© 2020 Journal of Pharmacy & Pharmacognosy Research, 8 (4), 336-345, 2020
ISSN 0719-4250
http://jppres.com/jppres

Original Article | Artículo Original

Characterization of microparticles prepared by the solvent evaporation method, use of alcohol-soluble cellulose acetate butyrate as a carrier

[Caracterización de micropartículas preparadas por el método de evaporación del solvente, uso de acetato butirato de celulosa soluble en alcohol como vehículo]

Aram Ibrahim and Rebaz Ali*

College of Pharmacy, University of Sulaimani, City Center Campus, Sulaimani, Kurdistan Region, Iraq.
*E-mail: rebaz.ali@univsul.edu.iq

Abstract

Context: Cellulose esters such as cellulose acetate, cellulose acetate butyrate and cellulose acetate propionate are used in solid pharmaceutical dosage forms for controlling drug delivery. The property of cellulose acetate butyrate (CAB) varies according to butyryl, acetyl and hydroxyl level. These polymers are soluble in flammable organic solvents such as acetone. CAB-553-0.4, however, is characterized by its solubility in a less harmful organic solvents such as low molecular weight alcohol.

Aims: To evaluate the use of CAB-553-0.4 as a new carrier for the preparation of microparticles by solvent evaporation method and comparing the result to the well-known carrier i.e., ethylcellulose (EC).

Methods: The polymer organic phase containing carbamazepine or propranolol HCl was dispersion in an aqueous media containing polyvinyl alcohol (PVA). Percent of encapsulation efficiency, EE%, was calculated and *in vitro* drug release from the microparticles was investigated.

Results: EE% of EC microparticles was relatively high (71%) for carbamazepine and low for propranolol HCl. However, the EE% of propranolol HCl increased by two folds when CAB used as a carrier. EE% of carbamazepine was decreased by increasing the volume of the aqueous phase from EC- and unchanged from CAB-microparticles. The optimum concentration of PVA was 0.25% w/v and the EE% was decreased with increasing temperature. Carbamazepine release from EC- and CAB-microparticles was similar, however, propranolol HCl release was slower from CAB- microparticles than EC microparticles.

Conclusions: CAB-553-0.4 is an interesting carrier for the formulation of microparticles, loaded with a water-soluble drug, by solvent evaporation.

Keywords: cellulose acetate butyrate; drug release; encapsulation efficiency; microparticles; solvent evaporation.

Resumen

Contexto: Los ésteres de celulosa tales como el acetato de celulosa, el butirato acetato de celulosa y el propionato acetato de celulosa se usan en formas farmacéuticas sólidas para controlar la administración de fármacos. La propiedad del butirato acetato de celulosa (CAB) varía según el nivel de butirilo, acetilo e hidroxilo. Estos polímeros son solubles en solventes orgánicos inflamables como la acetona. CAB-553-0.4, sin embargo, se caracteriza por su solubilidad en solventes orgánicos menos dañinos como el alcohol de bajo peso molecular.

Objetivos: Evaluar el uso de CAB-553-0.4 como un nuevo vehículo para la preparación de micropartículas por el método de evaporación del solvente y comparar el resultado con el vehículo conocido, es decir, etilcelulosa (EC).

Métodos: La fase orgánica del polímero que contenía carbamazepina (CZ) o propranolol HCl (PP) se dispersó en un medio acuoso que contenía alcohol polivinílico (PVA). Se calculó el porcentaje de eficiencia de encapsulación, %EE, y se investigó la liberación *in vitro* del fármaco desde las micropartículas.

Resultados: El %EE de las micropartículas de EC fue relativamente alto (71%) para CZ y bajo para PP. Sin embargo, el %EE del PP aumentó en dos veces cuando se usó CAB como vehículo. El %EE de CZ disminuyó al aumentar el volumen de la fase acuosa de las micropartículas CAB y sin cambios de las micropartículas CAB. La concentración óptima de PVA fue de 0,25% p/v y el %EE disminuyó al aumentar la temperatura. La liberación de CZ desde las micropartículas EC y CAB fue similar, sin embargo, la liberación de PP fue más lenta desde las micropartículas CAB que las micropartículas EC.

Conclusiones: CAB-553-0.4 es un vehículo interesante para la formulación de micropartículas, cargadas con un fármaco soluble en agua, por evaporación del disolvente.

Palabras Clave: acetato butirato de celulosa; eficiencia de encapsulación; evaporación de solvente; liberación de drogas; micropartículas.

ARTICLE INFO
Received: February 20, 2020.
Received in revised form: March 16, 2020.
Accepted: March 18, 2020.
Available Online: March 19, 2020.
Declaration of interests: The authors declare no conflict of interest.
Funding: This research was not funded and did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

INTRODUCTION

Microparticles are defined as solid particles with sizes in the range of micrometers (1 to 1000 µm) in which the drug is dissolved, entrapped, encapsulated or attached to a microparticles matrix (Nikam et al., 2016). They are formulated to protect the drug core from the environment, eliminate incompatibilities, masking of unpleasant taste, modifying the drug release, improving bioavailability and minimizing the side effects (Gattani, 2010).

Many methods such as coacervation (Sanders et al., 1984), spray drying (Bodmeier and Chen, 1988), supercritical fluid extraction (York, 1999), and solvent evaporation (Gharge and Bhandare, 2018) are used for the formulation of microparticles.

Despite spray drying is relatively simple, however, its use for highly temperature-sensitive compounds is limited. On the other hand, coacervation is frequently affected by residual solvents and coacervating agents found in the microspheres (Freitas et al., 2005).

Solvent evaporation technique is widely used in the preparation of microparticles nowadays. In this method, the drug-polymer organic solution is emulsified under agitation in a dispersing phase consisting of a non-solvent of the polymer and is immiscible with the organic solvent, which contains an appropriate emulsifying agent (Watts et al., 1990). Unlike other methods, solvent evaporation neither requires elevated temperatures nor phase separation inducing agents (Freitas et al., 2005). Selecting a particular method is primarily determined by the solubility of the drug and polymer. Solvent evaporation method is a common method for the encapsulation of water-insoluble drugs within water-insoluble polymers. Meanwhile, water-soluble drugs have been encapsulated by using an external oil phase instead of an aqueous phase (Alex and Bodmeier, 1990).

Many polymers such as ethylcellulose (Muhaimin and Bodmeier, 2017), cellulose acetate (Chandiran Irisappan et al., 2013), Eudragit® RS and RL (Lokhande et al., 2014), Eudragit® S (Lee et al., 2000), polylactic acid (Zhang et al., 2018) and poly lactic-co-glycolic acid (Hamishehkar et al., 2009) have been used for the preparation of microparticles by solvent evaporation technique.

Unlike other cellulose acetate butyrates, CAB-553-0.4 is soluble in low molecular weight alcohol due to higher hydroxyl content (Eastman, 2006). Additionally, it is stronger, more flexible and more permeable than ethylcellulose (Ali et al., 2018).

The main objective of the present work was to use CAB-553-0.4 as a carrier for the preparation of microparticles by the solvent evaporation method and determining the factors that may affect the encapsulation efficiency. Propranolol HCl and carbamazepine were used as model drugs, water-soluble and water-insoluble, respectively.

MATERIAL AND METHODS

Materials

Carbamazepine and propranolol HCl (BASF AG, Ludwigshafen, Germany); ethylcellulose standard 4 premium (Ethocel®, Colorcon Ltd, Dartford, Kent, UK); cellulose acetate butyrate (CAB-553-0.4, Krahn Chemie GmbH, Hamburg, Germany); sodium lauryl sulfate, SLS (Gainland chemical company, Deeside, UK); chloroform (Scharlau, Barcelona, Spain); polyvinyl alcohol, PVA (Mowiol® 4-88, Carl Roth GmbH + Co. KG, Karlsruhe, Germany); methanol and ethyl acetate (Merck, Darmstadt, Germany).

Preparation of microparticles

Cellulose acetate butyrate or ethylcellulose (0.6 g) and carbamazepine or propranolol HCl (0.4 g) were dissolved in 9 g of the organic solvent(s) to achieve the solid content of 10% w/w. The organic solvent was then emulsified into 800 mL of the aqueous phase containing 0.25% w/v (if not otherwise mentioned) PVA as an emulsifying agent at room temperature (if not otherwise mentioned). The resulting emulsion was agitated continuously by a propeller mixer (Heidolph Stirrer RZR1, Kelheim, Germany) until the organic solvent com-

pletely evaporated and solid microparticles were formed. The microparticles were then collected by filtration and washed with distilled water before drying in an oven (Binder, Tuttlingen, Germany) at 40°C for 24 h. The dried microparticles were screened through stainless steel sieves (Analysenieb, Haan, Germany), sizes of 315-725 µm were collected and stored at room temperature.

Viscosity measurement

The viscosity of 6% w/w polymers solution was determined using the viscometer (Visco basic plus, New York, USA) at 100 rpm using R2 spindle.

Encapsulation efficiency

In order to extract the drug, the microparticles were dissolved in the ethanol-water mixture and the drug content was determined by spectrophotometer (Shimadzu 1700, Japan) at λmax of 285.5 and 289 nm for carbamazepine and propranolol HCl, respectively.

The percent of encapsulation efficiency (EE%) was calculated according to the following equation [1]:

$$EE\ \% = \frac{actual\ drug\ content\ in\ the\ microparticles}{theoretical\ drug\ content} \times 100 \qquad [1]$$

Drug solubility measurement

An excess amount of carbamazepine was added to 0.1 N HCl with or without SLS (0.25% or 0.5%). Samples (n = 3) were shaken using laboratory shaker (GFL - Orbital Shaker - Model 3017, Burgwedel, Germany) until equilibrium achieved. The samples were filtered, and the drug concentration was measured by spectrophotometer after appropriate dilution.

Particle size measurement

Particle size of the microparticles is measured by a digital microscope (KKMOON Electronic microscope 1600×, China) and particle morphology was investigated with a scanning electron microscope SEM (CamScan 3200LV, Ashford, England) in which the microparticles were mounted on stubs and coated for 120 s with a layer of gold using a sputter coater.

Drug release study

The *in vitro* drug release from the microparticles was performed by the rotating bottle method using laboratory shaker (GFL - Orbital Shaker - Model 3017, Burgwedel, Germany) at room temperature. Samples (n = 3) of the drug-loaded microparticles (20-30 mg) were suspended in 100 mL of dark glass bottles containing 100 mL of the dissolution medium (0.1N HCl and 0.1N HCl containing 0.5% SLS). The glasses were sealed tightly and rotated at 100 rpm. Samples of 5 mL were withdrawn at predetermined time intervals and replaced with the fresh media to maintain the original volume (n = 3). The samples were assayed spectrophotometrically either directly or after appropriate dilution with the release medium.

Statistical analysis

The similarity factor (f_2) was used to establish the similarity of two release profiles [2] (Polli et al., 1997):

$$f_2 = 50 \times \log\left\{\left[1 + (1/n)\sum(R_t - T_t)^2\right]^{-0.5} \times 100\right\} \qquad [2]$$

n = number of pull points for tested samples, R_t = reference assay at time points t, T_t = test assay at time points t.

f_2 values higher than 50 (50–100) shows the similarity of the release profiles.

RESULTS AND DISCUSSION

Microparticles containing carbamazepine or propranolol HCl were prepared by the solvent evaporation technique. After the drug-polymer solution was emulsified into the aqueous phase, the organic solvent starts to evaporate from the droplet surface into the aqueous phase. The solvent loss resulted in an increase in polymer concentration at the phase boundary (Bodmeier and Mcginity, 1987a). Phase separation and polymer precipitation will be initiated at the droplet surface when the concentration limit for the polymer precipitation is reached. The drug partitioning into

the aqueous phase continues as long as the droplet is in a liquid state. Once the polymer precipitated at the droplet surface, the drug loss into the aqueous phase will not occur (Bodmeier and Mcginity, 1988).

Effect of formulation parameters on the encapsulation efficiency

To investigate the effect of organic solvent on the EE%, chloroform, methanol, and ethyl acetate were used and CAB, as a carrier, was compared to ethylcellulose (Table 1). The basic requirement for microparticles formation is the water immiscibility of the organic solvent. Due to miscibility with water, a fluffy irregular mass was obtained instead of microparticles when methanol was used as an organic solvent (Fig. 1). Regardless of the carrier and drug solubility, microparticles were achieved with chloroform and ethyl acetate (Fig. 2) and EE% was very similar (Table 1).

Carbamazepine loaded microparticles were rough and less spherical when prepared with chloroform and propranolol HCl loaded microparticles were more spherical and smoother especially when using ethyl acetate (Fig. 2). This is probably due to the higher solubility, faster evaporation rate, of ethyl acetate in water, namely, 8.7% and 0.8% for ethyl acetate and chloroform, respectively (Muhaimin and Bodmeier, 2017). Using the blend of organic solvents, namely chloroform:methanol at a ratio of 8:1, increased the EE% irrespective of the carrier and drug solubility, this is due to faster polymer precipitation at the droplet surface and decreasing drug partitioning.

Figure 1. Dispersion of CAB methanol solution in water containing PVA.

Table 1. Effect of organic solvents and polymer on the encapsulation efficiency.

Polymer (0.6 g)	Drug (0.4 g)	Organic solvents (g)			EE (%)
		Chloroform	Methanol	Ethyl acetate	
EC	Carbamazepine	-	9	-	-
		-	-	9	59.0 ± 2.1
		9	-	-	62.0 ± 2.0
		8	1	-	71.0 ± 3.2
	Propranolol HCl	-	9	-	-
		-	-	9	17.0 ± 2.3
		9	-	-	17.5 ± 2.1
		8	1	-	21.0 ± 3.1
CAB	Carbamazepine	-	9	-	-
		-	-	9	56.0 ± 2.0
		9	-	-	56.5 ± 2.6
		8	1	-	62.0 ± 3.2
	Propranolol HCl	-	9	-	-
		-	-	9	25.0 ± 2.5
		9	-	-	25.0 ± 2.1
		8	1	-	38.0 ± 3.0

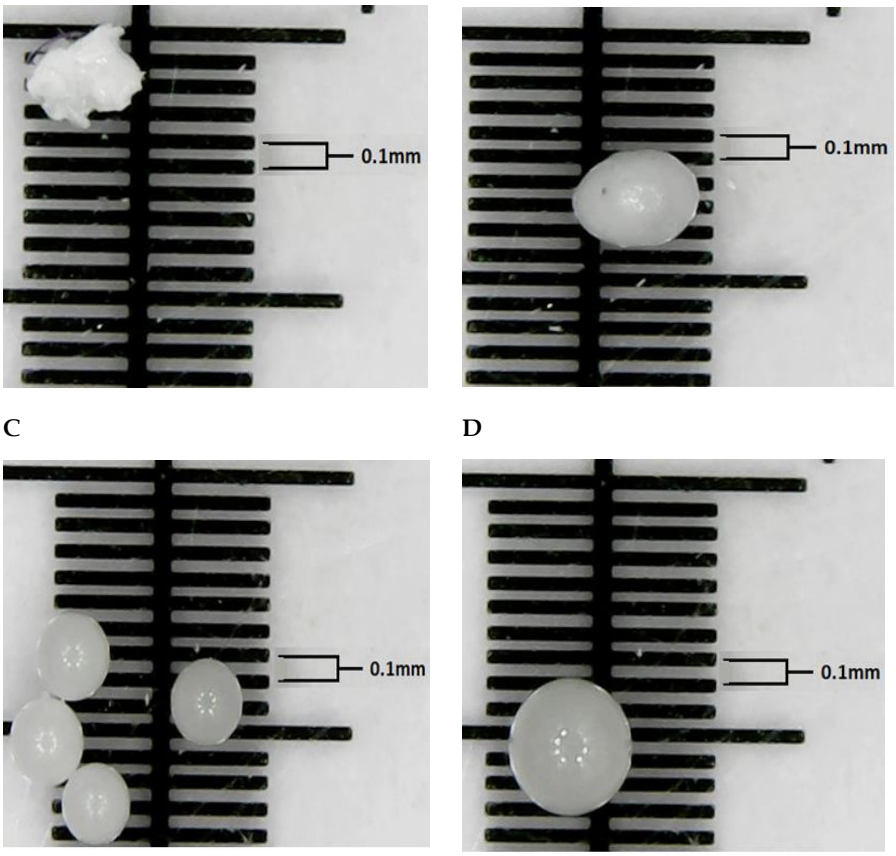

Figure 2. Carbamazepine (**A** and **B**) and propranolol HCl (**C** and **D**) loaded CAB microparticles when chloroform and ethyl acetate used as organic solvents, respectively.

Due to high water solubility and fast partitioning into the aqueous phase, EE% of the water-soluble drug, propranolol HCl, from ethylcellulose microparticles was low 21%. Interestingly, EE% of propranolol HCl was increased to 38% when CAB was used as a carrier. This is probably due to the physicochemical difference between these polymers (Ali et al., 2018). Additionally, the average size of CAB microparticles was larger than EC microparticles prepared under the same condition due to higher viscosity of the former than the latter, 64 cP vs 46 cP. With increased viscosity more energy is needed to divide the globules into smaller particles, which increase the mean particle size (Jelvehgari et al., 2011).

The volume of the external phase has a direct influence on the microparticle formation and encapsulation efficiency because the diffusion rate of the organic phase depends on the volume of the external phase (Bodmeier and Mcginity, 1987b). In the case of carbamazepine loaded microparticles, increasing volume of the external phase, decreased the EE% of EC microparticles, however, propranolol HCl was slightly affected (Table 2). This is probably due to increasing the amount of drug dissolved in the aqueous phase and, therefore, increasing the drug loss form organic phase results in the reduction of the encapsulation efficiency (Sharma et al., 2016). Meanwhile, the EE% was slightly increased from CAB microparticles with increasing external volume irrespective of the drug type. Because the EE% of the water-soluble drug from CAB microparticles was higher than EC microparticles, further study was undertaken on CAB microparticles.

In the emulsion solvent evaporation method, the emulsification and stabilization of the globules are two crucial factors. The surfactant molecules

Table 2. Effect of aqueous to organic phase ratios on the encapsulation efficiency using chloroform: methanol (8:1).

Polymer	Drug	Aqueous phase (L)	EE (%)
EC	Carbamazepine	0.8	71.0 ± 3.2
		1.2	49.0 ± 2.5
		1.6	45.5 ± 2.3
	Propranolol HCl	0.8	21.0 ± 3.1
		1.2	23.0 ± 2.6
		1.6	25.0 ± 2.1
CAB	Carbamazepine	0.8	62.0 ± 3.2
		1.2	69.0 ± 3.0
		1.6	70.0 ± 2.8
	Propranolol HCl	0.8	38.0 ± 3.0
		1.2	39.5 ± 2.5
		1.6	45.0 ± 2.0

tend to align themselves at the droplet surface lowering the free energy at the interface between two phases and resisting coalescence of the droplets (Sharma et al., 2016). The EE% was increased with increasing PVA content from 0.125 to 0.25% w/v and decreased with further increasing PVA content (Table 3). This could be explained by decreased average particle size, which increased the effective surface area exposed to the media and subsequently resulting in increased drug partitioning to the external phase (Bhagav et al., 2011).

Table 3. Effect of PVA concentration in the aqueous phase on the encapsulation efficiency of CAB microparticles loaded with carbamazepine.

PVA (%)	EE (%)
0.125	50.0 ± 2.6
0.25	62.0 ± 3.2
0.5	56.0 ± 2.5
1.0	49.0 ± 2.1

To investigate the effect of temperature, the aqueous phase was heated or cooled in an ice bath. As the temperature of the aqueous phase increased, the EE% was decreased (Table 4). This could be related to the increase of the vapor pressure of the organic solvent, which causes an increase in the flow of molecules across the phase boundary and a disturbance of the interface (Bodmeier and Mcginity, 1987b). In addition, the increase of the temperature may result in increasing the solubility of the water-insoluble drug, and this results in increasing drug partitioning to the aqueous phase (Bodmeier and Mcginity, 1987b).

Table 4. Effect of temperature of the aqueous phase on the encapsulation efficiency from CAB microparticles.

Drug	Temperature (°C)	EE (%)
Carbamazepine	0-5	81.0 ± 2.3
	15	75.0 ± 2.2
	25	62.0 ± 3.2
	40	16.5 ± 2.4
Propranolol HCl	0-5	54.0 ± 2.0
	15	47.0 ± 2.6
	25	38.0 ± 3.0
	40	31.0 ± 2.0

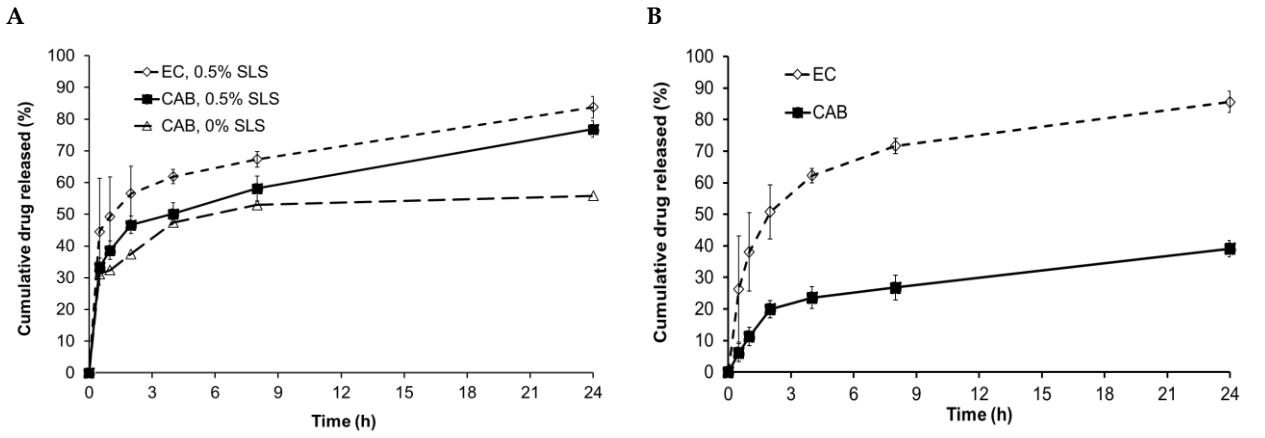

Figure 3. Drug release (**A)** carbamazepine and (**B)** propranolol HCl from EC and CAB microparticles (315-725 µm).

Drug release

Generally, the water solubility of the drug has an influence on the release, as the water solubility increase the rate of drug release is increased and with decreasing solubility the dissolution medium becomes saturated. The solubility was increased from 0.36 mg/mL to 1.71 mg/mL with the addition of 0.5% SLS. The *in vitro* release of carbamazepine and propranolol HCl from CAB and EC microparticle exhibited an initial burst effect, which may be due to the large surface area and the presence of some drug particles on the surface of the microspheres, followed by extended-release (Fig. 3).

The difference in carbamazepine release between CAB- and EC microparticles in 0.1 N HCl containing 0.5% SLS was not significant (f_2 = 52). However, the release was significantly decreased (f_2 = 32) in the media containing no SLS, this is due to poor solubility of carbamazepine and achieving equilibrium solubility (Fig 3A). Despite higher encapsulation efficiency (45% vs 25%), propranolol HCl release was significantly lower (f_2 = 25.8) than carbamazepine from CAB microparticles. Additionally, propranolol HCl release was slower (f_2 = 20.7) from CAB microparticles than EC microparticles (Fig. 3B). Because no change in infrared spectra was noticed (data is not shown), the microparticles were investigated with SEM. Microparticles formulated with EC were very rough, porous and irregular especially when loaded with carbamazepine (Fig 4A-B), hence carbamazepine release was relatively fast. Propranolol HCl microparticles, however, were more spherical and smoother. Cracks and pores were noticed at the surface of the propranolol HCl loaded EC microparticles but not for CAB microparticles (Fig. 4C-D), which explains the faster release of propranolol HCl from EC microparticles.

CONCLUSIONS

Cellulose acetate butyrate (CAB-553-0.4) was used as a carrier for the formulation of microparticles by solvent evaporation technique. The encapsulation efficiency and the drug release of the water-insoluble drug from CAB microparticle were similar to ethylcellulose microparticles. However, for the water-soluble drug, the encapsulation efficiency of CAB microparticles was higher by two folds and the release was slower. CAB is a promising carrier for the formulation of microparticles by solvent evaporation.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

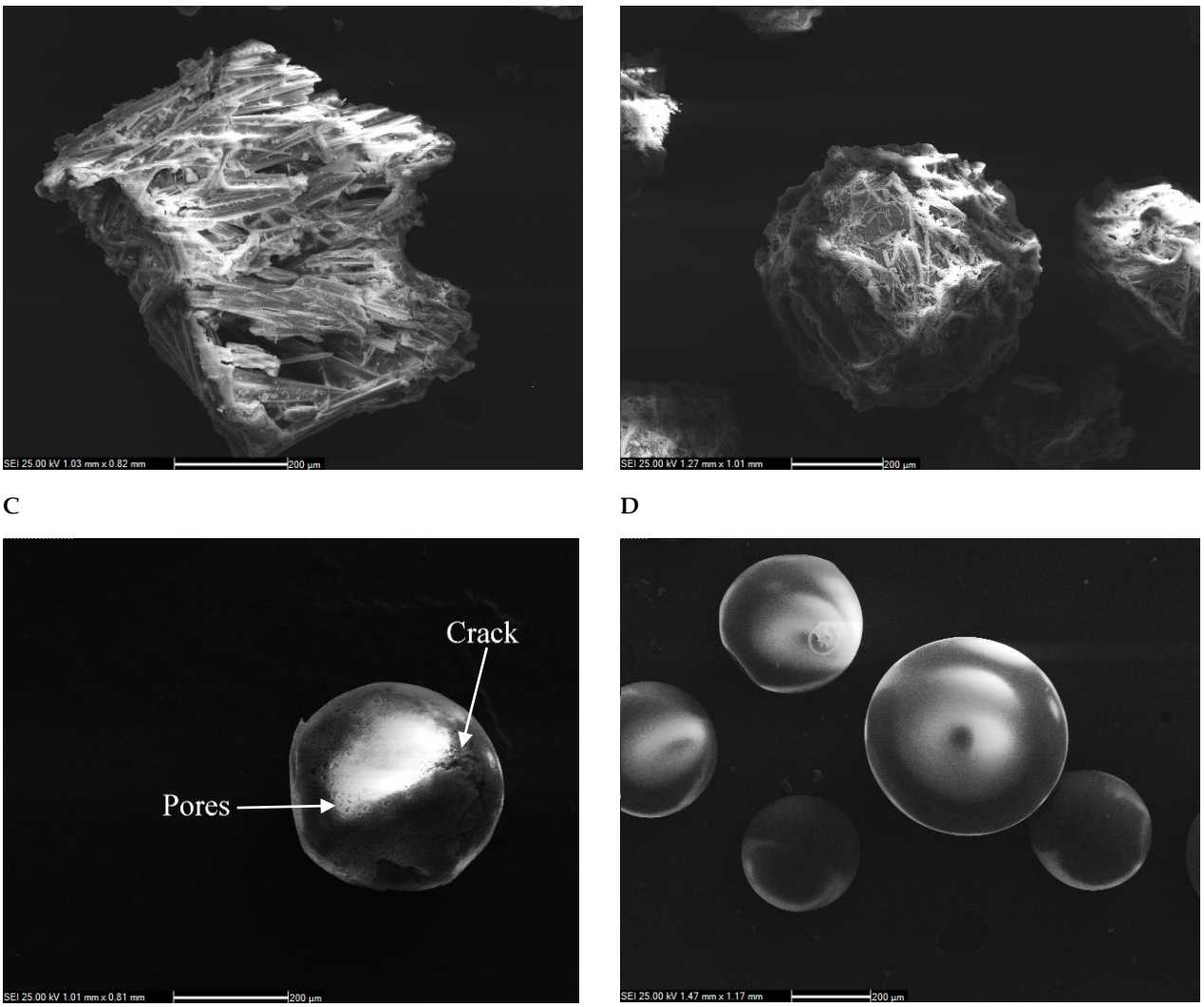

Figure 4. Scanning electron micrographs of carbamazepine loaded EC and CAB (**A** and **B**) microparticles and propranolol HCl loaded EC and CAB (**C** and **D**) microparticles, respectively.

ACKNOWLEDGMENTS

The authors are grateful to the College of Pharmacy, Ministry of Higher education, Kurdistan Region of Iraq. Data were partially obtained from Aram's Master Thesis with the title preparation and characterization of microparticles by the solvent evaporation method, comparing cellulose acetate butyrate to ethylcellulose as the carrier.

REFERENCES

Alex R, Bodmeier R (1990) Encapsulation of water-soluble drugs by a modified solvent evaporation Method. I. Effect of process and formulation variables on drug entrapment. J Microencapsul 7: 347–355.

Ali R, Walther M, Bodmeier R (2018) Cellulose acetate butyrate: Ammonio methacrylate copolymer blends as a novel coating in osmotic tablets. AAPS PharmSciTech 19: 148–154.

Bhagav P, Upadhyay H, Chandran S (2011) Brimonidine tartrate-eudragit long-acting nanoparticles: Formulation, optimization, *in vitro* and *in vivo* evaluation. AAPS PharmSciTech 12: 1087–1101.

Bodmeier R, Chen H (1988) Preparation of biodegradable poly(±)lactide microparticles using a spray-drying technique. J Pharm Pharmacol 40: 754–757.

Bodmeier R, Mcginity JW (1988) Polylactic acid microspheres containing quinidine base and quinidine sulphate prepared by the solvent evaporation method. III.

Morphology of the microspheres during dissolution studies. J Microencapsul 5: 325–330.

Bodmeier R, Mcginity JW (1987a) Polylactic acid microspheres containing quinidine base and quinidine sulphate prepared by the solvent evaporation technique. II. Some process parameters influencing the preparation and properties of microspheres. J Microencapsul 4: 289–297.

Bodmeier R, Mcginity JW (1987b) Polylactic acid microspheres containing quinidine base and quinidine sulphate prepared by the solvent evaporation technique. I. Methods and morphology. J Microencapsul 4: 279–288.

Chandiran Irisappan S, Pavan Kumar B, Narasimha Jayaveera K (2013) Characterization of Glibenclamide loaded cellulose acetate microparticles prepared by an emulsion solvent evaporation method. J Pharm Res 7: 766–773.

Eastman (2006) Technical Data Sheet Eastman™ Cellulose Acetate Butyrate (CAB-553-0.4). https://productcatalog.eastman.com/tds/ProdDatasheet.aspx?product=71001222&pn=Cellulose+Acetate+Butyrate+-+CAB-553-0.4#_ga=2.223635035.1562569450.1583226542-133426334.1583226542 [Consulted September 10, 2019].

Freitas S, Merkle HP, Gander B (2005) Microencapsulation by solvent extraction/evaporation: Reviewing the state of the art of microsphere preparation process technology. J Control Release 102: 313–332.

Gattani YS (2010) Floating multiparticulate drug delivery systems: An overview. Int J Pharma Bio Sci 1(2): 1–14.

Gharge VG, Bhandare PS (2018) Formulation and evaluation of microencapsulated glimepiride produced by the emulsion - solvent evaporation method. PharmaTutor 6: 27–30.

Hamishehkar H, Emami J, Najafabadi AR, Gilani K, Minaiyan M, Mahdavi H, Nokhodchi A (2009) The effect of formulation variables on the characteristics of insulin-loaded poly(lactic-co-glycolic acid) microspheres prepared by a single phase oil in oil solvent evaporation method. Colloids Surf B Biointerfaces 74: 340–349.

Jelvehgari M, Hassanzadeh D, Kiafar F, Loveymi BD, Amiri S (2011) Preparation and determination of drug-polymer interaction and in-vitro release of mefenamic acid microspheres made of cellulose acetate phthalate and/or ethylcellulose polymers. Iran. J Pharm Res 10: 457–467.

Lee J, Park TG, Choi H (2000) Effect of formulation and processing variables on the characteristics of microspheres for water-soluble drugs prepared by w/o/o double emulsion solvent diffusion method. Int J Pharm 196: 75–83.

Lokhande A, Mishra S, Kulkarni R, Naik J (2014) Effect of solvents, drug/polymer ratio and surfactant concentration on *in vitro* characteristic of repaglinide loaded poly (Meth) acrylate nanoparticles. Micro Nanosyst 6: 214–253.

Muhaimin, Bodmeier R (2017) Effect of solvent type on preparation of ethyl cellulose microparticles by solvent evaporation method with double emulsion system using focused beam reflectance measurement. Polym Int 66: 1448–1455.

Nikam PM, Gondkar SB, Saudagar RB (2016) Nanocrystal drug delivery system: A review. Res J Pharm Dos Forms Technol 8: 122–126.

Polli JE, Rekhi GS, Augsburger LL, Shah VP (1997) Methods to compare dissolution profiles and a rationale for wide dissolution specifications for metoprolol tartrate tablets. J Pharm Sci 86: 690–700.

Sanders LM, Kent JS, McRae GI, Vickery BH, Tice TR, Lewis DH (1984) Controlled release of a luteinizing hormone-releasing hormone analogue from poly(d,l-lactide—co-glycolide) microspheres. J Pharm Sci 73: 1294–1297.

Sharma N, Madan P, Lin S (2016) Effect of process and formulation variables on the preparation of parenteral paclitaxel-loaded biodegradable polymeric nanoparticles: A co-surfactant study. Asian J Pharm Sci 11: 404–416.

Watts PJ, Davies MC, Melia CD (1990) Microencapsulation using emulsification/solvent evaporation: An overview of techniques and applications. Crit Rev Ther Drug Carrier Syst 7(3):235–259.

York P (1999) Strategies for particle design using supercritical fluid technologies. Pharm Sci Technol Today 2: 430–440.

Zhang Y, Fei S, Yu M, Guo Y, He H, Zhang Y, Yin T, Xu H, Tang X (2018) Injectable sustained release PLA microparticles prepared by solvent evaporation-media milling technology. Drug Dev Ind Pharm 44: 1591–1597.

AUTHOR CONTRIBUTION:

Contribution	Ibrahim A	Ali R
Concepts or ideas		x
Design		x
Definition of intellectual content		x
Literature search	x	
Experimental studies	x	x
Data acquisition	x	x
Data analysis	x	x
Statistical analysis	x	x
Manuscript preparation	x	
Manuscript editing	x	x
Manuscript review	x	x

Citation Format: Ibrahim A, Ali R (2020) Characterization of microparticles prepared by the solvent evaporation method, use of alcohol-soluble cellulose acetate butyrate as a carrier. J Pharm Pharmacogn Res 8(4): 336–345.