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ABSTRACT BOOK

P-32
CEFDINIR SOLID DISPERSION WITH POLYVINYL ALCOHOL-POLYETHYLENE GLYCOL COPOLYMER (KOLLICOAT®): PREPARATION AND DETERMINATION OF SOLUBILITY AND RELEASE PROPERTIES

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1. INTRODUCTION

Cefdinir (CEF) is a semi synthetic third generation cephalosporin antibiotic used to treat bacterial infections. It has a short half-life of 1 to 2 hours with bioavailability of 20-25% [1]. CEF is a Biopharmaceutics Classification System (BCS) Class IV drug which means it has low solubility and low permeability. Even though it has marketed dosage forms, the challenge regarding treatment with CEF is that its solubility is much less than 1 mg/mL in water and highly dependent on pH. To overcome solubility problems, one of the solutions preferred is preparing solid dispersions (SDs). SDs can improve active pharmaceutical ingredient's dissolution profile and bioavailability by increasing its aqueous solubility. To prepare SDs, some of the preferred polymers are polyvinyl pyrrolidone, polyvinyl alcohol and carboxymethyl cellulose. Polymers used to prepare solid dispersions must be inert and compatible with active pharmaceutical ingredient [2]. Kollicoat®Protect is coprocessed blend of Polyvinyl alcohol-polyethylene glycol graft copolymer and polyvinyl alcohol. In this study, we aim to improve solubility of CEF by preparing solid dispersions using Kollicoat®Protect and evaluate its solubility and release properties.

2. MATERIALS AND METHODS

2.1. Materials

Cefdinir and Kollicoat®Protect (Polyvinyl alcohol-polyethylene glycol copolymer and polyvinyl alcohol) are kind gift from Sanovel İlaç (Istanbul, Turkey) and BASF (Ludwigshafen, Germany). All other chemicals used were of analytical grade.

2.2. Preparation of solid dispersions

SDs were prepared by lyophilization (Scanvac CoolSafePro Labogene, Denmark) following probe sonication (Sonics®, USA). To prepare SDs, Kollicoat®Protect (0,5 g) was dissolved in 50 mL water. CEF suspension in methanol (0,5 g in 50 mL) was added to the polymeric solution and mixed using magnetic stirrer. Then the mixture was sonicated. Afterwards, formulations were refrigerated at -80°C and lyophilized to obtain a fine powder. Physical mixture (PM-KOL) was prepared by mixing 0,5 g KOL and 0,5 g CEF. Formulation ingredients and conditions are summarized in Table 1.

Table 1. Formulation ingredients and preparation conditions

Code	K	Water	CEF	MeOH	Amp. & Min
PM-KOL	0.5 g	-	0.5 g	50 mL	-
KOl-1	0.5 g	50 mL	0.5 g	50 mL	75%, 4
KOL-2	0.5 g	50 mL	0.5 g	50 mL	75%, 8

*K: Kollicoat®Protect, Amp.: Amplitude %, Min: Minute

2.3. Characterization of solid dispersions

2.3.1. Solubility study

CEF (50 mg) was added to 10 mL of distilled water taken in falcon tube and shaken vigorously for 24 h in a horizontal shaker at 25°C at 250 rpm. Subsequently, the sample was centrifuged, and supernatant solution was filtered through 0.45 µm syringe filter. An aliquot of the filtrate was diluted with distilled water and analyzed in UV-Visible spectrophotometer (Shimad-

zu UV-160A, Japan) at 287 nm. Similar method was applied to analyze the solubility of PM-KOL, KOL-1 and KOL-2 coded solid dispersions. The experiment was performed in triplicate at 25°C.

2.3.2. Dissolution

In vitro dissolution study of the pure CEF and optimum SD formulation was investigated over 240 minutes using a dialysis membrane and performed in water, pH 1.2 buffer and simulated intestinal fluid (SIF, pH 6.8).

3. RESULTS AND DISCUSSION

3.1. Characterization of solid dispersions

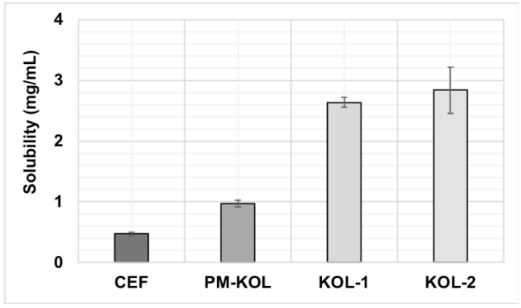

Figure 1. The water solubility of CEF, physical mixture, KOL-1 and KOL-2

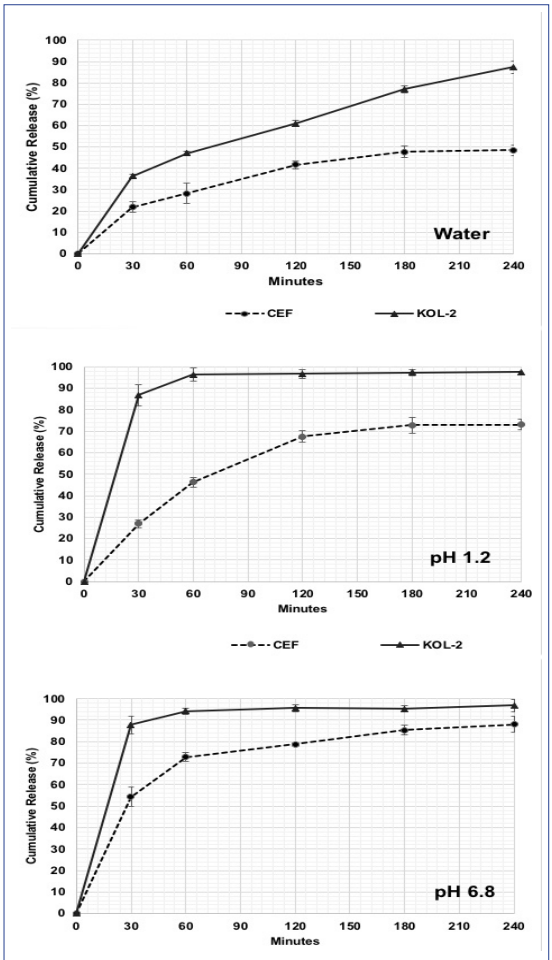

Figure 2. Drug release profile of pure CEF and KOL-2 in different media

Fig.1 shows water solubility of pure CEF, physical mixture and solid dispersion formulations. KOL-1 and KOL-2 coded solid dispersion formulations showed solubility of 2.63±0.08 mg/mL and 2.84±0.38 mg/mL, respectively, in the aqueous phase, whereas pure CEF showed lower solubility of 0.473±0.031 mg/mL. This represented a 5-fold increase in aqueous solubility of CEF by the solid dispersion process.

KOL-2 was chosen as the optimum formulation as it further increased the solubility of CEF. Fig. 2 shows *In Vitro* drug release profiles of pure CEF and KOL-2 coded SD formulation in distilled water, pH 1.2 buffer and simulated intestinal fluid (SIF, pH 6.8). When the results were examined, it was observed that CEF solubility in water and pH 1.2 medium was increased by KOL-2 coded SD formulation. However, it is clear that no excessive difference in pH 6.8 was observed. The reason for this can be explained as follows. The solubility of CEF in water is very low and its solubility increases with increasing pH (36) of the medium in which it dissolves [2].

4. CONCLUSION

In this study, we found that solid dispersion prepared with 'Kollicoat Protect' could increase the solubility of the lipophilic drug cefdinir. The developed solid dispersion commonly resulted in about 5-fold higher solubility of cefdinir and improved dissolution profile in water and pH 1.2, compared with pure. In addition, solid state characterizations anti-bacterial activity tests and in vivo studies should be performed to reach a complete result.

5. REFERENCES

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AUTHOR INDEX

I

IBRAHIM, YOUSIF H-E. Y. 109
IBRIĆ, SVETLANA 230, 253

İ

İLBASMIŞ TAMER, SIBEL 140, 293
İLEM ÖZDEMIR, DERYA 58
İMAMOĞLU ŞİRVANLI, NALAN 60
İNAL, OZGE 125
İNCECAYIR, TUBA 365
İZAT, NIHAN 332, 371

J

JIWA, NAILLA 260, 263
JÓZSA, LIZA 70
JR., GÉZA REGDON 109
JUHÁSZ, BÉLA 70
JUKIČ, MARKO 35

K

KABAN, KÜBRA 363
KAHRAMAN, EMINE 143, 302
KAIRANE, CESLAVA 354
KALAMI, ELMIRA 302
KALAYI, MOHAMMED 312
KANDILLI, BÜŞRA 166, 247
KANTARCI, GÜLTEN 363
KÁNTÁS, BOGLÁRKA 287, 352
KAPLAN, OZAN 332
KARA, ADNAN ALTUĞ 87, 273
KARA, ASLI 116, 221
KARABULUT, ERDEM 192
KARASULU, ERCÜMENT 134, 136, 216, 283, 358
KARASULU, HATİCE YEŞİM 373
KARASULU, H. YEŞIM 276, 280, 334, 358
KARATAŞ, AYŞEGÜL 237, 361
KARAVANA, SINEM YAPRAK 218
KARPUZ, MERVE 90
KÁSA, PÉTER 367
KAVAS, AYCAN 216
KAZANCI, ATILLA 20
KÉRI, GYÖRGY 352
KHALIL, RUQAIYA 66
KHAMIS, HALA 260
KIR, FATMA 332
KIRSIMÄE, KALLE 79
KISAND, VAMBOLA 289
KISA, ÖZGÜL 317
KOCBEK, PETRA 131
KOGERMANN, KARIN 27, 64, 79, 159, 289
KONDIC, JELENA 230
KORCZYK, PIOTR 64
KORHONEN, OSSI 30
KÕRKJAS, ARLE 159
KOSE OZKAN, CANSEL 114
KRISTL, JULIJANA 131, 155, 157
KRISTÓ, KATALIN 109
KRONSTRÖM, KAI 159
KUNT, SERIF TUGRUL 216
KÜÇÜKGÜZEL, Ş. GÜNIZ 60, 358
KÜÇÜKTÜRKMEN, BERRIN 171
KURALAY, FILIZ 20
KURT, NIHAT 348

L

LAIDMÄE, IVO 79, 159, 289
LALIĆ-POPOVIĆ, MLADENA 212
LANNO, GEORG-MARTEN 64
LAVRIČ, ZORAN 224
LEDNECZKI, ISTVÁN 31
LEHTO, VESA-PEKKA 32
LEPETRE-MOUELHI, SINDA 20
LÓPEZ-MACÍAS, CONSTANTINO 356
LORYAN, I. 26
LUDÁNYI, ZSÓFIA 328

M

MADŽAREVIĆ, MARIJANA 253
MÄEORG, UNO 289
MAHLAPUU, RIINA 354
MALEKGHASEMI, SOHEIL 195
MATJAŽ, MIRJAM GOSENCA 199, 268
MEDAREVIC, DJORDJE 230
MEHMETOGLU, AYCA 283
MEOS, ANDRES 289
MESUT, BURCU 72, 138, 285, 312
MIHELČIČ, ANJA 35
MIKOV, MOMIR 212
MIRTIČ, JANJA 131, 155, 157
MUT AŞKUN, MELIKE 197
MUTLU-AGARDAN, N. BASARAN 128

N

NAGY, SÁNDOR 153
NAJIB, NAJI M. 34
NAMLI, İREM 168, 175, 178, 226
NAZLI, HAKAN 138
NEMUTLU, EMIRHAN 20
NIEMCZYK-SOCZYNSK, BEATA 64
NIEMINEN, HEIKKI. J. 159

O

OBREZA, ALEŠ 35
OKTAY, AYSE NUR 140
OLGAÇ, SEVAL 74, 100
OMASA, TAKESHI 136
ONAYO, M. MAYOWA 325
ONGUN, MELIKE 270, 273
ONTIVEROS-PADILLA, LOUIS 356
ONUK GÖREN, FIGEN 337
ORAK, DUYGU 309

Ö

ÖLGEN, SUREYYA 350
ÖNER, LEVENT 20, 189, 192, 348
ÖZALP, YILDIZ 260, 263, 285, 322, 325
ÖZCAN BÜLBÜL, ECE 77
ÖZÇELIKAY, ARIF TANJU 92
ÖZDEMIR, ERTAN 371
ÖZDEM, SADI S. 37
ÖZER, A. YEKTA 62, 90, 102
ÖZER, ÖZGEN 214, 309
ÖZER, SINAN 148
ÖZGENÇ, EMRE 58
ÖZGÜNEY, IŞIK 210
ÖZKAN, YALCIN 107, 114
ÖZKÖSE, UMUT UGUR 221
ÖZKUL, AYKUT 356
ÖZLISELI, EZGI 235
ÖZMEN, GÜLÇE 134
ÖZPOLAT, LEYLA 216
ÖZSOY, YILDIZ 72, 77, 138, 143, 228, 285, 302, 312
ÖZTÜRK, A. ALPER 55, 168, 175, 226
ÖZTÜRK-ATAR, KIVILCIM 80, 173
ÖZTÜRK, NAILE 116, 221
ÖZTÜRK, ŞÜKRÜ 20
ÖZTÜRK, SÜLEYMAN CAN 90
ÖZ, UMUT CAN 171

P

PAAVER, URVE 289
PAKSOY, BAŞAK 182
PALA KARA, ZELIHA 112
PALCSÓ, BARNABÁS 297
PÁL, SZILÁRD 153, 367
PAVLOVIĆ, NEBOJŠA 212
PAYRITS, MAJA 287
PEKCAN, MERT 356
PESEN OKVUR, DEVRIM 38
PEZIK, ESRA 256, 258, 341, 343, 345, 369
PINTÉR, ERIKA 352
PINTYE-HÓDI, KLÁRA 153
PIRINÇCI, YAĞMUR 72
PIRNAT, SAŠA 155
POBIRK, ALENKA ZVONAR 199
POLAT, KEREM HEYBET 202, 205
POROSK, RANDO 354
POTOČNIK, ŠPELA 35
POTPARA, ZORICA 253
PREŠERN, ANJA 268
PURALI, NUHAN 356
PUTRINŠ, MARTA 64

R

RAJABALAYA, RAJAN 51
RAŠČAN, IRENA MLINARIČ 35
RENÇBER, SEDA 210
RIVERO-ARREDONDO, VANESSA 356
ROSENHOLM, JESSICA 235