonding between the formulations involved in the drug powder formulation. Thus, considering the results and the solutions presented in this project, it is hoped that solvent evaporation / emulsion method is a method used at the industrial scale. Given the gastrointestinal complications after long-term use of the drug orally and given its dermal absorption and reduction of undesired complications of this drug, it can be used to treat diseases such as hirsutism and so on.

References

1. Ansel, E. Et al. (2013). Pharmaceutical forms and drug delivery systems. Translation by Elham Khodaverdi, Mahdiad Shokib Azar, Ali Badie, Fatemeh Sadeghi, Ali Gholamzadeh, Alia Mousavian. Mashhad University of Medical Sciences
2. Shargel, L. Andrew B.C YU. (1999). Applied Biopharmaceutics & Pharmacokinetics.fourth edition. McGraw-Hill.Medical Publishing Division.
3. Haftek, M., Teillon, M.H., Schmitt, D. (1998). Stratum corneum, corneodesmosomes and ex vivo percutaneous penetration. Microscopy Research and Technique, 43 (3).242-249.

4. Aryane, N.s., N. Sultana., Sabah N. (2014). Fabrication of solid lipid nanoparticle for drug delivery. Pakistan Journal of Pharmaceutical Sciences, 20(3).251-259.
5. Krishna Sailja, A., Amareshwar, P., Chakravarty, P. (2011). Formulation of solid lipid nanoparticles and their applications, Current Pharma Research, Vol.1, pp.197-203
6. Partibha G., Kakadia, B., Conway, R. (2014). Solid Lipid Nanoparticles: A Potential Approach for Dermal Drug Delivery. American Journal of Pharmacological Sciences, vol.2, No. 5, A,1-7
7. Ekambaram, P., Abdul hasansathali, A., Priyanka, K. (2012). Solid Lipid Nanoparticles: A Review, Scientific Revews and Chemical Communications, Vol 2. pp 80-102.
8. Thassu, D., Deleers, M., Pathak, Y. (2007). Nanoparticulate Drug Delivery Systems. USA: Informa Healthcare Inc.
9. Wiesenthal, A., Hunter, L., Wang, S., Wickliffe, J., Wilkerson, M. (2011). Nanoparticles: small and mighty. The International Journal of Dermatology, 50.247-254.
10. Konradsdottir, F., ET. (2009). Drug targeting to the hair follicles: a cyclodextrin-based drug delivery. American Association of pharmaceutical Scienstists PharmSciTech, 10(1). 266-269.
11. Jenning, V., et al. (2000). vitamin A loaded solid lipid nanoparticle for topical use: occlusive properties and targeting to the upper skin. European Journal of Pharmaceutics and Biopharmaceutics, 49.211-218.
12. Lakashmi Sirisha Kotikalapudi, Laxminarayana Adepu, J VijayaRatna, Parkash V Diwan. (2012). Formulation and invitro characterization of domperidone loaded solid lipid nanoparticles. Int J Pharm Biomed Res, 3(1), 22-29.
13. Rawia, M. Khalid. Ahmad Abd, El-Bary., Nahfoz, A. Kasem., Mamdouh, M. Ghorab. Mona, B. Ahmed. (2013). Solid Lipid Nanoparticles for topical delivery of meloxicam: Development and in vitro characterization. Annual International Interdisciplinary Conference. AHC, 24-26 April. Azores. Portugal _ proceedings
14. Pakanti Pavan Kumar, Pankanti Gayatri, Reddy Sunil, Somagoni Jaganmohan and Yamasai Madhusudan Rao. (2012). Atorvastatin Loaded Solidlipid Nanoparticles: Formulation, Optimization, and In-vitro Characterization. IOSR Journal of pharmacy. Volume 2 Issue 5. Pp. 23-320
15. Trotta, M., Debernardi, F., Caputo, O. (2003). Preparation of solid lipid nanoparticles by a solvent emulsification-diffusion technique. Int J pharm, 12,257(1-2): 153-60. PMID: 1271117.
16. Laith hamza samein. Preparation and evaluation of nystatin loaded-solid-lipid nanoparticles for topical delivery. Int J pharm Sci, Vol 6, Suppl 2,592-597.
17. Moghimipour, Es. Salimi, A., Eftekhari, S. (2013). Design Characterization of Microemulsion System for Naproxen.Advanced Pharmaceutical Bulletin, 3(1), 63-71.