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A Comprehensive Review on Nose to Brain Drug Delivery via Development of Solid Lipid Nanoparticles

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ABSTRACT:
The nasal route has been used for many years for the local treatment of nasal diseases.More recently, this route has been gaining momentum, due to the possibility of targeting the central nervous system (CNS) from the nasal cavity, avoiding the blood−brain barrier (BBB).In these area solid lipid nanoparticle shows promising outcomes. The development of solid lipid nanoparticles(SLN)as a next-generation drug delivery technology has opened up new opportunities for the pharmaceutical industry, cosmetics, research, clinical medicine and other related fields of study. Recently, increasing attention has been focused on these SLN as colloidal drug carriers for incorporating hydrophilic or lipophilic drugs. Various general methods of preparation of SLN such as, high pressure homogenization, microemulsion based method, spray drying, precipitation method, solvent emulsification diffusion method, Film ultrasound dispersion, ultrasonication method. The present review focuses on nose to brain delivery on SLN in term of their methodology, characterization and survey of drugs.

Keyword: Solid Lipid Nanoparticles, Homogenization method, Nasal route, Brain targeting

I. INTRODUCTION:

Solid lipid nanoparticles were first time introduce in early 1990s. (1) Solid lipid nanoparticles are spherical in shape and particle size ranging from 10 to 1000 nm with diameter50 to 1000nm(2). The lipid-based drug delivery system, the main ingredient is phospholipids due to different types ofcharacteristics, are Amphiphilicin nature and Biocompatible etc. But,liposome's and lipospherehavedifferent types of disadvantages, such as- production method is difficult, entrapment efficiency (%EE) is less, large scale production does not easily possible, due to following reasons solid lipid nanoparticles are developed. The main ingredients of SLNs formulations, such as- lipids, surfactants or emulsifiers and/or mixture of both, Active Pharmaceutical Ingredients (APIs) with desired solvent system(3).The amount of absorption, the rate of absorption, and the drug's bioavailability are all strongly influenced by the drug's solubility in the solution and by its gastrointestinal permeability.The bioavailability of a drug is influenced by its solubility in water, rate of dissolution, drug permeability, sensitivity to efflux mechanisms, and first-pass metabolism(4). Compared to highly pure lipids, such as monoacid triglycerides, the use of mono- and di-glycerides as lipid matrix composition may boost medication solubility. Mono-, di-, and triglyceride mixes that contain fatty acids with different chain lengths and levels of unsaturation make up the oils and fats that are found in nature(5).Solid lipid nanoparticles having characteristics are smaller size, large surface area and gives controlled release action, better physical stability, good tolerability with the help of carriers. SLNs formulation are suitable for various route of administration, such as –Oral, Parenteral, Nasal, Rectal, Ocular.(2)

An ideal properties of Solid lipid nanoparticles are :

a) It shows controlled release action of drug.
b) Protect drug from chemical degradation.
c) Binding of drug to the target site.(6)

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STRUCTURE OF SOLID LIPID NANOPARTICLES:

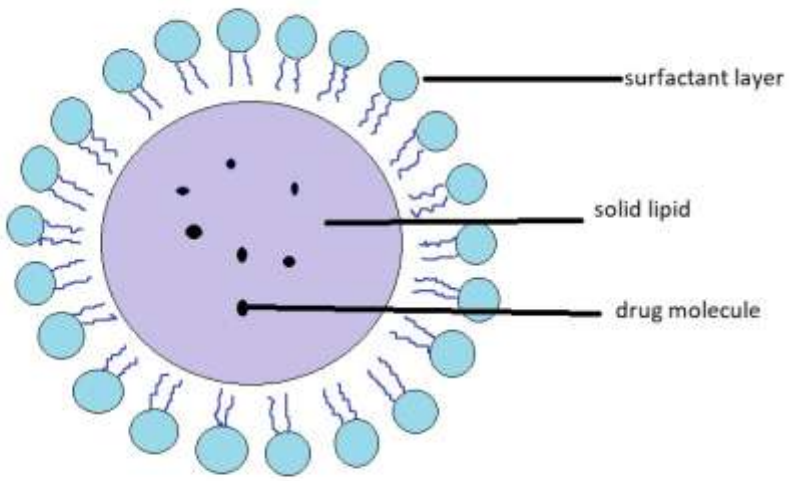

Diagram -1: Chemical structure of Solid lipid nanoparticles

Drug selection criteria for SLN formulation – (7)

In drug discovery, the proportion of drug candidates with low solubility has increased, and in recent years, about 70% of novel drug candidates have demonstrated poor aqueous solubility. BCS is a useful technique for formulation development decision-making from a biopharmaceutical perspective.Based on their solubility and intestinal permeability, pharmacological compounds are divided into one of four groups by the BCS. The following are these four groups: High solubility and high permeability define Class I; low solubility and high permeability define Class II; while high solubility and low permeability define Class III (Class IV).

GENERAL METHODS OF PREPARATION OF SLN:

1. High Pressure Homogenization
a) Hot homogenization
b) Cold homogenization
2. Microemulsion based method
3. Spray Drying method
4. Precipitation method
5. Solvent Emulsification Diffusion method
6. Film Ultrasound Dispersion
7. Ultrasonication

High Pressure Homogenization (8)

Hot Homogenization Technique:

Fordecrease the particle size in this techniquevery high pressure is applied (100 to 2000 bar). Solid lipid nanoparticles are get form either by high temperature or less than room temperature is known as Hot Homogenization and Cold Homogenization. In HPH technique, the drug and lipid both are heated at 5-10 ^{0}C, for dissolved drug into the melted lipid. In next step, the drug is dispersed or dissolved in melted lipid and form the emulsion. When high pressure is applied such as 100 to 1000 bar for 3-5 times then pre-emulsion is formed. After Homogenization process, firstly colloidal emulsion is formed, after cooling SLNs are formed.

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Table 1: Formation of Solid Lipid Nanoparticles by Hot Pressure Homogenization Technique

Drug	Lipid	Surfactant	Outcome	Ref.
Lopinavir	Compritol888ATO	Pluronic F 127, Mannitol	It improved bioavailability of drug	9
Lovastatin	Triglyceride, Phosphatidylcholine 95%	PluronicF68	Enhance the oral bioavailability of drug and provide controlled relase action.	10
Nitrendipine	Phosphatidylcholine	Pluronic F68	Enchanethe bioavailability of drug.	11
Praziquantel	Hydrogenated castor oil	Polyvinyl Alcohol (PVA)	Increase the pharmacological activity of drug.	12
Camptothecin	Stearic acid	PluronicF68, Tween 80	It shows sustained release effect.	13
Cyclosporine A	Imwitor 900	TagatS, Sodium cholate	Enhance the oral bioavailability of drug.	14
Fenofibrate	Vit.E TPGS, Vit.E 6-100	-	Enhance the bioavailability of drugs with low water solubility	15
Hydrocortosone	Dynasan 114, Dynasan 118, Tegin 4100	Tween80	The release properties and drug distribution in lipid particles are significantly influenced by the corticosteroid solubility in the lipid phase.	16

Cold Homogenization Technique: (17)

In Cold Homogenization Technique, firstly heated the lipid phase it contains the lipids and drug molecule. Due to heating lipid phase, suspension is formed it contains solid lipid drug mixture. After cooling the mixture in dry ice and/or liquid Nitrogen. Fine powder is formed the micro-particles by milling process. Solid lipid micro-particle dispersion is obtained by placing the micro-particles into the cold aqueous surfactant solution. At the last stage, SLNs are formed by homogenization at 1.5 × 108 Pa for at least 5 cycles.

Table 2: Formation ofSolid Lipid Nanoparticles by Cold Pressure Homogenization Technique

Drug	Lipid	Surfactant	Outcome	Ref.
Vinorelbin - bitartrate	Glyceryl monostearate	Methyl thiazolyl diphenyl tetrazolium bromide (MTT)	It shows high entrapment efficiency and drug release profile	18

Micro emulsion Based Method(19)

In micro emulsion technique, solid lipid nanoparticles are produced by addition of microemulsion in water it forms precipitation of lipids that leads to formation of SLNs. Microemulsion is a lipophilic in nature consist of surfactant, co-surfactant and water. In microemulsion technique, lipids are melted at a temperature 65-70^{0}C(above the M.P of lipids). Separately heated the mixture of surfactant, co-surfactant and water at a same temperature. Further added into the melted lipid with slowly stirring. Then transparent mixture is formed. In this mixture add excessive amount of cold water in the ratio of microemulsion to cold water (1:10) with continuous stirring. The solid lipid nanoparticles are produced and washed with distilled water for 2-3 times. After washing, filtration is done for removal of larger particles. The excessive amount of water is removed by either ultrafiltration or by lyophilisation

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Table 3: Formation of Solid Lipid Nanoparticles by Microemulsion Based Method

Drug	Lipid	Surfactant	Outcome	Ref.
Carvedilol	Stearic acid	Pluronic F68, Sodium taurocholate	Increase oral bioavailability of drug	20
Curcumin	Compritol 888 ATO	Soy lecithin, Tween 80	Improved oral bioavailability of drug.	21
Indarubicin	Stearic acid	Epikuron 200	It shows prolong release of action.	22
Ketoprofen	Bees wax, Carnauba wax	Tween 80, Egg lecithin	It shows high Entrapment Efficiency	23
Nevirapine	Stearic acid, Compritol 888 ATO	Tween 80, Lecithin	The Formulation shows better entrapment efficiency than plain drug.	24
Tobramycin	Stearic acid	Epikuron 200, Sodium taurocholate	It shows sustained release effect.	25

Spray Drying Method (26)

Spray drying is a cheaper process used for preparation of an aqueous solid lipid nanoparticle dispersion into a dry product, with the help of spray drying process powder is formed it generally used in I.V. injections. In this process, lipids are used with melting point>70^0 C. Further melting point of lipid can be minimized with dispersion medium. (Dispersion medium is used other than pure water).

Table 4: Formation of Solid Lipid Nanoparticles by Spray Drying Method

Drug	Lipid	Surfactant	Outcome	Ref.
Indomethacin or 5–fluorouracil	Glyceryl tristareate	Polyvinylpyrrolidone (PVP, 40)	It shows sustained release property	27
Bovine insulin	Dimyristoylphosphatidylcholine glycerol (DMPG)	Dipalmitoyl phosphatidylcholine (DPPC)	It shows controlled release of drug.	28

Precipitation Method (29)

Solid lipid nanoparticles are produced by precipitation method by using organic solvent. In this method of preparation lipid will be dissolved in an organic solvent and produced an aqueous phase. Then evaporation will be done for removal of organic solvent. When organic solvent will be removed the precipitation of Solid lipid nanoparticles were formed.

Table 5: Formation of Solid Lipid Nanoparticles by Precipitation Method

Drug	Lipid	Surfactant	Outcome	Ref.
Cloricromene	(Soya phosphatidylcholine 95%)	Epikuron 200 (surfactant) Taurocholate (cosurfactant)	It gives targeted delivery to drug.	30
Silibinin	Stearic acid	Brij 78 (Polyoxymethylene 20 stearyl ether)	It enhances solubility of drug.	31

Solvent Emulsification – Diffusion Method (32)

It is a combination of microemulsions and is used to prepare SLNs. This procedure involves dissolving the lipid phase in an organic solvent (acetone) before adding the organic phase tothe organic phase until it is entirely dissolved in the aqueous stage while being continuously mixed at 70–80°C The resulting nanoemulsion is then cooled

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to below 5°C to harden the lipid nanoparticles. The precipitation of the lipid in the evaporated aqueous medium causes nanoparticles to disperse as the solvent evaporates below condensed pressure. The average SLN diameters range between 30 and 100 nm, depending on the amount of lipid present in the organic phase, the emulsifier used, which also has the highest encapsulation efficiency at 67.9% and the solvent used.

Table 6: Formation of Solid Lipid Nanoparticles by Solvent Emulsification DiffusionMethod

Drug	Lipid	Surfactant	Outcome	Ref.
Doxorubicin	CapmulMCM C10	SolutolHS15	It improves solubility of drug.	33
Gonadorelin	Monostearin	Polyvinyl alcohol	It shows prolong release of drug.	34
Clobetasol propionate	Monostearin	Polyvinyl alcohol	It shows prolonged release for lipophilic drugs.	35

Film Ultrasound Dispersion (36)

The drug and lipid were combined with the appropriate organic solutions, and after the organic solutions were rotated, decompressed, and evaporated, a lipid film was created. Next, the emulsion-containing aqueous solution was added. SLN with small and homogeneous particle size is created by using ultrasound with the diffuser as the final step.

Table 7: Formation of Solid Lipid Nanoparticles by Film Ultrasound Dispersion Method

Drug	Lipid	Surfactant	Outcome	Ref.
Atazanavir	Stearic acid	Pluronic F-68	Increased brain uptake of atazanavir and potentially other than protease inhibitor.	37
Calcitonin	Stearic acid	Poloxamer 188 Pluronic F 68	Reduces the degradation of gastrointestinal enzymes	38

Ultrasonication

Solid lipid nanoparticles are prepared by using ultrasonication technique. For formation of small particle size ultrasonication and high-speed homogenization both techniques are used. Formation of SLNs with the help of ultrasonication method which does not use of organic solvent, large amount of surfactants or additives (39). In this technique, melted lipid is added and dispersed in an aqueous surfactant solution. Then primary emulsion gets formed. This emulsion temperature is cooled down at room temperature and ultrasonication is done with probe sonicatior.For ultrasonication, bath sonicatior and/or probe sonicatior is used. This method can be used at lab level but it shows the limitation like particle growth during storage. Metal contamination is the most important limitation of ultrasonication technique (40).

Table 8: Formation of Solid Lipid Nanoparticles by Ultrasonication Method

Drug	Lipid	Surfactant	Outcome	Ref.
Indomethacin	Glyceryl behenate & tribehenate	Lutrol F68	It shows controlled release of drugs.	41
Vipocetine	Glyceryl monostearate	Tween 80	It improve solubility of drugs.	42
Triptolide	Tristearin glyceride	Poloxamine 908	It enhances the anti-inflammatory activity	43
Mifepristone	Glycerol monostearate	Tween-80	It enhancesstability of	44

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			drug.	
Oridonin	Stearic acid, Lecithin	Pluronic F68	It improves solubility and bioavailability of drug.	45

CHARACTERIZATION OF SLNs:

Particle size Determination: (46)

Particle size can be measured by Photon Correlation Spectroscopy (PCS), Scanning Electron Microscopy (SEM), Transmission Electron Microscopy (TEM), Atomic Force Microscopy (AFM) and Laser Diffraction (LD). The physical stability of SLN is depend upon the size of the particle. There are two common techniques used for determination of size of particles- i) Laser Diffraction ii) Photon Correlation Spectroscopy.

Determination of particle size of Solid lipid nanoparticles: (47)

X-ray Diffraction and Differential Scanning Calorimeter

The scattering of radiation on the surface of solid and measures the degree of crystallinity. DSC can be used for evaluation of properties and degree of crystallinity of nanoparticles.

Electron Microscopy

Electron Microscopy gives direct information of particle shape of nanoparticles. For morphological examination of nanoparticles SEM and TEM mostly used.

Nuclear Magnetic Resonance (NMR)

NMR can be used for determination of particle size of nanoparticle along with its qualitative nature.

Surface charge and Zeta potential: (48)

Zeta potential analyser or zeta meter can be used for determination of surface charge. It is used for determination of stability of nanoparticles.

Atomic force Microscopy: (49)

It is a sophisticated microscopic approach used as a brand-new tool to visualize the particles natural, unaltered shape and surface characteristics.

Entrapment Efficiency and Drug loading: (50)

The encapsulation efficiency (EE) and drug loading are important parameters in formulation of solid lipid nanoparticles. The amount of drug entrapped in SLN is determined by centrifugation, filtration or gel chromatography after separation of free drug from medium. The absorbance of drug can be measured by standard analytical techniques such as UV Spectrophotometry, Spectroflurophotometry, High Performance Liquid Chromatography (HPLC), etc.

The percentage Entrapment Efficiency is calculated by following formula:

$$\% \text{ Entrapment Efficiency} = \frac{\text{Amount of drug in SLNs}}{\text{Total amount of Drug added}} \times 100$$

The percentage Drug loading is determined by following formula:

$$\%\text{Drug loading} = \frac{\text{Amount of drug in SLNs}}{\text{Total amount of drug, lipid, emulsifier}} \times 100$$

In Vitro Dissolution: (51)

In vitro dissolution method can be used for determination of drug release rate it can be achieved by using dialysis tubing. The SLN dispersion is placed in dialysis tubing. The suitable dissolution medium can be used at room temperature. The samples are withdrawn from dissolution medium at specific time interval along with centrifugation. The drug content can be measured by analytical method such as UV spectroscopy and High-Performance Liquid Chromatography.

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Table 9: Current Literature survey of SLN formulation of various route of administration:

Sr. No.	Route of Administration	Incorporated Drug	Therapeutic Use	Ref.
1.	OralAdministration	Efavirenz	Antiretroviral	52
		Idarubicin	Anticancer	22
		Camptothecin	Anticancer	13
		Tobramycin	Antibiotic	53
2.	Parenteral Administration	Camptothecin	Anticancer	54
		Cyclosporine A	Immunosuppressant	55
		Diazepam	Treatment of anxiety	56
		Doxorubicin	Anticancer	57,58
		Paclitaxel	Anticancer	59,60
3.	Topical Administration	Tretinoin	To treat Acne	61
		Clotrimazole	Antifungal	62
		Oxybenzone	To treat skin cancer	63
		Ketoconazole	Antifungal	64
4.	Pulmonary Administration	Insulin	Insulin	65
		Montelukast	To treat Asthma	66
		Levofloxacin&DNase	To treat bacterial infection	67
		Itraconazole	To treat infection in the lungs	68
		Tobramycin	To treat lung infection with cystic fibrosis	69

Nasal Route:

Since several years ago, corticosteroids, decongestants, and antihistamines have all been often administered via the nasal route to treat localised nasal illnesses. With thegoal of improving the treatment of disorders of the central nervous system (CNS), such as epilepsy, Alzheimer's disease, Parkinson's disease, multiple sclerosis, andgliomas, the possibility of bypassing the blood-brain barrier (BBB) and entering the brain throughthe nose has recently attracted attention.As the sole method of medication delivery to the brain that bypasses the BBB and the systemic circulation, intranasal administration uses the olfactory and trigeminal nerves. However, it's crucial to remember that some of the medication is absorbed into the bloodstream after being administered intravenously and then travels through the BBB to the brain.A possible alternative to current treatments for brain illnesses has been proposed using solid lipid nanoparticles (SLN) to help medications be targeted to the brain after being administered intranasally. (70)

Pathways for Delivery of drug fromNosetoBrain:

Nasal administration, different drug transport pathways from the nose to the brain can occur, which have been classified as direct transport, indirect transport, or a combination of both. Furthermore, some drugs can be eliminated by the mucociliary clearance mechanism before they reach the olfactory or respiratory regions. (70)

When a medicine is administered, drug-loaded particles go directly from the nose to the brain via the olfactory and trigeminal neurons and then indirectly into the bloodstream before crossing the blood-brain barrier to the brain.A drug is transported to the olfactory and respiratory areas when it enters the nasal cavity. Olfactory nerves in this area start in the olfactory epithelia and end at the olfactory bulb. Drugs in the olfactory region can enter the brain through one of four different pathways: (1) an extraneuronal route along olfactory neurons; (2) an intraneuronal route by olfactory neuron endocytosis; (3) through the intercellular space by endocytosis; (4) through supporting cells by endocytosis.The main direct method for drug transport from the nose to the

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brain, which can take up to 30 minutes, is the extraneuronal route (route 1). The intraneuronal method (route 2) involves olfactory neurons endocytosis the drugs, releasing it in the olfactory bulb, and then dispersing it to various brain regions.It can take several hours or even days to complete this process. Routes 3 and 4 (drug transport through or along supporting cells) are less significant. Additionally, although the trigeminal nerve pathway is less significant than the olfactory pathway, the drugs are enter the respiratory region can travel directly to the brain through extraneuronal or intraneuronal routes.Respiratory epithelia also allow drugs in the respiratory area to enter the bloodstream. This method, however, is only appropriate for lipophilic medications with low molecular weights and strong BBB permeability. Drugs that are not absorbed in the nasal cavity can travel through the lungs and digestive system before being absorbed into the systemic circulation. The BBB may allow the drug to penetrate into the brain from the blood.(71)

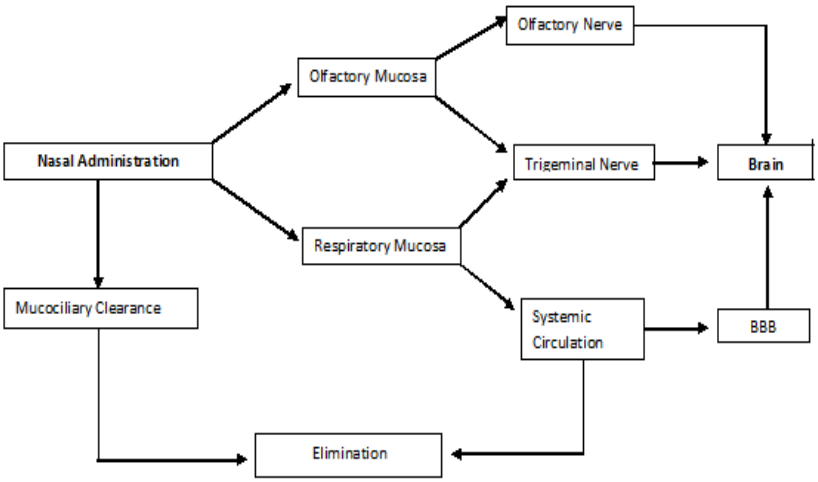

Diagram -2 : Different Pathways for Delivery of a Drug after Nasal Administration

Advantages of SLN for brain targeting through Nasal route(72)

1. Increase the bioavailability of entrapped drug. E.g. Zolmitriptan, Efavirenz
2. It shows the rapid and controlled drug delivery. E.g. Buspirone
3. Increase in tissue distribution and targeting action of drug E.g. Agomelatine
4.Avoid first pass metabolism .E.g. Rizatriptan

Drugselection criteria for Nose to brain drug delivery:

SLNs are suitable substitutes for polymeric nanoparticles, liposomes, micelles, and emulsions in drug delivery. Their expanded use for drug delivery via oral, parenteral, intranasal, ophthalmic, transdermal, and pulmonary routes is made possible by a number of specific advantages. The components of SLNs are safe, physiologically biocompatible, biodegradable, and suitable for nanotechnology drug delivery systems.SLNs are more stable than micelles, emulsions, or liposomes due to the effectiveness with which their solid matrices can shield the drugs that are embedded into them. Additionally, SLNs have greater entrapment efficiencies than liposomes for both hydrophilic and hydrophobic molecules. For nose-to-brain delivery, SLNs have a number of particular benefits.(1) Due to the lipophilic properties of SLNs, they can improve drug permeability and solubility. Additionally, they can increase the partition of nanoparticles into the lipid bilayer of the nasal epithelial cell membrane. The surfactants that can be used to open tight junctions between epithelial cells and improve the permeability of drug (E.g. Tween 80, Tween 20, and sodium lauryl sulphate).(2) When drugs are added to SLNs, their retention in the nasal cavity is increased. This retention can be increased by loading the SLNs into gel or coating them with the proper substances. For the manufacture of gels, poloxamer 407, poloxamer 188, methyl cellulose, and Hydroxy Propyl Methyl Cellulose (HPMC) are used for absorption of drugs and decrease the mucus viscosity.(3)

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Comparatively to solution-based dosage forms (such as solutions, suspensions), SLNs can minimize the enzymatic breakdown of drugs within nasal mucus. SLNs are safe, which makes nose-to-brain delivery apossible.(71)

II. LITERATURE SURVEY:

Table :10 Current research in the formulation of SLN-based on Nose to brain drug delivery

Drug	Excipient	Method of preparation	Outcome	Ref.
Risperidone	Compritol 888 ATO, Pluronic F-127	Solvent emulsification–solvent evaporation method	It overcome BBB for delivery of drug to brain	73
Rizatriptan	Glyeceryl Monostearate	Solvent diffusion method	Avoid first-pass metabolism, improve bioavailability of drug and shows sustained release effect.	74
Ferulic acid	Compritol 888 ATO, Transcutol and Gelucire 39/01, Stearic acid, Glyceryl monostearate, Chitosan	Hot homogenization method	Improved efficacy of drug in the treatment of Alzheimer's disease.	75
Haloperidol	Compritol ATO 888, Glyceryl monostearate (GMS),Precirol ATO 5, steric acid and palmitic acid	Emulsification–diffusion technique	The highest drug-targeting efficiency (2362.43%) and direct transport percentage (95.77%) was detected.	76
Alprazolam	Tween 80, Pluronic F68, and glyceryl monostearate (GMS)	solvent emulsification–diffusion technique	It protectthe encapsulated drugfrom degradation.	77
Clonazepam	Glycerol monostearate, Glyceryl monooleate, Glyceryl behenate	High pressure homogenization method	It gives prolong release of brain targeting action of drug.	78
Zolmitriptan	HPMC E15, Trimethylamine, Dimethylsulfoxide, Stearic acid, Cholesterol, and Lecithin	Emulsion Solvent Evaporation method	Improve systemic bioavailability and sustain release action of drug.	79
Astaxanthin	Stearic acid, Poloxamer 188, Lecithin, Citric acid	Solvent displacement method	Improve brain targeting action in neurological disorders	80
Donepezil	Compritol ATO 888, Glyceryl monostearate, Precirol ATO, Stearic acid, Palmitic acid	Solvent emulsification diffusion method	The optimised DP-SLN formulation was more sustained than DPL-Sol, according to an in vitro release study.	81
Nalbuphine	Phosphatidylcholine, Pluronic F-127, Tween 80, Hydrochloric acid,	Solvent injection technique	It isbiocompatible with lipid and shows rapid onset of action.	82

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	Sodium Hydroxide			
Paeonol	Pepsin, Trypsin, Glycerin monostearate	High-temperature emulsification–low-temperature with ultrasound.	The SLNs-ISG nose-brain drug delivery system is capable of delivering SLNs to brain regions.	83
Pueraria flavone	Stearic acid	Emulsification - evaporation-low temperature solidification method	Enhance the drug delivery to the brain with Borneol .	84
Rosmarinic acid	Tween 80 ,Glycerolmonostearate, soya lecithin	Hot homogenization Method	Improve the brain targeting efficiency of drug.	85
Ropinirole HCl	Dynasan 114, Pluronic F-68, glucose, sucrose, lactose,mannitol,Stearylamine, Phospholipon90 G	Emulsification-solvent diffusion Method	Avoid the hepatic first pass metabolism and improve therapeutic efficacy.	86
Agomelatine	Polyvinylalcohol, Glyceryl tripalmitate,	Emulsification solvent evaporation method	Enhance the bioavailability of drug and increase its brain delivery.	87
Agomelatine	Polyvinylalcohol, sodium deoxycholate,	Emulsification and Ultrasonication	Avoiding the first pass metabolism and gives direct brain targeting action.	88
Efavirenz	Glyceryl tripalmitate,Glyceryl monostearate, Glyceryl tristearate,	High Pressure Homogenization method	Increased permeability, enhanced bioavailability and brain targeting action of drug.	89
Buspirone	Compritol ATO 888, Glyceryl monostearate, Precirol ATO 5, Stearic acid, Palmitic acid, Tween 80	Melt-emulsification and ultrasonication Method	It gives sustain and continuous drug release action.	90
Ondansetron HCl	Glyceryl monostearate, Soya lecithin, Poloxamer 188	Solvent diffusion method	Quick and direct administration from the nose to the brain.	91
Almotriptan	Compritol ATO 888, Glyceryl monostearate, Precirol ATO 5, Stearic acid, Tween 80	Double emulsion-solvent evaporation method	It avoid the BBB and achieve rapid action.	92
Rivastigmine	Apifil,Compritol 888 ATO, Precirol ATO 5, Stearic acid, Tween 80	Homogenization and ultrasonication method	It is safe for intranasal delivery included intact nasal mucosa.	93
Tarenflurbil	Soya lecithin, stearic acid, Tween 20	Emulsification and solvent diffusion method	As compared to solution/suspension intravenous and oral routes of delivery,	94

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			nanoparticles enhanced the pharmacokinetic behaviour of drug.	
Geraniol/ Ursodeoxycholic acid	Sodium taurocholate hydrate, Compritol ATO 888, Carbodiimide hydrochloride	Emulsification/ evaporation solvent method	Penetration of a drugfromnose to CSF without causing mucosal irritation.	95
Piribedil	stearic acid, palmitic acid, Polyvinyl alcohol, Mannitol	Hot homogenization and ultrasonication method	It gives higher brain availability as compared to oral administration.	96
Meloxicam	Cholesterol, Phosphatidylcholine,Polycaprolactone	Double-emulsion solvent-evaporation method	It shows higher encapsulation efficacy and drug loading with enhancing the brain bioavailability	97
Levofloxacin/ Doxycycline	Stearic acid	Ultrasonication after emulsification via High-speed Homogenization	Long-lasting medication release from improved formulation.	98
Streptomycin	Tween 80, Soy lecithin, Compritol888 ATO	Nanocolloidal aqueous dispersion Method	Improve intrinsic permeability, stability and gives prolong release of action.	99
Dimethyl fumarate	stearic triglyceride, Dimethyl dioctadecyl ammonium chloride	Melt and ultrasonication method	Enhancing drug absorption and preventing first-pass metabolism.	100
Naloxone	Glyceryl Monostearate, Sodium Hydroxide, Hydrochloric acid, Compritol, Precirol, Poloxamer 407	Solvent evaporation method	The created formulation may serve as an effective vehicle for the intranasal administration of drug.	101
Quetiapine	Carboxymethyl cellulosesodium, sodium chloride, Glycerol monostearate, Span-80, Butanol	Microemulsion method	The clinical value of nasal QF-SLN-gel in the treatment of brain disorders.	102

III. CONCLUSION:

SLN is feasible to encapsulate both lipid-soluble and water-soluble pharmaceuticals, which combine the characteristics of polymer-based carriers and liposomes. Scaling up of SLN production is possible and affordable.The use of nasal cavity models has a lot of potential due to the efficiency of nasal formulations in penetrating the upper half of the nasal cavity, which is essential for optimal nose-to-brain transfer.In this review article highlight current research in nose to brain delivery and literature survey are mentioned.

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None.

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