Effect of Organogel Components on In Vitro Nasal Delivery of Propranolol Hydrochloride

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ABSTRACT

The purpose of this research was to evaluate in vitro transnasal sustained-release ability of sorbitan monostearate (SMS) organogels in isopropyl myristate (IM). Organogels were prepared containing SMS (2.5%-20%) and water (5%-25%) in IM and analyzed microscopically for phase behavior. The effect of Tween surfactants on gel strength and in vitro nasal diffusion of propranolol is reported. The in vitro nasal release retardant effect of SMS and Tween 20 was investigated using factorial design. The microscopic changes in structure of organogel during in vitro nasal diffusion were studied. The water-holding capacity of SMS organogels in IM increased with SMS concentration. The release retardant effect with incorporation of cosurfactant was of the order of Tween 80 > Tween 60 > Tween 20. Gel strengthening and increased viscosity were evident with increased concentration of SMS and Tween 20. The 3-dimensional network of SMS molecules controls the diffusional drug release. The organogel system on nasal mucosa during diffusion is dynamic in nature and changes continuously with the time of diffusion. The water penetration in the organogel network results in percolation and emulsification of organogel, thus affecting the release. Organogels provided an effective barrier for diffusion of propranolol. The surface epithelium lining and the granular cellular structure of treated nasal mucosa were intact.

KEYWORDS: sorbitan monostearate, organogel, nasal, propranolol, in vitro, retard release

INTRODUCTION

The greater permeability of drug through nasal mucosa has the potential to overcome the limitations of oral route and to approach the benefits of intravenous infusion (eg, ergotamine tartrate, calcitonin).[1,2] The nasal administration of nitroglycerin and melatonin as drops and sprays elicits the desired pharmacological response.[3] Powder form is suitable for number of nonpeptide and peptidal drugs. The transnasal absorption of insulin in powder form has been shown to give a better insulin uptake as compared with solution.[4] Bioadhesive excipients such as starch, albumin, and diethyl aminoethyl (DEAE)-sephadex have been successfully used to reduce rapid nasal mucociliary clearance of formulations (eg, gentamicin, insulin).[5,6] Propranolol hydrochloride has been absorbed effectively from solution via the nasal route in human volunteers.[7] However, its short biological half-life and rapid absorption are unfavorable to sustain the drug levels in the systemic circulation. An erythrocyte-based bioadhesive system and proliposomes containing propranolol hydrochloride have been reported with the sustained effect.[8,9] The manufacturing of these drug-loaded carriers requires specialized processing techniques.

Challenges in the development of a formulation for nasal administration include low residence time and nonreproducible absorption profiles. Researchers have improved bioadhesive properties and have reported applications of microemulsion-based hydrogels.[10,11] Hydrogels as drug-delivery carriers necessitates the use of penetration enhancers and has limited stability against temperature, moisture, and microbial contamination. The use of thermoreversible pluronic gels of vitamin B_{12} and melatonin for the treatment of pernicious anemia and chronobiological sleep disorders, respectively, has been reported by Pisal et al.[12,13]

The discoveries of several biocompatible substances capable of gelling organic solvents have been mentioned in reviews.[14] Organogels are emerging as carriers for drug molecules with diverse physicochemical properties and for macromolecules. Most studies have reported on gelling behavior of oils and structure of organogels.[15,16] Transdermal transport rates of scopolamine and broxaterol from lecithin organogels were faster than commercial patches.[17] Similarly, improved skin penetration of indomethacin and diclofenac has been observed with lecithin-based organogels in isopropyl palmitate.[18] Fresta et al[19] reported that using lecithin gels has sustained the ophthalmic pilocarpine release for 4 hours. These studies indicate renewed interest in organogels as carriers for transdermal and ophthalmic drug administration. However, its feasibility for transnasal absorption has not yet been determined.

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Figure 1. In vitro nasal diffusion cell (used with sheep nasal mucosa).

Florence et al[20] have observed a short depot release of antigen from sorbitan monostearate (SMS) gels after intramuscular (i.m.) injection in rats. These studies indicated that the pharmaceutically useful properties of these gels can be exploited for sustained delivery of hydrophilic drugs. Propranolol hydrochloride, a β-receptor blocking agent, undergoes extensive first pass metabolism (50%-70%) after oral administration. In the present study, the concept of gelling organic vehicle with nonionic surfactant, SMS, incorporating propranolol hydrochloride for sustained transnasal delivery is evaluated. The effect of gel-forming excipients on drug release is optimized. The microstructural changes in gel state during in vitro diffusion and the histopathological changes in nasal mucosa are investigated.

Materials and Methods

Materials

SMS was obtained from Loba Chemicals Ltd, Mumbai, India. Isopropyl myristate was a gift sample from S. D. Fine Chemicals, Mumbai, India. The polysorbate surfactants (Tween 20, Tween 60, and Tween 80) were purchased from Thomas Baker, Mumbai, India. Propranolol hydrochloride was kindly supplied by Sigma Labs, Tivim, Goa. All other chemicals used were of ultrapure grade.

Table 1. Factorial (2^3) Levels of Tween 20 and Sorbitan Monostearate in Optimization Organogels*

Coded Levels Variables	-1	0	+1
Tween 20 (X_1) (grams)	0.1	0.2	0.3
Sorbitan monostearate (X_2) (grams)	0.5	0.75	1.0

*Batch size is 10 mL.

Methods

Preformulation of Gelation Including Effect of Cosurfactant

Organogels were prepared containing 2.5%, 5%, 7.5%, 10%, 15%, and 20% wt/vol of SMS, 5% to 25% wt/vol of distilled water in IM using a method reported by Murdan et al.[21] These gels were then checked microscopically for isotropic solution, organogel, and oil/water (o/w) emulsion using a Zeiss universal microscope attached to a digital camera (Oberkochen, Germany). A 7.5% wt/vol of SMS containing 2% wt/vol each, separately, of Tween 20, Tween 60, Tween 80, water (up to 20% wt/vol), and 10% wt/vol of propranolol hydrochloride were prepared in IM. The aqueous drug solution was admixed with surfactant solution in oil, while vortexing and maintaining both the phases at 60°C.

The gel strength was determined employing the technique proposed by Choi[22] using 25 mL of gel in a measuring cylinder at 37°C and recording the minimal weight required to penetrate a piston of constant weight 5-cm deep into organogel.

Aqueous drug solution (10% wt/vol) was prepared separately by dissolving an accurately weighed amount of drug. An o/w emulsion of 7.5 wt/vol of sorbitan monooleate, 2% wt/vol of Tween 20, and 20% vol/vol of aqueous drug solution (10% wt/vol) was prepared in IM. In vitro diffusion of gels was performed (using jacketed nasal diffusion cell, sheep nasal mucosa) as shown in Figure 1.[23] The recipient chamber was filled with 60 mL, pH 6.8, phosphate buffer (37°C ± 2°C) and 0.1 mL of gel was placed on mucosa. Diffusion samples (0.5 mL) at predetermined intervals were transferred to amber-colored ampoules and analyzed at 254 nm.

Formulation Optimization

The simultaneous effect of concentration of Tween 20 (X_1) and SMS (X_2) on diffusion of propranolol hydrochloride from organogels was studied. The SMS and Tween 20 were used in the range of 5%, 7.5%, and 10% wt/vol and 1%, 2%, and 3% wt/vol, respectively, as per 2^3 factorial experiment (Table 1). Aqueous drug solution was incorporated (at 60°C) to get the final strength of 10% wt/vol of organogels. The gelation onset temperatures were recorded using Haake C 25 P cryostatic bath (Thermo Haake, Karlsouhe, Germany). The

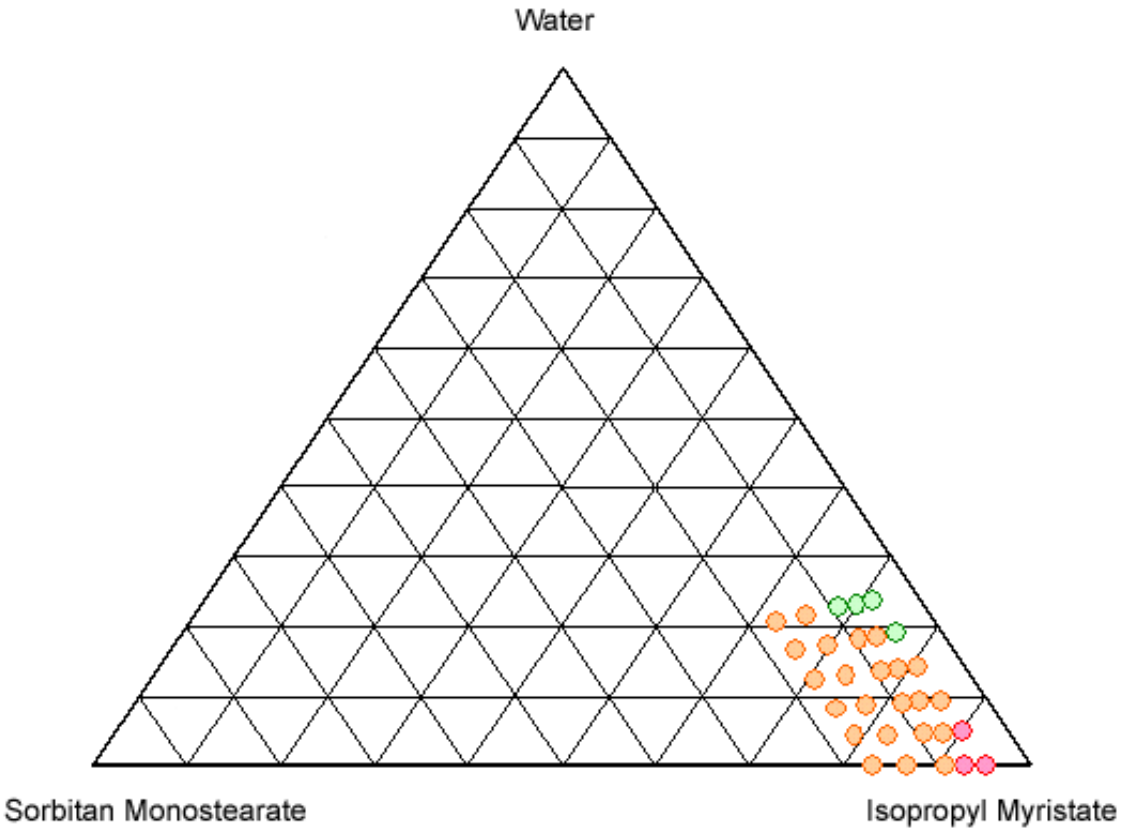

Figure 2. Phase diagram for SMS organogel in isopropyl myristate: Isotropic solution (), Organogels (), o/w emulsion ().

viscosity of the gels was measured at 37°C using Brookfield Synchro Viscometer (LVDV II$^+$) using Wingather software (Brookfield Instruments Ltd, Ontario, Canada). The gels were then subjected to in vitro diffusion with nasal cell. The 0.5 mL of diffusion samples withdrawn at 5 to 360 minutes, respectively, were analyzed at 254 nm. The diffusion data obtained were subjected to multiple-regression analysis using the following model:

$$\gamma = \beta_0 + \beta_1 X_1 + \beta_2 X_2 + \beta_{11} X_1^2 + \beta_{22} X_2^2 + \beta_{12} X_1 X_2 , \quad (1)$$

where β_0 is constant and β_1, β_2, β_{11}, β_{22}, β_{12} are regression coefficients. The response surfaces were plotted for the effect of X_1 and X_2 on time required for drug diffusion. Significance of each variable was checked.

Microstructure of Organogel During In Vitro Diffusion

A set of 3 diffusion cells with sheep nasal mucosa mounted on the donor chamber tube was used with experimental condition identical to in vitro diffusion. The 0.2 mL of organogel was placed on each of the 3 mounted nasal mucosa. Gel samples were removed at 2, 4, and 6 hours of diffusion. The microstructure of the gel was observed using a Zeiss universal microscope and recorded with a digital camera.

Effect of Organogel on Histology of Nasal Mucosa

Two nasal mucosa pieces (3 cm^2) were mounted on nasal diffusion cells. One mucosa was used as control (0.6 mL water) and the other was processed with 0.6 mL of optimized organogel (conditions similar to in vitro diffusion). The mucosa tissues were fixed in 10% neutral carbonate formalin (24 hours), and the vertical sections were dehydrated using graded solutions of ethanol. The subdivided tissues were stained with hematoxylin and eosin. The sections under microscope were photographed at original magnification × 100.

Results and Discussion

Preformulation of Organogelation

The formation of SMS organogel is affected by the concentration of gelator and addition of gelation-enhancing polar solvent. The effect of water fraction on the nature of phases present, viz isotropic solution, organogels, and o/w emulsion, in SMS-IM-water system is shown in 3-components triangular diagram (Figure 2). The concentration of SMS below 5% wt/vol in the presence or absence of water was insufficient to cause gelation, while more than 20% wt/vol could not be solubilized in IM at 60°C. The 5% wt/vol SMS showed an increase in viscosity, and the resultant gels were weak. However 10% wt/vol plain organogel without water was sufficient to form the gels. The water-holding capacity of SMS

Table 2. Effect of Tween on Strength of Sorbitan Monostearate Organogels*

Water % wt/vol in Organogel	Plain Gel (grams)	Tween 20 2% wt/vol (grams)	Tween 60 2% wt/vol (grams)	Tween 80 2% wt/vol (grams)
0	16.23 ± 0.15	22.35 ± 0.13	25.14 ± 0.14	28.15 ± 0.39
0.5	18.23 ± 0.12	24.32 ± 0.14	26.77 ± 0.11	30.22 ± 0.32
1	21.31 ± 0.21	27.52 ± 0.13	29.88 ± 0.23	32.94 ± 0.33
1.5	24.5 ± 0.14	30.91 ± 0.15	32.32 ± 0.55	34.83 ± 0.48
2	20.2 ± 0.13	32.52 ± 0.16	34.28 ± 0.22	37.12 ± 0.24
2.5	14.93 ± 0.14	21.32 ± 0.29	23.86 ± 0.51	28.95 ± 0.18

*Each value is average of 3 measurements with standard deviation.

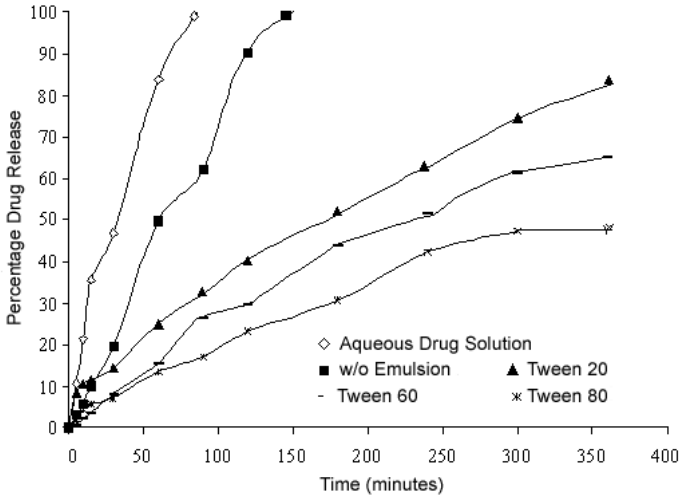

Figure 3. Effect of polysorbate cosurfactants on drug release from organogels.

organogel increased with the increase in SMS concentration. The water incorporated in excess of 20% wt/vol at 10% wt/vol of SMS resulted in an o/w emulsion rather than organogel.

The effect of hydrophilic cosurfactant viz 2% wt/vol each of Tween 20, Tween 60, and Tween 80, separately, on the strength of gels at various proportions of water in 7.5% wt/vol of SMS organogel is shown in Table 2. A small increment in gel strength with incorporation of Tween 20, Tween 60, and Tween 80 was observed. The gel-strengthening effect was of the order of Tween 80 > Tween 60 > Tween 20. The linear gel strength-enhancing effect was also observed with increasing water in organogels up to optimum level. The gel integrity and hence the gel strength of organogels was compromised when water in excess of holding capacity produced an o/w emulsion.

The standard curve for estimation of propranolol hydrochloride in diffusion media was prepared in a 5 to 30 µg/mL range with the equation of Y = 0.0182X + 0.0013 (R^2 = 0.9998). The drug release from organogels with 7.5% wt/vol of SMS containing 2% wt/vol of Tween 20, Tween 60, and Tween 80, separately, and 10% wt/vol of propranolol hydrochloride is shown in Figure 3. The release of drug from aqueous solution was completed within 90 minutes, and 92% release was obtained from o/w emulsion (prepared with sorbitan monooleate) within 2 hours. The initial peak flux of drug in organogels with Tween 20, Tween 60, and Tween 80 was found to be 90, 69, and 55 µg/min/cm^2 within 10 minutes of diffusion, respectively. The flux of diffusion in the case of Tween 20 thereafter remained constant between 45 and 51 µg/min/cm^2. The diffusional flux changed invariably in the case of Tween 60. The sustained drug release effect was of the increasing order of Tween 80 > Tween 60 > Tween 20. The cumulative amount diffused in 6 hours was found to be 44%, 58%, and 74%, respectively.

SMS has a linear structure and gels IM owing to tubular aggregation as temperature decreases.[20] The organic solvent has a prime role in gel formation as it provides the correct solubility-insolubility balance toward the gelator. Extensive joining of individual tubules finally creates a 3-dimensional network that immobilizes the solvent. The increased area of inverted micelle aggregates due to increased SMS may be the reason. Thus, the SMS concentrations of <5% wt/vol are insufficient to immobilize the bulk of organic solvent, while that of ≥20% wt/vol produces a nonhomogeneous gelator network. Water is added to promote gelation and as a solvent for incorporating hydrophilic propranolol hydrochloride. Water forms hydrogen bonding with head groups of surfactant. However, the capacity of surfactant aggregates of inverted bilayers to accommodate water is limited, and hence excess water appears as fine droplets producing an o/w emulsion. The integrity of organogels to be used as a drug delivery system is important during storage and uniform consistency is essential for reproducible release profile. Polysorbate surfactants participate in invert tubular aggregation of SMS and hence in the gel-strengthening effect and increased water-holding capacity. Excess water results in loss of gel integrity, thereby causing the decrease in gel strength. The longer fiber lengths of Tween 60 and Tween 80 can cause increased area of overlap of cross-linking and hence produce higher-strength gels.[21] Tween as cosurfactant participates in micellar gelation of SMS in IM. The longer fiber length of Tween surfactant in SMS gels has a profound effect on flux of drug diffusion. Hence, longer fiber length of Tween 80 has low diffusional flux.

Table 3. Gelation Onset Temperatures and Viscosity of Organogel Compositions*

Serial No.	Organogels With 20% wt/vol Water	Gelation Onset Temperature (°C)	Viscosity (cP) (at 37°C)
1	SMS 5% wt/vol + 1% wt/vol Tween 20	41-43	2014 ± 12
2	SMS 5% wt/vol + 2% wt/vol Tween 20	41-44	2788 ± 06
3	SMS 5% wt/vol + 3% wt/vol Tween 20	41-44	3842 ± 08
4	SMS 7.5% wt/vol + 1% wt/vol Tween 20	44-46	3924 ± 04
5	SMS 7.5% wt/vol + 2% wt/vol Tween 20	44-47	4213 ± 10
6	SMS 7.5% wt/vol + 3% wt/vol Tween 20	47-49	4523 ± 14
7	SMS 10% wt/vol + 1% wt/vol Tween 20	51-54	4492 ± 11
8	SMS 10% wt/vol + 2% wt/vol Tween 20	51-55	5224 ± 12
9	SMS 10% wt/vol + 3% wt/vol Tween 20	52-55	5928 ± 18

*SMS, sorbitan monostearate. Viscosity is average of 3 measurements with standard deviation.

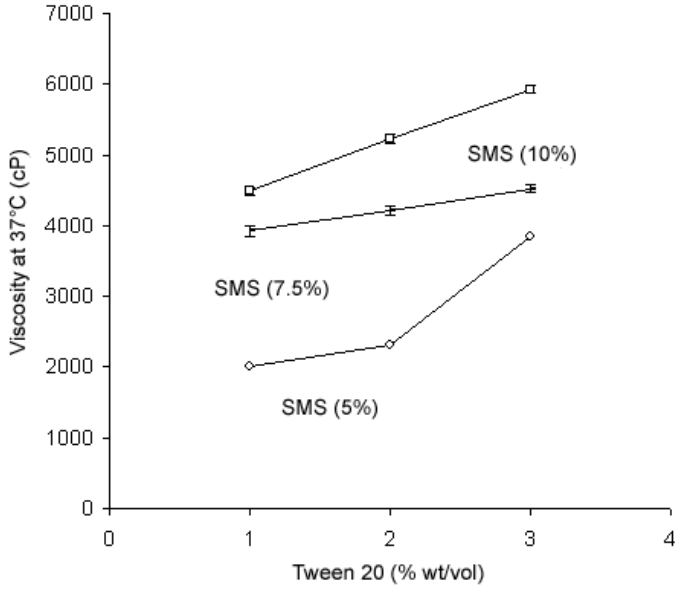

Figure 4. Effect of Tween 20 (X_1) and SMS (X_2) on viscosity of organogels at 37°C.

The changes in structure and strength of organogels with the addition of Tween surfactants and the incorporation of water show a profound effect on the release of drug from organogels. Propranolol hydrochloride is a hydrophilic drug with low molecular weight (295.81), and hence it diffuses freely from solution through leaky nasal mucosa. The o/w emulsion provides little barrier for simple diffusion process. However, release-retardant effect from organogels was dependent on the Tween (each at 2% wt/vol) used. The highest release-retardant effects with Tween 80, followed by Tween 60, are due to greater tubular networking and higher gel strength. Tween 20 has comparatively less gel-strengthening effect and hence has higher flux of 45 to 51 μg/min/cm^2. During diffusion of drug, hydrophilic Tweens are expected to leach from the mixed invert aggregates, thus changing the state of the gel. Although significant release-retardant effect was evident with Tween 60 and Tween 80, the nasal mucosal viability can be retained for 8 hours, and hence Tween 20 was selected for formulation optimization for a 6-hour duration.

Optimization of Drug Release From Organogels

The mechanism of drug release varies with the organogel system. The rectal release of salicylates, procaine, and ketoprofen from Eudragit-based organogels showed initial burst of drug release due to surface-deposited fraction of drug, and further release was governed by Eudragit concentration. Drug release from Eudragit L systems occurs by surface erosion of gel, while that from Eudragit S confirmed the diffusional model. The latter, containing linoleic or oleic acid, has proved useful as a sustained rectal preparation.[24] The transdermal permeation enhancement of indomethacin and diclofenac from lecithin-based organogels also followed diffusional drug release.[18] Shilpa et al have reported gelatin microemulsion-based organogels of Tween 85 in IM containing sodium salicylate. The iontophoretic drug permeation was significantly faster compared with passive diffusion.[25] Fresta et al, have reported diffusion-controlled ophthalmic release of pilocarpine from lecithin organogels in IM.[19] In a study by Florence et al, when SMS organogels were used for intramuscular delivery of vaccines, the percolation of interstitial fluid into the 3-dimensional network of the gel led to its breakdown into smaller fragments and subsequent short depot release of entrapped antigen.[20]

In the case of the majority of reported systems, the diffusional drug release is controlled by the 3- dimensional network of gelator molecules. The extensive cross-linking with higher concentration of gelator molecules decreases the flux of drug release. The properties of the gelator network, viz gelation onset temperature and viscosity at body temperature, significantly alter the drug release. The properties of organogels, in the present case at factorial concentrations of Tween 20 and SMS are shown in Table 3. At constant SMS concentration, as the Tween 20 concentration increased the gelation was evident at higher temperatures. Figure 4 reveals the viscosity trend is identical to the gel-strengthening effect. At constant SMS concentration, increased viscosity was evident with concentration of Tween 20. The viscosity data confirmed the gel-strengthening effect with increase in concentration of both the Tween 20 and SMS. The extensive 3-dimensional tubular net-

Table 4. Average Response of Diffusion From Factorial Batches of Propranolol Hydrochloride Organogels

Coded Level	t_{10} (minutes)	t_{30} (minutes)	t_{50} (minutes)	t_{70} (minutes)	t_{90} (minutes)
-1, -1	6.0	43.4	108.8	199.3	313.1
-1, 0	18.0	80.2	160.8	254.3	358.2
-1, +1	8.3	69.3	185.6	355.3	577.0
0, -1	8.5	53.9	127.0	223.4	340.8
0, 0	18.1	84.1	171.9	271.6	382.2
0, +1	9.5	79.3	212.7	407.5	662.2
+1, -1	9.4	63.3	153.7	275.6	426.4
+1, 0	19.9	89.6	179.2	303.8	450.7
+1, +1	12.6	98.2	255.4	479.3	767.1

working with concentration of SMS immobilizes the vehicle at higher temperature. The active participation of Tween in micelle formation, producing an increased area of micellar overlap, is the reason for linear increase in viscosity of the organogels.[26] These gels are expected to retain gel integrity during diffusion for extended time and retard drug release.

Average responses from in vitro nasal diffusion of factorial organogels containing propranolol hydrochloride are summarized in Table 4. More than 90% of drug is diffused in 5% SMS batches within 5 hours. The transnasal diffusion of propranolol hydrochloride in 7.5% SMS batches does not show significant variation up to 180 minutes. The sustained-release effect of drug was evident with 10% SMS batches. The complexity of transnasal propranolol hydrochloride release from SMS organogels containing polysorbate can be elucidated using response surface methodology (RSM). The results are analyzed on the basis of changes in these surfaces over the period of diffusion. The effect of Tween 20 (X_1) and SMS (X_2) on time required for 10% (t_{10}), 30% (t_{30}), 50% (t_{50}), 70%(t_{70}), and 90% (t_{90}) drug diffusion is shown in Figure 5.

The RSM for t_{10} (Figure 5A) shows a linear decrease in release with increase in concentration of Tween 20 ($t_{10} = 18.67 + 1.6X_1 + 1.08X_2 - 9.5X_2^2$, $R^2 = 0.985$). The SMS shows a curvilinear relationship for time to diffuse 10% of drug nasally. The $\beta 1$ is insignificant, and the effect is due to increased partition of Tween 20 in tubular aggregation of SMS. At low concentration of SMS, diffusion of free drug must be higher hence faster drug release. However, at zero level of SMS and higher level of Tween 20, the retardant effect of Tween 20 is predominant. This finding might be due to the increase in aggregation number as a result of micellar participation of Tween 20 and subsequent micellar drug portioning. Further increase in concentration of SMS develops the interconnected tubular contacts that provide an aqueous channel for faster drug diffusion.

The linear release-retardant effect of Tween 20 is continued at t_{30} (Figure 5B), while the curvilinear decrease in drug release with SMS was faster up to zero level and slowed down at higher levels ($t_{30} = 84.64 + 9.7X_1 + 14.37X_2 - 16.74X_2^2$, $R^2 = 0.955$). The optimum concentration of SMS is required to show the maximum release-retardant effects. At still higher concentration of SMS, an effect similar to t_{10} drug diffusion was observed. This might be due to partial fragmentation of gel structure as shown in Figure 6A. The SMS concentration has 2 opposing effects on drug release. The increased concentration of SMS in tubular aggregates increases drug partition in the micellar region, thereby showing a release-retardant effect. At still higher SMS concentration more tubular network develops (thus increasing the viscosity) and provides a tubular channel for drug release by diffusion process.

The RSM for t_{50} (Figure 5C) shows a linear decrease in the diffusion with increase in concentration of SMS and Tween 20 ($t_{50} = 172.83 + 22.17X_1 + 44.04X_2$, $R^2 = 0.9518$). This indicates that drug release at this point occurs from the micellar partitioned fraction of drug, with the coefficient of X_2 being predominant in controlling the release. This might be due to the diffusion of Tween 20 along with drug. The diffusion of Tween 20 between 100 and 200 minutes of diffusion nullifies the release-retardant effect of higher concentration of Tween 20, resulting in a linear relationship with release of drug.

The linear release-retardant effect of Tween 20 is constant at t_{70} ($t_{70} = 276.63 + 41.64X_1 + 90.63X_2 + 46.82X_2^2$, $R^2 = 0.948$, Figure 5D) and t_{90} ($t_{90} = 397.07 + 67.13X_1 + 154.34X_2 + 119.73X_2^2$, $R^2 = 0.983$); however, the slight curvilinear release-retardant effect was observed for SMS concentration. The curvilinear effect was potentiated at time for 90% of drug release (Figure 5E). The penetration of water after 200 minutes of diffusion of gels resulted in greater percolation of water in the gel structure (Figure 6B), which caused significant fragmentation and surface erosion by emulsification due to loss of Tween 20 and thus losing gel stability and producing emulsion.[27] The release of drug is expected purely from the micellar fraction of drug. The number of invert micellar aggregates of SMS decreases with time due to emulsification of gel. Organogel is progressively emulsified with the time of diffusion resulting in emulsion at the end of diffusion (Figure 6C).

Tween 20 and SMS are responsible for controlling transnasal in vitro diffusion of propranolol hydrochloride from organogels. The coefficient of significance for controlling drug release of both SMS and Tween 20 increases with time of diffusion. For 7.5% wt/vol of SMS, 85% release was obtained. Transnasal drug transport from organogels was compared with aqueous solution and emulsion. More than 90% of release was observed for 5% wt/vol batch of SMS. The release of propranolol hydrochloride was more sustained in the case of 10% wt/vol batches. However, the water pene-

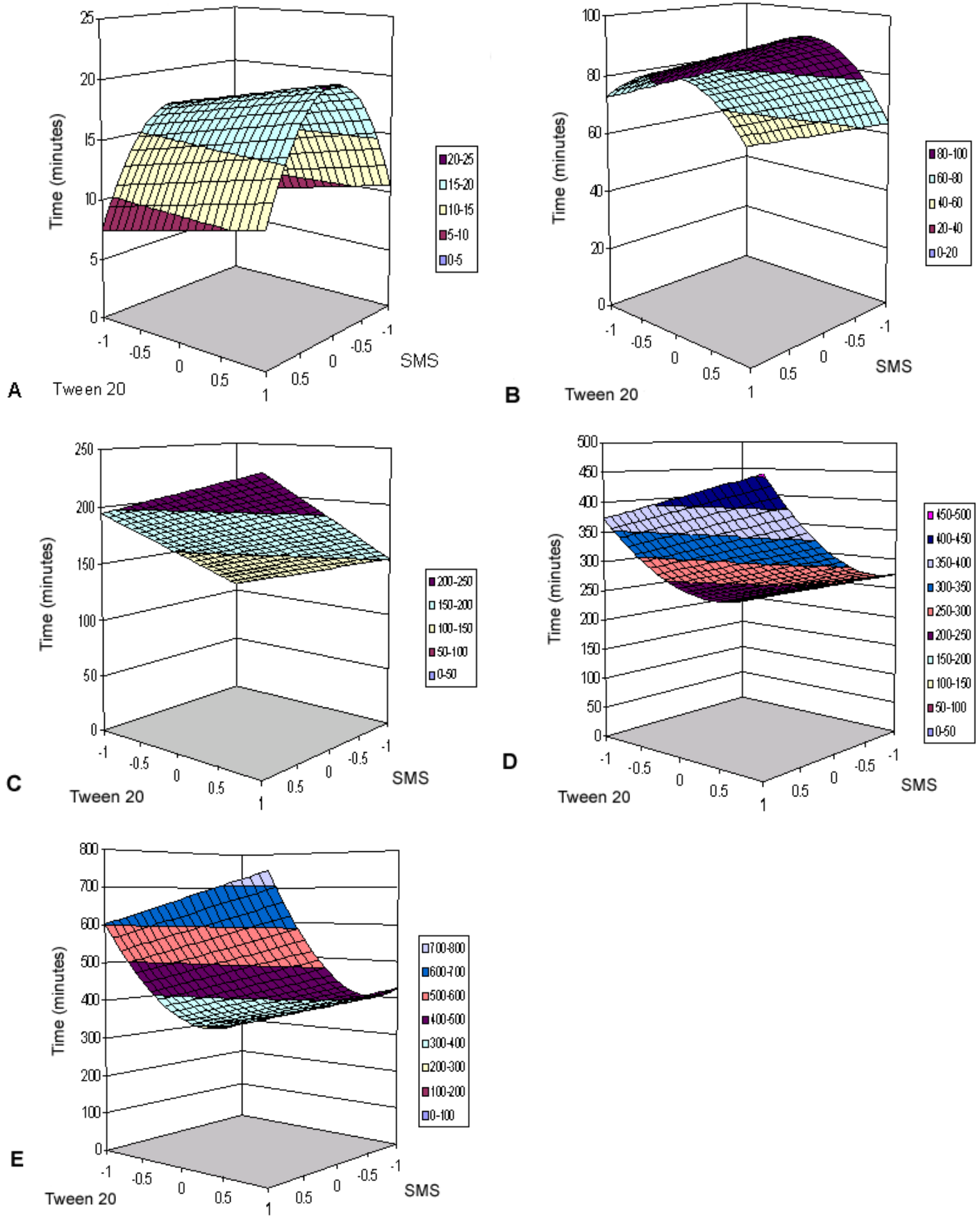

Figure 5. Effect of Tween 20 (X_1) and SMS (X_2) concentrations on time for (A) t_{10}, (B) t_{30}, (C) t_{50}, (D) t_{70}, and (E) t_{90} percentage drug diffusion.

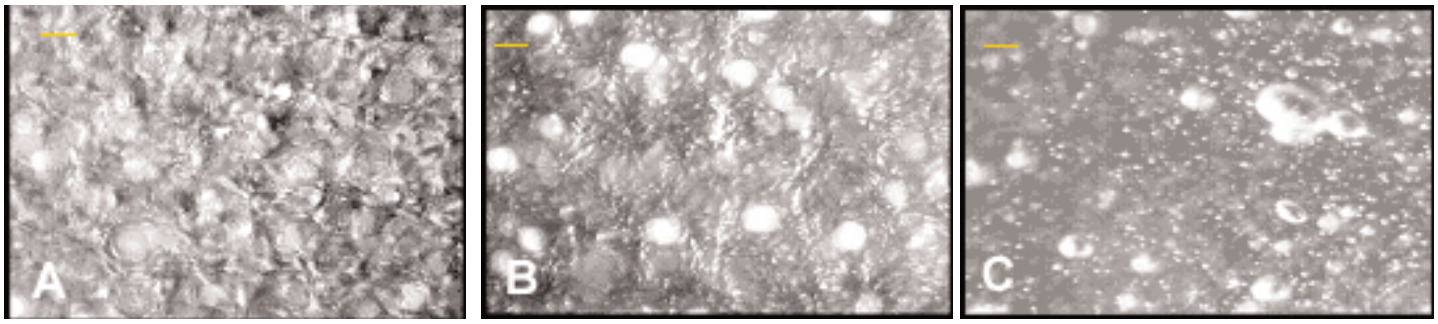

Figure 6. Microscopic structures of organogel at (A) 2 hours, (B) 4 hours, and (C) 6 hours during in vitro diffusion (bar indicates a micrometer).

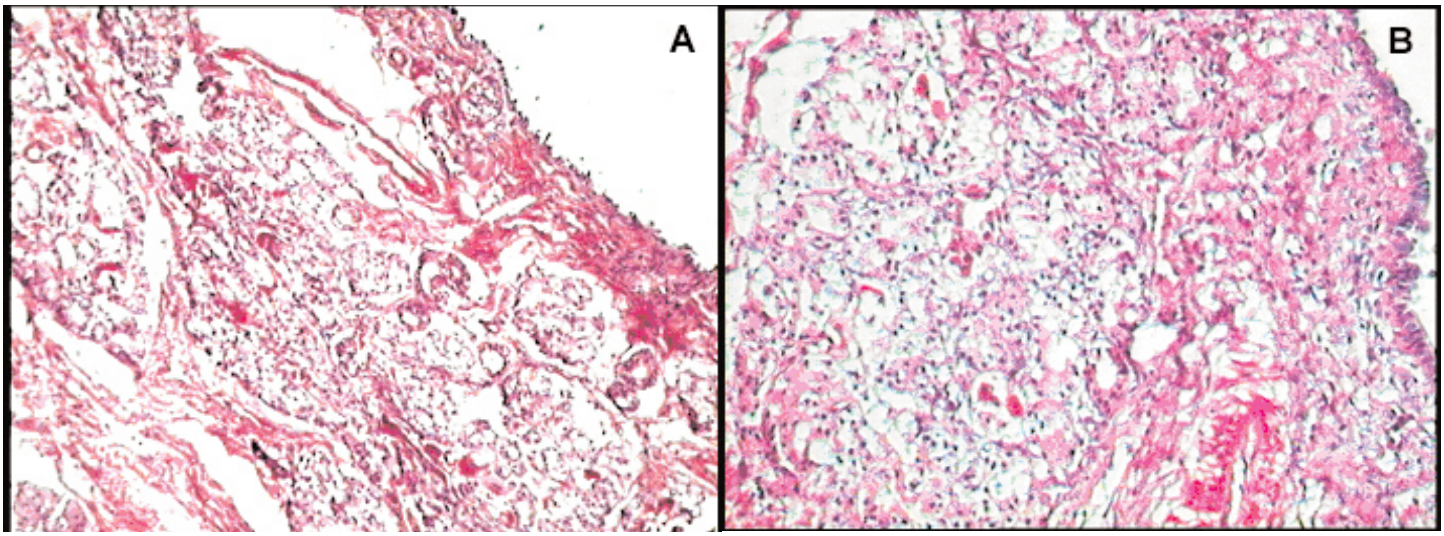

Figure 7. Histology of nasal mucosa. (A) Control, (B) Optimized Organogel.

tration rates in vivo are expected to be very low, and hence the desired release pattern of propranolol hydrochloride for 8-hour release can be obtained by the optimized batch of 7.5% wt/vol of SMS and 2% wt/vol of Tween 20 batch.

Histology of Treated Nasal Mucosa

The histology of nasal mucosa in control and treated with optimized batch of organogel after 6 hours is shown in Figure 7. The microscopic observations indicate that the optimized organogel has no significant effect on the microscopic structure of the mucosa. The surface epithelium lining and the granular cellular structure of the nasal mucosa were totally intact. No major changes in the ultrastructure of mucosa morphology could be seen and the epithelial cells appeared mostly unchanged. The nasal mucosa showed little hydration effect during diffusion. In the organogels under study, IM used as the organic vehicle is biodegradable and has been found nontoxic.[28] IM confers an intensive incrassate effect on mucosal membranes. The biocompatible ester serves as an effective vehicle for cutaneous oil elaboration. The cosurfactant in the gel, Tween 20, has GRAS status and sorbitan esters being widely used as emulsifiers in food and pharmaceuticals.[28]

Conclusion

The formation and properties of organogels are significantly altered by concentration of gelator and additives. These gels are capable of incorporating drug as a guest molecule and have the consistency desired for nasal application. Microstructural changes in the state of organogels with percolation of water cause emulsification. Drug diffusion is controlled by components participating in the invert micellar gels. Organogels provided an effective barrier for diffusion of propranolol, and hence short depot drug release.

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