ABSTRACT

Objective: The aim of this work was to determine the intestinal membrane transport parameters of eprosartan mesylate (EM) and to investigate self-nano emulsifying drug delivery systems (SNEDDS) and inclusion complexation with hydroxypropyl β-cyclodextrin (HPβCD) for enhanced intestinal absorption of eprosartan mesylate.

Methods: The intestinal absorption was monitored using the in situ rabbit intestinal perfusion technique. SNEDDS was developed using labrafail, Lauroglycol with a tween in the presence of ethanol. Inclusion complexation was achieved by construction of phase solubility diagram in the presence of HPβCD. The prepared complex was evaluated using Fourier Transform Infrared Spectroscopy (FTIR) and differential scanning calorimetry (DSC).

Results: The drug was found to be poorly absorbed from the jejun-ileum and the colon with the absorption being mainly through paracellular pathway. An inclusion complex was developed between the drug and HPβCD. Perfusion of the drug in the nanoemulsion formulation or as an inclusion complex resulted in a significant increase in the intestinal absorption of the drug compared with the control.

Conclusion: SNEDDS and inclusion complexation are promising strategies for enhanced intestinal absorption of eprosartan mesylate.

Keywords: Eprosartan, Self-nano emulsifying, Inclusion complexation, Hydroxypropyl β-cyclodextrin, Labrafail, Lauroglycol, Tween

INTRODUCTION

Eprosartan mesylate (EM) is chemically described as the mononemethane sulphonate salt of “(E)-2-butyl-1-(p-carboxybenzyl)-2-thienylmethylimidazole-5-acrylic acid” [1]. Its molecular weight equals to 520.62 g/mol [2]. Eprosartan mesylate is a highly selective angiotensin receptor blocker (ARB) with a unique molecular structure and physiological effects compared with other members of the group. It is a nonbenzopyran, nontetrazole competitive inhibitor with a high affinity for prejunctional subtype 1 angiotensin receptor (AT1) [3, 4]. It differs from other angiotensin receptor blockers (ARBs) in achieving its action via competitive inhibitory effect [4, 5]. Eprosartan is not substrate for cytochrome P450 (CYP450) and is mainly excreted unchanged by biliary or renal routes with no active metabolite being detected after oral or intravenous administration [6]. The drug is characterised by a relatively long elimination half-life which can reach 20 h but no accumulation was recorded after repeated dosing [6]. Eprosartan is an amphiphilic molecule containing aliphatic and phenylcarboxylic groups and one imidazole (basic) functional group. The latter will be protonated at pH values lower than 2 [7]. Increasing the pH will result in deprotonation of the aliphatic carboxylic group which has an estimated pKa of 2.9. The estimated pKα of the phenylcarboxylic group is 5.9 requiring higher pH values for deprotonation. Further increase in pH will result in deprotonation of the protonated imidazole which has an estimated pKα is 6.8.

According to the pH-partitioning theory, only unionised species or ion-neutral will be absorbed by passive diffusion [7]. Taking this into consideration together with the pH-dependent ionisation pattern of the drug, poor intestinal permeability may be considered an important reason for reduced bioavailability of eprosartan mesylate. In addition, eprosartan mesylate is poorly water soluble with slow dissolution rate which contributes to its low bioavailability after oral administration [8]. The drug thus exhibits low and variable bioavailability with the recorded absolute oral bioavailability being approximately 13% [6]. To date, the intestinal membrane transport parameters of this drug have not been identified.

The objective of this study was to characterise intestinal membrane permeability parameters of eprosartan mesylate and to enhance its intestinal absorption. This employed the in situ rabbit intestinal perfusion technique with the absorption enhancement depending on complexation with cyclodextrin as cyclodextrins are known to be used for enhancement of solubility, stability and bioavailability [9], and self-nano emulsifying formulation which are good candidates for oral drug delivery of hydrophobic drugs [10].

MATERIALS AND METHODS

Chemicals and reagents

Eprosartan mesylate (Hetero, India) was kindly donated by Pharmed healthcare pharmaceutical company (Hetero pharmed), El Sadat city, Egypt. Potassium dihydrogen orthophosphate, disodium hydrogen phosphate, sodium chloride and potassium chloride were purchased from Isocem, Vert-le-petit, France. Acetonitrile (HPLC grade) was obtained from Fischer scientific, Pennsylvania, USA. Hydroxypropyl β-cyclodextrin (HP-β-CD) was procured from China Eastar Holding Group, Shanghai, China. Absolute ethanol and polysorbate 80 were products of El-Nasr Pharmaceutical Chemicals Company, Cairo, Egypt. Linoleoyl polyoxyel-5 glycerides “Labrafail M 2125 CS®” and propylene glycol monolaurate “Lauroglyc 90®” were kindly donated as free samples from Gattefosse, Lyon, France. Ketamine HCl injections were from SigmaTec Pharmaceutical Industries, 6th of October city, Egypt. Chlorpromazine HCl was from Misr Company for Pharmaceutical Industries, Cairo, Egypt.

Chromatography

Perfusate samples were analysed for drug content by high-pressure liquid chromatography (HPLC). The method utilised an Agilent apparatus with a photodiode array detector. The separation was performed on zorbax SB-C8 column, 250 mm in length with 4.6 mm internal diameter and 5 µm particle size. The mobile phase was 0.2% v/v diluted orthophosphoric acid in highly purified water and
acetonitrile at a ratio of 68:32 (v/v), respectively. The mobile phase was pumped at a rate of 1 ml/minute and the effluent was monitored at 275 nm.

Phase solubility study

Phase solubility study is mentioned in details in the literature [11, 12]. The aim of this study was to monitor the kinetics of inclusion complexation of eprosartan mesylate/HPβCD. Solutions containing increasing concentration of HPβCD in water were prepared. Excess amounts of the drug were added to each of these solutions, and the resulting suspensions were maintained under continuous stirring at ambient temperature for 72 h. The suspended drug particles were separated by filtration before determining the solubility of the drug by HPLC. The solubility of the drug was plotted as a function of HPβCD concentration to provide the phase solubility diagram. The latter was used to identify the type of complex and to determine the stoichiometric ratio [13].

Fourier transform infra-red (FTIR) spectroscopy

This was used to study the interaction between the drug and the cyclodextrin. The same technique is used in the complexation study with another drug [14]. The spectra of eprosartan mesylate, HPβCD and their combinations were recorded using FTIR spectroscopy software.

Table 1: Absorbance at 600 nm (A) of different formulæ to determine the phase behaviour

| Formula | Lb* | Lg** | Tween 80 | T: E*** 2:1 | A       |
|---------|-----|------|----------|-------------|---------|
| F1      | 0.05| 0.05 | 0.40     | -           | 0.934   |
| F2      | 0.1 | 0.05 | 0.35     | -           | 1.172   |
| F3      | 0.05| 0.1  | 0.35     | -           | 1.175   |
| F4      | 0.15| 0.05 | 0.30     | -           | 1.286   |
| F5      | 0.1 | 0.1  | 0.30     | -           | 1.446   |
| F6      | 0.05| 0.15 | 0.30     | -           | 1.418   |
| F7      | 0.15| 0.10 | 0.25     | -           | 1.534   |
| F8      | 0.10| 0.15 | 0.25     | -           | 1.495   |
| F9      | 0.05| 0.05 | 0.40     | 0.35       | 1.459   |
| F10     | 0.05| 0.10 | -        | 0.25        | 1.462   |
| F11     | 0.15| 0.10 | -        | -           | 0.086   |
| F12     | 0.10| 0.40 | -        | -           | 1.476   |
| F13     | 0.40| 0.05 | 0.05     | -           | 1.085   |
| F14     | 0.05| 0.40 | 0.05     | -           | 0.824   |
| F15     | 0.05| 0.40 | 0.10     | -           | 0.645   |
| F16     | 0.05| 0.05 | 0.40     | 0.35        | 1.7     |
| F17     | 0.05| 0.10 | -        | 0.20        | 1.282   |
| F18     | 0.15| 0.15 | -        | 0.30        | 0.934   |
| F19     | 0.05| 0.05 | 0.40     | -           | 0.906   |
| F20     | 0.05| 0.05 | 0.50     | -           | 0.031   |

The amount of each material is presented as g/100 ml of the buffer; *Lb= labrafil M2125, **Lg= lauroglycol 90, ***T= tween 80; ethanol

The mixtures were vortex mixed before dispersing 100 mg of each system in 20 ml of hypotonic phosphate buffered saline. The resulting dispersions were evaluated visually for phase separation. Systems showing no phase separation were further characterised by the degree of turbidity by monitoring the absorbance at 600 nm using UV-VIS spectrophotometer (Shimadzu, UV-1800, Japan). Systems having an absorbance value below 0.1 were considered nanoemulsions with showing no phase separation were further characterised by the degree.

Preparation of perfusion solutions

Solutions of the drug (30 µg/ml) were prepared in a hypotonic phosphate buffered saline with pH adjusted to 7.4 and 6.6 for jejunum and ascending colon, respectively. This was used as the control. The system containing tween 80, labrafil, laurogol 90 and ethanol (1:6.0:2:0.2:2.2 w/w) was diluted (16 in 1000) with the same buffer and was used as a solvent for the drug to prepare test perfusion solution. Another perfusion solution was prepared using HPβCD which was added at a 1:1 molar ratio with the drug. This was prepared in the same buffer system with the pH being adjusted as before.

Isolated intestinal segment preparation

The study employed the in situ rabbit intestinal perfusion technique. The study protocol was approved by the ethical committee of the college of pharmacy, university of Tanta (approval number, 206014). The procedures for the preparation of isolated intestinal segments are well documented in literature with the detailed presentation being reported recently [15, 16]. The study employed 9 male albino rabbits with an average weight of 2-2.5 kg obtained from Tanta animal house. The rabbit was anaesthetized by intramuscular (i. m.) injections of ketamine HCl (2 doses of 45 mg/kg at 15 min intervals and repeated doses of 25 mg/kg when needed). Chlorpromazine HCl was used as a muscle relaxant and was given intramuscularly (2 mg/kg) before anaesthesia.

After induction of anaesthesia, the rabbit was laid down in a supine position on a heating pad to maintain physiologic body temperature. The abdominal area of interest was shaved with depilatory cream before making a midline longitudinal incision of 6-8 cm long. For jejunum ileum the proximal end (at least 25 cm from pylorus) was tied
off using a surgical thread and cannulated using a 3-way stopcock cannula. The desired length (30 cm) was measured, and the distal end was cannulated using an L-shaped glass cannula. For the ascending colon, the proximal end was tied off immediately after the ampulla coli and the distal end was tied off. Two small incisions were made, and the colon was cleaned by gentle hand squeezing of the segment. Both ends were then cannulated as before. Complete cleaning of the segment was achieved by infusing a 37 °C normal saline solution through the proximal end. The rabbit was utilised to study permeability in both segments simultaneously. The remaining parts of the intestine were returned into the abdominal cavity for better temperature control. Segments under study were arranged in a uniform S to multi-S-pattern to keep a regular flow without kinks or obstructions and were kept moistened and warm by covering with a gauze pad moistened regularly with a 37°C normal saline solution.

At the end of the experiment, the rabbit was sacrificed, and the intestinal segments under study were excised and accurately measured.

The perfusion solution was perfused into the intestinal segment at a flow rate of 0.27 ml/min using a constant rate perfusion pump (Harvard-22, Harvard apparatus, USA). The effluent from each segment was collected at 10 min intervals for 120 min in dry glass tubes. The volume of each sample was measured accurately.

**Data analysis**

The net water flux was calculated as the difference between the theoretical volume (based on the flow rate) and the actual volume of the perfusate collected. The recorded drug concentration was normalized on the base of the net water flux. The ratio between the theoretical volume (based on the flow rate) and the actual volume of the perfusate collected. The recorded drug concentration was measured.

The perfusion solution was regularly with a 37 °C normal saline solution moistened and warm by covering with a gauze pad moistened to keep a regular flow without kinks or obstructions and were kept.

**RESULTS AND DISCUSSION**

High-pressure liquid chromatography

The analytical method validation was conducted according to the guidelines of the International Conference of Harmonization [16]. The drug was eluted after a retention time of 5.6 min producing a symmetric peak. The USP tailing factor was 1.0 and number of plates per column was 8927 "on half-width method basis". The calibration curve of eprosartan mesylate was plotted from the recorded peak areas as a function of drug concentration (fig. 1).

The linear regression of the calibration curve of eprosartan mesylate was plotted an equation of y = 7.768 ± 0.06 x+1.874 ±2.8 and a value of (R²) of 0.99996. This high correlation reflects the linearity of the calibration curve in the tested range (9-100 µg/ml).

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asymmetric stretching vibration with the symmetric stretching being following equation \[17\].

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representing the conjugated aliphatic C=C. The characteristic absorption recorded as a weak peak at 1697 \text{cm}^{-1} absorption band of the second C=O (conjugated to an aromatic ring) was the first C=O stretching (conjugated to vinyl double bond). The FTIR spectroscopy vibration which was seen at 3413 \text{cm}^{-1} bands of the oligomer. These included the broadband of O-H stretching bands being similarly assigned \[19\]. The characteristic O-H band compared with that recorded in the case of unprocessed eprosartan mesylate reflecting the probability of intermolecular H-bonding with HPβCD. In addition, the absorption band corresponding to the C-S bond of the drug was not clearly defined in the spectra of the prospective complex. These findings highlight the complexation process. It is interesting to emphasise that the peak corresponding to the second carbonyl group of the drug becomes clearer compared with that recorded in the spectrum of the unprocessed drug. This reflects possible immobilisation of the group and provides additional evidence for complex formation (fig. 3).

The % recovery is a measure of accuracy, and %RSD are used as a measure of precision. All concentrations are shown as mean±SD (n=3). The limit of detection and limit of quantitation were calculated to be 0.34 µg/ml and 1.03 µg/ml respectively.

### Phase solubility diagram

The effect of HPβCD concentration on the aqueous solubility of eprosartan mesylate was used to construct the phase solubility diagram which was a plot of the molar solubility of the drug as a function of the molar concentration of HPβCD. This is shown in fig. 2 which reflects a linear relationship with \(R^2 = 0.979\) indicating an A\(_2\) type.

![Fig. 2: Phase solubility diagram](image)

This phase solubility diagram suggests a 1:1 molar ratio as the stoichiometric ratio. Complexation efficiency of eprosartan mesylate/HPβCD complex (CE) = 0.003 calculated according to the following equation \[17\]:

\[
\text{CE} = \frac{S_{\text{O}}}{K} = \frac{\text{Slope}}{(1 - \text{Slope})}
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### FTIR spectroscopy

FTIR spectra (fig. 3) were recorded to assess the possibility of the inclusion complex formation between eprosartan mesylate and HPβCD. The FTIR spectrum of unprocessed eprosartan mesylate showed a characteristic band at 3471 \text{cm}^{-1} for OH stretching two bands at 3134 \text{cm}^{-1} and 3041 \text{cm}^{-1} for aromatic =C-H stretching. The three bands at 2962 \text{cm}^{-1}, 2934 \text{cm}^{-1} and 2875 \text{cm}^{-1} can be due to C-H stretching vibrations. A strong, sharp band at 1706 \text{cm}^{-1} was recorded representing the first C=O stretching (conjugated to vinyl double bond). The absorption band of the second C=O (conjugated to an aromatic ring) was recorded as a weak peak at 1697 \text{cm}^{-1}, nearly fusing with that of the first C=O \[8\]. Two bands were recorded at 1643 \text{cm}^{-1} and 1615 \text{cm}^{-1} representing the conjugated aliphatic C=C. The characteristic absorption bands of SO\(_2\) (of the mesylate group) were detected at 1238 \text{cm}^{-1} for asymmetric stretching vibration with the symmetric stretching being recorded as two bands at 1161 \text{cm}^{-1} and 1042 \text{cm}^{-1}. An absorption peak was seen at 770 \text{cm}^{-1} for C-S linkage stretching.

The FTIR spectrum of HPβCD showed the characteristic absorption bands of the oligomer. These included the broadband of O-H stretching vibration which was seen at 3413 \text{cm}^{-1} with its bending vibrations being noticed at 1697 \text{cm}^{-1}. The C-H stretching vibrations were shown at 2970 \text{cm}^{-1} and 2890 \text{cm}^{-1} with the asymmetric C-H bending vibration appearing at 1457 \text{cm}^{-1} \[18\]. The C-O stretching vibrations were detected at 1155 \text{cm}^{-1} and 1084 \text{cm}^{-1}. A characteristic band at 854 \text{cm}^{-1} for α-1, 4-glycosidic bond was revealed by the spectrum. Similar spectrum was recorded by other investigators with the absorption bands being similarly assigned \[19\].

The FTIR spectra of the prospective complex prepared by kneading and co-evaporation produced FTIR spectra in which the absorption bands corresponding to aromatic =C-H stretching of the drug were absent. Both spectra showed an obvious broadening of the characteristic O-H band compared with that recorded in the case of unprocessed eprosartan mesylate reflecting the probability of intermolecular H-bonding with HPβCD. In addition, the absorption band corresponding to the C-S bond of the drug was not clearly defined in the spectra of the prospective complex. These findings highlight the complexation process. It is interesting to emphasise that the peak corresponding to the second carbonyl group of the drug becomes clearer compared with that recorded in the spectrum of the unprocessed drug. This reflects possible immobilisation of the group and provides additional evidence for complex formation (fig. 3).

### Table 2: The HPLC validation parameters of eprosartan mesylate

| Nominal Conc.(µg/ml) | Recovered Conc. µg/ml | % RSD | % recovery |
|----------------------|-----------------------|-------|------------|
|                      | Interday              |       |            |
| 15                   | 15.1 (±0.01)          | 0.1   | 100.7 (±0.1) |
| 30                   | 30.0 (±0.4)           | 1.4   | 100.0 (±1.3) |
| 60                   | 60.0 (±0.8)           | 1.3   | 100.1 (±1.4) |
| 100                  | 100.5 (±1.3)          | 1.3   | 100.5 (±1.4) |
|                      | Intraday              |       |            |
| 18                   | 17.9 (±0.1)           | 0.5   | 99.6 (±0.5) |
| 21                   | 21.0 (±0.1)           | 0.5   | 99.9 (±0.5) |
| 100                  | 99.8 (±0.2)           | 0.1   | 99.8 (±0.2) |

Intraday % recovery

100.5 (±0.4)

100.7 (±0.1)

100.0 (±1.3)

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DSC

The DSC traces of the unprocessed drug, HPβCD, and their prospective complex are shown in fig. 4. The thermogram of eprosartan mesylate showed two endothermic peaks in the range of 87 °C to 114 °C. These can be attributed to the liberation of the adsorbed water and/or the water of crystallisation. Dehydration behaviour of eprosartan mesylate dihydrate was reported in the literature showing gradual evaporation of the water of crystallisation upon heating [20].

The thermogram also revealed a sharp endothermic peak starting at 243 °C and ending at 258 °C with a transition midpoint Tm at 253 °C. This endothermic peak corresponds to the melting point of the drug and correlates well with suppliers’ specifications and the published data on the same drug [8].

The thermogram of HPβCD showed a broad endothermic peak starting at 32.47 °C and ending at 113.94 °C with a transition midpoint at 80.56 °C which can be attributed to the liberation of adsorbed moisture. The thermogram also showed another endothermic peak with a Tm at 340 °C due to complete melting with the decomposition of the oligomer (fig. 4). Similar thermal behaviour has been published for the same compound with a complete decomposition being noticed between 300 °C and 400 °C [19].

The thermograms of the drug/HPβCD complex were characterised by the absence of the main endothermic peak of the drug reflecting its presence in the form of molecular dispersion state. This strengthens the findings of the FTIR study and confirms the formation of the inclusion complex between the drug and the oligomer. Similar thermal changes were recorded after complexation of genistein with cyclodextrin with the findings being considered supportive for inclusion complexation [21]. A similar pattern was recorded for complexes prepared by co-evaporation and kneading (fig. 4).

Membrane transport parameters

The intestinal absorption of the drug was monitored using the in situ rabbit intestinal perfusion technique. This technique is being in use for a long period of time with many articles being published recently utilising the same method due to its advantages. The rabbit was selected as the test animal due to its intestinal physiology which simulates the human system [15]. Perfusion of an aqueous solution of eprosartan mesylate (control) through the selected intestinal segments produced membrane transport parameters highlighting the incomplete absorption of the drug from the tested intestinal segments (table 3).

Table 3: Membrane transport parameters of eprosartan mesylate after perfusion through rabbit intestinal segments (dilution with corresponding buffers was performed for each)

| Parameter     | Control* | Ascending colon | SNEDDS** | Ascending colon | HPβCD*** | Ascending colon |
|---------------|----------|-----------------|----------|-----------------|----------|----------------|
| Jejuno-ileum  | (±0.00115) | 0.00885 | 0.00164 | 0.00757 | 0.00161 | 0.00647 |
| cm            | (±0.0001)  | (±0.00449) | (±0.0002) | (±0.00081) | (±0.0001) | (±0.0014) |
| Rcm/Rm        | 0.85927±(±0.0164) | 0.75473±(±0.08496) | 0.79135±(±0.0272) | 0.73089±(±0.02624) | 0.79870±(±0.0166) | 0.84064±(±0.0180) |
| %Fa           | 14.1±(±64) | 24.5±(8.5) | 20.9±(2.7) | 26.9±(2.6) | 20.1±(1.7) | 15.9±(1.8) |
| LI5% (cm)     | 780.7±(79.66) | 235.2±(125.9) | 578.3±(163.6) | 116.8±(13.4) | 647.0±(169.7) | 142.9±(44.1) |
| ARL (cm)      | -600.7±(97.66) | -220.2±(125.9) | -398.3±(163.6) | -101.8±(13.4) | -467.0±(169.7) | -127.9±(44.1) |
| JW (ml/min)   | 0.11677±(±0.0187) | 0.09997±(±0.02026) | 0.12913±(±0.006) | 0.0936±(±0.00544) | 0.1300±(±0.0089) | 0.06573±(±0.0028) |
| JW/I (ml/min) | 0.00409 | 0.01301±(±0.00362) | 0.00429 | 0.01010 | 0.00455 | 0.01012 |
| PeA/I (ml/min. cm) | (±0.0003)  | (±0.0002) | (±0.00117) | (±0.0006) | (±0.0016) | (±0.0016) |

All results are shown as mean±SEM (n=3). *The control was the drug solution (30 µg/ml). **SNEDDS (30 µg/ml). ***The drug: HPβCD 1:1 inclusion complex (30 µg/ml).

Fig. 5: Absorptive clearance of eprosartan mesylate versus water flux. (a) control rabbits jejunoileum segment; (b) control rabbits Colon segment; (c) SNEDDS rabbits jejunoileum segment; (d) SNEDDS rabbits Colon segment; (e) HPβCD rabbits jejunoileum segment; (f) HPβCD rabbits Colon segment Parameters are normalized to segment length.
This incomplete absorption was manifested as low absorptive clearance with PeA/I being 0.00115 and 0.00885 ml/min/cm for the jejunoileum and colon, respectively. The fraction absorbed was 14.1 and 24.5% for the segments, respectively. The anatomical reserve length (ARL) was negative in both segments (table 3). These data confirm the poor absorption characteristic of the drug. This can be attributed to its existence in an ionised form in the pH of the tested intestinal segments. Dependence of drug absorption on the degree of ionisation was noticed by the same technique [15]. Comparing the intestinal membrane transport parameters recorded after perfusion through the jejunoileum with those recorded in case of the colon, the absorption pattern can be considered site dependent with the colon being superior per unit length.

To investigate the pathway of drug absorption, the absorptive clearance of the drug from each segment was correlated to with corresponding water flux according to Lifson’s model [16]. This was achieved by plotting the absorptive clearance as a function of the water flux (fig. 5). The linear regression analysis of such plots produced a slope equal to 0.62 with negative intercept. This slope was significantly different from zero in the jejunoileum segment and so, indicating the dependence of absorptive clearance of eprosartan mesylate on water flux. The same pattern was seen in the colon (fig. 5). This finding with the negative intercept indicates that the absorption is mainly convective which may explain the superiority of colonic absorption compared with the jejunoileum [22]. Calculated water flux values correlate with the suggested absorption pathway with the water flux per unit length being higher from the colon (table 3).

Perfusion of eprosartan mesylate in the form of nanoeulsion resulted in a significant increase in the intestinal absorption of the drug compared with the control. This was manifested as a trend of increased percentage fraction absorption from with a reduction in the 1.95%. The same trend was noticed in the jejunoileum and the colon (table 3). The same trend was shown after perfusion of the drug in the form of an inclusion complex with HPβCD. The use of nanoemulsion was able to extend the absorption window of furosemide is which known to be mainly ionised in the intestinal pH [15]. This agrees with the current finding which showed good potential for enhancing the intestinal absorption of eprosartan mesylate which is known to be mainly ionised at intestinal pH.

CONCLUSION

SNEDDS was successfully developed using labrafil, lauroglycol with Tween 80 in the presence of ethanol. Eprosartan mesylate formed an equinolar inclusion complex with HPβCD. Eprosartan mesylate is incompletely absorbed from the intestine. Self-nano emulsifying formulation and inclusion complexation were promising for enhanced intestinal absorption of eprosartan mesylate, and these techniques were thought to provide good tools for researchers in the field to expand its use in enhancing absorption of similar drugs.

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CONFLICTS OF INTERESTS

Declared none

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