Drug Development and Industrial Pharmacy, 2009; 35(12): 1430–1438

informa
healthcare

ORIGINAL ARTICLE

Design of a 24-hour controlled porosity osmotic pump system containing PVP: formulation variables

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Abstract

Purpose: The purpose of this study was to design a 24-hour controlled porosity osmotic pump system that utilizes polyvinyl pyrrolidone (PVP) as an osmotic-suspending/release retarding agent of drugs. *Methods*: Osmotic tablet cores containing various ratios of ketoprofen and PVP were prepared by wet granulation and initially spray coated with similar solution of cellulose acetate. A formulation containing ketoprofen and PVP at a ratio of 1:7 was selected for further studies. *Results*: The final formulation containing PVP K-30 in the tablet core augmented the release of ketoprofen (poorly water-soluble) up to 90 % over 24 hours much higher than either PVP K-25 or PVP K-90 and retarded the release of pseudoephedrine HCl (highly water-soluble) up to 18 hours. *Conclusion*: This study proposed the dual use of PVP in osmotic pump systems containing solids to modulate the release of either poorly or highly water-soluble drug.

Key words: *Controlled porosity osmotic pump design; formulation variables; ketoprofen; polyvinyl pyrrolidone; pseudoephedrine HCl*

Introduction

The coating permeability to water and the total solubility of osmotic core (containing drug and osmogent) are the key parameters considered in the design of any osmotic pump system. Bend Research Inc. (Bend, OR, USA) and Pfizer Inc. (New York, NY, USA) jointly developed a controlled porosity osmotic pump (CPOP) to enhance the coating permeability of dense membranes of elementary osmotic pump systems[1]. Even though the tablet core may contain an osmogent, drug solubility in water in the range of 10–15% (w/v) was reported as the most suitable for osmotic controlled release delivery[2]. In the design of conventional osmotic pump systems, drug solubility determines the choice of an osmogent[3]. However, new approaches are available for modifying or modulating solubility of drug substances to enhance their osmotic controlled release delivery[4–6].

In addition, attention has also been focused on either increasing or decreasing the rate of drug release from osmotic pump systems using hydrophilic polymer without modifying or modulating drug solubility. For the designing of these types of systems, the choice of a suitable hydrophilic polymer is crucial. Apart from the generation of driving force for the uptake of water, hydrophilic polymers assist in maintaining drug uniformity in the hydrated formulation[7]. For instance, polyethylene oxide and gum arabic were used as suspending agents to enhance the release of nifedipine and naproxen (poorly water-soluble drugs) from elementary osmotic pumps, respectively[8,9]. Contrarily, hydroxypropylmethylcellulose was used to retard the release of diltiazem hydrochloride, a highly water-soluble drug[2,10]. The drug release-retarding property of a hydrophilic polymer was related to its ability to form hydrogel within the tablet core that may restrict and delay solvent contact with the drug molecule, as well as increase the diffusional path length of the solvent[2].

Hitherto, a CPOP system containing a release-modulating hydrophilic polymer for the delivery of both poorly and highly water-soluble drugs has not yet been reported. Thus, the objective of this study was to employ the dual attributes of polyvinyl pyrrolidone (PVP) (povidone) as either a suspending agent or a release retardant for poorly and highly water-soluble drugs, respectively, in the design of a CPOP system.

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(Received 1 Oct 2008; accepted 21 Apr 2009)

ISSN 0363-9045 print/ISSN 1520-5762 online
DOI: 10.3109/03639040902988566

This polymer was chosen for the study because of its peculiar advantages. Firstly, it is freely soluble in water (1 g/mL) more than polyethylene oxide (miscible) and gum arabic (1 g/2.7 mL), thus possessing relatively higher osmotic strength. In the previous studies, the amount of gum arabic chosen as an optimal concentration for suspending the drug was high (naproxen/gum arabic; 1:9) using a fixed tablet weight of 500 mg and that of polyethylene oxide was even higher (nifedipine/polyethylene oxide; 1:34) using a fixed tablet weight of 700 mg. PVP is a readily available cheap pharmaceutical excipient, and it is not liable to microbial contamination in contrast to natural products such as gum arabic. Lastly, PVP is a nontoxic and safe additive; as such World Health Organization (WHO) recommends 25 mg/kg body weight as its acceptable daily intake[11].

The scope of the study covered formulation and preparation of 24-hour release CPOP tablets initially containing varying amounts of PVP at a fixed concentration of a poorly water-soluble model drug, ketoprofen; investigation of the influence of formulation variables (type and concentration of pore former, type of plasticizer, concentration of osmogent, drug loading, and molecular weight of PVP) on the drug release; and finally, investigation of the potential of the final design to control the release of a highly water-soluble drug pseudoephedrine hydrochloride.

Materials and methods

Materials

Ketoprofen (Wuxue Xunda Pharm, Wuxue, China) was used as a model drug, and pseudoephedrine hydrochloride (Emmellen Pharmaceuticals and Biotech, Mumbai, India) was used to investigate the release retarding of highly water-soluble drug by PVP. Three different viscosity grades of povidone (PVP K-25, 34,000 Da; PVP K-30, 58,000 Da; and PVP K-90, 1,300,000 Da) were used for osmotic-suspending/release-retarding property and were received for free from ISP Chemicals (M) Sdn Bhd (Kuala Lumpur, Malaysia). Dextrose monohydrate (R & M Chemicals, UK) was used as an osmogent and cellulose acetate (CA; Fluka, Essex, Germany) as a semipermeable membrane. PVP K-30, polyethylene glycol 8000 (PEG 8000; Sigma, St. Louis, MO, USA), and lactose monohydrate (Neisuikerfabriek, Vitgeest, Holland) were used as pore formers. Polyethylene glycol 400 (PEG 400; BDH, Poole, England), triacetin (Fluka, Germany), and triethyl citrate (TEC; Merck-schurchardt, Hohenbrunn, Germany) were used as plasticizers. Purified talc (Fluka, Germany) was used as an antiadherent and microcrystalline cellulose (MCC, Avicel PH101, Asahi Chem, Ikoma-Gun, Japan) as a filler. All the materials were used as received.

Preparation of tablet cores

The ingredients were weighed, sieved, and mixed in a planetary mixer (Kenwood Chef Classic KM800, Havant, UK) followed by wet granulation. The dried granules (loss on drying in the range of 2.0–2.5%) were compressed into tablets fixed at a weight of 600 mg using a single punch tableting machine (Surrey, Manesty, UK) with 12-mm diameter concave punches. The tablet hardness was maintained within a range of 8–9 kg/cm^2. Tablet cores were initially prepared with different drug/polymer ratio (Table 1). Tablet core V formulation (drug/polymer ratio, 1:7) was used throughout the study, simply by altering type or concentration (where applicable, increasing or decreasing amount of an excipient with an equivalent amount of microcrystalline cellulose, a filler) of a particular component variable while fixing the amounts of other ingredients (Table 2). Table 3 displays optimal tablet core formulation.

Coating of tablet cores

Dip coating of tablet core

Dip coating was employed to get preliminary data on the effect of concentration of PVP K-30 as osmotic-suspending agent in the preparations of osmotic pump tablets (Table 1). Subsequently, spray coating was

Table 1. Tablet core formulations containing varying concentration of PVP K-30 as an osmotic-suspending agent.

Ingredient (mg/tablet)	Formulation					
	I (1:0)	II (1:1)	III (1:3)	IV (1:5)	V (1:7)	VI (1:9)
Ketoprofen	25	25	25	25	25	25
PVP K-30	0	25	75	125	175	225
Dextrose monohydrate	240	240	240	240	240	240
MCC	329	304	254	204	154	104
Magnesium stearate	6	6	6	6	6	6
Isopropyl alcohol	qs	qs	qs	qs	qs	qs

Table 2. Tablet core V formulations used in investigating the influence of formulation variables on drug release.

	Ingredient (mg/tablet)	
Formulation	Dextrose monohydrate	Ketoprofen
V1	0	25
V2	180	25
V/V3	240	25
V4	300	25
V5	360	25
V4.1	300	50
V4.2	300	75
V4.3	300	100

Table 3. Final tablet core formulation (V4).

Ingredient	Composition (%, w/w)	Amount (mg/tablet)
Ketoprofen/pseudo-HCl	4.17	25
PVP K-30	29.17	175
Dextrose monohydrate	50	300
Microcrystalline cellulose	15.66	94
Magnesium stearate	1	6
Isopropyl alcohol	—	qs

employed through out the study. Coating dispersion was prepared by mixing the ethanol/acetone (1:2, v/v) solvent system with TEC (50%, w/w, of CA) followed by the addition of CA (8 g/100 mL) until completely dissolved. Purified talc (25%, w/w, of CA) and lactose monohydrate (100%, w/w, of CA) were added serially, resulting in the formation of a coating suspension. Lactose monohydrate was used as a pore former throughout the dip coating. Weighed amounts of tablet cores were placed in a stainless steel cookware strainer adopted as a dip-coating basket. The tablet cores inside the basket were dipped in the coating suspension under continuous stirring for 30 seconds, withdrawn, and dried in a coating pan (Kathori Teguh CP, Mumbai, India) for 15 minutes, maintained at 55 ± 5°C and a rotation speed of 8.5 rpm. Dipping and drying were repeated until a weight gain of 8% (w/w) was achieved. The coated tablets were finally dried in an oven (Carbolite PF60) at 40°C for 24 hours, and then reweighed to calculate coating weight gain.

Spray coating of tablet cores

Spray-coating dispersion was prepared by mixing the TEC (50%, w/w, of CA) with ethanol/acetone (1:2, v/v) solvent system followed by the addition of CA (2.5 g/100 mL). The solution of CA/plasticizer was mixed with a separate dispersion of pore former in the solvent system. The spray coating was carried out using Pilot 59 spray gun with 1.6-mm nozzle diameter at a coating pan rotation speed of 8.5 rpm. The coating conditions were as follows: inlet pressure (3 kg/cm^2), spray pressure (1 kg/cm^2), temperature (45 ± 2°C), and a spray rate of 13 ± 1 mL/min. The coated tablets were dried for an additional period of 10 minutes in the coating pan before final drying at 40°C in an oven for a period of 24 hours. Spray-coating formulations (containing different types/amounts of pore former or plasticizer at various coating weight gains) and an optimal spray-coating formulation (D2.2) are illustrated in Tables 4 and 5, respectively. Three different pore formers—PVP K-30, lactose monohydrate, and PEG 8000—were examined. PVP K-30 was dissolved, whereas lactose monohydrate was dispersed in the ethanol/acetone solvent system. PEG 8000 was first dissolved in dichloromethane and then the solution was mixed with the solution of CA/TEC in the solvent system.

Table 4. Spray-coating formulations used in investigating the influence of formulation variables on drug release.

Formulation	Pore-former: Type	Pore-former: Concentration (%, w/w, of CA)	Plasticizer type	Coating weight gain (%, w/w)
A	No pore-former	0	TEC	8
B	Lactose	100	TEC	8
C	PEG 8000	100	TEC	8
D	PVP K-30	100	TEC	8
D1	PVP K-30	25	TEC	8
D2	PVP K-30	40	TEC	8
D3	PVP K-30	50	TEC	8
D4	PVP K-30	150	TEC	8
D2.1	PVP K-30	40	TEC	6.5
D2.2	PVP K-30	40	TEC	5.0
D2.3	PVP K-30	40	PEG 400	5.0
D2.4	PVP K-30	40	Triacetin	5.0

Table 5. Final spray-coating formulation (D2.2).

Ingredient	Amount	% (w/w) of dried CA
Cellulose acetate (CA)	2.50 g/100 mL	—
PVP K-30	1.00 g/100 mL	40
Triethyl citrate	1.25 g/100 mL	50
Ethanol-acetone (1:2, v/v)	100 mL	—

In vitro drug release study

The in vitro drug release studies were conducted according to USP 26 Dissolution Test Apparatus I (Pharma Test PTWS 3CE, Hainburg, Germany) basket method. The volume of dissolution medium employed was 900 mL of pH 7.4 phosphate buffer solution[12]. The stirring rate was set at 100 rpm and maintained at a temperature of 37.0 ± 0.5°C. Samples of 5 mL were automatically collected from each vessel at time intervals of 0.5, 1.0, 1.5, 2.0, 4.0, 6.0, 8.0, 10.0, 12.0, 15.0, 18.0, 21.0, and 24.0 hours. The vessels were automatically refilled immediately with the same amount of fresh dissolution medium. Ketoprofen and pseudoephedrine HCl were both quantified using UV-spectrophotometer (U-2000 Hitachi, Japan) at detection wavelengths of 260 and 205 nm, respectively. The $T_{50\%}$ values of the drug release profiles were employed for comparison using one-way analysis of variance (ANOVA) ($P < 0.05$).

Results and discussion

The use of hydrophilic polymers as suspending agents or release retardants has attracted special attention in the field of osmotic pressure-controlled drug delivery[8–10].

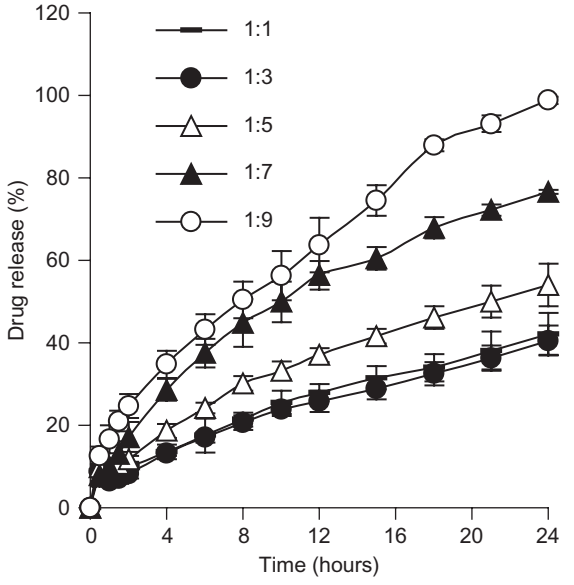

Figure 1. Influence of PVP K-30 concentration as an osmotic-suspending agent on ketoprofen release. Mean ± SD, $N = 6$.

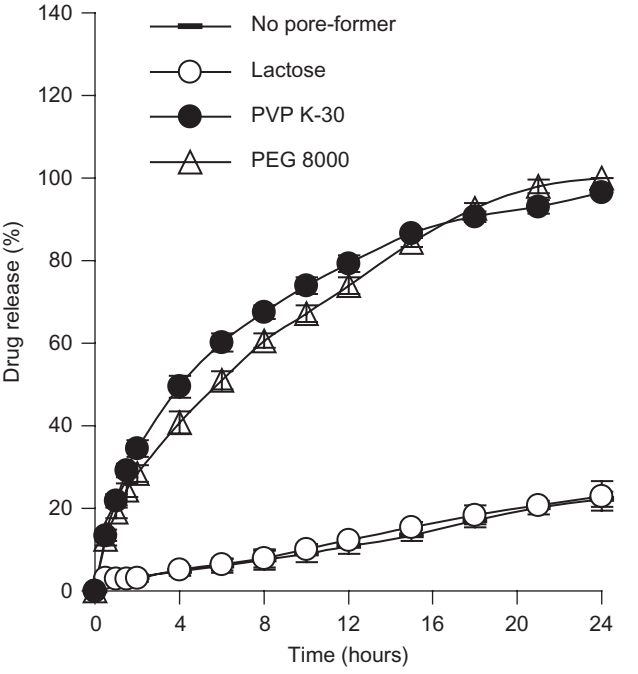

Figure 2. Influence of type of pore former on drug release. Mean ± SD, $N = 6$.

This study initially employed PVP as an osmotic as well as a suspending agent for ketoprofen in the design of CPOP system using various concentrations of the polymer at a fixed concentration of the drug (Table 1). Tablets having drug/polymer ratio ranging from 1:3 to 1:9 showed increased drug release as the polymer concentration increases (Figure 1). This was associated with increasing osmotic pressure generation as the number of moles of the polymeric osmogent increases vis-à-vis increasing driving force for the drug release, despite the presence of the primary osmogent, dextrose monohydrate. Furthermore, the result indicates that the amount of PVP used was sufficient enough to suspend ketoprofen in these hydrated tablets. In contrast, the release profiles of tablets containing drug/polymer ratio of 1:1 and 1:3 were the lowest and overlapped despite containing dextrose monohydrate at equal concentration relative to other formulations. The concentrations of PVP K-30 used in these tablets were within the normal range used as a binder in wet granulation. Thus, the amount of the polymer used may not cause sufficient suspension of the water-insoluble drug in the hydrated tablets and may eventually be unable to prevent precipitation of the drug resulting in slow release. For the tablets without povidone in the tablet core (coated tablet I), the coatings ruptured in about 10 minutes before sampling commenced, depicting the principle of osmotic pressure driving drug release. This indicated that for the tablets containing PVP K-30 in the tablet cores, the binding effect of the polymer might have prevented dextrose monohydrate from rapid dissolution upon hydration, thus avoiding the likely sudden boost in osmotic pressure that could rupture the tablet coats prematurely. Even though gum arabic and polyethylene oxide were used as osmotic-suspending agents in the design of osmotic pump tablets in the past, this study indicates that povidone could be used for the same purpose but at a lower concentration, thus enhancing drug loading.

CA is generally recognized as safe and among the first materials used to prepare semipermeable membrane for controlled drug release[12]. In this study, tablet core V were spray coated either with CA coating dispersion containing a pore former or without a pore former (Table 4). The drug release from the coating consisting of either PVP K-30 or PEG 8000 was over 95% in 24 hours (Figure 2). Contrarily, the drug released by the coating consisting of either lactose monohydrate or without pore former was low (~24% in 24 hours). PEG 8000 and PVP leached out of the coat resulting in the formation of drug delivery orifices. On the other hand, lactose monohydrate was only suspended in the solvent system and was largely lost as dust particles during spray-coating process, thus the resultant coating showed similar drug release profile with a coating without pore former. Even though lactose monohydrate-containing coating suspension was successfully used in dip coating, the use of solution in spray coating is crucial. The drug release from the coating in the absence of a pore former indicated that there might be a contribution of the plasticizer (another water-soluble component of this coating) and likely drug release resulting from diffusion process[13]. Also, the result indicated that PEG

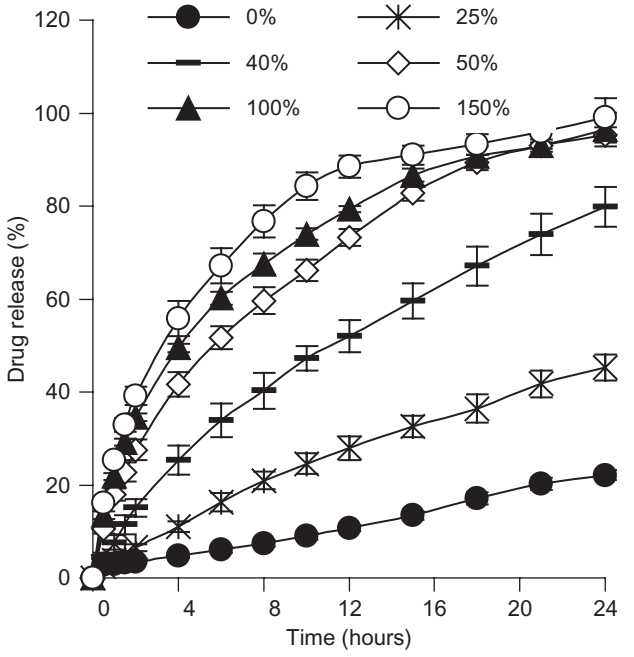

Figure 3. Influence of PVP K-30 concentration as a pore-former on drug release. Mean ± SD, $N = 6$.

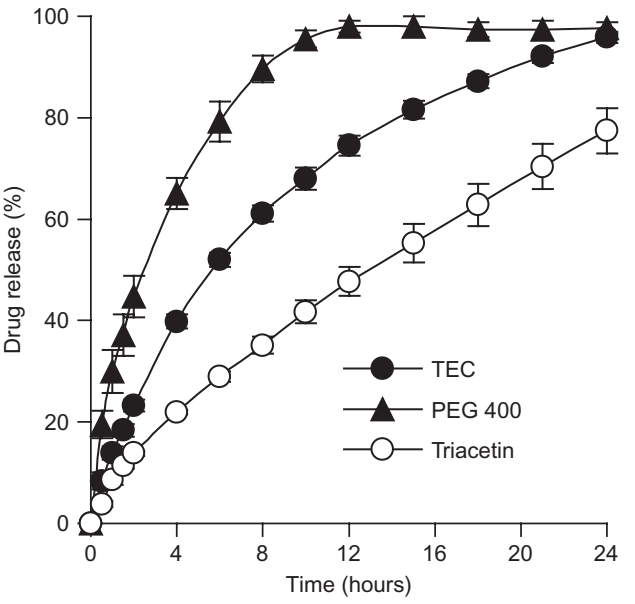

Figure 4. Influence of plasticizer type on drug permeation of cellulose acetate microporous membrane coating. Mean ± SD, $N = 6$.

8000 as a pore former could be used successfully in coating to tailor drug release. Furthermore, it was apparent that the amount of the drug released increased with an increase in the amount of PVP K-30 in the coating because of the increasing number of drug delivery orifices (Figure 3). The results obtained are in good agreement with findings of many researchers[14–20] but in contrast with the finding of Garg et al.[21] The linearity of ketoprofen release profiles decreases as the amount of PVP increases in the coating, indicating increased diffusional contribution resulting from leaching out of more pore former from the coating that gives rise to increased number of drug delivery orifices. CA microporous membrane-coating containing PVP (in combination of plasticizers) as a pore former was reported in the past, but contrarily at a higher optimal weight gain of 15% (w/w)[19].

Apart from the effects of a pore former, the presence of a plasticizer also augments the permeation of CA membrane coatings. For instance, triacetin, TEC, and PEG 400 were reported to have been used in polymeric coating[4,15,22]. This study employed the three plasticizers for comparison using CA (50%, w/w) microporous membrane (Table 4). Figure 4 shows the drug release profiles of tablets containing one of the plasticizers in the coating. The $T_{50\%}$ values of these release profiles were in ascending order of magnitude corresponding to decreasing release rate: PEG 400 (2.5 hours) < TEC (5.67 hours) < triacetin (12.0 hours). Also, the difference in drug release that exists among these plasticizers was statistically significant ($P < 0.05$). The higher drug release rate produced by PEG 400 (nonoily and highly water-soluble) in contrast to TEC (mobile oily liquid and water-soluble) and triacetin (oily liquid, water-soluble) relates to its relative faster leaching out of the coating. The rate at which a plasticizer leaches out of coating depends on its solubility in water, and this has a positive correlation with the rate of drug release. The hydrophobicity of a plasticizer significantly affects the water uptake characteristics of film coatings, subsequently changing the coating toughness and drug permeation[22]. Even though the TEC and triacetin have similar solubility in water (1 g/15 mL), the mobility of TEC might have increased its affinity to polymeric domain, thus resulting in tendency to weaken the intermolecular forces and creating more free volume responsible for the increased drug permeation. The results of this investigation showed a combination of physical effects a plasticizer may elicit on the rate of drug release, which may be useful in selecting a desirable plasticizer for osmotic pump drug delivery. Indeed, the inverse relationship between hydrophobicity of a plasticizer and drug release is consistent with the results obtained by Liu et al.[8] and Lecomte et al.[22] On the other hand, coating weight gain affects drug release inversely. In this study, at coating weight gains of 8%, 6.5% and 5%, the cumulative drug release at a 24-hour period was 78%, 84%, and 89%, respectively. On the other hand, the tablet core without coating released 100% of ketoprofen in approximately 2 hours only (Figure 5). The drug release profile of 6.5% coating weight gain was not statistically significantly different from the release profiles

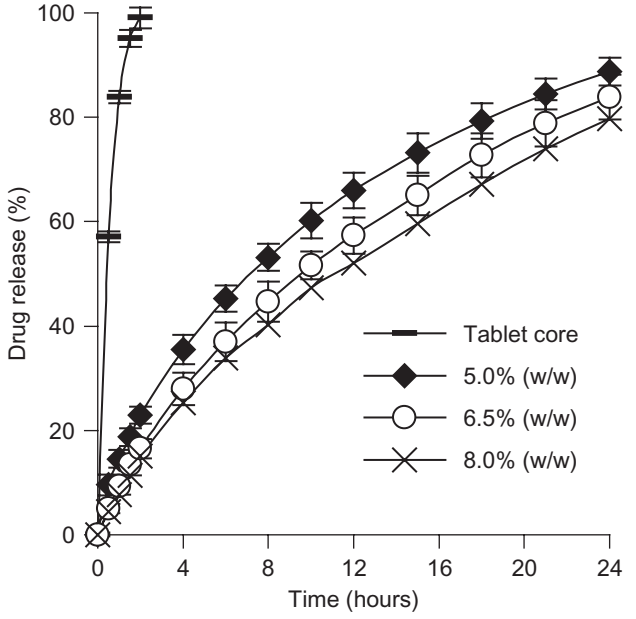

Figure 5. Influence of coating weight gain on drug release. Mean ± SD, $N = 6$.

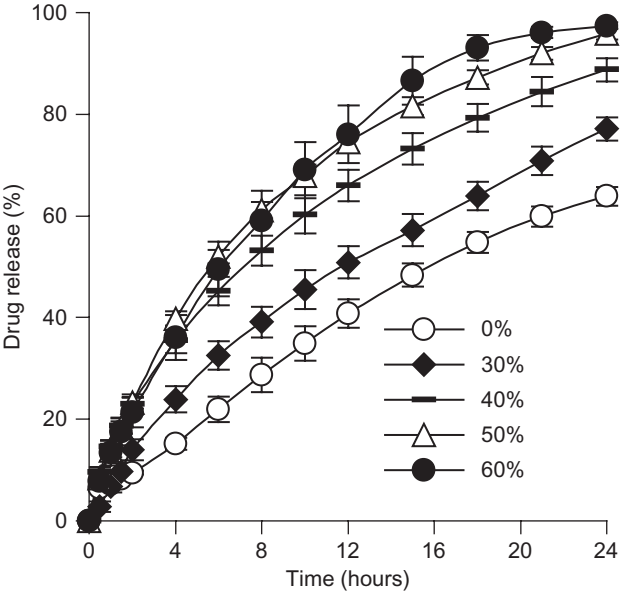

Figure 6. Influence of dextrose monohydrate concentration on drug release as an osmogent. Mean ± SD, $N = 6$.

of 8% and 5% ($P < 0.05$). Coating weight gain directly correlates to coating thickness, whereas the latter has a negative correlation with drug release from osmotic pump tablets[13,16,23–26].

Another subset of the formulation variables of the CPOP system relates to osmotic core. First, the influence of dextrose monohydrate concentration as an osmogent was studied using 0, 180, 240, 300, and 360 mg of the osmogent corresponding to 0%, 30%, 40%, 50%, and 60% (w/w) of a 600-mg tablet (Table 2). It was found that increased concentration of dextrose monohydrate (osmotic pressure of saturated solution = 82 atm) increased drug release significantly (Figure 6). Increase in number of moles of an osmogent increases the osmotic pressure inside a tablet resulting in an increase in osmotic pressure gradient with receptor medium that augments driving force for drug release. However, the rate of drug release was not augmented beyond 50% (w/w) of dextrose monohydrate. At this level of the osmogent, more than 90% of ketoprofen was released over a 24-hour period. There was no statistically significant difference in drug release between tablets containing 50% and 60% (w/w) levels of dextrose monohydrate, but statistically significant difference existed between this subset with the release profiles of the tablets containing less than 50% (w/w) level of this osmogent ($P < 0.05$). The finding of this investigation is in agreement with the mathematical expression on the rate of mass of drug release from osmotic pump systems[3,27–29] and also follows the trend of results obtained using other osmogents[30–32]. In contrast, drug release decreases as the drug loading was sequentially doubled from 4.17%

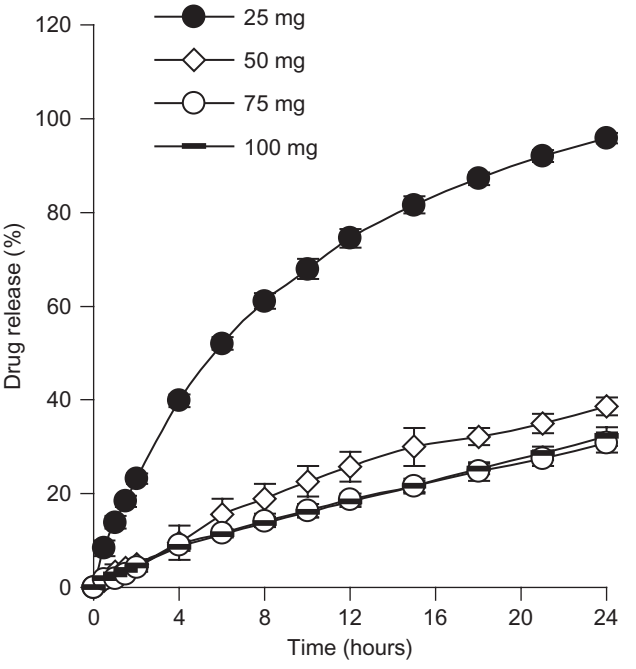

Figure 7. Influence of drug loading on drug release. Mean ± SD, $N = 6$.

(25 mg) to 16.67% (100 mg) (Figure 7). This might be because of the increase in the tendency of ketoprofen to precipitate out of the suspension inside the hydrated tablets because of increased condensed circumstances as the amount of the drug increases. In the design of this system, ketoprofen was used as a model drug only. Nonetheless, the design could be used to develop once-a-day formulations of other potential drug candidates

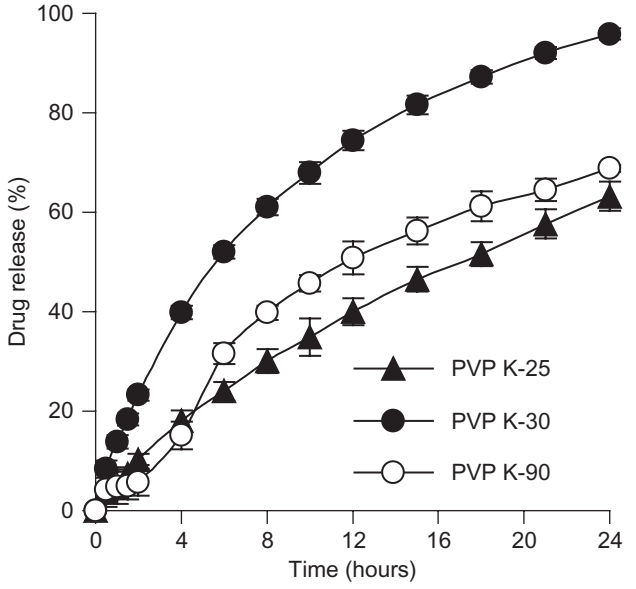

Figure 8. Influence of PVP molecular weight on drug release. Mean ± SD, $N = 6$.

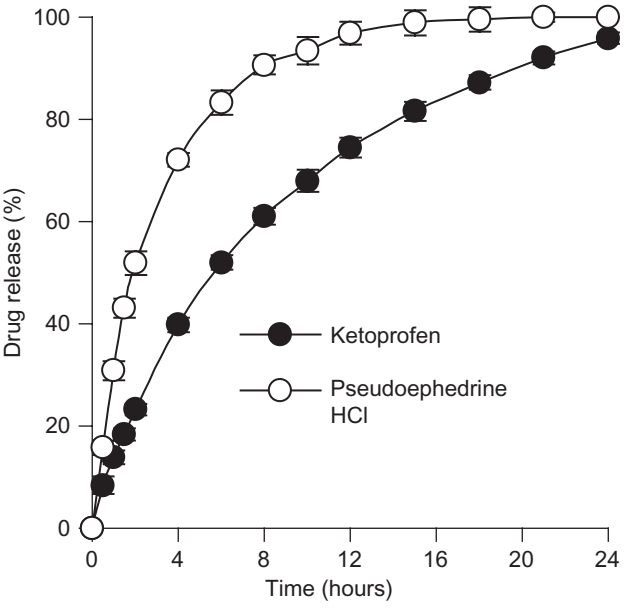

Figure 9. The release profile of pseudoephedrine HCl from the final formulation compared to the release of ketoprofen. Mean ± SD, $N = 6$.

having daily dosing of around 25 mg. Further increase in daily drug dose could be achieved by increasing the tablet weight, which directly correlates to drug loading. The rate of drug release from CPOP systems was reported to be generally dependent on drug loading[33,34] similar to results obtained from other monolithic osmotic pumps[8,35].

For a polymeric tablet core, molecular weight of a polymer could impact greater influence on rate of drug release. Although increasing the concentration of PVP K-30 in the tablet core increased drug release, other *k*-value grades of PVP affect drug release differently even at the same concentration (Figure 8). The three grades of plasdone K-30 used in the study affected the release of ketoprofen according to the following ascending order of magnitude of $T_{50\%}$ values corresponding to decrease in release rate: K-30 (5.67 hours) < K-90 (11.70 hours) < K-25 (17.05 hours). This difference is statistically significant ($P < 0.05$). The results indicated that the effect of molecular weight does not show a definite trend. For a hydrophilic polymer, the viscosity increases, but the solubility decreases with increasing molecular weight. As such, the typical viscosities of 5% solutions of PVP K-25, PVP K-30, and PVP K-90 in deionized water at 25°C were reported as 2.0, 2.5, and 55.0 mPas, respectively[36]. Although polymer solubility has positive correlation with osmotic pressure, the higher release produced by PVP K-90 relative to PVP K-25 indicated that viscosity factor has greater influence on the release of the poorly water-soluble drug than the polymer solubility. Similarly, the faster drug release produced by PVP K-30 relative to the other two grades might be due to its intermediate viscosity. This finding of the investigation suggests that although thickening effect of PVP is desirable for the release of poorly water-soluble drug, too much or too low viscosity would not produce desirable suspending effect. The findings are consistent with the results reported by other researchers using other hydrophilic polymers[8,10].

Lastly, the final formulation containing ketoprofen (KETO OPT Vd/D2.2) was used to study the influence of drug solubility on release characteristic. As such, ketoprofen was substituted from the formulation with highly water-soluble drug, pseudoephedrine HCl producing PSEUDO OPT Vd/D2.2 (Table 3). Pseudoephedrine HCl was relatively released faster (80% in 6 hours) initially, followed by a slow release phase (100% cumulative release in 18 hours) (Figure 9). The faster release phase might be because of the faster dissolution rate of pseudoephedrine HCl (0.5 g/mL) in water relative to the rate at which PVP K-30 (1.0 g/mL) dissolves to form viscous solution required to retard the release of the drug. During the slow release phase, sufficient amount of the polymer might have dissolved forming more viscous solution sufficient enough to retard the release of this drug. In contrast, the release of ketoprofen was slower (80% in 15 hours) relative to the release rate of pseudoephedrine HCl. Ketoprofen is practically insoluble in water, thus the rate at which PVP K-30 dissolves to suspend the drug (averting aggregation) determines the rate of release. However, 24-hour controlled release of pseudoephedrine HCl from the formulation could be achieved simply by increasing the coating weight gain.

Mechanism of drug release

An osmotic-suspending cocontrolled release might be the major mechanism of release of a poorly water-soluble ketoprofen from the design. The tablet initially imbibes water by diffusion because of water activity gradient, which results in an initial hydration followed by osmotic pressure generation produced by continuous dissolution of PVP K-30 and dextrose monohydrate. The osmotic pressure generation inside the tablet caused the imbibitions of more water through osmosis. As more water enters the tablet, a suspension of the drug and the excipients was formed, because of thickening effect of dissolved PVP K-30. The higher osmotic pressure inside the tablet exists in gradient with that of the external environment, thus forcing the drug through the delivery orifices formed by pore former as it leaches out of the coating. Also, despite faster solubility of pseudoephedrine HCl in water, the thickening of PVP K-30 solution in the hydrated tablets containing this drug retards its release from the system.

Conclusion

The CPOP tablets of ketoprofen were prepared using different concentrations of PVP K-30. The rate of the drug release from these tablets increased with increased concentrations of either the osmogent or the pore former but decreased with increased coating thickness or drug loading. Increased hydrophobicity among the different plasticizers used decreased ketoprofen release. However, possible physical interaction between CA and TEC enhanced 24-hour release profiling of ketoprofen relative to the coating containing triacetin that has similar solubility in water. The final formulation containing PVP K-30 in the tablet core augmented the release of ketoprofen up to 90% over 24 hours much higher than either PVP K-25- or PVP K-90-containing formulation and retarded the release of pseudoephedrine HCl up to 18 hours. The present findings indicate the dual attribute of PVP either as an osmotic-suspending or release-retarding agent of drugs in osmotic pump systems containing solids. This suggests that PVP could have potential use as a functional excipient in osmotic controlled release technology. It is also hoped that the present design could be evaluated and developed for the delivery of these types of hard-to-deliver compounds having low daily dosing.

Acknowledgment

The sponsorship received from the Jigawa State Government of Nigeria for the M.Sc study was appreciated.

Declaration of interest: The authors report no conflicts of interest.

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