Original Article

Naproxen sodium influence, excipients and the dissolution medium on the swelling of the tablets

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ABSTRACT

The study aims to investigate the influence of naproxen sodium, excipients, and the dissolution medium on the swelling of tablets. Naproxen sodium was the model drug used in the study. tablets were formulated from different types and ratios of polymers methylcellulose, sodium carboxymethylcellulose (hydrophilic polymers), and cellulose acetate phthalate (hydrophobic polymer) with another excipient. The dimensional changes and shapes were investigated in different dissolution mediums. The results showed that the diameter of naproxen sodium tablets with methylcellulose as an excipient in water reduced, while in the basic media with the buffer of pH 7.4, an increase in the diameter of tablets was observed. In the acidic buffer of pH 1.2, the diameter increased in the first hour from 1.1 cm at zero time to 1.25cm in the second hour and remains in the same diameter until the eighth hour. The results showed that in naproxen tablets with sodium carboxymethylcellulose in water the diameter of the tablets increased, while the higher increase in the tablet diameter was observed in the buffer of pH 7.4. Finally, in the buffer of pH 1.2, no change in the diameter of the tablet was observed during the time of the test. Naproxen tablets with cellulose acetate phthalate in water, diffusion of particles were observed around the tablets like beams, and the diameter of the tablets reduced by time.

Keywords: Naproxen sodium, Swelling rate, Excipients, Dissolution medium

Introduction

Naproxen sodium is an odorless crystalline powder, white to creamy in color, it is a nonsteroidal anti-inflammatory drug (NSAID), with analgesic and antipyretic properties, it is freely soluble in water [1, 2].

In the present study different formulas were prepared from the drug with hydrophilic and hydrophobic polymers to examine its effect on the swelling rate of the matrices in the different dissolution mediums.

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Cellulose Acetate Phthalate (CAP) a hydrophobic polymer is widely used in synthetic polymer and enteric-coated products [3-6]. Also, the effect of dissolution medium on drug release and swelling had been investigated by many researchers [7, 8].

Hydrophilic celluloses are widely used in the preparation of controlled release dosage forms. their ability to accommodate a large number of drugs, ease of compression, also they are not influenced by the processing variables are the reasons for their popularity [9-11]. Sodium Carboxy Methyl Cellulose (NaCMC) methylcellulose (MC) are available in a range of viscosities and good swelling to regulate the release of various drugs [12-16]. Cellulose Acetate Phthalate (CAP) a hydrophobic polymer is widely used in synthetic polymer and enteric-coated products [2, 3]. Several studies have discussed the combining of hydrophilic-hydrophobic polymers to produce controlled-release tablets [17-22].

Hydrogels and other polymer-carriers were developed to provide safe passage of drugs to the site of action in the body. Drugs have been incorporated in polymers to modify their

release or its half-life characteristics as well as to allow for passive and active targeting [14, 16, 23].

The application of polymers in drug delivery was used for more than 6 decades by compression, coating, and encapsulation. The polymers used were included cellulose derivatives, poly (ethylene glycol) PEG, and poly (N-vinyl pyrrolidone) [24]. From a drug delivery perspective, polymer devices can be categorized as diffusion-controlled devices, swelling- or osmotically-controlled devices [25], biodegradable systems, or systems that are affected by external factors such as pH, and temperature [26].

Materials and Methods

To prepare the matrices, the following materials were used: naproxen sodium a gift from Alhikma pharmaceutical manufacturing Jordan, sodium carboxymethylcellulose (NaCMC) (Carme lose) was sponsored by the Arab Pharmaceutical Manufacturing- Jordan (APM), methylcellulose from (GCC), cellulose Acetate Phthalate (CAP) from (Fluka) Magnesium stearate from (BDH). All the chemicals were reagent grade.

Preparation of tablets

The drugs and the excipients were blended for five minutes in a blender. The powders were compressed to prepare 400 mg tablets in a single tableting machine (Korch-Erweka). The ratio between the diameter and the thickness of the cylindrical flat-faced tablets was between 1.1and 0.4 cm. The hardness of the tablets was between 6 - 8 kg measured by Schleuniger-2 hardness tester. The physical evaluation of 20 tablets was made, such as weight deviation which was 1.6%, and the friability test which was less than 1% after 4 minutes.

formulations were prepared as listed in **Table 1** to evaluate the effect of the drug and the dissolution medium on the swelling rate of the tablet.

Table 1. The different formulations of tablets used in the study and the % composition of each tablet

ingredients	Formula 1	Formula 2	Formula 3
Naproxen sodium	50% (200 mg)	50% (200 mg)	50% (200 mg)
Methylcellulose	49 % (196mg)	-	
Sodium carboxymethyl cellulose	-	49 % (196)	
Cellulose acetate phthalate	-	-	49 % (196)
Mg stearate	1% (4mg)	1% (4mg)	1% (4mg)

Swelling and dimensional changes

The results showed that the diameter of the tablets with methylcellulose as an excipient in water reduced from 1.1 cm in the zero time to 0.80 cm in the eighth hour while in the basic media phosphate buffer pH 7.4 and increase in diameter of the tablets from 1.1 cm at zero time to 1.65 cm at the eighth hour. In the acidic buffer pH 1.2, the diameter of the tablets increased in the first hour from 1.1 cm at zero time to 1.25cm in the second hour and remains in the same diameter until the eighth hour **(Figures 1 and 2)**.

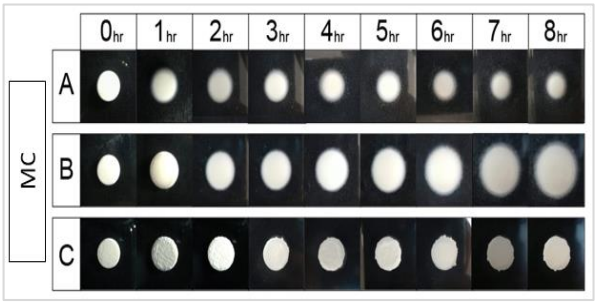

Figure 1. The swelling rate of tablets using MC in the different dissolution mediums (A- water, B- pH =7.4, and C - pH =1.2)

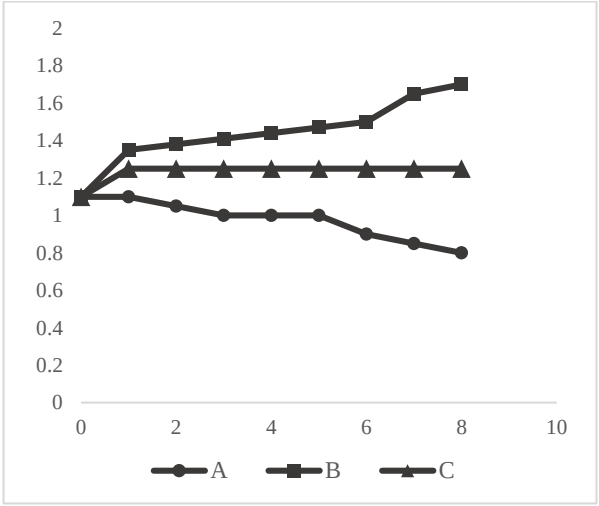

Figure 2. The graphical curve of the swelling rate of tablets using MC in the different dissolution mediums (A- water, B- pH =7.4, and C - pH =1.2)

Naproxen tablets with sodium carboxymethylcellulose in water the diameter of tablets increased from 1.1cm in the zero time to 1.45cm in the eighth hour while in the buffer of pH 7.4 an increase in the diameter of the tablets from 1.1 cm at zero time to 1.75 cm at the eighth hour. Finally in the buffer of pH 1.2 no change in the diameter of the tablets all the time **(Figures 3 and 4)**.

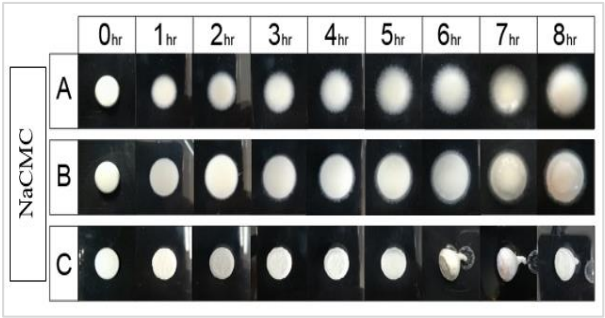

Figure 3. The swelling rate of tablets using NaCMC in the different dissolution mediums (A- water, B- pH =7.4, and C - pH =1.2)

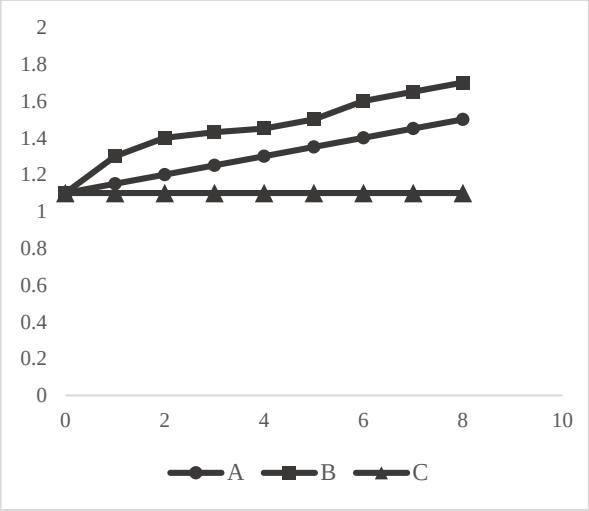

Figure 4. The graphical curve of the swelling rate of tablets using Na CMC in the different dissolution mediums (A- water, B- pH =7.4, and C - pH =1.2)

Naproxen tablets with cellulose acetate phthalate in water, diffusion of particles were observed around the tablets like beams, and the diameter of the tablets reduced by time **(Figure 5)**.

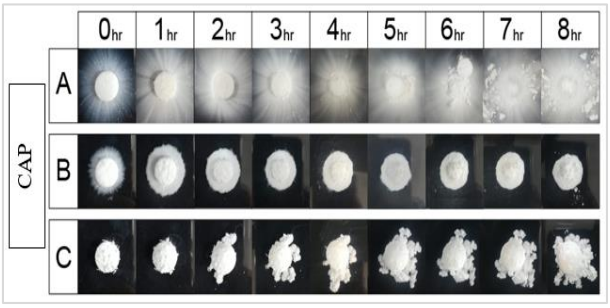

Figure 5. Shows the swelling rate of tablets using CAP in the different dissolution mediums (A- water, B- pH =7.4, and C - pH =1.2)

Results and Discussion

The results showed that the diameter of the tablets with methylcellulose as excipient when placed in Petri dishes containing 50 of water was reduced from 1.1 cm in the zero time to 1.08 in the first hour, to 1.06 in the third hour, 1.05 in the fourth hour, 1.03 in the fifth hour to 1.01 in the sixth hour, into 0.9 cm in the seventh hour and finally to 0.80 cm in the eighth hour as illustrated in **Figure 1** and the graphical **Figure 2** these results may be attributed to the freely soluble naproxen sodium [1] and the solubility of methylcellulose which is soluble in room temperature water more than the hot water [27].

Tablets of naproxen with MC excipients when the tablets were placed in Petri dishes each of 50 ml phosphate buffer pH 7.4 the diameter of the tablets increased from 1.1 to 1.15cm in the first hour. The diameter of the tablets increased to 1.25 cm in the second hour, 1.32 cm in the third hour to 1.39 cm in the fourth hour,145 cm in the fifth hour to 1.52 cm in the sixth hour, to 1.6 in the seventh hour, and 1.65 in the eighth hour, also gel layers was observed around the tablets. The slight and almost increase in the dimension of tablets was due to the slight penetration of water into the stagnant tablets in the dissolution medium and the free solubility of naproxen sodium in water [1] which resulted in the slow and regular swelling rate of the tablets and the tablets retain its cohesiveness [28, 29], also the solubility of methylcellulose in room temperature water is more than that of hot water [27]. The gel layer formed due to a slight release of naproxen in the outer layer of the stagnant tablets while the hydrophilic polymer retains its shape in a form of gel [30].

In the acidic buffer pH 1.2, the diameter of the tablets increased in the first hour from 1.1 cm at zero time to 1.25cm in the second hour and remains in the same diameter until the eighth hour **(Figures 1 and 2)**. this is due to the gel layer formed by NaCMC which is characterized by a rigid structure of a partially chemically cross-linked gel [27, 31, 32] which prevents the penetration of the dissolution medium to the tablets after the first hour.

Tablets of naproxen with NaCMC as excipients were placed in Petri dishes containing 50 ml of water as dissolution medium, the diameter of tablets increased from 1.1 to 1.15 cm in the first hour, to 1.2 cm in the second hour, to 1.25 cm in the third hour, to 1.3 cm in the fourth hour, 135 cm in the fifth hour to 1.4 cm in the sixth hour, to 1.43 in the seventh hour and 1.48 in the eighth hour with gel layers around the tablets. The slight and almost increase in the dimension of tablets was due to the slight penetration of water into the stagnant tablets in the dissolution medium and the free solubility of naproxen sodium in water [1] which resulted in the slow and regular swelling rate of the tablets and the tablets retain its cohesiveness [26]. The gel layer formed due to a slight release of naproxen in the outer layer of the stagnant tablets while the hydrophilic polymer retains its shape in a form of a gel [28].

When the tablet was placed in the Petri dishes with a dissolution medium of phosphate buffer pH 7,4 The increase of diameter was more than that of water. The increase from the first hour to the eighth hour was as follows 1.2 cm at the first hour, 1.3 cm at the second hour and 1.4 cm in the third hour, 1.45cm in the fourth hour, 1.55 in the fifth hour 1.6 in the sixth hour, it is observed that more drugs were released from the tablets. In the seventh hour, the diameter of the tablets increased to 1.7cm and 1.75 cm at the eighth hour and the thickness of the gel layer formed was more than that observed when the tablets were placed in water which is due to the more penetration of phosphate buffer pH 7.4 to the tablets and to more solubility of naproxen sodium which decreases the cohesiveness force of the polymer and the thickness of the gel layer increased, meanwhile the tablets retain their shape, **Figures 3 and 4** [26].

As illustrated in **Figure 3** and the graphical **Figure 4** when the tablets were placed in the dissolution medium acidic buffer pH = 1.2 with NaCMC as excipient there was no change in the diameter of the tablets all the time of placing tablets in the dissolution medium from the first to the eighth hour this is due to the gel layer formed by NaCMC which is characterized by a rigid structure of a partially chemically cross-linked gel [30, 31] which prevent the penetration of the medium to the tablets with a result of decreasing the density of the tablets, and formation of

the pyramidal shape with a tail that collapse the tablets as seen in **Figure 3-A**.

As illustrated in **Figure 5-A** when the tablets were placed in Petri dishes containing 50 ml of water diffusion of particles from the tablets was started from the first hour in a manner like beams around the tablets.

In the second hour the diffusion of the particles became wider and the dimension of the tablets reduced to about 1.05, also some particles were separated from the tablets, at the third hour the size of the particles became larger than the second hour and the diameter of the tablets reduced to 1 cm. from the fourth hour to the eighth hour there was no possibility to measure the diameter of the tablets due to the complete separation of the tablets. All these results may have been attributed to the moisturizing the hygroscopic CAP [32] which permeates water to penetrate the tablets to dissolve the free soluble naproxen sodium in water [1] with a result of tablets disintegration at the fourth hour.

When the tablets were placed in Petri dishes containing 50 ml of basic medium phosphate buffer pH 7.4 the dissolution medium penetrate the tablets and dissolve naproxen sodium within the tablets from the first hour to the fourth hour from the first and the second hour the diameter of the tablets reduced to 1 cm and dissolved drug accumulated around the tables in the third and fourth hour the tablet diameter reduced to 0.8 cm, after the fourth hour the tablets were disintegrated and we cannot obtain the diameter of the tablet because the drug within the tablets dissolved in the buffer [26] while CAP is soluble in buffer solutions at pH values more than pH= 6 [2], with a result of polymer solubility as illustrated in **Figure 5**.

When the tablets were placed in Petri dishes of pH = 1.2, it is observed that the tablets were disintegrated by time and there was no possibility to measure the diameter of the tablets due to the solubility of naproxen sodium which dissolves in the dissolution medium and the separation of the hydrophobic polymer (CAP).

Conclusion

the swelling rate of tablets was generally governed by the polymer type, the drug solubility, and the dissolution medium played a very important role in the swelling rate of the tablets depending on the hydrophilicity and hydrophobicity of the polymer used.

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Ethics statement: None

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