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Research paper

Enhanced oral bioavailability of dexibuprofen by a novel solid Self-emulsifying drug delivery system (SEDDS)

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ABSTRACT

The main objective of this study was to prepare a solid form of lipid-based self-emulsifying drug delivery system (SEDDS) by spray drying liquid SEDDS with an inert solid carrier Aerosil 200 to improve the oral bioavailability of poorly water-soluble drug dexibuprofen. The liquid SEDDS was a system that consisted of dexibuprofen, Labrasol, Capryol 90 and Labrafil M 1944 CS. The particle size analysis revealed no difference in the *z*-average particle diameter of the reconstituted emulsion between liquid and solid SEDDS. The solid SEDDS was characterized by SEM, DSC and XRD studies. In vivo results of solid SEDDS and dexibuprofen powder in rats at the dose of 10 mg/kg showed that the initial plasma concentrations of drug in solid SEDDS were significantly higher than those of dexibuprofen powder ($P < 0.05$). The solid SEDDS gave significantly higher AUC and Cmax than did dexibuprofen powder ($P < 0.05$). In particular, the AUC of solid SEDDS was about twofold higher than that of dexibuprofen powder. Our results suggested that this solid SEDDS could be used as an effective oral solid dosage form to improve the bioavailability of poorly water-soluble drug dexibuprofen.

1. Introduction

Dexibuprofen, S(+)-ibuprofen is a pharmacologically active form and is more potent than ibuprofen, which has equal quantities of R(−)- and S(+)-enantiomers [1]. On the rationale basis that a fraction of the dose of R(−)-ibuprofen undergoes "metabolic inversion" to an extent of 57–69% to yield S(+)-ibuprofen, it has been argued that a dose of 1:0.75 (rac-ibuprofen *vs.* dexibuprofen) would be needed to obtain comparable pharmacodynamic effects [2]. Therefore, the use of pure dexibuprofen may show distinct advantages. The effectiveness of dexibuprofen as an anti-inflammatory and analgesic agent was discounted like ibuprofen, due to its poor water solubility and low bioavailability after oral administration [3]. However, there were no reported studies on the enhancement of solubility and bioavailability of dexibuprofen. Instead, numerous studies were reported on ibuprofen [4–6].

In recent years much attention has been focused on lipid-microemulsion formulations with particular emphasis on self-microemulsifying or self-emulsifying drug delivery systems to improve oral bioavailability of poorly water-soluble drugs [7]. It was reported that the percentage release of biphenyl dimethyl dicarboxylate from SMEDDS was >12-fold higher than that from the tablet containing the drug [8]. A few other studies have reported of an enhancement in the bioavailability of poorly soluble drugs when formulated as SEDDS [7,9]. However, there exist a few limitations associated with this delivery system, including stability, manufacturing methods, interaction of the fill with the capsule shell, and storage temperature [10]. When the product is stored at a lower temperature, there may be some precipitation of the active ingredient and/or the excipients. The precipitated materials should therefore be dissolved again when warmed to room temperature; otherwise the drug will not be presented in a solution or as a fine emulsion droplet [11]. Moreover it has been suggested that the efficiency of the SEDDS or SMEDDS formulation is drug dependent in most instances [12]. Thus, the successful composition of the SEDDS or SMEDDS should be carefully explored.

Even though the researches focused on solid SEDDS area were increasing, very few publications were available for such attempts [13–15]. These solid SEDDS were almost prepared by extrusion/spheronization method or wet granulation in a high shear mixer. Recently, spray drying has been employed to prepare solid SMEDDS using dextran 40 as a water-soluble solid carrier by spray drying method [16]. However, in this study we intend to prepare solid SEDDS by spray drying liquid SEDDS with an inert solid carrier Aerosil 200. The objectives of the present study were there-

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fore: (1) to develop a novel solid SEDDS of dexibuprofen by spray drying, using Aerosil 200 as an inert solid carrier. Reconstitution properties of the spray-dried powders were investigated and correlated to solid state characterization of the powders performed by scanning electron microscopy (SEM), differential scanning calorimetry (DSC) and X-ray powder diffraction; (2) to determine whether the powder SEDDS maintained the absorption characteristics, a comparative bioavailability study was performed in rats with the solid SEDDS and dexibuprofen powder. Composition of SEDDS was optimized using solubility, phase diagram, particle size and drug release studies.

2. Materials and methods

2.1. Materials

Dexibuprofen was provided by Enzychem Co. (Seoul, South Korea). Polyglycolyzed glycerides (Capryol 90, Labrafac CC, Labrafac Lipophile WL 1349, Labrasol, Labrafil M 1944 CS, Labrafil M 2125 CS, Lauroglycol FCC, Peceol and Transcutol P) were obtained from Gattefosse (Saint-Priest Cedex, France). Castor oil, corn oil, cotton seed oil, sesame oil, soybean oil, sunflower oil and peanut oil were supplied by Sigma (St. Louis, USA). Span 20, Span 80, Tween 20 and Tween 80 were purchased from DC Chemical Co. (Seoul, South Korea). Aerosil 200 was obtained from Degussa (Frankfurt, Germany). All other chemicals and solvents were of reagent grade and were used without further purification.

2.2. Solubility studies

Solubility studies were conducted by placing an excess amount of dexibuprofen (approximately 1 g) in a 2 ml microtube (Axygen MCT-200) containing 1 ml of the vehicle (Table 1). Then, the mixture was vortexed and kept for 5 days at 25 °C in a shaking water bath to facilitate the solubilization. The samples were centrifuged at 3000*g* for 15 min to remove the undissolved dexibuprofen. The supernatant was taken and diluted with methanol for quantification of dexibuprofen by HPLC system (Shimadzu, Japan) consisting of Class VP computer software, LC 10AD VP pump and SPD 10A VP UVVIS detector. Column was Inertsil ODS-3 C18 column (5 μm, 150 * 4.6 mm). Mobile phase, a mixture of phosphate buffer (pH 3.5) and acetonitrile (4:6 v/v), was filtered through 0.45-μm membrane filter and was eluted at a flow rate of 1 ml/min. Effluents were monitored at 220 nm. The inter- and intra-day variance of this HPLC method were within the acceptable range of less than 6.3% (R^2 = 0.999).

2.3. Construction of ternary phase diagram

The existence of self-emulsifying oil formulation fields that could self-emulsify under dilution and gentle agitation was identified from ternary phase diagrams of systems containing oil-surfactant-cosurfactant. A series of self-emulsifying systems were prepared in the formula with varying concentrations of Labrafil M 1944 CS (5–40% *v/v*), Labrasol (40–95% *v/v*), Capryol 90 (0–25% *v/v*) and 100–300 mg/ml of dexibuprofen (10–30% *w/v*).

A formulation (0.2 ml) was introduced into 300 ml of water in a glass beaker at 37 °C and the contents were mixed gently with a magnetic stir bar. The tendency to emulsify spontaneously and also the progress of emulsion droplets were observed. The tendency to form an emulsion was judged as 'good' when droplets spread easily in water and formed a fine milky emulsion, and it was judged 'bad' when there was poor or no emulsion formation with immediate coalescence of oil droplets, especially when stirring was stopped [17]. Phase diagrams were constructed by identifying the good self-emulsifying region. All studies were repeated thrice, with similar observations being made between repeats. The self-emulsifying performance was visually assessed after infinite dilution using purified water.

Table 1
Solubility of dexibuprofen in various vehicles.

Vehicle	Solubility of dexibuprofen (mg/ml)
Surfactants	
Tween 20	>1 g
Tween 80	>1 g
Labrasol	>1 g
Transcutol P	>1 g
Oils	
Corn oil	130.91 ± 16.18
Castor oil	55.17 ± 2.33
Cotton seed oil	99.24 ± 13.03
Soybean oil	119.71 ± 15.03
Sunflower oil	114.03 ± 28.20
Sesame oil	134.48 ± 29.04
Peanut oil	144.19 ± 1.77
Peceol	105.09 ± 19.20
Labrafac CC	184.62 ± 21.06
Labrafac Lipophile WL 1349	179.90 ± 35.81
Labrafil M 1944 CS	163.90 ± 27.31
Labrafil M 2125 CS	184.90 ± 15.18
Co-surfactants	
Span 20	352.05 ± 28.53
Span 80	113.39 ± 15.77
Capryol 90	298.63 ± 31.61
Lauroglycol FCC	238.79 ± 36.99

Each value represents the mean ± SE (n = 3).

2.4. Preparation of liquid SEDDS formulations

The formulations were prepared by dissolving the formulation amount of dexibuprofen (20% *w/v*) in the mixture of surfactant, oil and cosurfactant at 25 °C (Table 2). The final mixture was vortexed until a clear solution was obtained. The final drug content of the liquid SEDDS was 17.9% w/w ratio. The formulations were examined for signs of turbidity or phase separation prior to self-emulsification and particle size studies.

2.5. Preparation of solid SEDDS formulations

Aerosil 200 (500 mg) was suspended in 100 ml ethanol by magnetic stirring. The liquid SEDDS (1 ml) was then added with constant stirring, and the solution was kept stirring at room temperature for 15 min to obtain a good suspension of Aerosil 200. The suspension was spray dried with a Buchi mini spray dryer B-190 apparatus (Buchi, Switzerland) under the following conditions: inlet temperature, 60 °C; outlet temperature, 35 °C; aspiration, 85%; feeding rate of the suspension, 5 ml/min. The final drug content of the solid SEDDS was 12.4% w/w ratio.

2.6. Characterization of the solid SEDDS

Liquid SEDDS (100 μl) or solid SEDDS (150 mg) was added to a volumetric flask containing 25 ml of distilled water. The flask was inverted and shaken gently to form a fine emulsion and was kept for 12 h at room temperature.

Table 2
Composition of optimized liquid SEDDS formulation.

Formulation (v/v)	
Labrafil M 1944 CS (%)	15
Labrasol (%)	80
Capryol 90 (%)	5

2.6.1. Droplet size of emulsions

The particle size of emulsion was determined by Zetasizer Nano ZS (Malvern Instruments, UK) dynamic light scattering particle size analyzer at a wavelength of 635 nm and at a scattering angle of 90° at 25 °C. All studies were repeated three times and the values of *z*-average diameters were used. The *z*-average diameter, also referred to as the harmonic intensity-weighted average hydrodynamic diameter, of the emulsions was derived from cumulated analysis by the Automeasure software (Malvern Instruments, Malvern, UK).

2.6.2. Morphological analysis of solid SEDDS

The outer macroscopic structure of the solid SEDDS was investigated by S-4100 scanning electron microscope (Hitachi, Japan). The samples were fixed on a brass stub using double-sided adhesive tape and were made electrically conductive by coating in vacuum (6 Pa) with platinum (6 nm/min) using Hitachi Ion Sputter (E-1030) for 240 s at 15 mA. The SEM images were analyzed with an image analysis system (ImageInside Ver 2.32) for particle size analysis.

2.6.3. Solid state characterization of solid SEDDS

The physical state of dexibuprofen in solid SEDDS was characterized by the differential scanning calorimetry (DSC Q200 v24.2 build 107, TA Instruments, USA). The samples (about 3.00 mg) were placed in standard aluminum pans, and dry nitrogen was used as effluent gas. All samples were scanned at a temperature ramp speed of 5 °C/min and at the heat flow from 0 to 120 °C. Furthermore, X-ray powder scattering measurements were carried out with an X'Pert PRO diffractometer (PAN analytical, The Netherlands) at room temperature using monochromatic CuK_{α}-radiation (λ = 1.5406 Å) at 30 mA and at 40 kV over a range of 2θ angles from 10° to 50° with an angular increment of 0.02° per second.

2.7. Drug release studies

Drug release studies from solid SEDDS were performed using USP XXIV, dissolution apparatus II with 900 ml of phosphate buffer pH 6.8 as a medium at 37 ± 0.5 °C. The speed of the paddle was adjusted to 100 rpm. Dexibuprofen-loaded solid SEDDS (equivalent to 80 mg of dexibuprofen) and 80 mg of powder dexibuprofen were placed in a dissolution tester (Shinseang Instrument Co., South Korea). At predetermined time intervals an aliquot (0.5 ml) of the sample was collected, filtered and analyzed for the content of dexibuprofen by high-performance liquid chromatography (HPLC) as mentioned above. An equivalent volume (0.5 ml) of fresh dissolution medium was added to compensate for the loss due to sampling.

2.8. In vivo study

The in vivo study of two formulations of dexibuprofen, an optimized solid SEDDS and control formulation (dexibuprofen powder) was performed in rats. Male Sprague–Dawley rats weighing 280 ± 20 g were fasted for 10–12 h prior to the experiments but were allowed free access to water. Twelve rats were divided into two groups. The rats in each group were administered with 2.6–3 mg of dexibuprofen powder or 21–25 mg of solid SEDDS equivalent to 10 mg/kg dose dexibuprofen filled in a mini hard capsule (SHIONOGI Qualicaps., Japan), respectively. Then, 0.25 ml of blood was collected from the right or left subclavian vein or artery using 1-ml needle at predetermined time intervals and 0.1 ml of plasma was separated by centrifuging blood samples at 3000*g* for 15 min. Plasma samples were stored at −20 °C until further analysis. All animals care and procedures were conducted according to the guiding principles in the use of animals in toxicology, as adopted by the Society of Toxicology (USP) in 1999 [18].

To 100 μl of plasma, 10 μl of internal standard (flufenamic acid 5 μg/ml acetonitrile) was added and vortex-mixed. The plasma was then deproteinized with 0.9 ml of acetonitrile and was vortex-mixed for 5 min and then centrifuged at 8000*g* for 2 min. The supernatant (0.8 ml) was evaporated in a rotary centrifugal vacuum evaporator. The residue was reconstituted with 100 μl of acetonitrile and 50 μl of the resulting solution was analyzed by HPLC as mentioned above.

Student's *t*-tests were performed to evaluate the significant differences between the two formulations. Values are reported as mean ± SD and the data were considered statistically significant at $P < 0.05$.

3. Results and discussion

3.1. Solubility study

The self-emulsifying formulations consisted of oil, surfactants, cosurfactants and drug should be a clear and monophasic liquid at ambient temperature when introduced to aqueous phase and should have good solvent properties to allow presentation of the drug in solution. The solubility of dexibuprofen in various vehicles is presented in Table 1. All the surfactants showed good solubility of the drug. Among the surfactants tested in this study, Labrasol, a medium-length alkyl chain surfactant with HLB 14 was selected as a surfactant because it was reported for its enhanced intestinal absorption of drugs [19].

Labrafac CC, Labrafac Lipophile WL 1349, Labrafil M 1944 CS and Labrafil M 2125 CS showed higher drug solubility than other oils. Moreover, the miscibility of these four oils with Labrasol at 1:1 volume ratio was investigated by clarity of oil/surfactant mixture. Labrafac Lipophile WL 1349 and Labrafac CC were poorly miscible with Labrasol, whereas Labrafil M 2125 CS (Linoleoyl macrogol glyceride) and Labrafil M 1944 CS (Oleoyl macrogol glyceride) were well miscible and formed clear solution with Labrasol. Even though Labrafil M 2125 CS showed better solubility for dexibuprofen than Labrafil M 1944 CS, the spontaneous emulsion formation and smaller *z*-average diameter of emulsion were observed with Labrafil M 1944 CS. Thus, Labrafil M 1944 CS was selected as an oily vehicle due to its good solubility and good emulsion-forming ability with Labrasol. Furthermore, Capryol 90, Propylene Glycol Monocaprylate (HLB 6) was selected as a cosurfactant for its good solubility, medium chain fatty acid and for preparing an optimal SEDDS formulation resulting in the improvement of drug loading and in the formation of spontaneous fine emulsion [20].

3.2. Construction of pseudo ternary phase diagrams

A series of SEDDS were prepared and their self-emulsifying properties were observed visually. It was reported that the drug incorporated in the SEDDS or SMEDDS might have some effect on the self-emulsifying performance [21]. Thus, pseudo-ternary phase diagrams were constructed in the presence of 100–300 mg of dexibuprofen (10–30% w/v) to identify the self-emulsifying regions with maximum drug loading and to optimize the concentration of oil, surfactant and cosurfactant in the SEDDS formulations. Labrafil M 1944 CS showed significant difference with different amounts of drug incorporation, it was observed that with increased drug loading, self-emulsification region and efficiency of the self-emulsification process decreased. Thus, the formulation was optimized to 20% w/v of drug incorporation (i.e. 17.9% w/w ratio). The phase diagram of the system containing Labrasol as a surfactant and Labrafil M 1944 CS as an oil and Capryol 90 as a cosurfac-

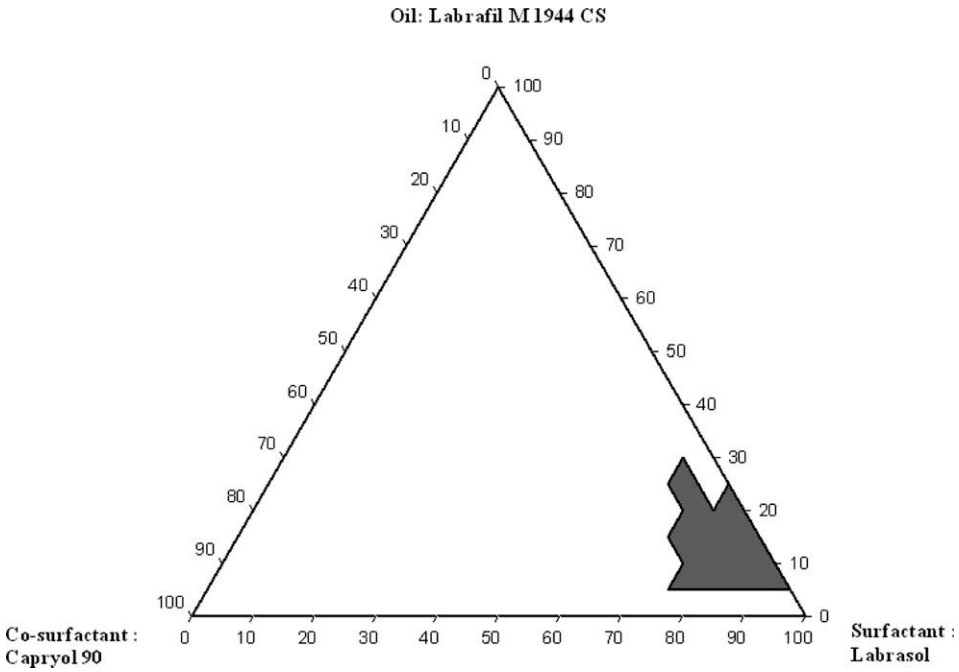

Fig. 1. Pseudo-ternary phase diagram of formula given in Table 1.

tant with 20% w/v drug loading is shown in Fig. 1. Moreover, it was observed that incorporation of cosurfactant, Capryol 90, within the self-emulsifying region increased the spontaneity of the self-emulsification process. The efficiency of emulsification was good when the surfactant/cosurfactant concentration was more than 75% v/v of SEDDS formulation. It was observed that the spontaneous emulsion formation was not efficient with less than 70% v/v of surfactant in SEDDS. In this system, the formulations surrounding the good self-emulsifying region in the phase diagram exhibited poor emulsion-forming ability.

3.3. Characterization of liquid SEDDS

In SMEDDS, the primary means of self-emulsification assessment is visual evaluation [22]. The efficiency of s elf-emulsification could be estimated by determining the rate of emulsification and droplet size distribution. The droplet size of the emulsion is a crucial factor in self-emulsification performance because it determines the rate and extent of drug release as well as absorption [23]. It was observed that increasing the surfactant concentration (from 60% to 80% v/v) in SEDDS formula (Table 1) decreased the *z*-average diameter of emulsion formed but above 80% with Labrafil M 1944 CS the *z*-average diameter slightly increased (Fig. 2). The effect of the cosurfactant (Capryol 90) concentration on the *z*-average diameter in SEDDS was similar to that of the surfactant (Labrasol) at concentrations of Capryol 90 from 0% to 15% v/v. A decrease in *z*-average diameter was observed with an increase in the cosurfactant concentration of Capryol 90 from 0% to 5%, after which the *z*-average diameter was not significantly different (Fig. 3). It was observed that the formulation composition ratio given in Table 2 gave smaller *z*-average diameter than other SEDDS formulations tested and chosen for further studies.

3.4. Reconstitution properties of solid SEDDS

The *z*-average diameter and polydispersity index of the solid and liquid SEDDS are presented in Table 3. As shown in the table, the *z*-average droplet sizes of both systems were less than 250 nm. The emulsion droplet size distribution in liquid and solid

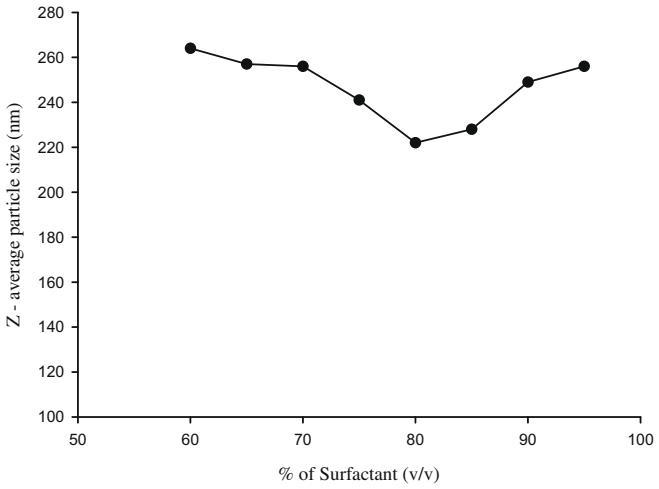

Fig. 2. Effect of the percentage volume ratio of surfactant to oil on the droplet size of emulsion formed from oil/surfactant mixture.

SEDDS (Fig. 4) further confirmed the self-emulsification nature of the solid SEDDS.

3.5. Solid state characterization of solid SEDDS

The scanning electron micrographs of dexibuprofen powder, Aerosil 200 and solid SEDDS are shown in Fig. 5. Dexibuprofen powder (Fig. 5B) appeared as smooth-surfaced rectangular crystalline in shape [24]. Aerosil 200 (Fig. 5A) appeared with a rough surface with porous particles. However, the solid SEDDS (Fig. 5C) appeared as smooth-surfaced Aerosil 200 particles, indicating that the liquid SEDDS is absorbed or coated inside the pores of Aerosil 200. Furthermore, the solid SEDDS had the mean particle size of 9.25 ± 4.84 μm.

The physical state of dexibuprofen in the solid SEDDS was investigated since it would have an important influence on the in vitro and in vivo release characteristics. DSC curves of pure dex-

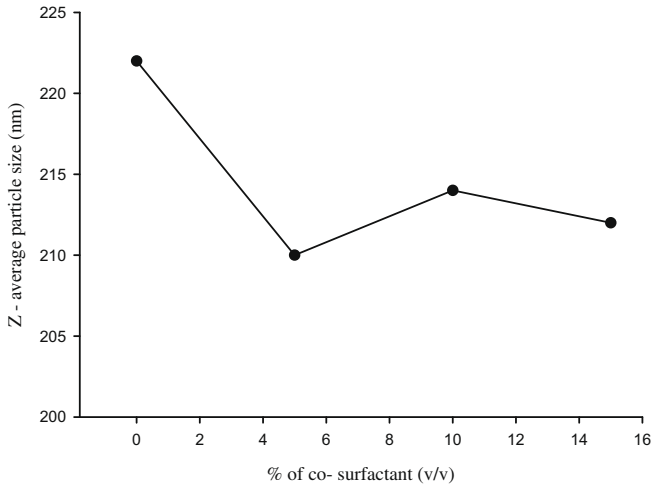

Fig. 3. Effect of cosurfactant percentage volume ratio on the mean emulsion droplet diameter of formulations containing 80% of constant surfactant volume.

Table 3
Mean emulsion droplet size and polydispersity index of the liquid and solid SEDDS.

Formulation	*z*-Average diameter (nm)	Polydispersity index (PDI)
Liquid SEDDS	212 ± 13	0.198 ± 0.018
Solid SEDDS	224 ± 19	0.219 ± 0.012

ibuprofen, Aerosil 200, physical mixture and solid SEDDS are shown in Fig. 6. The physical mixture was prepared by mixing well 500 mg of Aerosil 200 and 200 mg of dexibuprofen using mortar and pestle. Pure dexibuprofen showed a sharp endothermic peak at about 55 °C (curve D) [24]. Aerosil 200 did not show any peak over the entire range of the tested temperatures (curve C). The physical mixture exhibited a small endothermic peak for dexibuprofen (curve A). No obvious peak of the drug was found in the solid SEDDS of dexibuprofen (curve B), indicating that the drug must be present in molecularly dissolved state in solid SEDDS [25].

From X-ray powder diffractograms shown in Fig. 7, the internal physical state of dexibuprofen in the solid SEDDS was further verified. No obvious peaks representing crystals of dexibuprofen were seen for the solid SEDDS (curve D).

3.6. In vitro dissolution test

In the self-emulsifying systems, the free energy required to form an emulsion was very low, thereby allowing spontaneous formation of an interface between the oil droplets and water. It is suggested that the oil/surfactant/cosurfactant and water phases effectively swell, decrease the oil droplet size and eventually increase the release rate. In vitro drug release studies were performed for solid SEDDS and dexibuprofen powder, and are profiled in Fig. 8. As the emulsification time is below 30 s a maximum percentage of the drug released within 2 min from the solid SEDDS; however, the dissolution studies were conducted for 1 h to

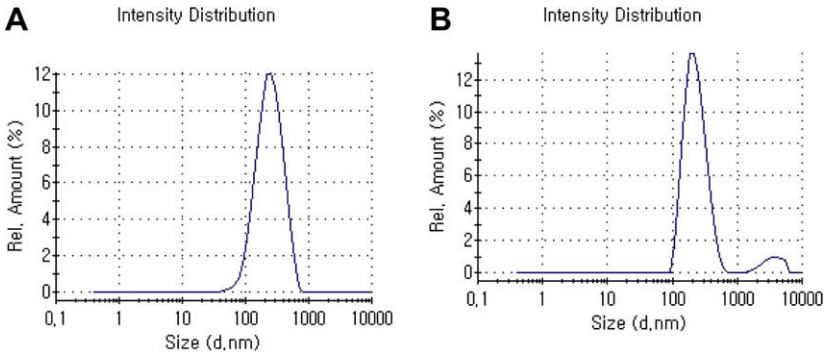

Fig. 4. Emulsion droplet size distribution: (A) liquid SEDDS; (B) solid SEDDS.

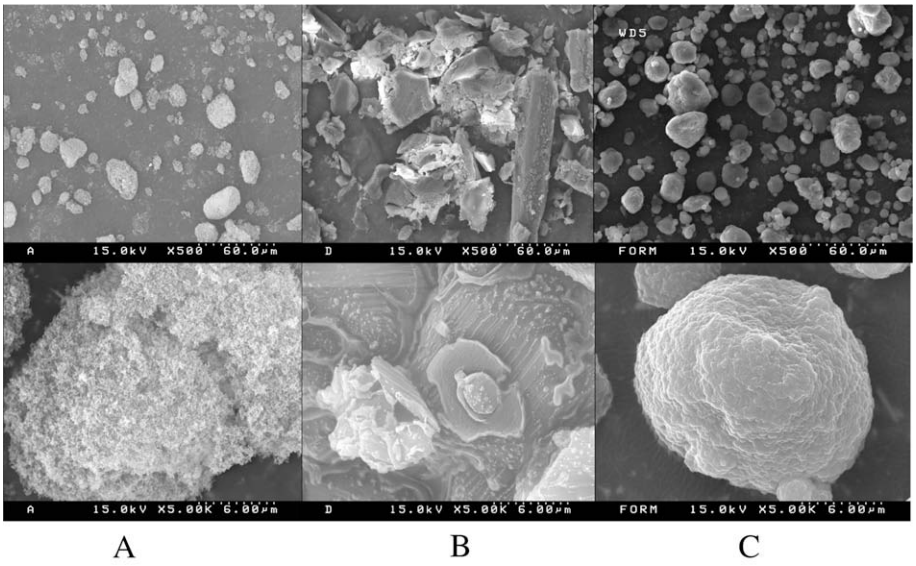

Fig. 5. Scanning electron micrographs: (A) Aerosil 200 (× 500 and 5000); (B) dexibuprofen powder (× 500 and 5000); (C) solid SEDDS (× 500 and 5000).

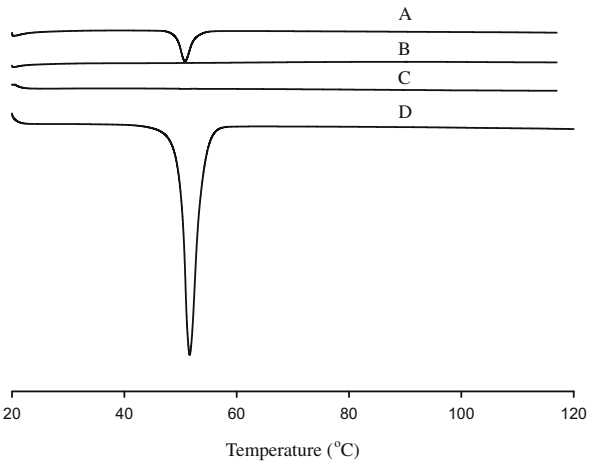

Fig. 6. Differential scanning calorimetric thermogram: (A) physical mixture; (B) solid SEDDS; (C) Aerosil 200; (D) dexibuprofen powder.

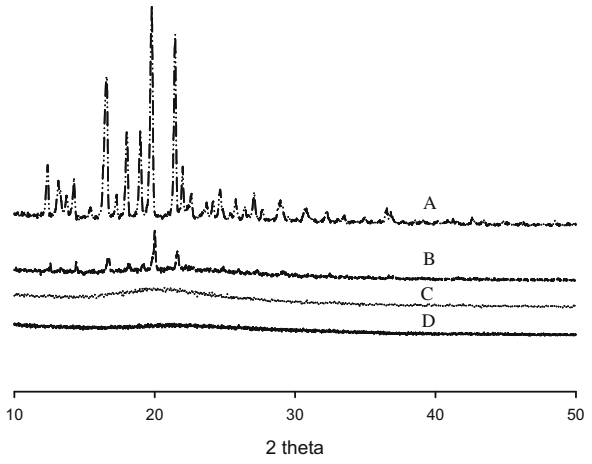

Fig. 7. X-ray powder diffraction: (A) dexibuprofen powder; (B) physical mixture; (C) Aerosil 200; (D) solid SEDDS.

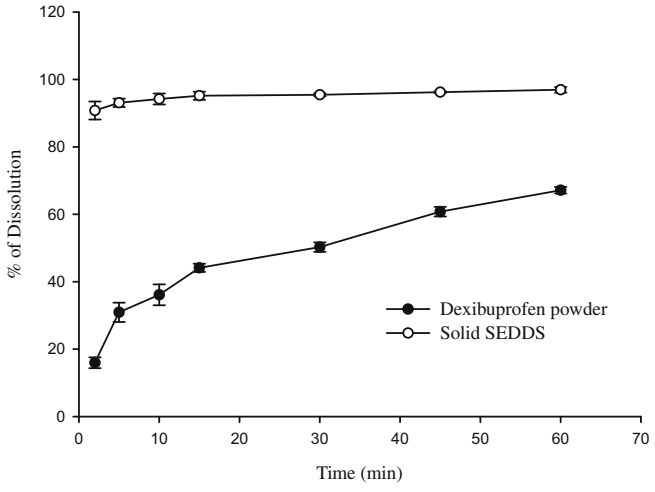

Fig. 8. Dissolution profile of dexibuprofen from powder and solid SEDDS in phosphate buffer pH 6.8. Each value represents the mean ± SD ($n = 6$).

see the variance or occurrence of precipitation over a period of time. In the present investigation drug release profile of solid SEDDS in buffer solution showed that the formulation had higher drug release profile than the dexibuprofen powder, ensuring that the solid SEDDS preserved the improvement of in vitro dissolution of liquid SEDDS.

Table 4
Pharmacokinetic parameters of solid SEDDS and dexibuprofen powder in rats.

Parameter	Powder	Solid SEDDS
tmax (h)	0.54 ± 0.1	0.50 ± 0
Cmax (μg/ml)	15.91 ± 5.89	34.02 ± 7.07*
$t½$ (h)	3.54 ± 0.45	3.93 ± 0.84
Ke (h^{-1})	0.19 ± 0.03	0.18 ± 0.02
AUC (μg h/ml)	58.34 ± 33.6	120.75 ± 29.38*

Each value represents the mean ± SE ($n = 3$).
* $P < 0.05$, when compared with those of dexibuprofen powder by Student's t-test.

3.7. In vivo study

The pharmacokinetic parameters of dexibuprofen (Table 4) were determined after oral administration of dexibuprofen powder or solid SEDDS in capsules to rats. Fig. 9 shows the change in mean plasma concentration of dexibuprofen after oral administration of preparations in rats. The total plasma concentrations of drug in solid SEDDS were higher than those in dexibuprofen powder. In particular, the initial plasma concentrations of dexibuprofen in solid SEDDS were significantly higher than those in dexibuprofen powder ($P < 0.05$). The solid SEDDS gave significantly higher AUC and Cmax of dexibuprofen than did dexibuprofen powder ($P < 0.05$). In particular, the AUC of dexibuprofen from solid SEDDS was about twofold higher than that of dexibuprofen powder. However, the tmax value of dexibuprofen from solid SEDDS was not different from those of dexibuprofen powder. These results showed that it is possible to improve the bioavailability of dexibuprofen if given in the solid SEDDS. Though, we have not performed in vivo study for the liquid SEDDS, the in vitro study showed no difference in the drug release profile from solid SEDDS (data not shown).

For the oral delivery of poor water-soluble drugs, there are two main barriers, i.e. the pre-epithelial, unstirred, aqueous layer and poor membrane permeability. Surfactants are known to increase the permeability of drugs by disturbing the cell membrane and modifying tight junctions between the cells [26], which are the primary barrier for the absorption of a majority of drugs. The very hydrophobic surfactants are poor enhancers, and very hydrophilic

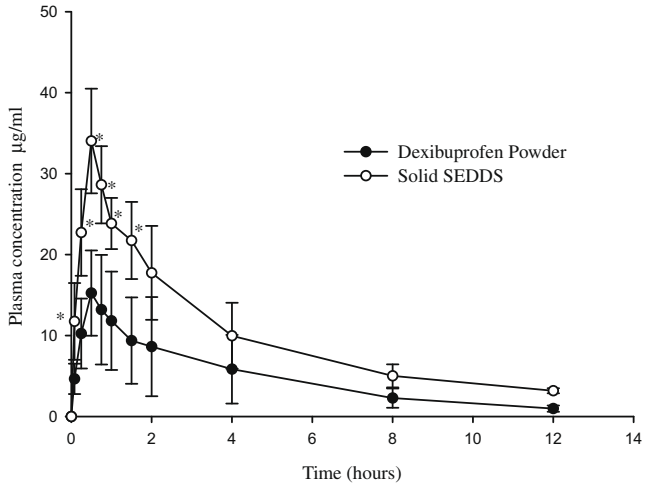

Fig. 9. Plasma concentration–time profiles of dexibuprofen after oral administration of powder and solid SEDDS in rats. Each value represents the mean ± SD ($n = 6$). *$P < 0.05$ when compared with those of dexibuprofen powder.

surfactants cannot partition into the hydrophobic environment of the lipid bi-layer [27]. A medium length alkyl chain surfactant may penetrate the lipid bi-layer easily, because its aqueous solubility has a greater monomer concentration and higher critical micellar concentration than a longer alkyl chain surfactant [23,28]. Labrasol is a surfactant that predominantly contains alkyl chain lengths of C_8 and C_{10}. Previous studies have indicated that Labrasol improves intestinal absorption of drugs [19]. In the present investigations, the superior performance of solid SEDDS may be attributed to the following factors: (a) larger surface area provided by the fine emulsion droplets (b) improved diffusion of the fine emulsion droplets and (c) increased mucosal permeability due to surfactants. Our results suggested that the solid SEDDS was kept well as a solid form of the liquid SEDDS.

4. Conclusion

In this study, the solid SEDDS of dexibuprofen was prepared by spray drying, using water-insoluble Aerosil 200 as a solid carrier. The solid SEDDS consisted of well-separated particles with smooth surface and preserved the self-emulsification performance of the liquid SEDDS. Both DSC measurements and X-ray diffraction analysis suggested that dexibuprofen in the solid SEDDS may be in the molecular dispersion state. In vitro dissolution test showed that the solid SEDDS had a faster in vitro release rate than the powder. In vivo absorption study in rats showed that solid SEDDS gave significant increase in the bioavailability of dexibuprofen compared to the powder formulation, indicating its preserved self-emulsification performance of liquid SEDDS. Thus, this solid self-emulsifying system may provide a useful oral solid dosage form for poorly water-soluble drug, dexibuprofen.

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