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Ex-*vivo* skin permeation studies of sumatriptan succinate using different solvent systems and its comparison with PLGA nanoparticles

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ABSTRACT

Sumatripatan succinate **(**SS) is a 5-HT_{1D} agonist used in migraine therapy. Its low oral bioavailability (~15 %) is due to extensive pre-systemic metabolism and low biological half-life. The frequent administration of SS is required to maintain effective plasma concentration. In the present investigation, polymeric nanoparticles of SS (SS-NPs) were prepared by $W_1/O/W_2$ double emulsion solvent evaporation method followed by probe sonication. Poly-(lactide-co-glycolide) (PLGA) and poloxamer 188 were used as polymer and surfactant respectively to formulate SS-NPs. The particle size, polydispersity index, zeta potential, percent entrapment efficiency of SS-NPs were found to be 126 nm, 0.06, (-) 24.1 mV, 32.52 ± 2.34 % respectively. Characterization of lyophilized SS-NPs revealed formation of drug entrapped amorphous SS-NPs. *Ex-vivo* skin permeation studies of SS were conducted using distilled water, ethanol (EtOH), propylene glycol (PG) and their binary combinations. The lag time, flux, permeability and steady state permeability coefficient and enhancement ratio were determined. The *ex-vivo* permeation profiles of SS in different solvent systems were compared with SS-NPs in distilled water. The maximum flux of 345.8 $\mu g.cm^{-2}.h^{-1}$ was obtained with solvent system comprising 33% PG in EtOH. The minimum lag time and a comparable flux value was obtained in *ex-vivo* diffusion studies of SS-NPs. Hence, it can be concluded that SS-NPs can be administered in transdermal drug delivery system using a solvent system comprising 33%PG in EtOH. The present investigation indicated that using suitable solvent system and PLGA nanoparticles, the skin permeation of SS can be enhanced.

Keywords: Migraine, sumatriptan succinate, poly-(lactide-co-glycolide), nanoparticles, transdermal patch

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INTRODUCTION

A migraine is a headache disorder affects approximately 15% of females and 6% of males. It is a neurobiological syndrome and the symptoms are unilateral throbbing headache. (*George M 2006).* A decreased level of vasoconstrictor amine 5-hydroxytryptamine vasodilates blood vessels of brain resulting in severe headache (*Villalón CM 2003).* Sumatriptan succinate (SS) is a serotonin agonist used in migraine therapy. SS is incompletely absorbed and undergoes pre-systemic metabolism. It therefore has a low oral bioavailability of about 15%. It exhibits a plasma half-life and elimination half-life of approximately 1.5 h and 2.5 h respectively (SC Jagdale 2014, *Ebell MH 2006).* Sumatriptan Succinate is freely soluble in water (US EPA 2009) having molecular weight 413.489 (g/mol) and log P value 0.93.

The mechanism of action of SS is vasoconstriction of meningeal arteries, inhibition of release of neurotransmitters from neurons in brain, prevention of the nociceptive transmission and reduction of the activity of trigeminal nerves (Hilaire 2004; Kolev 2007; Levy 2004; Silberstein 2000). SS is hydrophilic in nature and has been reported to cross the blood brain barrier (BBB) to certain extent (Tfelt-Hansen 2010).

The serotonin receptor (5-hydroxytryptamine [5-HT]) is believed to be the most important receptor in the headache pathway. Immunohistochemical studies have detected 5-hydroxytryptamine–1D (5-HT1D) receptors in trigeminal sensory neurons, including peripheral projections to the dura and within the trigeminal nucleus caudalis (TNC) and solitary tract, while 5-HT1B receptors are present on smooth muscle cells in meningeal vessels; however, both can be found in both tissues to some extent and even in coronary vessels.

All the currently available triptans are selective 5-HT1B/D full agonists. These agents may decrease headache by abolishing neuropeptide release in the periphery and blocking neurotransmission by acting on second-order neurons in the trigeminocervical complex.

The new techniques are required for crossing the blood brain barrier. The lipid soluble small molecules with

molecular weight less than 400 Da are able to cross the blood brain barrier via lipid-mediated free diffusion. Barrier layers are found at three main sites in the brain and spinal cord: the endothelium of parenchymal micro vessels, the epithelium of the choroid plexus secreting cerebrospinal fluid and arachnoid epithelium, the middle layer of the meninges forming the outer covering of the CNS (Abbott 2004a; Abbott et al 2010). At each of these sites, tight junctions significantly reduce permeation of ions and other small hydrophilic solutes through the intercellular cleft (Candela P 2010). Nanoparticles open tight junctions between endothelial cells resulting in penetration of free form of drug through BBB (X. Gao 2014, C.H.J. Choi 2010). Nanoparticulate drug delivery systems have been developed as an effective strategy for circumventing this barrier and targeting of drugs to the brain for better therapeutic efficacy (J. Kreuter 2001, 2002).

Poly (lactic-*co*-glycolic) acid (PLGA) is biocompatible biodegradable polymeric material and is approved for clinical use in humans by the U.S. Food and Drug Administration. PLGA has the potential to modify surface properties to provide better interaction with biological materials (Piergiorgio Gentile 2014). Transdermal drug delivery system (TDDS) avoids hepatic first pass metabolism of drug. Drug loaded polymeric nanoparticles can be administered by transdermal drug delivery system. TDDS maintains constant plasma levels of drug and enhances patient compliance by avoiding repeated administration of drug. The solvent system selection is important step in development of transdermal administration of drug as it affects the permeation of drug across skin by altering the barrier property of skin. In the view of physicochemical properties of SS, we envisaged to develop polymeric poly (lactic-*co*-glycolic) acid (PLGA) nanoparticles of SS (SS-NPs) and study the effect of solvent systems on *ex-vivo* permeation of SS and SS-NPs.

MATERIALS AND METHOD

Materials

Sumatriptan succinate (SS) was received as a gift sample from Natco Pharma Limited, Hyderabad, India. Purasorb PDLG 5002A was received as a gift sample from Corbion Purac Biomaterials, Netherlands, and U.S.A. Pluronic F-68 was received as gratis sample from BASF, Mumbai. Distilled water used for the preparation and processing purposes was double distilled water (Bio-Age, Direct Ultra TUVF5, Punjab, India).

All other chemical and reagents used during studies were of suitable analytical grade and were used as received.

Methods

Preparation of sumatriptan succinate polymeric nanoparticles (SS-NPs)

The PLGA polymeric nanoparticles containing sumatripatan succinate were prepared by double emulsion solvent evaporation technique (Ipek Baysal, 2013). The composition of formulation batches are shown in table 1. An accurately weighed amount of SS (5 mg) was dissolved in 2 mL distilled water to form aqueous phase (W_1). It was added drop wise into organic phase (O) consisting of PLGA dissolved in dichloromethane (5 mL) and mixed well using a magnetic stirrer (Labman Scientific Instruments, India) at speed of 800 rpm to form primary emulsion (W_1/O). The primary emulsion was further added drop wise with the help of syringe into aqueous phase (W_2) consisting of 15 mL Pluronic F 68 in 1 and 2 %w/v as a stabilizer and homogenized using a high speed homogenizer (IKA Ultra turrex T18, Germany) at speed 12,000 rpm followed by probe sonication (Sonics Vibra Cell ™) at 80 % amplitude for 5 min. Organic solvent was evaporated under continuous magnetic stirring at room temperature. The polymeric nanoparticles were recovered by refrigerated centrifugation at 20,000 rpm for 60 min at 15 °C, washed with distilled water to remove additives.

A cryoprotectant solution comprising 5 %w/v mannitol was added to nanoparticle pellet formed after centrifugation. It was vortexed (Impact, Icon Instruments Company, India) followed by bath sonication (PCi, India) for 5 min and filled in glass vials. The vials were freeze dried at (-) 40 °C and 850 mm/Hg vacuum for 72 h using a lyophilizer (Mac ®, Macro Scientific Works, India) and stored in refrigerator in airtight glass container sealed with parafilm.

Experimental procedure was repeated with varied drug and polymer ratios and surfactant concentrations.

Table 1 Compositions of SS-NP formulations

Screening Parameter	Formulations					
	PNP1	PNP2	PNP3	PNP4	PNP5	PNP6
SS : PLGA ratio SS (5 mg/2 mL)	1:3 (5:15)	1:3 (5:15)	1:3 (5:15)	1:3 (5:15)	1:5 (5:5)	1:5 (5:25)
Solvent (5 mL)	DCM	DCM	DCM	DCM	DCM	DCM
Surfactant (15 mL)	Pluronic F68	Pluronic F68	Pluronic F68	Pluronic F68	Pluronic F68	Pluronic F68
Concentration of surfactant (%w/v)	1	1	1	2	2	2
PNP = Polymeric nanoparticle, DCM = Dichloromethane						

Characterization of the SS-NPs

Percent entrapment efficiency and percent drug loading

The nanoparticle suspension was subjected to centrifugation at 20,000 rpm for 30 min. at 15 °C. Percent percent entrapment efficiency (% EE) was assessed using equation 1 (Deepti Mittal, 2014). Polymeric nanoparticle pellet was dissolved in specified volume of ethyl acetate and shaken for 4 h. Drug was extracted into equal quantity of water. This

solution was filtered to remove insoluble fractions of polymer and amount of drug was determined at 227 nm.

$$\% EE = \frac{Total\ drug\ content - Amount\ of\ free\ drug\ in\ supernatant}{Total\ drug\ content} \times 100$$

Physicochemical characterization of SS-NPs

For determination of mean particle size of SS-NPs, 5 mg sample of SS-NPs was dispersed in 10 mL deionized water. The mean particle size, polydispersity index and zeta potential were determined using Zetasizer Nano ZS 90 (Malvern Instruments, UK) (Wissing SA, 2004).

The surface morphology and structure of lyophilized SS-NPs were visualized by scanning electron microscopy (Zeiss SEM EVO-18, Carl Zeiss Microscopy). Water re-suspended nanoparticles were mounted on a glass slide as a thin smear and left to dry. The particles on the dried glass slide were subjected to gold sputtering and slide was attached on SEM holder using a double side carbon tape mounted on aluminium stud. The SEM photomicrographs were captured by operating at an accelerating voltage of 20 kV electron beam at desired magnification (Sharma G, 2015).

Characterization of lyophilized SS-NPs

Fourier Transform Infrared (FT-IR) Spectroscopy

The sample of lyophilized SS-NPs of was triturated and mixed well with IR grade potassium bromide in 1:100 ratio and the mixture was introduced in sample holder of FT-IR instrument (IRAffinity-1, Shimadzu, Japan) and scanned in the range 4000 to 400 cm^{-1}. The obtained spectrum was compared with the spectrum of SS and PLGA (Shu-Ben Sun, 2015).

Differential scanning calorimetry (DSC)

A sample of lyophilized SS-NPs was kept in desiccator for 24 h before thermal analysis. An accurately weighed 5 mg sample was hermetically sealed in aluminium crucible and heated at constant rate of 10 °C / min over a temperature range 40 to 300 °C using DSC (TA Instruments Trios V4.1). An inert atmosphere was maintained by purging nitrogen gas at a flow rate of 50 mL/min. An empty aluminium pan was used as a reference. The thermogram obtained was compared with the thermograms of SS and PLGA (Shu-Ben Sun, 2015).

X-ray diffraction (XRD) spectroscopy

X-ray diffraction spectrum of lyophilized SS-NPs was recorded by instrument (Brucker AXS D8 Advance, Germany) using Cu-Kα line as source of radiation at a voltage of 35 kV and current 25 mA. The sample was measured in 2θ angle range between 3-80^{0}and 0.0053 step size. The diffraction spectrum obtained was compared with the diffraction spectrum of SS and PLGA (Adeyinka Aina, 2016).

Ex-vivo skin permeation studies

Preparation of whole skin

Ex-vivo skin permeation studies were conducted to evaluate the effects of various vehicles (ethanol, propylene glycol and their binary combinations) on permeability profiles of SS. The permeability profile of SS-NPs. For preparation of whole skin, the animal was sacrificed by excess inhalation method. The dorsal skin of animal was shaved with the help of animal hair clipper in the direction of tail to head without causing damage to skin. The shaved skin was excised with the help of surgical blade (size 24) fitted in a surgical blade holder (size 4). The adhered tissues to the dermis was removed with the help of scalpel blade. The adhering fat to the dermis was also removed by cleaning with cotton swab moistened with isopropyl alcohol. The skin was washed with distilled water, wrapped in aluminum foil and stored in freezer at (-)20^{0}C till further use. The skin was thawed to room temperature. The skin was kept in thermostatic shaker bath at 37±1 ^{0}C temperature for 1 h. The receptor fluid containing 0.01% of sodium azide was sonicated for 15 min and filled in the receptor compartments and equilibrated to bring it to 37 ^{0}C temperature. The skin was cut into circular pieces to a size of external circumference of donor compartment and mounted on diffusion cell assembly, keeping Stratum corneum side towards donor compartment and equilibrated for one hour. From the receptor phase, 1 ml volume was withdrawn to check for the amount of drug present if any from previous experiment. The 2 ml of drug solution (40 mg) was applied in donor compartment. From the receptor compartment, 1 ml volume was withdrawn at 0,1,2,4,6,8,10,12, 16,20,24, 36, 48, 60, and 72 h and replaced with equal volume of fresh receptor phase every time. The withdrawn sample was analyzed for drug content. The lag time, flux, permeability, and enhancement ratio were calculated. Cartesian plots were made, taking time in hours on X-axis and cumulative amount of drug present in receptor fluid on Y-axis. Flux values (mg/cm^2.h) were calculated from the slopes of the steady states of above plots. Lag times were calculated from the intercepts of extrapolated steady state flux to X-axis. Permeability values were calculated by following equation 1 (Panchagnula 2001).

$$Permeability = \frac{Steady\ State\ Flux}{Concentration\ of\ drug\ in\ donor\ solution}$$

RESULTS AND DISCUSSION

Preparation of sumatriptan succinate nanoparticles (SS-NPs)

The polymeric nanoparticles containing sumatriptan succinate were prepared. A total six formulations with varying SS and PLGA ratios and varying Pluronic F-68 concentrations were developed and characterized for particle size, polydispersity index and zeta potential.

Characterization of SS-NPs

Percent entrapment efficiency and percent drug loading

The formulations PNP 1, PNP 2 and PNP 3 were found to be unstable. The entrapment efficiency in formulations PNP 1, PNP 2 and PNP 3 was found to be low as compared to formulation PNP4. The entrapment efficiency of formulation PNP 4 was found to be 32.52±2.34 %.

Particle size and Zeta Potential

The particle size (nm) and polydispersity index (PDI) of SS-NPs (Formulations PNP 4, PNP 5 and PNP 6) were found to be 126.0 nm, 281.8 nm, 188.0 nm and 0.060, 0.700, 0.378 respectively. The formulation containing 1:3 ratio of SS: PLGA with 2 (%w/v Pluronic F68 has shown the minimum particle size 126 nm with PDI value 0.060 (Ostertag F, 2012). The zeta potential (mV) of SS-NPs (formulations PNP 4, PNP 5 and PNP 6) were found to be (-) 24.1 mV, (-) 18.4 mV and (-) 12.1 mV respectively (Upadhyay S, 2012). Based on the values of % EE, % DL, particle size, PDI and zeta potential, PNP 4 was found to be optimized SS-NPs formulation (Figure 1).

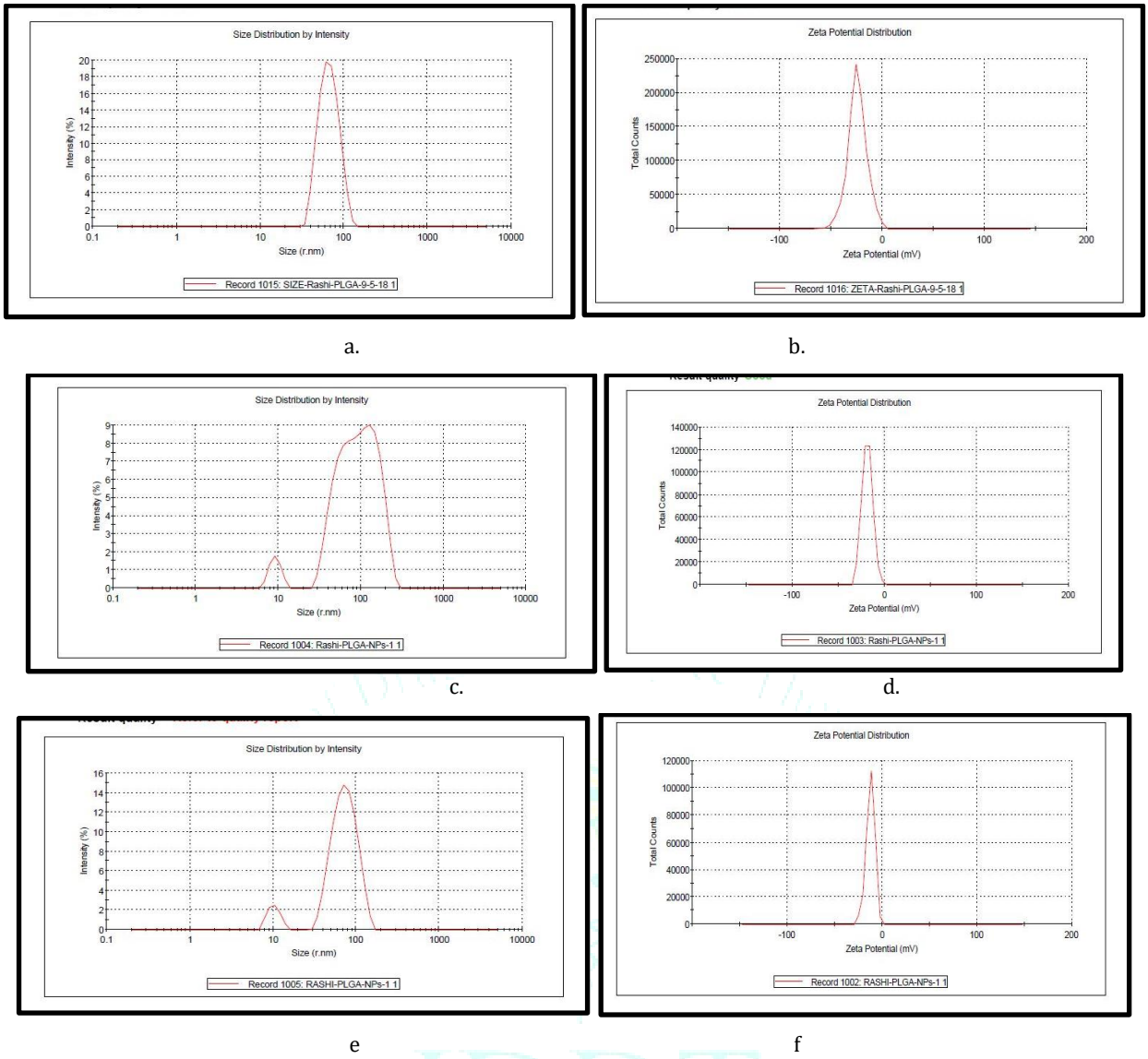

Figure 1 Graphs of particle size and PDI (a,c,e) Graphs of zeta potential (b,d,f) of formulations PNP 4, PNP 5, PNP 6

Drug-polymer interaction studies

FT-IR Spectroscopy

FT-IR spectra of the SS, PLGA and lyophilized SS-NPs are shown in figure 2,3 and 4 respectively. In comparison to the FT-IR spectrum of SS, the lyophilized SS-NPs exhibited disappearance of characteristic peaks and broadening of few peaks with reduction in intensity. The peak broadening phenomenon with hump in the FT-IR spectrum of lyophilized nanoparticles indicated formation of polymeric nanoparticles.

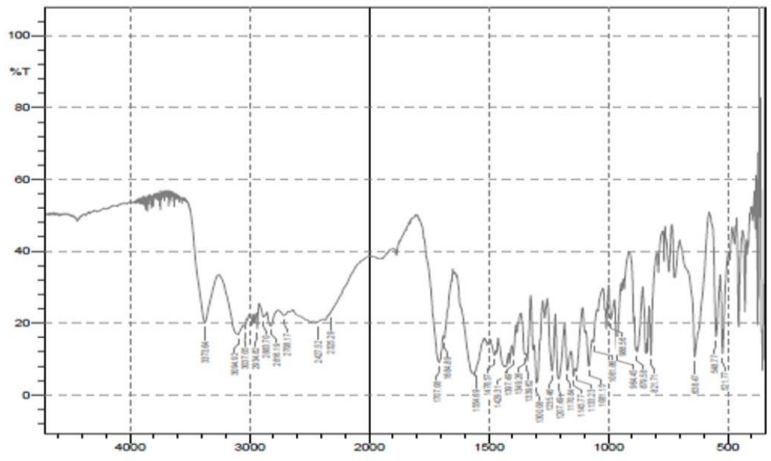

Figure 2 FT-IR spectrum of sumatriptan succinate

Figure 3 FT-IR spectrum of PLGA polymer

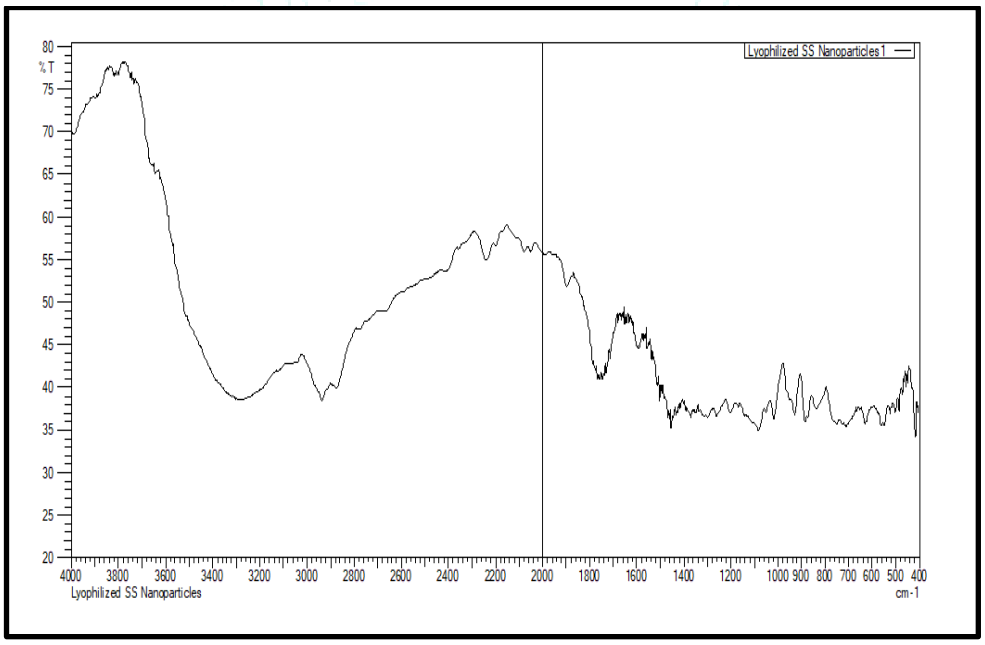

Figure 4 FT-IR Spectrum of lyophilized SS-NPs formulation batch PNP 4

Differential scanning calorimetry (DSC)

The DSC thermograms of SS, PLGA and lyophilized SS-NPs are shown in Figure 5,6, and 7 respectively .In comparison to the DSC thermogram of SS and PLGA, thermogram of lyophilized nanoparticles showed splitting of thermogram at 157.29 ℃ and 167.64 ℃ with enthalpy values 28.490 J/g and 46.285 J/g. The shifting of melting endotherm from 171.26 ℃ to 167.64 ℃ with reduction in the enthalpy from 141.48 J/g to 28.(SS-NPs) 490 J/g indicated the formation of nanoparticles. Also, the enthalpy of polymer was also found to significantly decreased from 804.47 J/g to 46.285 J/g indicating that energy has been utilized in the entrapment of SS within the formed polymeric nanoparticles. An endotherm at 167.64 ℃ signified the presence of free amount of drug on surface of SS-NPs.

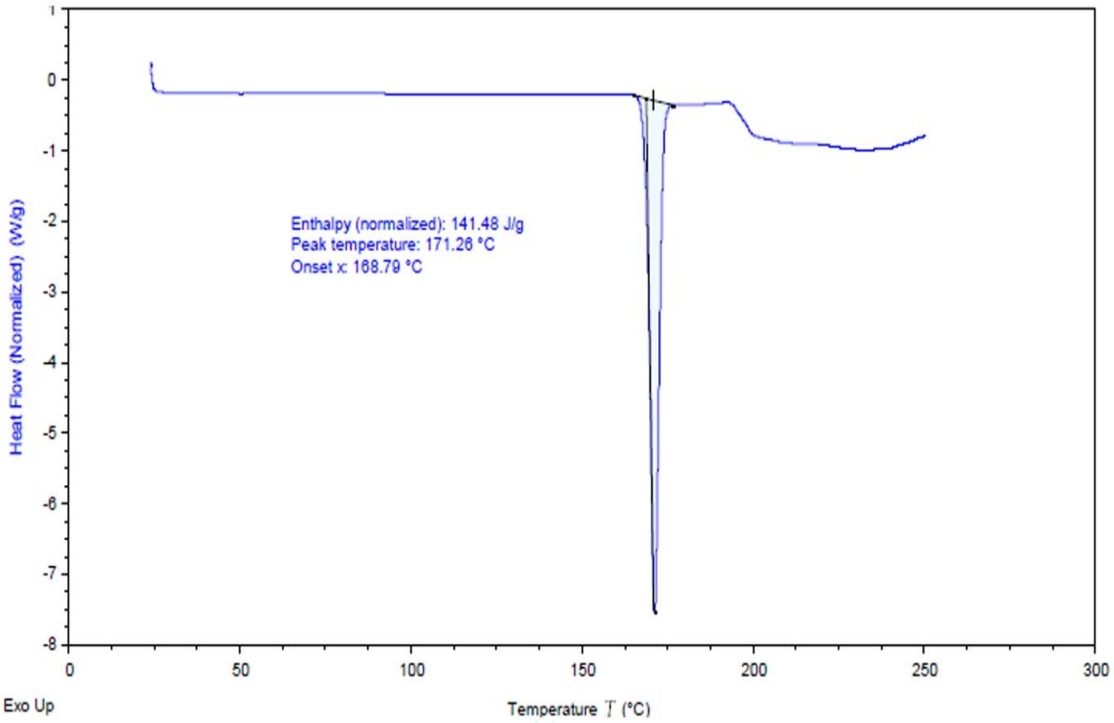

Figure 5 DSC thermogram of sumatriptan succinate

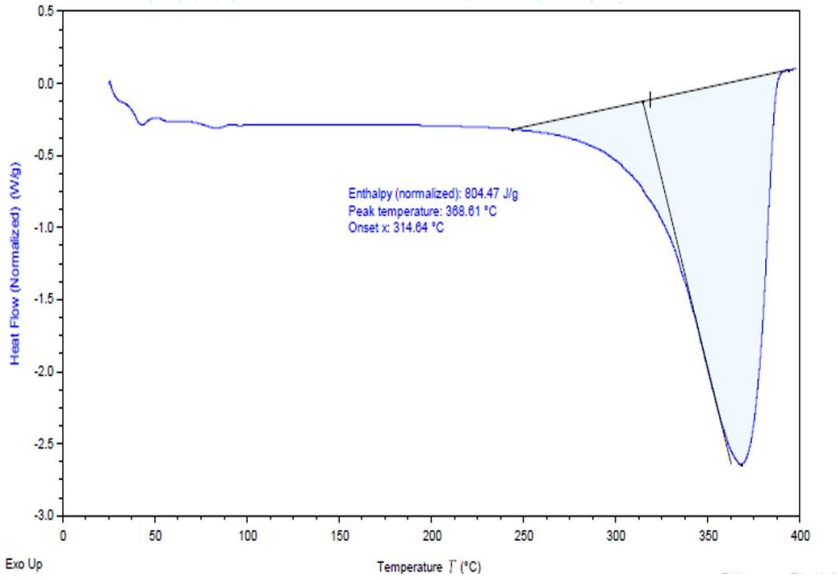

Figure 6 DSC thermogram of PLGA polymer

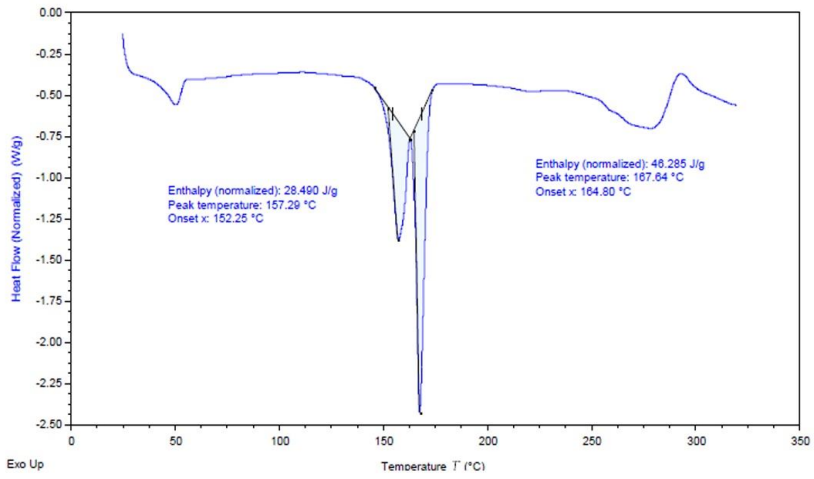

Figure 7 DSC thermogram of lyophilized SS-NPs formulation batch PNP 4

X-ray diffraction (XRD) spectroscopy

The XRD pattern of SS, PLGA and lyophilized SS-NPs are shown in figure 8,9 and 10 respectively. The diffraction pattern of lyophilized SS-NPs showed reduction in the number and intensity of peaks when compared with the spectrum of the SS and PLGA. The diffraction pattern of PLGA has shown complete absence of peaks at an angle 2θ indicating the amorphous nature of polymer. The peaks observed in XRD pattern at an angle 2θ of SS were 15.42, 16.22, 16.40. These peaks were found to be absent in XRD pattern of lyophilized SS-NPs and new peaks at 9.87, 17.47 were observed. A decrease in crystalline characteristic of SS and formation of partial amorphous characteristic of lyophilized SS-NPs was observed in XRD studies.

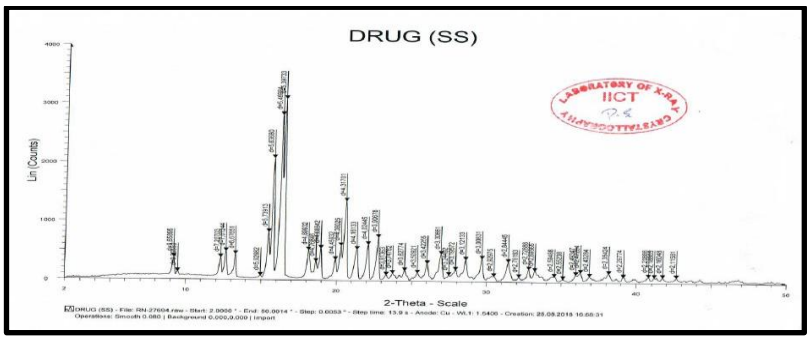

Figure 8 X-ray diffraction spectrum of SS

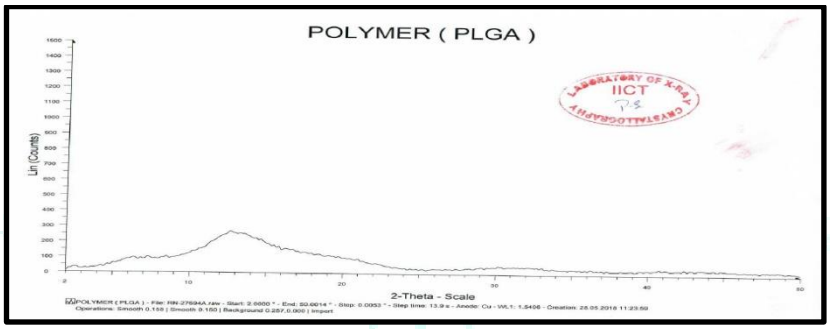

Figure 9 X-ray diffraction spectrum of PLGA polymer

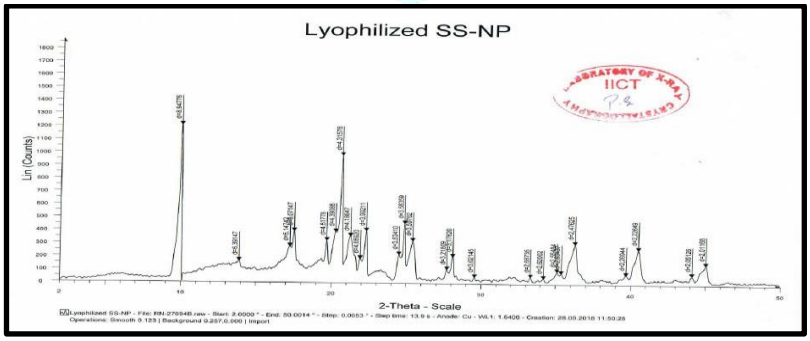

Figure 10 X-ray diffraction spectrum of lyophilized SS-NPs (formulation PNP 4)

Ex-vivo skin permeation studies

The *ex-vivo* skin permeation studies of sumatriptan succinate and sumatriptan succinate loaded polymeric nanoparticles (SS-NPs) were conducted using distilled water, ethanol, propylene glycol and their binary combinations. The *ex-vivo* permeation studies of SS conducted using distilled water were treated as control (group 1). The lag time, flux, permeability, steady state permeability coefficient and enhancement ratio were determined (Table 2).

The lag time in control group with water as solvent was found to be maximum as compared to the other solvent systems studied. The polymeric nanoparticles of sumatripatan succinate (SS-NPs) demonstrated minimum lag time of 6 h as compared to the control group and solvent systems studied. With increasing concentration of ethanol in water as observed in group S3 S4, S5, the lag time was found to be increased. It is due to stabilization and rigidization of intercellular lipids of stratum corneum membrane of skin hindering the passage of drug across the skin. No significant change in lag time was observed with increase in PG concentration in water (treatment group S6, and S7). However, with further enhancing of concentration of PG to 100%, the lag time was found to be slightly increased group S8). It is due to hygroscopic characteristic of PG which extracts water from bilayer lipids, increases tortuosity and diffusional path length for permeation of drug resulting in enhanced lag time. With PG and ethanol binary solvent system studied, the lag time was found to be decreased in group S9 to S10 and no change in lag time was observed in group S11. It is due to the thermodynamic activity of PG and ethanol on stratum corneum.

In the *ex-vivo* skin permeation studies of the polymeric nanoparticles of sumatritan succinate (SS-NPs) (group 2) in distilled water as solvent has shown an enhanced flux values as compared to permeation of control group. Also, the lag time was significantly decreased as compared to the control group. The enhanced permeation of SS-NPS was due to their small size in nonometer range which allowed for better penetration across the stratum corneum membrane

In group S3, S4, and S5, flux values of SS were found to increase proportionately with an increase in ethanol concentration in water from 33 to 66%. A significant increase in flux values were observed in ethanol treated groups as compared to control group. Ethanol exerts concentration dependent effect on the stratum corneum (Berner et al. 1989). The effect of ethanol on skin occurs by two mechanisms namely push effect whereby the evaporation of ethanol increases thermodynamic activity. (Kadir et al. 1987). The other mechanism exists whereby ethanol increases permeation of drug across skin due to reduction in barrier property of stratum corneum of skin. At lower concentration, ethanol exerts effect on lipoidal pathway while at higher ethanol concentration, effect on intercellular lipids as well as effect on polar pathway occurs.

The group S6, S7, the increasing concentration of PG in water has shown increase in flux values from 33 to 66%, while the formulation S8 containing 100% PG, a reduction in flux values was observed. A significant increase in flux values were observed in PG treated groups as compared to control group. PG exerts its effect as permeation enhancer effect due to its co-solvency effect. The thermodynamic activity of SS might have been increased due to effect of PG. The enhanced thermodynamic activity is the driving force for the permeation of SS across stratum corneum layer of skin. PG exerts its penetration enhancer effect by the carrier mechanism. The partitioning of PG into skin creates the movement of drug into the skin. At higher PG concentration (100%), the water present in the skin is drastically reduced hindering the movement of SS into skin resulting into decreased flux values. The hygroscopic property of PG takes water from binary combination with water. At higher concentration, PG takes water from skin lipids and corneocytes and complete dehydration of stratum corneum occurs resulting in increased barrier property of skin. Propylene glycol may also form a pool in the bilayer lipids hindering the passage of drug.

In group S9 containing 33% PG in ethanol, maximum flux was observed. It is due to thermodymanic activity of both PG and ethanol on epidermis. The decreased barrier property due to action of PG and EtOH on stratum corneum of skin has resulted in flux value. With increase in PG concentration as in group S10, the flux value was found to be decreased as compared to group S9. It is due to the dehydration effect of PG. In group S11, the flux value was increased as compared to group 10. It is due to co-solvency and partitioning effect of PG.

From the solvent systems studied for the *ex-vivo* permeation of sumatriptan succinate, the maximum flux values were obtained with solvent system comprising ethanol: PG in 33.5:66.5 ratio. The reduction in barrier property of stratum corneum and increased thermodynamic activity are the probable reasons for the highest flux of SS across skin. The flux of SS-NPs was found to be decreased as compared to flux value of SS with solvent system ethanol: PG in 33.5:66.5 ratio. However, the minimum lag time was observed with SS-NPs. Hence, it can be concluded that the SS-NPs can be administered with solvent system ethanol**:** PG in 33.5**:** 66.5 ratio for obtaining better control on lag time and flux values.

Table 2 *Ex-vivo* skin permeation parameters of sumatriptan succinate and its polymeric nanoparticles in various solvent systems

Sr. No.	Group code	Solvent System	Lag time (h)	Flux (µg/cm^2/h)	Permeability (=Slope/Concentration of drug in donor compartment)	Steady state permeability coefficient(K_p) (cm/h)	Enhancement ratio ER = (K_p of SS-NPs) / (K_p of drug)
1	S1	Control	20	140.4	3.15	89.42	0
2	S2	SS-NPs	6	331.8	8.29	211.33	2.36
3	S3	33% EtOH in Water	8	264.0	6.6	168.15	1.88
5	S4	50% EtOH in Water	13	286.9	7.17	182.73	2.04
6	S5	66% EtOH in Water	16	310.7	7.76	197.89	2.21
7	S6	33% PG in Water	9	189.3	4.73	120.57	1.34
8	S7	66% PG in water	8	209.3	5.23	133.31	1.49
9	S8	100% PG	10	199.7	4.99	127.19	1.42
10	S9	33 % PG in EtOH	12	345.8	8.64	220.25	2.46
11	S10	50% PG in EtOH	10	317.7	7.94	202.35	2.26
12	S11	66% PG in EtOH	10	336.2	8.40	214.14	2.39

CONCLUSION

The low oral bioavailability of sumatripatan succinate is due to extensive hepatic first pass metabolism metabolism and low biological half-life. The frequent administration of SS is required to maintain effective plasma concentration. Polymeric nanoparticles of SS (SS-NPs) were prepared by $W_1/O/W_2$ double emulsion solvent evaporation method followed by probe sonication. Poly-(lactide-co-glycolide) (PLGA) and poloxamer 188 were used as polymer and surfactant respectively to formulate SS-NPs. The particle size, polydispersity index, zeta potential, percent

entrapment efficiency of SS-NPs were found to be within acceptable range. Characterization of lyophilized SS-NPs by differential scanning calorimetry, FT-IR spectroscopy and X-ray diffraction spectroscopy revealed formation of drug entrapped amorphous SS-NPs. *Ex-vivo* skin permeation studies of SS were conducted using distilled water, ethanol (EtOH), propylene glycol (PG), and their binary combinations. The solvent system comprising 33% PG in EtOH was found to be the optimum solvent system for transdermal drug delivery of sumatriptan succinate. The minimum lag time and a comparable flux value was obtained in *ex-vivo* permeation studies of SS-NPs. Hence, it can be concluded that SS-NPs can be administered in transdermal drug delivery system using a solvent system comprising 33%PG in ethanol. The present investigation indicated that using suitable solvent system and PLGA nanoparticles, the skin permeation of sumatriptan succinate can be enhanced.

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