e - ISSN - 2348 - 2184
Print ISSN - 2348 - 2176

AMERICAN JOURNAL OF BIOLOGICAL AND PHARMACEUTICAL RESEARCH

Journal homepage: www.mcmed.us/journal/ajbpr

OPTIMIZATION OF PRODUCT AND PROCESS VARIABLE IN FORMULATION OF ISONIAZID SLN NANOPARTICLE

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Article Info

Received 25/03/2014
Revised 15/04/2014
Accepted 18/05/2014

Key words: Isoniazid, SLN, Zeta Size, PDI, Particle size etc.

ABSTRACT

The Aim of current study is to select optimized method for design of Solid Lipid Nanoparticle. The objective of the study is to optimize the solvent evaporation method for the preparation of Solid Lipid Nanoparticle by altering the product and process variable in the formulation. Here the independent product variable is surfactant and the dependent process variable is homogenization and ultrasonication. And then by varying this both independent and dependent variables Isoniazid SLN was formulated by using solvent evaporation method in order to decrease the dose, adverse effects and targeting effect. Evaluation variables like Particle size, Poly dispersibility index (PDI) and Zeta-potential are carried out by Malvern Zeta sizer. By the current results it was concluded that the optimized product and process variables that shown in the results are needed for the best formulation development technique for Isoniazid SLN.

INTRODUCTION

Physical, chemical and biological properties all must be given due consideration in the selection of components and processing steps for the dosage form. The final product must be one that meets not only the requirements placed on it from a bioavailability standpoint, but also the practical mass production criteria of process and product reproducibility. While undergoing formulation it should be understand the theoretical formulation and target processing parameter, as well the ranges for each excipients and processing parameter [1,2].

Optimization technique provides both the depth of understanding and a ability to explore and defend ranges for the formulation and processing factors. With the rational approaches to the selection of the several excipients and manufacturing steps for a given product, one qualitatively selects a formulation. Optimization was an useful tool to quantitate a formulation that can be qualitatively determined. The word optimize is defined as follows i.e., to make as perfect, effective and functional as possible [3].

In developing a dosage form one must be undergo logical steps, carefully control the variables and changing one at a time until a satisfactory system is produced. No matter how the dosage form is designs, but the trial and error method will be improve the quality of the dosage form [4].

MATERIALS AND METHODS

Isoniazid is acquired as a gift sample from Microlabs Pvt Ltd., Hosur, India. Stearic acid, Span 60, SLS and Cholesterol was received from Chem. Scientifics, Chennai. All the other solvents used in this project are belongs to analytical grade. Instruments like Malvern Zeta

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Sizer, High speed Homogenizer (CAT) was used for formulation and evaluation processes.

Optimization of Process variable (Homogenization and Ultra sonication) and Product variable (Surfactant) by solvent evaporation method

Solvent Evaporation followed by Sonication

Isoniazid, Cholesterol and Span 60 are dissolved in ethanol and kept for some time in bath sonicator .The aqueous medium is prepared by dissolving tween 80 in distilled water and kept for stirring in magnetic stirrer for 15 mins. Upon evaporation of the solvent, the lipid phase is slowly added into the aqueous phase under continuous stirring. The nanoparticles dispersion is formed in the aqueous medium. The solution was kept in Ultra probe sonicator at different pulse rate. Now repeat the same experiment with same amount of solvent, span 60 by adding stearic acid.

Solvent Evaporation followed by Homogenization

Isoniazid, Cholesterol and Span 60 are dissolved in ethanol and kept for some time in bath sonicator .The aqueous medium is prepared by dissolving Sodium lauryl sulfate (SLS) in distilled water and kept for stirring in magnetic stirrer for 15 mins. Upon evaporation of the solvent, the lipid phase is slowly added into the aqueous phase under continuous stirring. The nanoparticles dispersion is formed in the aqueous medium. The solution was kept in Homogenization at different RPM speed .Now repeat the same experiment with same amount of solvent, span 60 by adding stearic acid.[5-7]

Particle size determination

The average particle size, polydispersity index and zeta potential of the lipid particulate dispersions were determined using a Zetasizer (DTS Ver.4.10, Malvern Instruments, UK). The sample of dispersion was diluted to 1:9 v/v with double distilled water to ensure that the light scattering intensity was within the instrument's sensitivity range. Double distilled water was filtered through 0.45 µm membrane filters (Pall Life sciences, Mumbai, India) prior to particle size determination. [8-10]

Zeta Potential

Zeta potential is the difference in the potential between the surface of tightly bound layer and the electro neutral region of the solution.[9-12]

RESULTS AND DISCUSSION

Optimization of formulation based on effect of Sonication time and tween 80 on Average particle size, PDI and Zeta potential

The particle size analysis revealed that, the SLNs were in the nanometer range. The size of the nanoparticles was affected by the sonication time and the concentration of tween 80.

The size of the Isoniazid loaded SLNs were found to be between 273.3 nm to 368.6 nm. The stability of the formulated SLNs was evaluated by measuring the zeta potential of the SLNs by the Malvern particle size analyzer.

Zeta potential of isoniazid loaded formulations was in the range of -23.38 ± 2.40 to -38.33 ± 2.28 mV and Polydispersity index was found to be between 0.234±0.028 to 0.358±0.020. From the results it shows that as sonication time and surfactant concentration increases with decrease in particle size to nanometric range.

And if concentration of surfactant i.e.tween 80 increases with decrease in Poly Dispersibility index which shows good dispersibility particles and stability by increasing the concentration of tween 80. The results are shown in Table 3 and Figure No:1-4.

Optimization of formulation based on effect of Homogenization Time and SLS on Average particle size, PDI and Zeta potential

The particle size analysis revealed that, the SLNs were in the nanometer range. The size of the nanoparticles was affected by the Homogenization Time and the concentration of SLS.

The size of the Isoniazid loaded SLNs were found to be between 329.4 nm to 442.8nm.The stability of the formulated SLNs was evaluated by measuring the zeta potential of the SLNs by the Malvern particle size analyzer.

Zeta potential of isoniazid loaded formulations was in the range of -10.44 ± 2.08 to -16.48 ± 1.92 mV and Polydispersity index was found to be between 0.391±0.016 to 0.567±0.042.

From the results it shows that as Homogenization Time and surfactant concentration increases with decrease in particle size to nanometric range. And if concentration of surfactant i.e. SLS increases with decrease in Poly Dispersibility index which shows good dispersibility particles and stability by increasing the concentration of SLS. The results are shown in Table no 4 and Figure no 5-8.

Isoniazid Solid Lipid Nanoparticles was prepared and evaluates by Solvent Evaporation Method followed by Ultrasonication. From the results obtained from executed experiments it can be concluded that: Particle size parameter shows that, particle size of Isoniazid SLN decreases with increase in the concentration of the Tween 80. Polydispersity index was within the range of 0.244 to 0.326, which shows the prepared solid lipid nanoparticles formulation shows a homogeneous size distribution in all over the formulation.The results of Zeta potential in formulation FS3 shows -38.33 mV, that shows that FS3

formulation having high potential to conduct the surface charges with good stability, which confirms that FS3 Isoniazid - SLN shows better dispersion mechanism in the medium.

Isoniazid Solid Lipid Nanoparticles was prepared and evaluates by Solvent Evaporation Method followed by Homogenization. From the results obtained from executed experiments it can be concluded that: Particle size parameter shows that, particle size of Isoniazid SLN decreases with increase in the concentration of the SLS. Polydispersity index was within the range of 0.391 to 0.843, which shows the prepared solid lipid nanoparticles formulation shows a homogeneous size distribution in all over the formulation. The results of Zeta potential in formulation FH3 shows -16.48 mV, that shows that FH3 formulation having high potential to conduct the surface charges with good stability, which confirms that FH3 Isoniazid - SLN with SLS 1.5% shows better dispersion mechanism in the medium.

Table 1. Composition of various formulation of Isoniazid SLN-Solvent evaporation method (Ultrasonication)

Trial Formulation	FS1	FS2	FS3	FS4	FS5	FS6
Isoniazid (mg)	20	20	20	20	20	20
Cholesterol (mg)	200	200	200	-	-	-
Stearic acid (mg)	-	-	-	200	200	200
Span 60(mg)	100	100	100	100	100	100
Tween 80(ml)	0.5	1	1.5	0.5	1	1.5
Distilled Water(ml)	50	50	50	50	50	50
Ethanol(ml)	10	10	10	10	10	10
Sonication time (Pulse rate)	5 min	10 min	15 min	5 min	10 min	15 min

Table 2. Composition of various formulation of Isoniazid SLN-Solvent evaporation method (Homogenization)

Trial Formulation	FH1	FH2	FH3	FH4	FH5	FH6
Isoniazid (mg)	20	20	20	20	20	20
Cholesterol (mg)	200	200	200	-	-	-
Stearic acid (mg)	-	-	-	200	200	200
Span 60 (mg)	100	100	100	100	100	100
SLS (%)	0.5	1	1.5	0.5	1	1.5
Distilled Water (ml)	50	50	50	50	50	50
Ethanol (ml)	10	10	10	10	10	10
Homogenization (RPM)	1000	2000	3000	1000	2000	3000

Table 3. Effect of Sonication time &Tween 80 on Particle size, PDI and Zeta Potential

Formulation	Sonication time (min)	Tween 80 concentration %	Mean Particle size (nm)	Poly Dispersibility Index	Zeta Potential (mV)
FS1	5	0.5	368.6±3.9	0.326±0.012	-28.70 ± 2.28
FS2	10	1.0	346.4±1.8	0.312±0.018	-23.38 ± 2.40
FS3	15	1.5	273.2±4.1	0.263±0.024	-38.33 ± 1.84
FS4	5	0.5	340.5±3.1	0.358±0.020	-26.84 ± 1.82
FS5	10	1	288.6±1.4	0.244±0.018	-27.44 ± 2.80
FS6	15	1.5	278.00±1.8	0.234±0.028	-26.85± 1.80

Table 4. Effect of Homogenization Time &SLS on Particle size, PDI and Zeta Potential

Formulation	Homogenization Time (min)	SLS concentration %	Mean Particle size (nm)	Poly Dispersibility Index	Zeta Potential (mV)
FH1	1000	0.5	442.8±5.6	0.567±0.042	-12.86 ± 1.84
FH2	1500	1.0	386.50±4.0	0.456±0.034	-10.48 ± 2.08
FH3	2000	1.5	343.2±4.0	0.391±0.016	-16.48 ± 3.18
FH4	1000	0.5	402.8±3.8	0.478±0.018	-15.62 ± 1.84
FH5	1500	1	398.6.±3.0	0.386±0.028	-10.44 ± 1.48
FH6	2000	1.5	329.4±4.2	0.348±0.036	-12.54± 2.00

Table 5. Results of Best Isoniazid –SLN Formulations

Sl. No	Parameter	Result of SLN prepared by Sonication (15 min pulse) with 1.5 % Tween 80 as surfactant – FS3	Result of SLN prepared by Homogenization (3000 RPM) with 1.5 % SLS as surfactant – FH3
1	Particle Size	273.3 nm in diameter	343.2 nm in diameter
2	Zeta Potential	-38.33 mV	-16.48 mV
3	Polydispersity Index	0.263	0.391

Figure 1. Effect of Surfactant & Phospholipid, Sonication time on particle size on Isoniazid SLN formulation

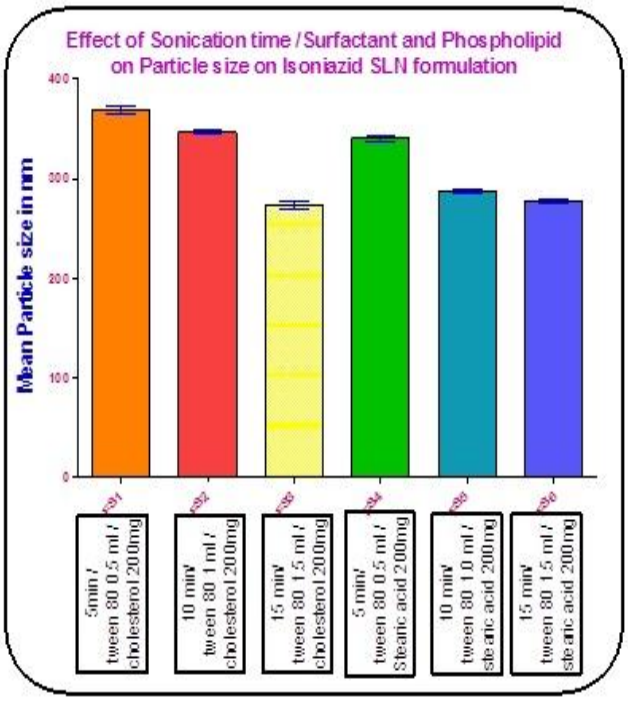


Figure 2. Effect of tween 80 on PDI of Isoniazid SLN

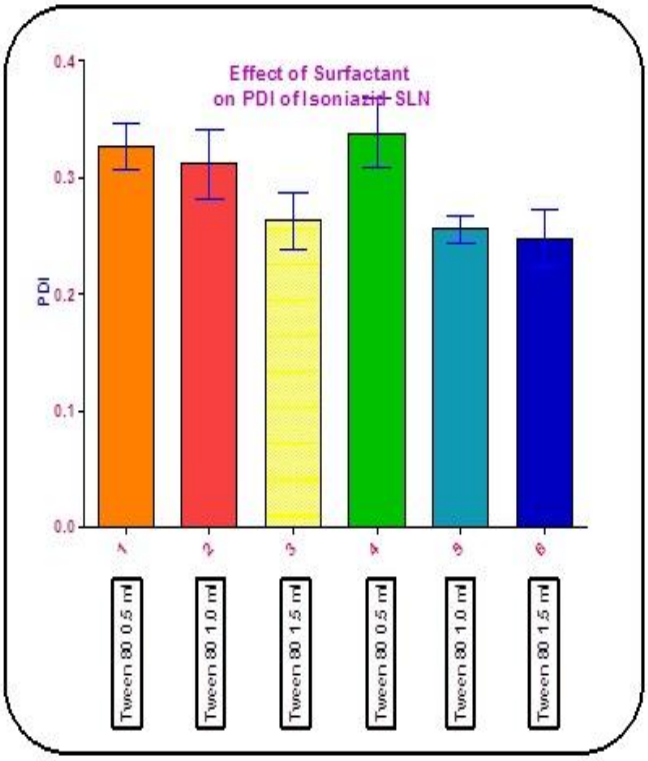


Figure 3. FS3 Isoniazid SLN Particle Size

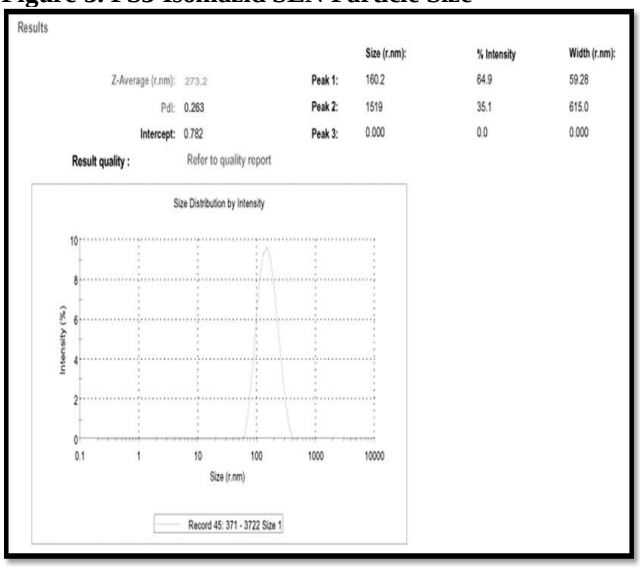


Figure 4. FS3 Isoniazid SLN Particle Zeta potential

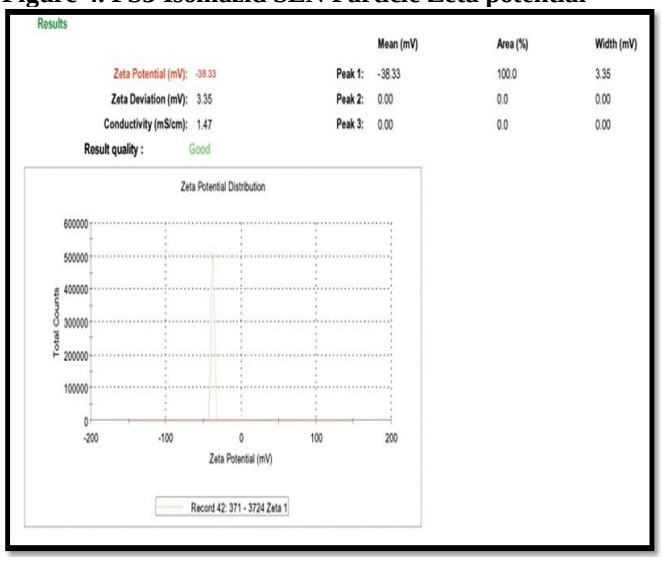


Figure 5. Effect of Surfactant & Phospholipid, Homogenization RPM on particle size on Isoniazid SLN formulation

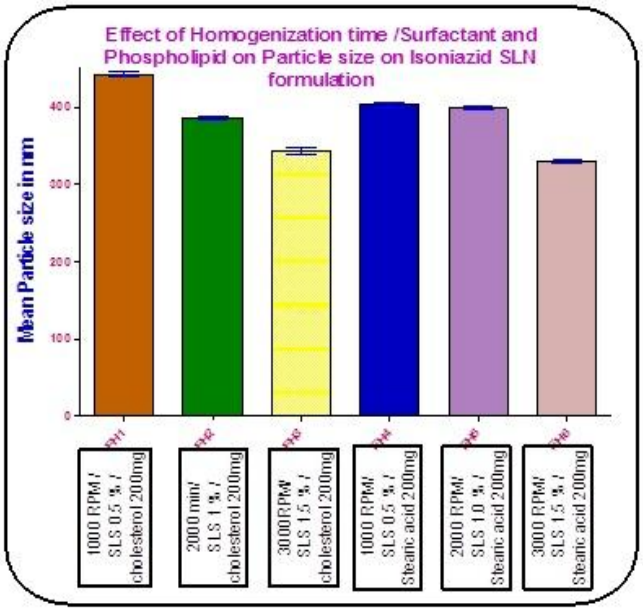


Figure 6. Effect of SLS, Cholesterol and stearic acid on PDI of Isoniazid SLN

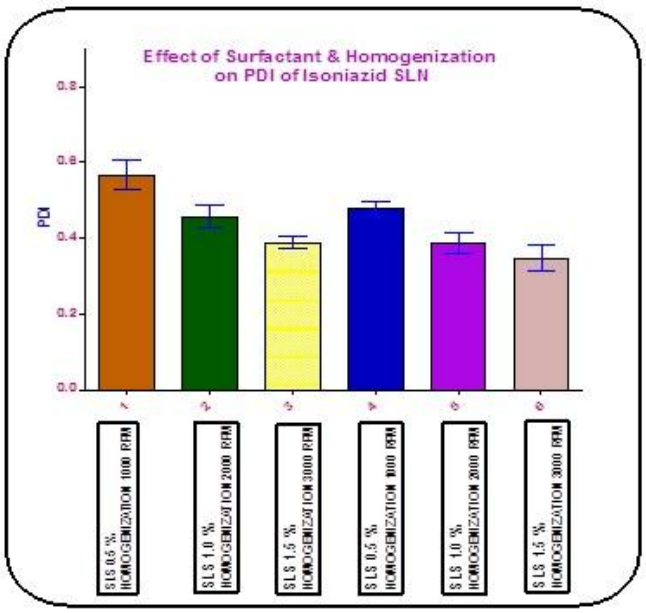


Figure 7. FH3 Isoniazid SLN Particle Size

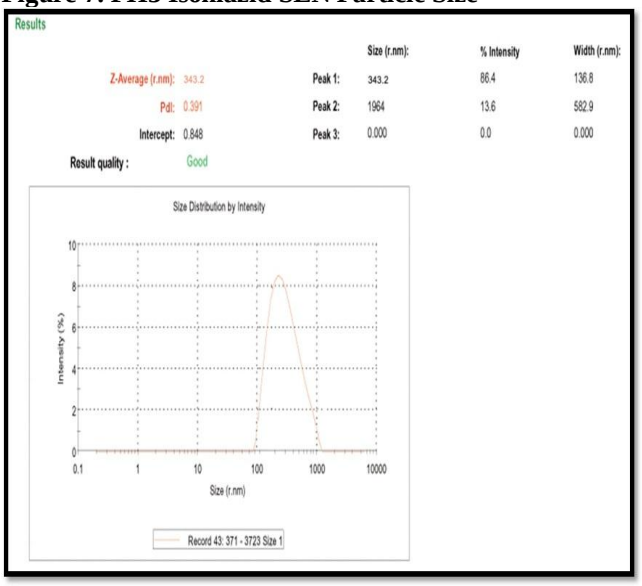
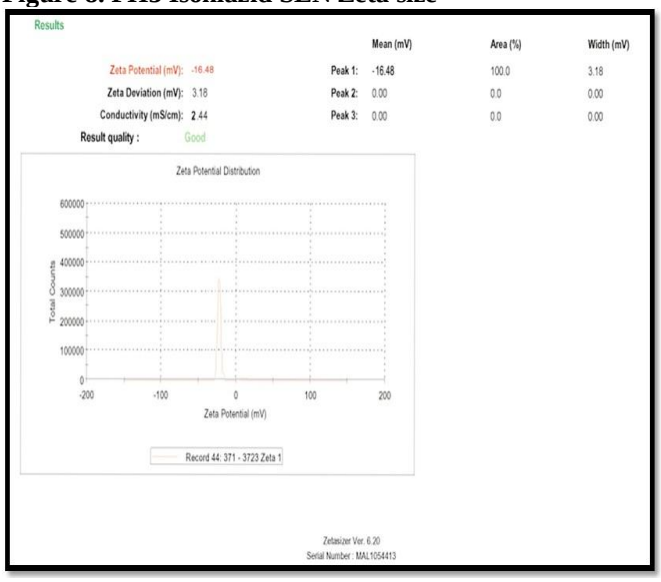


Figure 8. FH3 Isoniazid SLN Zeta size



CONCLUSION

SLN are formulated using with various excipients especially surfactant and process especially ultrasonication and homogenization time. Which are evaluated for Particle size, Zeta potential and Poly dispersibility index (PDI). It shows size of SLN decreases with increase in concentration of surfactant along with increased sonication and homogenization time. Concentration of surfactant (SLS/Tween 80) increases means, the size of SLN decreases and Zeta potential (surface charge) increases. From the results it was concluded that desired SLN was formed when the concentration of the surfactant (tween 80 and sodium lauryl sulfate) was maintained at 1.5% and Ultrasonication at 15 pulse/min, Homogenization (3000 RPM) under solvent evaporation method.

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