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COATED GELLAN GUM HYDROGEL AS A DRUG CARRIER FOR COLON TARGETED DRUG DELIVERY

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Abstract: Oral drug delivery system provides a simple mechanism and more convenient approach towards colon cancer treatment. Yet, oral drug administration also faced some limitation passing through in the gastrointestinal tract before reaching the targeted area. In this work, a coated gellan gum hydrogel was proposed to increase the treatment efficiency in colon cancer treatment through oral administration using dip coating process. Two types of coating materials, hydrocarbon (eicosane and docosane) and fatty acid (C12 and C16) were used. Single and mixed coating materials were tested using DSC and the results obtained showed that the best coating material was hydrocarbon with a weight ratio of 40:60 of eicosane and docosane (E:D).

Keywords: Coating materials, polymer, gastrointestinal tract, oral administration, colon cancer.

Introduction

Targeted oral colonic drug delivery system (CDDS) is to treat the colon site through oral administration. The drug delivery into the colon often encountered issues such as extreme pH environment in the GIT. The drug was either degraded or absorbed by colonic mucosa (Amidon *et al*., 2015). Hence, CDDS must have the ability to protect the drug so that no drug are released and absorbed in stomach or small intestine along the pathway to the colon and only triggered at the target site (Philip & Philip, 2010). Previously, Rangari and Puranik (2015), proposed pH sensitive polymer coating for colon site, however, this type of coating was pH dependent hence less efficient due to the uncertain pH inside the GIT.

In drug delivery system, hydrogel often used as drug carrier due to its versatile platform for the biomedical application (Tyagi *et al.,* 2004; Ranganath *et al.,* 2009).

In this work, gellan gum hydrogel was used because of its advantageous properties such as biocompatibility, biodegradability, non-toxicity and has been reported extensively in the literature (Prajapati *et al.,* 2013; Osma *et al.,* 2014; Pacelli *et al.,* 2015). Due to the challenges of drug delivery through oral administration in targeting the colon site a coated gellan gum hydrogel was proposed. Coated gellan gum hydrogel was never been used for the oral route in cancer treatment and this is the novelty of the research.

Materials and Methods

Materials

Gelzan and glycerin (Aldrich), paracetamol and calcium chloride (R&M Chemical), fatty acid (lauric acid, C12 and palmitic acid, C16) and hydrocarbon (eicosane and docosane) (Merck) were used in this reaserch.

Preparation of gellan gum hydrogel as drug carrier

The gellan gum and paracetamol (drug model) were weighed and dissolved in deionized water separately. Then, glycerin was added followed with calcium chloride (0.1 M). The hydrogel

was dried for 24 h prior to other characterization. The hydrogel was prepared following the same procedure as reported earlier (Mohd Sebri & Mat Amin, 2015). The hydrogel was then immersed into the basic and acidic medium. The absorbance peak was detected at 243 nm to confirm the drug loading ability.

Coating material for gellan gum hydrogel

Fatty acid (lauric and palmitic acid) and hydrocarbon (eicosane and docosane) were chosen as coating materials. The coating material was heated until it melted. Then, the hydrogel was dipped into the solution manually. Immediately, it was pulled up and allowed the coating to cooled down and stick to the surface of the hydrogel. The hydrogel was coated using dip coating process as reported by (Rose *et al*., 2016). Single and mixed coatings with different weight ratio were tested with a heating range of 38 ^{o}C to 42 ^{o}C and the best coating was identified using Perkin Elmer Pyris 6 Differential Scanning Calorimeter (DSC).

Dissolution Studies

Dissolution studies were performed using two solution medium that is basic medium (pH 6.80) and acidic medium (pH 1.20) as previously reported in (Rose *et al*., 2016). The sample was taken every 10 minutes for 2 hours in acidic medium (500 ml) and 6 hours in basic medium. The sample then tested using UV-1800 Shimadzu UV-vis Spectrophotometer at 243 nm and the amount of drug released were calculated using formula below:

$$\frac{\text{Amount of paracetamol in sample aliquot}}{\text{Amount of paracetamol loaded in hydrogel}} \times 100$$

Result and Discussion

Preparation of gellan gum hydrogel as drug carrier

Figure 1 showed the gellan gum hydrogel in a cylindrical shape formed due to the gelation of gellan gum solution by addition of Ca^{+} ions during its preparation. From the UV result (Figure 2), a peak at 243 nm was observed indicating that the gellan gum hydrogels were able to load drug inside it polymeric chain. This is in accordance to previous reported by Behera and coworkers (2012).

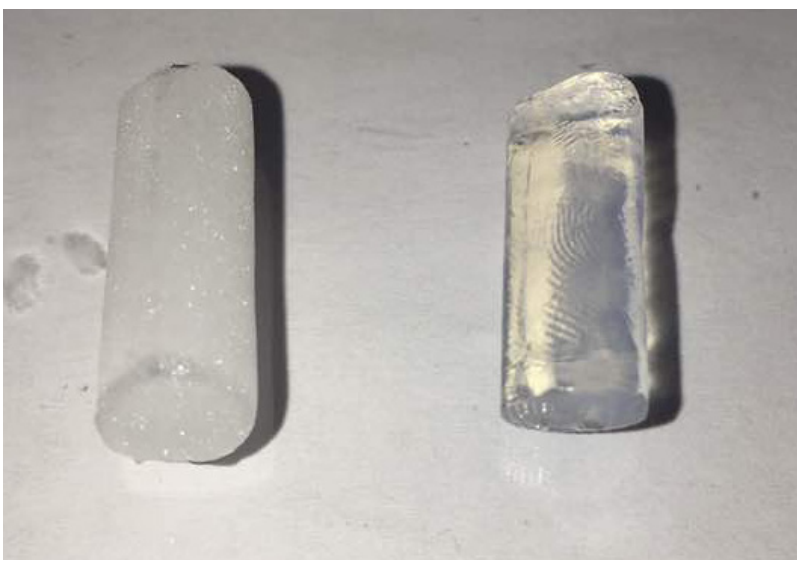


Figure 1: The gellan gum hydrogel obtained

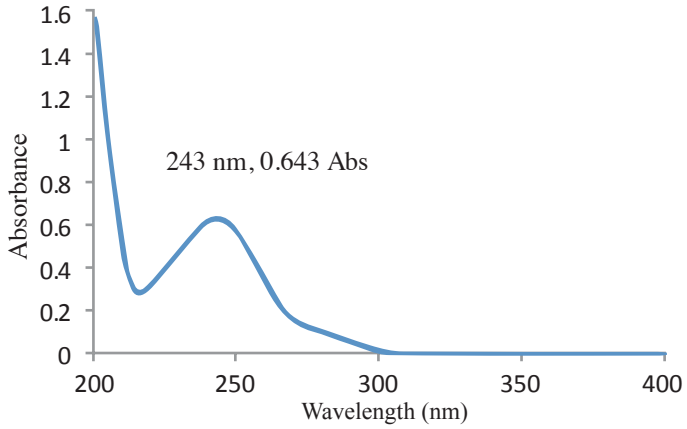


Figure 2: UV spectrum of paracetamol in the basic medium

Coating materials

Table 1 showed the melting temperature for single coating materials. Due to their melting point either low or too high making them were not suitable as a coating. The most important criteria in choosing the best coating material is the melting temperature of the materials must be in the range between 38 °C to 42 °C. This is because the coating material will not directly melt after consumed as body temperature is around 37 °C and the human cells tend to die with temperature more than 42 °C.

For mixed materials, the result obtained is shown in Figure 3 where the addition of C16 and docosane into C12 and eicosane respectively increased the melting point of the mixture due to their high melting temperature. It was observed that the melting point of mixed hydrocarbon and

Table 1: The melting temperature for the coating materials (Domalski & Hearing, 1996)

Coating Materials	Melting temperature, °C
Eicosane	37.70
Docosane	43.71
Lauric acid (C12)	44.56
Palmitic acid (C16)	63.23

mixed fatty acid at 40: 60 by weight ratio was at 41 °C and 39 °C respectively. Since the ratio falls in the range of 38 – 42 °C, these composition for coating materials were chosen for dissolution studies.

Dissolution studies

Figure 4 shows the drug released performance in the dissolution studies for the uncoated hydrogel. It showed that for the first two hours in acidic condition with pH 1.20 the drug was released continuously up to 40%. Then in the medium of pH 6.80, a sudden increased of drug released was observed and continued to increase until the last 6 hours up to about 50%. This was due to the variation of pH. The released was faster in the buffer medium compared to acidic medium. The same phenomenon was observed previously by Rana *et al.* (2011). Paracetamol (pKa 9.5) is weakly acidic drug, therefore the absorption should occurred more rapidly in small intestine since it is in a basic condition compared to stomach, which is acidic (Heading

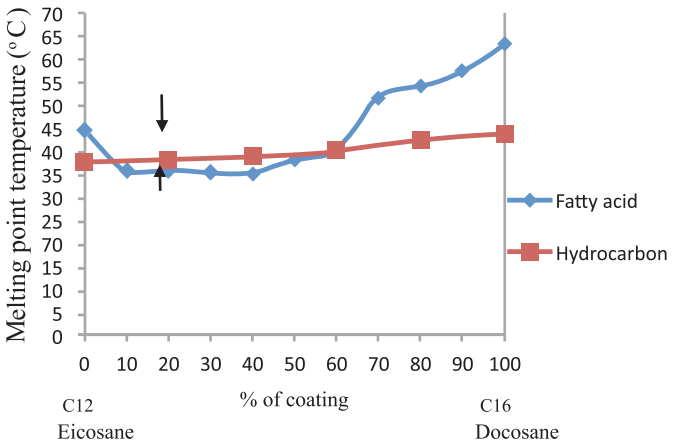


Figure 3: The variation of melting point of mixed coating materials at different percentage

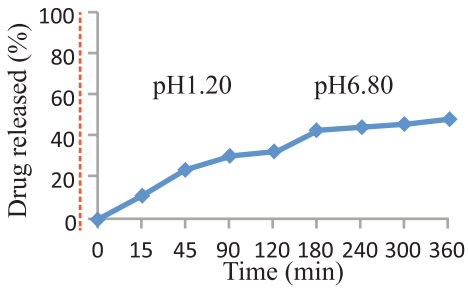


Figure 4: Drug release percentage of uncoated hydrogel

et al., 1973) in nature. This illustrated that the uncoated hydrogel was not efficient on its own and need to be supported with the coating materials to protect the drug inside the hydrogel from being released.

Figure 5 shows equivalent data but for coated hydrogel. Figure 5(a) showed the using of fatty acid as the coating where for the first two hours in acidic medium, there was no drug released. However, there was slight drug released in the buffer medium until the end of the process. Figure 5(b) showed equivalent data for hydrocarbon. It showed that for the first two hours, there were no drugs released in acidic medium. However, interestingly for the following hours in the buffer medium, there were no drugs released at all. Therefore, it showed that the use of hydrocarbon as the coating material is efficient to protect the drug because no drug released at all throughout the period of the experiment. Fatty acid and hydrocarbon are not easily affected by the aqueous solution of acid, alkalis, oxidizing and reducing agent making them stable in acid and basic medium.

Conclusion

The result showed that coated gellan gum hydrogel was suitable to be used as a drug carrier. Besides, the result also demonstrated the efficiency of coating material to protect the drug from being released at two pH conditions. As a summary, it can be concluded that the best ratio to use for both mixed coating materials of fatty acid and hydrocarbon were 40:60 by weight ratio and the best coating materials chosen was the mixture of eicosane and docosane.

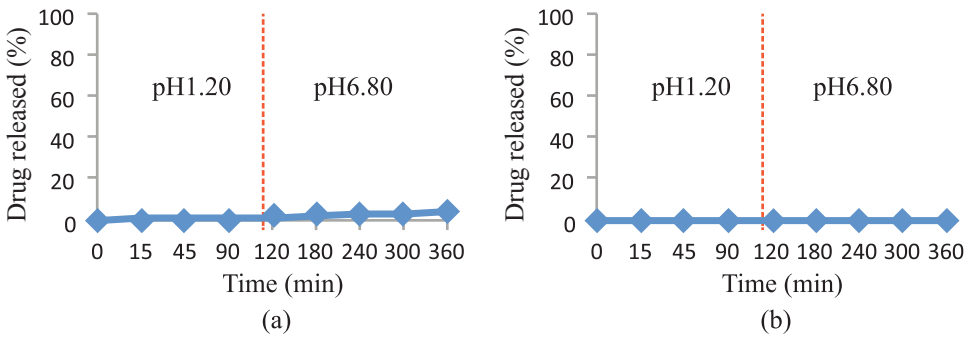


Figure 5: The percentage drug release from the coated hydrogel (a), coated with mixed fatty acid and (b), coated with mixed hydrocarbon

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