Available online on 15.07.2019 at http://jddtonline.info

Journal of Drug Delivery and Therapeutics

Open Access to Pharmaceutical and Medical Research

Open Access Research Article

Preformulation Studies of Intranasal Solid Lipid Nanoparticles of Mometasone Furoate

Madgulkar Ashwini R*., Padalkar Rahul R., Amale Sushant K.

Department of Pharmaceutics, All India Shri Shivaji Memorial Society's College of Pharmacy, Kennedy Road, Near R.T.O., Pune, Maharashtra, India-411001.

ABSTRACT

The objective of the present work was to prepare intranasal solid lipid nanoparticles (SLN) of mometasone furoate. Mometasone furoate is BCS class II drug having low aqueous solubility and highly sensitive to hepatic metabolism. Mometasone furoate loaded nanoparticles were prepared by high pressure homogenization technique. The preformulation studied was conducted by studying various selection criteria. Lipid was chosen on the basis of maximum solubility of the drug in lipid. Glyceryl monostearate was selected as the lipid phase which showed maximum drug solubility than other lipids. Selection of surfactant, homogenization pressure and no. of homogenization cycle was done on the basis of minimum particle size and maximum % entrapment efficiency. These results showed high entrapment efficiency and minimum particle size.

Keywords: Intranasal solid lipid nanoparticles, High pressure homogenization, Glyceryl monostearate.

Article Info: Received 13 May 2019; Review Completed 28 June 2019; Accepted 08 July 2019; Available online 15 July 2019

Cite this article as:

Madgulkar AR, Padalkar RR, Amale SK, Preformulation Studies of Intranasal Solid Lipid Nanoparticles of Mometasone Furoate, Journal of Drug Delivery and Therapeutics. 2019; 9(4):526-528 **http://dx.doi.org/10.22270/jddt.v9i4.3100**

***Address for Correspondence:**

Dr. Ashwini R. Madgulkar, Professor, AISSMS College of Pharmacy, Kennedy Road, Near R.T.O, Pune - 411001, Maharashtra, India.

INTRODUCTION:

Mometasone furoate is categorized as a potent vasoconstrictor, anti-inflammatory drug, selected for nasal solid lipid nanoparticle formulation. This is a corticosteroid hormone receptor agonist having anti-allergic and anti-inflammatory activity [1, 2].

The oral bioavailability of mometasone furoate is close to zero. Studies have reported that any amount of mometasone furoate that is ingested and absorbed undergoes extensive metabolism to multiple metabolites. Nasal absorption of the drug into the systemic circulation takes place very effectively. The recommended nasal dose of mometasone furoate is 400 mcg per day for an adult. It has the half-life of about 5.8 hrs with 99% plasma protein binding. The nasal administration of mometasone furoate SLN would be effective and it could be highly acceptable option for drug delivery [3-5].

Solid lipid nanoparticles can improve systemic drug delivery, since they are able to protect the encapsulated drug from biological or chemical degradation and from extracellular transport by P-gp efflux proteins [6]. Solid lipid nanoparticles are considered to be among the most effective lipid-based colloidal vehicles. They are constituted by a solid lipid matrix surrounded by a layer of surfactants in an aqueous dispersion [7].

MATERIALS AND METHODS:

Materials:

Mometasone was gifted by Glenmark Phamrmaceuticals, Baddi, HP, India IMWITOR® 900 K (glyceryl monostearate) gifted by IOI Oleo Gmbh , Germany. Tween 80 was obtained from Loba Chemie, Mumbai, India. Benzalkonium chloride was obtained from Molychem, Mumbai, India.

Methods:

Selection of excipients and their levels:

Selection of lipid:

Selection of lipid depends on the basis of solubility of drug in lipid and also on the melting point of lipid. For the preparation of solid lipid nanoparticles loaded with mometasone furate, drug should be completely soluble in lipid. Various lipids such as Dynasan 118 , Emulsire 61, Imwitor 900 k (GMS), Precirol ATO 5, Compritol 888 ATO, Gelucire, and Stearic acid were used to study the solubility of

drug. The total amount of lipid added to get a clear solution was recorded.

Selection of surfactant and its concentration:

Different surfactant were tried to prepare SLN. SLN are colloidal system of nanoparticles made up of solid lipid as matrix medium which is stabilize in aqueous media by surfactant. For preparation of SLN various surfactants used Such as Tween 80, Tween 20, Poloxamer 188 was used to observed particle size and entrapment efficiency. Surfactant concentration also influences particle size of formulation.

Selection of homogenization cycle and pressure:

Number of homogenization cycles and homogenization pressure were screened to get minimum particle size and maximum entrapment efficiency. Prepared pre-emulsion was passed into homogenization.

Preparation of SLN:

High pressure homogenization Method:

SLN formulation was prepared using HPH (high pressure homogenization) method. In this method, glyceryl monostearte was melted 5 to 10 ºC above the melting point of lipid. Mometasone furoate was dissolved in lipid under continuous stirring. Later surfactant water phase was added slowly and heated the same as drug lipid phase. Benzalkonium chloride was added to this pre-dispersion as a preservative. Pre-emulsion was obtained under stirring at high speed up to 1500 rpm. This pre-emulsion was passed through high pressure homogenizer. The obtained o/w dispersion formed was immediately cooled down to room temperature. Mometasone furoate loaded SLN dispersion was subjected to characterization.

RESULTS AND DISCUSSION:

Selection of lipid:

The maximum solubility of mometasone furoate was obtained in glyceryl monostearate (Figure 1). Greater solubility of the drug in lipid helps in formulation of matrix type of SLN. Maximum solubility of drug into the lipid phase is required for producing formulation with high drug load thus delivering maximum amount of drug to the site of action. 2 to 5 % lipid showed high viscosity and stability. Use of high concentration of lipid produced more viscous pre-emulsion and produced higher particle size. Lower concentration of lipid could not dissolve mometasone furoate.

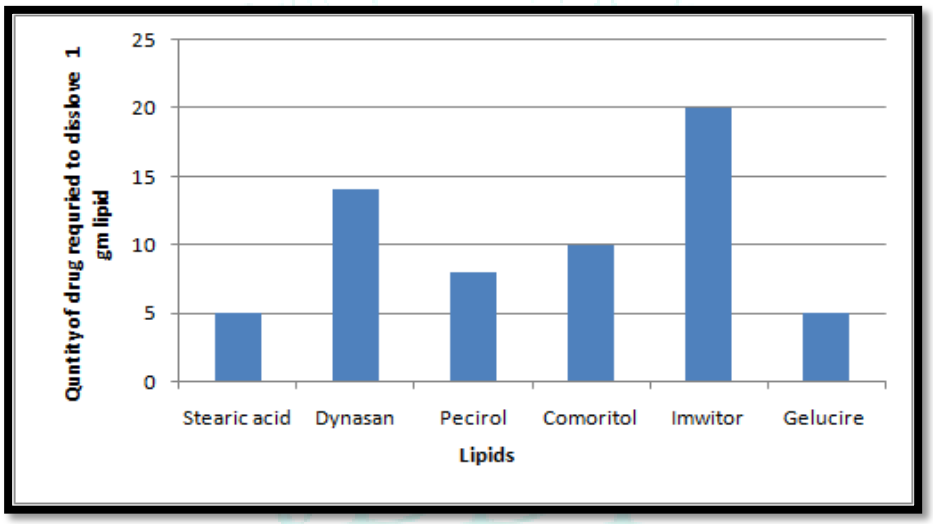

Figure 1: solubility of mometasone furoate in different lipid.

Selection of surfactant:

Different surfactants were screened to prepare SLN and the resultant particle size was observed in (table 1). Formulations containing Tween 20, Poloxamer 188 showed high particle size than Tween 80 and also gives low entrapment efficiency. Tween 80 resulted in particle size 218 ±1.7 and entrapment efficiency 72 % and hence it was selected as surfactant.

Table 1: Effect of surfactant on particle size and entrapment efficiency

Sr. no.	Type of surfactant	Particle size (nm)	Entrapment efficiency (%)
1	Poloxamer 188	480±5	65
2	Tween 80	218±4	72
3	Tween 20	319±3	64

n=3

Selection of surfactant concentration:

The surfactant concentration affects the particle size of SLN by causing the stabilization of the particles. It was observed that 0.5% concentration gives high particle size of 312 nm and when the concentration of surfactant was increased, there was a decreased in particle size (table 2). Surfactant concentration 4% and 5% reduced entrapment efficiency to 41%. Higher concentration of surfactant solubilizes drug in the micelles in the aqueous phase, leading to reduced entrapment efficiency.

Table 2: Effect of surfactant concentration particle size and entrapment efficiency

Sr. no.	Surfactant Concentrations (%)	Particle size (nm)	Entrapment efficiency (%)
1	0.5	312±3	38
2	1	272±4	48
3	2	240±6	64
4	3	116±3	70
5	4	110±2	51
6	5	112±1	41

n=3

Selection of homogenization cycles:

It was observed that as the no. of homogenization cycle increased, particle size was decreased (table 3). An increase in 9 to 12 the homogenization cycles resulted in increased particle size. This might be due to the high kinetic energy of small particles that showed aggregation of particles. It was observed that entrapment efficiency was not significantly affected by the homogenization cycles. After 5 homogenization cycles entrapment efficiency was reduced. Increasing number of homogenization cycles also decreased entrapment efficiency due to the aggregation of particles.

Table 3: Effect of surfactant on particle size and entrapment efficiency

Sr. no.	No. of homogenization cycles	Particle size (nm)	Entrapment efficiency (%)
1	1	348±3	80
2	3	240±2	75
3	5	180±4	74
4	7	148±4	71
5	9	212±3	68
6	10	388±7	66
7	12	412±2	61

n=3

Selection of homogenization pressure:

It was observed that applied homogenization pressure highly influences the particle size. When the applied homogenization pressure was increased from 200-1000 bar, particle size slowly decreased from 400nm to 138 nm (table 4). Increasing the homogenization pressure leads to an increase of particle size due to coalescence. This occurs because of the high kinetic energy of the particles [8].

Table 4: Effect of homogenization pressure on particle size

Sr. no.	homogenization pressure (bar)	Particle size (nm)
1	200	410±4
2	400	311±2
3	600	157±1
4	700	140±5
5	1000	138±3
6	1200	219±6

CONCLUSION:

Different formulations were developed and its particle size and % entrapment efficiency were studied.

As a result of the study the selection of lipid was done on the basis of maximum solubility of the drug in lipid. Glyceryl monostearate was selected as the lipid phase for mometasone furoate SLN preparation as it showed maximum drug solubility than other lipids. Selection of surfactant, homogenization pressure and no. of homogenization cycle was done on the basis of minimum particle size and maximum % entrapment efficiency. In the formulation study screening different surfactants were tried to prepare SLN. Tween 80 resulted in minimum particle size and maximum % entrapment efficiency and hence this was selected as a surfactant.

REFERENCES:

[1] Mandhane S, Shah J, Thennati R. Allergic rhinitis: An update on disease, present treatments and future prospects. International Immuno pharmacology. 2011; 11(11):1646-1662.

[2] Bousquet J, Schünemann H, Samolinski B, Demoly P, Baena-Cagnani C, Bachert C et al. Allergic Rhinitis and its Impact on Asthma (ARIA): Achievements in 10 years and future needs. Journal of Allergy and Clinical Immunology. 2012; 130(5):1049-1062.

[3] Galgatte U, Kumbhar A, Chaudhari P. Development of in situ gel for nasal delivery: design, optimization, in vitro and in vivo evaluation. Drug Delivery. 2013; 21(1):62-73.

[4] Mehta R, Surve A, Menon D. Novel Nasal in situ Gelling System for Treatment of Sinusitis. Indian Journal of Pharmaceutical Sciences. 2009; 71(6):721-722.

[5] Kosoglou T, Hubbell, Xuan, Cutler, Meehan, Comparison of the systemic bioavailability of mometasone furoate after oral inhalation from a mometasone furoate/formoterol fumarate metered-dose inhaler versus a mometasone furoate dry-powder inhaler in patients with chronic obstructive pulmonary disease. International Journal of Chronic Obstructive Pulmonary Disease. 2013:107.

[6] Alpesh M, Snjezana S, Lisbeth I. Nanoparticles for direct nose-to-brain delivery of drugs, International Journal of Pharmaceutics, 2009; 379:146–57.

[7] Battaglia L, Gallarate M. Lipid nanoparticles: state of the art, new preparation methods and challenges in drug delivery. Expert Opin. Drug Deliv. 2012;(9) 497–508.

[8] Chimmiri P ,Gankre K., Solid Lipid Nanoparticles: For Enhancement Of Oral Bioavailability. International Journal of Pharmaceutical Development & Technology. 2011; 1 (2), 2248 - 910.