Electronic Journal of University of Aden for Basic and Applied Sciences
EJUA-BA Vol. 3 No. 4 (2022)
https://doi.org/10.47372/ejua-ba.2022.4.204
ISSN: 2708-0684

RESEARCH ARTICLE

PREFORMULATION STUDY OF CEFTRIAXONE AND CIPROFLOXACIN FOR LIPID BASED DRUG DELIVERY SYSTEMS

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Received: 10 December 2022 / Accepted: 17 December 2022 / Published online: 31 December 2022

Abstract

Several tests should be performed to rule out any potential physical or chemical interactions between the active pharmaceutical ingredient and the various excipients that might be utilized in the manufacturing of the drug formula. Fourier Transform infrared spectroscopy is a simple technique for the detection of changes within excipient-drug mixtures. In addition to speeding up the aging process of drugs and their possible interactions with excipients, isothermal stress testing was achieved. In this study, Ceftriaxone sodium (CTX), and Ciprofloxacin hydrochloride (CIPRO) as active ingredients were subjected to several tests to exclude any interaction with the excipients that could be used in the formulation of lipid base biodegradable antibiotic for prevention of post-operative infection. The compatibility was tested by using Fourier Transform infrared spectroscopy (FT-IR) and isothermal stability testing (IST). As a result, the IR spectral interpretation showed that the spectra obtained from the binary mixtures match the original spectra of API. Generally, there was no obvious and influential change of any characteristic peaks which confirms the absence of chemical interaction between the CTX or CIPRO and excipients. In the IST, the API – excipient mixture shows no significant change in physical properties. There was no change in color, gas formation, and liquefaction of the mixture stored under stress conditions. There was no significant change in the amount of API after storage in stressed conditions at statistical significance ($p = 0.05$). In conclusion, there are no notable interactions between API and the various excipients that could be employed to create biodegradable lipid-based delivery systems that are effective at preventing post-operative infection.

Keywords: Pre-formulation, Ceftriaxone, Ciprofloxacin, Lipid base biodegradable, Spectra of API.

1. Introduction

To create dosage forms, pre-formulation investigations of the medicine and excipient are required. It may include many steps, processes, and experiments to exclude any physical or chemical interaction between Active pharmaceutical ingredients (API) and different excipients that could be used during the preparation of the drug formula. If there is any interaction between API and excipient it may cause alteration in the product efficacy, safety, therapeutic effect, stability, bioavailability, and side effect.

The first step toward the final pharmaceutical formulation is the selection of excipients after compatibility research. However, there are no universally accepted guidelines for evaluating and choosing appropriate excipients. Despite the fact that suboptimal combinations of API and excipients may change the formulation's stability and drug's bioavailability, a drug-excipient compatibility study is a significant part of the development of a stable pharmaceutical formulation. FT-IR is a simple technique for finding changes within excipient-drug mixtures. Clear evidence for interactions between the excipient and the API under investigation can be seen in the loss of an absorption peak or a decrease in peak strength paired with the emergence of additional peaks. Changes are undesirable as a first step, and drug-interacting excipients should be avoided wherever possible in the finished formulation. A deeper understanding of the mechanism of interaction can be achieved by the use of FT-IR, as the process allows the assignment of the peaks

and thereby offers valuable information about possible chemical changes.

FT-IR offers certain definite advantages over the other analytical techniques utilized in compatibility studies. , including:-

(i) Since there is no need to prepare the samples, it is non-disruptive.

(ii) The outcome is unaffected by the recording.

(iii) It is possible to identify changes in the crystal structure, such as desalting, hydrate formation, or polymorphism alterations [1].

In order to hasten API aging and interaction with excipients, IST entails storing API-excipient blends with or without moisture at high temperatures for a set amount of time (often 3–4 weeks). The samples are then visually detected and the API content is determined quantitatively. This method's drawback is that it takes a lot of time and calls for a quantitative analytical technique [2].

CTX with empirical formula $C_{18}H_{16}N_8Na_2O_7S_3$, $3.5H_2O$ & molecular weight [MW¼662 g/mol] belongs to the third spectrum cephalosporin's which are broad-spectrum β-lactam antibiotics [3]. CTX has acquired a high grade among the cephalosporin drugs. Like other third-generation cephalosporins, it has a substantially wider spectrum of activity against gram-negative organisms but is much less effective against gram-positive bacteria than first-generation medicines. [4]. Numerous infections brought on by susceptible organisms, such as those of the bone and joints, abdomen, lower respiratory tract, meninges, pelvic region, skin, and soft tissue, and urinary tract can be successfully treated with CTX. Septic arthritis, bacteremia, and gonorrhea, which are brought on by organisms susceptible to the antibiotic, can also be successfully treated with it. Additionally, it aids in preventing postoperative infections [5, 6].

CIPRO with empirical formula $C_{17}H_{18}FN_3O_3$, HCL & molecular weight [MW367.8 g/mol] belongs to fluoroquinolone antibacterial agent [7]. CIPRO is a well-known fluoroquinolone antibiotic with a broad spectrum that is active against both Gram-positive and Gram-negative bacteria infections [8, 9]. CIPRO is effective management for those infections most common in senior patients, including infections of the urinary tract, lower respiratory tract, skin and soft tissues, and bone and joints, and is an active agent for prophylaxis in transurethral surgery. In patients undergoing transurethral resection, a 300 mg intravenous dose was just as effective as a 1000 mg intravenous dose of Cefotaxime before surgery, and preoperative administration of a single oral dose of CIPRO 500 mg significantly decreased the incidence of postoperative UTI compared to a placebo [7].

To successfully get over physical and biological limitations relating to poor water solubility and stability, membrane permeability, drug efflux, and availability, lipid-based systems are increasingly being studied [10]. In these kinds of drug delivery systems, polymers, particularly poly-lacticco-glycolic acid (PLGA), are frequently utilized as matrix formers due to its biocompatibility and biodegradability. For instance, the teams of Benoit and Menei created PLGA-based microparticles with 5-fluorouracil loaded into them for the treatment of brain cancers [11-13]. However, because PLGA breaks down into acidic microclimates, it can have a major impact on the biological function of medications that are included, particularly proteins [14-16]. Several methods have been suggested to get over this limitation, such as using lipids as matrix formers rather than PLGA [17]. Lipids have the major benefit of not expanding to a significant level upon contact with aqueous media, in addition to avoiding acidic microclimates during decomposition [18]. A viable method for controlled, site-specific medication release is lipid-based drug delivery. Different molecular weights of lipids are accessible, and they have a higher level of biocompatibility [19]. The variety and adaptability of pharmaceutical grade lipid excipients and drug formulations, as well as their compatibility with liquid, semi-solid, and solid dosage forms, are the main causes of the rapidly expanding use of lipid-based drug delivery systems [20, 21].

In this study, CTX, and CIPRO as APIs were subjected to some investigations to exclude any interaction with the excipients that could be used in the formulation of lipid base biodegradable antibiotics for the prevention of post-operative infection.

2. MATERIALS AND METHODS

2.1. Materials:-

CTX (Gift from Medical Union Pharmaceuticals / Egypt), CIPRO (Gift from Modern Pharma & Global Pharma Companies / Yemen), Glyceryl monostearate (GMS), Polyethylene glycol 400 (PEG400), Polyethylene glycol 4000 (PEG 4000), Polyethylene glycol 6000 (PEG 6000), Glycerol, Sorbitol, tween 20, tween 80, Potassium bromide for infrared (KBr IR), FT-IR spectrophotometer (Varian, USA, Varian FT-IR), Oven (Gallenkamb, England, 3A 5048), Refrigerator (LG, Indonesia, GN-B262SLCL), and Spectrophotometric (Lasany ® advanced microprocessor UV-VIS-L1-295).

2.2 FT-IR spectrophotometer

2. 2.1. Scanning of API

10 mg of API (CTX or CIPRO) was mixed with 3000 mg KBr IR. The mixture was ground and filled in an appropriate die, and compressed manually to get the

translucent disc, which was scanned in the range of 2000 to 625 cm^{-1} by a Varian FT-IR spectrophotometer at room temperature.

2.2.2. Scanning of API and excipient

A binary mixture of API (CTX or CIPRO) with different excipients in a ratio of 1:1 w/w was arranged as in Table (1). A sample of the binary mixture (10 mg) was mixed with 3000 mg KBr IR. The mixture was ground and filled in an appropriate die, compressed manually to get a translucent disc, which was scanned in the range of 2000 to 625 cm^{-1} by a Varian FT-IR spectrophotometer at room temperature. The API spectrum was matched with the API-excipient spectrum and spectrums were examined for any interactions [22-23].

2.3. Isothermal stability testing (IST)

For IST testing, a binary mixture of API (CTX or CIPRO) was arranged in a ratio of 1:1 w/w as in Table (1). It was weighed precisely, mixed with mortar and pestle for 3 minutes, and sited in a glass vial (No =2). In each of the vials, a 10% (w/w) water was added and the API-excipients mixture was also mixed using a capillary tube (both the ends of which were closed). The capillary was broken and left within the vial to avoid material loss. A Teflon-lined screw cap was used to seal each vial, which was then kept at 50°C in a hot air oven. On the other hand, API-excipients blends without added water, stored in a refrigerator, functioned as controls. Each week, they were checked for any unexpected color changes. Utilizing a UV-visible spectrophotometer, samples were quantitatively examined after 3 weeks of storage under the aforementioned circumstances. To prepare the sample, the combination was mixed with enough distilled water to dissolve it, then it was transferred to a 100 mL volumetric flask. 2.5 mL of the created solution was then added to another 100 mL volumetric flask, and was filled with distilled water. Following the above-described steps, three sets of solutions were made, and the absorbance at (λ max) of API was determined. [2, 26-35].

Table (1): Amount of API – Excipient Mixture

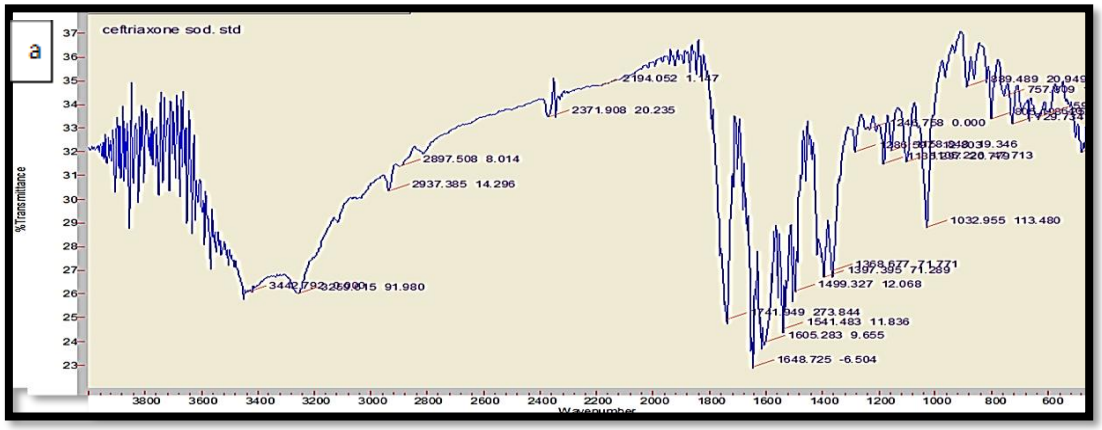
Sample	Ratio (API-excipient)	Sample	Ratio (API-excipient)
CTX	-	CIPRO	-
CTX – GMS	1:1	CIPRO – GMS	1:1
CTX – PEG 400	1:1	CIPR – PEG 400	1:1
CTX– PEG 4000	1:1	CIPRO –PEG 4000	1:1
CTX– PEG 6000	1:1	CIPRO – PEG 6000	1:1
CTX – Glycerol	1:1	CIPRO – Glycerol	1:1
CTX – Sorbitol	1:1	CIPRO – Sorbitol	1:1
CTX – PG	1:1	CIPRO – PG	1:1
CTX – Tween 20	1:1	CIPRO – Tween 20	1:1
CTX – Tween 80	1:1	CIPRO – Tween 80	1:1

3. Results and Discussion

The results of FT-IR spectra were used to estimate the possible interaction of API and excipients used. The results were represented as figures only.

3.1. Scanning of API

The obtained results are shown in Figures 1 (a, and b).



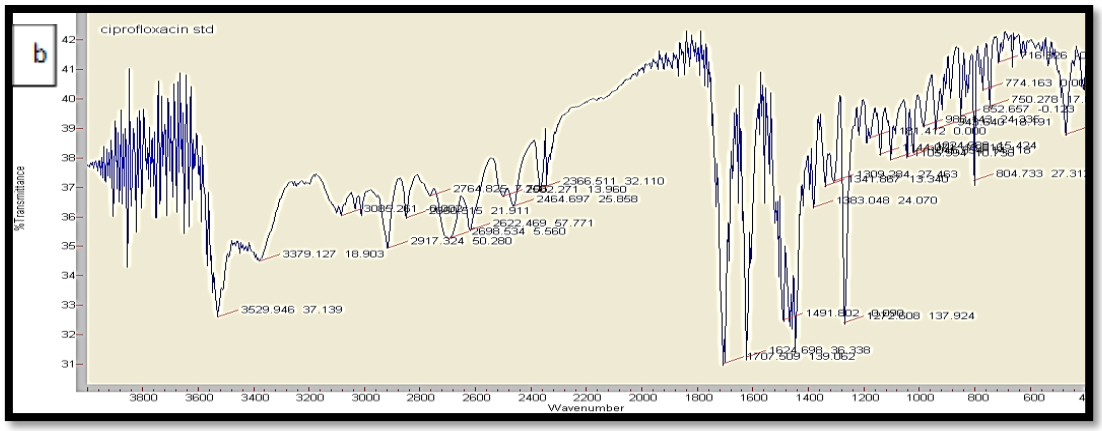


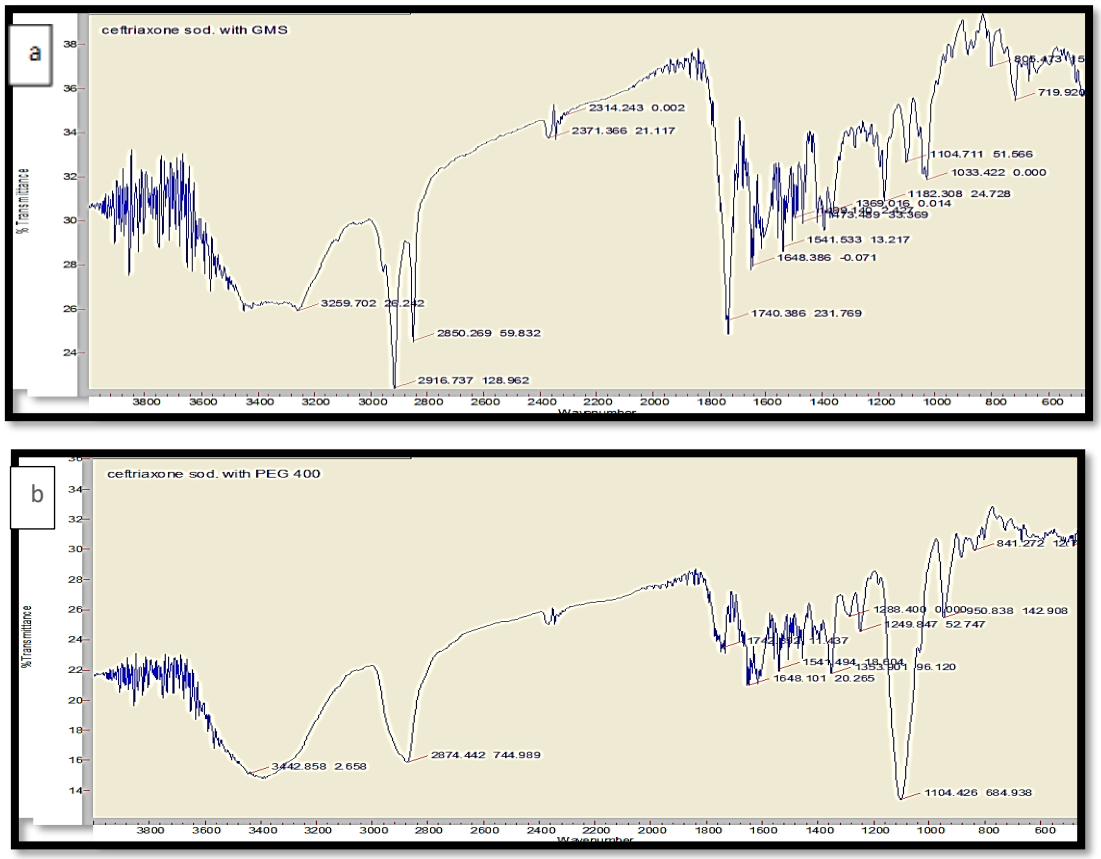
Fig. 1: FTIR Spectra of **(a)** CTX **(b)** CIPRO

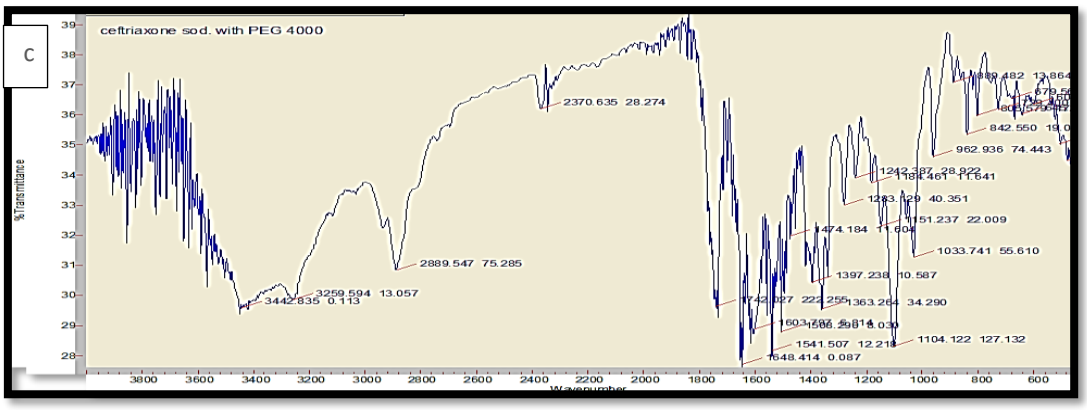
FTIR studies for CTX as represented in Figure (1-a) showed characteristic peaks at 3442 cm^{-1} (N-H stretching mode of H-bonded amide group), 1741 cm^{-1} (β-lactam C=O stretching vibrations), and 1648 cm^{-1} (oxime C=N stretching vibrations).

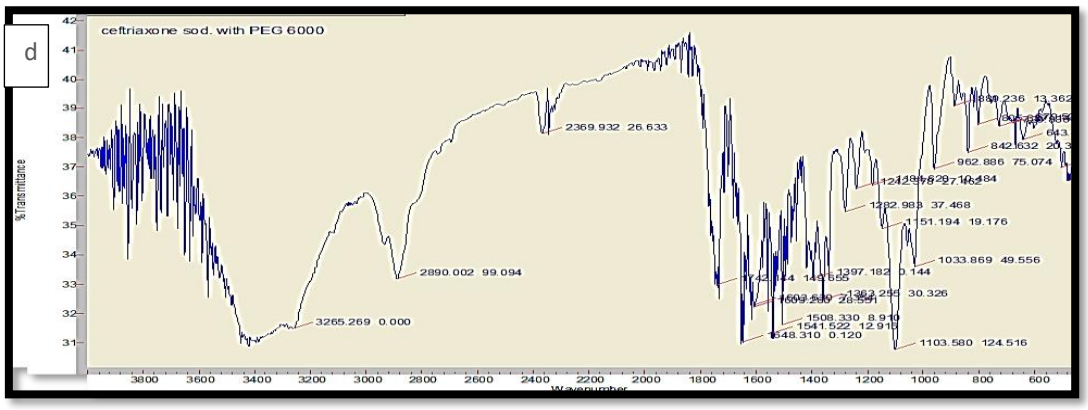
In the FTIR spectra of CIPRO as shown in Figure (1-b), one prominent characteristic peak was found at 3529 cm^{-1} and was assigned to OH stretching vibration (intermolecular hydrogen bonding). The bands at 1707 cm^{-1} represented -COOH stretching, while the peak at 1625 cm^{-1} was assigned to –C=O. The bands at the 1492 cm^{-1} represented C-H and the ones at 1383 cm^{-1} suggested bending vibration of the aromatic C=C group. In addition, a strong absorption peak between 1272 cm^{-1} was assigned to the C-F group.

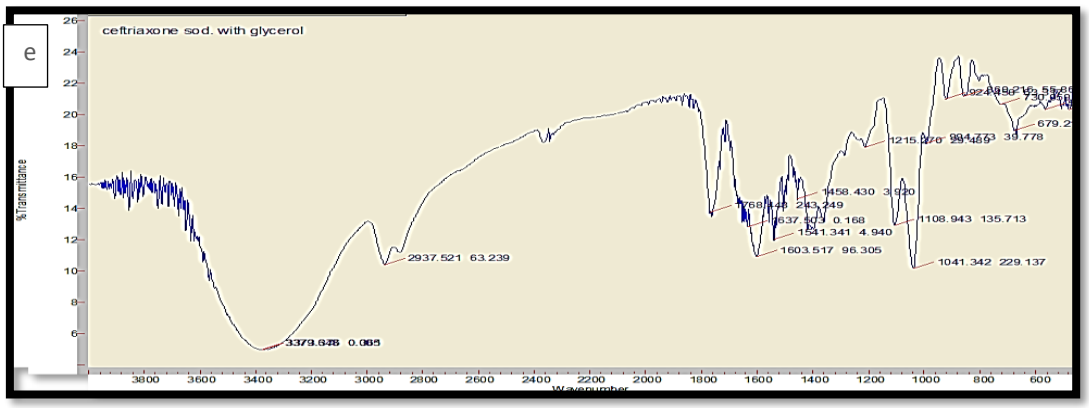
3.2. Scanning of API and excipients

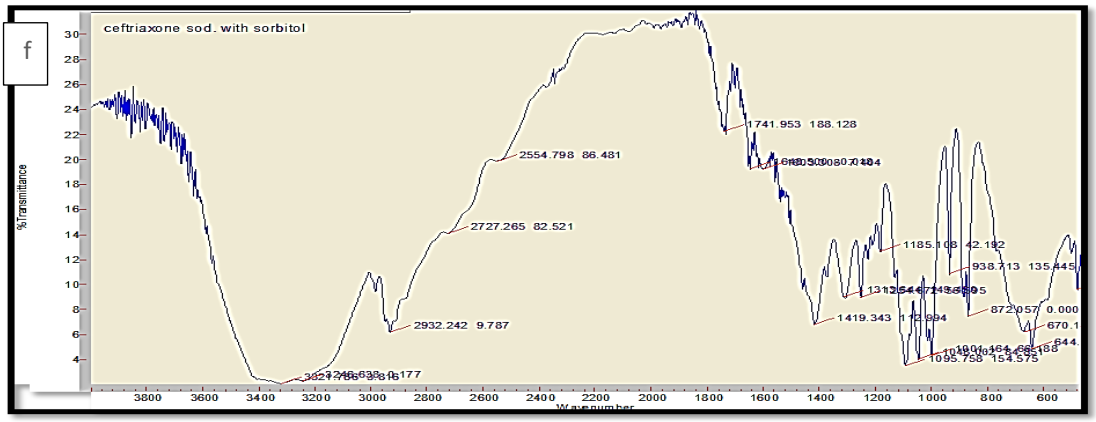
FTIR spectrum of the prepared mixture reveals the chemical interaction between the components. All the ingredients were studied for compatibility between them. For that purpose, the infrared spectra of individual drugs were compared with the infrared spectra of drug excipient binary mixtures represented in Figures 2 (a, b, c, d, e, f, g, h, and i) for CTX, and Figures 3 (a, b, c, d, e, f, g, h, and i) for CIPRO.




c
ceftriaxone sod. with PEG 4000
%Transmittance
Wavenumber
2370.635 28.274
2889.547 75.285
3259.594 13.057
3442.835 0.113
962.936 74.443
1033.741 55.610
1104.122 127.132
1541.507 12.218
1648.414 0.087


d
ceftriaxone sod. with PEG 6000
%Transmittance
Wavenumber
2369.932 26.633
2890.002 99.094
3265.269 0.000
962.886 75.074
1033.869 49.556
1103.580 124.516
1541.522 12.913
1648.310 0.120


e
ceftriaxone sod. with glycerol
%Transmittance
Wavenumber
2937.521 63.239
1603.517 96.305
1541.341 4.940
1108.943 135.713
1041.342 229.137


f
ceftriaxone sod. with sorbitol
%Transmittance
Wavenumber
2554.798 86.481
2727.265 82.521
2932.242 9.787
1741.953 188.128
1185.108 42.182
938.713 135.445
872.057 0.000
1419.343

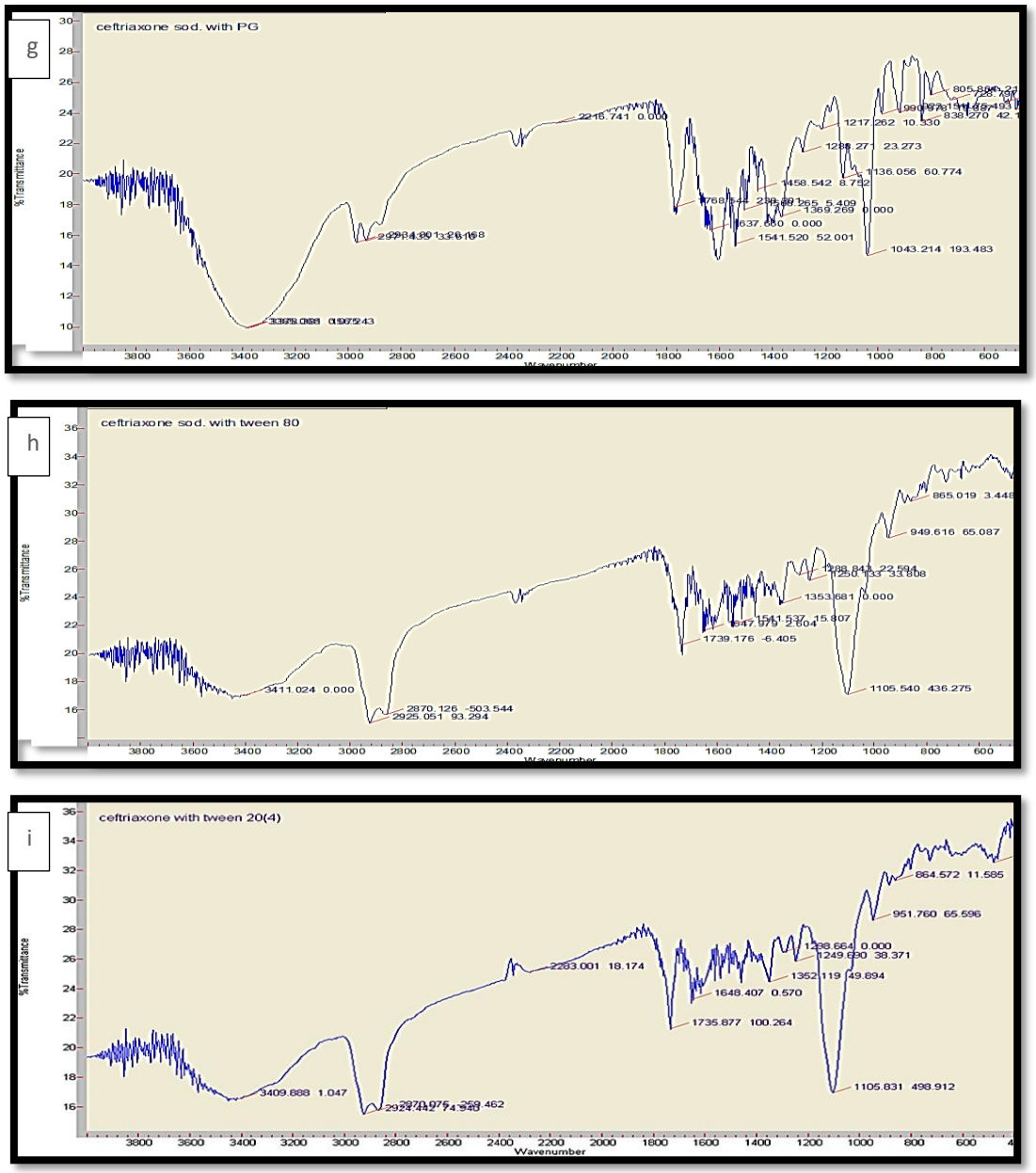
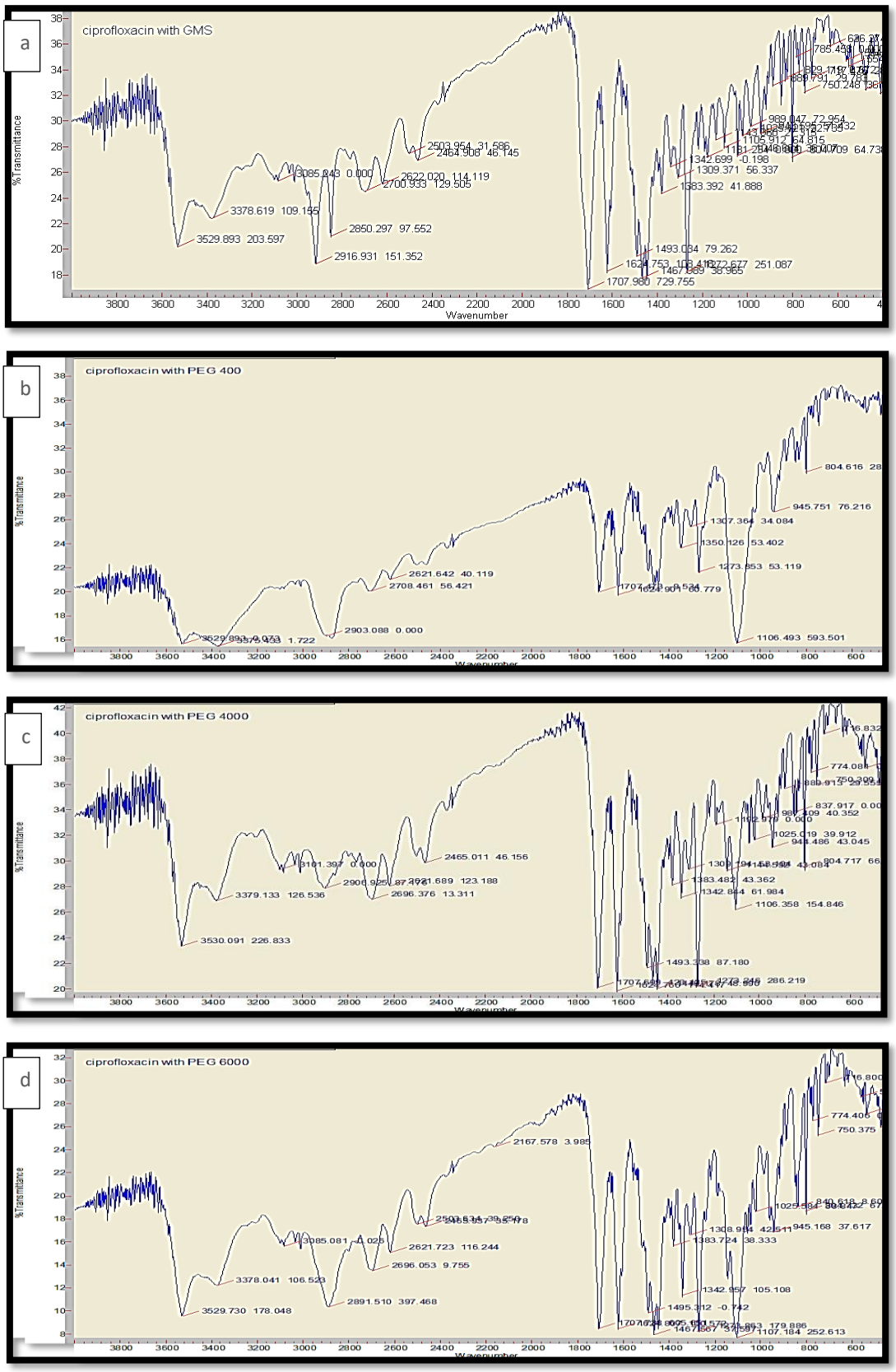
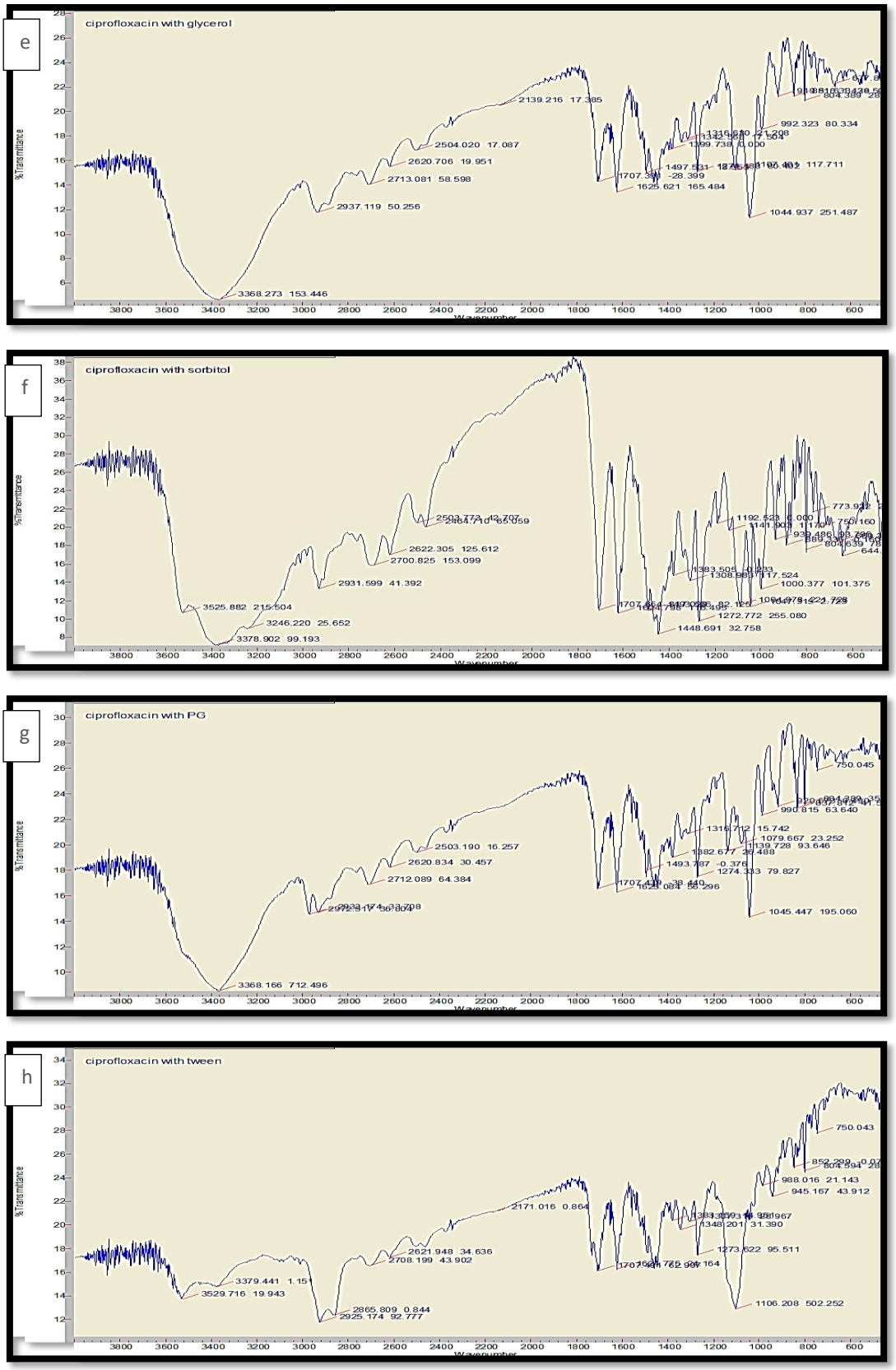


Fig. 2: Spectra of **(a)** CTX & GMS, **(b)** CTX & PEG 400, **(c)** CTX & PEG 4000, **(d)** CTX & PEG 6000, **(e)** CTX & Glycerol, **(f)** CTX & Sorbitol, **(g)** CTX & PG, **(h)** CTX & Tween 80, **(i)** CTX & Tween 20.

Regarding the FTIR spectra related to CTX represented in Figure 2 (a, b, c, d, e, f, g, h, and i), specifically, there are slight differences in the appearance of some bands such as β-lactam C=O stretching vibrations at 1735 to 1768 (normally must be at1745 ± 15), N-H stretching mode of H-bonded amide group which appearing at 3254 to 3411 (ideally must be appeared at 3700 - 3500) & oxime C=N stretching vibrations (usually appeared at 1665± 15) which only shifted toward a lower wavelength of 1637 cm^{-1}in case of propylene glycol confirms the existence of very low interaction of the CTX and excipient as shown in Figure 2 (g), which can be ignored because it is very simple and may be due to other things related to the device and not in the way of preparation such as when the instrument itself is flawed and provides inaccurate readings (systematic errors). As a result, the IR spectral interpretation showed that the spectra obtained from the binary mixtures in Figure 2 (a, b, c, d, e, f, g, h, and i) match with the original spectra of API in Figure 1(a). Generally, there was no obvious and influential change of any characteristic peaks which confirms the absence of chemical interaction between the CTX and excipients.


a
ciprofloxacin with GMS
%Transmittance
Wavenumber
3529.893 203.597
3378.619 109.155
2916.931 151.352
2850.297 97.552
3085.843 0.000
2700.933 129.505
2622.020 114.119
2503.954 31.586
2464.906 46.145
1707.980 729.755
1493.034 79.262
1342.699 -0.198
1309.371 56.337
1383.392 41.888
b
ciprofloxacin with PEG 400
2903.088 0.000
2708.461 56.421
2621.642 40.119
1106.493 593.501
1273.853 53.119
1350.126 53.402
1307.364 34.084
945.751 76.216
804.616
c
ciprofloxacin with PEG 4000
3530.091 226.833
3379.133 126.536
3101.397 0.000
2906.925 87.721
2696.376 13.311
2621.689 123.188
2465.011 46.156
1493.338 87.180
1383.482 43.362
1342.864 61.984
1106.358 154.846
1025.019 39.912
944.486 43.045
837.917 0.00
774.088
d
ciprofloxacin with PEG 6000
3529.730 178.048
3378.041 106.523
3085.081 -1.025
2891.510 397.468
2696.053 9.755
2621.723 116.244
2503.834 39.850
2167.578 3.985
1495.312 -0.742
1383.724 38.333
1342.957 105.108
1308.994 42.511
945.168 37.617
774.406
750.375


e
ciprofloxacin with glycerol
%Transmittance
Wavenumber
3368.273 153.446
2937.119 50.256
2713.081 58.598
2620.706 19.951
2504.020 17.087
2139.216 17.385
1625.621 165.484
1497.531
1044.937 251.487
992.323 80.334
f
ciprofloxacin with sorbitol
3525.882 215.504
3246.220 25.652
3378.902 99.193
2931.599 41.392
2700.825 153.099
2622.305 125.612
1448.691 32.758
1272.772 255.080
1000.377 101.375
g
ciprofloxacin with PG
3368.166 712.496
2712.089 64.384
2620.834 30.457
2503.190 16.257
1045.447 195.060
990.815 63.640
750.045
h
ciprofloxacin with tween
3529.716 19.943
3379.441 1.15
2865.809 0.844
2925.174 92.777
2621.948 34.636
2708.199 43.902
2171.016 0.864
1106.208 502.252
988.016 21.143
945.167 43.912
750.043

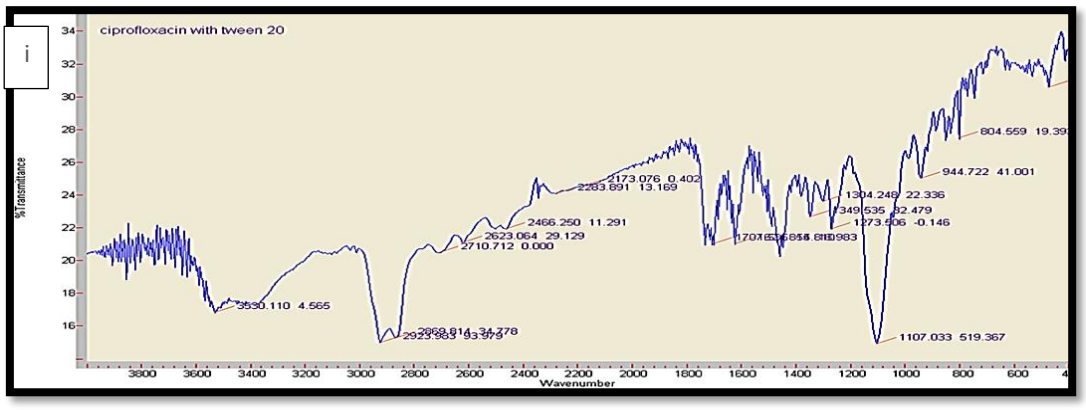


Fig. 3: Spectra of **(a)** CIPRO & GMS, **(b)** CIPRO & PEG 400, **(c)** CIPRO & PEG 4000, **(d)** CIPRO & PEG 6000, **(e)** CIPRO & Glycerol, **(f)** CIPRO & Sorbitol, **(g)** CIPRO & PG, **(h)** CIPRO & Tween 80, **(i)** CIPRO & Tween 20.

The compatibility test of CIPRO was performed using the FTIR instrument. The result was based on matching the peak of the pure API (CIPRO) with the drug excipient binary mixtures. From our results, it can be demonstrated that there was no interaction between CIPRO and excipients used in the formulations & was found to fulfill the criteria of typical binary mixtures as shown in Figures 3 (a, b, c, d, e, f, g, h, and i).

3.3. Isothermal stability testing (IST)

For the quantitative assessment, approved spectrophotometer techniques were employed [36,37]. The aqueous solutions of CTX or CIPRO showed maximum absorbance at 242, and 276 nm respectively, the water shows no significant absorbance at these wavelengths so more analysis was carried out at these wavelengths using water as a blank. The results of IST are shown in Table (2).

Table (2): Amount of API Remaining After IST

No	Samples	Ratio	% of API remaining after 3 weeks (mean ±SD)	
			Control sample [a]	Stressed sample [b]
1	CTX	1:0	105.946±6.763	102.884±2.733
2	CTX + GMS	1:1	105.746±8.157	102.645±5.073
3	CTX + PEG400	1:1	98.457±2.876	96.418±1.995
4	CTX + PEG4000	1:1	111.585±4.153	114.07±0.335
5	CTX + PEG6000	1:1	103.981±10.917	104.827±1.773
6	CTX + Glycerol	1:1	96.612 ± 0.321	95.287±2.605
7	CTX + Sorbitol	1:1	102.376±14.983	103.787±7.027
8	CTX + PG	1:1	95.932±7.446	93.590±9.113
9	CTX + Tween 20	1:1	111.956± 2.985	110.368±0.044
10	CTX + Tween 80	1:1	110.259±11.464	111.893±1.046
1	CIPRO	1:0	94.599±0.959	93.458±2.586
2	CIPRO + GMS	1:1	92.221±1.376	91.328±2.445
3	CIPRO+ PEG400	1:1	95.221±2.272	94.160±2.013
4	CIPRO+PEG4000	1:1	94.200±0.793	94.0924±0.597
5	CIPRO+PEG6000	1:1	92.288±1.493	91.176±1.480
6	CIPRO+ Glycerol	1:1	89.451±3.308	90.216±1.206
7	CIPRO + Sorbitol	1:1	93.405±1.839	92.758±2.032
8	CIPRO + PG	1:1	91.269±1.377	90.182±1.510
9	CIPRO+Tween20	1:1	92.197±0.546	91.648±0.866
10	CIPRO+Tween80	1:1	90.910±2.955	90.4578±1.062

a= control sample (API + excipient) were stored at refrigerator without adding water,
b= stressed sample (API + excipient) were stored at 50˚C with adding 10% w/w water.

In the IST, the API – excipient mixture showed no significant change in physical properties. There was no change in color, gas formation, and liquefaction of the mixture stored under stress conditions. The amount of API remaining after being stored in stressed condition was represented in Table 2. Also, there was no significant change in statistical significance (p = 0.05) in API content when analyzed after storage in stress conditions as data treated by independent T-test using SPSS version 20.

Mild liquefaction was observed in a mixture of CTX – PG but there was no significant change in drug content. As a result, the binary mixture of API and excipient could be used successfully in developing of biodegradable lipid base formulation for the prevention of post-operative infection.

The amount of API remaining after being stored in stressed condition was represented in Table 2. Also, there was no significant change at statistical significance (p = 0.05) in API content when analyzed after storage in stress conditions as data treated by independent T-test using SPSS version 20.

4. Conclusions

Based on the results obtained from the pre-formulation study, the FTIR spectrum of the prepared mixture revealed that there was no chemical interaction between the components. All the ingredients were studied for compatibility between them. For that purpose, the infrared spectra of the individual drug (CTX, CIPRO) were compared with the infrared spectra of API excipient binary mixtures. The IR spectral interpretation showed that the spectra obtained from the API excipient binary mixtures match the original spectra of the drug (CTX, CIPRO). Generally, there was no obvious and influential change of any characteristic peaks which confirms the absence of chemical interaction between the API and excipients, & was found to fulfill the criteria of typical binary mixtures. In conclusion, these results agree with the results of IST, in which there is no significant difference at (p 0.05) in API content after 21 days stored at stressed conditions.

5. Acknowledgment: -

I would like to express my extreme thanks for the teamwork in the research and development center at Modern Pharma and Global Pharma Company for their support and helps. Great thanks to my collagenous in the faculty of pharmacy, at Aden University for their help and patience.

References

[1] Liltorp, K., et al. “Solid state compatibility studies with tablet excipients using non-thermal methods”. *JPBA*, Vol. 55, No. 3: p. 424-428. 2011.

[2] Verma, R.K. and S. Garg, “Compatibility studies between isosorbide mononitrate and selected excipients used in the development of extended release formulations”. *JPBA*, Vol. 35, No. 3: p. 449-458. 2004.

[3] R Gaur, M.A., J Gan, P Hansal, K Harper, R Mannan, A Panchal, K Patel, M Patel, N Patel, J Rana, A Rogowska, “British Pharmacopoeia”. *BP*, Commission Laboratory, ed. Vol. 1, 2, London: The Crown Copyright. 1169-1173, 1381-1385. 2009.

[4] Balant, L.P., P. Dayer, and R. Auckenthaler, “Clinical pharmacokinetics of the third generation cephalosporins”. *Clin. Pharmacokinet* , Vol. 10, No. 2: p. 101-143. 1985.

[5] William A. Petri, J., “Penicillin's, Cephalosporin's, and Other β-Lactam Antibiotics”, in *Goodman & Gilman’s The Pharmacological Basis of therapeutics*, P. Laurence L. Brunton, Editor.The McGraw-Hill Companies: the United States. p. 1477-1503. 2011.

[6] Reynolds, J.E., Martindale: “the extra pharmacopoeia”. London, *UK*; The Pharmaceutical Press. 1982.

[7] Wiseman, L.R. and J.A. Balfour, “Ciprofloxacin, A Review of its Pharmacological Profile and Therapeutic Use in the Elderly”. *Drugs Aging*, Vol. 4, No. 2: p. 145-173. 1994.

[8] Ong, H.X., et al., “Ciprofloxacin is actively transported across bronchial lung epithelial cells using a Calu-3 air interface cell model”. *AAC*, Vol. 57, No. 6: p. 2535-2540. 2013.

[9] Landersdorfer, C.B., et al., “Competitive inhibition of renal tubular secretion of ciprofloxacin and metabolite by probenecid”. *BJCP*, Vol. 69, No. 2: p. 167-178. 2010.

[10] Westesen, K. and B. Siekmann, “Solid lipid particles, particles of bioactive agents and methods for the manufacture and use thereof”. *Google Patents*. 1998

[11] Menei, P., et al., “Local and sustained delivery of 5-fluorouracil from biodegradable microspheres for the radiosensitization of glioblastoma”: A pilot study. *Cancer*: Interdisciplinary International Journal of the ACS, Vol. 86, No. 2: p. 325-330. 1999.

[12] Menei, P., et al., "Stereotaxic implantation of 5-fluorouracil-releasing microspheres in malignant glioma: A Phase I study". *Cancer*, Vol. 100, No. 2: p. 405-410. 2004.

[13] Menei, P., et al., "Local and sustained delivery of 5-fluorouracil from biodegradable microspheres for the radiosensitization of malignant glioma: a randomized phase II trial". *Neurosurgery*, Vol. 56, No. 2: p. 242-248. 2005.

[14] Grizzi, I., et al., "Hydrolytic degradation of devices based on poly (DL-lactic acid) size-dependence". *Biomaterials*, Vol. 16, No. 4: p. 305-311. 1995.

[15] Lu, L., C.A. Garcia, and A.G. Mikos, "In vitro degradation of thin poly (DL-lactic-co-glycolic acid) films". *J. Biomed. Mater. Res*, Vol. 46, No. 2: p. 236-244. 1999.

[16] Kang, J. and S.P. Schwendeman, "Comparison of the effects of Mg (OH) 2 and sucrose on the stability of bovine serum albumin encapsulated in injectable poly (D, L-lactide-co-glycolide) implants". *Biomaterials*, Vol. 23, No. 1: p. 239-245. 2002.

[17] Guse, C., et al., "Programmable implants—From pulsatile to controlled release". *Int. J. Pharm*, Vol. 314, No. 2: p. 161-169. 2006.

[18] Guse, C., et al., "Drug release from lipid-based implants: elucidation of the underlying mass transport mechanisms". *Int. J. Pharm*, Vol. 314, No. 2: p. 137-144. 2006.

[19] Filipczak, N. Yalamarty, S.S.K. Li, X. Khan, M.M. Parveen, F. Torchilin, V., "Lipid-Based Drug Delivery Systems in Regenerative Medicine". *Materials (Basel)*, Vol. 14, No. 18: p. 6-7. 2021

[20] Attama, A.A. and M.O. Nkemnele, "In vitro evaluation of drug release from self micro-emulsifying drug delivery systems using a biodegradable homolipid from Capra hircus". *Int. J. Pharm*, Vol. 304, No. 1-2: p. 4-10. 2005.

[21] Craig, D., "Lipid matrices for sustained release: An academic overview". Bull. tech. Gattefossé, 97: p. 9-19. 2004.

[22] Lima, N.G., et al., "Compatibility studies of trioxsalen with excipients by DSC, DTA, and FTIR". *J Therm Anal Calorim*, Vol. 115, No. 3: p. 2311-2318. 2014.

[23] Aigner, Z., et al., "Compatibility studies of aceclofenac with retard tablet excipients by means of thermal and FT-IR spectroscopic methods". *J Therm Anal Calorim*, Vol. 104, No. 1: p. 265-271. 2011.

[24] Canbay, H.S. and M. Doğantürk, "Application of differential scanning calorimetry and fourier transform infrared spectroscopy to the study of metoprolol-excipient and lisinopril-excipient compatibility". *EJAC*, Vol. 13, No. 5: p. em39. 2018.

[25] Baru, R.T. and P. Bitla, "Cyclobenzaprine drug assay and Cyclobenzaprine-excipient interaction study by chromatography, thermal and spectral analysis". *J Pharm Chem Chem* Sci. 2017; Vol. 1, No. 1: 1-9, 2018.

[26] Pawar, A.Y., et al., "Compressed glyceryl monostearate based biodegradable implant of Gentamicin using melt granulation technique: In vitro evaluation & biocompatibility in animals". *DRUG INVENTION TODAY*, Vol. 5, No. 1: p. 39-49. 2013.

[27] Verma, R.K. and S. Garg, "Selection of excipients for extended release formulations of glipizide through drug–excipient compatibility testing". *JPBA*, Vol. 38, No. 4: p. 633-644. 2005.

[28] Karwa, P., P. Kasture, and R. Kimbahune, "Application of Thermal and Isothermal Methods for Compatibility Studies of Metoprolol Succinate with Carbopol Polymers". *IAJPR*, Vol. 3, No. 11: p. 9085-9092. 2013.

[29] Rosasco, M.A., et al., "Compatibility study of tobramycin and pharmaceutical excipients using differential scanning calorimetry, FTIR, DRX, and HPLC". *J Therm Anal Calorim*, Vol. 134, No. 3: p. 1929-1941. 2018.

[30] Shahe Mahammad, S., M. Chetty, and K. Ramana Murthy, "Preformulation studies of quetiapine fumarate". *J Pharm Res*, 5: p. 672-7. 2012.

[31] AHMED, A.B. and L.K. NATH, "Drug-excipients compatibility studies of nicorandil in controlled release floating tablet". *Int. J. Pharm. Pharm*. Sci, Vol. 6, No. 2: p. 468-475. 2014.

[32] Kunasekaran, V. and K. Krishnamoorthy, "Compatibility studies of rasagiline mesylate with selected excipients for an effective solid lipid nanoparticles formulation". *Int. J. Pharm. Pharm*. Sci, 7: p. 73-80. 2015.

[33] Pani, N.R., L.K. Nath, and B. Bhunia, "Formulation, development, and optimization of immediate release nateglinide tablets by factorial design". *ddtj*, Vol. 4, No. 6: p. 453-458. 2010.

[34] Manikandan, M., K. Kannan, and R. Manavalan, "Compatibility studies of camptothecin with various pharmaceutical excipients used in the development of nanoparticle formulation". *Int J Pharm Pharm* Sci, Vol. 5, No. 4: p. 315-321. 2013

[35] Sachin, T., M. Deodhar, and V. Prakya, "Advances in analytical techniques used in predicting drug-excipient interactions*". Int. J. Pharm*. Tech, Vol. 6, No. 1: p. 6388. 2014.

[36] Naveed, S. and N. Waheed, "Simple UV spectrophotometric assay of ciprofloxacin". *MJPMS*, 3: p. 10 -13. 2014.

[37] Patel, K., et al., "Development and validation of spectrophotometric method for determination of ceftriaxone sodium in pharmaceutical dosage forms". *Der Pharma Chemica*, Vol. 2, No. 5: p. 255-259. 2010.

مقالة بحثية

دراسة ما قبل الصياغة لسيفترايكسون و سيبروفلوكساسين لأنظمة توصيل الأدوية القائمة على الدهون

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المُلخّص

هناك عدة اختبارات لابد من اجراءها لاستبعاد أي تفاعلات فيزيائية أو كيميائية محتملة بين المادة الفعالة والسواغات المختلفة التي يمكن استخدامها في تصنيع الاشكال الصيدلانية. ان التحليل الطيفي باستخدام الأشعة تحت الحمراء هو تقنية بسيطة للكشف عن التغيرات داخل مخاليط الأدوية و السواغات. بالإضافة إلى تسريع عملية شيخوخة الأدوية وتفاعلاتها المحتملة مع السواغات تم إستخدام اختبار الإجهاد متساوي الحرارة. في هذه الدراسة خضعت المواد الفعالة (سيفترايكسون، سيبروفلوكساسين) لأختبارات وذلك لاستبعاد اي تفاعل مع السواغات المستخدمه في صياغة الدهون القابلة لتحلل وذلك للوقاية من العدوى المحتملة بعد العمليات الجراحية. تم اختبار التوافق باستخدام التحليل الطيفي للأشعة تحت الحمراء واختبار استقرار متساوي الحرا رة. ونتيجة لذلك يوضح التفسير الطيفي أن الاطياف التي تم الحصول عليها من المخاليط الثنائية تتطابق مع الأطياف الاصلية للمواد الفعالة كلا على حده. بشكل عام، لم يكن هناك تغيير واضح ومؤثر في أي قمم مميزة مما يؤكد عدم وجود تفاعل كيميائي بين السيفترايكسون او السيبروفلوكساسين و السواغات المستخدمة. في اختبار ثبات متساوي الحرارة، لم يظهر المزيج الثانئي أي تغير كبير في الخصائص الفيزيائية, حيث لم يكن هناك أي تغير في اللون او انطلاق الغازات او تحول الخليط المخزون الى سائل في ظروف الاجهاد. لم يحدث اي تغير معنوي في كمية المواد الفعالة بعد خزنها في الظروف المجهده عند القيمة المعنوبة (0.05).في الختام، لا توجد تفاعلات ملحوظة بين المواد الفعالة ومختلف السواغات التي يمكن استخدامها لإنشاء مضادات حيوية قائمة على الدهون قابلة للتحلل والتي تكون فعالة في منع العدوى بعد الجراحة.

الكلمات المفتاحية: دراسة ما قبل الصياغة، سيفترايكسون، سيبروفلوكساسين، دهون القابلة لتحلل، الأطياف للمواد الفعالة.

How to cite this article:

M. M .Alburyhi, A. A .Saif and R. M .Saif, "PREFORMULATION STUDY OF CEFTRIAXONE AND CIPROFLOXACIN FOR LIPID BASED DRUG DELIVERY SYSTEMS", *Electron. J. Univ. Aden Basic Appl. Sci.*, vol. 3, no. 4, pp. 339-350, Dec. 2022. DOI: https://doi.org/10.47372/ejua-ba.2022.4.204