the diffusion coefficients approach zero (Karrout et al., 2009a).With increasing water content, the mobility of the macromolecules increases and, thus, also the mobility of incorporated drug molecules increases. Fig. 1(a)& 1(b) shows the gravimetrically measured water uptake of thin polymeric films based on the different ratios of ECand starch nanocrystals blends upon exposure to simulated gastric fluid pH 1.2 and simulated intestinal fluid pH 6.8, respectively at 37 ^{o}C.Remarkably, the polymer blend ratio affected the resulting water penetration rate and extent. With increasing starch nanocrystals content, the amount of water taken up as well as the rate of this mass transport step was increased.

This phenomenon can be attributed to the more hydrophobic nature of EC compared to the starch nanocrystals. Thus, it can be expected that the mobility of a drug within this type of polymeric films significantly increases with increasing starch nanocrystals contents. There was no distinguishable difference in percentage of water uptake of the investigated films in simulated gastric acid pH 1.2 and simulated intestinal fluid pH 6.8.In addition to the water uptake kinetics, the weight loss behavior of polymeric films offers important insight into the latter's ability to suppress or allow drug release (Karrout et al., 2009b).

The effects of the EC: starch nanocrystals composite blend ratio on the resulting weight loss of thin films upon exposure to simulated gastric acid pH 1.2 and simulated intestinal fluid pH 6.8 are illustrated in Fig. 2(a) &2(b), respectively. Obviously, both the rate and the extent of the weight loss increased with increasing starch nanocrystals contents. This could at least partially be attributed to the leaching of this compound out into the bulk fluids. Due to the increasing water uptakes of the systems (Fig. 1), the mobility of the polymer chains increases and, thus, also cause to mobility of the starch nanocrystals into bulk media. Importantly, the dry mass loss is limited in all cases, and the presence of the water-insoluble EC in the

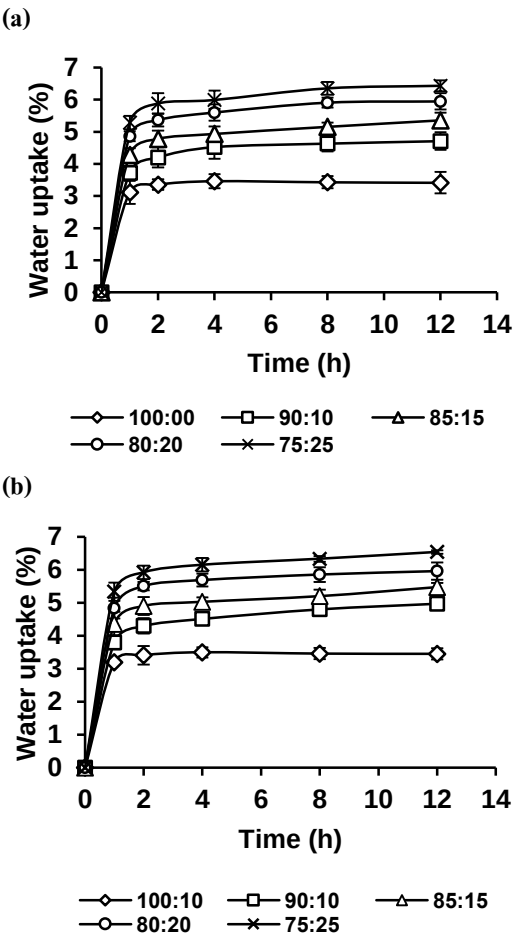

Figure 1 Water uptake of thin films consisting of EC: starch nanocrystals (the ratio is indicating in the figures) upon exposure to (a) simulated gastric fluid pH 1.2 and (b) simulated intestinal fluid pH 6.8 (DBS content, referred to polymer mass:10% w/w).

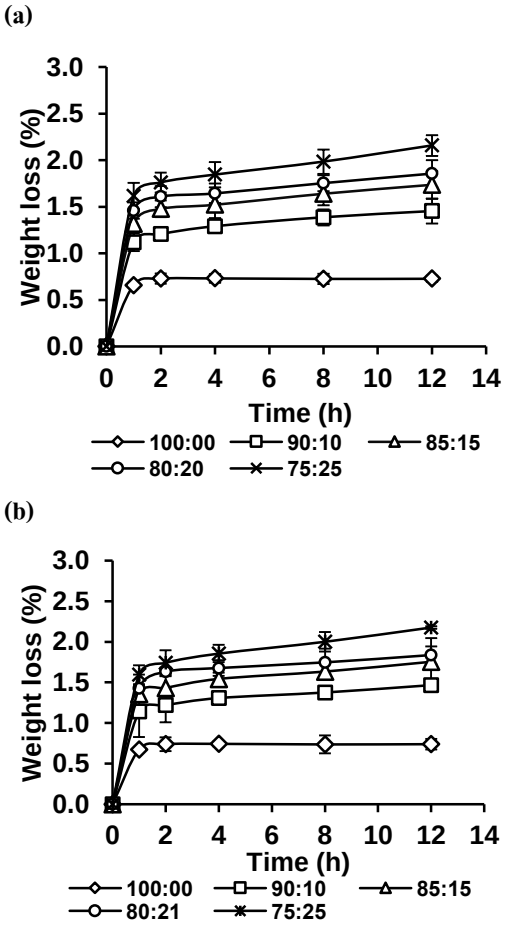

Figure 2 Weight loss of thin films consisting of EC: starch nanocrystals (the ratio is indicating in the figures) upon exposure to (a) simulated gastric fluid pH 1.2and (b) simulated intestinal fluid pH 6.8 (DBS content, referred to polymer mass:10% w/w)

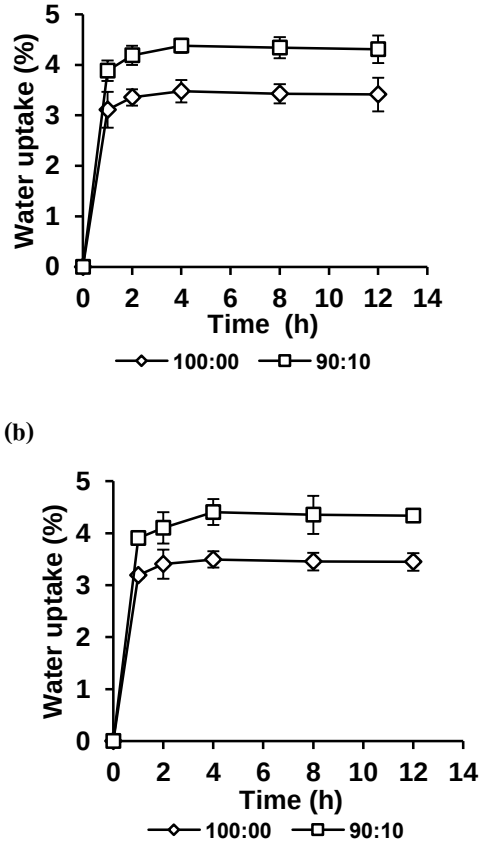

Figure 3 Water uptake of thin films consisting of EC: magnesium stearate (the ratio is indicating in the figures) upon exposure to (a) simulated gastric fluid pH 1.2and (b) simulated intestinal fluid pH 6.8 (DBS content, referred to polymer mass: 10% w/w).

films effectively hinders the leaching of the starch nanocrystals into the bulk fluids.

Fig. 3(a) &3(b) shows the gravimetrically measured water uptake of thin polymeric films based on EC: magnesium stearate (90:10) blends upon exposure to simulated gastric fluid pH 1.2 and simulated intestinal fluid pH 6.8 at 37 ^{o}C. The percentage of water uptake of the EC film containing magnesium stearate was higher than that of the EC film. A possible explanation was that the film containing magnesium stearate had more porous structure according to the phase separation of the filler(Sungthongjeen et al., 2004). Furthermore, there was no significant difference in % water uptake in these two media.

Mechanical properties of thin films

In addition to limited water uptake and weight loss in the upper GIT, a polymeric film coating

providing site-specific drug delivery must be sufficiently (mechanically) stable in order to avoid accidental crack formation due to the shear stress encountered in the stomach and small intestine *in vivo*(Karrout et al., 2009a). In addition, significant hydrostatic pressure might be built up within a coated dosage form due to the penetration of water into the system upon contact with aqueous body fluids. The presence/absence of somatically active drugs and/or excipients in the core formulation can strongly affect the importance of this phenomenon. Fragile film coatings are likely to rupture because of such shear forces from outside (caused by the motility of the GIT) and hydrostatic pressures from inside (caused by water penetration) they are exposed to. In order to be able to estimate the risk of such accidental crack formation, the energy required to break, puncture strength and percentage of elongation the investigated EC: starch nanocrystals composite films were measured in dry state using a texture analyzer. Fig. 4(a) &4(b) indicates the puncture strength and energy at break (mechanical stability) of thin EC: starch nanocrystals films (plasticized with 10% (w/w) DBS, referred to the ECcontent) in the dry state at room temperature as a function of the polymer blend ratio. Clearly, the energy at break of the films and tensile strength significantly were decreased with increasing starch nanocrystals content, indicating that made mechanically weak film under these conditions. It was observed that when adding the starch nanocrystals this may lead to break the ECpolymerinterchain interactions. This would be desirable for rupture of the coating of pulsatile drug delivery system. The film weakness can also be proved with the data of % elongation. According to Fig. 4(c) (% elongation), when increased the amount of starch nanocrystals films were ruptured at low probe

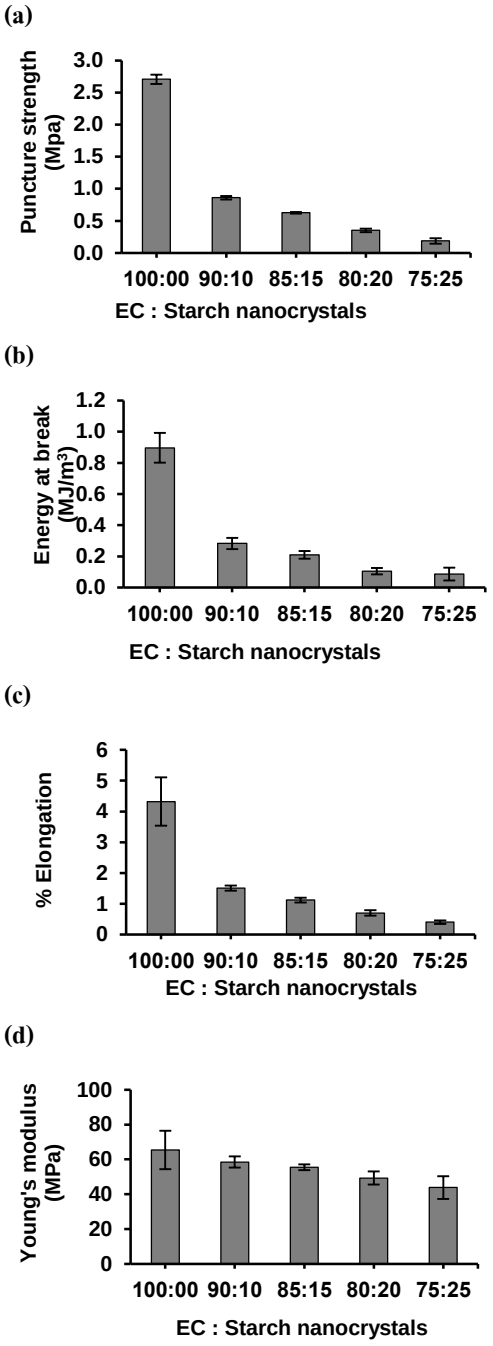

Figure 4 Effect of EC: starch nanocrystals blend ratio on (a) puncture strength, (b) energy at break, (c) % Elongation, and (d)Young's modulus (DBS content, referred to polymer mass:10% w/w).

displacement and resulted in a lower % elongation. This low % elongation can also be an advantageous to ensure a complete rupture in a rupturable pulsatile drug delivery system.

The addition of hydrophobic particulate material, magnesium stearate reduced the puncture strength and energy at break dramatically in dry state (Table 1). These results may be due to a reduced interaction between polymer chains by hydrophobic particles. The % elongation of the EC film with magnesium stearate significantly was decreased (Table 1). It was indicated that flexibility of the film was reduced.

Table1 Mechanical properties of EC and EC with magnesium stearate (90:10 w/w) films (DBS content, referred to polymer mass:10% w/w).

EC:MgStrfilms	Puncture strength (MPa)	Energy at break (mJ/m^3)	%Elongation (%)
100:00	2.71 ± 0.07	0.90 ± 0.10	4.31 ± 0.79
90:10	0.26 ± 0.03	0.10 ± 0.01	0.71 ± 0.23

Water vapor permeation of thin films:

The effects of the EC: starch nanocrystals composite blend ratios on the resulting water vapor permeation coefficient of thin films were illustrated in Fig.5. Clearly, the rate of water vapor permeation coefficient was increased with the higher amount of increasing starch nanocrystals contents. It was demonstrated that the addition of starch nanocrystals causes EC to reduce its hydrophorbicity and forms mechanically weak and soft films. Furthermore starch nanocrystals modify the polymer network more porous.

Conclusion

Cassava starch nanocrystals could improve mechanical properties of EC films, indicating a high potential to be used as a modifier for rupturable film for pulsatile drug delivery system.

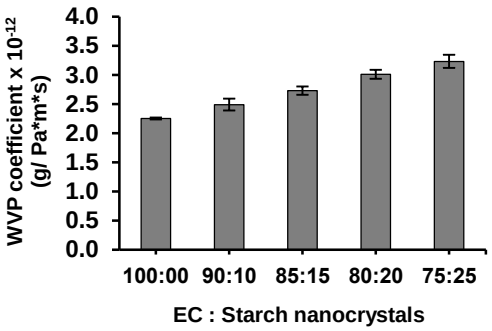

Figure 5 Water vapor permeability (WVP) of thin films consisting of EC: starch nanocrystals (DBS content, referred to polymer mass:10% w/w).

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