

## Effect of Hydroxy Propyl Methyl Cellulose (HPMC) on Amoxicillin Floating Tablet

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### Abstract

Amoxicillin is a broad spectrum antibiotic which has been used for treatment range of infections including *Helicobacter pylori*. Formulating a locally release drug delivery is preferred for better amoxicillin action. Floating dosage form is a candidate for carrying the drug which reserve drug in the upper gastrointestinal tract (GIT). Hydroxypropyl methyl cellulose (HPMC) was studied in this research to determine its effect on floating characteristics of amoxicillin tablet. Seven formulas of amoxicillin floating tablet were prepared by direct compression method. The results showed that using about 11% of the polymer gave better floating lag time (about 3 minutes) and floating duration (more than 5 hours) to be optimized formula in comparing with others.

تأثير هيدروكسي بروبيل ميثيل سيليلوز على طوفانية حبة الاموكسيسيلين

### الخلاصة

الاموكسيسيلين هو مضاد حيوي واسع الطيف يستخدم لعلاج الكثير من العدوى البكتيرية مثل التهاب المعدة ببكتريا هليكوباكتر بايلوري. للحصول على تأثير امثل للدواء لعلاج هذه العدوى يتطلب تصميم هيئة دوائية تبقى الدواء لفترة محددة داخل الجزء العلوي للجهاز الهضمي. الحبة الطافية هي واحدة من ابرز الطرق لذلك الغرض وهي تعتمد على البوليمرات المستخدمة. في هذه الدراسة تم استخدام هيدروكسي بروبيل ميثيل سيليلوز. سبعة تشكلات للحبة الطافية للاموكسيل قد حضرت بطريقة الكبس المباشر. وقد بينت النتائج ان استخدام هذا البوليمر بنسبة مايقارب 11% قد اعطت خواص طوفانية الافضل مقارنة ببقية النسب المستخدمة.

الكلمات المفتاحية: طوفانية، اموكسيسيلين، هيليكوباكتر بايلوري، هايدروكسي بروبيل مثل سيليلوز.

## 1. Introduction

Gastro retentive systems has significantly prolonged gastric residence time of drugs in the stomach. It can remain in the gastric region for hours to release the drug in a local area for absorption in upper GIT.<sup>1,2</sup> This enhances its solubility and increases the drug bioavailability. There are many strategies for formulating retentive drug delivery system for GIT including swelling and expandable systems, intragastric floating systems, modified shape systems, bioadhesive systems, low-density super porous systems high-density systems and delayed gastric-emptying systems.<sup>2,3</sup> Floating system has advantages for designing drug that absorbed from stomach and upper part of intestine. Furthermore, it is used for drugs that their absorption affected by the vigorous intestinal movement. Floating dosage form remains buoyant in the stomach for long period of time without affecting by gastric emptying time because it has less bulk density than the GIT fluid.<sup>4,5,6</sup>

Tablet is preferred dosage form for oral administration due to its ease of manufacturing and administration. Therefore, most of the floating dosage form has been formulated as tablet. This floating drug delivery depends mainly on the characteristics of employed polymers which entrap the drug within the formula. Many polymers have been used in floating formulation such as hydroxypropyl methyl cellulose (HPMC), carboxymethyl cellulose (CMC) and others.<sup>7,8</sup> Amoxicillin is a broad spectrum penicillin antibiotic which is used for wide range of infection including *Helicobacter pylori* (H. pylori). This bacteria is responsible on gastric and peptic ulcer. It has been demonstrated as one of the main line therapy for this infection for long time.<sup>9,10</sup> Amoxicillin is class III drug in biopharmaceutics classification system which has high solubility and low permeability. A local release of amoxicillin is required to treat this infection as floating system.<sup>11,12</sup> The aim of this research is to study the effect of HPMC on the floating characteristics of the amoxicillin tablet.

## 2. Materials and Methods

### 2.1. Materials

Amoxicillin was gift from Samaraa drug company (Iraq). HPMC was purchased from Baoji Guokang Bio-Technology Co., Ltd (China). Calcium carbonate (CaCO<sub>3</sub>) was from Carlo ERBA (France). Talc was purchased from Al-Rahma pharmaceutical Co. (Jordan). Magnesium stearate (MS) was from H. L. Blachford Ltd (United Kingdom).

## 2.2. Methods

### 2.2.1. Preparation of Single Unit Floating Matrix Tablet

A specific amount of HPMC, talc and the drug had been added in a mortar and mixed together with the pestle, as presented in Table 1. In another mortar, accurately an amount of  $\text{CaCO}_3$  crushed with pestle. All the ingredients were mixed together in the mortar then, MS was mixed for two minutes. Finally, the direct compression method was employed to compress the ingredient into tablets.<sup>13,14,15,16,17,18</sup>

**Table 1.** Formulations of Floating Tablet of amoxicillin.

Ingredient (mg)	F1	F2	F3	F4	F5	F6	F7
Amoxicillin	250	250	250	250	250	250	250
HPMC	5	10	25	50	75	100	125
$\text{CaCO}_3$	65	65	65	65	65	65	65
Talc	125.5	120.5	105.5	80.5	55.5	30.5	5.5
MS	4.5	4.5	4.5	4.5	4.5	4.5	4.5
Total weight	450	450	450	450	450	450	450

### 2.2.2. Evaluation of Floating Tablet

#### 2.2.2.1. Hardness test

Monsanto hardness tester had been used to measure this test (in  $\text{Kg/cm}^2$ ). Four floating tablets from each formula were picked randomly and the hardness was determined.<sup>13,14,15,16,17,18</sup>

#### 2.2.2.2. Weight variation test

Twenty tablets of the each prepared formulation were selected. The digital balance was used to measure their weights individually and collectively.<sup>13,14,15,16,17,18,19</sup>

### 2.2.2.3. Drug content

Ten tablet of each formula was powdered then 100 ml of 0.1 N HCl was added. The solution of amoxicillin was drawn and filtered with 0.45  $\mu$ m syringe filter. Then, amoxicillin was estimated by UV spectrophotometer (Carry win UV, Varian, Australia) at 230 nm.<sup>13,14,15,16,17,18,19</sup>

### 2.2.2.4. Thickness of the formulated tablets

Micrometer was used for this purpose. Three tablets of each amoxicillin batch was selected randomly and measured individually.<sup>13,14</sup>

### 2.2.2.5. In vitro buoyancy studies

In vitro buoyancy was evaluated by determining the floating lag time. Three tablets of each formula were taken. The tablet was placed in a beaker containing 100 ml of 0.1N HCl and the time required for the tablet to rise to the media surface and float was determined as floating lag time. The duration of time for each tablet dosage form remained on the surface of medium was determined as the total floating time.<sup>13,14,15,16,17</sup>

### 2.2.2.6. Swelling study

The swelling behavior of a tablet dosage form was measured by determination the difference in the weight before and after water (WU). The study was performed by immersing the tablet in 0.1N HCL at 37 °C and determining these factors at regular intervals up to 4 hours period. Water uptake was measured in terms of percent weight gain, as given by the equation.<sup>13,14,15,16,17</sup>

$$WU = (W_t - W_o) \times 100 / W_o$$

Where, WU is the water uptake,

$W_t$  is the weight of the dosage form at time.

$W_o$  is the initial weight of the dosage form

### 2.2.2.7. In vitro drug dissolution studies

The dissolution fluid was 900ml of 0.1N HCl, at speed of 50 rpm and a temperature of  $37 \pm 0.50$  °C were employed in each test. An aliquot 5 ml was withdrawn and filtered through a syringe filter of 45  $\mu$ m at different time intervals along 6 hours of the study, diluted and assayed using UV spectrophotometer.<sup>13,14,15,16,17</sup>

## 3. Results and discussion

All the formulations of the amoxicillin floating tablets were evaluated for their various physical parameters. The hardness test are represented in the range of 6.8 to 7.5  $Kg/Cm^2$ . These results refer to acceptable values within the normal ranges, as illustrated in Table 2.<sup>19</sup>

The weight variation of amoxicillin floating tablets were within the acceptable range and appeared to be uniform with low standard deviation value. Drug content uniformity of amoxicillin floating tablets have percentages which are in the acceptable range of 96.03 to 98.1%, as illustrated in Table 2.<sup>19</sup>

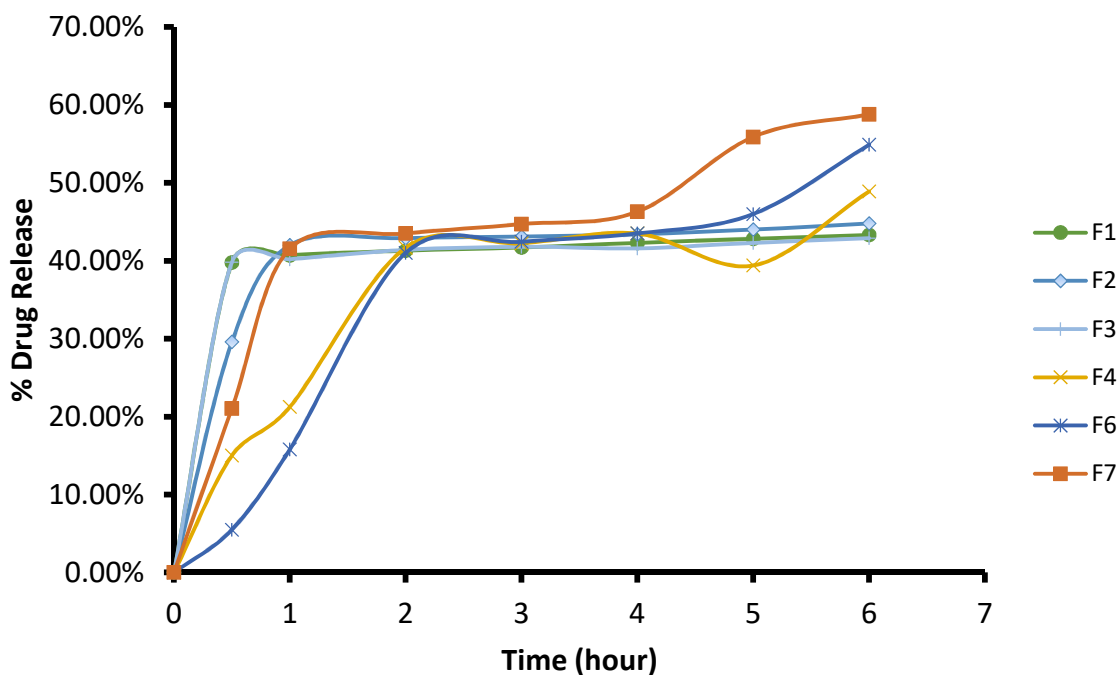
The magnitudes of the lag time of in vitro buoyancy study which were obtained a result experimentally are located within the range of 2 to 25 minutes. These results indicate that the floating lag time prolong when HPMC increases as observed in Table 2.<sup>15,16,19</sup>

**Table 2.** Post compression values of amoxicillin floating tablets

Batch code	Hardness* ( $Kg/Cm^2$ )	Weight variation* ( $mg$ )	Drug content uniformity*** (%)	Thickness* ( $mm$ )	Floating lag time * ( $min: second$ )	Total floating time* ( $hrs: min$ )
F1	6.8±1.0	451.2±0.2	98.05	7.01±0.02	4:38	4:49
F2	7.0±0.8	454.5±4.1	96.78	6.9±0.01	3	5:20
F3	7.3±0.5	448.2±3.2	96.03	7.0±0.03	16	4:15
F4	7.2±0.7	451±3.0	98.1	7.45±0.01	2:50	5:16
F5	7.2±0.9	455±5.1	96.3	6.98±0.35	19:47	4:38
F6	6.8±0.92	446±4.8	97.45	6.85±0.05	22:14	4:33
F7	7.5±1.1	453.4±3.4	96.23	7.58±0.08	25	4:55

\* $n=3$ , \*\* $n=4$ , \*\*\* $n=10$ , \*\*\*\* $n=20$

It was observed in the dissolution study that the release from matrix is relied on the amount of polymer, drug diffusion, and matrix erosion.<sup>13,16,17</sup> The drug release was carried out up to 6 hrs and the percentage of drug release from batch F1 to F7 varies from (5.5-58.8) %, as shown in Figure 1.



**Figure 1.** In-vitro drug release profile of amoxicillin floating tablets.

Swelling index which describes the amount of water uptake by polymer is considered as a function of network structure, hydrophilicity and ionization of functional groups of the polymer. In this study, the tablet weight increased experimentally with time gradually due to the water absorbed by the polymer and that depends on the polymer hydrophilicity where the outer layer of the polymer is the most part hydrated and swell, as explained in Table 3.<sup>20,21</sup>

**Table 3.** Swelling index of the amoxicillin floating tablets.

Batch code	Swelling Percentage in 2hrs (%)	Swelling Percentage in 4hrs (%)
F1	33.43	38.08
F2	35	42.9
F3	34.13	40.5
F4	32.01	35.8
F5	41	45.2
F6	39.9	40.5
F7	44.8	50.31

Table 2 shows that F4 has the best floating characteristics in dissolution media (gastric media at pH=1.2), good floating lag time (2:50) minutes, it seems that the amoxicillin tablets remain floats in the media of stomach without any cross to region of intestine. The drug release shows that it has fair sustained release at constant rate while the swelling index of the drug release is good, this translation is carried out by increasing the floating time. As mentioned above, the F4 is the optimized in comparison to other formulations as well as that F1, F2, F3, F4 have a good floating properties of 4:15 to 5:20 hrs with appropriate water uptake (the amount of needed water increases by adding more amount of HPMC) the drug release appears that they have sustained drug release. The F5, F6, F7 had prolonged lag time 20-25 minutes due to increase amount of HPMC. Its swelling capacity was high because of increase ratio of HPMC polymer, all these made drug release need sufficient time to be complete.<sup>20,21</sup>

#### 4. Conclusion

In this study it can conclude that gastro retentive floating tablet of amoxicillin is controlled by adding HPMC as a polymer. The floating tablet of amoxicillin is capable of maintaining the drug release for approximately 5 hrs. The formulation F4 has provided acceptable floating properties in comparison to the other formulations since it has rapid floating lag time.

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