A Study on the development and in-vivo evaluation of Exenatide Self-Emulsifying Drug Delivery System (SEDDS)

Aziz Unnisa

Department of Pharmaceutical Chemistry, College of Pharmacy, University of Hail, Hail, Kingdom Saudi Arabia.
Email: Khushiazeez@yahoo.co.in

Abstract

Introduction: The prevalence of diabetes has increased since 1980. This increased prevalence is responsible for a significant number of deaths. The advancement of different drug classes has been a practical solution, but the required pharmacological effect is not achieved due to the disadvantages of less bioavailability. One of the drugs, Exenatide, is being considered in this study. This current study aims to develop a SEDDS for Exenatide to make it stable and increase its ability to permeate through the enterocytes to enhance its bioavailability and eventually improve blood glucose level status. The study further investigated the cytotoxicity of the whole system and compared the SEDDS effect on blood glucose level (BGL), stress biomarkers, and body weight with that of healthy rats, diabetic rats, and rats who were given Metformin.

Materials and Methods: Exenatide is incorporated into the drug delivery system by ion-pairing method with sodium docusate (DOC) consisting of Labrafil, Cremophor-EL, propylene glycol and Capmul-PG. The study used rats for the classification of groups and analysis between the groups to find out the effect on BGL status, effect on stress biomarkers, and effect on body weight. The authors have performed the characterization, release, and cytotoxic studies of SEDDS to show that the validation of Exenatide administration is feasible using a drug delivery system.

Result: The study has found that SEDDS brings effective improvement in BGL status (P<0.001), prevents weight loss as compared to all other groups (P<0.001), and reduces stress biomarkers significantly (P<0.001). The authors also studied the permeation process and cytotoxicity of SEDDS to validate its usage.

Conclusion: Combining the findings, SEDDS (Exenatide and DOC) can be considered to manage diabetes type 2 effectively. However, there is a need to conduct more animal experiments and clinical trials. Unlike any previous study, detailed and analytically significant findings have been conducted and discussed in this current study to improve the management of diabetes type 2.

Keywords: SEDDS, Exenatide, type 2 diabetes, drug delivery system.

Introduction

There are several lipid-based formulations (LBF) to deliver water-soluble drugs. Some are nano-structure lipid carriers (NLC), nanoemulsions, and Solid Lipid Nanoparticles (SLN). From a commercial point of view, SEDDS can be of significant LBF, which has already been used to deliver poorly water-soluble drugs.

This is accomplished by forming the colloidal system with the drugs via self-emulsification by placing the drug inside an oily capsule, thus increasing the solubility and passing them smoothly through the gastrointestinal tract. This process leads to the improved bioavailability of the drug [1,2].

How to cite this article: Aziz Unnisa, A Study on the development and in-vivo evaluation of Exenatide Self-Emulsifying Drug Delivery System (SEDDS), J PHARM NEGATIVE RESULTS 2022;13:470-479.
For this purpose, lipid-based excipients are used in SEDDS, including vegetable oils or their derivatives, for efficient emulsification. Hydrophilic organic solvents in this drug delivery system impart sufficient drug solubility [3,4].

Figure 1: Overview of SEDDS: The drug is coated with micelles. They are then quickly delivered to the gastrointestinal system, where enterocytes absorb the drug into SEDDS. Again, the absorbed emulsified system breaks into its component drug and micelle, and the drug goes to the liver for first-pass metabolism and, after that, to the systemic circulation.

Although, in the past, there have been several pieces of research conducted on drug delivery from several aspects, including micronization, cyclodextrin, complexation, solid dispersion, and lipid delivery. Out of all these, the method of lipid delivery has gained popularity in [5,6], in which the molecules of the drug are dissolved in an emulsifier or co-emulsifier (oil phase) to form the oil-water emulsion (particle size of 10 to 500 nm) [7]. The SEDDS was first developed in the 1980s and is thought to be the solution for orally administered water-soluble drugs. SEDDS can serve the drug delivery, which are proteins, peptides, polysaccharides, etc. It is formed by pairing hydrophobic ions with oppositely charged lipophilic molecules. This results in the formation that protects the drug from the degradation of the intestinal enzyme. There are other benefits, like the drug can be targeted delivery, and the permeability of the drug through enterocytes can be increased significantly. Hence, SEDDS is now considered the center point of discussion in modern pharmaceutical drug delivery [8,9].

The prevalence of type 2 diabetes is playing a significant role in causing deaths worldwide. Recent advancement in drug introduction for type 2 diabetes is the development of Glucagon Like Peptide-1 (GLP-1) agonists. This drug class can increase insulin secretion, the hormone responsible for glucose uptake by the hepatocytes and muscle cells. In addition, GLP-1 can also suppress the release of another hormone called glucagon from the pancreas, which is responsible for glycogenolysis, leading to increased blood glucose [10]. The oral administration form of this drug is in massive demand from the perspective of patients' compliance and clinicians. However, there are many disadvantages of the oral formulation, due to which the bioavailability of the drug is lower than expected [11]. There are suggestions from different communities of scientists that the application of SEDDS is the ultimatum to increase the bioavailability of Exenatide.

Exenatide is primarily an analog of human GLP-1, which chemically consists of 39 amino acid peptides and enhances glucose-dependent insulin secretion. Exenatide binds and activates the GLP-1 receptor, leading to the in-vivo insulin secretion via the cyclic AMP pathway [12].

Figure 2: The chemical structure of Exenatide

This current study aims to develop SEDDS for Exenatide to make it stable and increase its ability to permeate through the enterocytes to enhance its bioavailability and positively impact BGL status. The study also characterized its formulation, studied the efficacy of the Exenatide SEDDS (including effective permeation through the gut epithelium and absorbance) and investigated the cytotoxicity of the whole system, compared SEDDS effect on Blood Glucose Level (BGL), stress biomarkers and body weight with that of healthy rats, diabetic rats, and rats who are given Metformin.

Materials and Methods

The materials used in this study are Exenatide, cremophor EL, primary alcohol ethoxylate, propylene glycol and sodium docusate (DOC), sodium dodecyl sulfate, sodium taurocholate, and sodium oleate. HPLC was employed to quantify the Exenatide. Samples containing Exenatide were kept on spherical silica (high quality) called Nucleosil C18 (250 x 4 mm) at 40 °C. Gradient elution (0.5 mL per minute) was employed for 15 minutes. The quantification limit was fixed at two µg/mL and 3.9 µg/mL. The study used the technique of hydrophobic ion pairing to impart lipophilicity to Exenatide. This can lead to easy incorporation of Exenatide into SEDDS. Firstly, Exenatide was dissolved with acetic acid (0.55 mM at pH 4), then dissolved Sodium docusate,
Sodium deoxycholate, Sodium taurocholate, and Sodium oleate in 0.555 mM of acetic acid (maintained at pH 4). Surfactant solutions were prepared and used at 1:1, 1:2, and 1:4. Centrifugation was carried out to precipitate the ion. The ion pair was washed and lyophilized at -30 °C and stored at -22 °C. Then, octanol was added to the ion pairs of Exenatide (maintained at the volume ratio of 1:1). This was mixed in a thermomixer and then centrifugation at 12000 RPM. The quantification of Exenatide in octanol was done by the HPLC method. For the adequate preparation of SEDDS, the ion pair of Exenatide with DOC was selected for this study. DOC and Exenatide were present in the ratio of 1:4. The mixture of Exenatide and DOC was concentrated at 0.08%, and the volume was maintained at 260 µL.

The study also conducted a release study by emulsifying Exenatide-DOC SEDDS in 50 mM, further diluted to obtain the Exenatide concentration of 1 mg/mL.

Mucus Permeation ability

For mucus permeation of SEDDS (Exenatide and DOC), it was taken into 24 well plates. 75 mg of mucus was added to it. In this, 260 µL of Exenatide and DOC SEDDS in 50 mM phosphate buffer (maintained at pH 6.8) was kept in the donor chamber of 24 healthy plates while the acceptor chamber was filled with phosphate buffer. This was incubated at 37 °C. The whole experiment was about 4 hours. Using the HPLC method, the amount of Exenatide that has passed through mucus (permeated) was determined and compared with a control obtained by the same method, which was kept in the donor chamber without the application of mucus.

Resazurin assaying for human cells viability

The SEDDS (Exenatide and DOC) cytotoxic properties were determined by the Alamar Blue assay (also known as resazurin assay), which investigates the viability of the cells. For this purpose, caco-2 cells were placed in 24-well plates along with fetal calf serum as a supplement. A mixture of penicillin and streptomycin at the dosage of 0.1 mg/L was added, and it was cultured for three weeks at an average body temperature (37 °C). The relative humidity of 95% maintained an atmosphere with 5% CO₂.

In-vivo evaluation of SEDDS:

The in-vivo study was conducted in two parts: inducing diabetes mellitus in the experimental animals (Sprague-Dawley rats) and the experiment itself. The animal ethics committee of JNT University (IAEC/ NCP/2022-001) approved the study.

Induction of diabetes mellitus type 2 was done among these Sprague-Dawley rats by intraperitoneal administration of Nicotinamide (NA) in saline solution at 110 mg/kg, followed by inoculation of single Streptozotocin (STZ) at the dosage of 60 mg/kg via the intraperitoneal route. The gap between the administration of NA ad STZ was maintained at half an hour. The administration of STZ was followed by the hypoglycaemic shock, which was interrupted by the inoculation of 5% glucose solution to the rats. Then after 4 to 5 days, the blood samples were withdrawn from the rats to determine the blood glucose level (BGL). The rats with BGL of more than 180 mg/dL were taken as diabetic rats and were considered for the study. The rats whose BGL came to be less than 100 mg/dL without any intervention were considered the control group for this study.

In this current study, there are four groups of rats. All the groups are administered twice a day for seven days following interventions.

Group 1 is the Normal Control group characterized by healthy rats (males), and they are first treated with 0.5% of carboxymethyl cellulose (CMC). Group 2 is the Diabetic control group characterized by the rats considered to have diabetes (induced) and treated with 0.5% of CMC. Group 3 is the Standard group comprising Metformin (100 mg/kg) treated diabetic rats (inoculated with standard drug) in 0.5 % oral CMC. Group 4 is the Experiment Group comprising rats receiving 150 µg of Exenatide (250 µL of Exenatide and DOC SEDDS) via the oral route. On day seventh (the last day of the experiments), the blood was withdrawn from each group. It was analyzed for Blood Glucose level (BGL), the level of stress biomarkers in each group, and body weight. However, BGL and stress biomarkers levels were assessed and recorded before the treatment, on the 0th day of the experiment, the first day of the experiment, and subsequently on the third and seventh day of the experiment.

Statistical analysis

The statistical analysis was conducted using ANOVA and t-test, considering p< 0.05 as the significance level. The study used SPSS 25 for statistical analysis, and other graphs were created using Excel software.

Results

The present study has shown a hydrophobic ion pairing method that is expected to increase the lipophilicity of SEDDS and thereby increase the solubility between Exenatide and SEDDS. However, no chemical reaction or mechanism is involved, so the peptide’s function is maintained. The study also involved surfactants in various ratios. The surfactant was added to peptide solution for the precipitation of Exenatide; after precipitation of Exenatide, it was isolated from the surfactant by centrifugation, and the leftover drug was analyzed by the method of HPLC.
The ion pair was precipitated in a 1:4 ratio (surfactant: Exenatide). As a surfactant, DOC had a higher rate of ion-pair formation and, hence, can be considered superior to SDS. The log P values of each ion pair also confirmed that DOC has a higher rate of ion pair formation than SDS. It was found that, with increasing amounts of surfactant, the values of logP increase to 2.1 for the Exenatide-DOC ion pair and 1.6 for the Exenatide-SDS ion pair.

At the ratio of 1:4, the lipophilicity of the surfactants (SDS and DOC) is at its highest. The lipophilicity reduces a little at the ratio of 1:6 due to the micelle formation that diffuses into the water phase. As per Figure 2 findings, the study considered Exenatide: DOC at 1:4 for further experiments.

The study required creating a stable ion pair structure to be functional in-vivo. So, the components that can withstand lipolysis and hydrolysis in the gastrointestinal environment were selected. For this, cremophor-EL was considered in this study. This study used SEDDS concentration at 7.8% (m/v). Table 1 below shows the pre-concentrate’s self-emulsifying properties with or without Exenatide. The mean size of the droplet increases due to the adding Exenatide as an ion pair which also prevents further precipitation. Zeta potential implies surface without any charge for SEDDS alone and with Exenatide-DOC.

The table shows the composition, percentage of its components, the size of droplets (mean±SD), Poly Dispersity Index (PDI), and zeta potential of SEDDS (with and without Exenatide). These parameters are assessed by using the light scattering method.

Figure 3: The Exenatide precipitation from 0.555 mM acetic acid (2 mg/mL) with DOC and SDS.

Figure 4: Log P of peptide and surfactant at pH 6.8 is plotted against the ratio of Exenatide and surfactant (1:0, 1:1, 1:4, 1:6). These values are the means of three experiments.
In this study, Exenatide is released from DOC by simple diffusion from the oily medium to the aqueous phase. The drug release is explained by logD or partition coefficient of ion-pair of SEDDS and release medium (phosphate medium). In our study, the ratio SEDDS: phosphate buffer (release medium) is 1:35. The values of the log D (SEDDS and phosphate buffer) of Exenatide and DOC (in the ratio of 1:4) are given.

Table 2: Obtained values of log D SEDDS and phosphate buffer of Exenatide and DOC at the ratio of 1:4

<table>
<thead>
<tr>
<th>Release Medium (phosphate buffer)</th>
<th>Log D</th>
</tr>
</thead>
<tbody>
<tr>
<td>Water</td>
<td>3.0±0.03</td>
</tr>
<tr>
<td>100 mM HCl*</td>
<td>3.3±0.02</td>
</tr>
<tr>
<td>50 mM phosphate buffer**</td>
<td>1.9±0.04</td>
</tr>
</tbody>
</table>

* maintained at pH 1; **maintained at pH 6.8

Figure 6: Radar graph showing values of log D SEDDS and phosphate buffer of Exenatide and DOC at the ratio of 1:4

The permeation ability assessment showed that the lipophilic nature of SEDDS could pass through the gastrointestinal epithelium and get absorbed. The result of this study has shown the improved permeation ability of the SEDDS with Exenatide. Figures 7 and 8 show the mucus permeation ability of the SEDDS and Exenatide over time.

The formulation's cytotoxic potential was studied to check the drug's accumulation inside the body. The study has shown that SEDDS concentration positively correlated with cell toxicity. The authors also used Triton x, which validates this method.
Aziz Unnisa: A Study on the development and *in-vivo* evaluation of Exenatide Self-Emulsifying Drug Delivery System (SEDDS)

Figure 7: 2D contour histogram showing permeation of Exenatide release from SEDDS over 4 hours at the temperature of 37 °C

Figure 8: The finding of permeation of Exenatide release from SEDDS over 4 hours at the temperature of 37 °C

Figure 9: The result of the assessment of the cytotoxic potential of SEDDS (Exenatide and DOC) at the specified concentration of 2.5 mg/mL, 3 mg/mL, 5 mg/ml, and 7 mg/mL in the experiment that was conducted for 12 hours

In-*vivo* experiment

The intraperitoneal administration of STZ and NA to induce diabetes in the rat population and subsequent monitoring of BGL were carried out. Although the *in-vivo* studies show the inclination and efficiency of Exenatide release, the *in-vivo* study comprises BGL analysis, bodyweight analysis, and analysis of the variation of oxidative stress biomarkers.

It was found that the effect of SEDDS on BGL (group 4) is insignificant as compared to group 1, but it is highly significant (P < 0.001) as compared to group 2 and group 3. The effect of group 3 is also insignificant compared to group 1 and significant compared to group 2 (P<0.005). Table 3 gives the detailed records of BGL in each group, and Figure 8 depicts the variation of BGL in each group over the days.

Table 4 shows the findings of the effect of SEDDS on bodyweight among different groups of rats. Prior to the treatment, the weight of each group was almost similar, and the weight of group 4 rats was slightly higher than other groups. In group 2 and group 3, the weight reduction is quite significant, whereas group 4 did not experience weight reduction. The body weight of group 4 on the seventh day of the experiment was not significantly reduced compared to group 1. In contrast, compared to group 2 and group 3, the weight loss prevention of group 4 on the seventh day is highly significant (P<0.001) in terms of prevention of weight reduction. Alternatively, the weight loss in group 2 and group 3 at the end of the experiment is quite significant compared to group 4.
A Study on the development and in-vivo evaluation of Exenatide Self-Emulsifying Drug Delivery System (SEDDS)

Table 3: Effect of SEDDS (Exenatide and DOC) on BGL after induction of diabetes mellitus type 2 with STZ+NA

<table>
<thead>
<tr>
<th></th>
<th>Group 1 (Normal control)</th>
<th>Group 2 (Diabetic control)</th>
<th>Group 3 (Standard group)</th>
<th>Group 4 (Experiment group)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prior STZ+NA</td>
<td>71.82±4.49</td>
<td>72.77±5.25</td>
<td>72.01±5.75</td>
<td>79.55±5.48</td>
</tr>
<tr>
<td>0th day</td>
<td>75.12±4.48</td>
<td>242.05±12.88</td>
<td>312.14±4.48</td>
<td>338.42±18.57</td>
</tr>
<tr>
<td>1st day</td>
<td>86.25±4.10</td>
<td>254.25±6.92</td>
<td>283.22±9.65</td>
<td>339.53±14.24</td>
</tr>
<tr>
<td>3rd day</td>
<td>83.12±4.62</td>
<td>306.09±8.66</td>
<td>160.11±5.42</td>
<td>167.11±6.23</td>
</tr>
<tr>
<td>7th day</td>
<td>76.55±3.43</td>
<td>271.05±13.58</td>
<td>83.22±5.15 [a,b]</td>
<td>90.42±5.85 [a,b**, c**]</td>
</tr>
</tbody>
</table>

a = compared with group 1; b = compared with group 2; c = compared with group 3; ns = not significant; *P<0.005; **P<0.001

Group 2 rats revealed increased stress biomarkers in hepatocytes compared to other groups. Again, SOD was lower in Group 4 rats than in groups 1 and 3. In the pancreas, the level of stress biomarkers in group 4 rats is almost similar to that of group 3, and as compared to group 2 rats, only SOD is higher. The detailed findings of biomarkers are given in Table 5. In group 2, it was observed that the MDA level was significantly higher than in group 1, group 3, and group 4 (P<0.001). Figure 10 and Figure 11 show the level of stress biomarkers (MDA, SOD, GSH) in each group found in hepatocytes and pancreatic tissues.

Figure 10: The effect of each group on Blood Glucose Level over the experiment days

Table 4: Effect of SEDDS on body weight in each group of rats

<table>
<thead>
<tr>
<th></th>
<th>Group 1 (Normal control)</th>
<th>Group 2 (Diabetic control)</th>
<th>Group 3 (Standard group)</th>
<th>Group 4 (Experiment group)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Before the treatment</td>
<td>178.58±4.29</td>
<td>168.71±3.85</td>
<td>168.64±3.12</td>
<td>191.61±5.33</td>
</tr>
<tr>
<td>0th day</td>
<td>179.11±4.12</td>
<td>155.63±3.85</td>
<td>158.84±3.04</td>
<td>184.21±6.18</td>
</tr>
<tr>
<td>1st day</td>
<td>180.44±4.29</td>
<td>154.58±5.11</td>
<td>155.64±2.25</td>
<td>183.14±6.21</td>
</tr>
<tr>
<td>3rd day</td>
<td>178.58±4.29</td>
<td>150.35±5.07</td>
<td>153.77±2.36</td>
<td>187.85±6.07</td>
</tr>
<tr>
<td>7th day</td>
<td>178.58±4.29</td>
<td>148.22±5.09</td>
<td>149.12±2.45</td>
<td>192.32±5.28 [b**, c**]</td>
</tr>
</tbody>
</table>

a = compared with group 1; b = compared with group 2; c = compared with group 3; *P<0.005; **P<0.001
A Study on the development and in-vivo evaluation of Exenatide Self-Emulsifying Drug Delivery System (SEDDS)

**Discussion**

Self-emulsifying drug delivery systems (SEDDS) are the present and future solutions for improving lipophilic drugs’ oral absorption. The efficacy of SEDDS depends upon its properties, including droplet size, charge, drug release, cytotoxicity, etc. The effective binding and formulation of the drug into SEDDS results in efficient absorption through the gastrointestinal mucosa and prevents damage to the drug molecules [13]. This current study has employed the SEDDS formulation to incorporate Exenatide, a GLP-1 agonist. In this study, the authors used Cremophor-EL as the surfactant because it can form a tiny droplet due to its higher hydrophilic-lipophile balance (HLB) value. Thus, it implies its self-emulsifying characteristics. In addition, cremophor-EL is a much less toxic in-vivo environment [14, 15]. The excellent absorption of drugs imparted by SEDDS is remarkable compared to other drugs.

In the case of other drugs, the mucous layer of the gastrointestinal mucosa is the primary hindrance, which

---

**Table 5:** Effect of SEDDS on the level of stress biomarkers like Malondialdehyde (MDA), Superoxide Dismutase (SOD), and Glutathione (GSH) in the liver and pancreatic tissues in each group of rats

<table>
<thead>
<tr>
<th>Group 1 (Normal control)</th>
<th>Group 2 (Diabetic control)</th>
<th>Group 3 (Standard group)</th>
<th>Group 4 (Experiment group)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Liver</td>
<td>Pancreas</td>
<td>Liver</td>
<td>Pancreas</td>
</tr>
<tr>
<td>MDA</td>
<td>10.35± 0.62</td>
<td>36.59± 0.36</td>
<td>29.77±1.4</td>
</tr>
<tr>
<td></td>
<td>[a**, c**, d**]</td>
<td></td>
<td>12.73±0.90</td>
</tr>
<tr>
<td>SOD</td>
<td>58.22±3.01</td>
<td>76.29±2.8</td>
<td>20.36±1.1</td>
</tr>
<tr>
<td></td>
<td>[a**]</td>
<td></td>
<td>53.83±2.88</td>
</tr>
<tr>
<td>GST</td>
<td>4.85±0.44</td>
<td>8.36±0.59</td>
<td>0.58±0.21</td>
</tr>
<tr>
<td></td>
<td>[a**, b, c, d**]</td>
<td></td>
<td>2.09±0.63</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>4.18±0.13</td>
</tr>
</tbody>
</table>

a = compared with group 1; b = compared with group 2; d = compared with group 4; *P<0.005; **P<0.001

---

**Figure 11:** The effect of each group on bodyweight over the experiment days

**Figure 12:** Level of stress biomarkers (in hepatocytes) in each group on the seventh day of the experiments

**Figure 13:** Level of stress biomarkers (in pancreatic tissues) in each group on the seventh day of the experiments
consists of negatively charged glycoproteins that prevent permeation by entrapping the drug molecules. The mucous layer achieves this by ionic interaction of the peptide drugs with the glycoproteins in this layer. SEDDS, in our study, escapes this check mainly due to the presence of Cremophor-EL by imparting the ability to open the tight junction for drug uptake by the mucous layer. However, the author suggests a need to conduct more in-depth biomolecular studies to understand the mechanism of drug uptake and the interaction with SEDDS in this regard. Previous studies have discussed that SEDDS helps droplet fusion with the bilayer cell membrane, endocytosis, or transcytosis by SEDDS droplets. However, these studies could not provide confirmed evidence [16, 17].

Daily administration of Exenatide (bid) at 5 mg or 10 mg has shown that body weight is maintained and prevents weight reduction compared to the controls. In addition, the status of the glycemic level was also improved compared to the control group [18]. Kadowaki et al. (2010) evaluated the therapeutic efficacy of Exenatide in Type 2 Diabetes. They concluded that the glycemic control was significantly improved by administration of Exenatide (twice a day at a dosage of 5 or 10 μg) compared to the control group [19]. Yesil et al. showed that oxidative stress markers like malondialdehyde (MDA) and superoxide dismutase (SOD) enzyme activities were reduced significantly in the rats administered with Exenatide compared to the control population. The study further highlights that the apoptotic markers are decreased due to Exenatide administration, reducing stress and subsequent cell death [20].

Conclusion

The current study has discussed an effective drug (Exenatide) delivery method via the oral route. The authors also conducted a Release Study showing the detailed observations of SEDDS (Exenatide and DOC). The study also shows the data related to the viability and cytotoxicity of the cells, which positively correlates with the previous studies. Significant mucus permeation validates that SEDDS of the cells, which positively correlates with the previous studies. Significant mucus permeation validates that SEDDS (Exenatide and DOC) can function effectively in the gastrointestinal epithelium and eventually get absorbed. The study also concluded that SEDDS significantly improves BGL, prevents weight loss due to diabetes, and decreases oxidative stress in diabetes. However, more animal experiments need to be conducted and should be conducted on a broader range of animals. Finally, clinical trials must be conducted to formulate SEDDS to function effectively in humans. However, this study has brought forward detailed and analytically significant findings regarding Exenatide in drug delivery systems among the rat population to show that SEDDS (Exenatide and DOC) can be developed and used in diabetes individuals' efficient drug delivery and its management.

References

Aziz Unnisa.: A Study on the development and *in-vivo* evaluation of Exenatide Self-Emulsifying Drug Delivery System (SEDDS)
