**INTRODUCTION**

*Diabetes mellitus* (DM) is considered a worldwide public health problem, it is estimated that by 2035, more than 590 million patients will be diagnosed.\(^1\) DM is a disease that depends on multiple factors and is characterized by a deficit in insulin secretion/action, resulting in hyperglycemia and macrovascular and microvascular complications.\(^2\) In addition to this condition, alterations in the metabolism of fats and proteins coexist. Type II or non-insulin dependent (T2DM) is the most common form and is often associated with obesity or increased visceral fat.\(^1\) Over the past years, studies investigating efficient drug delivery systems for T2DM therapy have increased, with drugs like insulin analogs, hypoglycemic drugs and genetic drugs.\(^3,4\) However, overcoming limitations such as rapid clearance, low biodistribution and solubility in physiological conditions and poor cell intake is still necessary. Drug delivery systems (DDS) have been found to have advantages such as higher stability and bioavailability.\(^3\) Floating drug delivery systems (FDDS) are a promising gastro-retentive tool for prolonged drug release, especially with drugs with low bioavailability and low solubility. Lately, it has been reported that the combination of lipids with hydrophilic polymers in the development of blends or composite hybrid materials may bring together the properties of individual components. This study proposed four formulations of effervescent lipid-polymer FDDS through a Taguchi experimental design for metformin’s prolonged release. Tablets were obtained by wet granulation, and the effect of HPMC, Compritol®, and sodium bicarbonate was studied. All formulations were evaluated with pharmacotechnical and biopharmaceutical properties such as *in-vitro* drug delivery, flotation, swelling, erosion and release kinetics. Effervescent lipid-polymer FDDS were obtained with prolonged release until 24 hours. Formulation F1 meets the acceptance criteria of USP extended delivery. Compritol®, combined with HPMC and sodium bicarbonate, impacted release behavior and buoyancy properties. Formulations with high amounts of HPMC and Compritol® were found to have the lowest release rates and followed the Peppas-Sahlin kinetic model. Successful preparation of effervescent lipid-polymer was achieved and evaluated through a Taguchi experimental design, expected to result in prolonged release and better therapeutic behavior.

**ABSTRACT**

Floating drug delivery systems (FDDS) formulated with hydrophilic polymers and effervescent agents are a promising gastro retentive tool for prolonged drug release, especially with drug with low bioavailability and low solubility. Lately, it has been reported that the combination of lipids with hydrophilic polymers in the development of blends or composite hybrid materials may bring together the properties of individual components. This study proposed four formulations of effervescent lipid-polymer FDDS through a Taguchi experimental design for metformin’s prolonged release. Tablets were obtained by wet granulation, and the effect of HPMC, Compritol®, and sodium bicarbonate was studied. All formulations were evaluated with pharmacotechnical and biopharmaceutical properties such as *in-vitro* drug delivery, flotation, swelling, erosion and release kinetics. Effervescent lipid-polymer FDDS were obtained with prolonged release until 24 hours. Formulation F1 meets the acceptance criteria of USP extended delivery. Compritol®, combined with HPMC and sodium bicarbonate, impacted release behavior and buoyancy properties. Formulations with high amounts of HPMC and Compritol® were found to have the lowest release rates and followed the Peppas-Sahlin kinetic model. Successful preparation of effervescent lipid-polymer was achieved and evaluated through a Taguchi experimental design, expected to result in prolonged release and better therapeutic behavior.

**Keywords**: Lipid-polymer, Floating tablet, Taguchi, Metformin, Diabetes, Kinetic release.


**Source of support**: Nil.

**Conflict of interest**: None.

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Flotation. Metformin hydrochloride (MEH) is a biguanide widely used as a first-line drug in clinical practice as an oral antidiabetic monotherapy and in combination with other drugs. MEH activates hepatic uptake of glucose and inhibits gluconeogenesis. It also helps to sensitize peripheral tissues to insulin, improving insulin sensitivity receptors. MEH is a Biopharmaceutical classification system (BCS) class III, with absorption in the gut by organic cationic transporters (OCTs), and appears to have limited gastrointestinal absorption due to permeability; the oral bioavailability of MEH is about 50 to 60% since its absorption occurs almost exclusively in the upper GIT with poor permeability in the lower GIT, and has a half-life of approximately 5 hours. The effect of gastroretention and prolonged release of FFDS is favorable for drugs such as MEH since its release is slow and prolonged, leading to an increase of in absorption. In the present study, we prepared lipid-polymer effervescent floating tablets for MEH for a prolonged release to improve its bioavailability. Four formulations were proposed through a Taguchi experimental design, and all formulations were evaluated with pharmacotechnical and biopharmaceutical properties such as in-vitro drug delivery, flotation, swelling, erosion, and profile release.

MATERIALS AND METHODS

Materials
MEH (Sinbiotik), Hydroxypropyl methylcellulose 90 SH-100000 (HPMC), (SHIN-ETSU Chemical), Compritol® ATO 888 (Compritol®) (GATTFEOSE®), Polyvinylpyrrolidone K-30 (PVP K-30) (Cosmopolitan Drugstore), sodium bicarbonate (J.T Baker), magnesium stearate (Lufra Chemistry).

Experimental Design
A Taguchi L4 2³ design was implemented and 4 formulations were obtained (n = 3) (Table 1). The factors of study were the proportion of HPMC, Compritol® ATO 888 (Compritol®) and sodium bicarbonate (SB). Constant values of metformin (MEH) (0.750 g), magnesium stearate (MS) (0.010 g) and PVP K-30 (0.015 g) were used. Statistical analysis was made using ANOVA (Statgraphics Centurion® XVII).

Table 1: Composition of formulations by Taguchi L4 2³ experimental design

<table>
<thead>
<tr>
<th>Component</th>
<th>F1</th>
<th>F2</th>
<th>F3</th>
<th>F4</th>
</tr>
</thead>
<tbody>
<tr>
<td>MEH (g)</td>
<td>0.750</td>
<td>0.750</td>
<td>0.750</td>
<td>0.750</td>
</tr>
<tr>
<td>HPMC (g)</td>
<td>0.200</td>
<td>0.200</td>
<td>0.250</td>
<td>0.250</td>
</tr>
<tr>
<td>Compritol® (g)</td>
<td>0.100</td>
<td>0.200</td>
<td>0.100</td>
<td>0.200</td>
</tr>
<tr>
<td>SB (g)</td>
<td>0.100</td>
<td>0.150</td>
<td>0.150</td>
<td>0.100</td>
</tr>
<tr>
<td>PVP K-30 (g)</td>
<td>0.015</td>
<td>0.015</td>
<td>0.015</td>
<td>0.015</td>
</tr>
<tr>
<td>MS (g)</td>
<td>0.010</td>
<td>0.010</td>
<td>0.010</td>
<td>0.010</td>
</tr>
</tbody>
</table>

Tablet Fabrication
Wet granulation method was used to obtain MEH tablets. Raw materials were sieved (mesh #40) and mixed (10 minutes at 30 rpm). The mixture was moistened with a PVP K-30 solution and sieved (mesh #14). The granulate was dried (BG drying oven) at 50°C until reaching a humidity of 1 to 3% (ROCA thermobalance), and sieved (mesh #14). MS (previously sifted in a #40 mesh) was added and mixed (2 minutes at 30 rpm). The final mixture was compressed in a hydraulic press (Enerpac P392 hydraulic press) using a pressure of 6500 psi for 30 seconds with round punches of 13 mm of diameter.

Characterization of Granules and Tablets
All formulations, including bulk and tapped density, Carr index, Hausner index and angle of repose with funnel method, were evaluated according to pharmacopeial methods (n = 3). Characterization of tablets included average weight and weight variation (CV%), hardness (Erweka durometer), Friability (ELECSA), drug content with a spectrophotometric method at 232 nm (n = 3) and a calibration curve in water from 1 to 20 μg/mL (UV-VIS Velab Spectrophotometer).

In-vitro Profile Release
The in-vitro profile was made with apparatus II (Dissolutor LABINDIA model DS 8000) at 100 rpm, with 900 mL of HCl 0.1 N at 37 ± 0.5°C previously degassed, which simulates gastric fluid. Samples (5 mL) were collected at 0.5, 1, 2, 3, 4, 6, 8, 10, 12 and 24 hours, and the medium was replenished. A 1 to 50 μg/mL calibration curve in 0.1 N HCl was used (n = 3) (UV-VIS Velab Spectrophotometer). Drug release data was modeled according to zero-order (Equation 1), first-order (Equation 2), Higuchi (Equation 3), Hixon–Crowell (Equation 4) and Korsmeyer-Peppas (Equation 5) kinetic equations with DDSolver.11

\[
\frac{M_t}{M_\infty} = k_t t \\
\frac{M_t}{M_\infty} = k_t t^{1/2} \\
\frac{M_t}{M_\infty} = k_t t^n \\
\frac{M_t}{M_\infty} = 1 - (1 - k_t t)^3 \\
\frac{M_t}{M_\infty} = k_d t^m + k_e t^{2m}
\]

Floating Behavior and Swelling and Erosion Index
Each tablet was placed individually in 100 mL of simulated gastric fluid at 37 ± 0.5°C and it was measured the floating lag time (time to rise to the surface) and the total floating duration of a tablet. The rates of swelling and erosion were determined by the gravimetric method. Dry tablets were weighed (Shimadzu Analytical Balance) and placed in HCl 0.1 N at 37 ± 0.5°C in separate experiments. The tablets were removed at 0.5, 1, 2, 4, 8, 12 and 24 hours and lightly dried with filter paper. The swollen tablets were weighed and dried at 40 ± 0.5°C for 12 hours (BG drying oven). Finally, the dry weight was determined. The swelling (Equation 6) and erosion (Equation 7) index were calculated using the following equations:
\[
\% \text{ swelling} = \frac{W_s - W_i}{W_i} \times 100 \quad \text{Eq. 6}
\]
\[
\% \text{ erosion} = \frac{W_r - W_t}{W_t} \times 100 \quad \text{Eq. 7}
\]

Where \( W_s \) is the weight of the swollen tablets at the time of sampling, \( W_i \) is the initial weight of the tablet, and \( W_t \) is the weight of the dry tablets at the time of sampling.

### RESULTS AND DISCUSSION

Gastroretentive DDS like floating tablets may increase transit time in GIT, improving the bioavailability of drugs with absorption in stomach or the intestine like MEH\textsuperscript{12,13}. In this study the effervescent floating tablets were obtained by wet granulation. Granule evaluation was performed to assess flow properties (Table 2). It was observed that all formulations presented acceptable to excellent flow behavior, according to the angle of repose (16–19\(^\circ\)) and Hausner ratio (1.11–1.28), also excellent compression properties, according to the Carr index (10–21). Their manufacture was carried out by wet granulation, which is the most common and widely used method, reaching granule humidity values from 2.3 to 2.8%. Wet granulation resulted in granules with homogeneous particle size and good rheological and compressibility properties suitable for the compression stage, regardless of the proportion of Compritol® SB or HPMC.

Round, flat, white and shiny tablets without strange particles were obtained. Table 3 summarizes the results of tablet characterization. All formulations complied with the established acceptance criterion CV \(\leq\) 5% for weight variation. Hardness values ranged from 9 to 12 Kp and all batches complied with the percentage of weight lost specification being no greater than 1% and any capping, cracking or chipping was observed. The results of the uniformity of content were between 95 to 105% according to specifications.

**In-vitro Profile Release**

Figure 1a shows the profile release of the 4 formulations, all batches showed floatability and prolonged release up to 24 hours. The profile release was dependent from the formulation established by the Taguchi L\(4\) experimental design where the effect of HPMC, Compritol® and SB was investigated in the dependent variables such as drug dissolved at 24 hours, swelling and erosion index (%). Formulations 1 to 3 showed a burst effect with a rapid initial release of around 40 to 60% at 3 hours, this effect may be due to the dissolution of MEH from the surface and the effervescent effect by SB, followed by a slow and continuous release until 24 hours. The gastro retentive effect may modify drug absorption, allowing the rate and amount of absorption to take place, especially for drugs with narrow absorption window in the first section of the intestine such as MEH.\textsuperscript{15} Formulation F1 with the three factors of study at low level showed the fastest release of MEH. However, it complied with the acceptance criteria by USP for the dissolution test for extended-release MEH tablets (Figure 1b). Formulation F4, containing HPMC and Compritol® at high level and SB at a low level presented the slowest release, while formulations F2 and F3 in which only one of the components at the high level had similar profiles. All formulations showed slower release of MEH than other flotation systems reported, such as matrix tablets based on cellulose with a dissolution rate of 40 to 80% in 2 hours.\textsuperscript{12} Other authors have obtained MEH effervescent floating tablets with a prolonged release for 12 hours.\textsuperscript{16} In this study, F2 to F4 may allow slower releases (>24 hours). The effects of factors on drug release are presented by principal effects (Figure 1c) and 3-D contour plots (Figure 1d).

#### Table 2: Rheological characterization of granules

<table>
<thead>
<tr>
<th>Formulation</th>
<th>Bulk density (g/mL)</th>
<th>Tapped density (g/mL)</th>
<th>Carr index</th>
<th>Hausner ratio</th>
<th>Angle of repose (°)</th>
</tr>
</thead>
<tbody>
<tr>
<td>F1</td>
<td>0.486 ± 0.009</td>
<td>0.541 ± 0.008</td>
<td>10.110 ± 1.280</td>
<td>1.110 ± 0.017</td>
<td>16.847 ± 2.111</td>
</tr>
<tr>
<td>F2</td>
<td>0.513 ± 0.007</td>
<td>0.588 ± 0.000</td>
<td>12.807 ± 1.120</td>
<td>1.147 ± 0.015</td>
<td>16.447 ± 0.272</td>
</tr>
<tr>
<td>F3</td>
<td>0.532 ± 0.022</td>
<td>0.600 ± 0.028</td>
<td>19.470 ± 0.256</td>
<td>1.243 ± 0.006</td>
<td>19.610 ± 0.572</td>
</tr>
<tr>
<td>F4</td>
<td>0.498 ± 0.009</td>
<td>0.639 ± 0.016</td>
<td>21.993 ± 0.766</td>
<td>1.280 ± 0.010</td>
<td>19.030 ± 1.750</td>
</tr>
</tbody>
</table>

*Mean ± standard deviation (n = 3)

#### Table 3: Characterization of tablet parameters

<table>
<thead>
<tr>
<th>Formulation</th>
<th>Average weight (g)</th>
<th>Weight variation (CV%)</th>
<th>Hardness (Kp)</th>
<th>Friability (%)</th>
<th>Drug content (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>F1</td>
<td>1.160 ± 0.004</td>
<td>0.357</td>
<td>9.156 ± 0.614</td>
<td>0.700</td>
<td>103.474 ± 1.252</td>
</tr>
<tr>
<td>F2</td>
<td>1.310 ± 0.003</td>
<td>0.235</td>
<td>10.767 ± 0.758</td>
<td>0.470</td>
<td>100.231 ± 0.462</td>
</tr>
<tr>
<td>F3</td>
<td>1.257 ± 0.004</td>
<td>0.329</td>
<td>10.055 ± 0.489</td>
<td>0.590</td>
<td>103.468 ± 1.726</td>
</tr>
<tr>
<td>F4</td>
<td>1.299 ± 0.017</td>
<td>1.343</td>
<td>11.903 ± 0.562</td>
<td>0.880</td>
<td>100.925 ± 3.876</td>
</tr>
</tbody>
</table>

*Mean ± standard deviation (n = 3)
eroding of the matrix.17 HPMC is a widely used polymer in floating tablet formulations such as those based on HPMC K15M and κ-Carrageenan with metformin release lasting <8.0 hours.18 Combinations of HPMC K15M with natural polysaccharides also showed that the tablet was maintained for >8 hours in the stomach.19 Combinations of HPMC with different grades of viscosity such as HPMC K4M and HPMC 100M with Carbopol also produced tablets that remained lastingly buoyant over 24 hours.15

**Compritol® ATO 888 effect**

Floating systems can also be obtained from non swellable lipophilic excipients, like waxes and lipids.20 Compritol® 888 ATO is a hydrophobic glyceride mixture21 that has been used as a sustained-release agent for high-dose drug delivery systems due to the formation of a hydrophobic barrier that limit drug diffusion.17,22,23 Figure 1c shows the effect of lipids; increasing the concentration of Compritol® 888 decreased MEH delivery. Several authors have reported sustained-release tablets based on Compritol® 888 ATO resulting in drug delivery during 12 hours22 and matrix tablets for sustained release until 20 hours.24 However, the excipient combination method for the obtention of floating tablets seems to provide DDS with excellent floating properties and satisfactory prolonged release behavior.25 The combination of hydrophilic polymers and lipophilic excipients has been reported to be a useful strategy for sustained release such as a non-effervescent floating matrix tablet based on cetlyl alcohol with HPMC K15M for sustained delivery of MEH during 24 hours26 and sustained-release pellets based on cellulose and Compritol® 888 ATO for 24 hours of delivery.27 Also extended-release non-effervescent tablets based on HPMC with different viscosity grades and Compritol® 888 ATO or Precirol ATO 5 as low-density lipids.28 It was observed that both HPMC and Compritol® decrease the drug release response, however, Compritol® has a greater effect in limiting drug release (Figure 1c and d).

**Sodium bicarbonate effect**

In effervescent floating systems, the most common effervescent components are tartaric acid, citric acid and sodium bicarbonate.29 Figure 1c shows the SB effect on drug release. An initial burst effect is observed attributed to the initial effervescent effect increasing pore formation and drug diffusion paths,15 then the drug release rate was retarded. CO₂ bubbles were extensively liberated and might be trapped in the gel barrier and obstructed diffusion paths, retarding diffusion of drug and dissolution medium.29 The potential role of SB in retarding drug release in combination with hydrophilic polymers such as HPMC was previously reported.14

**Mechanism and Kinetics of Drug Release**

The results of drug release kinetics are summarized in Table 4. Zero order, first order, and Higuchi were discarded due to lower R² values. All formulations showed a good fit into the Korsmeyer-Peppas (R² = 0.961–0.995). However, the higher values were obtained from the Peppas-Sahlin equation (R² = 0.994–0.996), indicating a combination of diffusion, swelling and erosion on drug release, similar to previous reports.12 Peppas and Sahlin proposed an equation to investigate the contribution of anomalous transport on release mechanisms, where Fickian diffusion predominates when k₁ > k₂, none the less when k₂ > k₁, polymer chain relaxation takes preference (Case II).27 Formulations F1 and F4 showed positive values for both constants with k₁>k₂, suggesting a combination of mechanisms (diffusion and erosion) where Fickian diffusion predominates, this result is in accordance with the n value (F1 = 0.522 and F4 = 0.506). F1 and F4 are combinations in which HPMC is in a greater proportion than Compritol® within the formulation, so the water inflow is slightly limited. They showed the same behavior. However, F1 release was faster (KKp = 31.233) than F4 (KKp = 19.241) due to the latter’s increase in polymer and lipid concentrations. Also, the contribution of relaxation is greater in F1 since HPMC is in a higher proportion than Compritol®. All of the above resulted in F1 showing a faster release. In F2, where k₁>>k₂ and n = 0.483, Fickian diffusion predominates over relaxation which is negligible (k₂ = -2.455) due to low levels of HPMC and high levels of Compritol®, which limited water entry and swelling. Compritol® is insoluble in water and does not swell, resulting in drug release taking place mainly by diffusion, as previously reported by some authors.22 F3 shows k₁<<k₂ and n = 0.613, corresponding to the relaxation of the chains being the predominant mechanism. Since the concentration of HPMC is in high level while Compritol® limited the entry of water, in addition the high level of SB which also favors this process and the progression of swelling and erosion of the matrix. Peppas-Sahlin constants shows that HPMC allows the release of the drug by diffusion in a first stage; however, as water begins to penetrate, the process of relaxation of the chains (swelling) with its subsequent erosion takes place. Swelling and erosion were limited according to the proportion of Compritol® used.11 These results are similar to previous reports where the effect of combinations of hydrophilic and lipophilic excipients on the profiles and mechanism release was investigated, indicating that the relaxation rate constant (k₂) decreased when the hydrophilic (F1 and F4) or the lipophilic proportions (F2) increase in tablets.11 It was observed that drug release is slower when only one release mechanism is present, either diffusion (F2) or erosion (F3), compared to when two mechanisms are involved (F1).

**Floating Behavior and Swelling and Erosion Index**

Table 5 shows the results of the flotation parameters of the tablets. Preferably, the FDDS should possess a short flotation lag time to avoid transiting to the small intestine.30 It has been reported that effervescent floating tablets improve buoyancy in high-dose tablets. Also, the use of low-density lipid excipients as Compritol® may improve buoyancy properties.14,28 Improvement in buoyancy has been reported as well when high-viscosity grade HPMC is present.25 F2 and F3, which contain high SB levels, showed short floating lag time due to rapid and higher CO₂ production. Additionally, F2 with high levels of SB and Compritol® showed the lowest float lag...
Lipid-Polymer Effervescent Floating Tablets

Table 4: Coefficient of determination for MEH release by fitting

<table>
<thead>
<tr>
<th>Formulation</th>
<th>Zero-order</th>
<th>First order</th>
<th>Higuchi</th>
<th>Korsmeyer-Peppas</th>
<th>Peppas-Sahlin</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>$R^2$</td>
<td>$R^2$</td>
<td>$R^2$</td>
<td>$n$</td>
<td>$R^2$</td>
</tr>
<tr>
<td>F1</td>
<td>-0.438</td>
<td>0.936</td>
<td>0.825</td>
<td>0.966</td>
<td>0.522</td>
</tr>
<tr>
<td>F2</td>
<td>-0.224</td>
<td>0.876</td>
<td>0.857</td>
<td>0.961</td>
<td>0.483</td>
</tr>
<tr>
<td>F3</td>
<td>0.049</td>
<td>0.948</td>
<td>0.907</td>
<td>0.987</td>
<td>0.613</td>
</tr>
<tr>
<td>F4</td>
<td>0.172</td>
<td>0.900</td>
<td>0.944</td>
<td>0.995</td>
<td>0.506</td>
</tr>
</tbody>
</table>

Figure 1: (a) MEH profile release of formulation F1 to F4, (b) F1 profile release with acceptance criteria by USP for dissolution test, (c) Effect of HPMC, Compritol® and SB on drug dissolved (24 hours) (d) 3-D contour plot of factors effect on drug dissolved (24 hours)

Table 5: Results of the tablet buoyancy properties assessment

<table>
<thead>
<tr>
<th>Formulation</th>
<th>Float lag time*</th>
<th>Total flotation time (Hours)</th>
</tr>
</thead>
<tbody>
<tr>
<td>F1</td>
<td>1.750 ± 0.270</td>
<td>24</td>
</tr>
<tr>
<td>F2</td>
<td>1.420 ± 0.070</td>
<td>24</td>
</tr>
<tr>
<td>F3</td>
<td>1.070 ± 0.740</td>
<td>24</td>
</tr>
<tr>
<td>F4</td>
<td>1.970 ± 0.390</td>
<td>24</td>
</tr>
</tbody>
</table>

*Mean ± standard deviation (n = 3)

All formulations show a total flotation time of 24 hours (Table 5), which can be attributed to the combination of excipients such as HPMC and Compritol®. HPMC was responsible for the entrapment and protection of the CO$_2$ within the gel layer. This process decreased the tablet density, consequently increasing flotation capacity in the stomach. On the other hand, Compritol® slowed water diffusion inside the matrix, resulting in the tablet floating for a longer period of time.

The evaluation of the swelling index (Figure 2a) is relevant because it corresponds with the formulation’s hydration capacity and affects tablet flotation and drug release. The swelling rate influences the release of the drug, as water gradually penetrates the tablet, a hydrated gel is generated, which the dissolved drug must overcome in its diffusion pathway. Thus, if water penetration to the tablet is insufficient, the diffusion of the active substance to the medium will be restricted. The swelling index was determined by measuring water absorption. Swelling was evaluated during 24 hours and analyzed as a dependent variable such as swelling at 12 hours (Figure 2c) and 24 hours (Figure 2e). At 12 hours, the lowest and highest swelling indexes were obtained in formulations F4 (120.00%) and F1 (154.47%), respectively, and the rate of swelling showed the tendency F1>F3>F2>F4. It was observed that both HPMC and Compritol® decreased swelling while SB increased the index values. At 24 hours, the lowest and highest swelling indexes were obtained in formulations.
Lipid-Polymer Effervescent Floating Tablets

CONCLUSION

Four formulations of lipid-polymer effervescent floating tablets were obtained and evaluated through a Taguchi experimental design. All tablets maintained metformin extended-release for 24 hours. Formulation F1 meets the acceptance criteria for extended delivery in the USP. Compritol® in combination with HPMC and SB significantly impacted the formulations by improving the physical properties, buoyancy and kinetic release characteristics of metformin tablets. Formulations with high amounts of HPMC and Compritol® were found to have the lowest release rates and the longest times. All the formulations followed Peppas-Sahlin kinetic model in which drug release depends on the combination of diffusion and relaxation-erosion mechanisms.

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