Design and *In-Vitro* Evaluation of Colon Targeted Prednisolone Solid Dispersion Tablets

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**Abstract**

In the present investigation an attempt was made to prepare colon targeted enteric coated tablet containing different prednisolone solid dispersion formulations, to prevent ulcerative colitis, improve the patient compliance and reduce the side effects of drug in the gastrointestinal tract (GIT). Solid dispersion is one of the most widely used approaches to enhance the solubility as well as dissolution rate of poorly water soluble drugs. Solid dispersions (SDs) of Prednisolone with D-mannitol, PEG 4000 and Kollicoat IR were prepared and evaluated to deliver Prednisolone to the colon in a pre-solubilized form. The selected formula using drug compatible excipients was compressed into fast disintegrating tablets and then coated with Eudragit S100 (pH-responsive polymer), several variables related to both solid dispersion preparation (carrier type and drug to the carrier ratio) and tablet coating (coat level) were studied to show their effects on drug solubility and dissolution. Different analytical techniques like differential scanning calorimetry (DSC), powder x-ray diffraction (PXRD) and scanning electron microscopy (SEM) were studied to prove the change of drug particle from crystal to amorphous form in SDs. The 1:3 Prednisolone/Kollicoat IR SDs showed the greatest improvement in the dissolution rate. The coating level was critical for determining the duration of the lag phase. Best result was given by the 16% coat (Eudragit S100/ Dibutyl phthalate/ talc). This coating level showed an acceptable lag time for the proposed colonic targeting (5 h) as the selected tablet resisted pre-colonic pH values, followed by an immediate release stage in pH 7.4. The suggested covered (coated) tablets may provide a colonic delivery system for prednisolone with enhanced solubility and bioavailability.

**Keywords:** Prednisolone, Colon Targeted, Solid dispersions

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1 Introduction

In the last few years, the development of the site specific drug delivery system has been introduced to be studied with great deal of research work which compromises numerous benefits over the traditional drug treatments. The principle goal of the site specific delivery is to deliver the drug in the specific organs of the body. Targeted drug delivery to the colon is highly required for local treatment of a variety of bowel diseases such as ulcerative colitis, Crohn's disease, amebiosis, and colonic cancer. The most critical challenge in such drug delivery approaches is to protect the formulation during its passage through the stomach and about first six meters of the small intestine arriving to colon with no loss of active ingredient by preventing the dissolution and the release till it reached the colon. Among the various pharmaceutical approaches used to target drugs to the colon are pH-dependent, time-dependent and bacterially degradable polymers.

Prednisolone (a potent synthetic corticosteroid that available for clinical use in 1955) making it useful for the treatment of a wide range of inflammatory and auto-immune conditions such as Crohn’s disease, Ulcerative colitis and Rheumatoid arthritis and others.

Peak plasma concentrations of prednisolone are obtained after 1-2 hours of an oral dose administration, and it has a usual plasma half-life of 2 to 4 hours.
Improvement of the dissolution rates of class II water-insoluble drugs is one of the most challenging issues of drug development, because the enhanced dissolution rates can enhance drug oral bioavailability. For water-insoluble drugs, the solid dispersion technique established by Chiou and Reigelman supplies an effective way to increase the dissolution rates of drugs.

In the present study, efforts were made to improve the dissolution behavior and consequently, absorption, of Prednisolone by applying the solid dispersion technique using three different hydrophilic carriers (PEG 4000, D-mannitol and Kollicoat IR) the solid dispersion formulations were compressed into tablets and further coated to deliver the drug to colon.

2 Materials and Methods

2.1 Materials

Prednisolone, D-mannitol, Crosspovidone, Croscarmellose sodium, magnesium stearate were obtained from Samara drug industry, Iraq; Kollicoat IR was obtained from Sigma-Aldrich Co., USA; Polyethylene glycol (PEG4000) from Sinopharm chemical reagent Co., China, Eudragit S100 was purchased from Evonik Company, Germany and Dibutyl phthalate was manufactured by Fluka Company, UK. All other chemicals, reagents and solutions used were of analytical grade. Marketed tablet Deltacortril® (Pfizer, Turkey) was purchased from local pharmacy.

2.2 Methods

2.2.1 Solubility determination of Prednisolone

For the determination of solubility of Prednisolone, an excess amount of the drug about 50 mg was added to 25 ml phosphate buffers pH 7.4. The flask was stirred for 24 hours using magnetic stirrer and maintained at 25°C. The sample was then filtered through 0.45 μm membrane filters, suitably diluted, and analyzed by UV-spectrophotometer at 247 nm for prednisolone. The study was performed in triplicate.

2.2.2 Preparation of Prednisolone solid dispersions

Solid dispersions of prednisolone in three hydrophilic carriers at three different weight ratios were prepared by solvent evaporation method by using ethanol as common solvent. The calculated amount of polymer and drug was dissolved separately in the required amount of solvent ethanol and mixed under mechanical agitation. The solvent was eliminated using a rotary evaporator under reduced pressure. The solid dispersions when dried were ground using a mortar and pestle then passed through 0.36 mm sieve and stored in desiccators till use, and the optimum one for each carrier was compared with the physical mixture and pure Prednisolone. Solid dispersion and physical mixture of different weight ratios are listed in Table 1.

2.2.3 Evaluation of the prepared solid dispersion

2.2.3.1 Determination of saturated solubility of Prednisolone in solid dispersions

Similar procedure mentioned in (2.2.1) was used to determine the saturation solubility of different solid dispersions in phosphate buffer pH 7.4 and compared to that of pure drug.

Table 1: Formulation code of Prednisolone solid dispersions and physical mixtures prepared with different carriers

<table>
<thead>
<tr>
<th>Formulation Codes</th>
<th>Carrier</th>
<th>Drug:Carrier ratio</th>
<th>Method of preparation</th>
</tr>
</thead>
<tbody>
<tr>
<td>SD1</td>
<td>PEG4000</td>
<td>1:1</td>
<td>Solvent Evaporation</td>
</tr>
<tr>
<td>SD2</td>
<td></td>
<td>1:2</td>
<td>Solvent Evaporation</td>
</tr>
<tr>
<td>SD3</td>
<td></td>
<td>1:3</td>
<td>Solvent Evaporation</td>
</tr>
<tr>
<td>PM1</td>
<td></td>
<td>1:3</td>
<td>Physical Mixture</td>
</tr>
<tr>
<td>SD4</td>
<td>D-Mannitol</td>
<td>1:1</td>
<td>Solvent Evaporation</td>
</tr>
<tr>
<td>SD5</td>
<td></td>
<td>1:2</td>
<td>Solvent Evaporation</td>
</tr>
<tr>
<td>SD6</td>
<td></td>
<td>1:3</td>
<td>Solvent Evaporation</td>
</tr>
<tr>
<td>PM2</td>
<td></td>
<td>1:3</td>
<td>Physical Mixture</td>
</tr>
<tr>
<td>SD7</td>
<td>Kollicoat IR</td>
<td>1:1</td>
<td>Solvent Evaporation</td>
</tr>
<tr>
<td>SD8</td>
<td></td>
<td>1:2</td>
<td>Solvent Evaporation</td>
</tr>
<tr>
<td>SD9</td>
<td></td>
<td>1:3</td>
<td>Solvent Evaporation</td>
</tr>
<tr>
<td>PM3</td>
<td></td>
<td>1:3</td>
<td>Physical Mixture</td>
</tr>
</tbody>
</table>

2.2.3.2 In-vitro dissolution study:

The in vitro dissolution study was carried out by using USP type II (paddle type) dissolution test apparatus (Cosmo Lab). Using 900 ml dissolution medium (pH 7.4) at 37°C and rotation speed of 50 rpm. Accurately weighted amount (5mg) of pure drug and equivalent amount from solid dispersions and physical mixtures to 5mg prednisolone were placed in the dissolution vessel for 90 min and at appropriate time intervals (2, 5, 10, 15, 20, 30, 45, 60 and 90 min), 5 ml samples were withdrawn and replenished with the same volume of fresh medium to keep the sink condition constant, samples then filtered and analyzed spectrophotometrically at (247 nm for Prednisolone). The procedure was performed in triplicate for each run test and the mean and standard deviation were calculated.
2.2.3.3 Determination of drug content

The drug content in each solid dispersion formulation was determined by placing the weighted amount of solid dispersion samples equivalent to 2mg of Prednisolone in 100ml volumetric flask containing phosphate buffer (pH 7.4), the samples were continuously shaking until completely dissolve them then filtered. The absorbance of the samples was determined at λmax 247 nm, using UV-visible spectrophotometer. Three readings were taken, and then mean and standard deviation was calculated.

2.2.3.4 Selection of the best formula

The phase solubility and in vitro dissolution test were used for selecting the best solid dispersion formula which will be subjected to further analysis.

2.2.4 Characterization of the selected solid dispersion formula

2.2.4.1 Fourier transforms infrared spectroscopy (FTIR):

Samples of pure drug, Kollicoat IR and SD9 (equivalent to about 5 mg of Prednisolone) were ground, mixed with dry potassium bromide and pressed in the form of discs using hydraulic press. The discs were analyzed by FTIR spectroscopy (4000-400 cm⁻¹).

2.2.4.2 Differential scanning calorimetry (DSC)

DSC was used to determine thermal behavior of Prednisolone, Kollicoat IR, and SD9 formulations. The pure drug, polymer and solid dispersions were examined by DSC 60 (Shimadzu, Japan), where 5-6 mg sample was placed in aluminum pan and scan at a heating rate of 10°C/min (in range of 0-350°C) with purging of dry nitrogen at a constant rate; an empty aluminium pan was used as a reference. Indium/Zinc standards were used to calibrate the DSC temperature and enthalpy scale.

2.2.4.3 Powder x-ray diffraction (PXRD)

The extent of crystallinity was determined for pure drug and prepared solid dispersion using X-ray (Shimadzu, Japan) powder diffraction system equipped with Cu radiation (λ=1.54060 A) at a voltage of (40 kV) and a current of (30 mA). The instrument was operated in the continuous scan mode and sample were analyzed in the range (5-80°C) with a step size of (0.05°C) at scanning speed of (5°C /min) and (2θ) axis.

2.2.4.4 Scanning electron microscopy (SEM):

The SEM analysis was carried out using a scanning electron microscope (SEM Tescan Vega III Czech). Before to examination, mounted the sample on an aluminum stub using a double sided adhesive tape, then coating with a thin layer of gold (approximately 20 nm) in the vacuum to make it electrically conductive. SEM provides a high resolution images that show details of a sample surface since a high energy beam of electrons typically from 0.5 kV to 40 kV is used to scan the surface of sample to give image in a raster scan pattern.

2.2.5 Manufacturing of colon targeted tablet of Prednisolone by direct compression method

Tablets of pure drug and solid dispersion formulations were prepared to evaluate the impact of solid dispersion on the release of the drug. Tablets ingredients used in tablet formulation (Table 2) were accurately weighed then passed through 0.36 mm sieve to get uniform particle size. The drug and all the ingredients except lubricants were mixed and blended for 5 min. Finally, magnesium stearate was added, mixed for 2 min to coat the particle surface by lubricant evenly. The blend was compressed using 6mm punch and die on a single punch tablet machine. The formulated tablets were stored in a tightly closed container until evaluated. Based on the results of dissolution study the best formulation was selected among the six formulations for further study.

Table 2: Formulation ingredient of pure and solid dispersions tablet of Prednisolone

<table>
<thead>
<tr>
<th>Ingredient</th>
<th>F1</th>
<th>F2</th>
<th>F3</th>
<th>F4</th>
<th>F5</th>
<th>F6</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>SD3</td>
<td>SD3</td>
<td>SD3</td>
<td>SD3</td>
<td>SD6</td>
<td>SD18</td>
</tr>
<tr>
<td>Prednisolone</td>
<td>5</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Solid Dispersion</td>
<td>-</td>
<td>20</td>
<td>20</td>
<td>20</td>
<td>20</td>
<td>20</td>
</tr>
<tr>
<td>Cros-carmellose Na</td>
<td>2</td>
<td>2</td>
<td>-</td>
<td>-</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Cros-povidone</td>
<td>-</td>
<td>-</td>
<td>2</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Magnesium stearate</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Avicel pH302</td>
<td>92</td>
<td>77</td>
<td>77</td>
<td>79</td>
<td>77</td>
<td>77</td>
</tr>
<tr>
<td>Total weight</td>
<td>100</td>
<td>100</td>
<td>100</td>
<td>100</td>
<td>100</td>
<td>100</td>
</tr>
</tbody>
</table>

2.2.5.1 Pre-compression parameters evaluation

Various micromeric parameters like angle of repose, bulk density, tap density, Carr’s (Compressibility) Index (CI), and Hausner’s ratio were measured for solid dispersions powders.

2.2.5.2 Post-compression parameters evaluation

Thickness of tablets prepared was calculated using Vernier caliper, the hardness of the tablets was determined using electrical hardness tester. It is expressed in Kg/cm². The hardness test was performed in which five tablets from each formula were tested randomly and the average reading ± sd was recorded. The friability test was done by UK J Pharm & Biosci, 2015: 3(6); 32.
placing 20 pre-weighed tablets in the friabilator which was then operated for 25 rpm for 4 minutes; the tablets were then dusted and reweighed. Tablets that lose a maximum of not more than 1% of their weight are generally considered acceptable\(^{29}\). In addition, weight variation was performed according to the USP specifications.

### 2.2.5.3 Content Uniformity test

Content uniformity was done by weighing and powdering 20 tablets. Weigh accurately a quantity of the powder equivalent to (5 mg of Prednisolone) and transferred to 100 mL volumetric flasks containing 50 mL of phosphate buffer pH 7.4. The flasks were shaken to solubilize the drug. The volume was completed to 100 mL with the buffer, allowed to stand for 24 h to make sure complete solubility of the drug. The solution was filtered, and 1 mL of the filtrate liquid was suitably diluted and analyzed for prednisolone content spectrophotometrically at 247 nm\(^{30,32}\).

### 2.2.5.4 In-vitro disintegration study

The in-vitro disintegration study of the uncoated tablets was determined using the disintegration test apparatus as per USP specifications. One tablet was placed in each of the six tubes of the basket, the disc was add to each tube and running the apparatus using 900 ml of phosphate buffer pH 7.4 maintained at 37\(^\circ\)C. The time in seconds for complete disintegration of the tablets with no palpable mass remaining in the apparatus was measured and recorded\(^{33}\).

### 2.2.5.5 In-vitro dissolution study

The in-vitro dissolution study was carried out as mentioned previously in section (2.2.3.2) except that one tablet of each prepared formula was placed in the dissolution vessel instead of powdered sample for 90min.

#### 2.2.5.5.1 Effect of different superdisintegrants addition on uncoated tablet release profile

Formulas F2SD3 and F3SD3 were designed to study the effect of different superdisintegrants addition on drug release of uncoated tablet compared with one without the addition of superdisintegrant (F4SD3), where 2% Croscarmellose, 2%Crospovidone and no superdisintegrant were used respectively.

### 2.2.6 Eudragit S100 coating of tablets for pH dependent release

For minimizing the drug release in upper GIT (stomach and small intestine) Eudragit S100 was selected as the pH dependent coating polymer. A 6% w/v Eudragit S100 coating solution was prepared using the mixture of isopropyl alcohol and acetone with the addition of 1% plasticizer- Dibutyl phthalate and used to coat tablet of optimized formula using dip coating method\(^{34}\).

#### 2.2.6.1 Evaluation of the prepared coated tablets

Tablet of optimum formula was coated and around the selected core tablet formula and the resulted coated tablets evaluated for thickness, hardness and friability in the same way for uncoated tablets.

#### 2.2.6.2 Disintegration test for enteric coated tablets

The disintegration test was carried out for all the formulations according to British Pharmacopeia method for enteric-coated tablets. 0.1N HCL and 7.4 pH phosphate buffer was used as disintegrating media. Six tablets were used in each case\(^{35}\).

#### 2.2.6.3 In-vitro drug release study of coated tablets of Prednisolone

Similar dissolution conditions mentioned for powder, and uncoated tablets were used. For simulating the gastric fluid in stomach, the dissolution was accomplished in 0.1 N HCl (pH 1.2) for 2hr, in the phosphate buffer (pH 6.8) to simulate the small intestinal fluid for three hours and for another two hours in phosphate buffer (pH 7.4), simulating the colonic environment. Sample aliquots withdrawn at specific time intervals, were analyzed at 247 nm using UV-Vis Spectrophotometer\(^{34,36}\).

#### 2.2.6.4 Drug-excipient interactions

The physicochemical compatibilities of the drug and the used excipients were tested by FTIR. Pure Prednisolone, selected core and press coated tablets (which were previously grinded); were mixed thoroughly with potassium bromide. The potassium bromide and press coated tablets (which were previously grinded); were mixed thoroughly with potassium bromide. The potassium bromide discs were prepared by compressing the powder at a pressure in a hydraulic press and analyse in the ranges (4000- 400 cm\(^{-1}\)).\(^{37}\)

#### 2.2.6.5 Statistical analysis

The results of the experiments are given as a mean values ± standard deviation (SD) and were analyzed according to one-way analysis of variance (ANOVA) at which significant results (p<0.05) and non-significant (p>0.05).

### 3 Results and Discussions

The measured solubility of Prednisolone in phosphate buffer pH7.4 (215±0.005 μg/ml) indicates that the drug is a very slightly soluble compound in this buffer. Solubility studies revealed a linear increase in drug solubility in the presence of an increasing carrier concentration this is because hydrophilic carriers are known to interact with drug molecules, mainly by electrostatic forces and occasionally by other types of forces like intermolecular hydrogen bonds\(^{38,39}\). The solubility enhancement of the various carriers was in the order of Kollicoat IR > PEG4000> D-Mannitol. The markedly higher solubility of Prednisolone in Kollicoat IR may be attributed to the higher solubilizing capacity as it is non-ionic polymer and its
solubility is pH-independent. The content of Prednisolone was determined in all the prepared formulas and was found to range from 98-101% of the theoretical calculated content which is within the limits of the official monographs of Prednisolone preparations of the British Pharmacopeia. The dissolution results of pure and solid dispersion of Prednisolone in the different carrier are presented in Figure 1. It is evident that all Prednisolone solid dispersions exhibit fast dissolution rate than pure drug. However, the rate of dissolution was varying among different Prednisolone solid dispersions (prepared using different types of carrier and ratios). The significant higher dissolution rate (p<0.05) obtained from solid dispersion formulations is a result of particle size reduction of the drug, formation of higher energy metastable state with higher degree of amorphization of the drug, improved drug’s wetting properties, local solubilization of the carrier at the diffusion layer, increased porosity, and the formation of intermolecular hydrogen bonding between the drug and the carrier.

Formula SD9 was chosen as the best formula since it showed higher drug solubility and percent drug release at the short period of time among other solid dispersion formulations; therefore, further characterization on this formula was done.

The FTIR spectrum (Figure 2) of Kollicoat IR showed a characteristic band at 3421 cm$^{-1}$, which is assigned for OH stretching. No appearance of new bands in SD9 FTIR spectrum suggesting no chemical interaction between the drug and the carrier. Reduction in the sharpness and smoothing of the peaks means a reduction of Prednisolone crystallinity which is further can be confirmed by DSC and PXRD analysis studies.

In general, there is a reduction in the intensity and sharpness of the absorption bands of SD9 compared to Prednisolone alone as a result of formation of intermolecular hydrogen bonding.

Thermal analysis using DSC showed the presence of single endothermic peak in the thermogram of SD9 (Figure 3) around the polymer melting point related to polymer fusion with the absence of a peak corresponding to melting endotherm of Prednisolone can be attributed to the possible dissolution of the drug in the molten carrier during heating cycle in DSC analysis, and PXRD result shown in figure 4 reveals the decrease in the intensity of prednisolone SD9 peak compared to pure drug which indicate decrease in crystallinity of the drug in SD9.

The results of SEM are shown in figure 5 SEM micrographs indicate that the pure drug is in the crystalline form whereas physical mixture contains both amorphous particles and some crystals of the drug. In the case of the solid dispersion, the drug particles reduced in size, some have spherical shape; which is might be one of the factors that are responsible for enhancing drug dissolution and solubility.

The values of angle of repose, bulk density, tapped density, Carr’s index, and Hausner ratio for the prepared uncoated powder blends of each formula was illustrated in table 3. These results estimated according to USP. The results show that the prepared uncoated mixtures have acceptable flow properties and compressibility.

The results of thickness, hardness and friability of all the prepared uncoated tablets are shown in table 4.

In vitro disintegration time for all prepared Prednisolone uncoated tablet was found to be in the range of (43-420 seconds). This short disintegration time is desirable since it facilitates the dissolution and

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releases of the drug from the tablet. In general disintegration of tablets achieved through overcoming the cohesive strength of tablets using different types and amount of Disintegrants in tablet formulation.

![Figure 2: FTIR spectra of A- Prednisolone, B- Kollicoat IR and C - SD9](image)

Figure 2: FTIR spectra of A- Prednisolone, B- Kollicoat IR and C - SD9

Figure 6 shows dissolution profiles of Prednisolone from 4 different SD tablets in the phosphate buffer (pH 7.4) compared to marketed one. These results are similar to those obtained from powdered Prednisolone, which indicates that the enhancement in the dissolution of drug from solid dispersion samples is maintained after manufacturing these samples into tablets.

The result of in vitro dissolution (F2, F3 and F4) uncoated tablet formula which was designed to show the effect of Croscarmellose sodium, Crospovidone and without addition of any disintegrants respectively on the drug release from the uncoated tablet shown in figure 7. There was significant difference (p<0.05) in the initial release of drug from these formulation among these formulas the F2 give the best result of 100% release due to the rapid increase in dissolution of Prednisolone with the use of Croscarmellose sodium may be attributed to rapid swelling and disintegration of tablet into apparently primary small particles while Crospovidone disintegrates the tablets quickly but into larger masses of accumulated particles. It exhibits high capillary activity and marked hydration with a little tendency to gel formation.

The developed formulation of coated tablet F6 was studied for its physical properties like thickness, hardness, friability and weight variation and the result was as follow thickness (3.66±0.002 mm), hardness (7±0.005 Kg/cm²), friability (0.18%) and weight variation (116±0.5 mg). The content uniformity test was done for the selected coated tablet formula and the result was 99.95%. This result agrees with the requirements of the United States pharmacopeia.

The coated tablet met pharmacopeial (BP/USP) requirements for the enteric performance test in the 0.1N HCl for 2hr. tablet disintegrate in phosphate buffer solution pH7.4 after 20±0.02 min. Also we found that tablet coated at higher levels had longer disintegration times than that coated at lower levels at the same medium as for 16% and 19% coat level was 20 and 60min respectively.

![Graph](image)

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UK J Pharm & Biosci, 2015: 3(6); 35
The requirement for in vitro release pattern selected for the colon targeting was no drug release up to the end of 5hrs to achieve this different Eudragit S100 coating level was examined, and the best result was using 16% coating level.

The concentration of polymer in solution and the % coating level was related to the drug release directly. Percent of drug release versus time plot illustrations that the dissolution rate was in reverse...
The percentage of drug released for different coating level showed significant differences. The lag time of coated tablet which have tablet thickness 3.66mm was 5 hours and 20 min while for the same tablet formula which have tablet thickness 3.75mm was 7 hours as shown in figure 8. These results showed that as the thickness of the coat increased, the lag time increased since the time required to complete the erosion of the outer shell would be longer. The same results were reported with other related studies. The FTIR spectra results showed that the drug bands didn't change significantly in the FTIR spectra of the grinded uncoated, and selected coated tablets as shown in figure 9.

Table 3: Pre-compression physical parameters for core powder blend

<table>
<thead>
<tr>
<th>Formula</th>
<th>Angle of repose (Degree)</th>
<th>Bulk density (g/cm³)</th>
<th>Tapped density (g/cm³)</th>
<th>Carr’s Index</th>
<th>Hausner ratio</th>
<th>Type of flow</th>
</tr>
</thead>
<tbody>
<tr>
<td>F1</td>
<td>33.78±0.66</td>
<td>0.323±0.04</td>
<td>0.37±0.01</td>
<td>12.7</td>
<td>1.15</td>
<td>Good</td>
</tr>
<tr>
<td>F2</td>
<td>31.21±0.51</td>
<td>0.323±0.01</td>
<td>0.364±0.06</td>
<td>11.26</td>
<td>1.13</td>
<td>Good</td>
</tr>
<tr>
<td>F3</td>
<td>31.21±0.51</td>
<td>0.323±0.01</td>
<td>0.364±0.06</td>
<td>11.26</td>
<td>1.13</td>
<td>Good</td>
</tr>
<tr>
<td>F4</td>
<td>31.15±0.63</td>
<td>0.364±0.04</td>
<td>0.408±0.01</td>
<td>10.78</td>
<td>1.12</td>
<td>Good</td>
</tr>
<tr>
<td>F5</td>
<td>24.52±0.62</td>
<td>0.385±0.02</td>
<td>0.417±0.03</td>
<td>7.67</td>
<td>1.08</td>
<td>Excellent</td>
</tr>
<tr>
<td>F6</td>
<td>33.17±0.64</td>
<td>0.345±0.03</td>
<td>0.408±0.04</td>
<td>15.44</td>
<td>1.18</td>
<td>Good</td>
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</table>

The FTIR spectra results showed that the drug bands didn't change significantly in the FTIR spectra of the grinded uncoated, and selected coated tablets as shown in figure 9. These results indicating that there is no significance evidence of chemical interaction between drug and polymer, which confirm the stability of drug.

4 Conclusion

Amorphous solid dispersions of prednisolone were successfully prepared by solvent evaporation method. The presence of amorphous form in SDs was confirmed by DSC, PXRD and SEM, and was reflected in the significant improvement in rate as well as the extent of in vitro drug dissolution. Proper selection of the
Eudragit® S100 coat level is essential to deliver prednisolone to the colon. The optimized prednisolone colon targeted tablets could be promising in reducing the drug dose and improving its bioavailability based on the protection from the intestinal metabolism. Such a delivery system could be applied for similar water insoluble drugs liable to intestinal enzymatic degradation. Additional studies are needed to assess its performance in vivo.

Table 4: Post compression parameter of Prednisolone tablets

<table>
<thead>
<tr>
<th>Formula</th>
<th>Thickness (mm)</th>
<th>Hardness (kg/cm²)</th>
<th>Friability (%)</th>
<th>Weight variation (mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>F1</td>
<td>3.19±0.01</td>
<td>4.5±0.02</td>
<td>0.46±0.04</td>
<td>99±0.04</td>
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<tr>
<td>F2</td>
<td>3.19±0.03</td>
<td>5.02±0.04</td>
<td>0.1±0.05</td>
<td>99.5±0.01</td>
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<tr>
<td>F3</td>
<td>3.19±0.02</td>
<td>5.8±0.01</td>
<td>0.2±0.03</td>
<td>100±0.02</td>
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<tr>
<td>F4</td>
<td>3.21±0.01</td>
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<td>98.5±0.01</td>
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<td>F5</td>
<td>3.19±0.01</td>
<td>4±0.03</td>
<td>0.51±0.02</td>
<td>98±0.02</td>
</tr>
<tr>
<td>F10</td>
<td>3.20±0.01</td>
<td>4±0.03</td>
<td>0.6±0.01</td>
<td>99.7±0.01</td>
</tr>
</tbody>
</table>

Figure 6: Dissolution profiles of Prednisolone from 4 different uncoated tablets in phosphate buffer (pH 7.4) compared to marketed one

5 Acknowledgements

We are grateful for the cooperation of Iraqi Ministry of Science and Technology for doing the required analytical measurements and Ibn-Sena center for drug research (Baghdad/Iraq) for providing chemicals from Samara drug industry.

6 Competing interests

Authors have no competing interests.

Table 5: Characteristic absorption bands of Prednisolone

<table>
<thead>
<tr>
<th>Characteristic Group</th>
<th>Pure Prednisolone cm⁻¹</th>
<th>Prednisolone core tablet cm⁻¹</th>
<th>Prednisolone coat tablet cm⁻¹</th>
</tr>
</thead>
<tbody>
<tr>
<td>-OH</td>
<td>3454 cm⁻¹</td>
<td>3379.4 cm⁻¹</td>
<td>3354 cm⁻¹</td>
</tr>
<tr>
<td>Sp3 C-H</td>
<td>2982 cm⁻¹</td>
<td>2910 cm⁻¹</td>
<td>2910 cm⁻¹</td>
</tr>
<tr>
<td>-C=O</td>
<td>1654 cm⁻¹</td>
<td>1654 cm⁻¹</td>
<td>1654 cm⁻¹</td>
</tr>
<tr>
<td>Aromatic C=C</td>
<td>1610 cm⁻¹</td>
<td>1612 cm⁻¹</td>
<td>1610 cm⁻¹</td>
</tr>
<tr>
<td>C-H bend</td>
<td>1446 cm⁻¹</td>
<td>1437 cm⁻¹</td>
<td>1431 cm⁻¹</td>
</tr>
<tr>
<td>OH bend</td>
<td>1348 cm⁻¹</td>
<td>1371 cm⁻¹</td>
<td>1371 cm⁻¹</td>
</tr>
<tr>
<td>-C-O</td>
<td>1236 cm⁻¹</td>
<td>1240 cm⁻¹</td>
<td>1242 cm⁻¹</td>
</tr>
<tr>
<td>Aromatic C=C bend</td>
<td>893 cm⁻¹</td>
<td>893 cm⁻¹</td>
<td>895 cm⁻¹</td>
</tr>
</tbody>
</table>

Figure 7: Effect of different superdisintegrant addition on uncoated tablet for F2, F3 and F4 in phosphate buffer pH 7.4

Figure 8: In-vitro release of uncoated tablet and Effect of coat thickness on percent of drug release in different dissolution media
7 Author’s contributions

The study was conceived, planned, performed and written in the form of manuscript by SZM, WKA participated in literature review and manuscript editing. Both authors read and approved on the final manuscript.

8 References


Alkazzaz et al. Design and In-Vitro Evaluation of Colon Targeted Prednisolone


